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Infectious Disease in Cervids of North America: Data, Models, and Management Challenges

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Abstract
Over the past two decades there has been a steady increase in the study and management of wildlife diseases. This trend has been driven by the perception of an increase in emerging zoonotic diseases and the recognition that wildlife can be a critical factor for controlling infectious diseases in domestic animals. Cervids are of recent concern because, as a group, they present a number of unique challenges. Their close ecological and phylogenetic relationship to livestock species places them at risk for receiving infections from, and reinfecting livestock. In addition, cervids are an important resource; revenue from hunting and viewing contribute substantially to agency budgets and local economies. A comprehensive coverage of infectious diseases in cervids is well beyond the scope of this chapter. In North America alone there are a number of infectious diseases that can potentially impact cervid populations, but for most of these, management is not feasible or the diseases are only a potential or future concern.We focus this chapter on three diseases that are of major management concern and the center of most disease research for cervids in North America: bovine tuberculosis, chronic wasting disease, and brucellosis.We discuss the available data and recent advances in modeling and management of these diseases.

Keywords
bovine tuberculosis, brucellosis, cervids, chronic wasting disease, North America, wildlife disease management, wildlife disease models, wildlife surveillance

Disciplines
Animal Diseases | Natural Resources Management and Policy | Veterinary Infectious Diseases | Zoology

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Infectious Disease in Cervids of North America

Data, Models, and Management Challenges

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Over the past two decades there has been a steady increase in the study and management of wildlife diseases. This trend has been driven by the perception of an increase in emerging zoonotic diseases and the recognition that wildlife can be a critical factor for controlling infectious diseases in domestic animals. Cervids are of recent concern because, as a group, they present a number of unique challenges. Their close ecological and phylogenetic relationship to livestock species places them at risk for receiving infections from, and reinfecting livestock. In addition, cervids are an important resource; revenue from hunting and viewing contribute substantially to agency budgets and local economies. A comprehensive coverage of infectious diseases in cervids is well beyond the scope of this chapter. In North America alone there are a number of infectious diseases that can potentially impact cervid populations, but for most of these, management is not feasible or the diseases are only a potential or future concern. We focus this chapter on three diseases that are of major management concern and the center of most disease research for cervids in North America: bovine tuberculosis, chronic wasting disease, and brucellosis. We discuss the available data and recent advances in modeling and management of these diseases.

Key words: **bovine tuberculosis; brucellosis; cervids; chronic wasting disease; North America; wildlife disease management; wildlife disease models; wildlife surveillance**

Introduction

Over the past two decades there has been a steady increase in the study and management of diseases in wild animals (Wobeser 2006). One driving factor in this trend is the perceived increase of emerging infectious diseases in humans and domesticated livestock that are linked to wild animals (Daszak *et al.* 2000; Wobeser 2006). From the wildlife perspective, substantial attention has recently been focused on cervids because, as a group, they present a number of unique challenges for wildlife disease management. Their close ecological and phylogenetic relationship to livestock species places them at greater risk for both receiving additional infections and reinfecting livestock. In addition, they are an important natural resource. For example, users of deer and elk contribute more than $20 billion annually to agency budgets and local economies (Opsahl 2003). Their simultaneous value as both consumptive and nonconsumptive resources places additional

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constraints on the ways that cervids can be managed. At times, the contrasting perspectives of managers, environmentalists, hunters, livestock industry, and the general public, along with the difficulty of understanding infectious diseases themselves, create substantial challenges to the management of cervid diseases.

To keep our review within reasonable limits, in this chapter we focus on the North American cervids: moose (*Alces alces*), elk (*Cervus elaphus*), caribou and reindeer (*Rangifer tarandus*), mule deer (*Odocoileus hemionus*), and white-tailed deer (*Odocoileus virginianus*). We begin with a general description of cervid ecology as it relates to disease management, before embarking on the specifics of the major cervid diseases of management concern today.

Cervids and Infectious Disease

It is difficult to create a simple framework for the discussion of cervid characteristics (e.g., ecology, behavior, demographics) important to infectious diseases. There are exceptions to every "rule," and our knowledge of how things fit together is in constant flux as we continue to gather more information. In this section we attempt to give readers unfamiliar with the specifics of cervid ecology and behavior a brief overview of important factors that impact disease processes and are relevant to the management of cervids. For clarity we divide these into three general categories: animal movements, behavior, and life-history characteristics. We also discuss how wildlife disease relates to domestic animals.

Animal Movements

Several aspects of cervid movement behavior and ecology have important ramifications for disease dynamics and the management of cervids. In particular, population level movements, such as migration and dispersal, are important because they can affect whether disease will spread and/or persist. In particular, population-level movements can influence the rate and spatial extent of the disease expansion.

Many North American cervids tend to form loose assemblages of individuals that fluctuate seasonally in size and space. Typically, migrating cervids in the temperate region choose a high-elevation summer range and low-elevation winter range (e.g., elk, moose, white-tailed deer, mule deer) (Mysterud 1999). This type of altitudinal migration is generally considered to be an adaptive response to snow cover and thus observed mostly in cervids inhabiting northern latitudes (Sabine *et al.* 2002). For example, in the Rocky Mountain region of North America, heavy snowfall makes seasonal migration to more suitable winter ranges necessary (Russell 1932; Garrott *et al.* 1987; Smith 2001; Sabine *et al.* 2002), while few mid-western or eastern cervid populations migrate (Sabine *et al.* 2002). Still, even the nonmigratory cervids of North America are subject to changes in environmental conditions and food availability during winter months. In response to these environmental changes animals are frequently forced to make short-distance movements to more suitable habitats/food sources. As a result, even nonmigratory cervids can usually be described as having distinctly different winter and summer ranges (location, size, or both) (Aycrigg & Porter 1997; Van Deelen *et al.* 1998; Sabine *et al.* 2002). In addition to migration, juvenile male dispersal from natal ranges appears to be the rule rather than the exception in most regions of North America (Robinette 1966; Bunnell & Harestad 1983; Nelson 1993; Smith 2001; Shaw *et al.* 2006).

Dispersal and migration (or seasonal movements) create different challenges for the understanding and management of cervid diseases. Seasonal movements typically result in constricted winter ranges which contain a relatively high density of animals compared to summer ranges. This winter gathering or "yarding" behavior of cervids is likely to increase interactions with contagion through direct contact with other individuals and contagious material in the environment. Furthermore, if infection occurs during winter yarding months, altitudinal migration provides the opportunity for

contagious material to travel to new regions (i.e., summer range). Unlike migration, dispersal generally does not create situations with increased risk of contact with contagion. Instead, dispersal provides a means of flow of infectious material to other regions. The role of dispersal in disease dynamics is not well understood. However, modeling exercises show that dispersal plays a critical role in the persistence of infectious disease in metapopulation frameworks (Hess 1996; Chavez & Yakubu 2001).

Animal Behavior

Animal behavior is an important aspect of disease/host dynamics that has not been well documented but may play an important role in the transmission in free-ranging wildlife populations. Cervid social behavior, including matrilineal social structure, birthing behavior, polygyny, male–male interactions, and olfactory signaling may all influence disease transmission. Elk, caribou, and deer live in some sort of matrilineal group that also includes juvenile males. Elk and caribou tend to live in larger groups where females of different matrilineal groups mix (Banfield 1951; Bergerud 1971; Geist 1982). Female white-tailed and mule deer live in stable matrilineal groups (Dasmann & Taber 1956; Hawkins & Klimstra 1970; Mathews & Porter 1993). Female moose are at the other end of the sociality spectrum; they are generally solitary and allow their offspring to stay with them for only a year (Houston 1951; Peterson 1955). In general, epidemiology models based on random mixing assumptions are not appropriate for cervids because of their matrilineal structure.

The birthing behavior of cervids is similar regardless of their natural social structure (i.e., gregarious versus solitary). Females of the nonsolitary cervids (caribou, elk, and deer) change their behavior and essentially take on a solitary existence prior to the fawning period. For the social cervids, matrilines temporarily dissolve and pregnant females segregate themselves from conspecifics by establishing and defending a fawning ground (Banfield 1951; Lent 1974; Geist 1981). In general, segregation during birthing may lead to lower disease transmission within populations of conspecifics, particularly for diseases like brucellosis that are transmitted via birthing products (Cheville *et al.* 1998). This segregation probably explains why brucellosis persists at high prevalence in bovids but is rarely found in cervids. However, the location of birthing areas may be important to transmission between wildlife and domestic stock.

North American cervids engage in some form of polygyny. Male elk and caribou build and maintain harems (Geist 1982), albeit loose harems for caribou (Banfield 1951; Bergerud 1971), while male moose and deer tend and court multiple females sequentially during the breeding season (Markgren 1971; Estes 1972; Lent 1974; Geist 1981). In either case, male cervids contact multiple females during the breeding season, which may bring breeding males into contact with infectious disease agents via infected females. Ritualized male combat occurs during the breeding season (Banfield 1951; Bergerud 1971; Markgren 1971; Lent 1974; Geist 1981,1982), which may enhance disease spread by bringing infected males into contact with susceptible males. Breeding interactions also may leave males in poor condition and more susceptible to disease infection. Finally, male cervids engage in olfactory marking. Grear *et al.* (2006) speculated that an added risk of chronic wasting disease (CWD) infection for white-tailed males during the breeding season may occur when susceptible males use scent stations (rubs or scrapes) used by infected males. In general, cervid breeding behaviors associated with polygyny are likely to increase a male's chance of contacting an infectious agent.

Life-History/Demographic Structure

Cervid demographic structure is another important component that influences disease dynamics. Demographically, it is difficult to classify cervids as either a k-selected or an r-selected species. However, for moose, elk, caribou, and deer in North America, a k-selected

classification seems the most applicable because they are characterized by long life spans, relatively advanced age of first breeding, and few (1–2) offspring at each breeding (Murie 1951; Geist 1974; Connolly 1981a; Taber *et al.* 1982; Valkenburg 2007). Although variation in elk calf survival may have an important effect on elk population growth rate (Raithel *et al.* 2007), adult female survival is typically considered the strongest driving factor in population regulation in cervids (Connolly 1981a; Freddy 1987; Conner, unpublished data). In general, North American cervids are more vulnerable to diseases operating on adult female mortality rather than those that affect reproduction (Wobeser 2006).

Cervids are a highly managed species, and hunting is one of the main management tools. Adult males are the primary target in the harvest management of cervids (Connolly 1981b; Mohler & Toweill 1982). Management objectives are varied; some herds are managed for population reduction, some for population maintenance, some for growth, and some for production of trophy males. Harvest is also used as a tool for disease management; in this case population reduction is the goal. From the perspective of management, understanding the demographic patterns of a disease may lead to the development of effective control strategies; for example, the high prevalence of CWD in older male deer suggests a harvest structure focused on this age class (Miller & Conner 2005).

Interaction with Domestic Stock

There are a number of infectious diseases that circulate between cervids and domestic animals. Two zoonotic diseases in particular, bovine tuberculosis (bTB) and brucellosis, are of major concern in the management of infectious disease in deer, elk, and domestic livestock in North America (Godfroid 2002; Wobeser 2006). The management problem involves the transmission of infection across the wildlife/livestock interface; that is the "spillover" (livestock infect wildlife) effect and its reverse condition, the "spillback" (wildlife reinfect livestock) effect (Daszak *et al.* 2000; Power & Mitchell 2004). Both spillover and spillback refer to situations where disease dynamics in the host population may be primarily driven not by intraspecific transmission, but by transmission from a reservoir species that maintains relatively high disease prevalence (Power & Mitchell 2004). The introduction of both bTB and brucellosis to wild cervid populations in North America are believed to be cases of spillover from domestic cattle in the early 1900s (Levine 1934). Today eradication programs have eliminated both diseases from most domestic herds, but complete eradication is impeded by spillback from wildlife reservoirs to domestic herds.

Objectives

A comprehensive coverage of infectious diseases in cervids is well beyond the scope of this chapter. In North America alone, there are a number of infectious diseases that can potentially impact cervid populations (Table 1). However, many of the infectious agents currently present situations where management is not feasible (e.g., epizootic hemorrhagic disease) or where management is only a *potential* or future management concern (e.g., meningeal brainworm). We focus this chapter on three cervid diseases that are the present focus of major management concerns in North America: bTB, CWD, and brucellosis. bTB is a bacterial disease that has infected or currently infects several North American cervid species including white-tailed deer, mule deer, elk, and moose. Management of bTB in cervids is generally aimed at controlling the disease (reducing prevalence to some low level) in order to minimize or eliminate the spillback of disease to domestic animals. CWD is classified as a transmissible spongiform encephalopathy (TSE), or prion disease. The known natural hosts are white-tailed deer, mule deer, elk (Williams & Young 1993; Williams & Miller 2002), and more recently, moose (Kreeger *et al.* 2006; Baeten

TABLE 1. The main infectious diseases of North America cervids

Disease	Affected cervids	Cervid role	Management
Bluetongue	deer	host	none
Bovine tuberculosis	deer, elk	reservoir, spillover	surveillance, control, eradication
Brucellosis	elk	reservoir, spillover	surveillance, control, eradication, prevention
Chronic wasting disease	deer, elk, moose	host	surveillance, control, eradication
Cranial abscessation syndrome[a]	deer	host	none
Elaeophorosis (arterial worm or lumpy jaw)	deer, elk, moose	host, spillover	none
Epizootic hemorrhagic disease	deer	host	limited surveillance
Foot and mouth disease[b]	deer, elk	reservoir, spillover	none
Leptospirosis	white-tailed deer	reservoir	none
Lyme disease	deer	host	none
Malignant catarrhal fever	deer	reservoir,[c] spillover	none
Meningeal brain worm	deer, elk, moose, caribou	host, resevoir[d]	none
Para tuberculosis (Johne's disease)	deer, elk	reservoir, spillover	none
Rabies	white-tailed deer, elk	host, reservoir,[e] spillover	none
Tularemia	deer	reservoir, spillover	none

[a]Does not appear to be very infectious; the only documented spread occurs between males during breeding skirmishes (through cuts in antler velvet).

[b]Almost nonexistent in North America; occurs in cervids in the United Kingdom.

[c]Cervids are a suspected, but not documented, reservoir for livestock.

[d]Deer are a reservoir for elk, moose, and caribou, as well as for domestic livestock.

[e]Rabies is extremely rare in white-tailed deer and even rarer in elk. Also, it is unclear whether these cervids are a are a host or reservoir.

et al. 2007). Management of CWD is generally aimed at eradicating or controlling it in free-ranging populations to mitigate potential future problems to cervid populations or potential spillover to livestock. Bovine brucellosis is caused mainly by *Brucella abortus,* and is the most common cause of brucellosis in cervids (Corbel 1997). The primary management concern is protecting cattle from spillback from infected elk in the Greater Yellowstone area. We present an in-depth review of available data and recent advances in modeling and management of these three diseases.

Bovine Tuberculosis

Disease Background

bTB originated in cattle and continues to be a problem in domestic animals worldwide. In the United States, for example, in the early 20th century, prevalence of bTB was high in domestic cattle across the country. Federal eradication programs began in 1917 and by 1940 had reduced prevalence in domestic herds by over 90% (Miller & Kaneene 2006). Sporadic cases of non-self-sustaining bTB in free-ranging cervids mostly associated with infected cattle were also detected during this time (Levine 1934; Hadwen 1942; Belli 1962; Friend *et al.* 1963; Sawa *et al.* 1974; Rhyan *et al.* 1992, 1995). By the late 20th century, most states had earned bTB-free accreditation for livestock, though remaining challenges include areas where the disease appears to be endemic, the importation of cattle from Mexico, and captive cervid operations (Essey & Koller 1994).

In the United States, bTB is endemic in the white-tailed deer population of Michigan's northeastern Lower Peninsula (Fig. 1A). The source of infection to deer was likely infected

Figure 1. General spatial distribution of (**A**) bTB, (**B**) CWD, and (**C**) brucellosis in the cervids of North America. No cervid has yet tested positive for bTB in Wood Buffalo National park; it is shown for reference because it is a referenced site for bTB in bison. Maps show only where the disease has been found; they do not portray disease intensity or prevalence.

cattle. In 1922, bTB prevalence in cattle in the northeastern Lower Peninsula was 20–32% (Miller & Kaneene 2006). Despite the USDA's eradication campaign during the early 20th century, prevalence was still 30% in Michigan cattle in 1950. Michigan livestock gained bTB-free accreditation in 1979. In 1975, however, a bTB-infected deer was identified, and following identification of an additional bTB-infected deer in 1994, surveillance during the mid-1990s led to the detection of additional infected individuals (Schmitt *et al.* 1997). Subsequent to detection of bTB in deer, bTB infection was identified in cattle on several farms, presumably due to spillback from infected deer populations. bTB has also been identified in a small, but growing number of white-tailed deer in Minnesota beginning in 2005. All infected deer have been found within 5 miles of infected cattle operations (cattle infection first detected in 2005) (Minnesota Department of Natural Resources 2007 Action Plan, http://www.dnr.state.mn.us /hunting/deer/tb/index.html). Surveillance of the deer population to determine the extent of infection is being conducted by collecting deer from hunters and sharpshooters. The current bTB infection in elk and white-tailed deer in and around Riding Mountain National Park (RMNP) in Canada (Fig. 1A) is also

hypothesized to have originated through spillover from cattle. In RMNP, bTB was identified in elk in 1992, and in deer in 2001, concurrent with four bTB outbreaks involving 11 cattle herds from 1991–2003 (Lees *et al.* 2003; Lees 2004; Nishi *et al.* 2006).

The causative agent of bTB, *Mycobacterium bovis*, is a relatively slow-growing bacterium that is resistant to freezing, enabling it to persist for fairly long periods in cold, dark, and damp environments (Whipple & Palmer 2000; Lees 2004; Palmer & Whipple 2006). Aerosol exposure (direct horizontal transmission) is the most common route of bTB infection in cervids (Francis 1958) and results in respiratory disease with pathology detectable in lymph nodes and the lungs. The disease is chronic and can lie dormant in the host for months or years, with most cervids rarely showing clinical signs of disease or developing disseminated lesions until late stages of infection (Renwick *et al.* 2006; Atwood *et al.* 2007).

Data—Surveillance Monitoring

Surveillance and monitoring of free-ranging cervid populations for bTB infection generally relie on examination and testing of hunter-harvested animals. Detection of bTB in cervids is difficult because prevalence is usually very low. In Michigan, lymph nodes in hunter-submitted deer heads are visually evaluated for indications of bTB infection (Schmitt *et al.* 1997; O'Brien *et al.* 2001). Testing goals aim at having 95% confidence of detecting at least one infected deer if prevalence in the population is greater than 1% (Martin *et al.* 1987; Schmitt *et al.* 1997; Nishi *et al.* 2006). Most managers agree that it would be desirable to detect diseases when they are at lower prevalence (e.g., 0.2%; Beal 1988), but sample sizes necessary to do so with high levels of confidence are almost never feasible. In RMNP, where elk and deer populations are not open to hunting, surveillance is conducted through live capture using helicopter net guns and testing (Lees 2004; Nishi *et al.* 2006).

A different strategy for bTB surveillance recently evaluated in both Michigan and RMNP is the use of coyotes as sentinel species. Species that can serve as effective sentinels must be easily detectable, become infected by direct contact with the reservoir host, and have a constrained space use so that spatial correlation between disease incidence in the sentinel and the host is high (Atwood *et al.* 2007). In Michigan, bTB prevalence in coyotes appears to be a good sentinel for disease in deer. Over a 10-year period across two counties, disease prevalence in coyotes (25%) was much higher than in white-tailed deer (0.46%) (Atwood *et al.* 2007). A similar evaluation conducted in RMNP failed to detect *M. bovis* in any coyote samples, suggesting that coyotes would not be effective sentinels in this circumstance (Sangster *et al.* 2007). One explanation for the difference between Michigan and RMNP may be that the primary reservoir for bTB in Michigan is white-tailed deer, while in RMNP the primary reservoir is elk, a species that is less likely to be preyed upon by coyotes (Sangster *et al.* 2007).

Models

Demographic patterns of bTB prevalence are similar across populations and species of cervids. Older animals have consistently higher bTB prevalence than younger animals (Lugton *et al.* 1998; O'Brien *et al.* 2002; Lees *et al.* 2003; Nishi *et al.* 2006; Delahay *et al.* 2007). In addition, in most, but not all cases males are more likely to be infected than females (O'Brien *et al.* 2002; Lees *et al.* 2003; Nishi *et al.* 2006). Behaviors in male white-tailed deer including ranging more widely than females, aggregating in temporary, seasonally variable all-male groups, and contacting many different females during their lifetime may explain their higher rate of infection and may be important for the spread of disease. In addition, stressors (such as those associated with male aggression and competition during the breeding season) have been demonstrated to increase deer susceptibility to

a variety of diseases including bTB (Thomson *et al.* 1994; Thomson & Griffin 1995). The effect of bTB on survival and population growth rates in cervids has not been well studied, though no major negative effects are immediately apparent. In bovids, cross-sectional studies of slaughtered African buffalo estimate an 11% reduction in survival and 27% reduction in fecundity (Jolles *et al.* 2005), but these effects are undetectable in longitudinal studies of known individuals (Cross *et al.*, unpublished manuscript). There is, however, some evidence that bTB and brucellosis may be contributing to the wood bison (*Bison bison athabascae*) population decline in Wood Buffalo National Park, Canada (Joly & Messier 2004) (Fig. 1A).

Strains of bTB identified in all species have been indistinguishable. As indicated above, in deer the disease is respiratory in nature and transmissible through aerosols (Francis 1958). Based on the respiratory nature of infection in deer and the continual high bTB prevalence in the population, deer are considered to be the wildlife reservoir of bTB in Michigan. Deer are responsible for spillback of disease to cattle and other wildlife species, such as coyotes (*Canis latrans*) and black bears (*Ursus americanus*) (Schmitt *et al.* 1997; Bruning-Fann *et al.* 2001; O'Brien *et al.* 2002). Carnivores and other species evaluated thus far are considered to be spillover hosts. Disease prevalence in species other than deer is low (Bruning-Fann *et al.* 2001). Additionally, in these species lesions occur primarily in the digestive tract, suggesting exposure occurs through ingestion of infected deer with little potential for further bTB transmission (Bruning-Fann *et al.* 2001).

Direct contact with infected individuals is the most common route of bTB transmission (Francis 1958). In bTB in white-tailed deer in Michigan and red deer in New Zealand, increasing deer density has been shown to be positively correlated with disease prevalence (Lugton *et al.* 1998; Hickling 2002). The social structure of cervids can also influence the transmission of bTB. For example, white-tailed deer have a matrilineal social structure in which females live in related groups (Hawkins & Klimstra 1970). Deer within groups come into high rates of contact, while deer from different groups rarely come into contact. In Michigan, Blanchong *et al.* (2007) found that bTB-infected deer harvested in close proximity were more closely related than were noninfected deer, suggesting that bTB transmission is occurring between relatives within social groups. The relationship between relatedness and probability of bTB infection was stronger following a ban on supplemental feeding. Supplemental feeding diluted the effect of relatedness by bringing together at feeding sites different social groups that otherwise would not have been expected to come into contact (Blanchong *et al.* 2006).

While direct contact is the most effective and important means of bTB transmission in cervids, indirect contact with food sources contaminated with saliva, nasal secretions, urine, or feces is also an important, though less efficient, route of infection (Palmer *et al.* 2001). *M. bovis* can survive on a variety of food items fed to deer (e.g., alfalfa, corn, sugar beets) for at least 7days and up to 112days in cold conditions (i.e., $\leq 23^{\circ}$F) (Palmer & Whipple 2006), and indirect transmission of bTB from deer to deer through shared food has been demonstrated (Palmer *et al.* 2004). In Michigan, in particular, bTB transmission appears to have been facilitated by a long history of supplemental feeding to maintain high deer densities for "hunt clubs" (Schmitt *et al.* 1997; Miller & Kaneene 2006; O'Brien *et al.* 2006). Supplemental feeding of white-tailed deer also resulted in high rates of face-to-face contact among deer at feeding sites (Garner 2001). Comparison of spatial genetic structure in the deer population during supplemental feeding and following its ban suggested that large aggregations of deer at feeding sites disrupted the natural tendency for different social groups to remain spatially segregated (Blanchong *et al.* 2006). These high rates of contact and overlap of normally segregated groups of deer are hypothesized to have enhanced bTB transmission and aided in the establishment of endemic disease in the deer population.

bTB in white-tailed deer in Michigan is clustered in a core-area (a 1500 km^2 region in the center of the four-county endemic area) in northeast Lower Peninsula. Analyses indicated that prevalence was 10 times higher in this area and deer in the core-area were 150 times more likely to be infected with bTB than deer elsewhere in Michigan (O'Brien *et al.* 2002). Within the northeast Lower Peninsula, bTB prevalence peaked in the center and rapidly declined outside this limited area, and a comparison over 1995–2000 found minimal changes in the spatial distribution of disease, with no significant spread out of the core area (Hickling 2002). These results suggest that conditions within the core area may support self-sustaining bTB in deer while conditions outside the core area do not. These findings conflict with a model that predicted bTB would increase in prevalence in Michigan regardless of the type of intervention taken to control the disease (McCarty & Miller 2001). The discrepancy between model predictions and observed trends in bTB may be due to a failure to consider the importance of both density-dependent and density-independent factors in disease transmission in the McCarty and Miller (2001) model.

Management

Several approaches have been used or are being developed to control bTB in free-ranging cervids. Approaches vary depending on the constraints of the particular circumstance and the feasibility of alternative methods. The management approach to bTB control in Michigan white-tailed deer has primarily focused on population reduction. The goal of bTB management has been to reduce the deer population to a level where the disease cannot persist (Schmitt *et al.* 1997). After 10 years and a $15 million investment, the deer population is estimated to have been reduced by 50%, and a declining trend in disease prevalence has been observed (4.9% in 1995 to 1.2% in 2005; figures are from the core-area of bTB in Michigan),but further population reduction is proving difficult due both to hunters' unwillingness to harvest high numbers of deer as they become rarer and to the public's resistance to high deer mortality (O'Brien *et al.* 2006). In addition to population reduction, supplemental feeding practices were banned in Michigan in order to reduce the aggregation of deer and reduce both direct and indirect transmission of bTB to both deer and cattle. This ban has been politically charged because of the long tradition of supplemental feeding in the area and the local economy built around this practice. Rudolph *et al.* (2006) suggested that successful control of bTB may require a balance between the biological risk of bTB transmission through baiting (a form of supplemental feeding) and the political risks of alienating the hunters on which bTB management relies. A mathematical model of the predicted outcomes of various levels of population reduction and feeding bans suggests that all management strategies will require more than a decade to reduce bTB in deer below a "detectable" level (Hickling 2002).

Because population reduction is often not a feasible disease-control option or may not be effective alone, other disease-control approaches are being explored. Surveillance and control efforts for bTB in RMNP rely on a test-and-cull approach because hunting is not allowed in the park (Nishi *et al.* 2006). In Michigan, a test-and-cull approach has been implemented in an effort to gain access to private land off limits to hunting that could become refugia for infected deer and to temper the politically distasteful mass mortality of deer (Schmitt *et al.* 2004). Studies of barrier fencing to limit cervid contact with cattle and cattle feed found contact rates between fences were very low (Nishi *et al.* 2006; VerCauteren *et al.* 2007). Protection dogs have also been effective at minimizing contact between deer and cattle, and minimizing use of cattle feed by deer (VerCauteren *et al.* 2005). Habitat modification and rehabilitation through prescribed burning in RMNP have been used to keep elk within the park and away from cattle (Nishi *et al.* 2006).

Future Directions

Ecological and anthropogenic factors that influence the rate of mixing in North American cervid populations and the transmission and spread of bTB have not been extensively investigated. Telemetry and social network modeling of bTB transmission in African buffalo were used to estimate the amount of time buffalo spent together and to investigate how movement of infected individuals affected disease spread (Cross *et al.* 2004). The nature of the social network was found to have a strong influence on simulated disease dynamics and indicated that diseases may spread faster during conditions that promote increased population mixing (Cross *et al.* 2004). This type of approach might be fruitfully applied to understanding the transmission and spread of bTB in cervids.

It is important to keep in mind that most efforts at bTB control in free-ranging cervids are motivated by the risk of transmission to domestic animals. A variety of approaches have been tested to minimize both direct and indirect contact between cervids and domestic animals. The development of an effective vaccine for bTB is an area of disease control that is under active exploration for both livestock and wildlife hosts. One of the major challenges associated with using a vaccination strategy to control disease is to identify effective and efficient delivery systems. Cross and Getz (2006) used sex- and age-structured modeling to evaluate the feasibility of a vaccination program for bTB in buffalo in Africa. Their models indicated that vaccinating young animals would be most efficient, but that the levels of vaccination necessary (>70% of calves every year) make it unlikely that vaccination could be a feasible or effective means to control the disease in this particular case. The efficacy and effectiveness of a bTB vaccine for free-ranging cervids are currently being examined.

In addition to management actions aimed at controlling bTB in wildlife, changes in cattle-management practices could also reduce risks to cattle of contact with bTB-infected cervids (Kaneene *et al.* 2002). Studies in Michigan, however, suggest that cattle producers are not taking sufficient actions to reduce contacts between cattle and deer (Kaneene *et al.* 2002; O'Brien *et al.* 2006). Kaneene *et al.* (2002) advocated examining and instituting farm biosecurity, feeding practices, and food-storage methods that could minimize wildlife contact with livestock to reduce the risk of bTB transmission from wildlife to livestock.

Chronic Wasting Disease

Disease Background

CWD is a relatively recently described disease that was first recognized as a TSE in 1978 (Williams & Young 1980). Although once thought to be restricted to cervids in north-central Colorado and southeastern Wyoming, CWD has been detected in free-ranging and captive herds in several areas in the United States and in two Canadian provinces. Of the relatively small number of known TSEs, CWD is one of the few that are contagious in their natural hosts and is the only one known to affect free-ranging species (Williams & Miller 2002).

No cases of human prion disease have been associated with CWD (Belay *et al.* 2001; World Health Organization 2007). However, CWD became a disease of concern to the general public because TSEs include bovine spongiform encephalopathy (BSE or mad cow disease) of cattle and because of the cattle link with variant Creutzfeldt–Jakob disease of humans (Williams *et al.* 2002). In addition to concern that CWD could behave similarly to BSE with respect to humans, there is some worry that CWD has the potential to cross the livestock barrier. Cattle intensively exposed to CWD-infected deer and elk via oral inoculation or confinement with infected captive mule deer have remained healthy (Williams *et al.* 2002). However, cattle have become infected with CWD via cerebral inoculation with material from diseased mule deer (Hamir *et al.* 2005, 2006) and white-tailed

deer (Hamir *et al.* 2007). Although this mode of transmission is not possible in a free-ranging situation, it forms the basis for the concern that CWD potentially could cross the species barrier and infect livestock. Thus, management of CWD in free-ranging cervids is focused on containing or eradicating the disease to minimize "potential future issues," such as spillover to livestock, human health impacts, or impacts on free-ranging cervid populations.

CWD was first recognized as a clinical syndrome of captive mule deer in research facilities in Colorado 1967 and was first recognized in the wild in 1981 (Williams & Miller 2002). Hunter harvest samples from the 1990s delineated a contiguous "endemic" area in north-central Colorado and southeastern Wyoming where prevalence was moderate (>2%) to high (>15%). During this period, CWD was also diagnosed in local mule deer populations in Saskatchewan, Canada (Williams & Miller 2002). During 2000–2002, CWD was diagnosed in free-ranging cervids from areas that were distant and discontinuous from the endemic area, including Wisconsin. At this point CWD went from being a localized western disease to a national one. Beginning in 2002, many states instituted CWD surveillance plans, and the disease was subsequently detected in several states east of the Mississippi River. By 2002 CWD was firmly established as a major cervid disease (Fig. 1B).

From empirical studies, the CWD transmission route has been well established as horizontal through both direct animal-to-animal contact (Miller & Williams 2003), potentially through saliva (Mathiason *et al.* 2006), and through indirect environmental contamination from pathways that include excreta and carcasses (M. Miller *et al.* 2004). Recent laboratory research suggests enhanced transmissibility of soil-bound prion particles for soils containing the common clay mineral motmorillonite, which may explain the indirect transmission of CWD despite the presumably low level of infectious prions shed into the environment (Johnson *et al.* 2007).

Data—Surveillance Monitoring

Surveillance programs for the detection and description of CWD vary from state to state, but most samples come from hunter-harvested cervids. Harvest samples come from regular hunts or special disease-management hunts. The other main source of surveillance data comes from cervids culled by agency or professional sharpshooters as part of CWD management programs. Field data consist primarily of the infectious status of harvested or culled samples, along with the date of collection (not date of infection), location, and demographic status. Originally location data were collected at a coarse scale, with a sample being located as being within a county or similar agency management area. Most surveillance data collected from 2002 onward have been collected at finer resolution (accuracy estimated to be $\leq$1 km of true locations) for improved spatial modeling.

Models

Over the course of research on CWD, the main questions first focused on its basic biology and ecology, as well as a spatial description of prevalence, and then on mechanism and predictions. The main questions of recent CWD research include spatial distribution and related environmental covariates/factors/risks, demographics of disease, transmission within populations, and spread across populations.

Initial modeling work focused on describing the spatial distribution of CWD prevalence. Due to improvements in the resolution of location data in CWD surveillance programs, recent research indicates that spatial distribution of CWD in deer is heterogeneous at relatively fine (<50 km^2) (Wolfe *et al.* 2002; Joly *et al.* 2003, 2006; Farnsworth *et al.* 2006) as well as broad resolutions (>1000 km^2) (Miller *et al.* 2000; Miller & Conner 2005). The finer resolution samples also allowed researchers to pursue more complex spatial modeling approaches. Analyses of recent data indicate that CWD

prevalence is spatially autocorrelated at a relatively fine resolution (<4.3 km) in white-tailed (Joly *et al.* 2006) and mule deer populations (Farnsworth *et al.* 2006). Based on these initial spatial analyses and mule deer ecology, Farnsworth *et al.* (2006) evaluated which of three spatial resolutions best described prevalence patterns in Colorado. There was strong support for local influences on observed patterns of CWD; only models at the finest resolution (<9 km^2) were plausible. These studies provide evidence that the spatial structure of CWD in free-ranging deer results from small-scale, local-contact processes between individuals or between individuals and a contaminated environment.

Recent spatial modeling work has also focused on environmental covariates and risk factors that may be linked to CWD prevalence. Farnsworth *et al.* (2005) examined how patterns of human land use were associated with variation in CWD, predicting urban development would enhance CWD transmission due to increased deer density on reduced range areas, as well as providing a hunting refuge. As predicted, male deer in urban areas were twice as likely to be CWD-infected as males in undeveloped areas. Based on field observations, Farnsworth *et al.* (2005) and Wolfe *et al.* (2002) suggested that higher prevalence among urban deer may be less related to deer density and more strongly related to local factors, such as artificial feeding and salt licks around residences, that concentrate deer at a few points and facilitate transmission. However, Farnsworth *et al.* (2005) considered the alternative hypothesis of increased deer densities plausible as well, though data were not available to estimate deer density in their study area.

Other environmental factors considered in the ecology and risk assessment of CWD have been proportion of mule deer winter range habitat, proportion of private land as refuge from hunting (Farnsworth *et al.* 2006), and proportion of white-tailed deer habitat (Joly *et al.* 2006). Proportion of mule deer winter range habitat was defined as the proportion of low-elevation grassland habitat in each grid cell in the study area, and proportion of white-tailed deer habitat was defined as the proportion of each grid cell in the study area that was forest, shrubland, and wetland >4 ha, or forest, shrubland, and wetland >1 ha and within 200 m of larger tracts of the same, or agricultural and grassland areas within 100 m of forest, shrubland, and wetland. These habitat measures were considered as proxies for deer density. Farnsworth *et al.* (2006) found little evidence that either percent mule deer winter range or percent private land refuge was related to CWD prevalence. In contrast, for white-tailed deer Joly *et al.* (2006) found a stronger positive relationship between CWD prevalence and percent deer habitat. Differences between white-tailed and mule deer biology and ecology relevant to disease modeling and that may shed light on these contrasting results are discussed in more detail below.

From an ecological perspective, age and sex variation in disease prevalence suggests common underlying mechanisms, such as reproductive behaviors, may drive infection patterns (Tomkins *et al.* 2002). One of the most intriguing recent demographic findings is that observed CWD prevalence in breeding-age males is 2–4 times higher than in younger males or females for both mule deer (Miller *et al.* 2000; Miller & Conner 2005) and white-tailed deer (Grear *et al.* 2006). Higher prevalence among breeding-age males may be due to higher susceptibility, lower disease mortality, or higher exposure risk. Data from captive cervid studies indicate males and females are equally susceptible to infection (Williams & Young 1980; Miller & Wild 2004; M. Miller *et al.* 2004). However, we note that free-ranging males may experience higher breeding stress than their captive counterparts, which could make them more susceptible to CWD infection, although stress may not play the same role with a prion infection because its role as an immunosuppressant may not be as important. In addition, no captive study notes differences between male and female survival times. This leaves higher exposure risk as

a likely explanation for gender-related differences in prevalence, although we cannot dismiss the potential for increased male susceptibility due to breeding stress in free-ranging deer.

It may be that deer social structure and breeding behaviors increase male exposure to the CWD agent (Miller & Conner 2005; Grear *et al.* 2006). In particular, male mule deer may range more widely during the breeding season (Geist 1981) and have more social interactions with different individuals than females (Kucera 1978; Koutnik 1981), potentially increasing their chance of either direct or indirect contact with infectious CWD agent. Perhaps more importantly, mature male mule deer practice polygyny, and breeding males canvas as many females as possible by sniffing and licking the vulva of females to detect estrus (Estes 1972; Geist 1981), which may bring breeding males into contact with infectious CWD agent shed via lymphoid tissue in the alimentary tract. Grear *et al.* (2006) speculated that an added risk for white-tailed males during the breeding season may occur when susceptible males use scent stations (rubs or scrapes) used by infected males. We propose that these behaviors may increase the contact of breeding males with infectious agent and, accordingly, explain the relatively high-prevalence rates observed in this class.

A recent forward movement in modeling transmission has come from a set of disease compartment models constructed by Miller *et al.* (2006) based on data from a group of captive mule deer. Models varied in structure to evaluate incubation and latency effects as well as the relative strength of direct versus indirect transmission. Based on this analysis, the main route of transmission was indirect, and there was limited support for a latent (animal infected but not infectious) period, but low support for an incubation (infected and infectious) period. This study, taken with earlier work, implies that direct contact is not required for CWD transmission (Miller *et al.* 2006) and that environmental contamination may be highly important to CWD transmission and dynamics.

For the CWD transmission function, the density dependent (DD) versus frequency dependent (FD) discussion continues unabated. Due to the matrilineal social structure of deer (Dasmann & Taber 1956; Hawkins & Klimstra 1970; Mathews & Porter 1993), FD transmission was initially used to model the direct animal-to-animal portion of CWD transmission (Miller *et al.* 2000; Gross & Miller 2001). These models predicted CWD could, over the course of 20–100 years, dramatically reduce free-ranging deer and elk populations (Gross & Miller 2001). Schauber and Woolf (2003) criticized Gross and Miller's (2001) CWD model and model interpretations because of their sole representation of FD disease transmission, which resulted in more dire predictions of population reduction than a DD model. Recent work on white-tailed deer contact rates suggests that indirect transmission is likely to be DD (Schauber *et al.* 2007). Schauber *et al.* (2007) note that high pathogen persistence in the environment, which is likely for CWD agent, is expected to result in delayed-density dependence. These issues remain unresolved; under representative field conditions (i.e., moderate to high population deer and elk densities and low to moderate disease prevalence), the behavior of models with DD and FD transmission is indistinguishable when compared to field data (Conner *et al.* 2007a).

The force of infection, or transmission rate, is another important parameter in disease models that can be overestimated if the assumption of homogeneous mixing is not met (Keeling 1999), regardless of the chosen transmission function. To evaluate whether deer randomly mix within relatively small areas, two recent studies on free-ranging deer estimated genetic relatedness, as a proxy for social structure, along with CWD infection status (Grear 2006; M.W. Miller, unpublished manuscript). In both studies, "closely related" female white-tailed and mule deer had markedly higher probabilities of being co-infected (i.e., both animals in a pair were infected) with CWD as compared to unrelated females (Grear 2006;

M.W. Miller, unpublished manuscript). In contrast to females, closely related male mule deer had similar co-infection probabilities compared to unrelated males (M.W. Miller, unpublished manuscript). However, while both studies found evidence for increased risk of infection between closely related females, the risk was lower for white-tailed deer (Grear 2006; M.W. Miller, unpublished manuscript). Grear (2006) speculated that in high-density situations, such as southern Wisconsin, female white-tailed deer may not restrict their contact to exclusive social groups, which would weaken barriers to direct transmission between social groups.

Transmission rate is also influenced by the proportion of susceptibles in a population. Earlier research documented that certain prion protein (PrP) genotypes are strongly associated with susceptibility to TSE infection for scrapie infection in sheep (O'Rourke 1998) and CWD infection in elk (O'Rourke *et al.* 1999). Recent research found a similar condition for mule deer. That is, CWD status was not independent of PrP genotype; the "susceptible" genotype was 30 times more likely to be CWD-infected than the other two genotypes (Jewell *et al.* 2005). A similar recent study of white-tailed deer found some evidence for differences in susceptibility to CWD infection, although the effect was not nearly as strong; the "susceptible" genotype was five times more likely to be CWD-infected as the two other genotypes (Johnson *et al.* 2006). However, there is no completely resistant genotype; despite some genotypes being more resistant than others, all genotypes have been observed in infected and noninfected white-tailed and mule deer (O'Rourke *et al.* 2004; Jewell *et al.* 2005; Fox *et al.* 2006; Johnson *et al.* 2006). In the more resistant PrP genotypes, the course of infection may be longer rather than nonlethal. A recent study of captive mule deer found the "resistant" genotype accumulated abnormal prions much more slowly than the "susceptible" genotype (Fox *et al.* 2006; Johnson *et al.* 2006). A result of this "slowed disease progression" resistance may lead to longer survival times of infected individuals, with a corresponding increase in their infectious period. This type of resistance could increase CWD transmission but greatly reduce its population-level impacts because deer could live long enough to approach their maximum reproductive potential.

Observed large-scale spatial patchiness of a wildlife disease could be the product of environmental factors that enhance the existence or transmission of the disease, or due to the predominant distribution and movement patterns of hosts or vectors of the disease. In north-central Colorado, CWD is patchily distributed without any obvious disease focal point or centroid. Because there was little dispersal (<2%) and most populations migrated seasonally, Conner and Miller (2004) concluded that seasonal migratory movement patterns were a plausible mechanism for geographic spread of CWD and the observed heterogeneous large-scale distribution of CWD. However, the spatial pattern of CWD in Wisconsin was quite different. There, CWD manifests a general diffusion pattern that is similar to (but not as striking as) bTB in white-tailed deer, which is another horizontally transmitted disease (Hickling 2002). Differences in CWD distribution patterns between mule and white-tailed deer may result from differences in deer densities, habitat, and movement patterns, or simply from differences in the age of the epidemics.

Management

CWD management goals vary with the situation and state, although all contain surveillance programs to monitor CWD distribution and prevalence. Besides surveillance, the main management approaches being used for CWD are control or eradication, both of which are implemented primarily by nonselective hunting and culling of deer. In the endemic area of Colorado, management programs focus on containing and reducing CWD prevalence in localized areas and reducing the risk of CWD spread along putative movement corridors (Colorado Division of Wildlife 2002).

In northwest Colorado, Saskatchewan, northwest Nebraska, and the core area of infection in Wisconsin, where CWD may not yet be endemic and areas of high prevalence are relatively small (<2000 km^2), eradication has been the focus of management (Colorado Division of Wildlife 2002; Blanchong *et al.* 2006). Wildlife managers in Colorado and Wyoming have not attempted eradication in the endemic area because it appears unattainable over such a large (>80,000 km^2) scale (Colorado Division of Wildlife 2002). CWD prevention measures have also been instituted by many states, including carcass regulations banning importation of brain or spinal column tissue, restrictions on the importation and raising of captive cervids, as well as bans on feeding or baiting stations for cervids (see http://www.cwd-info.org/index.php/fuseaction/policy.main for specific state policies).

There are few published studies evaluating the effect of management intervention on CWD. This is a result of the disease being relatively recently described, monitored, and managed, coupled with CWD's long disease course and relatively slow spatial spread. One of the few evaluations of management is from Colorado using a Before-After-Control-Impact (BACI) analysis. Nonselective culling of deer was done over 4 years on 16 relatively small (<17 km^2), high-prevalence areas. This management strategy was not effective; prevalence was not reduced after culling treatments (Conner *et al.* 2007b). Although the intensive culling was designed to remove all deer from small, high-prevalence areas, data were not available to evaluate whether culling reduced deer density on the treatment areas (Conner *et al.* 2007b). The general approach of culling in high-prevalence areas may be more applicable to white-tailed deer, where enough culling is being done to reduce population abundance and where DD transmission is more likely (Joly *et al.* 2006). Unfortunately, it will be several years before sufficient time-series data are collected to evaluate Wisconsin's management intervention.

Future Directions

Because our knowledge about CWD biology and disease ecology comes mainly from research on captive animals, much remains unknown about the disease course in free-ranging animals. We do not know whether captive cervids are good models for their free-ranging counterparts. For free-ranging cervids, the ultimate questions are whether CWD reduces population growth or detrimentally changes demographics in a biologically significant way. Penultimate to these questions are determination of the transmission parameters, such as length of infectious period, transmission function, transmission rate, intensity of environmental infectivity, and the relative contribution of direct versus indirect transmission to CWD infection, in free-ranging cervid populations.

Management of CWD would be improved by more efficient surveillance detection, both for direct contact and indirect contact components. Development of inexpensive, accurate, and quick-result antemortem tests will greatly facilitate the spatial monitoring and modeling of CWD. One promising new sampling technique is an antemortem rectal mucosa-associated lymphatic tissue test, which promises to be less expensive and simpler that antemortem testing of lymphoid tissue, as well as appearing to be suitable for rapid tests (Wolfe *et al.* 2007). In addition to tests to improve estimation and understanding of direct contact transmission, indirect transmission estimates would be improved by techniques that detect prions in the environment.

Brucellosis

Disease Background

Brucellosis, caused by *Brucella abortus*, is a chronic bacterial disease widespread in many livestock and wildlife populations and is among the most common zoonotic infections worldwide (Godfroid & Kasbohrer 2002;

Pappas *et al.* 2006). Transmission of *B. abortus* occurs when susceptible animals come into direct contact with contaminated aborted fetuses, birth membranes, uterine fluids, or vaginal discharges from infectious animals. Ingestion of contaminated material is the primary route of infection. Transmission within and among wildlife is far less documented than in cattle. However, it appears to follow a similar path as in domestic animals, with infected fetuses and placentas from abortion events the key vectors of transmission (Cheville *et al.* 1998). Prior to the introduction of pasteurization, dairy products were the primary source of infection in the human population, causing undulant fever, anxiety, and depression (Godfroid 2002).

Brucellosis was probably first introduced from cattle to bison and elk in the Greater Yellowstone Area shortly before 1917 (Meagher & Meyer 1994). Bovine brucellosis is caused mainly by *B. abortus*, and is the most widespread form in cervids (Corbel 1997). While rangiferine brucellosis (*B. suis* biovar 4) has been reported in caribou in Alaska and Canada, cases are rare (Tessaro 1986; Tessaro & Forbes 1986). While *B. suis* is pathogenic in caribou, it is reportedly nonpathogenic in livestock (Tessaro 1986), and consequently is not of great management concern. We restrict our discussion to *B. abortus* because research and management in North America focuses primarily on *B. abortus* in elk and bison.

Due to a successful eradication campaign, the cattle populations of most U.S. states are free of the disease (Ragan 2002). Brucellosis persists, however, in the Greater Yellowstone Ecosystem (GYE), USA, where elk (*Cervus elaphus*) and bison (*Bison bison*) are among the last reservoirs of infection, presenting a major hurdle for countrywide eradication (Cheville *et al.* 1998; Bienen & Tabor 2006). The disease appears to have minimal effects upon population dynamics of elk and bison, but rare abortion events by elk or bison on land used for livestock production can have a dramatic economic impact upon livestock producers. Infected cattle herds are depopulated, and if more than two properties are infected then the entire state looses its brucellosis-free status, which results in additional testing requirements.

Bison populations in Yellowstone National Park (YNP) and Grand Teton National Park (GTNP) maintain a seroprevalence of 40–70% (Dobson & Meagher 1996), while the seroprevalence in elk varies spatially. The average seroprevalence of brucellosis in elk that visit artificial feedgrounds in Wyoming is ~26%, while elk populations in other regions of the GYE tend to have a seroprevalence of 2–3% (Wyoming Game and Fish Department (WGFD), unpublished data; Aune *et al.* 2002; Etter & Drew 2006). The WGFD and the U.S. Fish and Wildlife Service maintain 23 supplemental elk feeding grounds in northwestern Wyoming, which appear to sustain the disease in elk by increasing elk aggregations during the time of transmission. Elk populations outside the GYE are not known to maintain the disease. This may be because the pathogen was never introduced to other elk populations. However, given that 11% of all cattle herds were infected in the 1930s (Ragan 2002), unintentional introductions of *B. abortus* to other elk populations may have occurred without persisting.

Supplemental feeding of elk began in 1910 to limit elk impacts on agricultural land and maintain elk populations, but had an added effect of shrinking native winter range (Smith 2001). Elk populations on (and off) feedgrounds have increased dramatically since feeding was instituted and are above management objectives in many places around the GYE (Fig. 1C; Dickson 2005). Feedgrounds are intended to minimize contact between elk and cattle during winter, but they also increase the concentration of elk between November and April. This winter concentration results in an overlap with the likely period of *B. abortus*–induced abortions, which occur from February to June (Roffe *et al.* 2004).

Data—Surveillance Monitoring

The diagnosis of *B. abortus* in elk and bison is a challenging issue. There are at least 20 serological tests for brucellosis (Nielsen 2002). The interpretation of a panel of these tests, for which there are no gold standards and not all agree, can be difficult, but Bayesian methods appear to be the next step (Gardner *et al.* 2000). Most tests are based on serology, so after a diagnosis is made the results still only indicate past exposure rather than whether the animal is currently infectious. Because most elk appear to recover from infection within a couple of years, seroprevalence will be much higher than the actual prevalence of infectious individuals (Thorne *et al.* 1978). In bison and elk roughly 50% of seropositive individuals will also be culture positive, which may be a better indication of whether an individual is infectious rather than just exposed or recovered (WGFD, unpublished data). Thus, test-and-remove programs based on serology will have to remove many recovered individuals along with the currently infectious individuals. Also, the persistence of antibodies in elk over long periods makes it difficult correlate temporal changes in, say, density or winter severity with changes in transmission and prevalence.

False-positive test results due to cross-reactions with other pathogens are an important issue that is usually ignored for convenience. The importance of false-positive tests recently came to a head however when managers in Montana noticed that brucellosis seroprevalence was increasing dramatically in an area west of YNP. This was of particular concern because of the increasing elk group sizes in this area and the lack of hunter access. Further investigations suggested that the increased brucellosis seroprevalence may have been due to cross-reactions with *Yersina enterocolitica* (Anderson *et al.* 2006).

Surveillance data on brucellosis are collected only in the GYE area and come from a number of sources. Annually, elk are captured and tested on a subset of feedgrounds in Wyoming. In addition, hunter-killed elk are collected and tested around the GYE to gather additional data on unfed elk. Bison brucellosis data come primarily from research-related captures in YNP as well as from bison that are culled along the borders of the park.

Models

Most of the brucellosis models created so far have focused on the potential efficacy of different management strategies, primarily with respect to bison. The modeling results of Peterson *et al.* (1991) as well as Dobson and Meagher (1996) suggest that controlling brucellosis in bison could be very difficult. These studies have investigated culling, test-and-remove, and vaccination as potential management strategies. However, for the particular case of brucellosis, models that investigate contraception may be enlightening. L.A. Miller *et al.* (2004) showed that gonadotropin-releasing hormone (GnRH) vaccine effectively reduced pregnancy in bison and could safely be administered during late pregnancy, and Conner *et al.* (2007c) showed GnRH effectively prevented pregnancy in free-ranging elk. Since *B. abortus* is primarily transmitted via abortions and calving, contraception could substantially reduce transmission from already infected individuals. Thus a combined strategy of contraception of seropositive females and vaccination of seronegative females may be a surprisingly effective management strategy for brucellosis in bison. Modeling efforts addressing some of the issues are currently under way.

Many disease models assume that parasite transmission is a function of host population size or density (for a review see McCallum *et al.* 2001). If transmission is related to density then management strategies that reduce host population density may decrease not only the total number of infectious individuals but also prevalence (Lloyd-Smith *et al.* 2005a). However, results from comparative analyses on the relationship between density and prevalence have

been mixed (Côté & Poulin 1995; Nunn *et al.* 2000; Nunn 2002, 2003a, b; Stanko *et al.* 2002; Tella 2002). Further, studies on brucellosis in elk and bison have found only weak to no evidence for a relationship between brucellosis seroprevalence and population size/density (Dobson & Meagher 1996; Joly & Messier 2004; Cross *et al.* 2007). These studies, however, attempted to correlate prevalence with population density rather than more directly measuring contact and/or transmission. Preliminary observations of fetuses placed on the feedgrounds suggest that contacts with abortions on elk feedgrounds are likely to increase with density (WGFD, unpublished data).

We believe the conflicting results are not due simply to different methodologies, but rather to differences of timescale. Prevalence is an index of cumulative exposure to the pathogen. Measurements of contact, however, relate to the particular point in time the observations were made. In many cases, transmission rates are likely to vary seasonally. For brucellosis, transmission is probably limited to the period of abortions, which are likely the months of February through May. Therefore, contact with aborted fetuses may be strongly correlated with density at the time of transmission, but seasonal fluctuations in density may result in no correlation between density and prevalence.

Management

Brucellosis causes little measurable morbidity or mortality in elk or bison, but it does reduce their productivity (Roffe *et al.* 2004). Even though *B. abortus* is a non-native parasite that may reduce elk and bison population growth, these are not the primary factors driving intense management and controversy. The primary motivation is protecting the profitability of the livestock industry, which has a strong constituency in the region. However livestock producers also help some conservation efforts by maintaining large open spaces in an area that is rapidly being converted to subdivisions (Hansen *et al.* 2002). To prevent transmission of *B. abortus* from bison to cattle, management agencies attempt to create spatiotemporal separation of bison and cattle by limiting bison movements via hazing as well as removing individuals at the border of the YNP. Periodically, this strategy leads to large population reductions of bison (~800–1000 out of 3000–5000 total). Despite the intensive management of bison, it was transmission from elk to cattle that caused Wyoming and Idaho cattle to lose their brucellosis-free status in 2004 and 2006, respectively (Galey *et al.* 2005), costing each state millions of dollars. As of 2007, Wyoming cattle have regained their brucellosis-free status, but the risk of transmission from wildlife to cattle remains.

The congregation of elk on feedgrounds facilitates a brucellosis vaccination program that began in 1985. Nearly all juveniles at every feedground except one are vaccinated annually with Strain 19 (WGFD, unpublished data). In captive studies, the Strain 19 vaccine reduced abortion events from 93% to 71% during the first pregnancy (Roffe *et al.* 2004). Over the longer term, reducing abortions, and thus transmission, should result in lower seroprevalence on the vaccinated feedgrounds. The one unvaccinated site has a higher seroprevalence than the average of the other 22 feedgrounds; however, its seroprevalence is no higher than expected given the length of its feeding season (Cross *et al.* 2007). Thus, the data (though indirect and based on a single population) are not suggestive of a strong protective effect of Strain 19 vaccination at a feedground level, which agrees with previous captive studies.

Managers have recognized the disease issues associated with the supplemental feeding of elk for many years. However, because the reduction in supplemental feeding can result in elk simply moving to nearby cattle feedlines, it remains unclear how to manage the problem without increasing the risk of transmission from elk to cattle. If the relationships between brucellosis seroprevalence and the duration of the feeding season are due to

a causative relationship, then the results from Cross *et al.* (2007) suggest that shortening the feeding season by 1 month may reduce brucellosis seroprevalence by as much as two-thirds. Cross *et al.* (2007) found that the seroprevalence of brucellosis was unrelated to the population size and density of elk at each feedground, but was highly correlated with the timing and duration of aggregation. Feedgrounds that fed elk longer and later into the spring had higher brucellosis seroprevalence. However, on most feedgrounds, elk rather than feedground personnel, appeared to determine when the feeding season ends by leaving the feeding areas for new green growth in spring. That is, elk leave the feedgrounds if managers stop feeding them, but often leave prior to the cessation of feeding. As a result, the ending date of the feeding season is highly correlated with snowpack. Thus, both management schedule and climate appear to drive the duration of the artificial feeding season, which is, in turn, correlated to brucellosis seroprevalence.

If shortening of the feeding season can successfully reduce seroprevalence, then the management question becomes where and when can the supplemental feeding be reduced in a way that elk respond by using native forage rather than drifting onto nearby cattle feedlines. Research is currently under way to document elk space-use patterns around the feedgrounds, which may help to identify sites and years that pose the most risk. In an effort to promote elk use of native forage during the critical time period, WGFD personnel are investigating whether habitat improvements may reduce the dependence of elk on the supplemental feedgrounds. Prescribed burning and mechanical thinning of aspen should increase vegetation recruitment and result in reduced dependence upon the feedgrounds. Prior to 1897, the mean fire return interval for sage-brush habitats in this region was 12–15 years, but post-settlement intervals have increased to >100 years (Miller & Rose 1999). It is unclear how long the benefits of these modifications may last, and the reintroduction of frequent fires to this landscape may result in some unexpected consequences.

Future Directions

Most of the past research on brucellosis in the GYE has focused on a single host–parasite combination (e.g., either bison or elk) despite the multihost nature of the system. As a result it remains unclear how much of the disease dynamics in either bison or elk is being driven by the alternate host. Elk outside the GYE are not known to sustain this disease. This may be due to a lack of *B. abortus* introductions to other areas, but the extent of brucellosis in cattle during the early to mid 1900s suggests that *B. abortus* may have been introduced to many elk populations around the United States and could only be sustained around the GYE. The most plausible hypothesis is that the supplemental feedgrounds maintain the infection in elk and brucellosis prevalence in surrounding elk populations reflects movement of previously exposed elk away from the feedgrounds. While there may be some spillover transmission between bison and elk, which would become problematic for eradication efforts, it probably does not affect the disease dynamics in either host (Ferrari & Garrott 2002).

However, our knowledge of disease interactions between bison and elk is mostly speculation. Understanding this relationship has direct relevance to management. If transmission between bison and elk is significant then management actions on one host may have cascading effects upon the other. Alternatively, the disease dynamics in each host may be completely independent of one another. Estimating the amount of transmission within a host species is challenging, and few, if any, studies have estimated the amount of transmission between host species. Parasite genetics and epidemiological modeling approaches may bring new insight to this system. For example, future genetic analyses may indicate whether *B. abortus* samples taken from elk in the northern areas of the GYE are more genetically related to samples taken from

nearby bison herds or from elk around other more distant feedgrounds. This sort of information would allow researchers to estimate the amount of transmission that occurs between elk and bison. Similarly, spatial epidemiological models that integrate elk movements with serological data could assess the likelihood that movement away from the feedgrounds is the primary determinant of elk seroprevalence in other areas of the GYE.

Future Issues and Conclusions

If our current patterns of increasing urbanization and agricultural development continue, we can expect further habitat loss and the alteration of remaining habitats into smaller, more isolated patches. At the same time, the value of cervids as a renewable natural resource is unlikely to change. This imbalance creates a difficult situation for managing cervid populations. While it is difficult to predict specific disease-related issues, we foresee several possible avenues.

One potential issue facing managers is the maintenance of present cervid population numbers in the face of increasingly reduced and fragmented habitats. This management strategy would lead to higher population densities in the remaining habitats—the most fundamental condition favorable to disease (Daszak *et al.* 2000; Wobeser 2006). Increasing urbanization and agricultural development may also result in increased contact and disease transmission between cervids and domestic livestock in residual areas of natural habitat. In all likelihood, some mixture of both of these scenarios will challenge wildlife managers in the years to come.

Not all disturbances are as visually obvious as habitat alteration. Climate change, if it occurs at the level projected by current global circulation models, may have important and far-reaching effects on infectious disease dynamics as well (Daszak *et al.* 2000). The mechanisms of change in disease dynamics may include impacts to the population size and range of hosts and pathogens, the length of transmission season, and the timing, speed, and intensity of outbreaks (Wobeser 2006). Climate changes may mean that known diseases that are not of management concern today may be forced to the forefront of management in the years to come.

This may be especially true in northern latitudes where some of the most dramatic changes in wildlife distribution could occur. For example, climate warming may result in the northern expansion of white-tailed deer range, which would bring white-tailed deer and their attendant meningeal worms into contact with moose and caribou herds in northeastern North America. The parasite does not harm white-tailed deer, but is highly virulent in other cervids causing fatal neurologic disease (Wobeser 2002). Thus, a climate driven range expansion of white-tailed deer could lead to serious declines in moose populations and especially devastating declines in caribou populations. Lyme disease is another zoonotic disease whose distribution is hypothesized to increase with global warming. Small arthropods are very sensitive to temperature, and temperature constrains the range of many vector borne diseases, such as Lyme disease. Although climate change is a relatively slow process, threshold levels may result in rapid changes in disease ecology. For example, in 2006 a surprising case of bluetongue, a midge-borne disease infecting domestic livestock and wild cervids, was detected in the Netherlands. This was not simply the virus creeping northwards, but a South African strain that spread rapidly across northern Europe (Daszak *et al.* 2000; Bluetongue licks northern Europe. *The New Scientist*, *Volume 191, Issue 2567*, 2 September 2006, Page 14). It is unknown how the disease appeared at this location with hundreds of miles of uninfected area between the new outbreak and the nearest bluetongue boundary. Regardless of how it arrived, the relatively mild 2006–2007 winter allowed the midges to overwinter and spread the following spring. This spread includes crossing the English Channel by midges blown there by the

wind (most likely), and the disease has killed almost 2 million sheep in Europe (Out of the blue. *The New Scientist*, Volume 196, Issue 2625, 13 October 2007, Page 3). Thus, even small climatic changes may result in large changes in disease distribution and create unexpected management problems.

For the diseases on which we focused, we speculate that climate change may reduce transmission of bTB and brucellosis if climate change leads to warmer temperatures. Because bTB survival declines with increasing temperatures, climate change could result in a reduction of infectious bTB in the environment or feed, and thus to a reduction in transmission rate. If climate change results in a decline in the winter snowpacks of the northern Rocky Mountains, then elk supplemental feeding seasons may be reduced. This in turn, may result in lower brucellosis prevalence due to a reduction in the overlap between feeding season and abortion/calving period, the period during which the disease is transmitted. However, we are speculating; it could be that climatic warming would change cervid grouping or movement behaviors in ways we do not expect and in ways that may somehow enhance transmission of these diseases.

Regardless of the effects of global warming on cervid disease, there are several critical research and management issues that need to be addressed. Most importantly, we need basic information on the impact of diseases on cervid population dynamics. Even for the three well studied and intensively managed cervid diseases presented here, it is not known whether diseases depress population growth rates or if disease is compensatory with respect to vital rates. From a management perspective, we need to know how well disease intervention measures work in free-ranging populations. At a minimum, we need information on the prevalence of the disease before and after intervention on treatment and control sites. And, more specifically for cervids, research also needs to address complexities in the relationship between transmission and host density. Cervid social structure may dilute within-group effects of density reduction strategies, such as hunting and culling, on disease control. For example, group sizes fluctuate seasonally for most cervids such that the number of groups may be related to population size while group size and within-group transmission rate remain relatively constant. However, because the number of groups may be DD, the overall direct contact rate between groups is likely to increase with population density (Schauber *et al.* 2007). In either case, epidemiology models based on random mixing assumptions will not be appropriate for cervids. Rather, future modeling should focus on alternative approaches such as metapopulation and network models, which can incorporate social structure and seasonal mixing (Keeling 1999; Cross *et al.* 2004; Lloyd-Smith *et al.* 2005b).

Finally, human dimension issues are fundamental to successful management of cervid disease in free-ranging populations. For example, in almost all situations, reducing or banning supplemental winter feeding would reduce disease transmission. However, feeding bans are often politically charged because of long traditions of supplemental feeding and local economies that are built around this practice. Risk modeling may help identify successful cervid disease strategies that balance the biological risks of disease transmission and the political risks of alienating hunters who assist with cervid management. Cervid disease management aimed at minimizing spillback and spillover to domestic animals will depend on development of secure livestock husbandry practices. Research on how best to separate livestock and cervids will be important to limit disease spillover. Disease management needs to be grounded in good science and implemented in the context of the political and human realities of the specific situation; in particular, stakeholders' views must be addressed in order for disease management to be successfully implemented.

In general, we conclude with the usual; we need more data. More specifically, we need

baseline data on the vital rates, demographics, and dynamics of diseased and disease-free cervid populations. Additionally, evaluating various models of disease transmission is critical to understanding cervid disease dynamics and accurately predicting its spread. We also need to frame all disease management intervention as well designed field studies that include disease monitoring. We also note that disease management programs should be carefully monitored with quantifiable benchmarks that can indicate management success or failure. Finally, we reiterate the importance of human dimensions; there is a continued need to bring together scientists, managers, livestock producers, ordinary citizens, and other stakeholders to successfully manage cervid diseases.

Conflicts of Interest

The authors declare no conflicts of interest.

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