Food Safety Concerns Regarding Paratuberculosis

Michael T. Collins, DVM, PhD

Concern about the possibility that *Mycobacterium avium* subsp. *paratuberculosis* (MAP) is a food-borne zoonotic pathogen has been the unspoken driving force behind establishment of national paratuberculosis control and herd certification programs in multiple countries including Australia, the Netherlands, Denmark, and the United States. It has also been a prime factor motivating large-scale funding of research programs like the Johne's Disease Integrated Program (JDIP) in the United States (more than US$8 million) and ParaTB Tools in the European Union (more than US$5 million). Some experts may disagree, but the true cost of paratuberculosis as a strictly animal health problem, in comparison with other infectious diseases and challenges in animal agriculture, cannot justify this magnitude of public expenditures for Johne's disease (JD) control and research unless one factors in the potential cost of paratuberculosis as a food-borne zoonotic pathogen.

IS MAP ZOONOTIC?

A wide array of animal species, including nonhuman primates, can be infected by MAP, making it quite plausible that it can also infect humans. MAP is consistently detected by PCR in humans with a disease epidemiologically and pathologically similar to JD, namely Crohn's disease (CD).[1,2] Multiple studies also detect antibody to MAP in humans with CD more often than controls. CD has been effectively treated, possibly even cured, by prolonged use of an appropriate combination of antimicrobial drugs.[3] The only significant piece of missing evidence preventing wider-spread recognition of MAP as one of the causes of CD is the inability of laboratories skilled in MAP culture to regularly grow MAP from CD patient samples.[4] That said, some laboratories have reported MAP recovery from 40 to 100% of CD patients.[5–7] MAP has also tentatively been linked with other human diseases such as type 1 diabetes mellitus.[8,9] While medical science may take more time to decide on the human health

consequences of MAP exposure, it is prudent for veterinary medicine to consider what can be done to mitigate the risk of human exposure to this potentially zoonotic ruminant pathogen.

RAW FOOD CONTAMINATION BY MAP

The majority of MAP infections occur in food-producing ruminants (ie, cattle, goats, and sheep) (see article by Lombard in this issue). Meat and milk derived from MAP-infected animals is commonly contaminated before harvesting (ie, ante mortem) during the disseminated stage of MAP infections when the organism is found in muscle meat, internal organs, colostrum and milk, and the unborn fetus of pregnant animals[10–12] (see the article by Sweeney in this issue). During harvesting of both milk and meat, there is a second opportunity for MAP contamination of food products in conjunction with fecal contamination.[13] Thus, raw products originating from herds or flocks of MAP-infected animals are likely to be contaminated with MAP.[14] Counts up to 560 MAP/mL of raw milk from individual cows have been reported.[13] The question then becomes whether manufacturing processes or cooking by the consumer will reliably kill MAP.

PASTEURIZED FOOD PRODUCTS

The preponderance of work on the ability of food manufacturing processes to kill MAP has focused on pasteurization, specifically high-temperature short-time (HTST) pasteurization.[15] Laboratory studies attempting to measure standard thermal tolerance parameters for MAP indicate that it is more heat-resistant than *Mycobacterium bovis* and *Coxiella burnetti*, the 2 milk-borne zoonotic pathogens designed to be killed by pasteurization.[16,17] Corroborating this are 3 independent retail milk surveys reporting recovery of viable MAP by culture from retail HTST pasteurized milk.[18–20] Clearly, HTST pasteurization kills large numbers of MAP in milk. However, evidence suggests that it does not kill 100% of MAP cells 100% of the time or that postpasteurization MAP contamination is frequently occurring.

Cheese

High-moisture, high-pH, "fresh" (short time from production to consumption) cheeses made from raw milk have the greatest likelihood of containing MAP as well as other milk-borne bacterial pathogens like *Listeria*.[21] However, MAP has been shown to persist even the processes involved in making low-moisture, low pH, aged cheese such as Swiss cheese, regardless of whether milk was first pasteurized.[22,23]

Yoghurt and Other Dairy Products

MAP numbers in spiked yoghurt were shown to persist during storage but decline somewhat in the presence of certain probiotic bacteria found in fermented milk products.[24] Other dairy products such as ice cream or powdered milk preparations have not been studied.

Meat

The effect of cooking on MAP viability in meat has been studied far less than pasteurization. Empirically, if meat is cooked to a condition known as "well-done" (defined as when the meat juices run clear), then the center of the product has attained a core temperature equivalent to that of HTST pasteurization. Hence, one could predict low or no MAP recovery from well-done meat. This prediction is supported by 2 studies attempting recovery of MAP from naturally and

intentionally contaminated meat.[25,26] Meat that is not well-done could harbor viable MAP.

Ground beef represents the greatest potential risk for harboring MAP in that (1) a significant proportion originates from culled dairy cattle, which have the highest animal-level prevalence of MAP infections; (2) dairy cattle are culled when they are no longer productive and late-stage MAP infections are a cause of low productivity; (3) fecal contamination of carcasses in the abattoir occurs despite efforts to minimize it; (4) ground beef includes lymph nodes where MAP are concentrated; and (5) the process of mixing and grinding beef to produce hamburger blends any MAP into the final product, away from the surface, which is exposed to the highest level of heat during cooking. However, the frequency of finding viable MAP in retail meat has not been assessed. Arguably, *Escherichia coli* O157 may serve as an indicator organism to gauge the frequency with which a zoonotic bacterial pathogen found in cattle feces contaminates ground beef. If one accepts this premise, then the frequent ground beef recalls due to *E. coli* O157 detection in the United States suggests that MAP contamination of ground beef may be common (Available at: http://www.fsis.usda.gov/Fsis_recalls/Open_Federal_Cases/index.asp; Accessed March 24, 2011).

Water

Although not traditionally considered "food," domestic water supplies must be considered in the context of food safety to ensure a balanced perspective on potential modes of human exposure to MAP. Domestic water sources vary among and within communities. Tap water may originate from surface water (ie, lakes and rivers) or underground (ie, wells). Surface waters are generally a mix of rainwater runoff and artesian spring water. Rainwater falling on land occupied by MAP-infected cattle has the potential to harbor MAP and the organism will persist in rainwater runoff for a prolonged time (eg, >1 year).[27] *Mycobacteria,* including MAP, are resistant to killing by the levels of chlorine commonly used to decontaminate domestic water.[28,29] Hence, water may exposure humans to MAP via either drinking or aerosolization and inhalation.[30–32]

SUMMARY

Two recent risk assessments concur in the conclusion that MAP contaminates raw products derived from MAP-infected animals and water runoff from MAP-infected farms and that MAP may survive food manufacturing processes or cooking.[33,34] The provocative discovery that MAP can produce spores explains its persistence in the environment and its tenacity in the face of industrial processes designed to control food-borne bacterial pathogens.[35] It remains to be proved what the real health consequences of MAP exposure or infection are for humans, and it will take considerable time and effort for medical science to resolve this question due, in part, to the chronic insidious nature of the diseases potentially involved and the lack of well-standardized assays for MAP infection in humans. However, given the weight of evidence and the severity and magnitude of potential human health problems, the precautionary principle suggests that it is time to take actions to limit "as low as reasonably achievable" human exposure to MAP.[36] All evidence suggests that the farm is the critical control point. Paratuberculosis control on farms serves to improve animal health and welfare, improve farm profitability, and lower MAP numbers in raw food products, thereby lessening the likelihood and level of human exposure to MAP whether in dairy products, meat, or domestic water supplies. With the rapid globalization of food production and trade, the challenge of MAP

control for both animal health and consumer confidence in the safety of their food is international.

REFERENCES

1. Abubakar I, Myhill D, Aliyu SH, et al. Detection of *Mycobacterium avium* subspecies *paratuberculosis* from patients with Crohn's disease using nucleic acid-based techniques: a systematic review and meta-analysis. Inflamm Bowel Dis 2008; 14(3):401–10.
2. Feller M, Huwiler K, Stephan R, et al. *Mycobacterium avium* subspecies *paratuberculosis* and Crohn's disease: a systematic review and meta-analysis. Lancet Infect Dis 2007;7(9):607–13.
3. Chamberlin W, Ghobrial G, Chehtane M, et al. Successful treatment of a Crohn's disease patient infected with bacteremic *Mycobacterium paratuberculosis*. Am J Gastroenterol 2007;102(3):689–91.
4. Behr MA. Paratuberculosis and Crohn's disease. In: Behr MA, Collins DM, editors. Paratuberculosis: organism,disease, control. Oxfordshire, UK: CABI; 2010. p. 40–9.
5. Mendoza JL, San-Pedro A, Culebras E, et al. High prevalence of vaible *Mycobacterium avium* subspecies *paratuberculosis* in Crohn's disease. World J Gastroenterol 2010;16(36):4558–63.
6. Naser SA, Collins MT, Crawford JT, et al. Culture of *Mycobacterium avium* subspecies *paratuberculosis* (MAP) from the blood of patients with Crohn's disease: A follow-up blind multi-center investigation. Open Inflamm J 2009;222-3.
7. Naser SA, Ghobrial G, Romero C, et al. Culture of *Mycobacterium avium* subspecies *paratuberculosis* from the blood of patients with Crohn's disease. Lancet 2004;364:1039–44.
8. Dow CT. Paratuberculosis and Type I diabetes: is this the trigger? Med Hypoth 2006;67(4):782–5.
9. Sechi LA, Rosu V, Pacifico A, et al. Humoral immune responses of Type 1 Diabetes patients to *Mycobacterium avium* subsp. *paratuberculosis* lend support to the infectious trigger hypothesis. Clin Vaccine Immunol 2008;15(2):320–6.
10. Alonso-Hearn M, Molina E, Geijo M, et al. Isolation of *Mycobacterium avium* subsp. *paratuberculosis* from muscle tissue of naturally infected cattle. Foodborne Pathogens Dis 2009;6(4):513–8.
11. Antognoli MC, Garry FB, Hirst HL, et al. Characterization of *Mycobacterium avium* subspecies *paratuberculosis* dissemination in dairy cattle and its association with antemortem test results. Vet Microbiol 2008;127;300–8.
12. Brady C, O'Grady D, O'Meara F, et al. Relationships between clinical signs, pathological changes and tissue distribution of *Mycobacterium avium* subspecies *paratuberculosis* in 21 cows from herds affected by Johne's disease. Vet Rec 2008;162(5): 147–52.
13. Grant IR. *Mycobacterium avium* subsp. *paratuberculosis* in animal-derived foods and the environment. In: Behr MA, Collins DM, editors. Paratuberculosis: organism,disease, control. Oxfordshire, UK: CABI; 2010. p. 29–39.
14. Eltholth MM, Marsh VR, Van Winden S, et al. Contamination of food products with *Mycobacterium avium paratuberculosis*: a systematic review. J Appl Microbiol 2009; 107;1061–71.
15. Grant IR, Hitchings EI, McCartney A, et al. Effect of commercial-scale high-temperature, short-time pasteurization on the viability of *Mycobacterium paratuberculosis* in naturally infected cows' milk. Appl Env Microbiol 2002;68(2):602–7.

16. Stumbo CR. Organisms of greatest importance in food pasteurization. In: Thermo-bacteriology in food processing. 2nd edition. New York: Academic Press; 1973. p. 31–45.

17. Sung N, Collins MT. Thermal tolerance of *Mycobacterium paratuberculosis*. Appl Env Microbiol 1998;64;999–1005.

18. Ayele WY, Svastova P, Roubal P, et al. *Mycobacterium avium* subspecies *paratuberculosis* cultured from locally and commercially pasteurized cow's milk in the Czech Republic. Appl Env Microbiol 2005;71;1210–4.

19. Ellingson JLE, Anderson JL, Koziczkowski JJ, et al. Detection of viable *Mycobacterium avium* subsp. *paratuberculosis* in retail pasteurized whole milk by two culture methods and PCR. J Food Prot 2005;67;966–72.

20. 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 Env Microbiol 2002;682;428–35.

21. Sung N, Collins MT. Effect of three factors in cheese production (pH, salt, and heat) on *Mycobacterium avium* subsp *paratuberculosis* viability. Appl Env Microbiol 2000; 66(4):1334–9.

22. Spahr U, Schafroth K. Fate of *Mycobacterium avium* subsp *paratuberculosis* in Swiss hard and semihard cheese manufactured from raw milk. Appl Env Microbiol 2001; 67(9):4199–205.

23. Williams AG, Withers SE. Microbiological characterisation of artisanal farmhouse cheeses manufacturered in Scotland. Int J Dairy Technol 2010;63(3):356–69.

24. Van Brandt L, Coudijzer K, Herman L, et al. Survival of *Mycobacterium avium* ssp. *paratuberculosis* in yoghurt and in commercial fermented milk products containing probiotic cultures. J Appl Microbiol 2011;110(5):1252–61.

25. Mutharia LM, Klassen MD, Fairles J, et al. *Mycobacterium avium* subsp. *paratuberculosis* in muscle, lymphatic and organ tissues from cows with advanced Johne's disease. Int J Food Microbiol 2010;136(3):340–4.

26. Whittington RJ, Waldron A, Warne D. Thermal inactivation profiles of *Mycobacterium avium* subsp. *paratuberculosis* in lamb skeletal muscle homogenate fluid. Int J Food Microbiol 2009.

27. Whittington RJ, Marsh IB, Reddacliff LA. Survival of *Mycobacterium avium* subsp. *paratuberculosis* in dam water and sediment. Appl Env Microbiol 2005;71(9):5304–8.

28. Le Dantec C, Duguet JP, Montiel A, et al. Chlorine disinfection of atypical mycobacteria isolated from a water distribution system. Appl Env Microbiol 2002;68(3):1025–32.

29. Whan LB, Grant IR, Ball HJ, et al. Bactericidal effect of chlorine on *Mycobacterium paratuberculosis* in drinking water. Lett Appl Microbiol 2001;33(3):227–31.

30. Beumer A, King D, Donohue M, et al. Detection of *Mycobacterium avium* subsp. *paratuberculosis* in drinking water and biofilms by quantitative PCR. Appl Env Microbiol 2010;76(21):7367–70.

31. Falkingham JO III. Nontuberculous mycobacteria from household plumbing of patients with nontuberculous mycobacteria disease. Emerg Infect Dis 2011;17(3): 419-4.

32. Pickup RW, Rhodes G, Arnott S, et al. *Mycobacterium avium* subspecies *paratuberculosis* in the catchment and water of the river Taff in South Wales, UK and its potential relationship to clustering of Crohn's disease in the city of Cardiff. Appl Env Microbiol 2005;71(4):2130–9.

33. Gill CO, Saucier L, Meadus WJ. *Mycobacterium avium* subsp. *paratuberculosis* in dairy products, meat, and drinking water. J Food Prot 2011;74(3):480–99.

34. National Advisory Committee on Microbiological Criteria for Foods. Assessment of food as a source of exposure to *Mycobacterium avium* subspecies *paratuberculosis* (MAP). J Food Prot 2010;73(7):1357–97.
35. Lamont EA, Bannantine JP, Armien A, et al. *Mycobacterium avium* subspecies *paratuberculosis* produces spores. Presented at the 110th Annual General Meeting of American Society of Microbiology. San Diego, CA, 2010 [abstract: U2932].
36. Weir E, Schabas R, Wilson K, et al. A Canadian framework for applying the precautionary principle to public health issues. Can J Pub Health 2010;101(5):396–8.