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Shot in the Dark

Autism and the Vaccines Controversy

Autism is a neurobiological disorder connected to a wide range of symptoms, from mild social and behavioral impairment to severe communication and cognitive disability. It is generally diagnosed in children before they turn three. Its causes are a mystery: while some specific genetic and environmental factors have been convincingly linked to autism, the complexity of the disorder and the variety of its manifestations have led researchers to suggest a bewildering array of potential causes, from diet to viruses to pesticide pollution. Perhaps the most controversial suggested cause—certainly the one that has garnered the most attention in the press—is vaccination. Since the 1980s, there has been a rapid rise in autism diagnoses (although it isn't clear whether that rise is due to an actual increase in autism rates or to more attentive screening). Various estimates suggest a tripling, quadrupling, or more; the most recent statistic from the Centers for Disease Control and Prevention (CDC) indicates that one in 150 children is autistic. Meanwhile, the number of standard childhood vaccinations has gone up from seven in the 1970s to sixteen today. That correlation, and the fact that the first detectable onset of symptoms occurs around the same time that vaccines are administered, has convinced many parents that there must be a connection between the two.

The theory that vaccines cause autism was first aired in 1998, when Dr. Andrew Wakefield of the Royal Free Hospital in London published a paper in the medical journal *The Lancet* claiming that the combination measles-mumps-rubella (MMR) vaccine had caused autism in several children. Until

just a decade earlier, the three vaccines had been administered separately in the United Kingdom. (Merck, the leading American vaccine manufacturer, had released the MMR vaccine in the U.K. in 1988, some seventeen years after its release in the United States.) Wakefield claimed that the measles strain in MMR damaged the intestinal lining, allowing harmful proteins to enter the bloodstream and cross over into the brain. He did not identify the specific proteins involved and did not explain why the measles vaccine was more dangerous in MMR than when administered alone. Wakefield also made no comparison of the rates of autism in children who had and had not been administered the MMR vaccine. In the paper, he noted that the study was preliminary, and cautiously called for further research. But at the press conference and the subsequent flurry of media interviews, caution was abandoned in favor of grandstanding; Wakefield and his sensational allegations made for good television.

Beyond its methodological flaws, Wakefield's study was ethically troubling. Six years after its publication, investigative reporter Brian Deer discovered that, unbeknownst to the editor of *The Lancet* or any of Wakefield's twelve coauthors, the study had been largely financed by a personal injuries lawyer representing several of the children in the study (and subsequently many of the seven hundred families who filed suits against pharmaceutical corporations after the study's publication). Wakefield had clear-cut conflicts of interest, with two patents pending—one for a new standalone measles vaccine and one for a "remedy" for MMR-caused autism. And even worse, the children in the study had been subjected to highly questionable procedures completely out of the realm of their normal treatment regimens, including blood collections, spinal taps, colonoscopies, and intestinal biopsies—never approved, despite Wakefield's claims to the contrary, by an ethical review committee. As Dr. Paul A. Offit, an American pediatrician and vaccine expert, explains in his new book *Vaccinated: One Man's Quest to Defeat the World's Deadliest Diseases*: "The fact that young children with autism were being subjected to biopsies and spinal taps for the purpose of generating evidence for a lawsuit caused many to wonder exactly who was looking out for their well-being"—and what was the real purpose of the study. When Wakefield's financial conflict of interest came to light in 2004, ten of his twelve coauthors formally retracted their support in the pages of *The Lancet*. Facing eleven charges of misconduct from the General Medical Council, Wakefield was dismissed from his post at the Royal Free Hospital and fled to Florida, where he resumed his practice at an alternative medicine clinic and styled himself a martyr, suppressed by the establishment but courageously standing firm for the sake of suffering children.

By that time, a vaccine scare was already well underway in the United States, where a short legislative

amendment in Congress had provoked an explosive series of hearings, thousands of lawsuits, and a coast-to-coast anti-vaccination campaign. In 1997, the FDA Modernization Act had instructed the Food and Drug Administration to "compile a list of drugs and foods that contain intentionally introduced mercury compounds and…provide a quantitative and qualitative analysis of the mercury compounds on the list." Two years later, the FDA requested that manufacturers disclose the data on mercury in their products. The level of mercury in infant vaccines caught the attention of Dr. Leslie Ball, a scientist at the FDA Center for Biological Evaluation and Research. At that time, three of the eleven routine childhood vaccines contained a mercury-based preservative called thimerosal: DTP (diphtheria-tetanus-pertussis), influenza, and hepatitis B. They contained 25 micrograms, 25 micrograms, and 12.5 micrograms of mercury, respectively. (A microgram is one-millionth of a gram—about the weight of a single speck of dust.) The influenza and hepatitis B vaccines had been added to the schedule relatively recently, in 1991 and 1993. All together, Ball figured, an infant receiving the normal course of vaccines would receive up to 187.5 micrograms of mercury within the first six months of life.

Thimerosal had been added as a preservative to some vaccines since the 1930s to prevent bacterial contamination in multi-dose vaccinations. By weight, it is 49.5 percent ethyl mercury. Unlike methyl mercury, the kind found in the environment, ethyl mercury does not accumulate in the body—it is metabolized more than five times as fast and has a much shorter half-life. Offit compares the difference between ethyl and methyl mercury to the difference between ethyl and methyl alcohol—ethyl (drinking) alcohol may cause a headache and a hangover; methyl (wood) alcohol causes blindness. However, ethyl mercury has not been extensively studied. In the late 1990s, there were no federal safety guidelines for acceptable levels of ethyl mercury, so, to interpret the results of her calculation, Ball turned to the guidelines for methyl mercury. While 187.5 micrograms did not exceed the acceptable standards promulgated by the FDA or the Agency for Toxic Substances Disease Registry, it was more than double the Environmental Protection Agency's recommended level. Disturbed by this finding, the American Academy of Pediatrics and the Public Health Service in June 1999 requested that pharmaceutical companies remove thimerosal from their vaccines. Hoping to "maintain the public's trust in immunization," they noted that there was no evidence that thimerosal was actually harmful, but that removing it would make "safe vaccines safer."

Maintaining the public's trust was hardly what this quizzical statement accomplished. Pharmaceutical corporations immediately complied, and discontinued thimerosal from all but the influenza vaccine. (Because of the high yearly demand for influenza

shots, switching to the more expensive single-dose vials was not financially feasible from the point of view of either the pharmaceutical corporations, for whom vaccine manufacturing is a net loss anyway, or the public that would need them.) In the meantime, the press leapt on the story, parents panicked, and the ears of personal injury lawyers pricked up. Mercury is a known neurotoxin, extremely harmful in large doses. (The phrase "mad as a hatter" was originally a reference to eighteenth- and nineteenth-century hat-makers who used mercury in the hat felt and absorbed poisonous quantities of it through their skin.) According to Offit, infants absorb about 360 micrograms of methyl mercury from their environment in the first six months of life—double what they would receive in the full complement of ethyl mercury-laced shots—but this is by gradual exposure. The idea of injecting more than trace amounts of *any* kind of mercury into small children distressed and sickened many parents. Twenty state legislatures banned mercury in vaccines. Parents of autistic children were outraged that a simple health measure they had taken in good faith might have caused their children's devastating disorder.

Congress soon stepped into the fray. Representative Dan Burton, a Republican from Indiana and then the chairman of the House Government Reform Committee, held a series of hearings on vaccines and autism from 1999 to 2002 that critics charged were heavily slanted and that, in any case, certainly added to the drama. Burton was convinced that MMR had caused his grandson's autism, and called in Wakefield and other outspoken opponents of vaccines to testify, while excluding the American Medical Association, the American Public Health Association, the Infectious Disease Society of America, the American Nurses' Association, Britain's Medical Research Council, the World Health Organization, and other experts and officials who had asked to testify. (Burton, it should be noted, had something of a familial conflict of interest: even as he was trying to revise and expand the compensation criteria for vaccine-related injury, his grandson had a case pending before the claims court.) California Congressman Henry Waxman, the ranking Democrat on the committee and a legislator who had in the past harshly criticized pharmaceutical companies, was in the unaccustomed position of defending the corporations that produced the vaccines. He said the congressional hearings were "called and structured to establish a point of view. And that's the point of view of the chairman." The political posturing and the alarmism uninformed by all the available facts posed, Waxman said, "a real danger.... Let's let the scientists decide where the truth may be."

Indeed, by then a growing body of scientific research was consistently refuting the purported link between vaccines and autism. In fourteen separate demographic studies of the medical records of 600,000 children in

the United States and Europe, the incidence of autism was exactly the same for the children that had received the MMR vaccine and those that hadn't. Even during the hearings, Wakefield's findings did not stand up to critical scrutiny; as Offit recounts, other investigators' inability to replicate his results even with the same study samples led some to question whether Wakefield's data had simply been fabricated.

But with Wakefield's MMR claims off the table, the growing anti-vaccine movement made a seamless transition to thimerosal. Here, too, evidence was piling up against the supposed link between ethyl mercury and autism. A special panel at the Institutes of Medicine issued a report in 2001 speculating that such a link was at least "biologically plausible" and calling for further research; three years later, a follow-up report concluded that a careful review of the evidence did not suggest any connection between thimerosal and autism. The panel added that, given other public health priorities, as well as the danger of alienating the public from essential vaccinations, no further research would be useful or necessary:

> From a public health perspective the committee does not consider a significant investment in studies of the theoretical vaccine-autism connection to be useful at this time…the benefits of vaccination are proven and the hypothesis of susceptible populations is presently speculative. Using an unsubstantiated hypothesis to question the safety of vaccination and the ethical behavior of those governmental agencies and scientists who advocate for vaccination could lead to widespread rejection of vaccines and inevitable increases of serious infectious diseases.

A major study of the subject undertaken by the CDC only worsened the controversy. The researchers at first seemed to find an apparent connection between thimerosal and neurological disorders, but then adjusted the study's sample size and controlled for factors like birthweight in such a way that the correlation disappeared. Skeptics interpreted these adjustments as a government effort to cook the books so as to protect the pharmaceutical industry from the fallout of one of the biggest public health disasters in history. In a widely-read 2005 article in *Salon* and *Rolling Stone*, environmental attorney Robert F. Kennedy, Jr. wrote of the "collusion" between the government and "Big Pharma"—what he called "a chilling case study of institutional arrogance, power, and greed."

The anti-thimerosal campaign has had its advocates in Washington, too. The House version of the 2008 Labor, Health and Human Services, and Education appropriations bill contained a provision prohibiting funds in the federal Vaccines for Children program from paying for vaccines that contain thimerosal. In a letter to House leaders, the Bush administration expressed strong opposition to the provision,

arguing it "could result in children not receiving any flu vaccine." The vaccine industry's current production capacity of the thimerosal-free single doses of the influenza vaccine is scarcely more than half of the amount necessary to vaccinate just infants, not to mention young children, pregnant women, and others endangered by the flu.

As of this writing, the budget has not yet been finalized, so it is not clear what will become of the provision, though the administration's insistent opposition is likely to win the day. But the administration has not always been so clear in its views. During the 2004 presidential campaign, President Bush was asked in a written questionnaire from an autism parents group whether he supported banning the use of thimerosal in all vaccines. His response was:

> I support the removal of thimerosal from vaccines on the childhood national vaccine schedule. During a second term as president, I will continue to support increased funding to support a wide variety of research initiatives aimed at seeking definitive causes and/or triggers of autism. It is important to note that while there are many possible theories about causes or triggers of autism, no one material has been definitely included or excluded.

While this reply refused to accept the claims of thimerosal alarmists, its commitment to remove thimerosal from vaccines and its groundless ambiguity about the evidence have been touted and used by vaccine alarmists ever since.

The best refutation of the alleged link, it turns out, is simply the passage of time. If heightened levels of mercury in vaccines were causing the explosion in autism diagnoses, incidences of autism should have dropped within a few years of its removal. This did not happen. Denmark eliminated thimerosal from childhood vaccines in 1992, Canada in 1996, and the United States in 1999. All these countries saw an unchecked rise in cases of autism. In California, for example, there was a 40 percent increase from 2002 to 2006 in the intake of autistic children to the state services system—a cohort of children who received no mercury in routine vaccinations.

To families with autistic children, however, the growing evidence against the mercury-autism link has had little impact. As journalist Arthur Allen explains in his new book *Vaccine: The Controversial Story of America's Greatest Lifesaver*,

> The fact that the mainstream medical community rejected this theory would not bother them much, for established medicine had so little to offer the parents of autistics that turning one's back on the advice of the American Academy of Pediatrics was almost no sacrifice at all. There seemed to be an epidemic of autism, and there were no drugs that consistently treated the disease. There was little money to

> meet the overwhelming demands of educating autistic children and, perhaps worst of all, there was no meaningful light to shed on the grievous mystery of autism itself.

As one mother put it, "When you get the diagnosis you fall off the map. They have nothing for you."

Being on the outs with the establishment meant that all the official studies and assurances of vaccine safety looked like nothing more than a collusive governmental effort to placate the public and avoid responsibility. Allen describes the experience of one family:

> By way of a medical problem the Meads had crossed a psychic divide, leaving behind the world of prosperous, reasonably contented professional people for the spooky realm of herbalists and populist mavericks and—not to put too fine a point on it, conspiracy kooks—who viewed America as a toxic hell. The Meads called it "going down the rabbit hole." In their world—dealing with a child who sometimes rocked for hours, banging his head on the wall, who chewed dirt and didn't speak but obsessively scratched his enormous welty mosquito bites—white was black and up was down. Unlike Alice they were not dreaming of Wonderland. They and thousands of other parents had become convinced that vaccines, which most of the world viewed as safe and wholesome and life-giving, were poison.

The Meads, like many other families in similar straits, resorted to alternative medicine, hoping it had something more to offer them than clinical medicine did. Many of the alternative therapies were designed as remedies for vaccine-inflicted harm; and when these treatments were in any way successful in alleviating symptoms, their proponents took it as proof that vaccines really were the culprit. A gluten-free, casein-free diet, for example, is a common and relatively helpful therapy for many autistic children, as digestive and immune problems are often co-inherited aspects of the disorder; but vaccine opponents took the diet's success as proof of intestinal damage inflicted by the measles vaccine. Other alternative treatments are somewhat bizarre—like injections of secretin, a pig hormone supposed to counteract the damage done by MMR; in 2003, a dozen studies showed secretin to be no more effective than a saline placebo in alleviating autism symptoms. And some therapies are outright hazardous, like the risky "chelation therapy" in which a powerful sulfur-based compound injected into the bloodstream binds to heavy metals and expels them from the body. The idea is to remove the extra mercury, but necessary minerals are excreted in the process, so chelated children must take an enormous number of supplements to compensate for their depletion. Among other risks, chelation can cause serious liver damage, hypocalcemia, and heart failure. In 2005, two children died within minutes of receiving the injection.

Some parents have turned to the legal system for relief and for answers. In June 2007, hearings began in the test case for the 4,800 claims that have been filed in the past few years seeking compensation in a special vaccine court established by Congress in 1986. The burden of proof is lighter than in a regular civil claims court, and the plaintiffs can retry their case in civil court if the vaccine court's three "special masters" do not rule to their satisfaction.

During those court proceedings, a barrage of expert testimony is expected over the next year—although now that institutionalized science has come down firmly against the theory, the plaintiffs' lawyers have come to rely on some fairly spurious sources. The mainstay of their case is the father-and-son team of Mark and David Geier, who work out of their basement in Maryland (a quack house crammed with cast-off lab equipment that Mark Geier told the *Washington Post* is "every bit as good as anything at NIH"), publish copiously in fringe journals, and are frequently called on to testify in Vaccine Injury Compensation Program hearings. Their testimony has been regularly disqualified for its lack of credibility—one judge in 2003 admonished that Mark Geier was "a professional witness in areas for which he has no training, expertise, and experience." Although Mark Geier holds a medical degree and formerly worked as a researcher at the National Institutes of Health, the mainstream scientific community views the Geiers as hacks whose work is sloppy, skewed, and, as the Institute of Medicine put it, "uninterpretable," and mainly geared to their lucrative expert testimony gig. "The problem with the Geiers' research is that they start with the answers and work backwards," Dr. Steven Black, director of the Kaiser Permanente Vaccine Study Center, commented to the *New York Times*. "They are doing voodoo science."

Scientific integrity, however, may not be necessary to win the case. An attorney for the plaintiffs said his legal argument is convincing enough to outweigh the shaky science. "There is a difference between scientific proof and legal proof," he told the *Washington Post*. "One is 95 percent certainty, and the other is…50 percent and a feather."

More unsettling than the prospect of a victory in a court of law is the prospect of a victory in the court of public opinion. If publicity surrounding the autism case spooks parents away from lifesaving vaccines, the consequences for public health could be disastrous. There is precedent for such skittishness about vaccines. In 1973, Dr. John Wilson, a British neurologist, presented a paper to the Royal Society of Medicine claiming that the whooping cough vaccine had caused permanent brain damage in 36 children. Although the study was full of holes—several of the children had pre-existing genetic conditions, others had developed symptoms before they received their shots, a couple of them actually had not been immunized at all—the media lapped up the story. Public alarm ensued. By 1978, the immunization rate in

England had dropped from 80 to 30 percent. The incidence of whooping cough more than quadrupled; 300,000 children were hospitalized, and at least seventy died. "Inherently we undervalue what vaccines do. When vaccines work well what happens? Nothing," said Dr. Bruce Gellin, a senior official at Health and Human Services. "And that's hard for people to value."

Similar hysteria is unlikely in this case, although there remains a very serious risk to vaccine manufacturers' incentive to continue to make them in sufficient quantities—or, indeed, at all. Forty years ago, there were twenty-six American companies producing vaccines. Now there are four. For some vaccines, such as measles, there is only one licensed manufacturer. The past few years have already seen regional shortages of MMR, DTP, influenza, and other vaccines. Companies always lose money on vaccines; meager profits, extremely complicated regulations, and factors such as the wildly unpredictable annual flu vaccine demand all discourage them from hanging onto their high risk, money-eating vaccine divisions. Add to that the potential for a bankrupting flood of lawsuits and it is remarkable that *any* corporations are still in the vaccine business at all. The idea behind the 1986 act establishing the special vaccine court, in fact, was to provide a place for those who had been genuinely harmed to receive compensation, while (partially) shielding a business absolutely crucial to the nation's health from being shut down entirely by frivolous lawsuits. Given the ever-increasing rates of international travel and the concomitant global patterns of disease, as well as the potential threat of bioterrorism, an adequate vaccine supply will only be increasingly important in the years ahead. And there is a worldwide need for cheap (multi-dose, thimerosal-preserved) vaccines; an "official" ruling declaring these toxic could cause a backlash against American vaccine exports, which would put them—"medicine's greatest lifesaver," in Arthur Allen's words—out of many, many people's reach.

Meanwhile, ever present behind the vaccines controversy raging from the Capitol to the courts, there remain the figures of those parents who have poured all their faith and fury into an explanation unsupported by the facts. That they have been misled by the claims of a connection between autism and vaccines seems clear; where they might turn now for hope and guidance is less so. "I am not a scientist. I am not a doctor," one mother involved in the court case has said. "We want to focus on Michelle and find out what happened and get the help for her that she needs." For so many of these parents, living and coping with autism is not enough; they can't help but question, and even seek vindication for, the baffling disorder that has upended so many lives.

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