

# THE USE OF PROBIOTICS ALONGSIDE ANTIBIOTICS



## INTRODUCTION

The introduction of antibiotics was a real turning point for mainstream medicine. Antibiotics have saved many lives and still play an extremely important role in combating bacterial infection. However, there is some concern that antibiotics, particularly broad-spectrum, have been used a little too often in both humans and animals. Conditions such as coughs, colds, sore throats and flu rarely require antibiotics. Antibiotic resistance is when a strain of bacteria no longer responds to treatment with one or more types of antibiotics. This is a growing concern, particularly because few new antibiotics are in development. Current Government strategy is to promote more responsible use of antibiotics among doctors, prescribing them only when they are really needed.

## ANTIBIOTICS EFFECT ON THE MICROFLORA & IMMUNITY

Whilst successfully inhibiting the growth of pathogenic bacteria, antibiotics are now well known to significantly disrupt protective intestinal and vaginal microbiota, significantly reducing bacteria considered to have health-promoting properties such as *Bifidobacterium* spp. and *Lactobacillus* spp.. A diverse microflora plays an important role in the functioning of strong immune and digestive systems. The predominance of lactobacilli in a healthy vagina is known to create an acidic environment that protects women from infection. *Candida* spp. overgrowth is often seen after a course of antibiotics when the defence layer of beneficial bacteria in the gut has been disturbed.

Additionally, antibiotics have been shown to specifically impair white blood cell function, a crucial line of defence<sup>1</sup> and slowing down their movement to the site of infection can delay healing<sup>2</sup>. Certain antibiotics have been shown to interfere with the production of mature T-cells by the thymus gland<sup>3</sup> and antibody production by B-lymphocytes<sup>1</sup>. However, these suppressive effects are beneficial qualities in treating some specific inflammatory conditions and preventing the rejection of transplants<sup>3</sup>.

## ANTIBIOTIC ASSOCIATED DIARRHOEA (AAD)

Antibiotics, as with any medication, can cause side effects such as nausea, vomiting and diarrhoea. By altering the microbial balance within the gastrointestinal tract, further pathogenic bacteria are able to selectively overgrow increasing the risk of developing a further intestinal infection; the main symptom of which being diarrhoea<sup>4</sup>. Rates of AAD vary from 5 to 39%<sup>5</sup>, with the young and the elderly most at risk and those more serious requiring hospitalisation.

## ANTIBIOTIC USE IN PREGNANCY AND INFANCY

In the first years after birth, the intestinal microbiota develops rapidly both in diversity and complexity. Many factors can influence this important early-life intestinal colonisation. Interestingly, early-life antibiotics have been associated with the later development of conditions considered gut related such as coeliac disease, allergies, obesity and autism<sup>6</sup>. Furthermore, maternal antibiotic use during pregnancy has been associated with an increased risk of cow's milk allergy, asthma, eczema and hay fever in their infants<sup>6</sup>.



## PROBIOTICS ALONGSIDE ANTIBIOTICS

A systematic review and meta-analysis by Hempel<sup>7</sup> in 2012, which analysed 63 randomised controlled trials (RCTs) including 11,811 participants, indicated a statistically significant association of probiotic (live bacteria) administration with reduction in AAD. Studies have indicated that probiotics may prevent AAD via restoration of the gut microflora<sup>4</sup>. Engelbrekton *et al*<sup>8</sup> demonstrated that a multi-strain probiotic containing bifidobacteria and lactobacilli strains, taken during and after antibiotic therapy, promoted a more rapid return to pre-antibiotic faecal bacteria. Probiotics may also provide such benefit by directly secreting antibacterial substances targeting pathogens and disrupting biofilm formation, making it easier for antibiotics to function; and by enhancing generalised mucosal immunity, which in turn aids in the eradication of the organisms at the mucosal site<sup>9</sup>.

A Cochrane review in 2011<sup>4</sup> noted that the most effective dose in protective studies appeared to be  $\geq 5$  billion CFUs a day. This protective effect could be evident during and after antibiotic treatment but it could take some time to rebalance the gut microflora and to restore normal gastrointestinal function. In a review in 2009 McFarland *et al*<sup>5</sup> pointed out that most studies only assign probiotics for the duration of the antibiotic treatment but that AAD may be delayed for up to two months (in up to 38% of patients) after antibiotics are discontinued. In a randomised controlled trial of a probiotic mixture given to prevent AAD, the rate of AAD was similar during antibiotic treatment (6.2% probiotic versus 8.1% control), but cases of delayed-onset AAD post-antibiotic treatment were significantly fewer in the probiotic group (5.7%) compared to the control group (27.5%)<sup>10</sup>.

Used alongside standard triple drug therapy for *Helicobacter pylori* a multi-strain probiotic (using Protexin strains) at a dose of 1 billion CFU significantly improved

eradication rate, whilst lowering side effects of nausea, vomiting and diarrhoea<sup>11</sup>. Another multi-strain probiotic (using Protexin strains) at a dose of 100 million CFU taken alongside antibiotics significantly improved symptoms of bacterial vaginosis at a higher rate of 87.5% compared to placebo at 67.5%<sup>12</sup>. Interestingly in 2005 Plummer *et al*<sup>13</sup> found that following antibiotic therapy, antibiotic resistant strains increased in the placebo group but not in those taking a daily probiotic. This could be due to the probiotics ability to clear antibiotic resistant strains thereby preventing the spread of infection, an effect demonstrated in a mouse study by Ubeda *et al* in 2013<sup>14</sup>.

## PROBIOTICS FOR IMMUNITY

A healthy immune system is primed to provide a defence mechanism against invading pathogens and their toxic by-products that could otherwise cause infection. Up to 70% of our immune cells are located in the gut<sup>15</sup>, and supported by a strong microflora<sup>16</sup>. One strategy to support the body's natural immunity to prevent initial infection, and reduce the need for antibiotics, is to consider regular consumption of fermented foods or probiotic supplements.

## CONCLUSION

During antibiotic therapy extra protection could be provided by consuming a probiotic supplement at the same time as antibiotic therapy, although at least 2 hours apart and continued for at least 2-4 weeks after completion of the antibiotic course at a dose of  $\geq 5$  billion CFUs/day. An additional strategy could be to support the body's natural immunity to prevent initial infection by considering regular consumption of probiotics as a daily preventative.

## References

1. Hauser WE Jr, Remington JS. 1982. Effect of antibiotics on the immune response. *Am J Med.* **72**(5):711-6.
2. Thong YH, Ferrante A. 1980. Effect of tetracycline treatment on immunological responses in mice. *Clin Exp Immunol.* **39**(3):728-32.
3. Kloppenburg M, Verweij CL, Miltenburg AM, Verhoeven AJ, Daha MR, Dijkmans BA, Breedveld FC. 1995. The influence of tetracyclines on T cell activation. *Clin Exp Immunol.* **102**(3):635-41.
4. Johnston BC, Goldenberg JZ, Vandvik PO, Sun X, Guyatt GH. 2011. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. *Cochrane Database Syst Rev.* **9**(11):CD004827.
5. McFarland LV. 2009. Evidence-based review of probiotics for antibiotic-associated diarrhea and Clostridium difficile infections. *Anaerobe.* **15**(6):274-80.
6. Nylund L, Satokari R, Salminen S, de Vos WM. 2014. Intestinal microbiota during early life - Impact on health and disease. *Proc Nutr Soc.* **73**(4):457-69.
7. Hempel S, Newberry SJ, Maher AR, Wang Z, Miles JN, Shanman R, Johnson B, Shekelle PG. 2012. Probiotics for the prevention and treatment of antibiotic-associated diarrhea: a systematic review and meta-analysis. *JAMA.* **307**(18):1959-69.
8. Engelbrekton A, Korzenik JR, Pittler A, Sanders ME, Klaenhammer TR, Leyer G, Kitts CL. 2009. Probiotics to minimize the disruption of faecal microbiota in healthy subjects undergoing antibiotic therapy. *J Med Microbiol.* **58**(Pt 5):663-70.
9. Reid G. 2006. Probiotics to prevent the need for, and augment the use of, antibiotics. *Can J Infect Dis Med Microbiol.* **17**(5):291-5.
10. Hickson M, D'Souza AL, Muthu N, Rogers TR, Want S, Rajkumar C, Bulpitt CJ. 2007. Use of probiotic Lactobacillus preparation to prevent diarrhoea associated with antibiotics: randomised double blind placebo controlled trial. *BMJ.* **4:335**(7610):80.
11. Ahmad K, Fatemeh F, Mehri N, Maryam S. 2013. Probiotics for the treatment of pediatric helicobacter pylori infection: a randomized double blind clinical trial. *Iran J Pediatr.* **23**(1):79-84.
12. Tafazzoli HH, Amiraliakbari S, Afrakhteh M, AlaviMajd H, Nouraei S, Ashari Z, Jamalfar H. 2014. Comparison of Metronidazole versus a Combination of Metronidazole plus Probiotics in the Treatment of Bacterial Vaginosis. *J Womens Health, Issues Care.* **3:3**, 2.
13. Plummer SF, Garaiova I, Sarvotham T, Cottrell SL, Le Scouiller S, Weaver MA, Tang J, Dee P, Hunter J. 2005. Effects of probiotics on the composition of the intestinal microbiota following antibiotic therapy. *Int J Antimicrob Agents.* **26**(1):69-74.
14. Ubeda C, Bucci V, Caballero S, Djukovic A, Toussaint NC, Equinda M, Lipuma L, Ling L, Gobourne A, No D, Taur Y, Jena RR, van den Brink MR, Xavier JB, Pamer EG. 2013. Intestinal Microbiota Containing Bacteriophage Species Cures Vancomycin-Resistant Enterococcus faecium Colonization. *Infect Immun.* **81**(3):965-73.
15. Vighi G, Marcucci F, Sensi L, Di Cara G, Frati F. 2008. Allergy and the gastrointestinal system. *Clin Exp Immunol.* **153** Suppl 1:3-6.
16. Cartwright P. 2011. Probiotic Allies. How to Maximise the Health Benefits of your Microflora. Prentice Publishing, Ilford. pp40.

