

NATIONAL VACCINE ADVISORY COMMITTEE

Report of the Subcommittee on Adverse Reactions
(Mrs. Fisher)

Approved By The Full Committee

September 18, 1990

GOAL:

1. To identify optimal strategies to prevent the occurrence of adverse reaction to vaccines.
2. To identify factors which hinder reduction in the occurrence of adverse reactions.

OVERVIEW:

Historically, U.S. mass vaccination programs have placed primary emphasis on the prevention and eradication of disease. During the early and mid-twentieth century when childhood diseases such as smallpox, diphtheria, pertussis, polio, measles, mumps and rubella were endemic in the U.S., preventing disease by vaccination was given a high priority. Because these programs contributed to reducing the incidence of these diseases, the occurrence of adverse reactions became more apparent. Today, concern and expectations for the safety and efficacy of vaccines has increased.

The optimal prevention of adverse reactions to vaccines is critical to the successful implementation of U.S. vaccination programs. It is essential that the public have confidence that government health agencies, vaccine manufacturers, and medical organizations are working together to assure that the safest and most effective vaccines are produced and available; that vaccines are being administered in the most effective and safest manner; that individuals at high risk for adverse reactions are identified; and that consumers are fully informed about the benefits and risks of vaccines and the risks of disease the vaccine is intended to prevent. All vaccines used in the U.S. today are licensed as safe and effective. However, none is perfectly safe nor perfectly effective. Adverse reactions to vaccines, including injuries and very rare deaths, are a reality. It is important that the U.S. have more and better information about the vaccines and the vaccination circumstances which result in adverse reactions. However, it must be recognized that misinformation about suspected vaccine reactions can impair vaccine use and result in a resurgence of preventable childhood disease. The public should be alerted to the fact that not all events that follow receipt of vaccines are caused by the vaccine itself. It is especially important for physicians to recognize the value of reporting adverse events.

FOCUS:

Several problems concerning the optimal prevention of adverse reactions were addressed by the National Childhood Vaccine Injury Act of 1986. These include the need for better adverse reaction data collection including factors predictive of such reactions; better recordkeeping by vaccine providers; better education of vaccine consumers and providers; and the need for better scientific data about the nature of adverse reactions and identification of high risk groups. The subcommittee chose to focus on four areas concerning the prevention of adverse reactions:

1. Data Collection/Analysis
2. Research
3. Education of Vaccine Providers and Consumers
4. Licensing and Testing of Vaccines

1. DATA COLLECTION/ANALYSIS--THE VACCINE ADVERSE EVENT REPORTING SYSTEM

In the U.S., approximately half of all immunizations are administered in private physicians offices and half in public health clinics. In the past, private physicians voluntarily reported vaccine reactions to the manufacturers and/or the Food and Drug Administration (FDA) while public health clinic physicians were requested to report reactions to the Centers for Disease Control (CDC).

A good example of how information generated by the Monitoring System for Adverse Events Following Immunization (MSAEFI), a passive reporting system, was used to help identify high risk children is the 1987 ACIP statement that infants and children with a personal or family history of convulsion have a three to six fold increased risk for neurologic events following DTP vaccination compared with those without such histories. Analysis of data from MSAEFI was used to arrive at this conclusion.

The National Childhood Vaccine Injury Act of 1986 mandated the reporting of vaccine reactions by all vaccine providers. Currently, the CDC and FDA are developing a unified Vaccine Adverse Event Reporting System (VAERS) for the nationwide collection of reports of adverse events temporally related to vaccination.

Scheduled to begin operation in 1990, VAERS is being designed to:

- o serve as a central repository for the reporting of adverse events temporally related to vaccination by providers and the public;
- o provide information on the number of adverse events reported and permit analysis of vaccine-specific information; and

- o serve as a sentinel for new or previously unrecognized or unreported vaccine-associated adverse events.

Other efforts to develop the linked database concept should be accelerated. The goal of such linkage is to better ascertain the number and rate of true reactions to vaccines and to identify background conditions occurring with the same frequency in vaccine-recipients and matched non-vaccinees, in the same population.

The NVAC Subcommittee on Adverse Events supports the implementation of VAERS. There are several points, however, which are of concern to the Committee.

- a. The quality and usefulness of vaccine reaction information generated by VAERS will depend upon whether vaccine providers and vaccine consumers recognize and report reactions. Experience in the U.S. and abroad with spontaneous reaction reporting systems, such as those for drugs, demonstrates that underreporting is a significant problem.

Therefore, utilization of VAERS will depend upon whether vaccine consumers and providers recognize adverse events when they occur following vaccination and perceive it is important to report these events to VAERS. Intensive promotion of VAERS in the media and by state health agencies and medical organizations is very important to ensure public and providers awareness and motivate utilization.

- b. Accurate and appropriate use of VAERS generated data is critical to successful vaccine use and prevention of vaccine reactions. The compilation, analysis and utilization of the data by the CDC, FDA, and other public and private groups or organizations compels the VAERS system to attempt to achieve a high degree of accuracy. For example, reaction rates cannot be generated by this passive system, but patterns of adverse reactions may be identified. Not all reactions reported will be true reactions caused by the vaccine, and may reflect conditions that would have occurred whether vaccine was given or not. The data may generate some idea of risk factors for individuals, could provide clues to lots of vaccines which are producing excessive numbers of reactions or unique disorders.

Data from the VAERS system should lead investigators to probe further into the relationship, or lack thereof, of reported reactions following receipt of vaccines and

the long term consequences of reactions. Prospective case-control or population-based studies may be indicated. The aim of these latter investigations is to ascertain frequency of reactions and mechanisms for their causation.

To further this end, the subcommittee suggests that:

- 1) Methods be specified for deciding if a specific VAERS report is vaccine related;
- 2) Methods be specified to assure long-term follow-up of individuals who experience adverse events following vaccination that may result in permanent sequelae. Follow-up of these patients to determine recovery status should be conducted after one or more years as well as shorter intervals;
- 3) Separate linked databases should be developed to determine the risk factors for adverse events and the nature of the relationship between vaccines and those adverse events.
- 4) The NVAC should be apprised of the protocol developed for VAERS information gathering and subsequent changes and have an opportunity to comment; and
- 5) Data from VAERS be used to evaluate and refine the reporting system.

2. RESEARCH

The subcommittee concluded that it would be desirable to have scientific studies to determine the mechanism of adverse reactions and to identify individual at risk for reaction including study to:

- a. determine the biological mechanism for adverse reactions for each recommended vaccine;
- b. determine the causes and outcome of encephalopathies occurring during the first two years of life including those temporally related to vaccination;
- c. determine the long-term outcome of seizures occurring in the first two years of life including those temporally related to vaccination;
- d. determine what genetic factors are predictive of vaccine response and reactions;

- e. determine whether environmental factors such as nutritional status, pregnancy, a coinciding viral or bacterial infection, a personal or family medical history of allergies, autoimmune or neurological disorders, or the administration of multiple antigens simultaneous are predictive of vaccine responses or reactions;
- f. determine if there are any effects of multiple immunization or total mass of antigen received by an individual;
- g. explore the feasibility and utility of a long-term cohort study of the safety and efficacy of vaccination in a defined population allowing lifetime follow-up;
- h. encourage development of linked databases which include all vaccination and medical outcome information to allow improved ascertainment of adverse events.

3. EDUCATION OF VACCINE PROVIDERS AND CONSUMERS:

Optimal prevention of vaccine reactions requires optimal education of vaccine providers; whom patients trust and rely upon to provide guidance, and of vaccine consumers. Educational efforts should be directed at improving provider knowledge of vaccines, vaccine preventable diseases, and particularly the importance of educating patients about vaccine reactions and monitoring patients for possible reactions. Methods to achieve the objectives include:

- a. Developing a model curriculum and materials (slides, videotapes) for use in physician, nurse and medical assistant training programs.
- b. Providing educational materials on immunization to Federal immunization grant recipients and publicizing their availability to vaccine providers.
- c. Recommending that knowledge of immunization practice be part of testing for professional licensing or certification.
- d. Assessing the knowledge of immunization practice and related issues among both vaccine providers and consumers.
- e. Promoting the knowledge of the Federal vaccine information pamphlets and the vaccine adverse event monitoring system (VAERS) among vaccine providers and consumers.

- f. Evaluating the Federal parent vaccine information pamphlets to determine the extent of their use in the public and private sectors and their impact on the knowledge and behavior of vaccine providers and consumers.
- g. Developing a range of materials, in addition to Federal parent vaccine information pamphlets, to inform parents regarding the risks and benefits of vaccines and the availability of the National Vaccine Injury Compensation Program.
- h. Supporting the work of the Interagency Group to develop a framework for looking at ways in which vaccine safety can be maximized.

4. LICENSING AND TESTING OF VACCINES

Questions remain about whether the FDA vaccine licensing process could be accelerated and whether that agency has adequate resources to fulfill its licensing and testing responsibilities. The NVAC should consider either establishing a separate subcommittee or seeking a consultant to evaluate the FDA's licensing and testing process. In addition, NVAC should inquire how additional resources might help the FDA facilitate the review and evaluation of new vaccines and enhance post-marketing surveillance of vaccine safety and efficacy.