

Adverse Events Following Immunization: Will It Happen Again?

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“Vaccines save lives.” “Vaccines are safe.”¹⁻³ These are critical concepts that pediatricians everywhere seek to convey to parents. However, for many reasons, primarily because of the successes in reduction of vaccine-preventable diseases, parents are increasingly concerned about the safety of and need for vaccines.^{4,5} Parents may come to well-child checkup appointments equipped with lists of questions about vaccine safety and effectiveness. In this context, pediatricians may struggle to explain the value of vaccines when confronted with a difficult situation: an actual untoward event after administration of childhood vaccines. Often referred to as an adverse event following immunization (AEFI),⁶ these events range from mild and uncommon to rare but serious. There are few experiences more challenging for a pediatrician than trying to convince a parent to continue vaccinating their child after they have witnessed a febrile seizure or a hypotonic-hyporesponsive episode (HHE) not long after a vaccination. Although studies have shown that these AEFI do not lead to adverse long-term consequences,⁷ and thus subsequent vaccination is not contraindicated,^{8,9} this information is often not enough to convince these parents that the benefits of future vaccination outweigh potential risks.

In this issue of *Pediatrics*, Zafack et al¹⁰ have provided valuable information to both pediatricians and parents confronted with such a situation. In the article, “Risk of Recurrence of Adverse Events Following Immunization: A Systematic Review,” the authors

quantify recurrence risk for numerous adverse events, including rare life-threatening events such as anaphylaxis, as well as to more common benign events such as injection pain and redness. The article offers accurate, immediately useful information for the practicing pediatrician regarding AEFI and revaccination.

HHEs represent a good example of how information from this article will be useful to pediatricians. Originally described as a “collapse” or “shock-like state” by a British public health officer in the early 1960s,¹¹ HHEs are characterized by the sudden onset of reduced muscle tone, hyporesponsiveness, and change of skin color, either pallor or cyanosis. These poorly-understood events can occur immediately after vaccination or up to 48 hours later, with a median of 3 to 4 hours, and most occurring with the first set of vaccines at ~2 months of age. HHEs have been associated with several different types of vaccines but are most conclusively linked with whole-cell pertussis-containing vaccines, as in the original description. These adverse events are frightening for parents¹² and may lead to extensive evaluation by providers to identify alternative causes, further compounding a parent’s negative vaccination experience. Unsurprisingly, parents whose children have experienced a vaccine-related adverse event may be reticent to revaccinate their child when the next set of immunizations is due. The question they want answered, of course, is, “Will it happen again?”

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Before the publication of the article by Zafack et al,¹⁰ estimates of the risk of recurrence of an HHE after vaccination using data from previous studies were lacking. For example, the American Academy of Pediatrics Report of the Committee on Infectious Diseases (Red Book) estimates the risk of HHE as 1 in 1750 doses but does not comment on the risk of recurrence after 1 has occurred.⁹ Even that estimate is based on administration of whole-cell diphtheria, tetanus, and pertussis vaccine rather than the currently used acellular pertussis vaccine, which is thought to be associated with a lower risk for HHE. The Zafack article¹⁰ includes 530 children and provides an estimate of the risk of recurrence: not 0, but <1%, thus allowing both pediatricians and

parents to be more comfortable with the decision to vaccinate. Equally useful and reassuring, information is now more readily available for other frightening events, such as the recurrence risk for seizures (0%) and anaphylaxis (0%). For more common but less severe AEFIs, such as redness, pain, and fever, more accurate estimates of the risks of AEFI recurrences are available for both pediatricians and parents.

This article also reinforces what vaccinologists and pediatricians have known for many years: vaccines are incredibly safe. Considering that the vaccines in the infant schedule are administered to millions of children each year, the list of known adverse events, even rare ones, is impressively short. Although this article does not address the

recurrence risk for all known AEFIs, particularly rare ones such as immune thrombocytopenic purpura¹³ after measles-containing vaccines and intussusception after rotavirus vaccine,¹⁴ it is impressively comprehensive and will be a useful reference for practicing pediatricians everywhere for years to come. This article will also help to reaffirm the overwhelming value and safety of vaccines in protecting infants and children from complications and death due to infectious diseases.

ABBREVIATIONS

AEFI: adverse event following immunization

HHE: hypotonic-hyporesponsive episode

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