The disease in cattle (Johne’s disease) caused by MAP and Crohn’s disease share a common target organ, the gastrointestinal tract. Epidemiologically, MAP infected animals may shed the mycobacterium into their biological fluids: specifically milk [1-3]. MAP is not killed by pasteurization [4-6]. Viable MAP has been both demonstrated and cultured from milk, infant formula, powdered milk, and other milk-based products [7-9]. MAP readily crosses species lines. MAP receptors line the entire small bowel [10]. Milk and related milk-based food items constitute the zoonotic vehicle by which a bovine pathogen accesses human hosts. Individuals whose genetic composition allows enhanced mycobacterium replication have a higher prevalence of Crohn’s disease than that projected for the general population. MAP DNA is more likely to be identified in diseased tissue and blood from individuals afflicted with Crohn’s disease than healthy individuals [11-15]. In immunocompromised individuals or individuals with markedly enhanced genetic susceptibility, MAP can cause infection. In these situations MAP can be identified by special stains and cultured using standard technology. This is not true for Crohn’s disease. The strongest argument for an infectious etiology is derived from isolated case studies and small clinical trials with a limited selection of anti-microbials that have produced a number of prolonged remissions, bordering upon “cures” [16-19]. In doing so, the observation leaves unanswered the question as to why do these selective drugs achieve apparent efficacy when other compounds effective against *M. tuberculosi*s were ineffective?

The infectious disease paradigm falls short of becoming an accepted medical pseudo-truth [20]. If MAP replication were the cause of Crohn’s disease, use of biologics and steroids would enhance the organism’s pathogenicity. Reactivation of *Mycobacterium tuberculosis* is a recognized complication of therapy with biologics. Instead of mucosal healing, exacerbating of signs and symptoms would occur. When infection is due to ingestion of milk containing a virulent mycobacterium, i.e., *Mycobacterium bovis*, gastrointestinal disease frequently ensues. In these situations, *Mycobacterium bovis* is readily demonstrated with special stain and cultured. This is not the case with Crohn’s disease. Despite the presence of MAP DNA in Crohn’s diseased tissue, both special stains for acid-fast bacilli and conventional culture isolation technology for mycobacteria are unable to identify or isolate MAP [21]. The occasional ability to demonstrate MAP DNA in healthy small bowel samples and from white blood cells of unaffected individuals further weakens the foundation of the infectious disease paradigm [11,14]. What can be argued is that given the widespread prevalence of MAP in the U.S. food supply, the probability of one having had contact with viable MAP is a function of diet and time; yet the correlation between human MAP infection and Crohn’s disease was not supportive of causation. The occasional demonstration of MAP DNA in a given control subject identifies an individual with current, active subclinical infection.

While providing a theoretical explanation for the spread, the infectious disease paradigm does not adequately address why the epidemic spread of a new disease, why breast feeding extends relative protection against the future development of Crohn’s disease [22-28], and why there is the near absence of Crohn’s disease in economically stressed populations [29-32]. In third world and economically stressed populations, breast milk is the principle source...
of affordable infant nutrition. In 2015, a third paradigm of causation for Crohn’s disease was proposed that united the autoimmunity and infectious disease paradigms [33]. The Hruska Postulate states that pathogenesis of Crohn’s disease is the consequence of two distinct interactions between MAP with the host’s immune system. First, adequate MAP infectious challenge had to occur in the absence of acquired immunity. Unlike *M. bovis*, MAP is a relatively weak mycobacterium. For Johnne’s disease to develop, infection needs to be ongoing for months or years. It is argued that inherent immunity is capable of aborting continued mycobacterium replication: but, at a price, loss of immunological tolerance to MAP’s antigenic array. The immune system’s pro-inflammatory response to MAP’s antigenic array becomes fixed within immunological memory. The third paradigm draws heavily from experiments in nature that document the importance of acquired immunity in arresting replication of organisms whose containment is primarily a function of cellular immunity, i.e. rubella, cytomegaloviruses, Herpes simplex viruses, *M. tuberculosis*. In the absence of acquired or ineffective immunity, the pathological consequences documented are markedly exaggerated in comparison to those observed when the same infections occur in the presence of intact immunity [34,35]. Acquired immunity is believed to be effectively functional late in the neonatal period. This fact puts into value the epidemiological studies indicating that breastfeeding confers a significant degree of protection against the future development of Crohn’s disease. Indirectly supportive of this concept is the paucity of individuals afflicted with Crohn’s disease in economically stressed populations where breast milk is the principle source of infant nutrition. It is argued that, in the absence of acquired immunity, MAP infection may so challenge inherent immunity that the resultant pro-inflammatory response required to abort continued mycobacterium replication becomes fixed within immunological memory. Immunological tolerance that would normally be anticipated to manifest upon re-exposure to MAP does not occur. In the immediate neonatal period, mucosal immunity is compromised by the relative absence of polysaccharide A (PSA) produced by the gastrointestinal microbiota. PSA is thought to promote mucosal tolerance by promoting the differentiation of functional Treg cells. What is theorized is that MAP challenge when Fox3+ Treg population induction of permanent remission from Crohn’s disease [40,41]. Therapeutic intervention points for the prevention and possible induction of permanent remission from Crohn’s disease [40,41].

Crohn’s disease has been labeled but never proven to be an autoimmune disease. The concept that, in the absence of acquired immunity, a pro-inflammatory response to a given antigen or antigens can become fixed within immunological memory opens to re-thinking other autoimmune diseases that have the classic tell: suppression of symptomology by biologics and steroids.

**References**


