Yakult Sponsorship

Bringing Science to Society: A Yakult Sponsored Public Forum

For the last 4 years the science department of Yakult Ireland has sponsored an event with the Alimentary Pharmabiotic Centre (APC) in Cork. The APC is a University College Cork(UCC)/Teagasc research centre funded by Science Foundation Ireland, focusing on gastrointestinal health and development of therapies for debilitating disorders such as Crohn's disease, colitis, irritable bowel syndrome (IBS) and food poisoning. On this occasion, the event was an APC Public Forum which took place on Tuesday November 9th 2010.

The focus of the forum was "TB: A re-emerging problem?". A panel of experts discussed the topic of tuberculosis (TB) in light of the recent outbreaks of TB in the Cork and Kerry region and specifically discussed the modern technologies used to detect, monitor and treat the disease. The forum was chaired by Dr Mary Horgan, Consultant Physician in Infectious Diseases, Cork University Hospital, with speakers Dr Dan Corcoran, Consultant Microbiologist, Cork University Hospital, Professor Mike Prentice, Medical Microbiologist, UCC & Principal Investigator APC and Professor Colin Hill, UCC & Principal Investigator, APC.

TB is commonly an infection of the lungs by *Mycobacterium tuberculosis* which causes a chronic respiratory disease that is spread by coughing and sneezing. Worldwide, there are over 9 million new cases diagnosed per year. Dr Dan Corcoran discussed the evolution of the disease and how landmark discoveries, such as the identification of the mycobacterium by Robert Koch in 1882, have influenced the disease. When active TB is diagnosed, it is usually curable, but involves antibiotic treatment for at least six months. Dr Corcoran, in his talk entitled "Tuberculosis: the resourceful opponent", discussed how antibiotic-resistant TB strains have emerged and what the global public health impact of this is. He pointed out that as the disease itself has adapted, so must we in terms of adequate diagnosis and effective regimens stating "lessons of the past must not be forgotten".

Ireland had a high incidence of TB in the 19th and 20th centuries, higher than Britain, with an average of 200 cases per 100,000 deaths. Nowadays, Ireland is classified as a low incidence country with the majority of worldwide cases reported in developing countries. Of the small number of cases reported in Ireland, 60% are in people born in Ireland. This figure increases to over 70% in the Cork/Kerry region.

In the UK, 73% of TB patients are born outside of the country, residing mostly in London and the Midlands. In his talk "TB: with special reference to Ireland" Professor Michael Prentice explained how advances in DNA sequencing now allow scientists to tell the difference between closely related bacteria that were previously indistinguishable. Using DNA techniques scientists can see that most of the TB bacteria that spread recently between people in Cork and Kerry are local strains persisting from the days when TB was common. DNA typing can assist with public health measures controlling the spread of TB.

Antibiotics have been the main weapon in our fight against infectious diseases for the last 60 years, saving millions of lives and turning previously fatal infections into relatively simple problems to treat. Unfortunately, many disease-causing bacteria have evolved to become antibiotic resistant, leaving many of our frontline antibiotics ineffective against these 'superbugs'. Professor Colin Hill in his presentation "Using microbes to PREVENT infection; an alternative to classic antibiotics?" illustrated how the APC have begun to look at alternative strategies to control infectious disease, looking to harness the power of our immune system, and taking advantage of the many strategies used by bacteria to kill other bacteria in the environment.

APC
Alimentary Pharmabiotic Centre
Mining Microbes for Mankind

Science team notice board

Probiotic Bulletin by E-mail

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Conferences and Events

International Yakult Symposium 2011: *The Gut and its Role in Health Maintenance*
This symposium will be held in Vienna, Austria on the 26th and 27th May. To see the full programme and to register visit www.yakultsumposium.com. Alternatively, for a chance to win a free place, including flights and accommodation, enter the draw at www.yakult.co.uk/hcp

International Yakult Symposium 2011

4–6 May INMO ADC
Hotel Kilkenny
www.inmo.ie/adc

7 May ICGP AGM
Radisson Hotel Galway
www.icgp.ie.go/courses/conferences

18-20 May INMED
Trinity College Dublin
www.medicine.tcd.ie/inmed

15–17 June NS Irish Section Meeting
University College Cork
www.nutritionsociety.org/node/32

22 June AIGNA Conference
Dublin
www.aigna.ie/events

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- Free educational talks by our team of nutritionists
- Advice on probiotics
- Free supply of Yakult for a trial period (subject to discussion)
- Probiotic Bulletin newsletter
- Dedicated website for healthcare professionals (www.yakult.ie/hcp) with nutritional information, FAQ and LcS scientific evidence:

  Synopses: Quick, digestible summaries of all the important studies

  Topics: Hyperlinked reference lists of all important LcS papers relevant for: gut-related infections, immune function, IBS & constipation, IBD, elderly, liver disease and cancer

Find the science behind Yakult **yakult.ie/hcp**

Contact us

If you have any questions about probiotics, please do not hesitate to get in touch.

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Probiotic Bulletin

AN UPDATE FOR HEALTHCARE PROFESSIONALS

Probiotics take on the common cold

Lactobacillus casei Shirota and placebo go head to head in a double-blind, randomised controlled trial in endurance athletes. Read on for the post-match interview with lead researcher Professor Mike Gleeson of Loughborough University.

Over the past 20 years Prof Gleeson has published over 150 papers on exercise physiology, immunology and sports nutrition. Prof Gleeson moved to Loughborough University in October 2002 as the Professor of Exercise Biochemistry. We caught up with him to find out more about his most recent study.

Thank you for speaking to us today. You have a new study that has just been published in the International Journal of Sport Nutrition and Exercise Metabolism – can you tell us what the study is about?

MG: The study investigated the effects of taking Yakult on a daily basis during four months of winter training, in a group of university based athletes. We wanted to see whether taking Yakult, compared with taking a matched placebo, had any effect on infection incidence, particularly the incidence of the common cold and gastrointestinal problems.

What were the main findings?

MG: We found that taking Yakult on a daily basis reduced the number of infection episodes by almost 50% compared with the placebo group. The proportion of people in the probiotic group who experienced one or more infections was significantly lower than those in the placebo group. Ninety percent of the subjects in the placebo group reported one or more infection episodes during the four months compared with 66% in the probiotic group. We also found that taking the probiotic helped to better maintain salivary IgA level whereas a significant fall in IgA level was shown in the placebo group.

What is the importance of salivary IgA levels?

MG: IgA is an antibody that is present in saliva. It is known that those individuals with low levels of IgA tend to get more infections, particularly upper respiratory tract infections. We suspect this is possibly the major mechanism by which this probiotic exerted a beneficial effect.

Why did you conduct the study in a group of athletes?

MG: Athletes, particularly endurance athletes tend to get more infections than the average sedentary person. This could be as a result of the hard exercise they do causing some stress and depressing immunity. Developing infections is a problem for athletes as it means they might have to miss important training sessions and they usually have to be isolated from the rest of the squad. If illness occurs around competition time they may under-perform or will not be able to compete in the event itself. We see probiotics as one possible nutritional means of boosting immunity and reducing infection incidence in athletes.

Could these findings have wider implications for the general population?

MG: Possibly. Occupational work related stress may have similar effects to the stress of exercise; the body may produce the same sort of hormonal and cytokine responses. We would suspect that anybody who is stressed might benefit from a supplement that potentially boosts immunity and reduces risk of infection.

Probiotics take on the common cold

"Nutritionists who work with the English Institute of Sport have been keeping an eye on current literature showing the benefits of reducing respiratory and gastrointestinal infection and have therefore been encouraging athletes to start taking probiotics."

...continued from P1

Do you think that all probiotics show the same effect in reducing the risk of colds?

MG: Almost certainly not. The effects of probiotics seem to be very strain-specific. It may be that some strains of probiotic have immune boosting, pro-inflammatory effects whereas others might have generally anti-inflammatory effects.

A number of athletes were unable to complete the study. Why was this?

MG: The main reason for drop-out was that the athletes picked up an injury which prevented them from training or had to go abroad to compete or to attend training camps in warm weather countries. They couldn't take the liquid supplement with them through airport security so that disallowed them from the study.

Do you think probiotics should be a routine aspect of nutrition for athletes?

MG: Yes, I can't see any sense in them not taking it. There are no detrimental effects and there is a good chance that they will have some positive effects in reducing respiratory and gastrointestinal infections.

Are probiotics widely consumed by elite athletes?

MG: Yes, I believe a significant number do [take probiotics]. Nutritionists who work with the English Institute of Sport have informed me that they have been keeping an eye on current literature showing the benefits of reducing respiratory and gastrointestinal infection and have therefore been encouraging athletes to start taking probiotics.

What other research are you involved in at Loughborough?

MG: As well as being interested in probiotics we are also interested in other supplements that are not on the banned list that might potentially boost immunity or reduce risk of infection. In the past we have examined the efficacy of taking carbohydrate during exercise to reduce the stress response to exercise. We also examine the impact of different types of exercise in periods of intensified training on immunity.

Loughborough University has fantastic sports facilities; are there any teams training at Loughborough during the Olympics?

MG: The majority of the British Olympic squad and also the Japanese Olympic squad are going to be based here at Loughborough in the months leading up to the games.

What are you looking forward to most about the Olympics?

MG: The fact that it is going to be based in this country, the potential of the Olympic legacy and the stimulation of a renewed focus on exercise for health.

Gleeson M *et al* (2011) Daily probiotic's (*Lactobacillus casei* Shirota) reduction of infection incidence in athletes. *International Journal of Sport Nutrition & Exercise Metabolism* **21**: 55–64

For the full interview, a synopsis of the study or to request a re-print of the full paper please visit the Yakult HCP website at www.yakult.ie/HCP

By Dr Heather Ford and Leanne Hewitt
Yakult UK Ltd

Behind the scenes of a large community study in India

In an urban slum in Kolkata, India a huge community study was conducted to evaluate the effect of the probiotic, *L. casei* Shirota, in preventing acute diarrhoea in children living in the slum.

I had the opportunity to hear presentations about this study at the 6th Yakult Shirota conference (Science of 'Kenchou Choujyu': Practice of Probiotics and Preventive Medicine) and the 19th Symposium on Intestinal Flora: Intestinal Microbiota and Health in Early Childhood, which is sponsored by Yakult's Bioscience Foundation.

The pictures taken during the study give a real insight and an appreciation of the task of organising a study on this scale and in this setting. With input from the researchers and with the pictures kindly sent by Dr Nair, I can give you a snapshot here.

The National Institute of Cholera and Enteric Diseases in Kolkata, evaluated the effect of *L. casei* Shirota in preventing acute diarrhoea in children aged 1–5 years living in an urban slum, using a double-blind, randomised field trial. The children (n=3585) were randomly grouped to receive either Yakult or a nutrient drink (fermented milk drink without the probiotic strain) for 12 weeks, with a further 12 week follow up.

Such a large study was a major undertaking. One of the first tasks was to train approximately 100 Community Health Workers (CHW) who would be delivering the drinks to the children and collecting faecal samples from any who developed diarrhoea. The study was conducted in five health outposts with each CHW responsible for about 40 subjects (image 1).

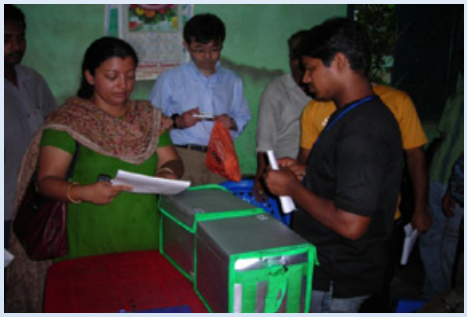
The CHW either gave the drinks directly to the child themselves, or watched the mothers do this (image 2). As the bottles were identical neither the subjects nor the researchers could tell whether the drink was the probiotic or the nutrient drink. The collected faecal samples were delivered back to the research institute in a coolbox and analysed for bacterial, viral and parasitic enteric pathogens using standard techniques.

The major findings of the study were that the proportion of children suffering diarrhoea was significantly lower in the probiotic group (608/1802 children or 33.7 %) compared to the nutrient group (674/1783 or 37.8%); the incidence of diarrhoea was also lower (0.88 cases/child/year vs 1.029/child/year. $P<0.01$), indicating a protective efficacy of 14%. Detection of Aeromonas and Cryptosporidium species was significantly lower in the probiotic group; other enteric pathogens showed little change.

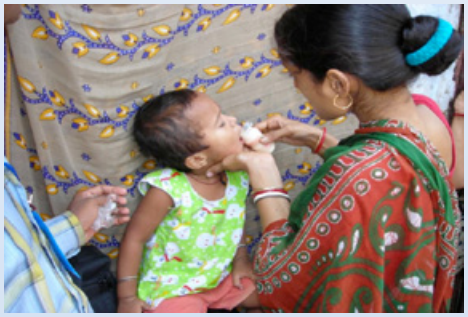
The authors concluded that daily intake of a probiotic drink can play an important role in the prevention of acute diarrhoea in young children in a community setting of a developing country like India.

It was clear that the researchers, from quite different parts of the world, have all become good friends and learnt a lot about each other's cultures (if you'll pardon the pun).

Sur D *et al* (2010) Role of probiotic in preventing acute diarrhoea in children: a community-based, randomized, double-blind placebo-controlled field trial in an urban slum. *Epidemiology and Infection* [Epub ahead of print]



1. A Project Medical Officer allocating coded drinks to Community Health workers at the project site for distribution to the study children



2. The drink being given to the children, under the supervision of one of the research staff

By Dr Linda Thomas
Yakult UK Ltd

Research round-up

Shaping of the immune system by the gut flora: a *Science* review

Observations of germ-free mice indicate that the contribution of the microbiota is fundamental; gut-associated lymphoid tissue (GALT) formation and multiple populations of immune cells require the microbiota for their proper development and function. The review focuses on the emerging knowledge of microbiological signalling which instructs $CD4^+$ T cell differentiation. A hypothetical model for the coevolution of adaptive immunity with the microbiota is proposed and the authors discuss how a shift in the balance of the commensal bacteria shapes the immune status of the host and may mediate the development of autoimmune disease.

Lee YK *et al* (2010) Has the microbiota played a critical role in the evolution of the adaptive immune system? *Science* **330**: 1768–1773

Acetate is crucial in bifidobacterial anti-infective effect

Certain bifidobacterial strains have been reported to prevent lethal death by *E.coli* O157:H7 infection in mice whereas other strains of this genus did not. By using 'omics' technology and gene knock out, this group demonstrated that the ability of the bifidobacteria to metabolise carbohydrate and to produce colonic acetate correlated with this protective effect. Acetate, at least *in vitro*, appears to block translocation of the *E.coli* O157:H7 Shiga toxin (Stx2) from the lumen into the blood. If the colonic concentration of acetate was increased (by simply feeding mice with acetylated starch), the mice became protected against *E.coli* O157-induced death.

Fukuda S *et al* (2011) Bifidobacteria can protect from enteropathogenic infection through production of acetate. *Nature* **469**: 543–547

New Cochrane review: Probiotics and infectious diarrhoea

Infectious diarrhoea is the fifth leading cause of death worldwide; it is a particular problem in children under the age of 5 in low- to middle-income countries and in industrialised countries death from infectious diarrhoea occurs mainly in the elderly. This systematic review assessed the effects of probiotics in infectious diarrhoea; 63 studies met the criteria with a total of 8014 participants. There was marked heterogeneity between studies in terms of participants, definition of diarrhoea, strain of probiotic and the treatment regimen. Remarkably however, nearly all studies reported shortened duration of diarrhoea and on average reduced the risk of diarrhoea lasting for four or more days by 59% in those who received probiotics compared to the controls.

Allen SJ *et al* (2010) Probiotics for treating acute infectious diarrhoea. *Cochrane Database of systematic reviews* **11**: CD003048

Review: Probiotics and ulcerative colitis (UC)

Many studies have indicated that a dysbiosis of the intestinal flora could contribute to the pathogenesis of UC. The potential role that probiotics may play in the treatment of UC has been widely discussed due to the positive effects probiotics have on stabilising the microbial ecosystem and regulating the immune response, yet studies to date have often been small scale. This meta-analysis evaluated thirteen studies that met the inclusion criteria; all were randomised, controlled trials that compared the benefit of probiotics with standard therapy for UC or placebo. The overall conclusion stated that probiotic auxiliary therapy during the maintenance therapy stage significantly reduced recurrence rates. Yet, using probiotics did not provide additional benefit in inducing remission.

Sang LX *et al* (2010) Remission induction and maintenance effect of probiotics and ulcerative colitis: a meta-analysis. *World Journal of Gastroenterology* **16 (15)**: 1908–1915