Global Journals LaTeX JournalKaleidoscope™
Artificial Intelligence formulated this projection for compatibility purposes from the original article published at Global Journals. However, this technology is currently in beta. *Therefore, kindly ignore odd layouts, missed formulae, text, tables, or figures.*

A Therapeutic Role for Diet in the Treatment of Crohn's Disease?

Gilles R. G. Monif

Received: 16 December 2015 Accepted: 2 January 2016 Published: 15 January 2016

Abstract

An unintended experiment in veterinary medicine and its follow up analysis have identified the ability for dietary supplements that enhance cellular immunity to destroy Mycobacterium avium subspecies paratuberculosis (MAP). The possible significance of this observation for Crohn's disease is discussed.An infectious disease is basically a statement of immune system failure. Either the pathogen's challenge inoculum was too great for the host's immune system to subjugate or the host's immune system was genetically designed to facilitate susceptibility to the mycobacterial pathogen in question. Within the Mycobacterium avium subspecies paratuberculosis (MAP) paradigm of causation of Crohn's disease, diet's therapeutic objectives have been reduction of MAP antigen challenges and the correction of diseased induced impairment of host immunity (1-3). The argument is presented that specifically targeted dietary supplementation may be therapeutic.

Index terms— crohn?s disease, diet, mycobacterium avium subspecies paratuberculosis.

1 I. Reduction/Elimination of map

Antigen Challenges he ability of immunomodulators and biologics to induce temporary remission had previously formed the foundation for the autoimmunity paradigm of causation. The current thesis of causation is that Crohn's disease is due to the interplay of two Mycobacterium avium subspecies paratuberculosis (MAP) mediated immunologically interactions (1,2). In the absence of acquired immunity, MAP causes fixation of the pro-inflammatory response that curtailed the infection. When the individual is subsequently MAP rechallenged, rather than exhibiting immune tolerance, the immune system again elaborates cytotoxic cytokines targeted against MAP. Unlike other mycobacterial diseases, MAP can't be identified within diseased tissues; nevertheless, MAP's DNA can be detected. This subliminal presence of MAP as spheroclasts is theorized to be the antigen template that sustains the anti-MAP cytokine cascade elicited upon re-exposure to MAP (2,3). In contrast to bacteria, occult sequestration of viruses and mycobacteria has been advanced to account for the persistence of immune markers for years after the initial infection (4). This persistence of specific antibodies is not a uniform occurrence in all cases, suggesting that, in some cases, immune destruction of the antigenic template has been achieved.

2 II. Immune System Enhancement by Diet

Prior to the advent of anti-mycobacterial drugs, the therapeutic modalities that could sometimes affect a clinical cure for infections due to Mycobacterium tuberculosis were stress reduction (negation of the effect of stress on the immune system), sunlight (correction of vitamin D deficiency), and nutrition (replacement of essential ingredients for optimum function of the immune system).

Unlike bacterial diseases, immunological and serological markers for mycobacteria and viruses may persist in some individuals for years after the initial infection. (4). When cell-mediated immunity is effectively compromise reactivation of organism replication may occur. in individual who retain immunological evidence of prior infection. The loss of immunological markers is presumed to correlate with destruction of its template.

Johne's disease is a reputedly incurable chronic granulomatous disease of the gastrointestinal tract caused by Mycobacterium avium subspecies paratuberculosis (MAP). Once a cow manifests with full blown liquid diarrhea associated with evidence of advanced malnutrition, death usually occurs in the ensuing two to three weeks. Just such a cow was removed from its herd and placed in a controlled, stress free environment. In order to obtain additional quantities of high-titer anti-MAP antibodies, the animal was put on boutique designed supplements composed of vitamins, minerals, and selected amino acids that targeted enhancing cellular immunity.

The animal thrived. During the four months of targeted dietary supplementation, her serological markers fell to near normal. When she was necropsied, neither gross nor histological evidence of MAP/Johne's disease were identified (5). Histological analysis of the diseased tissues identified the mechanism of MAP destruction (6).

The demonstrated ability of targeted dietary immune system enhancement to destroy MAP in Johne's disease makes a theoretical case for potential therapeutic synergy with anti-MAP drugs. Destruction of the MAP template required for the production of MAP targeted cytokines may be the requisite for transforming prolonged remissions into cures.

In Crohn's disease, MAP's DNA can be detected within diseased tissue, but MAP per se can't be identified. A secondary corollary of the Hruska Postulate is that the subliminal presence of MAP in spheroclastic form constitutes the template for anti-MAP cytokine (7). immunity.

Acquitted immunity is primarily derived from the symbiotic microbiological flora within the gastrointestinal tract. Once an individual experiences diarrhea of any etiology for a sustained period of time, his or her immune system becomes progressively compromised. Inflammatory changes and cell death alter the local microbiological environment and the inter-relationships within the governing bacterial hierarchy. Facultative anaerobic pathogenic bacteria escape the imposed suppression by dominant anaerobic bacteria. The governing symbiotic bacteria are replaced by more pathogenic organisms theoretically adversely affect gut acquired immunity. In Crohn's disease, the mucosal destruction and inflammatory infiltration of the lamina propria further impeded absorption of key elements needed to sustain an optimally functioning immune system.

Four of the nine ingredients included in cow #6142's dietary supplementation to counter diseaseimposed deficiencies are discussed.

Zinc is required for the catalytic activity of approximately 100 enzymes involved with immune function and protein and DNA synthesis. Zinc deficiencies result in adverse changes in cytokine production and T-cell subpopulations (12).). With infection, a redistribution of zinc occurs. Interlukin-1 (IL-1) tumor necrosis factor (TNF) and interlukin-6 (IL-6) cause a marked decrease in serum zinc concentration (13).

Even mild to moderate degrees of zinc deficiency can impair macrophage and neutrophil functions, natural killer cell activity and complement function. (13) The body requires zinc to develop and activate T-lymphocytes (14). Zinc is a critical component of the thymic hormone, thymosin that regulates cellmediated immunity. With prolonged zinc deficiency, thymic atrophy and lymphoid depletion of the spleen and lymph nodes occurs (14,15).

Among the major functional consequences of zinc deficiency are anorexia, diarrhea, and impaired immunological responsiveness. Zinc deficient individuals with significant diarrhea often have very high zinc loss in their feces.

The recommended daily amount of zinc recommended for health maintenance (15mg) is inadequate when systemic infection/disease is present and is totally inadequate with diarrhea.

Selenium: Selenium is an essential component of selenocyteine proteins within the immune system. Selenium is incorporated as selenocysteine into selenoproteins, one of which, glutathione peroxidase is considered essential in antioxidant defense mechanisms.

Selenium dependent glutathione peroxidases protect neutrophils from oxygen-derived radicals. Selenium acts as an anti-oxidase in the extracellular space, the cell cytosol, in association with cell membranes in the gastrointestinal tract. (**??**6) The selenium based antioxidants remove potentially damaging lipid hydroperoxidases and hydrogen peroxide and are considered essential in sustaining mucosal integrity. Selenium has been demonstrated to improve the killing ability of neutrophils (16).

Herds grazed on selenium poor soil have a high incidence of Johne's disease (a chronic granulomatous disease caused by MAAP) in comparison to those animals pastured on ground with good selenium levels. (**??**7) Vitamin E deficiency is frequently concomitantly present in selenium deficient animals (18). Deficiency of selenium undermines the integrity of the gastrointestinal mucosa by facilitating the action of pro-inflammatory compounds. In dairy cattle, deficiencies of selenium can cause poor growth and diarrhea (19).Individuals receiving zinc 20mg per day plus of selenium and 100ug per day plus anti-oxides appear to acquire fewer infections (20). Zinc: The body has no specialized system to store zinc. (8). Individuals with Crohn's disease very probably have zinc deficiency impairment affecting a broad spectrum of mechanisms involved in the killing of intra-cellular pathogens. Zinc generates oxidants that destroy viruses and mycobacterium (9).The zinc deficiency further sustains selective malnutrition through induced loss of appetite. With infection, a redistribution of zinc occurs. Interlukin-1 (IL-1) tumor necrosis factor (TNF) and interlukin-6 (IL-6) cause a marked decrease in serum zinc concentration (10), Crohn's disease can result in decreased zinc absorption and increased exogenous zinc loss (11). remained fixed at temporary disease palliation: arrestment of symptomology, with evidence of mucosal healing. The dysbiosis paradigm identified the second mechanism resulting from immune destruction of selected areas within the small bowel. The addition of antibiotics increases the number of remissions attained with biologics. The utilization of focused anti-MAP therapy has produced longer remission than had previously been attained

with biologics or immunomodulatory. Cow 6142 has added an additional therapeutic vehicle: auto-enhancement of MAP destruction through diet and of reduction the adverse effect of stress on the immune system.

Vitamin C: Vitamin C regenerates vitamin E from its oxidized form. The lipid soluble antioxidant vitamin E not only protects the integrity of cell membranes, but functions synergistically with other nutritional elements that beneficially influence cell-mediated immunity. The salvage of vitamin E influences the immune functions of selenium which in turn has a beneficial impact on copper and zinc utilization (24). The body's need for vitamin C dramatically increases with infection/disease (25)(26)(27)(28). Mega-doses can prevent and/or greatly speed the recovery from acute viral infections (29)(30).

3 III. Discussion -Destruction of the map Template

The Hruska Postulate and its modifications now constitute "error-up-to date" with respect to the pathogenesis of Crohn's disease. The incorporation of anti-MAP therapy into the treatment of Crohn's disease has resulted in remissions of longer durations than had been achieved with biologics, but also alleged cures (31)(32)(33)(34)(35). Warren et al. have noted the remission of Crohn's disease win individuals with tuberculosis who were treated with anti-tuberculosis therapy (36). In tuberculosis, pharmaceutical destruction of M. tuberculosis acted primarily to reduce the pathogen mass to a quantum that allowed the host's cellmediated immune system to achieve governance and sometime cure.

In the mid 1980s, Warren et al. described remission of Crohn's disease with anti-tuberculosis therapy (31). The implication of this experiment in medical care ultimately manifested a decade and a half later when Borody et al., Chamberlin et al., and Shafran et al., among others, incorporated anti-tuberculosis drugs into their therapeutic regimens for Crohn's disease (32)(33)(34)(35)(36). The importance of addressing therapy against the MAP template has been inferred by both statistical evidence derived from meta-analyses pf multiple formal studies and documented clinical and endoscopic responses in patients treat with anti-MAP combinations outside of formal clinical studies (36). Conversion of prolonged remissions to cure may require complete destruction of the sustaining immune template.

In Crohn's disease, the role of diet can go beyond reversing the induced catabolic state and reducing the number of MAP antigen challenges. In a consorted effort to destroy the sustaining MAP template in Crohn's disease, diet has the potential to be a synergistic therapeutic vehicle to anti-mycobacterial drugs. This demonstrated ability to, not render MAP inactive but to actually destroy the organism (5,6), introduces the potential of changing the therapeutic target in Crohn's disease from remission to cure.

4 IV. Conclusion

Cow #6142 has demonstrated that targeted dietary supplementation can affect destruction of MAP. This cow makes the case for dietary synergy with anti-MAP drugs in order to break the MAP template that is required for the elaboration of MAP targeting cytokines [1]

Figure 1: A

[Sever et al. ()] , J L Sever , J A Brody , G M Schiff . *Rubella epidemic on St. Paul Island in the Pribilofs* 1963.

[Am. J. Gastroenterol ()] , *Am. J. Gastroenterol* 2007. 102 p. .

[Almerighi ()] '1 Alpha, 25-edihydroxyvitamin D3 inhibits CD40L-induced pro-inflammatory and immunomodular activity in human monocytes'. C Almerighi . *Cytokines* 2009. 45 p. .

[Wichtel ()] 'A review of selenium deficiency in grazing ruminants, Part 1: new roles for selenium in ruminant metabolism'. J J Wichtel . *N.Z. Vet. J* 1998. 46 p. .

[Borody et al. ()] 'Antimycobacterial therapy in Crohn's disease heals mucosa with longitudinal scars'. T J Borody , S Bilkey , A R Wettstein . *Dig. Liver Dis* 2007. 39 p. .

[Biroulet et al. ()] 'Antimycobacterium therapy in Crohn's disease: the end of a long controversy?'. I P Biroulet , C Neut , J F Colombel . *Prac. Gastro* 2008. 1 p. .

[Walsh et al. ()] 'Antioxidant enzyme activity in the muscles of calves depleted of vitamin E or selenium or both'. D M Walsh , D G Kennedy , S Kennedy . *Br. J. Nutr* 1993. 70 p. .

[Furuya et al. ()] 'Antiviral effects of ascorbic and dehydroascorbic acid'. A Furuya , M Uozaki , H Yamasaki . *Int. J. Mol. Med* 2008. 22 p. .

[Tang ()] 'Calcitriol suppresses anti-retinal autoimmunity through inhibitory effects on the Th17 effector response'. J Tang . *J. Immunol* 2009. 182 p. .

[Clinical and laboratory findings for intense study population J. Am. Med. Assoc ()] 'Clinical and laboratory findings for intense study population'. *J. Am. Med. Assoc* 1965. 191 p. .

[Wintergerst et al. ()] 'Contribution of selected vitamins and trace elements to immune function'. E S Wintergerst , S Maggini , D H Hiornig . *Ann. Nutri. Metab* 2007. 51 p. .

[Hruska and Pavlik ()] 'Crohn's disease and related inflammatory diseases: from a single hypothesis to one "superhypothesis'. K Hruska , Pavlik . *Veterinarni Medicina* 2014. p. .

[Levy ()] *Curing the Incurable: Vitamin C, Infectious Diseases, and Toxins*, T E Levy . 2002.

[Webb and Villamor ()] 'Effects of antioxidant and non-antioxidant vitamins on the Immune system'. A L Webb , E Villamor . *Nutr. Rev* 2007. 65 p. .

[Gaetke et al. ()] 'Effects of endotoxin on zinc metabolism in human volunteers'. L Gaetke , C J Mcclain , R Talwalkar , S Shedlosky . *AM. J. Physiol* 1997. 272 p. .

[Prasad ()] 'Effects of zinc deficiency on Th1 and Th2 cytokine shifts'. A S Prasad . *J. Infect. Dis* 2000. 182 p. .

[Daniel ()] 'immune modulatory treatment of trinitrobenzene sulfonic acid colitis with calcitriol is associated with a change in T helper (Th) 1/17 to a Th2and regulatory T cell profile'. C Daniel . *J. Pharmacol. Exp. Ther* 2008. 324 p. .

[Wintergerst et al. ()] 'Immuneenhancing role of vitamin C and zinc and effect on clinical conditions Ann'. E S Wintergerst , S Maggini , D H Horning . *Nutri. Metab* 2006. 50 p. .

[Banc ()] 'Immunostimulation by vitamin C'. S Banc . *Int. J. Vitam. Nutr. Res. Suppl* 1982. 23 p. .

[Girodon et al. ()] 'Impact of trace elements and vitamin supplementation on immunity and infection in elderly institutionalized paitents: a randomized controlled trial MIN VIT AOX Geriatric network'. F Girodon , P Galan , A L Monget . *Arch Intern. Med* 1999. 159 p. .

[Murata et al. ()] 'Mechanism for inactivation of bacteriophage delta a containing single strand DNA by ascorbic acid'. A Murata , R Oyadomari , T Ohashi , K Kitagawa . *J. Nutr. Sci. Vitaminol* 1975. 21 p. .

[Chamberlin et al. ()] 'Primary treatment of Crohn's disease: combined antibiotics taking center stage'. W Chamberlin , T J Borody , J Campbell . *Expert Rev. Clin. Immunol* 2011. 7 p. .

[Chamberlin et al. ()] 'Primary treatment of Crohn's disease: combined antibiotics taking center stage'. W Chamberlin , T J Borody , J Campbell . *Expert Rev. Clin. Immunol* 2011. 7 p. .

[Monif and Williams ()] 'Relationship of intestinal eosinophilia and the acid-fast bacilli in Johne's disease. Intern'. G R G Monif , J E Williams . *J. Appl. Med* 2015. 13 p. .

[Warren et al.] 'Remission of Crohn's disease with tuberculosis therapy'. J Warren , H Rees , T Cox . 1886' 214: 182. *N. Engl. J/ Med*

[Shafran and Burgeunder ()] 'Rifaximin for the treatment of newly diagnosed Crohn's disease: a case series'. I Shafran , P Burgeunder . *Am. J. Gastroenterol* 2008. 103 p. .

[Hogen et al. ()] 'Role of vitamins and selenium in host defense against mastitis'. J S Hogen , W P Weiss , K L Smith . *J. Dairy Sci* 1993. 76 p. .

[Arthur et al. ()] 'Selenium in the immune system'. J R Arthur , R C Mckenzie , G J Beckett . *J. Nutri* 2003. 133 p. .

[Andrews et al. ()] 'Seleniumresponse disease of animals in New Zealand'. E D Andrews , W J Hartley , A R Grant . *N. Z. Vet. J* 1968. 16 p. .

[Buergelt et al. ()] 'Spontaneous clinical remission of John's disease in a Holstein cow'. C D Buergelt , J E Williams , G R G Monif . *Int. J. Applied Res. Vet. Med* 2004. 2 p. .

[Chamberlin et al.] *Successful treatment of a Crohn's disease patient with bacteremic Mycobacterium paratuberculosis*, W Chamberlin , G Ghobrial , M Chehtane .

[Powell ()] 'The anti-oxidant properties of zinc'. S Powell . *J. Nutr* 2000. 130 p. .

[Monif ()] *The Hruska postulate of Crohn's disease. Med Hypoth*, G R G Monif . 2015. 85 p. .

[Monif ()] 'The Mycobacterium avium subspecies paratuberculosis dilemma'. G R G Monif . 10.4172/0974-8369.1000270. *Biol. Med* 2016. 8 p. 279.

[Monif ()] 'Translation of Hypothesis to Therapy in Crohn's disease'. G R G Monif . *Inflam. Bowel Dis* 2016. 20 p. .

[Hickey and Saul ()] *Vitamin C: The Real Story, the Remarkable and Controversial Healing Factor*, S Hickey , A W Saul . 2008.

[Valberg et al. ()] 'Zinc absorption in inflammatory bowel disease'. L S Valberg , P R Flanagan , A Kertesz , D C Bondy . *Dig. Dis. Sci* 1986. 31 p. .

[Rink and Gabriel ()] 'Zinc and the immune system'. L Rink , P Gabriel . *Proc. Nut. Soc* 2000. 59 p. .

[Mcclain et al. ()] 'Zinc deficiency: a complication of Crohn's disease'. C J Mcclain , C Soutor , L Zieve . *Gatroenterol* 1980. 78 p. .

[Prasad et al. ()] 'Zinc deficiency: changes in cytokine production and T-cell subpopulations in patients with head and neck cancer and non-cancer patients'. A S Prasad , F W Beck , S M Grabowski , J Kaplin , R H Mathog . *Proc. Assoc. Am. Physicians* 1977. 109 p. .