The History of Vaccinations in the Light of the Autism Epidemic

Stephanie F. Cave, MD, MS, FAAFP

Autism has been characterized as a behavioral disorder since it was first described by Leo Kanner in 1943. The number of autistic children has increased over the last decade. The incidence of autism was 1 in 10,000 before the 1970s and has steadily increased to 1 in 150 in 2008 with a male:female predominance of 4:1. The cause of this epidemic has remained unknown, but several hypotheses have been studied. Many of these suggest an environmental trigger, such as the ethyl mercury contained in the preservative thimerosal, which has been used in vaccines since 1931. Other possible triggers associated with vaccinations are chemical toxins and live viruses. James has published studies suggesting a genetic predisposition in the families of autistic children, exposing them to a deficiency in glutathione and an inability to detoxify heavy metals. Vargas has shown autism to encompass ongoing inflammation in the brains of autistic children. The Hannah Poling vaccine decision was a landmark case. Poling's family was awarded funds for ongoing medical care of an autistic child who was found to have mitochondrial dysfunction exacerbated by vaccines that left her with autistic behavior and seizures. Several studies have emerged supporting the fact that a significant number of autistic children do have mitochondrial dysfunction. The impact that the Poling case will have on the ability of parents of autistic children to gain access to funds to enable them to properly care for their children remains to be seen.

English scientist Edward Jenner used a scientific approach to vaccination in the 18th century by inoculating people with cowpox to protect them against smallpox. This strategy helped but was short-lived because of the possibility of contamination. Louis Pasteur developed the first rabies vaccine for humans in 1885 and introduced the concept of attenuation or weakening the virus in the vaccine to avoid injuring the recipient.

The polio vaccines by Sabin and Salk followed. The injectable vaccine was used in 1955, sparking the use of mass vaccination in a free program for the public through the Poliomyelitis Vaccination Assistance Act. From 1906 to 1946, the diphtheria, tetanus, and pertussis vaccines were developed. The DTP combination vaccine was made available to the public in 1946.

The measles vaccine became available in 1963, followed in 1968 by the mumps vaccine and in 1969 by the rubella, or German measles, vaccine. Pneumococcal vaccine became available in 1978, and in 1979 the measles, mumps, and rubella vaccines were marketed as the combination MMR. The 1980s brought into use the hepatitis B and Haemophilus influenzae vaccines.

In 1991, the recombinant hepatitis B vaccine was recommended for use in newborns within 24 hours of birth. Also in 1991, the hepatitis B, Haemophilus influenzae B, and DTP vaccines were given together to children during the same office visit. All 3 of these contained the preservative thimerosal, which contained ethyl mercury. Additionally, administration of the Rho (D) immune globulin given to Rho (D) negative mothers was moved from postbirth to the 28th week of gestation. The immune globulin contained thimerosal until 2002. From 1991 to 1999, children inadvertently received up to 125 times the safe level of mercury recommended by the Environmental Protection Agency (EPA); this number is determined by the oral methylmercury standard on any given vaccine day that multiple vaccines were given. This level exceeded not only the EPA standard but also the safety standards of the US Food and Drug Administration, the Agency for Toxic Substances and Disease Registry, and the World Health Organization.

HISTORY OF AUTISM

Autism was first described by psychiatrist Leo Kanner, MD, in 1943 as a behavioral disorder of children. Around the same time, Hans Asperger was writing about children who had similar symptoms but no compromised speech. Many professionals and parents of autistic children have watched the number of autistic children rise to epidemic proportions while the toxic levels of ethyl mercury and other toxins persist in vaccines.

Autism has been classified by the disciplines of medicine as a psychiatric illness. Recently, autistic children have displayed symptoms of disease in many of the bodily systems. These include but are not limited to the gastrointestinal, neurological, and immune systems. In many cases there has been a regression in development closely following a round of vaccinations. The vaccinations in question contained a combination of thimerosal, aluminum, live viruses,
and other toxic chemicals such as formaldehyde, monosodium glutamate, and phenoxethanol.

**IATROGENIC EXPOSURE OF CHILDREN TO MERCURY THROUGH VACCINES**

Stajich et al studied iatrogenic exposure to mercury after the hepatitis B vaccine in preterm infants and reported much higher levels in the blood of preterm infants than that in the blood of full-term infants. Pichichero et al published a study in The Lancet in 2000 discussing the concentrations and metabolism of mercury in infants receiving vaccines containing thimerosal. This study discussed the loss of mercury from the body of the children following the vaccinations. Many thought after reading the study that thimerosal was not a threat to the children. Burbacher et al published a study in primes in 2005 showing that the mercury did not leave the body after an injection containing thimerosal but rather traveled to the brain, where the ethyl mercury became inorganic mercuroic chloride. The half-life in blood of the thimerosal mercury after the injection was 8.6 days and of the methylmercury, 21.5 days. There was a higher percentage of total brain mercury in the form of inorganic mercury in the thimerosal-exposed primates than in methyl-exposed primates.

**CLINICAL EFFECTS OF MERCURY TOXICITY**

Mercury is known to affect many body systems and organs, including the neurological, immune, gastrointestinal, and cardiovascular systems, as well as the kidneys and liver, and induces free radical pathology in all systems. Organic mercury (ethyl mercury and methylmercury) is lipid-soluble and stable and has a predilection for the nervous system. Ten percent of neonates have been exposed in utero to mercury levels that exceed what the EPA deems safe. Mercury alters the structure and function of enzymes and other proteins by binding to sulfhydryl (SH) groups, resulting in loss of enzyme activity and loss of structural integrity. According to verbal communication with Boyd Haley, PhD, Department of Chemistry, University of Kentucky, in October 2000, mercury destroys neuronal tubulin and axonal integrity.

Palmer et al found that for every 1000 lbs of environmentally released mercury, there was a 43% increase in the rate of special education services and a 61% increase in the rate of autism in Texas. Mercury interferes with serotonin release and transport, altered dopamine metabolism, elevated glutamate, elevated norepinephrine/epinephrine, and demyelination. Children with autism produce higher concentrations of serum autoantibodies to myelin basic protein and neurofilaments than control children. Their behavior mirrors that associated with neurochemistry abnormalities.

The immune system is also a target of mercury. In the presence of mercury, inflammatory cytokines are increased, early control of viruses is disabled, macrophages are inhibited, and T, B, and NK cells are inhibited. Mercury impairs cysteine regulation, glucose metabolism, and reduced glutathione availability in the liver.

Bernard et al studied clinical findings in autistic children that could be compared to the effects of mercury poisoning. These include but are not limited to psychiatric disturbances; speech, language, and hearing problems; sensory abnormalities; cognitive impairment; and unusual behavior.

**EVIDENCE OF IMPAIRED EFFLUX OF MERCURY IN AUTISTIC CHILDREN**

Holmes et al studied the concentration of mercury in hair samples from the first haircuts of autistic children vs those of an unaffected control population. They found an absence of mercury in the hair and concluded that this could indicate an efflux problem with this population of children. The mercury was readily found in the hair of the controls. Adams conducted a similar study with the teeth of autistic children and found higher levels of mercury in the teeth of autistic children than in controls.

Bradstreet et al followed this study in 2003 with a case control study of the mercury burden in autism. He treated autistic children and control children with dimercaptosuccinic acid (DMSA), an oral detoxifier of mercury. The autistic children's urine contained more mercury following a challenge with DMSA than did the controls' urine. This finding supported Holmes's hypothesis of an efflux problem.

Studies of urinary patterns of porphyrins have shown that the severity of the autism correlated to the degree of porphyrinuria. A prospective study of children with autism spectrum disorder (ASD) demonstrated significant increases in the precoproporphyrin fraction and pentacarboxypropophyrin when compared to control children. In a prospective study of 178 ASD children, Nataf et al showed that 53% had increased porphyrinuria compared to controls. The levels of precoproporphyrin and pentacarboxypropophyrin were significantly higher in the ASD children than in controls. The symptoms of autism correlated with the levels of coproporphyrin, which was 2.6-fold higher in the ASD children than in controls. The authors found these results consistent with an increase in mercury burden in the ASD children vs children in the control group.

**OXIDATIVE STRESS AND NEUROINFLAMMATION IN AUTISM**

In 2005, Vargas published a study in the Annals of Neurology that showed neurological activation and neuroinflammation in the brains of patients with autism. This result defined autism as something different—an ongoing neurological inflammation. From 2004 to 2006, James et al studied and published findings in autistic children showing metabolic biomarkers of oxidative stress and impaired methylation capacity. The genetic predisposition for inadequate methylation in autistic children leaves them open to damage by environmental toxins like heavy metals because their production of glutathione is compromised. Hornig et al showed neurotoxic effects of postnatal thimerosal in mice who had a predisposition for autoimmune diseases.

Geier and Geier have published studies during the past 4 years that supported the hypothesis that exposure to thimerosal can cause neurological impairment in children, leading to autistic behavior. In 2006, Herbert published a paper describing autism as a disorder that affects the brain rather than a primary brain disorder. Many clinicians are treating autistic children using a metabolic approach. The outcomes for children in the spectrum are very positive.
EVIDENCE OF A DECREASE IN THE PREVALENCE OF AUTISM WITH THE REDUCTION OF THIMEROSAL

The toxins in vaccines, including but not limited to ethyl mercury and aluminum, can have a devastating effect on children who are genetically predisposed to retain metals and environmental toxins. The oxidative stress caused by metals and other toxins precipitate an increase in inflammatory cytokines, which in turn can cause malfunction in the gastrointestinal tract, brain, and immune systems. The numbers of autistic children in California started to decrease as the thimerosal was removed in an initial move to reduce the toxin. It was around the same time, however, that the influenza vaccine, with a full complement of thimerosal, was recommended for children 6 to 60 months of age and for pregnant women.

EXPOSURE TO LIVE VIRUSES THROUGH VACCINES

The live viral vaccines, known to be contaminated with other viruses from growth media, have played a central role in the whole scheme of things. The weakened, oxidatively stressed immune systems are not able to mount an adequate fight. Some of these children have been shown to harbor live viruses in the gastrointestinal tract and spinal fluid and others still demonstrate a positive immunoglobulin M (IgM) response to viruses like Epstein-Barr and human herpes VI years after the initial infection.

Vaccines with multiple live viruses like the measles, mumps, rubella, varicella (MMRV) inoculation have been reported to cause so many reactions that the recommendation to give them together from the same vial has been withdrawn. The recent rotavirus vaccine has caused at least 28 cases of intussusception, with some requiring surgery.

With regard to autism, these questions arise: Would these children have been injured neurologically if the concentration of ethyl mercury had not reached the level that it did in the 1990s? Or if the recommendations of the 1980s for 23 doses of 7 vaccines by age 6 (the first at 2 months of age) had not changed over time to the current 48 doses of 14 vaccines by age 6 (the first at 12 hours)? Or if the measles, mumps, and rubella vaccines had not been injected as one MMR vaccine on the same day as the varicella or in the same bottle as in the case of the MMRV vaccine?

Throughout the years of the autism epidemic, US governmental agencies have maintained that thimerosal does not have any part to play in the cause of autism. The Institute of Medicine (IOM) issued a statement in 2004 refuting the connection between vaccines and autism. One of the studies used by this body to render a decision was the Centers for Disease Control and Prevention (CDC)-commissioned study by Verstraeten et al that in 2000 showed a significant increase in the risk of neurological impairment after mercury exposure. The implications of this study were discussed at the Simpsonwood meeting in June 2000, which was attended by representatives of the government agencies and the vaccine industry. A subsequent version of the study was published in 2003, and in it the statistical significance had disappeared. The CDC has never recommended the use of thimerosal-free vaccines over the ones containing thimerosal.

LANDMARK CASE: HANNAH POLING

The Hannah Poling case in 2008 was the landmark case for vaccine injury in an autistic child. The case was filed in the vaccine court but was decided in a private meeting of concerned individuals in the US Department of Health and Human Services. The case was awarded to the plaintiff because the child was found to have a mitochondrial disorder aggravated by the vaccines. This led to a regressive encephalopathy with autism spectrum disorder features. Recent published studies from Portugal show "a diversity of associated medical conditions was documented in 20%, with an unexpectedly high rate of mitochondrial respiratory chain disorders."

MITOCHONDRIAL DYSFUNCTION IN AUTISM

Bradstreet and Rossignol recently published a study in the American Journal of Biochemistry and Biotechnology discussing evidence of mitochondrial dysfunction in autism. The dysfunction that they report does not seem to be related to abnormalities in muscle biopsies even with objective evidence of mitochondrial dysfunction. They postulate that "exposure to environmental toxins is the likely etiology for [mitochondrial dysfunction] in autism. This dysfunction then contributes to a number of diagnostic symptoms and comorbidities observed in autism, including cognitive impairment, language deficits, abnormal energy metabolism, chronic gastrointestinal problems, abnormalities in fatty acid oxidation, and increased oxidative stress."

Hewitson recently reported developmental delays, behavioral problems and brain changes in macaque monkeys that mimic "certain neurological abnormalities of autism" after subjecting them to vaccines such as MMR and thimerosal-containing vaccines given in proportional doses, adjusted for age of the vaccines recommended between 1994 and 1999.

HOPE FOR THE FUTURE

Whether the Poling child had a genetic mitochondrial disorder or one precipitated by the toxins in the vaccines, her case may open the door for at least 4600 other children to have their cases heard. Dr Bernadine Healy, former director of the National Institutes of Health and a member of the Institute of Medicine, in an interview with CBS News discussed the fact that we have an opportunity to understand that there are groups of children who are more vulnerable to side effects of the vaccines. She offered the possibility that there may be a susceptible group that should not have a particular vaccine or should have vaccines on another schedule. She disagreed with the statement of the IOM in 2004 denying any causal link between vaccines and autism when it was clear that the possibility of susceptible groups was not pursued. She did not agree with the decision to abandon research in this area because there was fear about what might be found that may deter people from having their children vaccinated. When asked about the causation link between autism and vaccines, she said, "The question has not been answered." One might ask whether the Poling case and others like it will encourage the Academy of Pediatrics and the CDC to formulate a more reasonable vaccine schedule as more vaccines are added to the recommended list and, of course, to remove...
thimerosal from existing vaccines. These measures could hypothetically solve one of the most puzzling mysteries in medicine today—the autism epidemic.

REFERENCES
