Paratuberculosis and Crohn's Disease: Got Milk?

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Project Censored

Microbial foodborne illness is the largest class of emerging infectious diseases. In 1999, the Centers for Disease Control (CDC) released the latest figures on the incidence of US foodborne illness considered by the Food and Drug Administration (FDA) to be the most complete estimate ever compiled. Seventy-six million Americans every year get food poisoning, more than double the previous estimate. In today's food safety lottery there's a 1 in 4 chance you'll get sick, a 1 in 840 chance you'll be hospitalized, and a 1 in 55,000 chance that an American will die from foodborne illness annually.[174]

The CDC estimates 97% of foodborne illness is caused by animal foods.[17] The latest United States Department of Agriculture (USDA) survey, for example, found 9 out of 10 Thanksgiving turkeys contaminated with *Campylobacter,* the most common cause of bacterial food poisoning in the United States.[175] And 75% of the turkeys are contaminated with two or more foodborne diseases, most often *Salmonella* as well, which are becoming dangerously resistant to many of our best antibiotics.[55]

Although thousands die from food poisoning every year in the United States, most sufferers only experience acute self-limited episodes. Up to 15% of those that contract *Salmonella,* however, go on to get serious joint inflammation that can last for years. An estimated 100,000 to 200,000 people suffer from arthritis arising directly from foodborne infections each year in the United States.[101]

The most feared complication of food poisoning, however, is Guillain-Barré syndrome, in which infection with *Campylobacter* can lead to one being paralyzed for months on a ventilator. Up to 3800 cases of Guillain-Barré are triggered by infection with *Campylobacter* every year in the United States.[101]

Some scientists now fear, though, that an even more serious disease may be contaminating our food supply. Often touted as the Pulitzer Prize of alternative journalism, a Project Censored Award was given to what was considered one of the most censored stories of 1999—the connection between Crohn's Disease and paratuberculosis bacteria in milk.[20]

Crohn's Disease

Described as a human scourge,[33] over a half million[120] Americans suffer from this devastating, lifelong condition[95] with annual US medical costs in the billions.[189] Crohn's sufferers experience profuse urgent diarrhea, nausea, vomiting, and fevers.[78] Because of the diarrhea, many people are unable to leave their houses; others drive around in recreational vehicles or mobile homes to keep a bathroom close at hand.[98] The director of the National Association for Colitis and Crohn's Disease says the best way to describe to nonsufferers how bad the disease can get is to have them think of the worst stomach flu they ever had and then try to imagine living with that every day.[29]

What happens is that the immune system starts attacking the lining of the gut, which becomes swollen and inflamed.[24] In extreme cases this painful embarrassing condition can affect any part of the digestive system from the mouth to the anus.[27] This inflammation narrows the digestive tract and can result in excruciating pain during digestion as well as constant uncontrollable bowel movements. Added discomforts associated with Crohn's disease include severe joint pains, weight loss, and lack of energy.[92]

The intestines characteristically become so deeply ulcerated that they take on a "cobblestone" appearance. The ulcers can actually eat right through the gut wall and cause bleeding, abscesses, fistulas and perforation.[150] Passing food, sometimes even just drink, through Crohn's damaged intestines can be excruciatingly painful. In the words of one colorectal surgeon, "Crohn's is a surgical disease. We wait until the patient can no longer withstand the pain anymore, and then we perform surgery …and repeated surgeries over time…ultimately, as recurrences happen and intestinal damage occurs, we just cut and cut, in some cases, until there is no more intestine that can be cut out."[24]

Tragically, Crohn's disease typically strikes people in their teens and early twenties—destroying their health.[53] Children, adolescents, and young adults suddenly become faced with the harsh reality of a lifetime of chronic pain, in and out of hospitals their entire lives.[27]

The disease is mostly found in the United States, United Kingdom, and Scandinavia.[152] And it's on the increase. The incidence in the United States, which has been increasing steadily since the 1940s—doubling, then tripling, then quadrupling[89]—is now approaching that of an epidemic.[67] The most rapid increase has been seen in children. In the 1940s and early 1950s there were no recorded cases of Crohn's in teenagers. Currently, one in every six new cases diagnosed are under age twenty.[89] Dr. Crohn, who described one of the first series of cases back in 1932,[149] wrote decades later "From this small beginning, we have witnessed the evolution of a Frankenstein monster…."[25]

Johne's Disease

Crohn actually didn't discover Crohn's disease. The first person to give it a clear description was a Scottish surgeon named Kennedy Dalziel in 1913.[23] He wrote, "I can only regret that the etiology [cause] of the condition remains in obscurity, but I trust that before long, further consideration will clear up the difficulty."[42] Eighty-eight years later and the scientific community is still not sure what causes Crohn's, but Dalziel had a hunch which a growing number of prominent scientists now think may be correct.

About two decades earlier in 1895, German doctor H.A. Johne was the first to describe the cause of a disease in cattle characterized by chronic or intermittent profuse intractable diarrhea.[190] Clinically, the disease in cattle was virtually identical to that which we now know as human Crohn's disease.[25] The gross pathology of the infected cow's intestines likewise had the same cobblestone appearance; microscopically, the Crohn's diseased intestines and the diseased cattle intestines were dead ringers.[23] Dalziel wrote that the tissue characteristics were "so similar as to justify a proposition that the diseases may be the same."[42] He theorized that the disease in cattle and the disease in people were the same entity.

Mycobacterium Paratuberculosis

The cattle disease, which became known as Johne's disease (pronounced yo-neez), is known

to be caused by a bacteria called *Mycobacterium paratuberculosis,* also known as *Mycobacterium avium subspecies paratuberculosis,* or MAP.[183] MAP belongs to an infamous class of microbes called mycobacteria which cause diseases such as tuberculosis and leprosy. In fact, before Johne properly distinguished MAP from other mycobacteria, the disease in cattle was thought to be caused by intestinal bovine tuberculosis, hence the name paratuberculosis or "tuberculosis-like."

Mycobacterium paratuberculosis is one of the most enigmatic bacteria known.[121] It lives inside the hosts' cells, but has no known toxins and doesn't seem to damage the cells.[23] The damage, much like in diseases like hepatitis, comes from the hosts' reaction to it. MAP triggers a massive immune reaction against the body's own tissues in which MAP is hiding, in this case the gut.[26] It is known that *M. paratuberculosis*—MAP—causes Johne's disease in cattle, but does it cause Crohn's disease in people?

Spheroplasts

Paratuberculosis bacteria seem to cause disease in almost every species of animal so far studied.[75] It's reasonable to assume the same might happen in humans. ParaTB causes a specific chronic inflammation of the intestines of cattle, sheep, deer, rabbits, baboons, and three other species of primates.[115] The problem for Dalziel was that he couldn't visualize the bug microscopically in the surgically resected intestines of patients with Crohn's.[61]

While one can easily pick out MAP in most cases of Johne's disease with a simple light microscope, to this day attempts to stain and view MAP in Crohn's disease has been largely unsuccessful.[4] The landmark of most mycobacterial infections is the presence of acid-fast bacilli, so called because the mycobacterial cell wall soaks up and retains a particular acid stain.[27] Although failure to see acid-fast bacilli in general is not uncommon,[24] in the intestines of Johne's disease infected cattle, one can see swarms of acid-fast bacilli; in Crohn's there are none. The mystery wasn't solved until 1984, when Rodrick Chiodini, a microbiologist at Brown University's Rhode Island Hospital published a landmark study in which he actually cultured live paraTB germs from the gut walls of children with Crohn's disease.[23]

It has now been well established that paratuberculosis (and some other mycobacteria[186]) can shed their cell walls and exist as what has been termed "cell wall deficient" or "spheroplast" forms. Since it's the cell wall that picks up the stain, this form of the bacteria cannot be detected using the acid-fast stain test.[23] The bug, however, can then reform its cell wall even years later and revert back to its normal stainable self, which is what happened in Chiodini's lab.[65] It is thought that this cell wall deficient form is responsible for triggering the abnormal immune response which leads to Crohn's disease.[45]

Live Cultures

The next hurdle was the difficulty of consistently culturing the bug from Crohn's sufferers' intestines.[27] Although MAP has been independently isolated across three continents—cultured from Crohn's tissue in California, Texas, France, Australia, England, the Netherlands, and the Czech republic[27]—results are still relatively sparse and many labs have reported not being able to culture it at all.[115] This is not surprising.[24]

In order to isolate a specific bug from the multitude that exist naturally in the intestine, one has to devise a decontamination technique that kills other bacteria without harming the target bacterium, in this case MAP. Without their protective cell walls, however, cell wall deficient forms are almost impossible to culture because of the caustic processing techniques required to isolate them.[22]

Even once isolated, MAP is very difficult to grow.[68] Researchers have been trying since 1952 to grow mycobacteria from surgically removed Crohn's disease tissue.[46] It is thought that Chiodini succeeded where others had failed because of his many years of experience, combined with access to modern culture techniques and years of patient work.[126] Some human isolates took up to six years to grow, even under extremely precise culture and decontamination conditions.[66] Earlier researchers failed to meet these stringent standards for culturing the bacteria.[83]

Even modern labs have been found to be relying on faulty study design.[66] Moreover, the differences in methods used between labs can be vast.[24] Some labs still use fixed or frozen specimens or use only surface tissues from superficial biopsies, when it's been shown that one should optimally use fresh[66] resected tissue, as MAP tends to be found deep in the intestinal wall.[166] Some labs working with non-spheroplast forms of MAP from cattle haven't even been able to grow it. Even under the best circumstances, MAP is a tough bug to grow.[67]

To this day, many infectious agents have eluded our attempts to grow them in labs at all. For example, scientists have never been able to isolate *Mycobacterium leprae,* the microbe responsible for leprosy. Even *Campylobacter,* which we now know as the most significant bacteria in food poisoning, wasn't identified as a human pathogen until the 1970s, when culturing techniques enabling isolation were finally developed.[101]

Complicating attempts to culture the bug in Crohn's, there seem to be very few MAP actually involved in the disease process. This has a parallel in other animals—MAP bacteria in sheep and goat paratuberculosis are often sparse or even undetectable[147]—and in other mycobacterial human diseases like a type of leprosy in which just a few mycobacteria are capable of triggering a pathological immune response.[67]

DNA Fingerprinting

Obtaining Crohn's tissue samples is easy—patients are all too frequently having pieces of their bowel removed—but growing MAP from this tissue is so difficult that a nonculture-based method was needed. This advance came in the late 1980s when new DNA fingerprinting techniques arrived on the scene.[70] Using DNA probe technology similar to that used in forensic cases to pick up minute amounts of DNA, one can determine the definite presence of paraTB without needing to actually culture and grow it.[144] No longer would researchers have to wait months or years for the spheroplasts to revert back to normal and start growing again, one could just target, with 100% certainty, MAP DNA.

Sixty-five percent of bowel samples from Crohn's patients came up positive, compared to only 4% of those with the similar but different disease ulcerative colitis.[170] As techniques for extracting and isolating DNA have become better and better, MAP has been found in intestinal Crohn's tissue with increasingly positive results.[112] The reason more Crohn's cases were not detected is because the test has a limited sensitivity, especially when searching for a needle in a haystack in the gut which is awash in the DNA of billions of other bacteria.[153] DNA probe detection of other low abundance bacterial pathogens, particularly in chronically inflamed tissues—diseases like tuberculosis, Lyme disease, brucellosis, and lymphocytic leprosy—have similarly been fraught with difficulty.[155] Isolating chromosomal DNA from mycobacteria in general is experimentally difficult.[154] There are also other substances in the gut that have been found to inhibit the test such as bile salts and polysaccharides.[192]

Also accounting for uncertainty in the data[27] is the frequent misdiagnosing of Crohn's disease. For example, it's been shown that at least 20% of people diagnosed with Crohn's actually have a different disease, such as ulcerative colitis.[186] There is also considerable debate on whether or not Crohn's is a single disease entity in the first place.[23] Crohn's may be more of a catchall syndrome describing a number of different conditions, some of which may not be caused by MAP.[132] Either way, this makes it difficult to interpret data that show that not all of those we consider to have Crohn's disease test positive for MAP.

As expected, some people without Crohn's—healthy controls—test positive. Yet just because someone comes in contact with and harbors a specific germ doesn't necessarily mean that person will come down with the disease.[65] It is estimated, for example, that only a third of

calves that ingest MAP ever develop Johne's.[26] It is also possible, like closely related subspecies, that there are different strains of MAP, some of which cause disease and some of which don't.[163] The important point is that there has consistently been a highly significant specific association between *Mycobacterium paratuberculosis* and Crohn's disease.[24]

Association or Causation?

Just because Crohn's sufferers are much more likely to have MAP found in their gut does not necessarily mean that MAP caused the disease. Another explanation of the finding could be that this is just an opportunistic invasion of MAP into diseased tissue, leading to a chicken and egg scenario of which came first.[184] If MAP just has an affinity for inflamed tissue, however, one would expect that one would also find MAP more frequently in biopsies of similar diseases like ulcerative colitis, but this is not the case. Conversely, if you look for the DNA of other nonspecific mycobacteria, one finds that they are uniformly distributed between Crohn's patients versus controls. This finding is consistent with the known environmental distribution of mycobacteria, which are present in 30–50% of all environmental samplings—including water, soil, even air.[24] So other mycobacteria people routinely come in contact with, even the closely related *Mycobacterium avium subspecies silvaticum,* are equally distributed among people whether they have Crohn's disease, or colon cancer, or are completely healthy as one might expect.[109]

In medicine there is a method used to try to prove that a specific pathogen causes a specific disease. The first person to definitively prove that a disease was caused by a particular organism was Robert Koch, who uncovered the bacterial origin of anthrax in 1876. Koch cultured the bacteria from a diseased animal, gave anthrax to a healthy animal by inoculating her or him with a pure culture of the bacilli, and then was able to recover and reculture the bug once again.[14] These experiments fulfilled criteria proposed 36 years earlier by Henle as necessary to establish a causal relation between a specific agent and a specific disease. These criteria are now known as the Koch postulates.[90]

Not only are these experiments arguably unethical,[162] they also can be unreliable in clinical medicine, as other animals may not be susceptible to the same diseases that we are. For example, the case to prove that *H. pylori* caused ulcers was hindered by animal research, as rats and pigs were tested and seemed to be immune.[107] For this and other reasons, there are some recognized infectious diseases which have never fulfilled Koch's postulates. Leprosy, for example, has still never fulfilled more than one of the four criteria, because it is not possible to culture the culprit bacterium in the laboratory. Nonetheless, *Mycobacterium leprae* is known to be the cause of leprosy, and leprosy is known to be an infectious disease.[105] So while not absolutely necessary to fulfill Koch's postulates to prove causation, they are the most widely accepted method. So researchers set out to the task and they succeeded—twice.[126]

Chiodini fed chickens pure cultures of the paratuberculosis bacteria he recovered from the surgically removed intestines of children with Crohn's disease. The chickens then developed an intestinal disease resembling Crohn's.[108] In 1986, a different lab fed infant goats a human strain of paratuberculosis and also found that the bacteria induced a Crohn's-like intestinal disease in the goats. The same strain was then recovered back from all of them.[191] When asked why there continues to be so much resistance against the idea of MAP as a cause of Crohn's disease, Chiodini replied "What you have to realize is that there is a lot of politics in medicine. It's not whether you have the proof of something, but whether or not the medical community wants to accept it."[19]

Because there have been so many other failed attempts to figure out the cause of Crohn's, the medical community is very leery of new proposed causes, especially infectious ones.[24] The gastrointestinal community maintains a healthy skepticism regarding new pathogens as the cause of Crohn's disease, because different pathogens suspected in the past, such as chlamydia and measles, have since been disproven.[143] Of all the pathogens once thought associated with Crohn's in the 80 years it's been researched, MAP is the only one directly cultured and the only one capable of causing pathologically indistinguishable disease in other animals.[49]

The way that doctors test for the presence or absence of many infectious diseases is by looking for specific antibodies that our immune system uses to target the invader. When we test for HIV, for example, we are not usually testing for the virus directly, we are looking for the presence of anti-HIV antibodies.[173] If they're found, we can be relatively certain the person has been exposed to HIV. Similar searches have been launched for anti-MAP antibodies. Unfortunately, scientists have had difficulty finding an antibody which is specific for MAP.[186] There are some promising new suspects, however, which are thought to be unique to MAP and have been found in 90% of Crohn's patients, but in less than ten percent of those with ulcerative colitis.[165] These results not only support the theory, but open new research frontiers. A vaccine might be developed and the diagnosis of Crohn's may soon be just a blood test away.[120]

Epidemiology

Other potential lines of evidence include population studies. One would expect that if paratuberculosis was causing Crohn's disease, then the regions in which there is a high prevalence of Crohn's should overlap with the regions with a high prevalence of paratuberculosis. While sufficient data is lacking,[161] a review of the epidemiology of Johne's disease compared with the epidemiology of Crohn's disease found just that.[120] "Crohn's disease has a very spotty distribution in the world," notes Dr. Walter Thayer, an expert on the disease at Rhode Island Hospital who worked with Chiodini to culture MAP from Crohn's patients. "But it's seen only in milk-drinking areas—Australia, southern Africa, Europe, the United States, Canada, New Zealand. Interestingly, it's not seen in India, where they do drink milk, but they boil it first."[19]

Critics point to Sweden, which has its share of Crohn's, but whose cattle are reportedly paratuberculosis free. Unfortunately, the surveillance testing has been limited.[115] Michael Collins, veterinarian and microbiologist with the University of Wisconsin, has written "We believe no region in the world is free of *M. paratuberculosis* infection in its ruminant livestock. In all likelihood, Johne's disease is to be found in every country. Being free of the disease is probably more a function of how hard one has looked than a true lack of incidence."[35] We will see a prime example of this in the discussion of Ireland.

Another perceived inconsistency in the link between paraTB and Crohn's is the fact that Crohn's is found more often in urban, rather than rural populations.[143] Dairy farmers, for example, do not seem to have higher rates of Crohn's.[82] This is not dissimilar from other parallel diseases like bovine TB—tuberculosis not paratuberculosis—which, centuries ago, was responsible for the deaths of hundreds of thousands of children who drank unpasteurized milk.[7] The association between tuberculosis contracted by drinking milk and the rural community was also weak, presumably because of the commercial marketing and distribution of infected milk.[202]

Any explanation of Crohn's would have to account for the rapid increase seen in this disease this century.[178] The longest continuous study of the incidence of Crohn's disease is from Wales, which reports a 4000% increase of the disease since the 1930s.[140] This may be explained by the concurrent rise in paratuberculosis in intensively farmed dairy herds throughout the century.[66] Thayer asks also "What has happened to dairying in that time? Do you get milk from your local dairy? No. You get it from big conglomerates that buy from local dairies and pool all the milk. I think this is possibly the reason the disease has spread so quickly."[19]

Nick Barnes

Two centuries ago, when milk drinking children were dying en masse from bovine TB, one of the earliest signs that they had drunk milk

from a tuberculous cow was an infection of the lymph nodes that drained the throat. Scientists think milk is also the source for human exposure to paratuberculosis, so they wondered if the same thing happened with MAP.

Enter Nick Barnes, a 7-year-old boy who developed a painful swollen lump on the right side of his neck. His family took him to see their doctor, who decided it needed to be biopsied. The biopsy clearly showed he was infected with paratuberculosis. This is significant because it was the first definitive proof that paratuberculosis could infect human beings and cause disease. He and his family waited. Five years later, Nick Barnes came down with Crohn's disease.[68] Despite the clear-cut case description of a human paratuberculosis infection followed by the development of Crohn's, the medical community continued to ignore the growing evidence indicting MAP. There are many precedents of similar resistance to new ideas in the medical field.

H. pylori

Most ulcers are caused by the immune system attacking the lining of the stomach. Doctors blamed stress, thinking this led to too much stomach acid and the excess acid caused irritation which maybe triggered the attack. It was treated the same way as Crohn's has been treated: symptomatic relief of the inflammation and surgery. Then two Australian researchers cultured a tiny bacterium from the lining of the stomach and hypothesized heresy—that ulcers were actually caused by an infection.[99]

For almost a decade the researchers' ideas were dismissed and ridiculed.[39] The medical community scoffed at the notion that bacteria could survive in stomach acid.[107] One of the Australian researchers was so desperate that he actually drank a vial of the bacteria to prove his point.[99] What finally convinced the medical community, though, was that ulcers disappeared when patients were treated with the right antibiotics.[64] This discovery revolutionized thinking in medicine. The ulcer-causing bacteria, *H. pylori,* is now known as the cause of most ulcers in the world.[90]

Many scientists see a close parallel between the *H. pylori* story and paraTB. Just as *H. pylori* bacteria were the real reason the body was attacking the stomach lining in ulcers, researchers think that the MAP bacteria are the reason the body is attacking the intestinal lining in Crohn's. The proposition that ulcers were an infectious disease was met by nearly universal skepticism in the medical community.[107] As Dr. Hermon-Taylor, Chairman of the Department of Surgery at St. George's Medical School in London and leading proponent of the paraTB-Crohn's link, has noted, "And this [*H. pylori*] was a bug that you could see by looking down the microscope, grow in a simple culture system in the lab, test for immunologically pretty simply, and ordinary tablets readily available to doctors could make it go away. And it still took eight years for the penny to drop. Now we've got a bug [MAP] that you can't see, can't grow, hides under the immunological radar, is a bastard to kill, and the problem it's causing is far, far greater. If Rod Chiodini and I are wrong, the magnitude of the problem will only be the economic losses of farm animals, which is costing the United States somewhere between $1.5 and $2 billion a year. If Rod Chiodini and I are right, then, oh dear, oh dear. We have a big problem. It's going to take a lot to put it right."[19]

Antibiotics for Crohn's

The lesson researchers learned from stories like *H. pylori*[90] was that their best bet at convincing the world that MAP causes Crohn's lay in trying to cure Crohn's—a disease thought incurable—with appropriate antibiotics.[74] Of course, there was no guarantee that even if the disease were caused by MAP that it would respond to treatment.[156] For example, we can cure most pulmonary TB with antibiotics, but when TB bacteria move from the lung to the intestine and cause intestinal TB, it cannot typically be cured by antibiotics alone.[23] Researchers, though, set out to try.

Before we knew that ulcers were treatable with simple antibiotics, people underwent repeated grueling surgeries—some almost as risky and debilitating as Crohn's sufferers now undergo. Not only would a cure save Crohn's sufferers from the surgeon's knife, but it would also protect them from the toxic chemotherapy regimens currently used just for symptom relief, which can include immunosuppressants like steroids, cancer chemo agents,[136] and even thalidomide.[50]

Researchers started trying antibiotics they thought might kill MAP in Crohn's. Early results were disappointing,[156] leading to much of the deep-seated resistance among clinicians to accepting MAP as the cause of Crohn's.[14] Yet in hindsight, it turns out that doctors were using the wrong antibiotics, in the wrong combinations, for an inadequate period of time.

Perhaps because of the name similarity, many researchers assumed that antibiotics effective against *M. tuberculosis* should also be effective against *M. paratuberculosis*.[189] They were wrong; when one actually tested antibiotics against MAP in a lab, researchers found that it was in general resistant to antituberculous drugs.[22] They didn't work in cows;[23] they don't work in people.[120]

Another problem with some early studies was that they used monotherapy—meaning that they only used a single agent—which is rarely, if ever, effective in mycobacterial diseases because mycobacteria are so adept at developing resistance.[22] By giving multiple antibiotics at once, one decreases the chance that resistance will develop.

Adequate treatment duration had also been neglected. Mycobacterial infections in general are difficult to eradicate; prolonged treatment is required and relapses, either on treatment or off treatment, are common.[156] Tuberculosis takes months to treat; leprosy takes years—sometimes a lifetime—to treat. Our best estimate of how long it might take to rid the body of MAP can be made by studying pathogens in the same species. Infections caused by one of MAP's closest cousins (*M. avium intracellulare*) routinely require treatment for 3–4 years with 3 or 4 different antibiotics.[71] In some cases, it took five antibiotics all used in combination for 5 years before clinical improvement was achieved. We cannot expect trials using too few drugs, the wrong drugs, or even the right drugs for too short a time, to be successful.[21]

There are some factors which complicate any trial, even if the agents are chosen and used appropriately. Crohn's can be a cyclical disease, with periods of flare-ups and remissions, so approximately 20% of Crohn's patients during a treatment period will spontaneously improve on their own. The placebo effect is also expected to play a role in 30–40% of patients undergoing short-term therapy. And as mentioned previously, Crohn's is a poorly delineated disease—20% of people diagnosed with Crohn's may actually have something else.[186] There is also clinical, epidemiological, and molecular evidence indicating that there are two distinct clinical manifestations of Crohn's disease, which each may respond differently to treatment. These factors make it difficult to evaluate any therapeutic intervention.[150]

Despite these hurdles, the latest results are quite promising.[74] Instead of just blindly trying different antibiotics, scientists actually endured the laborious task of testing the antibiotics one by one on MAP in the lab. The breakthrough came in 1992 when the newly developed antibiotic clarithromycin was found to be the most effective known killer of *Mycobacterium paratuberculosis.* Many of the antibiotics used earlier worked by blocking cell wall synthesis. But Crohn's is thought to be caused by the spheroplast form of MAP which doesn't have a cell wall; it's therefore no wonder these earlier drugs didn't work. Clarithromycin, and an antibiotic called rifabutin, have a different mechanism of action, blocking protein synthesis.[157]

Another reason why drugs like clarithromycin (called macrolides) work against paraTB where others have failed is that MAP is an intracellular pathogen. They live inside our cells (another reason why they're so hard to see under a microscope). Only certain antibiotics, like macrolides, can penetrate inside human cells and still work effectively.[157] None of the previous MAP trials properly evaluated these newer macrolide antibiotics.[60] The time was ripe for a trial of these newer agents in Crohn's disease.

An Attempt at a Cure

The first trial took place in London, published 1997.[60] Researchers chose to use rifabutin and clarithromycin because they seem to complement or synergize with each other.[157] The treatment was named RMAT, Rifabutin and Macrolide Antibiotic Therapy.

Fifty-two patients with Crohn's disease, most of whom had persistent severe symptoms resistant to conventional treatment, were studied. Six patients had to be excluded, due mostly to intolerance to the antibiotics,[60] though in general the RMAT medications tend to have a much higher tolerance rate and far fewer side effects than the current immunosuppressive drugs used for Crohn's.[120] The remaining 46 patients were treated with RMAT for about a year. Of the 46 patients who were able to tolerate RMAT, 43 went into clinical remission, for a remission rate of 94%.[60]

A two-year follow-up was performed. The majority of patients in whom a clinical remission was initially induced remained symptom free off of all their previous medications.[60] Similar trials in other centers have reproduced these findings.[9,10,16,44,167] The fact that some patients relapsed after treatment was stopped may point to the difficulty in eradicating the organism or perhaps that they had been re-infected.[61] Hermon-Taylor, one of the principal investigators of the original trial, is currently recommending patients take RMAT regimen for at least 2 years. Among patients who respond to treatment, remission occurs slowly over the first three to six months of treatment. Symptoms often get worse before they get better, as in the drug treatment of other chronic mycobacterial diseases such as leprosy, perhaps due to the release of MAP antigens.[170]

Based on this pilot study, RMAT has the highest reported remission rate of any known treatment for Crohn's disease and the lowest reported relapse rate, including all current immunosuppressive treatments.[120] Thought to be an incurable disease, doctors seem to have been able to induce profound long-term remissions in the majority (68.7%) of patients with Crohn's disease.[12] Not only do patients stop having symptoms, but their intestines actually show evidence of healing, an unprecedented achievement.[164] "If this were cancer," said one RMAT researcher, "we would be calling these long remissions a cure."[98] Hermon-Taylor told the press "I've seen people who were without hope get better like magic. I've been a doctor for nearly 40 years, and it's the best thing I've ever seen in clinical medicine."[19]

Though the preliminary results of this and other pilot studies are encouraging, Hermon-Taylor is the first to point out the limitations of the study—it was too small and there were no controls.[185] "We were actually denied the funding to do a randomized control trial," he said. "So I did the best that I could with what I've got."[19] To date, according to the *Cleveland Free Times* article that won 1999's Project Censored Award, twenty-five of Hermon-Taylor's grant proposals submitted both here and abroad were rejected.[19]

Chiodini estimates he's similarly submitted over two dozen grant proposals to the National Institutes of Health, the USDA, and the Crohn's and Colitis Foundation of America, but to no avail.[19] Drug trials run in the United States have traditionally been supported by the pharmaceutical industry, but just as *H. pylori* threatened to deprive some of the largest corporations in the world of billions of dollars (anti-ulcer medications were the world's best-selling prescription drugs), the drug industry scores huge profits from increasingly complex and expensive maintenance Crohn's treatments, which must be administered for the rest of the patient's life.[107] Needless to say, financial support from the corporate sector has not been forthcoming.[120]

Nevertheless, these preliminary results must be reproduced to be seriously considered. Larger scale controlled studies are currently in progress to obtain better data.[161] The most promising is a phase III clinical trial of RMAT in Australia which has been designed as a double-blind, multi-center, controlled clinical trial involving over 200 patients with Crohn's in at least seven major cities across the continent.[125] Unfortunately, they seem to be having a problem securing patients for the study.[111] A controlled RMAT trial has also reportedly been initiated by the National Institutes of Health.[39]

Milk and Pus

Professor Hermon-Taylor, internationally known expert on Crohn's and MAP genetics, who has researched the illness for 20 years, said: "If there were no MAP I believe there would be almost no Crohn's disease. It is certainly responsible for between 60 per cent and 90 per cent of all cases and I would think that it is more likely to be 90 per cent."[110] Obviously, everyone who's exposed to paraTB doesn't come down with Crohn's disease, as is the case in virtually all infectious diseases. As mentioned previously, just because one comes in contact with a pathogen does not necessarily mean one comes down with the illness. Genetic and environmental factors facilitate establishment, persistence, and production of disease.[45]

H. pylori (the bacterium proven to cause ulcers), for example, is one of the most common of all bacterial infections[90]—a third of Americans have *H. pylori* in their stomachs.[99] A third of us, however, don't have ulcers;[64] some people are susceptible and some are not. Similarly, only about one in three hundred people exposed to tuberculosis actually come down with active disease.[19] Until we know why some and not others fall ill, all one can do is to try to minimize exposure to the pathogen. For example, people should not let those with tuberculosis cough in their face.

Drinking milk from cows infected with Johne's disease is how people are exposed to paratuberculosis. Based on DNA fingerprinting techniques, there are two strains of MAP: one that affects cattle, and one that affects goats and sheep. All human isolates so far have been of bovine origin,[24] implicating milk.[11] Milk is the "logical" focus of exposure[24] because cows with Johne's disease secrete paraTB abundantly in their milk.[158] Even sub-clinical cows—those that are infected but appear perfectly normal—shed paraTB bacteria into their milk.[24] Although these bacteria are found free-floating in milk, their transmission may be facilitated by their presence inside pus cells.[158] This is a particular problem in the United States, as we have the highest permitted upper limit of milk pus cell concentration in the world—almost twice the international standard of allowable pus cells (750,000/ml vs. 400,000/ml)[168] By US federal law, Grade A milk is allowed to have over a drop of pus per glass of milk.[6] These pus cells may facilitate the transmission of paraTB.[158]

Pasteurization

In England, researchers took milk off grocery shelves and tested it for the presence of paratuberculosis bacteria using DNA probes. Depending on the time of the year, up to 25% of milk cartons contained paratuberculosis DNA.[104] Interestingly, the seasonal variation coincided with the periods when Crohn's patients tend to suffer relapses.[61] The researchers tried to culture live paraTB bugs from the milk, but were largely unsuccessful, because cows' milk is such a stew of microbes that fungal overgrowth and faster multiplying bacteria took over the samples.[159] The question then remained, did the positive DNA samples in up to a quarter of the milk supply indicate live or dead paratuberculosis bacteria? Can paraTB survive pasteurization?

Historically, pasteurization had been established in order to kill paraTB's cousin, bovine tuberculosis.[179] TB was thought to be one of the most heat-resistant human pathogens, so the temperature was set at approximately 62° C (144° F) for a half an hour.[179] Later, the disease Q fever (caused by *Coxiella burnetii*) was discovered, so the temperature was increased to 63° C.[180] Now the HTST method, which stands for High Temperature, Short Time, is predominantly used—72° C (162° F), but only for 15 seconds.[93] While 72° C kills most bacteria, paratuberculosis has been shown to survive 15 seconds at 90° C (194° F).[58] By hiding in milk in fat droplets, pus cells, and fecal clumps,[189] paraTB might be able to survive at even higher temperatures.[59] Second only to prions[137] (which cause mad cow disease), paratuberculosis is considered the most heat-resistant pathogen in the human food supply.[115]

Johne's on the Rise

According to the Food and Agriculture Organization of the United Nations, Johne's disease is one of the most serious diseases affecting the cattle industry.[139] Although it is found in cattle populations throughout the world, the United States appears to have the worst paratuberculosis problem on the planet.[122] In 1997, the USDA released a long-awaited report of the national prevalence of Johne's disease. Surveying over 2500 dairy producers,[190] they showed that between 20 and 40% of US dairy herds were infected, a figure that they concede is probably an underestimate.[190] Since milk from an entire herd is likely to be pooled together in tankers for transport to processing plants, all the milk from 20 to 40% of US dairies is likely to be contaminated.[85]

Just as Crohn's disease is increasing in the human population—it may be no coincidence that the United States also has the world's highest incidence of Crohn's ever recorded[116]—Johne's disease is spreading among dairy cattle.[19] Johne's disease is spread primarily by the fecal-oral route. One can imagine how a cow with intractable diarrhea can thoroughly contaminate her surroundings[133] and just a few bits of swallowed manure can potentially infect a calf.[133] Overtly infected animals, losing up to 300 lb of body weight in one week[106] can shed as many as ten hundred trillion bugs a day.[30] One can also imagine what intensive modern farming practices have done for the disease.[85] Grazing bigger and bigger numbers of cattle on smaller and smaller plots of land is one of the reasons this dreaded disease is such a growing threat.[81] And every time animals are transported between farms, new herds may be infected. If no changes are made, the dairy herd infection rate is expected to reach 100%.[115]

USDA Farce?

With the growing Johne's epidemic, US governmental regulatory agencies have been in a bind. The only thing allegedly standing between people and the paratuberculosis bacterium are 15 seconds at 72° C.[37] The government has had to somehow convince the families of Crohn's patients who started to ask questions that pasteurization was foolproof. The problem was that the preponderance of the scientific evidence was against them—almost every study ever done simulating pasteurization conditions showed that paraTB survived the 15 seconds at 72° C.[67] So USDA scientists designed their own experiment, which they published in 1997.

Critics accuse the USDA of trying to ensure that no paraTB would survive in their pasteurization experiment by first crippling the bacteria. Very irregularly, with no precedent in the scientific literature for using this type of approach,[56] the USDA describes beginning their experiment by first "starving" the MAP bacteria,[124] exposing them to high-frequency sound waves, and freezing them—a technique that has been shown conclusively to weaken MAP.[56] They were also criticized for making a number of methodological mistakes and omissions.[18,124] Then, allegedly to make absolutely sure not a single bug would grow, they used an inadequate culture media[124] and report culturing them for only 2 to 3 months.[172] It is widely accepted that the minimum time it takes to ensure the growth of paraTB is 4 months.[124]

It is perhaps not surprising that no MAP grew from the pasteurized milk in their experiment. The researchers concluded: "Results indicate that the transmission of live paraTB bacteria via pasteurized milk is unlikely." Despite fifteen[19] years of better research to the contrary,[121] based on that single questionable study, in a letter dated February 9, 1998, Joseph Smucker, the leader of the FDA's Milk Safety Team wrote, "After a review of the available literature on this subject, it is the position of FDA that the latest research shows conclusively that commercial pasteurization does indeed eliminate this hazard."[201]

The FDA has argued that earlier pasteurization studies used unrealistically high levels of MAP that wouldn't be expected to exist naturally in the raw milk supply.[201] This is not a tenable criticism, primarily because the studies in question followed the published guidelines on the proper challenge concentration in the design of thermal inactivation studies.[57] Also, the concentration of MAP in raw milk is unknown. Cattle infected with Johne's disease have uncontrollable diarrhea, which "sprays" out from them in liquid form. Due to the close proximity of the cow's anus to her udders, it is unavoidable that an infected cow's udders will be smeared with feces, potentially leading to the contamination of her milk with high numbers of *Mycobacterium paratuberculosis*.[124] The feces contaminating her milk can have as many as a trillion paraTB bugs per gram.[142]

Off the Shelf

Despite its shortcomings, the USDA study continues to be cited and the rest of the scientific literature ignored by the government and the agricultural press.[62] *Hoard's Dairyman,* for example, cited the USDA study and concluded that "pasteurization destroys this dangerous disease."[100] The year after the USDA study was published, assertions such as this one were conclusively proven to be wrong.

The only way to demonstrate for sure that live paraTB bacteria survive pasteurization is to culture a colony of living paratuberculosis bacteria from retail pasteurized milk off the grocery shelf. In 1998, that is just what researchers did. Choosing Ireland, which has the highest per capita milk consumption in the European Union,[117] investigators went to 16 retail outlets and got 31 cartons of milk which were pasteurized at commercial dairies large and small.[36] Six grew out live paraTB, 19%—almost 1 in 5.[65] This caused a national food scare with daily front page headlines, not a word of which crossed the Atlantic.

In an editorial entitled "Media and Censorship," the editor-in-chief of the *Cleveland Free Times* wrote: "The dairy lobby is notoriously powerful inside the Washington DC beltway. And a tax on dairy farmers helps the dairy industry spread its advertising dollars around generously (most notably the 'Got Milk?' ad campaign), to the point where the wholesomeness of milk goes virtually unquestioned in the media. How else can it be explained that the possible link between a bacterium in milk and Crohn's disease is virtually unknown in the United States, despite front-page coverage in England and other places around the world?"[135]

When the results of the Irish study were released, crisis management specialists called the ramifications "enormous," "horrific." Dairy industry experts described it as a "significant blow to the industry," "accelerating the long-term decline of milk," and noting "It's not a market that can just bounce back."[198] Dairy industry leaders reacted angrily to the suggestion that pasteurization was inadequate. The British National Dairy Council's "Information Officer," said she wished the investigators had contacted the industry before publishing their scientific findings.[52]

Responding to public pressures, the British government initiated a nationwide thousand-sample survey of retail pasteurized milk. The announcement splashed headlines all over Europe, but there was still no word in the American press.[19] The preliminary findings of the British government's survey were released in April 2000. Three percent[92]—3 out of every one hundred cartons of milk off the shelves—grew out live paratuberculosis bacteria.[97,159] Based on the detection threshold of these tests, each quart had to contain at least about a million paraTB germs to come up positive.[66]

A year and a half earlier, after the announcement that milk was contaminated by at least paraTB DNA, the three British supermarket giants—Tesco, Sainsbury, and Safeway—announced that milk pasteurization time would be increased from 15 seconds to 25 seconds, to reassure the public that their products were safe.[13] The finding of live paratuberculosis bacteria in retail milk over a year later has fueled the skepticism that the 10 second change would make any difference.[94] The change was not based on science—in fact, there is a suggestion that some paraTB can survive pasteurization temperatures for 9 minutes[73] or longer.[172]

Public Relations

Despite the release of these findings, Nick Brown, the British agriculture minister said on national television: "I drink pasteurized milk and it is safe to do so…with confidence," a

claim reminiscent of a previous minister's assurances about beef from cattle infected with mad cow disease.[196] According to the Royal Statistical Society, contaminated beef still has the worst-case scenario potential of killing 13 million people who consumed it and are currently incubating the disease which Britain's health secretary called the worst form of death imaginable.[8]

The same assurances are echoed in the United States. For example, the director of the USDA National Animal Disease Center, feeling assured that pasteurization eliminated any health threat said, "I don't hesitate to feed [milk] to my 8-year-old."[187] The FDA chooses to continue to base national safety policy on the single flawed USDA study,[97] even now that the study has been superseded by proof that its conclusions are wrong (the United States mandates virtually the same pasteurization method that is used in Britain and Ireland).[2]

The FDA's continued insistence that pasteurization eliminates the risk of contracting paraTB—despite clear evidence to the contrary—puzzled Kurt Gutknecht, the editor of the highly respected industry publication *Wisconsin Agriculturist.* He called up Joe Smucker, the leader of the FDA's Milk Safety Team, and asked him about the FDA's official "commercial pasteurization does indeed eliminate this hazard" statement. Smucker replied that he did not have "clearance from the FDA" to speak to him on the subject. Surprised at Smucker's reluctance to talk to him, the editor went to the official FDA spokesperson, who described the refusal of an FDA official to not respond directly to press inquiries as "very unusual." Gutknecht turned his attention back to the Milk Safety Team which no longer returned his phone calls.[48]

The industry and/or[131] government knows, however, what kind of time bomb they're sitting on.[61] According to one industry expert, the incrimination of MAP in human disease would cause enormous economic damage to animal agriculture industries. An article in *Milk Science International* entitled "Is *Mycobacterium paratuberculosis* a possible agent in Crohn's Disease?" warns that "the present state of knowledge is…potentially catastrophic for the dairy industry should existing information be used in a sensationalist manner."[96]

Hidden Threat

Johne's disease is one of the most difficult diseases to recognize and control.[26] This is in part because of MAP's ability to resist destruction in the natural environment. It has reservoirs in pasture and, perhaps, in other animal populations. Paratuberculosis has spread, for example, from dairy cattle to wild, free-ranging white-tailed deer in the state of Connecticut.[28] The chief reason that paraTB is so hard to prevent and control, however, is its notoriously covert nature.

Paratuberculosis has been called a "spectral disease,"[139] a "hidden threat,"[171] an "insidious problem for the nation's dairy herds."[134] Although infections are usually initiated during calfhood, clinical disease does not appear until adulthood.[146] During this incubation period, which can last between 6 months[151] and 15 years,[186] the infection is invisible.[199] Subclinically infected animals don't have diarrhea or other typical visible signs of Johne's, but they are carriers and can shed the bacteria into the environment, giving paraTB ample opportunity to become entrenched in a herd before it is apparent that a problem even exists.[129]

In this way, the Johne's disease problem has been likened to the tip of an iceberg—the so-called "iceberg effect."[199] By the time a single clinical case surfaces, five[37] to fifteen[63] or twenty[190] others may be infected in the herd. If the clinically affected animal had been born on the farm, a minimum of 25 other animals are probably infected—perhaps as many as 50—and less than 30% of those would be detectable by currently available tests.[199]

Johne's may also be clinically hard to detect. While in some instances the disease progresses relatively rapidly, with the interval between the appearance of wasting and death measured in months, in other cases, after the initial loss of condition, there may be no clinical deterioration for long periods of time. Since the first signs of clinical disease are progressive weight loss and a drop in milk production, farmers may just cull the animal without requesting further diagnosis.[148] Also, like Crohn's, Johne's can go into periods of remission which can last for weeks or even months.[26] Finally, Johne's can mimic other diseases like intestinal parasitism, malnutrition, salmonellosis, winter dysentery, etc.[190]

Traditional control methods have involved culling infected animals and using hygiene methods to prevent new infections.[32] Removing infected animals alone has proven ineffective because of the latency period and because the bacteria survive so well outside the body. As one commentator noted, "An iceberg is not destroyed by the removal of the tip!"[138] Another proposal has been to kill off the entire herd, an option termed "herd disposal." The plan would then be to disinfect the barns and wait a year or so before new animals are allowed to pasture. This measure will likely never be initiated, though, because paraTB is so widespread that the resulting financial burden would be considered too great.[26]

After culling, the next most effective action is considered to be segregation of the infected animals.[142] Strict hygiene, down to the washing of boots, is necessary to prevent cross contamination—only a few grams of manure are needed to infect a calf.[133] Surveys show that many of these basic steps are not followed, however. For example, in approximately a third of operations, the cows' udders are not routinely washed prior to collecting colostrum or before nursing.[190]

While some calves are infected in utero,[32] removing newborn calves from the mother immediately upon birth is considered an effective control measure because it eliminates the newborn's attempt to nurse and risk ingesting infectious manure.[190] Currently, about two thirds of dairy operations report taking the calf away from the mother within 24 hours.[190] There are fears among the animal welfare community that Johne's disease management will intensify this irresponsible[69] practice.

Disposal of infectious feces creates quite a problem. Some industry specialists have advocated special landfills, while others have made the potentially hazardous proposal to "as a last resort, spread [it] on permanent cropland."[26]

Conspiracy of Silence

Despite its pervasiveness and its ability to severely impact milk production and destroy whole herds of cattle, Johne's disease remains an industry problem that is not openly discussed.[106] In an article entitled "Johne's Disease: A Dairy Industry Perspective," Johne's is described as "something that farmers talk about secretly—whisper behind hands." One dairy scientist stated that in all his years he had never heard an open, frank discussion of Johne's disease and calls for an end of the "whispering campaign."[5] Dairy farmers try to hide the fact that they have the disease in their dairy herds.[61] As an article in *Cornell Veterinarian* notes, "Farmers prefer not to acknowledge its presence and enshroud suspect cases with secrecy."[26] It is a problem that is kept out of sight and out of mind. As one dairy farmer put it, "It's [Johne's] a dirty word. It's like AIDS—you don't talk about it."[54]

This conspiracy of silence extends beyond the producers to encompass the entire industry to the point of interfering with scientific dialogue.[24] From the *Journal of Dairy Science:* "Fear of consumer reaction…can impede rational open discussion of scientific studies."[34] Without doubt, says Chiodini, "the dairy and regulatory industries are concerned vocally… but their concern is limited to the possibility of 'bad press' to the industry rather than a concern for the truth or public health."[24]

The secrecy has successfully bred ignorance. Over a century after the disease was identified, almost half of all dairy farmers nationally surveyed by the USDA didn't know anything about the disease.[106] And those with the largest herds—the herds most likely to be infected[106]—were found least likely to have known of the disease.[195] Karen Meyer, then executive director of the nonprofit Paratuberculosis Awareness & Research Association (PARA), placed the blame on the representatives of the dairy industry. At a meet-

ing of the USDA's United States Animal Health Association (USAHA), she challenged dairy producers to become more proactive. "If there are organizations you have been relying on for your information and to protect your interests, they have failed you miserably."[118] "I think we underestimate farmers," she told the *Wisconsin Agriculturist.* "If they even thought they were making someone sick, it would break their hearts."[61]

US Inaction

The USDA has been accused of continuing to keep its head in the sand. Industry specialists blame the federal government for "grossly underfunding" research, with less than one percent of its animal disease grant budget allocated to Johne's.[61] As Alan Kennedy, a co-founder of PARA and himself a sufferer of Crohn's disease remarked,"yet another case of CJD—Conflicting Job Description." The USDA is mandated to regulate animal industries and food safety, but it is also responsible for promoting these same agricultural products.[201]

The first US case of Johne's was discovered in Pennsylvania in 1908.[182] Almost a century later there is still no mandated control program,[138] even though as far back as 1922 scientists published warnings of the danger posed by the disease and outlined effective methods of controlling and eradicating it. Efforts to control and eradicate Johne's disease have been grossly inadequate.[61] "In the 75 years following the release of that publication, there's very little that any state has done to try to control the disease," says Collins, the University of Wisconsin veterinary researcher. Meanwhile, as predicted in 1922, the disease has continued to spread silently and surely. According to the USDA's figures, there are now three quarters of a million cattle infected with paraTB in the United States.[130]

The reason that Johne's has spread to such a degree is because there have been no direct constraints on the transport of infected animals.[142] Almost without exception, paratuberculosis is introduced into a herd through the addition of an asymptomatic, infected carrier animal. Almost every infected herd can trace the infection to the purchase of an infected cow[183] that appeared healthy when offered for sale.[194] Disturbingly, the USDA found that dairy farmers with infected herds were no less likely to sell replacement cows to other farms than owners of noninfected herds.[190]

Regulatory vets know and accept this fact, acknowledging that movement restrictions on infected animals must exist for an effective control program. However, as described in the *Veterinary Clinics of North America,* "if the voluntary program imposes movement restrictions, it could quickly become a regulatory program and not have widespread support and participation from the livestock industry."[169] In fact, the *Code of Federal Regulations* (part 80) was recently changed to remove restrictions on the interstate movement of Johne's disease positive animals.[127] The change was made because of pressure from the livestock industry.[169]

Though not putting its money where its mouth is, the USDA insists that the agency is doing everything it can with regard to Johne's disease.[61] The USDA, for example, cites the formation of the National Johne's Working Group (NJWG) in 1994. However, the executive committee of the group is composed of three people: one is John Adams of the National Milk Producers Federation and another is Gary Weber, a director of the National Cattleman's Beef Association.[201]

For those that remember the Oprah Winfrey mad cow fiasco, Weber was the cattleman defending cow cannibalism. "Now keep in mind," he said on that show, "before you—you view the ruminant animal, the cow, as simply a vegetarian—remember that they drink milk." Years earlier, in response to activists' requests that farmers discontinue the practice of feeding rendered animal protein to animals raised for slaughter, he told industry publication *Food Chemical News* that the cattle industry could indeed find economically feasible alternatives to such a practice, but that the cattlemen's association did not want to "set a precedent of being ruled by activists."[137]

Not surprisingly, the NJWG has officially come out against making Johne's a reportable disease, advocating that all attempts at control be voluntary.[169] In a moment of rare candor, one NJWG member explained why: "If the farmers have to report positive cows, then it will be like the sheep scrapie [mad sheep disease] program. Instead of reporting the disease, the farmers will 'shoot, shovel and shut up.'"[119]

A year earlier, a national paratuberculosis certification program had been started in order to identify low risk herds, but only 1% of dairy operations reported participating in the program, citing associated costs.[190] Less than 15% of the dairy producers appear to test for Johne's.[106] In 1997, the NJWG set up a similar program designed to be more affordable,[15] but again chose to keep it strictly optional, relying on the "livestock industry in each state to sell its economic advantage to its members."[169] As a concession to the industry, there is still no federally mandated Johne's disease control program.[169] Some states have Johne's control programs, but without exception they are noncompulsory.[123] Just as government deregulation of industry may have led to the mad cow disaster in Europe, the lack of industry accountability may also play a pivotal role in the human consequences of the paratuberculosis epidemic.[114]

The United States is being left behind in the worldwide race to eliminate paraTB.[118] The Netherlands, one of Europe's largest dairy exporters, has pledged to eradicate paratuberculosis by the end of this year by instigating a compulsory eradication program.[189] "To minimize the risk of human exposure to paratuberculosis" is one of the explicit reasons given for the Dutch program.[47] Sweden seems to be closest to winning the battle, probably because it was the first country whose control efforts were nonvoluntary.[141] Australia is currently also certifying herds with a view to eradication.[72] Although there are currently no restrictions on international trade as a result of the disease,[106] that may well change and potentially threaten America's $700 million dairy product export industry.[189]

Mike Collins began his messages to both the Johne's Disease Committee and the general session of the USAHA with the same words: "Don't shoot the messenger."[73] Rather than participating in serious dialogue around the issue, the dairy industry has been accused of spending its energies slinging mud at researchers in the field,[61] giving lip service, and vainly hoping it just all blows away.[24] Christine Rossiter, senior extension veterinarian with the Cornell University Veterinary Diagnostic Laboratory, told the *Wisconsin Agriculturist* that those who decide to address the issue are put at risk and there's "no value placed by the industry on a person who wants to do something about Johne's. Nobody wants to take it on."[61]

At an international colloquium on paratuberculosis, Chiodini expressed his view that the current focus of the American dairy industry "could put the industry in the same light as the tobacco industry, being accused of a cover-up and faced with all sorts of liabilities."[24] Paul Strandberg, Assistant Attorney General of the State of Minnesota warned the Johne's Disease Committee that if they chose to be less than forthright about the possible link between milk and beef and Crohn's Disease, they could wind up on *60 Minutes* in the middle of a media circus.[119]

Off the Shelf USA

In order to put the problem in perspective and get the issue out in the open, the consumer movement needs to get a study of retail milk supplies in the United States funded. That is the recommendation of PARA.[121] That is the recommendation of researchers in the field.[124] Not only has industry allegedly "totally ignored" this approach,[24] one observer wrote that it would be "political suicide" for a researcher in the United States to even suggest such a thing.[61] However, there have been two brave souls. Year after year, Chiodini and Hermon-Taylor, world-recognized authorities on MAP and Crohn's, have submitted proposals to the USDA and to the FDA to test retail milk supplies, and year after year their proposals have been rejected.[62]

At a meeting of the USAHA, a resolution was debated on whether or not to recommend that the USDA test retail dairy products in

the United States for the presence of live paraTB bacteria. John Adams, the National Milk Producers Federation executive member of the NJWG, was quite vocal in his opposition: "The FDA has already stated their position. They are confident that pasteurized milk is safe. We don't need to test retail milk."[119]

Steve Merkel, a founding member of PARA whose wife has suffered with Crohn's disease since 1960,[19] replied: "With all due respect, sir, if milk is as safe as you say it is, then retail testing will simply confirm that fact. Are you afraid of retail milk testing because you are afraid of what you might find?" The resolution was voted down by an overwhelming majority.[119]

PARA kept at it. Finally, in 1999, PARA successfully submitted two resolutions to the Johne's Disease Committee, one recommending the testing of retail milk and milk products for the presence of live MAP and another recommending research to determine what cooking temperatures are needed to reliably kill MAP in ground beef. Although both resolutions passed unanimously in open committee, they were later voted down behind closed doors. PARA saw this as the USAHA going on record as deliberately choosing ignorance about the presence of MAP in food products for human consumption.[119]

The USAHA tried to justify why the resolutions were quashed: "During the discussions of these resolutions, there was much concern about the feasibility of end-product testing of milk and meat for an organism that science has not confirmed as being the cause of Crohn's in humans, and the usage of this information." In the opinion of PARA, as expressed in a letter to the USAHA president-elect, "this statement presents USAHA as not only primarily self-serving, but further, is blatantly contemptuous of both its own member producers and the American public." The letter concludes "We at PARA are saddened that USAHA has chosen to be part of the problem rather than part of the solution."[119]

Gambling with Lives

The USAHA statement reveals the gamble the industry is willing to take. In Britain, when asked what the industry planned to do about paratuberculosis, spokespersons said that it was "something that bears watching"[201] but that they "preferred to defer action" until paraTB is proven to cause disease in humans.[84] This sounded all too familiar to the British public after the mad cow debacle, where the beef industry made the same wager—and lost.[177] According to some social science studies, it was the British public authorities' decade-long insistence on the safety of beef that did the most damage to the public trust.[79]

The American dairy industry is similarly gambling not only with the health of consumers, but with their own financial health. The financial impact of paraTB is enormous;[30] paratuberculosis currently costs the American livestock industry over a billion dollars a year.[61] A collapse in consumer confidence could raise that figure much higher.

"If MAP is ultimately shown not to be the cause of Crohn's disease," Chiodini argues, "then the industries have taken the appropriate position of 'lip-service', to give an image of concern."[24] If, however,—as PARA phrased it in an open letter to the industry—"dairy products become associated with the dreadful, life-destroying disease known as Crohn's disease, your markets may also collapse and may never recover. The image of dairy foods as being necessary for good nutrition, carefully propagated and nurtured by you for decades, may be destroyed."[124]

Other Dairy Products

At the present time, only testing of milk has been conducted (and only in the United Kingdom). All other dairy products have been neglected (cheese, yogurt, etc.). The only safe policy would be either to test all milk before it is used to make other dairy products or to test all dairy products. One third of cheese produced in the United States, for example, is made from raw unpasteurized milk, in which one could expect the highest levels of paraTB bacteria.[101] Cheese manufacturers rely on the salty acidic environment of cheese to inhibit bacterial growth,[181] but MAP is resistant to such conditions.[181] Even less robust mycobacteria can survive in soft cheese for at least 3 months and in hard cheese for up to 10 months.[76] Reportedly, at the University of Wisconsin, there is currently a research project which is investigating the survival of *Mycobacterium paratuberculosis* in cheese.[86]

Since MAP can survive freezing for at least a year,[88] products such as ice cream may also be implicated.[26] Ice cream may also come from less rigorously pasteurized milk.[121] Other dairy products like butter, yogurt, and infant formula must also be high research priorities.[124]

Beef

The standard veterinary recommendation when a cow is diagnosed with Johne's is to have her sent to slaughter. Beef from Johne's cattle is not prevented from being sold for human consumption because paratuberculosis is not officially considered a human pathogen. End-stage animals, their bodies dripping with literally trillions of paratuberculosis bacteria, are ground straight into hamburger meat.[123] When Crohn's patient advocates found out that infected tissues from animals with severe clinical paratuberculosis were funneled into the human food supply, they were described as, not surprisingly, "abhorred and nauseated."[201]

In the advanced stages of Johne's disease, MAP bacteria course through the cow's blood stream, infecting her internal organs, and possibly her muscle tissue (so far, no one has tried culturing MAP from a cow's muscle tissue). Even if the muscle tissue didn't contain large numbers of MAP before the infected cow's death, when she's slaughtered it seems impossible to ensure that feces do not contaminate the various tissues that are taken from her, as evidenced by the numerous *E. coli* food poisoning deaths in recent years.[123] As a scientist put it: "Consequently, both preharvest and postharvest contamination of food products originating from cattle is plausible."[34]

Although Americans eat 2.6 billion pounds of culled dairy cows annually, most hamburger meat comes from cattle raised for beef. In 1984, about one percent of US beef cattle were found positive for Johne's disease. Research is ongoing at the USDA to determine the current prevalence of Johne's disease in beef cattle, but since Johne's is such a hidden disease, is not reportable, and is not the subject of a mandatory control program, one might suspect that the incidence has increased significantly as it has in the dairy cattle population.[123] In spite of this situation, lack of awareness among beef producers is even greater than in dairy producers. The USDA Center for Animal Health Monitoring reports that 69.8% of US beef producers "had not heard of it [Johne's] before." And less then 10% of producers had any knowledge beyond name recognition.[43]

MAP bacteria probably survive standard cooking temperatures. *Mycobacterium paratuberculosis* is the most heat-resistant mycobacterium present in retail beef.[103] Even well-cooked meat may contain live paraTB. The USDA recommends that hamburgers be cooked to 71° C (160° F). An unpierced roast or steak need only reach an internal temperature of 63° C (145° F). Studies show prolonged exposure to at least 74° C (165° F) may be necessary to eliminate the paratuberculosis bug.[123] *Mycobacterium paratuberculosis* is also resistant to nitrites and the smoking process used in sausage production.[102] MAP may contaminate other meats as well—paratuberculosis is suspected in pigs and chickens.[139]

Milk may be more dangerous to consume than meat, though, in regards to paratuberculosis. MAP is thought to survive digestion when carried in a vehicle like milk, because—as designed by nature—milk buffers the stomach environment to a near-neutral pH. In meat however, MAP's ability to survive digestion by stomach acid is less certain.

Water

Municipal water supplies must also be assessed for risk because surface waters contaminated by agricultural run-off feed the domestic water supplies of many communities in the United States.[115] One of the reasons why paraTB has been called a "superbug" is because of its abil-

ity to survive in the environment for prolonged periods.[160] Mycobacteria like paraTB are one of the oldest forms of life. They have survived on this planet for over a billion years which has allowed them to adapt.[67] In the environment, MAP has a thick, waxy cell wall which protects it[121]—it can last for 9 months in mud,[139] almost a year in manure,[76] and two years in water. Standard domestic water treatment such as filtration and chlorination are probably ineffective against paraTB.[115]

There have been a few disconcerting[143] reports of MAP bacteria cultured from drinking water, both in Europe[188] and from the water supply of a major American city.[14] Europe's Drinking Water Inspectorate has commissioned a study into the distribution and fate of MAP in drinking water treatment;[91] the same inquiry should be happening here.

2000

The development last year with the most serious ramifications was published in the April 2000 issue of the *American Journal of Gastroenterology.* Knowing that cows with Johne's disease shed paratuberculosis into their breast milk, researchers wondered whether paratuberculosis bacteria could be detected in the milk of human mothers with Crohn's disease. Researchers also knew that there were reports of mothers with other mycobacterial diseases like leprosy shedding bacteria into their milk. So they examined two mothers with Crohn's who had just given birth and found paratuberculosis bacteria growing in both the mothers' breast milk, but not in the breast milk from control mothers without Crohn's. While breast-feeding has not been found to be a risk factor for Crohn's and may, for unknown reasons, actually have a protective effect,[143] the presence of MAP in the breast milk of mothers with Crohn's not only adds support to the role of MAP in the pathogenesis of Crohn's disease,[112] but shows how new generations could be exposed to paraTB.[158]

Recommendations for Action

Despite the fact that *M. paratuberculosis* is now a known human pathogen, it continues to be tolerated in our food supply.[74] After finding of MAP in their retail milk supply, the Food Safety Authority of Ireland (FSAI) now requires that cattle infected with Johne's be excluded from the food supply. The flesh from an infected cow is no longer considered fit for human consumption and her milk is simply dumped.[176] Karen Meyer of PARA commented, "The government of Ireland is to be commended for exercising the precautionary principle. Instead of trying to sweep the problem under the rug, they acted swiftly to give human health priority over special interests."[77]

The paratuberculosis problem in Ireland is minimal compared to that of the United States. According to the chief executive of the FSAI, of the 7.6 million cattle in Ireland, there are only 12 reported cases of Johne's disease. Nineteen percent of Irish retail milk samples grew out live paraTB and researchers only found 12 cases of Johne's disease in the entire country. Obviously, as the FSAI concedes, this may be an underestimate, but in the United States the paratuberculosis problem is exponentially worse. The estimated prevalence in the United States is some 20,000 times greater than that of Ireland.[1]

If any country should be preventing contamination of the human food supply it should be the United States, which has the highest prevalence of Johne's disease in the world.[122] At their Fall 2000 meeting, however, the NJWG continued to propose only voluntary measures to protect cattle health and no measures to protect human health.[197] The removal of clinically infected animals from the human food supply alone has been modeled as having a highly significant impact.[113] This could evidently be accomplished with relative ease, but as yet there has been little effort to do so.[74] When asked how long it would take to clean up America's herds if suddenly no milk from Johne's-positive cows could be sold, one Johne's Disease Committee member said, "About six months."[119]

The consumer movement also needs to fight to make Crohn's a reportable illness.[92] The official FDA stance that pasteurization eliminates MAP is no longer tenable and must be continuously confronted with the British retail milk studies which put an end to the pasteurization debate once and for all. An extensive Freedom of Information Act search must be initiated to unearth suppressed documents. For example, seven years ago, Canada's agriculture department produced a food safety risk assessment paper concluding that the paraTB-Crohn's link was something about which to be concerned. The document, however, was stamped "Protected. Not for Distribution" and was as such buried.[19] These are the kinds of documents the consumer movement needs to get a hold of.

In Dr. Hermon-Taylor's view, "There is overwhelming evidence that we are sitting on a public health disaster of tragic proportions."[40] Europe's Scientific Committee on Animal Health and Animal Welfare, however, concluded that the currently available evidence was insufficient to confirm or disprove the theory.[145] This uncertainty should not impede the government from taking concrete steps to prevent further potential human catastrophe. If the British government had acknowledged the precautionary principle, many lives may have been saved. The same exact things being said now about paraTB, "We'll wait and see," were those things said about mad cow disease. Once proof comes around, however, it may be too late.[177]

The precautionary principle is the basis for most European environmental law and is playing an increasingly important role in health policies worldwide.[51] Basically, it states, "If one has a reasonable suspicion that something bad might be going to happen, one has an obligation to try to stop it."[200] An ounce of prevention is worth a pound of cure.

On a Personal Level

On a personal level, the Crohn's advocacy group Action Research recommends that people who want to reduce their risk of infection or reinfection—especially those with Crohn's disease, or their close relatives (who might be genetically predisposed)—should stop eating dairy products unless they are effectively boiled first.[38] PARA recommends that cheese should be heated to the temperature of boiling water, 100° C (212° F), to reduce the threat. Thus, grilling cheese under direct heat for a few minutes (so that it "bubbles"), or cooking it in oven-baked meals, such as oven-baked lasagna, should effectively sterilize the cheese. The same applies to other dairy products, such as milk, yogurt, or butter.[86]

The reason the industry doesn't pasteurize all milk at that temperature to be safe, is because it could affect the taste of the milk. As the FSAI put it, "there is an upper temperature beyond which unacceptable changes to the taste of milk start to occur."[31] Steve Merkel of PARA would have governments mandate raising the minimum pasteurization temperature to levels that ensured safety regardless, "even if it means that milk doesn't taste the same as it did. Human health must take precedence over taste."[80]

Stricter pasteurization may not be the answer, though. Although there is recent evidence that living MAP bacteria cause Crohn's,[83] even dead MAP may be able to trigger disease.[31] For example, one of the reasons that the vaccine for Johne's is so seldom used is because it is so dangerous to handle.[106] Even though the vaccine is made out of killed MAP bacteria, the human immune system can react so violently just to the presence of MAP proteins, that accidentally injected into humans (or purposefully into other primates), the MAP vaccine causes a chronic progressive inflammation which can last for years[128] or may even necessitate amputation of the injection site.[22] Closely related bugs like leprosy can have similar effects.[115] So even if MAP is pasteurized to death, drinking the remnants of the bacteria may still cause a problem.

With this in mind, it may be more prudent to avoid dairy altogether. Although ingesting relatively few organisms may be able to cause infection, the human infective dose is not known.[186] It is also not known how heavily the milk supply is contaminated in this country. The most esteemed pediatrician of all time, Dr. Benjamin Spock, advised that children be raised vegan, with zero exposure to dairy products for a variety of reasons.[193] Especially considering

the risk of paratuberculosis in milk, this would seem sensible advice, particularly for children and adolescents.[110] There is a wide variety of dairy product substitutes—soy and rice milks, cheeses, ice creams, yogurts, etc.—making animal-derived dairy products unnecessary.

Conclusion

Because the spread of Johne's disease is related to stocking density, the epidemic of Johne's disease is one more indictment of factory farming.[3] The unnatural concentration of animals raised for slaughter, for example, has led to other human tragedies including the single worst epidemic in recorded world history, the 1918 influenza pandemic.[41] In that case, the unnatural density and proximity of pigs and ducks raised for slaughter led to the deaths of upwards of 40 million people.[87]

This potential crisis is also an indictment of an industry that continues to risk public safety and a government that seems to protect business interests over those of the consumer. As Karen Meyer recently told the *LA Times,* "There comes a point in time where consumer health takes precedence over commercial concerns."[97]

Every few hours, another child in this country is diagnosed with Crohn's disease and may be condemned to a life of chronic suffering.[62] The balance of evidence strongly suggests a causative link between *Mycobacterium paratuberculosis* and Crohn's disease.[145] This public health issue has been at the periphery of the dairy industry's agenda for years, a nagging concern on the back burner.[61] The consumer movement needs to move it to the front burner and needs to turn up the heat.

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