ENCYCLOPEDIA
on Early Childhood
Development

[Archived] Immunization and Its Impact on Child Neurodevelopment

Susan L. Hyman, PhD

University of Rochester, USA

October 2005

Introduction

Immunizations have dramatically decreased childhood disability from neurologic complications of infections such as congenital rubella syndrome, hemophilus influenza meningitis, measles meningoencephalitis, and the late effect of measles (subacute sclerosing panencephalitis), among many other examples. With the decreased prevalence of these infectious diseases, the real and potential neurodevelopmental complications of the immunizations themselves have become of greater concern to families.[1,2] Studies have linked discrete side effects such as benign febrile seizures with DTP (diphtheria, tetanus and pertussis) and MMR (measles, mumps and rubella) vaccines.[3] Among the most controversial allegations at present is whether childhood immunizations are associated with autism.

Subject

It would be a serious public health concern if the prevalence of disabilities in childhood increased because of the type or number of vaccines being administered. It would be a similarly

©2005-2026 ABILIO | IMMUNIZATION

serious concern if immunization rates declined and there were a resurgence of preventable childhood diseases due to concern about potential side effects that have not been substantiated by scientific data. This summary will describe the controversy linking immunizations and autism to date.

Problems

The biologic causes of autism are not known, but the evidence indicates a strong genetic component modified by environmental factors. The questions linking immunizations with autism spectrum disorders include: 1) Have the prevalence or symptoms of autism changed with the introduction of new vaccines? 2) Could vaccines given in the second year of life be associated with the regression in language and social behaviours seen in up to one-third of children with autism? 3) Do children with autism have more gastrointestinal symptoms and, if so, is it related to immunization? 4) If not the immune response to the viral antigen itself, could additives in some vaccines such as thimerosal produce an immune or toxic response that damages the brain?

Research Context

Pre-marketing evaluations of vaccines typically examine acute effects emerging over the two to three months after immunization.[4] Clinical data can identify uncommon side effects once larger numbers of children have been vaccinated. An example is an intestinal blockage called intussusception associated with the rotavirus vaccine, which resulted in the vaccine being withdrawn from the market.[5] A clinical case series reported a history of loss of milestones and onset of gastrointestinal symptoms in 12 children with autism after immunization with measles, mumps and rubella (MMR) vaccine.[6] Two lines of investigation have followed: one looking for evidence of viral infection or immunologic disorder after immunization in children with autism[7,8] and the other looking for epidemiologic evidence supporting or refuting the association of vaccination programs and the prevalence of autism on a population level.[9,10] A second hypothesis suggests that mercury exposure, either postnatally[11] or prenatally, results in brain damage leading to autism in susceptible individuals. This represents a separate hypothesis, since the ethylmercury preservative thimerosal has never been in MMR vaccine.

Research Results

A second case series of 42 children with developmental disabilities (40 with autism spectrum disorders) evaluated for GI (gastrointestinal) symptoms reported an increased prevalence of

lymphonodular hyperplasia, an enlargement of the regions of the intestine that produce cells that fight infection.[7] This may be a response to non-specific infections or may indicate specific immunologic abnormalities in the intestine in autism.[12] Initial reports of antibody response to measles virus were based on technology that was not specific.[4,13,14,15] It remains controversial whether measles virus related to the vaccine strain selectively affects the intestine. Measles virus may persist in multiple body tissues to maintain the immune response. There is controversy regarding whether the immune response to concurrently administered antigens such as in the MMR vaccine[8] or sequential natural viral infections[16] is associated with intestinal (GI) disease. Biologic data would suggest that the three vaccines given at once do not alter the immune response and that current vaccines are less antigenic than those used in the past.[17] A GI component of the autistic disorders may be an independent phenomenon. GE (gastroesophageal) reflux, increased permeability of the intestine, and increased pancreatic secretions have all been reported.[18] Whether or not GI disease is causally or biologically significant remains controversial, as does the underlying observation, since children with autism do not seek medical care for GI complaints any more frequently than children not diagnosed with autism.[19]

Epidemiologic data has examined whether the prevalence of autism has increased with introduction of the MMR in California, Finland and the U.K.[2,9,10] No increase in the rates of autism can be identified relative to the timing of vaccine introduction. No change in the reports of regression or GI symptoms in cases of children with autism was identified in the U.K. or France.[20,21,22,23] A recent study examining the rates of reported autism in Denmark among children receiving MMR reported rates comparable to the rate among children who had not been vaccinated.

Conclusion

Epidemiologic studies to date have not supported an association between MMR immunization and autism on a population level. The evidence based on studies examining viral, histologic and immunologic factors does not support, nor does it refute, the possibility of rare cases of association.[14,15] The Institute of Medicine did not identify evidence of an association of the preservative thimerosal and autism based on the currently available data, but noted that mercury is a known neurotoxin and more data were needed to investigate the potential of this agent to cause neurodevelopmental symptoms at the doses that were present in vaccines.[14,15] Based on the possible potential for harm and the presence of safe alternatives in terms of vaccine without a preservative, thimerosal has been removed from vaccinations commonly administered in

childhood while additional research is being completed. No alteration in the currently recommended immunization schedule has been suggested.

Implications for the Policy and Service Perspectives

Historically, infectious diseases have been a significant source of childhood morbidity and mortality. To prevent recurrence of these diseases, a high level of immunity is necessary in the general population. This is why there are rules for immunization at school entry. Since the epidemiologic data to date indicate that MMR vaccination is not associated with an increase in autism in the population, the known neurologic and other serious risks of these preventable diseases is considered to be greater than the risk of the vaccine. There are no data to suggest that separation of the components of the vaccine decreases the potential for neurologic side effects. Thimerosal has been removed from DTaP, H. Flu, and hepatitis B vaccinations. The current initiatives to determine the prevalence of autism, such as the centres funded by the Center for Disease Control in the United States, should be able to document whether the rates of diagnosis of autism spectrum disorders will decrease with the removal of thimerosal from routine immunizations given in infancy.

References

1. Patja A, Davidkin I, Kurki T, Kallio MJT, Valle M, Peltola H. Serious adverse events after measles-mumps-rubella vaccination during a fourteen-year prospective follow-up. *Pediatric Infectious DiseaseJournal* 2000;19(12):1127-1134.
2. Makela A, Nuorti JP, Peltola H. Neurologic disorders after measles-mumps-rubella vaccination. *Pediatrics* 2002;110(5):957-963.
3. Barlow WE, Davis RL, Glasser JW, Rhodes PH, Thompson RS, Mullooly JP, Black SB, Shinefield HR, Ward JI, Marcy SM, DeStefano F, Chen RT, Immanuel V, Pearson JA, Vadheim CM, Rebolledo V, Christakis D, Benson PJ, Lewis N. The risk of seizures after receipt of whole cell pertussis or measles, mumps, and rubella vaccine. *New England Journal of Medicine* 2001;345(9):656-661.
4. Halsey NA. The science of evaluation of adverse events associated with vaccination. *Seminars in Pediatric Infectious Diseases* 2002;13(3):205-214.
5. Peter G, Myers MG. Intussusception, rotavirus, and oral vaccines: Summary of a workshop. *Pediatrics* 2002;110(6):e67.
6. Wakefield AJ, Murch SH, Anthony A, Linnell J, Casson DM, Malik M, Berelowitz M, Dhillon AP, Thomson MA, Harvey P, Valentine A, Davies SE, Walker-Smith JA. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998;351(9103):637-641.
7. Wakefield AJ, Anthony A, Murch SH, Thomson M, Montgomery SM, Davies S, O'Leary JJ, Berelowitz M, Walker-Smith JA. Enterocolitis in children with developmental disorders. *American Journal of Gastroenterology* 2000;95(9):2285-

©2005-2026 ABILIO | IMMUNIZATION

2295.

8. Wakefield AJ, Montgomery SM. Measles, mumps, rubella vaccine: through a glass, darkly. *Adverse Drug Reactions and Toxicological Reviews* 2000;19(4):265-283.

9. Taylor B, Miller E, Farrington CP, Petropoulos MC, Favot-Mayaud I, Li J, Waight PA. Autism and measles, mumps, and rubella vaccine: No epidemiological evidence for a causal association. *Lancet* 1999;353(9169):2026-2029.

10. Dales L, Hammer SJ, Smith NJ. Time trends in autism and in MMR immunization coverage in California. *JAMA - Journal of the American Medical Association* 2001;285(9):1183-1185.

11. Bernard S, Enayati A, Redwood L, Roger H, Binstock T. Autism: a novel form of mercury poisoning. *Medical Hypotheses* 2001;56(4):462-471.

12. Torrente F, Ashwood P, Day R, Machado N, Furlano RI, Anthony A, Davies SE, Wakefield AJ, Thomson MA, Walker-Smith JA, Murch SH. Small intestinal enteropathy with epithelial IgG complement deposition in children with regressive autism. *Molecular Psychiatry* 2002;7(4):375-382.

13. Halsey NA, Hyman SL, Conference Writing Panel. Measles-mumps-rubella vaccine and autistic spectrum disorder: Report from the new challenges in childhood immunization conference convened in Oak Brook, Illinois, June 12-13, 2000. *Pediatrics* 2001;107(5):e84. Available at: http://pediatrics.aappublications.org/cgi/content/full/107/5/e84. Accessed June 23, 2005.

14. Stratton K, Gable A, Shetty P, McCormick MC, eds. *Immunization safety review: Measles-mumps-rubella vaccine and autism*. Washington, DC: National Academy Press; 2001.

15. Stratton K, Gable A, McCormick MC, eds. *Immunization safety review: Thimerosal-containing vaccines and neurodevelopmental disorders*. Washington, DC: National Academy Press; 2001.

16. Montgomery SM, Morris DL, Pounder RE, Wakefield AJ. Paramyxovirus infections in childhood and subsequent inflammatory bowel disease. *Gastroenterology* 1999;116(4):796-803.

17. Offit PA, Quarles J, Gerber MA, Hackett CJ, Marcuse EK, Kollman TR, Gellin BG, Landry S. Addressing parents' concerns: Do multiple vaccines overwhelm or weaken the infant's immune system? *Pediatrics* 2002;109(1):124-129.

18. Quigley EMM, Hurley D. Autism and the gastrointestinal tract. *American Journal of Gastroenterology* 2000;95(9):2154-2156.

19. Black C, Kaye JA, Jick H. Relation of childhood gastrointestinal disorders to autism: nested case-control study using data from the UK General Practice Research Database. *British Medical Journal* 2002;325(7361):419-421.

20. Taylor B, Miller, E, Lingam R, Andrews N, Simmons A, Stowe J. Measles, mumps, and rubella vaccination and bowel problems or developmental regression in children with autism: Population study. *British Medical Journal* 2002;324(7334):393-396.

21. Fombonne E, DuMazaubrun C, Cans, C, Granjean H. Autism and associated medical disorders in a French epidemiological survey. *Journal of the American Academy of Child and Adolescent Psychiatry* 1997;36(11):1561-1569.

22. Fombonne E, Chakrabarti S. No evidence for a new variant of measles-mumps-rubella-induced autism. *Pediatrics* 2001;108(4):e58.

23. Kaye JA, Melero-Montes MD, Jick H. Mumps, measles, and rubella vaccine and the incidence of autism recorded by general practitioners: a time trend analysis. British Medical Journal 2001;322(7284):460-463.

©2005-2026 ABILIO | IMMUNIZATION