

Mercury Containing Preservative Alters Immune Function

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Review

DAVIS, Calif., March 21 - Thimerosal, a mercury-containing organic no longer used as a preservative in many pediatric vaccines, can disrupt certain antigen presenting cells and may affect the immune response to external factors, reported investigators here.

Although far from the smoking gun that proponents of a Thimerosal-autism link seek, the finding suggested that Thimerosal exposure could cause dendritic cells to activate "aberrant and harmful immune responses," according to Isaac N. Pessah, Ph.D., and colleagues of the University of California at Davis. They reported the research online in *Environmental Health Perspectives*.

"This is the first time that thimerosal has been shown to selectively alter the normal functions of dendritic cells," said Dr. Pessah, a toxicologist and director of the Children's Center for Environmental Health and Disease Prevention at Cal Davis.

He added that dendritic cells "play pivotal roles in overcoming viral and bacterial invaders by coordinating the immune system's overall combat response."

Yet, Dr. Pessah emphasized, "Our findings do not directly implicate thimerosal as a single causative agent for triggering neurodevelopmental disorders such as autism."

"There is growing evidence that autism is several disorders that we now refer to as just one," he added. "There is also growing evidence that some children with autism have unique immune cell composition and responses to antigens. The results of our work provide a framework to test the hypothesis that the genetic background of some individuals may render them especially susceptible to thimerosal."

Dendritic cells are antigen-presenting cells that are potent activators of T-cells. But as Dr. Pessah and colleagues demonstrated in their study of cultured mouse cells, exposure to thimerosal disrupts calcium-channel signaling within dendritic cells, thereby altering growth patterns, maturation, and activation.

They determined this by exposing both mature and immature dendritic cells cultured from murine bone marrow to thimerosal at varying concentrations. The authors used immunocytofluorescence to visualize the effect of thimerosal exposure on calcium channels. Thimerosal contains approximately 50% ethylmercury by weight.

They found that at concentrations of 20 parts per billion, exposure of the dendritic cells to thimerosal altered the normal cross-talk between the calcium channels RyR12 and IP3R1, thereby "garbling the normal signaling system between them."

In addition, exposure to the compound resulted in irregular secretion by the dendritic cells of the pro-inflammatory cytokine interleukin-6.

When they ramped up thimerosal concentrations to 200 parts per billion, they found that it induced apoptosis of dendritic cells before they had fully matured, thereby preventing T-cell activation.

The finding suggests that in addition to its known neurotoxic properties, ethylmercury may also be an immunotoxicant, the authors said.

"A practical implication of the present findings has relevance to the commercial uses of thimerosal as an antimicrobial agent in vaccines and consumer products since they identify dendritic cells as sensitive targets for thimerosal and ethylmercury-mediated dysfunction," they wrote. "Given the importance of dendritic cells as a front line in regulating lymphocyte mediated immunity and tolerance, altering dendritic cell functions by forms of ethylmercury should be considered when assessing contributions to altered immune function."

They stopped short, however, of fingering thimerosal as a cause of autism. Thimerosal is still used in some commercial vaccines.

Other experts also advised drawing no final conclusions regarding thimerosal and autism on the basis of on this research.

"These findings should be interpreted cautiously. Although they suggest that thimerosal may affect dendritic cell function, the pathophysiological consequences of thimerosal remain unclear," said David A. Schwartz, M.D., director of the National Institute of Environmental Health Sciences, who was not involved in the study.