

# **The Paratuberculosis Newsletter**

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**DEADLINE FOR NEXT ISSUE: 15 August 2014**

All contributions should be sent to [saxmose@sund.ku.dk](mailto:saxmose@sund.ku.dk)

Søren Saxmose Nielsen  
Editor

## **1. IAP Business**

### **IAP Election Results 2014**

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### **Open Access publication subsidy**

The appearance of the Open Access publication system can help the IAP to better fulfill its main objective of promoting and spreading the knowledge on paratuberculosis. Although this system has increasingly become a business that is posing a higher pressure to publish on researchers with some risk of decreasing the quality of the material being published, it still is a way to make research available to less wealthy societies that should help their scientists to stay current in the continuous flux of newly generated information. This perspective is fully in line with other IAP policies like the Helping Hand awards and has been approved by the Board of Directors, as well as discussed in the last General Membership meeting. In order to take advantage of this system regarding the costs of maintaining the highest possible scientific standards while putting to work the funds collected by the IAP, the following rules have been established.

IAP can pay one Open Access publication fee for papers on paratuberculosis according to the following terms:

- 1) The paper has been accepted by a peer-reviewed Open Access journal in English and both a copy of the paper and of the invoice is sent to the IAP. Priority will be given to journals in order of last published impact index.
- 2) Only one paper per group and year will be subsidized. A paper will be considered from a different group in the same year if it has: a) different senior author (generally the one signing last, with the higher number of papers and/or with higher position in the institution), and b) no more than half the authors signed a previously funded paper.
- 3) At least one among the first, second or the senior authors must be a member of the IAP in good standing.
- 4) Applications are accepted until an IAP fund of US\$10.000 per year is exhausted in a first come, first serve schedule with a maximum of US\$1000 per paper.
- 5) A Selection Committee will make the decision on each submitted paper and will establish new rules and policies on any aspect not specified in this guideline. Initially this Committee will be constituted by the Officers of the IAP: President, Vice-president, Secretary-Treasurer and Editor-in-Chief.
- 6) The evaluation will be a continuous process that will be applied to all the applications submitted every three months until exhaustion of the provided fund.
- 7) Since these publications' copyright remain in the hands of the authors, the IAP might chose to include the subsidized papers in the Paratuberculosis Newsletter. At least the full bibliographic reference of all the subsidized papers will be published in it.
- 8) The IAP would require the following disclaimer to be added to any publication of the winning papers in its own media (The Paratuberculosis Newsletter): The IAP financial support of the Open Access publication does not mean IAP official endorsement of the published contents.
- 9) The call is open since its publication in The Paratuberculosis Newsletter and until otherwise noted in The Paratuberculosis Newsletter. Periodic reminders will also appear in its pages.
- 10) Submission must be sent by email to the Editor-in-Chief of the IAP ([saxmose@sund.ku.dk](mailto:saxmose@sund.ku.dk)) and must include a letter of application, a pdf copy of the published paper or its electronic address and a pdf copy of the publisher invoice.

Ramon A. Juste  
President of the IAP

## 2. Short Scientific Contributions

### The MAP Milk Tax

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Control of infection due to *Mycobacterium avium* subspecies *paratuberculosis* (Map) is a near oxymoron given that current non-control is too often the governing principle. USDA's decision not to require a Map ELISA test as part of an animal's certificate of health and the insensitivity of the USDA certified Map ELISA tests have permitted a progressive introduction of infected animals into uninfected herds. McKenna et al. have shown that commercial Map ELISA tests detect only 6.9 to 8.8% of tissue positive cattle (1). Monif and Williams demonstrated a 7.3% - 13.5% correlation between a positive commercial Map ELISA of cows and the presence of Map in the animal's feces. (2.) The prevalence of infection within large dairy herds has progressively increased from 20-30% in 2001 to an estimate of 70% in 2007 (3) and 90% in 2013.

Map infection negatively impacts on reproduction in beef cattle. Detectable Map infection results in lower cow fertility, lower calf weight, and lower calf weaning weight adjusted to 295 days (4). Map ELISA positive animals have a 10-17% reduction in slaughter weight. If the animal's fecal culture contains Map, the reduction in slaughter weight can be as high as 31% (5).

In dairy cows, the Map Milk Tax results in decreased milk production ranging from 0.02-1 kg/day for Map infected vs non-infected dairy cows. Heavily infected cows decreased their milk production by 4 kg/day (6-8). A large Danish study has demonstrated that declines in milk production attributable to Map occur over a long period of time and tend not to be realized by most producers (9). In 2007, the National Animal Health Monitoring System study of 515 dairy farms identified the fact that 31.2% of the participating dairy farms had bulk tank milk positive for Map DNA (11). Map is not killed by pasteurization (10-13). Map in concentrations from 48 to 32,500 live organisms per gram of powdered infant milk were found in 35% of 51 investigated samples (14). Map DNA can be detected in 4.2% to 31.7% of cheeses tested (15-17).

Because the effects on milk production and fat content are subtle, producers are paying a progressively larger Map infection tax each year. The on-going expansion of the number of subclinically, infected cows now rule the producer's bottom line. The paradigm is no longer control of Map, but rather management of the Map Milk Tax and its associated reproduction and slaughter weight penalties.

### Reducing the Map Milk Tax

The absence of information about a given cow's Map status has been the foundation of most herd management schema. The underlying reasons have been the direct and future cost of testing, the questionable value of the information derived from current Map ELISA tests (18), and the problems inherent in changing management practices (19). An unstated reason has been the elephant in the room: the thesis that Map is linked to gastrointestinal disease in humans.

Even though a circumstantial case exists that links Map exposure during the period of maximum immune vulnerability following with subsequent development of Crohn's disease, the definitive, prospective experiment to conclusively demonstrate causality can never be ethically done. The Food and Drug Administration's (FDA) working guidelines state that to label a substance as a potential health hazard, there has to be "credible evidence of, or reasonable grounds to suspect, adverse biological effects". This doctrine requires conclusiveness as witnessed by total consensus. The current lack of absolute scientific consensus has effectively shelved the decision as to whether Map is a public health hazard. The paralysis of decision making has created a window of opportunity for the dairy and dairy-dependent industries to develop creative solutions that will assure the continuing role of milk within national economies.

Advances in diagnostic technology now allow a producer to determine a) if an animal has been infected by Map, b) the magnitude of that animal's immune response to Map's antigen array, and c) an ability to assess the probability of whether the infection is recent or is active (20).

This new technology has resulted in a rethinking of the natural history of Map infection. Whitlock and Buergelt conceptualized Johne's disease as a three stage process due to unchecked replication of Map. Being focused on Johne's disease, their schema failed to embrace the natural history of Map infection. What the new technology has revealed is that Map infection and disease have strong parallels with infection/disease due to *Mycobacterium tuberculosis* in humans. In both situations, with exposure, infection is common, but disease is not. In either situation, organism containment is mediated by the host's cellular immunity which is the primary governor of whether infection or disease ensues. In both situations, an inverse relationship exists between disease development and age of infection acquisition. Significant compromise of host immunity, whether intrinsic or extrinsic, can cause a reactivation of mycobacterium replication.

A major difference between infection due to *M. tuberculosis* and Map is that in most Western nations, humans are not continually subjected to the anabolic stress of continuous milk production while in the throes of pregnancy. Consequently, reactivation of Map replication late in pregnancy or with calving is a common time for subclinical infection to clinically manifest.

The new technology offers producers the ability to assess the relative risk of a given animal to impose a Map Milk Tax. Herd access by new animals with potentially active infection can be blocked. Animals with defined risk within the herd can be managed for maximum production prior to their deletion from the herd. The primary short term goal of management is the identification of an animal's quantitatively and qualitatively risk of negatively affecting milk production over time.

The primary long term goal of future herd management schema needs to focus on increasing herd immunity to environmental mycobacterial challenges. Hereditary factors appear to influence the detectable incidence and severity of mycobacterial infection in cows (21). Serial serological surveillance allows producers to identify cows who demonstrate the ability to successfully handle Map environmental challenges. The retention of heifers from such cows over time will build a herd that is less likely, when infected, to shed Map into their milk or make the producer pay the Map Milk Tax.

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## In a Decade: Paratuberculosis in Egypt

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*Mycobacterium avium* subspecies *paratuberculosis* (MAP) is a global pathogen that causes huge economic losses to the veterinary field and possesses a climbing public health concern. Johne's disease (JD) is a serious, chronic and untreatable intestinal infection of ruminants caused by MAP. JD is considered a disease of socioeconomic and public health importance within countries and is significant for animal trade practice. Studies from various parts of the world have shown the widespread distribution of the disease. The disease has been reported on almost every continent and is listed as a notifiable disease in some countries. In Egypt, this title was largely ignored for several years as it was thought that Egypt was free from JD. In the past decade, concerns were raised by local field veterinarians and livestock producers in different localities across the country reporting clinical cases of JD. At that time, the recognition of the disease in Egypt was hampered by the lack of local information on the disease occurrence, distribution, economic impacts and risk factors. Additionally, it was not clear whether these concerns were based on diagnostic reports on some farms or it was due to clinical signs which could have been confused with other diseases. This concept was mostly believed until broken in 2005 after the successful isolation of MAP from diseased dairy cattle in three Governorates denoting the existence of the disease in Egypt. The disease was first identified in Ismailia, Menoufia and Cairo Governorates after investigating 2150 heads of cattle in which 75 of them (3.5%) were positive for MAP by culture and IS900 PCR on feces.

The current decade has seen increased interest and application of conventional and modern diagnostic methods for identifying MAP in multiple animal species within different Egyptian Governorates. Studies were conducted in multiple academic and research centers utilizing diagnostic methods like Ziehl-Neelsen staining, ELISA, culture or PCR to detect MAP in different field specimens including feces, milk, blood and tissues. In spite of that, available data on the incidence and the prevalence of the disease in Egypt are limited and few reports were published until now. The actual herd and animal-level prevalence is unknown. Reports vary according to the sensitivity and specificity of the applied diagnostic tests, the selection of clinical specimens and the bench mark or the gold standard used. Although different diagnostic techniques were used, comparison of data from previous reports might provide a quick insight into the disease distribution under the local conditions in Egypt. With regard to Governorate-based seropositivity using ELISA, MAP was mainly a problem reported in Cairo, Giza, Alexandria, Menoufia, Gharbia, Mansoura, Kafr El-sheikh, Ismailia and Fayoum with a prevalence ranging from 5% in some governorates up to 60% in

others. The relatively high positive percentage in some governorates, for example 60% in Ismailia, might be attributed to the sampling process and the inclusion of herds with a previous history of paratuberculosis. The highest prevalence was observed in herds where most of examined cattle were imported from some EU countries and USA, where the disease is considered endemic. On the other hand, animals reared on sporadic form have the lowest prevalence and this might be attributed to the long nature of this exotic disease that was recently introduced to Egypt. Infection was first recorded in exotic dairy cattle breeds, and then found to spread across Egyptian native breeds and other animal species with no restrictions. With regard to species, MAP was isolated from a variety of animal species in Egypt including cattle, water buffalo, Arabian camels, sheep, goat and non-domestic cats.

For sheep, the sero-prevalence is considered high especially in localities where sheep have replaced pigs in the elimination of organic wastes “including fecal matters” subjecting these animals to different pathogens specially those caused by robust microorganisms like MAP. Recently, MAP was detected by IS900 PCR in commercial baby milk powders in the Egyptian market that were imported from countries suffering from paratuberculosis problem. This finding has raised a speculation whether or not milk could act as a possible threat to the exposure of the general public to MAP and therefore the risk associated with the presence of cultivable MAP in retail dairy products should be taken into consideration by the veterinary stakeholders in Egypt. More recently, some authors have described a parallel increase in paratuberculosis and Crohn’s disease prevalence and discussed the possible links between them. It is noteworthy to mention that the information available is sufficient to support the possible risk associated with MAP to the ruminant industry in Egypt. Interestingly, from 2005 till 2012 Egypt was still reporting to be free from JD. It is not clear how the country came up with the disease absence with continuous reports on the disease from 2005 to date. Thus the information provided might not necessary mean freedom from the disease since it might reflect also a weak surveillance mechanism or a lack of an official capacity to monitor the disease. Paratuberculosis is considered a momentous problem to the animal population in Egypt and possess a climbing public health concern. Instead of reporting freedom from JD, it is noteworthy that MAP should be among the top animal health priorities in Egypt since the presence of the disease has been confirmed by direct specific means of diagnosis.

The actual losses in productivity and profit are difficult to be assessed making it likely that the impact of the disease is underestimated in Egypt. The prevalence of infection will definitely increase in countries that do not have mandatory control programs and hence there is a current need to conduct education and management components of successful control programs for paratuberculosis in Egypt. Government funding of a control program would likely be forthcoming. Initiating JD control programs now will lead to lower control costs in the future. There is a plethora of JD control programs within numerous countries. Scanning

international programs and facilitating communication between local JD working groups and veterinary industry bodies, reference laboratories, governmental and non-governmental institutions should be supported by the veterinary authorities as a foundation for the disease prevention and control in Egypt.

### **3. List of Recent Publications**

- Bradner L, Robbe-Austerman S, Beitz DC, Stabel JR. [Application of an N-acetyl-L-cysteine-NaOH decontamination method for the recovery of viable \*Mycobacterium avium\* subspecies \*paratuberculosis\* from milk of naturally infected cows](#). J Dairy Sci. 2014 Mar 20. [Epub ahead of print].
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