

AUTO-IMMUNITY AND THE GUT CONNECTION

INTRODUCTION

Auto-immunity is where the body's immune system mistakenly attacks and destroys the body's own healthy cells and tissues. An auto-immune disease is a disorder that occurs because of auto-immunity. There are over 70 classified diagnosable auto-immune conditions, with over 200 now suspected. Each condition relates to a specific area of the body that is being attacked, for example, the pancreas in type 1 diabetes mellitus, the joints in rheumatoid arthritis, the nervous system in multiple sclerosis and the gut lining in Crohn's disease. Over time, the immune system permanently damages and disables the structure under attack, leading to chronic disease. It is reported that autoimmune diseases are the third leading cause of morbidity and mortality in the industrialised world, surpassed only by cancer and heart disease¹. Each autoimmune disease is typically treated separately with immunosuppressive medication to suppress the body's own immune response.

POSSIBLE CAUSES OF AUTO-IMMUNITY

The etiology of most autoimmune diseases remains unknown. Although there is an underlying genetic link, studies suggest there is a combination of other factors included, like environmental factors². One theory is that some microorganisms (such as bacteria or viruses) or drugs may trigger some of these changes, especially in people who have genes that make them more likely to get auto-immune disorders².

THE CONNECTION BETWEEN AUTO-IMMUNITY AND THE GUT MICROFLORA

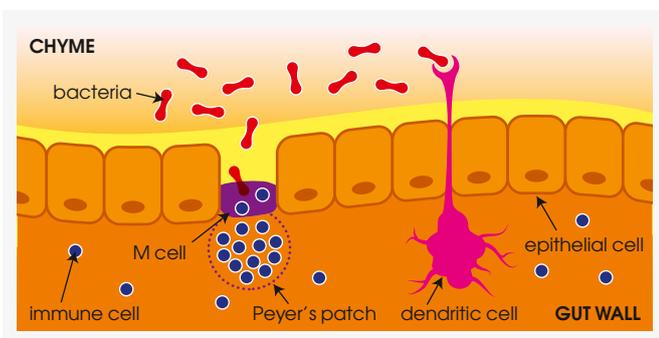


Diagram: Cartwright P. 2011.

As over 70% of our immune system is located within the gut³, many experts now believe that the development of auto-immune disorders begins here. A well-functioning immune system is able to provide protection against foreign substances such as harmful microbes and toxins. Our gastrointestinal tracts are home to trillions of organisms, mainly bacteria, and these form what is known as the gut microflora. It is known that the gut microflora

profoundly influences the continued development and health of the gut mucosal lining⁴ and the corresponding immune system^{5,6}. It appears that an infant's immune system is originally activated by the gut microflora received from the mother via vaginal birth and breast feeding, and from the surrounding environment⁷. Any disturbance to this protective gut flora could have severe impacts on the appropriate functioning of the gut immune system at any stage of life. The gut microflora could be damaged by a number of mechanisms such as antibiotics, infection, stress, diet and lifestyle. Recent epidemiologic data showed that children with autoimmune disease have a different intestinal flora from healthy ones⁸. In adults with auto-immune conditions alterations of intestinal flora have also been observed^{9,10}.

THE ROLE OF INTESTINAL BARRIER FUNCTION

A healthy gut mucosal lining with its intercellular tight junctions is our internal barrier against the outside world, protecting the body from foreign substances such as toxins or pathogens. Once food has been adequately digested along the various stages of the gastrointestinal tract, the final stage is completed by digestive enzymes produced by glands on the gut lining and by the accompanying gut microflora. These minute food particles are then absorbed across the gut lining into the blood stream, enabling us to get the necessary nutrients from our foods. It is believed the gut lining can be damaged in a number of ways such as by inflammation, toxins, pathogens, food sensitivities, alcohol, medications, stress etc. A healthy balanced gut microflora is one mechanism reported to protect against damage to the health and integrity of this gut mucosal barrier¹¹. However, if the gut microflora is imbalanced and the final stages of food digestion are not completed, mal-digested proteins appear to then cross a damaged gut lining in genetically susceptible individuals¹¹. When not recognised as beneficial nutrients the corresponding immune system appears to stimulate an immune response to destroy these unknown substances, and antibodies are created to remember this invader for the future, as in a food allergy. Various mal-digested proteins often look very similar to the body's own proteins which are the building blocks for every cell. These are then later attacked by the antibodies where ever they are found in the body, causing the long term damage seen in auto-immune diseases. This new theory suggests that the auto-immune process in genetically susceptible individuals can be arrested if the interplay between genes and environmental triggers is prevented. In 2005, Fasano *et al*¹¹ proposed this could be achieved by re-establishing intestinal barrier function, including rebalancing the gut microflora, ultimately leading to correct functioning of the immune system.

PROBIOTICS AND AUTO-IMMUNITY

Probiotics are live microorganisms which, when administered in adequate amounts, confer a health benefit on the host¹². As probiotics have been shown to positively influence gut microflora balance, the immune system¹³ and intestinal barrier function¹⁴, there is theoretical rationale for their use

in auto-immune diseases. However, there is a large amount of conflicting data on the preventive/therapeutic effects of probiotics in auto-immune diseases, although there is also fairly promising evidence to recommend them as well⁸. The table below summarises some of these:

Author	Species	Dosage	Study Details
Pineda <i>et al</i> , 2011 ¹⁵	<i>Lactobacillus rhamnosus</i> and <i>Lactobacillus reuteri</i>	2 x 10 ⁹ CFU / capsule twice daily for 3 months (4 billion/day)	29 patients with stable rheumatoid arthritis with chronic synovitis. Although probiotics did not clinically improve RA within the short time scale of 3 months, significant functional improvement was seen within the probiotic group compared to placebo.
Mandel <i>et al</i> , 2010 ¹⁶	<i>Bacillus coagulans</i>	2 x 10 ⁹ CFU / capsule daily for 60 days (2 billion)	45 adults with rheumatoid arthritis were randomly assigned to take a probiotic or placebo in addition to their standard anti-arthritis medications. The probiotic group saw statistically significant improvement in pain scale, greater improvement in patient global assessment and self-assessed disability, reduction in CRP (inflammation) ; as well as the ability to walk 2 miles, reach, and participate in daily activities .
Zocco <i>et al</i> , 2006 ¹⁷	<i>Lactobacillus rhamnosus</i>	18 x 10 ⁹ CFU/d For 12 months (18 billion)	187 ulcerative colitis patients with quiescent disease were randomised to receive a probiotic, mesalazine (standard maintenance treatment) or both. Although all patients relapsed the probiotic seemed to be effective and safe for maintaining a longer remission period .
Kato <i>et al</i> , 2004 ¹⁸	<i>Bifidobacterium breve</i> , <i>Bifidobacterium bifidum</i> and <i>Lactobacillus acidophilus</i>	1 x 10 ¹⁰ CFU/d for 12 weeks (10 billion)	20 patients with mild to moderate, active ulcerative colitis were randomly assigned to a fermented milk product alongside conventional treatment. The multi-strain probiotic was shown to be safe and more effective than conventional treatment alone at reducing UC activity scores.
Hatakka <i>et al</i> , 2003 ¹⁹	<i>Lactobacillus rhamnosus</i>	Twice daily for 12 months	In 21 rheumatoid arthritis patients the mean number of tender and swollen joints was reduced in 71% of the probiotic group vs. 30% of the placebo group, with more subjects in the probiotic group reporting subjective well-being .

CONCLUSION

Whilst there is clear, strong evidence to show that probiotics have a role to play in autoimmune disease, these study results vary in the strain used, the dosage given and for the limited time period of the study. A mixture, or multi-strain product, appears more beneficial than a single strain product in terms of clinical outcomes. This may be due to

synergy between the probiotic bacteria or the increased likelihood of the mixture containing a relevant probiotic for that individuals distinct gut flora or their condition. A multi-strain probiotic taken on a daily basis could therefore, be considered as an adjuvant to existing therapy in autoimmune disease.

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