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DOES AN UNHEALTHY DIET CAUSE INFLAMMATORY BOWEL DISEASE?

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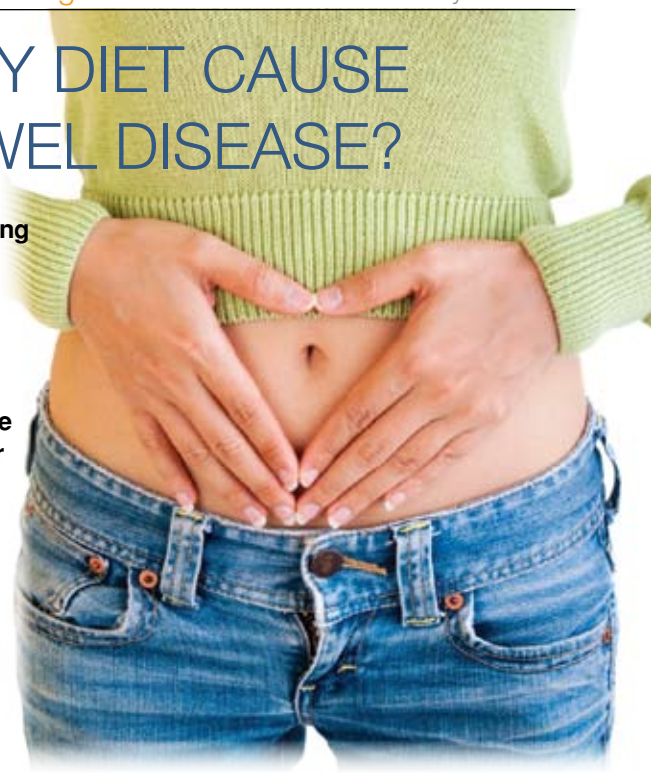

Inflammatory bowel disease (IBD) is a chronic relapsing condition presenting as inflammation of gut mucosa. Crohn's disease (CD) presents with transmural skip lesions at any point in the GI tract (1), whereas ulcerative colitis (UC) is a continuous inflammation of the mucosal layer of the large colon only. Both conditions have suspected dietary aetiology, therefore this article will look at the evidence to date of whether diet is implicated in IBD development.

The rates of IBD have been increasing over recent years and it now affects 0.5% of the population (2) leading to the suspicion that this increase is a result of an environmental factor. Changes in rates of diagnosis are reported to be too fast to be purely caused by changes in genetic composition (3.) An example of this is the increase in incidence of Crohn's disease in countries such as Japan (4), notable as a culture that has changed its dietary patterns to reflect western diets, which has led to diet being reported as a possible factor in CD development. Also migrants from areas of low incidence to high incidence have an increased risk in developing IBD (5). However, we live in interesting times and evidence and theories are growing of genetic factors that are implicated (6) and an area of rapid development is investigating how changes to natural gut flora produce effects for an individual's propensity to develop disease (7).

Identifying dietary factors that affect IBD development is a huge challenge. Observational prospective studies require large study groups to ensure adequate power and they are expensive as a result. Retrospective analysis can have recall bias (8) in a patient group that may be experiencing malnutrition as a consequence of diagnosed disease, or IBD patients who may experience a sharper focus on diet, when compared with a control population. Clinical experience has shown that patients will understandably self regulate their diet when they suspect that diet is influencing symptoms, to try to ameliorate diarrhoea, bloating and pain. Reduction of intake and exclusion of food groups appear commonly in IBD (9). This situation doesn't help when developing studies to research dietary causes of IBD, but you can empathise with the reasons why patients make these changes, as symptoms significantly affect quality of life. The best data comes from studying pre-diagnosis diet; in other words, prospective studies. There is a paucity of data available in this area. However, a large multi-centred trial (10) showed that for men and women, no association was found between diet and UC. It has been suggested that heterogeneity due to multi-centred design might have influenced the results (11) and a marginal positive association was found with total polyunsaturated fatty acid intake (10). It is difficult to recommend that pre-diagnosis diet doesn't affect risk of developing UC on evidence from one study alone and this study has nothing to add to theories of dietary intake and CD risk.

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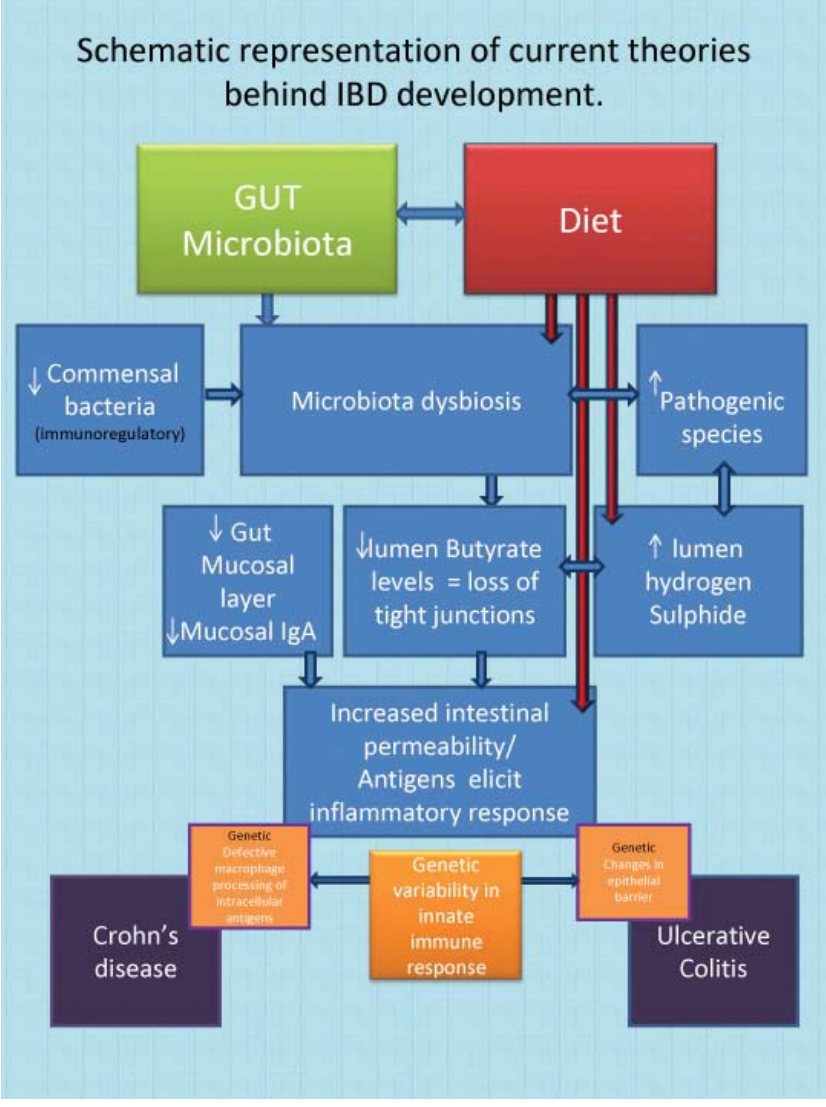
PROTEIN

Increases in risk of developing IBD with high protein intake are theorised to be caused by increases in intake of sulphur amino acids (methionine, cystine, cysteine and taurine) found in meat, fish, dairy and eggs. Sulphur compounds are suggested to be metabolised by gut bacteria to produce hydrogen sulphide, altering the membranes of colonocytes, leading to loss of gut barrier function and intestinal permeability in susceptible individuals (17).

Sulphur is also found in some other foods, such as cruciferous brassica vegetables, or foods high in glucosinolates. However, it has been suggested that high intakes are protective for gut health, in particular colon cancer (18), but interestingly, this study did not show exclusive protection in all groups. One large prospective study (8) was undertaken that showed an increased risk of IBD in French women, with high intakes of protein from meat and fish, but not protein from dairy foods. The study findings, when excluding individuals diagnosed with IBD within six to 12 months of completing the food questionnaire, were a hazard ratio of 3.63, 95 percent CI 1.32-10.01 (p trend = 0.01) total protein and 3.13; 95 percent CI, 1.34 – 7.31 (p trend = 0.01) for animal protein. A dose effect relationship with animal protein was only found in UC, but the authors reported this lack of dose effect in CD may have been due to lack of power. Also a systematic review, including prospective studies, showed high dietary consumption of meat was associated with an increased risk of both CD and UC (12) and De Silva et al (11) reported a positive association between high dietary intake of protein and IBD.



FATS

Retrospective studies have shown that western diets have a higher proportion of omega-6 as part of the diet, n-6:n-3 ratio of 8:1 was found in gastroenterology clinic patients (11) compared with an advised 2:1 (11). PUFA or more specifically the omega-6 fat linoleic acid (13) is converted to arachidonic acid, a precursor to lipid signalling molecules (11). PUFAs can modify inflammatory response; a diet high in omega-6 may result in pro-inflammatory prostaglandin synthesis in susceptible individuals (11). It is also possible that a higher intake of omega-6 to omega-3 can affect the population of gut bacteria; some PUFAs arrive in the colon intact and have been suggested to be bactericidal, thereby changing the flora population (11). The European Prospective Investigation into Cancer (EPIC) study group (13) looked at a subset of patients and found data supported a role for dietary linoleic acid in the aetiology of ulcerative colitis. The highest quartile of intake of linoleic acid was associated with an increased risk of ulcerative colitis (odds ratio (OR) = 2.49, 95 percent confidence interval (CI) = 1.23 to 5.07 p = 0.01) with a significant trend across quartiles (OR = 1.32 per quartile increase, 95 percent CI = 1.04 to 1.66, p = 0.02 for trend).

CARBOHYDRATES

Carbohydrates are composed of monosaccharides, disaccharides oligosaccharides and polysaccharides. Carbohydrates can be either be assimilated or pass to the colon where they are fermented by bacteria. Hypotheses that these substances are implicated in IBD development have been considered by a number of studies, but despite many retrospective reports of high intakes of sugar (disaccharides) associated with CD (14), prospective studies have found no link. Retrospective studies are suggested to represent an increase in intake due to recall bias as a consequence of changes in diet to ameliorate longstanding symptoms (9,15). Conflicting data exists with carbohydrate intake (11) as no consistent association between total carbohydrate intake was found, even at double the recommended intake in a systematic review (13). Also, no association of risk of developing Crohn's disease with intake of total dietary sugar or starch was reported (15) as part of the EPIC study. The E3N study (8) also showed no association with UC and sugar intake. However, taking into consideration knowledge of carbohydrate intake and the prebiotic effect on microbiota populations and the role of changes to populations in IBD, it might be prudent for researchers to investigate carbohydrates further.

Emerging evidence suggests that our individual population of microbiota are of real commensal value and changes to this population can lead to disease.

DIETARY ANTIGENS

Dietary antigens hypothesis for development of Crohn's, or provision of elemental diets free of substances that provoke antibody production and induce 'bowel rest', has been argued to be an unviable theory, as polymeric enteral formulas are just as effective in treatment (16). However, polymeric products are far from being the same as a 'normal' diet, De Silva (11) and Hansen (16) have suggested that the mechanism of treatment with enteral formulas is more likely to be changes in microbiota, which may be true. However, only a small amount of evidence is available, but more importantly, efficacy of treatment may not be the same as causation of disease, so the antigen theory should not be discounted.

BACTERIA AND GENETIC INFLUENCES

Emerging evidence suggests that our individual population of microbiota are of real commensal value and changes to this population can lead to disease (19). IBD is at the forefront of investigation of the Human Microbiome Project which has recently mapped the human microbiome population. The project has now been provided with funding to research the difference in populations of bacteria in patients with IBD. How are bacteria implicated in the development of IBD? Dysbiosis, or changes to the gut natural microbiota population is well established in IBD (19). Lower GI lumen dysbiosis means a reduction in available commensal bacteria, (e.g. lactobacillus and bifidobacteria) known to act as immunoregulators, and increases levels of pathogenic species, resulting in a lower level of production of the short chain fatty acid butyrate and higher lumen hydrogen sulphide levels. Butyrate provides energy to colonocytes and promotes production of tight junctions between epithelial cells preserving the impermeability and barrier of the gut (19). In IBD, when this barrier is weakened, by loss of tight junctions and a reduction in mucosal barrier defence mechanisms (IgA levels), bacterial translocation through the lamina propria elicits defensive macrophages. However, in IBD, genetically defective macrophages are ineffective in removing bacteria, increasing antigen levels. This increase in antigens promotes an inflammatory response by release of pro-inflammatory cytokines and activation of innate and T-Cell response, exacerbating the immune response leading to inflammation (19). The breakdown of this initial defensive barrier in combination with defective immunity and loss of tolerance to microbiota is suggested to lead to an abnormal inflammatory response in patients with IBD (19).

It is possible that a diet producing changes to microbiota profile has a very important role to play. Is diet just an antagonist to an already pro-inflammatory predisposition, which might be a more likely explanation, or is it the main culprit? The genetic and microbiota theories are complex, but diet is no exception, hypothesis of individual nutrients causing IBD are difficult to study, as foods often contain more than one suspected agent; for example, meat contains sulphur amino acids and fats. We are no nearer in being able to categorically offer preventative dietary advice, but recently published prospective studies suggest that high protein, high animal protein and high fat intakes are possible candidates and theories do suggest that diet may have a strong role to play. Further research is urgently needed and, in particular, it would be interesting to see if changes to genetically susceptible individuals' diets do in fact reduce the risk of developing IBD.

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Questions relating to: *Does an unhealthy diet cause inflammatory bowel disease?*
Type your answers below and then **print for your records.** Alternatively print and complete answers by hand.

Q.1	What is the difference between Crohn's disease and ulcerative colitis?
A	
Q.2	Why is diet now considered to be a factor in the development of CD?
A	
Q.3	Explain why identifying dietary factors in the development of IBD is such a difficult challenge.
A	
Q.4	What is the theory behind high protein intake increasing the risk of IBD?
A	
Q.5	How can omega-6 have an effect on gut bacteria?
A	
Q.6	What is the function of butyrate in the gut?
A	
Q.7	What happens when antigen levels increase in patients with IBD?
A	
Q.8	In what way is the Human Microbiome Project researching IBD?
A	
Q.9	What suggestions have been made in recent prospective studies into IBD?
A	

Please type additional notes here . . .