



Estimating Transmission and the Basic Reproductive Rate of *B. abortus* in Yellowstone Bison



Technical Report to the National Park Service
December 2011

YCR-2011-10



Suggested citation: Yellowstone Center for Resources. 2011. Estimating Transmission and the Basic Reproductive Rate of *B. abortus* in Yellowstone Bison. Technical Report for the National Park Service, December 2011. Mammoth Hot Springs, Wyoming, YCR-2011-10.

Cover Image: A bison shedding the final remnants of its winter coat grazes a Yellowstone meadow.

Estimating Transmission and the Basic Reproductive Rate of *B. abortus* in Yellowstone Bison

Chris Geremia

December 1, 2011

Abstract

Infectious diseases shape the dynamics of populations and communities of organisms. Knowledge of the parameters that regulate these dynamics is fundamental to building revealing models of the impacts of disease on ecological systems. We used hierarchical Bayesian techniques to estimate rates of exposure, latency, recovery, and return to the infective stage of *Brucella abortus* bacteria among Yellowstone bison (*Bison bison*) during 1995-2010. Effects of exposure on survival and reproduction were also estimated, and mean rates were unified in a simple SE_1E_2IR -model to determine the basic reproductive rate (R_0) of *B. abortus*. The median annual probability of infection was 0.19, and associated continuous time force of infection was 0.21. Median probabilities of horizontal (from unrelated bison) and vertical (from mother) exposure to calves were 0.10 and 0.08, respectively, though the distribution for vertical transmission was skewed left with most of the density closer to zero. Bison remained in the exposed stage for 1.97 years (SD = 0.67) and the duration of active infection was 1.30 years (SD = 0.19). The median probability of returning to the infective stage after recovering from the initial acute infection was 0.03 (0.00, 0.09). Median survival was high (0.91) and disease had lasting effects on fecundity with lower median probabilities of birth for infected (0.60) and recovered (0.61) animals. Our estimate of R_0 was 1.2 suggesting proper management intervention may break the infection cycle of *B. abortus* in bison. Given the competing interests of disease management and bison conservation in Yellowstone, management strategies that target young females (e.g. 2-5 years of age) will be most successful at influencing disease transmission.

INTRODUCTION

The ability of pathogens to influence the dynamics of wildlife populations by reducing the survival and fecundity of their hosts has long been recognized (Anderson and May 1979, Hudson et al. 1992, McCallum and Dobson 1995). However, most pathogens establish endemic infections that persist in their host populations without a noticeable effect on host vital rates. In contrast to epidemic diseases, which are characterized by rapid changes in infection prevalence that can lead to long periods without infective hosts, endemic diseases are described by a relatively constant proportion of the host population being infected with little fluctuation in prevalence of infection (Anderson and

May 1979). Endemic diseases in wildlife, such as bovine tuberculosis and brucellosis, are increasingly becoming a global problem due to the transmission risk to domestic livestock and humans. In free-ranging wildlife, endemic diseases are especially difficult to manage because the progression of infection can occur over a long period of time. Infected animals that harbor latent infections may not become infectious for years following exposure with some individuals developing long-term chronic infections. The interplay between the intensity of transmission and the degree of recovery from infection largely defines the level of endemic infection. Thus, effective control of endemic disease requires understanding how transmission and recovery rates influence the observed infection dynamics, which can be used to develop effective disease reduction strategies.

The Bison population in Yellowstone National Park has been affected by the disease bovine brucellosis for almost a century since it was introduced into the park by European cattle (Meagher and Meyer 1994). Bovine brucellosis is a contagious, infectious disease caused by the bacterium *Brucella abortus*, where infection of the reproductive organs during pregnancy can lead to late-term abortions with the highly infectious fetus serving as a transmission source (Williams et al. 1997). Brucellosis has not had a significant effect on survival within infected bison populations (Dobson and Meagher 1998, Joly and Messier 2005), but it is generally accepted that pregnant bison experience decreased fecundity during their first reproduction following infection (Thorne 2001, Rhyan et al. 2009). There is much uncertainty about the progression of the disease in wild bison, however the ability of *B. abortus* to establish long-term chronic infections is well documented in both humans and domesticated animals (Young and Corbel 1989) suggesting some contribution of chronically infected individuals toward *B. abortus* transmission and reductions in fecundity. Transmission maintaining *B. abortus* in Yellowstone bison is thought to occur primarily through contact with an aborted fetus or infected birth tissues shed during a live birth (i.e., horizontal transmission; Rhyan et al. 2009). Bison tend to give birth in close proximity to other group members, which increases the likelihood of horizontal transmission. The number of exposures that occur during these infectious events depends on the

behavior of the birthing female and associated group members at the time of parturition. However, *B. abortus* is also known to cause mammary gland infections and be transmitted through infected milk (i.e., vertical transmission; Rhyan and Drew 2002).

The intensity of transmission within these pathways and the duration of *B. abortus* infection are the primary factors that sustain the disease in Yellowstone bison. Understanding the rates at which infection is acquired and lost is necessary for implementing effective measures to reduce the risk of brucellosis transmission to cattle outside the parks boundaries. Yellowstone bison have been the target of brucellosis management in the northern portion of the greater Yellowstone area for several decades (Cheville et al. 1998), with current policy set by a court-mediated Interagency Bison Management Plan (IBMP) implemented collaboratively by the State of Montana and the federal government. The IBMP aims to conserve wild bison, while reducing the risk of brucellosis transmission to cattle (USDI and USDA 2000). Winter conditions influence bison movement to low elevation ranges outside IBMP tolerance areas established to minimize the risk of transmission through separation of cattle and bison (Geremia et al. 2011, USDA and USDI 2010). Approximately 3,200 bison were culled since 2001, with >20% of the population removed during 2006 and 2008 (White et al. 2011). These large culls have contributed to a skewed sex ratio, gaps in the populations age structure, and reduced productivity (White et al. 2011).

Management of Yellowstone bison receives worldwide attention, and several scientists have proposed ecological models to advise management decision-making (Dobson and Meagher 1998, Miller et al. 2004, Kilpatrick et al. 2009, Treanor et al. 2011). However, estimates of transmission probabilities and the duration of infection have generally been conjectured to lessen the efficacy of these tools. For example, high levels of horizontal transmission suggest that pregnant bison migrating into Montana near parturition could pose a transmission risk to cattle, while high levels of vertical transmission could reduce the effectiveness of vaccination in bison that are exposed to *B. abortus* prior to being

vaccinated.

Reliable estimates of disease transmission parameters require identifying the true disease state of individuals, which is usually complicated by the availability of information indicating exposure rather than true infection (Heisey et al. 2006, 2010). *B. abortus* infection is typically diagnosed using serologic tests, which indicate prior exposure but do not provide definitive proof of active infection (i.e., presence of *B. abortus*). Despite this shortcoming, serologic data collected from individual bison over time can be used to identify the window of *B. abortus* exposure (i.e., seroconversion) and estimate transmission routes influencing brucellosis dynamics. Similarly, bacterial culture of *B. abortus* from female bison following parturition indicates shedding of bacteria. If the same individuals are sampled following subsequent pregnancies, the information can be used to evaluate the duration of infection. Some bison may develop chronic brucellosis and shed bacteria for two or more years following the acute phase of infection, when an animal experiences their first reproductive cycle after exposure (Rhyan et al. 2009). The progression of brucellosis infection in chronically infected bison is similar to chronically infected cattle (Rhyan et al. 2009), and most chronically infected cattle recover by clearing the infection and exhibiting life-long immunity (Ficht 2003). However, a proportion of bison may develop persistent infections, from which they relapse back to an infectious state during periods of stress (e.g. pregnancy; Cheville et al. 1998), thereby increasing the duration of infection. Similarly, bison that previously cleared *B. abortus* infection may be re-exposed to an infectious dose that overwhelms existing immune defenses. The potential for bison to return to an infectious state during future pregnancies extends the transmission period at the individual level and may have a large effect on infection prevalence in the population.

Here, we present an epidemiological model to describe brucellosis infection in Yellowstone bison and assimilate data collected from Yellowstone bison with Bayesian hierarchical models to estimate probabilities of (1) horizontal transmission; (2) vertical transmission; (3) progression to the infective

stage; (4) recovery; (5) return to the infective stage; and effects on (6) reproduction and (7) survival. We then unify these estimates with our epidemiological model to determine the basic reproductive rate (R_0) of *B. abortus*.

METHODS

A DISEASE MODEL OF BRUCELLOSIS IN YELLOWSTONE BISON

We used an SE_1E_2IR model (suseptible-exposed(1)-exposed(2)-infective-recovered) to portray brucellosis dynamics in Yellowstone bison. Only female animals were considered since males are likely incapable of transmitting infection. Bison were born into the susceptible or exposed(2) stage (via vertical transmission), with all exposed individuals progressing through a latent period prior to active infection. Infective bison recovered from the initial acute infection or remained in the infective stage for subsequent year(s). Recovered bison also returned to the infective stage through recrudesence or loss from the recovered class followed by re-infection. Model parameters were μ mortality rate, f_1 fecundity of susceptible and exposed individuals, f_2 fecundity of infective individuals, f_3 fecundity of recovered individuals, λ_h per capita rate of new infections from horizontal exposure, λ_v per capita rate of new infections from vertical exposure, a progression into the infective stage, v recovery, and γ return to the infective stage.

$$\frac{dS}{dt} = f_1(S + E) + f_2R + f_3(1 - \lambda_v)I - (\mu + \lambda_h)S \quad (1)$$

$$\frac{dE_1}{dt} = \lambda_h S - (\mu + a)E \quad (2)$$

$$\frac{dE_2}{dt} = f_3\lambda_v I - (\mu + a)E \quad (3)$$

$$\frac{dI}{dt} = aE - (v + \mu)I + \gamma R \quad (4)$$

$$\frac{dR}{dt} = vI - (\gamma + \mu)R \quad (5)$$

ANIMAL HANDLING

The Animal and Plant Health Inspection Service (1995-2001) and National Park Service (2002-

2010) conducted a mark-recapture study of adult female bison in Yellowstone National Park and nearby areas of Montana. One hundred and forty-six bison >1 year of age were marked and monitored, with animals entering the study through the project. Bison were captured in autumn by immobilization with carfentanil and xylazine (Rhyan et al. 2009) or at handling facilities near the boundary of the park (USDI and USDA 2000). Whole blood was collected into vacutainer tubes and immediately centrifuged. Serum was then extracted and frozen at -70 F. During 1995-2001, sera were shipped to the National Veterinary Services Laboratory, Ames, Iowa, USA for testing for antibodies to *B. abortus* (Alton et al. 1988) and sero-status was determined using a panel of nine serologic tests including the standard card, standard plate, standard tube, rivanol, buffered acidified plate antigen, complement fixation, particle concentrate fluorescence immunoassay, rapid automated presumptive test, and competitive enzyme-linked immunoabsorbent assay. After 2001, sera were tested by park biologists (Yellowstone National Park) and/or the Montana Department of Livestock Diagnostics Laboratory (Bozeman, Montana, USA) using the quantitative fluorescent polarization assay (Neilsen and Gall 2001). Bison were fitted with a uniquely engraved metal ear tag and mortality-sensing telemetry collar (Advanced Telemetry Systems, Isanti, Minnesota, USA; Lotek, Newmarket, Ontario, Canada; Telonics, Mesa, Arizona, USA).

During 1995-2001, bison were located using ground-homing techniques and recaptured during fall (October-November), mid-winter (February) and within 5 days of parturition. Blood was collected for determining sero-status. We also collected heparinized blood, milk (if present), feces, and cervical swabs for culture of *B. abortus*. Isolation of *B. abortus* from samples was conducted at National Veterinary Services Laboratory according to established standard operating procedures. Attempts were made to catch neonatal calves of associated dams during post-parturition handling. Calves were marked with a unique metal ear tag and recaptured when associated with telemetered dams during the subsequent autumn. Blood was collected for determining sero-status and calves were fit with a telemetry device for long-term monitoring.

Throughout the study, survival status of individuals was determined by observing animals fit with telemetry devices. Females that were palpated as pregnant during 1995-2001 were implanted with a vaginal telemetry device. Observers regularly located females during the calving period and determined whether or not a viable calf was produced (Fullet et al. 2007, Geremia et al. 2009). We considered a viable calf as one observed nursing approximately one week after birth. All bison were observed and/or handled in compliance with the court-negotiated settlement for the Interagency Bison Management Plan and National Park Service research permit YELL-2008-SCI-5340, as well as guidelines recommended by the American Society of Mammalogists (Gannon and Sikes 2007). Animal care and welfare procedures were approved by veterinarians from the Biological Resource Management Division of the National Park Service and are outlined in the Yellowstone Bison Management Capture and Handling Protocol.

BAYESIAN ANALYSIS OF MARK-RECAPTURE HISTORIES

Bison were assumed to be exposed to *B. abortus* during the calving season and were tested for exposure approximately six months later. Testing coincided with gestation when the *B. abortus* organism is believed to begin replication and progression to the reproductive system. Therefore, timing of our tests should have allowed for a lag between exposure and the conversion to the positive sero-status (i.e., antibody presence). We defined λ_h^* as the probability that an adult bison was exposed to *B. abortus*. Bison entered the analysis seronegative and exited when we observed a positive sero-status. All bison were not handled annually, and we used a missing value structure to evaluate exposure probability (Clark 2007). Some bison were not tested for >2 years, but had converted to seropositive upon subsequent testing. We did not know when the individual was exposed, which is necessary for accurately estimating the probability of exposure. We defined t_i and T_i as years of entry and exit from the study, s_i as the subset of years during which we knew the sero-status of the individual, $z_{i,t}$ as the unobserved true sero-status, and $y_{i,t}$ as the observed

sero-status. Similar to the state space model framework (Calder et al. 2003, Newman et al. 2006), the true sero-status at time t was conditional on the probability of exposure λ_h^* and the preceding state of the individual $z_{i,t-1}$. Observations of states $y_{i,t}$ were conditional on true states $z_{i,t}$ (5).

$$[\mathbf{Z}, \lambda_h^* | \mathbf{Y}] \propto \prod_{i=1}^n \prod_{t \in s_i} [y_{i,t} | z_{i,t}] \prod_{i=1}^n \prod_{t=t_i+1}^{T_i} [z_{i,t} | z_{i,t-1} \lambda_h^*] [\lambda_h^*] \quad (6)$$

A total of thirty-eight calves associated with dams were captured during the fall capture period and tested for exposure to brucellosis. We defined $\lambda_{h_c}^*$ as the probability of horizontal transmission to calves and λ_v^* as the probability of vertical transmission to calves. We assumed that seronegative dams could not expose their calves to *B. abortus* and attributed all exposure of those bison to horizontal routes. Passive antibodies resulting from the transfer of antibodies from seropositive dams to calves are usually undetectable by 5-6 months of age (Rhyan et al. 2009). Calves born to seropositive dams remaining seropositive during October were likely exposed to *B. abortus* through either vertical or horizontal transmission, and routes of exposure were differentiated as $\lambda_{h_c}^* + \lambda_v^* - \lambda_{h_c}^* \lambda_v^*$. We defined y_n as the sum of seropositive calves born to seronegative dams, n_n as the number of tests of calves born to seronegative dams, y_p as the sum of seropositive calves born to seropositive dams, and n_p as the number of tests of calves born to seropositive dams (6).

$$[\lambda_{h_c}^*, \lambda_v^* | y_n, y_p, n_n, n_p] \propto [y_n | \lambda_{h_c}^*, n_n] [y_p | \lambda_v^*, \lambda_{h_c}^*, n_p] [\lambda_{h_c}^*] [\lambda_v^*] \quad (7)$$

We assumed that bison progressed through a latent period after exposure. Culture and serology data were available from nine animals (n_e) that were seronegative during the parturition season and converted to a positive sero-status by the beginning of the following gestation period. We considered a positive culture by the next parturition season (i.e, approximately one year since exposure) indicative of an animal that progressed into the infective stage. We summed results between individuals defining y_e as the number of culture positive tests and a^* as the probability of progressing into the infective stage (7).

$$[a^* | y_e, n_e] \propto [y_e | a^*, n_e] [a^*] \quad (8)$$

A similar approach was used for estimating recovery and we defined v^* as the probability of progression into the recovered stage. Eight individuals were observed as infective which was indicated by positive culture of *B. abortus* during the gestation period. Culture results were then obtained from six of these individuals (n_i) during the subsequent gestation period and we let y_i represent the number of culture-negative results (8).

$$[v^*|y_i, n_i] \propto [y_i|v^*, n_i][v^*] \quad (9)$$

We allowed bison to return directly from the recovered to infective stage. We considered bison that entered the study as seropositive (n=47) with an associated negative culture test. We also included seroconverting bison beginning the gestation period after the last sequential culture positive result associated with seroconversion (n=8). Observations were summed between individuals (n_r) and we defined γ^* as the probability of return to the infective stage (9).

$$[\gamma^*|y_r, n_r] \propto [y_r|\gamma^*, n_r][\gamma^*] \quad (10)$$

We did not anticipate that disease status would influence survival and we estimated a single annual mortality probability μ^* for the population (10). We estimated the probability of observing a birth as $\text{logit}(f)^{-1} = f_1 + f_2x_2 + f_3x_3$. x_2 and x_3 were (0,1) indicator variables for recovered and infective dams (11).

$$[\mu^*|y, n] \propto [y|\mu^*, n][\mu^*] \quad (11)$$

$$[f^*|y, n] \propto [y|f^*, n][f^*] \quad (12)$$

For each of these independent analyses, we treated unobserved and observed sero-statuses as random binomial variables, and specified diffuse prior distributions (i.e., Beta (1,1) or Normal (0,1000)) on model parameters. We obtained posterior distributions for model parameters using Monte Carlo Markov Chain methods in a Bayesian framework. Monte Carlo Markov Chain procedures were implemented using the RJAGS package to call JAGS version 2.3.0 from R (R Core Development Team). We ran each of the three models for 50,000 iterations using three different Monte Carlo

Markov chains. The first 10,000 iterations were excluded to allow for burn-in. We assessed convergence of chains using the Gelman and Heidelberg diagnostics using the `gelman.diag` and `heidel.diag` functions in R. The .975 quantile for Gelman potential scale reductions factors was < 1.05 for all parameter estimates. Chains for all parameters passed Heidel tests of stationary distribution and for accuracy of the mean.

We used the $*$ notation to refer to discrete time probabilities which were estimated directly in the mark-recapture analyses. However, we also needed to approximate the accompanying continuous time rates to input values into our disease model. Approximations were derived within each MCMC algorithm where $p^* = 1 - e^{-p}$, and p^* was the discrete probability and p was the continuous time rate.

RESULTS

We observed 139 female bison over 336 bison-years, and recorded 33 natural mortalities. Annual probability of mortality was 0.09 (0.06, 0.12; mean continuous time rate = 0.09). We also successfully determined the fate of 188 pregnancies of bison of known disease status. The probability of birth decreased for infective and recovered bison, with larger decreases in the probability of birth for infective individuals. The probability of birth for susceptible and exposed bison was 0.80 (0.70, 0.88; mean continuous time rate = 1.66), 0.60 (0.30, 0.86; mean continuous time rate = 0.92) for infective bison, and 0.61 (0.51, 0.70; mean continuous time rate = 0.92) for recovered bison.

Twenty-three seroconversions were observed out of 79 adult bison and occurred in animals between 2-10 years of age. The median annual probability of horizontal exposure (λ_h^*) was 0.19 (0.13, 0.26 95% credible interval). We cultured bacteria from five out of nine bison within a year of seroconversion and our estimated probability of transition to the infective stage (a^*) was 0.55 (0.26, 0.81). Animals that remained in the latent stage for more than one year were mostly exposed prior to reproductive

maturity. Also, eight (89%) bison tested culture positive within 30 months of seroconversion and we were unable to culture bacteria from one individual. Recovery was measured as obtaining a culture negative result during the gestation period after observing the initial culture positive test. A single bison was observed as infective during the subsequent gestation period. While these observations were limited to six individuals, we estimated the probability of recovery (v^*) as 0.77 (0.42, 0.96). Further, once bison were observed in the recovered stage (n=55) we only detected a single culture positive result and we estimated the probability of return to the infective stage (γ^*) as 0.035 (0.00, 0.09; Table 1).

Table 1: Marginal posterior distributions of disease parameters estimated from capture and recapture of female Yellowstone bison during 1995-2011. Parameters were annual probabilities determined in discrete time (1 year) and mean continuous time rates were estimated from these probabilities for determining R_0 .

Description	Parameter	Mean	95% Credible Interval	Mean Continuous Time Rate
horizontal transmission	λ_h	0.19	(0.13,0.26)	0.20
vertical transmission	λ_v	0.08	(0.00,0.28)	0.08
progression to the infective stage	a	0.55	(0.26, 0.81)	0.79
recovery	v	0.77	(0.42, 0.96)	1.46
return to the infective stage	γ	0.04	(0.00,0.09)	0.04

Serology was determined from both members of 38 calf and dam pairs approximately 6 months post-parturition. Horizontal brucellosis exposure to calves ($\lambda_{h_c}^*$) was 0.10 (0.03, 0.22) and vertical exposure (λ_v^*) was 0.08 (0.00, 0.28). The posterior distribution of vertical exposure was asymmetrical with 75% of the density <0.14 .

DISCUSSION

Bison calves were exposed to *Brucella* bacteria through both horizontal and vertical transmission routes. While the estimates for horizontal and vertical transmission to calves were similar, the skewed probability distribution for vertical transmission indicates that horizontal transmission is

most likely the dominant transmission mode. Nearly as many calves born to seronegative females were seropositive after 6 months of age compared to calves born to seropositive or seroconverting females. Nursing calves can receive maternal *B. abortus* antibodies passed through colostrum which will cause them to react positively on serologic tests. However, this passive immunity typically wanes by the time calves are 6 months of age (Rhyan et al. 2001). Thus, if *B. abortus* transmission to calves was dominated by vertical transmission, we would expect a stronger association of infected newborns (>6 months old) with infected mothers.

Earlier epidemiological models of *B. abortus* transmission suggested that 90% of calves born to infective dams were exposed (Dobson and Meagher 1998). We found that approximately 60% of infective bison give birth to a live calf. However, we were only able to track the fate of pregnancies of ten known infective individuals, and we are 95% certain that the probability of birth may be as low as 30%. Further, bison remained in the infective stage for 1.30 years (SD = 0.19) and there was a 0.03 probability of returning to the infective stage (i.e., infectious during a reproductive cycle followed by a period of non-infectiousness before becoming infectious again). Due to our observed high virulence of the *B. abortus* organism and relatively short duration of active infection, it is unlikely that disease could be maintained in bison if it was only transmitted vertically. Instead, contact by susceptible animals with infectious material shed onto the landscape likely serves as the dominant route of transmission (Rhyan et al. 2001) similar to infection in cattle (Davis et al. 1990, 1991) and elk (Thorne et al. 1971, Etter and Drew 2006).

Bison progressed from the exposed to infective stage in 1.97 years (SD = 0.67). Disease prevalence information suggests that many bison are exposed early in life with >40% of reproductively immature females testing seropositive to brucellosis (Treanor et al. 2011). Ingestion of the *Brucella* pathogen is the most common route of exposure where infection is initially limited to local lymph nodes. Timing of proliferation and spread, which is necessary for transmission, coincides with the

later stages of the gestation period. Therefore, bison exposed prior to reproductive maturity likely exhibit a lengthy incubation period, with transition to the infectious stage coinciding age of first reproduction.

Each bison (n=2) that was exposed more than one year prior to reaching reproductive maturity produced a viable calf during their first pregnancy. Perhaps, exposure early in life increases resistance against a full-blown brucellosis abortion. The host immune system has at least some capability to recognize the pathogen likely preventing unobstructed access to the placenta and diminishing the probability of abortion. Also, we were also unable to culture bacteria from one individual when exposure likely occurred after reproductive maturity. Heterogeneities in dose and/or individual susceptibility may prolong the incubation period to the extent that some seropositive individuals possess improved ability of containing infection.

Active infection diminished birth probability and these effects lasted beyond the period of initial active infection. A *B. abortus* induced abortion generally results in a retained placenta, which may serve as an entry route for new pathogens to the reproductive tract. Bison may develop metritis (or other intrauterine infection) as a by product of an abortion event having implications on future pregnancies (Geremia et al. 2009). Our research also suggests that the age of first reproduction is delayed when bison are exposed early in life.

We constructed next generation matrices of infection using our compartment equations to estimate R_0 (Diekmann et al. 2010). This approach necessitated that we defined the underlying form of the transmission process and that the bison population was at equilibrium (birth rate = death rate) at the time of disease introduction. Dobson and Meagher (1998) suggested that frequency dependent transmission, where the per capita rate of new infections depends on the prevalence rather than the abundance of infected individuals, better represented disease dynamics in Yellowstone bison. We

made this assumption, and represented 20% of adult female bison as actively infective during the extent of data collection efforts (Treanor et al. 2011). We populated our next generation matrix with mean continuous time values and estimated R_0 as 1.2. This value of R_0 suggests low level endemic infection in the bison population and is slightly lower than the previously recorded value (Dobson and Meagher, 1998).

Management Implications

Proposed brucellosis management strategies incorporate test and removal of seropositive and vaccination of seronegative individuals that migrate out of the park during winter [11,13]. Our confirmation that the dominant route of transmission is horizontal suggests vaccination may be a plausible disease control strategy. Also, targeted removal of serologically exposed primiparous (3 years old) and young mature female bison (4-5 years of age) may further suppress disease transmission by reducing the number of infective animals. Our estimate of R_0 suggests that management intervention has the potential to strongly influence disease dynamics, because of the 0.2 increment that R_0 is above the critical threshold necessary for disease proliferation. We strongly recommend further mathematical analysis of our proposed disease model to determine the degree to which each disease parameter must be reduced to decrease R_0 substantially below this critical threshold.

Our work represents one effort among several that attempts to portray brucellosis dynamics in Yellowstone bison. We conclude by reconciling data presented here with existing knowledge of the disease to offer a revised conceptual model of brucellosis in Yellowstone bison and outline future research. We treated each animal with identical susceptibility, progression into the infective stage, and recovery. Instead, the course of infection likely is affected by the timing of exposure, where animals exposed during gestation rapidly progress into the infective stage as conditions are favourable to bacteria proliferation and spread. Consequent attack of the placenta likely results in premature

birth, with the abortive material serving as a transmission source. The majority of these animals will completely recover from this acute infection. However, some will remain in the acute phase for subsequent pregnancies perhaps owing to genetic variations in the pathogen and host, and host condition. Other individuals may develop chronic brucellosis where the pathogen is contained in an inactive stage within the host. Conditions may again become favorable for bacteria proliferation and spread, timed with subsequent gestation. However, the host immune system has the capability to recognize the pathogen preventing unobstructed access to the placenta and diminishing the probability of abortion. Animals exposed prior to reproductive maturity may also develop some recognition ability for the pathogen providing similar protection against the brucella organism.

Literature Cited

- Alton GG, LM Jones, RD Angus, JM Verger. 1988. Techniques for the brucellosis laboratory. Institut National de la Recherche Agronomique, Paris, France, 190 pp.
- Anderson RM and RM May. 1979. Population biology of infectious diseases. *Nature* 280: 361-367.
- Calder C, M Lavine, P Muller, JS Clark. 2003. Incorporating multiple sources of stochasticity into dynamic population models. *Ecology* 84: 1395-1402.
- Chevillon NF, DR McCullough, LR Paulson. 1998. Brucellosis in the greater Yellowstone area. National Academy Press, Washington D.C., USA.
- Clark JS. 2007. Models for ecological data: an introduction. Princeton University Press, Princeton, New Jersey, USA.
- Davis DS, JW Templeton, TA Ficht, JD Williams, JD Kopec, et al. 1990. *Brucella abortus* in captive bison I. Serology, bacteriology, pathogenesis, and transmission to cattle. *Journal of Wildlife Diseases* 26: 360-371.
- Davis DS, JW Templeton, TA Ficht, JD Huber, RD Angus, et al. 1991. Evaluation of strain 19 in pregnant cows. *Journal of Wildlife Diseases* 27: 258-264.
- Diekmann O, AP Hesterbeek, MG Roberts. 2010 The construction of next generation matrices for compartmental epidemic models. *J. R. Soc Interface* 7: 873-885.
- Dobson A and M Meagher. 1998. The population dynamics of brucellosis in the Yellowstone Park. *Ecology* 77: 1026-1036.
- Etter RP and ML Drew. 2006. Brucellosis in elk of eastern Idaho. *Journal of Wildlife Diseases* 42: 271-278.
- Ficht TA. 2003. Intracellular survival of *Brucella*: defining the link with persistence. *Veterinary Microbiology* 92: 213-223.
- Fuller JA, RA Garrott, PJ White, K Aune, T Roffe, et al. 2007. Reproduction and survival of Yellowstone bison. *Journal of Wildlife Management* 71: 2365-2372.
- Gannon W L, Sikes RS, the Animal Care and Use Committee of the American Society of Mammalogists. 2007. Guidelines of the American Society of Mammalogists for the use of wild mammals in research. *Journal of Mammalogy* 88: 809-823.
- Geremia C, PJ White, RA Garrott, R Wallen, KE Aune, et al. 2009. Demography of central Yellowstone bison: effects of climate, density and disease. Pages 255-279 in RA Garrott, PJ White, FGR Watson, editors. *The ecology of large mammals in central Yellowstone: Sixteen years of integrated field studies*. Elsevier, San Diego, California, USA.
- Geremia C, PJ White, RL Wallen, FGR Watson, JJ Treanor et al. 2011. Predicting bison migration out of Yellowstone National Park using Bayesian models. *PLoS ONE* doi:10.1371/journal.pone.0016848.

Heisey DM, DO Joly, F Messier. 2006. The fitting of general force of infection models to wildlife disease prevalence data. *Journal of Ecology* 87: 2356-2365.

Heisey DM, EE Osnas, PC Cross, DO Joly, JA Langenberg et al. 2010. Linking process to pattern: estimating spatiotemporal dynamics of a wildlife epidemic from cross sectional data. *Ecological Monographs* 80: 221-240.

Hudson, P.J., D Newborn, and AP Dobson. .1992. Regulation and stability of a free-living host-parasite system: *Trichostrongylus evansi* in red grouse. I. Monitoring and parasite reduction experiments. *Journal of Animal Ecology* 61: 477-486.

Joly D and F Messier. 2005) The effect of bovine tuberculosis and brucellosis on reproduction and survival of wood bison in Wood Buffalo National Park. *Journal of Animal Ecology* 74: 541-551.

Kilpatrick AM, CM Gillian, P Daszak. 2009. Wildlife-livestock conflict: the risk of pathogen transmission from bison to cattle outside Yellowstone National Park. *Journal of Applied Ecology* 46: 476-485.

ADDMcCallum and Dobson 1995.

Meagher M and ME Meyer. 1994. On the origin of brucellosis in bison of Yellowstone National Park: a review. *Conservation Biology* 8: 645-653.

Miller LA, JC Rhyhan, M Drew. 2004. Contraception of bison by GnRH vaccine: a possible means of decreasing transmission of brucellosis in bison. *Journal of Wildlife Diseases* 40: 725-730.

Newman KB, ST Buckland, ST Lindley, L Thomas, C Fernandez. 2006 Hidden process models for animal population dynamics. *Ecological Applications* 16: 74-86.

Nielsen A and D Gall. 2001. Fluorescence polarization assay for the diagnosis of brucellosis: a review. *Journal of Immunoassay and Immunochemistry* 22: 183-201.

R Development Core Team. 201) R: a language and environment for statistical computing. Vienna Austria: R Foundation for Statistical Computing.

Rhyhan JC, T Gidlewski, TJ Roffe, K Aune, LM Philo, et al. 2001. Pathology of brucellosis in bison from Yellowstone National Park. *Journal of Wildlife Diseases* 37: 101-109.

Rhyhan JC and MD Drew. 2002. Contraception: a possible means of decreasing transmission of brucellosis in bison. Pages 99-108 in TJ Kreeger, editor. *Brucellosis in elk and bison in the greater Yellowstone area*. Wyoming Game and Fish, Cheyenne, Wyoming, USA.

Rhyhan J C, K Aune, T Roffe, D Ewalt, S Hennager, et al. 2009. Pathogenesis and epidemiology of brucellosis in Yellowstone: serologic and culture results from adult females and their progeny. *Journal of Wildlife Diseases* 45: 729-739.

Thorne ET, J Morton, FM Blunt, HA Dawson. 1978. Brucellosis in elk II clinical effects and means of transmission as determined through artificial infections. *Journal of Wildlife Diseases* 14: 260-291.

Thorne ET. 2001. Brucellosis. Pages 372-395 in ES Williams and IK Barker, editors. *Infectious diseases in wild mammals*. Blackwell Publishing, Ames, Iowa, USA.

Treanor J, J Johnson, RL Wallen, S Cilles, PH Crowley, et al. 2010. Vaccination strategies for

managing brucellosis in Yellowstone bison. Vaccine 28: F64-F72.

Treanor JJ, C Geremia, PH Crowley, JJ Cox, PJ White et al. 2011. Estimating probabilities of active brucellosis infection in Yellowstone bison through quantitative serology and tissue culture. Journal of Applied Ecology (in press)

United States Department of the Interior (USDI), National Park Service and United States Department of Agriculture (USDA), Forest Service, Animal, and Plant Health Inspection Service. 2000. Record of decision for final environmental impact statement and bison management plan for the state of Montana and Yellowstone National Park. Washington, D.C.

United States Department of the Interior, National Park Service. 2010. Brucellosis remote vaccination program for bison in Yellowstone National Park. Draft Environmental Impact Statement, Washington, D.C., USA.

White PJ, RL Wallen, C Geremia, JJ Treanor, D Blanton. 2011. Management of Yellowstone bison and brucellosis transmission risk expectations and realizations. Biological Conservation doi 10:10.1016/j.biocon.2011.01.003.

Williams ES, SL Cain, DS Davis. 1997. Brucellosis: the disease in bison. Pages 7-19 in ET Thorne, MS Boyce, P Nicoletti, TJ Kreeger, editors. Brucellosis, bison, elk, and cattle in the greater Yellowstone area: defining the problem, exploring solutions. Wyoming Game and Fish Department, Cheyenne, Wyoming, USA.

Young EJ and MJ Corbel. 1989. Brucellosis: Clinical and Laboratory Aspects. CRC Press, Inc. Boca, Raton, Florida. USA.