

CENTERS FOR DISEASE CONTROL AND PREVENTION

2009 Immunization Update—on MMR, HAV, and HBV Vaccines

This nonaccredited section highlights ACIP recommendations for the measles, mumps, and rubella (MMR) vaccine, and the hepatitis A (HAV) and hepatitis B (HBV) vaccines.

Measles, Mumps, and Rubella Vaccine

Measles is an acute viral infectious disease that was almost universal during childhood in the prevaccine era. By the time children were 15 years old, more than 90% were immune from having the disease. Following introduction of the first measles vaccine in 1963, measles incidence fell 98% in the United States. However, in developing countries, measles is still common and often fatal. According to World Health Organization data, more than 20 million cases and 242,000 deaths from measles occurred in 2006.¹

Measles is transmitted from person to person via respiratory droplets. It is highly communicable, with secondary attack rates more than 90% in susceptible individuals. Fever is followed by cough, coryza (runny nose), or conjunctivitis; then the classic maculopapular eruption, which usually lasts for 5 to 6 days. Anorexia, diarrhea (especially in infants), and lymphadenopathy also may occur. Complications of measles, occurring in about 30% of cases, include diarrhea, otitis media (almost exclusively in children), pneumonia, and acute encephalitis. From 1985 to 1992, death from measles was reported in approximately 2 per 1000 cases reported in the United States. Since 1995, an average of 1 measles-related death per year has been reported.¹

Although measles incidence has declined tremendously since the vaccine was introduced, disease resurgences have been observed. In 1989 to 1991, a dramatic rise in measles cases occurred, with more than 55,000 cases reported. In addition, the age distribution shifted from school-aged children to those <5 years of age. Over the 3-year resurgence period, there were 123 measles-related deaths; nearly half were in children <5 years of age, and 90% of deaths occurred among those with no history of measles vaccination. The measles resurgence was attributed largely to low vaccination coverage.^{1,2}

Measles incidence declined rapidly after the 1989 to 1991 flare-up, thanks to intensive efforts to vaccinate preschool-aged children. Among 2-year-olds, immunization rates rose from 70% in 1990 to 91% in 1997. Since then, <200 cases per year have been reported in the United States. In 2004, a record annual low of 37 cases was reached.¹ According to epidemiologic and virologic data, measles transmission had been interrupted in the United States and, in 2000, endogenous measles was declared eliminated.³ Cases

were imported from other countries or linked to imported cases. In 2001, 48% of all cases were in adults.¹

Although an average of 63 measles cases per year were reported during 2000 to 2007, Centers for Disease Control and Prevention (CDC) data for the first 6 months of 2008 show that 131 cases occurred in the United States. Of these, 89% were imported from or associated with importations from other countries, especially Europe, where measles outbreaks are ongoing and vaccine coverage is suboptimal.^{4,5} Among these cases, 76% occurred in individuals <20 years of age, and 91% were in people who were unvaccinated or had unknown vaccination status.⁴

Experts caution that as measles cases continue to be imported into the United States, endemic transmission may become re-established unless immunization coverage is sustained at high levels.⁶ Healthcare providers must remain attentive to ensuring that all appropriate candidates for measles vaccination—including themselves—are immunized or have documented evidence of immunity. Similar to that for varicella, acceptable evidence of immunity to measles (and rubella) includes the following:

- Written documentation of complete vaccination (2 doses of measles, mumps, and rubella [MMR] vaccine at least 4 weeks apart) or history of 1 rubella and 2 measles vaccine doses (with 2 doses of MMR being preferable)
- Documented laboratory evidence of measles and rubella immunity (an equivocal result represents nonimmunity)
- Clinician-diagnosed measles (does not apply to rubella)
- Born in the United States before 1957 (if born before 1957 and there is no measles disease history, consider 2 doses of MMR vaccine [5% to 9% test as nonimmune]). *Note:* presumptive immunity if born before 1957 does not apply to healthcare personnel.

Mumps

High MMR vaccination rates also must be sustained to control the occurrence of mumps. This viral infection also was very common in children and adults (especially in military personnel) in the prevaccine era. Clinical manifestations include nonspecific symptoms such as myalgias, anorexia, malaise, headache, and low-grade fever, as well as the characteristic parotitis (swollen parotid glands), which occurs in 30% to 40% of infected individuals. Transmitted via the respiratory route, mumps is highly contagious, although somewhat less so than measles or varicella.¹ Complications may include aseptic or symptomatic meningitis, orchitis in postpubertal males, and oophoritis in postpubertal females. Rare complications include pancreatitis, deafness, myocarditis, and arthralgia and arthritis. During 1980 to 1999, an average of 1 death per year from mumps was reported.

In 1964, approximately 212,000 cases of mumps occurred in the United States. After the mumps vaccine was licensed in 1967, the incidence of mumps quickly declined. For example, in 1983 to 1985, about 3000 cases were reported each year. However, in 1986 to 1987 there was a resurgence in the occurrence of mumps, with a peak of 12,848 cases in 1987. Many cases occurred in older high school and college-aged students who were born before routine

mumps vaccination was recommended. Mumps cases again steadily declined, reaching a low of 258 cases in 2004.

Then in 2006 more than 6000 cases occurred in a multistate outbreak, mostly in the Midwest. A large percentage of the cases occurred among college students, and many of them had been vaccinated with 1 or 2 doses of MMR.¹ The 2006 mumps resurgence prompted the CDC's Advisory Committee on Immunization Practices (ACIP) to issue an updated recommendation regarding acceptable presumptive evidence of immunity to mumps.

Redefined evidence of immunity now includes documentation of 2 doses of live mumps vaccine for school-aged children and adults at high risk (including persons who work in healthcare facilities, international travelers, and students in post-high-school institutions). Other criteria are unchanged (ie, birth before 1957, documentation of physician-diagnosed mumps, or laboratory evidence of immunity). In addition, healthcare facilities should consider recommending 1 dose of MMR vaccine to unvaccinated healthcare workers born before 1957 who do not have other evidence of mumps immunity.^{7,8}

Who Should Receive MMR Vaccine?

The ACIP recommends that the combination MMR vaccine be used when any of the individual components is indicated to ensure immunity to all 3 viruses. Adolescents 13 to 18 years of age without evidence of immunity should receive 2 doses of MMR vaccine, at least 28 days apart; those who received 1 dose should receive a second dose at the appropriate interval. Adults born before 1957 generally are considered immune to measles and mumps. Those born after 1957 should receive 1 or more doses of MMR unless they have a medical contraindication or evidence of immunity to measles or mumps. A second dose is recommended for those at high risk (eg, recent exposure to the virus, working in a healthcare facility, attending post-secondary educational institutions, planning international travel). For nonpregnant women whose rubella vaccination history is unreliable or who lack laboratory evidence of immunity, 1 dose of MMR vaccine is recommended for protection against rubella. (Detailed recommendations for each vaccine component are provided in the footnotes to the Adult Immunization schedule, available at: <http://www.cdc.gov/mmwr/PDF/wk/mm5753-Immunization.pdf>)

Contraindications, Precautions, and Adverse Reactions

Individuals with a severe allergic reaction to a vaccine component or following a prior dose of MMR vaccine generally should not be vaccinated with MMR. The vaccine is contraindicated in pregnancy and in people with severe immunocompromising conditions. As with other vaccinations, individuals with acute moderate or severe illness should wait until their condition improves before being vaccinated. For patients receiving antibody-containing blood products, MMR vaccine should be administered 2 weeks before or 3 months following administration. Mild adverse effects following vaccination include fever, mild rash, and swollen glands. Some patients experience moderate reactions such as temporary pain and stiffness, low platelet count, and seizure caused by fever. Severe reactions are rare.

Hepatitis A and B Vaccines

Hepatitis A and hepatitis B are distinctly different viral infections of the liver. Although the diseases have some clinical and epidemiologic features in common, such as symptoms and certain behavioral risk factors, they have different etiologic agents, routes of transmission, and courses of illness. Fortunately, both are vaccine-preventable.

Hepatitis A

Hepatitis A, formerly called “infectious hepatitis,” is caused by the hepatitis A virus (HAV) and is transmitted primarily by the fecal-oral route (eg, poor hand washing after bathroom use, sexual activities involving oral-anal contact with an infected person) or via contaminated food or water (more likely in countries where the disease is common and sanitary conditions are poor). Hepatitis A is self-limited and does not result in chronic infection or liver disease. However, disease severity can range from mild illness lasting a few weeks to severe, debilitating illness lasting several months. Further, approximately 10% to 15% of patients experience prolonged or relapsing symptoms that may persist for up to 6 months.¹

Hepatitis A has an approximately 28-day incubation period, with a range of 15 to 50 days. In adults and older children, symptoms typically include an abrupt onset of fever, malaise, anorexia, nausea, and abdominal discomfort, followed a few days later by dark urine and jaundice. In children <6 years of age, 70% of infections are asymptomatic and may go unrecognized. Youngsters who do exhibit symptoms rarely have jaundice. Fulminant hepatitis, although rare, can occur with HAV infection; the case-fatality rate among all age groups is 0.3%, but may be as high as 1.8% among adults >50 years of age.⁹ Individuals infected with hepatitis A are most likely to transmit the virus 1 to 2 weeks before they show signs of illness, because virus concentration in stool is highest during this time. Transmission risk thereafter decreases and is minimal by the week after jaundice appears. Infection with HAV confers life-long immunity. Management of hepatitis A is supportive, as there are no specific drug therapies for this infection.¹

In the United States, rates of hepatitis A have declined by 92% since the first hepatitis A vaccine was licensed in 1995.¹⁰ The largest number of cases reported in 1 year, in 1971, was 59,606. By 2004, the number of reported cases had fallen to 5970. In 2007, a record low 2979 acute symptomatic cases of hepatitis A were reported. This number reflects reported cases, and the actual number of cases—adjusting for underreporting and asymptomatic cases—is estimated to be much higher, approximately 25,000 for 2007. Still, the decreased incidence in hepatitis A is dramatic and likely attributable to wider vaccine use.^{1,10}

Two inactivated whole-virus hepatitis A vaccines were licensed in the United States in 1995 and 1996. Both vaccines are available in pediatric (1-18 years of age) and adult (≥19 years of age) formulations and provide long-term protection, possibly for 20 years or more, against HAV. In 2005, the ACIP recommended that routine hepatitis A vaccination for children 12 to 23 months of age be integrated into the childhood immunization schedule. Adults at increased risk for hepatitis A infection or complications from HAV infection should be

vaccinated, too. For both children and adults, 2 doses are administered intramuscularly (IM) into the deltoid muscle: a primary dose, followed by a second dose 6 to 12 or 18 months later (depending on which proprietary vaccine is used). The minimal interval between the first and second dose is 6 months. The dose formulation used must be based on the patient's age. For example, if an 18-year-old who received a first dose of pediatric formulation vaccine returns for the second dose at age 19, the second dose administered should be the adult formulation.

Another vaccine also is available for adults: a combination hepatitis A and hepatitis B vaccine licensed in 2001. The combination vaccine is approved for use in people ≥ 18 years of age who have indications for hepatitis A and hepatitis B vaccines. The 3-dose series is administered at 0, 1, and 6 months. An alternative accelerated dosing schedule also has been approved.¹

Who Should Receive Hepatitis A Vaccine?

The ACIP recommends hepatitis A vaccination for adolescents and adults who are at increased risk for hepatitis A or are at increased risk for complications from hepatitis A. Groups with the following risk factors should be vaccinated:

- **Medical:** chronic liver disease, including hepatitis C; clotting factor disorders
- **Behavioral:** men who have sex with men; users of illegal drugs (injection and noninjection)
- **Occupational:** people who work with HAV-infected primates; people working with HAV in a research laboratory setting (but not healthcare personnel, day-care workers, or food handlers)
- **Other:** people traveling to or working in areas where hepatitis A is endemic; any person wishing to obtain protection from hepatitis A

Hepatitis B

Hepatitis B, once known as “serum hepatitis,” is caused by the hepatitis B virus (HBV), and acute infection has some characteristics similar to those of hepatitis A. HBV, however, is transmitted primarily by parenteral or mucosal exposure to body fluids from people who have acute or chronic HBV infection. Blood and serous fluids contain the highest concentrations of HBV, while lower amounts of the virus are found in semen and saliva. In the United States, sexual contact (either heterosexual or homosexual) with an infected person is the most important way hepatitis B is spread. The virus also can be transmitted by percutaneous inoculation with contaminated needles during injection drug use. Healthcare workers may be exposed to the virus through needle sticks or injury from sharp instruments, as well as through eye splashes or mouth pipetting of infective serum or plasma. Babies born to HBV-infected mothers are at high risk for infection via perinatal transmission at birth.¹

The incubation period for hepatitis B ranges from 60 to 150 days, with an average of 90 days. Infants and children ≥ 5 years of age typically are asymptomatic, and only about 30% to 50% of children ≥ 5 years of age and adults experience clinical signs or symptoms.¹¹ When present, symptoms have an insidious onset and are often nonspecific, with malaise, anorexia, nausea, vomiting, abdominal pain, fever, headache, myalgias, skin rashes, arthralgia, or arthritis

for several days, followed by jaundice, light-colored stools, and hepatic tenderness that may last 1 to 3 weeks. Malaise and fatigue may last for weeks or months after jaundice and other symptoms resolve. Most immunocompetent adults with acute hepatitis B infection recover completely and become immune to future HBV infection. However, a fatality rate of 0.5% to 1.0% in reported cases of acute infection has been observed, with the highest rates in adults >60 years of age.¹¹ As with hepatitis A, management of hepatitis B includes supportive therapies.

An important aspect of hepatitis B infections is that they may progress to chronic hepatitis B, a serious disease that can result in long-term consequences such as liver damage, cirrhosis, liver failure, liver cancer, hepatocellular carcinoma, and death. The risk of chronic hepatitis B decreases with increasing age: about 90% of infants who acquire HBV at birth become chronically infected, and, of children infected between 1 and 5 years of age, 30% to 50% develop chronic infection. About 5% of adults with acute hepatitis B go on to develop chronic disease.¹ Immunosuppressed people, such as hemodialysis patients and those with the human immunodeficiency virus (HIV) infection, are at greater risk of developing chronic hepatitis B. Many people with chronic hepatitis B remain asymptomatic for years until they develop serious liver conditions such as cirrhosis or end-stage liver disease.¹¹ An estimated 1.2 million people in the United States have chronic hepatitis B; these individuals remain sources of HBV transmission to others.¹²

In 2005, there were an estimated 51,000 new acute hepatitis B infections in the United States (adjusted for under-reporting and asymptomatic infections), while in 1990, approximately 232,000 new cases occurred. This translates to an overall incidence of 1.9 per 100,000 population in 2005—a 78% decrease from 1990 rates (8.5 per 100,000 population).¹¹ The largest declines in incidence occurred among children and adolescents, reflecting the effect of routine childhood vaccinations. Although incidence also decreased among adults, the decline was smaller. By far, adults continue to account for the majority of hepatitis B cases. In addition, hepatitis B incidence has increased among some adult age groups.¹²

Public health programs and clinical care providers need to ensure that adults at high risk are offered hepatitis B vaccine.¹³ The ACIP has recommended an enhanced comprehensive hepatitis B immunization strategy for adults. One component calls for healthcare providers to implement standing orders to identify adults recommended for hepatitis B vaccination and administer vaccination as part of routine clinical services.¹¹

The first hepatitis B vaccine, a plasma-derived formulation, was licensed in 1981. This was replaced when 2 recombinant hepatitis B vaccines were licensed in 1986 and 1989; these vaccines cannot produce HBV infection because no viral DNA or complete viral particles are used to make them. Both vaccines are available in pediatric and adult formulations. Hepatitis B vaccine is a 3-dose series. For adolescents and adults, vaccine is administered by IM injection in the deltoid muscle of the arm. The usual schedule for adolescents and adults includes a first dose, followed 1 month later by the second dose (minimum interval of 4 weeks between doses 1 and 2), and the third dose 5 months after the second dose (minimum interval of 8 weeks between doses 2 and 3). There should be no less than 16 weeks between the first and

third doses. As mentioned previously, a combination hepatitis A and hepatitis B 3-dose vaccine is available for use in people ≥ 18 years of age who have indications for both hepatitis A and hepatitis B vaccines.¹

More than 90% of healthy adults and more than 95% of infants, children, and teenagers develop adequate antibody responses to hepatitis B vaccine after 3 doses.¹ Although postvaccination serologic testing is not routinely recommended for adults, it should be considered for certain groups, such as chronic hemodialysis patients, other immunocompromised patients, people with HIV infection, and sex partners of patients with hepatitis B infection. Healthcare workers who have contact with patients or blood and are at ongoing risk for needle stick injuries should be tested routinely for antibody 1 to 2 months after completion of the 3-dose series.

Individuals who do not respond to a primary series of hepatitis B vaccine should complete another 3-dose series (1 time only). Studies indicate that 15% to 25% of people will respond after 1 more dose, and 30% to 50% will respond after 3 more doses,¹ although response rates of 44% to 100% to a 3-dose revaccination series have also been reported.¹¹ Individuals who remain seronegative after 6 total doses of hepatitis B vaccine should be managed as a nonresponder.

Who Should Receive Hepatitis B Vaccine?

Risk for hepatitis B generally is highest when individuals are in frequent contact with blood from infected persons through lifestyle, occupational, or environmental circumstances. The ACIP recommends that adolescents and adults with the following risk factors be vaccinated:

- **Medical:** patients with chronic liver disease, end-stage renal disease, or HIV infection
- **Behavioral:** men who have sex with men; injection drug users; persons with >1 sex partner during the previous 6 months
- **Occupational:** healthcare personnel and public safety workers exposed to blood or body fluids
- **Other:** household contacts and sex partners; clients and staff of institutions for the developmentally delayed; international travelers to high-risk areas; any person wishing to obtain protection from hepatitis B—acknowledgment of a specific risk factor is not a requirement for vaccination

Contraindications, Precautions, and Adverse Reactions for Hepatitis A and Hepatitis B Vaccines

These are similar for both vaccines. Contraindications include severe allergic reaction to a vaccine component following a prior dose and moderate or severe acute illness. No special precautions are needed when vaccinating immunocompromised persons; however, vaccine response may be suboptimal. Safety studies in pregnancy have not been performed; benefit must be weighed against potential risks. Adverse reactions with both vaccines are generally mild and local (pain or erythema at the injection site). Mild systemic reactions (fatigue, headache, low-grade fever) occur at low rates.

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