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Emerging threats for public health associated with dairy cattle

Robert Tremblay, D.V.M., D.V.Sc., Dipl A.C.V.I.M.
Boehringer Ingelheim (Canada) Ltd, 5180 South Service Road, Burlington, ON, L7L 5H4
rtremblay@bur.boehringer–ingelheim.com

Introduction

Cattle have been domesticated for centuries and hence have had long history of close association with humans. Cattle harbor several microbes that have the potential to cause disease in humans. These zoonotic diseases consist of 2 groups, those transmitted primarily by direct contact with cattle and those spread indirectly. As the population in western society increasingly shifts from rural to urban, there is a reduced opportunity for transmission by direct contact but a relative increase in the transmission of zoonotic diseases that are spread by indirect contact, particularly diseases spread through food and water. This review will present information on three pathogens of dairy cattle that are increasingly considered as emerging zoonotic diseases.

Mycobacterium avium subsp paratuberculosis and Crohn's disease:

Probably the most controversial potential zoonotic pathogen of bovine origin is *Mycobactrium avium subsp* paratuberculosis (MAP). MAP bacteria are associated with Johne's disease in cattle and other ruminants. It has been proposed as a potential etiological agent in Crohn's disease in humans [2,9].

Crohn's disease is a disease complex that shares similar pathological features with Johne's disease. As a result, mycobacteria, particularly MAP have been suspected of being etiologic agents in Crohn's disease. Numerous studies have investigated this potential link. Recent reviews of the scientific literature have concluded that there is not enough evidence to clearly establish a causal relationship between MAP and Crohn's disease [6,17,18]. The authors in other reviews concluded that infection with MAP likely plays a causal role in a portion of Crohn's patients but that infection does not account for all cases and does not completely explain the pathogenesis of the condition [2,6,9].

Several lines of evidence have implicated MAP in Crohn's disease [2,17,18]. These include bacterial culture of tissues from patients with Crohn's disease, MAP-specific polymerase chain reaction and DNA hybridization to demonstrate MAP in tissues and bacterial isolates from Crohn's patients and in situ hybridization to demonstrate MAP in tissues of Crohn's patients. Studies have shown that MAP is more frequently detected in tissues of patients with Crohn's disease than in patients with other types of bowel disease. Additional evidence implicating MAP is the more frequent detection of a MAP-specific immune response in some Crohn's

patients than in patients with other bowel diseases. An infectious cause for Crohn's is further supported by reports of clinical improvement in a portion of Crohn's patients following anti-mycobacterial therapy. In addition, isolates of MAP have also been demonstrated in the breast milk of Crohn's patients [15]

Even if MAP is determined to play a causal role in Crohn's disease, the origin and reservoirs of the bacteria for human exposure will need to be determined. There are several potential sources of MAP and, accordingly, several potential mechanisms for human exposure. MAP is excreted in the milk of infected cows and infection is widespread in the cattle population [5,19]. There is then potential for human exposure through consumption of milk and other dairy products. MAP bacteria are also shed in the feces of infected animals, including cattle, leading for the potential for human exposure through direct contact with an infected animal, contact with MAP shed into the environment and consumption of water contaminated by run off from fields.

It may also transpire that humans are a source of MAP bacteria. As noted above, MAP can be cultured from the breast milk of patients with Crohn's disease [15]. Other research has detected MAP in the stool of Crohn's patients [3].

Coxiella burnetii and Q fever

Coxiella burnetii has several characteristics that make it a potential risk to human health [14]. It is highly infectious to susceptible people. It can persist because it survives well in the environment and it is highly resistant to heat and desiccation. Exposure of large numbers of people can easily occur because the organism is airborne leading to infection by inhalation of infectious aerosols. These attributes also give *Coxiella* the potential to be an agent of bioterrorism.

Coxiella burnetii causes Q fever in humans [12-14]. It is associated with a variety of clinical syndromes. In the majority of cases, infection is subclinical or associated with non-specific flu-like signs of fever, headache, muscle pain and cough. Other clinical manifestations include signs of pneumonia, hepatitis, meningoencephalitis and myocarditis. A small percentage of acute cases will develop chronic disease. The most frequent expression of chronic disease is endocarditis, although granulomatous hepatitis, pericarditis and osteoarticular infections may occur.

Coxiella burnetii is a pleomorphic obligate intracellular rickettsia organism that replicaties in monocytes and macrophages of the host. *Coxiella* has two life cycle stages, a large cell variant and a small cell variant. The small cell variant is the extracellular, infectious form that is long-lived once shed into the environment.

Outbreaks of Q fever are frequently associated with exposure to periparturient livestock [8,12,13]. *Coxiella burnetii* occurs in high concentrations in the placental tissue and birth fluids of several species including sheep, goats and cattle. It is also shed in milk, urine and feces of infected animals. Although human infection likely occurs primarily through inhalation of the organism in aerosols, infection is also believed to occur following the ingestion of unpasteurized dairy products.

Sheep and goats are considered to be the major source of human exposure to *Coxiella* but cattle may be of greater significance as a reservoir for the agent [9,14]. A limited number of surveys have shown the exposure is widespread in the cattle population [1,4,10,11]. In addition, cattle may represent a special risk group because they tend to shed *C. burnetii* continuously in milk compared to the intermittent shedding by sheep and goats [1]. Epidemiological studies of Q fever in England suggest that exposure among farm workers is more related to contact with cattle but not to other sources of *Coxiella* [22].

Cryptosporidium parvum

Cryptosporidium parvum is a protozoal parasite that causes gastrointestinal disease in several domesticated and wild animals and in humans. It is considered to be an emerging public health concern because it is associated with outbreaks of diarrhea affecting large numbers of people [16]. Its most severe manifestation in humans is in immunocompromised individuals where C. parvum can cause chronic disease that can be life threatening.

Cryptosporidium parvum is transmitted by ingestion of oocysts excreted in feces of infected humans and animals. Oocysts are long-lived in the environment. Human exposure occurs following ingestion of contaminated food or water, contact with an infectious animal or person or through contact with fomites contaminated with feces. Large outbreaks in humans are often associated with contaminated water or, less commonly, contaminated food.

C. parvum occurs in at least two genotypes [16,21,22]. Establishing genotypes is useful in determining the origin of particular isolates of *C. parvum*. Genotype 1 isolates occur only among humans. Genotype 2 isolates are recovered from cattle and from humans. Genotype 2 isolates have also been identified in sheep, goats and other mammals. The determination of genotype in clinical cases is a valuable tool in determining the likely origin of Cryptosporidia in human disease outbreaks. Outbreaks involving genotype 1 are likely human in origin; outbreaks of genotype 2 may originate from several species, including cattle.

Cattle and cattle manure have been frequently implicated as the likely source of cryptosporidiosis in humans. Analysis of genotype has determined that many of the high profile outbreaks of human cryptosporidiosis, such as the outbreak in Millwaukee in 1993, were due to C parvum genotype 1 and were, therefore, of human origin [16]. Outbreaks have also been associated with genotype 2 isolates. These outbreaks could be due to C parvum from cattle although they may also have originated from other animals or humans.

Cattle, and other livestock, are likely sources of C parvum for many of sporadic cases of cryptosporidiosis in people [19]. During the Foot and Mouth Disease (FMD) outbreak in the UK in 2001, control measures were implemented to limit animal movement and to limit human travel in rural areas. Coincidental with the outbreak, health officials observed a 35% decrease in cases of cryptosporidiosis among people. Cases were reduced by 63% in areas most affected by the FMD outbreak. Analysis of public health data concluded that the reduction in human cases could not be explained by variations in seasonal or yearly disease patterns or by changes in reporting protocols. Case counts returned to expected levels in the weeks following the

FMD outbreak. It was concluded that livestock were the likely source of many of the sporadic human cases of crytosporidiosis due to C parvum genotype 2.

Conclusions

Food borne and other zoonotic diseases will increasingly become issues for public health authorities. Effective prevention of zoonotic diseases will require the cooperative efforts of those working in public health and those working in agriculture. It is essential that actions taken to protect human health are based on appropriate scientific knowledge. An example of a situation where attacking animal agriculture is unlikely to have positive results is water-borne cryptosporidiosis. Because many water-borne outbreaks do not originate from cattle, preventive measures that solely target cattle are unlikely to be effective. Suitable prevention and control methods should consider all major sources of zoonotic pathogens.

Résumé français :

Les bovins ont été domestiqués depuis des siècles et en conséquence ont une longue histoire d'association étroite avec les humains. Les bovins hébergent plusieurs microbes qui ont le potentiel de causer des maladies chez les humains. Ces zoonoses se composent de 2 groupes, celles transmises principalement par contact direct avec les bovins et celles transmises indirectement. Comme la population dans notre société occidentale se déplace de plus en plus du milieu rural vers le milieu urbain, l'opportunité de transmission par contact direct est réduite mais il y a une augmentation relative dans la transmission des zoonoses qui sont transmises par contact indirect, particulièrement les maladies transmises par la nourriture et l'eau. Cette revue présentera des informations sur trois pathogènes des bovins laitiers qui sont de plus en plus considérés comme des zoonoses émergeantes.

References:

1 Biberstein EL, Behymer DE, Bushnell R, Crenshaw G, Reimann HP, Franti CE. A survey of Q fever (Coxiella burnetii) in California dairy cows. Am J Vet Res 1974;35:1577-1582

2 Chamberlin W, Graham DY, Hulten K, El-Zimaity HMT, Schwartz MR, Naser S, Shafran I, El-Zaatari FAK. Mycobacterium avium subsp paratuberculosis as one cause of Crohn's disease. Aliment Phermacol Ther 2001;15:337-346

3 Del Prete R, Quaranta M, Lippolis A, Giannuzzi V, Mosca A, Jirillo E, Miragliotta G. Detection of Mycobacterium paratuberculosis in stool samples of patients with inflammatory bowel disease by IS900-based PCR and colorimetric detection of amplified DNA. J Microbiol Methods 1998;33:105-114.

4 Dubovi EJ. New York State Veterinary Diagnostic Laboratory. Pers comm

5 Giese SB, Ahrens P. Detection of Mycobacterium avium subsp paratubeculosis in milk from clinically affected cows by PCR and culture. Vet Microbiol. 2000;20:291-297.

6 Greenstein RJ. Is Crohn's disease caused by a mycobacterium? Comparisons with leprosy, tuberculosis, and Johne's disease. Lancet Infect Dis 2003;3:507-514.

7 Harris JE, Lammerding AM. Crohn's disease and Mycobacterium avium subsp. paratuberculosis: current issues. J Food Prot. 2001;64:2103-2110.

8. Hellenbrand W, Breuer T, Petersen L. Changing epidemiology of Q fever in Germany, 1947-1999. Emerg Infect Dis 2001;7:789-796.

9 Hermon-Taylor J, Bull TJ, Sheridan JM, Cheng J, Stellakis ML, Sumar N. Causation of Crohn's disease by Mycobacterium avium subspecies paratuberculosis. Can J Gastroenterol 2000;14:521-539.
10 Hirai K, To H. Advances in the understanding of Coxiella burnetii infection in Japan. J Vet Med Sci 1998;60:781-790.
11 Lang GH. Serosurvey on the occurrence of Coxiella burnetii in Ontario cattle. Can J Public Health 1988;79:56-59.
12 Marrie TJ. Coxiella burnetii pneumonia. Eur Respir J 2003;21:713-719.
13 McQuiston JH, Childs JE. Q fever in humans and animals in the United States. Vector Borne Zoontic Dis 2002;2:179-191.
14 McQuiston JH, Childs JE, Thompson HA. Q fever. JAVMA 2002;221:796-799.
15 Naser SA, Schwartz D, Shafran I. Isolation of Mycobacterium avium subsp paratuberculosis from breast milk of Crohn's disease patients. Am J Gastroenterol 2000; 95:1094-1095.
16 Peng MM, Xiao L, Freeman AR, Arrowood MJ, Escalante AA, Weltman AC, Ong CSL, MacKenzie WR, Lai AA, Beard CB. Genetic polymorphism among Cryptosporidium parvum isolates: evidence of two distinct human transmission cycles. Emerg Infect Dis 1997;3:567-573.
17 Possible links between Crohn's disease and parartuberculosis. Report of the Committee on Animal Health and Animal Welfare, Directorate-General, Health & Consumer Protection, European Commission. 2000.
18 Rubery E. A review of the evidence for a link between exposure to Mycobacterium paratuberculosis (MAP) and Crohn's disease (CD) in humans. Food Standards Agency, London. 2001.
19 Smerdon WJ, Nichols T, Chalmers RM, Heine H, Reacher M. Foot and mouth disease in livestock and reduced cryptosporidiosis in humans, England and Wales. Emerg Infect Dis 2003:9:22-28
20 Sweeny RW, Whitlock RH, Rosenberger AE. Mycobacterium paratuberculosis cultured from supramammary lymph nodes of infected asymptomatic cow. J Clin Microbiol 1992;30:166-171.
21 Sulaiman IM, Xiao L, Yang C, Escalante L, Moore A, Beard CB, Arrowood MJ, Lai AA. Differentiating human from animal isolates of Cryptosporidium parvum. Emerg Infect Dis 1998;4:681-685.
22 Thomas DR, Treweek L, Salmon RL, Kench SM, Coleman TJ, Meadows D, Morgan-Capner P, Caul EO. The risk of acquiring Q fever on farms: a seroepidemiological study. Occup Environ Med 1995;52:644-647.