FACTSHEET

EVIDENCE FOR THE USE OF PROBIOTICS IN AUTISM

Autism is a developmental disease characterized by a spectrum of symptoms ranging from decreased verbal skills and social withdrawal, to repetitive behaviour and violent outbursts[1]. There is some evidence of a genetic predisposition to autism, but the number of autistic subjects with this background is unknown. It is clear that other factors, such as environmental influences, may play a role in this disease[2].

Children with autistic spectrum disorders (ASDs) tend to suffer from severe dietary and/or gastrointestinal (GI) problems (including abdominal pain, constipation, diarrhoea and bloating)[3,4]. In children with ASD, the presence of GI dysfunction is often associated with increased irritability, tantrums, aggressive behaviour, and sleep disturbances. Typically, parents claim that GI problems and behavioural symptoms manifest concurrently[3]. In 2011 Adams *et al*[5] found that GI symptoms were strongly correlated with the severity of autism, indicating that children with more severe autism are likely to have more severe GI symptoms and vice versa. He concluded that it is possible that autism symptoms are exacerbated or even partially due to the underlying GI problems.

Dietary intolerances have been seen, particularly the abnormal digestion of grain and dairy proteins, gluten and casein[6,7,8]. Restricted diets, such as gluten-free and/or casein-free (GF/CF) diets, have been associated with reduced GI disorders, and improved behaviour, in ASD individuals[6]. Many experts believe that these GI symptoms may be due to a disruption of the indigenous gut flora promoting the overgrowth of potentially pathogenic (toxin-producing) micro-organisms[3]. Activation of the mucosal immune response and the presence of abnormal gut microbiota are repeatedly observed in these children[4].

A study by Parracho *et al*[3] in 2005 compared the faecal flora of patients with ASDs with their healthy siblings and unrelated healthy children. The faecal flora of the ASD patients contained a higher incidence of a pathogenic toxin-producing bacterium (*Clostridium histolyticum*), with their siblings also showing some levels of this pathogen. It had been thought therefore that clostridia in the gut might be involved in autism because they are virulent organisms and spore-formers. Spores are known to resist antibacterial agents so that when antibiotics were discontinued the spores would germinate and by toxin production or by another mechanism could lead to autism[9]. However, a study in 2010 by Finegold *et al*[10] showed that *Desulfovibrio* and *Bacteroides vulgatus*, potentially pathogenic bacteria that are also resistant to antimicrobials, were more common in severely autistic subjects than in controls. These pathogenic bacteria species were also similarly found in the siblings of autistic children, again suggesting a possible connection to the family environment[10] or health of the mother.

Modulating gut bacteria with short-term antibiotic treatment has been shown to lead to temporary improvement in behavioural symptoms in some individuals with ASD[4]. It is however unlikely that the cause of the intestinal disturbance in autistic children is due solely to one pathogen but rather a disturbance of the individual's entire gut ecology and a reduction in the protective microflora. It is of concern to some that a significant percentage of individuals with autism have a history of extensive antibiotic use[11]. Oral antibiotics are now well known to significantly disrupt protective intestinal microbiota, creating a favourable environment for colonization by opportunistic pathogens[11,12,13] such as *Clostridium difficile* and *Desulfovibrio*[14].

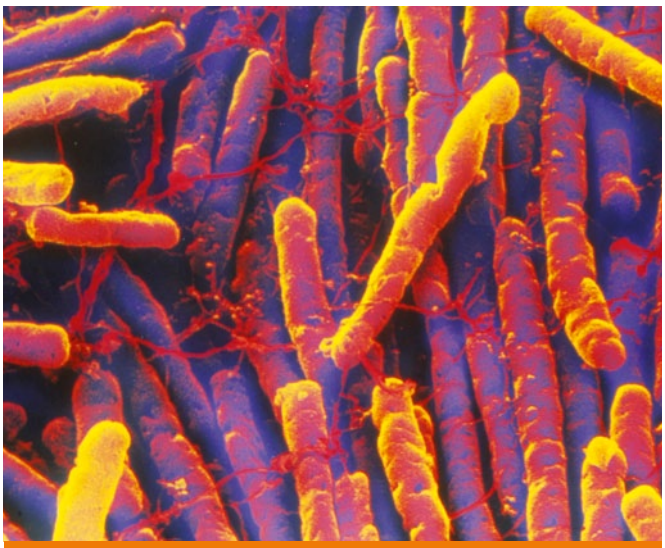

Figure 1: *Clostridium difficile*

Probiotics are believed to influence microbiota composition and intestinal barrier function, alter mucosal immune responses and aid digestion and detoxification. The administration of probiotic bacteria to address changes in the microbiota might, therefore, be a useful novel therapeutic tool and potentially ameliorate ASD behavioural symptoms[4]. In 2009 it was estimated that over half of children with autism were using complementary therapies including the use of probiotics[15], often chosen because they are perceived as treating the cause of symptoms rather than the symptoms themselves[16].

Bio-Kult is a unique multi-strain probiotic with 14 different strains of beneficial bacteria. As each different probiotic strain has a slightly different beneficial effect within the body a multi-strain is believed to have more positive benefits overall and therefore be able to help a more diverse range of GI disorders. *In vitro*[17] work has demonstrated the antibacterial activity of the Bio-Kult multi-strain mix on three common GI pathogens *Clostridium difficile, Escheria coli* and *Salmonella typhimurium.*

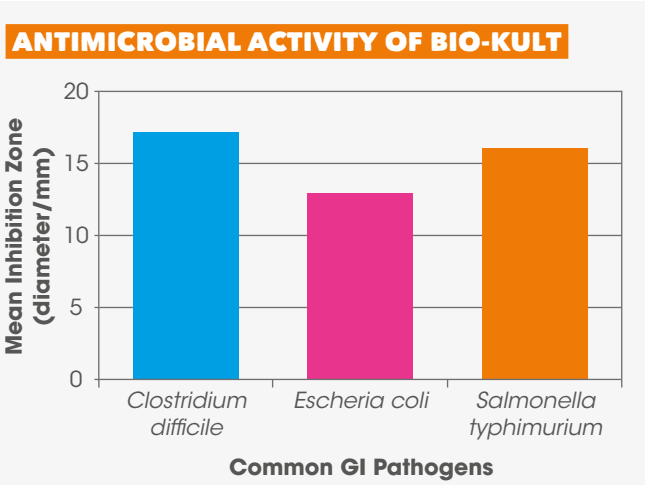

Figure 2: Probiotics International Limited: Data on file.

References

1. Brudnak MA. 2002. Probiotics as an adjuvant to detoxification protocols. *Med Hypotheses.* May;**58**(5):382-5.
2. Finegold SM, Dowd SE, Gontcharova V, Liu C, Henley KE, Wolcott RD, Youn E, Summanen PH, Granpeesheh D, Dixon D, Liu M, Molitoris DR, Green JA 3rd. 2010. Pyrosequencing study of fecal microflora of autistic and control children. *Anaerobe.* Aug;**16**(4):444-53.
3. Parracho HM, Bingham MO, Gibson GR, McCartney AL. 2005. Differences between the gut microflora of children with autistic spectrum disorders and that of healthy children. *J Med Microbiol.* Oct;**54**(Pt 10):987-91.
4. Critchfield JW, van Hemert S, Ash M, Mulder L, Ashwood P. 2011. The potential role of probiotics in the management of childhood autism spectrum disorders. *Gastroenterol Res Pract.* 2011:161358.
5. Adams JB, Johansen LJ, Powell LD, Quig D, Rubin RA. 2011. Gastrointestinal flora and gastrointestinal status in children with autism–comparisons to typical children and correlation with autism severity. *BMC Gastroenterol.* Mar **16**;11:22.
6. Knivsberg AM, Reichelt KL, Høien T, Nødland M. 2002. A randomised, controlled study of dietary intervention in autistic syndromes. *Nutr Neurosci.* Sep;**5**(4):251-61.
7. Garvey J. 2002. Diet in autism and associated disorders. *J Fam Health Care.***12**(2):34-8.
8. de Magistris L, Familiari V, Pascotto A, Sapone A, Frolli A, Iardino P, Carteni M, De Rosa M, Francavilla R, Riegler G, Militerni R, Bravaccio C. 2010. Alterations of the intestinal barrier in patients with autism spectrum disorders and in their first-degree relatives. *J Pediatr Gastroenterol Nutr.* **51**(4):418-24.
9. Finegold SM. 2011. Desulfovibrio species are potentially important in regressive autism. *Med Hypotheses.* Aug;**77**(2):270-4.
10. Finegold SM. 2011. State of the art; microbiology in health and disease. Intestinal bacterial flora in autism. *Anaerobe.* Dec;**17**(6):367-8.
11. Bolte ER. 1998. Autism and Clostridium tetani. *Med Hypotheses.* Aug;**51**(2):133-44.
12. Borchert D, Sheridan L, Papatsoris A, Faruquz Z, Barua JM, Junaid I, Pati Y, Chinegwundoh F, Buchholz N. 2008. Prevention and treatment of urinary tract infection with probiotics: Review and research perspective. *Indian J Urol.* **24**(2):139-44.
13. Johnston BC, Goldenberg JZ, Vandvik PO, Sun X, Guyatt GH. 2011. Probiotics for the prevention of pediatric antibiotic-associated diarrhea. *Cochrane Database Syst Rev.* Nov 9;(**11**):CD004827.
14. Finegold SM, Downes J, Summanen PH. 2012. Microbiology of regressive autism. *Anaerobe.* Apr;**18**(2):260-2.
15. Golnik AE, Ireland M. 2009. Complementary alternative medicine for children with autism: a physician survey. *J Autism Dev Disord.* Jul;**39**(7):996-1005.
16. Levy SE, Hyman SL. 2005. Novel treatments for autistic spectrum disorders. *Ment Retard Dev Disabil Res Rev.***11**(2):131-42.
17. Probiotics International Limited: *Data on file.*

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