Exploring the Role of Gut Health in Autoimmune Disease Management

By Leticia Torres

Autoimmune disorders are prevalent and often devastating. But lifestyle interventions to help treat flare-ups or manage high-risk patients are often vague, leaving doctors frustrated and unable to assist fully. Fortunately, emerging research suggests gut health may be crucial in improving treatment and outcomes, offering new tools to enhance patient prognosis.

Autoimmune disease (AD) cases are on the rise as a result of over-sanitized environments and constant exposure to toxins and chemicals.[1] ADs affect 1 in 10 people and disproportionately impact women.[2] These life-long conditions present symptoms that cannot always be managed effectively with medication alone. The unwanted side effects of treatment can take a heavy toll on patients' quality of life as well.[3,4]

Despite the increasing frequency of AD diagnoses, treatment guidelines haven't kept up with the needs of physicians or patients. Current strategies don't target the underlying cause of ADs, leading to frustration with disease management. Preventive guidelines remain similarly disconnected from the underlying mechanisms of the disease, making them ineffective in limiting flare-ups or delaying onset in high-risk patients.[5]

With the benefits unclear and a lack of specific, targeted strategies, these guidelines may seem unimportant to many patients. Ineffective guidelines lead to poor patient compliance. ADs can develop or worsen without simple, actionable strategies that help patients take an active role in preventing or managing the disease. Fortunately, a trait shared by many ADs could be the key to developing more effective prevention strategies.

Many ADs have been associated with an unhealthy gut microbiota. The gut microbiota plays a critical role in immune system function, mainly by maintaining the intestinal barrier and producing short-chain fatty acids (SCFAs). These SCFAs regulate immune cell differentiation and the development of regulatory T cells, both essential in controlling immune responses.[6] When the composition of the gut microbiota is imbalanced—a condition known as dysbiosis—the production of SCFAs is affected.[6] Microbiota dysbiosis is characteristic of several ADs.

Dysbiosis can trigger autoimmune responses and the development or flare-up of ADs through several mechanisms:

- Loss of a healthy intestinal barrier increases gut permeability, allowing microbial products, toxins, and food antigens to leak into the bloodstream, triggering inflammation.[7]
- Development of a pro-inflammatory state through loss of immune tolerance, overactivation of T cells, and overproduction of pro-inflammatory cytokines.[6]
- Production of mimics of host peptides or conversion of host proteins into antigens, triggering cross-reactive immune responses that target host tissues.[6,8]
- Alteration in the production of metabolites important for immune regulation.[6]

The effects of dysbiosis result in immune system chaos. A dysregulated immune response triggered by dysbiosis may be central to the development and worsening of ADs.

Remarkably, the degree or type of dysbiosis can be specific to certain autoimmune conditions, creating a microbiotic *signature*. For instance, in rheumatoid arthritis, patients tend to show an overgrowth of *Prevotella* spp. and a reduction in the abundance of *Bacteroides*, *Bifidobacterium*, and SCFA-producing bacteria.[9] This change is associated with the production of pro-inflammatory molecules and activation of autoreactive immune cells.[9] However, in multiple sclerosis, specific microbiotic metabolites aggravate symptoms by entering the bloodstream and altering the blood-brain barrier, causing neuroinflammation.[10] Gut microbiotic signatures can also help track disease activity. For example, disease progression correlates with an overgrowth of *Lactobacillus salivarius* in patients with rheumatoid arthritis and systemic lupus erythematosus.[6] This means that changes to the gut microbiota can lead to inflammation and autoimmune activity, helping predict disease trends.

Analyzing the microbiota can also benefit healthy people with an increased risk for ADs. Certain signatures are present before disease onset, as is the case with type 1 diabetes. A significant reduction in microbiotic diversity may be seen before the onset of the disease. This may explain why people who develop type 1 diabetes express fewer genes involved in the fermentation and synthesis of SCFAs.[11] These findings suggest periodic monitoring of the microbiota could alert doctors to impending flare-ups or AD onset. Microbiota modification strategies can then be initiated to help prevent progression.

Modifying the gut microbiota through lifestyle interventions such as diet, prebiotics, and probiotics can benefit immune function. Dietary non-digestible fibers that benefit the gut microbiota are known as prebiotics. Animal studies have shown supplementing specific prebiotics like inulin may slow disease progression in patients with rheumatoid arthritis and irritable bowel syndrome.[12,13] Incorporating non-digestible fiber from vegetables, legumes, fruits, nuts, and seeds into the diet provides the necessary nutrients to feed a diverse gut microbiota and is an actionable step for your patients with AD.[14]

Supplementing with probiotics can also benefit patients with ADs. For example, *Lactobacillus casei*, *Acidophilus*, and *Bifidobacterium* proved beneficial to patients with rheumatoid arthritis by enhancing B cell function, reducing inflammation, and improving disease prognosis.[15] An early probiotic intervention can also benefit at-risk people. For example, early probiotic supplementation in children at high risk of developing type 1 diabetes reduced their risk of islet autoimmunity.[16] Dietary intervention can give your at-risk patients concrete, achievable ways to help control or prevent autoimmune conditions.

Despite the potential benefits of gut microbiota biomarkers, some concerns, misconceptions, and limitations remain. A major hurdle is that a definitive cause-effect relationship has not been established, in part due to the multifactorial etiology of ADs.[6] Also, although dysbiosis is well-defined, the structure of a healthy microbiota can vary widely among individuals due to genetic and environmental factors. Therefore, additional considerations like microbiota-host interactions should be included when evaluating gut health.[6] Lastly, the use of probiotics is widespread, but the ideal bacterial strains for specific ADs and the long-term effects of probiotic use are yet to be defined.[6] Further research and validation are necessary to fully define the role of the gut microbiota in the diagnosis and treatment of ADs.

The world of gut health research is evolving rapidly, and the microbiota's connection to immune system development and function is becoming progressively clearer. Appreciating the microbiota's influence on ADs can empower you to suggest impactful lifestyle changes like incorporating a fiber-rich diet, prebiotics, and probiotics. Nurturing a healthy microbiota may help improve symptoms, prevent the onset of ADs, and significantly enhance the well-being of your patients. Learn more about the gut microbiota's association with the development and prognosis of autoimmune disorders here.

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