Review Article Compte rendu

Johne's disease in Canada Part II: Disease impacts, risk factors, and control programs for dairy producers

Shawn L.B. McKenna, Greg P. Keefe, Ashwani Tiwari, John VanLeeuwen, Herman W. Barkema

Abstract — Part I of this 2-part review examined the clinical stages, pathophysiology, diagnosis, and epidemiology of Johne's disease, providing information relevant to Canada, where available. In Part II, a critical review of the economic impacts of the disease, risk factors, and important control measures are presented to enable Canadian bovine practitioners to successfully implement control strategies and participate in control programs. In cattle positive by enzyme-linked immunosorbant assay, there is a 2.4 times increase in the risk of their being culled, and their lactational 305-day milk production is decreased by at least 370 kg. Reduced slaughter value and premature culling account for losses of CDN$1330 per year per infected 50-cow herd. Research has failed to show a consistent association between *Mycobacterium avium* subsp. *paratuberculosis* test status and reduced fertility or risk of clinical or subclinical mastitis. Host level factors include age and level of exposure, along with source of exposure, such as manure, colostrum, or milk. Agent factors involve the dose of infectious agent and strains of bacteria. Environmental management factors influence the persistence of the bacteria and the level of contamination in the environment. Emphasizing a risk factor approach, various control strategies are reviewed, including a number of national control programs currently in place throughout the world, specifically Australia, The Netherlands, and the United States. By reviewing the scientific literature about Johne's disease, control of the disease could be pursued through informed implementation of rational biosecurity efforts and the strategic use of testing and culling.

Résumé — Maladie de Johne au Canada, partie ll : Impacts de la maladie, facteurs de risques et programme de contrôle pour les producteurs laitiers. La partie I de cette revue en 2 parties portait sur les stades cliniques, la pathophysiologie, le diagnostic et l'épidémiologie de la maladie de Johne, fournissant, lorsque disponible, de l'information applicable au Canada. Dans la partie II, une revue critique des impacts économiques de la maladie, des facteurs de risques et des mesures importantes de contrôle sont présentés de manière à ce que les praticiens bovins canadiens puissent mettre en œuvre des stratégies efficaces de contrôle et participer à des programmes de lutte contre la maladie. Les bovins positifs au titrage immunoenzymatiques utilisant un antigène adsorbé avaient 2,4 fois plus de risques d'être réformés et leur production laitière, pour une lactation de 305 jours, était diminuée d'au moins 370 kg. Une valeur réduite à l'abattoir et une réforme prématurée contribuaient aux pertes annuelles de 1330 dollars canadiens par troupeau de 50 vaches. Les recherches n'ont pas trouvé d'associations évidentes entre un test positif à *Mycobacterium avium* subsp. *paratuberculosis* et une fertilité réduite ou un risque de mammite clinique ou subclinique. Les facteurs de risques reliés à l'hôte comprenaient l'âge et le niveau d'exposition ainsi que la source de l'exposition : fumier, colostrum ou lait. Les facteurs reliés à l'agent infectieux comprenaient la dose et la souche bactérienne. Les facteurs de gestion de l'environnement étaient impliqués dans la persistance de la bactérie et le niveau de contamination de l'environnement. En favorisant une approche par facteur de risques, diverses stratégies de lutte sont passées en revue dont plusieurs programmes déjà en place dans le monde, spécifiquement en Australie, aux Pays Bas et aux États-Unis. En se basant sur la littérature scientifique concernant la maladie de Johne, la lutte contre la maladie pourrait se poursuivre par l'implantation de mesures de sécurité rationnelles et par une utilisation stratégique de tests et de réformes.

(Traduit par Docteur André Blouin)

Can Vet J 2006;47:1089–1099

Department of Health Management, Atlantic Veterinary College, University of Prince Edward Island, 550 University Avenue, Charlottetown, Prince Edward Island C1A 4P3.

Address all correspondence and reprint requests to Dr. Shawn McKenna; e-mail: slmckenna@upei.ca

Introduction

Johne's Disease (JD) is a chronic, infectious, enteritis of ruminants caused by *Mycobacterium avium* subsp. *paratuberculosis* (MAP). In the clinical stage of this disease, the infection causes severe diarrhea and wasting of the affected animal. The clinical aspects, pathophysiology, and the currently available diagnostic tests for JD were discussed in the initial paper of this 2-part series (1). In this paper, the impact of the disease is discussed, including economic consequences on dairy production. Additionally, risk factors that are associated with the spread of the organism and the incidence of new infections on dairy farms are outlined. A review of control strategies that can be used to avoid new infections on a dairy farm is included.

Materials and methods

Due to substantial differences in management, production, and related control options between dairy and beef cattle, and the extensive literature on JD for both dairy and beef cattle, this paper focuses on dairy cattle. Also, because the intended audience for this paper is primarily veterinarians in Canada, Canadian references have been emphasized.

Medline (accessed via PubMed from 1950 to present), The Commonwealth Animal Bureaux (CAB) (accessed via VetCD and ParasiteCD sets from 1973 to present), and Agricola, produced by the National Agricultural Library of the US Department of Agriculture (from 1970 to present) were used to assemble the references. The keywords used in the search of the databases were *Mycobacteria,* paratuberculosis, Johne's, Canada, Canadian, dairy, and cattle. In addition, a small number of papers were identified from the reference lists of other papers and personal knowledge of reports or conference proceedings.

All relevant material collected from the process described was included in the review, provided that it was pertinent to the methods of production within the Canadian dairy industry. Exclusion of material was done only if information was redundant or outdated and had been directly refuted.

Impacts on productivity

Cattle that develop clinical JD have thickened intestinal mucosa, resulting in malabsorptive diarrhea and subsequent decreased intestinal absorption of nutrients. Reductions in milk production, infertility, premature culling, and lower slaughter value due to poor body condition have been reported as the common causes of economic loss associated with JD (2).

Losses associated with subclinical JD, defined as infected without overt clinical signs, have been more difficult to quantify because of the difficulty of accurately detecting subclinical paratuberculosis with the diagnostic tests currently available. Studies on subclinical impacts, as determined by identification of the organism through fecal culture, are less susceptible to misclassification bias than are those using identification of an immune response to the organism (enzyme linked immunosorbent assays — ELISAs), as explained below. However, due to the cost and long time lag between submission of samples for and results from fecal culture, ELISAs are frequently used in the field to identify subclinically infected animals. Therefore, observational studies on impacts based on positive ELISA results have been conducted and are also critically evaluated in the following section. An estimate of subclinical economic losses is necessary for assessing the cost-effectiveness of control strategies at the farm, region, and national levels.

Reported economic losses attributable to subclinical JD include decreased milk production (2,3), decreased milk fat and protein yield (4,5), reduced slaughter weight at culling (6), and premature culling (7). Decreased fertility (7) and increased incidence of clinical mastitis, subclinical mastitis, or both (8) may also be associated with MAP infections. In the following sections, each of these areas of loss is critically evaluated and summarized in Table 1.

Milk production, fat and protein yield

In 1 of only 2 published Canadian studies looking at the impacts of subclinical infection in dairy cattle, records from 2395 randomly selected dairy cattle in 90 randomly selected herds were examined (9). Overall, 305-day milk production for ELISA-seropositive cows was lower than that for seronegative cows. In their 1st and 5th lactations, ELISA-seropositive animals produced 573 and 1273 kg less than seronegative cows, respectively. Similar milk production losses were found in ELISA-based studies in Wisconsin (8) and Colorado (10). In the study from Wisconsin, positive cows were found to have a 376 kg (4%) decrease in 305-day mature equivalent milk production (305ME) (8), and in the study from Colorado, ELISA-positive cows were found to have had a 551 kg decrease in 305ME (10). In 2 studies, an association between paratuberculosis and decreased milk fat and protein yield has been reported (4,5), costing approximately US$205 per cow per lactation (4). In a study based in Ontario (11), associations between results from an experimental ELISA and milk production were inconsistent, perhaps owing to the experimental nature of the test utilized.

When culled dairy cows were diagnosed positive by histopathologic examination and culture of tissues, cows that showed no clinical signs but were positive had a 16% decrease in milk production in their last lactation compared with their lactation 2 y prior, and a 6% decrease in milk production compared with their lactation 1 y prior (2). However, production in uninfected cows was not studied for comparison. Assuming a lactation that produces 8000 kg of milk, these estimates would equate to 1280 and 480 kg, respectively. Similar results of milk production losses associated with subclinical paratuberculosis were determined for cattle that were positive on fecal or tissue culture (2,4,7). In a dairy herd of 210 cows in the USA with a high prevalence of MAP infection, fecal culture-positive cows produced 590 kg and 1270 kg less milk in their 3rd and 4th lactations, respectively, compared with their fecal culture-negative herdmates (3).

There is potential for bias in each of these studies. In the cull cow study (2), cull cows would likely include older cows, which, if infected, would be close to entering the clinical stage of infection. The use of cull cows, instead of a random sample of cows, in milking herds potentially overestimates the overall impact on milk production among the general population. Similarly, cows from a herd with a high prevalence of infection (fecal culture study) would also be more likely to include cows entering the

Table 1. Affects of paratuberculosis on health, production, and culling

Parameter	Diagnosis criteria	Affect of paratuberculosis	Reference
Milk production	Tissue positive	16% decrease in last lactation compared to two years prior and 6% decrease compared to one year prior	2
	Fecal positive	590 kg and 1270 kg less milk in third and fourth lactations, respectively	3
	ELISA positive	4% (376 kg) decrease in 305ME production	8
		551 kg decrease in 305ME production	10
		573 and 1273 kg less milk in first and fifth lactations, respectively	9
Risk of culling	Fecal positive	Greater culling rate cost infected herd US$75 per cow per year	16
	ELISA positive	Odds Ratio = 2.34 for risk of culling	15
Reduced slaughter value	Clinical JD	Reduced slaughter value of 20 to 30%	2
	Fecal positive	59 kg less weight at slaughter, for a loss of US$48 per head	6
	ELISA positive	Estimated losses of CAN$1330 per infected 50 cow herd	18
Fertility	Tissue positive	Higher fertility cull rate overall	7
	Fecal positive	No difference in fertility	22
	ELISA positive	49 day increase in days open in first lactation heifers	21
		No difference in fertility	22
Mastitis	Fecal positive	Lower somatic cell count	22
		Cull rate for mastitis was 22.6% versus 3.6% in culture-negative cows	7
	ELISA positive	Higher somatic cell count at the cow level and herd level	11
		Odds Ratio = 2.90 for risk of culling due to mastitis	15

ELISA — enzyme-linked immunosorbent assay
305ME — 305-day mature equivalent milk production
JD — Johne's disease

clinical stage of infection due to increased exposure to MAP compared with cows' exposure on lower prevalence farms.

However, there is a potential that this estimate of productivity loss may be an underestimation. The specificity of fecal culture is generally considered to be 100% (12); therefore, all culture-positive cattle are assumed to be infected (no false-positives). However, because sensitivity is less than 100% (estimated at 50% [11]), there are false-negatives in the culture-negative group. These false-negatives are likely to lower the average milk production of this group, bringing the mean productivity of the 2 groups closer, leading to an underestimation of the difference between test-positive and test-negative animals. Conversely, in a herd with a high prevalence of infection, the milk production effects for the industry may be overestimated, because heavy exposure to calves in this herd could lead to earlier clinical signs than would be seen for the rest of the industry.

As shown by these studies, the level of reduction in milk production in subclinically infected cows depends on a number of factors, including stage of subclinical infection (2); parity, with infection in older cows having a larger negative impact (3); sensitivity and specificity of the test utilized for identifying infected cattle, which varies with the stage of infection (13); and farm management (cow comfort, concurrent infections) (9). Further studies are needed to identify the onset, progression, and extent of milk production effects associated with JD in fecal culture-positive animals, controlling for these and other confounding variables at the cow, herd, and regional level. However, current knowledge supports the fact that subclinical JD has a considerable negative effect on milk production and udder-health, the only difference being the magnitude of this effect.

Premature culling and reduced slaughter value

Premature culling associated with paratuberculosis is 1 of the major economic burdens of this disease (14). In the only Canadian study estimating culling risk based on serological testing, results from randomly sampled cattle among randomly selected dairy herds in Maritime Canada indicated that after controlling for parity, 305-day milk production, and somatic cell count (SCC), the odds of being culled during the 3 y after testing were 2.3 times greater in ELISA-seropositive cows than in seronegative cows (15). While the owners in this study were informed of the test results 1 y after sampling, the difference in the odds of culling between seropositive and seronegative cattle was not significantly different before and after the results were communicated, indicating that the difference was for biological reasons, not simply due to the test results.

Similar results were found in a study comparing fecal culture-negative and culture-positive cows in 1 herd from New York, in which the estimated loss due to premature culling for MAP was US$75 per cow per year (16). Age at culling in tissue culture-positive cows showing clinical signs, tissue culture-positive cows not showing clinical signs, and noninfected cows has been demonstrated to be 4.3, 4.9, and 7.7 y, respectively (17).

In addition to premature culling, slaughter value has also been shown to be affected by JD. Clinical JD has resulted in a reduced slaughter value of from 20% to 30% in culled cattle (2). In addition, fecal culture-positive cattle without clinical signs have been shown to weigh approximately 59 kg less at slaughter, a loss of US$48 per head (6). By using economic modeling techniques, a loss of CDN$1330 per 50 cow herd (assuming an average apparent prevalence of 7%) due to reduced cull

value and premature culling associated with subclinical MAP seropositive cows was reported for dairy cattle in Maritime Canada (18). Further analysis is needed to verify that this estimate is appropriate for all of Canada.

Reduced fertility

Research has failed to show a consistent association between MAP test status and reduced fertility (19). In a study performed in a 900-cow herd spanning a total of 10 y, data were collected on reasons for culling, along with the results from fecal, ileum (ileal-cecal junction), and associated lymph node culture (7). A greater percentage of infected cows (68.8% or 106/155) than culture-negative cows (60.2% or 797/1324) were culled for infertility. The reliability of producer-reported reasons for culling have been questioned, because only 1 reason can be entered in most dairy herd improvement (DHI) systems when, in fact, multiple parameters often contribute to a culling decision (20). In the case of this 10-year study, however, producers were not restricted to picking 1 reason for culling, and multiple reasons were listed.

In 90 dairy herds from the Canadian Maritime provinces, seropositive 1st lactation heifers were open for 49 d more than seronegative 1st lactation heifers, but no association was found for other parities (21). In a study done in Michigan, seropositive cows had a 28-day increase in days open; however, there was no significant association when infected cows were identified with fecal culture (19). Furthermore, in studies done in 6 herds in New Zealand with fecal culture testing (22) and in 304 herds from Ontario with ELISA testing (11), no association was found between subclinical paratuberculosis and calving interval.

Overall, in 4 studies (2 ELISA and 2 culture-based), JD was found to have had a negative effect on reproduction, and in 3 studies (1 ELISA and 2 culture-based), to have had no negative effect on reproduction. As a result, it is difficult to draw strong conclusions regarding the impact of JD on fertility. From the available literature, seropositive cows appear to have some degree of diminished fertility; however, this impairment is not evident when the classification of disease status is based on fecal culture. Therefore, the implications of reduced fertility due to JD may not have anything to do with whether the cow is actively shedding bacteria.

If there truly is an impact of subclinical paratuberculosis on fertility, it has been hypothesized that the mechanism is related to the impaired immunological and gastrointestinal absorptive capacity and the accentuated negative energy balance sustained by infected cattle (19). Preliminary work has looked at the effect of energy on the metabolic and immune status of cows with JD around the time of parturition (23): fecal culture-positive cows were supplemented with a higher energy diet by means of "force feeding" through a rumen cannula, and it was found that although supplemented cows had the same periparturient decline in neutrophil function, in vitro immunoglobulin production was increased and the return to normal lymphocyte proliferation activity was less protracted. However, the major limitation of this study was that no uninfected cattle were included for comparison.

Mastitis

There has also been an inability to show a consistent association between MAP test status and the risk of clinical or subclinical mastitis. In 304 herds in Ontario, when an experimental ELISA was used to identify cattle with subclinical paratuberculosis (11), seropositivity was associated with higher SCC at the cow and herd level. Conversely, in a study of 6 dairy herds in New Zealand (NZ), subclinical, fecal culture-positive cows were found to have significantly lower SCC than did culture-negative cows (22). The differences in testing methodology make it difficult to make direct comparisons between the 2 studies. However, the results from NZ may be specific to the 6 herds that were sampled, which are unlikely to be comparable with most dairy farms in Canada, due to major differences in climate, management, and productivity between the 2 countries.

Results from a study of dairy cattle in Maritime Canada indicated that, after controlling for parity, 305-day milk production, and linear score SCC, the odds of being culled because of either decreased milk production, mastitis, or reproductive inefficiency was 2.9 times greater in MAP ELISA-positive cows than in ELISA-negative cows (15). These findings support previous reports where cull rates due to mastitis were higher for fecal culture-positive cows compared with culture-negative cows (7). In the previously mentioned culling study of a Guernsey herd, the risk of culling due to mastitis in the culture-positive cows was 22.6% (45 of 199 cows) versus 3.6% (49 of 1361 cows) in the culture-negative cows (7). However, due to the potentially unreliable nature of producer-reported reasons for culling in dairy herd improvement (DHI) data, mastitis-related culling evidence should be interpreted with caution. Nevertheless, in this case, where there are such dramatic differences, there is likely a real association present.

Overall, there appears to be more evidence for than against the theory that JD negatively affects udder health (Table 1). However, further research is needed to clarify and quantify this impact. The pathophysiology of how subclinical paratuberculosis could affect mastitis remains unclear and also requires further research. Speculation includes negative energy balance and reduced cellular immunity, which have been shown to occur, at least in periparturient cows, with JD (23).

Total economic losses at the farm, regional, and national level

Studies of annual economic losses associated with clinical and subclinical JD among dairy farms have indicated that there are substantial effects at the farm, regional, and national levels (16,18,22,24). As part of a survey by the USDA National Animal Health Monitoring System (NAHMS) conducted in 1996, it was estimated that, averaged across all herds in the United States (US), JD cost the US dairy industry US$200–250 million annually (24). Subsequently, a study conducted in the Canadian maritimes (18) found that based on ELISA, the losses were CDN$2472 per infected herd per year (average herd size of 50 cows with an average apparent prevalence of 7%) and CDN$0.84 million per year for the entire Canadian maritime provinces. Direct production losses included decreased milk production, increased culling risk,

reduced cull value, mortality, treatment costs, and reproductive loss. Assuming the prevalence of JD in the Maritimes were the same as in the rest of Canada, the national cost of JD could be estimated at CDN$15 million annually. However, these calculations most likely underestimate the actual losses associated with JD, because of misclassification of infected cattle by the ELISA and the authors' decision to not recognize other potentially relevant economic effects, such as mastitis, decreased feed efficiency, and restrictions on market access. Further data and improved diagnostic methods are needed in order to accurately determine economic losses associated with JD for the Canadian dairy industry.

Risk assessment

Various factors, such as host susceptibility and environmental factors (mode of transmission), interact to determine the prevalence and severity of MAP infection (24).

Host factors

Level of exposure (dose of organisms) and age at the time of exposure are major factors in determining whether an animal eventually becomes infected with JD. Although there is a paucity of scientific evidence on these factors, there is consensus that younger animals require a lower infective dose than do older animals (25–27), and an adult animal is quite unlikely to become infected unless there is extreme environmental contamination (28). Poor nutrition, stress related to transport, lactation, parturition, and immunosuppression by agents like bovine viral diarrhea virus have been proposed as biologically plausible factors accelerating or precipitating the onset of the clinical phase of infection (29).

Milk or colostrum may serve as the source of MAP organisms for neonates in 2 ways. Fecal contamination of these fluids may occur, allowing the milk or colostrum to act as the vehicle for infection. Additionally, MAP has been isolated from sterile collections of milk and colostrum from infected cows (30), indicating that there is potential for direct transmission through colostrum and milk from an infected dam (31). Infection can also occur directly across the placenta, as tissue-positive fetuses have been found in culled tissue-positive cows, although this occurrence is quite infrequent (32). This happens more often in cows displaying advanced clinical signs of JD; however, it can occur in cows that are heavy fecal shedders, yet not displaying clinical signs of disease (33).

It is suspected that, on rare occasions, certain animals that are exposed to MAP can generate a protective immune response resulting in full clearance of the MAP (28). It is unclear whether this capacity, if it exists, is restricted to mature animals, or whether some young animals also have this capability.

In some studies, Jersey and Shorthorn cows have been shown to have a higher susceptibility for paratuberculosis (34,35). However, these observed differences were confounded by the differences in these breeds being linked to husbandry practices in specific regions (herds with these breeds in these particular studies had worse hygiene). Due to these confounding circumstances, genetics and breed appear to be minor factors.

Agent factors

The specific number of organisms required to establish infection for specific age groups has not been determined. Infection can occur in calves with a dose of 1.6×10^7 organisms, which would easily be surpassed in a 2-gram sample of heavily infected feces (36). However, this number is likely to increase with increasing age as the resistance to infection of the animal increases (25).

Infection of animals may cause clinical disease, but this is not necessarily advantageous or essential to the organism. To survive, MAP only needs to colonize, replicate, and be shed, so that the rate of recruitment of new bacteria is equal to or greater than the loss of bacteria from the population. The presence of obvious clinical disease is not required for the spread of the organism in the animal population (31). It has been shown that, although the risk of individual cows being infected is higher on farms with clinical JD, there are still many herds that are infected yet display no clinical signs of JD (37).

Different strains of MAP exist, depending mainly on the species infected. Infections in cattle and sheep are considered to be caused by separate strains of MAP, sometimes classified as type C and type S, respectively. There has been some evidence of cross-infection of animals between these species (38), but more research is needed to determine the degree to which these 2 MAP types can actually cross the species barrier. There is also evidence that wildlife species, particularly rabbits (39), may play a role in the dispersion of MAP throughout the environment and cause contamination of feed for cattle (40).

Environmental factors

The primary method of MAP transmission is believed to be a direct fecal-oral cycle. The process is quite similar to the transmission of other enteric infections, whereby any exposure to manure from shedders can potentially lead to new infections. However, there is still a possibility of indirect transmission, such as through manure contamination of water bowls and machinery used for feed delivery. Therefore, any management activities that directly or indirectly lead to exposure of susceptible animals to manure from shedding animals could be considered risk factors of infection; these will be reviewed in detail in the section on disease control strategies. The efficiency of transmission by these pathways depends upon factors such as number of organisms shed in the feces and the organism's survival characteristics in the environment (41).

Factors that influence survival of the organism include substrate (feces, water, milk), temperature, and pH. The MAP organism can persist in the environment for at least 1 y (41), but it does not replicate in the environment. Although hardier than most other pathogens, the bacterium is susceptible to long-term desiccation, repeated freeze-thaw cycles, exposure to sunlight, and soils with an alkaline pH or low iron content (42). The MAP bacterium is more thermal resistant than other *Mycobacteria,* making pasteurization of milk and milk products somewhat problematic (43). Viable MAP was found in 2.1% of the pasteurized milk samples in Great Britain (44), but studies done in North America, including one using samples collected from retail stores and dairy plants in south-western Ontario, did not find viable MAP in pasteurized milk (45). This may be due

Table 2. Recommendations for decreasing the risk of new infections of *Mycobacterium avium* subsp. *paratuberculosis* in a dairy operation

Protect young stock from feces of mature cattle and feces-contaminated feed and water	Reduce the number of infected animals that may be shedding bacteria
a. Clean and disinfect maternity and calf pens after each use	a. Immediate cull of animals with clinical signs of JD
b. Calve cows in clean, dry, dedicated maternity pens	b. Consider testing adult cows with ELISA or fecal culture; positive ELISA should be confirmed with fecal culture in clinically normal cows
c. Immediate removal of calves from maternity pen (while calf still wet)	c. Cull fecal culture-positive cows; they are active shedders and are increasing the environmental challenge on the farm
d. Collect colostrum from cleaned udders	d. Maintain a closed herd or purchase animals only from source farms that have implemented similar or better control programs than purchasing farm (management practices and testing)
e. After colostrum feeding, use pasteurized milk or milk replacer	
f. Raise calves separate from the adult herd for first year of life	
g. Do not allow shared feed/water between adult cows and young stock	
h. Use separate equipment for handling feed and manure	
i. Feed-bunk and waterers should have no risk of fecal contamination	
j. Do not spread manure on grazing or hay land for young-stock	

JD — Johne's disease

to differences in pasteurization methods and temperature (46). However, recently, low numbers of viable organisms were found in 2.8% of 702 samples tested in commercially pasteurized milk purchased from stores in California, Minnesota, and Wisconsin (47). While these data have not been published in peer-reviewed journals, these occurrences have called into question the validity of feeding pasteurized milk products to calves as a possible means of lowering the risk of MAP infection.

Although relationships are not well defined among the numerous combinations of host, agent, and environment factors found on different farm situations, known risk factors and routes of transmission must be recognized and addressed for implementation of a control program.

Herd level control strategies

In general, every disease control program has 3 main objectives: decrease the number of new infections; decrease the number of clinically diseased or shedding animals; and decrease the duration of disease or its infective period. Controlling JD shares the same objectives; in order to achieve them, a complete understanding of the transmission and pathogenesis of the bacterium is crucial (34). It has been suggested that due to the prolonged preclinical phase of the life-long infection and the poor performance of diagnostic tests, identification of subclinical shedders is difficult, making exposure of the susceptible population to subclinical cows the main risk factor for spreading infection (48). Furthermore, the ability of the bacterium to survive for more than 1 y in the environment (42) makes it difficult to stop transmission within herds without stringent manure management control for young stock. Therefore, effective JD control programs involve 2 main objectives: to implement best management practices in order to decrease calf exposure to all manure (decrease occurrence of new infections), and to reduce the number of infected animals that may shed bacteria in their manure (decrease prevalence of existing infections).

Management practices have been identified as a vital aspect of pathogenesis within a herd (34). A JD control program for a farm needs to be customized to the goals and resources of the farm. While all farms should have a plan for implementing best management practices for reducing fecal-oral transmission, due to the challenges associated with the tests to identify infected animals, the intensity and focus of that plan will depend on the goals and resources of the farm. Recommended management practices for minimizing fecal-oral transmission of JD, adapted from numerous sources (34,49–54), are summarized in Table 2.

Due to the many possible ways in which calves can become exposed to MAP-infected manure and the long interval between exposure and detectable disease, it is both very difficult and costly to conduct clinical trials to test and quantify the importance of recommendations related to minimizing calf exposure to infected manure. There appears to be a significant lack of published knowledge in this area. However, poor manure management and hygiene around calves is universally accepted as leading to exposure and infection in herds with JD (53,54). Assessing and improving management practices that minimize calf exposure to infected manure will be cost-effective on most farms, not only for reducing the impacts of JD, but also for reducing the impacts of other fecal-orally transmitted diseases of cattle (*Escherichia coli, Campylobacter* spp., *Salmonella* spp., and *Cryptosporidium* spp.).

Because of differences in farm specific goals and resources, customized testing strategies that are farm specific have been suggested and widely adopted (52), based on which of the following 3 category types of the dairy farmer: 1) those that know they have a JD problem and want to decrease the prevalence; 2) those that have confirmed or suspected that they have JD but do not think it is present at a high prevalence; and 3) those that do not suspect they have JD and want it to remain that way.

Herds that have had at least 1 cow with clinical signs of JD and a positive fecal culture likely have an infection prevalence of at least 15% (48). This assumption is based on the premise that the cow was not recently purchased (was born on the farm) and, therefore, at the time this cow became infected, there was a high likelihood that others were also infected. Additionally, the clinical cow has likely had heifer calves of her own that are still in the herd and could have infected their calves along with other in-contact heifer calves. This statement, though highly generalized and not accounting for herd size, compels one to consider the true implications of 1 clinically infected cow. For those farms with a moderate to high prevalence ($> 30\%$), regular testing of the herd is likely warranted to identify cows that are shedding and dramatically increasing the environmental load of MAP (52). On these farms, fecal culturing will identify a substantial number of shedders. However, such farms should also consider using an ELISA, because the number of ELISA false-positives

will not outweigh the number of true-positives, producing a good predictive value of a positive test (55).

The most appropriate testing strategy to use in high prevalence herds depends on the goals of the producer and the time frame during which he or she wants to accomplish those goals. If the goal is reduction of prevalence to close to zero within a few years, an aggressive approach of annual fecal culture testing of all cows 2 y and older may be warranted. However, if the herd size is large (> 300 animals), more strategic measures may be necessary due to limitations of cost, time, and laboratory space for fecal culture. For example, ELISA testing the whole herd and then fecal culture testing all ELISA-positives plus all cows with sample-to-positive (S/P) ratios higher than 1 standard deviation below the cut-off value (cows that are more likely to be fecal culture-positive but ELISA-negative) may be an alternative approach (55). However this latter, less expensive approach will miss cows that are shedding MAP but have not yet mounted much of an immune response. With the improvements in fecal culture techniques during the last few decades, it is unlikely that fecal culture-negative cows are shedding significant numbers of bacteria in their feces. Simulation studies have reported that successful and simultaneous implementation of best management practices and strategic testing and culling leads to the largest and fastest reductions in infection levels (51).

In the past, the Dutch have attempted to decrease the number of clinically diseased animals on farms with a high prevalence of disease by use of a vaccination program, using a killed vaccine, on some farms, so that they would not have to rely on imperfect tests to detect the subclinical animals (50). However, their observations with this program have been that producers often become less vigilant with other management-related control measures and too reliant on the vaccine. For this reason, if vaccination is considered, it should be restricted to high prevalence farms that have numerous clinical cases of JD.

If there has not been a confirmed clinical case of JD on a farm, and it is suspected, based on herd history, husbandry practices, or testing, that the herd has a low to moderate prevalence (< 30%), then individual fecal cultures will seem quite costly for the low number of shedding cows detected. Furthermore, using an ELISA with less than optimal specificity will result in interpretation difficulties of test positives. The likelihood of a positive test being a true positive is low in herds with a low prevalence; therefore, a confirmatory test, such as a fecal culture, should always be performed. This approach can become quite costly in large herds and can be viewed as unrewarding, especially if the herd truly is negative and all confirmatory tests are negative. One viable strategy would be to perform pooled fecal cultures of the mature cows. The major benefit of pooling is the decreased testing cost; however, diluting the sample with too many cows could lead to false-negatives. Additionally, there is need for subsequent confirmation testing of individual cows in positive pools, taking additional time before culling can be implemented. The use of broth media for cultures has reduced the time required for incubation from 16 to 6 wk, which is one reason why this is becoming a viable option. The ideal number of cows per pool has not been well established, but available research results suggest that pools of 5 would likely be adequate (56,57). This strategy has been shown to identify 87% of positive animals, whereas individual culture found 96% of positive animals (56). However, cows with low level or intermittent shedding could be missed with pooled fecal cultures; therefore, management changes should also be implemented to minimize transmission between the missed cows and susceptible youngstock.

Another alternative for moderate to low prevalence herds would be to forego testing and focus on controlling the spread of the disease within the herd by focusing on the young animals. Implementing strict control measures along with a high turnover of cows should lead to a lower within herd prevalence after approximately 5 y. Considering the performance of available tests, individual testing may be more difficult and costly than the benefits derived from such a program. Simply implementing control procedures will decrease the risk associated with a low number of cows spreading the disease within the herd and eventually lead to a decreased prevalence.

For herds that have never identified a cow with clinical signs of JD on the farm, have had at least some of the herd tested for JD, and in which all tests have produced negative results for JD, the assumption would be that the prevalence of infection on these farms is likely either zero or very low. However, with the poor sensitivity of current tests for identifying MAP-infected cattle, there is no method that allows one to definitively state that a farm is free of JD. With repeated negative tests over many years, producers and their health advisors may assume that they have disease-free status, leading to the temptation to relax within farm management practices and concentrate on keeping the disease out. However, because JD-free status cannot be guaranteed, continued vigilance is needed to minimize calf exposure to manure to avoid spreading this insidious disease unknowingly (54).

For those farms where the data suggest a high likelihood of their being JD-free, along with on-farm biosecurity measures, it is likely more important to focus efforts on keeping the disease out of the herd (58). This could be accomplished by implementing all of the control points previously mentioned in the risk factor section (Table 2) and applying methods for keeping manure from cattle from other farms away from the herd by avoiding community or shared pasture and by restricting application of manure from other farms on the farm (51–54).

With the currently available tests for JD, the common movement of animals and equipment between herds, the difficulty of completely eliminating fecal-oral exposure of young stock on a dairy farm, and the long incubation period, it is questionable whether JD can truly be eradicated from an infected farm.

Existing control programs

A number of countries have developed national, government-funded animal health programs to provide logistical, administrative, and funding support to control JD. National, government-funded animal health programs are typically directed at exotic diseases and to the control of specific diseases of widely recognized economic or public health importance. Johne's disease has emerged as a disease requiring a national control program, due to mounting evidence and concern over production

losses and the possible restrictions to international movement of cattle, as some countries require testing. In addition, it has been suggested that because DNA from MAP has been found in 69% of patients with Crohn's disease, MAP may be a factor in the causation of the disease (59), although MAP may just be an opportunistic organism found in the intestines of Crohn's patients. If the relationship between JD and Crohn's disease were scientifically confirmed, government funding of a control program would likely be forthcoming. A review into this potential relationship is beyond the scope of this paper, but further information is available from the Crohn's disease Web site (60).

Australian national voluntary JD control program

Australia was among the first countries to implement a national JD control program, although many countries have a long history in JD education and extension. In 1996, the Australians launched the National Johne's Disease Market Assurance Program for Cattle (61,62). In this program, herds progress through levels of assurance on the basis of annual negative herd tests from monitored negative 1 (MN1) to monitored negative 3 (MN3), the highest level. The actual method of testing (ELISA, fecal culture, etc.) is not specified, but it is assessed for validity by the Chief Veterinary Officer (CVO). Annually, the supervising approved-veterinarian also uses auditing procedures to monitor critical herd management aspects to control the spread of JD. Herds can opt to stay at a level by carrying out a maintenance test every 2 y, when the entire herd, up to a maximum of 100 animals, is tested. Herds not participating in testing can be classified as a non-assessed herd (NA), which is a herd with no history of JD or in which any suspicion of infection has been resolved to the satisfaction of the CVO. A herd may be classified as a suspect herd (SU) for numerous reasons, including violations of the annual management audit; however, no diagnostic confirmation of positive animals has occurred in these herds. Infected herds (IN) are herds with a confirmed infected animal. Restricted herds (RD) are herds that were previously IN herds but are currently undertaking an approved test and control program under supervision of the CVO. In addition, RD herds have achieved 1 or more negative herd tests, commencing at least 12 mo after the last known infected animal was removed from the herd. There has been a linear increase in herds participating in the Australian JD control program from approximately 180 at the end of 1996, to around 1000 herds in 2000 (62), and by December 2003, 1623 herds were participating (63).

The Dutch national voluntary JD control program

The original JD control program in The Netherlands began in 1991. In 1997, it evolved into a pilot program based on fecal culture of 125 herds that were tested every 6 mo. After 5 rounds of testing (24 mo), only 58 herds (46%) remained clear of infection (64). The lessons gained from this experiment were that although these herds had no clinical signs in the last 5 y, more than half were infected. Secondly, fecal culture, regarded as the "gold standard," was not sensitive enough to detect all infected animals. Finally, producers were disappointed to find out that their herds were truly positive and labelled as such. As a result, highly motivated producers felt that they were penalized for participating.

The current Dutch JD control program, initiated in 1998, has an extensive program, based on management assessment only, and an intensive program, based on pooled fecal cultures and management assessment. The extensive program was developed for the dairy industry, but it has not yet been accepted by the industry as a whole (Kalis CHJ, Dutch Animal Health Service, personal communication). The rules of the management assessment are aimed at reducing the spread of infection to young calves. For example, pooled colostrum must not be used, milk replacer is required, and cows should calve separately in clean calving areas. There are also strict rules governing the purchase of animals and grazing practices, along with the contact of animals with different species that may carry MAP.

In the intensive program, there are 10 levels of classification of herd status. The program is categorized to certify herds as free (level 10) or unsuspected/low prevalence (level 6–9) and provides a control program for infected herds. The program employs annual testing of adult cattle. Fecal samples are pooled in batches of 5 for status advancement and the ELISA is used at various levels on individual animals for maintenance of levels. Positive ELISA results confirmed by positive fecal culture results lead to a decrease in status level. There is a well-defined program to assist farms that have been identified as infected, which encourages farmers to participate. Additionally, funds are provided to assist with the high cost of repetitive testing for farmers to reenter the certification program (64). From the original 350 infected herds, half are now unsuspected herds. There are now 1000 herds in the certification program for unsuspected and free herds and 250 are classified as infected herds (Kalis CHJ, Dutch Animal Health Service, personal communication).

United States national voluntary JD control program

In order to address disparities between existing programs among states and encourage nonparticipating states to participate, in April 2002, the US Department of Agriculture Veterinary Services section published the Uniform Program Standards for the Voluntary Bovine Johne's Disease Control Program (65). This program recommended an advisory committee in each state to assist the state veterinarian in establishing and operating a JD program. By the end of 2002, 40 states had established advisory committees for JD with federal representation on each committee (66).

The structure of the program has 3 parts. Part 1 is education of the producers, using a means that is at the discretion of the state advisory committee. Part 2 is an assessment of on-farm risk and herd management plans. Part 3 involves herd testing and classification into 4 levels. Under normal circumstances, 10 mo must pass before a herd can advance to the next level. If a herd does not test after 14 mo, it reverts to a herd of unknown status or, in some states, a maximum risk herd. Testing in the initial stage is done on 30 randomly selected animals 36 mo of age or older. The test used is specified as a screening test and is determined by the state administrator. At a recent US Animal Health Association-Johne's Committee meeting, a resolution was

passed to use environmental sampling as a potential screening test available to state administrators (67). The idea behind this is to decrease the cost of identifying positive herds without loss of herd sensitivity (68). However, if a herd is found positive, all animals must then be tested with an individual screening test. If an animal is found positive on the screening test, an appeal can be made to have that animal tested with an official Johne's test (either polymerase chain reaction [PCR] or fecal culture, upon the discretion of the state administrator). If the official test is negative, the herd regains its test-negative status, but the animal that was retested must be submitted for testing at the next assessment, if it still resides in the herd. If the appeal test is positive, the owner can request another appeal in which the animal must either be necropsied for further testing or undergo surgical biopsy of the ileum and lymph nodes. If the end of the testing and appeals process, the animal is found to be positive, the herd is assigned a positive status.

There is a fast track option in part 3 of the program that allows a herd to reach level 4 in 2 y with 3 tests; this was added at the insistence of the livestock industry. With this option, Level 1 is skipped with a signed declaration that no cows were seen, or diagnosed, with JD in the last 5 y (66).

At the end of 2002, approximately 2675 herds were enrolled in JD control programs with herd management plans, risk assessments filed with state programs, or both (66). As of the end of 2003, there were 4722 herds enrolled in JD control programs (Carter MMA. US Department of Agriculture, National Johne's Disease Control Program Coordinator, personal communication). Approximately 543 herds that tested negative and are considered less likely to have JD than untested herds were enrolled in state-specific herd status programs in 2003.

Again, there are some specific desirable components of this program. However, due to the poor performance of ELISAs, particularly in low prevalence herds, any program that relies primarily on ELISA testing is less likely to be applicable to the majority of low prevalence herds in Canada (69), due to low herd level specificity. Herd-level specificity (HSp) is the probability that an uninfected herd yields a negative herd-test result, while herd-level sensitivity (HSe) is the probability that an infected herd yields a positive herd-test result. With 30 cows tested in a herd, HSe will be 66% and HSp will be 49%, using the ELISA (assuming test Se and Sp of 45% and 98%, respectively). However, for fecal culture, the HSe will be 66% but the HSp will be 100% (assuming test Se and Sp of 45% and 100%, respectively). In 11 Dutch dairy herds, the reported HSe for fecal culture and pooled fecal-culture were 64% and 73%, respectively (55).

Alberta JD control program

In September 2001, Alberta Agriculture Food and Rural Development implemented a Voluntary Johne's Disease Herd Status Program. The testing protocol used in Alberta's program is similar to that of the American program, but it is more specific about what test can be used at each level (70). The Alberta program is heavily based upon education and awareness, both for producers and veterinarians. There is a veterinary accreditation program to ensure continuity of delivery throughout the program.

As a progression to the Alberta program, a proposed national program has been created for dairy herds in Canada (71). This proposed program was designed to build on the success of the Alberta program; however, it proposes 2 distinct pathways for participation in the program (testing versus no testing). This allows flexibility for herds to participate in a recognized program without the need of testing at all, focusing instead on risk management and disease avoidance.

Conclusions

Johne's disease continues to cause economic losses for dairy producers worldwide, particularly with respect to lost milk production, premature culling, reduced slaughter value, and perhaps increased infertility and mastitis. The cost of JD to the Canadian dairy industry is estimated at CDN$15 million annually. The control of JD nationally will be an immense task because of the insidious nature of the disease and the relatively poor performance of tests currently available. The industry must utilize knowledge of the biology of the disease and known risk factors in an attempt to control the spread of this disease through best management practices. Strategic testing can overcome the challenges with identifying infected cattle and herds. Johne's disease control programs initiated now will lead to lower control costs in the future, and will be seen as proactive steps for quality milk production, if the link between Crohn's disease and JD is confirmed in the future. CVJ

References

1. Tiwari A, VanLeeuwen JA, McKenna SLB, Keefe GP, Barkema HW. Johne's disease in Canada. Part I: Clinical symptoms, pathophysiology, diagnosis, and prevalence in dairy herds. Can Vet J 2006;47: 874–882.
2. Benedictus G, Dijkhuizen AA, Stelwagen J. Economic losses due to paratuberculosis in dairy cattle. Vet Rec 1987;121:142–146.
3. Wilson DJ, Rossiter C, Han HR, Sears PM. Association of *Mycobacterium paratuberculosis* infection with reduced mastitis, but with decreased milk production and increased cull rate in clinically normal dairy cows. Am J Vet Res 1993;54:1851–1857.
4. Collins MT, Nordlund K. Milk production levels in cows ELISA positive for serum antibodies to *M. paratuberculosis.* Proc. 3rd Int Colloq Paratuberculosis, Orlando, Florida, USA 1991:401–409.
5. Sweeny RW, Hutchinson LJ, Whitlock RH. Effects of *Mycobacterium paratuberculosis* infection on milk production in dairy cattle. Proc. 4th Int Colloq Paratuberculosis, Cambridge, UK 1994:133–139.
6. Whitlock RH, Hutchinson LT, Merkal RS, et al. Prevalence and economic consideration of Johne's disease in the northeastern U.S. Proc US Anim Health Assoc 1985;89:484–490.
7. Merkal RS, Larsen AB, Booth GD. Analysis of the effect of inapparent bovine paratuberculosis. Am J Vet Res 1975;36:837–838.
8. Nordlund KV, Goodger WJ, Pelletier J, Collins MT. Associations between subclinical paratuberculosis and milk production, milk components, and somatic cell counts in dairy herds. J Am Vet Med Assoc 1996;208:1872–1876.
9. Vanleeuwen JA, Keefe GP, Tiwari A. Seroprevalence and productivity effects of infection with bovine leukemia virus, *Mycobacterium avium subspecies paratuberculosis,* and *Neospora caninum* in maritime Canadian dairy cattle. Bov Pract 2002:86–91.
10. Goodle GM, Hirst H, Garry F, Dinsmore P. Comparison of cull rates and milk production of clinically normal dairy cows grouped by ELISA *Mycobacterium avium paratuberculosis* serum antibody results. Proc. 9th Int Symp Vet Epidemiol Econ, Breckenridge, Colorado, USA 2000: 897–899.

11. McNab WB, Meek AH, Martin SW, Duncan JR. Associations between dairy production indices and lipoarabinomannan enzyme-immunoassay results for paratuberculosis. Can J Vet Res 1991;55:356–361.
12. Sockett DC, Conrad TA, Thomas CB, Collins MT. Evaluation of four serological tests for bovine paratuberculosis. J Clin Microbiol 1992;30:1134–1139.
13. Dargatz DA, Byrum BA, Barber LK, et al. Evaluation of a commercial ELISA for diagnosis of paratuberculosis in cattle. J Am Vet Med Assoc 2001;218:1163–1166.
14. Hutchinson LJ. Economic impact of paratuberculosis. Vet Clin North Am Food Anim Pract 1996;12:373–381.
15. Tiwari A, Vanleeuwen JA, Dohoo IR, Keefe GP. Effects of seropositivity for *Mycobacterium avium* subspecies *paratuberculosis* on risk of culling in Maritime Canadian dairy cattle. Proc 54th Annu Conv Can Vet Med Assoc, Halifax, Nova Scotia 2002:264.
16. Wilson DJ, Rossiter C, Han HR, Sears PM. Financial effects of *Mycobacterium paratuberculosis* on mastitis, milk production, and cull rate in clinically normal cows. Agri Pract 1995;16:12–18.
17. Buergelt CD, Duncan JR. Age and milk production data of cattle culled from a dairy herd with paratuberculosis. J Am Vet Med Assoc 1978;173:478–480.
18. Chi J, VanLeeuwen JA, Weersink A, Keefe GP. Direct production losses and treatment costs from bovine viral diarrhoea virus, bovine leukosis virus, *Mycobacterium avium subspecies paratuberculosis,* and *Neospora caninum.* Prev Vet Med 2002;55:137–153.
19. Johnson-Ifearulundu YJ, Kaneene JB, Sprecher DJ, Gardiner JC, Lloyd JW. The effect of subclinical *Mycobacterium paratuberculosis* infection on days open in Michigan, USA, dairy cows. Prev Vet Med 2000;46:171–181.
20. Kelton D, Lissemore K. Reasons that dairy cows leave home — Valid or not? Proc 30th Annu Conv Am Assoc Bov Practit. Montreal, Quebec 1997:177.
21. Tiwari A, Vanleeuwen JA, Dohoo IR, Stryhn H, Keefe GP. Effects of seropositivity for bovine Leukemia virus, *Mycobacterium avium* subspecies *paratuberculosis,* and *Neospora caninum* on calving to conception interval in maritime Canadian dairy cattle. Proc Soc Vet Epidemiol Prev Vet Med, Warwick, UK 2003:243–252.
22. DeLisle GW, Milestone BA. The economic impact of Johne's disease in New Zealand. In: Milner A, Wood P, eds. Johne's disease. East Melbourne: CSIRO, 1989:41–45.
23. Stabel JR, Goff JP, Kimura K. Effects of supplemental energy on metabolic and immune measurements in periparturient dairy cows with Johne's disease. J Dairy Sci 2003;86:3527–3535.
24. Ott SL, Wells SJ, Wagner BA. Herd-level economic losses associated with Johne's disease on US dairy operations. Prev Vet Med 1999;40: 179–192.
25. Chiodini RJ. Immunology: Resistance to paratuberculosis. Vet Clin North Am Food Anim Pract 1996;12:313–343.
26. Chiodini RJ, Van Kruiningen HJ, Merkal RS. Ruminant paratuberculosis (Johne's disease): The current status and future prospects. Cornell Vet 1984;74:218–262.
27. Hagan WA. Age as a factor in susceptibility to Johne's disease. Cornell Vet 1938;28:34.
28. Rankin JD. The experimental infection of cattle with *Mycobacterium johnei.* IV: Adult cattle maintained in an infectious environment. J Comp Pathol 1962;72:133–117.
29. Kennedy DJ, Benedictus G. Control of *Mycobacterium avium* subsp. *paratuberculosis* infection in agricultural species. Rev Sci Tech 2001;20:151–179.
30. Streeter RN, Hoffsis GF, Bech-Nielsen S, Shulaw WP, Rings DM. Isolation of *Mycobacterium paratuberculosis* from colostrum and milk of subclinically infected cows. Am J Vet Res 1995;56:1322–1324.
31. Sweeney RW. Transmission of paratuberculosis. Vet Clin North Am Food Anim Pract 1996;12:305–312.
32. Seitz SE, Heider LE, Heuston WD, Bech-Nielsen S, Rings DM, Spangler L. Bovine fetal infection with *Mycobacterium paratuberculosis.* J Am Vet Med Assoc 1989;194:1423–1426.
33. Sweeney RW, Whitlock RH, Rosenberger AE. *Mycobacterium paratuberculosis* isolated from fetuses of infected cows not manifesting signs of the disease. Am J Vet Res 1992;53:477–480.
34. Cetinkaya B, Erdogan HM, Morgan KL. Relationships between the presence of Johne's disease and farm and management factors in dairy cattle in England. Prev Vet Med 1997;32:253–266.
35. Jakobsen MB, Alban L, Nielsen SS. A cross-sectional study of paratuberculosis in 1155 Danish dairy cows. Prev Vet Med 2000;46:15–27.
36. Waters WR, Miller JM, Palmer MV, et al. Early induction of humoral and cellular immune responses during experimental *Mycobacterium avium* subsp. *paratuberculosis* infection of calves. Infect Immun 2003;71:5130–5138.
37. Hirst HL, Garry FB, Morley PS, et al. Seroprevalence of *Mycobacterium avium* subsp *paratuberculosis* infection among dairy cows in Colorado and herd-level risk factors for seropositivity. J Am Vet Med Assoc 2004; 225:97–101.
38. Muskens J, Bakker D, de Boer J, van Keulen L. Paratuberculosis in sheep: Its possible role in the epidemiology of paratuberculosis in cattle. Vet Microbiol 2001;78:101–109.
39. Daniels MJ, Henderson D, Greig A, Stevenson K, Sharp JM, Hutchings MR. The potential role of wild rabbits *Oryctolagus cuniculus* in the epidemiology of paratuberculosis in domestic ruminants. Epidemiol Infect 2003;130:553–559.
40. Daniels MJ, Hutchings MR, Greig A. The risk of disease transmission to livestock posed by contamination of farm stored feed by wildlife excreta. Epidemiol Infect 2003;130:561–568.
41. Jorgensen JB. Survival of *Mycobacterium paratuberculosis* in slurry. Nord Vet Med 1977;29:267–270.
42. Lovell R, Levi M, Francis J. Studies on the survival of Johne's bacilli. J Comp Pathol 1944;54:120–129.
43. Lund BM, Donnelly CW, Rampling A. Heat resistance of *Mycobacterium paratuberculosis.* Lett Appl Microbiol 2000;31:184–185.
44. Grant IR, Ball HJ, Rowe MT. Incidence of *Mycobacterium paratuberculosis* in bulk raw and commercially pasteurized cows' milk from approved dairy processing establishments in the United Kingdom. Appl Environ Microbiol 2002;68:2428–2435.
45. Gao A, Mutharia L, Chen S, Rahn K, Odumeru J. Effect of pasteurization on survival of *Mycobacterium paratuberculosis* in milk. J Dairy Sci 2002;85:3198–3205.
46. Stabel JR. Johne's disease and milk: Do consumers need to worry? J Dairy Sci 2000;83:1659–1663.
47. Ellingson JL, Anderson JL, Kozickowski JJ, et al. Detection of viable *Mycobacterium avium* subsp. *paratuberculosis* in retail pasteruized whole milk by two culture methods and PCR. J Food Prot 2005;68: 966–972.
48. Whitlock RH. Preclinical and clinical manifestations of paratuberculosis (including pathology). Vet Clin North Am Food Anim Pract 1996;12:345–356.
49. Animal and Plant Health Inspection Services [page on the Internet]. Veterinary Services: Johne's Disease Fact Sheet. Available at: http://www.aphis.usda.gov/vs/nahps/johnes/ Last accessed on September 19, 2005.
50. Kalis CH, Hesselink JW, Barkema HW, Collins MT. Use of long-term vaccination with a killed vaccine to prevent fecal shedding of *Mycobacterium avium* subsp. *paratuberculosis* in dairy herds. Am J Vet Res 2001;62:270–274.
51. Wells SJ, Wagner BA. Herd-level risk factors for infection with *Mycobacterium paratuberculosis* in US dairies and association between familiarity of the herd manager with the disease or prior diagnosis of the disease in that herd and use of preventive measures. J Am Vet Med Assoc 2000;216:1450–1457.
52. Rossiter CA, Burhans WS. Farm-specific approach to paratuberculosis (Johne's disease) control. Vet Clin North Am Food Anim Pract 1996;12:383–415.
53. Johnson YJ, Kaneene JB. Management-related risk factors for *M. paratuberculosis* infection in Michigan, USA, dairy herds. Prev Vet Med 1998;37:41–54.
54. Goodger WJ, Collins MT, Nordlund KV, et al. Epidemiologic study of on-farm management practices associated with prevalence of *Mycobacterium paratuberculosis* infections in dairy cattle. J Am Vet Med Assoc 1996;208:1877–1881.
55. Collins MT. Interpretation of a commercial bovine paratuberculosis enzyme-linked immunosorbent assay by using likelihood ratios. Clin Diagn Lab Immunol 2002;9:1367–1371.
56. Kalis CH, Hesselink JW, Barkema HW, Collins MT. Culture of strategically pooled bovine fecal samples as a method to screen herds for paratuberculosis. J Vet Diag Invest 2000;12:547–551.
57. Van Schaik G, Rossiter CR, Stehman SM, Shin SJ, Schukken YH. Longitudinal study to investigate variation in results of repeated ELISA and culture of fecal samples for *Mycobacterium avium* subsp. *paratuberculosis* in commercial dairy herds. Am J Vet Res 2003;64:479–484.
58. Benedictus G, Kalis CJ. Paratuberculosis: Eradication, control and diagnostic methods. Acta Vet Scand 2003;44:231–241.

59. Sechi LA, Mura M, Tanda E, Lissia A, Fadda G, Zanetti S. *Mycobacterium avium* sub. *paratuberculosis* in tissue samples of Crohn's disease patients. New Microbiol 2004;27:75–77.
60. Paratuberculosis Awareness and Research Association [page on the Internet]. The Cause for a Cure for Crohn's Disease. Available at: http://www.crohns.org/aboutpara.htm Last accessed on July 25, 2006.
61. Animal Health Australia [page on the Internet]; National Johne's Disease Program: Standard Definitions and Rules for Cattle. c2003. Available from: http://www.animalhealthaustralia.com.au/programs/jd/njdcp.cfm Last accessed July 25, 2006.
62. Animal Health Australia [page on the Internet]; The New Market Assurance Programs for Johne's Disease. c2003. Available from: http://www.animalhealthaustralia.com.au/programs/jd/maps.cfm Last accessed July 25, 2006.
63. Animal Health Australia [page on the Internet]; National Johne's disease control program, National coordinators quarterly report. cOct–Dec 2003. Available from http://www.animalhealthaustralia.com.au/shadomx/apps/fms/fmsdownload.cfm?file_uuid=4EC0DEBC-EBE5-A0E2-48E1-7B736A870BA9&siteName=aahc Last accessed July 25, 2006.
64. Kalis CH, Hesselink JW, Russchen EW, Barkema HW, Collins MT, Visser IJ. Factors influencing the isolation of *Mycobacterium avium* subsp. *paratuberculosis* from bovine fecal samples. J Vet Diag Invest 1999;11:345–351.
65. United States Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services [page on Internet]; Disease Eradication, Johne's Disease, Uniform Standards for the Voluntary U.S. Johne's Control Program. c2002. Available from: http://www.aphis.usda.gov/vs/nahps/johnes/johnes-umr.pdf Last accessed July 25, 2006.
66. United States Department of Agriculture, Animal and Plant Health Inspection Service. Veterinary Services Annual Report [page on the Internet]; Johne's Program. Available from: http://www.aphis.usda.gov/vs/highlights/section3/section3-20.html Last accessed July 25, 2006.
67. United States Animal Health Association [page on the Internet]; New National Johne's Disease Herd Prevalence Study. c2004. Available from http://www.usaha.org/committees/resolutions/resolution01-2004.pdf Last accessed September 19, 2005.
68. Raizman EA, Wells SJ, Godden SM, et al. The distribution of *Mycobacterium avium* ssp. *paratuberculosis* in the environment surrounding Minnesota dairy farms. J Dairy Sci. 2004;87:2959–2966.
69. VanLeeuwen JA, Keefe GP, Tremblay R, Power C, Wichtel JJ. Seroprevalence of infection with *Mycobacterium avium* subspecies *paratuberculosis,* bovine leukemia virus, and bovine viral diarrhea virus in maritime Canada dairy cattle. Can Vet J 2001;42:193–198.
70. Alberta Agriculture, Food and Rural Development [page on the Internet]; Alberta's Johne's Disease Control Program. Available from http://www.wcds.afns.ualberta.ca/Proceedings/2002/Chapter%2006%20Mainali.htm Last accessed July 25, 2006.
71. McKenna SL, Vanleeuwen JA, Barkema HW, et al. Proposed Canadian Voluntary National Johne's Disease Prevention and Control Program. Can Vet J 2006;47:539–541.

Book Reviews
Comptes rendus de livres

Color Atlas of Canine and Feline Ophthalmology

Dziezyc J, Millichamp NJ. Elsevier Saunders, St. Louis, Missouri, USA, 2004, 256 pp. ISBN 0-7216-8239-1. $99.00.

This atlas contains over 800 color illustrations of both normal ocular structures and commonly encountered ocular lesions in dogs and cats. There are also illustrations to depict unique breed-related ocular conditions such as Collie eye anomaly, retinal dysplasia, and cataracts. Illustrations of less commonly observed ocular lesions, including optic nerve hypoplasia and staphylomas, are also provided. The illustrations are of excellent quality with vivid color to further highlight the key ocular findings. Typically, at least 2 images per normal ocular structure or ocular abnormality are provided to facilitate visual recognition of variations of normal and ocular problems, respectively.

The atlas is organized in a systematic manner from anterior to posterior segments of the eye. There are a total of 13 chapters commencing with Chapter 1 "Eyelid" and progressing to Chapter 13 "Orbit". Each chapter commences with a 1 introductory paragraph, which provides information regarding key anatomy and the most significant lesions affecting that portion of the ocular adnexa, globe, or orbit. There is a concise, yet informative, descriptive legend below each illustration. In certain cases, however, the key lesion may not be the sole ocular abnormality visible within the illustration, yet there is no reference made to the other apparent ocular lesion(s). As well, for further clarification, some of the illustrations would have benefited from an arrow or asterisk to highlight the main lesion. However, despite these minor flaws, this atlas illustrates clinically normal and diseased canine and feline eyes very well. There are also schematic illustrations throughout Chapter 11 "Retina, Choroid, Sclera" to enhance understanding of both the normal anatomy and ocular lesions affecting these ocular regions. The systematic organization of the atlas and its index, which lists ocular structures and lesions according to species, ocular diagnosis, ocular region, and breed, allow the reader to readily find illustrations accordingly.

Ophthalmology is heavily dependent upon the examiner's ability to visually recognize normal ocular features and ocular abnormalities. As such, this color atlas is helpful in aiding the clinician to identify and diagnose conditions encountered during an ophthalmic examination. Following accurate identification of the ocular abnormality, a more detailed veterinary ophthalmology textbook would need to be consulted for comprehensive information regarding etiology, pathophysiology, and treatment. The illustrations in this atlas would be particularly useful for small animal practitioners, veterinary undergraduate students, and veterinary ophthalmology residents.

Reviewed by ***Cheryl L. Cullen, DVM, MVetSc, DACVO,*** *Faculty of Veterinary Medicine, Health Sciences Centre, University of Calgary, 3330 Hospital Drive NW, Calgary, Alberta T2N 4N1, and Western Veterinary Specialist Centre, 1635-17th Avenue SW, Calgary, Alberta T2T 0E5.*