

Connecticut Epidemiologist

STATE OF CONNECTICUT DEPARTMENT OF HEALTH SERVICES

Vol. 2 No. 4

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April, 1983

GENERAL RECOMMENDATIONS ON IMMUNIZATION

Recommendations for immunization of infants, children, and adults are based on facts about immunobiologics and scientific knowledge about the principles of active and passive immunization and on judgements by public health officials and specialists in clinical and preventive medicine. Benefits and risks are associated with the use of all products--no vaccine is completely safe or completely effective. The benefits range from partial or complete protection from the consequences of disease, and the risks range from common, trivial, and inconvenient side effects to rare, severe, and life-threatening conditions. Thus, recommendations on immunization practices balance scientific evidence of benefits, costs, and risks to achieve optimal levels of protection against infectious or communicable diseases.

These recommendations describe this balance and attempt to minimize the risk by providing specific advice regarding dose, route, and spacing of immunobiologics by delineating situations warranting precautions or contraindicating their use. These recommendations may apply only in the United States, as epidemiological circumstances and vaccine may differ in other countries. The relative balance of benefits and risks may change as diseases are brought under control or eradicated. For example, because smallpox has been eradicated throughout the world, the very small risk from smallpox vaccine now exceeds the risk of smallpox; consequently, smallpox vaccination of civilians is now indicated only for laboratory workers directly involved with smallpox or closely related orthopox viruses (e.g., monkeypox, vaccinia, and others).

IMMUNOBIOLOGICS

The specific nature and content of immunobiologics may differ. When immunobiologics against the same infectious agents are produced by different manufacturers, active and inert ingredients among the various products may differ. Practitioners are urged to become familiar with the constituents of the products they use. These include: suspending fluid, preservatives, stabilizers, antibiotics and adjuvants. Subcutaneous or intracutaneous administration of vaccines with adjuvants may cause local irritation, inflammation, granuloma formation, or necrosis.

ROUTE, SITE, AND TECHNIQUE OF IMMUNIZATION

A. Route: There is a recommended route of administration for each immunobiologic. To avoid unnecessary local or systemic effects and/or ensure optimal efficacy, the practitioner should not deviate from the recommended route of administration.

B. Site: Injectable immunobiologics should be administered in an area where there is minimal opportunity for local, neural, vascular, or tissue injury. Subcutaneous injections are usually administered into the thigh of infants and the deltoid area of older children and adults. Intradermal injections are generally given on the volar surface of the forearms, except for human diploid cell rabies vaccine, with which reactions are less severe in the deltoid area.

In the past, the upper, outer quadrant of the buttocks was the usual site of intramuscular vaccine. The buttocks should not be routinely used as a vaccination site for infants and children; and, to avoid injury to the sciatic nerves, they are generally not used in adults. The central region of the buttocks should be avoided for all injections; the upper, outer quadrant should be used only for the largest volumes of injection or when multiple doses need to be given, such as when large doses of IG must be administered. The site selected should be well into the upper, outer mass of the gluteus maximus and away from the central region of the buttocks.

Currently, preferred sites for intramuscular injections are the anterolateral aspect of the upper thigh and the deltoid muscle of the upper arm. In most infants, the anterolateral aspect of the thigh provides the largest muscle mass and, therefore, is the preferred site. In older children, the deltoid mass is of sufficient size for intramuscular injection. An individual decision must be made for each child, based on the volume of the injected materials and the size of the muscle into which it is to be injected. Many practitioners prefer to continue using the anterolateral thigh until age 3 years before switching to the deltoid area. In adults, the deltoid is generally used for routine intramuscular vaccine administration.

C. Techniques: A separate needle and syringe should be used for each injection. Disposable needles and syringes should be discarded in labeled containers to prevent accidental inoculation or theft. If more than one vaccine preparation is administered, each should be given at a different site.

DOSAGE

The recommended doses of immunobiologics are derived from theoretical considerations, experimental trials, and clinical experience. Administration of dose volumes smaller than those recommended, such as split doses or intradermal administration (unless specifically recommended), may result in inadequate protection. Exceeding the recommended dose vol-

umes might be hazardous because of excessive local or systemic concentrations of antigens.

Some practitioners use divided doses of vaccine (particularly diphtheria and tetanus toxoids and pertussis vaccine (DTP) to reduce reaction rates. There has not been adequate study of the efficacy of such practices by serologic confirmation or clinical efficacy or of the effects on the subsequent frequency and severity of adverse reactions. The Committee does not recommend dividing doses of any vaccine.

AGE AT WHICH IMMUNOBIOLOGICS ARE ADMINISTERED

Several factors influence recommendations concerning the age at which vaccine is administered (Table 1-3). These include: age-specific risks of disease, age-specific risks of complications, ability of individuals of a given age to respond to the vaccine(s), and potential interference with the immune response by passively transferred maternal antibody. In general, vaccines are recommended for the youngest age group at risk with an acceptable level of antibody response following vaccine administration. For example, while infants as young as six months of age may be at risk for measles, most are protected by maternal antibody, which may inhibit successful active immunization at this age. In the United States, measles vaccine is routinely administered at 15 months of age, by which time maternal antibody is no longer detectable.

In certain measles epidemics, public health officials may recommend measles vaccine for infants as young as six months of age. Although a smaller proportion of those given vaccine before the first birthday develop antibody to measles, compared with older infants, the higher risk of disease during an epidemic may justify earlier immunization. Such infants should be reimmunized at the recommended age for measles vaccination to achieve protection.

SPACING OF IMMUNOBIOLOGICS

A. Multiple doses of same antigen: Some products require more than one dose for full protection. In addition, it is necessary to give periodic reinforcement (booster) doses of some preparations to maintain protection. In recommending the ages and/or intervals for multiple doses, the Committee takes into account current risks from disease and the objective of inducing satisfactory protection. Intervals between doses that are longer than those recommended do not lead to a reduction in final antibody levels. Therefore, it is unnecessary to restart an interrupted series of an immunobiologic or to add extra doses. By contrast, giving doses of a vaccine or toxoid at less than recommended intervals may lessen the antibody response; doses given at less than recommended intervals should not be counted as part of a primary series.

B. Different antigens: Experimental evidence and extensive clinical experience have strengthened the scientific basis for giving certain vaccines at the same time. Most of the widely used antigens can safely and effectively be given simultaneously. This knowledge is particularly helpful in circumstances that include imminent exposure to several infectious diseases, preparation for foreign travel, or uncertainty that the patient will return for further doses of vaccine.

In general, inactivated vaccines can be administered simultaneously at separate sites. It should be noted, however, that when vaccines commonly associated with local or systemic side effects (such as cholera, typhoid, and plague vaccines) are given simultaneously, the side effects theoretically might be accentuated. When practical, these vaccines should be given on separate occasions.

Field observations indicate that simultaneous administration (on the same day) of the most widely used live-virus vaccines has not resulted in impaired

TABLE 1. Recommended schedule for active immunization of normal infants and children (See individual ACIP recommendations for details.)

Recommended age*	Vaccine(s)†	Comments
2 mo.	DTP-1§, OPV-1¶	Can be given earlier in areas of high endemicity
4 mo.	DTP-2, OPV-2	6-wks-2 mo. interval desired between OPV doses to avoid interference
6 mo.	DTP-3	An additional dose of OPV at this time is optional for use in areas with a high risk of polio exposure
15 mo.**	M/R††	
18 mo.**	DTP-4, OPV-3	Completion of primary series
4-6 yr.§§	DTP-5, OPV-4	Preferably at or before school entry
14-16 yr.	Td¶¶	Repeat every 10 years throughout life

*These recommended ages should not be construed as absolute, i.e., 2 mos. can be 6-10 weeks, etc.

†For all products used, consult manufacturer's package enclosure for instructions for storage, handling, and administration. Immunobiologics prepared by different manufacturers may vary, and those of the same manufacturer may change from time to time. The package insert should be followed for a specific product.

§DTP - Diphtheria and tetanus toxoids and pertussis vaccine.

¶OPV - Oral, attenuated poliovirus vaccine contains poliovirus types 1, 2, and 3.

**Simultaneous administration of M/R, DTP, and OPV is appropriate for patients whose compliance with medical care recommendations cannot be assured.

††M/R - Live measles, mumps, and rubella viruses in a combined vaccine (see text for discussion of single vaccines versus combination).

§§Up to the seventh birthday.

¶¶Td - Adult tetanus toxoid and diphtheria toxoid in combination, which contains the same dose of tetanus toxoid as DTP or DT and a reduced dose of diphtheria toxoid.

antibody response or increased rates of adverse reactions. Observations of children indicates that antibody responses to trivalent oral polio vaccine (OPV) given simultaneously with licensed combination measles-mumps-rubella (MMR) vaccine are comparable to those obtained when the same vaccines are given at separate visits. It is reasonable to expect equivalent immunologic responses when other licensed combination or live, attenuated-virus vaccines or their component antigens are given simultaneously with OPV. While data are lacking on potential interference with antibody responses to measles, mumps, rubella and/or trivalent oral polio vaccines administered at different times within one month of one another, there are theoretical concerns and data showing that the immune response to a live virus vaccine might be impaired if the vaccine is administered within the month following another live virus vaccine. When feasible, live virus vaccines not administered on the same day should be given at least one month apart.

No data indicate that simultaneous administration of individual measles, mumps, or rubella antigens at different sites yields different results from administration of the combined vaccines in a single site.

Data on the response to simultaneous administration of diphtheria and tetanus toxoids and pertussis vaccine (DTP), OPV, and MMR vaccine are lacking. However, field experience and antibody data regarding simultaneous administration of either DTP and measles vaccine or DTP and OPV indicate that the protective response is satisfactory and adverse reactions do not increase. Therefore, simultaneous administration of all these antigens is recommended when individuals require multiple antigens and there is doubt that the recipient will return to receive further doses of vaccine. Children 15 months of age or older who have received fewer than the recommended number of DTP and OPV doses fall into this category (Table 2). Simultaneous administration of pneumococcal polysaccharide vaccine and whole-virus influenza vaccine gives satisfactory antibody response without increasing the occurrence of adverse reactions. Simultaneous administration of

the pneumococcal vaccine and split-virus influenza vaccine may also be expected to yield satisfactory results. However, it should be kept in mind that influenza vaccine should be administered annually to the target population, whereas, under current recommendations, pneumococcal polysaccharide vaccine should only be administered in a single dose.

An inactivated vaccine and a live, attenuated-virus vaccine can be administered simultaneously at separate sites, with the precautions that apply to the individual vaccines. Some data suggest that the simultaneous administration of cholera and yellow fever vaccines may interfere with the immune response to each other. Decreased levels of antibodies have been observed when the vaccines are administered within three weeks of each other, compared with administration of the vaccines at longer intervals. However, there is no evidence that protection to either of these diseases diminishes when these vaccines are administered simultaneously. Therefore, the Committee believes that yellow fever and cholera vaccines can be administered simultaneously, if necessary.

C. Immune globulin: Immune globulin (IG, formerly called Immune Serum Glublin, [ISG]) and various specific immune globulins contain antibodies common to the population from which the pooled plasma used in their preparation was obtained. These antibodies may interfere with the effectiveness of live, attenuated vaccines administered shortly after IG or specific IG has been given.

In general, such interference is of little practical importance with inactivated products. They can, therefore, be given anytime after IG use. With live, attenuated vaccines, passively acquired antibody may interfere with replication of vaccine virus and thus with the antibody response of the patient. Parenterally administered live vaccines (e.g., MMR or other combinations) should, therefore, not be given for at least six weeks, but preferably three months, after the administration of IG. Preliminary data indicate that IG does not interfere with the immune response either to OPV or yellow fever vaccine.

TABLE 2. Recommended immunization schedule for infants and children up to 7th birthday not immunized at the recommended time in early infancy* (See individual ACIP recommendations for details.)

Timing	Vaccine(s)	Comments
First visit	DTP-1, + OPV-1§ (if child is \geq 15 mo. of age, MMR)	DTP, OPV, and MMR can be administered simultaneously to children \geq 15 mo. of age
2 mo. after first DTP, OPV	DTP-2, OPV-2	
2 mo. after second DTP	DTP-3	An additional dose of OPV at this time is optional for use in areas with a high risk of polio exposure
6-12 mo. after third DTP	DTP-4, OPV-3	
Preschool** (4-6 yr.)	DTP-5, OPV-4	Preferably at or before school entry
14-16 yr.	Td††	Repeat every 10 years throughout life

*If initiated in the first year of life, give DTP-1, 2, and 3, OPV-1 and 2 according to this schedule and give MMR when the child becomes 15 months old.
 †DTP-Diphtheria and tetanus toxoids with pertussis vaccine. DTP may be used up to the seventh birthday.

§OPV-Oral, attenuated poliovirus vaccine contains poliovirus types 1, 2, and 3.
 ¶MMR-Live measles, mumps, and rubella viruses in a combined vaccine (see text for discussion of single vaccines versus combination).

**The preschool dose is not necessary if the fourth dose of DTP and third dose of OPV are administered after the fourth birthday.

††Td-Adult tetanus toxoid and diphtheria toxoid in combination, which contains the same dose of tetanus toxoid as DTP or DT and a reduced dose of diphtheria toxoid.

If IG administration becomes necessary after a live vaccine has been given, interference may occur. In general, vaccine virus replication and stimulation of immunity will occur within seven to 10 days. Thus, if the interval between vaccine and IG is less than 14 days, vaccine should be repeated about three months after IG was given, unless serologic testing indicates that antibodies have been produced; if the interval was longer, vaccine need not be readministered. If administration of IG becomes necessary because of imminent exposure to disease, live virus vaccines may be administered simultaneously with IG, with the recognition that vaccine-induced immunity may be compromised. The vaccine should be administered in a site remote from that chosen for IG inoculation. Vaccine should be repeated about three months later, unless serologic testing indicates antibodies have been produced.

HYPERSENSITIVITY TO VACCINE COMPONENTS

Vaccine antigens produced in systems or with substrates containing allergenic substances, e.g., antigens derived from growing microorganisms in embryonated chicken eggs, may cause hypersensitivity reactions. These reactions may include anaphylaxis when the final vaccine contains a substantial amount of the allergen. Yellow fever vaccine is such an antigen. Vaccines with such characteristics should not be given to persons with known hypersensitivity to components of the substrates. Contrary to this generalization, influenza vaccine antigens (whole or split), although prepared from viruses grown in embryonated eggs, are highly purified during preparation and have only very rarely been reported to be associated with hypersensitivity reactions.

Live virus vaccines prepared by growing viruses in cell cultures are essentially devoid of potentially allergenic substances related to host tissue. On very rare occasions, hypersensitivity reactions to measles vaccine have been reported in persons with anaphylactic hypersensitivity to eggs. Measles vaccine, however, can be given safely to egg-allergic individuals provided the allergies are not manifested by anaphylactic symptoms. Since mumps vaccine is grown in similar cell cultures, the same precautions apply.

Screening persons by history of ability to eat eggs without adverse effects is a reasonable way to

identify those possibly at risk from receiving measles, mumps, and influenza vaccine. Individuals with anaphylactic hypersensitivity to eggs (hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock)* should not be given these vaccines.

Rubella vaccine is grown in human diploid cell culture and can be safely given, regardless of a history of allergy to eggs or egg proteins.

Bacterial vaccines, such as cholera, DTP, plague, and typhoid, are frequently associated with local or systemic adverse effects; these common reactions do not appear to be allergic.

Some vaccines contain preservatives (e.g., thimerosal, a mercurial) or trace amounts of antibiotics (e.g., neomycin) to which patients may be hypersensitive. Those administering vaccines should carefully review the information provided with the package insert before deciding whether the rare patients with known hypersensitivity to such preservatives or antibiotics should be given the vaccine(s). No currently recommended vaccine contains penicillin or its derivatives.

Some vaccines (e.g., MMR vaccine or its individual component vaccines) contain trace amounts of neomycin. This amount is less than would usually be used for the skin test to determine hypersensitivity. Persons who have experienced anaphylactic reactions to neomycin should not receive these vaccines. Most often, neomycin allergy is a contact dermatitis, a manifestation of a delayed-type (cell-mediated) immune response rather than anaphylaxis. In such individuals, the adverse reaction, if any, to neomycin in the vaccines would be an erythematous, pruritic papule at 48-96 hours. A history of delayed-type reactions to neomycin is not a contraindication to receiving these vaccines.

ALTERED IMMUNOCOMPETENCE

Virus replication after administration of live, attenuated-virus vaccines may be enhanced in persons with immune deficiency diseases, and in those with suppressed capability for immune response, as occurs with leukemia, lymphoma, generalized malignancy, or therapy with corticosteroids, alkylating

*Any of these signs or symptoms constitutes a systemic anaphylactic response.

TABLE 3. Recommended immunization schedule for persons 7 years of age or older (See individual ACIP recommendations for details.)

Timing	Vaccine(s)	Comments
First visit	Td-1*, OPV-1† and MMR§	OPV not routinely administered to those \geq 18 years of age
2 mo. after first Td, OPV	Td-2, OPV-2	
6-12 mo. after second Td, OPV	Td-3, OPV-3	OPV-3 may be given as soon as 6 weeks after OPV-2
10 years after Td-3	Td	Repeat every 10 years throughout life

*Td-Tetanus and diphtheria toxoids (adult type) are used after the seventh birthday. The DTP doses given to children under 7 who remain incompletely immunized at age 7 or older should be counted as prior exposure to tetanus and diphtheria toxoids (e.g., a child who previously received 2 doses of DTP, only needs 1 dose of Td to complete a primary series).

†OPV-Oral, attenuated poliovirus vaccine contains poliovirus type 1, 2, and 3. When polio vaccine is to be given to individuals 18 years or older, IPV is preferred. See ACIP statement on polio vaccine for immunization schedule for IPV.

§MMR-Live measles, mumps, and rubella viruses in a combined vaccine. Persons born before 1957 can generally be considered immune to measles and mumps and need not be immunized. Rubella vaccine may be given to persons of any age, particularly to women of childbearing age. MMR may be used since administration of vaccine to persons already immune is not deleterious. (See text for discussion of single vaccines versus combination).

agents, antimetabolites, or radiation. Patients with such conditions should not be given live, attenuated-virus vaccines. Because of the possibility of familial immunodeficiency, live attenuated-virus vaccines should not be given to a member of a household in which there is a family history of congenital or hereditary immunodeficiency until the immune competence of the potential recipient is known. OPV should not be given to a member of a household in which there is a family history of immunodeficiency or immunosuppression, regardless whether acquired or hereditary, until the immune status of the recipient and the other family members is known. Individuals residing in the household of an immunocompromised individual should not receive OPV, because vaccine viruses are excreted by the recipient of the vaccine and may be communicable to other persons.

SEVERE FEBRILE ILLNESSES

Minor illnesses, such as mild upper-respiratory infections, should not postpone vaccine administration. However, immunization of persons with severe febrile illnesses should generally be deferred until they have recovered. This precaution is to avoid superimposing adverse effects from the vaccine on the underlying illness or mistakenly identifying a manifestation of the underlying illness as a result of the vaccine. In persons whose compliance with medical care cannot be assured, it is particularly important to take every opportunity to provide appropriate vaccinations.

VACCINATION DURING PREGNANCY

On the grounds of a theoretical risk to the developing fetus, live, attenuated-virus vaccines are not generally given to pregnant women or to those likely to become pregnant within three months after receiving vaccine(s). With some of these vaccines -- particularly rubella, measles, and mumps -- pregnancy is a contraindication. Both yellow fever vaccine and OPV can be given to pregnant women at substantial risk of exposure to natural infection. When vaccine is to be given during pregnancy, waiting until the second or third trimester to minimize any concern over teratogenicity is a reasonable precaution. If a pregnant woman receives a live, attenuated-virus vaccine, there is not necessarily any real risk to the fetus. In particular, although there are theoretical risks in giving rubella vaccine during pregnancy, data on previously and currently available rubella vaccines indicate that the risk, if any, of teratogenicity from live rubella vaccine is quite small. There has been no evidence of congenital rubella syndrome in infants born to susceptible mothers who received rubella vaccine during pregnancy.

Since persons given measles, mumps, or rubella vaccine viruses do not transmit them, these vaccines may be administered with safety to children of pregnant women. Although live polio virus is shed by children recently immunized with OPV (particularly following the first dose), this vaccine can also be administered to children of pregnant women. Polio immunization of children should not be delayed because of pregnancy in close adult contacts. Experience to date has not revealed any risks of poliovaccine virus to the fetus.

There is no convincing evidence of risk to the fetus from immunization of pregnant women using inactivated virus vaccines, bacterial vaccines, or toxoids. Tetanus and diphtheria toxoid (Td) should be given to inadequately immunized pregnant women because it affords protection against neonatal tetanus. There is no risk to the fetus from passive immunization of pregnant women with IG (see below). For further information regarding immunization of

pregnant women, refer to the American College of Obstetricians and Gynecologist (ACOG) Technical Bulletin Number 14, May 1982.

ADVERSE EVENTS FOLLOWING IMMUNIZATION

Modern vaccines are extremely safe and effective, but not completely so. Adverse events following immunization have been reported with all vaccines. These range from frequent, minor local reactions to extremely rare, severe, systemic illness such as paralysis associated with OPV. To improve knowledge about adverse reactions, all temporally associated events severe enough to require the recipient to seek medical attention should be evaluated and reported in detail to local or state health officials and to the vaccine manufacturer. It is frequently impossible to establish cause-and-effect relationships when untoward events occur after receiving vaccine(s) since temporal association alone does not necessarily indicate causation.

DISEASE CONTROL THROUGH CONTINUING PROGRAMS

The best means of reducing the occurrence of vaccine-preventable diseases of childhood (diphtheria, pertussis, tetanus, polio, measles, mumps, and rubella) is by having a highly immune population. Universal immunization is an important part of good health care and should be accomplished through routine and intensive programs carried out in physicians' offices and public health clinics. Programs aimed at ensuring that all children are immunized at the recommended age should be established and maintained in all communities. In addition, all other susceptible persons (regardless of age) should be immunized, unless vaccine is otherwise contraindicated.

Official health agencies should take whatever steps are necessary, including development and enforcement of school immunization requirements, to assure that all persons in schools at all grade levels and those in day-care centers are protected against the vaccine-preventable diseases of childhood.

Official personal immunization record cards have been adopted by every state and the District of Columbia to encourage uniformity of records and to facilitate the assessment of immunization status by schools and day-care centers. In many states, these cards are distributed to new mothers while they are still in the hospital following delivery. The records are used as one teaching tool in immunization education programs aimed at increasing parental awareness of the need for vaccines. The Committee recommends the use of these standard records by all health care providers.

A permanent, comprehensive immunization record should be established for each newborn infant and maintained by the parent. Physicians should encourage parents to use the record and should record all immunization data. Parents or guardians should be urged to bring the record every time the child sees a health care provider. Health care providers should review the immunization status of children at each visit. At a minimum, the type of immunobiologic administered and the date of administration should be entered into the patient's immunization record.

Maintenance of personal immunization records is very important, since persons in this country relocate frequently. This will facilitate accurate record-keeping for the patient, assist with physician encounters, and fulfill the need for documentation of immunization in schools and other institutions and organizations.

