Probiotics – A proactive approach for community health

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The intestinal microbiota is big news...

We are born wholly human but die 90 per cent microbial[1] because, immediately after birth, the sterile gut starts to develop what will become a vast and complex microbial population. Throughout life, the healthy human host and the microbiota constantly communicate with each other, maintaining what should be a mutually beneficial relationship.

Our understanding of this huge intestinal ecosystem is rapidly increasing as new analytic methods in microbiology develop. Pioneering work from the Human Microbiome Project[2,3] show that the variation in intestinal microbiota falls into three distinct classes ('enterotyopes') unrelated to age, gender, nationality or diet.[4] This has exciting implications – could your enterotype indicate your personal risk of disease or determine which medication or diet will be most effective for you? Even more personalised information could come from looking at specific bacteria within the intestines, which are influenced by the environment, lifestyle and diet. Getting to know one's intestinal microbiota could lead to a truly personalised healthcare approach in the future.

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Health in the community

People in the community seek healthcare for a multitude of reasons, from antibiotic treatment or vaccinations, to recurrent infections and age and lifestyle-related issues. Gut problems are especially common in primary care. Irritable bowel syndrome (IBS) affects 10-22 per cent of the population[5] and constipation affects a myriad of people as 40 per cent of pregnant women, 34 per cent of four to seven year old children and approximately one in five older people in the community will have symptoms of constipation.[6, 7]

All these health problems have been the focus of probiotic research. Here we provide a brief overview of the current evidence in key areas relevant to community health.

Irritable bowel syndrome (IBS)

IBS patients often have gut dysbiosis; for example, they may have decreased levels of lactobacilli in the gut[8] or small intestinal bowel overgrowth (SIBO), which occurs in up to 78 per cent of cases and has been linked to IBS development.[9, 10] This suggests that therapies targeting the intestinal microbiota may be beneficial. A small open trial with *Lactobacillus casei* Shirota, for example, showed reduction of SIBO that was associated with reduced symptoms.[11] Overall, most reviews conclude that there is good evidence for probiotics in IBS but more research is needed, particularly as benefits are strain-specific and may vary according to the predominant symptom (e.g. pain, flatulence, bloating, diarrhoea, etc).[12-14] NICE and BDA guidelines[15, 16] recommend that IBS patients wanting to take probiotics, should try for at least four weeks and monitor effects. This is sensible advice; patients can see for themselves if there is benefit to their set of symptoms and if a particular probiotic does not give improvement, consider trying another, perhaps of a different species or genus.

Constipation

The intestinal microbiota helps stimulate gut motility by lowering pH, due to production of short chain fatty acids and metabolism of bile acids, and producing neurotransmitters.[17] A large proportion of faecal bulk comprises bacteria.[18] Thus, there are many mechanisms whereby probiotics could help with constipation. For example, human studies with *Bifidobacterium lactis* DN-173010 show reduction of intestinal transit, independent of change in faecal bile mass or bile acid content.[19]

Evidence of probiotic benefit has reached the level where it is addressed in scientific reviews.[20, 21] Professor Eammon Quigley concluded this year that the available data suggest a favourable effect with *B. lactis* DN-173010, *L. casei* Shirota, and *Escherichia coli* Nissle on defecation frequency and stool consistency in adults but more research is needed.

Antibiotic-associated diarrhoea (AAD)

Antibiotics can have a profound and lasting effect on the intestinal microbiota, sometimes with immediate consequences.[22] Diarrhoea can result in five to 39 per cent of patients (particularly people >65 years in hospital), often due to outgrowth of *Clostridium difficile*. This can be an extremely serious disease: it increases healthcare costs, can be recurrent and extends inpatient stays. As antibiotics are usually first prescribed by a GP, can strategies be adopted in primary care that might help?

C. difficile rarely affects healthy adults as its growth is kept in check by the normal bacterial population of the intestine.[23] Probiotics can help ensure this protection is effective even after antibiotic treatment. There are now several large scale studies reporting probiotic benefit for AAD, and this is covered in numerous reviews.[24, 25] A study in the UK reported preventive effects with *L. casei* DN-144 001,[26] and this year Dr Hickson reviewed probiotic evidence for *C. Difficile*,[27] noting there were also good results with *L. rhamnosus* GG and *S. boulardii* (although the UK guidance raised issues of safety for the latter).[28] Other strains with human study evidence include *L. acidophilus* CL1285, and *L. casei* Shirota.

Adjuvant effect

Modulation of the immune system by probiotics is a well-established concept, known to be strain-dependent. Human studies have shown probiotic adjuvant effects with viral vaccines (e.g. influenza, hepatitis) and vaccines comprising attenuated bacterial pathogens (e.g. *Salmonella*, cholera, *Pneumococcus, Haemophilus*).[29-32] In most cases, the probiotic was consumed for a period of four to 13 weeks before vaccination. Current evidence is more promising for lactobacilli compared to bifidobacteria; effects seem stronger with viral vaccines and the strain must be live.

Susceptibility to infection

Stress, ill health and ageing are factors that cause transient depression of immune function, decreasing resistance to common infections. Athletes are good examples. Their increased physical and psychological stress, travel and competition mean they easily succumb to colds. Human studies showing reduction of incidence, duration and/or severity of colds have been conducted with *B. lactis* BB-12, *B. lactis* HN019, *Lactobacillus* GG, *L. casei* DN-114001, *L. casei* Shirota, *L. fermentum* VRI-003, *L. reuteri* ATCC 55730 and mixtures of probiotics +/- vitamins.[33-35] Subjects included students with exam stress, military cadets undertaking intensive training, elite athletes and older people.

Allergy

Reduced exposure to microbial allergens in early childhood is one theory explaining the rise in allergic disease in the western world. Children with allergies have also been shown to have an aberrant gut flora[36] so probiotic research has focussed on trials with mothers and babies with an atopic family history, so that the immune system can be targeted in its first stage of development. Results have sometimes conflicted but evidence is strongest for

children with atopic eczema, particularly with lactobacilli such as *L. rhamnosus* GG.[37] There is less evidence with adults but a recent trial with *L. casei* Shirota, for instance, showed down-regulation of the allergic response in adult hayfever sufferers.[38] Further research is ongoing to confirm clinical benefit.

And finally...

The current regulations on functional foods may, at least temporarily, restrict claims made for probiotic foods and supplements. This increases the importance of the healthcare professionals who are able to access and understand the supporting evidence for probiotics and, therefore, give informed advice to patients.

To understand which products to recommend and for what health conditions, look for the following: scientific evidence for specific strains or products; data which show that the strain survives transit through the gut; and human studies demonstrating one or more health benefits. And because probiotic benefits are strain-specific, look for the full name of the probiotic strain (i.e. genus, species, strain designator) on the label – it is difficult to check the supporting science without knowing this.

And finally, keep an eye on emerging areas of research, particularly in obesity-related disorders, liver disease, mood and behaviour, and urogenital infections.

> "... a recent trial with L. casei Shirota, for instance, showed down-regulation of the allergic response in adult hayfever sufferers.[38]"

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