# The Paratuberculosis Newsletter

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## Table of Contents



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Editor

# 1. IAP Business

## *Report on the 11th ICP*

*Richard Whittington*

The International Colloquium on Paratuberculosis 2012 (ICP) was held from 5-10 February 2012 at The Veterinary Science Conference Centre at The University of Sydney, Australia. The ICP is held every 2-3 years under the auspices of the IAP. It gathers together global expertise in the study and control of Johne's disease. The ICP enables people from around the world to discuss the latest findings, to stimulate new studies and to form new relationships and collaborations - with the ultimate goal of improving the control of Johne's disease.

In total **293 delegates** attended the Colloquium, from **36 countries**: Argentina 3; Australia 108; Austria 1; Brazil 2; Cameroon 2; Canada 20; Chile 2; Cyprus 1; Czech Republic 2; Denmark 7; France 7; Germany 5; Greece 2; India 8; Ireland 2; Iran 2; Israel 1; Italy 6; Japan 8; Netherlands 9; New Zealand 26; Norway 2; Qatar 1; Saudi Arabia 3; Singapore 1; Slovenia 1; South Korea 1; Spain 8; Sudan 1; Sweden 2; Switzerland 3; Syria 1; Thailand 4; United Arab Emirates 1; United Kingdom 14; United States 26.

The Colloquium attracted 11 Sponsors and Exhibitors, with 8 Exhibition Booths.

**Scientific program**
An engaging and science-rich program was developed by an International Scientific Committee and was delivered through 9 different theme areas. Sessions focused on diagnostics; the host immune response; genotyping and microbial diversity; microbiology; molecular biology; pathobiology; genomics; epidemiology; national and international disease control and public health. The program introduced a new session on the topic of sociology and its important influence on disease control.

A significant feature of this year's program was the Industry Special Focus Day which was sponsored by Animal Health Australia and brought together scientists, farmers, clinical veterinarians, veterinary consultants, the commercial sector and industry leaders.

The 11th ICP program included 35 Invited Speakers, 68 Oral Presenters and 139 Poster Presenters. The program brought together a large number of scientists and other professionals from around the world. It encompassed keynote and perspective speakers representing Australia, the United Kingdom, Denmark, Norway, United States of America, Canada, New Zealand and Japan.

**Sessions and invited speakers**
1. Diagnostics and Detection. Ian Gardner University of Prince Edward Island, Canada and John Bannantine National Animal Disease Centre, USA
2. Host Response and Immunology. Jayne Hope Institute for Animal Health, UK and Ingrid Olsen National Veterinary Institute, Norway
3. MAP Control Programs. David Kennedy Animal Health Services, Australia and Evan Sergeant Animal Health Services, Australia
4. Pathogenomics. Jeroen de Buck University of Calgary, Canada and Ad Koets Utrecht University, The Netherlands
5. Genotyping and MAP Diversity. Srinand Srivatsan University of Minnesota, USA And Karen Stevenson Moredun Research Institute, Scotland
6: Industry Special Focus Day.
7: Sociology and *Mycobacterium avium* Subsp. *Paratuberculosis* Control.

8. Epidemiology. Polychronis Kostoulas University of Thessaly, Greece
and Soren Nielsen University of Copenhagen, Denmark
9. Public Health and MAP in the Environment. Marcel Behr McGill University, Canada
and Eiichi Momotani National Institute of Animal Health, Japan
International Johne's Disease Initiatives. Vivek Kapur Pennsylvania State University, USA; Lorna Citer Animal Health Australia; Kaylene Larking Beef + Lamb New Zealand; Søren Nielsen University of Copenhagen
10. Colloquium Summary. Mike Collins University of Wisconsin, USA

**Social Program**
A vibrant social program contributed to the success of the meeting. It began with The Graduate Student Mixer, a very successful event, with students and key industry members in attendance. This event gave the Graduate Students the opportunity to meet some of the key professionals in the industry, whilst interacting with other student registrants. The event took place at North Sydney Lawn Bowls Club on the Sunday. The afternoon included a traditional Australian BBQ, as well as games of lawn bowls overlooking Sydney Harbour, the Opera House and Harbour Bridge.

The Welcome Reception took place at The Grandstand adjacent to the main oval of The University of Sydney. 196 delegates and 13 accompanying partners attended the event. During the two hour function, members enjoyed a wonderful warm summer's evening, with live music, drinks and canapés. Delegates enjoyed the opportunity to meet up with old friends and make new ones.

After an informative afternoon session on 'Mycobacterial Diseases of Wildlife' at Taronga Zoo, delegates were given one and half hours to wander the Zoo at their leisure, before boarding the Captain Cook III vessel for a 2 hour cruise on Sydney Harbour. After a short welcome speech by Greg Johnson from sponsor, Pfizer Animal Health, delegates enjoyed a leisurely cocktail cruise taking in the famous sights of Sydney Harbour.

To conclude the 11th International Colloquium on Paratuberculosis, 240 delegates (including partners) enjoyed a delicious three-course meal in one of Sydney old wharfs that has been converted into a spectacular location overlooking the harbour. The evening's theme reflected traditional Australian culture, captured in both the cuisine and the variety of entertainment. Delegates began the evening socialising with friends and colleagues, while enjoying predinner drinks on the picturesque deck. Once the delegates were ushered inside, upcoming Australian singer and pianist, Liam Cooper, commenced the entertainment for the night. Conference Chair Professor Richard Whittington and IAP President Ramon Juste welcomed members to the evening. Enthusiastic delegates were invited up on stage to take part in some very comical didgeridoo lessons. Guests were then treated to some beautiful and insightful poetry by Aussie bush poet, Bob Drake.

**Technical tours**
Two Technical Tours were offered as a part of the ICP 2012 program. The EMAI Laboratory and Belgenny Farm Technical Tour attracted 44 delegates who enjoyed a day out of Sydney visiting some of the most preeminent Science and Research facilities in Australia. The tour began with a trip to the NSW Centre for Animal and Plant Biosecurity at the Elizabeth Macarthur Agricultural Institute, followed by a visit to the historically significant Belgenny Farm. Delegates were able to relax over an Australian BBQ lunch, prior to visiting the last destination of the day, a visit to a modern, robotic "future dairy" farm.

The Arthursleigh Technical Tour was attended by 28 delegates who had a big day out. At 7:45am on Friday morning, 28 delegates met Professor Peter Windsor outside the Veterinary Conference Centre for the Arthursleigh Technical Tour. After a week of wet weather, the delegates were joined by the Australian sunshine on their journey to the Southern Highlands.

The first visit of the day was to a large, modern, commercial sheep and beef grazing property where the delegates engaged in discussions about animal husbandry and Johne's disease control with property managers. Delegates then experienced a heritage-listed wool shed from the early days of Australia's wool industry. After relaxing with a BBQ- style lunch, members got their hands dirty, as they took part in some true farm activities including whip cracking and sheep shearing.

**Feedback**
Based on the encouraging feedback received from many of the delegates, we can safely conclude that the 11th International Colloquium on Paratuberculosis was a success. The majority of the delegates were extremely positive about the events of the week and appeared to enjoy their time in Sydney.

**The bottom line**
A modest surplus in the 11ICP budget was returned to the IAP for investment in future meetings.

Conference dinner

The 11ICP delegates photograph

## *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

## *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/

## 2. Comments and Opinions

### Looking for Claude Bernard*

Gilles R. G. Monif, M.D.

The famous French physiologist, Claude Bernard, introduced to medicine what is basically a three step procedure by which observation is transformed into scientific truth: the scientific method. The first step involves gathering all the information relevant to the observation being analyzed. From the information gathered, a hypothesis is constructed to explain the observation. Finally, an experiment is designed, not to support the hypothesis, but to challenge it. A corollary within the scientific method is that the hypothesis must address the exceptions to the hypothesis if it is to be accepted as a scientific truth.

**Gathering All the Relevant Information:**
The United States Department of Agriculture (USDA) omitted from its synthesis consideration that *Mycobacterium avium* subspecies *paratuberculosis* (Map) had evolved with other pathogenic mycobacterium through an evolutionary bottle neck that partially connected them in terms of genetic material and pathogenic potential. Two errors, 1) that Map was THE cause of Johne's disease and 2) that *Mycobacterium avium* subspecies *avium* (Ma) and related mycobacterium where "environmental organisms" became assumptions central to the formulation of the hypothesis. These two conception errors were incorporated into the development of Map's diagnostic technologies and the subsequent interpretation of the resultant epidemiology data. The demand for specificity precluded the recognition that between Ma and Map pathogenic genomic variants exist. Basing all diagnostic technology of IS900 insertion sequence recognition, clinical isolates not confirmed by IS900 based primers or serum specimens not identified exclusively by antigens derived from an IS900 strain were either disregarded or not recognized.

USDA built its hypothesis for the natural history of herbivore infection by Map on fecal culture isolation data and industry-created Map ELISA tests. Fecal recovery of Map became the "gold standard" upon which USDA's scientists anchor their studies rather than the periodic use of necropsy to confirm or challenge presumptions derived from fecal culture data.

USDA permitted the manufacturers of Map serological tests to determine a given test's point of positivity without stating the exact meaning of a positive test. The unstated inference of a positive Map ELISA test was that an animal testing positive would develop chronic, granulomatous enteritis (Johne's disease). Approximately, 74% of animals testing positive will progress to clinical disease; however, the science requires an explanation as to why the other 26% of sero-positive animals fail to do so. USDA accepted, without asking the mandatory WHY, industry's explanation that an animal with a high positive titer that becomes subsequently sero-negative represented a false-positive test.

The net data derived from these two epidemiology tools should have launched different avenues of inquiry. The collective data of Collins et al., Whitlock et al., and Sweeney et al. had shown but a 13.5% TO 29% correlation between fecal recovery of Map and demonstration of anti-Map antibodies. The best correlation between the two diagnostic technologies was when the animal had advanced infection/disease. Even then, the correlation did not approach anything close approximating one standard deviation. By selective specimen selection, new diagnostic tests could demonstrate excellent specificity and sensitivity.

**The Governing Hypothesis:**
Elegant micro-molecular research delineated the pathogenesis of Johne's disease. The pathogenesis of diseases constitutes but an alternative terminal event within the natural history of Map infection.

USDA's contract acquired investigators advanced the hypothesis of a three stage natural history for progressive Map infection. Infection was presumed to be acquired early in an animal's life. Subsequently, Map was non-recoverable from fecal specimens as well as Map antibodies detected in sera. In the final stage, subclinical infection becomes documented by culture isolation of Map or serological demonstration of Map antibodies and capable of progression to overt disease.

Very quickly, observations were documented that seriously challenged the prevailing hypothesis. Individual cows lacking Map antibodies as well as evidence of clinical involvement transiently excreted Map in their feces and thereafter did not. This observation should have invalidated the hypothesis. Instead, USDA and its contract investigators proposed that what had been documented represented the incidental ingesting of fecal contaminated material. The term "pass-through" was coined to explain the apparent counter-evidence to the hypothesis. If anyone had calculated the amount of Map needed to overwhelm an animal's gastrointestinal Map receptor sites, this explanation would not have been accepted.

One clear acknowledgement of a flawed hypothesis was USDA's acceptance that intra-herd Map spread occurred. A system for quantifying the amount of Map in feces was put in place. Animals with a given amount of Map in their feces were termed "super-shedders" and marked for removal from the herd in order to reduce intra-herd dissemination of infection. While a good example of deductive reasoning, its formulation failed to take into consideration that Map grows in clumps. USDA allowed for the possibility of sample error to confound epidemiology data derived from quantified Map fecal data. When multiple samples were ultimately taken from the same specimen and analyzed using a variety of identification technologies, only 40% of culture identified "super shedders" were confirmed.

**Creation of an Experimental Design to Challenge the Hypothesis**
USDA chose neither to scientifically address the contradictions to its hypothesis nor to address Congress' reason for funding USDA over the National Institutes of Health (NIH) and the Centers for Diseases Control and Prevention (CDC).

Rather than designing experiments to seriously challenge its hypothesis, USDA initiated a five year program of "test-and-cull" (an approach previously employed in the controlling of anthrax as a veterinary and human problem). When it became apparent that identifying infected animals and removing them from the herd was neither economically feasible nor capable of eliminating Map from infected herds, the massive herd management demonstration project became primarily an expensive data gathering vehicle that lost its scientific identity. "Measurement without hypothesis is not science" (Louis Pasteur).

**What USDA's Johne's Disease Dairy Demonstration Program Taught Us**
The USDA Johne's Disease Dairy Demonstration Project and the associated relevant literature did produce useful information applicable to the veterinary portion of the Map dilemma.

1. Test-and-cull can markedly reduce the incidence of Johne's disease, but will not eliminate Map infection with the herd.

2. Monitoring for Map is economically beneficial to producer's bottom line.

3. Intra-herd dissemination of Map does occur.

4. More attention needs to be given to the supplemental feeding of calves.

5. Once Map is introduced into the pasture/production environment, its eradication is nearly impossible.

6. Significant polymorphism exists within Map and its genomic variants.

7. The IS*900* insertion sequence will not detect all pathogenic mycobacterium.

USDA is a branch of the United States government that is staffed by dedicated women and men who rigorously uphold the mission objective that led to its creation. The primary mission of USDA is the support and advancement of agriculture and agriculture-related business. Congress should have never asked USDA to address a problem that had the potential to violate its charter obligations and that exceed the credentialing of its designated scientists in the area of infectious diseases.

For Claude Bernard, science has a moral obligation to function within the public trust. A question that needs to be answered is when does bad science, masquerading as a scientific truth, becomes a violation of that trust?

**Expected date of publication September 2012*

## 3. List of Recent Publications

Abendaño N, Sevilla I, Prieto JM, Garrido JM, Juste RA, Alonso-Hearn M. Quantification of *Mycobacterium avium* subsp. *paratuberculosis* strains representing distinct genotypes and isolated from domestic and wildlife animal species by use of an automatic liquid culture system. J Clin Microbiol. 50:2609-17.

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