

Probioticbulletin

An update for healthcare professionals

Probiotics & irritable bowel syndrome

The rationale, the evidence and use in practice.

The National Institute for Health and Clinical Excellence (NICE) has produced new draft guidelines with regard to irritable bowel syndrome (IBS).

These state that “*Primary care clinicians should not discourage people with IBS from trying specific probiotic products. If people with IBS choose to do this, it should be for at least four weeks, and they should monitor their effect. The probiotic should be taken at the dose recommended by the manufacturer.*”



IBS is a condition that affects approximately 15% of the population. Diagnosis is based on symptoms and the exclusion of more serious pathology. Symptoms include abdominal pain and bloating, diarrhoea, constipation and flatulence. Although not life-threatening, it can severely disrupt a person's day-to-day life. The biggest challenge with IBS is that the precise aetiology is unknown and the disorder is multi-factorial; possibly involving inherited susceptibility, lifestyle factors such as stress and/or an unhealthy gut flora. Often the reason for the disorder is not known, and individuals may try a range of different lifestyle strategies or dietary changes in order to improve their quality of life.

The rationale

Probiotics are thought to benefit people with IBS by favourably altering the gut flora, and through immune support.

Madden & Hunter (2002) analysed the faeces of people with IBS and found they contained more streptococci, *E. coli* and clostridia and fewer bifidobacteria and bacteroides. Factors likely to cause an altered gut flora include:

- post-infective IBS
- post gastro-surgery
- use of antibiotics
- gastroenteritis

Antibiotics alone may wipe out as much as 60% of the gut flora, making the gut susceptible to colonisation with the less beneficial or even harmful species. Therefore

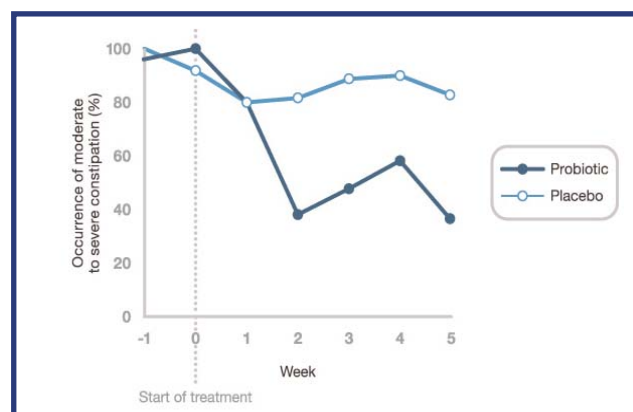
one theory of probiotic mechanism for IBS benefit is by modifying the microflora to a more favourable microbial population.

Evidence also suggests that probiotics may normalise inflammatory cytokine levels; for example Hart *et al* (2004) studied VSL#3 (a product containing a mixture of eight probiotic strains) and showed it promoted the secretion of IL-10 (anti-inflammatory) and suppressed IL-12 (pro-inflammatory) cytokines. Other studies have shown that IBS patients have an increased number of mast cells in their colonic nerves. Mast cells secrete tryptase and histamine which may contribute to the development of abdominal pain (Andresen & Baumgart 2006).

The evidence

There are numerous probiotic research studies on IBS, including those investigating constipation-dominant IBS. At the time of writing, a search on PubMed yielded 155 results using the term “irritable bowel syndrome and probiotics”.

An example of a constipation study is one reported by Koebnick *et al* (2003), with 70 volunteers who drank one bottle of a probiotic drink every day (containing 6.5×10^9 *Lactobacillus casei* Shirota) or a placebo for four weeks. Those in the treatment group reported a significant improvement in the severity of their constipation (see graph).



A more recent study investigated the use of a multi-species probiotic mixture on patients with more general symptoms of IBS. Kajander *et al* (2008) found that distension and abdominal pain improved in patients taking the probiotic compared to those on placebo, however no effects were observed on inflammatory markers.

Continued on page 2...

From page 1...

Probiotic benefits must be proven on a strain by strain basis. People with IBS may have to try a number of different products before finding one of benefit to them.

Difficulties of an IBS trial

One of the problems encountered whilst conducting any IBS trial - regardless of whether it is with probiotics - is the placebo effect; it has been estimated that there is a placebo response of 40% - 45%, making it harder to achieve a significant difference in these trials. Another problem is that due to the many possible causes of IBS, one treatment may work for a particular group and not for another. Although there are many published studies on probiotics and IBS, these differ widely in trial design, the type of strain investigated and the number of probiotic bacteria consumed daily – all of this makes it harder to draw strong conclusions and make recommendations.

Practicalities of using probiotics

The advice that many healthcare professionals (HCPs) give to patients when talking about probiotics is that it doesn't hurt to try them. A range of commercial probiotics are readily available and the well known products have scientific evidence to support survival through the gut, and safety records. If no benefit is seen after four weeks, one can either switch to another product, or try taking two bottles per day.

It is clear from the number of papers being published, that evidence is beginning to accumulate in this area but also that further large-scale, double-blind placebo controlled trials are needed, with harder and more objective endpoints. It is still worth remembering that there is a certain amount of anecdotal evidence for probiotics and IBS. For a fuller review of this area email science@yakult.co.uk to request your free copy of our new booklet '*An Introduction to the Potential of Probiotics in Primary Healthcare*'.

- Andresen V & Baumgart DC (2006) Role of probiotics in the treatment of irritable bowel syndrome: Potential mechanisms and current clinical evidence. *Int J Probiotics & Prebiotics* **1**, 11-18.
- Koebnick C *et al* (2003) Probiotic beverage containing *Lactobacillus casei* Shirota improves gastrointestinal symptoms in patients with chronic constipation. *Can J Gastroenterol* **17**, 655-659.
- Hart AL *et al* (2004) Modulation of human dendritic cell phenotype and function by probiotic bacteria. *Gut* **53**, 1602-9.
- Kajander *et al* (2008) Clinical trial: multispecies probiotic supplement alleviates the symptoms of irritable bowel syndrome and stabilizes intestinal flora. *Aliment Pharmacol Ther* **27**, 48-57.
- Madden JAJ & Hunter JO (2002) A review of the gut microflora in irritable bowel syndrome in patients and the effects of probiotics. *Br J Nutr* **88**, S67-72.

Centre of the Cell - Science team day visit

Centre of the Cell is a new interactive science education centre for children, young people, teachers and families. It is based in a working bio-medical research laboratory at Queen Mary, University of London. Although it doesn't open until later in the year the science team were lucky enough to be invited for a preview and a tour of the cell.



How the interior of the cell will look when completed.

The main part of the experience happens in a giant "cell" overlooking working laboratories. Children walk across a glass walkway into the cell. Once inside, the nucleus of the cell opens up to reveal interactive experiences including games, films and theatre. Each session lasts 1 hour 30 minutes and is free of charge. There is also an excellent website www.centreofthecell.org that works alongside and independently of the visit. It includes teaching tools, more interactive learning and details on how to book a tour.

We were shown round the cell and then given a short talk by Professor Fran Balkwill, who explained that the resources will help children understand cell science and how the latest developments in medical research affect them and their community.



*Members of the science team.
Left to right: Dang, Deirdre, Hannah, Miki and Becky*

We were particularly interested in a game that teaches children about good and bad bacteria. The children have to zap bad bacteria and leave the good ones alone; unfortunately this was still being made so were unable to play on it ourselves! After visiting Centre of the Cell we feel this is an excellent way to teach children about cells, the human body and microbiology.

Visit www.centreofthecell.org to book a tour.



Gut Week 2008: Love your gut - Could you share your expertise?

This summer marks the 10th anniversary of Gut Week – the annual digestive health awareness campaign. Organised in association with charities Core and The Gut Trust, the campaign has continually gathered momentum over the past nine years, attracting support from a wide range of respected figures and organisations.

Now a key fixture in the healthcare campaign calendar, Gut Week has, to date, provided valuable digestive help and advice to over 110,000 people via a dedicated website and specialist nurse helpline.

This year Gut Week will take place from 14th to 20th July - and we're asking for your help. Gut problems affect many people, in 2006; two million people in the UK were diagnosed with a digestive disease/condition.¹



Yakult and the Gut Week campaign are committed to educating people about gut health – and if you are a healthcare professional, you could help us by displaying Gut Week posters in your health centre and/or sharing your expertise with regional media via press interviews. If you would be willing to help us during this week please email Jane at jpower@yakult.co.uk - we would really appreciate your support!

For more information, visit the new comprehensive gut health website www.loveyourgut.com (from end April 2008) or www.gutweek.org.uk

¹ Primary diagnosis, Hospital Episode Statistics, 2005/06. DoH, England

University of Reading Postgrad Student Award

Last year we introduced a new award at the University of Reading for best post-graduate student within the School of Food Biosciences. The award is intended to inspire and encourage young researchers, and is judged on the quality of their research by the university.

In December 2007, the award was given to Trevor George, chosen for his excellent contribution to the university. Trevor has published a paper, a peer reviewed proceedings paper and also presented at four scientific meetings in the last year. He was presented with the award and the prize money at the department dinner in December by Professor Bob Rastall, Head of the Food Biosciences department.



Trevor George receiving his award from Prof Bob Rastall

Yakult

UK Symposium 2008

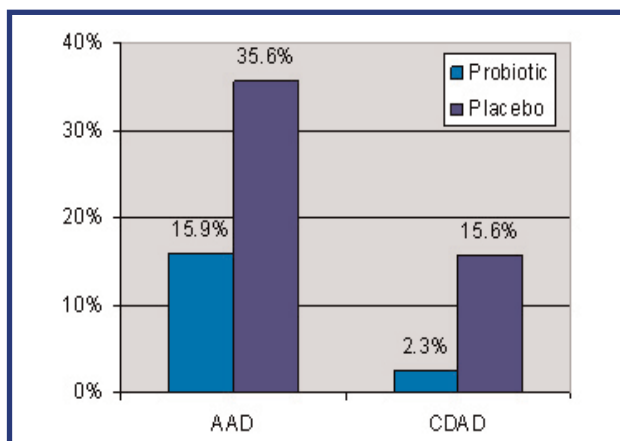
Following on from our successful symposium in 2006, we are pleased to announce that on Tuesday 21st October we will be holding another symposium themed *Probiotic Relevance: Putting Theory into Practice*. The symposium will be held at 76 Portland Place, London and will bring together eminent scientists and clinicians to review and update you on the latest probiotic research. The programme also includes a closing discussion session – your opportunity to ask the experts! The day will close with wine and nibbles.

Email science@yakult.co.uk for more details and to reserve your place. There are generous price discounts for NHS staff and early bird bookings.

Research round up

Probiotics and *Clostridium difficile*

This study is the latest in a long line of trials indicating that probiotics may be beneficial for hospitalised patients taking antibiotics. In the study, involving 89 patients, those in the probiotic group were given a fermented milk drink containing 50×10^9 CFU (50 billion) of the probiotic strains *Lactobacillus acidophilus* and *Lactobacillus casei*. Significantly less patients developed antibiotic-associated diarrhoea in the probiotic group compared to the placebo group ($p=0.05$). The incidence of *Clostridium difficile* associated diarrhoea was also lower in the probiotic group, although not significantly.



- Beausolei M *et al* (2007) Effect of a fermented milk combining *Lactobacillus acidophilus* CL1285 and *Lactobacillus casei* in the prevention of antibiotic-associated diarrhea: A randomized, double-blind, placebo-controlled trial. *Can J Gastroenterol* **21**, 11, 732-735.

Can probiotics reduce gastrointestinal symptoms associated with stress?

Stress can result in many gastrointestinal symptoms, such as bloating, constipation and diarrhoea; in fact 60% of British adults will experience digestive problems when undergoing stressful situations (Gut Omnibus survey 2006).

Previous studies have shown that the balance of our gut flora is linked with stress, with one study showing that stress appeared to result in a reduction of bifidobacteria and an increase of the harmful bacteria such as clostridia (Lizko NN, 1991).

New results published in the journal *Nutrition Research* showed that a probiotic mix of *Lactobacillus acidophilus* Rosell-52 and *Bifidobacterium longum* Rosell-175 significantly reduced abdominal pain and nausea or vomiting in stressed subjects. In the double-blind trial, 75 volunteers were given a placebo or 3×10^9 CFU of the probiotic daily for three weeks.

- Gut Omnibus Survey Tickbox.net, July 2006; 1,281 respondents.

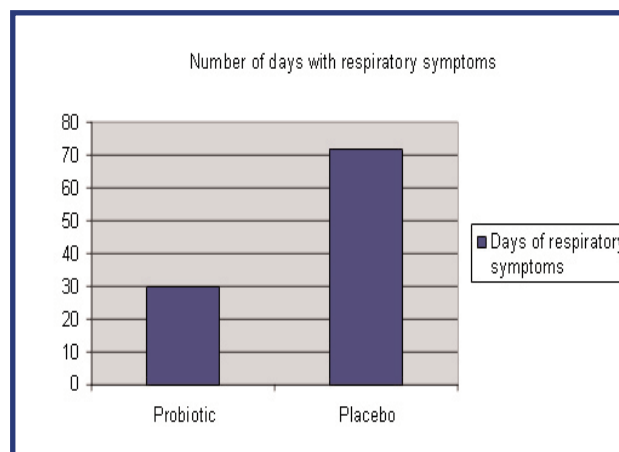
- Lizko NN (1991) Problems of microbial ecology in man space mission, *Acta Astronaut* **23**, 163-9.

- Diop L *et al* (2008) Probiotic supplement reduces stress-induced gastrointestinal symptoms in volunteers: a double-blind, placebo controlled, randomized trial, *Nutr Res* **28**, 1-5.

Possible probiotic benefit for endurance athletes

This Australian study received a lot of press coverage, with headlines such as "Probiotics 'protect top athletes'" (BBC news online 14th February 2008). The double-blind, placebo-controlled trial investigated the immune benefits of a daily probiotic (*Lactobacillus fermentum* VRI 003 at 1.2×10^{10} CFU) in 20 healthy elite runners.

Elite athletes are known to be prone to infections as a result of exercise-induced immunosuppression. As there is evidence to suggest that probiotics may stimulate mucosal immune function the researchers hypothesised that a probiotic might reduce the incidence, severity and/or duration of respiratory illness in these endurance athletes.



The subjects in the probiotic group experienced significantly less respiratory symptoms compared to the placebo group ($p = 0.00006$, see graph). Illness severity was also lower in the probiotic group. Although there was no significant difference in salivary IgA, IgA1, IL-4 and IL-12 between treatments, there was a greater change in whole-blood culture IFN-alpha compared with the placebo, suggesting that maintaining IFN-alpha levels could be the mechanism contributing to the reduction in respiratory symptoms.

The results of a small, pilot trial investigating immune benefit with *L.casei* Shirota in elite athletes (cyclists) conducted at Loughborough University by Professor Mike Gleeson will be presented at the 13th European College of Sport Science annual meeting in Portugal in July.

- Cox AJ *et al* (2008) Oral administration of the probiotic *Lactobacillus fermentum* VRI-003 and mucosal immunity in endurance athletes, *Br J Sports Med*; Epublication 13 February 2008.



Probiotics in the spotlight

By Dr Linda Thomas, Science Manager of Yakult UK

Probiotics featured in the BBC 2 Horizon programme: 'Prof Regan's Supermarket Secrets', in which the science and marketing of various products with above average technical claims were examined. A pot marked

'Probiotics - Live Forever' started the section on probiotics and Professor Glenn Gibson spoke positively and constructively about probiotic evidence and health benefits – even he and all his family take them.

The programme then presented a study where 21 volunteers drank an anonymous probiotic for three weeks, and measured any metabolic changes in the gut. Only one set of results was discussed: in the study, levels of a harmful clostridial metabolite, para-cresol, were not always changed for the better after taking the probiotic, leading to the conclusion that probiotics were not relevant for healthy people. That is a conclusion I can certainly argue against, but it was the statement that probiotics appeared to increase the presence of creosote in the stomach that was clearly designed to be sensational.



The fact that the findings of this uncontrolled study did not agree with numerous published, controlled studies demonstrating efficacy, safety and benefit of probiotics to the public was ignored. The references below are particularly relevant to this programme since they describe studies that found significant reduction of para-cresol associated with consumption of the probiotic *L. casei* Shirota.

■ De Preter V *et al* (2004) The *in vivo* use of the stable isotope-labelled biomarkers lactose-[¹⁵N]ureide and [²H₄]tyrosine to assess the effects of pro- and prebiotics on the intestinal flora of healthy human volunteers, *Br J Nutr* **92**, 439-446.

■ De Preter *et al* (2007) Effects of *Lactobacillus casei* Shirota, *Bifidobacterium breve*, and oligofructose-enriched inulin on the colonic nitrogen-protein metabolism in healthy humans, *Am J Physiol Gastrointest Liver Physiol* **292**, 358-368.

Where to find us

May and June are going to be very busy months for us; come and meet us with our stand at the following conferences:

- Primary Care Live, Birmingham, 21st – 22nd May
- BDA conference, Liverpool, 17th - 19th June
- HPA conference, London, 26th - 27th June
- Nutrition Society Summer Meeting, Nottingham, 30th June - 3rd July

How we can support you

- free literature – new primary care booklet
- free educational DVD of digestive system
- Probiotic Bulletin
- supply of product for limited trial period
- Yakult Symposium 21 Oct 2008, London
- free educational talks by our team of nutritionists and dietitians
- advice on probiotics
- dedicated website - www.yakult.co.uk/hcp

*subject to agreement

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