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## Pasteurellosis Transmission Risks between Domestic and Wild Sheep

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### Introduction

Disease has contributed significantly to the decline of bighorn sheep (*Ovis canadensis*) populations throughout much of western North America, decreasing many native herds to less than 10% of their historical size and imperiling some populations and subspecies.

Disease has contributed significantly to the decline of bighorn sheep (*Ovis canadensis*) populations throughout much of western North America, decreasing many native herds to less than 10% of their historical size and imperiling some populations and subspecies (Valdez and Krausman 1999). According to historical accounts (e.g., Grinnell 1928; Honess and Frost 1942; Shillinger 1937; Warren 1910), epidemics in some locations coincided with the advent of domestic livestock grazing in bighorn ranges, suggesting that novel pathogens may have been introduced into some bighorn populations beginning in the 1800s.

Native North American wild sheep species—bighorn sheep and thinhorn (Dall's and Stone's) sheep (*O. dalli*)—are very susceptible to pneumonia and particularly to pasteurellosis (Miller 2001). The generic term “pasteurellosis” is used here for disease (often respiratory) caused by bacteria in the family *Pasteurellaceae* but now classified in the genera *Pasteurella*, *Mannheimia*, or *Bibersteinia*. In some recent pneumonia epidemics in bighorns, the cause has been attributed to endemic respiratory pathogens or strains of *Pasteurellaceae* (Rudolph et al. 2007), and in other epidemics the cause has been attributed to *Pasteurellaceae* strains or other pathogens introduced via interactions with domestic sheep (*O. aires*; George et al. 2008). This Commentary reviews current knowledge on pneumonic pasteurellosis in domestic and wild sheep, the risks of transmission between these species, and approaches for lowering the overall risk of epidemics in wild sheep.

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## Pneumonic Pasteurellosis in Domestic Sheep

Respiratory disease is a serious problem in domestic sheep that can result in substantial economic losses. Pneumonia in domestic sheep is more common in lambs than in adults, and affected animals often die if not treated.

Pasteurellosis in domestic sheep generally is thought to result from invasion of the lung by *Pasteurellaceae* following a compromise of the respiratory tract.

The effects of psychological, physiological, and physical environmental stressors are believed to be important components of pasteurellosis in many domestic ruminants.

Early treatment with antibiotics effective against *Pasteurellaceae* generally stops a pneumonia outbreak, suggesting that these bacteria are important in the disease process.

The diversity of commensal and disease-associated *Pasteurellaceae* further complicates the epidemiology and control of pasteurellosis.

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Pasteurellosis in domestic sheep often is described as a disease complex (Alley, Ionas, and Clarke 1999; Donachie 2007; Gilmour and Gilmour 1989) and generally is thought to result from invasion of the lung by *Pasteurellaceae* following a compromise of the respiratory tract. The initiating insult can be from respiratory infection by mildly pathogenic agents such as parainfluenza-3 (PI-3) virus, adenoviruses, respiratory syncytial viruses (RSV), *Chlamydia pecorum*, and *Mycoplasma ovipneumoniae*, as well as from mechanical irritants such as dust (Alley, Ionas, and Clarke 1999; Brogden, Lehmkuhl, and Cutlip 1998; Donachie 2007) and lungworms. In most instances, these insults alone do not result in significant epidemics with high morbidity or mortality; however, when these and other stressors are compounded by infection with *Pasteurellaceae*, the result can be increased disease and death.

The effects of psychological, physiological, and physical environmental stressors are believed to be important components of pasteurellosis in many domestic ruminants (Brogden, Lehmkuhl, and Cutlip 1998; Carroll and Forsberg 2007; Donachie 2007; Gilmour and Gilmour 1989). Although the effects of stressors are difficult to measure, some indicators including increased body temperature, heart rate, and plasma cortisol have been correlated with disease (Carroll and Forsberg 2007; Knowles et al. 1995). Physiological response to stressors (collectively called "stress") includes suppression of the immune system; consequently, prolonged stress may increase susceptibility to pathogens and to morbidity and mortality. Environmental stressors most commonly associated with pasteurellosis in livestock include heat, cold, wind chill, crowding, mixing with new animals, poor ventilation, handling, and transport (Brogden, Lehmkuhl, and Cutlip 1998; Carroll and Forsberg 2007; Knowles et al. 1995). Other predisposing factors, such as lack of sufficient energy or protein, inadequate colostrum consumption, specific vitamins, or certain minerals, also may compromise immunity further (Carroll and Forsberg 2007).

*Pasteurella multocida*, *Mannheimia haemolytica*, and *Bibersteinia trehalosi* (all formerly in the genus *Pasteurella*) are the three most commonly isolated bacterial agents from pneumonias that result in high rates of illness, morbidity, and mortality in domestic sheep (Brogden, Lehmkuhl, and Cutlip 1998; Donachie 2007; Gilmour and Gilmour 1989). Early treatment with antibiotics effective against *Pasteurellaceae* generally stops a pneumonia outbreak, suggesting that these bacteria are important in the disease process. *Pasteurellaceae* are common inhabitants of the tonsils and oropharynx of a variety of healthy domestic and wild species (Gilmour, Thompson, and Fraser 1974; Jaworski, Hunter, and Ward 1998). In domestic sheep, *Pasteurellaceae* are believed to be opportunistic bacteria that colonize the lung after some predisposing insult (Brogden, Lehmkuhl, and Cutlip 1998). Some *Pasteurellaceae* strains make products (including leukotoxin and endotoxin) that exacerbate disease in the host after colonization of lung tissue (Ackermann and Brogden 2000; Gilmour and Gilmour 1989) and result in increased morbidity and mortality.

The diversity of commensal and disease-associated *Pasteurellaceae* further complicates the epidemiology and control of pasteurellosis. Serotyping and phenotyping based on variations in fermentation patterns (Angen et al. 1999; Frank 1982; Jaworski, Hunter, and Ward 1998) and gene sequencing (Angen et al. 1999; Jaworski et al. 1993;

Kelley et al. 2007) have been used to distinguish among *Pasteurellaceae* strains. Studies using these approaches have shown that domestic sheep may carry numerous strains of *Pasteurellaceae* (Jaworski, Hunter, and Ward 1998; Ward et al. 1997).

Most *Pasteurellaceae* of sheep are obligate bacteria that die rapidly in the environment outside a living host (Dixon et al. 2002). Environmental sources such as water and soil are not thought to be important in maintaining or spreading these bacteria; consequently, transmission is most likely to occur through direct contact among animals. Because many healthy domestic sheep carry strains associated with disease (Jaworski, Hunter, and Ward 1998), transmission of a specific pathogenic *Pasteurellaceae* strain may not be necessary for a disease outbreak to occur. In some instances, however, mixing individuals from different sources and possibly carrying different strains of *Pasteurellaceae* seems to precipitate outbreaks (Gilmour and Gilmour 1989).

As in domestic sheep, *Pasteurellaceae* commonly are associated with pneumonia epidemics in bighorn sheep, and pasteurellosis frequently results in both all-age die-offs and persistent high rates of pneumonia in lambs.

### Pasteurellosis in Wild Sheep

As in domestic sheep, *Pasteurellaceae* commonly are associated with pneumonia epidemics in bighorn sheep (Miller 2001), and pasteurellosis frequently results in both all-age die-offs and persistent high rates of pneumonia in lambs (Cassirer and Sinclair 2007; Monello, Murray, and Cassirer 2001). Thinhorn sheep also are susceptible to pneumonia (Black et al. 1988; Foreyt, Silflow, and Lagerquist 1996; Jenkins et al. 2007), but epidemics have not been reported in free-ranging populations.

The observed differences in susceptibility to experimental and natural pasteurellosis between domestic and wild sheep are thought to result from differences in pulmonary host defense mechanisms and greater vulnerability of phagocytes to leukotoxin that apparently increase overall susceptibility to pasteurellosis.

*Pasteurellaceae* alone seem to have a more severe effect on wild sheep than on domestic sheep in experimental situations. Wild sheep experience high morbidity and mortality after being intratracheally or intradermally inoculated with relatively high doses ( $10^4$  organisms) of field strains or attenuated strains of *M. haemolytica* from domestic sheep or cattle (*Bos taurus*), or with *B. trehalosi* strains originating from other wild sheep (Foreyt, Silflow, and Lagerquist 1996; Foreyt, Snipes, and Kasten 1994; Onderka, Rawluk, and Wishart 1988). The resulting pathology from experimental inoculations of wild sheep varied among strains used, but all strains caused some form of pneumonia. The observed differences in susceptibility to experimental and natural pasteurellosis between domestic and wild sheep are thought to result from differences in pulmonary host defense mechanisms and greater vulnerability of phagocytes to leukotoxin that apparently increase overall susceptibility to pasteurellosis (Foreyt, Silflow, and Lagerquist 1996; Silflow, Foreyt, and Leid 1993; Silflow et al. 1989).

Both endemic and introduced pathogens are believed to contribute to contemporary pasteurellosis epidemics in bighorn sheep.

*Pasteurellaceae* have been isolated from both healthy and pneumonic wild sheep (Jaworski, Hunter, and Ward 1998; Jenkins et al. 2007; Kelley et al. 2007; Rudolph et al. 2007). Although field investigations often are complicated by delays in detecting cases and by sample availability, two broad epidemic patterns in bighorns have emerged. In some bighorn epidemics, endemic respiratory pathogens including *Pasteurellaceae*, PI-3, RSV, and *M. ovipneumoniae*, as well as lungworms (*Protostrongylus* spp.), with or without other environmental stressors, are believed to have contributed to disease (Rudolph et al. 2007; Spraker et al. 1986). These outbreaks resemble the patterns described in some pasteurellosis epidemics in feedlot lambs (Gilmour and Gilmour 1989). Other epidemics, however, are believed to have been initiated by introductions of novel respiratory pathogens into bighorn populations (Foreyt and Jessup 1982; George et al. 2008). These patterns resemble some pasteurellosis epidemics reported in domestic sheep, particularly feedlot lambs, after transportation and mixing of different groups in confinement settings (Gilmour and Gilmour 1989). Thus, both endemic and introduced pathogens are believed to contribute to contemporary pasteurellosis epidemics in bighorn sheep.

Based on evidence from empirical studies and field observations, interactions between wild sheep and domestic sheep increase the probability of mortality and reduced lamb survival in wild sheep populations, primarily because of respiratory disease.

Pneumonia in wild sheep developed after contact with domestic sheep in captive conditions.

Quantifying the risk of interspecies disease transmission between wild sheep and domestic sheep in a natural setting is problematic.

Further work is needed to understand better the magnitude of potential risk to wild sheep arising from interactions with domestic goats, cattle, and other wild ruminant species, as well as potential influences of seasonal and environmental factors on these risks.

The most practical approaches identified thus far for minimizing risk involve preventing interspecies interactions that could result in respiratory pathogen transmission.

## Risks to Wild Sheep Associated with Domestic Sheep Interactions

Based on evidence from empirical studies and field observations, interactions between wild sheep and domestic sheep increase the probability of mortality and reduced lamb survival in wild sheep populations, primarily because of respiratory disease (USDA–FS 2006). Interactions between wild sheep and domestic goats (*Capra hircus*), although not as widely reported, seem to pose comparable risks (Garde et al. 2005; Jansen et al. 2006). Similarities in social behavior and physiology between wild and domestic sheep (and, to a lesser extent, goats) probably create a natural attraction that fosters intimate contact between these species.

Pneumonia in wild sheep developed after contact with domestic sheep in captive conditions (Black et al. 1988; Callan et al. 1991; Foreyt 1989; Onderka and Wishart 1988). Moreover, relationships between the onset of some pneumonia epidemics in wild sheep and the concurrent presence of domestic sheep on bighorn ranges have been described (George et al. 2008; Monello, Murray, and Cassirer 2001). Whether introduced *Pasteurellaceae* strains, introduced virulence factors, or other introduced pathogens contribute to precipitating these epidemics remains unclear (Besser et al. 2008; George et al. 2008; Kelley et al. 2007).

Quantifying the risk of interspecies disease transmission between wild sheep and domestic sheep in a natural setting is problematic. Movements of wild sheep may influence the potential for pathogen introductions and transmission from domestic to wild sheep, as may the proximity, duration, movements, management, seasonality, reproductive status, and straying rates of domestic sheep grazing in occupied wild sheep habitats. The increased risk of a pneumonia epidemic in a wild sheep population associated with domestic sheep interaction seems to be the product of the probabilities of multiple events, namely: interactions of sufficient duration and proximity to transmit one or more pathogens; pathogen shedding by the domestic sheep; the ability to transmit an infectious dose to one or more wild sheep; the survival of newly infected wild sheep; and, further shedding and secondary transmission. Seasonal or environmental factors also may somehow modulate the probability of epidemics occurring (Cassirer and Sinclair 2007; George et al. 2008), and the risk attributable to interactions between these species probably is additive and may vary widely among wild sheep populations. Indeed, a common *Pasteurellaceae* strain or other agent directly linking bighorn epidemics to either domestic sheep interactions or to emergence of endemic pathogens has not been demonstrated to date, and thus unequivocal evidence for either process remains elusive. Consequently, the magnitude of such risks may be assessed best on a case-by-case basis (Clifford et al. 2007; Garde et al. 2005). Further work is needed to understand better the magnitude of potential risk to wild sheep arising from interactions with domestic goats, cattle, and other wild ruminant species, as well as potential influences of seasonal and environmental factors on these risks.

## Strategies for Minimizing Risk of Interspecies Disease Transmission and Managing Wild Sheep Health

Available data suggest that interactions between wild and domestic sheep carry some inherent risk of precipitating pneumonia in wild sheep under range conditions (USDA–FS 2006). Given the limitations of today's tools, the most practical approaches identified thus far for minimizing this risk involve simply preventing interspecies interactions that could result in respiratory pathogen transmission between wild and domestic sheep (WAFWA 2007). Incomplete knowledge about the epidemiology and some details

To achieve “effective separation” (i.e., separation sufficient to minimize opportunities for pathogen transmission), herdsman and wildlife managers can actively discourage wild sheep from approaching or commingling with domestic sheep, and vice versa.

The risk of interspecies pathogen transmission may be decreased further by ensuring that domestic sheep grazing in wild sheep habitats are healthy and by removing ill sheep of either species.

Not all pasteurellosis epidemics in bighorn sheep can be attributed to contact with domestic sheep.

Wildlife managers should recognize the potential for moving pathogens via translocations and should monitor wild sheep herds routinely for pathogens of concern, using only healthy herds as source stock.

of processes contributing to the risk of interspecies disease transmission, however, remains an obstacle to consensus on acceptable and “best” management approaches.

To achieve “effective separation” (i.e., separation sufficient to minimize opportunities for pathogen transmission [WAFWA 2007]), herdsman and wildlife managers can actively discourage wild sheep from approaching or commingling with domestic sheep, and vice versa. Domestic sheep should be monitored closely and herded to prevent straying and should not be left unattended in wild sheep habitats. In some instances, truck transport may be the best means for moving domestic sheep through critical wild sheep habitats. Similarly, wild sheep that have contacted domestic sheep should not be left to commingle with other wild sheep. On common public lands, land management agencies, wildlife agencies, and domestic sheep producers with grazing leases should develop and agree on plans for handling interactions between the species, with emphasis on preventing interactions that could result in respiratory pathogen transmission between domestic and wild sheep. Ideally, similar plans also should be established between private landowners and wildlife managers where wild sheep may stray onto private land.

The risk of interspecies pathogen transmission may be decreased further by ensuring that domestic sheep grazing in wild sheep habitats are healthy and by removing ill sheep of either species. As vaccines and therapeutics for the prevention and control of infection or disease caused by *Pasteurellaceae* in domestic or wild sheep become available, producers and wildlife managers should seek practical ways to use them. In some instances where these approaches are not effective, one species or the other may need to be given management priority in, or excluded from, a particular range (WAFWA 2007). Although seemingly simple, the latter approach has several potential consequences, including lack of rangeland available to one or the other species, economic impacts, and limitations on restoration efforts.

Not all pasteurellosis epidemics in bighorn sheep can be attributed to contact with domestic sheep (USDA–FS 2006). Because some potentially pathogenic *Pasteurellaceae* and other pathogens are endemic in some wild sheep populations, wildlife managers should examine the implications of interactions between different herds of wild sheep. In doing so, the benefits of outbreeding and genetic diversity must be weighed against the increased risk of disease transmission (WAFWA 2007). In certain instances, wild sheep may need to be maintained at herd densities that minimize dispersal to help lower the risk of pathogen spread.

Augmenting wild sheep herds with individuals from other herds also poses a risk for moving pathogens. Consequently, wildlife managers should recognize the potential for moving pathogens via translocations and should monitor wild sheep herds routinely for pathogens of concern, using only healthy herds as source stock. Protocols for sampling, testing for transplant, and responding to disease outbreaks should be standardized to the extent possible and reviewed and updated as necessary. Moreover, data should be shared and interagency and interdisciplinary communications should be encouraged to develop better strategies for improving overall herd health.

## Research Needs

Current understanding about causative agents and the factors allowing these agents to lead to pasteurellosis epidemics in wild sheep is incomplete. Previous work, however, provides some clarity for future research directions. Further study of mechanisms underlying the increased susceptibility of wild sheep to respiratory diseases, as compared with domestic sheep and cattle, could aid in developing and refining approaches for improving

Developing methods that decrease the occurrence or severity of pneumonia and pasteurellosis in either domestic or wild sheep might lead to advances in managing all impacted species.

A broad approach to population health management currently may be the most practical way to decrease the overall likelihood of epidemics in wild sheep populations. Such an approach includes, but does not rely solely on, practices that prevent interactions between wild and domestic sheep that could result in respiratory pathogen transmission.

and maintaining herd health. For developing better disease prevention and control strategies, more information is needed concerning host genetics and immune responses, virulence mechanisms, pathogen transmission dynamics, and the epidemiology of the diseases. The full influence and potential for control or mitigation of other factors such as environmental stressors and nutrition, which seem important in pasteurellosis epidemics in domestic ruminants, also need to be understood better for wild sheep.

Developing methods that decrease the occurrence or severity of pneumonia and pasteurellosis in either domestic or wild sheep, including the development and use of vaccines, immunostimulants, or long-acting therapeutic agents, might lead to advances in managing all impacted species. Outcomes of such research could help decrease risks posed by interspecies interactions, or decrease wild sheep susceptibility to pathogens. In developing biologic and therapeutic agents as tools, the research should focus not only on safety and efficacy of the products, but also on the potential for practical use in free-ranging populations.

## Conclusions

Although the authors acknowledge that the current understanding about pasteurellosis in wild and domestic sheep is incomplete, respiratory disease clearly is a serious problem in both. Because the onset of some pneumonia epidemics in bighorn sheep has been associated with the presence of domestic sheep on native range, and because other outbreaks seem to have resulted from pathogens already endemic in affected wild sheep herds, accurately quantifying the risk of interspecies disease transmission in range conditions is problematic. Consequently, a broad approach to population health management currently may be the most practical way to decrease the overall likelihood of epidemics in wild sheep populations. Such an approach includes, but does not rely solely on, practices that prevent interactions between wild and domestic sheep that could result in respiratory pathogen transmission. Preventing contact between wild and domestic sheep, better monitoring of exchanges and interactions between wild sheep populations, and managing population and habitat quality all have some value in improving and maintaining the overall health of wild sheep populations and preventing pneumonia epidemics. Ongoing and planned research also is likely to provide a better understanding and new tools that may further improve approaches for wild and domestic sheep health management on native ranges.

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