

INSTITUTE OF MEDICINE

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IMMUNIZATION SAFETY REVIEW: MEASLES-MUMPS-RUBELLA VACCINE AND AUTISM

Immunization is widely regarded as one of the world's most effective tools for protecting public health. In the United States alone, child-vaccination programs have resulted in the elimination of smallpox and polio and rendered once-common, often debilitating, and potentially life-threatening infectious diseases—such as diphtheria, pertussis, and measles—exceedingly *uncommon*.

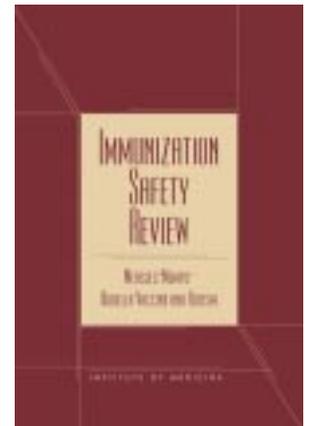
But along with these benefits have come concerns about safety, making some immunization policies a subject of public debate. One such issue is whether or not the measles-mumps-rubella (MMR) vaccine causes autistic spectrum disorders (ASD), frequently referred to simply as autism.

The MMR vaccine, which comprises three vaccines given in a single shot, has been extremely successful in virtually eliminating measles, mumps, and rubella in the United States. Measles cases, for example, dropped from over 400,000 per year in the pre-vaccine era to only 100 in 1999. However, these diseases remain a serious threat in other parts of the world where children are not routinely vaccinated. Measles alone resulted in over a million deaths in children around the world last year.

Some parents and researchers are concerned though that the MMR vaccine might cause ASD. Autistic spectrum disorders are incurable, permanent diseases that result in serious developmental problems in children. Although scientists generally agree that most cases of ASD result from events that occur in the prenatal period or shortly after birth, there is considerable concern because autistic symptoms typically do not emerge until the child's second year—about the same time the MMR vaccine is first administered. In addition, there are concerns that the introduction of wide-scale use of MMR coincides with an apparent increase in the incidence of autism.

Recent research in Britain provides suggestive evidence of such a link. In a highly publicized study, published in *The Lancet* in 1998, researchers describe 12 children who developed behavioral problems, including ASD, shortly after receiving the MMR vaccine. While the authors note that their study did not prove an association between MMR and ASD, it suggests the need for further research on this hypothesis. Since then, this group and other scientists have further examined this potential relationship.

The CDC and the National Institutes of Health recognized the need for an independent group to carefully examine the hypothesized MMR-autism link and address other vaccine-safety issues as well, in order to give some guidance to themselves, health care providers, researchers, and a concerned public. These agencies engaged the Institute of Medicine (IOM), which in turn appointed the Immunization Safety Review Committee, a 15-member body of health professionals with wide-ranging



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expertise in areas relevant to the problem. To preclude any real or perceived conflicts of interest, candidate members were subject to strict selection criteria that excluded anyone who had participated in research on vaccine safety, received funding from vaccine manufacturers or their parent companies, or served on vaccine advisory committees. The results of the committee's assessment of the issue are described in the report titled *Immunization Safety Review: Measles-Mumps-Rubella Vaccine and Autism*.

The committee has reviewed the numerous research efforts on the MMR-autism hypothesis. "The evidence favors rejection of a causal relationship at the population level between MMR vaccine and autistic spectrum disorders," the committee concludes in its report. "A consistent body of epidemiological evidence shows no association at a population level between MMR and ASD," the report says.

Moreover, the committee can find no proven biological mechanisms that would explain such a relationship. Scientists have suggested some theories, but none have been demonstrated. For example, though it is possible that a viral infection caused by the vaccine could invade the central nervous system, provoke an autoimmune response and ultimately produce autism, researchers have observed no evidence of this kind of injury. Finally, scientists have not been able to make inferences by studying the hypothesis in laboratory animals because of the difficulty of mimicking these conditions in animals.

Other leading medical groups—the American Academy of Pediatrics, the World Health Organization, and British health authorities—have come to similar conclusions for largely the same reasons.

Though the MMR-autism question might appear to be resolved, science is always a work in progress; a conclusion is only as good as the methods of the analysis. The epidemiological studies, traditional public health tools used to examine the risk factors for a disease on a population level, were at a disadvantage here because there is little variation in exposure to MMR since children in most developed countries are vaccinated similarly. Furthermore, the difficulties in diagnosing and determining the exact onset of autism in children make it difficult to design appropriate studies and compare the results from those studies.

The committee acknowledges they could not rule out another possibility—that MMR vaccine could contribute to ASD in a small number of children—because existing epidemiological tools may not have enough precision to detect the occurrence of rare effects like ASD.

The significance of this set of issues transcends the science alone. Infectious diseases like measles, mumps, and rubella, left unchecked, could cause considerable sickness and death. Public-health officials fear a repetition of the pertussis-vaccine history of the 1970s, when the combination of low numbers of pertussis cases and public concerns about the vaccine's safety caused immunization rates around the world to plummet, with sobering results. In Japan, for instance, pertussis vaccine coverage dropped from 80% to 10% in the mid-1970's resulting in epidemic involving 13,000 reported cases and 41 deaths. "Similar disease outbreaks could easily occur, with devastating effects," says the committee, "were immunization rates to decline as a result of fears regarding MMR vaccine."

Still, "the responsibility of the government to ensure the safety of [the MMR] vaccine is high, even if the adverse outcome is rare," the committee notes. The seriousness of autism - an incurable and serious behavioral disorder - requires rigorous consideration of all possible etiologies. And in any case, it adds, the level of public concern about MMR vaccine safety is high and must be meaningfully addressed.

This is especially important in that MMR vaccination is required by law in all 50 states for entry into school and day care, in part, to protect the health of others. These factors, the committee concludes, suggest the need for continued attention to this issue.

At present, however, no change of MMR immunization procedures is warranted. The report plainly states that "The committee does not recommend a policy review at this

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The committee does propose targeted research efforts and more rigorous data-gathering procedures. These would give scientists a firmer understanding of MMR vaccination and any possible side effects. In particular, the committee recommends the use of common definitions for autism cases; more detail and documentation in their reporting; comparing the effects of different immunization exposures; and clinical and epidemiological studies to identify risk factors and biological markers of ASD.

Further, the committee notes that government agencies responsible for immunization should recognize that most members of the public currently get their information on this and other health issues from the news media and the Internet. As a result, agencies such as the CDC and Food and Drug Administration must actively work at providing helpful public communications, beginning with the improved accessibility of their own Web sites.

“Attention should be given to how the material is perceived and used by those with the right and desire to know—the parents of children about to be immunized or those who believe their child has been adversely affected,” the committee says. “Direct input from parents and other stakeholders would be invaluable in conducting a systematic and effective evaluation of current communication tools.”

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For More Information...

Information on the Immunization Safety Review Committee can be found at www.iom.edu/ImSafety

Copies of *Immunization Safety Review: Measles-Mumps-Rubella Vaccine and Autism* are available for sale from the National Academy Press; call (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area), or visit the NAP home page at www.nap.edu.

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