The Paratuberculosis Newsletter - Online

January 2005

An Official Publication of the INTERNATIONAL ASSOCIATION for PARATUBERCULOSIS and Other Intestinal Mycobacterioses
Notes from the editor

2005 has the makings of an exciting year for the International Association for Paratuberculosis. The major event of the year will be the 8th Colloquium to be held in Copenhagen in August. Members are urged to attend what will be a stimulating conference and they should visit the Colloquium’s website for details.

This Newsletter is once again a mixed bag. There is a fascinating story behind the description by Crohn and Ginzburg of what is now know as Crohn’s disease. If circumstances had been slightly different it could now be known as Ginzburg’s rather than Crohn’s disease.

I have included a picture, taken by my colleague Terry Ryan, of the macroscopic lesions of a farmed deer with paratuberculosis (still to be confirmed by culture). The reason for including these photographs is to highlight that different hosts can respond quite differently to infection with *Mycobacterium paratuberculosis*. This deer lesion, where the predominant presenting sign is a liquefactive necrosis is not uncommon in farmed deer but is extremely rare in other hosts infected with this organism.

Paratuberculosis has attracted its share of controversy. In the last few years this has principally related to the debate over whether or not *M. paratuberculosis* is a human pathogen and the cause of Crohn’s disease. There can be little debate that the growing interest in paratuberculosis relates in very large part to this issue. The recent publication in the Lancet by Naser et al. where they describe the isolation of *M. paratuberculosis* from the blood of Crohn’s patients has attracted considerable amount of attention. There are a couple of letters to the Lancet in response to this publication in which are raised some serious questions as to the significance of the findings of Naser et al.. Associated with the issue of *M. paratuberculosis* and Crohn’s disease has been the question of how effective pasteurisation is in killing this organism. The International Life Science Institute has recently published a report entitled “*Mycobacterium avium* subsp. paratuberculosis (MAP) and the Food Chain”. The major strength of this report is a review of the studies relating to the effects of pasteurisation on the survival of *M. paratuberculosis* in milk. The literature on this subject tends to be confusing and an independent report on this subject is timely.

Geoffrey W. de Lisle,
Editor

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Message from the President:

January 27, 2005

Best wishes for the new year. 2005 is going to be a busy year for the International Association for Paratuberculosis. We meet again in Copenhagen this coming August. The Colloquium organizers have several important deadlines that you need to be aware of. Our Colloquium also triggers many important business functions of the Association, notably election of people to represent you on the Governing Board and operate the Association until the next Colloquium. Many times these dates and deadlines sneak up on us. To try and help, I am taking this space to itemize for you several critical dates that include both presentations at the Colloquium and Association business deadlines. **Please mark your calendars:**

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
<th>Details</th>
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<tr>
<td>February 1</td>
<td>2005 dues payment notice.</td>
<td>This notice will come via email, through the Association’s website. Please pay promptly and directly to Dr. Claus Buergelt. We accept credit card payments but our website does not take online payments. To pay your dues, simply go to the Association’s membership form on our website <a href="http://paratuberculosis.org/member/memform.htm">http://paratuberculosis.org/member/memform.htm</a> complete the form, print the form, and then fax (if you pay by credit card) or mail the form with your payment. The fax number and mailing address are on the bottom of the form. It is simple, fast and easy! If you think the Association should institute acceptance of online payments in the future, please let the Governing Board know. This would add some cost to the association would make payments for dues and books must more simple. If enough members like the idea, the Board will evaluate the costs and benefits.</td>
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<tr>
<td>February 14</td>
<td>Deadline for nominations from the membership for people to serve on the Board of Directors.</td>
<td>Countries are granted one seat on the Board if they have five or more members in good standing. When we hold elections, we will count members by country that have paid dues for 2004 and 2005. An additional seat on the Board is granted for each additional 25 members in good standing. Don’t let your country lose a seat on the Board because you failed to pay your dues on time!</td>
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<tr>
<td>March 15</td>
<td>Deadline for receipt of abstracts for the 8ICP.</td>
<td>These abstracts must be submitted electronically through the Association’s website. See the 8ICP website for more details. <a href="http://www.8icp.dk/">http://www.8icp.dk/</a></td>
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<td>April 14</td>
<td>Deadline for the Board of Directors to provide to the Secretary-Treasurer a slate of candidates for officers of the Association: President, Vice-President, Secretary-Treasurer, and Editor-in-Chief.</td>
<td>If you have people you wish to nominate, including yourself, please let a member of the Board know.</td>
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<td>April 30</td>
<td>Deadline for receipt of dues payment for the purposes of counting members in good standing and representation by countries on the Board of Directors.</td>
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May 1 Notification to authors if their submitted abstract has been selected for presentation at the 8ICP.

June 14 Deadline to mail ballots for the Board of Directors and Officers to the general membership. Look for the ballot in your email. And, deadline for members to submit proposals to change the Association’s Laws & By Laws. Contact Dr. Claus Buergelt, Secretary-Treasurer if you have suggestions @ buergeltc@mail.vetmed.ufl.edu

July 4 Deadline for the membership to suggest items for the agenda of the general membership meeting. Contact Claus @ buergeltc@mail.vetmed.ufl.edu

August 1 Secretary-Treasurer sends a draft of the agendas for both the Governing Board and general membership meetings to the full membership.

August 1 Full manuscript are due from all authors with papers accepted for presentation at the 8ICP.

August 13 Electronic presentations, i.e., PowerPoint files, for the Colloquium must be submitted to the organizers of the 8ICP at 8icp@kvl.dk

August 13 Meeting of the Governing Board (Officers and Board of Directors) in Copenhagen.

August 14 Start of the 8th International Colloquium on Paratuberculosis in Copenhagen.

August 17 International Association for Paratuberculosis general membership meeting beginning at 16:30.

At the 7ICP it was decided that we will set our Colloquia on a two year schedule, reflecting the accelerating pace of work in the field of paratuberculosis. Therefore, the 9ICP will be held in 2009. As of now, we have not established where this meeting will be held and are seeking proposals from countries interesting in hosting either the 9th or 10th ICP. It would be helpful to have an expression of interest by May. This can be sent to any officer or member of the Board of Directors. The Board will then decide which countries to invite to make more formal presentations in their bids to host a Colloquium at the Governing Board meeting August 13.

Watch your email for further updates as we approach our next Colloquium.

Sincerely,

Michael T. Collins mcollin5@wisc.edu
President, International Association for Paratuberculosis
What is your diagnosis?

Lesions identified at slaughter in the mesenteric lymph nodes of an approximately 2 year old farmed deer. This deer was not showing any clinical signs of disease.

While not the most common lesion seen in deer with paratuberculosis, this liquefactive-type of lesion is frequently seen in deer infected with *M. paratuberculosis*. Importantly, almost identical lesions are seen in some deer infected with *Mycobacterium bovis*. I have never seen this type of lesion in cattle, sheep or goats infected with *M. paratuberculosis*. Editor.

Dr T.J. Ryan is thanked for supplying the photographs.
Burrill B. Crohn (1884-1983)

The history of the first descriptions of what is now known as Crohn’s disease is fascinating and touched with a little controversy. The whole saga has recently been reviewed in The Mount Sinai Journal of Medicine, and the two central articles originally published in 1932 have been reprinted. J.H. Baron has produced a complete account of the events. The summary of Baron’s paper is presented below.

“Inflammatory bowel diseases have been a major interest of generations of Mount Sinai Hospital gastroenterologists. Although clinical descriptions of diarrhea with or without blood go back thousands of years, clear distinctions between enteritis and ulcerative colitis were possible only in the 19th century. At that time, many case reports were published of, in retrospect, classical regional enteritis. The term "ulcerative colitis" dates from 1888; the introduction of the electric sigmoidoscope soon after made it possible to make proper diagnosis of ulcerative colitis and distinguish it from infective dysentery, membranous mucous or catarrhal colitis, and nervous diarrhea. Doctors at The Mount Sinai Hospital adopted this diagnostic approach in the 1870s and 1880s, and were particularly interested in patients with tuberculosis-like ileocecal disease without tubercle bacilli. Articles were written by Weiner in 1914, Moschowitz and Wilensky in 1923 and 1927, and Goldfarb and Suisse in 1931. Dr. A.A. Berg, in 1925, encouraged his assistant Leon Ginzburg to conduct a study of the inflammatory granulomatous diseases of the bowel, when Ginzburg and Gordon Oppenheimer were working in Dr. Paul Klemperer's laboratory. Initial reports came in 1927 and 1928, but Ginzburg and Oppenheimer "in conjunction with Dr. Burrill B. Crohn" presented a definitive paper, "Non-specific Granulomata of the Intestine," on May 2, 1932, to the American Gastro-Enterological Association. On
May 13, 1932, Dr. Crohn presented a paper on "Terminal Ileitis" to the American Medical Association; this was published later that year with the title "Regional Ileitis: A Pathologic and Chronic Entity," under the authorship of Crohn, Ginzburg and Oppenheimer.

Baron’s conclusion was that the Ginzburg and Oppenheimer American Gastro-Enterological Association presentation in 1932 and subsequent papers were the definitive clinicopathological studies which established the entity of regional enteritis in both small and large intestine.

http://www.mssm.edu/msjournal/67/673174.shtml

Drs Oppenheimer, Crohn and Ginzburg

Non-specific Granulomata of the Intestine (Inflammatory Tumors and Strictures of Bowel) Leon Ginzburg and Gordon D. Oppenheimer


Regional Ileitis: A Pathologic and Clinical Entity
Burrill B. Crohn, Leon Ginzburg, and Gordon D. Oppenheimer
JAMA (1932) 99:1323-1329

DEADLINES

The following deadlines should be noted by authors

Abstract Submission
March 15, 2005 at 23.59 CET
No abstracts will be accepted after this date, irrespective that it may be customary at some conferences

Keynote presentation: Notification to authors if their submission has been selected
May 1, 2005
Note will be sent by e-mail to corresponding author

Short oral presentation: Notification to authors if their submission has been selected
May 1, 2005
Note will be sent by e-mail to corresponding author

Full paper submission
August 1, 2005 at 23.59 CET

Submission of presentations by e-mail
August 13, 2005 at 23.59 CET
Should be sent to 8icp@kvl.dk

For further details visit the 8ICP website

http://www.8icp.dk/
The Editor’s selection

The following are some recent publications that have attracted the interest of the Editor. The selection is heavily biased by the background and interests of the editor.

Use of multilocus variable-number tandem-repeat analysis for typing Mycobacterium avium subsp. paratuberculosis.


The etiology of Crohn's disease in humans is largely unknown. Clinical signs of Crohn's disease partly resemble the clinical picture of Johne's disease in ruminants caused by Mycobacterium avium subsp. paratuberculosis. Because of the high prevalence of these bacteria in (products of) ruminants and their remarkable thermostability, concern has been raised about the possible role of these bacteria in the pathogenesis of Crohn's disease. In an attempt to develop a molecular typing method to facilitate meaningful comparative DNA fingerprinting of M. avium subsp. paratuberculosis isolates from the human and animal reservoirs, multilocus variable-number tandem-repeat analysis (MLVA) was explored and compared to IS900 restriction fragment length polymorphism (RFLP) typing. MLVA typing subdivided the most predominant RFLP type, R01, into six subtypes and thus provides a promising molecular subtyping approach to study the diversity of M. avium subsp. paratuberculosis.

Analysis of the immune response to Mycobacterium avium subsp. paratuberculosis in experimentally infected calves.


Department of Veterinary Microbiology, College of Veterinary Medicine, Seoul National University, Seoul, Korea.

Infect Immun. 2004 Dec;72(12):6870-83
Johne's disease of cattle is widespread and causes significant economic loss to producers. Control has been hindered by limited understanding of the immune response to the causative agent, Mycobacterium avium subsp. paratuberculosis, and lack of an effective vaccine and sensitive specific diagnostic assays. The present study was conducted to gain insight into factors affecting the immune response to M. avium subsp. paratuberculosis. A persistent proliferative response to M. avium subsp. paratuberculosis purified protein derivative and soluble M. avium subsp. paratuberculosis antigens was detected in orally infected neonatal calves 6 months postinfection (p.i.) by flow cytometry (FC). CD4(+) T cells with a memory phenotype (CD45R0(+)) expressing CD25 and CD26 were the predominant cell type responding to antigens. Few CD8(+) T cells proliferated in response to antigens until 18 months p.i. gammadelta T cells did not appear to respond to antigen until 18 months p.i. The majority of WC1(+) CD2(-) and a few WC1(-) CD2(+) gammadelta T cells expressed CD25 at time zero. By 18 months, however, subsets of gammadelta T cells from both control and infected animals showed an increase in expression of CD25, ACT2, and CD26 in the presence of the antigens. Two populations of CD3(-) non-T non-B null cells, CD2(+) and CD2(-), proliferated in cell cultures from some control and infected animals during the study, with and without antigen. The studies clearly show multicolor FC offers a consistent reliable way to monitor the evolution and changes in the immune response to M. avium subsp. paratuberculosis that occur during disease progression.

An evaluation of mycophage therapy, chemotherapy and vaccination for control of Mycobacterium avium subsp. paratuberculosis infection.

Emery DL, Whittington RJ.

Faculty of Veterinary Science, University of Sydney Locked Bag 3, Camden, NSW 2570, Australia. david.emery@camden.usyd.edu.au


The control of ovine Johne's disease (OJD) is important for domestic trade, the viability of farming units and possibly also for public health. Current strategies in Australia have included quarantine and pasture spelling to decrease prevalence and shedding rates and reduce numbers of Mycobacterium paratuberculosis (Mptb) ingested by susceptible sheep. However, alternative procedures are needed and vaccination with Gudair has recently commenced. This review examines prospects for the control of OJD by chemotherapy,
vaccination and mycophages. Current chemotherapeutic regimes for treatment of M. paratuberculosis in ruminants are prohibitively expensive and of dubious efficacy, and apart from environmental concerns, mycophage therapy lacks a track record of success against intracellular bacteria. There is substantial evidence that live and killed mycobacterial vaccines reduce the incidence of clinical disease and shedding rates in OJD. An appraisal of recent experimental results suggests that neonatal vaccination with a defined dose of M. paratuberculosis offers the best prospects for the induction of protective Th1-type immunity.

**Efficacy of pasteurization conditions for the inactivation of Mycobacterium avium subsp. paratuberculosis in milk.**

Stabel JR, Lambertz A.

US Department of Agriculture, Animal Research Service, National Animal Disease Center, Bacterial Diseases of Livestock Research Unit, Ames, Iowa 50010, USA. jstabel@nadc.ars.usda.gov


Mycobacterium avium subsp. paratuberculosis, the causative agent of a chronic enteritis in ruminants (Johne's disease), has been linked to Crohn's disease in humans. This microorganism is shed by infected animals primarily in the feces but is also shed in the milk at much lower levels. Therefore, dairy products from infected animals may be one mode of transmission of this animal pathogen. This study was designed to evaluate the effectiveness of the holder and high-temperature short-time pasteurization standards on the destruction of M. paratuberculosis. One hundred eighty experiments were conducted in this study using a slug-flow pasteurizer unit and a laboratory scale pasteurizer unit. Ultrahigh-temperature milk was inoculated at two concentrations, 10^8 and 10^5 CFU/ml, with three different field strains of M. paratuberculosis. Five different time-temperature combinations were evaluated: 62.7 degrees C for 30 min, 65.5 degrees C for 16 s, 71.7 degrees C for 15 s, 71.7 degrees C for 20 s, and 74.4 degrees C for 15 s. Three replicates of each experiment were run for the pasteurizer unit, time-temperature combination, and strain of M. paratuberculosis. Treatment of milk regardless of bacterial strain or pasteurizer unit resulted in an average 5.0- and 7.7-log kill for the low and high concentrations of inoculum, respectively. Milk treated for cheese production (65.5 degrees C for 16 s) resulted in a much lower and more variable kill. Results from this study indicate that the current U.S. minimum standards for batch and high-temperature short-time pasteurization of grade A milk significantly reduced the survivability of M. paratuberculosis, but some bacteria survived subpasteurization heat treatment of milk used for cheese manufacture.
The following have been written in response to the article published in September 2004 by Naser et al. in which they describe the isolation of M. paratuberculosis from the blood of patients with Crohn’s disease. The two responses to Naser’s paper question his statement that the finding of M. paratuberculosis in the bloodstream of patients with Crohn’s disease adds to the evidence that this organism is “a leading candidate pathogen” in this complex disease. Editor.

Crohn's disease and MAP.

Gaya DR, Black RA, MacKenzie JF.


Comment on: 
Lancet. 2004 Sep 18;364(9439):1039-44.

Crohn's disease and MAP.

Huggett J, Dheda K, Zumla A, Rook G.


Comment on: 
Lancet. 2004 Sep 18;364(9439):1039-44.

Culture of Mycobacterium avium subspecies paratuberculosis from the blood of patients with Crohn’s disease.

Naser SA, Ghobrial G, Romero C, Valentine JF.

Lancet. 2004 Sep 18;364(9439):1039-44.

Department of Molecular Biology and Microbiology and Biomolecular Science Center, Burnett College of Biomedical Sciences, University of Central Florida, Orlando, FL 32816, USA. nasers@mail.ucf.edu
International Life Sciences Institute (ILSI)

Founded in 1978, the International Life Sciences Institute (ILSI) is a nonprofit, worldwide foundation that seeks to improve the well-being of the general public through the advancement of science. Its goal is to further the understanding of scientific issues relating to nutrition, food safety, toxicology, risk assessment, and the environment by bringing together scientists from academia, government, and industry. ILSI's work is guided by its Code of Ethics and Organizational Standards of Conduct.

Emerging Pathogens Task Force

The major goal of this Task Force is to collect information on emerging pathogens in order to predict their occurrence and fate during processing methodologies more reliably, and to give recommendations on how contamination of the food supply can best be prevented in future. The Task Force reviews different emerging pathogens, and publishes the outcome in the ILSI Europe Report Series. Reports have been published on Salmonella typhimurium DT104, Entero-haemorrhagic E. coli, food-borne viruses, food-borne parasites and transmissible spongiform encephalopathy (TSE).

Mycobacterium avium subsp. paratuberculosis (MAP) and the Food Chain

2004

Grahame Gould


*Mycobacterium avium* subsp. *paratuberculosis* (MAP) is the causative agent of Johne’s disease in cattle, sheep and goats, and occurs in some non-ruminants, including primates. Heat treatment is the most effective measure to reduce MAP during the manufacture of milk and milk products, and of meat and products derived from meat. However, anomalously high heat tolerances of fractions of MAP populations have been reported, though not explained, and low level survival has been demonstrated in some surveys of commercially pasteurised milk.
There have been reports of a potential association between MAP and Crohn’s disease in humans. At present the complexity of the human disease is such that definitive answers cannot be given, though most recent studies do not support a causal link. However, the possibility should not be ignored. Issues that remain include the possibility of an association of MAP with the disease and, should there prove to be an association, the dose response relationship that would allow a proper risk assessment to be undertaken, targeting all possible sources of MAP. The report has identified a number of gaps, particularly with respect to the heat tolerance of MAP, and to sources of MAP other than dairy, especially water and meat.


A major emphasis and strength of this report is a review of the studies on the heat resistance of MAP. These studies have used a variety of different methods that may have had a major influence on the results. This point is discussed in some detail but the overall conclusion is that current pasteurisation procedures will markedly reduce the number of viable MAP present in milk. The conclusions in regards to MAP being a human pathogen are very similar to those of previous reviews such as the European Commission, 2000 and Rubery 2002.

The review of on-farm control measures is relatively brief and superficial and is a weakness of this report. Editor.

References


“Conclusions

MAP shed by infected cattle and other animals contaminates the environment and, whilst not multiplying there, gains irregular access to a number of foods, of which milk has received the most attention. Small fractions of populations of MAP cells appear, unexpectedly, to show greatly enhanced heat resistance, and MAP may occasionally be recoverable from pasteurised milk, though the reason for this remain unknown. In contrast to the many studies of MAP contamination of milk that have been undertaken, other potential sources, especially water and meat, have so far received too little attention.

The public health importance of such survival of MAP depends on their possible involvement in human disease, in particular Crohn’s disease. At the present time, despite substantial research the possible involvement of
MAP in human disease remains under discussion. Further studies are needed to clarify the issue.

**Recommendations**

While further studies are underway, it has been suggested that the food industry should adopt a precautionary approach and support programmes and new initiatives aimed at reducing the chance of MAP contamination of foods so that more effective control measures can be developed. There is a need to learn more about MAP occurrence in meat and water.

The most effective and long lasting actions are likely to be the on-farm management programmes aimed at reducing infection in cattle. While food processing, predominantly by heating, is effective in reducing numbers of any contaminant MAP, normally by approximately 5 log, the occasional occurrence of survivors remains unexplained, and requires further research.”
Animal health and welfare

The following are links to the DEFRA (Department for environment and rural affairs, UK) website and relate to issues about paratuberculosis. Included is a recent review on the assessment of surveillance and control of Johne’s disease in farm animals in Great Britain. Editor.

Johne's Disease in Dairy Herds

- **News release**: Launch of Guidance to Control Johne's Disease in Dairy Herds.
- **Assessment of surveillance and control of Johne's disease in farm animals in GB** (5.5 MB - Please note, this is a very large file) report by the SAC Veterinary Science Division
- Guidance Notes on the control of Johne’s disease in dairy herds in both English (2.7 MB) and Welsh (1.4 MB) versions.
- Introductory Leaflet for farmers on Johne’s disease in dairy herds in both English (1.4 MB) and Welsh (2.9 MB) versions.
- **Question & Answers (Q&A)** on M.paratuberculosis / Johne’s Disease / Crohn’s Disease / Future Policy.

- What is Johne’s disease?
- Why should farmers care about Johne’s disease?
- How is Map spread?
- How can you spot Johne’s disease?

You can download information on Johne’s Disease from this website or call the Defra Publications line on 0845 955 6000 quoting publication number PB9990.

**Why should farmers care about Johne’s disease?**

The disease can have a significant financial impact on herds through loss of output and early culling. It has been suggested that this organism may also be a possible cause of Crohn’s Disease in humans. Such a causal link between the two conditions has yet to be proved or disproved, however the Government is taking a precautionary approach in this area. A possible route to infection in humans could be through consumption of milk containing Map.

Control and prevention of Johne’s disease makes sound long term sense for three reasons:

1. To reduce or prevent your production losses and income that result from this disease;
2. to increase the value of your breeding stock if your herd is certified as
free of the disease and
3. to reduce the level of Map in milk and the environment.
The Food Standards Agency has published a strategy for reducing the
levels of Map in milk. The strategy includes the following components:

- Hygienic milking practices;
- Effective pasteurisation of milk;
- Reducing the level of Map in dairy herds.

For more information visit
www.food.gov.uk/science/sciencetopics/microbiology/mapinmilk and for
more
information on dairy hygiene refer to
www.defra.gov.uk/corporate/rds/shortguide.pdf. The guidance is based on
a detailed study undertaken for Defra by the Scottish Agricultural College.

JDCP National Coordinators
Quarterly Report

Quarterly Newsletter - JD News

This report gives an up-to-date summary of the paratuberculosis situation in
Australia. Editor.

- July - September 2004 [PDF] 134 KB LATEST

Paratuberculosis – Commercial websites

The following is a website address that refers to a site of a company that is selling products and or services relating to paratuberculosis. This site was not included in the September 2004 listing. The listing of the services is not an endorsement of them by the International Association for Paratuberculosis. The Association does not have an official opinion as to the value of the services or products described in the websites. The editor encourages members to forward to him any relevant websites that are not included in previous lists or any corrections of fact. These will be included in subsequent issues of the Newsletter.

Genekam Biotechnology AG

http://www.genekam.de/tex_e/main/mycoplama/mycobacteriumaviumrtu_e.html

Product

PCR kit ready to use, *Mycobacterium avium* subsp. *paratuberculosis*