

Irritable Bowel Syndrome

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ABSTRACTS

Early abuse, psychiatric diagnoses and irritable bowel syndrome.

Blanchard EB, Keefer L, Payne A, et al.

Behav Res Ther. 2002 Mar; 40(3):289-98.

In a population of 71 (57 female, 14 male) IBS patients seeking psychological treatment, we found expected levels of childhood sexual and physical abuse (57.7%) and expected levels of current Axis I psychiatric disorders (54.9%). Moreover, we found those who had been victims of early abuse had higher current Beck Depression Inventory scores. However, contrary to expectations, there were no significant associations between early abuse and current psychiatric disorder in this population, suggesting that those individuals with psychological distress are not exactly the same group with a history of abuse

[Irritable bowel syndrome. Survey of definitions, differential diagnosis and pathogenesis].

Bodemar G, Ragnarsson G.

Lakartidningen. 2001 Feb 14; 98(7):666-71.

Abdominal pain/discomfort, bloating, need to rush to the toilet, straining, feeling of incomplete bowel emptying and alternating periods of diarrhea and constipation is the clinical definition of the irritable bowel syndrome. The internationally used syndrome definition is based on expert opinions and answers to patient questionnaires. When symptoms are registered prospectively, abdominal pain starts or worsens after meals and is not relieved by defecation. As in the general population patients with the syndrome define diarrhea as loose stools and constipation as hard stools regardless of stool frequencies. Variation in defecatory symptoms and discrepancies between these symptoms and stool consistency are the hallmarks of the syndrome, and the degree of variation per fortnight is relatively stable in the individual patient. Fermentation of carbohydrates by colonic bacteria, increased sensitivity to bowel distention by gas, gas-producing food, increased secretion of cholecystokinin after fatty meals and/or increased sympathetic nerve tone at stress can give rise to symptoms. Symptoms can start after a single period of bacterial gastroenteritis. Although patients seeking medical care for the syndrome are more often anxious, the syndrome itself is not psychosomatic. Symptoms are possibly mediated through partial degranulation of mast cells in bowel mucosa, but this does not make it an allergic disease. If bowel dysmotility can be measured, early stage or a mild case of intestinal pseudoobstruction should be considered. Hyperreactivity in the enteric nervous system and/or in the brain is the likely main cause of the symptoms. More widespread activity in the brain after exposure to stimuli originating from bowel nerves or less inhibition of this stimulation in the brain are possible mechanisms

What is the benefit of coarse wheat bran in patients with irritable bowel syndrome?

Cann PA, Read NW, Holdsworth CD.

Gut. 1984 Feb; 25(2):168-73.

The effect of open treatment with coarse wheat bran was compared with response to placebo, given in the form of a double blind, cross over drug trial, in patients with irritable bowel syndrome. Both bran and placebo significantly reduced the severity of most of the symptoms. Constipation was the only symptom that improved significantly with bran, but not with placebo, and was the only symptom that predicted a successful outcome with bran. Diarrhoea did not improve with bran. In fact, stools became less formed in patients presenting with this symptom. The incidence of pain and urgency was significantly more frequent on bran compared with placebo. Compared with a baseline period, bran treatment resulted in an acceleration of whole gut transit time (p less than 0.05) increases in daily stool weight (p less than 0.01) and the proportion of unformed stools (p less than 0.01) but no change in stool frequency. Coarse wheat bran was no better than placebo for most symptoms in irritable bowel syndrome, although its efficacy in constipation was confirmed

The utility of diagnostic tests in irritable bowel syndrome patients: a systematic review.

Cash BD, Schoenfeld P, Chey WD.

Am J Gastroenterol. 2002 Nov; 97(11):2812-9.

OBJECTIVE: The aim of this study was to determine the pretest probability of organic GI disease and the accuracy of diagnostic tests for organic GI disease in patients who meet symptom-based criteria for irritable bowel syndrome (IBS). **METHODS:** After a comprehensive literature search for studies examining the accuracy of diagnostic tests for organic GI disease among patients who meet symptom-based criteria for IBS, two independent observers qualitatively assessed the methodology of selected studies and extracted data. Data on the pretest probability of organic GI disease in this population and the accuracy of currently recommended diagnostic tests were converted to descriptive tables. **RESULTS:** Among patients meeting symptom-based criteria for IBS, the pretest probability of inflammatory bowel disease, colorectal cancer, or infectious diarrhea is less than 1%. Currently recommended diagnostic tests rarely identify organic GI disease in patients fulfilling symptom-based criteria for IBS. However, the pretest probability of celiac disease in patients meeting symptom-based criteria for IBS was 10 times higher than the prevalence of celiac disease in the general population. **CONCLUSIONS:** There is insufficient evidence to recommend the routine performance of a standardized battery of diagnostic tests in patients who meet symptom-based criteria for IBS. Based upon the increased pretest probability of celiac disease, routine performance of serological tests for celiac disease may be useful in this patient population, though additional study is needed in this area

Gender differences in irritable bowel syndrome.

Chang L, Heitkemper MM.

Gastroenterology. 2002 Nov; 123(5):1686-701.

In the United States and other Western cultures, a greater number of women seek health care services for symptoms of functional pain disorders, including irritable bowel syndrome, than men. Recent clinical trials indicate that gender differences in responsiveness to drug therapy also occur. Several lines of inquiry have focused on explaining this gender-related difference due to the higher prevalence of these disorders in women. Evidence of a physiologic component is based on gender differences in gastrointestinal transit time, visceral sensitivity, central nervous system pain processing, and specific effects of estrogen and progesterone on gut function. Additional factors may play a role, including gender-related differences in neuroendocrine, autonomic nervous system, and stress reactivity, which are related to bowel function and pain. However, the link between these measures and gut motility or sensitivity remains to be clarified. Psychological characteristics, including somatization, depression, and anxiety as well as a history of sexual abuse, may also contribute to gender-related differences in the prevalence of irritable bowel syndrome. Although gender differences in the therapeutic benefit of serotonergic agents have been observed, less is known about potential differences in responsiveness to nondrug therapies for irritable bowel syndrome

New developments in the treatment of irritable bowel syndrome.

De Schryver AM, Samsom M.

Scand J Gastroenterol Suppl. 2000;(232):38-42.

The irritable bowel syndrome (IBS) is one of the most common gastrointestinal conditions encountered by general practitioners, and it accounts for a great deal of the workload of gastroenterologists in secondary care. Research to date indicates that several factors contribute to the development of IBS, of which disturbed gastrointestinal motility, altered visceral perception and psychosocial factors are regarded as the three most important mechanisms interacting in the development of this disorder. Most pharmacological research has been based on these insights. Several agents capable of modulating either motility or sensitivity are currently under investigation. Potential drugs in the treatment of diarrhoea-predominant IBS are the more selective antispasmodics, such as the M3-receptor antagonists (e.g. zamifenacin, darifenacin). In constipation-predominant IBS the colokinetic effects of the selective 5HT₄ agonists prucalopride and tegaserod are of great interest. Since altered visceral perception is thought to play an important role in the genesis of abdominal pain and bloating in many patients with IBS, new drugs are targeted at modulating the sensitivity, such as 5HT₃ antagonists (e.g. alosetron), kappa-agonists (e.g. fedotozine) and somatostatin analogues. Furthermore, psychosocial factors should not be overlooked, since these appear to be of great influence on the clinical outcome of IBS

Stress and visceral perception.

Delvaux MM.

Can J Gastroenterol. 1999 Mar; 13 Suppl A:32A-6A.

Functional bowel disorders are characterized by the presence of a visceral hyperalgesia in most patients. This visceral hyperalgesia is related to an enhanced perception of sensations originating from the gut. Stressful events can dramatically influence the course of functional bowel disorders, and patients suffering from these syndromes appear to be more susceptible to the stressful events of daily life. However, until now, few studies have evaluated the relationship between stress and visceral perception. Some studies of healthy volunteers indicated contradictory results, but the studies used different methodologies. During stress conditions, either physical or mental, thresholds of perception of rectal distension were increased, suggesting a 'distraction effect', or were decreased, supporting a sensitizing effect of stress. In most studies, rectal compliance was not affected, but stress has been shown to alter the rectal tone, as measured by a barostat. One study comparing irritable bowel syndrome patients with controls demonstrated the importance of cognitive processes in the modulation of visceral perception by stress. Animal studies have also demonstrated the sensitizing effect of stress on the perception of rectal distension. Mediators involved may be numerous, but corticotropin-releasing factor has been demonstrated to play a major role at the central level. Mast cells and histamine release may play a role at the peripheral level. Stress can thus be included in an integrative model explaining the pathophysiology of functional bowel disorders. Advances in the understanding of the relationship between stress and visceral perception may constitute a basis for a therapeutic approach of functional bowel disorders targeted on the central nervous system

Peppermint oil for the irritable bowel syndrome: a multicentre trial.

Dew MJ, Evans BK, Rhodes J.

Br J Clin Pract. 1984 Nov; 38(11-12):394, 398.

Bran and irritable bowel syndrome: time for reappraisal.

Francis CY, Whorwell PJ.

Lancet. 1994 Jul 2; 344(8914):39-40.

Whilst following up large numbers of patients with irritable bowel syndrome we got the impression that wholemeal wheat and bran products made people with the condition worse rather than better. One hundred consecutive new referrals, all of whom had tried bran, were questioned to resolve this issue. 55% of patients were made worse by bran whereas only 10% had found it helpful. With the exception of fruit, other forms of dietary fibre were not as detrimental and proprietary supplements were found to be beneficial. All symptoms of irritable bowel syndrome were exacerbated by bran, with bowel disturbance most often adversely affected, followed by abdominal distension and pain. The results of this study suggest that the use of bran in irritable bowel syndrome should be reconsidered. The study also raises the possibility that excessive consumption of bran in the community may actually be creating patients with irritable bowel syndrome by exacerbating mild, non-complaining cases

Modification of visceral sensitivity and pain in irritable bowel syndrome by 5-HT₃ antagonism (ondansetron).

Goldberg PA, Kamm MA, Setti-Carraro P, et al.

Digestion. 1996 Nov; 57(6):478-83.

Intrinsic neurons containing serotonin (5-HT) are involved in the regulation of gastrointestinal motor function and are also thought to be important in the modulation of visceral sensory function. We have evaluated the effect of a specific 5-HT₃ antagonist (ondansetron, O) on visceral sensation and rectal compliance in a randomized, double-blind, cross-over, placebo (P) controlled study of O 16 mg 3 times/day, in healthy volunteers and patients with irritable bowel syndrome (IBS). Symptoms were also evaluated in the latter group. A 2-week run-in period was followed by two 2-week treatment arms of P and O, separated by a 2-week wash-out period. Twelve healthy subjects and 9 patients with IBS were recruited. Assessment was by daily symptom and bowel function diary, and physiological tests of anal manometry, rectal sensory testing to distension and electrical stimulation, and rectal compliance. Ten healthy subjects completed the entire study, and 6 IBS patients completed the diary card evaluation, including 5 who also completed the physiological evaluation. O caused significantly ($p < 0.01$) firmer stools when considering both subject groups together. In the healthy subjects no physiological parameters were altered by O. In IBS patients the rectal sensory threshold to electrical stimulation tended to increase with O (20 vs. 28 mA, P vs. O, median, $p = 0.06$) while the urge (80 vs. 60 ml, $p = 0.05$) and maximum tolerated volumes (130 vs. 90, $p = 0.03$) to distension tended to decrease with O. Patients with IBS experienced significantly fewer daily episodes of pain while on O (2 vs. 1, $p = 0.03$). Serotonin-3 antagonism (O) causes firmer bowel actions in all subjects, and may affect gut sensitivity and pain in patients with IBS

Interleukin 10 genotypes in irritable bowel syndrome: evidence for an inflammatory component?

Gonsalkorale WM, Perrey C, Pravica V, et al.

BACKGROUND AND AIMS: Inflammation may play a role in the pathogenesis of irritable bowel syndrome in some individuals, such as in those who develop symptoms following a dysenteric illness. Persisting inflammation, resulting from an imbalance of cytokines regulating the inflammatory response, is one possible mechanism. As the elaboration of cytokines is under genetic control, this study was designed to establish whether there might be a genetic predisposition to an altered pattern of anti-inflammatory cytokine production in patients with irritable bowel syndrome. **SUBJECTS:** A total of 230 unselected patients with irritable bowel syndrome and 450 healthy, ethnically matched controls were studied. **METHODS:** DNA was extracted from peripheral blood leucocytes of subjects. Allele and genotype frequencies were determined for the anti-inflammatory cytokine interleukin 10 at the site (-1082) concerned with production in lymphocytes. Transforming growth factor beta(1) (codons 10 and 25) genotypes were also examined in a smaller group of subjects. **RESULTS:** Patients with irritable bowel syndrome had significantly reduced frequencies of the high producer genotype for interleukin 10 than controls (21% v 32%; $p=0.003$). There was no apparent relationship with any particular bowel habit subtype. Genotypes for transforming growth factor beta(1) were not altered. **CONCLUSIONS:** These preliminary results suggest that at least some patients with irritable bowel syndrome may be genetically predisposed to produce lower amounts of the anti-inflammatory cytokine interleukin 10. This lends some support to the hypothesis that there may be an inflammatory or genetic component in some cases of this condition and that further studies in specific irritable bowel syndrome subgroups are justified

5-HT₄ receptor antagonism in irritable bowel syndrome: effect of SB-207266-A on rectal sensitivity and small bowel transit.

Houghton LA, Jackson NA, Whorwell PJ, et al.

Aliment Pharmacol Ther. 1999 Nov; 13(11):1437-44.

BACKGROUND: Pre-clinical studies indicate that the 5-hydroxytryptamine (5-HT)₄ receptor may be involved in the pathophysiology of irritable bowel syndrome and that antagonism of this receptor may be an effective therapeutic strategy. **AIM:** To investigate the effects of SB-207266-A, a selective 5-HT₄ receptor antagonist on rectal sensitivity and small bowel transit in patients with irritable bowel syndrome. **METHODS:** Eighteen patients with diarrhoea-predominant irritable bowel syndrome and a history of increased rectal sensitivity were randomized to receive either SB-207266-A (20 mg) or placebo for 10 days. Following a washout period, patients were then crossed over to receive the alternative therapy for 10 days. Rectal sensitivity and oro-caecal transit time were assessed on day 10 of each treatment period. In addition, patients were asked whether they had experienced any changes in their symptoms. **RESULTS:** Fifteen patients completed the study. SB-207266-A significantly increased oro-caecal transit time towards normal (placebo: 5.3 h (4.0-7.2 h), mean (IQR) vs. SB-207266-A: 6.5 h (4.8-8.0 h); $P=0.027$) and tended to decrease rectal sensitivity (volume to discomfort 89 mL (60-150 mL), geometric mean (IQR) vs. 107 mL (75-150 mL); $P=0.134$). Eleven out of 15 patients reported symptomatic improvements with SB-207266-A but none with placebo. SB-207266-A was well tolerated. **CONCLUSION:** Our results support a role for the 5-HT₄ receptor in the pathophysiology of irritable bowel syndrome and suggest that the selective 5-HT₄ antagonist, SB-207266-A, is worthy of further evaluation in this disorder

Intergenerational transmission of gastrointestinal illness behavior.

Levy RL, Whitehead WE, Von Korff MR, et al.

Am J Gastroenterol. 2000 Feb; 95(2):451-6.

OBJECTIVE: Previous research, based on retrospective reporting, suggests that parental reinforcement and modeling may be important mechanisms in the development of gastrointestinal illness behavior in children and adults. The aim of this study was to determine the relationship between the illness behavior of parents, in the form of health care use for irritable bowel symptoms, and the illness behavior of their children, without relying on retrospective recall. **METHODS:** A comparison of two matched groups was made. Groups included 631 children of parents who were diagnosed with irritable bowel syndrome during 1 calendar yr and 646 children of parents matched by parental age, gender, and number of children in the family who did not receive an IBS diagnosis during the same 1 yr. Health care use and costs over a 3-yr calendar period for all children and their parents collected from the health care database of a large health maintenance organization were evaluated. **RESULTS:** Case children had significantly more ambulatory care visits for all causes (mean 12.26 vs. 9.81, $p = 0.0001$) and more ambulatory visits for gastrointestinal symptoms (0.35 vs. 0.18, $p = 0.0001$). Outpatient health care costs over the 3-yr period were also significantly higher for case than control children (\$1979 vs. \$1546, $p = 0.0001$). Controlling for the total number of ambulatory visits of the parents, excluding gastrointestinal visits, did not alter the findings. Gender of the IBS parent was not related to children's gastrointestinal visits. **CONCLUSION:** This study extends previous research by showing that specific types of illness behavior may be learned through modeling

Alosetron for irritable bowel syndrome.

Lievre M.

BMJ. 2002 Sep 14; 325(7364):555-6.

Comorbid conditions in patients with irritable syndrome: data from a national IBS awareness registry.

Markowitz MHWRFHCGSHWACEGAA.

Gastroenterology. 2001;(120(Suppl. 1)):105.

Probiotics in clinical conditions.

Marteau PR.

Clin Rev Allergy Immunol. 2002 Jun; 22(3):255-73.

Probiotics are nonpathogenic microorganisms which, when ingested, exert a positive influence on the health or physiology of the host. Their mechanisms of action and effects are now studied using the same pharmacological approach as for drugs. This article summarizes and comments on evidence for the positive effects of probiotics in various clinical situations. Substantial evidence can be achieved when randomized controlled trials or meta-analyses show positive results. The clinical situations studied include prevention or treatment of antibiotic-associated disorders, gastroenteritis, and diarrhea, lactose intolerance, intestinal infections and colonization by pathogenic bacteria (including *Helicobacter pylori* and *Clostridium difficile*), traveler's diarrhea, irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), colonic cancer, urogenital infections and tumors, allergy (especially atopic eczema), vaccination, and cholesterol lowering. Current probiotics have an excellent safety record--another topic discussed in this article

Efficacy of a fixed peppermint oil/caraway oil combination in non-ulcer dyspepsia.

May B, Kuntz HD, Kieser M, et al.

Arzneimittelforschung. 1996 Dec; 46(12):1149-53.

The efficacy and safety of the standardized herbal combination preparation of Enteroplant, consisting of peppermint oil (90 mg) and caraway (50 mg) in an enteric coated capsule, have been studied in a double-blind, placebo-controlled multicentre trial in patients with non-ulcer dyspepsia. A total of 45 patients were included in the trial after thorough physical and gastroenterological examination. The primary outcome variables were the change in the intensity of pain and the global clinical impression (Clinical Global Impression [CGI], Item 2), which were evaluated for 39 patients (test preparation: 19, placebo: 20). After four weeks of treatment both target parameters were significantly improved for the group of patients treated with the peppermint oil/caraway oil combination compared to the placebo group ($p = 0.015$ and 0.008 , respectively). Before the start of treatment all patients in the test preparation group reported moderate to severe pain, while by the end of the study 63.2% of these patients were free of pain. The pain symptoms had improved in a total of 89.5% of the patients in the active treatment group. After 4 weeks the Clinical Global Impressions were improved for 94.5% of the patients treated with the peppermint oil/caraway oil combination. The trial medication was also superior to placebo with respect to pain frequency, medical prognosis, the severity of the disorder and the efficacy index (CGI, Items 1 and 3), which were adopted as secondary end-points for evaluation of efficacy. There were similarly favourable findings for the herbal combination, compared with placebo, with respect to the reduction of other gastrointestinal symptoms. The combination preparation was found to be excellently tolerated. There was a total of 7 adverse events (test preparation: 4, placebo: 3), with a causal association with the treatment being ascribed in one case for the test preparation group and one case for the placebo group

Depression, anxiety, and the gastrointestinal system.

Mayer EA, Craske M, Naliboff BD.

J Clin Psychiatry. 2001; 62 Suppl 8:28-36.

Functional disorders of the digestive system, such as irritable bowel syndrome, are often associated with affective disorders, such as depression, anxiety, panic, and posttraumatic stress disorder (PTSD). Some of these associations are observed not only in clinical populations, but also in population-based samples, suggesting a relationship with pathophysiologic mechanisms underlying both gastrointestinal (GI) dysfunction and certain affective disorders. Sustained and acute life-threatening stressors play an important role in the onset and modulation of GI symptoms as well as in the development of affective disorders and PTSD. A neurobiological model is proposed that attempts to explain the development of visceral hypersensitivity, the

neuroendocrine and autonomic dysfunction characteristic of functional GI disorders, as well as the overlap with affective disorders

Basic pathophysiologic mechanisms in irritable bowel syndrome.

Mayer EA, Naliboff BD, Chang L.

Dig Dis. 2001; 19(3):212-8.

Converging evidence supports the concept that the irritable bowel syndrome (IBS) symptom complex results from altered regulation of gastrointestinal motility and epithelial function, as well as an altered perception of visceral events. Despite similar symptoms, there is likely heterogeneity of underlying dysfunction and pathogenesis in different subgroups of IBS patients: the syndrome may be produced by primary alterations in the central nervous system (CNS; top down model), or by primary alterations in the periphery (bottom up model), or by a combination of both. One plausible mechanism by which alterations in the CNS result in symptoms, is the enhanced responsiveness of central stress/emotion circuits. The physiological effects of psychological and physical stressors on gut function and brain-gut interactions are mediated by outputs of the emotional motor system in terms of autonomic, neuroendocrine, attentional and pain modulatory responses. IBS patients show an enhanced responsiveness of this system manifesting in altered modulation of gastrointestinal motility, secretion, immune function and in alterations in the perceptual and emotional response to visceral events

Is there an irritable bladder in the irritable bowel syndrome?

Monga AK, Marrero JM, Stanton SL, et al.

Br J Obstet Gynaecol. 1997 Dec; 104(12):1409-12.

In this prospective case controlled study 16 premenopausal women with documented irritable bowel syndrome were recruited from the gastroenterology clinic and 16 premenopausal controls without symptoms of irritable bowel syndrome were recruited from the gynaecology clinic. All women answered a standardised bowel and urinary symptom questionnaire and underwent twin channel subtracted cystometry. Women with irritable bowel syndrome also underwent oesophageal balloon distension studies for perception and pain. Oesophageal and bladder sensory thresholds were compared. Urinary frequency and urgency and the urodynamic finding of detrusor instability were significantly more common in women with irritable bowel syndrome ($P < 0.05$). We were unable to demonstrate a relationship between first sensation of bladder fullness and oesophageal perception or between maximum bladder capacity and oesophageal pain thresholds. These findings suggest that there is an irritable bladder in the irritable bowel syndrome and support the concept that irritable bowel syndrome is part of a generalised disorder of smooth muscle

Role of stress in functional gastrointestinal disorders. Evidence for stress-induced alterations in gastrointestinal motility and sensitivity.

Monnikes H, Tebbe JJ, Hildebrandt M, et al.

Dig Dis. 2001; 19(3):201-11.

Psychological stress is widely believed to play a major role in functional gastrointestinal (GI) disorders, especially irritable bowel syndrome (IBS), by precipitating exacerbation of symptoms. The available data clearly demonstrate that inhibition of gastric emptying and stimulation of colonic transit is the most consistent pattern in the motility response of the GI tract to acute or short-term stress. Thus, one might propose that these alterations might play a pathophysiological role in dyspeptic symptoms and alterations in stool frequency and consistency in patients with stress-related functional GI disorders. Taken together, the above-mentioned studies suggest that the colonic motor response to stress is exaggerated in IBS. There is evidence that an increased emotional response is associated with this difference in colonic, and perhaps also gastric motor responses to certain stressors. However, almost no valid data are available so far from human studies addressing the question if differences in motility responses to stress between patients with functional GI disorders and healthy subjects are due to an altered stress response associated with an imbalance of the autonomic nervous system or increased stress susceptibility. We can summarize that in experimental animals the most consistent pattern of GI motor alterations induced by various psychological and physical stressors is that of delaying gastric emptying and accelerating colonic transit. Endogenous corticotropin-releasing factor (CRF) in the brain plays a significant role in the central nervous system mediation of stress-induced inhibition of upper GI and stimulation of lower GI motor function through activation of brain CRF receptors. The inhibition of gastric emptying by CRF may be mediated by interaction with the CRF-2 receptor, while CRF-1 receptors are involved in the colonic and angiogenic responses to stress. Endogenous serotonin, peripherally released in response to stress, seems to be involved in stress- and central CRF-induced stimulation of colonic motility by acting on 5HT-3 receptors. Taken together, the limited data available from investigations in healthy subjects and patients with functional GI disorders provide some evidence that stress affects visceral

sensitivity in humans. Acute psychological stress seems to facilitate increased sensitivity to experimental visceral stimuli, if the stressor induces a significant emotional change. In summary, studies in experimental animals suggest that stress-induced visceral hypersensitivity is centrally mediated by endogenous CRF and involvement of structures of the emotional motor system, e.g. the amygdala. Stress-induced activation or sensitization of mucosal mast cells in the GI tract seem to be involved in stress-associated alterations of visceral sensitivity

A controlled, double-blind, randomized study on the efficacy of *Lactobacillus plantarum* 299V in patients with irritable bowel syndrome.

Niedzielin K, Kordecki H, Birkenfeld B.

Eur J Gastroenterol Hepatol. 2001 Oct; 13(10):1143-7.

BACKGROUND: Irritable bowel syndrome (IBS) is a widespread functional disorder of the digestive tract. Its aetiology is unknown and therapeutic options are limited. Recent reports suggest that probiotics may have a role in regulating the motility of the digestive tract. **AIM:** To assess the efficacy of *Lactobacillus plantarum* 299V (LP299V) in patients with IBS. **PATIENTS AND METHODS:** Forty patients were randomized to receive either LP299V in liquid suspension (20 patients) or placebo (20 patients) over a period of 4 weeks. Clinical examination was performed at baseline and at the end of the study. Additionally, patients assessed their symptoms by applying a scoring system. **RESULTS:** All patients treated with LP299V reported resolution of their abdominal pain as compared to 11 patients from a placebo group ($P = 0.0012$). There was also a trend towards normalization of stools frequency in constipated patients in six out of 10 patients treated with LP299V compared with two out of 11 treated with placebo ($P = 0.17$). With regards to all IBS symptoms an improvement was noted in 95% of patients in the LP299V group vs 15% of patients in the placebo group ($P < 0.0001$). **CONCLUSIONS:** LP299V seems to have a beneficial effect in patients with IBS. Further studies on larger cohorts of patients and with longer duration of therapy are required in order to establish the place of *L. plantarum* in the treatment of IBS

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5-HT₄ receptor antagonism does not affect motor and reward mechanisms in the rat.

Reavill C, Hatcher JP, Lewis VA, et al.

Eur J Pharmacol. 1998 Sep 18; 357(2-3):115-20.

5-HT₄ receptors are concentrated in areas of the brain which are rich in dopamine neuronal markers, which may suggest that they influence motor and reward processes. We tested this hypothesis by examining the effects of a 5-HT₄ receptor antagonist, 8-amino-7-chloro-(N-butyl-4-piperidyl)methylbenzo-1,4-dioxan-5-carboxylate hydrochloride (SB-204070-A) on amphetamine- and nicotine-induced locomotor stimulation in intact rats. In rats with unilateral 6-hydroxydopamine-induced lesions of the ascending nigrostriatal dopaminergic projection, SB-204070-A was tested for its effects on amphetamine-induced rotation. SB-204070-A was also tested for its effects on rewarded behaviour maintained by intracranial self-stimulation. SB-204070-A did not alter behaviour under any of these conditions, suggesting a lack of involvement of the 5-HT₄ receptor in motor and reward processes

Treating irritable bowel syndrome with peppermint oil.

Rees WD, Evans BK, Rhodes J.

Br Med J. 1979 Oct 6; 2(6194):835-6.

Irritable bowel syndrome.

Ringel Y, Sperber AD, Drossman DA.

Annu Rev Med. 2001; 52:319-38.

The irritable bowel syndrome (IBS) is a functional gastrointestinal disorder whose hallmark is abdominal pain or discomfort associated with a change in the consistency or frequency of stools. In the western world, 8% to 23% of adults have IBS and its

socioeconomic cost is substantial. Research-generated insights have led to the understanding of IBS as a disorder of brain-gut regulation. The experience of symptoms derives from dysregulation of the bidirectional communication system between the gastrointestinal tract and the brain, mediated by neuroendocrine and immunological factors and modulated by psychosocial factors. The biopsychosocial model integrates the various physical and psychosocial factors that contribute to the patient's illness. This model and the recently revised symptom-based criteria (i.e. the "Rome II criteria") form the basis for establishing a comprehensive and effective approach for the diagnosis and management of the disorder

Irritable Bowel Syndrome.

Sach JA, Chang L.

Curr Treat Options Gastroenterol. 2002 Aug; 5(4):267-78.

Because treatment of irritable bowel syndrome (IBS) patients can be frustrating to the clinician and patient as well, the physician should strive to gain the patient's confidence with a concise, appropriate work-up and by offering reassurance and education that IBS is a functional disorder without significant long-term health risks. First-line treatment should be aimed at treating the most bothersome symptom. Tricyclic antidepressants are superior to placebo in reducing abdominal pain scores, as well as improving global symptom severity. Loperamide is superior to placebo in managing IBS-associated diarrhea. Whereas fiber has a role in treating constipation, its value for IBS or, specifically, in the relief of abdominal pain or diarrhea associated with IBS is controversial. Although certain antispasmodics have demonstrated superiority over placebo in managing abdominal pain, none of these agents are available in the United States. Probiotic therapy using *Lactobacillus plantarum* has demonstrated superiority to placebo in improving pain, regulating bowel habits, and decreasing flatulence. As studied in a recent placebo-controlled prospective study, Chinese herbal medicines significantly improved bowel symptom scores and global symptom profile, and reduced IBS-related quality of life impairment. Some of the most promising emerging therapies in IBS revolve around targeted pharmacotherapeutic modulation of serotonin receptors (ie, 5-HT₃ and 5-HT₄ subtypes), which are involved in sensory and motor functions of the gut. Other investigational agents that are also being explored include cholecystokinin antagonists, alpha₂-adrenergic agonists (eg, clonidine), serotonin reuptake inhibitors (eg, citalopram), and neurokinin antagonists. IBS is best understood through the biopsychosocial paradigm, and therefore, its effective management requires a comprehensive multidisciplinary approach based on patient education and reassurance, enhanced by diet recommendations and lifestyle modifications, and complemented by pharmacotherapy and psychosocial intervention in more severe cases

Continuous culture selection of bifidobacteria and lactobacilli from human faecal samples using fructooligosaccharide as selective substrate.

Sghir A, Chow JM, Mackie RI.

J Appl Microbiol. 1998 Oct; 85(4):769-77.

The human large intestine contains a large and diverse population of bacteria. Certain genera, namely *Bifidobacterium* and *Lactobacillus*, are thought to exert health-promoting effects. Prebiotics such as fructooligosaccharides (FOS) have been shown to stimulate the growth of endogenous bifidobacteria. In this study, changes of lactic acid producing bacteria in continuous culture fermentors (semi-defined, anaerobic medium containing 5 g l⁻¹ FOS, dilution rate of 0.1 h⁻¹, pH 5.5) were followed over a 21 d period after inoculation with blended human faeces from four healthy adults. Samples were also taken every 3 d for influent/effluent FOS, short chain fatty acid (SCFA), lactate and microbiological analyses. Results showed that SCFA concentrations decreased abruptly 1 d after inoculation while lactate concentrations increased. Classical methods of enumeration using selective media showed that the proportion of total culturable count represented by bifidobacteria and lactobacilli increased from 11.9% on day 1 to 98.1% on day 21. However, molecular methods using genus-specific 16S rRNA oligonucleotide probes indicated that the bifidobacterial population maintained a level between 10 and 20% of total 16S rRNA during the first 6 d and disappeared rapidly when the maximum concentration of lactate was reached. Lactobacilli, which were initially present in low numbers, increased until day 9 and remained at high levels (20-42% of total 16S rRNA) to day 21, with the exception of day 18. Although FOS has usually been regarded as a selective substrate for bifidobacteria, these observations suggest that: (1) lactobacilli are also able to use FOS, (2) lactobacilli can out-compete bifidobacteria in continuous culture at pH 5.2-5.4 when FOS is the primary carbon and energy source, and (3) bifidobacteria can grow faster on FOS than lactobacilli under controlled conditions

Turbo probiotics for IBD.

Shanahan F.

Gastroenterology. 2001 Apr; 120(5):1297-8.

Bran supplementation in the treatment of irritable bowel syndrome.

Snook J, Shepherd HA.

Aliment Pharmacol Ther. 1994 Oct; 8(5):511-4.

BACKGROUND: Irritable bowel syndrome remains the commonest reason for referral to a gastroenterology clinic. Patients with irritable bowel syndrome are frequently advised to increase their intake of bran fibre, despite inconclusive experimental evidence of benefit. **METHODS:** The effect of dietary supplementation with a bolus of bran fibre (12 g/day) was studied in a block-randomized, placebo-controlled, crossover study of 80 patients with irritable bowel syndrome referred to a District General Hospital outpatient clinic. Comparison of the benefits of bran and placebo was based upon personal assessment of individual and overall symptom profiles, determined from a simple daily symptom score and post-treatment interview. **RESULTS:** Overall symptomatic improvement was reported with bran by 52% and with placebo by 54% of patients. Bran supplementation was no more effective than placebo in improving individual symptoms of irritable bowel syndrome, and for wind-related symptoms it was significantly less effective ($P < 0.001$). **CONCLUSION:** Dietary supplementation with bran is of no value in the treatment of patients with irritable bowel syndrome referred to a hospital clinic

The sense of coherence index and the irritable bowel syndrome. A cross-sectional comparison among irritable bowel syndrome patients with and without coexisting fibromyalgia, irritable bowel syndrome non-patients, and controls.

Sperber AD, Carmel S, Atzmon Y, et al.

Scand J Gastroenterol. 1999 Mar; 34(3):259-63.

BACKGROUND: Sense of Coherence (SOC) is a global orientation that affects coping with stressors. A strong SOC is associated with better health outcomes. The purpose of this study was to evaluate SOC among patients with irritable bowel syndrome (IBS) and matched controls. **METHODS:** Seventy-nine IBS patients and 72 matched controls completed questionnaires and were tested for fibromyalgia (FS). The controls were subdivided into healthy controls ($n = 49$) or IBS non-patients ($n = 23$), and the patients into IBS only ($n = 54$) or IBS and FS ($n = 25$). **RESULTS:** The mean SOC score was higher for the controls than for the IBS patients (65.7 ± 1.2 and 59.6 ± 1.1 , respectively; $P = 0.003$). There was no significant difference between the healthy controls and the IBS non-patients. The controls had a higher SOC than patients with IBS only and patients with IBS and FS ($P = 0.0004$). **CONCLUSIONS:** An association was found between IBS and SOC. No causality can be inferred from this study. Individuals with low SOC may be more likely to express symptoms in terms of psychological distress and increased health care utilization because of poor coping skills. Conversely, the presence of IBS may affect SOC negatively. Further longitudinal studies could clarify the potential of SOC as a predictor variable (for example, for treatment results) or an outcome variable

Self-reported abuse and gastrointestinal disease in outpatients: association with irritable bowel-type symptoms.

Talley NJ, Fett SL, Zinsmeister AR.

Am J Gastroenterol. 1995 Mar; 90(3):366-71.

OBJECTIVE: A link between functional bowel disease and sexual, physical, emotional, or verbal abuse remains controversial. We aimed to determine whether abuse is associated with functional bowel disease in outpatients. **METHODS:** A consecutive sample of outpatients completed a validated questionnaire; 997 responded. Using standard criteria, we obtained data on symptoms, psychosocial factors, and abuse (sexual, physical, and emotional or verbal). Logistic regression analysis was used to determine whether abuse was associated with functional bowel disease (versus organic disease) and with irritable bowel syndrome (IBS)-type symptoms defined by the Manning criteria. Adjustments were made for age, gender, marital status, education level, psychological distress, and social support. **RESULTS:** Of those with a physician-based diagnosis of functional bowel disease ($n = 440$), 22% reported some form of abuse (13% sexual and/or physical abuse), compared with those with organic disease ($n = 557$), 16% of whom reported some form of abuse; this difference was not significant. However, abused patients were significantly more likely to report IBS-type symptoms than those who did not report a history of abuse (odds ratio = 1.7, 95% confidence interval = 1.2, 2.5). **CONCLUSION:** Outpatients who report abuse are more likely to have IBS-type symptoms

Irritable bowel syndrome: a little understood organic bowel disease?

Talley NJ, Spiller R.

Lancet. 2002 Aug 17; 360(9332):555-64.

Irritable bowel syndrome affects 10% of adults with an unexplained female predominance. Although only a few people see their family doctor, the disease causes reduced quality of life and represents a multi-billion pound health-care problem. The disorder clusters in families, which is possibly because of intra-familial learning and a genetic predisposition. Visceral hypersensitivity is a key feature in most patients. Results of imaging studies of regional cerebral blood flow during rectal distension suggest underlying disturbances of central processing of afferent signals, though this is not unique to the disorder, since it is seen in other chronic pain syndromes. Environmental factors that are strongly implicated in at least some patients include gastrointestinal infection and inflammation and chronic stress. Diagnosis is based on positive symptoms and absence of any alarm indicators. Treatment remains unsatisfactory and hinges on an excellent doctor-patient relationship, with drugs for symptom exacerbations. Cognitive behavioural treatment, psychotherapy, and hypnosis could provide long-lasting benefit in some patients. Tricyclic antidepressants in low doses seem to be the most effective class of drugs for the disorder on the basis of limited data

Full-thickness biopsy of the jejunum reveals inflammation and enteric neuropathy in irritable bowel syndrome.

Tornblom H, Lindberg G, Nyberg B, et al.

Gastroenterology. 2002 Dec; 123(6):1972-9.

BACKGROUND & AIMS: Irritable bowel syndrome (IBS) is regarded as a functional bowel disorder. Few studies have looked for histopathologic changes in the gut and only then in biopsy specimens from intestinal mucosa. Because bowel function is governed mainly by nerve plexuses in the bowel wall, we have investigated full-thickness bowel biopsy specimens in patients with severe IBS. **METHODS:** We used a laparoscopy-assisted technique to obtain full-thickness biopsy specimens from the proximal jejunum. Tissue specimens were investigated with light microscopy using routine stainings and immunohistochemical techniques. Horizontal sectioning was done to visualize large areas of the myenteric plexus. Fifteen autopsy specimens were used as controls regarding the myenteric plexus. Colorectal adenoma controls with terminal ileum biopsy specimens and full-thickness jejunal biopsy specimens from patients with degenerative enteric neuropathy were used as control groups for intraepithelial lymphocyte counts. **RESULTS:** Ten patients (2 males, 8 females) were studied. In 9 patients, we found low-grade infiltration of lymphocytes in the myenteric plexus. Lymphocytes had peri- and intraganglionic location. The mean number of lymphocytes per ganglion ranged from 1.9 to 7.1 per patient, with an overall mean of 3.4. No intraganglionic lymphocytes were found in the control group and only a few periganglionic lymphocytes (mean, 0.2). Four patients had concomitant intraepithelial lymphocytosis. Neuron degeneration was evident in 6 of 9 patients with and 1 patient without ganglionic lymphocyte infiltration. **CONCLUSIONS:** Our findings indicate that inflammation and neuronal degeneration in the myenteric plexus are involved in the pathogenesis of IBS

Histories of sexual victimization in patients with irritable bowel syndrome or inflammatory bowel disease.

Walker EA, Katon WJ, Roy-Byrne PP, et al.

Am J Psychiatry. 1993 Oct; 150(10):1502-6.

OBJECTIVE: Two reports have suggested a possible association between a history of sexual trauma and irritable bowel syndrome, but several factors in their study designs limited their generalizability. The authors used a more rigorous methodology to confirm this association. **METHOD:** They administered structured psychiatric and sexual trauma interviews to 28 patients with irritable bowel syndrome and 19 patients with inflammatory bowel disease and compared prevalence rates of sexual victimization in the two groups. **RESULTS:** Compared with patients diagnosed as having inflammatory bowel disease, patients with irritable bowel syndrome had a significantly higher rate of severe lifetime sexual trauma (32% versus 0%), severe childhood sexual abuse (11% versus 0%), and any lifetime sexual victimization (54% versus 5%). The nine patients who had experienced severe lifetime victimization had significantly higher odds ratios for lifetime depression, panic disorder, phobia, somatization disorder, alcohol abuse, functional dyspareunia, and inhibited sexual desire than the 38 patients who had experienced less severe sexual trauma or no trauma. A logistic regression analysis showed that gender, the number of medically unexplained physical symptoms, and self-reported anxiety and hostility accounted for all of the variance in the victimized group. **CONCLUSIONS:** These preliminary results suggest that sexual victimization may be an important factor in the development of irritable bowel syndrome in some patients. Future studies attempting to categorize subgroups of patients with irritable bowel syndrome should inquire into past histories of sexual victimization

Systematic review of the comorbidity of irritable bowel syndrome with other disorders: what are the causes and implications?

Whitehead WE, Palsson O, Jones KR.

Gastroenterology. 2002 Apr; 122(4):1140-56.

BACKGROUND & AIMS: Comorbid or extraintestinal symptoms occur frequently with irritable bowel syndrome and account for

up to three fourths of excess health care visits. This challenges the assumption that irritable bowel is a distinct disorder. The aims of this study were to (1) assess comorbidity in 3 areas: gastrointestinal disorders, psychiatric disorders, and nongastrointestinal somatic disorders; and (2) evaluate explanatory hypotheses. METHODS: The scientific literature since 1966 in all languages cited in Medline was systematically reviewed. RESULTS: Comorbidity with other functional gastrointestinal disorders is high and may be caused by shared pathophysiological mechanisms such as visceral hypersensitivity. Psychiatric disorders, especially major depression, anxiety, and somatoform disorders, occur in up to 94%. The nongastrointestinal nonpsychiatric disorders with the best-documented association are fibromyalgia (median of 49% have IBS), chronic fatigue syndrome (51%), temporomandibular joint disorder (64%), and chronic pelvic pain (50%). CONCLUSIONS: Multivariate statistical analyses suggest that these are distinct disorders and not manifestations of a common somatization disorder, but their strong comorbidity suggests a common feature important to their expression, which is most likely psychological. Some models explain the comorbidity of irritable bowel with other disorders by suggesting that each disorder is the manifestation of varying combinations of interacting physiological and psychological factors. An alternative hypothesis is that the irritable bowel diagnosis is applied to a heterogeneous group of patients, some of whom have a predominantly psychological etiology, whereas others have a predominantly biological etiology, and that the presence of multiple comorbid disorders is a marker for psychological influences on etiology

[Mast cells of ileocecal junction in irritable bowel syndrome].

Yang Y, Zhou D, Zhang W.

Zhonghua Nei Ke Za Zhi. 1997 Apr; 36(4):231-3.

To investigate whether the mast cells (MC) of the ileocecal junction (ICJ) is elevated in the irritable bowel syndrome (IBS) and the possible roles of the MC in IBS, the biopsies of ICJ were stained specifically by histochemistry for the MC in the IBS group (n = 20) and the normal group (n = 19). The structure relation between MC and nerves was studied through an electronic microscopy and an immunohistochemical method demonstrating neuron-specific enolase. The results demonstrated that the number of the MC of ICJ was significantly elevated in the IBS (P = 0.019) and that mast cells were close to nerves which were often unmyelinated nerves in lamina propria. The results indicate that the MC of ICJ may be responsible for the pathophysiology of the IBS. We conclude that the MC of ICJ may be a mediator between the gut and the nervous system in the IBS, and that the mast cell stabilizer or the antagonists of the mast cell products may have potential treatment effects on the IBS

Medscape: Inflammation Infection and IBS.

Yehuda RDD.

2002;An Update 2002

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