

# Probiotic Bulletin

A Newsletter for Healthcare Professionals



## Human immunodeficiency virus (HIV)

Does the gut microbiota have any influence on disease?

The clue is in the name – the human immunodeficiency virus (HIV) destroys or impairs the immune system. So, as the majority of the immune system is located in the gut (the gut-associated lymphoid tissue), how does HIV infection affect the commensal bacteria there (or vice versa), and could there be benefit from interventions that modulate the gut microbiota?

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Dr Marcella Reale (University "G. d'Annunzio" Chieti-Pescara, Italy), a researcher in immunology, explains further: 'HIV attacks and destroys T helper lymphocytes (CD4+ T helper cells). The lower a person's CD4+ T-cell count, the more susceptible they are to infections that an otherwise healthy body could fight. Initially the decline is gradual: in the first few months and years, counts may remain near normal or only slightly decreased. But people living with HIV/AIDS (acquired immunodeficiency syndrome) face serious health threats from opportunistic infections that can be life-threatening when the CD4 count falls below 200 cells/mm<sup>3</sup>; these infections are the most common cause of death.'

As early as 1993, the gut was identified as the site of significant HIV replication early in the infection process.<sup>1</sup> The virus disrupts the gut's barrier function and its commensal microbiota, increasing the likelihood of translocation from the gut to the bloodstream of microbial products such as lipopolysaccharide (LPS), an endotoxin found in the outer cell wall of Gram-negative bacteria.<sup>2</sup> The discovery that patients have elevated levels of plasma LPS<sup>3</sup> has implicated the gut microbiota in disease progression, because endotoxin activates the T cells that HIV preferentially targets.

## Did you know....?

- In 1981, an unusual illness was first described by the US Centre for Disease Control and Prevention; the following year it was named acquired immunodeficiency syndrome (AIDS).
- In 1987 the World Health Organisation launched a worldwide campaign to raise awareness, support research, devise policies and champion the rights of patients.
- In 2008, Françoise Barré-Sinoussi and Luc Montagnier were awarded a Nobel Prize for their discovery of HIV. The US researcher Robert Gallo was later recognised as a co-discoverer.
- Public Health England reported that ~100,000 people in the UK were infected with HIV in 2012. About 21,900 did not know they were infected.<sup>4</sup>
- In 2013 a global HIV survey reported 1.8 million new infections, 29.2 million prevalent cases, and 1.3 million HIV-related deaths, (an improvement on 2005 results).<sup>5</sup>
- A three-year old child (the 'Mississippi baby'), infected at birth and treated with aggressive antiretroviral treatment (ART), has now been off treatment for more than two years and is no longer testing positive for HIV.<sup>6</sup>

## The gut microbiota and HIV

The gut microbiome of healthy people is distinctly different from that of people living with HIV; in the latter case, it may be less diverse with loss/ reduction of key species, increased numbers/ changed profile of Gram-negative bacteria, and reduced levels of certain Gram-positive bacteria.<sup>7-13</sup> If diagnosed promptly, HIV can be managed with antiretroviral therapy (ART)<sup>14-15</sup> but even people on long term successful therapy rarely have a 'healthy' gut microbiota. Dysbiosis has been linked to disease progression, and vice versa. A study of newly infected, untreated men found an association between higher levels of lactic acid bacteria and higher CD4 cell count, lower viral load and reduced microbial translocation<sup>16</sup> (all predictors of a better clinical prognosis<sup>17-18</sup>).

observed in HIV-positive women and conversely, a *Lactobacillus*-dominated microbiota has been associated with reduced HIV prevalence and viral load.<sup>24-26</sup> A *Lactobacillus*-predominant microbiota not only makes the vagina more hostile to HIV, it could also lower risk of transfer to male partners by reducing viral shedding.<sup>27-28</sup>

## Probiotics and HIV

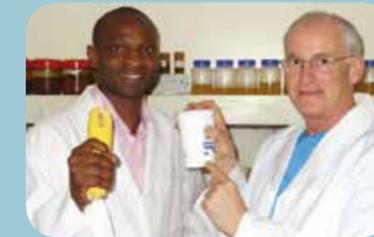
Although research is still in its infancy, interesting findings have come from investigations either into preserving immune function or improving the associated gut-related problems.<sup>29</sup> Such research is underpinned by mechanistic studies that have shown, for example, that expression of the CD4 receptor by lactobacilli enables these bacteria to bind to the virus and block HIV infection.<sup>30</sup>

## Probiotic yogurt in Africa

A community kitchen project started in Tanzania is now being expanded across Africa thanks to the Western Heads East charity ([www.westernheadseast.ca](http://www.westernheadseast.ca)) and YobaforLife ([www.yoba4life.com](http://www.yoba4life.com)).<sup>40</sup> Professor Gregor Reid (University of Western Ontario, Canada), the main driver behind this initiative, told us: 'Probiotic yogurt that is affordable to all, has the potential to save and improve many lives in the developing world: the challenge is to get it there in a sustainable manner.'



Professor Gregor Reid with the yogurt mamas of Mwanza



Nicholas Nduti (PhD student) and Professor Gregor Reid

## The vaginal microbiota and HIV

Bacterial vaginosis (characterised by reduced numbers of the dominant commensal lactobacilli<sup>19-20</sup> and overgrowth with anaerobes<sup>21</sup>), is strongly associated with increased risk of HIV infection.<sup>22</sup> Normal levels of lactic acid should kill HIV; fewer lactobacilli invariably means the vagina is not sufficiently acidic.<sup>23</sup> A disturbed vaginal microbiota has been

In a small pilot study in Nigeria, consumption of yogurt containing *L. rhamnosus* GR-1 and *L. reuteri* RC-14 (strains previously shown to be beneficial for bacterial vaginosis)<sup>31</sup> was linked to cessation of diarrhoea and a trend for delayed decline of CD4 T cells.<sup>32</sup> A later 3-year retrospective study found that the probiotic yogurt (*L. rhamnosus* GR-1) made by local women in a low income community in

Tanzania significantly increased CD4 count<sup>33</sup> although a large controlled study (n=112) did not show any more health benefit than that associated with consumption of a micronutrient-enriched yogurt.<sup>34</sup>

Probiotic studies conducted with children have also shown positive indications, including improved CD4 counts, improved growth and reduced diarrhoea.<sup>36-38</sup> Several other strains, a prebiotic<sup>39</sup> and synbiotic combinations have been investigated with adults in both developed and developing countries.<sup>40-43</sup>

Dr Reale and colleague Dr Falasca told us about their new research in Italy. 'Immune-modulation is an important potential mechanism for probiotics, and pro-inflammatory cytokines such as IL-6 and TNF $\alpha$ , and TGF $\beta$  levels are elevated in HIV-infected patients, so we decided to conduct a small study in HIV-infected subjects (20 clinically stable and on ART, and 8 naive for treatment) to investigate the effects of a probiotic (*Lactobacillus casei* Shirota; LcS) on immune cell counts, and expression of cytokines in human peripheral blood mononuclear cells (PBMC) and their circulating levels in the plasma. We presented preliminary results at two conferences in Italy this year.<sup>44</sup> Encouragingly, we saw an average increase in CD4+, CD8+ and CD56+ cell count, and modulation of cytokine levels. The probiotic was well tolerated by the patients. Of course, larger and longer term studies are needed in order to confirm and understand these findings. It would be interesting, for example, to analyse a broader panel of immune markers, to better define their role in the HIV infection process.'

**We would like to pay our respects to the HIV/AIDS research scientists, activists and health workers who lost their lives in the recent plane crash in Ukraine, and offer condolences to all those affected.**

## The first London microbiome meeting

The first London microbiome meeting at St Thomas' Hospital in June was organised by PhD students Michelle Beaumont and Tiphaine Martin.

Talks from microbiome experts ranged from general overviews to more specific topics (eg, cardiometabolic disease, the oral microbiome and antibiotic dysbiosis). An excellent evening, an ambitious programme, and hopefully to be repeated.



## Symposium report

Thomas et al (2014) Exploring the influence of the gut microbiota and probiotics on health: a symposium report. *British Journal of Nutrition* 112 Suppl 1:S1-S18.

This open access paper describes talks at the International Yakult Symposium in London last year. Reprints are also available from [science@yakult.co.uk](mailto:science@yakult.co.uk).



## A consensus paper on probiotics

Hill et al (2014) *Nature Reviews Gastroenterology & Hepatology* 11:506-514

Leading international probiotic experts gathered in London in October last year to re-examine the probiotic concept; this paper describes the outcome of their debate.

Apart from endorsing (but making a minor grammatical correction to) the FAO/WHO definition,<sup>45</sup> they distinguished three categories of these beneficial microorganisms:

- Probiotics that belong to safe species supported by sufficient evidence of general benefit in humans or with a beneficial property;
- Probiotics in food or supplements that are defined strains with proof of delivery of viable numbers at the end of shelf-life, and convincing evidence for a specific health benefit;
- Probiotic drugs: similar to the latter group but with appropriate trials to meet regulatory standards for drugs.

Undefined consortia, such as those used in faecal microbiota transplantation, were not considered to be probiotic nor were live microbial cultures used to produce fermented foods.

## Yakult: Watch this space!

Yakult and the Japan Aerospace Exploration Agency (JAXA) are collaborating on a research project in the International Space Station that will last until 2020.

They will investigate whether *Lactobacillus casei* Shirota can help support the immune function and gut microbiota of astronauts living in space for extended periods.



## Love Your Gut Cookery School – Cooking for a Sensitive Gut

Earlier this summer, on behalf of the Love Your Gut partners (Yakult UK Limited, Core and the IBS Network), we organised an innovative Cookery School event entitled 'Cooking for a Sensitive Gut'. Based on a concept devised by Dr Nick Read of the IBS Network, the aim was to educate and inform guests about food sensitivity and intolerance, specifically with regard to digestive symptoms.

Up to 33% of the UK's adult population is estimated to have some form of food intolerance; and a 2010 survey found that 43% of the UK experience digestive discomfort (YouGov; n=2,287). Of these, 41% had never visited a doctor, which increased to 61% in 25-35 year olds. Compared to men, women experienced more constipation (53% vs 32%), bloating (62% vs 41%), flatulence (47% vs 41%) and pain (67% vs 58%).

The Cookery School was led by chef and nutritionist Dr Joan Ransley, who had devised a range of original recipes designed to be gentle on the gut – whilst still tickling the taste buds!



Love Your Gut Cookery School guests

Joan led the assembled guests (healthcare professionals, bloggers and food journalists) through a lively demonstration of a starter, main course and dessert, explaining why certain foods might aggravate a delicate digestive system, and suggesting clever 'gut-friendly' alternatives. Guests then paired off and cooked the meals for themselves within the bright and airy surroundings of Cactus Kitchens, home to Michel Roux Jr's Cookery School and Saturday Kitchen. Two nutritionists also answered questions and provided additional advice. The event ended with all guests enjoying the food they had prepared.

To see the recipes, tips – and even a video of the event – please visit [www.loveyourgut.com/recipes](http://www.loveyourgut.com/recipes).

## FODMAPs and irritable bowel syndrome (IBS): an examination of the evidence

Staudacher HM et al (2014) *Nature Reviews Gastroenterology & Hepatology* 11:256-266

**Fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) are short-chain carbohydrates that reach the colon undigested, where they are fermented rapidly by the commensal bacteria that reside there. As they are small molecules, they are also osmotically active in the gut.**

The low FODMAP diet has become increasingly popular since the concept was first explored by researchers in Australia.<sup>46-47</sup> This informative review from the dietetic group at King's College London explains (with the help of a clear diagram) how these

compounds trigger gastrointestinal symptoms, and summarises the clinical evidence for dietary exclusion of fermentable carbohydrates. Ten clinical studies are cited, ranging from retrospective uncontrolled trials to two of randomised, blinded, controlled, crossover design; all report benefit for one or more symptoms. The review concludes with a discussion of the difficulties of conducting such trials, and acknowledges the need to investigate how the diet may affect patients' nutritional intake and their gut microbiota, in particular bifidobacteria.

## Coral reef - probiotics: a new line of research?

Coral reefs are home to an extremely diverse fauna; over 25% of marine species may live in these 'sea rainforests'.<sup>48-50</sup> White Band Disease is killing reefs in the Caribbean, and a University of Derby team has identified three bacteria and one ciliate as possible culprits. Although antibiotics could be a control strategy, large-scale dosing of reefs is not feasible and would increase antibiotic resistance. Coral is similar to the gut in that it produces mucus and has a commensal microbiota that is disrupted when the reef is diseased. This suggests another strategy, as lead researcher Dr Michael Sweet commented: 'We'd like to try and develop a probiotic, basically like a Yakult, where you can dose a coral that has a disease with a community of healthy good bacteria and let the coral fight off the pathogen itself.'



## Pint of Science

It's official - science is cool!

The 'Pint of Science' festival, which combines cutting-edge science talks with a trip to the pub, enables researchers to discuss their work with the general public.

We were delighted to sponsor one of the 'Understanding our Bodies' events in London this May, with talks from University College London researchers Dr Nathan Davies (*Loving your liver – why we should all become hepatophiles*) and Dr Jane MacNaughtan (*Better bacteria for a better you*).

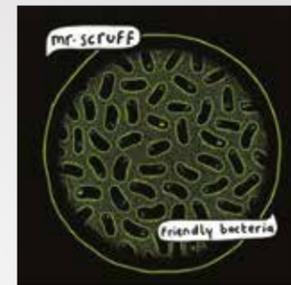
For further details, visit [www.pintofscience.com](http://www.pintofscience.com)



## These 'friendly bacteria' are music to our ears!

We were delighted to see that British DJ and music producer mr. scruff's new album is entitled 'Friendly Bacteria' and features an image of some very friendly-looking bacteria!

To listen to his music and for further details visit: <http://www.mrscruff.com/>



## Crowdsourcing – helping fight ash dieback disease

The power of the people is helping researchers analyse genetic data from the fungal pathogen (*Hymenoscyphus fraxinea*) and the trees themselves (*Fraxinus excelsior*).

Get involved by going to [oadb.tsl.ac.uk](http://oadb.tsl.ac.uk) and playing the Fraxinus Facebook game, an initiative of The Sainsbury Laboratory, Norwich. Each contributor will be acknowledged.

L to R: Allan Downie, Anne Edwards, Dan MacLean, Sophien Kamoun, Kentaro Yoshida, Dianne Saunders.

## Nursing Standard Awards

This year marked the 25th anniversary for these awards - and Yakult was proud to sponsor the 'Patients' Choice Award.'

Congratulations to Susan Lovett, an oncology nurse at the Shrewsbury and Telford Hospital NHS Trust, who won for the 'unbelievably kind and empathetic care' she gave to a patient and his family.

L to R: Katie Griffith (Yakult); Jane Cummings (Chief Nursing Officer, NHS England); Susan Lovett (award winner); Professor Viv Bennett (Director of Nursing, Public Health England); Fiona Phillips (TV presenter and journalist)



## Love Your Gut campaign: an update from our partners



The IBS Network has just launched an e-newsletter, *The Inside Story*, for healthcare professionals interested in IBS. It contains a leading article by an IBS opinion leader/practitioner, an editorial on a controversial topic, and notices of key publications and meetings on IBS.

Take a look at their new healthcare professionals' page at: [www.theibsnetwork.org/healthcare-professionals/](http://www.theibsnetwork.org/healthcare-professionals/) and sign up for a free copy.



Core is a national charity that funds medical research into the prevention, cure and treatment of digestive disorders, and provides information for patients and sufferers.

Check out their recent event Exploring the Science of Digestion at: [www.corecharity.org.uk/video](http://www.corecharity.org.uk/video)

## | Research Round-up

### Recent studies, including those with *Lactobacillus casei* Shirota (LcS)

#### Abdominal symptoms in patients with part or all of their stomachs removed

This study involved 134 gastrectomised patients, who were given a daily probiotic (LcS) or placebo for four weeks. The probiotic (compared to placebo) group showed an improvement in the degree of constipation, for those who had been suffering from it. The group who had been suffering from diarrhoea also showed an improvement (probiotic; comparison between pre- and post-intervention).

Aoki et al (2014) *Scand J Gastroenterol* 49(5):552-63.

#### A retrospective look at habitual consumers of probiotics

This study compared women who worked for a probiotic company and routinely took probiotics, with women who did not regularly take any probiotic. The probiotic strains (LcS and *Bifidobacterium breve* Yakult [BbY]) were detected more frequently in the probiotic group's faecal microbiota, which had a profile generally considered more conducive to health. The habitual probiotic consumers were observed to have a better bowel habit (ie, increased defecation frequency and significantly softer stools, within the normal range).

Tsuji et al (2014) *Int J Probiotics Prebiotics* 9(1/2):31-38.

#### Patients with chronic kidney disease

Thirty-one patients enrolled into this exploratory randomised controlled trial; they were divided into two groups and given different doses of probiotic (LcS) for eight weeks. The higher dose of LcS was associated with a reduction of over 10% in blood urea concentrations (compared to baseline).

Miranda Alariste et al (2014) *Nutr Hosp* 29:582-590.

#### Dysbiosis in patients with type 2 diabetes (T2D)

The faecal gut microbiota of 50 patients with T2D and 50 control subjects was analysed using a reverse transcription-quantitative PCR method. The patients had lower counts of *Clostridium coccooides* group, *Atopobium* cluster and *Prevotella*, and higher lactobacilli counts. Gut bacteria were also found more often in the blood of the patients, suggesting translocation from the gut had occurred.

Sato et al (2014) *Diabetes Care* Aug;37(8):2343-50

#### Does small intestinal permeability deteriorate with age?

In this cross-sectional study, 215 non-smoking healthy adults went on a 12-hour fast, then consumed lactulose and mannitol. This was followed by an analysis of their urine for the sugars. Gut permeability was similar for older and younger adults, but the gut appeared impaired in people who had a combination of low-grade inflammation and noninsulin-dependent type 2 diabetes.

Valentini et al (2014) *Physiological Reports* 2(4):e00281.

#### Babies undergoing surgery for congenital heart disease

This pilot study investigated 21 neonates, randomised to receive either enteral probiotic (BbY) or not. The probiotic appeared to be safe, and improved the faecal microbiota and faecal levels of organic and acetic acids. There were indications that it helped postoperative recovery.

Umenai et al (2014) *J Intensive Care* 2:36.

#### Yakult-FINA consensus statement on nutrition for the aquatic sports

These recommendations were agreed by an international panel of nutrition experts, and explain the importance of an effective nutrition plan, with specific advice for different disciplines: swimming, open water swimming, water polo, diving and synchronised swimming.

Mountjoy et al (2014) *Int J Sport Nutr Exercise Metab* 24(4):349-350.

#### Malnutrition in children damages the gut microbiota

In this study in Bangladesh, nutritional supplements were given to children with severe acute malnourishment in Bangladesh (for 1.3 ± 0.7 weeks). Whilst the children did gain weight, only a temporary improvement in the profile of their poorly-developed gut microbiota was observed. The association of severe acute malnutrition to significant relative microbiota immaturity may explain why such children often fail to grow normally, and indicates that nutritional supplementation should be long-term. And/ or adding gut microbes may be needed.

Subramanian et al (2014) *Nature* 510:417-421.

#### Is an aberrant gut microbiota a risk factor for sudden infant death syndrome (SIDS)?

The intestinal microbiota of SIDS babies was analysed and compared with faecal analysis of live babies. Dual colonisation with *Clostridium difficile* and *Clostridium perfringens* occurred more frequently in SIDS babies, who were also more often colonised with *Staphylococcus aureus*.

Hight et al (2014) *Int J Med Microbiol* 304:735-741.

# Yakult Study Day

## 1st October, 2014

Current insights into the gut microbiota and its influence on health: An independent and expert review examining different patient groups.

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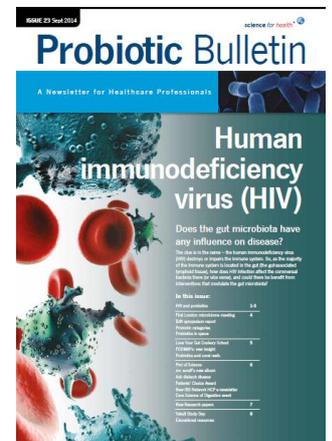
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This booklet is intended for healthcare professionals. Not to be distributed to patients.

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## References for Probiotic Bulletin, Issue 23

### Page 1-3 Human immunodeficiency virus (HIV)

1. Lim S *et al* (1993) Audit of endoscopic surveillance biopsy specimens in HIV positive patients with gastrointestinal symptoms. *Gut* **34(10)**: 1429–1432
2. Klatt NR *et al* (2013) Microbial translocation, immune activation, and HIV disease. *Trends Microbiol* **21**:6-13.
3. Merlini E *et al* (2011) Evidence for polymicrobial flora translocating in peripheral blood of HIV-infected patients with poor response to antiretroviral therapy. *PlosOne* **6(4)**:e18580.
4. Public Health England. HIV in the United Kingdom: 2013 report. [www.gov.uk/phe](http://www.gov.uk/phe)
5. Murray CJ *et al* (2014) Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* pii: S0140-6736(14)60844-8.
6. Persaud D *et al* (2013) Absence of detectable HIV-1 viremia after treatment cessation in an infant. *N Eng J Med* **369**:1828-35.
7. Vujkovic-Cvijin I *et al* (2013) Dysbiosis of the gut microbiota is associated with HIV disease progression and tryptophan catabolism. *Sci Transl Med* **5**:193ra91.
8. Mutlu EA *et al* (2014) A compositional look at the human gastrointestinal microbiome and immune activation parameters in HIV infected subjects. *PlosPathogens* **10(2)**:e1003829.
9. Dillon SM *et al* (2014) An altered intestinal mucosal microbiome in HIV-1 infection is associated with mucosal and systemic immune activation and endotoxaemia. *Mucosal Immunol* **7(4)**:983-994.
10. McHardy IH *et al* (2013) HIV infection is associated with compositional and functional shifts in the rectal mucosal microbiota. *Microbiome* **1**:26.
11. Ellis CL *et al* (2011) Molecular characterization of stool microbiota in HIV-infected subjects by panbacterial and order-level 16S ribosomal DNA (rDNA) quantification and correlations with immune activation. *J Acquir Immune Defic Syndr* **57(5)**:363-370.
12. Lozupone CA *et al* (2013) Alterations in the gut microbiota associated with HIV-1 infection. *Cell Host Microbe* **14**:329 – 39.
13. Cunningham-Rundles S *et al* (2011) Effect of probiotic bacteria on microbial host defense, growth, and immune function in human immunodeficiency virus Type-1 infection. *Nutrients* **3**:1042-1070.
14. Lifson JD & Engleman EG (1989) Role of CD4 in normal immunity and HIV infection. *Immunol Rev* **109**:93-117.
15. Donahue D, Wainberg MA (2013) Cellular and molecular mechanisms involved in the establishment of HIV-1 latency. *Retrovirology* **10**:11
16. Perez-Santago J *et al* (2013) Gut Lactobacillales are associated with higher CD4 and less microbial translocation during HIV infection. *AIDS* **27(12)**:1921-1931.
17. Graham NM (1996) The role of immunologic and viral markers in predicting clinical outcome in HIV infection. *AIDS* **10(Suppl 5)**:S21-S25.
18. Fahey JL *et al* (1990) The prognostic value of cellular and serologica markers in infection with human immunodeficiency virus type 1. *N Engl J Med* **322**:166-172.
19. Lamont RF *et al* (2011) The vaginal microbiome: new information about genital tract flora using molecular based techniques. *BJOG* **118**:533-549.
20. Ravel J *et al* (2011) Vaginal microbiome of reproductive-age women. *PNAS* **108(Suppl 1)**:4680-4687.
21. Fredricks DN *et al* (2005) Molecular identification of bacteria associated with bacterial vaginosis. *N Engl J Med* **353**:1899-1911.
22. Atashili J *et al* (2008) Bacterial vaginosis and HIV acquisition: A meta-analysis of published studies. *AIDS* **22(12)**:1493-1501.

23. Aldunate M *et al* (2013) Vaginal concentrations of lactic acid potentially inactivate HIV. *J Antimicrob Chemother* **68**:2015-2025.
24. Petrova M *et al* (2013) Vaginal microbiota and its role in HIV transmission and infection. *FEMS Microbiol Rev* **37(5)**:762-792.
25. Spear GT *et al* (2008) Comparison of the diversity of the vaginal microbiota in HIV-infected and –uninfected women with and without Bacterial Vaginosis. *J Infect Dis* **198(8)**:1131-1140.
26. Borgdorff H *et al* (2014) *Lactobacillus*-dominated cervicovaginal microbiota associated with reduced HIV/STI prevalence and genital HIV viral load in African women. *ISME J* March 6 [Epub ahead off print]
27. Nardis C *et al* (2013) Vaginal microbiota and viral sexually transmitted disease. *An Ig* **25**:443-456.
28. Mitchell C *et al* (2013) Interaction between lactobacilli, bacterial vaginosis-associated bacteria, and HIV type 1 RNA and DNA genital shedding in U.S. and Kenyan women. *AIDS Res Hum Retroviruses* **29(1)**:13-19.
29. Irvine SL *et al* (2011) Probiotic yogurt consumption may improve gastrointestinal symptoms, productivity, and nutritional intake of people living with human immunodeficiency virus in Mwanza, Tanzania. *Nutr Res* **31(12)**:875-881.
30. Su Y *et al* (2013) CD4 detected from *Lactobacillus* helps understand the interaction between *Lactobacillus* and HIV. *Microbiol Res* **168**:273-277.
31. Anukam KC *et al* (2006) Clinical study comparing probiotic *Lactobacillus* GR-1 and RC-14 with metronidazole vaginal gel to treat symptomatic bacterial vaginosis. *Microbes Infect* **8(12-13)**:2772-2776.
32. Anukam KC *et al* (2008) Yogurt containing probiotic *Lactobacillus rhamnosus* GR-1 and *L. reuteri* RC-14 helps resolve moderate diarrhea and increases CD4 count in HIV/AIDS patients. *J Clin Gastroenterol* **42(3)**:239-243.
33. Irvine SL *et al* (2010) Probiotic consumption is associated with an increase of CD4 count among people living with HIV/AIDS. *J Clin Gastroenterol* **44(9)**:e201-5.
34. Hummelmen R *et al* (2011) Effect of micronutrient and probiotic fortified yogurt on immune-function of anti-retroviral therapy naïve HIV patients. *Nutrients* **3**:897-909.
35. Whaling MA *et al* (2012) Perceptions about probiotic yogurt for health and nutrition in the context of HIV/AIDS in Mwanza, Tanzania. *J Health Popul Nutr* **30(1)**:31-40.
36. Gautam N *et al* (2014) Role of multivitamins, micronutrients and probiotics supplementation in management of HIV infected children. *Indian J Pediatr* April 24 [Epub ahead of print]
37. Trois L *et al* (2008) Use of probiotics in HIV-infected children: a randomized double-blind controlled study. *J Trop Pediatr* **54**:19-24.
38. Cunningham-Rundles S *et al* (2000) Probiotics and immune response. *Am J Gastroenterol* **95**:S22-S25.
39. Gori A *et al* (2011) Specific prebiotics modulate gut microbiota and immune activation in HAART-naïve HIV infected adults: results of the 'COPA' pilot randomized trial. *Mucosal Immunol* **4(5)**:554-563.
40. Hemsworth JC *et al* (2012) Micronutrient supplemented probiotic yogurt for HIV-infected adults taking HAART in London, Canada. *Gut Microb* **3(5)**:414-9.
41. Hummelmen R *et al* (2010) Micronutrients, *n*-acetyl cysteine, probiotics and prebiotics, a review of effectiveness in reducing HIV progression. *Nutrients* **2**:626-651.
42. Gonzalez-Hernandez LA *et al* (2012) Synbiotic therapy decreases microbial translocation and inflammation and improves immunological status in HIV-infected patients: a double-blind randomized controlled pilot trial. *Nutr J* **11**:90.
43. Schunter M *et al* (2012) Randomized pilot trial of a synbiotic dietary supplement in chronic HIV-1 infection. *Compliment Alt Medicine* **12**:84.

44. Chiara D *et al* (2014) Effect of probiotic *Lactobacillus casei* Shirota on immune function of people living with HIV. IX National Conference of the Italian Society of Immunology, Clinical Immunology,
45. Food and Agricultural Organization of the United Nations and World Health Organization (2001) Health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria. *World Health Organization* [online]  
[http://www.who.int/foodsafety/publications/fs\\_management/probiotics/en/](http://www.who.int/foodsafety/publications/fs_management/probiotics/en/)
46. Shepherd SJ *et al* (2006) [Fructose malabsorption and symptoms of irritable bowel syndrome: guidelines for effective dietary management.](#) *J Am Diet Assoc* **106(10)**:1631
47. Shepherd SJ *et al* (2008) Dietary triggers of abdominal symptoms in patients with irritable bowel syndrome: randomized placebo-controlled evidence. *Clin Gastroenterol Hepatol* **6(7)**:765-771.
48. JH Connell (1978) Diversity in Tropical Rain Forests and Coral Reefs *Science* **199**(4335):1302-1310
49. MD Spalding, EP Green and C Ravilious (2001). *World Atlas of Coral Reefs*. Berkeley, CA: University of California Press and UNEP/WCMC ISBN 0520232550.
50. Mulhall M (2009) Saving rainforests of the sea: An analysis of international efforts to conserve coral reefs. *Duke Environmental Law and Policy Forum* **19**:321–351.

#### **OTHER REFERENCES AND LINKS**

**Page 6 Nursing Standard Awards** Lynne Pearce (2014) Introducing the Patients Choice. *Nursing Standard* **28(37)**:24. Image: <http://www.nurseawards.co.uk/256>

**Page 7 Cookery School** YouGov. Online survey carried out in April 2010 involving a nationally representative sample of 2,287 adults (aged 18+ years).

**Page 7 Yakult Space** Yakult Honsha Ltd press release March 2014 (JAXA to start joint research regarding study of the effect by probiotics on human immune function and gut microbiota in a microgravity environment. [http://global.jaxa.jp/press/2014/03/20140319\\_yakult\\_e.html](http://global.jaxa.jp/press/2014/03/20140319_yakult_e.html)  
Image: [http://www.nasa.gov/mission\\_pages/station/multimedia/config.html](http://www.nasa.gov/mission_pages/station/multimedia/config.html)

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