

# Mercury, Vaccines, and Autism

## One Controversy, Three Histories

The controversy regarding the once widely used mercury-containing preservative thimerosal in childhood vaccines has raised many historical questions that have not been adequately explored. Why was this preservative incorporated in the first place? Was there any real evidence that it caused harm? And how did thimerosal become linked in the public mind to the “autism epidemic”?

I examine the origins of the thimerosal controversy and their legacy for the debate that has followed. More specifically, I explore the parallel histories of three factors that converged to create the crisis: vaccine preservatives, mercury poisoning, and autism.

An understanding of this history provides important lessons for physicians and policymakers seeking to preserve the public's trust in the nation's vaccine system. (*Am J Public Health*. 2008;98:244–253. doi:10.2105/AJPH.2007.113159)

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### DESPITE THE REASSURANCE

of no less than eight safety review panels conducted by the Institute of Medicine (IOM) since 2001, many parents continue to fear that childhood vaccines can cause a host of adverse effects ranging from immune dysfunction to attention deficit disorder and autism.<sup>1</sup> Several trends no doubt contribute to this anxiety: fading memory of vaccine-preventable diseases, adverse media coverage, misinformation on the Internet, and litigation.<sup>2</sup> Yet global explanations of this sort fail to do justice to the fact that controversies over vaccines have often followed quite disparate trajectories in different settings. For example, although the alleged relationship

between childhood vaccines and autism has been the dominant controversy over child immunization of recent years, British anxiety has centered on the measles-mumps-rubella vaccine, whereas Americans have focused much more on the role of mercury in vaccine preservatives.<sup>3</sup>

I examine the origins of the American debate surrounding vaccines, mercury, and autism to illuminate how historical analysis can contribute to understanding public attitudes toward vaccine safety. It is not my intent to answer whether mercury in vaccines explains the increasing prevalence of autism; the IOM has already determined over the course of two reviews that available evidence fails to support such a conclusion.<sup>4</sup> Instead, I examine the historical questions that have been raised in the debate but only superficially addressed by the IOM. Why was the mercury-containing preservative thimerosal introduced in infant vaccines in the first place? Why was its use not questioned until the late 1990s, long after the toxic effects of mercury had been recognized? Why was autism perceived to be “epidemic” in the 1990s, and how

did it become linked to vaccines in the public's mind?

I argue that the thimerosal story is best envisioned in terms of three historical “streams” dating back to the early 20th century that converged unexpectedly and momentarily in the summer of 1999. These three tributaries, corresponding to the histories of vaccine preservatives, mercury poisoning, and autism, are examined successively to illuminate why various groups responded so differently to the debates beginning in that year.

### THIMEROSAL AND VACCINES

Understanding why mercury was first incorporated into childhood vaccines leads back to the preantibiotic era, a time when physicians employed a variety of compounds known as “germicides” to combat bacteria. Perhaps the best known was Joseph Lister's carbolic acid, developed in the 1860s for surgical antiseptics and later employed as a germicide and preservative known as phenol.<sup>5</sup> Yet a variety of mercury compounds were also used for the same purpose. No less an

authority than Robert Koch championed the use of mercury chloride as an antiseptic, although the product's propensity to cause tissue irritation limited its use. In the early 20th century, investigators synthesized a new class of compounds they claimed to be both more effective and less toxic, the organomercurials. Often brilliantly colored, these products soon found widespread usage, from operating suites to home medicine cabinets.<sup>6</sup>

Thimerosal was one of the most promising new organomercurials that excited the pharmaceutical industry after World War I. It was a white, crystalline powder, approximately 50% mercury by weight, in the form of ethylmercury bound to thiosalicylate. The emerging pharmaceutical giant Eli Lilly and Company provided grant support for its synthesis at the University of Chicago and in 1928 patented it under the trade name Merthiolate.<sup>7</sup> Over the next several years, Lilly's investigators H.M. Powell and W.A. Jamieson conducted extensive *in vitro* testing, showing that thimerosal was 40 to 50 times as effective as phenol against *Staphylococcus aureus*. The two men evaluated toxicity by injecting the compound into over 300 rabbits and a variety of other animals observed for a week's time. The animals appeared to tolerate significant doses—up to 20 mg per kg body weight in rabbits and still higher in rats—without apparent injury.<sup>8</sup>

These encouraging results prompted the Lilly team in 1929 to offer their product to the Indiana General Hospital during an epidemic of meningococcal meningitis. Hospital physicians gave 22 patients as much as 180 mL of a 1% solution of thimerosal intravenously divided over five doses.

From a therapeutic standpoint, the trial was a failure, but investigators were struck by how well the patients seemed to tolerate such high doses.<sup>9</sup> Combined with the animal studies, the data further reinforced the impression that thimerosal was far more benign than earlier mercurials, preparing the way for its incorporation at low concentrations into a wide range of biological products as a preservative. Vaccines would become an especially important niche.

One of the most troublesome safety issues afflicting early 20th-century child immunization was that of bacterial contamination. This could easily occur on a sporadic basis, when general practitioners might have to draw vaccines from multidose vials under poor hygienic conditions. Contamination of entire lots could be much more spectacular. In Columbia, South Carolina, in 1916, a tainted batch of typhoid vaccine stored at room temperature caused 68 severe reactions, 26 abscesses, and 4 deaths. A still more disturbing incident took place in 1928 in Queensland, Australia, where 12 of 21 children inoculated with contaminated diphtheria vaccine died of multiple staphylococcal abscesses and toxemia. The need for effective preservatives was readily apparent and represented one of the most important safety issues for the promoters of new vaccines.<sup>10</sup>

In this context, Powell and Jamieson's studies suggested that Merthiolate had an unexpected advantage. The problem with existing preservatives such as phenol and cresol was that they often reduced the potency of the biological products they were intended to protect. By contrast, thimerosal not only inhibited bacterial growth in vaccines and antisera at concentrations as low as

1:10 000 but also had no such deleterious effects.<sup>11</sup> A series of other investigators confirmed these findings over the next several years, and by 1940 thimerosal was incorporated into diphtheria toxoid, meningococcal serum, pertussis vaccine, and a host of other biological products.<sup>12</sup> Indeed, in 1938 Lilly's assistant director of research listed Merthiolate along with insulin as one of the five most important drugs ever developed by the company.<sup>13</sup>

Thimerosal's efficacy was sometimes challenged during the first 50 years following its synthesis, but rarely its safety. In 1948,

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the American Medical Association's (AMA's) Council on Pharmacy and Chemistry issued a report calling attention to a series of investigations asking whether organomercurials were any more effective as germicides than inorganic mercury compounds had previously been.<sup>14</sup> The AMA's council, it should be noted, played an important role before 1950 in providing independent assessments and approvals of drugs; the US Food and Drug Administration (FDA) did not require manufacturers to submit prelicensure safety testing until 1938 or efficacy testing until the 1960s.<sup>15</sup> Despite these voices of dissent, thimerosal remained popular in practice. Its defenders pointed to their own studies and the simple fact that contamination incidents

had become exceedingly uncommon following its introduction.<sup>16</sup> Although Jonas Salk's experience with inactivated polio vaccine in field trials from 1954 to 1955 suggested that in some cases thimerosal, contrary to expectation, did in fact harm vaccine immunogenicity, this case was regarded as an exception to the rule.<sup>17</sup>

The first real questions regarding thimerosal's safety were raised in the 1970s, provoked (as will be described in the next section) by rising awareness of the dangers of organic mercury poisoning. Although the latter debate centered on the organomercurial methylmercury found in fish and industrial pollution, ethylmercury did not escape scrutiny. A series of case reports demonstrated the compound's potential for neurotoxicity when given in large volumes, such as when used as a topical antiseptic to "paint" large omphaloceles.<sup>18,19</sup> These exposures exceeded those in vaccines, however, by many orders of magnitude. Only one routine infant vaccine in the 1970s, the diphtheria-tetanus-pertussis combination, contained thimerosal. A formal review of thimerosal by the FDA concluded in 1976 that no dangerous quantity of mercury was likely to be received from vaccines and other biological products over a lifetime.<sup>20</sup>

Concerns over neurotoxicity in infants receiving thimerosal from vaccines were never raised by medical or governmental authorities before the late 1990s. To be sure, some bacteriologists continued to question its efficacy in the laboratory. As noted by dermatologists (and eventually the FDA), skin testing revealed that contact with thimerosal caused hypersensitivity in many people. There was no evidence, however, that this

phenomenon had any medical significance.<sup>21</sup> Thimerosal's toxicity at high doses was clearly established by the 1970s, but the comparatively miniscule exposures involved in vaccines were well within all published guidelines for mercury exposure. The overwhelming consensus was that ethylmercury in low concentrations was safe and effective in practice.

What broke this consensus was the convergence of the history of ethylmercury with the parallel history of methylmercury in the mid-1990s. This story, known better to environmental scientists than vaccinologists, evolved in a direction that eventually suggested that even relatively low exposures to organic mercury could be dangerous to the fetus and young infant.

## METHYLMERCURY AND THE DEVELOPING BRAIN

Methylmercury, the form of mercury linked most closely in the public mind with environmental pollution, has a history as public and infamous as the history of ethylmercury has been quiet and inconspicuous. Much in the thimerosal debate hinges on the alleged similarity, or dissimilarity, of ethylmercury to methylmercury. The two compounds sound alike, differ by only one methylated side chain in their structure, and tend to be mentioned interchangeably in the popular press. Yet the chemical distinction is not trivial; it may be compared with that between ethanol (the form of alcohol in wine) and its highly lethal counterpart methanol. Methylmercury was once used widely in developing countries as a fungicide as part of the "Green Revolution" that transformed agriculture after 1945. It is also synthesized by bacteria living in mercury-polluted waters, where it

is passed up the food chain and concentrated in fish. The dangers of methylmercury in both contexts have been vividly demonstrated in a series of environmental disasters.

The first and best remembered of these took place in the fishing community of Minamata Bay, Japan. In the early 1950s, the Chisso chemical company constructed a factory that began expelling large quantities of effluent into the bay. The area's inhabitants soon began witnessing a variety of disturbing events. Seagulls fell from the sky, dead fish washed ashore, and frenzied cats were seen whirling in a mad dance ending in death. Soon thereafter, doctors began seeing patients with a staggering gait, numbness in the hands and feet, and more profound neurological impairments. A new form of viral encephalitis was initially suspected. An investigation by Kumamoto University, however, pointed instead to the similarity of the symptoms to those described in an obscure 1940 case report of four workers in a manufacturing plant producing methylmercury as a seed disinfectant. Bacteria in the bay, the researchers concluded, had converted inorganic mercury discharged from the plant into methylmercury.<sup>22</sup>

The Minamata Bay disaster became one of the defining events in the rise of environmental awareness of the toxic effects of mercury. The Chisso company long resisted pressure to improve its discharge system, and victims continued to appear in the 1960s both in Minamata and in Niigata, Japan, the site of a second outbreak. Only in 1968 did the Japanese government release a formal statement implicating methylmercury in the outbreaks. A series of lawsuits began

shortly thereafter that would last until the end of the century. The magnitude of the disaster remains hard to determine, but as of 2003, over 2265 patients had been certified to have had Minamata disease.<sup>23</sup> The spectacle was brought to American eyes in the 1960s on the pages of *Life* magazine through the poignant work of documentary photographer and activist W. Eugene Smith.<sup>24</sup>

Some of Smith's most enduring images depicted children with mercury poisoning, some of whom, born to asymptomatic mothers, had been exposed in utero. Here was the first indication that the fetus was more vulnerable than the adult. Infants with "congenital Minamata disease" manifested the hallmarks of profound neurological injury: spasticity, seizures, deafness, and severe mental deficiency. So great was the shame associated with the syndrome, however, that investigators had a great deal of difficulty enrolling patients for formal studies.<sup>25</sup>

Tragically, a still greater disaster soon provided researchers another opportunity. In Iraq in 1971 and 1972, an estimated 6530 farmers and family members were hospitalized for methylmercury poisoning, of whom 459 died. The source was homemade bread derived from seed wheat that had been contaminated by fungicide.<sup>26</sup> Extensive study of the Iraqi victims provided the basis for the first standards defining safe organic mercury exposure for adults. Specifically, the FDA drew upon this data, as well as a variety of animal studies and reports from other mercury poisoning incidents, when it proposed in the 1970s an acceptable daily intake of 0.4 µg per kg of body weight per day, based on the threshold at

which paresthesia occurs in adults.<sup>27</sup>

Determining safe exposure for the fetus and newborn proved much more challenging.<sup>28</sup> At an early point, investigators in Iraq identified cases of severe congenital mercury poisoning characterized by profound retardation and spasticity similar to those that had been described in Japan.<sup>29</sup> Only gradually did it become apparent that these infants represented the extreme of a continuum of toxicity. The first published studies of apparently asymptomatic Iraqi infants exposed to intrauterine or postnatal (through breastmilk) methylmercury were reassuring, with tests revealing normal development at age 1 year. As surveillance of these children continued into the 1980s, however, a disproportionate number began to show signs of delays in language acquisition.<sup>30</sup> The probability that mercury might be analogous to lead, which was also shown to have more subtle yet real cognitive effects by researchers in the same time period, was becoming more compelling.<sup>31</sup>

Two major longitudinal studies were launched during the 1980s in the hope of answering whether relatively low maternal methylmercury exposures could result in any degree of neurological injury to the fetus. Both were conducted in isolated island populations consuming large quantities of fish. The first, based in the Seychelles in the Indian Ocean, used global measures such as overall IQ and the Denver Developmental Screening test, whereas the second, based in the Faroe Islands in the North Atlantic, employed more-specialized, domain-related tests of function.

The two studies produced different results. The Seychelles children did not appear to suffer any

adverse outcomes. By contrast, the Faroe children demonstrated deficits in language, attention, and memory at age 7 years. It is unclear whether these differences reflect testing strategies, different genetic vulnerabilities, or the source of mercury. The Faroe Islanders consumed mercury in more of a "bolus" fashion in the form of meals, including pilot whale blubber, which is heavily contaminated with fat-soluble pollutants such as polychlorinated biphenyl (PCB) and pesticides. Still, the more-specific types of testing in the Faroes led many environmental experts to give the results there precedence.<sup>32,33</sup>

The stage was now set for the confusing array of advisory recommendations on methylmercury that emerged in the 1990s. Agencies differed with respect to directing recommendations at adults or pregnant women, balancing the conflicting data for the Seychelles and Faroes, and determining how much of an uncertainty factor to take into account the extent to which individuals may metabolize mercury differently. As of 1999, the FDA continued to set its acceptable daily intake at 0.4 µg per kg of body weight per day, the standard proposed for adults in the 1970s. It noted that this figure should probably be set lower for pregnant women. By contrast, the Environmental Protection Agency in 1994 lowered its reference dose for methylmercury exposure to 0.1 µg per kg of body weight per day on the basis of the Iraqi data on women and children. To make the situation still more confusing, the Agency for Toxic Substances and Disease Registry lowered its minimal risk level to 0.1 µg per kg of body weight per day in 1994, only to raise it back to 0.3 µg per kg of body weight per

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day in 1999, prioritizing the Seychelles over the Faroes studies.<sup>34</sup>

Beyond the discrepancy between official recommendations, two other points deserve emphasis. First, there was an emerging consensus among environmental scientists that the fetus was indeed more sensitive to methylmercury than the adult and that this toxicity was better expressed as a continuum than a clear-cut syndrome. The second point is that this concern had to do with relatively subtle cognitive and language delays, detectable in older children through domain-specific testing. Autism was not even discussed. It was not described among either the profoundly injured children in disasters such as Minamata Bay and Iraq or the milder delays described in the Faroes. Autism only entered the discourse in 1999, represented by a third set of communities with their own historical memories.

### AUTISM AND ITS HISTORIES

The hypothesis that thimerosal-containing vaccines could explain the remarkable rise in the prevalence of autism arose not among environmental scientists but among the communities that have emerged over the past 20 years of parents and professionals caring for autistic children.<sup>35</sup> Specifically, parents and clinicians who have framed autism in biomedical terms (such as immune or gastrointestinal dysfunction) have been critical agents in promoting

both the concept of the “autism epidemic” and the primacy of vaccines as its cause. The passion behind their arguments stems from a long history of advocacy on behalf of their children, often in the face of psychiatric theories perceived as “parent blaming” and inadequately funded developmental and educational resources in many communities.

The psychoanalyst Leo Kanner first coined the term “autistic” in a classic 1948 case report of 11 children exhibiting what he characterized as “an extreme autistic aloneness” shutting out all social contact, as well as an “obsessive desire for the maintenance of sameness” in their play and daily routines. The typical autistic child in his series eventually acquired language but used it in a mechanical way devoid of emotion, sometimes combined with striking rote memory. One preschool child could recite 25 questions of the Presbyterian Catechism, another could distinguish 18 symphonies from one another. Kanner (along with his contemporary Hans Asperger, who described a similar syndrome in 1944) was especially struck that all the children were born to highly intelligent parents.<sup>36</sup> Over the next two decades, autism researchers such as Bruno Bettelheim developed an explicitly Freudian explanation to account for the association: autism arose in infancy in response to rejection by an emotionally distant (although typically well-educated) parent—a so-called “refrigerator mother.”<sup>37</sup>

In 1965, psychologist Bernard Rimland (himself the father of an autistic child) rejected the psychogenic model of autism in his ground-breaking *Infantile Autism*, proposing that the condition was instead rooted in biology.<sup>38</sup> The collapse of the psychoanalytic model gave rise, however, to two rather different explanatory frameworks in its place. The ways in which these have diverged and have been embraced by different communities of parents and professionals is of critical importance to understanding the current debate over the existence of an autism epidemic.

What might be characterized as the “mainline” community of autism researchers has reconceptualized autism as a neurodevelopmental condition.<sup>39</sup> Four tenets have characterized most approaches by these researchers. First, the cause of autism is fundamentally biological and no more attributable to parental behavior than is cerebral palsy or Down syndrome. Although the nature of the cause remains unknown, a variety of studies (ranging from radiographic imaging to genetic twin studies and family pedigree analysis) have increasingly highlighted the importance of genetics.<sup>40</sup> Second, autism is conceptualized as a spectrum of disorders. In the 1970s, investigators modified Kanner’s original restrictive diagnosis to encompass children with greater intellectual and language impairment and then expanded it in the opposite direction to encompass higher-functioning children with labels such as “pervasive developmental disorders” and “autistic spectrum disorders.”<sup>41</sup>

Third, if autism represents a spectrum disorder rooted in biology as proffered in the first two tenets, its treatment must be largely rehabilitative rather than

curative. For example, Eric Schopler of the University of North Carolina developed the influential TEACCH (Teaching and Education of Autistic and related Communication-handicapped Children) program as a model combining parental education and therapy to assist parents in understanding their children prior to setting realistic management approaches.<sup>42</sup> Fourth, as with other developmental disorders, early referral and intervention offer the greatest hope for a positive outcome. Many autism researchers and parent allies have worked tirelessly to promote screening tools and special education programs in the schools. In 1991, autism was officially added to the list of covered disabilities in the Individuals with Disabilities Education Act passed the preceding year, providing a major boost to its diagnosis and early treatment.<sup>43</sup>

The essential point to understand is that the rise of autism diagnoses in the 1990s was exactly what the mainline researchers expected.<sup>44</sup> It represented the logical consequence of their ongoing efforts to expand its definition and promote its recognition in developmental evaluation centers and the schools. What perhaps was not expected, and certainly not welcome, was the gap that frequently appeared between the supply of and rising demand for autistic services. All too often, parents confronted with their child's diagnosis in the 1990s were met with long waiting lists and primary care doctors who seemed barely familiar with the condition. Placed in this predicament, parents not surprisingly turned to one another and the Internet.

Parents frustrated by the mainline approach to autism were likely to meet what might be characterized as the “alternative”

community of autism research. This approach viewed autism in biomedical terms. Rather than viewing autism as a continuum of disability, it characterized the condition as a heterogeneous collection of discrete entities with different etiologies sharing a common presentation. Most importantly, this viewpoint offered hope that at least some forms of autism are not simply treatable, but curable. Many such cures have been proposed. Among the most popular were those focusing on special diets, based on studies suggesting that an abnormality in intestinal permeability (a so-called “leaky gut”) may admit intestinal toxins or opioids affecting the nervous system at an early age. Although promoted by researchers who viewed themselves as “dissident” with respect to mainline thinking, these theories recast autism as biomedical in origin and potentially curable in ways that profoundly reflected late 20th-century American hopes in the power of medical technology.<sup>45</sup>

The most notable organization promoting this framework is the Autism Research Institute in San Diego, Calif, which through its Defeat Autism Now! conferences and educational materials seeks to provide parents with the tools to understand and treat their own child. Parents provide much of the leadership and energy in this and related organizations. A smaller cadre of professionals participate as well, some of whom are very prominent in their own right. The Autism Research Institute was organized with the full support of psychologist Bernard Rimland, who had earlier played such a pivotal role in dethroning the psychogenic approach.<sup>46</sup>

It was among these parental advocacy groups, not the medical or educational professions, that

the notion of an autism “epidemic” first took root. These organizations provided a context to bring parents out of isolation and into a realization that others—many others—shared their hopes and frustrations. Against this background, an alarming possibility became more plausible: the cause of autism was not only biological but environmental, the consequence of some new exposure faced by young children. Indeed, it seemed fair to speak of an autism epidemic as a means of summoning the sense of urgency the situation required.

In 1998, British gastroenterologist Andrew Wakefield proposed a hypothesis linking the “leaky gut” etiologic framework of autism to a new environmental factor explaining its rise. In that year, he published a report describing a small number of patients who developed autistic regression and diarrhea following their measles-mumps-rubella immunization.<sup>47</sup> Wakefield's study launched a major controversy in Britain, despite the failure of large epidemiological studies to confirm its results.<sup>48</sup> Aided by the Internet, the controversy soon crossed the Atlantic and was viewed with concern by many parents of autistic children as well as the parallel network of parent groups opposing compulsory immunization. Both groups gained a powerful ally when Congressman Dan Burton (D, Ind) began a series of congressional hearings on autism and vaccine safety after his own grandchild was diagnosed with autism following the 12-month vaccinations.<sup>49</sup>

By 1999, a growing body of articulate and well-organized parents of autistic children were set on a trajectory destined to collide with that of the vaccine community. Their collective experience had

taught them the importance of challenging conventional wisdom and expertise. Many were highly capable individuals, such as Rick Rollens, an associate of California Governor Gray Davis (and, again, the father of an autistic child), who persuaded the legislature to fund millions of dollars for autism research at the University of California at Davis, as well as a study examining the historical trend in children receiving services for autism in the state's public school system.<sup>50</sup> Released on March 1, 1999, the report indicated that the rate of autism had increased 273% over the past 10 years. Reported widely in the press, the California Department of Developmental Services study gave new urgency to calls for investigation of an autism "epidemic" as the summer approached.<sup>51</sup>

## CONFLUENCE

The events that would bring these three histories together began in 1997, when New Jersey Representative Frank Pallone, representing a district concerned about environmental mercury poisoning, appended a rider to the FDA Modernization Act of that year to assess all of the agency's products for mercury content.<sup>52</sup> In response, the Center for Biologics Evaluation and Research (CBER) at the FDA initiated a formal risk assessment of thimerosal in vaccines beginning in April 1998. By this point, the vaccine schedule had expanded, and three of the vaccines routinely given to infants (diphtheria-tetanus-acellular pertussis, *Haemophilus influenzae* type b conjugate, and hepatitis B) potentially contained thimerosal. The analysis was completed in the spring of 1999. The actual cumulative exposure varied considerably, given that not all manufacturers used the preservative,

but the CBER scientists calculated that a minority of infants could receive as much as 187.5 mg of ethylmercury during the first 6 months of life. Lacking any standard for ethylmercury, the CBER team compared this exposure to standards for methylmercury and discovered that it exceeded that set by the Environmental Protection Agency. Although acknowledging the many uncertainties involved, the FDA responded by inviting vaccine advisory bodies for consultation in June 1999.<sup>53</sup>

There followed a rapid series of meetings and conference calls involving representatives of the American Academy of Pediatrics and the Centers for Disease Control and Prevention (CDC), culminating in a joint statement released on July 9, 1999. Although noting that there was no evidence that the use of thimerosal as a vaccine preservative had caused any true harm, the groups agreed that "thimerosal-containing vaccines should be removed as soon as possible" given the concerns raised by the Environmental Protection Agency's guidelines.<sup>54</sup> The controversy was now out in the open.

Many have criticized the process leading to the release of the joint statement, charging that it took place too rapidly and without proper consultation from important parties.<sup>55</sup> Its call to suspend the use of hepatitis B virus vaccine in infants younger than 6 months until thimerosal-free vaccine became widely available was particularly contentious. Although the ban lasted only for several months, it resulted in considerable confusion and inconsistency in hepatitis B virus vaccine delivery in some hospital nurseries.<sup>56</sup> One study later found that the proportion of hospitals failing to vaccinate infants born to seropositive mothers rose by over 6 times

(from 1% to 7%) during the suspension.<sup>57</sup> The consequences of this were harder to calculate but clearly worrisome given the very high (up to 90%) chance that infants who acquire hepatitis B infection at birth will develop the infection in a chronic form, with a significant (25%) risk of liver cancer.<sup>58</sup> By contrast, the statement's defenders asserted the prime importance of preserving the public's trust in the vaccine system, particularly given the rising influence of populist "vaccine safety" groups since the 1970s. Manufacturers, moreover, did successfully mobilize to remove thimerosal from their routine infant vaccines in a remarkably short time; the effort was largely complete by the summer of 2001.<sup>59,60</sup>

Meanwhile, the third of the historical streams, represented by parents within the "alternative" autism community, rapidly entered the debate. As detailed by journalist David Kirby, it was in fact a group of parents of autistic children (rather than parental organizations critical of vaccination such as the National Vaccine Information Center) who first seized upon thimerosal as an explanation for the autism epidemic. In keeping with their identity as participants in shaping research, some spent long hours on the computer or in libraries researching studies on mercury. Eventually, their efforts led to a published study in *Medical Hypotheses* that compared the features of autism to various signs reported in past studies and case reports of mercury exposure.<sup>61</sup> The publication of this study in turn helped to legitimize the hypothesis and thereby reinforce a growing body of individual testimonies across the Internet and in conferences.

Parents organized effectively in the political realm as well. The

self-designated “Mercury Moms” created an advocacy organization, Safe Minds. They were instrumental in persuading Congressman Burton to shift his focus from measles–mumps–rubella to thimerosal in his congressional hearings. And they organized successfully to oppose a rider to the Homeland Security Bill in 2003 that would protect thimerosal’s manufacturer from legal action.<sup>62</sup>

These events are chosen among many that have taken place since 1999 that illustrate the polarization that soon characterized the entire debate. Although a full analysis cannot be provided here, two themes deserve emphasis. One is the issue of trust. Physicians and public health leaders have generally turned to the scientific process to sort out the controversy and have been reassured by the negative conclusions of the IOM reports. Vaccine opponents have repeatedly rejected these studies, charging that the data have been manipulated for political reasons.<sup>63</sup> The second factor has been the entry of personal injury lawyers into the debate, accompanied by full-page advertisements in prominent newspapers and an infusion of financial support. Although hardly the primary agent in the story, litigation has without doubt fueled the polarization of the debate and further obscured scientific testimony through the promotion of expert witnesses dissenting from the IOM position.<sup>64</sup> Today, the mercury–autism hypothesis continues to be accepted widely among the parents of autistic children.

## CONCLUSION

At this point, it is fair to ask whether this narrative should more properly have focused on

the story of the thimerosal controversy since 1999. Has not a new group of actors, including members of Congress, professional groups, antivaccine organizations, and personal injury lawyers, assumed central relevance since that time? Is it really that necessary to understand the long-term historical trends that converged just prior to the 1999 joint statement?

There are three answers, each corresponding to one of the historical streams already examined. The first is directed at the insinuation prevalent on the Internet that thimerosal was a dubious product smuggled into vaccines by avaricious drug companies bent on profits rather than the welfare of children. A more sober assessment would suggest that thimerosal was the result of ethical scientific and corporate research in the 1920s and 1930s, specifically to improve vaccine safety. Despite questions regarding its efficacy, it has performed well in practice and posed toxicity so low as to be considered negligible until recent years.

The second point concerns the history of mercury poisoning. Central to the public story of thimerosal has been a battle over the meaning of “mercury.” Those in the scientific community take it as axiomatic that all forms of mercury are not created equal; in particular, there are good reasons to believe that the ethylmercury used in vaccines is very different from the methylmercury studied in environmental science. In public discourse, however, such distinctions are subsumed under a single entity, mercury, with a long and very public history. Perhaps unfairly, history has endowed mercury in all of its forms with a notoriety that is not easy to erase, as will quickly be discovered by any pediatrician trying to convince an

anxious mother that a “trace” of mercury in a vaccine is safe. One cannot simply brush aside this perception in constructing policy.

Finally, however important personal injury lawyers, vaccine skeptics, and their allies in Congress may have been in shaping the thimerosal controversy since 1999, they did not create it. Parents within the “alternative” wing of the autism community were the primary agents in popularizing the concepts that autism had become epidemic and that vaccines were its cause. Jumping from the first to the second proposition may have been highly conjectural, but the question of whether the rise in autism is real or defined (or both) remains open to reasonable debate. There is genuine anger in the autism community that has fueled the polarization of the thimerosal debate, but this anger is best understood in terms of frustration with the medical and educational systems, not the cynical manipulation of lawyers.

Although historical understanding may not readily translate into policy guidelines, it is essential for those responsible for conducting and implementing such policy. A polarized debate both draws upon and contributes to polarized understandings of history. Participants within each of this story’s three streams judged the same data using different sets of assumptions, each shaped by history. Articulating and sharing these narratives represent a first step toward transcending the powerful boundaries shaping today’s vaccine controversies. ■

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### ENDNOTES

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