

The Not-So-Crackpot Autism Theory

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Neal Halsey's life was dedicated to promoting vaccination. In June 1999, the Johns Hopkins pediatrician and scholar had completed a decade of service on the influential committees that decide which inoculations will be jabbed into the arms and thighs and buttocks of eight million American children each year. At the urging of Halsey and others, the number of vaccines mandated for children under 2 in the 90's soared to 20, from 8. Kids were healthier for it, according to him. These simple, safe injections against hepatitis B and germs like haemophilus bacteria would help thousands grow up free of diseases like meningitis and liver cancer.

Halsey's view, however, was not shared by a small but vocal faction of parents who questioned whether all these shots did more harm than good. While many of the childhood infections that vaccines were designed to prevent -- among them diphtheria, mumps, chickenpox and polio -- seemed to be either antique or innocuous, serious chronic diseases like asthma, juvenile diabetes and autism were on the rise. And on the Internet, especially, a growing number of self-styled health activists blamed vaccines for these increases.

Like all medical interventions, vaccines sometimes cause adverse reactions. But unlike pills, vaccines come packaged with high expectations, which make them particularly vulnerable to public criticism. Vaccines don't cure people, and they are administered to healthy children, which gives them few opportunities for good press. When they work, nothing happens. When vaccinated children become ill, their parents are grief-stricken and often enraged, even if vaccines aren't proved to be at fault. All of this puts public-health advocates like Halsey on the defensive. Most

attacks on vaccines, they say, are based on hysteria, bad science and dubious politics.

Halsey, 57, has green eyes, a white beard that makes him look like a ship's captain and an air of careful authority. As chairman of the American Academy of Pediatrics committee on infectious diseases from 1995 through June 1999, he often appeared in the media administering calm reassurance. "Many of the allegations against vaccines," Halsey said in one interview, "are based on unproven hypotheses and causal associations with little evidence."

And then suddenly in June 1999, during a visit to the Food and Drug Administration, a squall appeared on the horizon of Halsey's confidence. Halsey attended a meeting to discuss thimerosal, a mercury-containing preservative that at the time was being used in several vaccines -- including the hepatitis B shot that Halsey had fought so hard to have administered to American babies. By the time the dust kicked up in that meeting had settled, Halsey would be forced to reckon with the hypothesis that thimerosal had damaged the brains of immunized infants and may have contributed to the unexplained explosion in the number of cases of autism being diagnosed in children.

That Halsey was willing even to entertain this possibility enraged some of his fellow vaccinologists, who couldn't fathom how a doctor who had spent so much energy dismantling the arguments of people who attacked vaccines could now be changing sides. But to Halsey's mind, his actions were perfectly consistent: he was simply working from the data. And the numbers deeply troubled him. "From the beginning, I saw thimerosal as something different," he says. "It was the first strong evidence of a causal association with neurological impairment. I was very concerned."

The investigation into mercury vaccines was instigated in 1997 by Representative Frank Pallone Jr., a New Jersey Democrat whose district includes a string of shore towns where mercury in fish is one of many environmental concerns. Pallone, who had been pressing the government to re-evaluate its overall guidelines on mercury toxicity, attached an amendment to an F.D.A. bill requiring the agency to inventory all mercury contained in licensed drugs and vaccines.

The job of adding up the amount of mercury in vaccines and assessing its risk fell to Robert Ball, an F.D.A. scientist, and two F.D.A. pediatricians, Leslie Ball, Robert's wife, and R. Douglas Pratt. Thimerosal, which is 50 percent ethyl mercury by weight, had been used as a vaccine preservative since the 1930's in the

diphtheria-tetanus-pertussis shot, known as D.T.P., and it was later added to some vaccines for hepatitis B and haemophilus bacteria, which by the early 1990's had become routine immunizations for infants.

The F.D.A. team's conclusions were frightening. Vaccines added under Halsey's watch had tripled the dose of mercury that infants got in their first few months of life. As many as 30 million American children may have been exposed to mercury in excess of Environmental Protection Agency guidelines -- levels of mercury that, in theory, could have killed enough brain cells to scramble thinking or hex behavior.

"My first reaction was simply disbelief, which was the reaction of almost everybody involved in vaccines," Halsey says. "In most vaccine containers, thimerosal is listed as a mercury derivative, a hundredth of a percent. And what I believed, and what everybody else believed, was that it was truly a trace, a biologically insignificant amount. My honest belief is that if the labels had had the mercury content in micrograms, this would have been uncovered years ago. But the fact is, no one did the calculation."

Making matters worse, the latest science on mercury damage suggested that even small amounts of organic mercury could do harm to the fetal brain. Some of the federal safety guidelines on mercury were relaxed in the 90's, even as the amount of mercury that children received in vaccines increased. The more Halsey learned about these mercury studies, the more he worried.

"My first concern was that it would harm the credibility of the immunization program," he says. "But gradually it came home to me that maybe there was some real risk to the children." Mercury was turning out to be like lead, which had been studied extensively in the homes of the Baltimore poor during Halsey's tenure at Hopkins. "As they got more sophisticated at testing for lead, the safe level marched down and down, and they continued to find subtle neurological impairment," Halsey says. "And that's almost exactly what happened with mercury."

Halsey was beginning to think that it would be prudent to limit thimerosal-containing vaccines and urge pediatricians to use thimerosal-free shots when possible. But his decision inflamed some of his peers. After all, although the thimerosal data was worrisome to Halsey, the available science offered no clear proof that the preservative posed a genuine danger to children when given in parts per million. Moreover, it wasn't clear that there were enough thimerosal-free vaccines available for diseases like

pertussis and hepatitis B. Should an unproven fear justify the cessation of a procedure that protected children from proven dangers?

Halsey looked into the matter further and found only complexity. In the medical literature, most cases of acute mercury poisoning result from doses hundreds or thousands of times higher than what infants received with thimerosal-laden vaccines. And although the thimerosal levels in vaccines exceeded the E.P.A.'s guidelines for methyl mercury, thimerosal contained ethyl mercury, a compound that behaves somewhat differently in the body. The E.P.A. based its guidelines on a series of studies of 917 children born in 1987 in the Faeroe Islands, a windswept North Atlantic archipelago, to women who ate methyl-mercury-tainted whale meat. The Faeroes children, whose umbilical cord blood averaged four times the E.P.A.'s daily "safe" dose -- which was 0.1 micrograms per kilo -- exhibited small but measurable neurological deficits seven years later. They had slower reaction times and diminished attention spans and their word choice and memorization were less keen than those of their classmates who had been exposed to less mercury, according to Philippe Grandjean, a Danish researcher who leads the continuing Faeroes study and teaches at Boston University.

During most of the 90's, many American 6-month-olds received a total of 187.5 micrograms of ethyl mercury through vaccination. While the Faeroes children were exposed to mercury as developing fetuses, and therefore were more vulnerable than the vaccinated American infants, the American babies included about 60,000 each year who had already been exposed to high mercury levels because their mothers had eaten a lot of contaminated fish. What's more, hundreds of thousands of Rh-negative pregnant women and their unborn Rh-positive babies received additional thimerosal each year through injections designed to keep the mothers' immune systems from attacking the fetuses.

The Faeroes studies, though they dealt with methyl mercury, unnerved Halsey. Other researchers were troubled, too. George Lucier, a toxicologist who led a 1998 White House review of mercury's dangers, went so far as to say it was "very likely" that thimerosal had damaged some children. There was precious little data to back up that precise suspicion -- and little to dismiss it -- because of the lack of toxicology research on ethyl mercury.

On July 7, 1999, at Halsey's urging, the American Academy of Pediatrics and the Public Health Service released a statement urging vaccine manufacturers to remove thimerosal as quickly as possible and advising pediatricians to postpone giving most

newborns the birth dose of the hepatitis B vaccine. The decision, which helped to create vaccine shortages and led some babies to become infected with hepatitis B, outraged some senior vaccine experts. Walter Orenstein, director of the National Immunization Program at the Centers for Disease Control and Prevention, would charge that the rush to remove thimerosal-containing vaccines was "precipitous." Stanley Plotkin, a renowned vaccine developer, said that it was fruitless to try to soothe vaccination critics. "If antivaccinationists did not have mercury, they would have another issue," he said at one meeting. "One cannot prevent them from making hay regardless of whether the sun is shining or not."

In Halsey's view, however, thimerosal wasn't simply a bone for rabid vaccine opponents to gnaw on. In the middle of that hectic summer he took a vacation in Maine. Canoeing on a lake, he came across posters that advised fishermen to "protect your children -- release your catch." Halsey took that message to heart. If the government was warning people against eating fish with mercury, he asked his colleagues, "does it make sense to allow it to be injected into infants?"

Although other vaccinologists criticized Halsey, many of his colleagues rallied around him. "Neal put kids ahead of the vaccination program, which was gutsy," says Lynn Goldman, a former E.P.A. official who has been on the Hopkins faculty since 1999 and worked with Halsey on thimerosal. "It would have been easier for him to line up on the other side."

Few scientists believe that the spike in autism could have been caused solely by the thimerosal in vaccines, but in October 2001, a vaccine-safety committee at the starchy Institute of Medicine confirmed that it was "biologically plausible" -- though by no means proved -- that thimerosal could be related to neurodevelopmental delays in some children. The committee recommended that thimerosal be removed from vaccines and called for extensive research to determine any damage it had caused.

Halsey's fellow researchers were right about one thing. Antivaccine advocates immediately seized upon the thimerosal theory, and Halsey became something of an unwilling hero to the vaccine-safety advocates with whom he had so often sparred. In fact, thousands of parents with autistic children have responded to the Institute of Medicine report by filing lawsuits. Michael Williams, who has won millions in toxic tort settlements from pharmaceutical companies, was among the first lawyers to sue vaccine manufacturers, on behalf of William Mead, a 4-year-old

Portland, Ore., boy with autism. Williams also filed a separate class-action lawsuit with William's healthy older sister, Eleanor, as lead plaintiff, demanding that vaccine makers also pay for studies to determine thimerosal's effects on millions of children who might have lower I.Q.'s or other less obvious signs of mercury poisoning. Past studies have shown that mercury's effects vary tremendously from person to person, presumably because of genetic differences in the body's capacity to protect delicate organs from it.

"In order to win the Eleanor lawsuit you need to establish liability, but I don't think that is going to be that hard," Williams said in a recent chat in his Portland office. "Organic mercury is a very serious neurotoxin."

Williams embodies the vaccine establishment's worst fear about Halsey's course of action -- which is that taking the precautionary step of eliminating thimerosal would be read as an admission of fault. "The agenda was set by the lawyers and the antivaccine activists," a source close to a number of manufacturers complained to me. "The scientists responded to it scientifically, and that put them behind the eight ball right away. You had Neal Halsey running around saying: 'We've got to do something! We've got to show we're concerned!'"

Paul Offit, a vaccinologist at the Children's Hospital of Philadelphia, takes it a step further. "In some instances I think full disclosure can be harmful," he says. "Is it safe to say there is zero risk with thimerosal, when it is remotely possible that one child would get sick? Well, since we say that mercury is a neurotoxin, we have to do everything we can to get rid of it. But I would argue that removing thimerosal didn't make vaccines safer -- it only made them perceptibly safer."

For Halsey, thimerosal injury is a possibility that must be addressed -- but by science, not by the courts. The scientific agenda, however, is already deeply politicized. From the start, the C.D.C.'s efforts to examine the possibility of thimerosal damage became snarled in acrimony. Critics of the vaccination system don't trust the C.D.C., which monitors evidence of adverse reactions to vaccines through the Vaccine Safety Datalink, a computerized set of 7.5 million medical records. Safe Minds, an advocacy group of parents who believe that their autistic children were damaged by thimerosal, has used the Freedom of Information Act to obtain documents showing that as early as December 1999 the C.D.C. had reason to believe that thimerosal caused developmental delays in some children. It was far from conclusive evidence, but vaccine critics charged that the C.D.C. tried to play it

down. One of those critics was Dan Burton, a Republican congressman from Indiana, who says he firmly believes that his grandson's autism is a result of vaccines. "I'm so ticked off about my grandson, and to think that the public-health people have been circling the wagons to cover up the facts!" Burton fumed at a June hearing. "Why, it just makes me want to vomit!"

What comes through in an examination of the documents uncovered by Safe Minds is less a coverup than an impression of scientists anxiously watching over their shoulders as they work. One document, for example, records comments made by Robert Brent, a Philadelphia pediatrician who served as a consultant for the thimerosal study. "The medical-legal findings in this study, causal or not, are horrendous," Brent said. "If an allegation was made that a child's neurobehavioral findings were caused by thimerosal-containing vaccines, you could readily find a junk scientist who would support the claim with a reasonable degree of certainty. But you will not find a scientist with any integrity who would say the reverse with the data that is available. . . . So we are in a bad position from the standpoint of defending any lawsuits if they were initiated."

More research is in the works. The C.D.C. is setting up a study of neurodevelopmental effects based in part on the Faeroe Islands model. The N.I.H. is financing studies of thimerosal metabolism in animals and children. (An early University of Rochester study was reassuring: it indicated that children eliminate thimerosal much more quickly than expected.)

Clearly, a lot is riding on this research, and pressure is being brought to bear on both sides. Can the vaccine authorities accept a positive answer? Can the vaccine opponents accept a negative one? "No one wants to think that harm might have been done," Halsey says. "I don't want to think harm might have been done."

American children still receive up to 20 vaccines in the first two years of life. The first symptoms of autism often appear between the ages of 12 and 24 months. Most autism experts say that the two facts are coincidental, but as a major California study recently confirmed, autism is being diagnosed in numbers far higher than ever before, suggesting that a nongenetic cause may be partly to blame. In some children, the behavioral traits of autism present themselves along with physical problems like sensory dysfunction and motor disorders that have rough correlates in the mercury-poisoning literature. For some parents, thimerosal provides a grand unifying theory that squarely points the finger at the government and vaccine makers.

During much of the 20th-century, children suffered from an ailment called pink disease, which caused peeling skin on the extremities as well as regressive behavior. In 1948, a keen-eyed Cincinnati pediatrician named Josef Warkany noticed a common risk factor in these children: they had all been given teething powders containing calomel, a mercury derivative. Only about 1 in 500 children whose parents gave them calomel got pink disease -- suggesting that a constitutional vulnerability to mercury was part of the clinical picture. Soon after the powders were taken off the market, pink disease disappeared.

Autism is a global phenomenon that was first reported in America in 1943, long before the potential dangers of thimerosal vaccines were raised. Removing the preservative won't -- even in the best case -- eliminate the illness. But scientists estimate that the current rate of autism in its various forms might be as high as 1 in 500. If the autism trend begins to recede now that thimerosal has been removed, it could certainly suggest a cause. If it does decline, we might have Neal Halsey to thank. If it doesn't, his colleagues in the vaccine establishment may blame him for stoking an irrational protest from the public.

Halsey, who still heads the Hopkins Institute for Vaccine Safety, which he was a founder of in 1997, is on the fence. "I don't believe the evidence is convincing now that there has definitely been harm done by thimerosal," he says, absently stroking his balding head. But to keep the vaccine program on a steady keel, Halsey says, the public-health authorities simply must follow through with the studies and face the consequences without flinching. If there is damage, he says, "there should be some kind of compensation, though I don't know how." He pauses, and sighs. "I empathize with families of children with these disorders. How are you going to put dollar values on that?"

