Biomedical Update:

Study detects no link between thimerosal, autistic autoimmunity

A recent study casts doubts on an association between the autoimmune symptoms seen in autism and exposure to thimerosal, the mercury-laden preservative formerly used in many childhood vaccines.

Animal research has shown that toxic levels of mercury can cause autoimmunity, with associated high levels of antinuclear and antilaminin antibodies. In the new study, Vijendra Singh and Wyatt Rivas tested levels of these antibodies in 60 autistic children, 9 nondisabled siblings of the autistic children, and 46 other nondisabled children. (Not all children received all tests.) All of the children had received a typical schedule of thimerosal-containing vaccines.

The researchers report that their analysis showed no significant differences in levels of the two antibodies in autistic and nondisabled children. They note as well that the abnormal levels of antibodies to myelin basic protein or neuron-axonal filament 200-Kd protein which have been reported in autistic individuals are not seen in industrial workers with autoimmunity due to mercury exposure.

"Accordingly," the researchers say, "we think that the chance of setting up an autoimmune response from exposure to small amounts of mercury is rather rare, unless some other factor concurrently contributes and increases the susceptibility to mercurial effects."

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"Detection of antinuclear and antilaminin antibodies in autistic children who received thimerosal-containing vaccines," Vijendra K. Singh and Wyatt H. Rivas, *Journal of Biomedical Science*, Vol. 11. No. 5, September-October 2004, 607-10. Address: Vijendra K. Singh, Biotechnology Center Building, Utah State University, UMC 4700, Logan, UT 84322.

Low vitamin B6 levels linked to depression

Vitamin B6 is highly beneficial for a large percentage of autistic children (see ARRI 1/4, 10/3, 11/4), and a new study indicates that high B6 levels may also protect against depression.

Anne-Mette Hvas and colleagues studied 140 individuals, comparing those with symptoms of depression to those who were depression-free. The researchers found a significant correlation between a low plasma level of PLP (pyridoxal phosphate, a metabolite of vitamin B6) and depressive symptoms.

Hvas et al. note that depression is strongly associated with reduced levels of serotonin or catecholamines. "The synthesis of serotonin and catecholamines is PLP dependent," they say, "and for this reason vitamin B6 has been considered a therapeutic adjunct in a variety of conditions with known or suspected neurotransmitter abnormalities."

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"Vitamin B6 level is associated with symptoms of depression," Anne-Mette Hvas, Svend Juul, Per Bech, and Ebba Nexø, *Psychotherapy and Psychosomatics*, Vol. 73, 2004, 340-3. Address: Anne-Mette Hvas, Department of Clinical Biochemistry, Aarhus University Hospital, AKH, Noerrebrogade 44, DK-8000 Århus C, Denmark, am.hvas@dadlnet.dk.

Risperidone reduces PDD symptoms, but side effects seen

A recent study confirms that risperidone (Risperdal) can reduce behavior problems in children with pervasive developmental disorders, but with significant side effects.

In an eight-week double-blind trial, Sarah Shea and colleagues administered the drug (mean dosage 0.04 mg/kg/day) or a placebo to 79 children with PDD, ranging in age from 5 to 12. They report that compared to children taking the placebo, children taking risperidone exhibited significantly less irritability and decreases in other symptoms. In addition, more subjects in the risperidone group showed global improvement. Side effects included sleepiness, marked weight gain (an average of nearly six pounds over the brief study), and increases in pulse rate and systolic blood pressure.

Although no other side effects were reported in this study, risperidone and other atypical antipsychotics are linked to dangerous dysregulation of blood glucose levels, which can lead to diabetes, and to an increased risk of cardiac irregularities. Many patients experience rapid weight gain while taking risperidone, and the drug can cause hyperprolactinemia (an elevation of the hormone prolactin) which can lead to abnormal lactation in both males and females.

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"Risperidone in the treatment of disruptive behavioral symptoms in children with autistic and other pervasive developmental disorders," S. Shea, A. Turgay, A. Carroll, M. Schulz, H. Orlik, I. Smith, and F. Dunbar, *Pediatrics*, October 18, 2004 (epub ahead of print). Address: Sarah Shea, Department of Pediatrics, Dalhousie Medical School, 5850 University Avenue, Halifax, NS, Canada B3J 3G9.

Drugs' adverse effects grossly underreported

Typically, the adverse effects of psychotropic drugs do not become apparent until the drugs are in widespread use. For example, millions of children received prescriptions for antidepressants before research revealed that they dramatically increase the risk of suicide in this population (see ARRI 18/1, 18/3), and atypical antipsychotics such as olanzapine and risperidone—now linked to diabetes, massive weight gain, cardiac irregularities, and other serious health problems—were initially reported to be far safer than older drugs.

A primary reason for this information lag, according to a study by P. N. Papanikolaou and colleagues, is that early drug trials are grossly deficient in reporting adverse events. The researchers analyzed 103 drug trials randomly selected from a registry of mental-health-related controlled trials, and found that:

- Only 21.4 percent adequately reported clinical adverse events
- Only 16.5 percent adequately reported laboratory-determined toxicity
- Only one third reported both the numbers of participants quitting the study and the reasons for withdrawals due to toxicity.

"On average," Papanikolaou et al. say, "drug trials devoted one tenth of a page in their results sections to safety, and 58.3 percent devoted more space to the names and affiliations of authors than to safety." Long-term trials and trials conducted in the U.S. contained the least amount of information regarding drug safety.

The researchers conclude, "Safety reporting is largely neglected across trials of mental health-related interventions, thus hindering the assessment of risk-benefit ratios for rational decision making in mental health care."

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"Safety reporting in randomized trials of mental health interventions," P. N. Papanikolaou, R. Churchill, K. Wahlbeck, and J. P. Ioannidis, *American Journal of Psychiatry*, Vol. 161, No. 9, September 2004, 1692-7. Address: P. N. Papanikolaou, Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina 45110, Greece.

SCHOOLS AND SERVICES: The Autism Research Institute maintains a list of schools and services for autistic individuals. If your facility should be included on our list, and you believe it may not be, please send a self-addressed, stamped envelope to receive our referral list questionnaire.