

Adverse Reactions to Vaccines

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Abstract

(The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.)

Immunization healthcare is becoming increasingly complex as the number and types of vaccines have continued to expand. Like all prescription drugs, vaccines may be associated with adverse events. The majority of these reactions are self-limited and not associated with prolonged disability. The media, Internet and public advocacy groups have focused on potentially serious vaccine-associated adverse events with questions raised about causal linkages to increasing frequencies of diseases such as autism and asthma. Despite a lack of evidence of a causal relationship to a variety of vaccine safety concerns, including extensive reviews by the Institute of Medicine, questions regarding vaccine safety continue to threaten the success of immunization programs. Risk communication and individual risk assessment is further challenged by the public health success of vaccine programs creating the perception that certain vaccines are no longer necessary or justified because of the rare reaction risk.

There is a need for improved understanding of true vaccine contraindications and precautions as well as host factors and disease threat in order to develop a patient specific balanced risk communication intervention. When they occur, vaccine related adverse events must be treated, documented and reported through the VAERS system. The increasing complexity of vaccination health care has led the Center of Disease Control and Prevention (CDC) to identify Vaccine Safety Assessment and Evaluation as a potential new specialty.

Index Entries:

Adverse reactions; adjuvants; gelatin; allergy; risk communication; temporal association.

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Background

The success of large-scale population-based vaccination programs is undisputed. Smallpox was eradicated by 1980, and today the World Health Organization (WHO) targets global eradication of polio as an achievable goal. Since the time of Edward Jenner, immunization programs have controlled—at least in parts of the world—13 major diseases (smallpox, diphtheria, tetanus, yellow fever, pertussis, *Haemophilus influenza* type b disease, poliomyelitis, measles, mumps, rubella, influenza, and select pneumococcal and meningococcal disease). Annual reported cases of diphtheria, measles, mumps, rubella, congenital rubella syndrome, and *Haemophilus influenza* type b have been reduced by over 99% from prevaccine-era levels during the twentieth century (1).

Despite the success of large-scale vaccination programs in diminishing or eliminating disease, some people have come to fear vaccines and possible serious (even if rare) adverse reactions more than the diseases that were once viewed with such dread. Many vaccine-preventable diseases once had great potential for long-term morbidity and death. The fear of vaccines arises in part from their success and a decrease in the tolerance for any undesirable outcome from modern medicine.

When smallpox disfigured many and had a case-fatality rate of approx 30%, nearly everyone knew a friend or family member who had been affected. The ravages of polio were easily seen on the streets of nearly any city. In this setting, potential vaccine-related adverse events were considered acceptable. However, as the incidence of disease diminished following large-scale mandatory vaccinations, adverse reactions became an increasing concern and were the single most important factor to bring mandatory smallpox vaccination to an end. When polio complications were no longer a visible problem, the rare cases of paralytic disease complicating live polio vaccination became unacceptable. We have now reached a

state in which it is not uncommon for parents to ask, “Are vaccinations hurting my child?” Despite this public concern, improved immunization coverage has been recognized as a national priority by the Department of Health and Human Services and outlined in the Healthy People 2010 goals (2).

Adverse Reactions

Vaccines, like all other prescription drugs, may be associated with adverse events that may or may not be caused by the immunizing agent. There is substantial public focus on rare vaccine-associated adverse events (2) and a widespread lack of understanding and trust in evidence-based benefit-risk considerations in vaccination programs. A growing political and public minority is calling for voluntary childhood immunizations despite evidence of recurrent disease outbreaks in subgroups of unvaccinated populations. Managing individual patient risk factors, such as a prior history of anaphylaxis, is critical to the future of immunization healthcare and calls for clinical guidelines and research agendas focused on the development of evidence-based recommendations, particularly in regard to special patient categories such as post-transplantation, immunodeficiency, or secondary immunosuppression. Twenty-first century challenges involving bioterrorism-related vaccines such as anthrax and smallpox highlight the importance of vaccine-risk identification, communication, and management for all providers involved in immunization services and adverse events management.

Although vaccine adverse reactions are usually minor, they may be serious or even life-threatening. Mild, expected side effects include local reactions and systemic reactions such as low-grade fever, malaise, or “flu-like” illness lasting a few days but resolving without sequelae. These types of reactions are not contraindications to future vaccination and generally do not raise concern for the patient or

Table 1

Safety Concerns Under Review by the Institute of Medicine Immunization Safety Review Committee

COMPLETED: NO EVIDENCE FOR EPIDEMIOLOGICAL CAUSALITY

MMR and autism

Thimerosal and autism, developmental disorders

Immune system overload from exposure to increased number of antigens in vaccines

RECOMMENDED FOR REVIEW IN 2003

Encephalopathy/encephalitis and MMR

Encephalopathy/encephalitis and pertussis

Reverse transcriptase—potential risk MMR and influenza vaccines?

Seizure disorder and vaccines: MMR, pertussis

Subdural hematoma or intracranial hemorrhage

Hepatitis B and other childhood vaccines

SCHEDULED FOR REVIEW IN 2003 (BOLD = HIGHEST PRIORITY)**Allergies, asthma, and vaccines****Arthritis and hepatitis B vaccine****Arthritis and Lyme disease vaccine**

Autoimmune illness and aluminum in vaccines

Cancer from SV40 contamination of polio

Chronic fatigue-like syndrome and Hepatitis B vaccine

CJD-bovine-derived gelatin in vaccines as a risk factor for transmitting new variant CJD (prion disease)**Diabetes and timing of childhood vaccines****Neurological disorders and influenza vaccines****Sudden unexpected infant deaths and vaccines**

provider. However, if the large local reactions extend to the entire limb or the systemic symptoms last more than 30 d and interfere with quality of life, vaccinees may be averse to receiving further vaccine doses.

Serious adverse reactions such as anaphylaxis are rare, but are considered an absolute contraindication for further routine immunization with the suspected vaccine. Severe adverse reactions such as encephalitis with pertussis-containing vaccines are extremely rare, but can be disabling and even deadly. The public concern about adverse events related to vaccines has generated a major public health commitment to continuously improve vaccine safety monitoring and to establish an ongoing process of credible, non-conflicted expert review of the evidence for or against a causal link between observed reactions and specific vaccines or immunization practices (Table 1).

Contraindications and Precautions

A contraindication is a condition that greatly increases the chances of a serious adverse reaction in the recipient. With a contraindication present, a vaccine should not be administered unless a provider experienced in vaccine safety assessment evaluates all the considerations of the situation and recommends immunization with informed consent, perhaps with modified strategies for vaccination and close monitoring. For example, a history of severe allergic reaction to a vaccine or to one of its components is a contraindication, unless a specialist determines that a desensitization or dose-challenge procedure is indicated despite the risk.

A precaution is a condition that might increase the risk for a serious adverse reaction or cause the immune response to be less than optimal. The risk is less than with a contraindication, but vaccine administration should be

deferred if possible. If the benefit of avoiding the disease outweighs the risk of possible adverse reactions or muted immune response, then the vaccine can be given.

Any acute or serious systemic disease may impact on vaccine efficacy and safety. However, minor illness or infectious disease in the recovery phase should not be a barrier to an opportunity to vaccinate when indicated. Failure to vaccinate children because of minor illness at the time of the health care visit can impact adversely on immunization program success (3–5). Improved education about what is and what is not a contraindication or precaution for a vaccine administration is crucial in order to prevent underutilization of vaccines proven to prevent serious disease consequences (6) (Table 2).

Vaccine Components That May Cause Adverse Reactions

Adverse reactions to vaccines are not well-characterized. One may see immediate or delayed hypersensitivity reactions to vaccines or their components. Immediate hypersensitivity reactions to vaccines range from local wheal-and-flare responses to systemic anaphylaxis with respiratory and/or cardiovascular compromise. The cause of the reaction may be vaccine antigen, residual animal protein, gelatin, antimicrobial agents as preservatives, stabilizers, or other vaccine components. Protein allergens within vaccine products may cause serious anaphylactic reactions, whereas polysaccharide antigens tend to have much lower immediate hypersensitivity reaction rates. An extensive listing of vaccine components and their use is available on the CDC National Immunization Program website at <http://www.cdc.gov/nip>.

Egg Protein

Influenza and yellow fever vaccines are prepared by using embryonated chicken eggs and present a risk for individuals with anaphylaxis to eggs or egg proteins. However, most

allergic patients, even with evidence of egg-specific IgE, tolerate the vaccines without difficulty when the vaccine is administered using progressive dose challenge under controlled conditions. Skin testing with vaccine using the prick full-strength vaccine followed by a 1:100 dilution intradermally may be helpful, although systematic data for the positive predictive value of a positive skin test for most of the specific vaccine preparations is limited.

Measles and mumps vaccines are grown in chick embryo fibroblast tissue culture with no measurable egg protein and do not pose a problem for egg allergic patients (6,7). Rubella, varicella, or rabies vaccines are grown in human diploid-cell cultures and do not contain egg proteins.

Gelatin

Severe hypersensitivity reactions to measles, mumps, rubella vaccines have been linked to gelatin protein. Individual vaccine products (manufacturer-specific) vary in component contents, and checking the package insert for the presence of gelatin will determine if a reaction could be linked to gelatin. A history of hypersensitivity to gelatin-containing foods or to another vaccine containing gelatin along with a positive skin test to gelatin supports the diagnosis (8–11). However, a history of food-associated reactions is not essential, and skin testing with the actual vaccine preparation is advisable. Hypersensitivity is not an absolute contraindication, and may be managed with either an alternative vaccine product (gelatin-free) or with a desensitization procedure under controlled conditions if a gelatin-free vaccine preparation is not available.

Antibiotics/Preservatives

Trace amounts of antibiotics, preservatives, or other ingredients may be associated with hypersensitivity reactions. No licensed vaccine contains penicillin or penicillin derivatives, but some contain other antibiotics such as neomycin, streptomycin, polymyxin B, and chlortet-

Table 2
Vaccines and Their True and Untrue Contraindications and Precautions*

Vaccine	Contraindications and Precautions	Incorrect Contraindications (Vaccine can be administered)
General for all vaccines: DTaP, DT, IPV, Td, MMR, Hib, HAV, HBV, VAR, PCV, PPV, including Anthrax	Contraindications - Serious allergic reaction after a previous vaccine dose - Serious allergic reaction to a vaccine component Precautions - Moderate or severe acute illness with or without fever - Partial immunodeficiency, primary or secondary to disease, treatments - Pregnancy Prior DTaP dose: $T \geq 40.5^{\circ}\text{C}$. within 48 h; continuous crying ≥ 3 h within 48 h; pale or limp episode or collapse within 48 h; unstable progressive neurologic problems (defer until stable)	- Mild acute illness - Prior vaccine reaction: mild-moderate local, systemic - Convalescent illness phase - Premature birth if indicated - Recent infection exposure - History of penicillin allergy, relative with allergies
Live virus OPV, MMR, VAR	Contraindications - Serious allergic reaction after a previous vaccine dose - Serious allergic reaction to a vaccine component - Severe immunodeficiency, primary or secondary; immunosuppressive therapy Precautions - Immune globulin containing products ≤ 11 mo (only for vaccines for which population has IgG to vaccine antigen, therefore not relevant to yellow fever, anthrax) - Vaccinee close contact at risk from vaccine strain of virus - Moderate or severe acute illness with or without fever - Partial immunodeficiency, primary or secondary to disease, treatments - Pregnancy	- MMR: asymptomatic HIV infection - Varicella: avoidance of salicylates for 6 wk following vaccine recommended by manufacturer but not a contraindication if needed - Varicella vaccine recommended in patients with antibody deficiency if cellular immunity is intact (6)
Smallpox/Vaccinia	Contraindications - Same as for other live viruses - Atopic dermatitis Precautions - Skin rash or topical anti-inflammatory therapy - Contact with atopic dermatitis or immunodeficiency	
Live bacteria BCG, Typhoid Ty21 (oral)	Contraindications - Same as for general Precautions - Vaccine close contact at risk from vaccine strain of bacteria	

*Adapted from MMWR 2002;51(RR02):1–36

racycline (Dryvax® smallpox vaccine contains all of these in trace amounts). A history of anaphylactic reaction to neomycin is a contraindication to receiving vaccines containing neomycin. However, neomycin allergy is usually a contact dermatitis, which is not a contraindication for administration of these vaccines (12,13).

Thimerosal is an organic mercurial compound used as a preservative, and is the focus of recent controversy because of fear that mercury release in low-birthweight infants (<2 kg) might, with multiple vaccinations, exceed a defined safety limit in terms of exposure per kg body wt (14,15). Although there is no evidence of adverse effects, increasing autism rates in the population have raised the concern of a possible linkage. The U.S. Public Health Service, the American Academy of Pediatrics, and the American Academy of Family Physicians established the goal of removing thimerosal from infant vaccines and this is actively being accomplished. As with neomycin, hypersensitivity reactions have been largely limited to contact dermatitis, and the amount in vaccines is significantly less than that used in a standard patch test (usually 1:20,000 dilution as opposed to 0.1% or 1:1000 in the traditional dermatology patch test). The majority of patch test-positive individuals are able to tolerate thimerosal-containing vaccines.

Adjuvants

An adjuvant is any substance that enhances immunogenicity when mixed with an antigen. Aluminum salts such as aluminum hydroxide and aluminum sulfate are used to enhance the immune response to vaccines containing inactivated (non-living) microorganisms or their products (e.g., toxoids or hepatitis B). These agents act by depot formation, increasing the time of contact between antigen and immune-response cells. Associated with increasing side effects locally—especially if given subcutaneously rather than intramuscularly—vaccines with such adjuvants must usually be injected

deeply into muscle mass in order to avoid local irritation, inflammation, necrosis, or granuloma formation (16–18).

Protein conjugates—carrier proteins such as mutant diphtheria toxoid conjugated to a less immunogenic polysaccharide antigen—are considered adjuvants because they enhance immunologic response to the polysaccharide antigen, particularly in infants and children. The newly conjugated seven valent pneumococcal vaccine (PRevnar™) is an example of such a vaccine construct, which has improved seroconversion in children less than 2 yr of age who are unable to respond effectively to the pneumococcal polysaccharide 23-valent vaccine (6).

Host Factors

Although vaccine additives may cause reactions, host-specific factors can influence vaccine responses and, potentially, adverse event risks.

Latex allergy, if severe, may require special handling, although the majority of vaccine vials now use synthetic rubber, which does not contain natural latex antigens. The old smallpox vaccine is stored in vials with rubber stoppers and may present a risk for severely latex-allergic patients. There is only one case report of an allergic reaction following hepatitis B vaccine in the setting of anaphylactic hypersensitivity to latex (19).

Pregnancy has traditionally been a reason for providers to avoid immunization. However, the data that support this practice is largely theoretical, and inadvertent vaccination is not a reason to terminate a pregnancy. Safety data regarding birth defects with current recommended vaccines is reassuring, even for live virus vaccines such as measles, mumps, and rubella (20). Thus, pregnancy is a relative rather than absolute contraindication to immunization. The decision to immunize should be based on the benefit vs theoretical risk (including patient concerns). In addition, the disease risk to the mother and/or fetus should

be considered, and in many instances the enhancement of maternal immunity can provide passive immunity to the infant. Influenza vaccine is now recommended in the second and third trimester of pregnancy because the benefit far outweighs any evidence of risk (21).

Current guidelines for contraindicated vaccines during pregnancy include varicella and measles, mumps, rubella despite the fact that no cases of congenital rubella or varicella syndrome or abnormalities attributable to fetal infection have been observed among infants born to susceptible women who received rubella or varicella vaccines during pregnancy (20). Revised immunization guidelines have changed to recommend only 1-mo (rather than 3-mo) delay in pregnancy following exposure to these vaccines, and no intervention is required if inadvertent immunization occurs, even in the first trimester.

Smallpox vaccine during pregnancy poses a serious risk to the fetus. Fetal vaccinia during the smallpox era was almost universally fatal and was linked to maternal vaccinee transmission. However, there is no evidence of teratogenicity associated with vaccinia, and inadvertent vaccination is not a reason for pregnancy termination. In the face of a smallpox outbreak with direct exposure, vaccination may be life-saving, and most experts from the smallpox era recommend vaccination despite risk.

Breast feeding is not a contraindication to immunization with either live or inactivated vaccines, and both mother and infant should receive routine recommended vaccines. Some mothers will refuse vaccination—particularly with live vaccines—because of continued safety concerns, despite an overall lack of data. Successful immunization of the mother enhances her immunity and her ability to pass protective antibody to her infant. This additional information may reassure some mothers about the value of vaccinations.

Immunodeficiency states can impact on vaccination strategies and risk assessment. Persons who are severely immunocompromised

(e.g., congenital severe combined immunodeficiency, leukemia, lymphoma, acquired immunodeficiency secondary to chronic or severe disease or disease therapy, or AIDS) are at increased risk for one or more of these adverse outcomes:

- Failure to respond to the vaccine with no protection from the targeted disease (mostly with severe cellular immunodeficiencies but also with profound hypogammaglobulinemia if the protective mechanism depends on neutralizing antibodies);
- Partial immune response to the vaccine with short-term protection but rapid loss of immune response, necessitating more frequent vaccine doses;
- More severe or more frequent adverse events with the vaccine, particularly in the setting of live virus vaccines

Persons with conditions that cause limited immune deficits (e.g., asplenia, renal failure, IgA deficiency, post-transplantation or immunosuppressive therapy patients, asymptomatic HIV infection) may require use of special vaccines, special vaccine strategies (e.g., repeating a primary dose series) or higher doses of vaccines (e.g., dialysis patients and hepatitis B vaccine) without an absolute contraindication to any particular vaccine. For patients with asymptomatic human immunodeficiency virus (HIV), the risk of an adverse event from vaccination with mumps measles rubella (MMR) is outweighed by the benefit of avoiding severe complications from measles infection (22).

Many immunodeficiency states are partial and may be associated with some benefit from immunization. Although the WHO has indicated that congenital immunodeficiency is a contraindication to immunization, some immunodeficiencies (e.g., chronic granulomatous disease, IgA deficiency) can respond to vaccines, and may benefit by the enhanced disease protection.

The responsibility for determining how severely a patient is immunocompromised

ultimately lies with the physician and remains a challenge because the level of immune compromise is dynamic and affected by a variety of co-factors such as malnutrition. Drug-specific immunosuppression is also highly variable, from profound suppression with generalized malignancy and therapy with alkylating agents, anti-metabolites, radiation, or large amounts of corticosteroid to less severe suppression during recovery phases of disease activity or disease therapy. Anergy panel skin testing may be helpful in identifying patients at greatest risk for live virus vaccine failures and complications, but has not yet been fully standardized for clinical use. Individual patient evaluation is required in order to develop a benefit-risk analysis with patient informed consent for or against specific vaccination strategies.

Corticosteroid therapy, depending on dose and duration, is usually not a contraindication to live-virus vaccines if the following conditions apply (adapted from Recommendations for Immunization, 22):

- Limited in dose and/or duration;
- Short-term (e.g., <2 wk) with low to moderate dosing;
- Long-term, alternative-day single-dose treatment with short-acting preparations (e.g., prednisone) and low to moderate doses;
- Maintenance physiologic doses (replacement therapy);
- Limited administration such as by intra-articular, bursal, or tendon injection, topical administration to airway (aerosol), eye or skin topical applications;
- Otherwise relatively immunocompetent.

Corticosteroids used in greater than physiologic doses can reduce the immune response to some vaccines in some individuals. Ideally, providers should wait ≥ 1 mo after discontinuation of therapy before administering a live-virus vaccine to patients who have received high, systemically absorbed doses of corticosteroids for ≥ 2 wk. Passive immunization rather than active may be indicated during post-corticosteroid therapy recovery.

Persons with bleeding disorders (e.g., hemophilia) or who are receiving anticoagulant therapy may be at increased risk for bleeding and hematoma formation with intramuscular (im) injection vaccines such as hepatitis B. Hepatitis B vaccine can be administered by the intradermal route with prolonged pressure, avoiding this complication risk, but serologic response should be monitored for adequacy and duration of the immune response. Repeated dosing may be required to maintain serologic evidence of immunity.

Risk Perception, Communication, and Patient Education

Unlike most drugs, vaccines are given to defend against potential, rather than existing disease. Individuals who have adverse reactions to vaccines are healthy individuals whose disease was introduced by the therapeutic intervention. This has led some to question the overall safety of vaccines. When viewed on a population basis the risk of an individual rare adverse reaction such as Guillan Barré is outweighed by the benefit provided to the community.

The frequency of serious vaccine adverse events is low, often little more than the background rate, and causality is difficult to prove or disprove. Often there is only the temporal association of vaccination and the onset of disease but no proof of causality. The two factors—rare incidence and inability to prove or disprove causality—can make the risk-benefit analysis complex. Autism and autism-like disorders in relation to MMR and hepatitis B vaccine continue to cause concern. The Institute of Medicine (IOM) reviewed the evidence and did not find an association.

Concentration on potential adverse events may diminish vaccination rates, either through refusal of vaccinations or because of discon-

tinuation of a vaccine that cannot be proven to be completely safe. Some complementary or alternative medicine literature has stoked fears about childhood vaccinations that potentially increase the risk of asthma and allergic disease (23,24), despite the value of influenza vaccine for asthmatics and others with chronic lung disease. This question has been posed to the IOM for review and public hearing discussions.

Public perception of risk can be a powerful force. Fear of disease will drive the public to clamor for a vaccine that may have a less than optimal safety record, and fear of adverse reactions to the vaccine may prompt the public to avoid a good vaccine when the incidence of disease is low. This is well-illustrated by the bioterrorist threat and the public desire for access to vaccines against possible bioterrorist agents when the threat of terrorism is high. As with any other prescription drug, vaccine administration necessitates patient and/or guardian education about risks and benefits in the context of the patient's medical history and complicating medical conditions, a skill that requires training and competency development.

Documenting the patient education process for routine vaccines makes sense and is a part of informed consent, but is not required under current national guidelines (22). Written consent is required for any vaccine that is offered under protocol (investigational new drug or IND status with the Food and Drug Administration [FDA]). Some vaccines have a long history of use and safety as an IND drug, such as Venezuelan equine encephalitis or Rift Valley Fever vaccines, but have not achieved full licensure because there is no economic incentive for a manufacturer to complete all the costly requirements of the FDA. This is particularly true for diseases that are mainly a problem in parts of the world outside the United States. In this instance, travelers and military personnel are the main recipients of these vaccines. Parents, guardians, legal representatives,

and adolescent and adult patients should be informed about the benefits and risks of vaccines in understandable language. An opportunity for questions should be provided before each vaccination. Discussion of the benefits and risks of vaccination is sound medical practice, and is required by law.

The National Childhood Vaccine Injury Compensation Act (NCVICA, 1986 Public Law 99-660, Sec. 2114a) requires that vaccine information materials be developed for each vaccine covered by the Act. These materials, known as Vaccine Information Statements or VIS, must be given out by all public and private vaccination providers each time a vaccine is administered. Copies of Vaccine Information Statements are available from state health authorities responsible for immunization, or they can be obtained from Centers for Disease Control's (CDC's) National Immunization Program website at <http://www.cdc.gov/nip>. Translations of VIS in languages other than English are available from certain state immunization programs and from the Immunization Action Coalition website at <http://www.immunize.org>. The standard of providing drug-related information applies to all vaccines, but VIS resources have not been developed for all travel-relevant vaccines. Other sources of information are available through the resource listing provided at the end of this article. Increasingly, through the media and the barrage of Internet sites addressing vaccine fears (including personal testimonials that are highly emotional), decisions regarding risk are based on inaccurate information and fear. Only through direct dialogue with parents or patients and by using available evidence-based resources can health-care professionals hope to aid the patient and/or parent in making an informed decision that optimizes clinical benefits. However, the credibility of health care providers is enhanced when the provider acknowledges those areas in which data may be lacking and safety concerns may have biological plausibility.

Documenting an Adverse Reaction

Therapy for vaccine-related adverse reactions is primarily focused on symptomatic care and characterization and reporting of the adverse event. An important part of management is reporting the adverse event to the Vaccine Adverse Events Reporting System (VAERS), the passive surveillance system for adverse events associated with vaccines. The VAERS system should be used for all vaccines, pediatric and adult, with no requirement for proof of causality, but only temporal association. Particularly for more serious events such as hospitalization or prolonged illness, reporting is critical even if the individual provider cannot determine causality. The VAERS system was effective in signaling the association of intussusception with rotavirus vaccination, but still is in need of quality improvement. Electronic VAERS reporting is now available online at www.vaers.org; continuing education on the history and importance of VAERS is encouraged for all providers via this same website. Direct access to assistance with VAERS filing is also available at toll-free 1-800-822-7967 or by toll-free fax at 1-877-721-0366.

The National Vaccine Compensation Law of 1990 and the National Childhood Vaccine Injury Compensation Act (NCVICA) of 1986 provide a mechanism for compensation if a severe adverse event occurs after mandatory childhood vaccination. Adults may also apply to the fund if the adverse event is related to a required childhood vaccine (as defined by the Advisory Committee on Immunization Practices or ACIP), but not if related to a non-mandated vaccine, even if occupationally required.

Vaccine safety assessment and evaluations of vaccine temporally associated adverse events are increasing in complexity for the consulting physician, calling for an expert opinion on the probability of causation. The National Immunization Program Office (The Centers for Disease Control, or CDC) has identified this area as potentially a “new specialty” in medical

practice and is sponsoring centers of excellence known as CISA (clinical immunization safety assessment) centers. The Department of Defense, in collaboration with the CDC, is establishing similar centers of excellence known as the Vaccine Healthcare Centers (VHC) Network.

Revaccination with a Past History of a Vaccine Temporally Associated Adverse Event

Benefit-risk communication in relation to a recommended vaccine is further complicated by any history of an adverse event following past immunization. Current CDC guidelines only make severe allergic reaction (e.g., anaphylaxis) and encephalopathy (in the case of pertussis) absolute contraindications to the majority of vaccines listed.

Drug desensitization for anaphylaxis may overcome this contraindication when clinically indicated by vaccine requirement with no alternative therapies available. Other adverse events are considered an item of relative precaution in which individual benefit-risk considerations must be applied to determine need for additional vaccine. Guillain-Barré syndrome less than 6 wk following diphtheria (DT) and tetanus diphtheria (Td) is listed as a precaution, not an absolute contraindication, but many providers and patients find the risk of repeat vaccination generally unacceptable in this setting, particularly since alternative therapies are available (documentation of immune status with antibody measurement or passive immunity with acute disease risk). For many adverse events, there are no data on the outcomes of continued immunization, causing uncertainty about safety for both provider and patient. Thus, the outcomes study in which 421 Australian children with a past history of an adverse vaccine reaction were revaccinated provides valuable information that can be used in the risk communication encounter and in deciding about vaccine exemptions vs continued immunization. Ninety percent of children

who experienced reactions (421/469) after immunization received additional doses of vaccine under informed consent with only one significant neurological event that was transient and resolved spontaneously (25).

There are currently no large-scale revaccination outcomes data for adults with vaccine-associated adverse events, making counseling about risk and safety more difficult, particularly for more serious reactions. Worries about disease exacerbation or initiation in genetically predisposed individuals have driven political support for voluntary rather than required immunization programs. Negative studies, such as those recently reported for multiple sclerosis and influenza, pneumococcal, and hepatitis B vaccines, are critical for improving evidence-based risk communication (26).

Summary

Although the possibility of an adverse reaction exists with any vaccine, the challenge for health care providers is how to communicate credible benefit-risk considerations to facilitate immunization compliance in which the benefits are well-established and the risks are acceptable. The allergist-immunologist can play an important role in managing those patients whose adverse event risks may be significant or in whom the degree of risk is not well-defined. It would be a tragedy if preventable diseases reappeared with their associated morbidity and mortality because the misperception of risk clouded the reality of benefits.

Providers must familiarize themselves with the increasing requirements for patient education and documentation, and must ensure full compliance with the VAERS program. Informed patients will be able to understand and accept the risks associated with vaccinations if they perceive that the benefit outweighs the known risk.

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Information Resources

National Immunization Information Hotline

The National Immunization Information Hotline is supported by CDC's National Immunization Program and provides vaccination information for health-care providers and the public, 8:00 am–11:00 pm, Monday–Friday:

Telephone (English): 800–232–2522

Telephone (Spanish): 800–232–0233

Telephone (TTY): 800–243–7889

Internet: <http://www.ashastd.org> (accessed February 25, 2002)

CDC's National Immunization Program

CDC's National Immunization Program website provides direct access to immunization recommendations of the Advisory Committee on Immunization Practices (ACIP), vaccination schedules, vaccine safety information, publications, provider education and training, and links to other immunization-related websites. It is located at <http://www.cdc.gov/nip> (accessed November 7, 2001).

Morbidity and Mortality Weekly Report

ACIP recommendations regarding vaccine use, statements of vaccine policy as they are developed, and reports of specific disease activity are published by CDC in the Morbidity and Mortality Weekly Report (MMWR) series. Electronic subscriptions are free and available at <http://www.cdc.gov/subscribe.html> (accessed November 7, 2001).

Printed subscriptions are available at

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American Academy of Pediatrics (AAP)

Every 3 years, AAP issues the Red Book: Report of the Committee on Infectious Diseases, which contains a composite summary of AAP recommendations concerning infectious diseases and immunizations for infants, children, and adolescents.

Telephone: 888–227–1770

Internet: <http://www.aap.org> (accessed November 7, 2001)

American Academy of Family Physicians (AAFP)

Information from the professional organization of family physicians is available at <http://www.aafp.org> (accessed November 7, 2001).

Immunization Action Coalition

This source provides extensive free provider and patient information, including translations of Vaccine Information Statements into multiple languages. The Internet address is <http://www.immunize.org> (accessed November 7, 2001).

National Network for Immunization Information

This information source is provided by the Infectious Diseases Society of America, Pediatric Infectious Diseases Society, AAP, American Nurses Association, and other professional organizations. It provides objective, science-based information regarding vaccines for the public and providers. The Internet site is <http://www.immunization-nfo.org> (accessed November 7, 2001).

Vaccine Education Center

Located at the Children's Hospital of Philadelphia, this source provides patient and provider information. The Internet address is <http://www.vaccine.chop.edu> (accessed November 7, 2001).

Institute for Vaccine Safety

Located at Johns Hopkins University School of Public Health, this source provides information regarding vaccine safety concerns and objectives and timely information to health-care providers and parents. It is available at <http://www.vaccinesafety.edu> (accessed November 7, 2001).

National Partnership for Immunization

This national organization encourages greater acceptance and use of vaccinations for all ages through partnerships with public and private organizations. Their Internet address is <http://www.partnersforimmunization.org> (accessed November 7, 2001).

State and Local Health Departments

State and local health departments provide technical advice through hotlines, electronic

mail, and Internet sites, including printed information regarding vaccines and immunization schedules, posters, and other educational materials.

US Army Center for Health Promotion and Preventive Medicine. <http://chppm-www.apgea.army.mil/>

CHPPM provides worldwide technical support for implementing preventive medicine, public health, and health promotion/wellness services into all aspects of America's Army and the Army Community anticipating and rapidly responding to operational needs and adaptable to a changing world environment.