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Gluten and Its Relationship to Immunological Function
This issue is Part II in a series on gluten sensitivity and immunological function. Dr. Bland begins the issue with an interview with Dr. Kristina Harris of the University of Maryland School of Medicine.

Clinician/Researcher of the Month

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Dr. Kristina Harris has recently received her PhD from the University of Maryland Graduate School. After receiving her undergraduate degree from Southern Illinois University in 2001 and gaining laboratory experience there as a histology technician, Dr. Harris moved on to the University of Maryland, where she originally worked with Dr. Dean Mann on cancer immunotherapy. She was recruited by Dr. Alessio Fasano, director of the Center for Celiac Research at the University of Maryland, to collaborate on studies being conducted on celiac disease. REF #1

Dr. Harris has already published several articles about her work. She and Dr. Bland specifically discuss a 2008 article published in *The Journal of Immunology* (co-authored by Dr. Fasano and Dr. Mann) titled "Cutting Edge: IL-1 Controls the IL-23 Response Induced by Gliadin, the Etiologic Agent in Celiac Disease." This study explores the role of Interleukin-23 (IL-23) in the pathogenesis of celiac disease (CD). The article states, "CD provides a unique model for investigating autoimmunity because both the major genetic (95% HLA-DQ2+) and etiologic factors (dietary glutens) for susceptibility are known. Although the HLA-DQ2/DQ8-restricted T cell response to gluten-derived gliadin peptides has been extensively documented in CD, little is known regarding the innate immune response to dietary gluten in these patients. Because the majority of individuals with these alleles are exposed to the etiologic agent but never develop CD, we set out to test the hypothesis that disease susceptibility might be related to differences in IL-23 responses to dietary glutens in HLA-DQ2+ individuals with CD compared to those without disease." REF #2-3

Dr. Bland and Dr. Harris methodically discuss her research, with Dr. Bland highlighting clinically important observations throughout and suggesting how the research ties in to the functional medicine model of patient care. They discuss potential future directions for

gluten research, including some preliminary reports (from other researchers) suggesting that probiotic and prebiotic organisms may play a role in modulating the influence of gluten in some individuals with gluten sensitivity. REF #4-5

Dr. Bland's Takeaways

Following his discussion with Dr. Harris, Dr. Bland summarizes his takeaways and thoughts:

- Celiac disease is categorized as a member of the autoimmune disease family related to auto-antibodies of the small intestine that lead to local and regional inflammatory response.
- There are certain genetic linkages to this condition through polymorphisms that code for increasing susceptibility to adverse or immunological response to gluten.
- Gluten is a term that applies to a family of different proteins, and we really should be talking about the specific members within the gluten family that are the antigenic determinants that create these autoimmune-type responses in genetically susceptible people.
- There are many people who are carriers of the HLA-DQ2+ polymorphism that never experience celiac disease, even when consuming gluten in their diet. There are other variables that relate to the specific personality of these antigenic determinants and autoimmune disease in these individuals that modify the expression of these characteristics.
- The Interleukin-23 (IL-23) immune response pathway may be involved in the cascade of events that manifest as celiac disease.
- IL-23 is a potent cytokine that is related to innate immunity. It has been implicated in the pathogenesis of other tissue-specific autoimmune diseases. This is where (according to Dr. Bland) the topic becomes more broadly implicated for looking at a wide variety of immune-related dysfunctions, possibly even those of the nervous system.

Autism and Oxidative Stress

Dr. Bland closes this issue with a discussion of autism. He recounts some of his personal experiences from his long association with the Institutes for the Achievement of Human Potential (www.iahp.org) in Philadelphia, and specifically discusses a 2009 article published in *BMC Pediatrics* titled, "Hyperbaric Treatment for Children with Autism: A Multicenter, Randomized, Double-Blind, Controlled Trial." In this trial, 62 children with autism, age 2 – 7, were recruited from six centers. The children were randomly assigned to 40 hourly treatments of either hyperbaric treatment at 1.3 atmospheres (atm) and 24% oxygen or slightly pressurized room air at 1.03 atm and 21% oxygen. Outcome measures included Clinical Global Impression scale, Aberrant Behavior Checklist (ABC), and Autism Treatment Evaluation Checklist (ATEC). The conclusions of this study were that children with autism who received hyperbaric treatment at 1.3 atm and 24% oxygen for 40 hourly sessions had significant improvements in overall functioning, receptive language, social interaction, eye contact, and sensory/cognitive awareness compared to children who received slightly pressurized room air. Dr. Bland briefly provides some background on oxidative biochemistry and discusses some of the variables that can affect oxygen delivery to the brain. REF #6

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