

The Paratuberculosis Newsletter

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DEADLINE FOR NEXT ISSUE: 15 November 2014

All contributions should be sent to saxmose@sund.ku.dk

Søren Saxmose Nielsen
Editor

1. IAP Business

Notes from the IAP Annual General Meeting 25 June 2014 in Parma, Italy

1. Presidents report

President Ramon Juste presented the Board of Directors and the Executive Officers, and explained that we have slightly fewer members compared to the previous colloquium.

Board of Directors

Australia:	Richard Whittington
Canada:	Jeroen de Buck
Denmark:	Gregers Jungersen
France:	Christine Fourichon
Germany:	Heike Köhler
India:	Shoorvir Singh
Ireland:	Peter Mallowney
Italy:	Norma Arrigoni
Netherlands:	Victor Rutten
New Zealand:	Frank Griffin
Spain:	Joseba Garrido
United Kingdom:	Karen Stevenson
United States:	Judy Stabel and Murray Hines

Executive Officers

President:	Ramon Juste
Vice-President:	Eiichi Momotani
Editor in Chief:	Søren Saxmose Nielsen
Secretary-Treasurer:	Ray Sweeney

Further issues from the President:

- Only one application was received for Open Access subsidy of papers.
- There has been a proposal for a Paratuberculosis day, a topic that still needs to be developed. Members were invited to contribute ideas.
- The Board of Directors had decided that the dues will increase to 100 USD/2 years, which is at the same level as at the last colloquium, where the level was briefly reduced to 50 USD/2 years.
- Helping hands policies will be revised following a discussion among Board of Directors in the upcoming months
- Five bids had been received and reviewed by the Board of Directors, and it was decided that Mexico will host the 2018 colloquium.

2. Secretary-Treasurer's report

Presented by Raymond Sweeney, whom went through the number of members and list of countries entitled to have a representative on the Board of Directors.

Furthermore, the treasury was accounted for, resulting in the current balance of 42,871 USD.

3. Editor-in-Chief's report

Søren S. Nielsen reported that The Paratuberculosis Newsletter has been published quarterly, on the March 5, June 5, September 5 and December 5 each year. A survey about the newsletter is expected to be conducted within a couple of months to assess needs and wishes for the newsletter in the future. Future issues may contain brief non-peer-reviewed abstracts from members, along with position statements.

Proceedings of the colloquia have been made available at the IAP website www.paratuberculosis.info.

The 12ICP proceedings are expected online within a few weeks from the meeting.

4. 11ICP report

Richard Whittington briefly summarized his written report to the President. This report mentions that a colloquium with some nice science and a good social programme had been held in Sydney in 2012. A surplus from the meeting had been transferred to the IAP treasury.

5. 12ICP report

Norma Arrigoni reported that 304 people had registered for the meeting. Of these, 271 were paying participants, 16 were invited speakers, and 18 were company representatives. Of the 271 paying participants, 109 were members. A total of 256 abstracts had been received. The Gala dinner had 203 registrants.

The finances look healthy and a small surplus is expected.

A list of attendees was requested by David Kennedy and Norma promised to circulate a list. It was mentioned that a Flickr profile still exist from 11ICP, and this might be useful.

6. 13ICP report

Christine Fourichon briefly presented the 13ICP, where information will be put on the colloquium website www.icp2016.eu. The colloquium will be held on 20-24th June 2016 in Nantes, France.

7. 14ICP report

The 14ICP will be held in Cancun, Mexico.

8. 15ICP

Ramon Juste invited for bids for the following colloquium to be presented in Nantes.

9. IAP Member Recognition and Support Committee

This committee consists of Judy Stabel, Allen Roussel, Douwe Bakker, Lucy Mutharia, Douglas Begg and Ramon Juste. Ramon thanked the committee for their work for the different awards. Thanks were also given to the past member David Kennedy.

The committee had selected Naiara Abendaño and Rienske Mortier for the Merkal Awards, Ratna Gurung (Bhutan), Aneesh Thakur (India), Fernando Leite (Brazil), Nathalia Correa (Colombia) and Saurabh Gupta (India) for Helping Hand Awards.

Mike Sharp, Eugenio Lilini and John Hermon-Taylor were all made IAP Emeritii.

Rod Chiodini and Mike Collins were awarded Service Awards for their services to the IAP.

10. New activities.

Website facilities are slowly improving to better adhere to the needs of payments.

Furthermore, reviews for the website or the newsletter are considered to increase the activity level in the IAP.

11. New business

David Kennedy: Suggested various consensus statements could originate from the IAP, e.g. genotyping guidelines as mentioned by Srinand Sreevatsan, PCR guidelines mentioned by Ian Marsh and Movement restriction guidelines proposed by David Kennedy. Ramon Juste in principle supported such initiatives, although the form might differ from case to case.

It was mentioned that expert groups are often attempted established, but experts were not always easily identifiable. IAP could play a role in establishment of such groups.

Gregers Jungersen suggested that IAP could have a Facebook page as a way for members to network and discuss ideas. An alternative suggestion from Judy Stabel was a LinkedIn page, since US government employees are not permitted to use Facebook for work related activity.

Shoor Vir Singh mentioned that IAP could do something in relation to OIE.

Petr Kralik noted that a meeting will be held at the OIE Reference Laboratory in Brno in the Autumn, and he could provide suggestions to the OIE there.

Maarten Weber asked if auditors should be used to audit the IAP Treasury. Rod Chiodini mentioned that this would be fairly expensive and Ray Sweeney responded that the Board of Directors receive a financial report quarterly.

Judy Stabel suggested that awards are granted e.g. at the opening ceremony or something alike rather than at the membership meeting. It will make it a bit more exiting to receive the awards. A special half hour could be allocated for this purpose.

Tim Bull requested that more emphasis was given to the posters, with special poster sessions allocated for poster viewing.

Ramon Juste mentioned that Norma Arrigoni has accepted the responsibility of updating the colloquium organizing guidelines.

It was suggested to ask poster presenters to make their posters available at www.paratuberculosis.info. This will be investigated further.

Meeting ended 18.15 /Notes made by Søren Saxmose Nielsen.

Continued worldwide efforts address Johne's disease

In this article, Ken Olson summarises the 12th International Colloquium in Parma.

http://www.progressivedairy.com/index.php?option=com_content&view=article&id=12493:continued-worldwide-efforts-address-johnes-disease&catid=38:progressive-events&Itemid=64

The paper is at the end of the newsletter, where it is reprinted with permission from Progressive Dairyman, Issue 13, August 7, 2014.

Thank you to Ken for this nice summary.

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) 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 *Mycobacterium avium* subspecies *paratuberculosis* (MAP) infection in camel (*Camelus dromedarius*) in Saudi Arabia: Questions wait to be addressed

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Introduction

Dromedary camel (*Camelus dromedarius*) can survive and produce considerable amount of milk during recurrent and prolonged hot and dry environment (Bekele et al., 2011). Thus, camel milk is considered one of the most valuable food sources due to its nutritional value and medicinal properties (Lorenzen et al., 2011). Camel milk and meat are considered an important source of proteins for wide range of population (Breulmann et al., 2007). It was estimated that world camel milk market worth 10 billion dollars (Breulmann et al., 2007).

In Saudi Arabia, the camel population in 2010 was estimated 850000 heads of different breeds (Aljumaah et al., 2012a). The daily milk production by the indigenous breeds ranges from 6-8 liter/head. The total annual production was estimated 2500-4900 liter (Aljumaah et al., 2012b).

The MAP infection was reported in camel in Saudi Arabia (Alhebab and Alluwaimi, 2010). In the last years, MAP infection in camel has attracted a considerable attention (Alluwaimi, 2011; Alharbi et al., 2012).

Although the research interest in the camel MAP infection is continuously increasing, the approaches to address this problem were less than the expectations. Here we present several questions that are essential in understanding the nature of the problem for this disease in camel. The posted questions are based on the major gaps exist in the knowledge of the camel MAP infection in Saudi Arabia. These questions are related to nature of the camel immune responses, the environmental factors, public health risk potentials and possible camel genetic susceptibility to the MAP infection.

The questions are:

1. What is the nature of the camel immune responses to the MAP infection?
2. How MAP maintains its survival and persistence in the harsh camel environment?
3. Is there breed related susceptibility to the MAP infection?
4. Does consumption of meat and milk of MAP-infected camel state public health risks?

1. What is the nature of the camel immune responses to the MAP infection?

A gap of knowledge still exists about wide range of immune response mechanisms of the camel immune system. The mechanism of cellular immune responses cannot be apprehended in view of complete lack of understanding the major histocompatibility complex (MHC) structure and diversity. In addition, the role of the humoral responses to the infection requires further delineation. Thus, in view of this large black hole in the knowledge of camel immune system, a vaccination trial could face major set back in assessing and evaluation of the immune responses. Furthermore, ELISA and PCR could play crucial role in monitoring the disease in camel but they are indecisive tools in providing clear picture on the extent of the MAP infection in the camel herds in Saudi Arabia (Alluwaimi, 2011). Therefore, design of the efficient approach in detecting MAP infection in camel is hindered by comprehensive research on basic and applied aspects of the camel immune system. It is potentially important to conduct MAP experimental infection to compensate for the major lack of details of the camel immune response to MAP.

The nature of the camel immune responses could be influenced by distinct physiological and immunogenetical factors. Recently evidence were accumulated that the nature of cellular trafficking to the camel mammary glands is most probably of mucosal origin (AL-Mohammed Salem et al., 2012a; b; Al-Ashqar, 2014). Extensive expression of mucosal addressin cell-adhesion molecule-1 (MAdCAM-1) in the mammary glands tissue and the mesenteric lymph node as well as the expression of the $\alpha 4\beta 7$ Peyer's patches adhesion molecule-1 (LPAM-1) on the lymphocytes of normal milk cells and cells from glands with mastitis (AL-Mohammed Salem et al., 2012a; b; Al-Ashqar, 2014). It is possible, therefore, in depth and explicit studies on camel immune system could reveal more unexpected and extraordinary immune response mechanisms.

In general, line of research of camel immunology is vitally required to decipher puzzles still exist in the camel immune system.

2. How MAP maintains its survival and persistence in the harsh camel environment?

The major landscape of the Saudi Arabia is desert (2,330,000 Km² [900,000mile²]). Three major deserts are located on the three sides of country's central plateau (Wikipedia). In the north part is An-Nafud desert and Rub Al khali (empty quarter) is to the south, which extends to about 650,000 km² [250,000 mile²], The third desert is Ad Dahna, located to the east part of the country.

Climate of the country is characterized with extreme heat in summer that could reach above 50 °C (120 F). The summer season could extend to more than six months of the year.

In this harsh and arid environment, what are the physico-physiological properties that enable MAP to stand and maintain its transmission? Study on the camel MAP shedding indicated that young camels shed MAP continuously with low tendency to develop infection.

High level of positive PCR results probably reflects the capability of the young camels to recirculate MAP in their environment rather than succumb to its infection (Al hebabi et al., 2012). But the major obstacle is the period the organism could remain intact in this environment and how?

Majority of camel flocks are kept in free grazing in an empty desert and in almost complete isolation from contact with other animals. Is it plausible to assume that certain desert rodents (Daniels et al., 2003) act as backup for the continuous supply of MAP in the environment (Al hebabi et al., 2012)?

Hence, extensive studies appear urgent to draw a detailed picture of the MAP survival in the camel's arid environment.

3. Is there breed related susceptibility to the MAP infection?

It is widely documented that the severity of the MAP infection is correlated with the host genetic background (Singh et al., 2013; Kirkpatrick and Shook, 2011; Stevenson and Sharp, 1997; Morris, 2007). Fortunately, the full camel (*Camelus dromidarius*) genome was sequenced in Saudi Arabia (Al-Swailem et al., 2010). Attempts were carried out to identify the genetic variation of different breeds of the Saudi Arabian camel (Mahrous et al., 2011; Al-Swailem et al., 2007). The traditional way of breed classification is mainly based on the phenotypic differences. The indigenous camels in Saudi Arabia are traditionally classified into four different breeds; they are Maghatier, Shu'l, Majahiem and Soffer, in which certain breeds are considered more appropriate for milk production (Aljumaah et al., 2012b; 2011).

In view of this important achievement in disclosing the camel genome and efforts to draw the genetic relationship between the different conventionally designated camel breeds, it is important to conduct epidemiological studies to reveal if variation in the susceptibility to MAP infection is exist among the camel breeds. This has important impact on the decision of the breeding methods. Breeding could play effective approach in controlling the MAP infection among camel population.

4. Does consumption of meat and milk of MAP-infected camel state public health risks?

It is becoming clearly evident that MAP has important role in the pathogenesis of Crohn's disease (Alluwaimi, 2007; Singh et al., 2013). These accumulated evidence definitely exert public health concern about consumption of the camel dairy and meat products. The reports on MAP resistance to milk pasteurization (Over et al., 2011), the process of milk formula (Hruska et al, 2011) and meat (Gill et al., 2011) state imminent potential risks on the public health.

It is greatly critical to design new approaches and undertake effective amendments on the public health inspection policies to eradicate any food contaminated with MAP. Proposal in this wide scale and details definitely requires longitudinal public health studies on the

extent, sources and methods that cause serious contamination of the camel meat and milk products.

In conclusion, the heritage and economical value of the camel in Saudi Arabia urge for overwhelming attention to research in the field of camel MAP infection. There are out numbered shortages in tools and strategies that necessitate better organization and long lasting road map to tackle this national problem.

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3. List of Recent Publications

- Abendaño N, Tyukalova L, Barandika JF, Balseiro A, Sevilla IA, Garrido JM, Juste RA, Alonso-Hearn M. [Mycobacterium avium subsp. paratuberculosis isolates induce in vitro granuloma formation and show successful survival phenotype, common anti-inflammatory and antiapoptotic responses within ovine macrophages regardless of genotype or host of origin](#). PLoS One. 9:e104238.
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Continued worldwide efforts address Johne's disease

Ken Olson for *Progressive Dairyman*

The 12th International Colloquium on Paratuberculosis (ICP) was held June 22-27, 2014, in Parma, Italy. It was also a celebration of the 25th anniversary of the founding of the International Association for Paratuberculosis (IAP) (www.paratuberculosis.org), the sponsoring organization. The ICP brings together veterinary and human medical researchers, educators and livestock industry representatives to share current work on paratuberculosis (Johne's disease). Johne's impacts many species, so there were reports on dairy and beef cattle, sheep, goats, deer and camels. More than 320 individuals from 20 countries participated, affirming the worldwide interest in the disease.

The ICP is a major scientific event with 76 oral and 194 poster presentations during the meeting. One of the strong points of the meeting is that it brings together such a wide range of expertise related to better understanding *Mycobacterium avium subspecies paratuberculosis* (MAP), the cause of Johne's disease, and developing ways to control and combat it. Presentations range from very basic science in molecular genetics and cell biology to diagnostics and vaccine development to practical application of that science at the farm level and concluded with an update on public health and food safety aspects.

Some common challenges and concerns noted included:

- ◆ Difficulty in developing effective diagnostics and vaccines
- ◆ Reduced funding for research and control programs in many countries
- ◆ Increasing indication of an association with several human diseases and increases in the prevalence of those diseases

In an invited presentation, Hernan Barkema of the University of Calgary highlighted bottlenecks in the prevention and control of MAP infection. He noted an

“Johne's is a disease we have known for over a century, but much remains to be learned about it. We know it is a costly disease for producers, and the potential links to human disease remain a concern.”

essential parameter for control programs is the baseline prevalence of the disease, but in most regions of the world this is unknown, or if estimated, it is underestimated. Slaughterhouse data can provide a good estimate, but little is being collected. He noted there are different genotypes of MAP that may result in differences in shedding, transmission, clinical disease, virulence and the effectiveness of vaccines. Cow-to-cow, cow-to-calf and calf-to-calf transmission have all been confirmed.

It has also been shown that MAP survives for extended periods in the environment and that it is found in wildlife. These challenges all confirm the need for continued research to address the disease. While much remains to be learned, we do have tools that can help address the disease on the farm. He shared two videos, developed by the Ontario Johne's Education & Management Assistance Program (www.johnes.ca) that discuss preventing Johne's and what it means for farmers.

While many challenges and unknowns related to MAP exist, presentations showed progress is being made. In recent years, environmental sampling from six areas on a dairy has been found to be a useful tool for identifying infection at the herd level. Work from Canada and Germany demonstrated that “sample socks,” when worn by the veterinarian during herd work, provide a quick and easy sampling that was similar in accuracy to that of the environmental sampling.

Whole-herd prevalence as low as 2.4 percent was detected. The “socks” are the same as those used in salmonella evaluation in poultry. Relative to improved diagnostics, Irene Grant of the Queen's University Belfast reported

on enhanced techniques to more accurately identify the number of viable MAP in raw milk samples. Tim Bull of St. George's University of London Medical School reported on a new culture medium that improves the growth and isolation of MAP found in human blood and tissue.

MAP vaccines have been shown to be somewhat effective in reducing clinical disease and delaying or reducing shedding by infected animals; however, they have limited success in reducing overall prevalence and they do interfere with tuberculosis (TB) testing. Several projects reported some success in development of more effective vaccines.

Tim Bull and co-workers reported initial success with a new vaccine that uses a virus delivery system. Tested in calves, it reduced shedding and allowed differentiation of vaccinated and non-vaccinated animals. Workers from Denmark reported on a new vaccine developed from antigens of infected animals that was tested in calves after exposure to MAP. Calves received two doses of the vaccine during the trial. It was seen to be effective and it did not interfere with TB testing.

Murray Hines of the University of Georgia Diagnostic Lab reported on the Johne's Disease Integrated Program (JDIP) vaccine development project. The project put 20 candidate vaccines through a rigorous screening process. The five top candidates were tested in goats using an oral delivery system, and two have shown promise. It is encouraging that workers in several countries are identifying potentially effective new vaccines, but it must be noted that all require additional testing before possible approval for use in the field, meaning they are at least several years away from being available.

Genetic selection is another tool being studied. Resistance or susceptibility to Johne's is known to exist, but heritability has generally been found to be low, meaning that selection is possible, but progress is slow. Frank Griffin of the University of Otago in New Zealand reported on work in farmed deer where genetic markers were identified that did allow more rapid progress in selecting for immunity. Work is ongoing in other labs to identify similar markers in cattle. It is likely to be an area of interest in the future.

Johne's is a disease we have known for over a century, but much remains to be learned about it. We know it is a costly disease for producers, and the potential links to human disease remain a concern. Both are good reasons to address it at the farm. Current tools are far from perfect, but work reported at the ICP shows progress is being made. In many other countries, producer groups are working together to provide research funds and program resources to help address the disease. It bears watching, and perhaps emulation, as they provide competition in the global dairy market. **PD**

Full proceedings from the ICP are available on the IAP site (www.paratuberculosis.org) and in the Searchable Proceeding of Animal Conferences (www.spac.adsa.org).

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 **PROGRESSIVE DAIRYMAN**

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