

Autism Research Review

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Reviewing biomedical and educational research in the field of autism and related disorders

Two databases confirm autism rates rose, dropped in parallel with thimerosal exposure

Two large, independent databases reveal that rates of autism and speech disorders began dropping following the removal of the mercury-laden preservative thimerosal from most childhood vaccines. The data also confirm that cases of both disorders rose consistently in earlier years, as children received

growing numbers of thimerosal-containing vaccines.

David Geier and Mark Geier identified cases of autism and speech disorders reported to the national Vaccine Adverse Event Reporting System (VAERS), which contains nationwide reports (nearly all from doctors) about adverse vaccine reactions. They also identified cases of autism reported by California's Department of Developmental Services (CDDS). The researchers then analyzed the trends for autism and speech disorders during the period from 1994 through 2002, and compared it with the trends for the period from 2002 to June 2005.

Children's exposure to thimerosal rose throughout the 1990s, as U.S. officials continued to add vaccines to the pediatric schedule. Drug companies began gradually phasing

out thimerosal from vaccines in 1999, and children are typically diagnosed with neurological disorders at the age of three or four. Thus, a thimerosal-autism link would result in escalating numbers of cases of autism and related disorders through 2002, followed by a steady decline.

This trend, according to Geier and Geier, is exactly what both databases show. They report, "The trends in newly diagnosed neurological disorders correspond directly with the expansion and subsequent contraction of the cumulative mercury dose to which children were exposed from thimerosal-containing vaccines through the U.S. immunization schedule." Moreover, they say, "The magnitude of the change in the trend lines is substantial." (See graphs on next page.)

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Why vitamin B6 works: study offers new clues

Vitamin B6, reported in 21 of 22 studies to be helpful for autism, benefits about half of the autistic children and adults who take it in high doses (typically along with magnesium, which enhances its effects). A new study helps to explain why the vitamin is so beneficial.

James Adams and colleagues compared 35 children with autism spectrum disorders to 11 unrelated, non-disabled children. None of the children were taking supplemental B6 at the time of the study.

The researchers measured blood levels of vitamin B6 in both groups and report that "the children with autism spectrum disorders had much higher levels of vitamin B6 than the controls," a finding that was true for both males and females. Overall, children with autism had a 75% higher level of total vitamin B6 than the controls.

To be used by the body, vitamin B6 must be converted from pyridoxine to pyridoxal-5-phosphate (P5P). Earlier research by Adams and colleagues revealed lower levels of P5P in autistic children than in controls, and also found low activity of an enzyme (pyridoxal kinase) that converts B6 into P5P. Adams et al. theorize that low activity of pyridoxal kinase ultimately results in high levels of inactive B6 and low levels of P5P, consistent with the results of their studies.

Adams and colleagues note that P5P is an enzymatic cofactor for 113 enzymes, and plays a key role in the formation of major neurotransmitters. "Thus, low levels of P5P could have wide-ranging effects on human metabolism, including mental function. Normalization of P5P would be expected to improve mental and physical function in some

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UC Davis study links thimerosal to immune dysregulation

A new study of mice reveals that antigen-presenting cells known as dendritic cells are exquisitely sensitive to thimerosal, and that exposure to even extremely small concentrations of the vaccine preservative can fundamentally change the immune system's ability to respond to a challenge. The study adds to evidence linking thimerosal to autism and other neurodevelopmental disabilities (see related articles above and on page 5).

Isaac Pessah and colleagues found that within minutes, exposure to thimerosal alters the connections between calcium channels in dendritic cells. The researchers say immature cells are particularly sensitive to thimerosal.

"The slightest fluctuation in how calcium channels 'communicate' can alter the growth, maturation and activation of dendritic cells," Pessah says. "Thimerosal dramatically alters how two key calcium channels, code-named RyR1 and IP3R1, found in dendritic cells function as a team by 'garbling' the normal signaling system between them." When this occurs, Pessah notes, dendritic cells respond by secreting abnormal amounts of IL-6 cytokine, a potent chemical that initiates inflammatory responses. Higher concentrations of thimerosal cause programmed death of dendritic cells, preventing them from carrying

out their proper role of activating T cells.

Dendritic cells that receive improper signals can become rogues, Pessah says, "producing misinformation that could activate aberrant and harmful immune responses. Even one rogue dendritic cell can activate many inappropriate immune responses."

Pessah and colleagues used concentrations of thimerosal comparable to those contained in childhood vaccines containing the preservative. Moreover, the mice they studied were not particularly susceptible to immune disorders.

The researchers next plan to study dendritic cells isolated from the blood of autistic and non-autistic children, to see if these cells reveal a similar response to thimerosal.

"Uncoupling of ATP-mediated calcium signaling and dysregulated IL-6 secretion in dendritic cells by nanomolar thimerosal," Samuel R. Goth, Ruth A. Chu, Jeffrey P. Gregg, Gennady Cherednichenko, and Isaac N. Pessah, *Environmental Health Perspectives*, in press. Address: Isaac N. Pessah, Department of Veterinary Medicine: Molecular Biosciences, 1311 Haring Hall, One Shields Avenue, University of California, Davis, CA 95616, inpessah@ucdavis.edu.

—and—

"UC Davis study with mice links thimerosal with immune system dysfunction," news release, UC Davis, March 21, 2006.