

Vaccine Safety and Efficacy Issues

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Neal A. Halsey, M.D.

Professor of International Health and Pediatrics - Johns Hopkins University
Director, Division of Disease Control
Director, Institute for Vaccine Safety
Department of International Health, Johns Hopkins University School of Public Health

My name is Dr. Neal Halsey. I am a pediatrician specializing in the study of infectious diseases and vaccines at the Johns Hopkins University School of Public Health. Thank you Mr. Chairman for the opportunity to provide this committee with my perspective on the important issue of vaccine safety. I have had the opportunity to care for children who have suffered from each of the infections that can be prevented through vaccination. I have also cared for children who have developed serious adverse reactions to vaccines. These experiences, coupled with my research over 27 years, have resulted in my current focus of interest on vaccine safety and the founding of the Institute for Vaccine Safety at Johns Hopkins University. My objective, and I believe the objective of most people in this room, is to ensure that both children and adults receive the safest vaccines possible to protect them against serious infectious diseases.

I have had the opportunity to review the written testimonies of Drs Harold Margolis, Samuel Katz, and David Satcher in their appearances before this committee and Congressman Mica's subcommittee. These witnesses have detailed the enormous benefits from immunizations and I agree with their statements. Therefore, I will not reiterate the benefits of vaccines in my testimony today, but I will be happy to address any questions regarding this issue.

Since this committee has expressed concern about possible conflicts of interest I provide the following information. I have never owned stock from any vaccine company or any other corporation. My retirement account is in mutual funds. I own no patents and I have no vested interest in any specific vaccine made by any company. My salary is generated from teaching and research grants and contracts, including studies to evaluate vaccine safety issues supported by the World Health Organization, the US Agency for International Development, the Food and Drug Administration and the manufacturer of Lyme disease vaccine. The Institute for Vaccine safety has received support from individuals concerned about vaccine safety, and in 1997 and 1998 we received unrestricted educational grants from several vaccine manufacturers.

I have served on the Advisory Committee for Immunization Practices for the Centers for Disease Control and Prevention (CDC) and the Committee on Infectious Diseases of the Academy of Pediatrics (AAP). During my tenure on the advisory committees to the CDC and the AAP, I was a strong advocate for changes in policy to encourage the use of the safest vaccines possible, including the change to use of inactivated polio vaccine and acellular pertussis vaccines. I no longer serve on these committees and I appear before you today representing myself and the Institute for Vaccine safety.

Today I was asked to comment on three issues: the number of vaccines children receive, combination vaccines, and diabetes.

I am not concerned about the number of vaccines children receive, and I look forward to the availability of several other vaccines that will help us prevent serious infections and cancer. The human immune system is remarkable in its capacity to respond to millions of different antigens. Children are exposed to many thousands of bacteria, fungi and viruses beginning at the moment of birth. In the first few months of life the human immune system responds to many foreign antigens from these organisms. Each bacterium contains hundreds of different antigens including carbohydrates, fatty substances, proteins, RNA and DNA. Children develop antibodies to 17 different proteins in one common bacterium

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(*Moraxella catarrhalis*) and a strep throat infection results in immune responses to 25-50 different antigens.¹

Some new, highly effective vaccines are made using only one or two bacterial antigens. For example, *Haemophilus influenzae* type b vaccines, or Hib as they are commonly called, contain only a single bacterial antigen attached to a protein. Children immunized with these vaccines are protected against meningitis and sepsis caused by the *Haemophilus influenzae* type b organism. Therefore, the immune systems of children who receive this vaccine are exposed to far fewer antigens than children naturally infected with the bacterium. Since all children would be exposed to the bacterium if they were not immunized, the use of the Hib vaccine actually reduces the burden on the immune system.

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Questions have been raised about the benefits and problems associated with administering several vaccines at the same time or combining vaccines in the same syringe. There are factors that can limit the ability to combine vaccines and there are theoretical concerns that have been reviewed in detail in a workshop sponsored by the FDA, the National Vaccine Program Office, CDC and NIH². These factors are taken into account in the FDA review of combination products. Numerous studies have been conducted to evaluate the safety and effectiveness of vaccines administered simultaneously or in the same syringe. Several efforts to produce new combined vaccines have not been successful, but those vaccines that have been approved by the FDA have been carefully evaluated and found to be safe and effective. Experts serving on advisory committees for the CDC and the AAP review the data from these studies prior to making recommendations for general use.

Children benefit from combined vaccines because they are protected against several different diseases with a single injection, thereby reducing pain and discomfort from multiple injections. If we did not have combined vaccines, children would need to be brought to physician's offices or clinics far more often, perhaps even weekly during the first few months of life, in order to protect them against serious infections. The use of combined vaccines can simplify the immunization process and record keeping for parents, physicians and public health officials.³

Recently, concerns have been raised about the amounts of thimerosal preservative and other products in some vaccines. Manufacturers, the FDA, the CDC and the AAP have responded rapidly to these concerns to make new products available that reduce infant's exposure to these components. I anticipate that further steps will be taken in the near future to eliminate these concerns. The use of combination products reduces the total exposure to these components and theoretical concerns about these issues.

If vaccines that are currently given in combination were separated and administered at separate visits, children would be left unprotected against some diseases for varying periods of time. As we learned a decade ago with the resurgence of measles in this country, leaving children unprotected even for a few weeks or months can lead to epidemics and unnecessary suffering and death. We do not need to learn the same lessons over again.

I know that Congressman Burton is concerned about combining measles, mumps, and rubella vaccines in the same syringe. This issue was raised first in the United Kingdom by

Dr. Andrew Wakefield. Dr. Wakefield's unfortunate statements at a press conference about separating measles mumps and rubella vaccines were based upon theory, not fact. Part of this theory was based upon his studies of children with inflammatory bowel disease. His original studies suggesting persistent measles infection in the inflamed intestinal tissue have not held up to careful review by investigators at the University of Connecticut and in Japan where his findings were not replicated.⁴⁻⁶ A review by highly qualified professionals in the United Kingdom found no evidence of a causal association between autism and MMR.⁷

Autism is a complex disease and there undoubtedly are several factors that contribute to children acquiring this unfortunate disorder. Unraveling the complex etiology will require research into the basic causes by highly qualified scientists. We do know that encephalitis is one of the factors that pre-disposes children to autism. All three of the diseases prevented by the MMR vaccine, measles, mumps and rubella, can cause encephalitis. We would not want to leave children unprotected against these diseases for even a short period of time. The routine use of MMR has resulted in the prevention of many thousands of cases of congenital rubella syndrome, a recognized cause of autism. I support the continued use of the combined measles, mumps and rubella vaccines as the safest and most effective means to protect children against these diseases.

Many hypotheses about causal factors have been offered to explain the increasing incidence of autism and diabetes. Statements made about hepatitis B vaccines before Congressman Mica's subcommittee on May 18, 1999 have been refuted by letters submitted to the committee by the State Epidemiologist of New Hampshire and the Director-General of Health of New Zealand. Also, the study in Finland referred to by Dr. Classen was published in the British Medical Journal and reveals no evidence of any effect from Hib vaccination on the risk of diabetes.⁸ The increasing incidence of diabetes, autism, and other medical conditions for which no specific etiology has been identified parallels the increase in many other factors such as the use of wireless communications, computers, and fast food restaurants. One could easily hypothesize that these factors or many other changes in our lifestyles contributed to the increases in these diseases, but there is no scientific evidence to support these ideas.

Two workshops have been conducted to investigate the possible link between childhood diabetes and vaccines, one at the Institute for Vaccine Safety and the other at the National Institutes of Health.^{9,10} The conclusions from both inquiries revealed no scientific evidence to support the hypothesis that vaccines cause diabetes. There are studies indicating the selective use of some vaccines early in life can prevent diabetes in animals, but to date, studies in humans have not confirmed this finding. Additional studies are in progress and other research is needed to identify methods for preventing this important cause of disease.

The history of medicine is filled with stories of physicians and others who have been quick to claim that they have the answers to complex medical problems based on inadequate studies. Just as people should not be misled by promises of cures from fake medications, we should not mislead people with false villains to blame when unexpected illnesses occur. The parents of children with diabetes, autism and other disorders that we do not fully understand deserve answers as to why this happened to their child. These answers should be based on sound scientific inquiries. Congress should support increased funding for research to identify the basic causes of these disorders.

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Identifying the safest possible vaccines is a process; there are no absolutes. We must constantly reassess vaccines using appropriate experts and make adjustments when indicated. This situation is similar to safety evaluation of other products such as automobiles. Modifications are constantly being made in automobile design to improve safety. These efforts require constant study, reassessment, and innovation through a competitive marketplace. Hepatitis B vaccine has been the target of several anti-vaccination groups. Hepatitis B vaccine prevents acute and chronic liver disease and this vaccine is the first successful cancer preventing vaccine. I hope that this committee would encourage the development of other cancer preventing vaccines through objective scientifically based inquiries. Promoting unproven hypotheses and hearsay about vaccine safety could have a negative effect on the willingness of vaccine manufacturers to invest the large amount of resources necessary to develop new vaccines that will protect our children against cancer and other serious diseases.

The primary message I would like to convey to this committee is that decisions about vaccine safety should be based on good science, not on hypotheses, opinion, individual beliefs, or observations. Federal agencies responsible for vaccine safety and major universities have procedures to assure high quality scientific research and reviews of vaccine safety issues. Congress should be concerned about vaccine safety and should provide sufficient resources to assure that the best possible science is conducted to assist with development of vaccine policy.

Assuring the safest possible vaccines requires constant vigilance and periodic reviews of all vaccines. Rapid advances in biotechnology are being made that have created new tools for developing and evaluating vaccines. We need highly qualified scientists who are on the cutting-edge of their fields to be conducting reviews of new and existing vaccines. Therefore, it is disconcerting to learn that the research budget for the agency responsible for approving vaccines, the Center for Biologics and Evaluation Research (CBER) of the FDA, has been cut to one-third of the level that it was just five years ago. You cannot expect an agency to do its job effectively if you deprive the scientists of research support. If this committee is truly concerned with assuring that the safest possible vaccines are used for children and adults, I urge you to investigate this issue and restore funding for vaccine safety research. The NIH, CDC, and FDA should be queried to determine the funding needed to support all aspects of vaccine safety research.

Thank you for the opportunity to share my views on these subjects. I will be happy to answer any questions.

References:

1. Institute of Medicine (US). Immunologic Reactions. In: Stratton KR, Howe C J, Johnston Jr., RB, editors. Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality. Washington DC: National Academy Press; 1994. p. 63.
2. Williams JC, Goldenthal KL, Burns DL, Lewis Jr. BP, editors. Combined Vaccines and Simultaneous Administration: Current Issues and Perspectives. Vol 754. New York: New York Academy of Sciences; 1995.
3. Advisory Committee on Immunization Practices, American Academy of Pediatrics and the American Academy of Family Physicians. Combination Vaccines for Childhood Immunization. *Pediatrics* 1999;103(5):1064.
4. Lizuka M, Masamune O. Measles vaccination and inflammatory bowel disease (letter; comment). *Lancet* 1997;350(9093):1775.
5. Liu Y, van Kruiningen H J, West AB, Cartun RW, Cortot A, Colombel JF. Immunocytochemical evidence of Listeria, Escherichia coli, and Streptococcus antigens in Crohn's disease. *Gastroenterology* 1995;108(5):1396-404.
6. Lizuka M, Nakagomi O, Chiba M, Ueda S, Masamune O. Absence of measles virus in Crohn's disease (letter). *Lancet* 1995;345(8943):199.
7. 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):2026-29.
8. Karvonen M, Cepaitis Z, Tuomilehto J. Association between type 1 diabetes and Haemophilus influenzae type b vaccination: birth cohort study. *BMJ* 1999;318(7192):1169-72.
9. The Institute for Vaccine safety Diabetes Workshop Panel. Childhood immunizations and type 1 diabetes: summary of an Institute for Vaccine safety Workshop. *Pediatr Infect Dis J* 1999;18(3):217-22.
10. Jefferson TO, Rabinovich R, Tuomilehto J. Vaccines and their real or perceived adverse effects. *BMJ* 1999; 318: 1487.