Wakefield: gut-brain connection increasingly clear

Awareness is growing among experts, says Andrew Wakefield in a new review article, that in a large proportion of children with developmental disorders "gut-brain interactions may be central to abnormal neural development and the subsequent expression of aberrant behaviors."

Wakefield, who recently identified a unique form of inflammatory bowel disease in a high percentage of autistic children (see ARRI 12/1, 15/1), says that mounting evidence points to a link between digestive system abnormalities and aberrant behavior in autism. For instance, he notes:

• Approximately half of autistic children exhibit clinically significant gastrointestinal symptoms, as compared to about 10 percent of developmentally normal children.

• Laboratory studies consistently reveal abnormal gut findings in autism, indicating inflammation, abnormal intestinal permeability and/or abnormal digestive enzyme activity in many cases.

• Autistic children often exhibit deterioration of behavior and gastrointestinal function when given certain foods (e.g., gluten).

• Autistic children also "often manifest complex biochemical, metabolic, and immunologic abnormalities that a primary genetic cause cannot readily account for." Biochemical studies of the bowel abnormalities found in autistic children, for instance, show that they are consistent with an autoimmune pathology.

Wakefield notes that bowel abnormalities similar to those detected by his research group were recently reported in some children with attention deficit hyperactivity disorder, "suggesting that gastrointestinal pathology may be relevant to a broader spectrum of childhood developmental/behavioral disorders."

Wakefield says physicians skeptical of a gut-brain connection in autism may be unaware that such a link is already well established for several other disorders. These include:

• Untreated celiac disease, which causes both intestinal dysfunction and neurological disturbances (including autistic symptoms).

• D-lactic acidosis, in which acid-tolerant bacterial overgrowth in the bowel can lead to neurological symptoms including altered mental state, aggression, stupor, movement disorders, and asterixis (a "flapping" tremor).

• Hepatic encephalopathy, in which a damaged liver fails to metabolize or eliminate toxic gut products, leading to personality changes and mental impairment. Hepatic encephalopathy leads to changes in neurotransmitter (GABA and serotonergic) systems, which are also seen in autism.

Further evidence for a gut-brain connection in autism, Wakefield says, comes from the effects of treating autistic children's bowel problems. "During the course of clinical assessment and management of these children," he says, "we have been impressed by the symptomatic improvement in their behavior and general well-being after bowel clearance before colonoscopy; treatment of intestinal inflammation... relief of chronic constipation; and in particular the elimination of certain proteins (casein or gluten) from the diet." He also cites studies showing that treatment for abnormal gut flora can lead to temporary improvement in autistic children's behavior, and theorizes that the transient nature of this improvement "suggest[s] that any colonic dysbiosis and associated toxic sequelae probably were secondary to underlying intestinal disease rather than the primary problem."

Wakefield says, "In summary, within the autistic spectrum, a substantial group of children have what may be primary intestinal pathology." He notes that a greater understanding of this pathology may lead to more rational treatment approaches.

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"The gut-brain axis in childhood developmental disorders," Andrew J. Wakefield, *Journal of Pediatric Gastroenterology and Nutrition*, Vol. 34, Suppl 1, May-June 2002, S14-7. Address: Andrew Wakefield, International Autism Research Center, 1663 Georgie St. NE, Ste. 700, Palm Bay, FL 32907, wakers@aol.com.

High heavy metal levels seen in autistic children

New research from Britain reveals toxic levels of several heavy metals in a large percentage of autistic children.

Biochemist Gordon Bell tested 37 children (24 with autism, 5 with Asperger syndrome, and 8 with no disability) for toxic metals. Analyzing hair samples, he found that the autistic children's levels of antimony were five times higher than the maximum amount considered safe, and levels of lead and aluminum were three times higher. All 24 autistic children had elevated levels of antimony, compared to about half of the nondisabled children and those with Asperger syndrome. Ninety-two percent of the autistic children had elevated lead levels (vs. 25 percent of nondisabled and 20 percent of Asperger subjects), and 54 percent of the autistic children had elevated aluminum levels (vs 12 percent of nondisabled controls and none of the children with Asperger's).

Noting that all three of these metals weaken immune system function, Bell suggests that high levels of them could impair the body's ability to react in a healthy way to the MMR (measles-mumps-rubella) vaccine—a possible explanation for the apparent link, in many cases, between MMR immunization and autism.

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"Scots study on autism poses new question of MMR link," V. Collins, *The Herald* (UK), July 22, 2002.

Secretin more beneficial for autistic children with chronic diarrhea

Many parents report that their children improve markedly when given infusions of the hormone secretin, but a number of studies have reported little or no overall benefit to subjects. A new double-blind, placebo-controlled, crossover study offers one explanation: secretin appears to improve symptoms in autistic children with chronic diarrhea more than it helps those without this problem.

Janet Kern and colleagues studied 19 autistic children, giving each child one infusion of porcine secretin (2CUs/kg) and one infusion of a placebo saline solution. The researchers report that children with chronic diarrhea (5 boys) showed decreases in irritability, agitation, crying, hyperactivity, and noncompliance when treated with secretin but not in response to placebo, while other subjects did not respond to either secretin or placebo infusions. In addition, the autistic/chronic diarrhea subjects, unlike other subjects, showed an increase in vocabulary, and decreases in withdrawal and stereotypic behavior, after treatment—responses seen in few of the controls. The only significant worsening was seen in one child with no GI symptoms, whose behavior problems escalated.

Kern et al. say secretin may benefit children with chronic diarrhea by increasing the volume and bicarbonate content of secreted pancreatic juices, which in turn may improve bowel integrity. In addition, by decreasing plasma motilin levels, secretin decreases bowel activity and reduces the frequency of diarrhea.

"How GI dysfunction relates to the neurological problems in autism is unclear," Kern et al. say. "However, it is interesting to note that inflammatory bowel disease is associated with neurological disorders." *(See related story on p. 2.)* The researchers note that GI abnormalities are common in autism, and that "the most commonly stated concern of parents of children with autism/PDD is the presence of abnormal stools and bowel movements in their children."

They conclude that the pattern of improvement seen in their study "suggests that there may be a subtype of children with autism/PDD and chronic diarrhea who benefit from secretin."

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"Efficacy of porcine secretin in children with autism and pervasive developmental disorder," Janet K. Kern, Van S. Miller, Patricia A. Evans, and Madhukar H. Trivedi, *Journal of Autism and Developmental Disorders*, Vol. 32, No. 3, June 2002, 153-60. Address: Janet Kern, University of Texas Southwestern Medical Center, St. Paul Professional Building I, 5959 Harry Hines Blvd., Suite 520, Dallas, TX 75390-9101.