

67. Postexposure Prophylaxis for Selected Infectious Diseases

RECOMMENDATION

Postexposure prophylaxis should be provided to selected persons with exposure or possible exposure to *Haemophilus influenzae* type b, hepatitis A, hepatitis B, meningococcal, rabies, or tetanus pathogens (see *Clinical Intervention*). See Chapter 66 for recommendations on postexposure prophylaxis against influenza A.

HAEMOPHILUS INFLUENZAETYPE B DISEASE

Burden of Suffering

The incidence of invasive *H. influenzae* type b (Hib) disease (e.g., meningitis, epiglottitis, septic arthritis) has decreased dramatically in recent years, most likely due to the immunization of infants and young children with effective vaccines, with 1,174 cases reported in 1994.¹ The incidence of invasive Hib disease among children less than 5 years of age decreased from 41/100,000 in 1987 to fewer than 2/100,000 in 1994.² Most cases occur during infancy,^{3,4} but many children remain susceptible to infection until age 4–5 years. Young children are at especially increased risk if they are exposed to infected persons at home or in day care.^{3,5–7} Most secondary cases of Hib disease in household contacts occur within 1–2 weeks of the primary case.⁵

Efficacy of Prophylaxis

Rifampin prophylaxis can reduce the risk of secondary infection in persons exposed to Hib. A randomized controlled clinical trial and an uncontrolled trial have shown that a 4-day antibiotic regimen can reduce both the rate of asymptomatic carriage of Hib and the incidence of secondary infection in household and day care contacts of infected persons.^{8,9} Postexposure prophylaxis for Hib may prove unnecessary eventually, given widespread childhood immunization with the Hib conjugate vaccine (see Chapter 65). In addition to protecting the vaccinated child against Hib infection, conjugate vaccine appears to decrease Hib pharyngeal colonization,^{10,11} which would also reduce Hib transmission to unvaccinated children.

HEPATITIS A AND B

Burden of Suffering

Epidemics caused by hepatitis A virus (HAV) remain a major public health problem, with 26,796 cases reported in 1994 in the U.S.¹ HAV is transmitted through the fecal-oral route, and the most frequent source of infection is household or sexual contact with a person who has hepatitis A. Day care centers have become an important source of epidemic HAV infection.¹² In the U.S. each year, hepatitis B virus (HBV) causes an estimated 200,000 to 300,000 acute infections and 4,000–5,000 deaths from chronic liver disease and hepatocellular carcinoma.¹³ More than 1 million Americans have chronic HBV infection. HBV may be transmitted by perinatal (see Chapter 24), percutaneous, sexual, or mucosal exposure.¹⁴

Efficacy of Prophylaxis

Since the 1940s, passive immunization with immune globulin (IG), administered within 2 weeks of exposure, has been shown to be an effective means of preventing or markedly attenuating clinical hepatitis A in persons exposed to HAV.¹⁵ Studies in household contacts have shown that IG can reduce the incidence of clinical hepatitis A by 80–90%.¹⁶ The earlier that IG is given after exposure the more likely it is that protection will result.¹⁶ Adverse effects of IG include local symptoms and, less commonly, systemic symptoms such as headache, chills, and nausea.¹² Serious adverse effects with IG have been rare.¹³ There is no evidence of transmission of HBV, human immunodeficiency virus, or other viruses in the U.S. by IG prepared for intramuscular injection.¹³ Hepatitis C transmission has been reported with intravenous administration of an immune globulin product.^{16a}

Immunogenic inactivated hepatitis A vaccines, recently licensed in the U.S., have been shown to be highly protective against hepatitis A (see Chapters 65 and 66).^{17,18} Because an adequate immune response does not develop for 1–2 weeks after vaccine administration,^{17,19–22} the vaccine alone is likely to be inadequate for postexposure prophylaxis. Vaccine may be given simultaneously with IG for individuals with both immediate and continued risk of hepatitis A. Although studies have reported lower mean antibody titers when the vaccine is administered concomitantly with IG, vaccine seroconversion rates appear to be adequate.^{20,23,24}

Administration of hepatitis B immune globulin (HBIG) promptly after exposure and 1 month later has a combined efficacy of about 75% in protecting susceptible persons with perinatal, percutaneous, sexual, or mucosal exposure to HBV.^{25–28} Hepatitis B vaccine is highly immunogenic and efficacious and can be used to provide both preexposure and postexposure protection (see Chapters 24, 65, and 66).²⁹ Two recombinant DNA hepatitis B vaccines are currently licensed in the U.S. and, in recom-

mended dosages, provide similar seroconversion rates. Combined active-passive immunization has the advantage of providing both immediate and long-term protection.³⁰ For infants born to mothers who are infected with HBV, the combination of HBIG given at birth and hepatitis B vaccine given at birth and ages 1 and 6 months is 85–90% effective in preventing perinatal HBV transmission (see Chapter 24).^{31–34} Regimens involving a vaccine series alone have shown 70–85% efficacy in preventing perinatal transmission (see Chapters 24 and 65).

MENINGOCOCCAL INFECTION

Burden of Suffering

Infection with *Neisseria meningitidis* serotypes A, B, C, X, Y, Z, 29-E, and W-135 can lead to meningitis and fulminant septicemia. Meningococcal infections occur sporadically, with 2,886 cases reported in the U.S. in 1994.¹ The estimated incidence during 1989–1991 in the U.S. was 1/100,000 persons annually.³⁵ The potential exists for epidemic meningococcal disease.

Efficacy of Prophylaxis

Both chemoprophylaxis and vaccination are available for postexposure prophylaxis against meningococcal infection, although vaccines are not routinely recommended for postexposure prophylaxis. Rifampin prophylaxis in contacts of patients with meningococcal infection can reduce the rate of meningococcal colonization, thereby reducing the risk of secondary infection.^{36–38} Rifampin dosage schedules effective in eliminating meningococci in adults have included 600 mg taken once daily for 4 days or twice daily for 2 days.^{36–40} One study has shown that a single intramuscular dose of ceftriaxone is at least as effective as oral rifampin in eliminating pharyngeal carriage in family contacts;³⁹ its efficacy has only been confirmed for serogroup A strains.

Due to the relatively long interval (as long as 14–30 days) that can occur between primary and secondary cases,^{41,42} meningococcal vaccines also may be efficacious for postexposure prophylaxis against serogroups contained in the vaccine.⁴³ A quadrivalent vaccine effective against meningococcal serogroups A, C, Y, and W-135,^{12,44} is available in the U.S. and has been effective in interrupting epidemic disease in other developed countries.^{45,46} The serogroup A component is immunogenic in children 3 months of age,⁴⁷ but children less than 2 years of age do not always respond to the vaccine's other components. The current vaccine does not provide adequate long-term protection. A satisfactory vaccine to prevent group B meningococcal disease has yet to be developed. One vaccine against group B meningococcus was estimated to be 74% effective in children aged 4–6 years but was not proven ef-

fective in younger children.⁴⁸ Conjugate meningococcal vaccines, which may be more immunogenic, are currently being evaluated.^{49,50} The serogroup specificity of currently available meningococcal vaccines requires that the infecting organism be properly characterized.

RABIES

Burden of Suffering

In the absence of adequate prophylaxis, persons infected with rabies almost always die from rabies encephalitis.⁵¹ Human rabies is an uncommon disease in the U.S., with only 33 cases diagnosed from 1977 to 1994, 15 of which were associated with exposure to dogs outside the country or at the U.S.-Mexican border.⁵² Bat-associated rabies virus has been associated with at least 10 cases.⁵² Wild animals now constitute the largest source of human infection acquired in the U.S. A recent outbreak among raccoons in the northeastern states has been responsible for a large increase in the incidence of animal rabies, although no human transmission has been reported.⁵³ In the U.S., squirrels, chipmunks, and other rodents have not been implicated in any human cases.⁵¹ More than 18,000 persons receive postexposure prophylaxis yearly for rabies.⁵⁴ Another 10,000 persons at increased risk receive preexposure prophylaxis.

Efficacy of Prophylaxis

Currently recommended postexposure prophylaxis consists of wound cleansing, human rabies immune globulin (HRIG) administered at the site of the bite and into the gluteal muscle, and a vaccination series administered into the deltoid muscle. Two vaccine preparations, human diploid cell vaccine (HDCV) and rabies vaccine, adsorbed (RVA) are available in the U.S. No vaccine failure has been reported in the U.S. in anyone who received postexposure prophylaxis using the current regimen.⁵⁵ Field experience has shown that this regimen provides adequate virus-neutralizing antibody titers.⁵⁶⁻⁵⁹ Studies from developing countries have reported adequate antibody titers and clinical efficacy with varied dosages, schedules, and routes of administration of potent rabies vaccines (HDCV and others).^{55,60-62b} Deviations from current recommendations, including gluteal HDCV administration, inadequate wound cleansing, and incorrect use of HRIG, may have been responsible for 13 rabies cases that occurred after administration of postexposure prophylaxis in other countries.⁶³⁻⁶⁶ Two cohort studies have shown that gluteal, as opposed to deltoid, administration of HDCV results in lower antibody titers.^{67,68} Reported adverse effects of HDCV include systemic allergic reactions⁶⁹ and, rarely, Guillain-Barré-like illnesses.⁷⁰⁻⁷²

Preexposure rabies vaccination is recommended for persons at high risk of rabies exposure. A three-dose series of HDCV (1.0 mL intramuscularly [IM] or 0.1 mL intradermally) or RVA (1.0 mL IM), given in the deltoid region on days 0, 7, and 21 or 28, provides an antibody response in virtually all individuals, lasting at least 2 years.⁷³⁻⁷⁶ Recent studies have reported a continuous decline in antibody levels over time.^{77,78} A two-dose booster is therefore recommended after an exposure. One rabies case has been reported following preexposure rabies vaccination;⁷⁹ this patient did not receive the recommended two-dose booster following exposure. Immune complex hypersensitivity develops in 6% of persons given a HDCV booster dose after the initial series.^{69,80,81} A recent randomized clinical trial reports that purified HDCV used for boosters causes fewer severe and urticarial reactions.⁸²

TETANUS

Burden of Suffering

Largely as a result of childhood immunization, tetanus has become uncommon in the U.S., with only 51 cases reported in 1994.¹ Tetanus remains a serious disease with 24% of recent cases resulting in death. Reports may underrepresent tetanus mortality by as much as 60%.⁸³ Most persons with tetanus had not received a primary immunization series.⁸⁴ Seventy-eight percent of cases followed an acute injury, half of which were puncture wounds. At least half of cases of tetanus and deaths from tetanus occur in persons over the age of 60.^{1,84} In the third National Health and Nutrition Examination Survey (NHANES III), the prevalence of immunity to tetanus declined with increasing age beginning at age 40.⁸⁵ More than 80% of persons aged 6-39 years, but only 28% of persons 70 years and older, had protective antibody levels.

Efficacy of Prophylaxis

The use of equine tetanus immune globulin (TIG) resulted in a dramatic decline in the incidence of clinical tetanus during World War I.^{86,87} Numerous animal trials^{88,89} and an uncontrolled experiment involving two humans⁹⁰ established the protective serum antitoxin level at 0.01 unit/mL, although there have been several case reports of clinical tetanus despite higher serum antitoxin levels.⁹¹⁻⁹³ In unimmunized individuals, the combination of 250 units human TIG and 0.5 mL adsorbed tetanus toxoid provides a serum antitoxin level of 0.01 unit/mL immediately that lasts beyond 4 weeks.⁹⁴⁻⁹⁸ Individuals who have completed a primary vaccination series (three doses and one booster) have serum antitoxin levels of 0.01 unit/mL for at least 20 years.⁹⁹⁻¹⁰¹ Booster immunization results in

a vigorous anamnestic response after periods as long as 20–30 years following a three-dose primary vaccination series,^{100,101} recent data suggest, however, that some individuals who receive their first booster 17–20 years after a primary vaccination series may not develop protective antitoxin levels immediately.¹⁰² There is animal evidence to suggest that protection begins before a rise in antitoxin is detected.¹⁰³ Furthermore, tetanus is unlikely in persons who have received a primary vaccination series at any time.^{83,104} Serious adverse effects of tetanus toxoid are rare, although several case reports and a case series have described allergic or Arthus-like reactions and peripheral neuropathy following frequent boosters.^{105,106}

Recommendations of Other Groups

The Advisory Committee on Immunization Practices,^{13,54,55,74,107–109} the American Academy of Pediatrics,¹² and the American College of Physicians¹¹⁰ have issued recommendations on postexposure prophylaxis for Hib disease, hepatitis A and B, meningococcal infection, rabies, and tetanus that are similar to those described below. The American College of Obstetricians and Gynecologists has issued detailed guidelines on the use of vaccines during pregnancy.¹¹¹

CLINICAL INTERVENTION

Postexposure prophylaxis is recommended for selected persons with exposure or possible exposure to *H. influenzae* type b, hepatitis A, hepatitis B, meningococcal, rabies, or tetanus pathogens (“A” recommendation). Details are given below.

H. influenzae Type b Disease Oral rifampin prophylaxis should be prescribed promptly for patients with Hib disease and for all their household contacts regardless of age, if at least one of the contacts is a child less than 4 years of age who has not been fully vaccinated with a licensed Hib conjugate vaccine. Experts define a household contact as a person residing with the index patient or a nonresident who spent 4 hours or more with the index patient for at least 5 of the 7 days preceding the day of hospital admission of the index patient.¹² The dosage of rifampin for children and adults is 20 mg/kg (maximum 600 mg) as a single daily dose for 4 days. The dose for infants younger than 1 month of age has not been established, but experts recommend reducing the dose to 10 mg/kg/day.¹² Published guidelines also recommend postexposure prophylaxis for all day care attendees and staff, regardless of vaccination status, when 2 or more cases have occurred within 60 days and unvaccinated or incompletely vaccinated children attend.¹² When a single case has occurred in a day care center, rifampin prophylaxis should be given to all attendees and staff

only if unvaccinated or incompletely vaccinated children less than 2 years of age are present in the center for at least 25 hours per week.¹² Day care contacts of children with Hib disease should receive rifampin prophylaxis using the same regimen as for household contacts. All children who are less than 5 years of age and who are unvaccinated or incompletely vaccinated should be brought up to date by administration of the recommended doses of a licensed Hib conjugate vaccine (see Chapter 65).

Hepatitis A. Immune globulin should be administered at a dose of 0.02 mL/kg IM as soon as possible within 2 weeks of exposure to sexual and close household contacts of persons with hepatitis A, staff and children at day care centers where a hepatitis A case is recognized, staff and patients at custodial institutions where HAV transmission is documented, and food handlers at food service establishments where a food handler is diagnosed with hepatitis A. Detailed published protocols are available.^{12,13,110} Hepatitis A vaccine is recommended for persons \geq 2 years of age who are at high risk for infection (see Chapters 65 and 66).

Hepatitis B. The use of HBIG and hepatitis B vaccine is recommended to prevent HBV infection in the following circumstances: birth of an infant to a hepatitis B surface antigen (HBsAg)-positive mother (see Chapter 24), percutaneous or permucosal exposure to HBsAg-positive blood, sexual exposure to an HBsAg-positive person, and household exposure of an infant less than 1 year of age to a primary caregiver who has acute HBV infection. For needlesticks and other percutaneous exposures, and for sexual exposures, the precise protocol for postexposure prophylaxis against hepatitis B depends on the nature of the exposure, the availability from the source of exposure of blood for testing, the HBsAg status of the source, and the hepatitis B vaccination and vaccine-response status of the exposed person. Detailed guidelines are available.^{12,13} See Chapter 24 for detailed recommendations on prenatal screening and perinatal postexposure prophylaxis against HBV infection, and Chapters 65 and 66 for recommendations regarding routine use of hepatitis B vaccine in children and adults.

Meningococcal Infection. Oral rifampin prophylaxis is indicated for household or day care contacts of persons with meningococcal infection, as well as for those with direct exposure to oral secretions (e.g., kissing) of an index patient. The dose is 600 mg for adults, 10 mg/kg for children 1–12 years of age, and 5 mg/kg for infants 3 months to 1 year of age, given twice daily for 2 days (for a total of four doses). Rifampin is contraindicated during pregnancy. There is currently insufficient evidence to recommend for or against the use of ceftriaxone for routine meningococcal prophylaxis (“C” recommendation). Ceftriaxone at a dose of 250 mg IM for adults and 125 mg IM for children is efficacious for eliminating meningococcal carriage of serogroup A strains of meningococcus. In outbreaks

caused by serogroup A strains, the use of meningococcal vaccine is recommended in addition to antibiotic prophylaxis for all persons 3 months of age. In outbreaks caused by serogroup C, Y, and W-135 strains, vaccination is recommended for persons 2 years of age.¹²

Rabies. Postexposure prophylaxis against rabies should be instituted if a possible exposure to rabies has occurred. Criteria for making this assessment, which include the type of animal (e.g., carnivorous wild animals, bats), the circumstances of the attack (e.g., unprovoked attack), and the type of exposure (e.g., bite), are available in published guidelines^{55,110} and from local health departments. HRIG is given at a dose of 20 IU/kg; half of the dose is infiltrated around the wound, and the remainder is given intramuscularly at another site. The upper outer gluteal region of the buttocks is preferred because of the large volume administered. HDCV or RVA is administered in the deltoid muscle in five 1.0 mL injections on days 0, 3, 7, 14, and 28. Persons who were immunized before the incident require only two 1.0 mL doses of vaccine on days 0 and 3, and do not require HRIG. Preexposure prophylaxis with three injections (1.0 mL IM or 0.1 mL intradermally) of vaccine (days 0, 7, and 21 or 28) is recommended for those at high risk of contact with rabies virus, including rabies laboratory workers, veterinarians, animal handlers, and persons planning to spend more than 1 month in countries where rabies is endemic. Persons with frequent exposure should have their antibody level checked every 6 months and receive booster injections if antibody titers are below protective levels. Published guidelines suggest more frequent testing for certain continuously exposed laboratory workers.^{55,110}

Tetanus. All individuals who have not completed a primary vaccination series of at least three doses and who present with wounds should receive 0.5 mL IM adsorbed tetanus toxoid. Diphtheria and tetanus toxoids and whole-cell or acellular pertussis vaccine adsorbed (DTP or DTaP, respectively) or diphtheria and tetanus toxoids adsorbed (DT) (as appropriate) for patients less than 7 years old and tetanus and diphtheria toxoids adsorbed (Td) for patients 7 years old, are preferred so that adequate levels of diphtheria and pertussis immunity are maintained (see Chapters 65 and 66). For a wound that is serious and/or contaminated (e.g., with dirt, feces), the incompletely vaccinated patient should receive both vaccine and human TIG (250 units IM at a separate site). Although there is inadequate evidence on which to make a recommendation for or against TIG prophylaxis for clean, minor wounds in inadequately immunized persons, experts recommend against the routine use of human TIG.^{12,109,110} For individuals presenting with a wound who have completed a primary vaccination series of at least three doses, tetanus toxoid is recommended if more than 10 years have elapsed since the last dose or if only three doses of fluid

toxoid (which was used prior to the availability of adsorbed toxoid) were received. There is insufficient evidence to document increased risk after a shorter interval for major or contaminated wounds, but expert opinion supports vaccination when more than 5 years have elapsed.^{12,109,110} Human TIG is not recommended for persons who have completed a primary vaccination series. All wounds should be properly cleaned and debrided.

Influenza. See Chapter 66 for recommendations regarding the use of amantadine and rimantadine to protect against influenza A.

The draft update of this chapter was prepared for the U.S. Preventive Services Task Force by Robert Reid, MD, MPH, Carolyn DiGiuseppi, MD, MPH, Cameron Grant, MBChB, and Modena Wilson, MD, MPH.

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