

## **AU1 Autism, An Extreme Challenge to Integrate Medicine. Part II: Medical Management**

Parris M. Kidd, PhD. *Altern Med Rev* 2002;7(6):472-499)

Autism and allied autistic spectrum disorders (ASD) present myriad behavioral, clinical, and biochemical abnormalities. Parental participation, advanced testing protocols, and eclectic treatment strategies have driven progress toward cure. Behavioral modification and structured education are beneficial but insufficient. Dietary restrictions, including removal of milk and other casein dairy products, wheat and other gluten sources, sugar, chocolate, preservatives, and food coloring are beneficial and prerequisite to benefit from other interventions. Individualized IgG or IgE testing can identify other troublesome foods but not non-immune mediated food sensitivities. Gastrointestinal improvement rests on controlling *Candida* and other parasites, and using probiotic bacteria and nutrients to correct dysbiosis and decrease gut permeability. Detoxification of mercury and other heavy metals by DMSA/ DMPS chelation can have marked benefit. Documented sulfoxidation-sulfation inadequacies call for sulfur-sulphydryl repletion and other liver p450 support. Many nutrient supplements are beneficial and well tolerated, including dimethylglycine (DMG) and a combination of pyridoxine (vitamin B6) and magnesium, both of which benefit roughly half of ASD cases. Vitamins A, B3, C, and folic acid; the minerals calcium and zinc; cod liver oil; and digestive enzymes, all offer benefit. Secretin, a triggering factor for digestion, is presently under investigation. Immune therapies (pentoxifyllin, intravenous immunoglobulin, transfer factor, and colostrum) benefit selected cases. Long-chain omega-3 fatty acids offer great promise. Current pharmaceuticals fail to benefit the primary symptoms and can have marked adverse effects. Individualized, indepth clinical and laboratory assessments and integrative parent-physician-scientist cooperation are the keys to successful ASD management.'

## **AU2 Autism and Schizophrenia: Intestinal Disorders**

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We examined Dohan's hypothesis that schizophrenia is associated with the absorption of uexorphins" contained in gluten and casein. In addition, because of the work of Reichelt et al. (Reichelt, K.L., Saelid, G., Lindback, J. and Orbeck, H. (1986) *Biological Psychiatry* 21: 1279-1290) and Rodriguezetal. (Rodriguez, Trav, A.L., Barreiro Marin, P., Galvez, Borrero, I.M., del Olmo Romero-Nieva, F. and Diaz Alvarez, A. (1994) *Journal of Nervous and Mental Disease* Aug; 182(8): 478-479), we carried out similar studies on a group of children with autism. In both syndromes we found similar patterns of peptide containing peaks (Ninhydrin positive) after molecular screening with Sephadex G-15. Immunoglobulin assay of IgA and IgG against gliadin and casein in serum was done. High titer IgG antibodies to gliadin were found in 87% of autistic and 86% of schizophrenic patients and high titer IgG antibodies to bovine casein were found in 90% of autistic and in 93% of schizophrenic patients. High titer IgA antibodies to gluten or casein were found in 30% of children with autism while in schizophrenic patients 86% had elevated IgA antibodies to gluten and 67% to casein; some normal children and adults have these antibodies but only in trace amounts.'

## **AU3 Neuroglial Activation and Neuroinflammation in the Brain of Patients with Autism**

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Autism is a neurodevelopmental disorder characterized by impaired communication and social interaction and may be accompanied by mental retardation and epilepsy. Its cause remains unknown, despite evidence that genetic, environmental, and immunological factors may play a role in its pathogenesis. To investigate whether immune-mediated mechanisms are involved in the pathogenesis of autism, we used immunocytochemistry, cytokine protein arrays, and enzyme-linked immunosorbent assays to study brain tissues and cerebrospinal fluid (CSF) from autistic patients and determined the magnitude of neuroglial and inflammatory reactions and their cytokine expression profiles. Brain tissues from cerebellum, midfrontal, and cingulate gyrus obtained at autopsy from 11 patients with autism were used for morphological studies. Fresh-frozen tissues available from seven patients and CSF from six living autistic patients were used for cytokine protein profiling. We demonstrate an active neuroinflammatory process in the cerebral cortex, white matter, and notably in cerebellum of autistic patients. Immunocytochemical studies showed marked activation of microglia and astroglia, and cytokine profiling indicated that macrophage chemoattractant protein (MCP)-1 and tumor growth factor-1, derived from neuroglia, were the most prevalent cytokines in brain tissues. CSF showed a unique proinflammatory profile of cytokines, including a marked increase in MCP-1. Our findings indicate that innate neuroimmune reactions play a pathogenic role in an undefined proportion of autistic patients, suggesting that future therapies might involve modifying neuroglial responses in the brain.'