

## EPIDEMIOLOGY

## Vaccine-Autism Link Dealt Blow

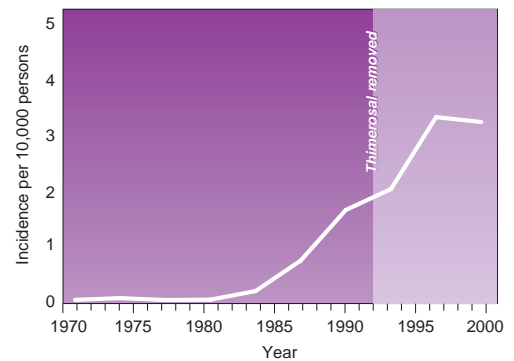
Two new studies cast further doubt on the theory that a mercury-based preservative in vaccines causes autism. Called thimerosal, the preservative has already been phased out in many industrialized countries but is still used in the developing world. The new findings “provide additional, extremely reassuring data,” says William Schaffner of Vanderbilt University School of Medicine in Nashville, Tennessee.

Thimerosal first attracted attention in the United States in 1999, when the Food and Drug Administration realized that toddlers, who are typically injected with several vaccines simultaneously, might be receiving higher doses of mercury than allowed by one federal standard. As a precaution, vaccine-makers began to phase out thimerosal that year.

Not long after, parent advocate groups from Safe Minds proposed that mercury, from the preservative and other sources, might be a factor in the rising incidence of autism, which often appears at about the same time that 2-year-olds get a round of

shots. Many scientists were skeptical, given the minute amount of mercury and the different symptoms of mercury poisoning and autism. But in 2001 an Institute of Medicine panel concluded that there wasn't enough evidence to rule out (or accept) the link.

Now the first big epidemiological studies weigh in. One comes from Denmark, which eliminated thimerosal from childhood vaccines in 1992. A team led by Kreesten Madsen of the Danish Epidemiology Science Centre in Aarhus reasoned that if thimerosal were a major cause of autism, incidence of new cases should drop once it was removed. In the September issue of the journal *Pediatrics*, they report that, instead of declining, the incidence continued to skyrocket after 1992. Like many epidemiologists, Madsen says the rising incidence could be a result of increased awareness and broader definitions of the disease. In any case, Madsen says, because incidence



**Disconnect.** New cases of autism continued to rise in Denmark after a vaccine preservative was removed.

didn't even slacken, thimerosal is not a major cause of autism.

But Mark Blaxill of Safe Minds argues that the study is “distorted and misleading.” He notes that in 1995, the Danish health registry began tracking a new category of patient, called autism outpatients. This and other factors, he says, are artifacts that confound the interpretation. Madsen responds that an unpublished analysis without outpatients showed the ▶

## RETRACTION

## Paper on Toxic Party Drug Is Pulled Over Vial Mix-Up

Last year scientists at Johns Hopkins University School of Medicine created a stir with a report in *Science* suggesting that people who use the party drug ecstasy may damage their dopamine neurons, raising their risk of Parkinson's disease. This week on page 1479 they publish a retraction: Owing to a mislabeled bottle, they say, they were using the wrong drug in their experiments. The toxic effects they ascribed to ecstasy (methylenedioxymethamphetamine, or MDMA) were caused by a sister drug, methamphetamine,

which is known to be toxic to dopamine neurons. Both drugs were delivered to the lab on the same day and in identical bottles, but the labels were switched.

A spokesperson for the drug supplier, Research Triangle Institute (RTI) in Research Triangle Park, North Carolina, says, “We are conducting a thorough review of our procedures, even though we do not have any evidence that an error occurred at RTI.”

Cognitive neuroscientist Jon Cole of the University of Liverpool, U.K., expressed doubts from the beginning about the study's implications for disease risk (*Science*, 27 September 2002, p. 2185). “If MDMA and [Parkinson's] were linked, we would be seeing hundreds, if not thousands, more young-onset Parkinson's disease cases,” he says. Now, he says, “I think they should ... abandon” the quest to link the two.

Study author George Ricaurte insists, however, that the retraction is by no means the last word on the issue of MDMA-induced dopamine neurotoxicity in primates, which he says “is [still] an open question.” He also notes that the retraction doesn't affect the well-established find that MDMA is toxic to neurons that communicate by means of the messenger serotonin.

The study in question found surprisingly strong reactions—including two deaths—and “profound dopamine toxicity” in primates given injections of what the researchers thought was MDMA (*Science*, 27 September 2002, p. 2260). The doses were no higher than the equivalent of what a human would get in one all-night “rave.” They concluded that even brief exposure to MDMA may cause brain damage and raise a person's risk of developing Parkinson's disease, which is the result of dead dopamine neurons.

But the team's subsequent attempts to replicate the results with oral doses, from a different batch of MDMA, failed. So did a repeat of the injection approach. The researchers then became suspicious of their original drug supply. Although the bottle labeled MDMA had been discarded, they discovered that their bottle of “methamphetamine” actually contained MDMA. A check of preserved animal brains from the experiment revealed methamphetamine and not a trace of MDMA.

Ricaurte says he's not planning to abandon this line of inquiry. MDMA is toxic to dopamine neurons in mice, he says. “In what we've done so far, we do not see an effect in monkeys,” but various regimens remain to be tested. From now on, he says, lab members will test selected chemicals to be sure they are what they say they are. —CONSTANCE HOLDEN



**A bad rap.** Primates with damaged dopamine neurons had received methamphetamine, not ecstasy (above).

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