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Diphtheria, Tetanus, and Pertussis: Preventive Measures

This revision of the Immunization Practices Advisory Committee (ACIP) statement on diphtheria, tetanus, and pertussis updates the statement issued in 1981 (1) *and incorporates the 1984 supplementary statement on the risks of pertussis disease and pertussis vaccine for infants and children with personal histories of convulsions* (2). *It includes a review of the epidemiology of the three diseases, a description of the available immunobiologic preparations, and the appropriate immunization schedules. Also included are revisions in the schedule for combined diphtheria and tetanus toxoids (DT), when pertussis vaccine is contraindicated, and revisions in the recommendations on precautions and contraindications to vaccine use, on immunization for infants and children who have underlying neurologic disorders, and on tetanus prophylaxis in wound management.*

INTRODUCTION

Simultaneous immunization against diphtheria, tetanus, and pertussis during infancy and childhood has been a routine practice in the United States since the late 1940s. This practice has played a major role in markedly reducing the incidence rates of cases and deaths from each of these diseases.

DIPHTHERIA

At one time, diphtheria was common in the United States. More than 200,000 cases, primarily among children, were reported in 1921. Approximately 5%-10% of cases were fatal; the highest case-fatality ratios were in the very young and the elderly. Reported cases of diphtheria of all types declined from 306 in 1975 to 59 in 1979; most were cutaneous diphtheria reported from a single state. After 1979, cutaneous diphtheria was no longer reportable. From 1980 through 1983, only 15 cases of respiratory diphtheria were reported; 11 occurred among persons 20 years of age or older.

The current rarity of diphtheria in the United States is due primarily to the high level of appropriate immunization among children (96% of children entering school have received three or more doses of diphtheria and tetanus toxoids and pertussis vaccine [DTP]) and to an apparent reduction of the circulation of toxigenic strains of *Corynebacterium diphtheriae*. Most cases occur among unimmunized or inadequately immunized persons. The age distribution of recent cases and the results of serosurveys indicate that many adults in the United States are not protected against diphtheria. Thus, it appears that more emphasis should be placed on adult immunization programs.

Both toxigenic and nontoxigenic strains of *C. diphtheriae* can cause disease, but only strains that produce toxin cause myocarditis and neuritis. Furthermore, toxigenic strains are more often associated with severe or fatal illness in noncutaneous (respiratory or other mucosal surface) infections and are more commonly recovered from respiratory than from cutaneous infections.

C. diphtheriae can contaminate the skin of certain individuals, usually at the site of a wound. Although a sharply demarcated lesion with a pseudomembranous base often results, the appearance may not be distinctive, and the infection can be confirmed only by culture. Usually, other bacterial species can also be isolated. Cutaneous diphtheria has most commonly affected indigent adults and certain groups of Native Americans.

Complete immunization significantly reduces the risk of developing diphtheria, and immunized persons who develop disease have milder illnesses. Protection is thought to last at least 10 years. Immunization does not, however, eliminate carriage of *C.*

diphtheriae in the pharynx or nose or on the skin.

TETANUS

The occurrence of tetanus in the United States has decreased markedly because of the routine use of tetanus toxoid. Nevertheless, the number of reported cases has remained relatively constant in the last decade at an annual average of 90 cases. In 1983, 91 tetanus cases were reported from 29 states. In recent years, approximately two-thirds of patients have been 50 years of age or older. The age distribution of recent cases and the results of serosurveys indicate that many U.S. adults are not protected against tetanus. The disease has occurred almost exclusively among persons who are unimmunized or inadequately immunized or whose immunization histories are unknown or uncertain.

In 6% of tetanus cases reported during 1982 and 1983, no wound or other condition could be implicated. Nonacute skin lesions, such as ulcers, or medical conditions, such as abscesses, were reported in 17% of cases.

Neonatal tetanus occurs among infants born under unhygienic conditions to inadequately immunized mothers. Immune pregnant women confer protection to their infants through transplacental maternal antibody. From 1974 through 1983, 20 cases of neonatal tetanus were reported in the United States.

Spores of *Clostridium tetani* are ubiquitous. Serologic tests indicate that naturally acquired immunity to tetanus toxin does not occur in the United States. Thus, universal primary immunization, with subsequent maintenance of adequate antitoxin levels by means of appropriately timed boosters, is necessary to protect persons in all age groups. Tetanus toxoid is a highly effective antigen, and a completed primary series generally induces protective levels of serum antitoxin that persist for 10 or more years.

PERTUSSIS

General use of standardized pertussis vaccine has resulted in a substantial reduction in cases and deaths from pertussis disease. However, the annual number of reported cases has changed relatively little during the last 10 years, when annual averages of 1,835 cases and 10 fatalities have occurred. In 1983, 2,463 cases were reported; in 1981, the latest year for which final national mortality statistics are available from the National Center for Health Statistics, six deaths were recorded. More precise data do not exist, since many cases go unrecognized or unreported, and diagnostic tests for *Bordetella pertussis*—culture and direct-immunofluorescence assay (DFA)—may be unavailable, difficult to perform, or incorrectly interpreted.

For 1982 and 1983, 53% of reported illnesses from *B. pertussis* occurred among children under 1 year of age, and 78%, among children under 5 years of age; 13 of 15 deaths reported to CDC occurred among children under 1 year old. Before widespread use of DTP, about 20% of cases and 50% of pertussis-related deaths occurred among children under 1 year old.

Pertussis is highly communicable (attack rates of over 90% have been reported in unimmunized household contacts) and can cause severe disease, particularly in very young children. Of patients under 1 year of age reported to CDC during 1982 and 1983, 75% were hospitalized; approximately 22% had pneumonia; 2% had one or more seizures; and 0.7% died. Because of the substantial risks of complications of the disease, completion of a primary series of DTP early in life is essential.

In older children and adults—including, in some instances, those previously immunized—infection may result in nonspecific symptoms of bronchitis or an upper respiratory tract infection, and pertussis may not be diagnosed because classic signs, especially the inspiratory whoop, may be absent. Older preschool-aged children and school-aged siblings who are not fully immunized and develop pertussis can be important sources of infection for young infants, the group at highest risk of disease and disease severity. The importance of the infected adult in overall transmission remains to be defined.

Controversy regarding use of pertussis vaccine led to a formal reevaluation of the benefits and risks of this vaccine. The analysis indicated that the benefits of the vaccine continue to outweigh its risks *(3)*.

Because the incidence rate and severity of pertussis decrease with age, and because the vaccine may cause side effects and adverse reactions, pertussis immunization is not recommended for children after the seventh birthday, except under unusual circumstances (see **VACCINE USAGE**).

PREPARATIONS USED FOR IMMUNIZATION

Diphtheria and tetanus toxoids are prepared by formaldehyde treatment of the respective toxins and are standardized for potency according to the regulations of the U.S. Food and Drug Administration (FDA). The Lf content of each toxoid (quantity of toxoid as assessed by flocculation) may vary among different products. Because adverse reactions to diphtheria toxoid are apparently directly related to the quantity of antigen and to the age of the recipient, the concentration of diphtheria toxoid in preparations intended for use in adults is reduced.

Pertussis vaccine is a suspension of inactivated *B. pertussis* cells. Potency is assayed by comparison with the U.S. Standard Pertussis Vaccine in the intracerebral mouse protection test. The protective efficacy of pertussis vaccines in humans has been shown to correlate with the potency of vaccines.

Diphtheria and tetanus toxoids and pertussis vaccine, as single antigens or various combinations, are available as aluminum salt adsorbed preparations. Only tetanus toxoid is available in nonadsorbed (fluid) form. Although the rate of seroconversion is essentially equivalent with either type of tetanus toxoid, the adsorbed toxoid induces a more persistent antitoxin titer.

The two toxoids and the pertussis vaccine are currently available in the United States as the following preparations:

1. Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed (DTP) and Diphtheria and Tetanus Toxoids Adsorbed (For Pediatric Use) (DT)* are combinations for use in infants and children under 7 years old.
2. Tetanus and Diphtheria Toxoids Adsorbed (For Adult Use) (Td) is a combined preparation for use in persons 7 years old and older.
3. Pertussis Vaccine Adsorbed (P)†, Tetanus Toxoid (Fluid), Tetanus Toxoid Adsorbed (T), and Diphtheria Toxoid Adsorbed (D), are single-antigen products for use in instances when combined antigen preparations are not indicated.

Work is in progress to develop an effective acellular pertussis vaccine with a reduced reaction rate. Current

research is directed toward development of a vaccine consisting principally of one or more of the bacterial components thought to provide protection. Prominent candidate antigens include filamentous hemagglutinin and lymphocytosis promoting factor (pertussis toxin). However, several years will be necessary to complete development and to document the potency, safety, and efficacy of a new vaccine.

VACCINE USAGE

The standard single-dose volume of DTP, DT, Td, single-antigen adsorbed preparations of pertussis vaccine, tetanus toxoid, and diphtheria toxoid, and the nonadsorbed tetanus toxoid is 0.5 ml. Adsorbed preparations should be administered intramuscularly (IM). Vaccine administration by jet injection may be associated with more frequent local reactions. (See also: ACIP: General recommendations on immunization. *MMWR* 1983;32:1-8,13-7.)

Primary Immunization

Children 6 weeks through 6 years old (up to the seventh birthday) (Table 1). One dose of DTP should be given IM on four occasions—the first three doses at 4- to 8-week intervals, beginning when the infant is approximately 6 weeks-2 months old. The fourth dose is given approximately 6-12 months after the third to maintain adequate immunity for the ensuing preschool years. This dose is an integral part of the primary immunizing course. If a contraindication to pertussis vaccination exists (see **PRECAUTIONS AND CONTRAINDICATIONS),** DT should be substituted for DTP as outlined under **Special Considerations** below.

Persons 7 years old and older (Table 2). Pertussis-containing preparations are not recommended routinely in these age groups. A series of three doses of Td should be given IM; the second dose is given 4-8 weeks after the first; and the third dose, 6-12 months after the second. Td rather than DT is the agent of choice for immunization of all patients 7 years old and older, because side effects from higher doses of diphtheria toxoid are more common in older children and adults.

Interruption of primary immunization schedule. Interrupting the recommended schedule or delaying subsequent doses probably does not lead to a reduction in the level of immunity reached on completion of the primary series. Therefore, there is no need to restart a series regardless of the time elapsed between doses.

Booster Immunization

Children 4-6 years old (up to the seventh birthday). Those who received all four primary immunizing doses before the fourth birthday should receive a single dose of DTP just before entering kindergarten or elementary school. This booster dose is not necessary if the fourth dose in the primary series was given on or after the fourth birthday.

Persons 7 years old and older. Tetanus toxoid should be given with diphtheria toxoid as Td every 10 years. If a dose is given sooner as part of wound management, the next booster is not needed for 10 years thereafter (see **TETANUS PROPHYLAXIS IN WOUND MANAGEMENT).** More frequent boosters are not indicated and have been reported to result in an increased occurrence and severity of adverse reactions. One means of ensuring that persons receive boosters every 10 years is to vaccinate persons routinely at mid-decade ages, i.e., 15 years, 25 years, 35 years, etc.

Special Considerations

Children with a contraindication to pertussis vaccination (see PRECAUTIONS AND CONTRAINDICATIONS). For children under 7 years old with a contraindication to pertussis vaccine, DT should be used rather than DTP. To ensure that there will be no interference with the antigens from maternal antibodies, unimmunized children under 1 year of age receiving their first DT dose should receive a total of four doses of DT as the primary series, the first three doses at 4- to 8-week intervals and the fourth dose 6-12 months later (similar to the recommended DTP schedule). If further doses of pertussis vaccine become contraindicated after beginning a DTP series in the first year of life, DT should be substituted for each of the remaining scheduled DTP doses.

Unimmunized children 1 year of age or older for whom DTP is contraindicated should receive two doses of DT 4-8 weeks apart, followed by a third dose 6-12 months later to complete the primary series. Children 1 year of age or older who have received one or two doses of DT or DTP and for whom further pertussis vaccine is contraindicated should receive a total of three doses of a preparation containing diphtheria and tetanus toxoids, with the third dose administered

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TABLE 1. Routine diphtheria, tetanus, and pertussis immunization schedule summary for children under 7 years old—United States, 1985*

Dose	Age/interval†	Product
Primary 1	6 weeks old or older	DTP†¶
Primary 2	4-8 weeks after first dose§	DTP¶
Primary 3	4-8 weeks after second dose§	DTP¶
Primary 4	6-12 months after third dose§	DTP¶
Booster	4-6 years old, before entering kindergarten or elementary school (not necessary if fourth primary immunizing dose administered on or after fourth birthday)	DTP¶
Additional boosters	Every 10 years after last dose	Td

**Important details are in the text.*
†Customarily begun at 8 weeks of age, with second and third doses given at 8-week intervals.
§Prolonging the interval does not require restarting series.
¶DT, if pertussis vaccine is contraindicated. If the child is 1 year of age or older at the time the primary dose is given, a third dose 6-12 months after the second completes primary immunization with DT.

*TABLE 2. Routine diphtheria and tetanus immunization schedule summary for persons 7 years old and older—United States, 1985**

Dose	Age/interval	Product
Primary 1	First dose	Td
Primary 2	4-8 weeks after first dose†	Td
Primary 3	6-12 months after second dose†	Td
Boosters	Every 10 years after last dose	Td

**Important details are in the text.*
†Prolonging the interval does not require restarting series.

6-12 months after the second dose.

Children who complete a primary series of DT before the fourth birthday should receive a single dose of DT just before entering kindergarten or elementary school. This dose is not necessary if the last dose of the primary series was given on or after the fourth birthday.

Pertussis immunization for persons 7 years old or older. Routine immunization against pertussis is not recommended for persons 7 years old and older. In exceptional cases, such as persons with chronic pulmonary disease exposed to children with pertussis or health-care personnel exposed during nosocomial or community outbreaks, a booster dose of adsorbed pertussis vaccine may be considered. A reduced dose is used for adults *(4)*. Routine pertussis vaccination of hospital personnel is not recommended.

Persons recovering from tetanus or diphtheria. Tetanus or diphtheria infection may not confer immunity; therefore, active immunization should be initiated at the time of recovery from the illness, and arrangements made to ensure that the remaining doses of a primary series are administered as early as possible.

Children recovering from pertussis. Children who have recovered from culture-confirmed pertussis need not receive further doses of pertussis vaccine. Lacking culture confirmation of the diagnosis, DTP immunization should be completed, because a pertussis-like syndrome may have been caused by other *Bordetella* species, chlamydia, or some viruses.

Neonatal tetanus prevention. There is no evidence that tetanus and diphtheria toxoids are teratogenic. A previously unimmunized pregnant woman who may deliver her child under unhygienic circumstances or surroundings should receive two properly spaced doses of Td before delivery, preferably during the last two trimesters. Incompletely immunized pregnant women should complete the three-dose series. Those immunized more than 10 years previously should have a booster dose.

Adult immunization with Td. Limited serosurveys done since 1977 indicate that the proportion of the population lacking protective levels of circulating antitoxin against diphtheria and tetanus increases with increasing age and that at least 40% of persons 60 years of age or older lack protective levels of antitoxins. Every visit of an adult to a health-care provider should be an opportunity to assess the patient's immunization status and, if indicated, to provide protection against tetanus and diphtheria using the combined toxoid, Td. Adults with uncertain histories of a complete primary series should receive a primary series. To ensure continued adequate protection in the individual, booster doses of Td could be given routinely at mid-decade ages, i.e., 15 years, 25 years, 35 years, etc.

Use of Single-Antigen Preparations

Multiple-antigen preparations should be used, unless there is a contraindication to one or more antigens in a preparation.

A single-antigen adsorbed pertussis vaccine preparation may be used to complete immunization against pertussis for children under 7 years of age who have received fewer than the recommended number of doses of pertussis vaccine but have received the recommended number of doses of diphtheria and tetanus toxoids for their age. Alternatively, doses of DTP can be given for protection against pertussis, although it is suggested that the total number of doses of diphtheria and tetanus toxoids not exceed six each before the seventh birthday.

Available data do not indicate substantially more reactions following receipt of Td than following receipt of single-antigen, adsorbed tetanus toxoid. Furthermore, adults, in general, are even less likely to have adequate circulating levels of diphtheria antitoxin than adequate circulating levels of tetanus antitoxin. The routine use of Td in all medical settings, e.g., private practice, clinics, and emergency rooms, for all persons 7 years of age or older requiring primary immunization or booster doses will improve levels of protection against both tetanus and diphtheria, especially among adults.

SIDE EFFECTS AND ADVERSE REACTIONS

Local reactions, generally erythema and induration with or without tenderness, are common after the administration of vaccines containing diphtheria, tetanus, or pertussis antigens. Occasionally, a nodule may be palpable at the injection site of adsorbed products for several weeks. Abscesses at the site of injection have been reported (6-10 per million doses). Mild systemic reactions, such as fever, drowsiness, fretfulness, and anorexia, occur quite frequently. These reactions are significantly more common following DTP than following DT, are usually self-limited, and need no therapy other than, perhaps, symptomatic treatment (e.g., antipyretics).

Moderate to severe systemic events, such as fever of 40.5 C (105 F) or higher, persistent, inconsolable crying lasting 3 hours or more, unusual high-pitched crying, collapse, or convulsions, occur relatively infrequently. Other more severe neurologic complications, such as a prolonged convulsion or an encephalopathy, occasionally fatal, have been reported to be associated with DTP administration, although rarely.

Approximate rates for adverse events following receipt of DTP vaccine (regardless of dose number in the series) are indicated in Table 3 *(5,6)*.

The frequency of local reactions and fever following DTP vaccination is significantly higher with increasing numbers of doses of DTP, while other mild to moderate systemic reactions (e.g., fretfulness, vomiting) are significantly less frequent *(5)*. If local redness of 2.5 cm or greater occurs, the likelihood of recurrence after another DTP dose increases significantly *(7)*.

In the National Childhood Enceph-

alopathy Study (NCES), a large, case-control study in England (*6*), children 2-35 months of age with serious, acute neurologic disorders, such as encephalopathy or complicated convulsion(s), were more likely to have received DTP in the 7 days preceding onset than their age-, sex-, and neighborhood-matched controls. Among children known to be neurologically normal before entering the study, the relative risk§ of a neurologic illness occurring within the 7-day period following receipt of DTP dose, compared to children not receiving DTP vaccine in the 7-day period before onset of their illness, was 3.3 ($p < 0.001$). Within this 7-day period, the risk was significantly increased for immunized children only within 3 days of vaccination (relative risk 4.2, $p < 0.001$). The relative risk for illness occurring 4-7 days after vaccination was 2.1 ($0.05 < p < 0.1$). The attributable risk estimates for a serious acute neurologic disorder within 7 days after DTP vaccine (regardless of outcome) was one in 110,000 doses of DTP, and for a permanent neurologic deficit, one in 310,000 doses. No specific clinical syndrome was identified. Overall, DTP vaccine accounted for only a small proportion of cases of serious neurologic disorders reported in the population studied.

Although there are uncertainties in the reported studies, recent data suggest that infants and young children who have had previous convulsions (whether febrile or nonfebrile) are more likely to have seizures following DTP than those without such histories (*8*).

Rarely, an anaphylactic reaction (i.e., hives, swelling of the mouth, difficulty breathing, hypotension, or shock) has been reported after receiving preparations containing diphtheria, tetanus, and/or pertussis antigens. The ACIP finds no good evidence for a causal relationship between DTP and hemolytic anemia or thrombocytopenic purpura.

Arthus-type hypersensitivity reactions, characterized by severe local reactions (generally starting 2-8 hours after an injection), may follow receipt of tetanus toxoid, particularly in adults who have received frequent (e.g., annual) boosters of tetanus toxoid. A few cases of peripheral neuropathy have been reported following tetanus toxoid administration, although a causal relationship has not been established.

Sudden infant death syndrome (SIDS) has occurred in infants following administration of DTP. A large case-control study of SIDS in the United States showed that receipt of DTP was not causally related to SIDS (*9*). It should be recognized that the first three primary immunizing doses of DTP are usually administered to infants 2-6 months old and that approximately 85% of SIDS cases occur at ages 1-6 months, with the peak incidence occurring at 6 weeks-4 months of age. By chance alone, some SIDS victims can be expected to have recently received vaccine.

Onset of infantile spasms has occurred in infants who have recently received DTP or DT. Analysis of data from the NCES on children with infantile spasms showed that receipt of DTP or DT was not causally related to infantile spasms (*10*). The incidence of onset of infantile spasms increases at 3-9 months of age, the time period in which the second and third doses of DTP are generally given. Therefore, some cases of infantile spasms can be expected to be related by chance alone to recent receipt of DTP.

Reporting of Adverse Events

Reporting by parents and patients of all adverse events occurring within 4 weeks of antigen administration should be encouraged. Adverse events that require a visit to a health-care provider should be reported by health-care providers to manufacturers and local or state health departments. The information will be forwarded to an appropriate federal agency (the Bureau of Biologics Research and Review, FDA, or CDC).

COMMENTS ON USING REDUCED DOSAGE SCHEDULES OR MULTIPLE SMALL DOSES

The ACIP recommends giving only the full dose of DTP; if a specific contraindication to DTP exists, none should be given. In the United States, the full course of primary immunization is considered to be four 0.5-ml doses of DTP.

Concern about adverse events following pertussis vaccination has led some practitioners to reduce the volume of DTP administered to less than 0.5 ml per dose in an attempt to reduce side effects. There is no evidence that a reduction in dosage decreases the frequency of severe events, such as seizures, hypotonic-hyporesponsive episodes, and encephalopathy. The mechanisms for these reactions are not known. Some studies reported significantly lower rates of local reactions to one-half the

§Relative risk was estimated by odds ratio.

TABLE 3. Adverse events occurring within 48 hours of DTP immunizations

Event	Frequency*
Local	
Redness	1/3 doses
Swelling	2/5 doses
Pain	1/2 doses
Mild/moderate systemic	
Fever ≥ 38 C (100.4 F)	1/2 doses
Drowsiness	1/3 doses
Fretfulness	1/2 doses
Vomiting	1/15 doses
Anorexia	1/5 doses
More serious systemic	
Persistent, inconsolable crying duration ≥ 3 hours)	1/100 doses
High-pitched, unusual cry	1/900 doses
Fever ≥ 40.5 C (≥ 105 F)	1/330 doses
Collapse (hypotonic-hyporesponsive episode)	1/1,750 doses
Convulsions (with or without fever)	1/1,750 doses
Acute encephalopathy†	1/110,000 doses
Permanent neurologic deficit†	1/310,000 doses

**Number of adverse events per total number of doses regardless of dose number in DTP series.*
†Occurring within 7 days of DTP immunization.

recommended dose (0.25 ml), compared to those following a full dose (*7,11*). A recent study also showed significantly lower pertussis serologic responses after the second and third half-doses, although the differences were small (*11*). This investigation used pertussis agglutinins as a measure of clinical protection; however, agglutinins are not absolute measures of clinical protection against pertussis disease. Furthermore, there is no evidence that the low screening titer used in this investigation (1:16) is indicative of protection. Currently, there are no reliable measures of efficacy other than clinical protection. Further evidence against the use of reduced doses comes from earlier studies of vaccine (*12,13*) with potency equivalent to that of half-doses of current vaccine. Attack rates of pertussis for exposed household contacts who received a lower potency vaccine (equivalent to a half-dose of the current vaccine) were approximately twice as high as attack rates for exposed household contacts who had received vaccines of potency equivalent to full doses of current vaccine (29%, compared to 14% or lower).

The use of an increased number of reduced-volume doses of DTP to equal the total volume of the five recommended doses of DTP vaccine is not recommended. It is unknown whether such a practice reduces the likelihood of vaccine-related events. In addition, by increasing the number of immunizations, the likelihood of a temporally associated but etiologically unrelated event may be enhanced.

Neither the use of reduced individual DTP doses nor the use of multiple doses of reduced volume that, in total, equal a full immunizing dose has been adequately studied. Neither the efficacy of such practices in reducing the frequency of associated serious adverse events nor the resulting protection against disease have been determined.

SIMULTANEOUS ADMINISTRATION OF VACCINES

The simultaneous administration of DTP, oral polio virus vaccine (OPV), and/or measles-mumps-rubella vaccine (MMR) has resulted in seroconversion rates and rates of side effects similar to those observed when the vaccines are administered separately (*14*). Therefore, if there is any doubt that a vaccine recipient will return for further vaccine doses, the ACIP recommends the simultaneous administration of all vaccines appropriate to the age and previous vaccination status of the recipient. This would especially include the simultaneous administration of DTP, OPV, and MMR to such persons at 15 months of age or older.

PRECAUTIONS AND CONTRAINDICATIONS

A febrile illness is reason to defer routine vaccination. Minor illness, such as mild upper respiratory infection, should not ordinarily be a reason for postponing vaccination. A history of prematurity generally is not a reason to defer vaccination (*15*).

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune response to vaccines. Short-term (less than 2 weeks) corticosteroid therapy or intraarticular, bursal, or tendon injections with corticosteroids should not be immunosuppressive. Although no specific studies with pertussis vaccine are available, if immunosuppressive therapy will be discontinued shortly, it would be reasonable to defer immunization until the patient has been off therapy for 1 month (*16*); otherwise, the patient should be vaccinated while still on therapy.

When an infant or child returns for the next dose of DTP, the parent should be questioned about any adverse events occurring after the previous dose.

Pertussis-Containing Preparations

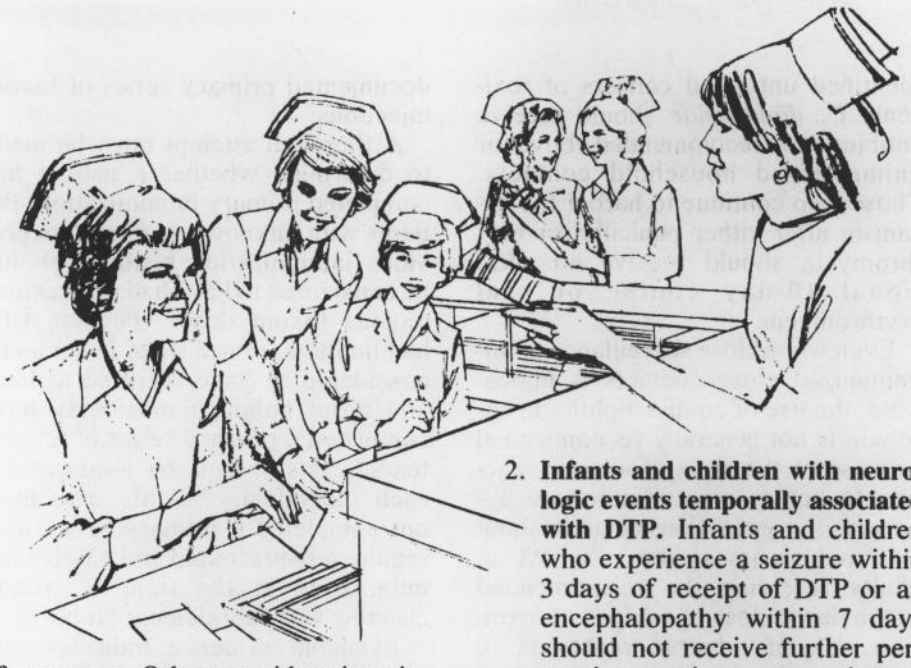
Absolute contraindications. If any of the following adverse events occur after DTP or single-antigen pertussis vaccination, further vaccination with a vaccine containing pertussis antigen is contraindicated:

1. Allergic hypersensitivity.
2. Fever of 40.5 C (105 F) or greater within 48 hours.
3. Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours.
4. Persisting, inconsolable crying lasting 3 hours or more or an unusual, high-pitched cry occurring within 48 hours.
5. Convulsion(s) with or without fever occurring within 3 days. (All children with convulsions, especially those with convulsions occurring within 4-7 days of receipt of DTP, should be fully evaluated to clarify their medical and neurologic status before a decision is made on initiating or continuing vaccination with DTP [see next section, item 3]).
6. Encephalopathy occurring within 7 days; this includes severe alterations in consciousness with generalized or focal neurologic signs. (A small but significantly increased risk of encephalopathy has been shown only within the 3-day period following DTP receipt. However, most authorities believe that an encephalopathy occurring within 7 days of DTP should be considered a contraindication to further doses of DTP.)

Immunization of infants and young children who have underlying neurologic disorders. The presence of a neurologic condition characterized by changing developmental or neurologic findings, regardless of whether a definitive diagnosis has been made, is also considered a contraindication to receipt of pertussis vaccine, because administration of DTP may coincide with or possibly even aggravate manifestations of the disease. Such disorders include uncontrolled epilepsy, infantile spasms, and progressive encephalopathy. Stable conditions, such as cerebral palsy and developmental delay, are not considered contraindications to receipt of pertussis vaccination.

Although there are uncertainties in the reported studies, recent data suggest that infants and young children who have had previous convulsions (whether febrile or nonfebrile) are more likely to have seizures following DTP receipt than those without such histories (*8*). A convulsion within 3 days of DTP receipt in a child with a history of convulsion(s) may be initiated by fever caused by the vaccine in a child prone to febrile convulsions, induced by the pertussis component, or unrelated to the vaccination. Available data do not indicate that seizures alone, temporally associated with DTP administration, induce permanent brain damage in these children.

Whether to administer DTP to children with proven or suspected underlying neurologic disorders, and when, must be decided on an individual basis. An important consideration is the current low frequency of pertussis reported in most areas of the United States, indicating a relatively low risk



of exposure. Other considerations include the current near absence of diphtheria in the United States and the low risk that an infant will acquire an infection with *C. tetani*. Based on these considerations and the nature of the child's disorder, the following approaches are recommended:

1. **Infants as yet unimmunized who are suspected of having underlying neurologic disease.** Possible latent central nervous system disorders that are suspected because of perinatal complications or other phenomena may become evident as they evolve over time. Because DTP administration may coincide with onset of overt manifestations of such disorders and result in confusion about causation, it is prudent to delay initiation of immunization with DTP or DT (but not OPV) until further observation and study have clarified the child's neurologic status. In addition, the effect of treatment, if any, can be assessed. The decision whether to commence immunization with DTP or DT should be made no later than the child's first birthday. In making this decision, it should be recognized that children with severe neurologic disorders may be at enhanced risk of exposure to pertussis from institutionalization or from attendance at clinics and special schools in which many of the children may be unimmunized. In addition, because of neurologic handicaps, these children may be in greater jeopardy from complications of the disease.
2. **Infants and children with neurologic events temporally associated with DTP.** Infants and children who experience a seizure within 3 days of receipt of DTP or an encephalopathy within 7 days should not receive further pertussis vaccine, even though cause and effect may not be established (see **PRECAUTIONS AND CONTRAINDICATIONS**).
3. **Incompletely immunized children with neurologic events occurring between doses.** Infants and children who have received one or more doses of DTP and who experience a neurologic disorder, e.g., a seizure, temporally unassociated with the administration of vaccine but before the next scheduled dose, present a special problem. If the seizure or other disorder occurs before the first birthday and completion of the first three doses of the primary series of DTP, deferral of further doses of DTP or DT (but not OPV) is recommended until the infant's status has been clarified. The decision whether to use DTP or DT to complete the series should be made no later than the child's first birthday and should take into consideration the nature of the child's problem and the benefits and risks of the vaccine. If the seizure or other disorder occurs after the first birthday, the child's neurologic status should be evaluated to ensure the disorder is stable before a subsequent dose of DTP is given (see next section).
4. **Infants and children with stable neurologic conditions.** Infants and children with stable neurologic conditions, including well-controlled seizures, may be vaccinated. The occurrence of single seizures (temporally unassociated with DTP) in infants and young children, while necessitating evaluation, need not contraindicate DTP immunization, particularly if the seizures can be satisfactorily explained. Anticonvulsant prophylaxis should be considered when giving DTP to such children. Parents of infants and children with histories of convulsions should be made aware of the slightly increased chance of postimmunization seizures.
5. **Children with resolved or corrected neurologic disorders.** DTP administration is recommended for infants with certain neurologic problems that have clearly subsided without residua or have been corrected, such as neonatal hypocalcemic tetany or hydrocephalus (following placement of a shunt and without seizures).

Immunization of infants and young children with family histories of convulsion or other central nervous system disorders. The ACIP, after evaluating the evidence available concerning the risk of a neurologic illness following pertussis vaccination of a child with a family history of convulsion or other central nervous system disorder, does not believe that such a history is a contraindication to pertussis vaccination.

Preparations Containing Diphtheria Toxoid and Tetanus Toxoid

The only contraindication to tetanus and diphtheria toxoids is a history of a neurologic or severe hypersensitivity reaction following a previous dose. Immunization with tetanus and diphtheria toxoids is not known to be associated with an increased risk of convulsions. Local side effects alone do not preclude continued use. If an anaphylactic reaction to a previous dose of tetanus toxoid is suspected, intradermal skin testing with appropriately diluted tetanus toxoid may be useful before a decision is made to discontinue tetanus toxoid immunization (*17*). In one study, 94 of 95 persons giving histories of anaphylactic symptoms following a previous tetanus toxoid dose were nonreactive following intradermal testing and tolerated a further tetanus toxoid challenge without a reaction (*17*). One person had immediate erythema and induration following skin testing but tolerated a full intramuscular dose without adverse effects. Mild, nonspecific skin-test reactivity to tetanus toxoid, particularly if used undiluted, appears to be fairly common. Most

vaccinees develop inconsequential cutaneous delayed hypersensitivity to the toxoid.

Persons who experienced Arthus-type hypersensitivity reactions or fever greater than 39.4 C (103 F) following a prior dose of tetanus toxoid usually have very high serum tetanus antitoxin levels and should not be given even emergency doses of Td more frequently than every 10 years, even if they have a wound that is neither clean nor minor.

If a contraindication to using tetanus toxoid-containing preparations exists in a person who has not completed a primary immunizing course of tetanus toxoid and other than a clean, minor wound is sustained, *only* passive immunization should be given using tetanus immune globulin (TIG) (see **TETANUS PROPHYLAXIS IN WOUND MANAGEMENT**).

Although there is no evidence that tetanus and diphtheria toxoids are teratogenic, waiting until the second trimester of pregnancy to administer Td is a reasonable precaution to minimize any theoretical concern.

DIPHTHERIA PROPHYLAXIS FOR CASE CONTACTS

All close contacts, household and other, with less than three doses of diphtheria toxoid should receive an immediate dose of a diphtheria toxoid-containing preparation and should complete the series according to schedule (Tables 1 and 2). Close contacts with three or more doses who have not received a dose of a preparation containing diphtheria toxoid within the previous 5 years should receive a booster dose of a diphtheria toxoid-containing preparation appropriate for their age.

All close contacts should be examined daily for 7 days for evidence of disease. Asymptomatic unimmunized or inadequately immunized close contacts should receive prompt chemoprophylaxis with either an IM injection of benzathine penicillin (600,000 units for persons under 6 years old and 1,200,000 units for those 6 years old or older) or a 7- to 10-day course of oral erythromycin (children: 40 mg/kg/day; adults: 1 g/day). Erythromycin may be slightly more effective, but IM benzathine penicillin may be preferred, since it avoids possible problems of noncompliance with a multiday oral drug regimen. Bacteriologic cultures before and after antibiotic prophylaxis may be useful in the follow-up and management of contacts. Identified untreated carriers of toxigenic *C. diphtheriae* should receive antibiotics as recommended above for unimmunized household contacts. Those who continue to harbor the organism after either penicillin or erythromycin should receive an additional 10-day course of oral erythromycin.

Even when close surveillance of unimmunized close contacts is impossible, the use of equine diphtheria antitoxin is not generally recommended because of the risks of allergic reaction to horse serum. Immediate hypersensitivity reactions occur in about 7%, and serum sickness, in 5% of adults receiving the recommended prophylactic dose of equine antitoxin. The risk of adverse reactions to equine antitoxin must be weighed against the small risk of diphtheria occurring in an unimmunized household contact who receives chemoprophylaxis. If antitoxin is to be used, the usually recommended dose is 5,000-10,000 units IM—after appropriate testing for sensitivity—at a site different from that of toxoid injection. The immune responses to simultaneous diphtheria antitoxin and toxoid inoculation is unlikely to be impaired, but this has not been adequately studied.

Cases of cutaneous diphtheria generally are caused by infections with nontoxigenic strains of *C. diphtheriae*. However, a lesion suspected of being cutaneous diphtheria should be considered to be caused by a toxigenic strain until proven otherwise. Recommendations for prophylaxis of close case contacts are the same as for respiratory diphtheria, since cutaneous diphtheria may be more contagious than respiratory infection for close contacts. If a cutaneous case is known to be due to a nontoxigenic strain, routine investigation or prophylaxis of contacts is not necessary.

TETANUS PROPHYLAXIS IN WOUND MANAGEMENT

Chemoprophylaxis against tetanus is neither practical nor useful in managing wounds; wound cleaning, debridement when indicated, and proper immunization are important. The need for tetanus toxoid (active immunization), with or without tetanus immune globulin (TIG) (passive immunization), depends on both the condition of the wound and the patient's immunization history (Table 4; see also **PRECAUTIONS AND CONTRAINDICATIONS**). Rarely has tetanus occurred among persons with a documented primary series of toxoid injections.

A thorough attempt must be made to determine whether a patient has completed primary immunization. Patients with unknown or uncertain previous immunization histories should be considered to have had no previous tetanus toxoid doses. Persons who had military service since 1941 can be considered to have received at least one dose; although most may have completed a primary series of tetanus toxoid, this cannot be assumed for each individual. Patients who have not completed a primary series may require tetanus toxoid and passive immunization at the time of wound cleaning and debridement (Table 4).

Available evidence indicates that complete primary immunization with tetanus toxoid provides long-lasting protection—10 years or more in most recipients. Consequently, after complete primary tetanus immunization, boosters—even for wound management—need to be given only every 10 years when wounds are minor and uncontaminated. For other wounds, a booster is appropriate if the patient has not received tetanus toxoid within the preceding 5 years. Antitoxin antibodies develop rapidly in persons who have previously received at least two doses of tetanus toxoid.

Td is the preferred preparation for active tetanus immunization in wound management of patients 7 years old or older. This is to enhance diphtheria protection, since a large proportion of adults are susceptible. Thus, by taking advantage of acute health-care visits, such as for wound management, some patients can be protected who otherwise would remain susceptible. For routine wound management of children under 7 years old who are not adequately immunized, DTP should be used instead of single-antigen tetanus toxoid. If pertussis vaccine is contraindicated or individual circumstances are such that potential febrile reactions following DTP might confound the management of the patient, DT may be used. For inadequately immunized patients of all ages, completion of primary vaccination at the time of discharge or at follow-up visits should be ensured (Tables 1 and 2).

If passive immunization is needed, human TIG is the product of choice. It provides longer protection than antitoxin of animal origin and causes few adverse reactions. The currently recommended prophylactic dose of TIG

for wounds of average severity is 250 units IM. When tetanus toxoid and TIG are given concurrently, separate syringes and separate sites should be used. The ACIP recommends the use of only adsorbed toxoid in this situation.

PERTUSSIS PROPHYLAXIS FOR CASE CONTACTS

Spread of pertussis can be limited by decreasing infectivity of the patient and by protecting close contacts of that patient. To reduce infectivity as quickly as possible, a course of oral erythromycin (children: 40 mg/kg/day; adults: 1 g/day) or trimethoprim/sulfamethoxazole (children: trimethoprim 8 mg/kg/day, sulfamethoxazole 40 mg/kg/day; adults: trimethoprim 320 mg/day, sulfamethoxazole 1,600 mg/day) is recommended for patients with clinical pertussis. The antibiotic should be administered for 14 days to minimize any chance of antibiotic failure. Chemotherapy, however, probably does not affect the duration or severity of disease.

There are two approaches for protecting close contacts (such as children exposed in a household or day-care center) of patients with pertussis—active immunization and chemoprophylaxis. Close contacts under 7 years old who have not completed the four-dose primary series of DTP injections or who have not received a dose of DTP within 3 years of exposure should be given a dose of vaccine and should complete a primary series with the minimal intervals (Table 1). While the usefulness of chemoprophylaxis has not been well demonstrated, it may be prudent to consider a 14-day course of erythromycin or trimethoprim/sulfamethoxazole for close contacts under 1 year old, regardless of immunization status, and for unimmunized close contacts under 7 years old.

Prophylactic postexposure passive immunization is not recommended. Studies have shown that use of human pertussis immune globulin neither prevents illness nor reduces its severity. This product is no longer available in the United States.

Reverences

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Adapted from MMWR 1985;34:405-14, 419-26.

TABLE 4. Summary guide to tetanus prophylaxis in routine wound management—United States, 1985*

History of adsorbed tetanus toxoid (doses)	Clean, minor wounds		All other wounds†	
	Td§	TIG	Td§	TIG
Unknown or < three	Yes	No	Yes	Yes
≥ three¶	No**	No	No††	No

**Important details are in the text.*

†Such as, but not limited to, wounds contaminated with dirt, feces, soil, saliva, etc.; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns and frostbite.

§For children under 7 years old; DTP (DT, if pertussis vaccine is contraindicated) is preferred to tetanus toxoid alone. For persons 7 years old and older, Td is preferred to tetanus toxoid alone.

¶If only three doses of fluid *toxoid have been received, a fourth dose of toxoid, preferably an adsorbed toxoid, should be given.*

***Yes, if more than 10 years since last dose.*

††Yes, if more than 5 years since last dose. (More frequent boosters are not needed and can accentuate side effects.)

Cases of selected notifiable diseases, Virginia, for the period September 1 through September 30, 1985

Disease	State					Regions				
	This Month	Last Month	Total to Date 1985	Total to Date 1984	Mean 5 Year To Date	This Month N.W.	This Month N.	This Month S.W.	This Month C.	This Month E.
Measles	2	4	27	5	71	0	0	0	2	0
Mumps	1	10	42	18	53	0	0	0	0	1
Pertussis	6	3	14	19	20	0	0	3	0	3
Rubella	0	0	2	0	12	0	0	0	0	0
Meningitis—Aseptic	79	35	237	192	173	7	8	19	26	19
*Bacterial	18	21	191	172	163	1	0	5	4	8
Hepatitis A (Infectious)	8	8	125	78	143	2	0	3	1	2
B (Serum)	53	42	435	377	390	5	4	9	13	22
Non-A, Non-B	3	3	65	73	48	0	0	3	0	0
Salmonellosis	130	201	1213	972	1069	18	15	19	38	40
Shigellosis	8	14	65	172	322	0	7	0	0	1
Campylobacter Infections	54	133	560	470	262	10	8	11	14	11
Tuberculosis	52	25	297	343	—	—	—	—	—	—
Syphilis (Primary & Secondary)	22	30	225	316	429	0	2	5	8	7
Gonorrhea	1655	2083	14,376	14,973	15,738	—	—	—	—	—
Rocky Mountain Spotted Fever	0	6	18	45	72	0	0	0	0	0
Rabies in Animals	20	14	139	174	248	8	7	4	1	0
Meningococcal Infections	3	0	43	48	58	0	0	2	1	0
Influenza	1	16	944	1102	1601	0	0	1	0	0
Toxic Shock Syndrome	0	0	1	7	7	0	0	0	0	0
Reyes Syndrome	0	0	2	6	9	0	0	0	0	0
Legionellosis	1	4	12	22	16	0	0	1	0	0
Kawasaki's Disease	1	2	25	12	17	0	0	0	0	1
Other: Acquired Immunodeficiency Syndrome	17	10	72	26	—	0	13	1	1	2

Counties Reporting Animal Rabies: Augusta 1 gray fox; Frederick 1 raccoon; King George 1 fox, 1 skunk, 1 raccoon; Louisa 1 raccoon; Rockingham 1 skunk; Stafford 1 raccoon, Arlington 1 raccoon; Fairfax 1 bat; Loudoun 1 bat, 4 raccoons; Lee 2 foxes; Russell 2 skunks; Henrico 1 bat.

Occupational Illnesses: Pneumoconioses 18; Carpal tunnel syndrome 15; Silicosis 10; Loss of hearing 9; Dermatoses 4; Asbestosis 3; Mesothelioma 1; Chlorine gas inhalation 1.

*other than meningococcal

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