

Editors' Introduction: Vaccine Safety Throughout the Product Life Cycle

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The development and widespread use, in the United States and globally, of safe and effective vaccines has been one of the greatest achievements in science, medicine, and public health—saving lives, preventing disabilities, contributing to improvements in life expectancy, and reducing health care costs. Serious and once common childhood infections are increasingly joining the ranks of “vaccine-preventable diseases.” The number of childhood and adolescent diseases prevented by vaccines has increased from 10 to 16 in just the last 10 years. Moreover, we now have vaccines that can prevent the infections that can lead to cervical and liver cancer.

Ironically, as the threat of disease has been diminished by vaccines, there has been increasing attention on the risks, both real and perceived, from vaccines. When vaccines are used effectively, the incidence of vaccine-preventable diseases declines, and over time, the diseases that vaccines have prevented are less common. The result is that there is a subtle shift in the benefit/risk ratio. With the recent addition of new vaccines to the recommended childhood immunization schedule, an increasing number of parents have raised concerns that their children are receiving more vaccines than they need. Changes in information technology, such as the Internet, provide more access to information, both accurate and inaccurate.

The safety standards for vaccines are arguably higher than those of any other medical product because vaccines are given to healthy persons to prevent disease, are recommended for near-universal use, and are often required by state laws for school entrance. Nevertheless, no medical product, including vaccines, is risk free.

Similar to other infrastructures, the components of the US vaccine-safety system may not be familiar to many people. Because the quality and transparency of this system are critical to maintaining public confidence in our immunization program, this supplement to *Pediatrics* has been assembled to help everyone better understand each of the elements of this system, how they work separately and synergistically to detect and prevent adverse events from vaccination, and what is being done to strengthen the system.

Adverse events after vaccination are medical events that may or may not be caused by the vaccine. Because medical histories provide insights into exposures that may have contributed to the presenting chief complaint, it is not surprising that childhood diseases that are diagnosed during the time period when many vaccines are given may be attributed to a vaccine. For many people, a temporal association between childhood diseases and vaccines is often perceived as a causal association, especially when faced with an otherwise unexplained increase in the reported incidence of many diseases.

One key element of vaccine-safety science is to determine if such temporal relationships are occurring by chance alone or whether they may be caused by the vaccine (and how commonly this may be occurring). With rare exceptions (eg, vaccine-associated paralytic polio), the adverse events are not clinical syndromes unique to a vaccine and may be caused by a long list of diseases of interest. For events that are caused by the vaccine, it is important to quantify that risk (eg, how much of the disease burden may be attributed to the vaccine), determine if there are any subpopulations at increased risk, and identify the biological mechanism responsible for the adverse reaction.

Although patients are increasingly getting medical information from a variety of sources, as with other aspects of medicine and medical advice, health care providers are often looked to as the most credible and frequently consulted sources for questions about vaccines. Many parents want to know how vaccines are made, how they work, why they are needed, who makes them, and who monitors how well they are working, including both their effectiveness and safety over time. Health care providers are needed to accurately inform parents regarding each of these issues and particularly to help parents understand and balance the risks and benefits of vaccination for making an informed vaccination decision. Health care providers who administer vaccine or provide counseling on vaccine issues are increasingly challenged to find the time and materials to inform patients and address their concerns. This supplement was developed to inform and improve this dialogue and to address the call from health care providers for better tools to help more effectively communicate with their patients (and parents) about vaccines and vaccine safety.

This supplement is divided into 2 broad sections: a description of the nation's vaccine-safety system and a series of articles that focus on identifying and addressing specific vaccine-safety concerns that many providers have heard from their patients (and parents).

The vaccine-safety system comprises a number of activities under the direction of a broad range of organizations, including government-sponsored and government-conducted programs, that are often invisible to the public. An understanding by health care providers of the components of the nation's vaccine-safety systems will not only help in discussion with patients but will also clarify how providers play an important role in contributing to the safety system (eg, making reports to the Vaccine Adverse Event Reporting System).

The supplement starts with a powerful account of an everyday mother dealing with the decision to vaccinate; she decided to forgo vaccination and experienced the impact of a vaccine-preventable disease when her child contracted *Haemophilus influenzae* type b meningitis.¹

After this personal story, the first section of this supplement includes a series of articles in which the authors describe key programs and activities conducted by a broad range of groups that make substantial contributions to the nation's vaccine-safety system:

- research conducted by the National Institutes of Health, which often plays a critical role in the development of safe and effective vaccines, including laboratory studies, clinical studies, and related research projects²;
- vaccine research, development, and manufacturing conducted by vaccine companies³;
- the role of the US Food and Drug Administration and the regulatory

process by which vaccines are approved for use, including oversight of the vaccine-manufacturing process⁴;

- postlicensure safety surveillance conducted by the Food and Drug Administration⁵;
- Internet enhancement to the Vaccine Adverse Event Reporting System, the passive surveillance system used primarily to detect possible vaccine-safety "signals" that warrant further investigation⁶;
- the Vaccine Safety Datalink, described by many as the backbone of our nation's vaccine-safety system, which has explored associations between vaccines and a broad range of health outcomes by linking health records of nearly 3% of the US population⁷;
- the Vaccine Safety Datalink rapid cycle analysis, a methodology that has been used increasingly by the Vaccine Safety Datalink and other active surveillance systems to provide rapid and ongoing assessment of potential vaccine-safety signals⁸;
- the Clinical Immunization Safety Assessment Network, which provides a clinically oriented assessment of vaccine adverse events, designed in part to help understand the role of human variation in these events⁹;
- the National Vaccine Injury Compensation Program, which provides financial compensation to people who may have experienced a serious adverse reaction from vaccination¹⁰; and
- recent enhancements made to our vaccine-safety system to monitor the safety of H1N1 vaccines.¹¹

The second section of this supplement is focused on identifying and addressing vaccine-safety concerns among parents:

- a study that tracked vaccine-safety inquiries to detect signals and monitor public concerns about vaccines¹²;
- a report on audience segmentation research to understand vaccine attitudes and concerns among parents and highlight the need to tailor communications toward the specific needs of parents¹³;
- a systematic review of immunization safety print media over a 10-year period, including types of news stories being reported, the messages of these stories, and trends over time¹⁴;
- sources used and those considered credible by parents for vaccine information, which further highlights the important role of health care providers¹⁵;
- a timely study that examined acceptance of pandemic 2009 influenza (H1N1) vaccine in a minority population in Atlanta, Georgia¹⁶;
- a study that examined the impact of timing of vaccine information on the

attitudes of parents with vaccine concerns¹⁷;

- practical advice on how to communicate with vaccine-hesitant parents, including the importance of an open, nonconfrontational dialogue from an early stage, and provide unambiguous, comprehensible information¹⁸; and
- strategies for finding reliable information about vaccines, including substantial discussion of online sources.¹⁹

Throughout the history of vaccines, there have always been concerns raised by the public about vaccine effectiveness, safety, and necessity. Because vaccine safety is an integral part of any immunization program, vaccine safety will continue to be a component of the immunization dialogue. Improved communications and the broad availability of a variety of clear educational materials about vaccines can address some of these concerns.

The opportunities for vaccines—those that are already available and those that

are in the development pipeline—to further prevent morbidity and mortality have never been greater. However, the recent experience with the H1N1 vaccine program highlights the need for communication to improve public understanding of and confidence in our vaccine-safety system. To achieve this, we will need to continue to close gaps in our basic scientific understanding of the underlying mechanisms by which vaccines can, in some people, result in adverse events and continue to refine our ability to rapidly detect, quantify, and investigate possible adverse events after immunization. The H1N1 vaccine program also offers us the opportunity to institutionalize enhancements made to our safety-monitoring program.

Health care providers play a critical role in maintaining and improving public confidence in vaccines so that the full potential of vaccines to prevent serious infectious diseases and their complications can be realized. We are hopeful that this supplement to *Pediatrics* will advance that effort.

REFERENCES

1. Walther S. A parent's decision on immunization: making the right choice. *Pediatrics*. 2011;127(3 suppl):55–58
2. Curlin G, Landry S, Bernstein J, et al. Integrating safety and efficacy evaluation throughout vaccine research and development. *Pediatrics*. 2011;127(3 suppl):S9–S15
3. Kanasa-thasan N, Shaw A, Stoddard JJ, Vernon TM. Ensuring the optimal safety of licensed vaccines: a perspective of the vaccine research, development, and manufacturing companies. *Pediatrics*. 2011;127(3 suppl):S16–S22
4. Marshall V, Baylor NW. Food and Drug Administration regulation and evaluation of vaccines. *Pediatrics*. 2011;127(3 suppl):S23–S30
5. Ball R, Horne D, Izurieta H, Sutherland A, Walderhaug M, Hsu H. Statistical, epidemiological, and risk-assessment approaches to evaluating safety of vaccines throughout the life cycle at the Food and Drug Administration. *Pediatrics*. 2011;127(3 suppl):S31–S38
6. Haber P, Iskander J, Walton K, Campbell SR, Kohl KS. Internet-based reporting to the Vaccine Adverse Event Reporting System: a more timely and complete way for providers to support vaccine safety. *Pediatrics*. 2011;127(3 suppl):S39–S44
7. Baggs J, Gee J, Lewis E, et al. The Vaccine Safety Datalink: a model for monitoring immunization safety. *Pediatrics*. 2011;127(3 suppl):S45–S53
8. Yih WK, Kulldorff M, Fireman BH, et al. Active surveillance for adverse events: the experience of the Vaccine Safety Datalink Project. *Pediatrics*. 2011;127(3 suppl):S54–S64
9. LaRussa PS, Edwards KM, Dekker CL, et al. Understanding the role of human variation in vaccine adverse events: the Clinical Immunization Safety Assessment Network. *Pediatrics*. 2011;127(3 suppl):S65–S73
10. Cook KM, Evans G. The National Vaccine Injury Compensation Program. *Pediatrics*. 2011;127(3 suppl):S74–S77
11. Salmon DA, Akhtar A, Mergler MJ, et al; H1N1 Working Group of the Federal Immunization Safety Task Force. Immunization-safety monitoring systems for the 2009 H1N1 monovalent influenza vaccination program. *Pediatrics*. 2011;127(3 suppl):S78–S86
12. Miller E, Batten B, Hampton L, Campbell SR, Gao J, Iskander J. Tracking vaccine-safety inquiries to detect signals and monitor public concerns. *Pediatrics*. 2011;127(3 suppl):S87–S91
13. Kennedy A, Basket M, Sheedy K. Vaccine attitudes, concerns, and information sources reported by parents of young children: results from the 2009 HealthStyles survey. *Pediatrics*. 2011;127(3 suppl):S92–S99
14. Hussain H, Omer SB, Manganello JA, et al. Immunization safety in US print media, 1995–2005. *Pediatrics*. 2011;127(3 suppl):S100–S106
15. Freed GL, Clark SJ, Butchart AT, Singer DC, Davis MM. Sources and perceived credibility of vaccine-safety information for

- parents. *Pediatrics*. 2011;127(3 suppl):S107–S112
16. Frew PM, Hixson B, del Rio C, Esteves-Jaramillo A, Omer SB. Acceptance of pandemic 2009 influenza A (H1N1) vaccine in a minority population: determinants and potential points of intervention. *Pediatrics*. 2011;127(3 suppl):S113–S119
 17. Vannice KS, Salmon DA, Shui I, et al. Attitudes and beliefs of parents concerned about vaccines: impact of timing of immunization information. *Pediatrics*. 2011;127(3 suppl):S120–S126
 18. Healy CM, Pickering LK. How to communicate with vaccine-hesitant parents. *Pediatrics*. 2011;127(3 suppl):S127–S133
 19. Pineda D, Myers MG. Finding reliable information about vaccines. *Pediatrics*. 2011;127(3 suppl):S134–S137

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