Subjects

Animal Health

Disease Cards

- Bluetongue
- Contagious bovine pleuropneumonia (CBPP)
- Contagious caprine pleuropneumonia (CCPP)
- Sheep and goat pox (SGP)

Zoonotic Diseases

- Anthrax
- Avian Influenza
- Botulism
- Bovine Spongiform Encephalopathy - BSE [Spanish only]
- **Brucellosis, bovine**
- Brucellosis, ovine/ caprine
- Cysticercosis (bovine)
- Cysticercosis (porcine)
- Escherichia coli [Spanish only]
- Hydatid disease
- Leptospirosis
- Listeria monocytogenes [Spanish only]
- Q fever
- Rabies
- Rift valley fever (RVF)
- Sarcocystosis
- Toxoplasmosis
- Trichinosis
- Tuberculosis

ANIMAL HEALTH DISEASE CARDS

Bovine Brucellosis

Names

Pathogen(s)

Preferred Name : Brucellosis (Brucella abortus)

Disease/Parasitosis

Preferred Name : Brucellosis (Brucella abortus)

Common Names (English):

Bang's disease
Malta fever (man)
Contagious abortion
Infectious abortion
Undulent fever (man)

Overview

Brucella abortus was isolated from cattle in 1897 by the Danish veterinarian Bernard Bang (Bang, 1897). The disease caused by Brucella abortus (B. abortus) is known as brucellosis, Bang's disease, contagious abortion, or infectious abortion. It affects many animal species on every continent and is a zoonose of economic importance, as well as a public health hazard.

Brucellosis is primarily a reproductive disease characterized by abortion, retained placenta and impaired fertility in the principal animal host. Brucella abortus is to a certain extent distinguishable from other brucellae by biochemical reactions and by serological means. The serological differences are related to the amounts of A and M antigens that a Brucella strain possesses.

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Animals Affected Table

See Table

Animals Affected

Brucellae have definite host preferences. Secondary hosts play a small part if any in the maintenance or spread of a particular Brucella species. Brucella abortus mainly infects cattle and is the main cause of contagious abortion in cattle (Manthei and Carter, 1950; Dekeijzer, 1981; Crawford et al., 1990). However, sheep, goats, dogs, camels, buffaloes as well as feral animals may also contract B. abortus infections .

Although sheep do not easily become infected with B. abortus (Collier and Molello, 1964; Allsup, 1974) they may become carriers and excrete Brucellae for up to 40 months once they have acquired the infection (Luchsinger and Anderson, 1967). The low prevalence of naturally acquired B. abortus infections reported in goats makes this animal species irrelevant as a host for B. abortus (Mathur, 1967).

Isolation of B. abortus from swine (Ray, 1979), horses (Robertson et al., 1973), and camels (Al-Khalaf and El-Khaladi, 1989) in areas with enzootic brucellosis clearly indicates that these species may acquire infection with B. abortus . However, their significance as a host for B. abortus is doubtful, as these animal species usually do not intermingle with cattle. Dogs with naturally acquired B. abortus infections play an important role in the epidemiology of cattle brucellosis (Chary, 1970). The relationship between infected dogs and outbreaks of brucellosis in cattle has not only been reported but has also been demonstrated (Prior, 1976; Forbes, 1990).

Studies indicate that feral animal such as buffalo, swine, deer, fox, hare and rodents are susceptible to Brucellae . However, their role as a host for Brucella particularly in intensive cattle

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Related Links

Medline

farming is not clearly established (Cook et al., 1966; Moore and Schnurrenberger, 1981; Schnurrenberger et al., 1985). In fact, data compiled during brucellosis control and eradication campaigns suggest that brucellosis disappears form wildlife when it is eradicated from domestic animals (Ray, 1979).

The significance of fowl as a reservoir of Brucella is unclear (Anezykowski, 1972). The role of small feral animals is also not clear although studies of experimentally induced and naturally occurring Brucella -infection in flies, arthropods and other parasites suggest that they may be susceptible to infection with Brucella (Thorpe et al., 1965; Britov et al., 1979).

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Epidemiology

Transmission and dissemination

Transmission of B. abortus is very likely to occur via the oral route because cattle tend to lick aborted foetuses and the genital discharge of an aborting cow (Cunningham, 1977). Exposure to Brucella organisms is also likely to occur in utero (Fensterbank, 1978) or when calves born to healthy dams are fed on colostrum or milk from infected dams (Bercovich et al., 1990).

It has been established that brucellosis in bulls does not always result in infertility, although semen quality may be affected. Bulls that remain fertile and functionally active will shed Brucella organisms with the semen during the acute phase of the disease. Shedding, however, may cease or become intermittent (McCaughey et al., 1973). In contrast to artificial insemination, bulls used in natural service may fail to spread the infection, as the infected semen is not deposited in the uterus (Ray, 1979).

While indirect exposure to Brucella organisms could be mediated by wildlife, birds and waterways (contaminated with urine, uterine discharge, or slurry from aborting cattle) it seems that only dogs carry pieces of placenta or aborted foetuses from one place to another (Forbes, 1990) causing direct exposure.

Contamination of a cowshed or pasture takes place when infected cattle abort or have a full-term parturition. Although it is generally accepted that B. abortus is not excreted for any considerable time before abortion occurs, excretion in the vaginal discharge of infected cattle may occur as early as 39 days after exposure (Philippon et al., 1970). A massive excretion of Brucellae starts after abortion and may continue for 15 days. Once the foetal membranes are expelled the uterine discharge diminishes and the number of Brucella organisms excreted decreases rapidly (Nicoletti, 1980). Although the infectious material from the genital tract usually clears after 2-3 months, some infected cattle become carriers of Brucella and excrete it intermittently for many years (Philippon et al., 1970; Herr et al., 1990).

Survival of Brucella in the environment

The survival of the organism in the environment may play a role in the epidemiology of the disease. Wray (1975) reviewed many studies conducted to determine the ability of Brucella organisms to survive under various experimental and environmental conditions. Temperature, humidity, and pH influence the organism's ability to survive in the environment. Brucellae are sensitive to direct sunlight, disinfectant and pasteurization. In dry conditions they survive only if embedded in protein (Davies and Casey, 1973). Brucellae can survive in tap water for several months at 4-8 ÌC, 2.5 years at 0 ÌC, and several years in frozen tissues or medium. Brucellae can also survive up to 60 days in damp soil, and up to 144 days at 20 ÌC and 40% relative humidity.

Brucellae can survive 30 days in urine, 75 days in aborted foetuses and more than 200 days in uterine exudate. In bedding contaminated with infected faecal material Brucella will be destroyed at 56 ÌC-61 ÌC within 4.5 hours (King, 1957). However, there are conflicting reports as to its survival in liquid manure. According to one study B. abortus can survive at least 8 months at 12 ÌC (Plommet, 1972) whereas another study indicates that Brucellae could not be recovered from slurry after 3 months (Rankin and Taylor ,1969). Yet another study indicates that the survival of Brucella is subject to seasonal influences. It has been found that Brucella can survive in faeces, slurry, or liquid manure 85-103 days in the winter, 120-210 days in spring, 30-180 days in summer, and 50-120 days in autumn (Kerimov, 1983). Although B. abortus is relatively resistant and may survive for a considerable time, the environment is not considered to be an important source of infection (Wray, 1975).

Resistance to infection

Age, sex, stage of pregnancy and natural resistance to Brucella may influence the progression of infection. Heifers born to infected dams usually test seronegative for Brucella for a long period (Bercovich et al., 1990). Because the stage of pregnancy at the time of infection determines the incubation period abortions in cattle caused by B. abortus seldom occur before the fourth or fifth month of pregnancy (Thomsen, 1950). Pregnant females are more likely to become infected than non-pregnant cattle or males. This is because a gravid uterus sustains growth of the organism (Crawford et al., 1990). Furthermore, the course and incidence of the disease is also influenced by natural resistance to infection with Brucella (Hellmann et al., 1984).

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Distribution Table

See Table

Distribution

Data on the prevalence of brucellosis and the success or failure to control or eradicate the disease are published in a great number of scientific papers. However, a substantial number of those publications are now only of historical value since eradication programs employed in various countries have successfully eliminated B. abortus infection from cattle. For this reason only selected relevant data published in the last decade has been used for the distribution table.

Re-appearance of the disease in brucellosis free areas is usually limited and the infected herds are immediately slaughtered, to prevent spread of brucellosis. Therefore, reports on the prevalence of brucellosis do not always appear in the literature. It usually depends on the frequency of surveillance for brucellosis in each country, and whether the results are published. Therefore, the literature references given in the geographical distribution tables are not always up to date and for countries where no information is given are not always free from brucellosis.

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Economic Importance and Impact

The economic loss from brucellosis in developed counties arises from the slaughter of cattle herds that are infected with Brucella. The economic loss from brucellosis in developing countries arises from the actual abortion of calves and resulting decreased milk yield, birth of weak calves that die soon after birth, retention of the placenta, impaired fertility and sometimes arthritis or bursitis. It is difficult to estimate the financial loss caused by brucellosis, as it depends on the type of cattle farming, herd size, and whether it is an intensive or extensive cattle farm. Furthermore, although it is very difficult to estimate the financial loss incurred by human brucellosis there is no doubt that it is substantial.

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Disease Systems

See Table

Disease Course

Brucellae are facultative intracellular bacteria that can survive within host cells causing a chronic infectious disease that may persist throughout the life of an animal. Enright (1990) extensively reviewed the pathogenesis and pathology of Brucella infection in domestic animals. It seems that the initiation of Brucella infection depends on exposure dose, virulence of the organism and natural resistance of the animal to Brucella . Resistance to infection is based on the hostÿs ability to prevent the establishment of a mucosal infection by the destruction of the invading organism. Invading Brucella usually localize in the lymph nodes, draining the invasion site, resulting in hyperplasia of lymphoid and reticuloendothelial tissue, and the infiltration of inflammatory cells. Survival of the first-line of defence by the bacteria, results in a local infection and the escape of brucellae from the lymph nodes into the blood. During the bacteraemic phase (which may last 2-8 weeks) the bones, joints, eye and brain can be infected, but the bacteria are most frequently isolated from supramammary lymph nodes, mammary lymph nodes, milk, iliac lymph nodes, the spleen and uterus.

The tropism of Brucella to the male or female reproductive tract

was thought to be by erythritol, which stimulates the growth of the organism, but Brucella has also been found in the reproductive tract of animals with no detectable levels of erythritol. In the acute stage of infection, abortion occurs at four or five months into pregnancy, and cattle usually abort only once. Abortion and retention of the placenta, late abortions or birth of infected full-time calves is common in herds with endemic brucellosis. Excretion of Brucella after parturition may persist for months or years and may re-occur after any consecutive normal parturition. Infected cattle excrete Brucellae in the colostrum or milk although it cannot always be detected (Manthei and Deyoe, 1970; Ray, 1979).

In bulls the predilection sites for infection are the reproductive organs and the associated lymph nodes. During the acute phase of infection the semen contains large numbers of Brucella but as the infection becomes more chronic the number of brucellae excreted decreases and excretion may cease altogether. However, it also may continue to be excreted for years or just become intermittent. Usually, orchitis, epididymitis and infection of the accessory sex glands also occur (Jubb and Kennedy, 1963).

Abortion and expulsion of the foetus was thought to be the results of a placentitis caused by Brucella . Proliferation of Brucella in the uterus induces necrosis and destruction of the foetal and maternal placental membranes resulting in death and then expulsion of the foetus. The pathologic changes in the caruncles and cotyledons prevent normal separation and expulsion of the placenta (Jubb and Kennedy, 1963). Although placentitis impairs the normal function of the placenta Brucella endotoxins may also play a role in inducing abortion (Anderson et al., 1986). Brucella abortus may induce production of high concentration of cortisol that decrease progesterone production and increase oestrogen production. Decreases in progesterone level and increases in oestrogen levels induce a premature parturition (Enright et al., 1984).

Symptoms Table

See Table

Diagnosis

Clinical signs

An outbreak of brucellosis is hardly ever confined to one animal and there are no pathognomonic signs. Therefore, clinical examination of aborted material is not of great diagnostic value. Demonstration of characteristic clumps of Brucella organisms in stained smears of hygroma fluid, chorionic epithelium, or the use of fluorescent antibody techniques to examine foetal stomach content and uterine, or vaginal exudate may provide a tentative diagnosis (Corbel, 1973).

Bacteriological examination

Bacteriological examination of lochia of aborting cattle is the method of choice for diagnosing early infections (Erasmus, 1986). However, the procedure is laborious, time consuming, costly and cannot routinely be used as a diagnostic procedure in developed or developing countries. Moreover, the probability of successful recovery of B. abortus is strongly reduced when the material is heavily contaminated and negative culture results do not exclude infection.

Serological tests

Body fluids such as serum, uterine discharge, vaginal mucus, milk, or semen plasma from suspected cattle may contain different quantities of antibodies of the M, G 1, G 2, and A types directed against Brucella (Beh, 1974). Because infected cattle may or may not produce all antibody types in detectable quantities several tests are used to detect brucellosis. The commonly used tests are the milk ring test (MRT), serum agglutination test (SAT), complement fixation test (CFT), Rose Bengal (RB) plate test, anti-globulin (Coombs) test, 2-mercaptoethanol, rivanol and the enzyme-linked immunosorbent assay (ELISA). The use of several tests to reliably detect brucellosis suggests shortcomings in each of the tests.

The milk ring test (MRT) is cheap, easy, simple and quick to perform. It detects lacteal anti- Brucella IgM and IgA bound to milk fat globules. However, it tests false positive when milk that contains colostrum, milk at the end of the lactation period, milk from cows suffering from a hormonal disorder or milk from cows with mastitis are tested (Bercovich and Moerman, 1979). Milk that contains low concentrations of lacteal IgM and IgA or which is lacking the fat-clustering factors tests false-negative (Keer et al., 1959; Tanwani and Pathak, 1971; Patterson and Deyoe, 1978). Because lacteal antibodies rapidly decline after abortion or

parturition, the reliability of the MRT, using 1 ml milk, to detect Brucella antibodies in individual cattle or in tank milk is strongly reduced (Hill, 1966). Although the MRT performed with 8 ml milk it improved the detection of brucellosis in tank milk (Bercovich and Lagendijk, 1978), it may test false positive when traces of colostrum are present in tank milk (Bercovich and Moerman, 1979).

The serum agglutination test (SAT), which historically has been the principal serological test used to detect brucellosis, measures agglutinating antibodies of the IgM, IgG 1, IgG 2, and IgA types (Levieux, 1974). The SAT is relatively simple and easy to perform but it requires basic laboratory equipment. It can be used to detects acute infections, as antibodies of the IgM type usually appear first after infection and are more reactive in the SAT than antibodies of the IgG 1and IgG 2types (Beh, 1974; Levieux, 1974). However, because the SAT may yield both false negative or false positive results (Corbel et al., 1984) it effectively detects

brucellosis only on a herd basis. The complement fixation test (CFT) detects specific antibodies of the IgM and IgG 1type that fix complement (Hill, 1963a; Levieux, 1974). The CFT is highly specific (Hill, 1963b) but it is laborious and requires highly trained personnel as well as suitable laboratory facilities. This makes the CFT less suitable for use in developing countries. Although its specificity is very important for the control and eradication of brucellosis it may test false negative when antibodies of the IgG 2type hinder complement fixation (MacMillan, 1990). The CFT measures more antibodies of the IgG 1type than antibodies of the IgM type, as the latter are partially destroyed during inactivation. Since antibodies of the IgG 1type usually appear after antibodies of the IgM type control and surveillance for brucellosis is best done with SAT and CFT (EU directive 64/432/EC (F2) AnnexA. II, and C).

The Rose Bengal plate test is a spot agglutination technique. Because the test does not need special laboratory facilities and it is simple and easy to perform it is used to screen sera for Brucella antibodies. The test detects specific antibodies of the IgM and IgG types and is more effective in detecting antibodies of the IgG 1type than IgM and IgG 2types (Levieux, 1974). The test may yield negative results in infected cattle that give positive results with the CFT (Rose and Roepke, 1957). Although the low pH (+3.6) of the antigen enhances the specificity of the test, the temperature of the antigen and the ambient temperature at which the reaction takes place may influence the sensitivity and specificity of the RB test (MacMillan, 1990).

The anti-globulin (Coombs) test detects (incomplete Brucella) antibodies of the IgG 2type and is used to confirm SAT results (Hill, 1963b). The Coombs test, although laborious, is particularly important when the SAT is positive and CFT results are negative or inconclusive (Kiss, 1971). However, Coombs test results are indicative for infection only when its titres are at least two times the titres of the SAT (Hill, 1963b). This is the tests main limitation, as not all infected cattle show this ratio. The 2-mercaptoethanol and the rivanol tests detect specific IgG (Rossi and Cantini, 1969) and are usually used to differentiate between infected and vaccinated cattle.

Nielsen et al. (1981) reviewed several ELISA procedures and the antigens, conjugates and substrates that can be used in the assay. The ELISA has proven to be specific and as sensitive as the MRT and SAT in detecting Brucella antibodies in milk and serum. ELISA results are usually also in agreement with CFT results (Ruppanner and Taaijke, 1980; Stemshorn et al., 1980; Bercovich and Taaijke, 1990). The test can be used for screening and confirmation of brucellosis in both milk and serum (Bercovich and Taaijke, 1990). However, depending on the presence of traces of colostrum in the milk, or the presence of low concentrations of lacteal immunoglobulin the ELISA may test false positive or false negative (Bercovich and Taaijke, 1990; Kerkhofs et al., 1990). It seems that the ELISA is less sensitive than the CFT, as some infected cattle that test positive with the CFT may test negative with the ELISA (Cargill et al., 1985; Sutherland, 1984). Some researchers imply that the main advantage of the ELISA when compared with the CFT lies in its relative simple test procedure (Sutherland et al., 1986). The assay is very costly when only a few samples are tested, therefore, it is unsuitable for testing individual animals but it is the ideal test for screening suspected herds.

Since the reliability of serological tests to detect brucellosis depends on antibodies that may or may not be present at the time of examination, inevitably some infected animals may elude detection. Because the skin-delayed-type-hypersensitivity (SDTH) test is independent of circulating antibodies it should be added to the serological tests to improve detection of brucellosis. The SDTH test confirms serologic test results, confirms brucellosis in cattle with ambivalent serologic test results and detects latent carriers of Brucella. Furthermore, the SDTH test does not sensitize cattle for several consecutive SDTH tests (Bercovich, 1999). Therefore, the SDTH test should be the test of choice in developing countries, as cattle in those countries are usually not tagged so

that serological test results could be related to the individual animal. Where the animals are tagged a combined use of the SAT and SDTH tests increase the reliability of brucellosis diagnosis (Bercovich, 1999).

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Disease Treatment Table

No data

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Disease Prevention and Control

Prolonged treatment of infected domestic animals with a high dosage of antibiotics is not used due to the appearance of antibiotics in the human food chain and its interferes with the production of milk products. Moreover, as Brucellae are facultative intracellular bacteria, relapses after treatment usually occur. Therefore, efforts are directed at prevention or eradication of brucellosis.

Legislation is needed to effectively control and eradicate brucellosis. There are various combinations of diagnostic tests that can be used to detect cattle infected with B. abortus in tagged animals. Untagged animals can repeatedly (every 5-6 weeks) be tested with the SDTH test, as the test does not sensitize cattle for subsequent SDTH tests (Bercovich et al., 1992). Suspect herds must be tested at regular intervals until all animals test negative. Animals that test positive should be removed from the herd.

In areas with endemic brucellosis only vaccination will control brucellosis. Vaccination reduces the number of infected animals and eventually permits disease control. Brucella vaccines in use are the live B. abortus Strain-19 vaccine and to a lesser extent the whole cell killed adjuvant B. abortus 45/20 vaccine. In the last decade a new B. abortus vaccine RB51 has been introduced.

Vaccination with 40-120 x 10 9CFU (classical dose) of living Brucella abortus Strain-19 gives a fair to good protection but it also has some disadvantages (Plommet, 1991). It may cause abortion in pregnant cattle and/or induce an antibody response that confuses the serological diagnosis of brucellosis for 12-36 months. It is excreted in the milk and may induce brucellosis in humans. To diminish these undesirable effects of vaccination with S-19, two vaccination procedures have been suggested. In one procedure calves are vaccinated once with 3-10 x 10 9CFU (¬reduced doseÿ) at an age of 4-8 month and for the second time with 3-10 x 10 9CFU as adults. The second procedure suggests a conjunctival vaccination of calves with two drops of vaccine containing 4-10 x 10 9CFU at an age of 4-10 months and a second conjunctival vaccination with the same dose six months later.

Brucella abortus strain RB51 used for vaccination was selected by growth of B. abortus strain 2308 in the presence of rifampicin. The protective effect of this vaccine in cattle is similar to that of S-19. Compared with S-19 B. abortus RB51 vaccine causes less abortion (Cheville et al., 1996) and does not induce production of agglutinating antibodies of the IgM type, although specific IgG is produced (Stevens and Olsen, 1996). Depending on the doses used it may cause placentitis that leads to pre-term expulsion of the foetus. The vaccine has been approved for use in the USA to allow additional data on filed use under controlled conditions (Information Circular, WHO Mediterranean Zoonoses Control Center).

The use of Brucella abortus 45/20 vaccine is less common than S-19 because in comparison to S-19 it does not give lasting immunity. The vaccine does not induce detectable agglutinating antibodies and is not harmful but it gives a marked skin reaction on the injection site. Two initial vaccinations at specific intervals and an annual booster are needed for good protection (Plommet, 1991).

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Vaccines

See Table

Zoonoses and Food Safety

Brucellosis known as ¬Malta feverÿ or ¬undulant feverÿ are synonyms for brucellosis in man (Ansorg et al., 1983). Symptoms of acute brucellosis caused by Brucella abortus are 'flu-like' and highly nonspecific. Chronic brucellosis is an insidious disease with vague symptoms that might be confused with other diseases affecting various organ systems (Yinnon et al., 1993). Humans usually acquire brucellosis by consumption of raw milk or milk products. Brucellosis is also recognized as an occupational hazard for farmers, veterinarians, and workers in the meat industry within areas with enzootic B. abortus. Farmers and workers in the meat industry may contract brucellosis percutaneous, conjunctival or by nasal mucous membrane infection. Veterinarians may become infected when handling aborted foetuses or apparently healthy calves born to infected cows and by performing gynaecological and obstetric manipulations, or rectal examination of infected cattle (Schnurrenberger et al., 1975; Dekeijzer, 1981; Peelman and Dekeyser ,1987). Because cattle and small ruminants are the major source of human infection, programmes to eradicate human brucellosis have been largely aimed at these animal species.

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Taxonomic Tree

Kingdom Proteobacteria [01PROT]

Class Rhodospirilli [21RHOD]

Order Rhizobiales [31RHIZ]

Family Brucellaceae [41BRUC]

Genus Brucella [51BRUC]

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Hosts Table

See Table

Pathogen Characteristics

The organism responsible for brucellosis is a small Gram-negative coccobacillus that is non-motile, non-encapsulated and non-spore-forming. In infected tissue it normally occurs singly or in small groups. The colonies are circular and 2-4 mm in diameter. Smooth colonies appear translucent, honey-coloured and bluish-green or unstained when stained with crystal violet. Rough colonies appear granular, reddish-yellow and deep violet-red when stained with crystal violet. Mucoid colonies are stringy and appear transparent, greyish and light bluish-red when stained with crystal violet.

Several commercial firms produce media suitable for the isolation of Brucella . On primary isolation it usually requires the addition of 5-10% carbon dioxide and takes 3-5 days incubation at 37 ÌC for visible colonies to appear. Brucella abortus produces H 2S. It usually grows in the presence of basic fuchsin, but not always in the presence of thionin at standard concentrations, and is catalase and oxidase positive. It is lyzed by brucella-phages Weybridge (Wb), Firenze (Fz), Tbilisi (Tb) and Berkeley (Bk).

Each Brucella has a specific oxidative metabolic pattern that can be used to determine the ability of an isolate to utilize oxygen on various amino acid and carbohydrate substrates. Currently there are eight recognized Brucella abortus biovars (Corbel et al., 1978; Ray, 1979).

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