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Opinion

The Curing of Crohn's Disease

Gilles R. G. Monif [1, 2, *]

1. Infectious Diseases Incorporated, Bellevue, NE, United States
2. University of Florida, College of Veterinary Medicine, Gainesville, FL, United States; E-Mail: gmonif@AOL.com

* **Correspondence:** Gilles R. G. Monif; E-Mail: gmonif@AOL.com

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Abstract

Using the therapeutic intervention points identified by the Hruska Postulate, Infectious Disease Incorporated's designated therapeutic priorities for Crohn's disease via are presented. Central to the curing of Crohn's disease is destruction of the anti-MAP template.

Keywords

Crohn's disease; therapy; Hruska Postulate; dietary manipulation; anti-mycobacterial therapy

1. Introduction

In Crohn's disease, understanding the cause of the loss of gastrointestinal mucosal integrity and the consequences of this loss underlies the ability to cure it.

Due to the inability to define the events that combine to produce disease, the current therapy of Crohn's disease evolved from a digest of therapeutic trials and errors. Demonstration that the

disruption of the immune system's pro-inflammatory response could abort disease symptomology and result in mucosal healing became the foundational pieces of therapy. Unable to identify the target antigen or antigens of what is an immune-mediated process, conceptual ignorance has been sustained by attributing causation to the unsubstantiated myth of autoimmunity [1, 2]. Labelling a disease as being due to autoimmunity has effectively shifted the burden of proof from proving it to disproving it.

Under the cover of assumed autoimmunity, the therapy of Crohn's disease has arrested with pharmaceutical plication of disease. The 2018 American College of Gastroenterology's Clinical Guideline states "*Despite the recent advances in the treatment of patients with CD, there still remains a large group of patients who do not respond adequately to our current medication armamentarium.*" … *We will certainly expand our medical treatment war chest and uncover effective biologics with different mechanisms of action to treat our patient. If the initial biologic drug fails, the patient will be able to be switch to another agent and even combination biologics may become a reality*" [3]. In another world, continuing to do basically the same thing therapeutically for two decades and expecting a different outcome would be deemed insanity.

In 2015, work done by Infectious Disease Incorporated (IDI) in conjunction with the Veterinary Research Institute of The Czech Republic and the University of Florida College of Veterinary Medicine produced the Hruska Postulate of causation [3-6].

What the Hruska Postulate states is that the genesis of Crohn's disease begins when a newborn experiences a significant infectious challenge by Mycobacterium avium subspecies paratuberculosis (MAP) at a time when its acquired immunity has yet to develop. In order to abort continued MAP replication, genetically determined, inherent immunity can become so stressed that its pro-inflammatory TH 1 response against MAP becomes fixed within its immunological memory. Every time its immune system is presented with MAP, rather than responding with primarily a nonaggressive TH 2 response (known as immunological tolerance), it again initiates a pro-inflammatory release of substances that attack MAP.

The absence of functional acquired immunity, gives MAP infection the potential to convert itself from an infectious disease into an immune-mediated disease.

The loss of mucosal integrity gives the gastrointestinal tract's microbial flora an open portal for invasion. If left undertreated or untreated, the resultant polymicrobial bacterial invasion follows the principles of the anaerobic progression in which the many initial bacterial participants self-condense down to a few and within abscesses to one organism. Continuing bacterial replication creates the second pathological mechanism of disease production within Crohn's disease [3, 7]. The permanent sequelae of Crohn's disease, submucosal fibrosis, strictures, bowel to bowel fistulae, bowel perforations, and perianal fistulae, are attributable to inadequately antimicrobial counter-acting the pathology induced by the gastrointestinal microbiota [7-9].

2. The Curing of Crohn's Disease

The implied thesis embedded in the Hruska Postulate is that to cure Crohn's disease, destruction of the MAP template sustaining the dysfunctional pro-inflammatory response requires destruction. Validation of this thesis resides with the only two therapeutic approaches that have produced permanent remission: therapy with selective anti-mycobacterial compounds and exclusion diets.

2.1 Antimicrobial Therapy

Since the 1990's, MAP had been cited as the possible cause of Crohn's disease. The death blow to the MAP infectious disease paradigm came from the inability, using standard culture technology, to isolate or identify using special stains MAP in diseased gastrointestinal tissue [6]. In contrast, MAP is readily cultured and demonstrable in diseased gastrointestinal tissue from domestic animals with Johne's disease.

A byproduct arising from the direct infectious disease causation of Crohn's disease was the occasional achievement of a permanent remission with the administration of anti-mycobacterial compounds [10-12]. The explanation for why the prior failures and why the occasional successes partially resided in the selection of anti-mycobacterial compounds. MAP template is MAP in its spheroblastic form. To be effective against spheroblasts, the drug's mechanism of action must disrupt ribosomal function.

2.2 Dietary Manipulation

In Japan, dietary therapy has long been a standard part of Crohn's disease treatment. Within pediatric gastroenterology, beneficial results have been achieved with selective dietary regimens [13-17]. The dietary discipline implemented by isolated individuals afflicted with Crohn's disease has produced permanent cures. The common thread uniting these observations is the elimination of foods that have the potential to have been adulterated with MAP. Reduction of the antigen challenge load is insufficient to produce permanent cure. Fortunately, an animal with far advanced gastrointestinal infection due to MAP provided the answer as to why dietary exclusion can achieve a potential cure of Crohn's disease in humans: immune destruction of MAP [18-19]. The inflammatory destruction of gastrointestinal mucosa alters the composition of the gastrointestinal microbiota which plays an important role I n maintaining acquired immunity. The loss of mucosal surface in a strategic area for absorption and increased fecal transit time result in loss of vitamins and minerals essential to optimal immune system function [20-24].

The answer as to how dietary manipulations have produced occasional permanent remissions was initially supplied by a cow with far advanced, well documented Johne's disease due to MAP. A boutique diet that specifically targeted enhancement of cellular immunity was administered. An animal that should have died in a matter of a few week regained full health. When finally necropsied, the animal had neither microbiological nor pathological evidence of disease. Tens of millions of mycobacteria had been destroyed. What histological analysis did reveal was the mechanism by which mycobacteria can be destroyed [19].

Both anti-MAP drug administration and dietary exclusion with immune system enhancement require a significant tincture of time in order to achieve their ultimate therapeutic objective. Shortening the time required for the re-establishment of mucosal integrity being of primary therapeutic importance argues for the short-term use of a biologic. Neither anti-MAP therapy nor dietary manipulations alone adequately addressed therapy of established polymicrobial infection. Aggressive, targeted antibiotic therapy is needed to preclude the permanent sequela observed in individuals afflicted with Crohn's disease

3. The Therapy of Crohn's Disease

Having identified the primary therapeutic objectives, the immediate focus needs to be the reconstitution of mucosal integrity in the shortest time frame possible [25-26]. The following suggested recommendations are adapted from Infectious Diseases Incorporated's (IDI) therapeutic guidelines for Crohn's disease.

The therapy of Crohn's disease is a team endeavor that includes a gastroenterologist, an internist with specialized training in infectious diseases, a dietician, and a competent clinical laboratory.

3.1 Designated Priorities

3.1.1 Rapid Establishment the Diagnosis of Crohn's Disease

There is a correlation between the duration of clinically overt disease and the rapidity with which a remission is achieved. After over two decades, the absence of a relatively non-invasive diagnostic test for Crohn's disease is an unpardonable blemish on medicine.

3.1.2 Dietary Manipulations

Elimination of all dairy and other foods having the potential of being adulterated by live or nonviable MAP organisms (basically a vegetarian diet to which a fish source of protein is added).

3.1.3 Dietary Immune System Enhancement

In addition to replacing deficiencies in factors known to be essential to optimal immune system function, consideration should be given to putting cellular immunity in hyper-drive through dietary supplementation.

3.1.4 Antibacterial Therapy

The initial poly-antibiotic therapy advocated should comprehensively cover the *Enterobacteriaceae, Bacteroides fragilis*, the peptostreptococci, and the enterococci. The duration of anti-bacterial therapy can be monitored using established indicators of inflammation. Pre- and intra-therapy monitoring for *Clostridium difficile* toxin is imperative.

3.1.5 Restoration of Mucosal Integrity

Biologics can effectively restore mucosal integrity; however, not all biologics may not be of comparable efficacy.

3.1.6 Anti-*Mycobacterium* Therapy

In transitioning from anti-bacterial to anti-mycobacterial therapy, the initial use of clarithromycin should be continued.

3.1.7 Probiotics

The role of the designated probiotic has little to do with curing Crohn's disease. Its role is to positively influence the intraluminal bacterial flora so as to enhance the individual's acquired immunity.

4. Commentary

Crohn's disease research is primarily funded by the pharmaceutical industry. Academic medicine can be adversely influenced by third parties [27-29]. Government agencies that reputedly function within the public trust are castrates in front of political will. The validation that Crohn's disease is a curable disease will not come from expensive, large, double blinded, randomized, placebo controlled comparative studies (FDA's definition of "evidence-based data"). Documentation will come from small, independently funded clinical trials whose end titration point is sustained remission period.

Infectious Diseases Incorporated stated opinion is that Crohn's disease is both a curable and preventable disease [25, 26, 30].

Author Contributions

Gilles R. G. Monif did all work.

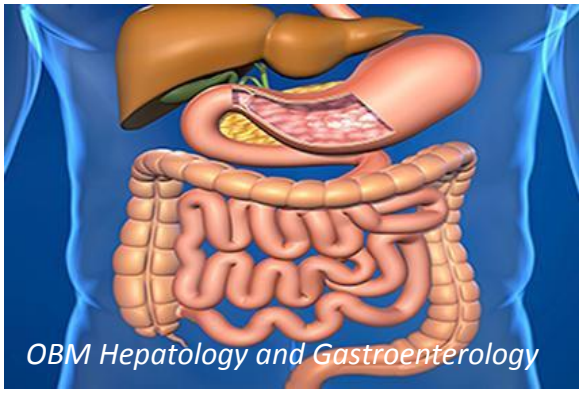
Competing Interests

The author has declared that no competing interests exist.

References

1. Monif GRG. The myth of autoimmunity. Med Hypothesis. 2018; 121: 78-79.
2. Monif GRG. The paradigms for causation of Crohn's disease. Crohn's Colitis. 2016; 22: E6-10.
3. Lichenstein GR, Loftus EVJr, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACCG Clinical Guidelines: Management of Cohn's disease in adults. Amer J Gastroenterol. 2018; 113: 481-517.
4. Monif GRG. The Hruska postulate. Med Hypothesis. 2015; 85: 878-881.
5. Monif GRG. The WHY? of Crohn's disease. Adv Res Gastroenterol Hepatol. 2018; 10: 555798.
6. Monif GRG. The Mycobacterium avium subspecies paratuberculosis dilemma. Bio Med. 2016; 8: 2.
7. Monif GRG. Translation of hypotheses to therapy in Crohn's disease. Inflamm Bowel Dis. 2016; 22: E8-9.
8. Monif GRG. An infectious disease process within an immune-mediated disease process: Role of the gastrointestinal microbiota in Crohn's disease. Adv Res Gastroenterol Hepatol. 2017; 5: 1-2.
9. Monif GRG. Are the permanent sequelae of Crohn's disease a failure to treat the gastrointestinal microbiota? Med Hypothesis. 2018; 122: 198-199.
10. Behr MA, Hanley J. Anti-mycobacterial therapy for Crohn's disease: A reanalysis. Lancet Infect Dis. 2008; 8: 344.

11. Chamberlin W, Borody T, Campell J. Primary treatment of Crohn's disease: Combined antibiotics taking center stage. Expert Rev Clin Immunol. 2011; 76: 751-760.
12. Biroulet IP, Neut C, Colombel JF. Anti-mycobacterium therapy in Crohn's disease: The end of a long controversy? Prac Gastroenterol. 2008; 1: 11-17.
13. Suskind DL, Wahbeh G, Cohen SA, Damman CJ, Klein J, Braly K, et al. Patients perceive clinical benefit with specific carbohydrate diet for inflammatory bowel disease. Dig Dis Sci. 2016; 61: 3255-3260.
14. Cohen SA, Gold DB, Oliva S, Lewis J, Stallworth A, Koch B, et al. Clinical and mucosal improvement with specific carbohydrate diet in pediatric Crohn's disease. J Pediatr Gastroenterol Nultr. 2014; 59: 516-521.
15. Burgis JC, Nguten K, Park KT, Cox K. Response to strict and liberalized specific carbohydrate diet in Pediatric Crohn's disease. World J Gastroenterol. 2016; 22: 2111-2117.
16. Penagin F, Dilillo D, Borsani B, Cococcioni L, Galli E, Bedogni G, et al. Nutrition in pediatric inflammatory bowel disease: From etiology to treatment. A systemic review. Nutrients. 2016; 1: 8.
17. Romano A, Castagna V. Human nutrition from the gastroenterologist's perspective. Gastroenterol Clin N Amer. 2016; 79-86.
18. Monif GRG, Williams JE. Relationship of intestinal eosinophilia and acid-fast bacilli in Johne's disease. Int J Appl Res Vet Med. 2015; 13: 147-149.
19. Buergelt CD, Williams JE, Monif GRG. Spontaneous clinical remission of Johne's disease in a Holstein cow. Int J Appl Res Vet Med. 2004; 2: 126-128.
20. Monif GRG. The enhanced role of diet in Crohn's disease. Adv Res Gastroenterol Hepatol. 2017; 3: ARGH NS55529
21. Valberg LS, Flanagan PR, Kertesz A, Bondy DC. Zinc absorption in inflammatory bowel disease. Dig Dis Sci. 1986; 32: 724-731
22. McClain CJ, Soutor C, Hiornig DH. Zinc deficiency: A complication of Crohn's disease. Gastroenterol. 1980; 78: 273-279.
23. Girodon F, Galan P, Monget AL, Boutron-Ruault MC, Brunet-Lecomte P, Preziosi P, et al. Impact of trace elements and vitamin supplementation on immunity and infection in the elderly institutionalized patients: a randomized controlled trial. MIN. VIT. AOX. geriatric network. Arch Intern Med. 1999; 159: 748-754.
24. Wintergerst ES, Maggini S, Hiornig DH. Contribution of selected vitamins and trace elements to immune function. Ann Nutri Metab. 2007; 51: 301-323.
25. Monif GRG. Understanding therapeutic concepts in Crohn's disease. Clin Med Insights Gastroenterol. 2018; 20: 1-3.
26. Monif GRG. The quest for a cure to Crohn's disease. Adv Med Biol. 2018; 129: 187-204.
27. Botkin JR. Should failure to disclose significant financial conflict of interest be considered research misconduct. JAMA. 2018; 320: 2307-2308.
28. Cigarro FG, Masters BS, Sharphorn D. Institutional conflict of interest and the public trust. JAMA. 2018; 329: 2305-2306.
29. Ornstein C. Thomas K. What these medical journals don't reveal: Top doctor's ties to industry. The New York Times; 2018.
30. Monif GRG. The prevention of Crohn's disease. Adv Res Gastroenterol Hepatol. 2017; 8: 555738.



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