

Note from the Editor

In 2016, there were about 150 publications relating to paratuberculosis. The themes discussed in the scientific literature from the last three months are reflected in the cover image of this issue of the newsletter. Does this reflect your research activities?

What this image does not capture adequately is the global situation for paratuberculosis. Is this a disease of importance compared to the prevalence of other animal diseases in your region? How does each country attempt to control paratuberculosis? In this edition, Søren Nielsen discusses details of the Danish control program over the past ten years. Contact me if you would like to share news from your part of the world.

This edition also includes a draft document on guidelines for movement of livestock in relation to MAP infection. The IAP governing board would like your thoughts on this document.

As the end of the year approaches, whether you are sheltering from the summer heat like I am in the southern hemisphere or keeping warm at the other end of the world, I would like to wish you a very happy and safe holiday season!

Kumi de Silva



IAP business

IAP General Membership Meeting Minutes 13ICP, Nantes, France; July 22, 2016

Presiding: Dr. Ramon Juste

- 1) Meeting called to order at 17:30

- 2) President's report (brief synopsis of Board activities since 12ICP and of the Governing Board meeting:
 - a. Governing Board set member's discount for the meeting to be roughly equal to 2 years' dues
 - b. 12ICP was a scientific and financial success. The LOC returned the cash advanced for start-up funds, and returned an additional USD8000 profit.
 - c. Open Access subsidy has been discontinued. Board will be investigating a new initiative to provide a subsidy to foster international collaboration in research.
 - d. The issue of information disclosure during ICP scientific discussions was discussed. Some members expressed concern about presenters unwilling to disclose proprietary information (eg culture media composition) during their presentations. The Board did not recommend a policy on this subject, but did offer the suggestion to LOC's that speakers should be required to provide a financial disclosure/conflict-of-interest statement at the start of each presentation.

- e. Membership initiative – the new Editor in Chief, Kumi de Silva when compiling the bibliography of recent publications for the Newsletter, will check to see if authors are members of the IAP, and invite those who are not members to join.

- 3) Secretary-Treasurer report:

- a. Financial - the balance remains stable since the same time before 12ICP at ~\$60,000. Revenues consist of meeting profits and dues, which are offset by ICP expenses such as Helping Hands and Merkal scholarships, and some PayPal service fees.

- b. The membership totals 161 members, down slightly from 12ICP. Further discussion below in New Business.

- 4) International Trade Guidelines

- a. At the request of the Membership at the 12ICP, a task force, headed by Dr. David Kennedy, was charged with creating Guidelines for International Trade document. This was submitted to the Board for approval. However, the Board determined that if this document was to be an official position or consensus paper of the IAP, that the General membership should have the opportunity to comment.

The document will be placed on our website with an open comment period.

5) Helping Hands Awards – The 5 winners of the Helping Hands awards were presented their certificates and recognized:

- a. Kundan Kumar Chahubey – India
- b. Sujata Hariharan – India
- c. Kamal Raj Acharya – Nepal
- d. Ana Carolina Silva Faria – Brazil
- e. Marat Kuibagarov – Kazakhstan

6) The Merkal Awards were presented their plaques during the scientific sessions.

The winners were:

- a. Hannah B. Pooley – Australia
- b. Caroline Ritter – Canada

7) 13ICP Report – Christine Fourichon, LOC Chair

- a. 256 attendees from 29 countries
- b. The budget is expected to return a positive balance to the ICP treasury
- c. Dr. Fourichon recognized the 20 members of the Scientific Committee

8) 14ICP Report

- a. The 14 ICP will be held in Cancun, Mexico, organized by Dr. Gilberto Chavez-Gris. The dates will be June 3-7 2018. The presentation was postponed to the closing session of the Congress.

9) 15ICP Report

- a. The 15ICP will be held in Dublin Ireland in 2020, hosted by Dr. Peter Mullaney. Excellent bids were also received from Jaipur India (Jagdip Singh Sohal and Shoorvir Singh) and Edinburgh, Scotland (Karen Stevenson).

10) President's comments

- a. Dr. Juste expressed the importance of younger members, and younger conference delegates that are not IAP members to become involved in the IAP.

11) New Business

- a. A discussion ensued regarding membership and the need for a strategic evaluation of gaps in our membership (eg. Geographical, age demographics, scientific disciplines such as human health, etc) and how these potential members can be recruited.

- b. Motion (Ray Sweeney, seconded Mike Collins): The President shall appoint a committee to develop and implement a strategic plan to expand/improve the IAP membership. Discussion against the motion suggested this should be a Board activity. Discussion in favor pointed out that some of the underdeveloped nations do not have Board representation. [Secretary's note—the motion did not state

whether the composition of the committee would be from the Board only or include General members]. The motion carried 36-10.

c. Motion from Dr. Robert Greenstein (seconded) that the President appoint a committee of 3 members to establish scientific goals for the association. Discussion included the point that the motion would contradict the one of the missions of the IAP as stated in the bylaws, specifically to “foster scientific freedom”. The motion was defeated.

12) Webmaster Report - Rod Chiodini

a. A new website for the organization has been created:

www.paratuberculosis.net

b. Dr. Chiodini demonstrated some features of the website, including the

members-only area which has a discussion area which he hopes will foster exchange of ideas amongst members.

c. The demonstration included the emphasis that when making payment, the user must return to the IAP website from the Paypal site to insure that payment is credited to the members account. Comprehensive instructions were published in the Newsletter of December 2015. http://www.paratuberculosis.net/newsletters/PtbNL_12-2015.pdf

13) Adjournment

a. The meeting was adjourned at 19:10

*Recorded by:
Raymond W. Sweeney, VMD
Secretary-Treasurer IAP*

Guidelines for certification for movement of livestock for *Mycobacterium avium* subsp. *paratuberculosis* (MAP) infection

This document was requested by the IAP Governing Board and was prepared by a working group of IAP members headed by Dr. David Kennedy. The Board seeks comments from the IAP membership prior to consideration for approval. Please forward all comments to Prof. Ray Sweeney (rsweeney@vet.upenn.edu) by 01 March 2017.

Internal Association for Paratuberculosis

Guidelines for certification for movement of livestock for

***Mycobacterium avium* subsp *paratuberculosis* (MAP) infection**

Purpose

To provide guidance for scientifically sound risk assessment of MAP infection that can be used by risk managers to reduce the risk of spread of MAP between populations of **livestock**, consistent with WTO standards for international trade.

NOTE: These guidelines do **not** consider the risks of

- MAP infecting people, nor
- Transmission via bovine semen (EFSA 2004).

Introduction

Despite increasing understanding of MAP and paratuberculosis (Johne's disease), little progress has been made in limiting the spread of MAP between regions and countries. Interest in MAP often only increases in countries and regions as they realise, too late, that they have endemic Johne's disease (JD) or when another country wants to include MAP in health certification for animals or products.

Article 3 of the World Trade Organization *Agreement on the Application of Sanitary and Phytosanitary Measures* (the SPS Agreement, Ref) states that

“To harmonize sanitary and phytosanitary measures on as wide a basis as possible, Members shall base their sanitary or phytosanitary measures on international standards, guidelines or recommendations, where they exist.”

There has also been little progress in developing and applying scientifically sound movement requirements for MAP. Since 2001, efforts through official channels such as OIE have not borne fruit and, for the past decade, the OIE Terrestrial Animal Health Code Chapter on Paratuberculosis has provided little guidance in this area (OIEa 2015). Concern about the low accuracy of diagnostic tests in individual animals has been a major reason that the Code chapter has not been developed further. However, the OIE Diagnostic Manual (OIEb 2015) has been updated to also refer to diagnostic testing at herd level. Herd level testing and other certification based on large scale surveillance has been implemented for other diseases for which negative individual animal tests provide limited assurance, such as bovine brucellosis, bovine tuberculosis and the prion diseases.

The International Association for Paratuberculosis (IAP) agreed in 2015 to develop its own guidelines for importers and exporters who want to implement rational movement requirements,

based on current understanding of managing MAP risks and consistent with the principles of the SPS Agreement. These recognise and recommend risk management that is justified and appropriate for different situations.

Rationale

One of the *Basic Obligations* outlined in Article 2 of the SPS Agreement is that.

“Members shall ensure that any sanitary or phytosanitary measure is applied only to the extent necessary to protect human, animal or plant life or health, is based on scientific principles and is not maintained without sufficient scientific evidence, except as provided for in paragraph 7 of Article 5.”

which states that,

“In cases where relevant scientific evidence is insufficient, a Member may provisionally adopt sanitary or phytosanitary measures on the basis of available pertinent information, including that from the relevant international organizations as well as from sanitary or phytosanitary measures applied by other Members. In such circumstances, Members shall seek to obtain the additional information necessary for a more objective assessment of risk and review the sanitary or phytosanitary measure accordingly within a reasonable period of time.”

Flawed Requirements

Many official movement protocols have hindered, rather than enhanced, control of MAP infection as they are scientifically flawed and ineffective.

Certification based on the recent herd or flock history of clinical disease and on testing of the individual animals to be moved is still common for a broad range of types of animals. However, the *negative predictive value* of such certification from endemically infected regions (ie the probability that a test negative animal is truly free from MAP) approaches zero.

- Clinical disease is not a sensitive indicator of MAP infection and requiring a negative clinical history discourages farmers who want to trade from investigating or reporting suspect cases.
- It encourages traders to move, or falsify the identity of, animals so as not to exclude farms with a positive history from trading opportunities.
- Movement testing is often of consignments of young animals and sometimes with outdated tests.

Such protocols also have perverse effects by discouraging participation in herd classification programs and by penalising regions and herd owners actively trying to control MAP through surveillance, testing and vaccination.

Unjustified Requirements

The World Trade Organization Agreement on the Application of Sanitary and Phytosanitary Measures (the SPS Agreement, Ref) opens,

“*Reaffirming* that no Member should be prevented from adopting or enforcing measures necessary to protect human, animal or plant life or health, subject to the requirement that these measures are not applied in a manner which would constitute a means of arbitrary or unjustifiable discrimination between Members where the same conditions prevail or a disguised restriction on international trade”

Furthermore, Article 2 paragraph 3 states that,

“Members shall ensure that their sanitary and phytosanitary measures do not arbitrarily or unjustifiably discriminate between Members where identical or similar conditions prevail, including between their own territory and that of other Members.”

And Article 5 paragraph 4 includes,

“Members should, when determining the appropriate level of sanitary or phytosanitary protection, take into account the objective of minimizing negative trade effects.”

Yet some countries, in which MAP is endemic, require certification when they themselves have no significant surveillance or control programs in place. And some markets require negative farm level assurance for young animals destined for slaughter in the short term.

In contrast, the few regions that have vigorously controlled and stamped out MAP, may struggle for recognition and acceptance that they should set an allowable level of protection and require appropriate entry requirements based on risk analysis.

MAP Risk Assessment

Risk assessment and management programs (RAMPs) have become the keystone of modern on-farm JD control programs. Many of the same principles can be applied at a regional level.

Article 5 of the SPS Agreement defines risk assessment as

1. “Members shall ensure that their sanitary or phytosanitary measures are based on an assessment, as appropriate to the circumstances, of the risks to human, animal or plant life or health, taking into account risk assessment techniques developed by the relevant international organizations.
2. “In the assessment of risks, Members shall take into account available scientific evidence; relevant processes and production methods; relevant inspection, sampling and testing methods; prevalence of specific diseases or pests; existence of pest- or

disease-free areas; relevant ecological and environmental conditions; and quarantine or other treatment.”

The epidemiology and pathogenesis of MAP infection is complex and varies between species. However, on balance, the scientific evidence indicates that the following key characteristics of MAP infection should be considered in assessing the risks of livestock being infected with MAP

At the **herd or population level**:

1. MAP is endemic in developed livestock industries worldwide and has been spreading around the world with the movement of livestock for over a century.
2. Any country that has imported large numbers of livestock in recent decades from developed livestock industries is likely to have endemic MAP infection unless it has taken sound and vigorous action to reduce the risk of entry and/or to stamp it out.
3. The likelihood that a country, region or herd/flock is not infected can only be demonstrated by ongoing negative herd or population testing and active surveillance on a large scale over long periods.
4. A negative clinical history of MAP infection has a low negative predictive value of herd or flock status.

At the **individual animal level**:

1. Animals may become infected at any age but are most susceptible to becoming infected in the first few months of life.
2. Infected animals may excrete some MAP organisms at any stage but the likelihood and rate and amount of excretion increases as the infection progresses with age.
3. Diagnostic tests usually have low sensitivity until the later stages of infection and so a negative test of an individual animal has a low predictive value.
4. Clinical signs of Johne’s disease occur late in infection and are not pathognomonic; the absence of clinical signs usually has a low predictive value in determining whether an animal is infected.
5. The most important source of MAP is faeces.
6. Infectious MAP organisms survive in the environment in large numbers for months with longer survival in areas protected from extreme heat (Jørgensen, 1977; Whittington et al 2004; Eppleston et al 2014).
7. MAP strains that have adapted to one species can infect others, but usually at a lower incidence (Verna et al 2007).

MAP Risk Management

The results of risk assessments are not perfect, largely because of uncertainties in the input parameters and assumptions. Therefore importing countries and regions that require certification for MAP should take responsibility for preventing MAP spreading in their own areas, both from local animals and from imported animals, should it be inadvertently introduced.

The likelihood of MAP infection spreading from introduced animals and infecting populations into which they are introduced may be **managed** by:

1. Preventing exposure of susceptible animals to infectious sources, especially feed, water and other materials contaminated by faeces.
2. Removing from the population introduced and exposed animals that are suspected of being infected.
3. Removing MAP from contaminated environments and disposing of contaminated materials.
4. Importing regions may determine that MAP strains that are adapted to different species (eg cattle and sheep strains) constitute epidemiologically distinct infections for the purposes of managing their risk.

Although not permitted in all countries, increasing the immunity of susceptible animals by vaccination has also been successfully used to reduce the risk of disease spread in exposed sheep and goats. However, evidence of the efficacy of MAP vaccination is still missing in some species, notably cattle.

Risk Classifications of Areas

Free and low-prevalence areas are recognised under Article 6 of the SPS Agreement:

2. “Members shall, in particular, recognize the concepts of pest- or disease-free areas and areas of low pest or disease prevalence. Determination of such areas shall be based on factors such as geography, ecosystems, epidemiological surveillance, and the effectiveness of sanitary or phytosanitary controls.
3. Exporting Members claiming that areas within their territories are pest- or disease-free areas or areas of low pest or disease prevalence shall provide the necessary evidence thereof in order to objectively demonstrate to the importing Member that such areas are, and are likely to remain, pest- or disease-free areas or areas of low pest or disease prevalence, respectively. For this purpose, reasonable access shall be given, upon request, to the importing Member for inspection, testing and other relevant procedures.”

For the purpose of these guidelines it is recommended that four concepts for area classifications be used:

Free Area: A country, zone or compartment in which MAP infection is notifiable and extensive and large scale surveillance for MAP infection by the animal health authority has not identified endemic infection for ten years or where infection has been introduced it has been demonstrably stamped out by slaughter and intensive tracing of suspect infection and intensive surveillance has not identified MAP for 2 years. A Free Area will retain its status as long as appropriate area biosecurity and surveillance are maintained.

Eradication Area: A country, zone or compartment in which MAP infection is notifiable and extensive and large scale compulsory surveillance for MAP infection by the animal health authority continues to demonstrate a low herd prevalence of infection and where the herd prevalence of infection is demonstrably being reduced as infection is stamped out.

Officially sanctioned and recognised voluntary or compulsory herd certification programs based on negative herd and/or flock testing and surveillance may also operate to objectively classify herds and/or flocks for MAP risk.

Certification Area: A country, zone or compartment in which an officially sanctioned and recognised voluntary certification program based on sound farm biosecurity and negative herd and/or flock testing and surveillance operates to objectively classify herds and/or flocks for MAP risk.

Other Area: All other countries and regions.

Herd Classification

A herd classification program should satisfy the following criteria:

- a. Sanctioned and recognised by the official animal health authority of the Area.
- b. Herds and flocks are under the supervision of a veterinarian who has been trained and approved for the purpose of the program.
- c. An officially recognised register of classified herds and flocks.
- d. Within each herd or flock the program will include:
 - permanent individual animal identification.
 - traceability of animals entering and leaving.
 - a farm-level biosecurity and management component to minimise the probability of MAP entering and spreading.
 - screening of adult animals by a sensitive and specific diagnostic test that is recommended by the IAP and approved by the regulator for the purpose.
 - a test-strategy that appropriately documents a specific probability of freedom from infection

For the purposes of these guidelines a single herd or flock classification is proposed, **MAP Certified**, which satisfies the importing Area's appropriate level of protection and is defined as follows:

- a. Located within an Eradication Area or a Certification Area which is under the control of the animal health authority which also sanctions and recognises the herd classification program for MAP, and
- b. Taking into consideration its location, history and management, the herd or flock has

- i. implemented biosecurity measures to minimise the likelihood of introduction and/or spread of MAP, and
- ii. repeatedly screened a representative sample of adult animals from the herd or flock (or the whole adult herd/flock) using OIE recommended tests and appropriate sample sizes to provide a specified level of confidence of detecting a specified low prevalence of infection (if present). See Martin et al (1993) and MacDiarmid (1988) and More et al (2013) for more information.

Individual programs may use other and/or additional classifications to denote various risk statuses.

Recommended tests

Numerous tests have been developed for detection of statuses related to MAP, but few have been evaluated using state-of-the-art diagnostic test evaluations. (See Table 1 Test methods available for diagnosis of paratuberculosis and their purpose in the OIE Terrestrial Manual Chapter 2.1.11 adopted 2014).

One or two target conditions are relevant to trade of livestock:

- **MAP infected animal** is any animal carrying MAP intracellularly,
- **MAP exposed animal** is any animal that has been exposed to MAP in their lifetime. They can thus be MAP infected or merely have immune responses following exposure to MAP.

For **MAP infection**, OIE recognises four diagnostic tests: indirect antibody ELISA (for serum or milk), faecal PCR and faecal bacteriological culture and the agar gel immunodiffusion AGID for serology in small ruminants.

For **MAP exposure**, interferon-gamma ELISA is also a potential option (Nielsen, 2014). However, the latter has so far been insufficiently evaluated and is thus not a current option.

Therefore, the antibody ELISA, the faecal PCR and faecal culture are the current tests of interest. It is important to decide if MAP exposure should be included as a target condition, because PCR and faecal culture may be considered 100% specific if “exposure” is the target condition. However, if exposure should be excluded, then it is possible that false-positive reactions occur, particularly in animals originating from high-prevalence herds (Kralik et al., 2014; Whitlock et al., 2009). The result is a specificity which may be around 98% for culture (Nielsen et al., 2002), and perhaps even lower for PCR, if the analytical sensitivity is lower than for culture.

For the combined target condition, ie MAP exposure or MAP infection, the sensitivity of PCR is likely to be the highest, followed by culture and ELISA. However, the specific test that is used should be evaluated for the specific purpose prior to use in a certification programme.

Test strategies

The diagnostic sensitivity of does not only depend on the diagnostic test, but also the target population. The age-distribution affects test sensitivity, so a young population will have a lower average sensitivity, because some infections will not have progressed to detectable stages, whereas a very old population may have many animals that are more likely to have survived because they were un-infected (healthy worker survivor bias should be avoided). Therefore, the highest sensitivity can likely be achieved in the age-groups where most animals start excreting detectable amounts of bacteria or sero-converting, that is from approximately 2 to 6 years of age (Nielsen and Ersbøll, 2006).

The negative predictive value of a test on a single animal is of limited value, whereas it is possible to estimate the probability of an animal being free of MAP infection if multiple animals from the same herd or flock have been tested (Sergeant et al., 2008; More et al., 2013). Although herd level sensitivity may be higher than sensitivity at the individual level, sampling on one occasion is usually not sufficient to achieve a high probability that the herd is free from MAP. In such cases, repeated sampling can be applied until the desired level of confidence is reached.

Prior information about the prevalence of MAP in the region and herd of origin and the probability of introduction of MAP into the herd can then be used to infer about the individual. Higher probabilities of existing infection, or of introduction of infection, will increase both the number of samplings and the period of time required to attain a high level of confidence of freedom.

Acceptable Level of Protection/ MAP Certification

Livestock

Based on these principles the following levels of protection and certification requirements are recommended for Areas importing different types of livestock from different Areas.

MAP status of Importing Area	MAP status of Exporting Area	Type of animal	Acceptable Level of Protection/ MAP Certification
Free Area	Free Area	All	Throughout their lifetimes the animals have only resided in a Free Area or have satisfied the requirements to be introduced to the Free Area.
	Eradication Area	Animals for breeding Other restocking (including feeding for slaughter, but not in quarantine).	Throughout their lifetimes the animals have only resided in a MAP Certified herd or flock.
		Animals for confined feeding for slaughter, in quarantine. Animals for immediate slaughter	No requirements. (The importing regulator will enact quarantine procedures that are sufficient to manage the risk)
	Certification Area	Animals for breeding Other restocking (including feeding for slaughter but not in quarantine).	Throughout their lifetimes the animals have only resided in a MAP Certified herd or flock

		Animals for confined feeding for slaughter, in quarantine. Animals for immediate slaughter	No requirements. (The importing regulator will enact quarantine procedures that are sufficient to manage the risk)
	Other Areas	Animals for breeding Other restocking (including unconfined feeding for slaughter).	Not permitted
		Animals for confined feeding for slaughter, in quarantine. Animals for immediate slaughter	No requirements (The importing regulator will enact quarantine procedures that are sufficient to manage the risk)
Eradication Area	Free Area	All	Throughout their lifetimes the animals have only resided in a Free Area or have satisfied the requirements to be introduced to the Free Area.
	Eradication Area	Animals for breeding Other restocking (including unconfined feeding for slaughter).	Throughout their lifetimes the animals have only resided in a MAP Certified herd or flock.
		Animals for confined feeding for slaughter Animals for immediate slaughter	No requirements (The importing regulator will enact quarantine procedures that are sufficient to manage the risk)
	Certification Area	Animals for breeding Other restocking (including unconfined feeding for slaughter).	No requirements. (The importing owner will manage the risk.)

		Animals for confined feeding for slaughter Animals for immediate slaughter	.
	Other Areas	Animals for breeding Other restocking (including unconfined feeding for slaughter).	Not permitted
		Animals for confined feeding for slaughter Animals for immediate slaughter	No requirements
Certification Area	All Areas	All	No requirements. (The importing owner will manage the risk.)
Other Area	All Areas	All	No requirements

Embryos that have been sourced from donors that were clinically healthy at the time of collection and have been treated, handled and stored according to the procedures of the International Embryo Transfer Society (Ref) may be imported into any Area.

Manure. Faeces is the most important carrier of MAP. The identification and traceability of manure is problematic and therefore all manure should be assessed as high risk unless it is derived from a Free Area. Managing the risk presented by manure is also difficult as large numbers of MAP organisms can be dispersed over large areas by the movement of contaminated dust and water (Refs). The risk may be reduced by containing and composting manure at high temperatures (Detail and refs)

References

- Anon. The Risk of Transmission of Mycobacterium avium subsp. paratuberculosis via Bovine Semen. *The EFSA Journal* (2004) **110**, 1-59.
- Eppleston J, Begg DJ, Dhand NK, Watt B, Whittington RJ, 2014. Environmental survival of Mycobacterium avium subsp. paratuberculosis in different climatic zones of eastern Australia. *Appl Environ Microbiol.* 80:2337-42.
- Jørgensen JB., 1977. Survival of Mycobacterium paratuberculosis in slurry. *Nord. Vet.-Med.*, 29: 267-270.
- Kralik P, Pribylova-Dziedzinska R, Kralova A, Kovarcik K, Slana I, 2014. Evidence of passive faecal shedding of Mycobacterium avium subsp. paratuberculosis in a Limousin cattle herd. *Vet J.* 201:91-4.
- MacDiarmid, S.C., 1988. Future options for brucellosis surveillance in New Zealand beef herds. *New-Zealand-Veterinary-Journal* 36, 39-42.
- Martin, S.W., Shoukri, M., Thorburn, M.A., 1992. Evaluating the health status of herds based on tests applied to individuals. *Prev. Vet. Med.* 14, 33-43.
- More SJ, Sergeant ES, Strain S, Cashman W, Kenny K, Graham D, 2013. The effect of alternative testing strategies and bio-exclusion practices on Johne's disease risk in test-negative herds. *J Dairy Sci.* 96:1581-90.
- Nielsen SS, Ersbøll AK, 2006. Age at occurrence of Mycobacterium avium subspecies paratuberculosis in naturally infected dairy cows. *J Dairy Sci.* 89:4557-66.
- Nielsen SS, Grønbaek C, Agger JF, Houe H, 2002. Maximum-likelihood estimation of sensitivity and specificity of ELISAs and faecal culture for diagnosis of paratuberculosis. *Prev Vet Med.* 53:191-204.
- OIE a. *Terrestrial Animal Health Code 2015*. Chapter 8.12 Paratuberculosis. http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_paratuberculosis.htm. (Accessed 17 Feb 2016).
- OIE b. *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2015*. Chapter 2.1.11. Paratuberculosis (Johne's disease). http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.11_PARATB.pdf. (Accessed 17 Feb 2016).
- Sergeant ES, Nielsen SS, Toft N, 2008. Evaluation of test-strategies for estimating probability of low prevalence of paratuberculosis in Danish dairy herds. *Prev Vet Med.* 85:92-106.
- Verna AE, Garcia-Pariente C, Muñoz M, Moreno O, García-Marin JF, Romano MI, Paolicchi F, Pérez V, 2007. Variation in the immuno-pathological responses of lambs after experimental infection with different strains of Mycobacterium avium subsp. paratuberculosis. *Zoonoses Public Health.* 54:243-52

Whittington RJ, Marshall DJ, Nicholls PJ, Marsh IB, Reddacliff LA, 2004. Survival and dormancy of Mycobacterium avium subsp. paratuberculosis in the environment. Appl Environ Microbiol. 70:2989-3004.

Whitlock RH, Fyock T, Schukken Y, Van Kessel J, Karns J, Hovingh E, Smith J, 2009. Passive MAP fecal shedding in dairy cattle. Proceedings of the 10th International Colloquium on Paratuberculosis, 9-14 August 2009, Minneapolis, Minnesota, USA, p. 196.

World Trade Organisation. Agreement on the Application of Sanitary and Phytosanitary Measures

https://www.wto.org/english/docs_e/legal_e/15-sps.pdf (Accessed 17 Feb 2016)

END

13 May 2016

FOR IAP BOARD APPROVAL

Developments in the Danish control programme on paratuberculosis 2006-2016

Søren Saxmose Nielsen
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Paratuberculosis has been a topic of attention in Denmark ever since Professor Bernhard Bang was first notified by veterinarians P.H. Nielsen and J. Hansen about cases of chronic diarrhoea on farms in the island of Lolland that had occurred in the 1880s and 1890s (Bang, 1909). Although paratuberculosis has been present in many European countries such as Belgium, England, Germany, Switzerland, and the Netherlands for more than a century (Bang, 1909), the prevalence is still largely uncertain in most countries, although many herds are presumed to be infected although generally with a low within-herd prevalence (Nielsen and Toft, 2009). The European Productivity Agency of the Organisation for European Economic Co-operation in 1956 provided a report on control of paratuberculosis because it had been concluded that the infection had a severe impact on productivity in many member countries (European Productivity Agency, 1956).



In Denmark, the veterinary authorities in the 1980s noted that many herds were in “peaceful coexistence” with the causative bacterium, *Mycobacterium avium* subsp. *paratuberculosis* (MAP), the prevalence of clinical cases is low and results in a limited financial loss of 1%, and a highly dynamic cattle sector with many cattle movements would make it difficult to control paratuberculosis. In the following two decades, the control efforts were therefore largely limited to individual herds suffering severe losses, while few centralised efforts were in place.



The prevalence of infected herds was largely unknown towards the end of the century, but in 1998 and 1999, a number of prevalence studies were carried out suggesting that more than half of the Danish dairy herds were infected. More “precisely” (but still not very precise), the prevalence of infected herds was probably 80-90%, and the median within-herd prevalence perhaps 10-15%. These estimates were associated with a high degree of uncertainty, but were nonetheless used by the Danish dairy industry to decide that a control programme should be established. The Danish programme, Operation Paratuberculosis, was launched in 2006 as

a voluntary risk-based control programme aiming to reduce the prevalence of paratuberculosis in Denmark and to provide farmers and advisors with tools to do so (Nielsen et al., 2007), and the programme is still in existence today.

The programme is risk-based meaning that high-risk animals are identified and should be managed according to a specific set of guidelines, whereas low-risk animals can be managed without specific requirements (Nielsen, 2009). Separation of high and low risk animals is a requirement, and milk antibody ELISA of samples from the milk recording scheme is used for this purpose. The test strategy was decided centrally to include 4 annual herd screenings of all lactating animals. Whether farmers actually implemented the recommended practices following receipt of the test-results in the tools provided, were up to the individual, but they could not avoid the testing and thus also testing costs. All test costs have been carried by the farmer throughout the programme. The farmers have been informed that false-positive reactions are highly likely. The specificity of the test used since October 2008 has in practice been estimated to 98.7% (Nielsen et al., 2013), but when interpreted based on repeated testing, the risk of false-positives should be reduced significantly. Still, farmers were advised to

do follow-up culture of faecal samples if they were uncomfortable with the risk of false-positives. Limited, if any, follow-up diagnosis using culture has been used since 2006, while approximately 5.6 million ELISA results have been reported from 1.1 million animals in more than 2000 different herds.

Not all herds follow the recommendations and only one recommendation has been associated with a decrease in the test-prevalence, namely test-and-cull (Nielsen and Toft, 2011).

There can be multiple reasons for this, but a main reason may be failure to actually capture how well farmers follow the recommendations. Nonetheless, the true within-herd and between-herd prevalences have been estimated to decrease (Verdugo et al., 2015).

Recently the within-herd apparent prevalence has started to increase (Figure 1). The level of participation has also decreased significantly the past 5 years, both cow- and herd-level participation (Figure 1). The reasons that farmers are

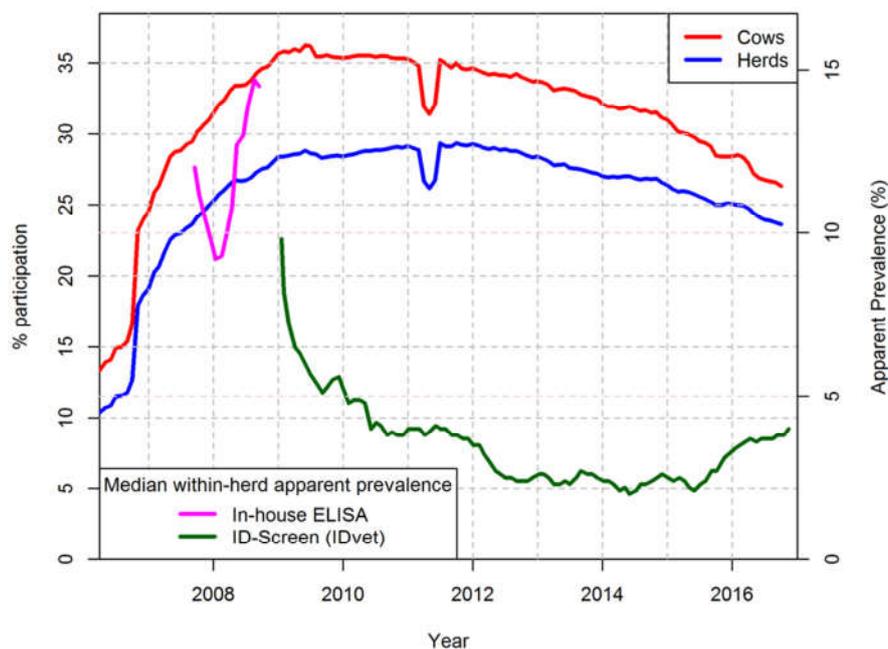


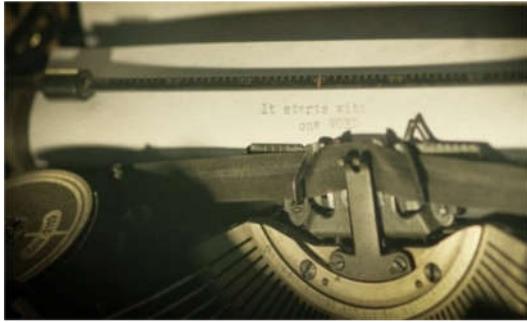
Figure 1. Developments in the level of participation and the apparent prevalence in the Danish programme on paratuberculosis from 2006 to 2016

By 1 October 2016, 3106 dairy herds including 562000 cows were present in Denmark, while 5413 herds had 552000 cows when the programme started in March 2006.

leaving the programme are largely unknown, but it could be speculated that a decreasing prevalence and lack of noticeable effects from the infection could lead many farmers to leave the programme. Furthermore, a financial crisis in dairy farming requests that many farmers cut costs, and test costs can be high, especially if they are not used for managing the infection anyway. Lastly, the programme is a control programme with no options for surveillance. This may be changed in the near future, so that both farmers wishing control and surveillance can be included in the programme at costs that suit their specific needs.

References

- Bang, B., 1909. Kvægets smitsomme kroniske Tarmbetændelse. *Maanedsskrift for Dyr læger*, 21: 513-548 (in Danish).
- European Productivity Agency, 1956. Control of Johne's disease in cattle, sheep and goats. Project no. 207. 202 pp.
- Flensburg J. C.; Munck C., 1980. Erfaringer fra veterinærdirektoratets arbejde med paratuberkulose. *Dansk Veterinærtidsskrift*, 63: 806-811 (in Danish).
- Nielsen SS, 2009. Use of diagnostics for risk-based control of paratuberculosis in dairy herds. *In Practice*, 31, 150-154.
- Nielsen SS, Toft N, 2009. A review of prevalences of paratuberculosis in farmed animals in Europe. *Prev Vet Med*, 88, 1-14.
- Nielsen SS, Toft N, 2011. Effect of management practices on paratuberculosis test-prevalence in Danish dairy herds. *J Dairy Sci*, 94, 1849-1857.
- Nielsen SS, Jepsen ØR, Aagaard K, 2007. Control programme for paratuberculosis in Denmark. *Proceedings of the 1st ParaTB Forum, Shanghai, China, Oct. 19, 2006. Bulletin of International Dairy Federation*, 410, 23-29.
- Verdugo C, Toft N, Nielsen SS, 2015. Within- and between-herd prevalence variation of *Mycobacterium avium* subsp. *paratuberculosis* infection among control programme herds in Denmark (2011 - 2013). *Prev Vet Med*, 121: 282-287.



The success of our Association depends heavily on the continued involvement of its members; we need to interact not just at the biannual meetings but also in the years in-between. I would like to encourage you to engage in these discussions via the [website](#).

Paratuberculosis news



Emeritus Professor William H. Fales of the University of Missouri College of Veterinary Medicine was recently inducted into the Missouri Veterinary Medical Foundation (MVMF) Veterinary Honor Roll. Dr. Fales has been a member of the IAP for many years.

The IAP newsletter invites articles about your research group or research activities. Please [email](#) the Editor if you would like to contribute.

Upcoming events

The 14th International Colloquium on Paratuberculosis will be held in Cancun, Mexico from June 3-7 2018



More information at <http://14thicp.mx/>

The 15th ICP will be held Dublin, Ireland in 2020

Recent publications

- Al-Mamun, M. A., R. L. Smith, Y. H. Schukken and Y. T. Grohn (2016). "[Modeling of Mycobacterium avium subsp. paratuberculosis dynamics in a dairy herd: An individual based approach.](#)" J Theor Biol 408: 105-117.
- Albuquerque, P. P., A. S. Santos, O. L. Souza Neto, P. C. Kim, E. F. Cavalcanti, J. M. Oliveira, R. A. Mota and J. W. Junior (2016). "[Detection of Mycobacterium avium subsp. paratuberculosis in bovine milk from the state of Pernambuco, Brazil.](#)" Braz J Microbiol.
- Arango-Sabogal, J. C., O. Labrecque, J. Pare, J. H. Fairbrother, J. P. Roy, V. Wellemans and G. Fecteau (2016). "[Evaluation of a PCR assay on overgrown environmental samples cultured for Mycobacterium avium subsp. paratuberculosis.](#)" J Vet Diagn Invest 28(6): 638-645.
- Bauman, C. A., A. Jones-Bitton, J. Jansen, D. Kelton and P. Menzies (2016). "[Evaluation of fecal culture and fecal RT-PCR to detect Mycobacterium avium ssp. paratuberculosis fecal shedding in dairy goats and dairy sheep using latent class Bayesian modeling.](#)" BMC Vet Res 12: 212.
- Beaver, A., P. L. Ruegg, Y. T. Grohn and Y. H. Schukken (2016). "[Comparative risk assessment for new cow-level Mycobacterium avium ssp. paratuberculosis infections between 3 dairy production types: Organic, conventional, and conventional-grazing systems.](#)" J Dairy Sci 99(12): 9885-9899.
- Chaubey, K. K., R. D. Gupta, S. Gupta, S. V. Singh, A. K. Bhatia, S. Jayaraman, N. Kumar, A. Goel, A. S. Rathore, Sahzad, J. S. Sohal, B. J. Stephen, M. Singh, M. Goyal, K. Dhama and A. Derakhshandeh (2016). "[Trends and advances in the diagnosis and control of paratuberculosis in domestic livestock.](#)" Vet Q 36(4): 203-227.
- Devitt, C., D. A. Graham, J. O'Flaherty and S. A. Strain (2016). "[Herd owners' experiences of a voluntary Johne's disease eradication programme in Ireland.](#)" Vet Rec 179(11): 276.
- Dhand, N. K., J. Eppleston, R. J. Whittington and P. A. Windsor (2016). "[Changes in prevalence of ovine paratuberculosis following vaccination with Gudair\(R\): Results of a longitudinal study conducted over a decade.](#)" Vaccine 34(42): 5107-5113.
- Dukkipati, V. S., A. L. Ridler, K. G. Thompson, B. M. Buddle, B. A. Hedgespeth, M. Price-Carter, D. J. Begg, R. J. Whittington, B. Gicquel and A. Murray (2016). "[Experimental infection of New Zealand Merino sheep with a suspension of Mycobacterium avium subspecies paratuberculosis \(Map\) strain Telford: Kinetics of the immune response, histopathology and Map culture.](#)" Vet Microbiol 195: 136-143.
- Fawzy, A., A. Fayed, H. Youssef, A. El-Sayed and M. Zschock (2016). "[First report of MIRU-VNTR genotyping of Mycobacterium avium subsp. paratuberculosis isolates from Egypt.](#)" Iran J Vet Res 17(2): 130-133.

- Fock-Chow-Tho, D., E. Topp, E. A. Ibeagha-Awemu and N. Bissonnette (2016). "[Comparison of commercial DNA extraction kits and quantitative PCR systems for better sensitivity in detecting the causative agent of paratuberculosis in dairy cow fecal samples.](#)" J Dairy Sci.
- Foster, D. M., K. P. Poulsen, H. J. Sylvester, M. E. Jacob, K. E. Casulli and B. E. Farkas (2016). "[Effect of high-pressure processing of bovine colostrum on immunoglobulin G concentration, pathogens, viscosity, and transfer of passive immunity to calves.](#)" J Dairy Sci 99(11): 8575-8588.
- Graesboll, K., L. O. Andresen, T. Halasa and N. Toft (2016). "[Opportunities and challenges when pooling milk samples using ELISA.](#)" Prev Vet Med.
- Hesam Shariati, S., A. Alaei, R. Keshavarz, N. Mosavari, A. Rabbani, M. Niegowska, L. A. Sechi and M. M. Feizabadi (2016). "[Detection of Mycobacterium avium subsp. paratuberculosis in Iranian patients with type 1 diabetes mellitus by PCR and ELISA.](#)" J Infect Dev Ctries 10(8): 857-862.
- Jurkovich, V., B. Bogнар, K. Balogh, M. Kovacs-Weber, K. Fornoyos, R. T. Szabo, P. Kovacs, L. Konyves and M. Mezes (2016). "[Effects of subclinical Mycobacterium avium ssp. paratuberculosis infection on some physiological parameters, health status and production in dairy cows.](#)" Acta Vet Hung 64(3): 301-312.
- Khare, S., K. L. Drake, S. D. Lawhon, J. E. Nunes, J. F. Figueiredo, C. A. Rossetti, T. Gull, R. E. Everts, H. A. Lewin and L. G. Adams (2016). "[Systems Analysis of Early Host Gene Expression Provides Clues for Transient Mycobacterium avium ssp avium vs. Persistent Mycobacterium avium ssp paratuberculosis Intestinal Infections.](#)" PLoS One 11(9): e0161946.
- Kirkeby, C., K. Graesboll, S. S. Nielsen, L. E. Christiansen, N. Toft, E. Rattenborg and T. Halasa (2016). "[Simulating the Epidemiological and Economic Impact of Paratuberculosis Control Actions in Dairy Cattle.](#)" Front Vet Sci 3: 90.
- Konnai, S., S. Murata and K. Ohashi (2016). "[Immune exhaustion during chronic infections in cattle.](#)" J Vet Med Sci.
- Krueger, L. A., D. C. Beitz, S. B. Humphrey and J. R. Stabel (2016). "[Gamma delta T cells are early responders to Mycobacterium avium ssp. paratuberculosis in colostrum-replete Holstein calves.](#)" J Dairy Sci 99(11): 9040-9050.
- Kugadas, A., E. A. Lamont, J. P. Bannantine, F. M. Shoyama, E. Brenner, H. K. Janagama and S. Sreevatsan (2016). "[A Mycobacterium avium subsp. paratuberculosis Predicted Serine Protease Is Associated with Acid Stress and Intraphagosomal Survival.](#)" Front Cell Infect Microbiol 6: 85.
- Kuntzel, A., S. Fischer, A. Bergmann, P. Oertel, M. Steffens, P. Trefz, W. Miekisch, J. K. Schubert, P. Reinhold and H. Kohler (2016). "[Effects of biological and methodological factors on volatile organic compound patterns during cultural growth of Mycobacterium avium ssp. paratuberculosis.](#)" J Breath Res 10(3): 037103.

Laurin, E. L., J. Sanchez, M. Chaffer, S. L. McKenna and G. P. Keefe (2016). "[Assessment of the relative sensitivity of milk ELISA for detection of Mycobacterium avium subspecies paratuberculosis infectious dairy cows.](#)" J Dairy Sci.

Malik, I., J. Csollei, J. Jampilek, L. Stanzel, I. Zadrazilova, J. Hosek, S. Pospisilova, A. Cizek, A. Coffey and J. O'Mahony (2016). "[The Structure-Antimicrobial Activity Relationships of a Promising Class of the Compounds Containing the N-Arylpiperazine Scaffold.](#)" Molecules 21(10).

Malvisi, M., F. Palazzo, N. Morandi, B. Lazzari, J. L. Williams, G. Pagnacco and G. Minozzi (2016). "[Responses of Bovine Innate Immunity to Mycobacterium avium subsp. paratuberculosis Infection Revealed by Changes in Gene Expression and Levels of MicroRNA.](#)" PLoS One 11(10): e0164461.

Marquetoux, N., C. Heuer, P. Wilson, A. Ridler and M. Stevenson (2016). "[Merging DNA typing and network analysis to assess the transmission of paratuberculosis between farms.](#)" Prev Vet Med 134: 113-121.

Mercier, P., S. Freret, K. Laroucau, M. P. Gautier, I. Bremaud, C. Bertin, C. Rossignol, A. Souriau and L. A. Guilloteau (2016). "[A longitudinal study of the Mycobacterium avium subspecies paratuberculosis infection status in young goats and their mothers.](#)" Vet Microbiol 195: 9-16.

Nicol, L., H. Wilkie, A. Gossner, C. Watkins, R. Dalziel and J. Hopkins (2016). "[Variations in T cell transcription factor gene structure and expression associated with the two disease forms of sheep paratuberculosis.](#)" Vet Res 47(1): 83.

Pritchard, T. C., M. P. Coffey, K. S. Bond, M. R. Hutchings and E. Wall (2016). "[Phenotypic effects of subclinical paratuberculosis \(Johne's disease\) in dairy cattle.](#)" J Dairy Sci.

Qasem, A., M. Safavikhasraghi and S. A. Naser (2016). "[A single capsule formulation of RHB-104 demonstrates higher anti-microbial growth potency for effective treatment of Crohn's disease associated with Mycobacterium avium subspecies paratuberculosis.](#)" Gut Pathog 8: 45.

Ricchi, M., A. Mazzarelli, A. Piscini, A. Di Caro, A. Cannas, S. Leo, S. Russo and N. Arrigoni (2016). "[Exploring MALDI-TOF MS approach for a rapid identification of Mycobacterium avium subsp. paratuberculosis field isolates.](#)" J Appl Microbiol.

Ritter, C., J. Jansen, K. Roth, J. P. Kastelic, C. L. Adams and H. W. Barkema (2016). "[Dairy farmers' perceptions toward the implementation of on-farm Johne's disease prevention and control strategies.](#)" J Dairy Sci 99(11): 9114-9125.

Serraino, A., P. Bonilauri, F. Giacometti, M. Ricchi, G. Cammi, S. Piva, V. Zambrini, A. Canever and N. Arrigoni (2016). "[Short communication: Investigation into Mycobacterium avium ssp. paratuberculosis in pasteurized milk in Italy.](#)" J Dairy Sci.

Shippy, D. C., J. J. Lemke, A. Berry, K. Nelson, M. E. Hines, 2nd and A. M. Talaat (2016). "[Superior protection from live-attenuated vaccines directed against Johne's disease.](#)" Clin Vaccine Immunol.

Singh, S. V., J. T. Kuenstner, W. C. Davis, P. Agarwal, N. Kumar, D. Singh, S. Gupta, K. K. Chaubey, A. Kumar, J. Misri, S. Jayaraman, J. S. Sohal and K. Dhama (2016). "[Concurrent Resolution of Chronic Diarrhea Likely Due to Crohn's Disease and Infection with Mycobacterium avium paratuberculosis.](#)" Front Med (Lausanne) 3: 49.

Songini, M., C. Mannu, C. Targhetta and G. Bruno (2016). "[Type 1 diabetes in Sardinia: facts and hypotheses in the context of worldwide epidemiological data.](#)" Acta Diabetol.

Tahir, A. H., J. Wan, M. K. Shah, H. Janyaro, X. J. Li and M. X. Ding (2016). "[A novel model for studying ileitis-induced visceral hypersensitivity in goats.](#)" Acta Vet Scand 58(1): 72.

Waddell, L., A. Rajic, K. Stark and S. A. McEwen (2016). "[Mycobacterium avium ssp. paratuberculosis detection in animals, food, water and other sources or vehicles of human exposure: A scoping review of the existing evidence.](#)" Prev Vet Med 132: 32-48.

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