

## Probiotics in pregnancy could have diabetes benefits

Combining probiotics with perinatal dietary counselling could help reduce the risk of diabetes in mothers, according to a new study from Finland.<sup>39</sup>

The study recruited 256 women, who were randomized during their first trimester of pregnancy into a dietary intervention and a control group. All these women, none of whom had chronic metabolic diseases, received dietary counselling provided by welfare clinics according to a national programme. The intervention group received additionally intensive dietary counselling at every study visit provided by a nutritionist and were further randomized in a double-blind manner to receive either probiotics, *Lactobacillus rhamnosus* GG and *Bifidobacterium lactis* BB-12 at a dose of  $10^{10}$  CFU/d each (diet/probiotics group), or placebo capsules (diet/placebo group). The capsules were taken once daily and the intervention period extended from the first trimester of pregnancy to the end of exclusive breastfeeding.

The researchers evaluated pregnancy outcome and fetal and infant growth during the 24 months' follow-up. 93% of the women (238/256) completed the study, while 79% of the children delivered (191/241) completed the 24 months' follow-up.

Results of the study showed that the frequency of gestational diabetes mellitus (GDM) was significantly different between the study groups ( $p=0.003$ ). The risk of GDM was significantly reduced in the diet/probiotics group when compared to the control group (OR=0.27; 95% CI 0.11, 0.62;  $p=0.002$ ), whereas in the diet/placebo group, the risk was not significantly different when compared to the control group (OR=1.08; 95% CI 0.55, 2.12,  $p=0.823$ ). Women who had taken probiotics had a reduced frequency of GDM: 13% for the diet/probiotics group, compared to 36% in the diet/placebo group and 34% for the control group.

Although no significant differences in fetal growth were observed among the study groups, dietary intervention was found to diminish the risk of larger birth size in affected cases ( $p=0.035$  for birth weight and  $p=0.028$  for birth length), indicating that dietary intervention modified the effect of GDM.

Interestingly, this study demonstrates that probiotic intervention and nutrition counselling have a distinct effect on GDM; probiotics diminish the risk of disorder and dietary counselling during pregnancy reduced the risk of fetal overgrowth associated with it. All pregnancies were of normal duration and there were no adverse events noted in mothers and children, attesting the long-term safety of this approach. Considering that the maternal microbiota is a first inoculum to the development of the child's microbiota, it is important to recognize that the gut microbiota has come to be seen as a key organ involved in host energy homeostasis.

Based on the findings of the study, perinatal dietary counselling combined with probiotics could provide a safe and cost-effective tool in modifying the risk of metabolic epidemic.

## Probiotics may protect infants from respiratory illness

Infectious diseases are the most significant illnesses for infants worldwide. In developed countries, most children experience several respiratory tract infections during the first year of their life. Respiratory tract infections often coincide with or precede acute otitis media, the most common cause for antibiotic use in children. Gastrointestinal infections are the second-most common diseases in childhood and even cause increased mortality in developing countries.

In the August 2010 issue of the British Journal of Nutrition, Finnish researchers found that daily supplements of a probiotic (*Bifidobacterium animalis* subsp. *lactis* BB-12) may reduce the incidence of respiratory illness for infants during their first eight months of life.<sup>40</sup>

109 one-month-old infants were assigned randomly to a probiotic group receiving a BB-12-containing tablet ( $n=55$ ) or to a control group receiving a control tablet ( $n=54$ ). The test tablets were administered to the infants twice a day (daily dose of BB-12  $10^9$  CFU) from the age of 1-2 months to 8 months with a novel slow-release pacifier or a spoon.

While no significant differences were observed between the probiotic and control groups for gastrointestinal symptoms, otitis media or use of antibiotics, a significant reduction in respiratory infections were observed in the probiotic-fed infants. Only 65% of the infants who received daily doses of BB-12 experienced respiratory infections compared to 94% in the control group (RR=0.69; 95% CI 0.53, 0.89;  $p=0.014$ ). The baseline characteristics of the two groups were similar, as was the duration of exclusive breastfeeding. No serious adverse effects were detected during the administration period and the daily duration of pacifier sucking was not associated with the occurrence of acute otitis media.

These findings agree with the results of previous studies which also found a reduction in the occurrence of respiratory infections with the supplementation of probiotic in infants. This is the first study to report probiotic administration by means of a pacifier. The study concluded that this modality may offer a safe and controlled way to reduce early respiratory infections. Nevertheless, clinical trials with larger numbers of infants are required to corroborate the aforementioned findings.

## Quick Facts

For colonization to occur, probiotics must contain living, viable organisms and must be ingested on a regular basis in order to maintain effective concentrations.<sup>41</sup>

### References:

1. Gwee KA, Png DJ. The prevalence, symptom characteristics, and impact of irritable bowel syndrome in an Asian urban community. *Am J Gastroenterol* 2004
2. Simrén M, Månsson A, Langkilde AM, et al. Food-related gastrointestinal symptoms in the irritable bowel syndrome. *Digestion* 2001;63:108-115
3. Heizer WD, Southern S, McGovern S. The role of diet in symptoms of irritable bowel syndrome in adults: a narrative review. *J. Am. Diet. Assoc.* 2009; 109: 1204-14
4. Bernstein CN. The placebo effect for gastroenterology: Tool or torment. *Clin Gastroenterol Hepatol.* 2006;4:1302-1308
5. Martin H, Hoch, M.D., MACG, and Rathi Narayan, M.D. Diet in the Irritable Bowel Syndrome. *J Clin Gastroenterol* 2002;35(Suppl.):S45-S52
6. Giannini EG, Mansi C, Dulbecco P, Savarino V. Role of partially hydrolyzed guar gum in the treatment of irritable bowel syndrome. *Nutrition.* 2006;22:334-342
7. Hunter JO, Tuffnell Q, Lee AJ. Controlled trial of oligofructose in the management of irritable bowel syndrome. *J Nutr.* 1999;129(suppl): 1451S-1453S
8. Olesen M, Gudmand-Hoyer E. Efficacy, safety, and tolerability of fructooligosaccharides in the treatment of irritable bowel syndrome. *Am J Clin Nutr.* 2000;72:1570-1575
9. Paineau D, Payen F, Panserieu S, Coulombier G, Sobaszek A, Lartigau I, Brabet M, Galmiche JP, Tripodi D, Sacher-Huvelin S, Chapalain V, Zourabichvili O, Respondek F, Wagner A, Borner FR. The effects of regular consumption of short-chain fructo-oligosaccharides on digestive comfort of subjects with minor functional bowel disorders. *Br J Nutr.* 2008;99:311-318
10. Cook LJ, Irvine EJ, Campbell D, Shannon S, Reddy SN, Collins SM. Effect of dietary fiber on symptoms and rectosigmoid motility in patients with irritable bowel syndrome. *Gastroenterology* 1990;98:66-72

11. Feldman W, McGrath P, Hodgson C, Ritter H, Shipman RT. The use of dietary fiber in the management of simple, childhood, idiopathic, recurrent abdominal pain: results in a prospective, double-blind, randomized, controlled trial. *Am J Dis Child* 1995;138:1216-8
12. Homann H, Kernen M, Fuessinich C, et al. Reduction in diarrhea incidence by soluble fiber in patients receiving total or supplemental enteral nutrition. *J Parent Enteral Nut* 1994; 18:486-90
13. Parkman HP Irritable bowel syndrome: diagnosis and management. *Practical Gastroenterol* May 2007
14. Camilleri M Is there a role for probiotics in irritable bowel syndrome? *Dig Liver Dis* 2006
15. P Moayyedi, A C Ford, N J Talley, et al. The efficacy of probiotics in the treatment of irritable bowel syndrome: a systematic review. *Gut* 2010 59: 325-332
16. Andriulli A, Neri M, Loguercio C, Terreni N, Merla A, Cardarella MP, Federico A, Chilovi F, Milandri GL, De Bona M, Cavenati S, Gullini S, Abbiati R, Garbagna N, Cerutti R, Grossi E. Clinical trial on the efficacy of a new symbiotic formulation, Flortec, in patients with irritable bowel syndrome: A multicenter, randomized study. *J Clin Gastroenterol.* 2008;42:S218-223
17. Grigoleit HG, Grigoleit P. Peppermint oil in irritable bowel syndrome. *Phytomedicine.* 2005;12:601-606
18. Cappello G, Spezzafiero M, Grossi L, Manzoli L, Marzio L. Peppermint oil (Mintoil) in the treatment of irritable bowel syndrome: A prospective double blind placebo-controlled randomized trial. *Dig Liver Dis.* 2007;39:530-536
19. Ford AC, Talley NJ, Spiegel BM, Fox-Orenstein AE, Schiller L, Quigley EM, Moayyedi P. Effect of fibre, antispasmodics, and peppermint oil in the treatment of irritable bowel syndrome: Systematic review and meta-analysis. *BMJ.* 2008;337:a2313
20. Bundy R, Walker AF, Middleton RW, Booth J. Turmeric extract may improve irritable bowel syndrome symptomatology in otherwise healthy adults: A pilot study. *J Altern Complement Med.* 2004;10: 1015-1018
21. Gonlacharvit. Are Rice and Spicy Diet Good for Functional Gastrointestinal Disorders? *J Neurogastroenterol Motil.* Vol. 16 No. 2 April, 2010
22. Zuo XL, Li YQ, Li WJ, et al. Alterations of food antigen-specific serum immunoglobulins G and E antibodies in patients with irritable bowel syndrome and functional dyspepsia. *Clin Exp Allergy* 2007;37:823-830
23. King TS, Elia M, Hunter JO. Abnormal colonic fermentation in irritable bowel syndrome. *Lancet* 1998;352:1187-1189
24. Vernia P, Ricciardi MR, Frandina C, Bilotta T, Frieri G. Lactose malabsorption and irritable bowel syndrome. Effect of a long-term lactose-free diet. *Ital J Gastroenterol.* 1995;27:117-121
25. Suarez F, Levitt MD. Abdominal symptoms and lactose: The discrepancy between patients' claims and the results of blinded trials. *Am J Clin Nutr.* 1996;64:251-252
26. Lisker R, Solomons NW, Perez Briceno R, Ramirez Mata M. Lactase and placebo in the management of the irritable bowel syndrome: A double-blind, cross-over study. *Am J Gastroenterol.* 1989;84:756-762
27. Rao SS, Welch K, Zimmerman B, Stumbo P. Is coffee a colonic stimulant? *Eur J Gastroenterol Hepatol.* 1998;10:113-118
28. Nanda R, James R, Smith H, Dudley CR, Jewell DP. Food intolerance and the irritable bowel syndrome. *Gut.* 1989;30:1099-1104
29. Jones VA, McLaughlan P, Shorthouse M, Workman E, Hunter JO. Food intolerance: A major factor in the pathogenesis of irritable bowel syndrome. *Lancet.* 1982;2:1115-1117
30. Petitpierre M, Gumowski P, Girard JP. Irritable bowel syndrome and hypersensitivity to food. *Ann Allergy.* 1985;54:538-540
31. Hunter JO, Workman EM, Jones AV. Dietary studies. In: Gibson PR, Jewell DP, eds. *Topics in Gastroenterology.* Vol 12. Oxford, UK: Blackwell Scientific Publications; 1995:305-313
32. Hawthorne B, Lambert S, Scott D, Scott B. Food intolerance and the irritable bowel syndrome. *J Hum Nutr Diet.* 1991;3:19-23
33. Parker TJ, Naylor SJ, Riordan AM, Hunter JO. Management of patients with food intolerance in irritable bowel syndrome: The development and use of an exclusion diet. *J Hum Nutr Diet.* 1995; 8:159-166
34. Serra J, Azpiroz F, Malagelada JR. Impaired transit and tolerance of intestinal gas in the irritable bowel syndrome. *Gut.* 2001;48:14-19
35. Serra J, Sakvioti B, Azpiroz F, Malagelada JR. Lipid-induced intestinal gas retention in irritable bowel syndrome. *Gastroenterology.* 2002;123:700-706
36. Simren M, Agerforz P, Björnsson ES, Abrahamsson H. Nutrient dependent enhancement of rectal sensitivity in irritable bowel syndrome (IBS). *Neurogastroenterol Motil.* 2007;19:20-29
37. Drossman DA, Camilleri M, Mayer EA, Whitehead WE. AGA technical review on irritable bowel syndrome. *Gastroenterology.* 2002; 123:2108-2131
38. Atkinson W, Sheldon TA, Shaath N, Whorwell PJ. Food elimination based on IgG antibodies in irritable bowel syndrome: A randomised controlled trial. *Gut* 2004; 53: 1459-64
39. Luoto R, Laitinen K, Nermes M, Isolauri E. Impact of maternal probiotic-supplemented dietary counselling on pregnancy outcome and prenatal and postnatal growth: a double-blind, placebo-controlled study. *Br J Nutr* 2010 doi: 10.1017/S0007114509993808.
40. Taipale T, Pienihäkkinen K, Isolauri E, Larsen C, Brockmann E. Bifidobacterium animalis subsp. lactis BB-12 in reducing the risk of infections in infancy. *Br J Nutr* 2010 doi:10.1017/S0007114510003685.
41. Williams NT. Probiotics. *Am J Health Syst Pharm* 2010;67(6):449-458.

The contents are not to be reproduced in part or in whole, without prior written approval from the editor. Whilst every effort is made in compiling the content of this publication, the publishers, editors and authors accept no liability whatsoever for the consequences of any inaccurate or misleading data, opinions or statements.



### Medical Advisors

**Dr Charles Vu**  
*MBBS (Monash), FRACP,  
FAMS (Gastroenterology)*



Head & Senior Consultant,  
Dept of Gastroenterology & Hepatology (TTSH)  
Adjunct Assistant Professor,  
National University of Singapore

**Dr Francis Seow-Choen**  
*MBBS, FRCSed, FAMS, FRCS*



Colorectal Surgeon & Director  
Seow-Choen Colorectal Centre PLC  
President, Eurasian (European-Asian) Colorectal Technology Association (ECTA)  
President, Guide Dogs Association of the Blind Singapore  
Chairman, Board of Directors City College Singapore  
Vice-President, Singapore-China Association for the Advancement of Science and Technology (SCAAST)  
Visiting Consultant, Department of Colorectal Surgery, Singapore General Hospital  
Visiting Consultant, Alexandra Hospital  
Visiting Professor, Tianjin Police Hospital, Tianjin, China  
Visiting Professor, Tianjin Union Medical College, Tianjin Colorectal Centre, Tianjin PRC  
Visiting Professor, National Ctr for Colorectal Disease, Nanjing TCM University, Nanjing, China  
Visiting Professor, Wenzhou Medical College, Wenzhou, China,  
Visiting Professor, Dept of Colorectal Surgery, Guigang Renmin Hospital, GuangXi, China

**Dr Steven J. Mesenas**  
*MBBS (S'pore), MRCP (UK),  
FAMS (Gastroenterology)*



Senior Consultant,  
Dept of Gastroenterology & Hepatology (SGH)  
Director, SGH Endoscopy Centre  
Clinical Lecturer, National University of Singapore

**Editor-in-Chief**  
Mr Melvin Wong, CEO

**Executive Editors**  
Ms Nah Li Ching, B.Sc. (Pharm), Hons  
Mr Leong Wai Sin

**Editorial Board**  
Ms Nang Moon Moon Tint, B.Pharm  
Ms Sindy Wong  
Ms Gladius Neo

For enquiries, comments, suggestions or article contribution, please write to:

**The Editor (The Probiotics News)**  
**MD Pharmaceuticals Pte Ltd**  
**896 Dunearn Road #02-01A**  
**Sime Darby Centre Singapore 589472**

**Tel: (65) 6465 4321**  
**Fax: (65) 6469 8979**

Website: <http://www.mdpharm.com>  
Email: [liching.nah@mdpharm.com](mailto:liching.nah@mdpharm.com) or [waisin.leong@mdpharm.com](mailto:waisin.leong@mdpharm.com)

Printed by Chin Hiap Hong Corporation Pte Ltd

# The Probiotics news

MICA (P) 079/06/2010



An educational project by MD Pharmaceuticals Pte Ltd

### Message from the Editor

For the past three years, nearly 5500 medical practitioners in Singapore have received our probiotic newsletters since 2008. MD Pharmaceuticals would like to thank some of the readers for their encouraging and favourable feedbacks.

To many tourists, Singapore is reputed as a food haven. In this 6<sup>th</sup> issue, the editorial team would like to thank Drs SJ Mesenas and SW Chuah from the Gastroenterology and Hepatology Department of SGH for their informative article on "Food & IBS".

In addition, two interesting short write-ups on the possible role of probiotics on diabetes in pregnancy and respiratory illness in infants are being included.

Wishing one and all a joyous, peaceful & family centered Lunar New Year.

God Bless!

Melvin Wong  
Editor-in-Chief

### Food and Irritable Bowel Syndrome (IBS)

**Dr SW Chuah, Dr SJ Mesenas**  
*Dept of Gastroenterology & Hepatology (SGH)*

Irritable Bowel Syndrome (IBS) is one of the most common problems seen in the Gastroenterology clinic. This disorder is highly prevalent affecting up to 10% of Singapore population.<sup>1</sup> It can be associated with significant emotional distress, impaired health-related quality of life, disability, and high direct and indirect associated health care costs.

IBS patients commonly report the precipitation of symptoms on food ingestion. Complaints of gastrointestinal symptoms after food ingestion are reported in 25-64% of IBS patients.<sup>2</sup> Studies suggest that 20-67% of IBS patients might have dietary triggers, and a substantial number report improvement upon dietary management.<sup>3</sup>

Given the primary function of the gut, it should come as no surprise that food ingestion is the most potent stimulus of such gastrointestinal functions as motility and secretion. The provocation of either of these could induce symptoms in IBS. Proposed mechanisms include abnormal gas handling in the gastrointestinal tract, abnormal colonic fermentation, exaggerated motor responses after meals, psychological factors, and intolerance to specific foods.<sup>2</sup>

Addressing the dietary aspects of IBS is important and many IBS patients are interested to know what foods to avoid. There is considerable interest in the potential roles of diet and food supplements in IBS therapy. However, the evidence base for dietary recommendations remains slim as there are very few studies that carefully analyse diet intake in these patients before intervention and therapy. Clinical trials of treatment for IBS present significant challenges because of a high and variable placebo response ranging from 0% to 84%, median 47%, which is greater than most treatment effects.<sup>4</sup> Trials involving diets are even more challenging because they may be difficult to control adequately.

### Food to be encouraged?

#### A) Fiber

Dietary fiber is non-starch polysaccharide derived from plant foods that are poorly digested by human enzymes. It occurs in grains, fruits, and vegetables. Fiber deficiency was widely believed to be the primary cause of IBS. To evaluate which fiber diet is best for any given patient, it is important to understand that fibers can be divided from the chemical analysis process into soluble and insoluble fibers.

#### a) Soluble fiber (Prebiotic)

Derived primarily from fruits and grains and is composed of hemicelluloses. Soluble fibers commonly studied are psyllium or ispaghula, partially hydrolyzed guar gum, fructo-oligosaccharide, oligosaccharide, and calcium polycarbophil. Oats contain 50% soluble, psyllium seed contains 80% soluble, and substances such as pectin and guar are 100% soluble.<sup>5</sup>





Soluble fibers are fermented in the colon to form short-chain fatty acids. Because the fermentation process is markedly increased by soluble fibers, the microflora that performs the fermentation is nurtured and proliferates. This nurturing can define soluble fiber as a prebiotic, because it improves the colonic flora. Prebiotics are non-digestible food substances or supplements that are fermented by host bacteria and alter the intestinal flora and stimulate the growth of healthy bacteria.

The increase in the size of the stool that results from increasing soluble fiber intake is largely an increase in the fecal bacterial mass. This increase in the fecal mass results in a softer stool with ease of passage.

Some patients will experience a mild bloating or "increased gas" sensation when they rapidly increase the intake of soluble fibers. Therefore, these supplements should be started slowly and increased gradually.

The use of partially hydrolyzed guar gum (prebiotic), to treat IBS was reviewed in 2005.<sup>6</sup> Despite decreased abdominal pain and increased quality of life scores in the three studies reviewed, the lack of placebo-control and blinding precluded valid conclusions from these studies. Another prebiotic fiber, fructo-oligosaccharide (oligofructose), has been investigated. Two studies showed no benefit from 6 g/day or from either 10 g/day or 20 g/day.<sup>7,8</sup> In contrast, a recent randomised, double-blind, placebo controlled trial of short-chain fructo-oligosaccharides in subjects with minor functional bowel disorders showed significant reduction of intensity of abdominal pain, constipation, and diarrhea, as well as improvement in performance of daily activities.<sup>9</sup>

Further randomised, controlled trials of the effects of various prebiotic fibers on IBS symptoms are needed. The dose and fermentability of the prebiotic fiber may be key factors in the effectiveness of these proposed dietary treatments.

#### b) Insoluble fibers

Largely found in grains. They are part of the shell of the grain, and their chemical makeup is primarily cellulose, hemicelluloses, and lignin. Products rich in insoluble fiber that have been studied are wheat bran, corn bran, and defatted ground flaxseed.

Their major physiologic effect is to hold onto water and, thereby, increase the bulk and size of the stool. They clearly decrease transit time. However, marked increase in intake of insoluble fiber without a slow adjustment can also give a sensation of bloating. Although insoluble fibers are poorly fermented, they are partially fermented and can produce an increased amount of both short-chain fatty acids and expelled gases.

Some patients will tolerate soluble fiber better than insoluble, and others will tolerate insoluble better than soluble. Finding the right mix of fiber foods or supplements requires careful monitoring by the physician or dietitian.

The study performed by Cook which supplemented the diet with 20 grams of corn fiber per day, revealed significant improvement in symptoms of irritable bowel with less pain severity, increased stool frequency, and a careful measurement of rectosigmoid pressures correlated with the pain severity. In that study, the results did reveal the trend to decrease rectosigmoid pressures after fiber therapy and the patients had less symptoms.<sup>10</sup>

There is recommendation for fiber intake of 20 to 30 grams of dietary fiber per day for constipation. However, the amount of fiber that is necessary to correct constipation or stabilize bowel movements varies in different people. Ispaghula has been used successfully in the treatment of constipation. Ispaghula is primarily soluble fiber, and therefore benefit may also be gained by increasing the proportion of soluble fiber via dietary manipulation in patients with IBS.

There are no diet recommendations in the guidelines published by the American Gastroenterological Association (AGA) for diarrhea. A trial of increasing soluble fiber may be helpful. Often some patients are helped by increasing the fecal mass with the use of soluble fibers. Psyllium seed can be used and in many parts of the world partially hydrolyzed guar gum is used. Although there are limited studies on the use of dietary fiber substances, partially hydrolyzed guar gum has been shown to decrease diarrhea both in children suffering from acute diarrhea and in adults on enteral feeding.<sup>12</sup> To date, this experience is anecdotal and there are no trials that demonstrate a clear benefit.

It is theorised that dietary fiber can reduce pain by gradually increasing the size of the fecal mass and slowly decreasing wall tension pressure by transferring the wall pressure to the lumen contents. Animal studies clearly demonstrate that high fiber intake can affect colonic motility and increase propulsive activity. A study in children revealed that abdominal pain, similar to the pain of IBS, can be relieved by a high-fiber diet although studies in adults have variable outcomes.<sup>11</sup>

There is a contradiction in the fact that fiber may increase gas production, but yet increased dietary fiber intake may help the symptoms. Obviously, patients vary, symptoms vary, and the effect of dietary fiber to help one patient but may not help another. At this point in time, there is inadequate evidence to make recommendations on diet where pain and bloating are the major symptoms.

The use of fiber or bulking agents for treatment of IBS has been reviewed in meta-analyses and systematic reviews. The reviews uniformly concluded that fiber either has no efficacy for treatment of IBS or possible limited benefits for patients who have IBS with constipation. Soluble fiber showed a tendency to greater global symptom improvements than insoluble fiber.

#### B) Probiotics

Probiotics are a live microbial food supplement which, when administered in adequate amounts, confer a health benefit to the host by improving the balance in the intestinal microflora. Many mechanisms by which probiotics might improve IBS symptoms have been hypothesised. Rationale for using probiotics in the treatment of IBS is based on epidemiological studies suggesting a role in the intestinal infection or inflammation in the pathogenesis of IBS and anecdotal observations demonstrating alterations in stool cultures in patients with IBS compared with controls.<sup>13,14</sup> It has been suggested that abnormal colonic flora could be relevant in the pathogenesis of IBS, which has led to the interest in using probiotics to try and naturally alter the flora. The mechanisms influenced by probiotics that are of potential relevance to the development and treatment of IBS include alteration in the immune function, motility, and the intraluminal milieu.<sup>14</sup>

*Lactobacillus paracasei* was reported to attenuate post-infectious intestinal dysmotility in a mouse model.<sup>15</sup> A number of animal models have also shown that probiotics improve visceral hypersensitivity. *Lactobacillus acidophilus* administration induces the expression of cannabinoid and opioid receptors on intestinal cells, and this may explain the effect of probiotics on visceral hypersensitivity. Probiotics can have potent anti-inflammatory properties, and *Bifidobacterium infantis* 35624 normalised circulating interleukin 10 (IL10) and interleukin 12 (IL12) levels in IBS patients in randomised controlled trials.<sup>15</sup>

Studies have reported an improvement in global symptoms with probiotics, whilst others have failed to demonstrate any benefit. Other trials have not found a clear effect of probiotics on primary endpoints, but have found benefits for secondary endpoints such as bloating. Some of this variation may be attributable to the type of probiotic used, as well as methodological differences between trials.



A systemic review looking at the efficacy of probiotics in the treatment of IBS indicates that probiotics have a therapeutic benefit in improving IBS symptoms.<sup>16</sup> The main limitation of this review is that there were a variety of species, strains and doses of probiotics used, and therefore it was difficult to come to any conclusion about the optimum probiotic strategy to use in IBS. Individual probiotics may differ greatly in their effects on host immune function, and the reason for their potential therapeutic efficacy remains unclear. There was a trend for *Bifidobacteria* to improve IBS symptoms, but this effect did not reach statistical significance. It is therefore possible that *Bifidobacteria* constitute the active treatment in probiotic combinations. Alternatively it is possible that different species of probiotics are synergistic in promoting a therapeutic effect on IBS. While we need more information, this systematic review suggests that probiotic treatment is a promising strategy to treat patients with IBS.

Meta-analyses on the use of probiotics in the treatment of IBS all concluded that probiotics may be useful but there are many variables affecting the results such as the type, dose, and formulation of bacteria comprising the probiotic preparation, the outcome measured, and size and characteristics of the IBS population studied. Additional studies are needed with well-characterised bacterial preparations, longer treatment and follow-up durations, and standardised outcome measures. Factorial designed randomised controlled trials that compare individual bacterial species with combinations are also required to establish whether probiotics can have a synergistic effect.

Symbiotics (or synbiotics), which are combinations of a prebiotic fiber and a probiotic, have also been tested for treatment of IBS but have not shown efficacy or have not been placebo controlled.<sup>16</sup>

#### C) Peppermint oil

Peppermint oil relaxes the smooth muscle of the intestinal tract. A review summarised the effect of 15 studies in patients with IBS.<sup>17</sup> Twelve of the studies were randomised, double-blind, and placebo-controlled. In eight of these studies peppermint oil relieved symptoms significantly better than placebo, but in four studies it did not. In the three additional studies, peppermint oil was no better than an anticholinergic medication in relieving symptoms. The authors concluded that peppermint oil "may be the drug of first choice" for patients with relatively mild IBS symptoms.

In a randomised, placebo-controlled study of 57 patients published after the review, symptom improvement from baseline after 4 weeks was 75% for those receiving peppermint oil and 38% for those on placebo, a significant difference.<sup>18</sup> A very recent review also concluded that peppermint oil is more effective than placebo in relieving IBS symptoms.<sup>19</sup>

#### D) Turmeric

Turmeric is a member of the ginger family and its extract, curcumin, has anti-inflammatory effects. In a partially blinded, randomised, 8-week trial of oral turmeric in 207 individuals with IBS, overall symptoms improved more than 65%.<sup>20</sup> However, there was no placebo control and, therefore, no conclusions can be drawn from this study.

#### E) Rice and high-carbohydrate diet

Rice is the major source of carbohydrate in Asian populations. In contrast to wheat and other sources of carbohydrate, rice is completely absorbed in the small bowel and produces very little intestinal gas after ingestion. A previous study demonstrated that the amount of hydrogen, a maker of carbohydrate metabolism by intestinal bacteria, in breath samples after rice ingestion is minimally increased and not significantly different from the fasting period.<sup>21</sup> Furthermore, rice has been shown to have a low allergenicity. Previous studies demonstrated that serum IgG levels produced in reaction to several kinds of food such as wheat, beef, pork, lamb, soybean, shrimp, egg, and crab were increased in IBS patients compared to healthy humans, but the serum IgG levels produced to rice in IBS patients is mild or not increased.<sup>22</sup> In addition, a small crossover controlled study supports its benefit in IBS.<sup>23</sup>

All together, rice may be the best source of carbohydrate for patients with functional bowel disorder because of its low allergenicity and its nearly complete absorption in the small bowel.



#### Food to avoid?

##### A) Lactose

The prevalence of lactose deficiency varies considerably, from 5% of the population in England and Scandinavia, 15% among Caucasians in the USA, 40% in Italy, 75% in Greece and up to 100% in Africa and Asia.<sup>24</sup>

In a study including 427 healthy individuals, 101 people were found to be lactose maldigesters and 15% of both the lactose maldigesters and the digesters had IBS. One-third of those with IBS reported lactose intolerance to 20 g of lactose although only half were lactose maldigesters. The IBS patients who were not lactose maldigesters and reported lactose intolerance were described as having 'subjective lactose intolerance'. The percentage of lactose maldigesters with IBS was the same as in the healthy population, which was 24%, but the number of subjects reporting lactose intolerance was higher, 60% compared to 27% (P < 0.001). The author concluded that there was a strong relationship between subjective lactose intolerance and IBS.<sup>24</sup>

Individuals with and without IBS may report increased symptoms, including bloating, flatulence, abdominal discomfort, nausea and loose stools, following ingestion of lactose-containing foods such as milk and ice cream. This is attributed to low levels of the enzyme lactase in the intestinal mucosa, although symptoms correlate poorly with the lactase level and are often not reproducible following lactose ingestion.<sup>25</sup>

In uncontrolled, unblinded trials of lactose restricted diets, 40% to 85% of IBS patients reported significant improvement.<sup>24</sup> The improvement could be because some IBS patients have low levels of lactase in their intestinal mucosa, because some are intolerant to another component in the restricted diet, or because of a placebo effect. Lactase supplementation did not improve IBS symptoms in a small double-blind, placebo-controlled study.<sup>26</sup> Lactose malabsorption can be misdiagnosed as IBS and the two conditions can coexist.

##### B) Other poorly absorbed carbohydrates

Poorly absorbed carbohydrates include fructose, fructose-containing compounds, and sorbitol and other sugar-alcohols. A significant portion of the ingested carbohydrate may enter the distal small bowel and colon. This will increase the osmotic load and provide substrate for bacterial fermentation, which can result in gas production, a change in bacterial populations and a change in motility.

While there is evidence that fructose and sorbitol malabsorption are all common in IBS patients, malabsorption of these sugars is similarly prevalent in healthy volunteers.<sup>27</sup> Nevertheless, restriction of carbohydrates in subjects with IBS does seem to help improve symptoms.

##### C) Caffeine

Caffeine has often been cited as a gastric irritant. It has been concluded from an investigation that caffeinated coffee stimulated colonic motor activity and can cause diarrhea in normal individuals, the magnitude of which was similar to that of a meal and 60% stronger than water.<sup>27</sup>

Evidence directly relating caffeine and gastrointestinal symptoms suffered by IBS patients is lacking in the literature. Six studies in which patients improved on an exclusion diet and had recurrence of symptoms during open reintroduction of foods reported that coffee caused a recurrence of symptoms in 14% to 33% of IBS patients.<sup>28,29,30,31,32,33</sup> Four of the same studies reported that tea caused recurrence of symptoms in 18% to 28% of IBS patients and chocolate in 6% to 28%. All of these percentages are well within the range of placebo responses in IBS. There are no reported randomised, controlled trials of a reduced coffee or caffeine diet for treatment of IBS.

However, from the evidence available on the effect of caffeine as a gut stimulant and a gastric irritant, it would seem sensible to assess the intake of IBS patients and advice accordingly.

##### D) Gas-Forming foods

Most foods increase gas production in the colon due to fermentation, but the amount can vary by more than 10-fold depending on the food ingested and the individual. Foods reported to produce large amounts of gas include beans, Brussels sprouts, onions, celery, carrots, raisins, bananas, prune juice, apricots, wheat germ, and bagels.

There is no clear evidence that IBS patients generate more gas than normal individuals, but they may be more troubled by intestinal gas due to abnormal gas handling or increased gastrointestinal sensitivity.<sup>34</sup> There is no reported double-blind, controlled trial comparing a diet low in gas-producing foods with a control diet but, based on the above study, a trial of eliminating highly gas-forming foods may be appropriate.

##### E) Fat

Compared to controls, individuals with IBS may consume a higher proportion of energy as fat although the data are not consistent.<sup>35</sup> Dietary fat is a potent modulator of gut motor function. This has been shown by Serra et al, who conducted a series of studies that demonstrated that in contrast to healthy volunteers, IBS patients have increased intestinal sensitivity to fat and exhibited retention of gas that had been infused into the small intestine.<sup>35</sup> Following administration of enteral fat, the volume of retained gas increased from 289 to 505 mL. Infusion of fat into the duodenum slows gas movement in the jejunum and increases rectal sensitivity significantly more in patients with IBS than in normal controls.<sup>36</sup>

There has been no prospective, randomised, controlled trial of a low-fat diet for treatment of IBS.



### General Recommendation

The cause of IBS is unknown but it is unlikely that food is responsible for all the symptoms and this is not supported in the literature. A very large number (60 or more) of foods have been implicated in IBS, and many patients report intolerance to a large number of foods (40% of patients in one study had intolerance to six or more foods; in another study the mean number of foods patients were sensitive to was six).<sup>38</sup> Hence, it is not possible to recommend a standard diet for all IBS patients.

Prescriptive diets without prior assessment are of limited value as dietary manipulation needs to be geared to the individual patient. All dietary recommendations for IBS are based on the patient's symptom complex. Therefore, taking a detailed dietary history and the use of a food diary are important first steps. Dietary modifications can then be suggested if this assessment identifies potential dietary factors. It is important to take care that dietary modification does not lead to an inadequate diet. The tendency to an eating disorder might be present, particularly among female IBS patients. The dietitian has to assess the patient's global nutrient intake and to ensure that physicians' recommendations are not misinterpreted and that important nutrients are not omitted.

Modification of either eating habits (reducing meal size and/or the time of meals) or the composition of meals (avoiding specific food items) may benefit IBS patients. Take note of foods that seem to be followed by increased symptoms within 1 to 3 days, paying particular attention to milk, lactose, fructose, sorbitol, gas-forming foods, wheat, fat, and coffee.

The AGA guidelines recommend constipation should be first treated with an increase in dietary fiber. However, there are no diet recommendations to treat diarrhea or pain/gas/bloating.

Fiber-mixed, soluble, or insoluble-may have to be increased or decreased to affect stool size and character as well as gas production. Dietary fiber is most helpful in a patient with constipation. For some patients with constipation predominant IBS, improvement can be achieved by increasing the intake of soluble fiber by 10 to 20 g/day in the form of supplements such as ispaghula, psyllium, and probably other supplements and foods high in soluble fiber. Increasing the amount of insoluble fiber in the diet, especially in patients without constipation, may worsen IBS symptoms. Fibers which are commonly thought to be beneficial in IBS should be carefully used as they are able to induce or increase symptoms in IBS patients, potentially via gas production.

In patients with diarrhea predominant IBS, the intake of sugars such as fructose and sorbitol needs to be assessed and advice given regarding reduction of the intake of apple juice, soft drinks and sugarless chewing gum. It could be useful to assess the patient's intake of coffee, regardless of its caffeine content, and use of other stimuli. In cases of lactose intolerance, it is important to identify sources of lactose other than in dairy produce (e.g. food preservatives and drug additives) and teach patients to carefully study product labels in this respect.

Probiotic treatment is a promising strategy to treat patients with IBS. Although there are some trials which showed equivocal or inconclusive results, many studies have reported a trend towards an improvement in global symptoms with probiotics.

The diet that relieves symptoms will not be the same for each patient, and there are currently no reliable laboratory tests or other simple, clinically applicable methods to determine what dietary restrictions will be helpful for a particular patient. It can be frustrating for the patient to find that the initial prescription is not working, but manipulation of the foods and supplements can result in a rewarding outcome if monitored carefully.

### Conclusion

Food, diet and food supplements are an important, but poorly studied, aspect of IBS. Food undoubtedly precipitates symptoms in many IBS patients; the precise mode of this effect remains unclear and may vary from one individual to another.

Food is not responsible for all IBS symptoms but dietary manipulation targeted to individual IBS patients could help them to keep some control on well-being. By further understanding the mechanisms involved in dietary intolerance, it should be possible to optimise the benefits of this approach to treatment.

The role of food as an inducer of allergic or inflammatory responses in IBS deserves further study. While a sheer lack of good data currently precludes the provision of evidence based dietary advice to an individual IBS patient, recent studies provide good evidence for a role for certain specific probiotics and prebiotics in the management of IBS.

