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Dietary Manipulation in Crohn's Disease?

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ABSTRACT

In isolated cases of Crohn's disease, dietary manipulations have produced what biologics and steroids have yet to document: permanent remissions/cures. The questions of how and why are addressed. The postulates advanced are 1) that clinical amelioration remissions achieved through dietary manipulation are the consequence of limiting MAP antigen/cytokine interactions at the sites of Mycobacterium avium subspecies paratuberculosis mucosal attachment and ultimately, 2) by dietary restoration and enhancement of host cellular immunity, resulting in the destruction of the MAP-template which drives the dysfunctional pro-inflammatory immune response. The syngergistic coupling of diet and biologics is discussed.

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Crohn's disease is a zoonotic food-borne disease

Mycobacterium avium subspecies paratuberculosis (MAP) is a significant pathogen for milk-producing domestic animals. Infected animals have the ability to shed the mycobacterium into their milk. MAP survives pasteurization. USDA's failure to address the growing prevalence of MAP in dairy herds has resulted in widespread dissemination of the mycobacterium, particularly within milk-based food products. MAP has been identified in infant formula, powdered milk, milk, cheese, etc. [1-13].

In contrast to their pathogenicity as replication pathogens in domestic animals, MAP and other atypical mycobacteria have limited pathogenicity for humans unless a form of immunodeficiency is present [14,15].

At birth, lacking acquired immunity newborn infants are analogous to a germ-free animal. Acquired immunity is central to establishing immunological governance over viral and mycobacterial infections. The Hruska postulate introduced the concept that, if a newborn becomes infected with MAP in its period of immunological vulnerability, the ability of its inherent immune system to abort mycobacterial replication could be severely challenged [16]. Depending on the baby's genetic profile, the magnitude of the infectious MAP inoculum, and the status of its developing acquired immunity, the baby's inherent immune system can become so taxed that its TH1 pro-inflammatory response to MAP becomes fixed within immunological memory. Whenever the body is again presented with MAP's antigenic array, rather than responding by exhibiting immunological tolerance, immunity re-initiates its original pro-inflammatory cytokine responses and attacks MAP at its site of attachment and antigen processing. Fecal stasis concentrates MAP challenges in the ileocecum. The focal destruction of the gastrointestinal mucosa allows for penetration of the gastrointestinal microbiota into the lamina propria and underlying tissues [17, 18] (which imposes a secondary disease process).

Dietary Manipulation Therapeutic

Things happen for a reason. Isolated unstructured observations without implied mechanism of action are rarely published in the medical literature. Most cases of permanent resolution of Crohn's disease through dietary manipulation are found in the lay literature. What is in the medical literature is the demonstration that dietary use of specific carbohydrates (the SCD diet) can produce demonstrable clinical amelioration in cases of pediatric Crohn's disease. While the SCD diet improved mucosal inflammation, healing could not be documented [19-22].

Central to re-establishing mucosal integrity is aborting antigen/antibody cytotoxicity at MAP's sites of mucosal attachment. The pathogenesis of Crohn's disease argues for the removal from diet of all foods that have the potential of having been adulterated by MAP, more specifically all dairy based products and red meat. By so doing, the number of cytotoxic antigen/antibody interactions within the gastrointestinal tracts are markedly reduced. Biologics act by dismantling the cytotoxic cytokine response to MAP. Dietary exclusions utilize prevention of, rather than immune response interference to achieve the same objective, reconstitution of mucosal integrity. It being nearly impossible to identify and/or eliminate all MAP-adulterated foods, dietary exclusion and biologics can be complementary to each other in re-establishing mucosal reconstitution.

Dietary Supplementation Therapeutics

In Crohn's disease, the induced alterations of gastrointestinal structure and function compromise the quantitative availability of vitamins, minerals and selected amino acids essential to the maintenance of effective immune system function.

Minerals

Zinc is a prime example of how deficiency of a single mineral can undermine immune system integrity. The body has no specialized system to store zinc. Individuals with Crohn's disease have zinc

deficiency impairment affecting a broad spectrum of immune mechanisms owing to decreased absorption and increased exogenous loss. Individuals with a diarrheal disease will have high fecal zinc loss. Zinc is important to the catalytic activity of approximately 100 enzymes involved with immune system function and DNA synthesis. Zinc deficiencies result in adverse changes in cytokine production and T-cell subpopulations. A side effect of zinc deficiency is anorexia which in itself can create its own negative feedback [23-26].

Vitamins

The vitamin C and E interactions are central to immune system maintenance. 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.

Like zinc, vitamin C has limited storage within the human body. Through its antioxidant effect, vitamin C plays a central role in the containment of mycobacteria. The body's need for vitamin C dramatically increases with infection/disease [27, 28].

Destruction of the MAP Immune Template

The reason for acute therapeutic focus on vitamins, minerals, and amino acids central to maintenance of optimal host immunity is the postulate that the curing of Crohn's disease is contingent upon destruction of the MAP templates (spheroplasts) sustaining the dysfunctional immune response that is characteristic of Crohn's disease.

The evidence relating to destruction of the MAP template through specific enhancement of host immunity is derived in part from a four-month study of a cow with near terminal Johne's disease. In an attempt to prolong her life in order to collect high-titer anti-MAP serum, a specialized diet was designed that targeted enhancement of cellular immunity. When finally necropsied four months later, the cow had regained all her body weight. The serological markers for MAP infection had dropped to near normal status. No gross or histological evidence of Johne's disease could be identified. Evidence of acid-fast bacilli in diseased tissue was totally absent. What was present was a clue as to how the body can actually destroy mycobacteria. The significance of this observation, which was subsequently confirmed by field trials in diseased animals, provided insight as to how dietary manipulation had, more likely than not, attained permanent remissions [29-31].

A secondary substantiation of MAP spheroplasts driving the dysfunctional proinflammatory immune-mediate response comes from the only other therapeutic regimen that has produced isolated cures of Crohn's disease: anti-mycobacterium drugs [32-38]. As a general rule, anti-tuberculosis drugs have not produced cures. When they have, the mechanism of action of one or more of the compounds used involved disruption of RNA function. For an antibiotic to destroy bacteria without a cell wall (spheroplasts), the drug must act on the organism's ribosomes.

Why Dietary Manipulation or Biologics Alone Can Fail

Crohn's disease is the consequence of two inter-related but separate disease processes; a dysfunctional immune-mediated response to MAP's antigen array and a localized polymicrobial bacterial infection of the small bowel [39]. Failure to appropriately negate the latter through comprehensive antibiotic therapy is responsible for the late sequela of Crohn's disease: strictures, loop-to-loop anastomoses, peri-anal fistula, bowel perforations, etc. [40,41]. Once in place, surgical intervention is often required.

Dietary Manipulation's Risk-Benefit Ratio

In contrast to biologics and steroids, proper dietary manipulation is a therapeutic modality with literally no indefinable adverse consequences. The key to termination of symptomology is re-establishment of mucosal integrity. The therapeutic coupling of diet and biologics is one of logic. Reducing the frequency of MAP/immune system interactions stands to enhance the efficacy of biologics to abort cytokine consequences. Theoretical template destruction using dietary manipulation alone is projected to require significantly more time. A better coupling after mucosal healing has been documented, is that of selected antimicrobials that target MAP RNA and dietary manipulation. Individually, these two therapeutic are the only therapeutic modalities that have induced permanent remissions in isolated cases.

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