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# The MAP Gap

Bridging The Space Between The Science And You

TheCrohnsInfection.org Quarterly Newsletter

April 2016

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## Site News

If you haven't visited the site recently, you are in for a treat! We have added new Tabs, Pages and even a Patient Story. Although we focus on treating Crohn's disease as a mycobacterial infection, **we've added a Page which discusses Traditional Treatment of Crohn's Disease.** While the page lays out the standard information about each treatment, some medications will be hyperlinked to their own, more detailed page in the future. We hope this enhancement provides our readers with accessible information to guide their treatment decisions.

While you're exploring the site, see the new **Documentary section** of videos. More will be added as they become available.

Also new is the **For Clinicians tab.** We felt strongly about having a place where doctors and health care practitioners could learn about this research in their own language directly from the doctors involved with our site. In this section, an exclusive analysis of the Selby study explains its design flaws, and indicates that the Selby study is an unreliable assessment of AMAT.

Lastly, **introducing our new Facebook Group!** We've enjoyed enhancing excellent research content but now we want to hear from you. We want to connect Crohn's patients and learn from our shared experiences. The Facebook group will feature real time information from a broader base, and allows everyone to join in the discussion. Tell us what you want to see and who you want to hear from in the future. We love comments and suggestions. Our free site exists to help Crohn's patients everywhere. All are welcome!❖

### INSIDE THIS ISSUE

1	Site News
1-4	Research Corner
3	Other News
3	Just for Fun

## Research Corner

Below we have summarized some recent mycobacterial research articles. While we've simplified the content in an attempt to make it accessible to everyone, we've also provided links if you'd like to view the source and read the full article/abstract. While this is not an exhaustive list, we thought these articles were the most pertinent to the focus of the site.

### **On deaf ears, *Mycobacterium avium paratuberculosis* in pathogenesis Crohn's and other diseases. (December 2015)**

Historically, a large problem with research in Crohn's disease surrounding MAP has been a reliable detection method. Now that more advanced detection methods are available, MAP has been found in a greater percentage of Crohn's disease patients than in controls.

**What is more concerning is the number of MAP infected healthy controls;** those who show no symptoms of disease. Difficulty in understanding the mechanism of

how some mycobacterial species cause disease in only a portion of those exposed is also at issue in the MAP in Crohn's debate. Why do some get disease while others who were similarly exposed don't? Only about 10% of those exposed develop active tuberculosis. How MAP triggers Crohn's disease needs to be studied further.

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*Humans like other species, are equally susceptible to infection with MAP regardless of health status.*

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By studying the role of MAP in Johne's disease, we've learned that MAP has a long latency period, and exposure needs to be constant to cause disease. Younger animals seem more susceptible. Generally, humans and cattle seem to have a protective immune response when introduced to MAP which protects the patient from disease. At some point this protective immune response breaks down, and the disease process begins.

[William C. Davis, World J Gastroenterol. 2015 Dec 28; 21\(48\).](#) ❖

### **Seroprevalence of IgG1 and IgG4 class antibodies against *Mycobacterium avium* subsp. *paratuberculosis* in Japanese population. (October 2015)**

Researchers measured the MAP serum IgG antibody levels of 126 healthy Japanese. Elevated antibody responses were seen in 14% of the samples. This provides evidence that the Japanese population is exposed to MAP from a foodborne chain of exposure. No cross reaction with BCG antigens were observed.

[Otsubo S, Foodborne Pathog. Dis. 2015 Oct;12\(10\):851-6.](#) ❖

### **The association of *Mycobacterium avium* subspecies *paratuberculosis* with Inflammatory Bowel Disease. (February 2016)**

Colonoscopy biopsies of 105 subjects (42 controls) were tested for the MAP via three different PCR assays. While only 29% of Crohn's patients were positive for all three PCR assays, this was a significant association that was unrelated to age, gender, place of birth, smoking and alcohol intake. No evidence of MAP was detected in the patients with aphthous (mouth) ulcers, which have been

suggested as a precursor to Crohn's disease. One of the cultures, from a UC patient, grew at 5°C and was resistant to ethambutol, streptomycin, clofazamine and rifampin. The authors made note of this culture and raised the Selby Study, wherein this isolate would have been resistant to the antibiotic regime and deemed ineffective. This highlights the need for improved detection and monitoring MAP in humans.

[Timms VJ, Daskalopoulos G, Mitchell HM, Neilan BA \(2016\) PLoS ONE 11\(2\): e0148731. doi:10.1371/journal.pone.0148731.](#) ❖

### **Oxidative stress due to *Mycobacterium avium* subspecies *paratuberculosis* (MAP) infection upregulates selenium-dependent GPx activity. (March 2016)**

The authors studied the relationship between MAP infection and selenium-dependent glutathione peroxidase (GPx) in both cattle and humans. GPx is an antioxidant enzyme thought to prevent GI tract inflammation. The results showed a strong correlation between MAP infected humans and increased GPx activity. This means that Crohn's patients had more oxidative stress than controls. This correlation may even be useful for predicting MAP infection status. GPx levels were also significantly higher in MAP infected cattle.

Interestingly, a similar strong correlation was shown in MAP infected pre-diabetes patients. The authors posit that MAP could be involved in the development of insulin resistance.

[Qasem A, Abdel-Aty A et al, Gut Pathogens 2016 8:12, DOI: 10.1186/s13099-016-0090-8.](#) ❖

### **Genome-Wide Diversity and Phylogeography of *Mycobacterium avium* subsp. *paratuberculosis* in Canadian Dairy Cattle. (February 2016)**

In this study, 182 MAP samples from Canada were differentiated using full genome DNA sequencing. MAP is generally classified into two broad types: Type I and Type II. Of the nine subtypes identified, eight were classified as Type II. One of the subtypes, Type Bison, indicates that there was a recent transmission of MAP between bison and dairy cattle. The article concludes: "The large number of

shared subtypes among provinces suggests that cattle movement is a major driver of MAP transmission at the herd level."

[Ahlstrom C. et al. \(2016\) PLoS ONE 11\(2\): e0149017. doi:10.1371/journal.pone.0149017.](#) ❖

### Assessment of yeast *Saccharomyces cerevisiae* component binding to *Mycobacterium avium* subspecies *paratuberculosis* using bovine epithelial cells. (March 2016)

The authors here postulated that since dairy producers often use yeast to combat pathogens and alleviate the need for antibiotics, yeast may have some preventative effect against Johne's disease. They concluded that two forms of a dead yeast strain showed a significant impact in preventing MAP from adhering to epithelial (skin) cells in vitro. However, more investigation needs to be done using small intestinal epithelial cells, which were not readily available and the mechanism of action of reduced MAP adhesion by yeast remains to be discovered.

[Ziwei, L. et al, BMC Veterinary Research 2016 12:42 DOI: 10.1186/s12917-016-0665-0.](#) ❖

### Possible Airborne Person-to-Person Transmission of *Mycobacterium bovis*. (March 2016)

The CDC issued this notice which details an airborne cluster of *Mycobacterium bovis* infections, previously thought to be transmitted to humans solely by unpasteurized dairy products.

[Buss, B. et al, Morbidity and Mortality Weekly Report, March 4, 2016 / 65\(8\):197-201.](#) ❖

## Other News

In a [February 2016 press release](#), Martinis BioPharma received FDA approval to begin a Phase I study of **amikacin**, an antibiotic used in the treatment of Non-Tuberculosis mycobacteria. Phase I, scheduled to begin in the first half of 2016, will evaluate the drug's safety in health subjects.

Two press releases from **RedHill Biopharma** offer hope for both Crohn's and Multiple Sclerosis patients worldwide. Not only has RedHill [secured a 5th patent](#) for RHB-104 (the triple antibiotic cocktail for Crohn's disease), but they just released positive results from the [Phase IIa study](#) using RHB-104 to treat multiple sclerosis. Congrats to RedHill!

In a [February 24, 2016 press release](#), GeneThera names **Prof. Karel Hruska** as their new scientific advisor.

New Zealand patient Kimberley Coleman made news in February with [her story](#) of nearly 20 years of AMAT remission! ❖

## Just for Fun

Wish your ostomy bag had more style? One young entrepreneur is turning lemons into lemonade with [these fashionable ostomy bags!](#)

Need to find a toilet in no time? There's an app for that! Multiple apps like Take a Break and Flush cater to this critical need of IBD patients around the world. This [latest addition](#) gives information for Belgium and allows users to rate the location for cleanliness. ❖

Do you enjoy this newsletter? Sign up for our [mailing list](#) to get the latest content. We value your privacy as much as you do, your information will never be sold or shared.

Have a question or comment? We'd love to hear from you! Visit our [Contact page](#).

### **Crohn's disease diagnosis difficult to obtain, life altering, new national study finds. (March 2016)**

A study of more than 2000 United States Crohn's disease patients reveals some insightful information about what it's like to live with the disease:

- 22.5% say that they had their first symptoms prior to age 15.
- 44% needed 10 or more office visits for initial diagnosis.
- Less than 3% of respondents were not experiencing symptoms.
- One quarter say they've never been in remission, and three quarters report a flare every few months.
- 85% report complications, the three most prevalent being swollen joints, malnutrition and anemia

[Health Union. ScienceDaily, 1 March 2016.](#) ❖

### **Curcumin enhances human macrophage control of *Mycobacterium tuberculosis* infection. (March 2016)**

Curcumin, which is generally found in the spice curry, was found to induce apoptosis (cell death), which is the mechanism used by macrophages to kill intracellular tuberculosis. The conclusion was that curcumin protects human macrophages against tuberculosis infection.

[Bai, X, et al, Respiriology, 2016; DOI:10.1111/resp.12762.](#) ❖

### **Gut Bacterial DNA Translocation is an Independent Risk Factor of Flare at Short Term in Patients With Crohn's Disease. (February 2016)**

Bacterial DNA (bactDNA) was detected in the blood of 98 of 288 Crohn's disease patients who were in remission. The presence of bactDNA was determined to be a significant, independent, predictive factor for relapse measured by hospitalization, steroid start-up and treatment switch at 6 months. Patients with bactDNA had increased levels of inflammatory cytokines in their blood.

[Gutiérrez, A et al, \(23 February 2016\)|doi:10.1038/ajg.2016.8.](#) ❖

### **Tracking of *Mycobacterium Avium Paratuberculosis* Load in Milk Production Chain: A Real Time QPCR Culture Assay. (March 2016)**

This study looked at the MAP levels at various stages of the milk production chain in dairy herds to determine potential sources of contamination. Testing was done on milk at the individual cow level, at the farm collection tank and at the local collection center. Fecal contamination during hand milking or at the farm level was found to play a major role in increasing the MAP levels in the bulk collection tanks.

[Hanifian, S et al, Journal of Food Safety, March 2015, doi: 10.1111/jfs.12243.](#)

### **The Economic and Health-related Impact of Crohn's Disease in the United States: Evidence from a Nationally Representative Survey. (March 2016)**

Although this may not come as much of a surprise to sufferers, Crohn's disease is associated with higher medical costs, lost earnings and is responsible for \$3.48 billion in yearly national costs in the United States alone. However, the numbers do not tell the full story of the cost of Crohn's disease to individual patients like our readers.

[Ganz, ML et al, Inflamm Bowel Dis. 2016 March 10, epub ahead of print.](#)