Probiotics for Gut Health

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It is widely accepted that probiotics (beneficial microbes) improve the health of the intestine, but what is the evidence in specific conditions? This article will describe nine conditions that are improved by probiotics, listed in order of strength of evidence, with the strongest first.

Infectious Diarrhoea

Infectious diarrhoea is an intestinal disturbance caused by a pathogenic microbe. One of the body's responses to such an infection is to try to flush the microbe out of the intestine. This occurs by water flowing from the body into the intestinal space and by increased intestinal muscle contractions. With more water in the intestine and the content travelling more quickly, the person experiences fluid bowel movements, as well as stomach cramps as the intestinal muscles strain against the fluid.

In developed countries, infectious diarrhoea is much less common than it used to be, because of improved sanitation and hygiene. It usually resolves itself in three or four days, and therefore for most people in developed countries infectious diarrhoea does not cause great concern. It is more of an unpleasant nuisance, especially if it occurs on holiday. However, infectious diarrhoea is more serious in those who are vulnerable, including infants, the elderly, and the hospitalised.

In particular, young children are vulnerable to dehydration from the loss of fluid through diarrhoea, and this is why it is important to give them oral rehydration solution. Probiotics also have a role, because it is certain that they accelerate recovery from both viral and bacterial infection.

More than 25 randomised controlled trials (RCTs) have been undertaken on people with infectious diarrhoea, the majority with children. Almost every study has shown a positive benefit from probiotics. The duration of the intestinal diarrhoea was reduced on average by 31 hours.

Necrotising Enterocolitis (NE)

This is an intestinal condition that affects about 10% of infants of very low birth-weight. It is dangerous, because there is a death-rate of up to one-fifth of those affected. Nine RCTs have been undertaken involving 1,400 pre-term infants, and in every study there has been a substantially lower rate of NE in those consuming probiotics. On average, the rate was two-thirds lower than that of infants not consuming a probiotic.

Lactose Intolerance

The term ‘lactose intolerance’ refers to the inability of some adults to digest the sugar lactose, which is present in milk. Lactose is digested by the enzyme lactase, and if too little lactase is produced then the undigested lactose causes intestinal difficulties.

Most of the world's adult population are lactose intolerant, although they may be able to digest small amounts of milk (up to 25 grams a day) without difficulty. Greater amounts than this cause symptoms of excess gas, bloating, diarrhoea cramps, abdominal rumblings and flatulence. In severe cases, there may be nausea and vomiting.

The excess gas is probably caused by the resident gut microflora fermenting the lactose. The diarrhoea may be caused by an osmotic response to the lactose, leading to the maintenance of high water content in the faeces.

Numerous studies have shown better lactose digestion and less flatulence in lactose-intolerant people who have consumed live yoghurt rather than milk. Symptoms have been reduced by about two-thirds. The reason why yoghurt is helpful is because the two bacteria that turn milk into yoghurt, *Lactobacillus bulgaricus* and *Streptococcus thermophilus,* produce significant quantities of the lactase enzyme. They are able to digest lactose in the live yoghurt product, but also to continue such digestion in the small intestine once the yoghurt has been eaten. Furthermore, yoghurt moves more slowly along the intestine compared with milk, therefore allowing more time for intestinal lactase to digest lactose.

Freeze-dried probiotic products that contain strains known to produce the lactase enzyme may also help to reduce lactose intolerance.

Antibiotic associated Diarrhoea

Despite the huge benefits that antibiotics have provided since the Second World War in the treatment of bacterial infection, saving countless lives, they can produce a number of side effects. One is the tendency to promote the rise of resistant strains of bacteria and so reduce the effectiveness of the antibiotic. Another side effect is the tendency of antibiotics to disturb the gut microflora, making the person vulnerable to subsequent pathogenic infection.

Such an infection of the intestine usually leads to diarrhoea and, as such, it is described as 'antibiotic associated diarrhoea' (AAD). The proportion of people developing AAD after taking a course of antibiotics is about 20%. Many of such infections are quite mild, but others can be severe. In about one-fifth of cases of AAD, the microbial pathogen involved is *Clostridium difficile*. This can be a difficult pathogen to eradicate because it can form spores, which remain dormant and then grow again at a later date. *C. difficile* infection may also cause a serious condition known as pseudomembranous colitis.

There have been a number of studies in which probiotics have prevented AAD, although not all studies have shown probiotics to be effective. In the successful studies, probiotics were mostly taken at the same time as the antibiotic and usually continued for at least one week after completion of the course of antibiotics. In those studies, people taking probiotics reduced the risk of developing AAD by about two-thirds.

Ulcerative Colitis

Ulcerative colitis (UC) is a chronic condition affecting the large intestine, especially the sigmoid colon and the rectum. It involves persistent inflammation of the lining of the gut wall, leading to ulcers (open sores). The symptoms are severe diarrhoea and false urges to have a bowel motion. Sometimes blood, mucus and pus is found in the stool. There may also be crampy abdominal pain, tiredness and fever.

In the UK, there are about 90,000 people with UC. It most commonly starts during young adulthood, although it may start at any age. It is not an infectious condition. In severe cases, it may be necessary to surgically remove the whole of the large intestine.

Usually, there are periods when the symptoms are in abeyance. The goal of treatment is to control active disease and increase the time when the disease is in remission. Anti-inflammatory drugs are prescribed, but there is substantial scope for improvement of treatment.

Probiotics were considered as a support to standard drug treatment when it was found that the microbes that live on the gut wall surface (mucosa) were different in people with UC compared with the general population. The gut microflora in people with UC had fewer lactobacilli and bifidobacteria (which are probiotic bacteria), and more pathogenic strains of *E. coli*.

There have been eight RCTs involving people with UC and seven of these showed significant benefit. Of the seven successful trials, probiotics were shown to extend periods of remission or reduce active disease.

Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a common condition affecting 10-15% of the population. Like UC, it affects the large intestine, but unlike UC there is no apparent damage to the intestinal wall. Its cause is unknown, and the symptoms are: altered bowel habit (diarrhoea or constipation), bloating and flatulence, and abdominal discomfort relieved by the passing of wind or stool.

Treatment of IBS is often unsuccessful, although changes to diet sometimes help. One of the hypotheses about the cause is that people with IBS have 'low-grade' inflammation of the intestine, possibly arising from a bout of microbial infection of the bowel. This is thought to make the intestine 'hyper-sensitive'.

It is thought that an intestinal infection that was overcome by the body's immune system has led to a residual effect. It is as if the immune system has not fully turned off the inflammation required to defeat the pathogen. Supporting this explanation are the statistics that 25-30% of IBS patients have had acute infectious diarrhoea before developing their IBS. Also, such patients are more likely to have a 'leaky gut', whereby it is easier for microbes to cross into the gut wall and beyond. It is not therefore surprising to find that post-infective IBS patients have more lymphocytes (immune cells) in the mucosa of their intestine, indicating an inflammatory process at work.

Studies using probiotics have had mixed results in IBS, but the more recent studies have been positive. In those more recent studies, symptoms have reduced, especially bloating and flatulence. In one study, one probiotic species (*Bifidobacterium infantis*) reduced symptoms while another species (*Lactobacillus salivarius*) had little or no effect. It may be, therefore, that not all probiotics will help IBS. More large-scale studies should help clarify this question.

Gastritis and Stomach Ulcers

Helicobacter pylori is a bacterium that causes gastritis, which is an inflammation of the lining of the stomach. Such infection is very common, with about half of the world's population infected. In developed countries, it is present in about 20% of people under the age of 30, and in about half of those over the age of 60.

The great majority of infected individuals (about 85%) have no symptoms and are unaware of any infection. The symptoms of gastritis are abdominal pain, nausea and vomiting.

The standard treatment for eradicating *H. pylori* is the use of three drugs simultaneously. The need for three drugs indicates how difficult it is to eliminate the infection. Two of the drugs are antibiotics and increasingly there are *Helicobacter* strains appearing that are resistant to those antibiotics. In such cases, another antibiotic is added to the drug treatment, making it a 'quadruple' therapy.

As it involves multiple drugs, the treatment is very expensive, and in about 10% of cases it fails. Side effects, such as diarrhoea, vomiting, nausea, and taste disturbance, are also common with the drug treatment.

Probiotics have been tried, but have been unsuccessful in eradicating *H. pylori* when used alone. However, several studies have found that if probiotics are used in conjunction with the standard drugs, the rate of eradication is greater than by drug therapy alone. Furthermore, the incidence of adverse side-effects is halved.

Constipation

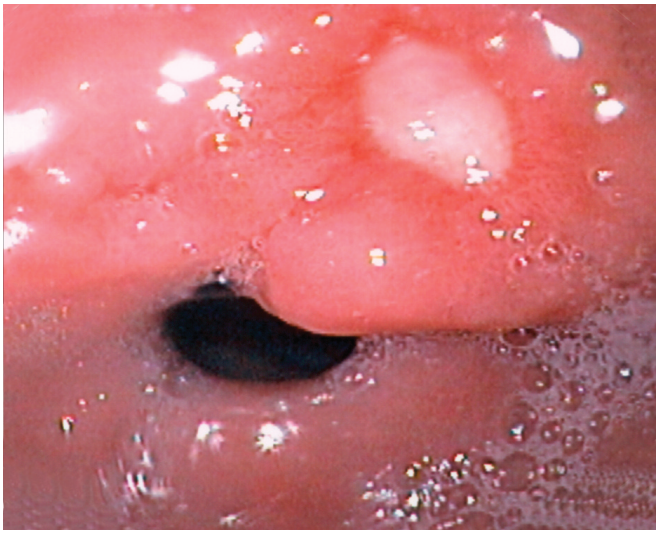
Constipation is the infrequent and difficult passing of hardened stool. Based on surveys in developed countries, the proportion of the population suffering from constipation at any one time is about 15%. The proportion among women is greater. Not only does constipation give a general feeling of abdominal discomfort, but straining to pass stool may put pressure on the anal area with the potential for negative consequences, such as haemorrhoids (piles).

A major cause of constipation is the shortage of fibre in the diet. Other factors may be lack of exercise, or the consumption of certain drugs, such as antidepressants.

The main approach in relieving constipation is to increase the amount of fibre in the diet, by eating more vegetables and fruit, plus wholemeal bread and whole grain breakfast cereals. The only disadvantage with a high fibre diet is that sometimes it leads to uncomfortable bloating and flatulence, which is excessive gas in the intestines produced by some of the microfloral bacteria.

In a small proportion of people, a high fibre diet does not fully resolve the constipation problem. In such cases, there are various medicines that have a laxative effect, but laxatives should not be used for long periods as they may encourage a weakening of natural gut muscle contractions. Relief of abdominal pain that occasionally arises from constipation is something of a problem, because the main painkiller drugs, the non-steroidal anti-inflammatory drugs (NSAIDs), have a constipating effect.

There are several studies which show probiotics relieving constipation. The improvements were in the range of a 20-50% increase in the number of bowel movements a week.



The majority (85%) of individuals with *H. pylori* infection are unaware of their infection

Colo-rectal cancer

One of the most common areas of the body to be affected by cancer is the large intestine, especially the latter part of the colon and the rectum. The cause of colo-rectal cancer is not clear, although diet is believed to be a factor. The gut microflora may also be involved. The mixture of microfloral species in the stool of people at high risk of colo-rectal cancer was found to differ from those at low risk.

Some types of bacteria in the gut microflora convert substances into potential cancer-causing molecules. They do this through the use of certain enzymes. In laboratory experiments, probiotics have been shown to reduce the production of such harmful enzymes.

Animals at high risk of developing colon cancer were given probiotics and the researchers looked for the appearance of tumours, or early signs of damage to the intestinal surface (aberrant crypt foci – ACF). Ten animal studies have been undertaken and all demonstrated a protective effect from the probiotics, with a reduction of almost 50% in the numbers of ACF appearing.

One human study tested the effect of probiotics on patients with colon cancer or who had previously had malignant polyps removed. A probiotic and prebiotic mixture was consumed for 12 weeks, and blood and other samples were taken. The probiotic group had reduced amounts of substances that are believed to be markers for cancer risk.

Conclusion

The information in this article is summarised in Table 1.

	Positive RCTs*	How strong evidence?	Average benefit	Other comments
Infectious diarrhoea	> 25[1]	Very strong, with almost all studies positive[2]. 2,000 participants.	Duration of diarrhoea reduced by 31 hours[3].	Most studies with children. Reduces both viral and bacterial infection.
Necrotising enterocolitis (NE)	9[4]	Strong, with all studies positive. 1,400 participants.	Rate of severe NE reduced by two-thirds.	NE is dangerous condition common in pre-term infants.
Lactose intolerance	> 20[5]	Strong, with yoghurt the most effective probiotic.	Lactose and symptoms reduced by two-thirds.	Yoghurt bacteria (L. bulgaricus and S. thermophilus) very helpful.
Antibiotic associated diarrhoea (AAD)	13[6]	Good, but some studies failed.	AAD rate reduced by half.	Higher dosage more effective (i.e. >5 billion cells per day).
Ulcerative colitis	7[7]	Good, but one study failed.	Prolonged remission equivalent to standard drug.	Some evidence of active disease reduction.
Irritable bowel syndrome (IBS)	7[1,8]	Mixed results, but more recent studies positive.	Symptoms reduced, especially bloating and flatulence.	More large studies needed.
Gastritis and stomach ulcers	3[1,9]	Similar number of positive and neutral results.	Standard drugs more effective in eliminating H. pylori.	Consistently fewer side effects from drugs.
Constipation	5[10]	Moderate improvement.	20-50% increase in bowel movements.	Prebiotics may also help.
Colo-rectal cancer	1[11]	Some markers reduced. Animal studies positive.	Cancer risk halved in ten animal studies[12].	Prebiotics may also help.

* Number of randomised controlled trials (RCTs) that have given positive results for probiotics.

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Peter Cartwright has 17 years experience of working for patient and self-help associations, as Assistant Director of the National Association for Colitis and Crohn's Disease, Director of the British Stammering Association and National Development Officer of the Self-Help Alliance. Currently he is a Trustee of the Bladder & Bowel Foundation. Peter has an MSc in Microbiology and an MA in Sociology. He is the author of three books for the general public on intestinal health, including *Probiotics for Crohn's and Colitis* and has given over 40 lectures on probiotics to doctors in 10 countries.

Probiotics International Ltd is one of the largest manufacturers and suppliers of probiotics for the healthcare, veterinary and animal health industry. Products are marketed under the brand name of Protexin.

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