



## Vaccines and Autism Revisited — The Hannah Poling Case

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On April 11, 2008, the National Vaccine Advisory Committee took an unusual step: in the name of transparency, trust, and collaboration, it asked members of the public to help set its vaccine-safety

research agenda for the next 5 years. Several parents, given this opportunity, expressed concern that vaccines might cause autism — a fear that had recently been fueled by extensive media coverage of a press conference involving a 9-year-old girl named Hannah Poling.

When she was 19 months old, Hannah, the daughter of Jon and Terry Poling, received five vaccines — diphtheria–tetanus–acellular pertussis, *Haemophilus influenzae* type b (Hib), measles–mumps–rubella (MMR), varicella, and inactivated polio. At the time, Hannah was interactive, playful, and communicative. Two days later, she was lethargic, irritable, and febrile. Ten days after vaccination,

she developed a rash consistent with vaccine-induced varicella.

Months later, with delays in neurologic and psychological development, Hannah was diagnosed with encephalopathy caused by a mitochondrial enzyme deficit. Hannah's signs included problems with language, communication, and behavior — all features of autism spectrum disorder. Although it is not unusual for children with mitochondrial enzyme deficiencies to develop neurologic signs between their first and second years of life, Hannah's parents believed that vaccines had triggered her encephalopathy. They sued the Department of Health and Human Services (DHHS) for compensation under the Vaccine

Injury Compensation Program (VICP) and won.

On March 6, 2008, the Polings took their case to the public. Standing before a bank of microphones from several major news organizations, Jon Poling said that “the results in this case may well signify a landmark decision with children developing autism following vaccinations.”<sup>1</sup> For years, federal health agencies and professional organizations had reassured the public that vaccines didn't cause autism. Now, with DHHS making this concession in a federal claims court, the government appeared to be saying exactly the opposite. Caught in the middle, clinicians were at a loss to explain the reasoning behind the VICP's decision.

The Poling case is best understood in the context of the decision-making process of this unusual vaccine court. In the late 1970s and early 1980s, American

lawyers successfully sued pharmaceutical companies claiming that vaccines caused a variety of illnesses, including unexplained coma, sudden infant death syndrome, Reye's syndrome, transverse myelitis, mental retardation, and epilepsy. By 1986, all but one manufacturer of the diphtheria-tetanus-pertussis vaccine had left the market. The federal government stepped in, passing the National Childhood Vaccine Injury Act, which included the creation of the VICP. Funded by a federal excise tax on each dose of vaccine, the VICP compiled a list of compensable injuries. If scientific studies supported the notion that vaccines caused an adverse event — such as thrombocytopenia after receipt of measles-containing vaccine or paralysis after receipt of oral polio vaccine — children and their families were compensated quickly, generously, and fairly. The number of lawsuits against vaccine makers decreased dramatically.

Unfortunately, in recent years the VICP seems to have turned its back on science. In 2005, Margaret Althen successfully claimed that a tetanus vaccine had caused her optic neuritis. Although there was no evidence to support her claim, the VICP ruled that if a petitioner proposed a biologically plausible mechanism by which a vaccine could cause harm, as well as a logical sequence of cause and effect, an award should be granted. The door opened by this and other rulings allowed petitioners to claim successfully that the MMR vaccine caused fibromyalgia and epilepsy, the hepatitis B vaccine caused Guillain-Barré syndrome and chronic demyelinating polyneuropathy, and the Hib vaccine caused transverse myelitis.

No case, however, represented a greater deviation from the VICP's original standards than that of Dorothy Werderitsh, who in 2006 successfully claimed that a hepatitis B vaccine had caused her multiple sclerosis. By the time of the ruling, several studies had shown that hepatitis B vaccine neither caused nor exacerbated the disease, and the Institute of Medicine had concluded that "evidence favors rejection of a causal relationship between hepatitis B vaccine and multiple sclerosis."<sup>22</sup> But the VICP was less impressed with the scientific literature than it was with an expert's proposal of a mechanism by which hepatitis B vaccine could induce autoimmunity (an ironic conclusion, given that Dorothy Werderitsh never had a detectable immune response to the vaccine).

Like the Werderitsh decision, the VICP's concession to Hannah Poling was poorly reasoned. First, whereas it is clear that natural infections can exacerbate symptoms of encephalopathy in patients with mitochondrial enzyme deficiencies, no clear evidence exists that vaccines cause similar exacerbations. Indeed, because children with such deficiencies are particularly susceptible to infections, it is recommended that they receive all vaccines.

Second, the belief that the administration of multiple vaccines can overwhelm or weaken the immune system of a susceptible child is at variance with the number of immunologic components contained in modern vaccines. A century ago, children received one vaccine, smallpox, which contained about 200 structural and nonstructural viral proteins. Today, thanks to advances in protein purification and recombinant DNA

technology, the 14 vaccines given to young children contain a total of about 150 immunologic components.<sup>3</sup>

Third, although experts testifying on behalf of the Polings could reasonably argue that development of fever and a varicella-vaccine rash after the administration of nine vaccines was enough to stress a child with mitochondrial enzyme deficiency, Hannah had other immunologic challenges that were not related to vaccines. She had frequent episodes of fever and otitis media, eventually necessitating placement of bilateral polyethylene tubes. Nor is such a medical history unusual. Children typically have four to six febrile illnesses each year during their first few years of life<sup>4</sup>; vaccines are a minuscule contributor to this antigenic challenge.

Fourth, without data that clearly exonerate vaccines, it could be argued that children with mitochondrial enzyme deficiencies might have a lower risk of exacerbations if vaccines were withheld, delayed, or separated. But such changes would come at a price. Even spacing out vaccinations would increase the period during which children were susceptible to natural infections, giving a theoretical risk from vaccines priority over a known risk from vaccine-preventable diseases. These diseases aren't merely historical: pneumococcus, varicella, and pertussis are still common in the United States. Recent measles outbreaks in California, Arizona, and Wisconsin among children whose parents had chosen not to vaccinate them show the real risks of public distrust of immunization.

After the Polings' press con-

ference, Julie Gerberding, director of the Centers for Disease Control and Prevention, responded to their claims that vaccines had caused their daughter's autism. "Let me be very clear that the government has made absolutely no statement . . . indicating that vaccines are a cause of autism," she said.<sup>5</sup> Gerberding's biggest challenge was defining the term "autism." Because autism is a clinical diagnosis, children are labeled as autistic on the basis of a collection of clinical features. Hannah Poling clearly had difficulties with language, speech, and communication. But those features of her condition considered autistic were part of a global encephalopathy caused by a mitochondrial enzyme deficit. Rett's syndrome, tuberous sclerosis, fragile X syndrome, and Down's

syndrome in children can also have autistic features. Indeed, features reminiscent of autism are evident in all children with profound impairments in cognition; but these similarities are superficial, and their causal mechanisms and genetic influences are different from those of classic autism.

Going forward, the VICP should more rigorously define the criteria by which it determines that a vaccine has caused harm. Otherwise, the message that the program inadvertently sends to the public will further erode confidence in vaccines and hurt those whom it is charged with protecting.

Dr. Offit reports being a co-inventor and co-holder of a patent on the rotavirus vaccine RotaTeq, from which he and his institution receive royalties, as well as serving on a scientific advisory board for Merck.

No other potential conflict of interest relevant to this article was reported.

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## Like Night and Day — Shedding Light on Off-Hours Care

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Lately, I've been coming to work at midnight. You see, I've begun making late-night administrative rounds at the hospital where I am president and chief executive officer. No, I'm not nostalgic for my harrowing days as a resident. Rather, these middle-of-the-nighters are part of an initiative of mine intended to address a matter that is of increasing concern at hospitals throughout the country: the stark discrepancy in quality between daytime and nighttime inpatient services.

Like many hospital executives, I've come to appreciate the fact that I work in two distinct places,

though they share the same address. One is a hospital that operates from approximately 7 a.m. until 7 p.m., Monday through Friday. The other is a hospital that operates in the evening, through the night, and on weekends. Although these facilities appear to be one and the same, they in fact represent two very different medical environments.

The weekday hospital has a full administrative team, department chairs and service chiefs, experienced nurse managers, and a full complement of professional staff. The off-hours hospital, on the other hand, rarely, if ever, has senior managers present. Nurse-

to-patient ratios are significantly lower. Even the number of residents is considerably lower — certainly lower than during my days of training — because of mandated work-hour restrictions.

The positive spin on these differences is that we are trying to achieve a calmer and quieter environment at night and on the weekend so that our patients can rest and recuperate. But there are serious downsides. Silent hospital corridors can also reflect sparse staffing and a lack of institutional leadership, which make important hospital services and consultative expertise difficult to obtain. This discrepancy in pro-