



BRUCELLOSIS (BANG'S DISEASE) IN CATTLE AND WILDLIFE

Questions and answers from the Wyoming State Veterinary Laboratory
December 2003

These questions and answers were developed in response to questions from producers in Wyoming after the recognition of a positive herd of cattle in Sublette County, Wyoming in November 2003.

Q. What is brucellosis?

A. In cattle, brucellosis is a chronic bacterial disease caused by *Brucella abortus*. Its main effect is abortion. It can cause decreased milk production, weight loss, loss of young, infertility, and lameness.

Q. What are the signs of brucellosis in cattle?

A. The most obvious sign in pregnant animals is abortion, retained placentas, and birth of weak calves. Not all infected cows abort, but most do so between the 5th - 7th months of pregnancy. Most infected cows abort once, but some may abort during additional pregnancies. Calves born from later pregnancies may be weak and unhealthy. Other signs of brucellosis include an apparent lowering of fertility with poor conception rates, retained afterbirths with resulting uterine infections,

Q. Why is brucellosis a big deal?

A. The disease is highly contagious and historically was a major source of production loss to livestock owners in the United States. As recently as 1957, there were 124,000 infected *herds* in the United States. Today the country is nearly free of the disease. Recognition of brucellosis in a brucellosis-free state has serious economic impacts on domestic livestock markets and threatens export markets. *Brucella abortus* can infect people and cause disease. It is a high-category (Biosafety Level-3) pathogen and listed as a potential bioterrorism agent (i.e., it is a Select Agent). Clinical signs in people resemble influenza, and signs include fever, sweats, malaise, anorexia, headache, muscle and back pain. Less common signs are undulant fever, arthritis, and inflammation of the testicles. Neurological symptoms occur acutely in up to 5% of cases. In the chronic form (>1 year from onset), symptoms include chronic fatigue, depression, and arthritis. Treatment usually consists of doxycycline and rifampin used in combination for 6 weeks to prevent recurring infection. Depending on the timing of treatment and severity of illness, recovery takes several weeks to several months. Mortality is low (<2%), and generally associated with endocarditis.

Additional information on brucellosis in people is available at the CDC web site:

http://www.cdc.gov/ncidod/dbmd/diseaseinfo/brucellosis_g.htm

Q. Who calls the shots when brucellosis is identified in a herd?

A. Control of brucellosis in a state is regulated jointly by the USDA's Area-Veterinarian-in-Charge and the state veterinarian under the Cooperative State-Federal Brucellosis Eradication Program,

Q. What is the strategy for testing a cattle herd suspected to have brucellosis?

A. This is a two step process. Initial laboratory screening uses inexpensive, easy to perform, rapid, *highly sensitive and fairly specific* tests. Sensitivity is crucial for screening, so the occurrence of some false positive samples is tolerated in order to detect all infected animals. Then, to identify the false positive reactions, a second set of tests is then performed. Secondary tests are more expensive and complicated, and designed to *maximize specificity*. Generally, screening tests for Wyoming cattle are done at the WSVL and confirmatory tests are done at the USDA's National Veterinary Services Laboratory in Ames IA.

Q. Why is the WSVL involved in testing for brucellosis?

A. It is important that Wyoming has independent testing capability for the disease in cattle. The WSVL signed an agreement with the USDA to perform front line screening tests such as the rivenol test. The

WSVL bacteriology laboratory has the ability to culture *B. abortus* from tissues. Personnel who perform the serological testing are monitored on a continuing basis and are formally certified by the USDA on their knowledge of accepted testing procedures. Considerable brucellosis research has been done in the laboratory in collaboration with other agencies.

Q. What do blood tests detect?

A. Blood tests detect antibodies to *Brucella abortus*. The most useful antibody to measure is IgG1. Some antibodies produced in response to vaccination cause false positives, particularly IgM. Many tests were developed so that IgM is precipitated or otherwise eliminated so it does not cause false positive reactions.

Q. Why are there so many blood tests to *Brucella abortus*?

A. Various tests were developed so that they maximize ease of use, sensitivity, specificity, cost-effectiveness and ability to distinguish vaccinated from naturally infected cattle. No one test combines all these attributes. For that reason, the number of tests run on individual samples is determined by the Area-Veterinarian-in-Charge and his/her superiors and the state veterinarian, based on circumstances of the herd.

Q. What tests does the WSVL run for *Brucella abortus*?

A. We run 4 tests: the standard tube agglutination test (“STT”), the buffered acidified plate antigen (“BAPA”) test, the card test (“CARD”) and the rivenol test (“RIVENOL”).

Q. How are these tests interpreted?

A. Interpretation is based on the test reaction (“negative,” “suspect,” or “reactor”) AND vaccination status of the animal being tested. Details about interpretation of specific tests are provided in a USDA document dated Feb 1, 1998, *Brucellosis Eradication: Uniform Methods and Rules*, <http://www.aphis.usda.gov/oa/pubs/bruumr.pdf>

Q. What is the gold standard for diagnosis of brucellosis in cattle?

A. The confirmatory serological tests done at the USDA’s National Veterinary Services Laboratory are helpful in establishing the status of a herd. But the definitive test is isolation of *Brucella abortus* from tissues of infected animals, either at slaughter or at necropsy. Culture allows the agent to be subtyped as to biovar. Culture takes ~2 weeks since the organism is fastidious and slow to grow. Newer tests, such as polymerase chain reaction (PCR), can supplement bacterial culture as a “gold standard” method.

Q. How do I stay abreast of the current brucellosis situation in Wyoming?

A. The office of the state veterinarian for Wyoming is posting updates on brucellosis on the Wyoming Livestock Board’s web site at <http://wlsb.state.wy.us/>. This is the most current and accurate source of information. The WSVL does not pass out confidential information about test status of individual herds to third parties, including the press. As tests are completed, results are relayed to the state veterinarian and the USDA’s area veterinarian in charge. Tests are NOT reported via the Web, so there is no way that third parties can see raw test results from individual herds.

Q. Where can I find reliable generic information on the Web about brucellosis in cattle?

A. There is a good clearing house on the VetGate site in the United Kingdom which carries information from various countries (USA, UK, Israel and South Africa). The site is at <http://vetgate.ac.uk/browse/cabi/detail/ac86a3d1a3b4ca5fcb5b57a54da15103.html>

Q. Where can I or my veterinarian find current scientific information on brucellosis in cattle?

A. A good collection of current articles on brucellosis is in the journal *Veterinary Microbiology* issues 1 – 4, pp. 1 – 603, dated 20 Dec 2002. Articles are written by international specialists and represent the state of the art in brucellosis research and testing as of last year. Copies of the articles are available from medical libraries or – for a fee – from the publisher Elsevier via its Science Direct web site: <http://www.sciencedirect.com/>

Q. How does USDA APHIS decide whether to depopulate a herd?

A. Once infection is found, the herds are tested and positive animals are removed. Additional tests are conducted every 30 – 180 days until a herd is negative. Depopulation of affected herds was adopted in the mid-1970s as a management option for intractable, heavily affected herds. The decision about depopulation is made at a state and federal level, based on the risk that a reactor herd presents.

Q. Is it possible to prove cattle acquired infection from a wildlife source, such as elk or bison?

A. There are techniques that can help in fingerprinting strains, but scientists have limited experience in locking in firm conclusions that infection originated from wildlife, particularly elk and bison, since such

events are relatively rare. Promising techniques have been developed, such on multi-locus analysis of variable number tandem repeats (VNTRs) in DNA of *Brucella abortus* isolates. The VNTR method requires that researchers have bacterial isolates from the suspect wildlife source and cattle in order to undertake a comparison. Epidemiological studies, such as proximity of infected elk to cattle, and incidence of infection in elk, are helpful for establishing where infection originated.

Q. Is it possible to prove cattle acquired infection from vaccination?

A. Provided the organism is cultured from the reactor cattle, yes. Growth characteristics in the laboratory help to distinguish vaccine strains (Strain 19 and RB51) from wild-type strains. Polymerase chain reaction (PCR) methods can also help recognize wild biovars and vaccinal strains (*J. Clin. Microbiol* 38: 3085-3086).

Q. Can bacteriophages (viruses that infect bacteria) be used to successfully treat brucellosis in cattle?

A. We are not aware of any published, peer-reviewed studies on the use of bacteriophages to treat cattle with brucellosis. Indeed there are no recognized successful medical treatments for cattle chronically infected with *Brucella abortus*. Test and culling reactor cattle is the standard method to control and eradicate brucellosis in the United States and other countries.

Q. Why won't state and federal authorities allow treatment with bacteriophages for brucellosis in cattle?

A. There are practical, regulatory and theoretical reasons for rejecting bacteriophage treatment for brucellosis at this time. The method has never been shown to work for this disease, whereas testing and culling of positive cattle does. Environmental impacts of bacteriophages are unknown. The safety of using biological agents of undefined concentration, purity and potency is a major consideration, which is why the USDA and FDA tightly regulate the medical use of experimental treatments such as bacteriophage therapy in animals and people, respectively. The organism that causes brucellosis lives inside cells, not free in the body, so it not clear how (or whether) bacteriophages could enter infected cells to attack *B. abortus*. Phage genetic material, under some conditions, can integrate into the bacterial genetic code, conferring resistance to further infection as well as endowing bacteria such as *B. abortus* with new antigenic and/or toxigenic properties. Unless established to be safe and effective in controlled experimental studies, the use of bacteriophages must be considered an unproved technology to treat cattle with brucellosis.

Q. Why did the USDA switch from vaccination with Strain 19 to RB51?

A. Strain RB51 is associated with fewer adverse post-vaccination reactions in cattle, such as abortions and localized inflammation at vaccine injection sites, compared to Strain 19. More importantly, and unlike Strain 19, RB51 does not stimulate the production of antibodies that can be confused on standard diagnostic tests with antibodies produced in natural infection.

Q. Is RB51 as good as Strain 19 in providing protection against brucellosis in cattle?

A. Yes. Studies indicate that both vaccines protect 70– 80% of animals in herds against challenge with wild-type *B. abortus*. Like all vaccines, protection is never perfect and the probability of infection is determined in appreciable part by the challenge dose of wild-type *Brucella abortus*.

Q. Why hasn't vaccination of wildlife controlled the problem in elk and bison?

A. Only a limited number of vaccines have been studied in wildlife, mostly S19 and RB51, both of which were developed for domestic livestock. Neither is as effective in wildlife as they are in cattle. RB51 provides lower levels of protection to vaccinated wildlife.

Q. How does the USDA classify states based on their brucellosis status?

A. There are 3 classes. Class Free status for a state or area means it is essentially brucellosis free. Class A and B states or areas have 0.25% and 1.5% *Brucella*-positive herds, respectively. Currently the US has only free states. If Wyoming loses its Class Free status, this imposes additional costs due to testing and possible import restrictions on Wyoming stock growers.

Dr. Donal O'Toole
Director, WSVL

Dr. Ken Mills
Bacteriologist, WSVL

December 14, 2003