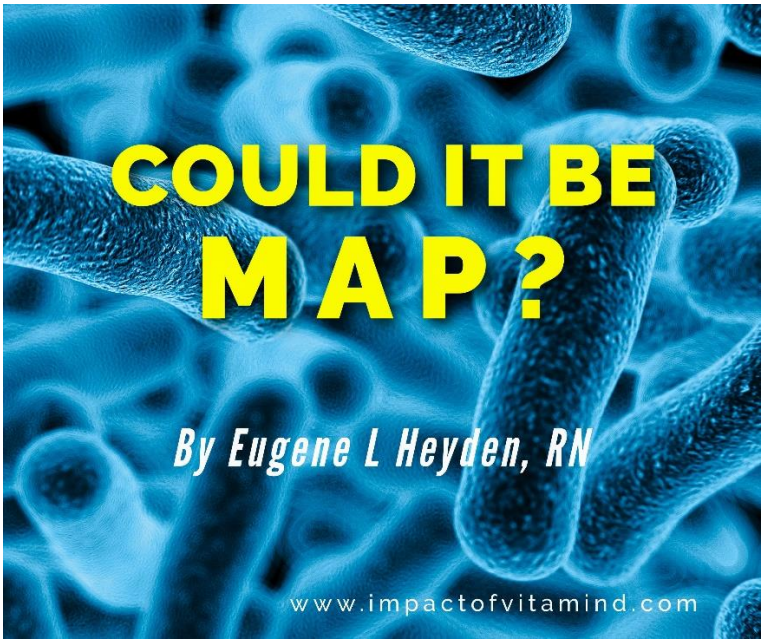

Could it be MAP?

By Eugene L. Heyden, RN

I have been following a controversy for years: Is a pathogen called ***Mycobacterium avium*** **subspecies** ***paratuberculosis***, **MAP** for short, the cause of Crohn's? I must confess, at times I had my doubts (little tiny doubts), but the latest evidence for this is very strong. And then I stumbled across the work of Dr. Horatio Bach—it's all over folks! No more little tiny doubts for me! The research that he and his colleagues have conducted should help lay this controversy to rest . . . eventually. But first, let's back up a little and see what the MAP controversy is all about. Then I will share with you what I regard as a "landmark" discovery, or more accurately, series of discoveries, made by Dr. Bach and associates.

When Crohn's disease was first characterized in the early 1930s as a distinct disease entity, it was exceedingly rare. Most physicians at the time had never seen such a thing! But collectively they were ready for a new challenge, now that falling off a horse was no longer the leading cause of death. And if a physician at this point in time did happen to run across a patient exhibiting the signs and symptoms of this disease before it was formally characterized by Dr. Burrell B. Crohn and associates, he or she may have called it intestinal tuberculosis. But Crohn's was a different animal. It looked and acted so much

like a devastating disease in cattle called **Johne's disease**—an infectious disease unquestionably caused by MAP. Many investigators at the time, including Dr. Crohn himself, believed that Crohn's was caused by MAP. But since all efforts in the early days of Crohn's research failed to discover the pathogen in human tissue samples yet the similarities between Crohn's and Johne's disease were so compelling, two camps were eventually formed: one camp of believers, one camp of nonbelievers. And just like that, a controversy was born.

As time passed, those who did not believe became the majority, perhaps unduly influenced by their previously-held assumptions. MAP infection simply did not fit within with their "psychosomatic" or their "autoimmune" disease theories, theories now laid to rest. Even today, if you believe that Crohn's disease is caused by an abnormal reactivity to ordinary gut microbes, the commonly-held belief today, you are unlikely to consider MAP to be the pathogen behind the disease. Enter Dr. Bach and team. What did they discover that I believe will help put an end to the controversy?

What this team of investigators found was this: Within the immune cell called the macrophage—a cell known to be dysfunctional in Crohn's and central to the disease process—a unique foreign protein can be found after it is infected with MAP (Bach et al., 2006; Xai et al., 2011). It is a protein called **PtpA**. This protein is created and released by MAP only when it wants to survive within a host cell and interfere with host cell function. Additionally, Dr. Bach and associates found that antibodies to PtpA were *"significantly higher"* in the blood of patients with CD compared to patients with ulcerative colitis and healthy controls (Xai et al., 2011). This is quite a finding! But there is more to the story.

In an earlier study, Dr. Bach and team found that "live" MAP pathogens secrete PtpA after being enclosed within an isolation membrane formed by the macrophage, a membrane called a **phagosome** (Bach et al., 2006). Just so you know, a phagosome is created by the cell to envelope and isolate an invading pathogen. (For the macrophage, phagosome formation is business as usual.) According to plan, the macrophage systematically wraps a bacterium within a phagosome to first contain it, then later to destroy it. Enter PtpA. **PtpA secretion by MAP occurs after its capture. Its job is to leave the phagosome and block further efforts by the macrophage to destroy the invader within (Xia et al., 2011). The pathogen gets to live. To find PtpA in significant amounts is to find MAP, or similar pathogen, alive and taking the sophisticated steps it takes to prevent its destruction. It tells us that pathogens are being captured and pathogens are taking the measures it takes to establish and perpetuate an infection. In my view, this is a very important and most relevant finding!** And

all this was worked out in an actual human macrophage cell line. Taken together, the discoveries of Dr. Bach and associates present compelling evidence that MAP is actively involved in the disease we call Crohn's. But then, there is compelling evidence everywhere!

> *MAP is present in **86%** of surgically resected tissue compared to 20% of biopsy specimens of CD patients **compared to 0% of controls**. These data suggest that MAP may be residing in the submucosal layer of ulcerated tissue in CD patients rather than in biopsies obtained from the surface of the mucosal layer. The fact that MAP was cultured in several weeks from resected tissue of CD patients, rather than several months as seen in some positive biopsies, may indicate that MAP in deep tissue is virulent and metabolically active.* **(Schwartz et al., 2000, emphasis added)**

And consider this:

> *Recent technical advances . . . [have] allowed for more accurate identification of MAP via DNA amplification, identifying MAP DNA in up to 92% of CD [Crohn's disease] tissues versus only 26% in healthy controls. Another study of resected bowel tissues from 300 CD patients identified MAP DNA in 52% of CD patients, 2% of UC [ulcerative colitis] patients and 5% of controls, further supporting a similar study that identified MAP DNA in 6/7 (86 %) resected tissue, and 4/20 (20%) biopsy specimens from CD patients, versus 2/36 (5.6%) control biopsy specimens.* **(Campbell et al., 2012)**

No wonder investigators are beginning to say things like,

> *Although there has been a century-long debate, the role of MAP in Crohn's has evolved from controversial to compelling.* **(Dow, 2012)**

And speaking of compelling, there is a new report out of India I must share with you. (Singh et al., 2016) This is the first case report of its kind. It tells the story of an individual who was found to be sheading massive numbers of MAP cells in his stool, similar to what happens in livestock during the later stage of Johne's disease.

In the report, we meet a 61-year-old gentleman who had been experiencing all the classic symptoms of Crohn's, diarrhea included, for quite some time. Despite consulting with gastroenterologists over a period of years, he did not receive a diagnosis that lead to effective treatment. For some reason, the diagnosis of Crohn's was not made. Did I mention diarrhea? I would say passing loose stool or mucus every half hour, day in and day out, is a sure sign that something is wrong. Well, you can't put up with this forever! In addition, this gentleman was suffering from weight loss, weakness, and depression.

Fortunately for the gentleman of our story, he had a relative who was a state official familiar with the screening of animals for MAP, goats included. Eventually, a conversation occurred between these two individuals. It must have gone something like this: "If the doctor for humans can't help you, maybe a good goat doctor could get to the bottom of things?" This line of reasoning makes perfect sense to me, and apparently made perfect sense to the gentleman of our story, who promptly scheduled an appointment with the local Central Institute for Goat Research.

At the Central Institute for Goat Research, after patiently waited his turn, our gentleman produced a stool sample for testing. (It didn't take long.) Subsequently, the stool sample was found to be loaded with MAP cells. Blood work, drawn at the time of the initial visit, also revealed the presence of MAP.

Well you can't take a gentleman out and shoot him (you can do this to a goat) so the kind folks at Central Institute for Goat Research found a local physician who agreed to medically manage this clear case of human Johne's disease. But not just any physician. The new physician just happened to be familiar with the use of antibiotics to treat MAP infection in humans. The gentleman of our story was undoubtedly infected with MAP. In view of this finding, no other therapy would be reasonable to pursue.

After consulting a world-renowned expert in the treatment of Crohn's disease with anti-MAP antibiotics (Dr. Thomas J. Broody), the new physician started the new patient on an aggressive antibiotic regimen. After four months, stool frequency was reduced from every half hour to two to three times a day. And after a year of therapy, *"recovery was complete,"* with post-treatment studies finding no evidence of MAP in his stool. I guess one might say he was cured. Apparently, his Johne's disease (Crohn's) became a thing of the past.

Certainly, this report out of India will cause many to pause and take notice. Perhaps MAP is the pathogen behind the disease. The case for this is only getting stronger.

If you wish to learn more about the relationship between MAP and Crohn's disease, I have a plan. If you click on the link provided immediately below, you can read and excerpt from my book ***More to Consider in the Battle against Crohn's***.

Click here to read Crohn's and the MAP Controversy**.**

I will close with this:

> *The concept of CD being triggered by a Mycobacterium is gaining momentum with the advent of new molecular techniques and cytogenetics. Mycobacterium avium subspecies paratuberculosis (MAP) is once again coming under the microscope due to the increased ability to detect its genetic signature.* **(Agrawal et al., 2014)**

> *In due course, informed public opinion will judge Gastroenterology harshly if a culture of neglect on this issue, and an inadequate understanding and misinterpretation of available scientific information, in the field, occasionally exemplified in contemporary writing, continues to prevail.* **(Hermon-Taylor, 2002**)

Suggested reading

I have a friend who has been severely damaged by Crohn's disease. My friend is also a physician. She has studied the Crohn's/MAP controversy relentlessly and has written several papers on the subject. Her mission in life is to convince others that MAP *is* the pathogen behind the disease. If you want to learn more about MAP, her papers will get you off to a great start. They are all available free, and easy to find on the internet.

Pierce ES 2009 Where Are All the *Mycobacterium avium* subspecies *paratuberculosis* in Patients with Crohn's Disease? PLoS Pathogens; March; 5(3):1–11

Pierce ES 2010 *Mycobacterium avium* subspecies *paratuberculosis* the Common Villain? Gut Pathogens 2:21

Pierce ES 2009 Possible Transmission of *Mycobacterium avium s*ubspecies *paratuberculosis* through Potable Water: Lessons from an Urban Cluster of Crohn's Disease. Gut Pathogens; September 23; 1(7):1–5

Pierce ES, Borowitz SM, Naser SA 2011 The Broad Street Pump Revisited: Dairy Farms and an Ongoing Outbreak of Inflammatory Bowel Disease in Forrest, Virginia. Gut Pathogens 3(20):1–5

Pierce ES 2012 Free-Ranging Rocky Mountain Bighorn Sheep and an Outbreak of Inflammatory Bowel Disease along the Clark Fork River in Plains, Montana. Virulence; October 2; 3(6):546–550

Also recommended

Agrawal G, Borody TJ, Chamberlin W 2014 "Global Warming" to *Mycobacterium avium* subspecies *paratuberculosis.* Future Medicine 9(7):829– 832 http://www.futuremedicine.com/doi/pdf/10.2217/fmb.14.52

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Bach H, Ko HH, Raizman EA, Attarian R, Cho B, Biet F, Enns R, Bressler B 2011 Immunogenicity of Mycobacterium avium subsp. paratuberculosis Proteins in Crohn's Disease Patients. Scandinavian Journal of Gastroenterology; Jan 1; 46(1):30–39.

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Campbell J, Borody TJ, Leis S 2012 The Many Faces of Crohn's Disease: Latest Concepts in Etiology. Open Journal of Internal Medicine (2):107–115

Dow CT 2012 *Mycobacterium avium* subspecies paratuberculosis—An Environmental Trigger of Type 1 Diabetes Mellitus. Journal of Diabetes Mellitus 2(1):88–95

Schwartz D, Shafran I, Romero C, Piromalli C, Biggerstaff J, Naser N, Naser SA 2001 Use of Short-Term Culture for Identification of *Mycobacterium avium* subsp. *paratuberculosis* in Tissue from Crohn's Disease Patients. Clinical Microbiol Infect 6(6):303–307

Singh SV, Kuenstner JT, Davis WC, Agarwal P, Kumar N, Singh D, Gupta S, Chaubey KK, Kumar A, Misri J, Jayaraman S. 2016 Concurrent Resolution of Chronic Diarrhea Likely Due to Crohn's Disease and Infection with Mycobacterium avium paratuberculosis. Frontiers in Medicine, 3
http://journal.frontiersin.org/article/10.3389/fmed.2016.00049/full

Xia A, Stempak JM, Grist J, Bressler B, Silverberg MS, Bach H 2014 Effect of Inflammatory Bowel Disease Therapies on Immunogenicity of *Mycobacterium paratuberculosis* Proteins. Scandinavian Journal of Gastroenterology; Feb 1; 49(2):157–163.

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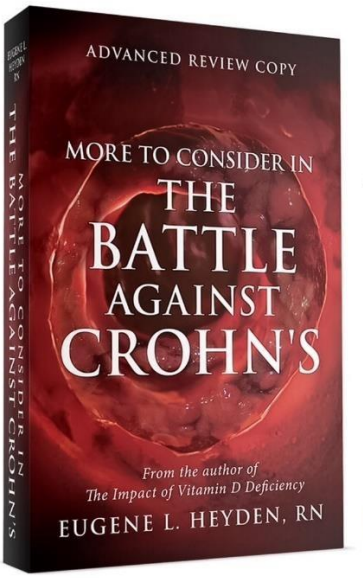

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