The Brucellosis Program in the United States: Lessons Learned and Considerations for Success

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History

The first State-Federal cooperative efforts towards eradication of brucellosis caused by *Brucella abortus* in the United States began in 1934 as part of a recovery program to reduce the cattle population during severe drought conditions. A number of states saw this as an opportunity to reduce losses due to brucellosis. In 1934 and 1935, the reactor rate in adult cattle tested was 11.5%.

The magnitude of the brucellosis problem in the United States in terms of economics to the cattle industry and human health prompted Congress, in 1954, to appropriate funds for a comprehensive national effort to eradicate brucellosis. The eradication program was designed as a cooperative effort between the federal government, the state, and livestock producers. Since its inception, the brucellosis eradication program has undergone many modifications that have allowed it to progress to the stage it is today.

Overview of Brucellosis

Brucella abortus, the bacteria that causes brucellosis, is shed at or around the time of parturition or abortion. A susceptible animal ingests the organism, which progresses through the local oral mucosa to regional lymph nodes, where it resides during the incubation period. The incubation period, which is the time between exposure to the organism and the ability to detect the disease, may range from 2 weeks to 2 months, or even considerably longer. After a subsequent brief bacteremic phase, the organism localizes in the uterus, placenta, udder and/or regional lymph nodes. Although the most common clinical sign of brucellosis in cattle is abortion, the brucellosis infected cow is often asymptomatic. She is often sero-negative due to the lag time between exposure and seroconversion or clinical disease. She is generally non-infective to other animals until calving or parturition, when she then becomes a highly efficient transmitter of disease via products of parturition. After parturition, she rapidly loses the ability to infect other animals, generally within 30 days. She remains relatively non-infectious until her next parturition.

Brucellosis is not primarily a human disease, although it is a serious disease of humans worldwide. Man acquires the disease either directly or indirectly from animals. It has

been associated with certain occupations involving contact with infected animals, and may also be food borne, associated with consumption of unpasteurized dairy products. The disease in man is also known as undulant fever or Malta fever. Human brucellosis is distributed worldwide. The close association of mankind to cattle, goats, sheep, and swine as major food sources predisposes to human infection so long as brucellosis exists in these animal populations.

Current Status of Brucellosis in the United States

As of April 1, 2011 there were three affected cattle herds and two affected domestic bison herds remaining in the United States, all disclosed in a small area in the three states around Yellowstone National Park, where the disease has spilled over from affected elk. Wild bison and elk in the Greater Yellowstone Area are the last remaining known reservoir of *Brucella abortus* in the United States. Eliminating brucellosis from this area is a challenge due to the fact that these animals are on public lands, and there are many players with many different viewpoints involved in the management of these animals. A joint agency management plan for bison that wander out of Yellowstone National Park into the vicinity has been in effect since 2000, and there has been no apparent spread from bison to cattle. Elk which are fed on feedgrounds in the vicinity have maintained the disease and have transmitted it to cattle in the vicinity in recent years. Elk in a natural environment, where they are not artificially congregated by feeding do not normally maintain brucellosis. A number of research projects and vaccination trials in elk are underway in the vicinity in an effort to better manage the disease in elk in the region.

In December 2000, the United States had no known brucellosis affected herds for the first time. Although that accomplishment was significant, it is recognized that the accomplishment had to be put in the proper context. Brucellosis has a variable, sometimes quite lengthy incubation period, so it was expected that additional affected herds would be disclosed. Recognizing this possibility, animal health officials remained prepared to aggressively pursue any newly disclosed affected herds to eliminate the disease as quickly as possible. A few additional affected herds were disclosed as expected.

In January 2011, an affected cattle herd was disclosed in a state outside of the Greater Yellowstone Area for the first time since 2005. This herd was in Texas, and has been depopulated. The herd was disclosed through livestock market surveillance testing and no further infection in the vicinity has been found. It appears that this was an old affected herd, and had not been detected previously as the owner had not sold any test-eligible adult animals for a number of years. The discovery of this case demonstrates the importance of continued surveillance for a number of years after the apparent

elimination of brucellosis from an area. Therefore, other than in the immediate vicinity of the Greater Yellowstone Area, there are no affected cattle herds in the United States.

This current status is quite an achievement, especially when one considers that in Fiscal Year 1957, almost 124,000 brucellosis affected cattle herds were found. It is estimated that this was only one-third to one-half of what actually existed at the time, since at that time, surveillance activities were not at an optimal level.

At this time, all 50 states are officially classified as Class Free states. In the United States, a state must not have any herds with brucellosis reactors for a minimum of one full year, plus fulfill certain surveillance criteria to be awarded Class Free status. Until recently, if a state classified as brucellosis Class Free subsequently disclosed an additional affected herd, the state was allowed to maintain its Class Free status if the herd was depopulated within 60 days, an epidemiologic investigation was completed, and there was no further indication of spread of disease. This provision could be applied once every two years; in other words if two affected herds were disclosed in a two year time frame, the state would automatically lose its Class Free status.

In December 2010, an interim rule was enacted to amend the brucellosis regulations. Today, the disease is mostly eliminated from the United States, with the exception of the known wildlife reservoir of brucellosis in the Greater Yellowstone area. These new regulations reflect a recognition of the changed status of the country relative to brucellosis, and a move towards more efficient and streamlined surveillance as a result. It also reflects a move towards risk-based testing and decision-making as opposed to rigid guidelines applicable in all cases. These changes include reducing the amount of testing required to maintain Class Free status for states that have been Class Free for five or more years and have no *Brucella abortus* in wildlife; removing the provision for automatic reclassification of any Class Free state or area to a lower status if two or more herds are found to have brucellosis within a two-year period or if a single brucellosis-affected herd is not depopulated within 60 days (depending on the epidemiology and response to the occurrence, and other changes). In addition, a requirement was added that any Class Free state or area with *Brucella abortus* in wildlife must develop and implement a brucellosis management plan approved by the United States Department of Agriculture (USDA) in order to maintain Class Free status.

Turning Points of the Brucellosis Eradication Program

As the brucellosis eradication program progressed, there were a number of key developments that were major turning points in the program. Some of these were actually advancements in technology, while others could feasibly be considered “things we did that made a difference after we learned what we were doing wrong”.

In the beginning, the standard tube and plate agglutination tests were the only ones practical for routine program use. As the program progressed, new, better presumptive tests, as well as more specific diagnostic tests were added. They have continued to be added and now a battery of tests is available and used by epidemiologists. The most recently approved brucellosis test in the United States was the Fluorescence Polarization Assay (FPA) which was approved in 2004.

In the mid-1970s, blood testing of cattle at the first point of assembly of cattle (livestock markets, stockyards) was initiated in all high incidence states to enhance surveillance procedures. This provided for the identification of reactor and exposed animals before they had the opportunity to be moved to other areas. It also allowed for more accurate identification of these animals back to the farm of origin, which resulted in more efficient and accurate disclosure of affected herds.

Also in the mid-1970s, depopulation of affected herds was adopted as a management option that provided a solution for intractable and heavily affected herds. Depopulation of affected herds has been especially emphasized in the latter years of the program as the number of affected herds was decreased significantly.

Wide area testing in the vicinities of affected herds was instituted as well as increased testing of herds adjacent to affected herds and high-risk herds identified through epidemiological traces. These procedures were critical in ensuring that a brucellosis affected herd could be found and appropriately handled before the disease was allowed to spread.

The use of vaccination has also been a major factor in the success of the brucellosis eradication program. For many years, Strain 19 vaccine was used in calves only. The use of a reduced dose of Strain 19 in adult cows provided a new and effective procedure for use in large and heavily affected herds. One of the problems with Strain 19 vaccine was the fact that in a number of animals, the vaccine induced vaccinal titers that could not be distinguished from true field strain brucellosis. That problem was resolved with the advent of a new vaccine, RB51, which was initially conditionally approved in 1996. This vaccine has the advantage of producing comparable protection as Strain 19, without inducing the titers that cause diagnostic confusion. RB51 has been used extensively since its introduction and played a large role in clearing the disease from communities with long-standing brucellosis infection that cycled in the community.

In 1997, the Brucellosis Emergency Action Plan was developed and implemented. The plan emphasized depopulation of newly disclosed herds, enhanced surveillance, excellent epidemiology and herd management of all newly disclosed herds, and rapid response when an affected herd was disclosed. At the time this plan was developed, there were 31 known affected herds, and 54 newly affected herds disclosed during the

year. The actions clearly delineated in the Emergency Action Plan are all critical elements in the success of an eradication program.

A major factor in the success of the approaches developed and implemented during the course of the brucellosis eradication program, was owner acceptance of these new program procedures, in spite of the inconveniences, cost, and additional work required.

The Role of Surveillance in the Brucellosis Eradication Program

The classical action plan for disease control and eradication is as follows:

1. Find - Surveillance.
2. Contain - Prevent spread from infected herds.
3. Eradicate - Elimination of the disease.

Prevention might be added as a fourth consideration to include vaccination and other preventive measures. The point is, that **any plan that will affect whether or not disease exists, begins with surveillance.**

Current standard surveillance programs in the United States

More often than not brucellosis manifests itself as a chronic disease with variable and sometimes quite long incubation periods. There may or may not be indicative signs or symptoms, and even when present, there are none specific for brucellosis alone. Effective surveillance, because of the nature of brucellosis, must be ongoing and must utilize multiple methods. Some methods can be performed through the day-to-day marketing of livestock or milk. Other surveillance is accomplished as a result of finding new infected herds or by the movement of livestock.

Two very effective surveillance programs for brucellosis historically used in the United States are the market livestock testing program and the milk ring testing program. These are accomplished on an ongoing basis and, over a period of time, can survey virtually all of a specific animal population.

1. **Market Cattle Testing**: Surveillance by this method is done as a part of the marketing process. Testing can be accomplished at livestock markets, slaughterhouses, livestock buying stations or dealer premises. This type of testing is very effective, especially if required at the first point of assembly of cattle from the farm of origin. Absolutely essential ingredients are good animal identification and records so that infected animals (reactors) can be traced to the correct farm of origin. As more and more states became free of brucellosis, testing at livestock markets was decreased. However, in the

United States, 95 % or more of cows and bull two years of age or older have been required to be tested at slaughter for brucellosis. That requirement is now being modified in states that have been Class Free for five years or more, and have no brucellosis-infected wildlife reservoirs, per an interim rule published in December 2010.

2. **Milk Ring Testing**: Surveillance by this method involves the regular, periodic testing of milk or cream from dairy herds that commercially produce these products. The test for this procedure is very sensitive and is performed on a small sample of milk from the entire herd. The milk ring test itself is simple and cheap. A well-managed milk ring testing program is important to public health and can reduce the exposure potential of contaminated milk products to humans by identifying affected herds. In the United States, milk ring testing has been required two times per year in commercial diaries in states officially declared free of brucellosis, and four times per year in states not officially free of brucellosis.

The new interim rule published in December 2010, on which a comment period recently closed modifies the surveillance slaughter and milk ring testing requirements in states that have been Class Free for 5 years or more. Slaughter surveillance will become more risk-based, and laboratories are being consolidated to reflect the changing brucellosis status of the country.

A. Increased Surveillance in States as They Approached Class Free Status

As states approached Class Free status, and in light of the Emergency Action Plan, Class A states generally greatly increased their active surveillance in order to achieve Class Free status, and to ensure that they have not left any infection behind. This work was done in addition to the routine market and slaughter surveillance that was ongoing in these states. Some examples of this increased active surveillance are the following:

1. Testing community herds at a greater distance from affected herds, and for a longer period of time.

2. Testing animals at a younger age. This became much more common as the use of RB51 increased. Instead of testing at approximately two years of age in calfhood vaccinated animals, some states reduced the test age to 18 months or even younger.

3. Revisiting communities that have had previous infection. States reviewed the epidemiology and testing history in those communities. In a majority of cases,

herds that were not tested adequately, or herds that were not found on the original round of testing were identified and retested.

4. Other methods of finding herds that may have been missed by standard passive surveillance techniques were put in to place. Identifying owners who only sold calves and had never had a herd test, and surveys on management practices were also used.

Lessons Learned

As the Brucellosis Eradication Program progressed and evolved over the years, a number of lessons were learned.

One of the lessons is the **importance of communication and cooperation** in all efforts. The Brucellosis Eradication Program in the United States is a state-federal-industry partnership. That partnership has been key in the accomplishments that have been made thus far. Although governments can write rules and regulations, without industry participation, involvement and commitment, very little progress will be made.

Flexibility and modification of the program as the disease status changes is essential. The program must have constant oversight and be adjusted and fine-tuned as needed to ensure continued progress. Actions and approaches would be very different when prevalence is high and the focus is to reduce the number of affected herds, as opposed to when the focus is to find and eliminate the last few remaining herds near the end of a program.

An additional lesson was that **quarantine times** utilized at the outset of the program were insufficient and resulted in brucellosis being left in herds and communities. Initially, herds were quarantined for 30 days. The time was then incrementally increased up to quarantine times of six months. We learned that even when herds were quarantined for six months, recrudescence of brucellosis occurred. Now, herds that are not depopulated are quarantined for one year, which appears to be a sufficient length of time to disclose animals that are incubating.

We learned that appropriate **heifer management** is critical. Heifers are very high-risk animals and often were the reason that recrudescence of brucellosis occurred in herds that previously had apparently eliminated brucellosis. Once we managed heifers more closely to remove them from affected herds, or to minimize their exposure to infection during their most susceptible times and managed them properly at calving so they did not expose other animals, herds became negative and stayed negative for the duration.

We learned that **vaccination alone does not work**. Vaccination is one tool, and a very good one, but brucella vaccines are not 100% effective and can be overwhelmed with a high enough exposure dose to the brucella organism. Vaccination works very well when combined with effective herd management designed to minimize transmission and exposure to brucella.

We learned that **surveillance must be multi-faceted and on-going**. By utilizing multiple surveillance streams, we were able to detect infected animals from different production systems and stages of infection. The key to eliminating brucellosis is to find it early, before it has had a chance to spread. Utilizing various types of surveillance concurrently increases the likelihood of finding infected herds early.

Continuation of Surveillance in the Latter Stages of an Eradication Program

One of the primary challenges with continued progress of an eradication program is to ensure that surveillance activities that are continued will not only be economically feasible, but will be effective as well. Once a state has been declared brucellosis free, there is usually a push to drastically reduce surveillance, especially if first point of assembly, or market testing, has been used as a primary method of surveillance. This is frequently an issue because of the economics of conducting that kind of surveillance, but there are also concerns regarding the necessity of maintaining surveillance once a state has achieved Class Free status. It is important to recognize the reasons for continued surveillance, as this question is one that will continue to be raised as eradication programs progress.

As the country is largely free of brucellosis in livestock (with the exception of occasional spill-over from wildlife in the Greater Yellowstone Area), the United States is moving towards streamlining surveillance, using a risk-based approach and sampling schemes that more appropriately reflect the disease status of the country. These modifications are under development currently.

The reasons for continuing surveillance after a state or the country is declared brucellosis free include;

- To find the last few cases in cattle, or to find infections, which may have been introduced into cattle from wildlife. Experience in other countries has shown that new cases may be found for several years after a country is officially declared free of brucellosis.

- To find any cases of infection which may have been imported into the United States. Although import testing requirements are designed to ensure that only negative, non-incubating animals are imported into the US, there is always the

possibility that an incubating animal may actually be imported, or that animals may be imported illegally.

- As international trade continues to expand, countries will demand surveillance to varying degrees in order to accept our classification of brucellosis free for export purposes. An adequate surveillance system nationwide will undoubtedly be a necessary aspect of the ability of the United States to be recognized world-wide as truly brucellosis free.

Conclusion

The State-Federal Brucellosis Eradication Program has made tremendous progress since its inception. Recently, a review of the countries of the world that have eradicated brucellosis from cattle disclosed that this accomplishment in the United States will have involved more cattle, in more herds, under more diverse circumstances than in any other country (Barton, per comm.). In an eradication program, it is critically important to recognize that, despite all the tools that are available to eliminate the disease, an effective surveillance system is a critical first step that must be in place in order to be successful. Surveillance will need to be monitored continually to assess effectiveness, as well as to determine when surveillance may need to be altered as requirements change. It is imperative to not only be able to find the disease in order to eliminate it, but it is critically important to find the disease before it has had a chance to spread. Once adequate surveillance is in place, the next step is local control to ensure that disease spread does not occur. If the disease can be identified, contained, and eliminated before spread occurs, eradication can be achieved.

Program oversight and refinement is critical as progress continues. Brucellosis eradication programs should frequently be reviewed and modified as needed to reflect current prevalence level and to ensure continued progress towards the ultimate goal of elimination of the disease from livestock.