

## **Brucellosis in Captive Bison**

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## LETTER TO THE EDITOR . . .

### Brucellosis in Captive Bison

Davis et al. (1990) experimentally infected each of 12 pregnant bison and bovine cows with *Brucella abortus* biovar 1, strain 2308 and from the serologic, bacteriologic, pathologic, and transmissibility data they concluded that brucellosis in bison (*Bison bison*) did not differ from that observed in other ruminant species, i.e., cattle, sheep, and goats. In contrast, Meyer (1992) and Meyer and Meagher (1993) found that under natural (field) conditions, brucellosis of bison is not mimetic of bovine brucellosis. The fact that the bison used experimentally by Davis et al. (1990) were artificially exposed, “captive” animals, and the reports by Meyer (1992) and Meyer and Meagher (1993) concerned animals naturally exposed under field conditions, does not account for such differing conclusions. The question that needs to be considered is why the results from experimental infections are at such odds with the manifestations of the disease as it occurs in free-ranging bison.

As stated by Davis et al. (1990), the objectives of their experimental study were to (1) “document the serologic response to non-brucellosis [sic] vaccinated, pregnant bison after challenge with a standard bovine infective dose of *B. abortus* strain 2308 by 11 diagnostic techniques, (2) compare the susceptibility of bison and cattle to *B. abortus* infection, (3) determine the pathogenesis of *B. abortus* in bison, and (4) determine the potential for transmission of *B. abortus* [from] infected bison to susceptible pregnant cattle as compared with *B. abortus* between cattle under identical experimental conditions.”

It long has been known that bison are susceptible to infection with *B. abortus* and may abort therefrom (Mohler, 1917) and that the infecting species or organism is *Brucella abortus* (Creech, 1930) and is biovar 1 (Meyer, 1964). However, the dose

of organisms required to induce infection and abortion in bison has never been ascertained. Thus, in the Davis et al. (1990) study on captive bison, objective 2 should have been the primary objective because the results of the other three objectives depended upon the dose used to assess the comparative susceptibility of bison and cattle to infection with *B. abortus*, in this instance, strain 2308.

To ascertain this comparative susceptibility, each of the 12 pregnant bison and bovine cows were exposed to what Davis et al. (1990) described as “a standard bovine challenge dose (Davies et al., 1973) of  $1 \times 10^7$  colony forming units (CFU) of *B. abortus* 2308 by bilateral conjunctival inoculation.” However, the cited reference for this challenge dose details the preservation of *B. abortus*, strain 544 in liquid nitrogen and then describes how to assess its virulence by challenge of female guinea pigs.

The dose of  $1 \times 10^7$  CFU is in excess of the number of organisms recommended for use in the standard dose to challenge immunity, as measured by abortion or lack thereof, in previously immunized animals (Manthei, 1959). Thus, the dose Davis et al. (1990) used was the dosage for testing the efficacy of immunization. It was not the dose that would measure comparative susceptibility, and in fact, was a severe overdose.

The long established, conventional, and accepted standard method for determining susceptibility to, or infectivity of, pathogenic microorganisms is to assess the dose response of the host by administering graded doses and determining the ( $ID_{50}$ ), dose infective to 50% of the test animals, sometimes called the effective dose ( $ED_{50}$ ) (Freeman, 1979). In brucellosis research the  $ID_{50}$  is the minimum number of organisms which will cause 50% of non-im-

munized cows to abort. For *B. abortus*, strain 2308 the ID<sub>50</sub> is approximately 350,000 organisms, and 700,000 is the recommended number for a standard challenge dose to test the efficacy of immunizing agents in cattle (Mantei, 1959).

To determine the appropriate number of organisms of *B. abortus*, strain 544 to use for challenging the efficacy of immunizing agents, McEwen et al. (1939) administered graded doses from a low of 1,460 organisms to a high of  $1,460 \times 10^6$  to groups of pregnant cattle. The low dose caused only a minimal response and the highest dose, which the authors described as a severe dose, induced abortions, necrotic placentae, and high serotiters of prolonged duration. Other investigators also have explored and commented on low and high doses of *Brucella* organisms (Edington, et al., 1952; King and Frank, 1961). Berman et al. (1949) cautioned that it was of primary importance in research on brucellosis that an adequate but not overwhelming number of organisms be used for artificial exposure.

A small sampling of the literature available in the standard array of veterinary journals reveals reports on determining vaccine efficacy using *B. abortus*, strain 2308 challenge doses of 660,000 organisms (Lambert et al., 1961); 750,000 (Edington et al., 1952), 714,000 to 900,000 (King and Frank, 1961; Redman et al., 1967); and 6 million organisms (Deyoe et al., 1979).

In nature, the majority of bison and cattle undoubtedly become infected via the oral route (Manthei and Deyoe, 1970; Nicoletti and Milward, 1983; Meyer, 1992; Meyer and Meagher, 1993). As far as can be determined in cattle, exposure to infection via the conjunctiva essentially duplicates the pathogenesis of oral exposure and is certainly the route routinely used for experimental purposes. For bison, it is not known whether the outcome of exposure is identical by each of these routes. However, evidence has been accumulating from field (natural) infections to indicate that the host response of bison to *B. abortus*

does not duplicate that of cattle (Meyer, 1992; Meyer and Meagher, 1993). It also is known that, depending on the species of host animal, the route of exposure can have a profound influence on the outcome of exposure, that is, production of immunity versus causing abortion. A good example of this phenomenon is the response of various animals to *B. suis*, biovar 1, strain 2. This strain is used extensively by the Chinese and to a lesser extent by others, for oral immunization of cattle, sheep, and goats against brucellosis. When injected intramuscularly or subcutaneously, it causes abortion in sheep and goats, but not in cattle (Xin, 1986). Since there was no experimental work on brucellosis in bison prior to that of Davies et al. (1990), a well-designed experiment should have included additional groups of bison given an exposure orally to imitate exposure as it occurs in nature.

Davis et al. (1990) concluded that "brucellosis in bison does not differ from that observed in other ruminant species," i.e., cattle, sheep, and goats. Yet, under their experimental circumstances, all the animals in the trial were massively overdosed; this causes distortion and magnification of the results. Because no controls were included, we do not believe it is possible for them to reach this conclusion.

Davis et al. (1990) reported the results of 11 serologic tests and stated that "The antibody response of bison to *B. abortus* challenge, as measured by all serologic tests, lagged approximately 2 to 3 wk behind that seen in cattle at the same time." Because the conclusion has been drawn that brucellosis in bison does not differ from that in cattle, then at least the results of the three standard tests routinely used for identifying infected cattle, i.e., card, standard tube agglutination (SAT), and Rivanol, should be essentially the same in bison. By examination of their data on their Tables 2 and 3 it obviously is not just a simple matter of a 2 to 3 wk lag period. The antibody response of bison, as measured by these three tests, clearly differed from

that of cattle. Irrespective of the ramifications this may have on the usefulness of these tests for diagnostic purposes, it should have alerted these investigators to the possibility that bison may well differ immunologically from cattle in their response to *B. abortus*.

In a further statement on their results, Davis et al. (1990) reported that "Multiple testing periods in which the Card test was used in combination with bison the conjugated enzyme linked immunosorbent assay [BisELISA] and hemolysis-in-gel [HIG] proved to be a useful battery of serologic techniques to diagnose brucellosis in bison after the initial 8 wk PE [post-exposure]." This conclusion is not defensible because 25% of the bison remained negative to the card test at 8 wk PE. Davis et al. (1990) should have recognized and discussed this because these are the bison that gave birth to live calves. Stating that these tests were useful after 8 wk PE is futile because the record presented to the reader terminated at 8 wk, PE.

Based on examination of their Tables 2 and 3, it is evident that even with the severe challenge dose, 25% fewer bison than cattle aborted. The differences in these abortion rates do not support the conclusion of Davis et al. (1990) regarding the similarity of response to brucellosis by bison and cattle. Remarkably, abortion is not mentioned in the results or discussed by the investigators.

The title of the Davis et al. (1990) paper purports it to be devoted to brucellosis in captive bison and to the serology, bacteriology, pathogenesis, and transmissibility of *B. abortus* from bison to cattle. Curiously, in the results and discussion of the paper, abortions are ignored, pathogenesis is covered in two sentences, data on which the final conclusions were drawn regarding serology are not presented, and a key paper on natural (non-experimental) transmission of brucellosis from bison to cattle (Flagg, 1983) is not cited. So, what led Davis et al. (1990) to their conclusions? The initial step in their rationale appears

to be based upon the statement (p. 369) that "*Brucella abortus* was cultured from a wide variety of bison tissues following experimental inoculation, as was described in cattle with brucellosis (Davies et al., 1980)." This reference, however, concerns immunizing calves 3 to 6 mo of age with different doses of *B. abortus*, strain 19, some with and some without administration of hyperimmune sera, and challenging them when they were 13 to 16 mo of age. Although there was an unvaccinated control group of calves, none of the animals were bred and only abdominal and cranial lymph nodes and spleen were cultured. Needless to say, this is not a valid comparison to adult, pregnant, unvaccinated bison, that have been administered a severe dose of field strain of *B. abortus*.

Davis et al. (1990) also pointed out that the histopathology of lymph nodes of infected bison was the same as that of infected cattle. However, microlesions are not definitive of brucellosis in ruminants and certainly cannot be used for definition of the disease. Identical lesions occur in other infections, one example is campylobacteriosis (Jubb et al., 1985).

Finally, Davis et al. (1990) state that "The fetal and placental lesions parallel those previously described in cattle (Jubb and Kennedy [sic], 1985), sheep (Morello [sic] et al., 1963), and goats (Anderson et al., 1986) and this supports the conclusion that brucellosis in bison does not differ from that observed in other ruminant species" such as cattle, goats, and sheep. However, it should be noted that fetal and placental microlesions are not pathognomonic for brucellosis (Jubb et al., 1985). Additionally, there are some marked differences between the response of cattle to exposure and infection with *B. abortus* and that of sheep and goats. One of the differences is in the disparate susceptibilities to *B. abortus*. Cattle are a natural reservoir of this species of *Brucella*, while sheep and goats are not. Under natural (field) conditions, infection and abortion in sheep or goats is uncommon. As previously indicated, the

ID<sub>50</sub> of virulent *B. abortus* for cattle is 360,000 colony-forming units (CFU) (Manthel, 1959). Davis et al. (1990) compare this to abortion in sheep as described by Molello et al. (1963) and in goats, as described by Anderson et al. (1986). To induce abortion experimentally in pregnant sheep, Molello et al. (1963) had to administer  $2.4 \times 10^9$  organisms intravenously. Goats are even less susceptible to *B. abortus* than are sheep. Anderson et al. (1986) induced abortion in only four of ten goats by performing laparotomies and inoculating each goat with 1 billion ( $1 \times 10^9$ ) organisms intravenously in the uterine artery. In contrast, the ID<sub>50</sub> of the standard virulent strain of *B. melitensis* (strain 6015) for goats is 20,000 to 50,000 CFU (Renoux et al., 1955; Elberg, 1959) and approximately 400,000 CFU for sheep (Renoux et al., 1955).

Davis et al. (1990) also clearly stated "Gross lesions were not observed in bison cows or their fetuses." However, gross lesions of the placenta are characteristic of bovine infections with *B. abortus* (Jubb et al., 1985). Both Molello et al. (1963) and Anderson et al. (1986) described at length gross pathological placental lesions in sheep and in goats.

In summary, one of the primary objectives of the study by Davis et al. (1990) was to determine the comparative susceptibility of bison and bovine cows to infection and abortion following exposure to *B. abortus*. A fundamental flaw was introduced into the experiment when a massive dose was administered, causing distortion, magnification, and alteration in pathogenesis and in serologic, bacteriologic, and pathologic results. Thus, the conclusion that brucellosis of bison does not differ from that in cattle or other ruminants cannot be made on the basis of the experimental conditions described by Davis et al. (1990).

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