

Biomedical Update:

Thimerosal again linked to neuronal death

More evidence that the vaccine preservative thimerosal damages neurons comes from a study by Leman Yel and colleagues.

Using neuroblastoma cells as a model for neurons, the researchers found that “thimerosal, at nanomolecular concentrations, induces neuronal cell death through the mitochondrial pathway.” Thimerosal appears to cause the mitochondria, which are the “energy factories” inside cells, to release chemicals that cause a form of cell death called apoptosis. Thimerosal damaged the neurons, the researchers say, “in a concentration- and time-dependent manner.”

The findings are consistent with an earlier study by M. L. Humphrey and colleagues (see ARRI 19/2), who found that exposure to thimerosal damaged or killed neuroblastoma cells, with the amount of harm depending on the dosage and length of exposure. The research group also found evidence that this process involved changes in mitochondrial function.

“Thimerosal induces neuronal cell apoptosis by causing cytochrome c and apoptosis-inducing factor release from mitochondria,” L. Yel, L. E. Brown, K. Su, S. Gollapudi, and S. Gupta, *International Journal of Molecular Medicine*, Vol. 16, No. 6, December 2005, 971-7. Address: L. Yel, Department of Medicine, University of California, Irvine, CA 92697, lyel@uci.edu.

Mercury levels in U.S. women: more bad news

More than one in five U.S. women of childbearing age may have mercury levels that exceed the Environmental Protection Agency’s recommended threshold, according to a study that raises new concerns about the levels of mercury in pregnant women and the effects on their children’s neurological development.

The Environmental Quality Institute (EQI) at the University of North Carolina-Asheville tested hair samples from more than 6,600 people around the country. They report that 23 percent of women between the ages of 16 and 49 had mercury levels equal to or higher than one microgram of mercury per gram of hair, the EPA’s recommended limit. The researchers caution that their study subjects were recruited through media notices and special events, and that people most concerned about mercury issues were likely to be overrepresented.

The findings of this study follow those of a 2004 study by the EPA (see ARRI 18/1), which found that one in six pregnant women

have mercury levels that could put their children at risk for neurological disorders.

“An investigation of factors related to levels of mercury in human hair,” Technical Report #05-150, Steven C. Patch, Richard P. Maas, and Kimberly R. Sergeant, Environmental Quality Institute, University of North Carolina-Asheville. Address: Steven C Patch, Environmental Quality Institute, University of North Carolina-Asheville, One University Heights, Asheville, NC 28804.

Antibiotics in infancy linked to immune ills

Mainstream doctors almost universally dismiss the theory that heavy exposure to antibiotics in infancy and early childhood can alter immune function, causing or exacerbating diseases such as autism. A new study, however, supports this theory, showing that children given antibiotics during infancy are twice as likely as other children to develop asthma, another disease linked to immune dysfunction.

Fawziah Marra and colleagues performed a meta-analysis of eight studies evaluating the association between early antibiotic exposure and subsequent development of childhood asthma. Overall, the researchers found, receiving at least one antibiotic before turning one year old doubled a child’s risk of developing childhood asthma. The risk was dose-dependent, with each extra course of antibiotics during the first year of life making the child 1.16 times more likely to develop asthma. Retrospective studies showed a much stronger link than did prospective studies.

The data are consistent with the theory that by killing off beneficial bacteria, antibiotic use early in life alters the balance of intestinal flora. “The prevalence of asthma has been increasing over time in the western countries,” Marra says. “What has been proposed is that we’re too hygienic. We need, at a young age, to be exposed to a number of bacteria and infections for the immune system to develop.”

“Does antibiotic exposure during infancy lead to development of asthma? A systematic review and metaanalysis,” Fawziah Marra, Larry Lynd, Megan Coombes, Kathryn Richardson, Michael Legal, J. Mark FitzGerald, and Carlo Marra, *Chest*, Vol. 129, 2006, 610-18. Address: Carlo A. Marra, Health Economics Program, Centre for Clinical Epidemiology and Evaluation, Vancouver Coastal Health Research Institute, Faculty of Pharmaceutical Sciences, University of BC, 828 W. Tenth Avenue, Vancouver, BC, V5Z 1L8 Canada, carlo.marra@ubc.ca.

“The kids are alright... or are they?” *Your Health*, British Columbia Lung Association, Fall 2005.

FDA panel calls for “black box” warning for ADHD drugs

A panel convened by the Food and Drug Administration recommended in February that Ritalin and other drugs for attention deficit hyperactivity disorder (ADHD) carry a black box warning—the strongest warning possible for pharmaceuticals. The action surprised the FDA, which had asked the panel merely to propose studies regarding the drugs’ risks.

The panel based its recommendation on an FDA review which uncovered 25 sudden deaths due to cardiac arrest involving children and adults taking stimulant drugs between 1999 and 2003. The same review cited 54 non-fatal cases of heart attack, stroke, hypertension, arrhythmia, or heart palpitations occurring in patients taking these drugs. Drugs included in the review included both methylphenidate drugs such as Ritalin, Concerta, Methylin, and Metadate, and amphetamine drugs such as Adderall, Dextrostat, Dexedrine, and Desoxyn.

Doctors who presented evidence to the panel noted that stimulant drugs increase blood pressure and heart rate, and appear to increase the risk of strokes and arrhythmias. Researcher David Graham commented, “The number of arrhythmia hospitalizations really struck us as surprising. Arrhythmia is believed to be the pathway for sudden unexplained death.”

Current data suggest that stimulant drugs may more than double the risk of heart problems, Statistician Thomas Fleming commented that the drugs may prove to be more dangerous than Vioxx, the arthritis drug recently removed from the market due to its link to strokes and heart attacks. Drug safety expert Andrew Mosholder noted that the chemical structures of stimulants resemble those of ephedrine, the diet drug banned after it caused several fatalities.

The FDA is not required to take the advice of the panel, and one FDA official said, “We don’t think anything different needs to be done right now. We think the labeling right now is adequate.” The FDA plans to follow this panel, which consisted primarily of drug safety specialists, with another panel of pediatricians and psychiatrists.

Warning urged on stimulants like Ritalin,” Gardiner Harris, *New York Times*, February 10, 2006.

“ADHD drug medication guide on potential cardiac risks recommended by committee,” Food and Drug Administration, text at FDAAdvisory-Committee.com.

“Strongest warning suggested for ADHD drugs,” CNN, February 10, 2006.