Control of Mycobacterium avium subsp. paratuberculosis infection in agricultural species

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Summary
Paratuberculosis or Johne's disease is a chronic intestinal disease caused by Mycobacterium avium subsp. paratuberculosis, which continues to spread in agricultural species. Control of paratuberculosis is challenging and should not be underestimated. Due to the long incubation period of the infection, disease is largely subclinical in domesticated livestock. Hence, direct effects on animal productivity and welfare are often masked and may appear insufficient to justify large investments in control programmes by individual farmers, livestock industries or governments. Furthermore, in some countries the main effects of the disease are indirect, resulting from the impact of market discrimination against herds and flocks known to be infected, or from the control measures enforced to reduce transmission. In such circumstances, producers may be unwilling to co-operate with surveillance that may detect infection in herds or flocks. As control programmes are rarely successful in eliminating the infection from a herd or flock in the short term without an aggressive and costly programme, financial and community support assists producers to deal with the challenge.

Successful prevention and control depends on animal health authorities and livestock industries acquiring a good understanding of the nature and epidemiology of infection, and of the application of tools for diagnosis and control. Building support for control programmes under the leadership of the affected livestock industries is critical, as programmes are unlikely to be successful without ongoing political will, supported by funding for research, surveillance and control.

Keywords

Introduction

Mycobacterium avium subsp. paratuberculosis is the cause of paratuberculosis or Johne's disease, a chronic intestinal disease which has been detected in livestock world-wide. The previous paper in this issue of the Review describes the diagnosis and pathogenesis of paratuberculosis (111). The present paper complements it and aims to discuss the principal factors that are important in understanding the effects and epidemiology of the infection, in addition to the control options available.

History

In 1895, Johne and Frothingham published a case report of what was considered to be 'Ein eigenthümlicher Fall von Tuberculose beim Rind' ('A singular case of bovine tuberculosis') (81). A six-year-old cow with a history of weight loss and diarrhoea was suspected by the local veterinarian of having intestinal tuberculosis. However, the animal was tuberculin negative. The animal died in the following spring and post-mortem examination revealed a chronic enteritis; the mucosa of the small intestines was thickened and had a corrugated aspect. Histological
examination identified abundant acid-fast bacilli in poorly organised granulomatous lesions, comparable to lesions observed in leprosy. The authors concluded that the disease was caused by the avian tubercle bacillus and proposed the name pseudotuberculosis. However, Bang recognised this as another disease which he called paratuberculosis, although it strongly resembled intestinal tuberculosis (11). McFadyean introduced the name Johne's disease (105). The causative organism of paratuberculosis was first isolated in 1910 by Twort and Ingram (181) and is presently classified as *Mycobacterium avium* subspecies *paratuberculosis* (*M. paratuberculosis*).

The involvement of *M. paratuberculosis* in the pathogenesis of Crohn's disease, an intestinal disease in humans, was suggested as early as 1913. Similarities exist between the pathological and clinical features of Crohn's disease and paratuberculosis (30), although research has not demonstrated a causal association at this stage (56).

**Nature of infection**

Paratuberculosis is a chronic infectious disorder of the intestinal tract, principally in domestic ruminants, but also in wild ruminants. The causative organism can also infect a wide range of other domestic and wild (free-living and captive) species, including primates. *Mycobacterium paratuberculosis* has recently been isolated in wild rabbits suffering a chronic granulomatous enteropathy (68), in foxes, weasels and stoats (13), in macaques and in humans (46). The identification of a genetic element, insertion sequence (IS)900, which is highly specific for *M. paratuberculosis*, has facilitated the identification of different strains of the bacteria by restriction endonuclease analysis.

The infection can be transmitted by either direct or indirect contact between infected and susceptible animals. Bacilli are ingested, usually in large numbers, when young animals nurse on teats which have been contaminated by faeces of shedding animals. Young susceptible animals also ingest the organism in infected macrophages that may be present in colostrum and milk, as well as in milk contaminated by faeces. Contaminated feed, water and surfaces may also be sources of infection. *Mycobacterium paratuberculosis* can also be recovered from uterine fluid and placental tissue, and foetal infection has been reported. Although the organism has been recovered from semen, venereal transmission seems to be unlikely (41).

Animals are most susceptible to infection in the first few months of life. Adult cattle are difficult to infect, as an age-related resistance to infection develops during the first year of life. The precise nature of this age-related resistance is unknown, but may be linked to the developmental physiology of the 'gut-associated lymphoid tissue'.

After crossing the intestinal barrier, *M. paratuberculosis* invades macrophages, in which the organisms persist. Whether or not the infection becomes established in the exposed animal depends on the number of organisms ingested, the number of times the animals are exposed to infection and the defence mechanisms of the animal (174). The infection progresses slowly, but in advanced clinical cases, the infection can be disseminated in macrophages throughout the body (97) and the animal begins to shed bacteria via the faeces, colostrum, milk or semen. Clinical disease rarely appears until adulthood, and then only in a minority of infected animals. Once clinical disease occurs, the condition of the animal deteriorates until natural death or slaughter.

**Global spread and distribution**

Since the first description of paratuberculosis, the disease has been recognised virtually world-wide (94), and in an increasing range of animals. Paratuberculosis is an increasing problem in dairy herds and in other domestic livestock such as sheep, goats, farmed deer and camelids, in many countries (33). However, the disease does not occur in all species in all parts of the world, and some countries or regions have very little or no endemic infection. Notably, in more than twenty of the nearly sixty countries in which paratuberculosis has been described, the disease was introduced by imported cattle or sheep (94). Difficulty in diagnosing paratuberculosis means that accurate estimates of the true prevalence and distribution are difficult to obtain (30).

From the 1950s to the 1980s, prevalence was generally estimated by isolation of *M. paratuberculosis* from tissue specimens obtained from cattle at slaughter. Results of these types of studies are summarised in Table I (190). Reported prevalence ranged from 0% (reported in 1955, in Australia) to 18% (reported in 1983, in Connecticut, United States of America [USA]).

Several recent surveys in Europe have principally used serological testing to estimate the prevalence of infection in cattle (Tables II and III).

In the study in the Netherlands, the test sensitivity and specificity were considered in calculating the true prevalences. Based on a test sensitivity of 0.3 to 0.4, and a specificity that ranged from 0.985 to 0.995, the true prevalences at animal level and at herd level were estimated to be 3%-7% and 31%-71%, respectively (121). In Austria, positive test results were obtained in 2% of animals and in 7% of herds (65), but on 87.5% of the positive farms only one positive animal was detected.

More recent work in the USA revealed that 50% of the dairy herds and 7.3% of the individual animals in Wisconsin were serologically positive (38). In 1996, 22% of dairy herds in the USA were estimated to be infected (187).
Table I
Prevalence of paratuberculosis based on isolation of *Mycobacterium paratuberculosis* from tissues of cattle taken at slaughter

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Number of samples</th>
<th>Positive (%)</th>
<th>Specimens cultured</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Great Britain</td>
<td>1949</td>
<td>243</td>
<td>15</td>
<td>l/c Ln</td>
<td>175</td>
</tr>
<tr>
<td></td>
<td>1952</td>
<td>665</td>
<td>15</td>
<td>l/c Ln</td>
<td>176</td>
</tr>
<tr>
<td></td>
<td>1954</td>
<td>552</td>
<td>6</td>
<td>l/c Ln</td>
<td>148</td>
</tr>
<tr>
<td></td>
<td>1954</td>
<td>358</td>
<td>7.5</td>
<td>l/c Ln</td>
<td>148</td>
</tr>
<tr>
<td></td>
<td>1954</td>
<td>300</td>
<td>17</td>
<td>l/c Ln</td>
<td>195</td>
</tr>
<tr>
<td>Ireland</td>
<td>1954</td>
<td>256</td>
<td>0.8</td>
<td>l/c Ln</td>
<td>148</td>
</tr>
<tr>
<td>Australia</td>
<td>1955</td>
<td>355</td>
<td>0</td>
<td>l/c Ln</td>
<td>146</td>
</tr>
<tr>
<td>Germany</td>
<td>1961</td>
<td>NA</td>
<td>1.7</td>
<td>l/c Ln</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>1961</td>
<td>NA</td>
<td>3.3</td>
<td>l/c Ln</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>1961</td>
<td>NA</td>
<td>3.4</td>
<td>l/c Ln</td>
<td>86</td>
</tr>
<tr>
<td>Denmark</td>
<td>1965</td>
<td>662</td>
<td>2.3</td>
<td>l/c Ln</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>1972</td>
<td>10,118</td>
<td>9.8</td>
<td>l/c Ln</td>
<td>87</td>
</tr>
<tr>
<td>United States of America</td>
<td>1987</td>
<td>7,540</td>
<td>1.5</td>
<td>l/c Ln</td>
<td>117</td>
</tr>
<tr>
<td>California</td>
<td>1975</td>
<td>313</td>
<td>1.6</td>
<td>l/c Ln, l/c valve and ileum</td>
<td>1</td>
</tr>
<tr>
<td>Connecticut</td>
<td>1986</td>
<td>100</td>
<td>18</td>
<td>6 tissues per animal</td>
<td>31</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>1983</td>
<td>591</td>
<td>10.8</td>
<td>l/c valve</td>
<td>8</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>1985</td>
<td>1,224</td>
<td>7.2</td>
<td>l/c Ln, ileum, faeces</td>
<td>191</td>
</tr>
<tr>
<td>Wisconsin</td>
<td>1985</td>
<td>205</td>
<td>7.8</td>
<td>l/c Ln, ileum, faeces</td>
<td>61</td>
</tr>
<tr>
<td>Beef</td>
<td></td>
<td>3,522</td>
<td>0.8</td>
<td>l/c Ln</td>
<td>117</td>
</tr>
<tr>
<td>Dairy</td>
<td></td>
<td>2,827</td>
<td>2.9</td>
<td>l/c Ln</td>
<td>117</td>
</tr>
<tr>
<td>Canada</td>
<td>1991</td>
<td>400</td>
<td>5.5</td>
<td>l/c Ln, ileum</td>
<td>108</td>
</tr>
</tbody>
</table>

l/c : ileocaecal
ln : lymph node(s)
NA: not available

Source: adapted from Whipple (190)

In Greece, 9.8% of sheep tested were positive to delayed type hypersensitivity tests (48). In Spain, a study identified 46.7% of flocks as infected. Within flocks, prevalence levels of affected animals ranged from 33% to 46%, based on an enzyme-linked immunosorbent assay (ELISA) (89).

However, the potential distribution of the infection has not yet been reached, and the disease continues to spread. Indications of the way in which the infection can slowly spread and become endemic over a wide area can be observed in countries in the southern hemisphere to which domestic livestock have been introduced relatively recently. In Australia, paratuberculosis was first diagnosed in cattle seventy-five years ago and in sheep in 1980. Both types of infection now occur over a large part of temperate south-eastern Australia in dairy and beef cattle, sheep, goats, alpacas and deer. Approximately 2,150 cattle herds were known to be infected in early 2000, and the known herd prevalence among dairy herds in south-eastern Australia was 14%. Overall, approximately 750 infected sheep flocks had been identified by early 2000. Infections in alpaca were only diagnosed in Australia in the early 1990s (152), and infections in deer in the late 1990s. However, stamping out of introduced infections and controls on movements have contributed to the current situation where neither bovine nor ovine infection is endemic in northern and western parts of the continent (5, 96).

Paratuberculosis has also been diagnosed in cattle, sheep, goats and deer in New Zealand (189). The first bovine case was diagnosed in 1912, and by the 1990s, paratuberculosis was diagnosed by post-mortem examination in 16% of investigated dairy herds (44). However, a much higher estimate of dairy herd prevalence (60%) was recently used in an official economic analysis (22). Paratuberculosis was first reported in sheep in New Zealand forty years ago, but an exponential increase in the number of flocks known to be infected in subsequent years led to 6.4% of sheep flocks being officially classified as infected by 1996 (189). Again, a higher estimate, of 70%, was used in the economic study by Brett (22).

**Clinical and economic effects of infection**

**Introduction**

Paratuberculosis is principally a subclinical infection. The disease has a protracted incubation period and clinical signs are only the terminal manifestation of the infection, which develop in a minority of infected animals. The key factors contributing to the time of onset of clinical disease are probably the age of the animal at the time of infection and the initial dose of infection. However, a range of risk factors have...
Table II
Prevalence estimates of bovine paratuberculosis in selected countries of Western Europe

<table>
<thead>
<tr>
<th>Country</th>
<th>Region</th>
<th>Year(s) of survey</th>
<th>Number tested</th>
<th>Apparent prevalence (%)</th>
<th>True prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>All</td>
<td>1995-1997</td>
<td>2,757</td>
<td>Herd 7 (a)</td>
<td>Herd 2 (a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Individual 7 (b)</td>
<td>Individual 2 (b)</td>
</tr>
<tr>
<td>Belgium</td>
<td>All</td>
<td>1997-1998</td>
<td>442</td>
<td>Herd 17.42 (d)</td>
<td>Herd 25</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Individual 11.8 (d)</td>
<td>Individual 17 (d)</td>
</tr>
<tr>
<td>Denmark</td>
<td>All</td>
<td>1998</td>
<td>900</td>
<td>Herd 55 (e)</td>
<td>Herd 47</td>
</tr>
<tr>
<td>Southern Jutland</td>
<td>1999-2000</td>
<td></td>
<td>6,071</td>
<td></td>
<td></td>
</tr>
<tr>
<td>England and Wales</td>
<td>All</td>
<td>1997</td>
<td>2,953</td>
<td>Herd 17 (d)</td>
<td></td>
</tr>
<tr>
<td>Finland</td>
<td></td>
<td>1993-1998</td>
<td>6,922</td>
<td>Herd 7 (b)</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>Arnberg</td>
<td>1993-1998</td>
<td>10-30 (a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>11.9 (a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>Umbria and Marche</td>
<td>1990</td>
<td>106</td>
<td>Herd 2.8 (d)</td>
<td></td>
</tr>
<tr>
<td>Brescia</td>
<td>1990</td>
<td></td>
<td>3,652</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweden</td>
<td>All</td>
<td>1993</td>
<td>4,000</td>
<td>Herd 1.2 (b)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Individual 0.47 (f)</td>
<td>Individual 0 (f)</td>
</tr>
<tr>
<td>Switzerland</td>
<td>All</td>
<td>1995-1996</td>
<td>3,166</td>
<td>Herd 8.0 (b)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The Netherlands</td>
<td>Three northern provinces</td>
<td>1995</td>
<td>113</td>
<td>Herd 0.7 (d)</td>
<td></td>
</tr>
<tr>
<td>Northern region</td>
<td>1998</td>
<td></td>
<td>1,863</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(a) seroprevalence on herd level
(b) seroprevalence on individual animal level
(c) postal survey of farmers; no diagnostic tests were used
(d) prevalence of faecal culture on individual level
(e) repeated faecal cultures from all cows in herds under investigation; all herds had no history of paratuberculosis
(f) Johne's absorbed enzyme-linked immunosorbent assay (ELISA), assuming a sensitivity of 0.43 and a specificity of 0.98

Source: courtesy of S.S. Nielsen

been proposed as accelerating or precipitating the onset of the clinical phase of the infection, including intensive farming systems, acid soils, poor nutrition, stress related to transport, lactation, parturition and immunosuppression by agents such as bovine virus diarrhoea virus or by deficiency of essential elements. Dietary iron and vitamin D may modulate the course of the disease. In vitro studies have demonstrated that growth hormone and prolactin appear to influence uptake and subsequent killing of bacteria by bovine macrophages (59).

In cattle, clinical signs rarely appear before two years of age and most cases develop between the ages of two and six years. However, the range is truncated by herd culling practices, and the reported ages of animals with clinical signs vary from six months to fifteen years (30). Estimates suggest that for each animal with clinical signs of paratuberculosis in dairy herds in the USA, twenty-five subclinically infected cows are present, of which nine can be detected with the current diagnostic tests (192). Only a proportion (5%-10%) of the chronically infected animals are likely to progress to the clinical stage. The morbidity rate in infected herds and flocks is usually less than 1% per year. The incubation period in sheep and goats is generally at least one year and is usually longer.

Subclinically infected animals can shed very large numbers of M. paratuberculosis for long periods, resulting in a highly contaminated environment. Shedding of bacteria may reach $1 \times 10^8$ bacteria per gram of faeces in cows and sheep with clinical signs of disease (30, 198). Young animals born into a heavily contaminated environment are very likely to be exposed to bacteria while in the susceptible age range.

**Clinical effects**

In ruminants, clinical disease is characterised by a progressive, afebrile weight loss that leads to emaciation, submandibular oedema and poor coat quality, despite a good appetite. A drop in milk yield has been reported in the lactation preceding that in which clinical disease becomes apparent. However, the major clinical sign of the disease in cattle is a chronic, intractable diarrhoea, which in some animals may be intermittent. In contrast to cattle, diarrhoea in small ruminants does not occur or is not severe, although in advanced cases in sheep and goats the faeces may be sufficiently soft to lose the usual pelleted form.

The duration of the clinical phase of paratuberculosis varies considerably, from weeks to months. A temporary improvement may also occur when cattle are removed from
The damaged intestine may also leak serum albumin into the lumen. The increased amount of nutrients available to the damaged intestine to digest and absorb nutrients is impaired, causing malabsorption. Electrolytes and other osmotically active nutrients remain in the gut in higher concentrations, causing water to be retained in the lumen. These clinical signs reflect the intestinal pathology. The ability of the damaged intestine to digest and absorb nutrients is impaired, causing malabsorption. Electrolytes and other osmotically active nutrients remain in the gut in higher concentrations, causing water to be retained in the lumen.

In cattle, a significantly elevated incidence of mastitis and infertility has been associated with bovine paratuberculosis (116). Longer calving intervals have also been reported (1, 82). Cows that are infected with M. paratuberculosis may have an increased risk of being in a metabolic state that is characterized by a negative energy balance due to reduced intestinal absorption. This state may be compounded by endoparasites (52).

In an infected herd or flock, infected animals can be classified into four categories, as detailed below (32,102).

- **Asymptomatic shedders:**
  - in late subclinical phase, no clinical signs except reduction in milk yield, intermittent shedding, high antibody responses and a low level of cell-mediated immunity.

- **Clinically ill animals** characterised by clinical signs, heavy shedding, high antibody responses and a low level of cell-mediated immunity.

- **Carrier animals:** a latent phase which cannot be diagnosed using immunological methods and faecal culture. Diagnosis may be achieved by surgical biopsy of mesenteric lymph nodes (15). These animals do not shed the bacteria and no immunological response is detectable.

- **Uninfected animals:** these animals are healthy and do not shed the bacteria.

In goats, a variety of presenting problems may be observed, including poor reproductive performance and/or milk production. In some herds, the effects of paratuberculosis may be compounded by endoparasites (52).

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Economic impact

Losses attributed to paratuberculosis can be classified as direct, indirect and inapparent costs for the different species. The economic losses vary according to the region, the farm unit and the species involved. In herds affected with paratuberculosis, the losses can be so great that profitable farming cannot be continued (114).

Direct costs

Direct economic losses are due to the following:

a) clinical disease
b) subclinical disease
c) increased susceptibility to disease, infertility and a shortened life expectancy
d) the costs of controlling the disease.

Clinical disease

The economic losses due to clinical disease in dairy cattle herds comprise the following:

a) losses prior to culling, due to the loss of milk production and costs of examination and treatment
b) losses at culling or death, due to the reduced slaughter value of the animals and the resulting suboptimal utilisation of capital equipment on-farm
c) losses due to premature culling or death, i.e. the unrealised future income.

Highly productive cows which are infected with M. paratuberculosis are more likely to develop clinical disease (16, 47, 50).

The relative productive potential of mature cows with paratuberculosis is approximately 8% to 9% greater than that of the herd average. There is therefore a relationship between the production capacity and the likelihood of culling for paratuberculosis. Many studies describe a decrease in milk production in cattle with clinical paratuberculosis when compared with other herd members, varying from 14.6% to 15.9%, and reaching 19.5% in the last lactation (16, 25, 83). According to Wilson et al., in New York State, USA, financial differences in milk production associated with paratuberculosis ranged from no significant effect in the first lactation to a loss of US$248 per cow per year in fourth-plus lactation (200).

Malabsorption also causes poorer feed conversion, so an infected animal has to consume more per unit of product than unaffected peers.

Subclinical infection

In the penultimate lactation before culling, subclinically infected cows were found to produce 6% less milk than the previous lactation (with a lower fat and protein content); in the last lactation, milk production was reduced by 16% (14, 200).

Other losses

Losses associated with subclinical paratuberculosis can be caused by higher rates of mastitis and infertility and increased culling rates (1, 82, 116, 200). Economic losses generally appear to commence in the second lactation (200). Culling losses are approximately US$75 per cow per year in infected dairy herds. In addition, the age of infected cattle is significantly lower than that of non-infected cattle, indicating that infected cattle have a shorter life expectancy.

Control costs

The costs of controlling paratuberculosis consist of the costs of private and other veterinary services, costs of diagnostic testing programmes and the costs of management changes instituted by the farmer, especially to calf rearing facilities. However, these management changes may also result in control of other diseases and be offset by improved calf health and growth.

Indirect costs

The indirect costs of paratuberculosis result from restrictions on market access, movement testing of live animals for domestic trade and export (laboratory and veterinary fees) and funding for paratuberculosis research. The costs of incorporating recommended preventive management practices in group rearing and artificial breeding centres are another source of economic loss.

In some regions, a large proportion of the cost is caused by market-driven or regulatory trading restrictions on herds and flocks known or suspected to be infected (170). Animals from farms or areas known to be infected may suffer price penalties or may sell only for slaughter. Stringent conditions are often placed for movement to areas in which the disease is less prevalent or not recognised. Such costs are incurred at several different levels, from the individual farm through to the interzone and international levels, where quarantine and movement restrictions increase the costs of trading at a national and international level.

Inapparent costs

Other less obvious losses include the loss of genetic potential through early culling and through trading restrictions. Opportunities to sell animals with a high genetic value from infected herds or flocks are limited. In addition, owners of herds and flocks wishing to avoid infection by maintaining totally closed herds have a limited access to superior genetics (70). Limited selection may also occur where animals are introduced only from test-negative herds.

Overall estimates of the economic loss caused by paratuberculosis vary considerably depending on production and pricing systems. Accurate data is limited, but the estimated annual losses due to paratuberculosis in the dairy industries of different countries are presented in Table IV.
bacteria can also survive for long periods in the environment. *M. paratuberculosis* is potentially transmitted by four routes, *M. avium* is the necessary cause of *M. paratuberculosis*, but various factors combine to influence whether infection establishes and progresses (29).

**Agent**

*Mycobacterium paratuberculosis* is closely related to *M. avium* subsp. *avium*. In some species, and notably in deer (45), the two infections cause similar pathology. *Mycobacterium paratuberculosis* is an obligate parasite, dependent on animal hosts to provide a source of iron on which growth and multiplication of the organism depend. Other members of the *M. avium* complex are common in the environment, hence the ability to differentiate *M. paratuberculosis* from the other subspecies is important for paratuberculosis surveillance and control (57, 58).

The genome of *M. paratuberculosis* contains several copies of a highly specific insertion sequence, IS900, that facilitates differentiation from *M. avium* and other mycobacterial species (67). However, Cousins *et al.* have identified non-mycobactin dependent mycobacteria that were IS900 positive (39) and recommended that restriction digests of the PCR product should be undertaken to confirm the identity of *M. paratuberculosis*. Recently, Whittington *et al.* (196) and Marsh *et al.* (112) described another insertion sequence (IS1311) that differentiated between *M. paratuberculosis* and *M. avium* after the restriction digestion of PCR product. Ellingson *et al.* have also reported a thirty-three base-pair oligonucleotide that is unique to *M. paratuberculosis* (53).

Extensive field and laboratory experience has indicated that differences exist among the organisms causing paratuberculosis in different host species. The disease commonly occurs in one species but not in other susceptible species grazing in the same area. In Australia, paratuberculosis was first diagnosed in cattle in 1925 (3), but was not observed in sheep for more than fifty years (162). Conversely, when paratuberculosis was diagnosed in sheep flocks in Australia in 1980, cattle that were grazing alongside the sheep had no obvious disease. Under very different management systems in Iceland, the same observations were reported (60). The disease has occurred regularly in goat herds in Norway, but has only recently been detected in a small number of cattle herds (132). In the laboratory, strains of *M. paratuberculosis* from sheep have been generally more difficult to culture than those from cattle (35).

The molecular basis for these differences has been identified by restriction endonuclease analysis. Two principal types, a cattle type (C) and a sheep type (S), were initially identified in 1990 by Collins *et al.* (34), who also reported that two goat isolates from Norway differed from these two main types. Restriction fragment length polymorphism analyses using different enzymes to fragment the deoxyribonucleic acid (DNA) have also identified variations within the main C and S types. Moreira *et al.* found that isolates from Argentina differed from isolates obtained in Europe (119), and Bauerfiend *et al.* reported significant variation in cattle and...
sheep isolates from Morocco and South Africa (12). Pavlik et al. reported considerable heterogeneity in the types isolated from a range of animal species in Europe and elsewhere (137). This presents an opportunity to use molecular epidemiology as a tool to study the spread of the disease in those regions. Less heterogeneity occurs within the main C and S strains in Australia and New Zealand (40). However, Whittington et al. found differences in the occurrence of types C1 and C3 among cattle isolates between two regions and between dairy and beef cattle in one region (197). The great majority of isolates from sheep were S1. The limited range of types may be a result of these countries having restricted imports of livestock for many years to maintain a favourable status with regard to other important animal diseases.

Host preferences of types of M. paratuberculosis are important in managing the disease in mixed grazing situations. Paratuberculosis in cattle, goats and camels is mainly caused by C type M. paratuberculosis, whereas sheep are usually infected with S types. Although some types appear to have a strong host preference, this is not absolute, and sheep types can infect cattle and vice versa. In New Zealand, sheep grazed on ground contaminated by clinically diseased cattle for two years excreted viable bacteria, and bacteria were isolated from the lymph nodes and ileum, although no pathological lesions were observed (154). Similar findings have recently been reported in sheep on infected cattle farms in the Netherlands (122). In Iceland, sheep strains have infected cattle and goats (60) and in Australia, a small number of cattle and goats have been confirmed to be infected with S types on relatively extensive grazing systems within which the disease is established in the sheep flocks (195). In infected environments in which two or more species are grazed together, the evolution of types of M. paratuberculosis that are adapted to more than one species is feasible.

Host factors

Most of the current knowledge of the epidemiology of paratuberculosis has been derived from studies in cattle, and particularly dairy cattle, although the disease has been common in sheep and goats in many countries for decades. Epidemiological research on infection in sheep is still in the early stages, possibly because of the relative economic value of the species. In addition, ovine paratuberculosis is a comparatively recent problem in several countries and techniques for routine culture of S types have been only comparatively recent problem in several countries and techniques for routine culture of S types have been only

Susceptible species

Mycobacterium paratuberculosis infects a very wide range of animal species. However, the disease is most common among domestic ruminants (especially cattle, goats, sheep, and deer). Reports of infections in other animals, domesticated, in zoos and in the wild, include pigs and primates (140, 163, 168). A small number of isolates have been reported in humans (56).

The bacterium has also been isolated from wild deer in contact with livestock, in the USA (153) and Europe (140), but the epidemiological significance of infection in wild animals has not been determined. The potential for a wildlife reservoir of paratuberculosis in Scotland was illustrated by the detection of gross lesions of paratuberculosis in a wild European rabbit (Oryctolagus cuniculus) (4). Infection and lesions have since been found commonly in rabbits in Scotland (68) and have also been detected recently in predators (13). At this stage, most wildlife infections are thought likely to be spill-overs from infection in farm species. However, some types of the organism could adapt sufficiently to develop sylvatic life cycles and possibly act as reservoirs to infect domestic animals in areas in which sufficient contact occurs.

Mycobacterium paratuberculosis has also been isolated from humans, and an association with Crohn's disease has been suggested (56). Although these findings are important in the consideration of whether M. paratuberculosis causes disease in humans, and in decisions as to the appropriate degree of control of animal paratuberculosis, any infection in humans is highly unlikely to be an important epidemiological factor in the infection of agricultural animals.

Breeds

Although paratuberculosis has been observed to occur more commonly in some breeds of cattle and sheep, genetics appears to be a minor factor in susceptibility (98). The difference in observed occurrence of the disease among various breeds is confounded by husbandry factors such as animal movements within breeds and management practices in certain enterprises that favour the transmission or the clinical expression of disease. For instance, in most countries, the prevalence of paratuberculosis is higher in dairy populations which are usually managed more intensively than beef herds. However, in Sweden, infection has been confined to beef cattle following the introduction of infection by imported cattle and subsequent spread of infection by movements between herds of one or two beef breeds (184).

Resistance and age

The pathogenesis of infection is the subject of the previous paper in this issue of the Review (111). In summary, the probability that M. paratuberculosis infection will establish and persist in an individual animal will vary according to the following factors:

- the innate susceptibility and resistance of the host
- the immune status of the host
- the number of organisms to which the host is exposed, the number of times exposure occurs and the period of time over which the host is exposed
- the infectivity and pathogenicity of the particular type of organism for the host species in question (29, 173).
Most infections occur in young animals by the oral route. The active gut lymphoid tissue of neonates and suckling animals provides access for the invading bacteria (173). A strong and effective resistance to infection develops with age in cattle. Although no definitive evidence has been obtained, young animals of other agricultural species are assumed to be also more susceptible to infection (168).

Infection of adult cattle has been reported experimentally and naturally in contaminated environments (149). Morgan reviewed the literature on age resistance and concluded that older cattle may be infected with *M. paratuberculosis* given sufficient challenge, but that clinical disease is unlikely to develop (41).

**Excretion and transmission**

The principal route of exit of *M. paratuberculosis* from infected animals is faeces, but organisms are also excreted via milk and colostrum, uterine fluids and semen to a lesser extent.

*Mycobacterium paratuberculosis* is primarily an inhabitant of the gut and associated lymph nodes, thus faecal excretion is the most important route for the sheer volume and persistence of the material in the environment and the numbers of organisms shed. As infection progresses, the concentration of organisms in the faeces rises dramatically. The number of organisms excreted per gram of faeces from clinically affected dairy cattle and from sheep with subclinical multibacillary infection is approximately $10^8$ organisms per gram of faeces (30, 198). As infection progresses and dissemination occurs throughout the body, organisms are also excreted in increasing numbers by other routes (194).

Foetal infection has been reported in sheep and goats (168), and approximately 10% of subclinically infected cows produce infected foetuses; this rises to approximately half of clinically affected cows (151, 173). Schaaf and Beerwerth reported that approximately 80% of foetuses from clinically affected cows were infected with *M. paratuberculosis* (161). The increasing rate of foetal infection in clinical cases and the probability that a calf is infected at birth are consistent with dissemination of infection as the disease advances in the body. The stage of gestation at which the foetus becomes infected is not yet known. Furthermore, whether the course of disease in these animals differs from that in animals infected post-natally also remains to be elucidated.

The neonate is at particular risk of being infected as the animal naïvely enters an environment potentially contaminated with high concentrations of *M. paratuberculosis*, from the faeces of the mother or other adults in the herd or flock. Organisms may be ingested from the following sources:
- the colostrum and milk of the mother
- cross suckling other cows or multiple rearing on suckler cows
- pooled colostrum and milk from other cows in the herd or from other herds
- teats, skin and other surfaces, fixtures, water and feedstuffs contaminated with faeces.

Excretion of *M. paratuberculosis* in colostrum and milk, even in comparatively low concentrations, is potentially as important as faecal excretion, given that the young susceptible animal is intimately exposed to this source until weaning (171, 177). Where feasible, early removal of the neonate from adults and the contaminated environment, followed by careful rearing, is recommended as a fundamental component of paratuberculosis control. In systems in which this is not feasible, a serious constraint is placed on the successful reduction of the incidence of infection.

As the dependence of young animals on the dam or on milk feeding diminishes, faecal contamination of pastures, other feedstuffs and water, presents a relatively higher risk. Faecal deposits may directly contaminate pastures and water supplies. Indirect contamination may result from drainage or splashing of contaminated effluent or water, or transfer on boots, clothing, machinery, buckets and similar materials. In intensive farming systems, irrigation water, dairy effluent and manure fertiliser are potentially significant sources of infection.

In favourable environments and management systems, contamination of the farm environment and the incidence of infection will usually rise in the absence of effective control procedures. Factors that expedite infection in the animal and favour shedding earlier in life will increase excretion and the rate of spread of infection. Although clinical disease and heavy faecal shedding usually occur in older animals, significant faecal excretion may occur in young animals in heavily infected herds (93).

*Mycobacterium paratuberculosis* is found in low concentrations in the uterine fluids and semen of infected cattle, particularly in advanced infection (41). Experimental infection of one-year-old heifers by intrauterine inoculation of high doses of *M. paratuberculosis* has been demonstrated (131), but venereal infection of mature cattle is unlikely (159). However, contaminated semen may contaminate embryos and, theoretically, result in pre-natal infection and the birth of infected animals. The risk of infection of dam or embryo by artificial insemination is probably extremely low, given that the volume of semen used is small, and that health certification and testing of donors for paratuberculosis should greatly reduce the likelihood of bulls at commercial semen centres shedding organisms in semen. Recommended washing procedures remove the vast majority of organisms from the surface of intact embryos (155), but Morgan concluded that embryos without an intact zona pellucida may be infected (41).
Overall, the risk of transmission of paratuberculosis through artificial breeding techniques appears to be very low. However, the status of embryo recipients is important, as the recipient may transmit infection to the transplanted offspring, as foetuses or as neonates, and subsequently to other young animals in the herd or flock.

Environmental factors
Survival
The ability of M. paratuberculosis to survive for long periods in the agricultural environment presents a significant challenge to the successful control of paratuberculosis. Contaminated areas may be infective to animals for several months. The organism has been isolated from a wide range of sites on infected farms, both outdoors and in animal houses (192). In laboratory studies, viable bacteria have been recovered in water for up to seventeen months (103) and in slurry for several months at low temperatures of 5°C and 15°C (88), but high temperatures, for instance over 35°C, appear to markedly reduce the longevity of the bacteria (128). The relative significance of moisture, temperature, ultraviolet radiation and desiccation has not yet been determined.

Detection of viable bacteria in the environment does not necessarily signify that the environment is infectious to animals. To establish infection, live organisms must have sufficient contact in high numbers with susceptible animals. At this stage, no tool exists to determine the risk posed by contaminated environments or whether previously contaminated pastures or fodders are still infectious. Methods are currently being evaluated, based on findings that infection in young lambs was detectable bacteriologically soon after oral inoculation (23). Cell-mediated immune responses in young sheep and goats may also prove useful in determining the infectivity of contaminated environments (169).

The dependence of M. paratuberculosis on iron, in addition to field observations of the distribution of paratuberculosis, has led to the hypothesis that soil and water chemistry may affect the distribution of infection. Soil acidity may affect iron solubility and availability, hence influencing the occurrence of paratuberculosis in dairy herds (85, 99). The observation that the liming of pastures is associated with a lower incidence of infection appears to corroborate this hypothesis (85). However, the association may not necessarily be causal, as other agronomic management factors may be confounding (83). Recently, paratuberculosis in small ruminants has been observed to be associated with acidic soils in South Africa and Spain (118, 150).

Spread of infection between farms
Animal movement
The most important means of transmission from an infected premises is the movement of infected animals. Infected animals may enter herds and flocks as planned introductions or by uncontrolled movements of stray domestic stock or of wild animals. The risk posed by these introductions will vary according to the following:

- the origin of the animals introduced
- the prevalence of infection in the source population
- the numbers introduced
- the age to which the animals are retained
- whether the animals are used for breeding
- the effective contact with susceptible animals.

Introduction of infected breeding females poses the highest risk, as these animals are often introduced to a herd or flock in large numbers, remain for prolonged periods and have intimate contact with progeny and other neonates. The risk posed by introduced sires will vary according to the management system. In controlled mating systems, such as dairy or alpaca herds, sires may effectively be held in isolation and mating managed in such a way as to almost eliminate the risk of infection to other animals. In more extensive paddock mating systems, the degree of contact with young animals will vary according to the gestation period of the species and the age at which young animals are weaned. For instance, in enterprises with restricted mating periods, young sheep would normally be weaned before rams are joined with the ewe flock. In contrast, in beef cattle, a bull would normally be joined with cows that are still suckling calves.

In most circumstances, a lower risk is posed by non-breeding animals, such as young castrate males. Meat animals are usually reared on a high plane of nutrition and removed from the herd or flock for slaughter before two years of age. Such animals are unlikely to develop advanced infection or excrete significant concentrations of bacteria. In contrast, castrate sheep or goats for fibre production may be reared on a lower plane of nutrition and retained for several years. In some systems, castrate male cattle may be retained and worked heavily as draft animals.

Exposure to other infected animals or environments may result from animals from a herd or flock being moved off the farm for short periods. Reasons for movement include the following:

- sharing sires with other farms
- group rearing of female replacement stock, especially in the dairy industry
- group breeding schemes, especially in the sheep industry
- movement to artificial breeding centres
- exhibitions, shows and sales
- straying.

In addition to grazing with infected animals, contaminated pasture, fodder and water present the main risks. Although aggregations and mixing of animals present a potential opportunity for infectious diseases to spread, paratuberculosis is not highly infectious.
Manure and water flow
Given the potentially very high concentrations of organisms in faeces and the ability of organisms to survive in water, infection may be spread mechanically between farms by drainage of contaminated water or effluent or by faecal material being washed across fencelines. Fertilising pastures and fodder crops with fresh manure and effluent from other farms is a hazardous practice.

Feedstuffs
Grass or crops grown for animal feedstuffs may be contaminated by grazing animals or by contaminated fertiliser or irrigation water. Old faecal material may also be collected by mechanical harvesters and be incorporated into fodder. Many bacteria in fresh green chop are likely to remain viable and infectious. Silage production does not generate high temperatures unless oxidative spoilage and composting occurs, but the process is anaerobic and acidic (A. Kayser, personal communication). However, no definitive work appears to be available regarding the impact of hay curing and silage fermentation on the survival of M. paratuberculosis. In a heavily contaminated farm environment, these feeds could be accidentally re-contaminated by faeces during post-harvest storage or handling.

Relative importance of epidemiological factors
The relative importance of risk factors will vary according to the species and the systems under which the animals are managed. A small number of multivariate analyses have been undertaken at the herd level in dairy populations in the USA, to rank risk factors and their impact on the occurrence of paratuberculosis (66, 84, 125, 187). In these systems, a range of different factors has been significantly associated with a higher prevalence of infection within herds. These factors have included large herd size, introduction of replacement animals, calf management and soil acidity. In Spain, flock size and high replacement rates were associated with seropositive flocks of sheep and goats (109).

Although these studies are not definitive, the knowledge of the epidemiology of paratuberculosis is adequate to assess the principal risk factors for the spread of infection between regions and premises and for transmission of infections within a particular enterprise. Paratuberculosis primarily spreads between premises by the movement of animals, and spreads within premises by direct and indirect contact between adults and young animals. Communicating and implementing strategies that effectively address these key messages remains a significant challenge.

Control strategies
Paratuberculosis spreads slowly within and between herds and flocks or regions if not controlled effectively. Experiences such as those of the sheep industries of Australia and New Zealand (130, 189) and the deer industry of New Zealand (73, 106, 107) have demonstrated that initial expectations that the disease would not become widespread were overly optimistic. Similarly, continued detection of paratuberculosis in supposed uninfected herds in the Netherlands demonstrates the insidious nature of the infection (92).

The increasing prevalence of the disease not only results in increased economic losses and elevated costs of control, but leads to a situation where effective prevention and control become increasingly difficult. The higher the prevalence of infection in a herd or flock, the less likely that all infected animals will be identified and removed before infecting others. The level of bacterial shedding rises, as does environmental contamination and the infectious load to which susceptible animals are exposed. Within regions, as the proportion of infected herds or flocks increases, animal movements become more likely to further spread disease, and sourcing of disease-free animals for restocking becomes more difficult. For these reasons, prevention should be encouraged where the disease is not already established.

The reasons for preventing paratuberculosis or controlling the disease where it is endemic may vary between regions and enterprises. The potentially severe effects of the known presence of infection on market access for livestock and on land values are significant driving-forces for prevention in regions in which the disease is uncommon. Where the disease is endemic, the potential economic losses noted previously should be considered when planning control options.

In considering control options for an infectious animal disease, the following factors and capabilities are important:
- an adequate understanding of the epidemiology of the disease
- adequate tools to halt transmission
- the diagnostic capability to discriminate between infected and non-infected animals
- an understanding of the distribution and occurrence of the disease through surveillance
- sources of disease-free replacement stock
- producer and community attitudes and support
- public health considerations
- environmental considerations
- economic benefits relative to costs
- adequate veterinary services
- adequate legislation
- adequate funding (adapted from Thrusfield [178]).

Successful control of paratuberculosis requires risk assessment and the implementation of a combination of imperfect risk management strategies aimed at preventing infection at the regional, herd and individual animal level. The
relative importance of causal factors and a range of risk management procedures will vary among different livestock industries and enterprises.

Current understanding of the epidemiology of paratuberculosis is incomplete, and although the range of diagnostic and immunological tools is limited, these tools are adequate to successfully prevent the spread of infection and to reduce the impact of the disease, especially where infection is not well established. However, no cost-effective therapy is available for the disease in agricultural species, hence eradication, other than by depopulation and decontamination of the environment, is very costly, slow and/or difficult. As demonstrated by experience in some regions of Australia, sporadic infection can be stamped-out if the available tools are aggressively applied (54, 145). In Iceland, vaccination has reduced the incidence of ovine paratuberculosis to very low levels (60). However, few cost-benefit analyses of control options for paratuberculosis appear to have been undertaken (22).

The Scientific Committee on Animal Health and Animal Welfare of the European Commission (56) recently concluded that 'the currently available evidence is insufficient to confirm or disprove that Mycobacterium paratuberculosis is a causative agent of at least some cases of Crohn's disease in man' and that 'there are sufficient grounds for concern to warrant increased and urgent research activity to resolve the issue'. Ongoing perceptions and publicity regarding a possible link between paratuberculosis infection in animals and Crohn's disease in humans is an additional factor that cannot be ignored in a world that is becoming increasingly concerned with consumer protection and the marketing of wholesome foods. Therefore, consideration of the approaches to disease control that may reduce potential contamination of animal products and the environment by M. paratuberculosis may be prudent.

Regional surveillance

Surveillance underpins prevention and control of paratuberculosis. Depending on the objectives of the control programme, surveillance may provide data for planning and monitoring disease control and may be used to identify infected populations in which control activities are to be initiated. Negative surveillance data may be used to assign some form of recognised status to a region, herd or flock. Surveillance may be based on opportunistic or passive surveillance methods, such as the following:
- notification of suspicion
- investigation of suspected clinical cases
- investigation of high-risk herds and flocks
- movement testing
- accreditation testing

The nature of these methods results in significant selection and measurement bias. Paratuberculosis is a notifiable disease in many countries, and records are maintained of herds or flocks known to be infected. However, most infections are subclinical and disincentives often exist to notifying suspicion of clinical disease. In addition, the interest and diagnostic capability of Veterinary Services vary. Records and prevalence estimates based on notification alone are therefore likely to significantly underestimate the occurrence of disease in most cases. Records of movement testing are also of limited value, as diagnostic tests for paratuberculosis have modest sensitivity. Most traded animals are healthy and young, so the predictive value of such negative tests is low. Accreditation testing may be based on higher herd level sensitivity, but participants in voluntary schemes such as the Market Assurance Programs in Australia are self-selected and data will be biased towards breeding herds and flocks that the owners believe are unlikely to be infected.

Reliable estimates of prevalence of paratuberculosis can only be achieved by implementing a surveillance strategy designed for the purpose. Such a strategy should include information collected by opportunistic methods, but also by less biased methods that have a higher herd level sensitivity over time. These include purposive surveys and abattoir surveillance for gross changes or serology and faecal culture.

Random cross-sectional surveys can produce accurate estimates of prevalence at the herd or individual animal level, but are usually relatively expensive to undertake. Achieving adequate participation in such surveys may also be difficult where known infected herds or flocks are penalised by regulatory action or restrictions on market access. Where the disease is thought to be rare, investigations should be deliberately biased to increase the pre-test probability of disease and the probability of detecting disease if present. Those areas, herds and individuals that are most likely to be infected and to react to the testing regime employed should be targeted. For instance, animals introduced from areas of higher prevalence may be targeted for investigation, and diagnostic laboratory accessions from adult cases of illthrift and diarrhoea could be routinely screened for paratuberculosis. Selection of older animals for test will usually include those with more advanced infection that are more likely to react in the tests.

Testing composite samples or screening aggregations of animals are potentially powerful and comparatively inexpensive surveillance tools. Post-mortem inspection of older animals at abattoirs has potential as a sensitive method of detecting sheep flocks with established infection (J. Denholm, unpublished findings), if complemented by animal identification systems which allow relatively easy traceback to the flock of origin. For dairy farms, regular screening for antibody of composite herd samples, such as raw milk from farm tanks (123), or antigen detection methods, such as immunomagnetic polymerase chain reaction (PCR) (113), may be used in future. Although Nielsen et al. (123) tested milk using an ELISA to estimate
approximate herd prevalence (by using sensitivity and specificity estimates to adjust the apparent prevalence), the correlation between individual serum and milk ELISA results is low (75), and the test is not sufficiently accurate to determine the status of individual herds. Methods that use PCR are highly sensitive and can be highly specific if quality control is of a high standard.

Depending on the local jurisdiction and disease control policies, screening results may be used anonymously for summary information or to detect infected herds and flocks for follow-up investigation and possibly regulatory action. The purpose and regulatory implications of surveillance are likely to be significant political and legal issues which will require resolution before testing is undertaken.

Regional risk management
Although paratuberculosis occurs virtually world-wide in agricultural species, recognised paratuberculosis-free areas exist in Australia, and some regions or countries, for instance in Scandinavia, appear to be free of ovine and/or bovine strains of the infection. As types of M. paratuberculosis vary in distribution and ability to infect different species (12, 119, 140), these types may be considered, and to some extent managed, as separate diseases. Where practicable, the protection of populations from infection with new types should be considered, if the endemic types have narrow host preferences.

Zoning is an internationally accepted means of managing animal diseases. Australia formally declared zones for sheep and cattle types of paratuberculosis in 1999 under the provisions of the nationally agreed standards for control of ovine and bovine Johne's disease. Western Australia was declared officially free of both infections on the basis of the disease control history and targeted surveillance (54, 77). Large areas of Australia where the cattle infection was known to be rare or absent were declared protected zones (145), while control zones were established in which the diseases were more common and regulatory disease control was undertaken. Relatively small regions with a high herd or flock prevalence, or no system of regulatory disease control, were declared residual zones.

Zoning can only be effective if movements of potentially infected animals can be managed to protect the status of herds and flocks in zones with higher status. Although movement controls interfere with trade and can be abused as trade barriers, zoning based on sound surveillance allows the technically justifiable regulation of movements of animals, consistent with the International Agreements on the Application of Sanitary and Phytosanitary Measures and on Technical Barriers to Trade (201).

Current international movement requirements for breeding animals, outlined in the Chapter 2.2.6. of the International Animal Health Code of the OIE, recommend certification of a negative herd history of paratuberculosis for the previous five years and a movement test on individual animals (127). As an official record of infection in a breeding herd or flock may result in restricted market access, livestock exporters may be understandably reluctant to investigate initial or later suspected cases. Furthermore, this insidious infection is highly unlikely to simply disappear from an infected herd or flock over a five year period. Therefore, the subclinical nature of paratuberculosis in most infected animals and the poor sensitivity of diagnostic tests, particularly in young animals, combine to negate the effectiveness of certification based on a negative history of clinical disease and a negative test prior to movement of the animals.

Greater confidence in the true paratuberculosis status of individual animals can be gained from assessing the status of the zone and herd or flock of origin. For instance, individual animals from a disease-free zone should be considered uninfected without further herd or individual animal testing. In regions or zones in which the disease does occur, certification of animals as negative for paratuberculosis should be based on the objectively assessed status of the herd using approved diagnostic tests.

Given the modest sensitivity of tests for paratuberculosis in individual animals, a high level of confidence in a negative herd status requires repeated herd testing over a period of time combined with biosecurity measures to prevent introduction of infection. This is the basis of herd and flock accreditation programmes such as the Voluntary Johne's Disease Herd Status Program for cattle in the USA (26), the Paratuberculosis Program for Cattle in the Netherlands (17) and the Johne's Disease Market Assurance Programs in Australia for cattle, sheep, goats and alpaca (96).

Herd-level risk management
To manage the risk posed by introduced animals at a regional level, the regulatory authority must understand and apply appropriate risk management procedures. At the herd or flock level, the owner must understand and apply similar management to an individual farm enterprise. Effective communication of the principles of paratuberculosis prevention to owners and to veterinary and non-veterinary advisers is an important component of a successful control strategy.

The risks that infection will be introduced to, and become established within a herd or flock have been outlined earlier in the section entitled 'Spread of infection between farms'.

Purchasers of breeding animals wishing to avoid paratuberculosis should be encouraged to buy from low risk areas and from herds and flocks with a negative status in recognised, transparent, high-standard market assurance or accreditation programmes. A written declaration of the paratuberculosis status of the herd or flock of origin, signed by the vendor, can be a powerful tool in further reducing the
risk. In the Netherlands, a poll-fax service and a voice response service assist the public in identifying herds within the Paratuberculosis Program, and in Australia, herds and flocks in Johne’s Disease Market Assurance Programs are listed on a public website and on a poll-fax service. A distinctive logo is used in advertisements and sale catalogues to promote these herds and flocks (Fig. 1).

Fig. 1
Logo for herds and flocks with an assessed status in the Australian Johne’s Disease Market Assurance Program

In areas in which paratuberculosis is endemic, herds and flocks that have not been objectively assessed (sometimes called ‘non-assessed’ or ‘non-suspect’) may have a high probability of being infected. Animals from these herds and flocks may present a higher risk than similar animals from known-infected herds and flocks that are successfully controlling the infection under official programmes. Similarly, non-assessed herds that rear replacements in a manner that minimises the risk of calves becoming infected should be a lower risk source of replacement animals than similar herds in the area that do nothing to protect calves.

As outlined previously, the risk posed by different classes of introduced animals varies according to the age of these animals and the degree of contact with the herd or flock.

The risk presented by animals straying from neighbouring farms will depend on the true status of the herd or flock of origin, the number and age of animals that stray and the length of time that these animals are on the farm. The true status will often not be known, but may be subjectively assessed on the bases of local prevalence and management of the herd or flock. If the risk of strays contaminating land is high, action may be warranted to restrict grazing by susceptible animals. Adult animals is not simple, especially in environments where M. paratuberculosis can survive for long periods. Collins and Morgan used a Reed-Frost approach to model this contact in dairy herds and studied the impact of herd characteristics such as herd size and replacement rates on the rate of spread (36, 37). If uncontrolled, the model indicated that paratuberculosis could infect approximately half of the herd. In practice, reducing the effective contact rate was probably between two and three in most dairy herds in the USA (37), while in the highly intensive dairy industry of the Netherlands, data from control projects indicated that the contact rate was as high as 4.2 (17).

Reducing the incidence of clinical disease and preventing infection within herds and flocks

Infectious agents spread by direct or indirect contact between infected and susceptible animals. To reduce the incidence of new infections, the effective rate of contact or the reproduction ratio, which is the average number of susceptible animals that will be infected by a single infectious animal, must be lowered to less than one. Collins and Morgan considered that the effective contact rate was theoretically likely under favourable circumstances, although this has not been proven. The risk of infection from the movement of contaminated water, dairy effluent and faecal pellets across property boundaries may be managed by placing barriers such as levee banks or fenced off buffer areas of trees or bushes across drainage lines and by limiting the access of susceptible animals to potentially contaminated areas. Using manure from other farms is an obvious potential source of infection, although effective composting will reduce the concentration of viable bacteria (144).

The prolonged survival of M. paratuberculosis in the environment makes environmental spread of infection theoretically likely under favourable circumstances, although this has not been proven. The risk of infection from the movement of contaminated water, dairy effluent and faecal pellets across property boundaries may be managed by placing barriers such as levee banks or fenced off buffer areas of trees or bushes across drainage lines and by limiting the access of susceptible animals to potentially contaminated areas. Using manure from other farms is an obvious potential source of infection, although effective composting will reduce the concentration of viable bacteria (144).

The keys to reducing the effective contact rate in infected herds and flocks are to minimise the exposure of susceptible animals to potentially infected animals and potentially contaminated environments, and to reduce the numbers of animals progressing to advanced stages of infection. This may be supplemented by increasing the herd immunity by vaccination. The mix of practicable and economically feasible solutions will vary between enterprises, so that relatively easy
changes in an intensive dairy herd may be virtually impossible in a grazing beef cattle herd. Where possible, risk assessments and management plans should be developed for individual premises.

Although experimental work has demonstrated that anti-mycobacterial therapy can lead to recovery (159), no cost-effective treatment is available for clinically infected agricultural animals (76) which invariably die or are slaughtered. Not only does this entail significant cost, but clinically affected animals are also the most potent source of infectious bacteria. Lowering the incidence of clinical disease in a herd or flock will therefore reduce environmental contamination and the incidence of new infections. Managing adult herds and flocks to reduce nutritional and lactation stress and parasite loads may also contribute to the prevention of heavy environmental contamination.

Removal of a large proportion of those animals with advanced infection may be achieved by test and slaughter programmes, but the success of these programmes in eradicating infection is limited by the relatively poor sensitivity of the available screening tests in carrier and subclinically infected animals. Therefore, identification and aggressive removal of whole groups of high-risk animals may be advisable. These may include all the progeny of an infected cow, the members of a cohort reared with infected animals, or animals that have had close contact as young animals with an infected individual. Profiling a herd based on the distribution of serological results can also be used to identify animals for early culling (80). Test and slaughter programmes are unlikely to be successful without complementary management procedures to reduce the effective exposure of young animals to infected adults and contaminated environments (37, 71).

In infected regions, the risk of inadvertently introducing infection to previously non-infected farms is constant, and many herds and flocks will be subclinically infected without the owners being aware. The implementation of practical risk management in all herds and flocks in infected regions should be encouraged.

In intensively managed herds and flocks the basic practices are as follows:
- to provide a clean environment for the delivery of young
- to ensure that a neonate receives colostrum only from its mother or from animals that have tested negative
- to separate neonate and mother within 12 h-24 h of birth
- to rear young in a clean environment, free of adult faecal contamination, on milk replacer, pasteurised or sterilised waste milk. Contamination of water and pasture used for rearing replacement animals must be avoided.

In many grazing enterprises, such as extensively grazed sheep flocks, such intervention is not possible. In addition, low test sensitivity at the individual animal level, combined with the size of herds and flocks in some regions and the costs of testing relative to the individual value of the animals, limit the available control options. In these situations, reducing contact or exposure of young animals to the more heavily contaminated environments on the farm and preparation of low-risk pastures for neonates and weaners may reduce the incidence of paratuberculosis. Lowering the stocking density on these pastures and early weaning are additional means of reducing effective contact. Vaccination may also reduce the proportion of susceptible animals in the herd or flock.

**Farm-specific control programmes**

The degree of efficacy with which an individual farm owner or manager can implement the principal biosecurity and management procedures will significantly affect the probability of success in controlling and potentially eradicating paratuberculosis from a farm. Studies of compliance with generic calf management programmes in dairy herds in the Netherlands and Australia have found compliance to be very poor (122, 202). Wells and Wagner reported that dairy farmers in the USA who were familiar with paratuberculosis did not manage herds very differently from other farmers (188).

These results indicate that a significant gap remains between recommendations for control and the successful implementation of these recommendations on farms. A programme must not only be technically sound, but must also be communicated effectively and be affordable and practicable. To be successful, the owner or manager must be committed to implementing the programme in his or her enterprise for at least one generation, so that replacement animals have a significantly lower prevalence of infection. Therefore, the personal objectives of the farmer for the farm enterprise are paramount considerations when planning an on-farm paratuberculosis management programme. Programme planning methods recently developed in the USA attempt to address this for dairy and beef cattle owners (157, 158). Individual Property Disease Eradication Plans are also prepared by sheep flock owners and advisers in Australia, and farm-specific control programmes are being trialed in dairy herds in the Netherlands.

The models developed by Collins and Morgan (36, 37) and by Groenendaal et al. (71), and adapted to Pennsylvania by Groenendaal and Galligan (69), are tools which offer the potential to prioritise control strategies, thereby allowing farmers to concentrate efforts in the most effective areas. The models emphasise the importance of management of replacement heifers to prevent infection. In intensive dairy production systems, Groenendaal and Galligan have proposed that test and slaughter strategies are unlikely to significantly affect within-herd prevalence, but that hygienic calf rearing is critical. In Pennsylvania, specialist contract rearing of heifers is thought likely to be more effective in
preventing paratuberculosis than attempting the same management on the home farm (69).

**Vaccination**

Vaccination, using attenuated and killed vaccines, does not produce a high level of protective immunity in individual animals and does not prevent infection in all animals (91). Vaccination has been demonstrated to reduce the incidence of clinical disease in cattle, sheep and goats and to reduce or delay the excretion of high concentrations of bacteria (62, 104, 160, 183). As herd immunity develops and environmental contamination declines over time, vaccination may significantly reduce the incidence of infection and clinical disease and the associated economic losses. If possible, vaccination should be used with other management procedures to reduce the exposure of susceptible animals, although the practice may be most valuable in extensively managed enterprises in which these cannot be successfully implemented.

As vaccinated animals continue to shed mycobacteria, react to serological tests for paratuberculosis (100, 166), and remain sensitised to the purified protein derivative used for the skin test for bovine tuberculosis (172), these animals should be permanently identified. Vaccines also cause a local granulomatous reaction at the site of inoculation, therefore the vaccine should be administered carefully in meat animals, in sites that can easily be trimmed from the carcass. This local reaction may be serious in humans who are accidentally inoculated (18, 133). Some countries, such as Sweden and the Republic of Ireland have prohibited the use of vaccines, while others, including Denmark and Australia, have restricted use. France was the first country to organise the control of paratuberculosis in cattle in the 1920s, by vaccination with a live attenuated vaccine. However, because the programme interfered with the eradication of tuberculosis, it was abandoned in the 1930s (182).

Vaccination of young animals remains a potentially important component of control, especially in sheep and goats, and has played a central role in many programmes. In Iceland, successful control of ovine paratuberculosis was achieved in the 1950s and 1960s by a single dose vaccination of lambs using a killed vaccine, and restricting sheep to one specific region during the eradication campaign (164). The control of paratuberculosis in sheep in Cyprus was based on vaccination of all stock with an attenuated live vaccine. No clinical cases of paratuberculosis were detected within three months of the commencement of the programme (42).

In 1942, a programme for the organised control of paratuberculosis in 138 dairy herds was implemented in the Netherlands, based on annual intradermal Johnin testing and culture of faeces from suspect cases. From 1952, a system of subsidies was implemented, through which farmers received financial compensation for the culling of clinically suspect animals. From 1958, all animals over eighteen months of age were tested using the complement fixation test and Johnin, followed by slaughter of animals with positive test results. As this approach did not lead to the desired results and costs increased substantially, a new programme was initiated, focusing on the vaccination of calves and all animals in heavily infected herds, with a killed vaccine (17). However, long-term vaccination alone did not prevent paratuberculosis transmission, therefore management and testing strategies were re-introduced to improve control (93).

In 1964, a scheme was introduced in Great Britain for voluntary vaccination of stock under the age of thirty days on infected farms with a live attenuated vaccine. Freedom from clinical disease was achieved after an average of four years, but the time taken to achieve this appeared to be strongly influenced by management practices (199).

In Norway, after several years of unsuccessful efforts to control paratuberculosis in goats by hygienic measures and the isolation and slaughter of clinically affected animals, a vaccination programme using an attenuated live vaccine in kids aged from two to four weeks was initiated in 1967. The prevalence of infection was reduced from 53% to 1%, based on post-mortem examination. Moreover, infection occurred almost exclusively in goats that had been vaccinated at over four weeks of age, or not vaccinated at all (160).

Vaccination is also used in infected sheep flocks in Spain and New Zealand, and a killed vaccine is currently being trialed for use in heavily infected sheep flocks suffering high mortality in an endemic region in Australia.

**Implementing national and regional control programmes**

In the past, several countries have developed programmes for the control and eradication of paratuberculosis in sheep, goats and/or cattle. Almost all of these programmes stressed the early identification and rapid elimination of clinically infected and excreting animals, and the implementation of preventive measures. In various states of the USA, such as Wisconsin, New York and Pennsylvania, voluntary control programmes commenced in the 1980s, based on various diagnostic methods supplemented by management recommendations for appropriate measures to prevent further transmission of *M. paratuberculosis* within and between herds (120, 156). None of these programmes has resulted in eradication or successful regional control of the disease.

Successful control at a regional or national level requires not only technical, legal and management capability, but clear achievable objectives and a strong, long-term commitment from both the affected animal industries and from governments. As cross-infection may occur among several agricultural species in a region or country, co-operation between the affected livestock industries may be essential. The goat, camelid and deer industries may be affected by
programmes primarily directed to control paratuberculosis in cattle herds and, if infection is left uncontrolled in these species, a potential reservoir for reinfection of cattle remains. Programme management structures should involve these industries.

Governments continue to support animal health programmes through technical advice and standards and by providing legislative support. However, in developed countries, the responsibility for funding operational aspects of animal health programmes is increasingly being transferred to the livestock industries. Experience in the USA (193) and Australia has demonstrated that mechanisms of equitable collection and transparent management of adequate industry funds over a prolonged period are critical elements in both initiating and maintaining support for livestock disease control programmes. As control is difficult and success or failure may only be demonstrated over a long period of time, progress must be carefully monitored and reported to interested parties (particularly to the livestock industries and individual producers involved).

Where control aims to reduce the direct impact of the disease in infected herds and flocks, the economic benefits may be largely private and sufficient to justify that the costs of control be paid by the owner. However, where quarantine and movement restrictions are imposed with the aim of reducing the spread of infection between farms and between regions, the benefits are shared by the broader livestock industry, and particularly by those producers whose negative status is being protected. Therefore, the broader industry should be expected to contribute to funding and adequately supporting those affected by the programme. If financial and social support is not provided, co-operation with surveillance and control programmes will not be sustained.

Major programmes for the control of paratuberculosis are currently operating in several countries, particularly in the cattle industries. In the USA, industry has recently been closely involved in developing national standards and guidelines (26), and in Australia, seven affected industries have a major commitment to the management and funding of control and evaluation programmes for ovine and bovine paratuberculosis (64). In the Netherlands, Sweden and France, livestock producer organisations both manage and implement cattle health programmes (17; A. Holmstrom and E. Vindel, personal communications).

A significant development in recent years has been accreditation programmes for negative herds such as the Voluntary Herd Status Program in the USA (26) and the Johne's Disease Market Assurance Programs in Australia (96). Similar programmes are operating in the Netherlands and Sweden. These utilise the high herd level sensitivity that can be gained from using the available moderately sensitive, but highly specific tests, on large numbers of animals. These accreditation programmes provide a source of low risk livestock from herds and flocks that have been tested negative and are managed to reduce the risk of infection being introduced. The highest level of accreditation is achieved after a series of negative tests for the full adult herd or flock, or a large sample of it. Some of these programmes allow an inexpensive entry level, of comparatively low assurance, based on negative testing of thirty or fifty animals. The sample sizes for large herds and flock tests are typically designed to detect a prevalence of 2% with 95% confidence. Herd testing must be complemented by management to reduce the risk of infection being introduced and spread within the herd. As the passing of time allows any infection present in the herd to progress in animals, and as older animals are replaced by animals reared under improved management, repeated negative herd tests increase the confidence that a herd is free of infection.

Paratuberculosis control and accreditation programmes rely heavily on a range of diagnostic tests, and the results of these tests can have a serious implication for the status of a region, herd or flock. Where market and/or regulatory restrictions apply to herds and flocks that are known or suspected to be infected, the financial and social impact of positive test results can be significant. Therefore, intra- and inter-laboratory quality control programmes should be an important component of any regional programme. The Johne's Disease Laboratory Approval Program in the USA (143) and the Australian National Quality Assurance Program (186) are two examples of schemes established to monitor the performance of approved laboratories by conducting serological and cultural tests on a standard sample panel.

**Developments in national paratuberculosis control activities**

**Western Europe**

Paratuberculosis is notifiable in Greece, the Republic of Ireland, Luxembourg, Norway, Switzerland, Spain and Sweden. Most countries of Western Europe do not have a strategically planned control programme. Programmes are advanced in Sweden and Norway, where the prevalence of paratuberculosis is very low and the aim is to prevent infection of non-infected populations. Sweden has performed extensive testing, and in addition, follow-up of all imported beef cattle and intensive surveillance of the contact herds have been undertaken (20, 184). Herd testing involving beef herds was initiated in 1998 and includes annual faecal sampling and culture. In Norway, paratuberculosis has been relatively common in goats, but also a small number of cattle herds have recently been found to be infected. Most of these appear to have been associated with imported cattle. Transmission from goats is thought to be the source in one case (49). Serological testing of risk populations, including all dairy herds in contact with goats, and a representative sample of the remaining cattle population has been initiated.
The Netherlands initiated a voluntary certification programme in the dairy industry in 1998 which has been strongly supported (17). The testing programme includes ten certification levels, comprising six levels for test-negative herds and four levels for herds infected or of unknown status. In negative herds, the programme aims to prevent infection and to supply low-risk replacement stock. Control in infected herds is based on education and management assistance to reduce transmission. Animals that are shedding organisms are culled as early as possible.

Denmark and France have implemented non-government industry-supported programmes in cattle herds. The programme in France is in the early phase and the main objective of the programme is to control clinical disease and reduce the risk of transmission. Only a small number of herds are currently enrolled in the programme in Denmark. Clinically suspect and faecal culture positive cows are culled, with compensation available from cattle organisations for herds which annually test all cows and implement management procedures appropriate for the farm (S. Nielsen, personal communication).

The only official programme to control paratuberculosis in small ruminants is that undertaken in Iceland (60). In many countries, the impacts of clinical disease are controlled principally by voluntary vaccination.

Central Europe

Poland, the Czech Republic, Slovakia, Hungary, Slovenia and the Republic of Croatia are the countries discussed below in relation to paratuberculosis in Central Europe.

Paratuberculosis was first diagnosed in the former Yugoslavia at the beginning of the 20th Century (185). The disease was diagnosed only occasionally in the 1960s and 1970s in imported cattle; in 1961, in Slovenia in imported Jersey cows (89); in Bosnia and Herzegovina between 1962 and 1970 (9, 10), during the same period in other parts of Yugoslavia (110, 179, 180) and in Poland in 1970 (147). The disease was described in the former Czechoslovakia: in one cow in the Czech Republic in 1962 (51), and in several animals in Slovakia in 1966 (State Veterinary Administration records).

The reported incidence increased significantly in the 1980s and 1990s, when importation of dairy and beef cattle from Western Europe commenced. Paratuberculosis was diagnosed in Hungary in imported Jersey, Holstein and Limousin cattle (101; B. Körmendy, personal communication; G. Nagy, personal communication) and in various breeds of cattle imported into the Czech Republic (79, 139, 141). The disease has been diagnosed predominantly in imported Holsteins in Slovakia (I. Melicharek, personal communication), Poland (J. Kaba, personal communication) and Slovenia (M. Ocepek, personal communication). From these imported animals, paratuberculosis has been transmitted to indigenous cattle, sheep and goat herds (134, 135, 136, 137, 138). Available data on prevalence of paratuberculosis in some countries of Central Europe are presented in Table III.

Although paratuberculosis is a notifiable disease in all countries of Central Europe, control measures vary due to limited financial resources. Testing is undertaken by serology and/or faecal culture. Vaccination against paratuberculosis is not permitted in any of these countries.

All cattle imported into the Czech Republic after 1994 were subjected to intensive surveillance for two years. Animals were examined twice a year serologically, and faecal culture was performed in the reactors. Fifty-two infected cattle herds were identified and were enrolled in a control programme (141). Approved programmes of twice-yearly serological testing and faecal culture in all animals over eighteen months of age are fully financed by the state. Serological reactors and animals shedding M. paratuberculosis are culled, with the cost borne by the herd owner or in part by an insurance company (I. Pavlik, personal communication). This programme has been successful in controlling the disease in infected herds (142).

Americas

During the 1990s, surveillance in eastern Argentina has detected a significant occurrence of paratuberculosis in cattle and sheep. Bovine paratuberculosis is subject to official disease control regulations and research is being undertaken to improve diagnostic testing for sheep and cattle (A. Bernadelli and G. Traveria, personal communications). In Mexico, bovine and ovine paratuberculosis occur as separate diseases. Vaccination is being trialled in heavily infected goat herds, and a test and slaughter approach has been attempted in some heavily infected flocks of sheep. During the current tuberculosis eradication programme, authorities have recognised the importance of paratuberculosis and the National Animal Health Committee is currently considering whether to undertake a national control programme (G. Chavez Gris and R. Cervantes, personal communication).

Since 1997, efforts to monitor and control paratuberculosis in the USA have steadily gained momentum in the individual states. This has been driven by the commitment of both national cattle organisations to educate the industries about Johne's disease and state agricultural departments dealing with the disease at a state-level. The 'education first' strategy has encouraged producers to take an active role in supporting state and federal governments to develop programmes and policies to control and eliminate paratuberculosis from dairy and beef herds. In 1998, national guidelines were developed and approved by the United States Animal Health Association (USAHA) to identify test negative status herds. In 1999, the USAHA approved a set of minimum recommendations guiding the states towards establishing complementary programmes. To date, twenty-five states have formed Johne's disease advisory committees to help develop and manage the
programme within the state, and eight state governments have donated funds to support these activities. Eleven states have control programmes in place, with 3,600 herds enrolled. Nine states have initiated herd status/certification programmes for Johne’s disease and another five are about to implement similar programmes. Overall, 525 herds have enrolled to date, and 139 herds are advancing through the herd status levels (M. Carter, personal communication).

Africa, Asia and the Pacific
In South Africa, bovine paratuberculosis is a notifiable disease, but is believed to occur only sporadically. Between 1990 and 1999, infection was confirmed in only four of seventy-four bovine cases submitted to the paratuberculosis laboratory (A. Michel, personal communication). Cases are slaughtered and compensation is provided. Ovine paratuberculosis was first confirmed in 1967, and a national survey in 1996 detected fifty-two infected flocks in the Cape Provinces (118). However, no control programme has been implemented.

In Hokkaido, Japan, an aggressive test and slaughter programme in the dairy and beef industries, with compensation for reactors, commenced in the late 1990s. Testing of all adult cattle by the absorbed ELISA was planned over a period of two years. In infected herds, testing is undertaken quarterly until a negative herd test is achieved. Herds will be declared free if four consecutive negative tests are achieved over three years. This programme is being extended to other provinces (K. Nishimori and S. Tachibana, personal communication).

Paratuberculosis is common in the cattle and sheep industries in New Zealand, and has recently become an increasing concern in the deer industry (107). Voluntary vaccination is practised in infected cattle and sheep. Although the beef cattle industry may have a relatively low prevalence of infection, more than half the dairy herds and sheep flocks in the country are thought to be infected (22). An economic assessment of control options and a consultative review with the livestock industries in the late 1990s has resulted in a decision not to pursue a national control programme.

Protection of non-infected regions and farms is a high priority of the approach in Australia. Voluntary herd and flock accreditation programmes are complemented by zoning and movement restrictions. The first Johne’s Disease Market Assurance Program was implemented in 1996 (95), and by early 2000, over 1,000 cattle herds, 700 sheep flocks, 100 alpaca herds and twenty-five goat herds had achieved a ‘monitored - negative’ status. Zoning was formally implemented in 1999 and Western Australia was declared a disease-free zone for both ovine and bovine paratuberculosis. Much of Australia is a protected zone for bovine paratuberculosis. The intensity of on-farm disease control and/or stamping-out varies according to zone status, the livestock industry involved and the funding provided in the states. In Victoria, approximately 600 cattle herds are enrolled in an official test and control programme. In south-eastern Australia, over 200 sheep flocks have been depopulated to stamp-out the infection. A major six-year research, surveillance and control programme is underway to determine the best approach for the long-term control of ovine paratuberculosis (5).

Conclusion
Paratuberculosis caused by a large variety of types of M. paratuberculosis continues to spread slowly among livestock populations worldwide. Control may be implemented to protect non-infected populations, reduce the direct impacts of the disease or to reduce contamination of animal products and the environment with M. paratuberculosis. Successful control regionally or on the farm depends on a clear understanding of the known epidemiology and pathogenesis of the infection and on the appropriate use of diagnostic and immunogenic tools.

However, the particular characteristics that make effective prevention and control of paratuberculosis a difficult long-term objective must be recognised. Inapparent infection and poor sensitivity of diagnostic tests, prolonged survival of the organism in the environment, the lack of effective therapy and limited immunogenicity of current vaccines have combined to challenge and often defeat disease control efforts. However, understanding of the disease and application of diagnostic tools are slowly improving, allowing a potentially more intelligent and scientific approach to control. To be successful, sustained community, financial and political support is required, and this will only be maintained where there is equitable support for those most affected by the control programmes.

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Prophylaxie de l'infection à *Mycobacterium avium* subsp. *paratuberculosis* chez les animaux de rente

D.J. Kennedy & G. Benedictus

Résumé
La paratuberculose ou maladie de Johne, entérite chronique due à *Mycobacterium avium* subsp. *paratuberculosis*, ne cesse de se propager parmi les animaux de rente. La prophylaxie de la paratuberculose présente des difficultés qui ne doivent pas être sous-estimées. En raison de la longue période d'incubation de l'infection, les animaux domestiques infectés ne présentent généralement pas de signes cliniques. C'est pourquoi les effets directs sur la productivité et sur le bien-être des animaux ne sont pas identifiés comme tels, ou sont jugés insuffisants pour inciter les éleveurs, l'industrie de l'élevage ou les gouvernements à s'engager dans de coûteux programmes de prévention. De plus, dans certains pays, la maladie a un impact essentiellement indirect, dû à la suspension des échanges de produits de l'élevage ou de troupeaux infectés ou au coût des mesures de prophylaxie. Dans ces conditions, les éleveurs ne sont pas toujours disposés à coopérer avec les services de surveillance, car ils craignent la détection de l'infection dans leurs troupeaux. Comme la seule politique de prophylaxie efficace rapidement est, le plus souvent, celle qui engage des programmes coûteux et à grande échelle, l'éleveur dépend de l'aide financière et du soutien de la collectivité pour affronter ce problème.

Pour que les mesures de prévention et de prophylaxie soient efficaces, les autorités sanitaires et les éleveurs doivent bien connaître la maladie de Johne et son épidémiologie, ainsi que les mesures diagnostiques et prophylactiques qui lui sont applicables. Les programmes de prophylaxie doivent être renforcés et conduits par les professionnels des secteurs concernés, car l'efficacité de ces programmes dépend d'une volonté politique soutenue et du financement adéquat des programmes de recherche, de surveillance et de prophylaxie.

Mots-clés

Lucha contra la infección de animales de renta por *Mycobacterium avium* subesp. *paratuberculosis*

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Resumen
La paratuberculosis o enfermedad de Johne, afección intestinal crónica causada por *Mycobacterium avium* subesp. *paratuberculosis*, sigue extendiéndose entre las especies de animales domésticos. La lucha contra esa enfermedad plantea dificultades que no cabe subestimar. Debido a su largo período de incubación, la paratuberculosis generalmente reviste en los animales de renta un carácter subclínico, y por ello la incidencia directa de la enfermedad en la productividad y el bienestar de los animales suele quedar enmascarada y puede parecer insuficiente para justificar que los ganaderos, la industria pecuaria o las autoridades públicas inviertan recursos considerables en programas de control. En algunos países, además, los principales efectos de la enfermedad son de tipo indirecto, fruto de la discriminación de los mercados con respecto a hatos o
rebaños infectados o de las medidas de control impuestas para reducir la transmisión de la infección. En tales circunstancias, los productores pueden ser reacios a colaborar con actividades de vigilancia susceptibles de detectar la presencia de la infección en sus rebaños. Los programas de lucha consiguen rara vez eliminar en poco tiempo la infección de un rebaño o un hato, a menos que se acompañen de un conjunto de medidas enérgicas y costosas. De ahí la necesidad de que los productores gocen de apoyo financiero y comunitario para hacer frente al problema.

Condición necesaria para el éxito de la prevención y el control de la enfermedad es que las autoridades de sanidad animal y el sector de la industria agropecuaria entiendan cabalmente no sólo la naturaleza y la epidemiología de la infección sino también la mejor forma de aplicar medidas de diagnóstico y control. Es fundamental que se instituyan mecanismos de apoyo a los programas de lucha liderados por los sectores ganaderos afectados, ya que sin voluntad política continuada y sin los fondos necesarios para la investigación, la vigilancia y el control, esos programas tienen escasas probabilidades de éxito.

**Palabras clave**

**References**


172


