Dr Bengt Jeppsson discusses the research into gut bacteria that could help to relieve the strain of the age-related illnesses which are increasingly impacting health services worldwide.

To begin, could you explain how you came to develop an interest in the health benefits of probiotics for elderly populations?

This project started a long time ago in a completely different area that dealt with patients in intensive care units suffering multiple organ failure. This is a group of patients that usually have complications following surgery or trauma; or else have undergone other therapies such as oncologic treatment. They exhibit a severe inflammatory process that leads to the failure of organs outside the site of injury, usually starting with the lungs, then kidneys and later the heart and gastrointestinal (GI) tract.

The failing respiratory, kidney and heart functions can be supported, but many patients continue to exhibit a state of severe inflammation which turns into sepsis. All the patients involved in this work were on heavy antibiotics, but no focus for the infection could be found. It was then proposed that perhaps the gut is the origin of this multiple organ failure; with the intestines non-functional as a result of paralysis, breakdown of the intestinal barrier and leaking of bacteria or bacterial products to organs outside the gut. In order to combat this condition we focused on the health-promoting gut bacteria lactobacilli and bifidobacteria.

What are some of the most common GI issues that can arise in older age, and to what extent do these impact health and quality of life?

Malnutrition is a big problem with increasing age, and its origins are multifactorial: difficulty swallowing, poor absorption because of mucosal atrophy and constipation all play a role. Many conditions associated with increasing age are disease-related, but gut malfunction, muscle waste and poor immune function seem to be age-related. These afflictions lead to immobility, weight loss and increased risk of infection; as well as generally leading to a poorer quality of life.

With our knowledge of gut microflora and its importance for gut and immune function, it was easy to see the benefits of using probiotics in elderly patients. Furthermore, I thought that our knowledge of alterations in gut bacteria was insufficient, owing largely to the difficulty of studying flora in population. As well as such studies being highly labour intensive, microflora can be affected by many factors that are hard to standardise, such as diet and mobility.

It has been reported that 10-20 per cent of residents in nursing and residential homes for the elderly are receiving antibiotic therapies. How could this impact GI microflora?

We know that a simple course of ordinary antibiotics for upper respiratory infection or urinary tract infection will upset the microbial balance for several months, and during this time the gut mucosa may be exposed to pathogenic bacteria that can dominate and have a negative impact on the body. There is a strong need to decrease the use of antibiotics in general, but especially for the elderly. Doing so will help reduce problems of diarrhoea, as well as clostridial infections which are difficult to manage and may force the temporary closure of patient wards. Then, of course, we have the major problem of emerging multi-resistant bacteria. We can limit these challenges through restricted use of antibiotics, strict hygiene among staff and perhaps the use of probiotics in certain conditions.

Could you outline the central aims of your current project; what are the anticipated applications?

With the above in mind we wanted to design a probiotic for elderly patients that stimulates immune function and reduces the atrophy of gut mucosa to facilitate absorption and alleviate constipation. Gut microbiota have been studied very little but there are some reports that in old age there is a general decrease in bifidobacteria and lactobacilli. We have a long tradition of working with lactobacilli and know their behaviour in the human GI-tract, so we can easily identify and handle them in a clinical situation.

We hope that a new product specifically designed for elderly patients will improve their GI function. We know that GI problems are very common, but are not talked about much; it is not good dinnertime conversation, after all.
The benefits of bacteria

Researchers at Lund University and the bioscience company Probi in Sweden are developing a probiotic drink to help restore the diverse populations of microflora in the gut and combat the onset of age-related disease.

As we age, our risk of suffering from a variety of diseases increases hugely. Alterations to the body’s physiological processes that occur around the time someone enters their seventies open the door to conditions such as cancer, cardiovascular disease, Type 2 diabetes and dementia. With the elderly population growing across the globe, it is critical that coping strategies are developed to handle the burden on healthcare systems that is expected to result from universally rising incidences of age-related disease.

Studies of patients suffering multiple organ dysfunction syndrome (MODS) have led scientists in Sweden to focus their attention on microflora in the gastrointestinal (GI) tract in their efforts to combat the sharp rise in age-related physiological alterations. It is now known that the interactions between the gut’s diverse populations of microflora deeply affect the function, inflammation and immune response of the GI tract, implicating them in the initiation of MODS. Just as states of disease can be characterised by reduced levels of microflora diversity, old age also leads to a population shift in favour of harmful bacteria like Escherichia coli. Maintaining a normal, balanced bacterial interplay in the GI tract could therefore help reduce the inevitability of age-related diseases.

A different view

Dr Bengt Jeppsson, Professor of Surgery at Lund University in Sweden and a Fellow of the Royal College of Surgeons, is using the lessons learned from patients with MODS to develop a method for supplementing probiotics in the elderly. A co-founder of the Swedish biotechnology company Probi, Jeppsson is scaling down his duties at Lund University to focus on the company’s probiotic drink products, an area greatly benefiting from his capacity as a consultant and his contribution to clinical testing.

Maintaining a balanced bacterial interplay in the gut could help reduce the inevitability of age-related diseases

The development of a dietary method of treatment has naturally brought Jeppsson into contact with disciplines which are less surgical in nature but fundamental to the project’s success nonetheless. Professors Göran Molin and Siv Ahrne of Lund University’s Department of Food Technology, Engineering and Nutrition provide a perspective on probiotics that medical microbiologists lack. “Food microbiologists have the ability to work with bacteria that, because they are non-pathogenic, are of no interest to medicine,” explains Jeppsson. Even experts at the Swedish University of Agricultural Science (SLU) have come into the fold as the project begins to explore the uses of fruit and vegetables in creating a drink to promote diversity and balance among the gut’s microflora.

Lactobacillus plantarum

Enterobacteria like E. coli induce inflammation via the upregulation of proinflammatory cytokines which decrease the phagocytic activity of granulocytes. In this state the risks of disease are greatly enhanced and a cause for concern in elderly patients as old age leads to the occurrence of low-level, continuous inflammation. To counteract this mechanism, Jeppsson aims to promote bacteria from the Lactobacillus genus to test their anti-inflammatory qualities. With the ten Lactobacillus species occurring most frequently in samples of gut mucosa being made available for consumption, finding the best probiotic contender has been a very hands-on approach. Taking the first drink, Jeppsson and his colleagues later identified from their own gut mucosal biopsies Lactobacillus plantarum 299 (Lp299v) as the bacterium to follow. An inhabitant of lactic acid-fermented cereals, fruits and vegetables, Lp299v is well known for its ability to break down tannins to anti-inflammatory and antimicrobial compounds. This microorganism is a tenacious coloniser of the GI-tract, and its role in mucin production, bacterial translocation, inflammation and the immune system helps it to suppress the growth of potentially pathogenic bacteria. Heightened levels of imbibed lactobacilli drop off when their consumption is stopped, allowing a return to the gut’s bacterial status quo.
BETTER FOOD FOR THE ELDERLY?
PROBIOTICS WITH ANTI-INFLAMMATORY ACTION

OBJECTIVES
To design a probiotic for elderly patients that stimulates good gastrointestinal health and function, as well as reducing the need for antibiotics.

KEY COLLABORATORS
Probi Ltd., Sweden
Professor Göran Molin, Professor Siv Ahrné, Dr Åsa Häkansson, Lund University, Lund, Sweden
Professor Sölve Elmståhl, Professor Lennart Minthon, Lund University, Malmö, Sweden
Professor Beatriz Alsanius; Professor Marie Olsson, Swedish University of Agricultural Sciences, Alnarp, Sweden

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CONTACT
Professor Bengt Jeppsson
Professor of Surgery
Lund University
Department of Clinical Sciences
Surgery Research Unit
Skåne University Hospital
Inga Marie Nilssons gata 47, floor 3
SE-205 02 Malmö, Sweden
T +46 706 563760
E bengt.jeppsson@med.lu.se
www.probi.se

PROFESSOR BENGT JEPSSON is a graduate of Lund University. He is Professor of Surgery and Senior Consultant at the Surgical Department of the University Hospital. He has previously trained for three years in the US at Harvard Medical School, Massachusetts General Hospital, Boston and at University of Cincinnati Medical School. In addition, he has had further experience at Centre Chirurgie Digestive, Hôpital Saint Antoine, Université de Paris, France. He has devoted his professional life to diseases of the gastrointestinal tract and has produced over 300 scientific publications. He is a fellow of the Royal College of Surgeons, and a member of the American Gastroenterological Association, American Association for Cancer Research, European Surgical Association and International Hepato-Pancreato-Biliary Association. He has also served as President of the European Society of Surgical Research.

PROSPECTIVE PROBIOTIC RESULTS
Randomised controlled studies into the effects of Lp299v are testament to its potentially therapeutic and preventative qualities. It is essential for the maintenance of proper barrier function in the gut in order to prevent hostile bacteria from taking over and allowing greater ease of infection. In analysing the excretion ratios of lactulose, a synthetic non-digestible sugar, and rhamnose, a naturally-occurring dextrose sugar, in patients with and without the probiotic formula, a clear difference in outcome can be observed. With both groups tested before and after administration, the excretion ratios for five of the seven patients on Lp299v became normal whereas the controls generally started badly and got worse.

Perhaps the most deadly consequence of low diversity among microflora populations is the translocation of bacteria through the mucosal lining, from its correct place inside the gut to the outside. Rats given a range of Lactobacillus and Bifidobacterium strains over eight days were measured for rates of translocation after inducing an inflammation in the liver. At over 2500 colony forming units (CFU) per gram of liver tissue, the control animals were significantly worse off than those on Lp299v, whose bacterial translocation was shown to be almost negligible at less than 0.05 CFU/g of liver tissue. This is a remarkable drop in the rate of CFU translocation, which could have lifesaving consequences for older individuals whose age alone increases the risk of bacterial leakage from the GI-tract.

One indication of an imbalance in the gut’s floral composition is the presence of the proinflammatory cytokine interleukin six (IL-6) and eight (IL-8), which are responsible for the continuous, low-level inflammation in the elderly. To establish whether or not probiotic treatment has an effect, its impact has been measured on the elevated levels of inflammation in 18 smokers. Before administering Lp299v, the smokers displayed over 2.5 nanograms (ng) per litre of IL-6 in their blood – an amount which was marginally reduced following a placebo treatment. After probiotic treatment, however, a reduction close to 1.5 ng/L was observed. As Jeppsson points out, the potential for efficacious treatment with this species of Lactobacillus is great: “It can improve gut function, tighten a leaky gut, reduce systematic inflammation, colonise the gut mucosa and reduce the number of pathogenic bacteria,” he enthuses. Though patients suffering from MODS are not the intended beneficiaries, it has certainly provided Jeppsson and his colleagues with an important proof of concept.

Having established these clear health benefits, Jeppsson and his colleagues continue to investigate the use of probiotics to further ascertain their effects on the proper functioning of the gut. Their far-reaching collaborative work with SLU is yielding some palatable treatments, and with human testing planned to start as soon as possible, the development of Probi’s new products for the promotion of health in older adults could soon be easing the projected burden on health services the world over.