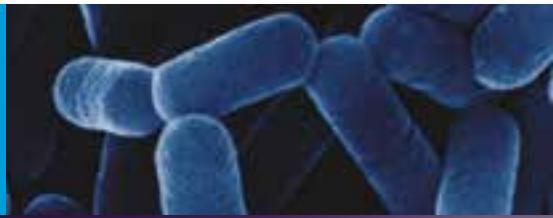


Probiotic Bulletin

A Newsletter for Healthcare Professionals



Probiotics & Women's Health

Exploring the research

In this issue, we explore research conducted in the field of the microbiota and probiotics that is of relevance to women's health, with articles on the use of probiotics for urogenital infections and in pregnancy.

We also take the opportunity to highlight programmes in place to support women in science, share new research and resources, celebrate award winning healthcare professionals and tell you more about the upcoming International Yakult Symposium.

In this issue:



- | | |
|---------------------------------------|-----|
| • Probiotics & Urogenital Infections | 1-3 |
| • Probiotics in Pregnancy | 1-3 |
| <hr/> | |
| • Women & their Microbes | 4-5 |
| • Bacteria & Fashion | 4-5 |
| • Women in STEM | 4-5 |
| <hr/> | |
| • HCP Awards | 6 |
| <hr/> | |
| • Research Round-up | 7 |
| • IPA Guide to Probiotics | 7 |
| <hr/> | |
| • International Yakult Symposium 2018 | 8 |
| <hr/> | |

Probiotics & Urogenital Infections

Urogenital infections present a challenge for healthcare providers, as it has been estimated that around half of all women suffer from a urinary tract infection (UTI) at least once in their lifetime,¹ and around 40% will experience an episode of vulvovaginal candidiasis (VVC) before the age of 50 years.² Although there are antimicrobial treatments available, increasing concerns about antibiotic resistance mean that alternative or complementary therapies to support the treatment or prevention of urogenital infections are sought after.



Probiotics may be one of those potential alternative or adjunct therapies.³ In 1973, a study in healthy women found an association between the presence of non-pathogenic organisms, such as coagulase-negative *Staphylococcus*, in the vaginal microbiota and no history of UTIs;⁴ this is where the basis for the use of probiotics for urogenital infections stemmed from. Although originally it was vaginal application of probiotics that was studied, research has more recently shown that oral probiotics, which result in changes to intestinal microbiota, can also influence the composition of vaginal microbiota too.⁵

A recent systematic review looked at randomised-controlled trials (RCTs) that have explored the use of probiotics in the treatment and prevention of urogenital infections in women.⁶ Here, we describe the overall outcomes from this systematic review across four key urogenital infections: urinary tract infections (UTIs), bacterial vaginosis (BV), vulvovaginal candidiasis (VCC) and human papilloma virus (HPV).

To date, clinical efficacy for the use of probiotics to reduce recurrence of UTIs exists for strains within the *Lactobacillus* (L) genus: *L. crispatus* (CTV-05) delivered in vaginal capsules for three months showed a significant reduction in UTI recurrence ($P<0.01$), and *L. rhamnosus* GR-1 and *L. reuteri* RC-14 given orally for six months showed a significant reduction in recurrence in those with uncomplicated UTI ($P<0.001$).

Of the 14 RCTs trialing probiotics in BV identified in the systematic review, eight focused on the treatment of BV and six focused on the prevention of BV. Across all the RCTs, although probiotic strain, dose, delivery route and duration varied across the interventions, the predominant probiotic strain/s used across all RCTs were from the *Lactobacillus* genus. Intervention findings included a significant increase in the clearance of BV in the probiotic groups compared to controls, and a significant reduction in BV recurrence and time to BV recurrence.

Findings from the three RCTs that investigated probiotics in the treatment and/or prevention of VVC were variable, and they did not show an effectiveness in treating acute VVC. However, a trend towards a reduction in VVC recurrence was shown in the probiotic groups when delivered via vaginal tablet ($P=0.083$), and oral capsule ($P<0.057$).

There is only one RCT that has studied the use of probiotics in HPV. In this intervention, *Lactobacillus casei* Shirota was given for a six-month period to participants who had low-grade squamous intraepithelial lesions identified during cervical smears, and in the probiotic group there was twice the clearance of HPV lesions compared to the controls ($P=0.05$). HPV clearance was also higher in the probiotic group compared to control (29% vs 19%), although this was not statistically significant.

Summary

- Interventions investigating the use of probiotics in the treatment and prevention of urogenital infections, as an alternative or co-treatment, have shown some interesting results.
- The probiotic interventions were not associated with any serious adverse event.
- There remains a need for well-designed clinical research on probiotic use in the treatment and prevention of urogenital infections in women, to develop clear clinical recommendations.

References

- ¹ Foxman B (2002) *Am J Med* 113(1):5–13. ² Blostein F et al. (2017) *Annals of Epidemiology* 27(9):575–82. ³ Reid G & Bruce AW (2003) *Postgraduate Medical Journal* 79(934):428–32. ⁴ Bruce AW et al. (1973) *Can Med Assoc J* 108:973. ⁵ Reid G et al. (2001) *FEMS Immunol Med Microbiol* 30(1):49–52. ⁶ Hanson L et al. (2016) *J Midwifery Women's Health* 61(3):339–55.

Probiotics in Pregnancy

Pregnancy is a remarkable biological process that involves changes in many physiological systems to support the growth and development of a healthy foetus. Whilst some of the hormonal and metabolic changes associated with pregnancy have been known for many years, it has only recently been appreciated that during pregnancy there are also significant changes in not just the gut microbiota, but also the vaginal and oral microbiota.¹

The use of probiotics during pregnancy and breastfeeding presents a unique opportunity to potentially not only influence maternal health, but also that of the offspring, and so it has increasingly become an area of interest. In this summary, we focus on gestational diabetes and childhood allergies.

Gestational Diabetes

Gestational diabetes mellitus (GDM) is associated with a range of short and long-term consequences for both the mother and the infant, and the few studies that have explored the impact of probiotic supplementation on maternal rates of GDM have shown mixed results. In a Finnish study, in which *Lactobacillus rhamnosus* GG and *Bifidobacterium lactis* Bb12 was given daily from the first trimester until the end of exclusive breastfeeding, showed a significantly lower prevalence of GDM in those taking the probiotic.² However, in a more recent trial where *Lactobacillus salivarius* UCC118 was given from 24 to 28 weeks' gestation in obese pregnant women, there was no effect on fasting glucose or other maternal outcomes.³

These data suggest that the impact of probiotics on the prevalence of GDM may be dependent on the species and strain, as well as the stage of pregnancy at which the intervention begins, the duration of the intervention and the concurrent diet.

Allergy

There is a body of research examining the use of probiotics in the prevention of allergic disease, particularly atopic dermatitis/eczema, which is increasingly prevalent in children worldwide and is associated with sensitisation to other allergens.⁴

Meta-analyses of randomised controlled trials have indicated that consumption of probiotics containing *Lactobacillus* alone or *Lactobacillus* with *Bifidobacterium* during pregnancy and early life appear to be protective against atopic dermatitis/eczema,^{5,6} however a Cochrane review found that the effect does not seem to be significant for immunoglobulin E (IgE) associated atopic dermatitis.⁷ Of importance to note is that almost all the trials conducted so far have probiotic interventions that started within the final 2 months of pregnancy, after foetal production of IgE antibodies and allergen-specific IgE antibodies, which may explain the general lack of effect of probiotics on infant sensitisation.⁸

References

- ¹ Nuriel-Ohayon et al. (2016) *Front Microbiol* 7:1031. ² Luoto et al. (2010) *Br J Nutr* 103: 1792-9. ³ Lindsay et al. (2014) *Am J Clin Nutr* 99:1432-9.
- ⁴ Pawankar et al. (2013) World Allergy Organisation (WAO) White Book on Allergy: update 2013. Milwaukee: WAO. ⁵ Pelucchi et al. (2012) *Epidemiology* 23:402-14. ⁶ Panduru et al. (2015) *J Eur Acad Dermatol Venereol* 29:232-42. ⁷ Osborn et al. (2007) *Cochrane Database Syst Rev* Art. No.: CD006475.
- ⁸ Barthow et al. (2016) *BMC Pregnancy and Childbirth* 16:133.

Conclusion

The use of probiotics in the primary prenatal care of pregnant women would be easy to establish, and may have the potential to influence both maternal and infant health, however further research and evidence is required. There are trials currently underway that will help to develop the evidence base, such as the Probiotics in Pregnancy study in New Zealand, which is designed to explore the outcomes discussed, but also post-natal depression and anxiety.⁹



Women & their Microbes

This scientific conference has taken place annually since 2015, and aims to promote knowledge about the essential role of microbes in women's health among healthcare professionals, scientists, and the public too. This year's meeting took place on 2nd June in Amsterdam and the theme was 'External Influences on Female Microbiomes'. The lectures covered several aspects including the female oral microbiome, the role of the breast microbiome in breastfeeding success and women's health, the role of vaginal microbiota in health and disease, and even a talk on how men influence the female microbiome.

For summaries and slides from the past meetings, and details of the 2018 meeting, visit: womenandtheirmicrobes.com



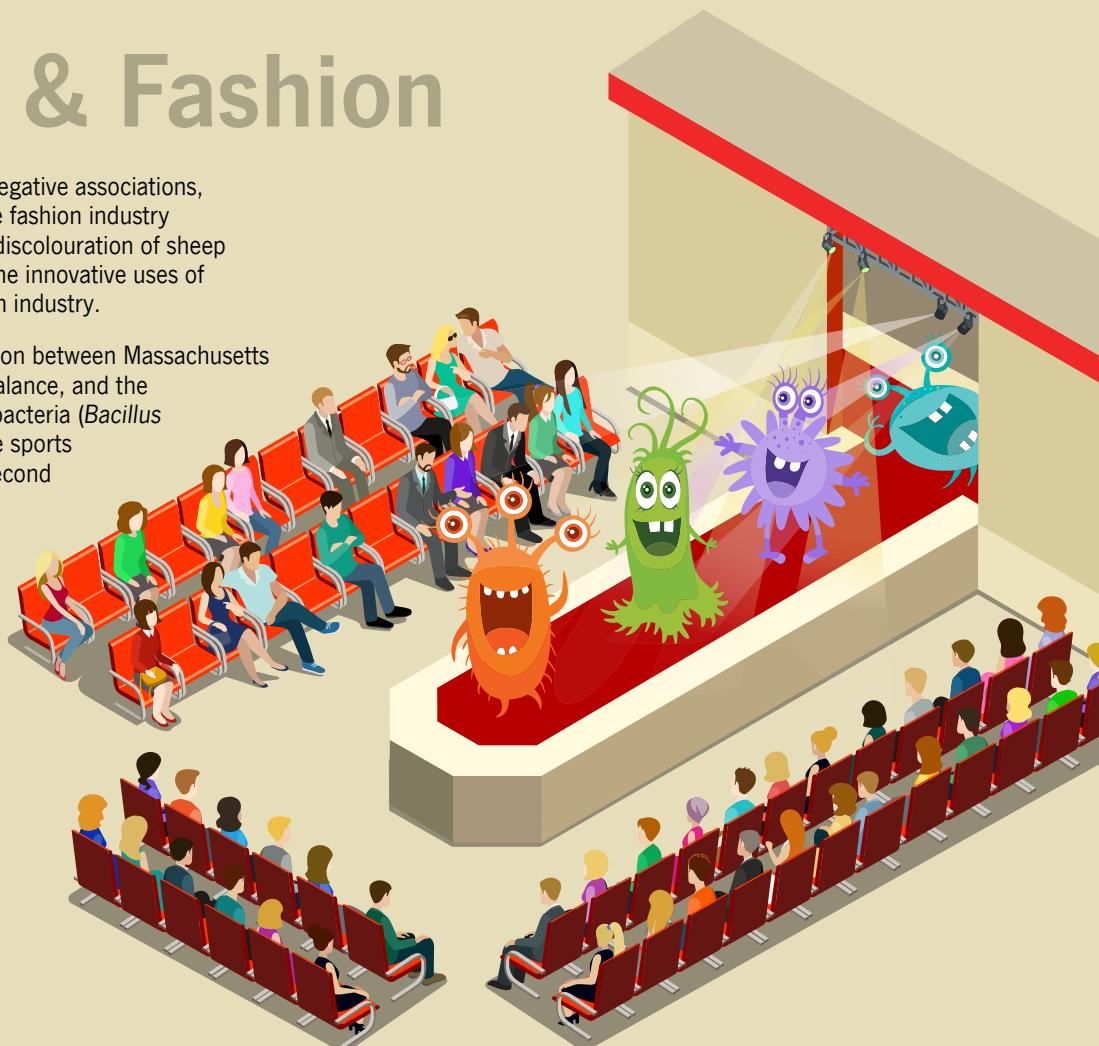
Bacteria & Fashion

The word 'bacteria' can often have negative associations, and not just for health but also in the fashion industry

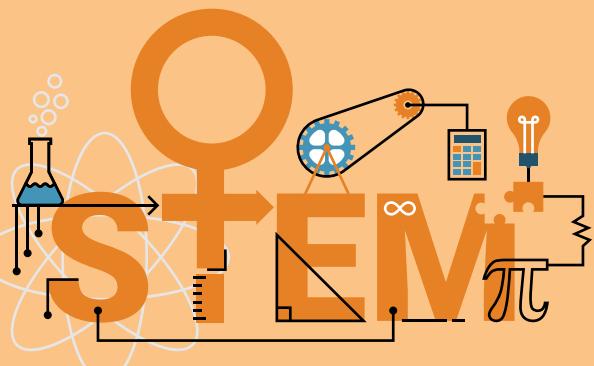
- *Pseudomonas* bacteria can cause discolouration of sheep fleeces. However, there are also some innovative uses of bacteria within the textile and fashion industry.

The 'bioLogic' project is a collaboration between Massachusetts Institute of Technology (MIT), New Balance, and the Royal College of Art, which is using bacteria (*Bacillus substillis natto*) to create a responsive sports clothing which they have called a 'Second Skin'. Second Skin is created using a bioprinter to deposit a bio-hybrid film containing the bacteria. The bacteria cells expand or contract in response to the body's heat and sweat, causing ventilation zones to open and close accordingly, allowing sweat to evaporate.

For more information, visit:
arts.mit.edu/artists/biologic/



Women in STEM



According to statistics published in October 2017, the core science, technology, engineering and mathematic (STEM) workforces remains predominantly male, with women filling just 23% of the roles.¹ In this women's health edition, we highlight some of the organisations, networks and programmes that are in place to support and increase the participation, success and recognition of women in the STEM workforce, all the way from the classroom to a boardroom.



The WISE Campaign

WISE enables and energises people in business, industry and education to increase the participation, contribution and success of women in STEM. They offer a number of resources, provide training and run events and workshops throughout the UK. Membership is open to educational institutes at all levels, but also for individuals free of charge. So, if you are committed to improving gender diversity in the STEM sector, why not become a member?



Athena SWAN Charter

Athena SWAN (Scientific Women's Academic Network) is a charter established by the Equality Challenge Unit in 2005 that recognises institutions good practice towards gender equality, and their commitment to advancing women's careers in STEM and medicine in higher education and research. By joining the charter, institutions commit to adopting a number of principles including addressing the loss of women across the career pipeline, removing obstacles faced by women and tackling the gender pay gap.



Women in Technology & Science – Ireland

Women in Technology and Science (WITS) Ireland is an independent voluntary membership organisation supporting women in STEM to reach their full potential. Individual membership gives access to social events, evening lectures, training workshops and networking events.



L'Oreal-UNESCO for Women in Science Programme

L'Oréal and UNESCO founded the Women In Science programme to promote and highlight the critical importance of ensuring greater participation of women in science. Each year, the programme recognises the achievements of exceptional female scientists across the globe and awards them with Fellowships to help further their research. The L'Oréal-UNESCO UK and Ireland Fellowships for Women in Science are annual awards offered to promote, enhance and encourage the contribution of women pursuing their research careers in the UK or Ireland, in the fields of the life and physical sciences.

And with 'Little Miss Inventor' – a female engineer – joining the Mr Men and Little Miss series as a positive role model for girls in March 2018, let's continue to encourage female participation in STEM!

¹ WISE (2017) Women in STEM Workforce 2017. Available at: www.wisecampaign.org.uk/resources/2017/10/women-in-stem-workforce-2017 [accessed 25 Nov 2017]



Healthcare Professional Awards

In 2017, we were delighted to continue our sponsorship of a number of national awards for healthcare professionals, including the *Complete Nutrition (CN) Clinical Nutrition Professional of the Year Award* and the *RCNi Patients Choice Award*.



CN Community Nutrition Professional of the Year

This CN Award gives recognition to the achievements of a clinical nutrition professional whose great work has made a significant contribution to the nutrition field.

We would like to congratulate the 2017 winner, Professor David Sanders, Professor of Gastroenterology at the University of Sheffield and a NHS Consultant Gastroenterologist at Royal Hallamshire Hospital. Professor Sanders has made significant contributions to advancing gastroenterology research and, alongside his colleagues in the Sheffield Gastroenterology Team, has translated research into practice to truly transform services and improve patient care.

Our congratulations extend to all the nominees and award winners across the categories of the CN Awards.

For further information about the awards visit: nutrition2me.com/cn-awards

RCNi Patient's Choice Award

Yakult were also proud to have sponsored the *RCNi Patient Choice Award* for a fourth year running. This award gives patients the opportunity to thank a healthcare professional within the nursing profession who has made a real difference to their, or a loved one's, care.

Our congratulations and admiration go to this year's winner, Joanne O'Toole. Joanne was a children's nurse for over 38 years and most recently worked as a children's respiratory nurse specialist at Royal Manchester Children's Hospital. Lesley Chan nominated her daughter's 'wonderful and courageous' respiratory specialist nurse for the comfort, support and compassion she had shown the family.

We would also like to congratulate Karen Coutts, Nadine MacArthur, Sarah Moody and Sian Bodman on their truly deserving nominations.

The awards ceremony was an inspirational evening, showcasing exceptional nurses who have enhanced patient care, improved health outcomes and transformed nursing practise.

For further information visit: rcni.com/nurse-awards



Recent studies with *Lactobacillus casei* Shirota

LcS and osteoarthritis symptoms

This study examined the efficacy of LcS in 537 patients with knee osteoarthritis. The patients were randomly assigned to LcS or placebo for a 6-month period. Compared to baseline and placebo, the LcS group had significantly lower total and subscale Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores and pain visual analogue scale (VAS) scores. These improvements in symptoms could be attributable to C-reactive protein (CRP) levels, which were significantly reduced in the LcS group post-intervention ($P<0.05$).

Lei et al. (2017) The effect of probiotic *Lactobacillus casei* Shirota on knee osteoarthritis: a randomised double-blind, placebo-controlled clinical trial. *Beneficial Microbes* 8(5):697-703

LcS and academic stress-induced sleep disturbances

In this randomised, double-blind, placebo controlled trial, LcS was examined for its effects on improving stress-induced sleep disturbances in medical students ($n=98$) preparing to sit a national examination. Participants were randomly assigned to an 11-week intervention of either LcS-fermented milk drink or placebo, in the 8-week period before, and for 3-weeks after taking the exam. Sleep quality, measured using the Oguri-Shirakawa-Azumi (OSA) sleep inventory, was impaired in both groups in the period before the examination, and recovered after the exam. However, the OSA sub-categories of 'sleep length' and 'sleepiness on rising' were both significantly improved in the LcS group compared to placebo ($P<0.01$ and $P<0.05$ respectively). Further assessment, using electroencephalography (EEG), found LcS intervention also had favourable effects in preserving the time taken to fall asleep (sleep latency) and depth of sleep (stage 3 non-REM sleep), compared to placebo.

Takada et al. (2017) Beneficial effects of *Lactobacillus casei* strain Shirota on academic stress-induced sleep disturbance in healthy adults: a double-blind, randomised, placebo-controlled trial. *Beneficial Microbes* 8(2):153-162

LcS and obesity in children: a pilot study

This pilot study examined the effects of LcS on the intestinal microbiota in 12 obese children, who received diet and exercise therapy for 12 months, and drank an LcS fermented milk drink daily for the latter 6 months. Within this study, they also included a single measurement from 22 healthy weight children to act as a control group. Pre-intervention the obese group had significantly lower *Bifidobacterium* and total bacteria count in the faeces compared with the healthy weight group ($P<0.05$). In the obese intervention group, body weight was significantly lower and HDL cholesterol levels were significantly higher only after the 12 months when compared with baseline ($P<0.05$). LcS consumption for 6 months also led to a significant increase in total bacteria ($P<0.05$), LcS ($P<0.01$) and *Bifidobacteria* ($P<0.01$) in the faecal microbiota.

Nagata et al. (2017) The effects of the *Lactobacillus casei* strain on obesity in children: a pilot study. *Beneficial Microbes* 8(4):535 - 543

Systematic Reviews & Meta-Analyses on Constipation

Probiotics as treatment for constipation in the elderly

A systematic review of nine studies (four randomised-controlled trials and five observational studies) concluded that probiotic administration can improve chronic constipation by 10-40% in elderly people, compared to control.*

Martinez-Martinez et al. (2017) The effect of probiotics as a treatment for constipation in elderly people: A systematic review. *Arch Gerontol Geriatr.* 71:142-149.

Probiotics in childhood constipation

A meta-analysis of six randomised controlled trials ($n=498$), found that probiotic interventions, compared to control, significantly improves stool frequency in children with constipation (mean difference = 0.73, $P=0.02$).*

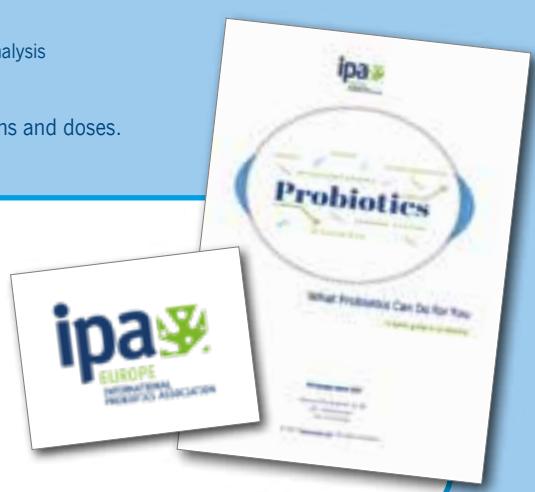
Huang & Hu (2017) Positive Effect of Probiotics on Constipation in Children: A Systematic Review and Meta-Analysis of Six Randomized Controlled Trials. *Front Cell Infect Microbiol.* 7:153

*Both reviews highlighted the need for further studies to identify efficacy of specific probiotic strains and doses.

New 'Quick Guide' to Probiotics

The International Probiotics Association (IPA) Europe have developed a new 'quick guide' brochure, highlighting insights based on the latest probiotics research and discussing what current science says about the effects of probiotics on human health.

To download a copy visit: ipa-europe.org/about.php?ID=7



REGISTRATION & CALL FOR ABSTRACTS OPEN!



International Yakult Symposium

The Role of Probiotics on the Roadmap to a Healthy Microbiota

19th-20th April 2018, Ghent, Belgium

The 9th International Yakult Symposium provides a unique opportunity to learn about the latest insights into the interaction of probiotic with the microbiota and their influence on host health, engage in scientific debate, and network with experts and colleagues in the field.

Confirmed speakers include Professor Colin Hill (University College Cork, Ireland), Professor Julian Marchesi (Imperial College London, UK) and Dr Masanobu Nanno (Yakult Central Institute, Japan).

For the full programme information and to register, visit yakultsymposium.com

Places are limited and early bird rates apply. We would also encourage you to submit an abstract for a poster presentation and the opportunity to be selected for a 'flash talk'.

We look forward to welcoming you in Ghent!



Interested in learning more about probiotics and the gut microbiota? We offer **FREE** educational workplace sessions for you and your colleagues. Contact a member of the Yakult science team today to arrange a session at your place of work: **+44 (0)20 8842 7600, science@yakult.co.uk or science@yakult.ie**.

We also offer:

- Advice on probiotics
- Copies of our newsletter, reprints and other material
- Free trial period of product (subject to discussion)

To receive future copies of this bulletin
contact science@yakult.co.uk or science@yakult.ie
We can also send paper copies (in bulk if required).

www.yakult.co.uk/hcp

www.yakult.ie/hcp

This booklet is intended for healthcare professionals. Not to be distributed to patients.

© Yakult UK Limited, Science Department, Anteros, Odyssey Business Park, West End Road, South Ruislip, Mddx HA4 6QQ

Tel: +44 (0)20 8842 7600; Email: science@yakult.co.uk or science@yakult.ie

