Wakefield: intestinal abnormalities confirmed

A large-scale study confirms initial findings of a unique form of inflammatory bowel disease, ileo-colonic lymphoid nodular hyperplasia (LNH), in autistic children.

Andrew Wakefield and colleagues assessed 148 autistic children undergoing ileocolonoscopy for gastrointestinal complaints such as diarrhea or abdominal pain. The majority of the children, who ranged in age from 2 to 16, had regressed following normal early development. The autistic children were compared to 30 nondisabled children also undergoing testing for gastrointestinal problems.

The researchers report that the prevalence of LNH was far greater in autism spectrum disorder children than in controls, both in the ileum (90 percent of autistic children vs. 30 percent of controls) and in the colon (59 percent of autistic children vs. 23 percent of controls), whether or not the controls exhibited colon inflammation. The severity of ileal LNH also was significantly greater than in controls, with 68 percent of autistic children but only 15 percent of controls exhibiting moderate to severe ileal LNH.

Wakefield, the first researcher to identify LNH in autistic children (see ARRI 12/1), says, "The findings of this new study add to the clear evidence of a novel and treatable disease of the intestinal immune system in children with developmental disorders. These are medical diseases which should be treated as such. Children are suffering needlessly and this has got to change."

The researchers note that special diets did not influence the existence or severity of swollen lymph glands, indicating that food intolerance were not a cause. They suggest, instead, that the intestinal inflammation may be associated with a smoldering viral infection.

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"The significance of ileo-colonic lymphoid nodular hyperplasia in children with autistic spectrum disorder," Andrew Wakefield, Paul Ashwood, Kirsten Limb, and Andrew Anthony, *European Journal of Gastroenterology and Hepatology*, Vol. 17, No. 8, August 2005, 827-36. Address: Andrew Wakefield, Thoughtful House for Children, 3001 Bee Caves Road, Austin, TX 78746.

New therapy: Low-dose naltrexone for immunomodulation

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night, the body attempts to overcome the opioid block and the endorphins rise, to stay elevated throughout the next 18 hours. Studies in human cancer patients show that LDN acts to increase natural killer cells and other healthy immune defenses against cancer. Restoration of the body's normal production of endorphins in those with cancer or autoimmune diseases is the major therapeutic action of LDN.

The use of LDN for children with autism spectrum disorders was previously studied in the 1990s, with researchers using from 5 to 50mg daily or every other day. In these trials, researchers were looking for opioid antagonism. Panksepp and other researchers noted better results with low doses; studies on higher doses were more equivocal in children, with non-compliance due to the bitterness of the drug. For my study, Dr. Tyrus Smith at Coastal Compounding agreed to create a transdermal cream. This allowed us to adjust the dose easily (some of the smaller kids did better with only 1-1/2mg), the bitter taste was no problem, and the cream could be put on the patients' bodies while they slept. The cream is put into syringes, with ½ cc providing 3mg for children or 4.5mg for adults.

I recently completed an eight-week informal clinical study on 15 of my autism spectrum disorder patients using 3mg of LDN transdermally between 9 and 12 p.m. Several adults participated also, one with Crohn's Disease and one with Chronic Fatigue Syndrome using 4.5mg nightly. Parents reported weekly on the results of the treatment.

Eight of the 15 children in this study had positive responses, with five of these eight having results considered quite phenomenal according to their parents. The primary positive responses have been in the area of mood, cognition, language, and socialization. Five of the children had equivocal results and three children dropped out, one because of no response after four weeks and the others for non-drug related issues. Two small children responded better when changed to 1-1/2mg dosing. No allergic reactions were noted, and the primary negative side effect was insomnia and earlier awakening when the cream was first administered. The two adults in the study had very positive responses, and the Crohn's participant says she has been in remission since starting LDN (almost three months now).

All of the children in my study were on well-controlled dietary restriction. I am receiving reports from the e-lists I monitor of about five percent of other children having side effects such as irritability, agitation, and restlessness, subsiding as soon as the drug is withdrawn. I am querying these parents about gluten/casein/soy in the children's diets, as this response is very likely indicative of withdrawal symptoms of opioid block. I suspect that children on a strict GF/CF/SF diet are less apt to show this response.

I do not know the cause of the immediate positive mood/cognitive/relating effects seen in the children in my study; it is unlikely the immune benefits are showing this quickly. For other autoimmune groups, the evidence is that the optimum immune response can take four to six months.

I am hoping LDN will be another weapon in our ever-expanding arsenal to help children with autism spectrum disorders become as immune-efficient as possible. Clinical responses must be what we go on for now, as it will take time to get a research study done. Evaluative lab tests show that the majority of our children have autoimmune issues. In my opinion an intervention that is effective, non-toxic, non-invasive, and inexpensive is worth a try.

I want to thank my trusting patients who participated in the study, as well as Dr. Tyrus Smith at Coastal Compounding for helping devise a successful form of LDN to use for our children. (Dr. Smith has offered to share his formula with any compounding pharmacist who wishes to call him; his number is 912-354-5188.) I have started a yahoo e-list for reporting and discussion of this intervention at Autism_LDN@yahoogroups.com.

Mounting evidence points to oxidative stress as a culprit in autism spectrum disorders

Oxidative stress occurs when excessive numbers of molecules in the body lose electrons (a process called oxidation), changing their structure and function and resulting in tissue injury. Indicators of oxidative stress, which is believed to stem from a combination of environmental stressors and genetic vulnerability, include an increase in byproducts of oxidation (oxidized cell parts in urine, blood, or tissues); a decrease in "antioxidant" nutrients, molecules, and enzymes that neutralize oxidants; and elevated levels of toxins.

In 2004 (see ARRI 18/4), Jill James and colleagues reported evidence that autistic children have reduced levels of glutathione—a molecule that protects against oxidation—leading to oxidative stress and making these children highly vulnerable to the effects of the mercury-containing preservative thimerosal. New findings, summarized at two recent conferences, offer powerful support for the autism/oxidative stress link. These findings include:

—Research by George Perry and Robert Salomon revealing evidence of oxidative injury to the axons and dendrites of neurons in the brains of autistic individuals. The researchers found carboxyethylpyrrole, a product of lipid oxidation, in the cortex of autistic individuals but not control subjects.

—The finding by Edith Lopez-Hurtado of elevated levels of another oxidative marker, lipofuscin, in three language-related areas of the brain—and particularly in an area associated with speech recognition. This finding

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