

**Aliment Pharmacol Ther. 2001 Apr;15(4):439-49.**

**Food hypersensitivity and irritable bowel syndrome.**

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**Irritable bowel syndrome is a common condition but its pathophysiology remains poorly understood. Many irritable bowel syndrome patients give a history of food intolerance, but data from dietary elimination and re-challenge studies are inconclusive. Multiple aetio-pathological mechanisms have been postulated. The gut has an extensive immune system but current understanding of processing of food antigens in health and disease is limited. There is no clinically useful marker available to test for food hypersensitivity in irritable bowel syndrome. Researchers have employed both skin tests and serum immunoglobulins (IgG and IgE) as markers of food hypersensitivity in various disorders including irritable bowel syndrome, but published data are equivocal. In this article, the evidence for the role of food hypersensitivity in irritable bowel syndrome is reviewed and, based on the available data, a possible pathophysiological hypothesis has been formulated.**

**Gut. 1994 Apr;35(4):571-2**

**Food intolerance and Crohn's disease.**

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**It has been claimed that prolonged remissions of Crohn's disease can be achieved after enteral or parenteral nutrition, by identifying and excluding foods that exacerbate a patient's symptoms. The occurrence of food intolerances were assessed after induction of remission with elemental diet in 42 eligible patients to whom single foods were introduced over five days. Suspect foods were reinvestigated with open and if possible, double blind rechallenge. Fourteen patients (33%) dropped out of the study because of relapse of disease unrelated to food (n = 8) or because of difficulties in complying with the regimen (n = 6). Twenty (48%) of the patients identified food sensitivities whereas eight (19%) did not. Seventeen of the patients who identified food sensitivities had an open rechallenge with recurrence of symptoms in 10 (24% of total). Food sensitivity was confirmed in three**

patients on double blind challenge. There was no significant difference in the duration of remission between patients who did or did not identify food sensitivities. During the study three cases of intolerance to the formula diet, and one of severe salicylate sensitivity were encountered. In conclusion food sensitivities are evident after treatment of Crohn's disease with elemental diet but are variable, often do not persist, and are of insufficient importance to warrant putting all patients through elimination diets

Can J Gastroenterol. 2003 Jun;17(6):363-8; quiz 405-6.

Irritable bowel syndrome in primary care: the patients' and doctors' views on symptoms, etiology and management.

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**BACKGROUND:** To facilitate the development of clinical guidelines and to direct future irritable bowel syndrome (IBS) research, insight into the perceptions of patients and general practitioners (GPs) regarding IBS is required. **OBJECTIVES:** To compare patients' and GPs' views on the symptomatology, etiology and treatment of IBS. **METHODS:** One hundred forty-two IBS patients and 100 GPs were requested to complete a structured questionnaire. **RESULTS:** The response rates of the patients and GPs were 80% and 47%, respectively. Abdominal pain and bloating were considered to be the most bothersome symptoms in IBS, by both patients and GPs. Although all patients were diagnosed by their GP as having IBS, and 62% met the Manning criteria, only 18% fulfilled the Rome II criteria for IBS. Patients consider food intolerance and GPs regard lack of fibre as the main etiologic dietary factor. Many IBS patients expect a diagnostic work-up, but GPs generally restrict this to elderly patients. GPs start IBS management with dietary advice (94%), counselling (77%) and drug therapy (55%). Patients expect reassurance (47%) and drug treatment (37%), but dietary interventions are less appreciated (9%). **CONCLUSIONS:** Patients and GPs have different perceptions of the efficacy of diagnostic and dietary interventions in IBS. GPs should explore the patients expectations and incorporate these in their approach to IBS patients.

Arch Intern Med. 2003 Feb 10;163(3):265-74.

**A systematic review of alternative therapies in the irritable bowel syndrome.**

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**The irritable bowel syndrome is a common disorder associated with a significant burden of illness, poor quality of life, high rates of absenteeism, and high health care utilization. Management can be difficult and treatment unrewarding; these facts have led physicians and patients toward alternative therapies. We explored a variety of treatments that exist beyond the scope of commonly used therapies for irritable bowel syndrome. Guarded optimism exists for traditional Chinese medicine and psychological therapies, but further well-designed trials are needed. Oral cromolyn sodium may be useful in chronic unexplained diarrhea and appears as effective as and safer than elimination diets. The roles of lactose and fructose intolerance remain poorly understood. Alterations of enteric flora may play a role in irritable bowel syndrome, but supporting evidence for bacterial overgrowth or probiotic therapy is lacking.**

**Ann Ital Med Int. 2002 Jul-Sep;17(3):157-65.**

**[Probiotics: history, definition, requirements and possible therapeutic applications]**

**[Article in Italian]**

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**The ingestion of probiotics is associated with various beneficial effects on human health and modifies the physiological homeostasis of the intestinal flora. Probiotics are microorganisms with some particular characteristics: human origin, safety in human use, bile and acid resistance, survival in the intestine, at least temporary colonization of the human gut, adhesion to the mucosa and bacteriocine production. Thanks to these characteristics, probiotics block the invasion of human intestinal cells by the enteroinvasive bacteria. Furthermore, they should be able to stimulate and modulate**

the intestinal immune response, and to protect and stabilize the mucosal barrier. Finally, the efficacy of probiotics should be evident and documented with valid studies. All their properties should be maintained during processing and storage. Probiotics are usually used to protect the host from pathogens. With regard to this, they are useful in the prevention of antibiotic and traveler's diarrhea and they may play a role in the management of gastric *Helicobacter pylori* infection. Furthermore, their efficacy in the treatment of infectious diarrhea, in inflammatory bowel diseases, in pouchitis and in food allergy has been shown. Probiotics can improve the symptoms of irritable bowel syndrome and of lactose malabsorption. Finally, it has been suggested that such microorganisms may play a role in the prevention of carcinogenesis and of tumor growth.

**J Hum Nutr Diet. 2001 Jun;14(3):231-41.**

**Dietary treatment of irritable bowel syndrome: current evidence and guidelines for future practice.**

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The aim of this literature review is to produce guidelines for dietetic practice in irritable bowel syndrome (IBS) by evaluating the research available. In this area randomized control trials (RCT) only account for a small proportion of the literature and have been concentrated in the modification of dietary fibre in patients with IBS. The bulk of the literature is mainly observational trials from which no indisputable conclusions can be extracted. In this review, the evidence available has been interpreted within the context of the current knowledge base. Conclusions are drawn to facilitate the development of guidelines, enabling a starting point for discussion and an evaluation of current practice. The literature available on therapeutic dietary manipulation in IBS patients is centred around non-starch polysaccharides (NSPs), mono and disaccharide sensitivity and food intolerance. The production of these guidelines has focused on research examining the role of dietary components in the therapeutic management of patients with IBS. However, where there is a deficiency in the literature directly relating dietary intake to management of IBS patients, physiological function in relation to dietary components has been relied upon to produce practical guidelines which can be applied realistically in a clinical environment. An interpretation of the evidence has revealed a limited role for exclusion diets, a move away from high-fibre diets towards

the manipulation of fibre fractions in the diet, an evaluation of the effects of caffeine on gut function and the necessity for individual dietary assessment to identify dietary issues pertinent to the patient's symptoms. These guidelines outline a positive role for dietitians in the treatment of IBS patients which draws on the unique skills possessed by dietitians regarding the assessment of habitual eating habits and therapeutic dietary manipulation.

Am J Gastroenterol. 2000 Jan;95(1):157-65.

Locke GR 3rd, Zinsmeister AR, Talley NJ, Fett SL, Melton LJ.

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**OBJECTIVE:** Symptoms of irritable bowel syndrome (IBS) are reported by 10% of the general population; however, evaluation of traditional risk factors has not provided any insight into the pathogenesis of this condition. The objective of this study was to identify additional risk factors for irritable bowel syndrome.

**METHODS:** A valid self-report questionnaire that records the gastrointestinal (GI) symptoms required for a diagnosis of IBS, self-reported measures of potential risk factors, and a psychosomatic symptom checklist was mailed to an age-and gender-stratified random sample of Olmsted County, Minnesota residents aged 30-64 yr. A logistic regression model that adjusted for age, gender, and psychosomatic symptom score was used to identify factors significantly associated with IBS. **RESULTS:** A total of 643 (72%) of 892 eligible subjects returned the survey. IBS symptoms were reported by 12% of the respondents. IBS was significantly associated with use of analgesics (acetaminophen, aspirin, or nonaspirin nonsteroidal antiinflammatory drugs) for reasons other than IBS, reporting a food allergy or sensitivity, and ratings of somatic symptoms. No association was detected for age, gender, body mass index, smoking history, alcohol use, educational level, exposure to pets in the household, or water supply. Among subjects reporting the use of just one type of analgesic, IBS was associated with acetaminophen but not aspirin or nonaspirin nonsteroidal antiinflammatory drugs used alone. The odds of having IBS were higher among subjects reporting more reasons for taking analgesics and intolerance to a higher number of foods. **CONCLUSIONS:** IBS is significantly associated with analgesic use. However, this is confounded by other somatic pain complaints. IBS symptoms are associated with the reporting of many food allergies or sensitivities. The role of food-induced symptoms in IBS requires further investigation.

Am J Gastroenterol. 1999 Jul;94(7):1892-7.

**Discrepancies between reported food intolerance and sensitization test findings in irritable bowel syndrome patients.**

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**OBJECTIVE:** Irritable bowel syndrome (IBS) is a common gastrointestinal disorder with clinical signs typical of "intestinal" food allergies or intolerance. The aim of this study was to characterize the clinical features of IBS patients suspected of suffering from adverse reactions to food. **METHODS:** The study involved 128 consecutive IBS patients divided into four groups according to their main symptom on presentation at our outpatient clinic. A detailed medical history was recorded, paying particular attention to any allergies and reported intolerance to food. Each patient was screened for allergies; intestinal permeability tests were performed in randomly selected patients from different groups. Findings were analyzed using the chi<sup>2</sup> test. **RESULTS:** Adverse reactions to one or more foods were reported by 80 patients (62.5%); skin prick tests (SPT) were positive in 67 patients (52.3%) with no significant differences between patients complaining of different symptoms. Patients who reported a food intolerance had more positive SPTs than those who did not (47 of 80 [58.7%] vs 20 of 48 [41.7%]); this difference was not statistically significant, although it suggests a trend ( $p < 0.0610$ ). There was little consistency between the specific foods reported to cause intolerance and those resulting from the tests (11 of 80 patients, 13.7%). The intestinal permeability test was normal in 29 of 33 patients (87.9%). **CONCLUSIONS:** More than 50% of IBS patients were found sensitized to some food or inhalant without any typical clinical signs. Patients were unable to identify potentially offending foods. The lack of a correlation between SPT results and reported food allergies needs further investigation to clarify the pathophysiology and improve the diagnosis of intestinal food allergies

**Lancet. 1998 Oct 10;352(9135):1187-9.**

**Abnormal colonic fermentation in irritable bowel syndrome.**

**King TS, Elia M, Hunter JO.**

**Department of Gastroenterology, Addenbrooke's Hospital, Cambridge, UK.**

**BACKGROUND:** The cause of irritable bowel syndrome (IBS) is unknown. It may follow gastroenteritis and be associated with an abnormal gut flora and with food intolerance. Our study was designed to assess whether these factors were associated with colonic malfermentation. **METHODS:** We carried out a crossover controlled trial of a standard diet and an exclusion diet matched for macronutrients in six female IBS patients and six female controls. During the final 72 h on each diet, faecal excretion of fat, nitrogen, starch, and non-starch polysaccharide NSP was measured, and total excretion of hydrogen and methane collected over 24 h in a purpose-built 1.4 m<sup>3</sup> whole-body calorimeter. Breath hydrogen and methane excretion were then measured for 3 h after 20 g oral lactulose. **FINDINGS:** The maximum rate of gas excretion was significantly greater in patients than in controls (2.4 mL/min IQR 1.7-2.6 vs 0.6, 0.4-1.1). Although total gas production in patients was not greater than in controls (median 527 mL/24 h IQR 387-660 vs 412, 234-507), hydrogen production was higher (332, 318-478 vs 162, 126-217, p=0.009). In patients, the exclusion diet reduced symptoms and produced a fall in maximum gas excretion (0.5 mL/min IQR 0.3-0.7). After lactulose, breath hydrogen was greater on the standard than on the exclusion diet. **INTERPRETATION:** Colonic-gas production, particularly of hydrogen, is greater in patients with IBS than in controls, and both symptoms and gas production are reduced by an exclusion diet. This reduction may be associated with alterations in the activity of hydrogen-consuming bacteria. Fermentation may be an important factor in the pathogenesis of IBS.

Baillieres Clin Gastroenterol. 1996 Sep;10(3):443-59.

**Mucosal allergy: role of mast cells and eosinophil granulocytes in the gut.**

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Despite the progress made in understanding the mechanisms of allergic disease, the pathophysiology and clinical significance of intestinal allergic reactions is largely unclear. The intestinal mucosa is pre-destined for allergic reactions against food proteins and other antigens, and a number of studies indicate that allergic reactions occur in the GI tract. However, only a few epidemiological data are available, and the mechanisms are poorly understood. Intestinal allergic reactions may be different to classical IgE-mediated

reactions because patients with intestinal allergy often have negative skin tests and low levels of serum IgE. There is increasing evidence that, as with the findings in the skin and lung, mast cells and eosinophils play a central role in mediating intestinal allergic reactions. Furthermore, both types of cell are found to be activated in a number of other GI inflammatory diseases such as inflammatory bowel disease, celiac disease and eosinophilic gastroenteritis. However, the relationship between these pathologies and intestinal allergy is largely unclear. A major clinical problem is the lack of appropriate means for confirming the diagnosis of intestinal allergy. However, new test systems have been developed--such as the measurement of eosinophil mediators in stool samples or endoscopic provocation tests performed locally at the intestinal mucosa, which may improve the possibility of identifying afflicted patients on an objective basis. Since symptoms of intestinal allergic reactions are variable and non-specific, the diagnosis requires the use of multiple tests and the exclusion of other pathologies such as infectious disease or non-immunological intolerance reactions. The preferred therapeutic option is avoidance of the allergens of relevance; however, this approach can be realized only in some patients, whereas others require additional treatment, for example, with oral cromoglycate or corticosteroids. Although we do not yet know to what extent intestinal allergic reactions may be an aetiological factor in GI diseases, such reactions should be considered in the differential diagnosis of unclear intestinal inflammation and irritable bowel syndrome.

Scand J Gastroenterol. 1995 Jun;30(6):535-41.

Oral cromolyn sodium in comparison with elimination diet in the irritable bowel syndrome, diarrheic type. Multicenter study of 428 patients.

Stefanini GF, Saggiaro A, Alvisi V, Angelini G, Capurso L, di Lorenzo G, Dobrilla G, Doderio M, Galimberti M, Gasbarrini G, et al.

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**BACKGROUND:** In a significant number of patients affected by the irritable bowel syndrome, an adverse reaction to food is proposed to be a causative factor. A diet that eliminates the offending foods is the obvious treatment for such adverse reactions. Compliance with a dietetic regimen is often poor and sometimes not completely free from risks. **METHODS:** Since the diarrheic type of irritable bowel syndrome seems mainly affected by food intolerance, and previous observations suggested that oral cromolyn sodium is effective in

such patients, a multicenter therapeutic trial in the diarrheic type of irritable bowel syndrome was carried out in 346 of 409 patients with this disease, to evaluate the effects of oral cromolyn sodium and compare its efficacy with that of an elimination diet. **RESULTS:** Symptoms related to the irritable bowel syndrome improved in 60% of patients treated with elimination diet and in 67% of those treated with oral cromolyn sodium (1500 mg/day) for 1 month. Moreover, in both groups clinical results were significantly better in the patients positive to the skin prick test than in the negative ones. **CONCLUSIONS:** These results confirm the high prevalence of adverse reactions to foods in diarrheic irritable bowel syndrome and the usefulness of cromolyn sodium treatment in these patients

Practitioner. 1994 Jul;238(1540):499-502, 504.

Irritable bowel syndrome and food intolerance.

Gertner D, Powell-Tuck J.

Royal London Hospital.

Minerva Pediatr. 1993 Jun;45(6):253-8.

[Food intolerance and irritable bowel syndrome of childhood: clinical efficacy of oral sodium cromoglycate and elimination diet]

[Article in Italian]

Grazioli I, Melzi G, Balsamo V, Castellucci G, Castro M, Catassi C, Ratsch JM, Scotta S.

Schiapparelli Searle, Torino.

Irritable bowel syndrome (IBS) is recognized to be a common cause of chronic diarrhea without failure to thrive in childhood. Several studies stressed the role of food intolerance as a major factor in the pathogenesis of IBS. The aim of this multicenter study was to investigate the offending role of food in IBS and to compare the therapeutic role of oral sodium cromoglycate versus elimination diet. 153 patients (mean age 4 years) with diarrhea (> 3 stools per day for four days in a week) and abdominal pain for about 10 months were enrolled in this trial. About half of the patients had a family history positive for atopy and 70% of the cases complained of intestinal symptoms after food ingestion. In 17% of the patients Skin Prick test (SPT) resulted positive to at least one food allergen and 87% of positive reactions to SPT was provoked by common foodstuffs. 87%

of patients treated with elimination diet (rice, lamb, turkey, lettuce, carrots, sweet potatoes, pears, oil, tea, salt, mineral water, brown sugar) and 97% of patients treated with SCG (mean 63 mg/kg/day) for one month showed a significant improvement of intestinal symptoms. An elimination diet for several weeks can produce, beside a bad compliance (23% of patients admitted to our study didn't strictly follow diet regimen) also a nutritional deprivation. The results of this trial suggest that it's correct to investigate the role of food in children with diarrhea not due to organic diseases and diagnosed such as IBS and to use oral SCG to obtain the improvement of these symptoms.

**Clin Exp Allergy. 1991 Sep;21(5):569-72.**

**Double-blind cross-over trial of oral sodium cromoglycate in patients with irritable bowel syndrome due to food intolerance.**

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**Twenty patients with irritable bowel syndrome due to food intolerance were randomized to either oral sodium cromoglycate or placebo in a double-blind cross-over trial. The study consisted of treatment with either sodium cromoglycate or placebo for 8 weeks, followed by the cross-over treatment for 8 further weeks. Patients were allowed to eat the offending foods during the study. Eighteen patients completed the study. Analysis of patients' diary card scores showed a statistically significant difference in favour of sodium cromoglycate. There was a long carry-over effect in the active-placebo order group. Therefore oral sodium cromoglycate seems to be a useful treatment in patients with irritable bowel syndrome and proven food intolerance.**

**Gastroenterol Clin North Am. 1991 Jun;20(2):335-49.**

**New directions in the irritable bowel syndrome.**

**Bailey LD Jr, Stewart WR Jr, McCallum RW.**

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The irritable bowel syndrome (IBS) is an umbrella for the diagnosis of heterogeneous conditions that are awaiting better identification of specific manometric causes. This article focuses on the concept that future therapy for IBS will rely on identification of subgroups and in turn tailor the specific therapeutic approaches to an appreciation of the pathophysiology and symptom predominance of these subgroups. Future therapies will rely on the following principles: (1) prokinetic agents to coordinate upper gastrointestinal and colonic motility as well as improve the propulsive nature of colonic contractions; (2) gastrointestinal hormone agonists such as erythromycin and antagonists such as sandostatin and cholecystikinin antagonists; (3) spasmolytic therapy incorporating calcium channel blocking and anticholinergic agents; (4) inhibition of ovulatory cycle changes in circulating concentrations of gonadal hormones in women, who tend to dominate the IBS population; (5) incorporation of concepts relating to the role of subtypes of 5-hydroxytryptamine receptors in control of neural and myogenic function; (6) reassessment of food intolerance and sensitivity; and (7) incorporation of concepts relating to psychologic profiles and psychologic treatment approaches. IBS is a rich and fertile area for application of the exciting new pharmacologic advances relating to gastrointestinal smooth-muscle and neural innervation of the gut. Improvement in the understanding and treatment of IBS will be one of the major accomplishments of this decade

Minerva Dietol Gastroenterol. 1989 Oct-Dec;35(4):219-24.

[Irritable colon syndrome in intolerance to food additives]

[Article in Italian]

Antico A, Soana R, Clivio L, Baioni R.

The rate of the irritable bowel syndrome (IBS) and the follow-up of its symptoms on diet and in therapy with disodium cromoglycate have been studied in a group of patients suffering from mainly extra-digestive symptoms related to food intolerance. Following our observation, we can draw the conclusion that food additives intolerance may be a major factor in the pathogenesis of IBS.

Gut. 1989 Aug;30(8):1099-104.

Food intolerance and the irritable bowel syndrome.

**Nanda R, James R, Smith H, Dudley CR, Jewell DP.**

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**Two hundred patients (156 women) with the irritable bowel syndrome were treated with dietary exclusion for three weeks. Of the 189 who completed this study, 91 (48.2%) showed symptomatic improvement. Subsequent challenge with individual foods showed that 73 of these 91 responders were able to identify one or more food intolerances and 72 remained well on a modified diet during the follow up period (mean (SD), 14.7 (7.98) months). Of the 98 patients who showed no symptomatic improvement after three weeks of strict exclusion only three were symptomatically well at follow up (mean (SD), 12.48 (8.09) months). There was no close correlation between response and symptom complex. There was a wide range of food intolerance. The majority (50%) identified two to five foods which upset them (range 1-14). The foods most commonly incriminated were dairy products (40.7%) and grains (39.4%).**

**Lancet. 1985 Nov 9;2(8463):1064.**

**Food intolerance, atopy, and irritable bowel syndrome.**

**Smith MA, Youngs GR, Finn R.**

**Scand J Gastroenterol Suppl. 1985;109:117-21.**

**Food intolerance.**

**Lessof MH.**

**Food intolerant symptoms can have various causes, including enzyme deficiencies (of lactase or aldehyde dehydrogenase) and pharmacological effects (e.g., caffeine, salicylates). The irritable bowel syndrome can also be associated with intolerance to specific foods in some cases, but the mechanism is unclear. Immunological causes are less common but may explain the small bowel mucosal changes associated with gluten enteropathy, as well as the childhood enteropathy provoked by cow's milk or, rarely, by other foods. Food allergy of the more immediate and classical type is associated with reactions both within and outside the gastrointestinal tract. Where these include urticaria, asthma and eczema, immunoglobulin E antibodies are often demonstrable by skin or radioallergosorbent tests, but pseudo-allergic reactions can produce a similar clinical picture. Diagnosis of food intolerance depends on withdrawing the food concerned and assessing the**

**response to a blind challenge. Objective ways of detecting subclinical reactions are also useful, including the detection of a mediator response involving prostaglandins, histamine or serotonin.**