



Spokeswoman. Actress Jenny McCarthy (center) has described on talk shows and at rallies, such as this one held in Washington, D.C., in June, how chelation helped her son recover from autism.

MEDICINE

Stalled Trial for Autism Highlights Dilemma of Alternative Treatments

The tension between parents desperate to help their sick children and researchers who worry about quack medicine has long put public health agencies in a bind. Last week, a long-simmering controversy boiled over when newspapers across the country ran an Associated Press story claiming that “government researchers are pushing to test an unproven treatment on autistic children, a move some scientists see as an unethical experiment in voodoo medicine.” In fact, a trial of the controversial treatment was halted last year, and Thomas Insel, director of the National Institute of Mental Health (NIMH) in Bethesda, Maryland, says he’s not pushing to restart it. The case, and the publicity surrounding it, illustrates the difficulty of deciding whether to test these questionable therapies, especially in children.

The “voodoo” here is chelation therapy. Believing that mercury in vaccines triggers autism, thousands of parents, often at the advice of their physicians, have given their autistic children drugs to bind, or chelate, and remove heavy metals from the body. Some say the over-the-counter or off-label treatment can improve poor language skills, social problems, and other symptoms of the disorder. And yet the drugs are not risk-free, and the underlying rationale—that mercury from vaccines causes or worsens autism—has been roundly rejected by many scientific studies.

NIMH has argued that the widespread use of the drugs creates a “public health imperative” to conduct a rigorous trial so that the institute can inform parents and physicians about any merits or dangers of the drugs. But some researchers and ethicists oppose studies that they say have no

chance of working—and little chance of persuading the most zealous advocates—especially if the drug poses a substantial risk. “On balance, it’s not an ethical study,” says vaccine researcher Paul Offit of the University of Pennsylvania.

This isn’t the first time researchers at the National Institutes of Health (NIH) have felt compelled to react to the use of dubious autism treatments. In the late 1990s, a wave of media publicity touted the abilities of a gastrointestinal drug called secretin to “cure” symptoms of autism (*Science*, 5 October 2001, p. 37). So many parents were buying the drug that NIH decided to do a series of small, rapid clinical trials. Secretin flopped, and most parents eventually stopped clamoring for it. “It was a meteoric rise, and it fell just as quickly,” says one autism researcher, who asked not to be named to avoid offending advocates. “I haven’t heard of anyone using secretin in years.”

Chelation therapy remains widely used. Some surveys have suggested that 2% to 8% of children with autism have had it, perhaps several thousand per year. Parents either buy unregulated supplements or have a doctor use a treatment for lead poisoning. Not only do the drugs bind to toxic metals, but they can also remove essential minerals such as calcium and iron.

NIMH wanted to conduct a study of the common chelator DMSA, which is approved by the Food and Drug Administration for treating lead poisoning. The idea was to give 120 children, aged 4 to 10, with a range of autism symptoms either DMSA or a placebo. After 12 weeks, NIMH researchers would evaluate the children to see if their social and language skills had improved. It would be the

first controlled study of a chelator on autism.

But first the study had to pass ethical muster with a so-called institutional review board (IRB). Putting children at risk of side effects is considered unethical if they are unlikely to receive any direct benefit from the drug. And Insel acknowledges that “it is difficult to make the case” that a chelator would help children with autism. On the other hand, a well-conducted trial with negative results could help parents better choose whether to use a chelator, says pediatrician and bioethicist Douglas Diekema of the University of Washington, Seattle, who was not part of the IRB. The NIMH study, which included multivitamins to safeguard against most of the risks of the drug, passed review and was launched in September 2006.

A few months later, new research raised a red flag. An October 2006 online study in *Environmental Health Perspectives* examined the impact of DMSA on rodents. Although the drug helped rodents overcome lead poisoning, when it was given to rodents without lead it caused lasting cognitive and emotional problems. The finding “raises concerns about the use of chelating agents in treating autistic children without elevated levels of heavy metals,” says senior author Barbara Strupp of Cornell University, although she notes that it’s not known what the threshold might be for such adverse effects. The children in the autism trial would not have had elevated levels of mercury in their blood (otherwise, they could not ethically be given a placebo).

NIMH officials halted the trial in February 2007 and sent it back to the IRB for further review. Given the new risks, the IRB concluded it did not have the authority to approve the trial, although NIMH’s parent agency, the Department of Health and Human Services (HHS), could if it felt the societal benefit were large enough. Rather than appeal to HHS, Insel says, the principal investigator, NIMH’s Susan Swedo, decided that NIMH’s intramural resources were better focused elsewhere, on the possible benefit of reducing inflammation with an antibiotic called minocycline in children with so-called regressive autism. Some critics of the chelation therapy say it was a good call because there is some preliminary evidence to suggest why inflammation—as opposed to mercury—might be involved in autism.

—ERIK STOKSTAD

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