The Paratuberculosis Newsletter

March 2013

An official publication of the
International Association for Paratuberculosis

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DEADLINE FOR NEXT ISSUE: 15 May 2013

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

Søren Saxmose Nielsen
Editor

1. IAP Business

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

Tackling Johne's around the world

A summary of the 11th International Colloquium on Paratuberculosis was provided by Ken Olsen in Hoard's Dairyman in January 2013.
The summary is available via the JDIP website at:
http://www.jdip.org/index.php?option=com_content&task=view&id=94&Itemid=142

12th International Colloquium on Paratuberculosis

The 12th International Colloquium on Paratuberculosis will take place in Parma 22-26 June 2014. Visit the official website at: http://www.icp2014.eu/

Financial Report – End of Year 2012

International Association for Paratuberculosis

112 Barnview Road
Kennett Square, PA 19348 USA

	Checking	Money Market	Cert. Dep.	PayPal	Total
Open (1/1/12)	$33,403.01	$18,516.30	$57,959.79	$3.75	$109,892.85
Q2 (6/30/12)	$12,685.64	$35,001.83		$189.10	$47,876.57
Close (12/31/12)	$12,740.08	$35,019.48		$189.10	$47,948.66

Income

	Q1 & Q2	Q3 & Q4	Total
Dues	$350.00	$100.00	$450.00
Interest	$ 92.61	$ 17.65	$ 11.26
Book sales		$ 15.00	$ 15.00
Total	**$442.61**	**$132.65**	**$575.26**

Expenses

	Q1 & Q2	Q3 & Q4	Total
Expenses CreditCard/PayPal	$110.58	$60.56	$171.14
11ICP advance	$15,045.00*		$15,045.00**
HH Awards	$28,527.60		$28,527.60
ICP Merkal, Officers travel	$14,042.64		$14,042.64
Webmaster	$ 4,733.07		$ 4,733.07
Total	**$62,458.89**	**$60.56 $**	
62,519.45			

*Note: Anticipated net revenue from 11ICP to be applied in 3rd financial quarter

**11ICP net revenue remains outstanding, due to Australian taxing authority delay

Respectfully Submitted,
(signed)
Raymond W. Sweeney, VMD
Secretary-Treasurer

IAP Book Purchases

The association has a number of past International Colloquium proceedings available for distribution. We currently have the following in stock:

8ICP Proceedings – Book
8ICP Proceedings – CD-ROM
7ICP Proceedings – Book
6ICP Proceedings – Book
5ICP Proceedings – Book
4ICP Proceedings – Book

Proceedings are available FREE to members, but shipping charges of $15 (USA) or $35 (outside of USA) will apply. Non-members may purchase the Proceedings for $25 plus shipping costs.

Furthermore,
The History of Paratuberculosis compiled by Rod Chiodini
is available for 50 USD + shipping for members, and $125 +shipping for non-members.

To order please send an e-mail to Secretary-Treasurer Ray Sweeney at:
rsweeney@vet.upenn.edu

and include the following information:

- Item and no. of each
- Shipping address
- Preferred method of payment
- E-mail address

The number of proceedings is limited so we operate by first-come-first-served principle. Please place your order no later than 1 April 2012.

Also note that the 7th, 8th, 9th, 10th, and 11th Proceedings are available on-line at www.paratuberculosis.info.
Starting with the 9th ICP, a print version of the Proceedings are no longer produced by IAP. However, print versions of 9th, 10th, and 11th ICP can be purchased at
http://www.proceedings.com/6219.html

2. Short Scientific Reports

Mycobacterium avium subsp. *paratuberculosis* cells are surprisingly resistant to ensiling process

KL Cook[1], SA Flis[2], CS Ballard[2]

[1]*USDA-ARS, Bowling Green, KY, 42104*
[2]*William H. Miner Agricultural Research Institute, Chazy, NY, 12921-2402*

Silage is a valuable source of nutrients for dairy and beef cattle in non-forage months. The most commonly ensiled crops include corn and grass forage, both of which are often fertilized with livestock manure spread by broadcasting onto the soil or by spray irrigation. Pathogen contamination may result from application of contaminated manure or wash waters to silage crops. Die-off of undesirable microbial populations in materials undergoing the ensiling process occurs as a result of production of weak organic acids (including lactic, acetic and propionic) and concomitant decreases in pH. Pathogens of concern in silage, therefore, are those like *Mycobacterium avium* subsp. *paratuberculosis* (*M. paratuberculosis*) which are resistant to acids and are able to withstand harsh conditions encountered in the natural environment and within the host during pathogenesis. ARS scientists in the USDA Agricultural Research Service Animal Waste Management Research Unit at Bowling Green, KY in collaboration with scientists from the William H. Miner Agricultural Research Institute in Chazy, NY evaluated the ability of *M. paratuberculosis* to survive the low pH and high organic acid concentrations encountered as part of the ensiling process. Researchers found that *M. paratuberculosis* was extremely sensitive to direct intracellular acidification by organic acids at pH 4.0, however the organism was seven times less sensitive when exposed to silage exudates at the same pH. In fact, *M. paratuberculosis* cells showed no significant decrease in repeated silage experiments (Fig. 1). It is important to note that dead M. paratuberculosis also showed no decrease in silage (DNA from other control cells, dead *E. coli* and *S. Typhimurium*, was never detected).

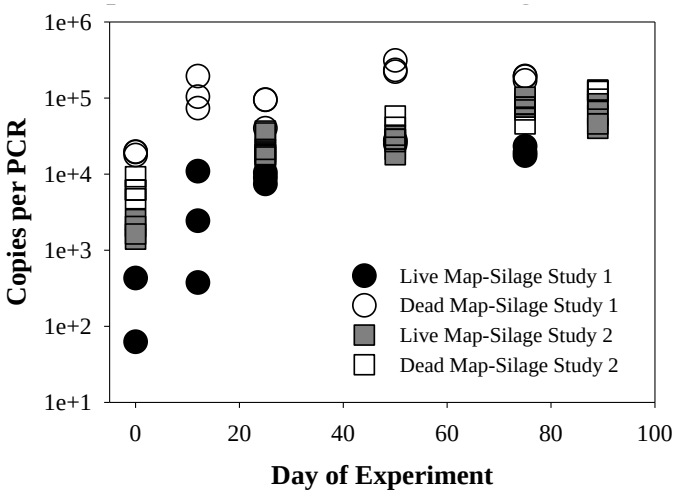

Figure 1. Copies of *M. paratuberculosis* IS*900* gene per gram of silage. Triplicate quantitative real-time PCR values from three different silage bags and two different studies are shown for live or dead *M. paratuberculosis* per sample time.

Results from this series of studies suggest that cells of M. paratuberculosis may persist when exposed to the low pH and high organic acids that are important to the ensilaging process. Silage may be a potential route of exposure if viable M. paratuberculosis cells survive and are ingested by a susceptible animal. Given the organisms importance as a dairy pathogen, further research is needed to better understand persistence of this organism in livestock feeds.

For further information contact Dr. Kim Cook (kim.coook@ars.usda.gov)

3. Comments and Opinions

Mycobacterial Diseases of Animals– the Multi-State Initiative

Kenneth E Olson PhD, PAS

Johne's Disease Integrated Program (JDIP) efforts are well known around the world. Primary funding has been through two USDA competitive grants that were also used by members to leverage additional public and private funding that expand the effort. Our funding through current grants has come to an end and JDIP leadership has been looking to the future.

JDIP has successfully addressed many knowledge gaps relative to Johne's disease, but much work remains to be done. Rather than allow the effort to fade away, JDIP evaluated a range of options for the future of the consortium. Primary objectives were to maintain the networking, collaboration and basic infrastructure developed through JDIP, allowing participants to identify, obtain and share resources needed to address issues related to Johne's and other mycobacterial diseases. To this end, JDIP, in collaboration with other interested parties, developed a proposal that received final approval from USDA's National Institute for Food and Agriculture (NIFA) and officially began operation as Multistate Initiative - NE1201, "**Mycobacterial Diseases of Animals (MDA**)"), on October 1, 2012.

The new ***multi-state initiative (MI)*** is focused on two mycobacterial disease complexes - paratuberculosis (Johne's disease; JD) and the tuberculosis complex of diseases (TBc; i.e bovine tuberculosis). The initiative includes five objectives:

Objective 1: Increase understanding of the epidemiology and transmission of Mycobacterial diseases in animals, including predictive modeling;

Objective 2: Develop and implement new generations of diagnostic tests for JD and TBc;

Objective 3: Improving our understanding of the biology and pathogenesis of Mycobacterial diseases, as well as the host response to infection;

Objective 4: Develop programs to evaluate and develop new generations of vaccines for JD and TBc; and,

Extension/Outreach: Develop and deliver education and outreach material related to JD and TBc in electronic and print form for use by extension specialists, veterinarians, government agencies, producers and other stakeholders. Utilize trade media, producer organizations and other outlets to aid in dissemination of information generated through the initiative.

Projects within each of these objectives, with cross-cutting contributions, will be designed to address the major animal, human, and societal issues surrounding detection and control of mycobacterial infection, including how these organisms move and spread within cattle, small ruminant and wildlife populations.

NEXT STEPS: The MI organizational structure, including an Executive Committee (EC) and an External Advisory Board (EAB) is in place. Work is progressing on transitioning JDIP Core resources to the new initiative and identifying of other resources that will be needed as we move forward, broadening our focus to include other mycobacterial diseases.

While approved by USDA, the Initiative comes with no research funding, so an important function will be facilitating the collaboration of participants as they seek funding through competitive grants and other sources. This was a strength of JDIP that will be carried forward through the MI. To aid this effort the MI EC is currently developing a not for profit organization that will work in conjunction with the MI to facilitate meeting and funding efforts.

We are strongly encouraging participation by JDIP members and invite others to join the effort. Our initial Annual Meeting was held on Sunday December 2, 2012 in Chicago in conjunction with the Conference of Research Workers in Animal Diseases (CRWAD). Visit our website www.jdip.org, under “Multistate Initiative/ Annual Conference” to see slides from the meeting presentations. For more information on the MI visit the website or contact us directly.

Contact: Ken Olson PhD, JDIP Outreach Coordinator, Ph. 1-630-237-4961 e-mail: keolson@prodigy.net or
Robab Katani, Penn State Project Assistant, Ph. 1- 814-867-0256 e-mail: rxk104@psu.edu

Failed Goals within the National Johne's Disease Control Program

Gilles R. G. Monif, M.D.

The 2008 National Johne's Disease Control Program Strategic Plan identified three specific goals (*Schwartz A.: National Johne's Disease Control Program Strategic Plan. October 23, 2008. Page 1*):

1. Reduce the prevalence of Map/Johne's disease in the national herd
2. Reduce the impact of Johne's disease on individual herds
3. Reduce the risk of introducing Johne's Disease to uninfected herds

The National Johne's Disease Control Program has failed in meeting two of the three of its stated goal objectives.

Central in the herd monitoring schema proposed by the National Johne's Disease Control Program for Johne's disease was identification and removal of infected animals from the herd. The current commercial Map ELISA tests certified by the United States Department of Agriculture (USDA) measure anti-Map antibodies, but the interpretation of a positive test is predicated on the identification of a level of antibody that predicts a high probability of a progression of Map infection to clinically overt enteritis or confirmation of its presence. A negative commercial Map ELISA test does not address the issue of whether or not a given animal is or ever has been infected by Map. The decision by USDA to have the Map ELISA tests represent a statement of probability rather than a valid measurement of the amount of antibody present permitted infected cows to be transported across state lines and national borders with relative impunity. The net result is not only the introduction of infected animal into uninfected herds, but an increased prevalence of Map infection in the national herds. In 2007, USDA acknowledged that an estimated 70% of U.S. dairy herds contained one or more infected animals (USDA-APHIS Johne's Disease in U.S. Dairies 1991-2007. http://nahms.aphis.usda.gov/dairy/dairyo7/Dairy 2007-Johnes.pdf.2007).

Reducing the introduction of Map infection and potentially Johne's disease into uninfected herds is largely contingent upon the buyer having the proper information to go along with eyeball analysis of the animal's body condition score (BSC). Quality of merchandise is theoretically addressed through the animal's health certificate. On the United States federal level, revision to part 71 and 80 of the Code of Federal Regulations (CFR) is supposed to restrict the interstate movement of Map-infected animals except to recognized slaughter establishments (*United States Department of Agriculture Animal Plant Health Inspection Service. 9, Parts 71 and 80.2000. Johne's disease in domestic animals: interstate movement. Federal register 65:18875-188879*). With an artificially constitute threshold for a

positive test, the pertinent CFR regulations do not truly address the quality of merchandise issue. Too often on the states level, state animal health certificates merely require that the certificate be signed by a veterinarian attesting to the apparent absence of any contagious or otherwise transmissible disease. The language in many state health certificates tends to minimize any requirement that the animal be free of underlying infectious diseases. The principle exception is the Wisconsin Implied Warranty law that stipulates that cattle to be sold are guaranteed to be Map-free unless sellers provide a written retraction of this guarantee at the time of the sale (*Sockett D. C.: Johne's disease eradication and control: regulatory implications. 1996. Vet. Clin. North Am. Food Anim. Pract. 12:431-440*).

By not stipulating on the animal's certificate of health its Map status in a manner comparable to *Mycobacterium bovis*, animals with subclinical disease animal are and have been transported across state and national boundaries. The decision by USDA not to require a statement as to an animal's Map status has undermined its avowed intent to prevent dissemination of Map into uninfected herds.

The Japanese perception that Map constitutes a potential public health hazard has engendered a different schema (*Eiichi M.2012. Epidemiological situation and control strategies for paratuberculosis in Japan. Japanese J. Vrt. Res. 60:19s-29s*). In accordance with the Act on Domestic Animal Infectious Disease Control, after 1998, every Japanese dairy farm is examined for Map every five years. Imported cattle are subjected to quarantine in which they are screened using a Map ELISA test, fecal bacterial culture, PCR analysis for fecal Map DNA, and Johnin skin test. If a new cow is to be introduced into a herd, the recommended procedure is that the cow should be negative in more than two ELISA tests within three-month interval during the last six months, negative at least once in culture for Map, and kept in quarantine until proven non-infectious. Fifty-four percent of diseased animal detected by the Japanese Animal Quarantine Service came from the United States. Owing to the high antibody threshold of a current positive Map ELISA test, the real number of infected cows shipped from the United States escaping detection is open to speculation.

Once Map is introduced into the pasture/production environment, its elimination is extraordinarily difficult (*Eisenberg S. W. F., Nielen M., Santema W. Houwers D. L., Heederik D., Koets A. P.: Detection of spatial and temporal spread of Mycobacterium avium subsp. paratuberculosis in the environment of a cattle farm through bio-aerosols. Vet. Microbiol. 2010; 143:284-292*). Even if elimination of Map could be achieved, the ultimate reservoir of infection cannot be eradicated. What has now been shown is that *Mycobacterium avum* subspecies *paratuberculosis* infection in dairy herds acts much like *Mycobacterium tuberculosis* in human: Disease is a small percentage of infection (*Monif G. R. G., Williams J.E.: The natural history of Mycobacterium avium subspecies paratuberculosis as interpreted by the FUIDI #2Map test. Proceedings of 10th ICP. 2009; p. 164*). Once a resident animal within a confined herd develops clinical signs, a significant number of animals within the herd will have had antigenic exposure to Map.

The veterinary world looks to the USDA for conceptual leadership. With privilege comes responsibility. To do nothing is to do something (*"In any moment of decision, the best thing you can do is the right thing, the next best thing is the wrong thing, and the worst thing you can do is nothing"*- Theodore Roosevelt). The cost of doing nothing has been the widespread dissemination of Map within the nation's dairy and beef herds in the name of protecting agriculture.

4. List of Recent Publications

Abendaño N, Sevilla IA, Prieto JM, Garrido JM, Juste RA, Alonso-Hearn M. *Mycobacterium avium* subspecies *paratuberculosis* isolates from sheep and goats show reduced persistence in bovine macrophages than cattle, bison, deer and wild boar strains regardless of genotype. Vet Microbiol. 2013 Jan 29. [Epub ahead of print].

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Bull TJ, Schock A, Sharp JM, Greene M, McKendrick IJ, Sales J, Linedale R, Stevenson K. Genomic variations associated with attenuation in *Mycobacterium avium* subsp. *paratuberculosis* vaccine strains. BMC Microbiol. 13:11.

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