Biomedical Update:

Harvard researchers confirm GI/autism link

Harvard physician Timothy Buie recently reported that biopsies performed by him revealed the presence of chronic inflammation of the gastrointestinal tract, as well as the presence of lymphoid nodular hyperplasia, in 15 of 89 autistic children. The findings parallel those of Andrew Wakefield, the researcher who first identified the presence of a unique type of gastrointestinal disorder in children with autism spectrum disorders. Buie told a conference in December, "These children are ill, in distress and pain, and not just mentally, neurologically dysfunctional."

Buie, Rafail Kushak, and colleagues also have measured the activity of dissaccharidases (enzymes that break down carbohydrates in the intestine) in tissues obtained from duodenal biopsies from 308 autistic individuals, comparing them to samples from 206 non-autistic controls. All of the subjects underwent endoscopy for suspected gastrointestinal problems. The researchers report, "Autistic individuals with diarrhea [206 individuals] demonstrated significantly lower maltase activity than nonautistic individuals with diarrhea. Frequency of lactase deficiency in autistic individuals with failure to thrive [five individuals] was significantly higher (80% vs. 25%) than in non-autistic individuals with failure to thrive, and frequency of palatinase deficiency in autistic individuals with diarrhea was significantly higher than in nonautistic individuals with the same gastrointestinal problem." Autistic and nonautistic individuals with other gastrointestinal problems exhibited similar frequencies of disaccharidase deficiencies.

These findings further support the link between autism and a novel form of gastrointestinal disease, and are consistent with clinical evidence that many autistic children improve physically and behaviorally when they are placed on gluten- and casein-free diets and receive supplements of disaccharidase enzymes.

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"Gastrointestinal symptoms and intestinal disaccharidase activities in children with autism," Rafail Kushak, Harland Winter, Nathan Farber, and Timothy Buie, Abstract of presentation to the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition, Annual Meeting, October 20-22, 2005, Salt Lake City, Utah.

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"Gastrointestinal symptoms and intestinal disaccharidase activities in children with autism," Rafail Kushak, Harland Winter, Nathan Farber, and Timothy Buie, *Journal of Pediatric Gastroenterology and Nutrition*, Vol. 41, No. 4, October 2005.

—and—

"Harvard Clinic scientist finds gut/autism link, like Wakefield findings," *FEAT Newsletter*, December 2005.

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Clue to gold's effects on autoimmune disease symptoms uncovered

Interest in gold as a potential treatment for autism has increased following a report by Dan Olmsted of United Press International, who discovered that the first individual diagnosed with autism, more than half a century ago, recovered after being treated with gold salts for juvenile rheumatoid arthritis.

Several months ago, Olmsted reported that an experiment conducted by chemist Boyd Haley (see ARRI 19/4) revealed the ability of gold salts to break the bonds between thiols (a class of molecules found in most enzymes) and mercury, a toxin strongly implicated in autism. The finding suggested that gold salts can reactivate critical enzymes by stripping them of the mercury that impairs their function.

A new report from Harvard indicates that gold's effects may also be related to another of the metal's traits: its ability to disrupt the activity of MHC class II proteins. These proteins normally hold pieces of bacteria, viruses, or other foreign molecules on the surface of specialized cells, alerting lymphocytes to began an immune response—but this process can go awry and cause autoimmune disorders, in which the body attacks its own cells. There is evidence that such processes may play a role in autism.

Brian DeDecker et al. screened thousands of chemical compounds in search of one that would strip foreign molecules from MHC class II proteins. To their surprise, the researchers found that gold, palladium, and platinum all were effective.

The researchers hope the new findings will allow scientists to develop gold-based compounds that are more effective, and less prone to side effects, than gold salts.

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"Noble metals strip peptides from class II MHC proteins," Stephen L. De Wall, Corrie Painter, Jennifer D. Stone, Rajintha Bandaranayake, Don C. Wiley, Timothy J. Mitchison, Lawrence J. Stern, and Brian S. DeDecker, *Nature Chemical Biology*, February 26, 2006 (epub ahead of print publication).

—and—

"Harvard Medical School researchers discover how gold and other medicinal metals in its class function against rheumatoid arthritis and other autoimmune diseases," news release, Harvard Medical School, February 26, 2006.

AS parents show signs of hyper-male brain

Parents of children with Asperger syndrome, a variant of high-functioning autism, show evidence of "extreme male brains," according to a new study by Simon Baron-Cohen and colleagues.

Baron-Cohen et al. have theorized that autism involves excess exposure to testosterone before birth, "masculinizing" the brain. They note that autistic children show an exaggeration of abilities and interests associated with males, such as systemizing, and a deficit of traits associated with females, such as empathy. Their earlier experiments showed that on two mental tests where men and women typically score differently, the test scores of both autistic individuals and their parents are indicative of hyper-masculinization.

In the new study, Baron-Cohen and colleagues used the same two tests—the Embedded Figures Test (EFT) and the "Reading the Mind in the Eyes" task. This time, the researchers used fMRI (functional magnetic resonance imaging) to study the brain activity of 12 parents of individuals with Asperger syndrome and 12 sex-matched controls as they completed the tasks.

The researchers report, "Parents of children with Asperger syndrome show atypical brain function during both visual search and emotion recognition, in the direction of hyper-masculinization of the brain." This pattern, the researchers say, "is assumed to arise from their genetic status as first-degree relatives of people with an autism spectrum condition, that is, as one aspect of the broader autism phenotype."

Editor's note: A different way to interpret Baron-Cohen et al.'s findings is that elevated exposure to testosterone leads to only slight variants in personality and skills, such as those seen in the parents of children with autism or Asperger syndrome—unless an environment insult, to which children with high testosterone levels are particularly sensitive, enters the picture. There is, indeed, one such environmental insult: exposure to mercury, such as that in thimerosal-containing vaccines. It is well established (see ARRI 19/1) that testosterone exacerbates mercury toxicity, while estrogen is protective.

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"fMRI of parents of children with Asperger syndrome: A pilot study," Simon Baron-Cohen, Howard Ring, Xavier Chitnis, Sally Wheelwright, Lloyd Gregory, Steve Williams, Mick Brammer, and Ed Bullmore, *Brain and Cognition*, in press. Address: Simon Baron-Cohen, Autism Research Centre, Dep.t of Psychiatry, University of Cambridge, Douglas House, 18b Trumpington Road, Cambridge CB2 2AH, UK.