International Efforts at Paratuberculosis Control

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KEYWORDS

- Paratuberculosis • Johne's • International • Control
- Assurance

Johne's disease is now playing on a truly global stage thanks to the trucks, ships, and aircraft that have moved animals around the world in the past century. In late 2010, only 26 countries were listed as reporting that the disease had never occurred in their country.[1] *Mycobacterium avium* subsp. *paratuberculosis* (MAP) slowly spread out from western Europe in live animal exports to colonies and other markets. This year is the centenary of the first confirmed case in Australia—an imported bull in a quarantine station.[2] As the livestock industries matured in countries in the Americas and Pacific, they in turn contributed to Johne's disease spreading to trading partners that had only more recently developed their domestic livestock production systems. The increased incidence of Johne's disease in eastern Europe was largely attributed to the development of the livestock trade from western Europe after the fall of the "Iron Curtain."[3] Recently, Johne's disease, caused by various subtypes of MAP, has been recognised as a developing problem in a diverse range of countries including Iran,[4] South Africa,[5] India,[6] and Korea.[7]

This progressive, inadvertent spread of MAP over long distances has been favored by 2 of its key characteristics: the largely subclinical nature of infection and the poor sensitivity of diagnostic tests. In the past 20 years, the international community has attempted to limit this spread and its impacts.

INTERNATIONAL COLLABORATION

International interest in Johne's disease increased toward the end of the twentieth century, following the publication of work by Chiodini and others associating MAP with Crohn's disease in people in the United States.[8] Multinational groups have addressed various aspects of understanding and managing paratuberculosis, much of it stimulated by ongoing debate about this hypothesis.

Founded in 1989, The International Association for Paratuberculosis is a "scientific organization devoted to the advancement of scientific progress on paratuberculosis

and related diseases." From a small organization of laboratory scientists, the association has grown to embrace members from over 30 countries and from diverse fields of interest, including livestock production, animal disease control, public health, and human gastroenterology (www.paratuberculosis.org). The association hosts and publishes the proceedings of its international colloquia every 2 to 3 years to update members and other interested people on developments in the knowledge, technology, and control of Johne's disease. Recent colloquia have been held in Spain, Denmark and Japan with the most recent in Minneapolis in 2009. The 11th colloquium will be held in Australia in 2012.

RESEARCH

The International Association for Paratuberculosis and its regular colloquia have stimulated collaborative discussion and research among members, many of whom have extended the knowledge on Johne's disease internationally through postgraduate study and sabbatical exchanges. Researchers in Asia, the Pacific, and the Americas are also participating in or benefiting from 2 large research programs recently initiated in the United States and in Europe.

The Johne's Disease Integrated Program (JDIP) has coordinated a large collaborative research and extension program since 2004 involving academic institutions across the United States (http://www.jdip.org). The 4 main collaborative research programs aim to:

1. Better understand Johne's disease epidemiology and the process of disease transmission.
2. Develop and implement new generations of diagnostic tests and methods for strain differentiation.
3. Improve understanding of the biology and pathogenesis of MAP.
4. Elucidate the immune response to MAP and evaluate and develop new generations of vaccines.

The European Union's Food Quality and Safety collaborative research program, ParaTB Tools, commenced in 2006 with 28 partner institutions from 16 countries and has projects covering 5 themes[9]:

1. Standardization, harmonization, and improvement of laboratory diagnosis of paratuberculosis in livestock
2. Interaction between host and pathogen in ruminants infected with MAP: development of improved diagnostic tests
3. Inactivation of MAP in milk and dairy products
4. Risk and control
5. Characterization of the interaction between humans with Crohn's disease (CD) and MAP to establish whether a causal relationship is present.

CONTROL

The desire to provide the dairy industry worldwide with up to date advice on Johne's disease and its control led the International Dairy Federation to sponsor a series of collaborative activities from 1999. The resulting proceedings outlined the then-current state of knowledge and its application to on-farm control in several countries.[10,11] In turn, the World Organization for Animal Health (OIE) then sought to improve its guidelines on population-level disease control in the chapter on paratuberculosis in the Terrestrial Animal Health Code. The existing Code chapter recommended movement certification, based on the recent known history of Johne's disease in the herd of

origin, supplemented by negative tests on the animals being traded. Given the subclinical nature of Johne's disease and the low sensitivity of diagnostic tests at the individual animal level, certification based on these requirements is of limited value and may inadvertently contribute to increased spread.

The OIE subsequently considered a new Code chapter that recommended more valid herd level assessments but, 5 years ago, removed the text of the old chapter. Following another review in 2009, the OIE confirmed this position[12] so that the code chapter now only contains a reference to the terrestrial manual.[13] Inappropriate movement requirements, on one hand, do little to validly assess and manage high-risk movements of breeding animals, while, on the other hand, can impose unwarranted restrictions on low-risk movements.

While the movement standards have not been resolved, the OIE continues to provide guidance and support for diagnostic standards for Johne's disease through its *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2010*[14] supported by, reference laboratories and experts in several countries.

Also flowing from the IDF's work ten years ago has been an informal ParaTB Forum that has been held in association with the World Dairy Congress in Shanghai in 2006 and with the International Colloquium on Paratuberculosis in 2009.[15] These forums bring together managers from countries that have implemented Johne's disease control programs to review and critique how improved knowledge and tools have been applied in their national control and assurance programs and to learn from one another's challenges and successes. As outlined below, successfully controlling Johne's disease has posed formidable challenges in several countries.

NATIONAL APPROACHES

Several countries have developed and refined national strategies to deal with Johne's disease during the past 2 decades. These have varied depending on the particular country's livestock production and trading environment and whether livestock industry and/or governments have been the major drivers. In general, government animal health services have largely led programs aimed at protecting uninfected regions (such as northern and western Australia) or at eradicating infection from populations with low prevalences of Johne's disease such as in Sweden and Japan. In other countries, such as Austria,[16] governments have recently been heavily involved in the early stages of response to rapidly increasing occurrence of disease.

In contrast, programs aimed at managing the risk of spread and contamination in endemically infected livestock populations in western Europe have been largely led by the national livestock industry organizations or, as is happening in Australia, are now becoming increasingly dependent on industry leadership and funding as government commitment changes. Food safety authorities in several developed countries have been monitoring developments related to Crohn's disease but have generally not mandated standards to manage human exposure to MAP, preferring to encourage ongoing on-farm risk management programs and good food processing practice.

National strategies generally have one or more of the following aims:

- Improving knowledge and understanding of MAP and developing tools to better manage MAP infection and contamination and its impacts
- Managing the risk of unacceptable levels of MAP occurring in food products

- Preventing and controlling the effects of Johne's disease on animal production and welfare
- Preventing and reducing the occurrence of MAP in herds and regions
- Demonstrating the low-risk status of breeding herds and flocks
- Eradicating MAP from herds and/or regional livestock populations.

In the majority of countries, programs have been directed at the dairy and beef cattle industries but significant Johne's disease programs have also been implemented for sheep (eg, in Australia), goats (Norway), deer (New Zealand) and South American camelids (Australia).

CONTROL AND RISK ASSESSMENT IN ENDEMICALLY INFECTED POPULATIONS

Johne's disease is well established in intensive cattle production systems in most countries, especially in dairy herds. The Netherlands, the United States, and Australia have been in the vanguard of controlling endemic Johne's disease, and each country's strategies have evolved substantially over time. In the United States and Australia, animal disease control is largely a constitutional responsibility of the states, rather than the federal government, and the initial steps to control Johne's disease were largely unilateral state-based regulatory programs. Interstate movement regulations were also implemented in the United States and Australia in the hope of reducing spread between regions.

A major problem for these types of regulatory programs resulted from a focus on and discrimination against herds that were officially known to be infected. Test-and-cull programs also were optimistic that MAP-infected herds could transition out of their infected status to "freedom" over several years. Regrettably, the sensitivity of tests and the cost effectiveness of programs were poor, so most owners saw little benefit in, and many downsides from, confirming MAP infection in their herds. A consequence was that most infected herds remained undetected. They were not engaged in actively controlling the infection and continued to sell infected animals.

In the mid to late 1990s the Dutch, U.S., and Australian programs took an important step towards more modern risk assessment and management of Johne's disease as a subclinical infection in endemically infected regions. For instance, within infected herds, a common recommendation to cull all test-positive cows before their next calving was refined to using the individual serologic or fecal culture results as indicators of the risk that a particular cow was a major contributor to shedding of MAP and therefore to contamination of milk and to infection of replacement calves. The focus also shifted from a focus on whether a herd was known to be MAP-infected toward probabilities that herds may be infected or that the prevalence would exceed a certain prevalence. The Australian Market Assurance Programs and the U.S. Voluntary Herd Status Program outlined how herd owners could objectively and transparently demonstrate a specified low risk of their herds being infected with MAP.[17,18]

The Dutch animal health service has taken this risk assessment a step further after a 1990s longitudinal study of test negative herds found that most of them were actually infected.[19] The Netherlands has moved to a program that classifies milk-producing herds as high risk (red herds) or low risk (green), not of being infected per se, but rather of contaminating bulk milk at a level above which pasteurization would eliminate organisms.[20] Risk assessment is also the basis of control programs in Ontario and the western provinces in Canada.[21]

In the face of a high prevalence of infection, the voluntary Danish cattle industry program has also taken a probabilistic approach to classifying herds and cows by

risk, depending on antibody levels in milk.[22] Quarterly herd recording samples are tested for evidence of a range of infections including Johne's disease and the participating herds' risks published on the industry website.

Although most international attention has been paid to Johne's disease in cattle, infection with S type MAP, is endemic in major sheep-producing countries including Spain,[23] Australia,[24] New Zealand,[25] and South Africa,[5] and an Indian Bison type organism is common in sheep and goats in India.[6] Small ruminant production systems often provide few opportunities to manage individual animals and vaccination has been a more important tool to reduce the impact of disease within infected flocks and herds. From 1966, Iceland enforced a strict vaccination program in sheep, combined with movement controls that eliminated clinical disease however subsequent surveillance confirmed that the S-type infection had not been eradicated.[26]

ASSURANCE FOR DOMESTIC ANIMAL TRADE

Unlike most developed livestock-producing countries, the livestock populations over a large part of northern and western Australia have demonstrably little or no Johne's disease. To protect that status, movements are regulated into those areas so that introduced animals have only a low probability of being infected with paratuberculosis. In turn, this pressure gradient has extended southward and eastward through pedigree breeding herds and flocks, encouraging many to provide an appropriate level of assurance. To this end, the Australian Johne's Disease Market Assurance Programs commenced in 1996 to provide a transparent national standard for owner declarations based on herd and flock biosecurity and negative testing.[17] In the past 5 years, more broadly applicable and attractive herd and flock risk scoring schemes have been developed for the dairy, sheep, and goat industries.[27,28] These cover a wider range of herd statuses from herds and flocks that are infected but undertaking no control (score 0) through to high-level market assurance program herds and flocks. The "pure beef" sector (that has little or no contact with dairy cattle) and alpaca populations in Australia have very little Johne's and have developed assurance schemes based on herd biosecurity. Farmers are encouraged to use nationally agreed animal health statements to declare their assurance level when selling stock. The effectiveness of these schemes is about to be critically reviewed but suffice to say that there have been very different outcomes in different livestock sectors and in different regions.

REGIONAL DISEASE PREVENTION AND ERADICATION

Most countries have struggled to effectively control the spread of endemic Johne's disease once it has established in its livestock populations. In Australia, for instance, the sheep strain was probably introduced about 50 years ago but its known distribution remained quite localized in central New South Wales for a further 15 years. Since then, however, it has been progressively detected over a wide area of southern Australia, despite the efforts of initial regulatory programs and later voluntary industry–government programs to control it.[29] The estimated prevalence of infected flocks in large parts of New South Wales and Victoria is now over 30%.[30]

Several regions and countries have adopted energetic programs to protect their livestock populations and limit the spread of Johne's disease before it has established widely. Sweden has successfully eradicated the cattle strain that was introduced in imported cattle in the 1970s,[31] and Norway maintains a program to control Johne's disease in goats and prevent its spillover into cattle.[32] Japan commenced a national program of surveillance testing of all cattle herds every 5 years in 1997, with follow-up

test and cull programs in herds identified as infected with a view to eradicating Johne's disease.[33] Northern and western Australia are officially declared protected and free zones for the cattle strain of MAP, and these regions have successfully prevented the establishment of infection by movement controls and stamping out infection when detected. Queensland and South Australia have taken similar action to protect their sheep flocks from ovine infection.

SUMMARY

The epidemiology and pathogenesis of Johne's disease facilitated its spread with livestock movements across the globe during the twentieth century, initially from Europe and subsequently from other developed livestock exporting countries. In the past 20 years, international collaboration in research and disease control methods has increased. The previous international guidelines on movement certification for Johne's disease have been removed from the OIE Terrestrial Animal Health Code but are yet to be replaced by standards that will effectively contribute to reducing the risk of international spread. Over the past 2 decades, individual countries have conducted a range of programs aimed at controlling the spread of Johne's disease between herds and flocks, with the more successful being those that have energetically addressed the disease before it has established. In endemically infected regions, control of the disease within infected herds and flocks focuses on reducing the impacts on animal welfare and productivity and in reducing contamination of the farm environment and of farm products. This is undertaken through reducing the exposure of young animals, vaccination, and/or identifying and removing animals that are most likely contributing to heavy contamination of the farm and environment. Collaboration among the international community of researchers, government regulators, and livestock industry leaders has significantly contributed to improved understanding of Johne's disease and to more innovative strategies to deal with it.

ACKNOWLEDGMENTS

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