

The first descriptions of hepatitis (epidemic jaundice) are generally attributed to Hippocrates. Outbreaks of jaundice, probably hepatitis A, were reported in the 17th and 18th centuries, particularly in association with military campaigns. Hepatitis A (formerly called infectious hepatitis) was differentiated epidemiologically from long-incubation period hepatitis B in the 1940s. The development of serologic tests allowed definitive diagnosis of hepatitis B. Identification of the virus, and development of serologic tests in the 1970s helped differentiate hepatitis A from other types of non-B hepatitis.

Hepatitis A is the most common type of hepatitis reported in the United States. Until recently, the primary methods used for preventing hepatitis A have been hygienic measures and passive immunization with immune globulin (IG) to provide short-term protection. Hepatitis A vaccines were licensed in 1995 and 1996 for use in persons  $\geq 2$  years of age, and can provide long-term protection against hepatitis A virus (HAV) infection. The similarities between the epidemiology of hepatitis A and poliomyelitis suggest that widespread vaccination of appropriate susceptible populations can substantially lower disease incidence, eliminate virus transmission, and ultimately, eradicate HAV infection.

## HEPATITIS A VIRUS

Hepatitis A is caused by infection with HAV, a nonenveloped RNA virus that is classified as a picornavirus. It was first isolated in 1979. Humans are the only natural host, although several nonhuman primates may be experimentally infected. Depending on conditions, HAV can be stable in the environment for months. The virus is relatively stable at low pH levels and moderate temperatures, but can be inactivated by high temperature ( $>185^{\circ}\text{F}$ ), formalin, and chlorine.

## PATHOGENESIS

HAV is acquired by mouth (fecal-oral) and replicates in the liver. After 10-12 days, virus is present in blood and is excreted via the biliary system into the feces. Peak titers occur during the 2 weeks before onset of illness. Although virus is present in serum, its concentration is several orders of magnitude less than in feces. Virus excretion begins to decline at the onset of clinical illness, and has decreased significantly 7-10 days after onset of symptoms. Most infected people no longer excrete virus in the feces by the third week of illness. Children may excrete virus longer than adults.

## CLINICAL FEATURES

The **incubation period** of hepatitis A is 28 days (range 15–50 days). The clinical course of acute hepatitis A is indistinguishable from that of other types of acute viral hepatitis. The illness typically has an abrupt onset of signs and symptoms that include fever, malaise, anorexia, nausea, abdominal discomfort, dark urine and jaundice. Clinical illness usually does not last longer than 2

### Hepatitis A

- Epidemic jaundice described by Hippocrates
- Differentiated from hepatitis B in 1940s
- Serologic tests developed in 1970s
- Most commonly reported type of hepatitis in the United States

### Hepatitis A Virus

- Picornavirus (RNA)
- Humans are only natural host
- Stable at low pH
- Inactivated by high temperature, formalin, chlorine

### Hepatitis A Pathogenesis

- Entry into mouth
- Viral replication in the liver
- Virus present in blood and feces 10-12 days after infection
- Virus excretion may continue for up to 3 weeks after onset of symptoms

## Hepatitis A Clinical Features

- Incubation period 28 days (range 15-50 days)
- Illness not specific for hepatitis A
- Likelihood of symptomatic illness directly related to age
- Children generally asymptomatic, adults symptomatic

months, although 10%-15% of persons have prolonged or relapsing signs and symptoms for up to 6 months. Virus may be excreted during a relapse.

The likelihood of symptomatic illness from HAV infection is directly related to age. Among children <6 years of age, most (70%) infections are asymptomatic. Among older children and adults, infection is usually symptomatic with jaundice occurring in >70% of patients. HAV infection occasionally produces fulminant hepatitis A.

## COMPLICATIONS

Fulminant hepatitis A causes about 100 deaths per year in the U.S. The case-fatality rate among reported cases of all ages is approximately 0.3%, but can be higher among older persons (approximately 2% among persons >40 years of age).

Hepatitis A results in substantial morbidity with associated costs caused by medical care and work loss. Hospitalization rates for hepatitis A are 11%-22%. Adults who become ill lose an average of 27 work days per illness and health departments incur the costs of postexposure prophylaxis for 11 contacts per case. Average direct and indirect costs of hepatitis A range from \$1,817 to \$2,459 per adult case and \$433 to \$1,492 per pediatric case. In 1989, the estimated annual U.S. total cost of hepatitis A was >\$200 million.

## LABORATORY DIAGNOSIS

Hepatitis A cannot be distinguished from other types of viral hepatitis on the basis of clinical or epidemiologic features alone. Serologic testing is required to confirm the diagnosis. Virtually all patients with acute hepatitis A have detectable anti-HAV IgM antibody. Acute HAV infection is confirmed during the acute or early convalescent phase of infection by the presence of **anti-HAV IgM** antibody in serum. IgM generally becomes detectable 5-10 days before the onset of symptoms and can persist for up to 6 months.

**Anti-HAV IgG** antibody appears in the convalescent phase of infection, remains present in serum for the lifetime of the person and confers enduring protection against disease. The antibody test for total anti-HAV measures both anti-HAV IgG and anti-HAV IgM. Persons who are total anti-HAV positive and anti-HAV IgM negative have serologic markers indicating immunity consistent with either past infection or vaccination.

Molecular virology methods such as polymerase chain reaction (PCR)-based assays may be used to amplify and sequence viral genomes. These assays are helpful to investigate common source outbreaks of hepatitis A. Providers with questions about molecular virology methods should consult with their state health department or the Division of Viral Hepatitis, CDC.

## MEDICAL MANAGEMENT

There is no specific treatment for hepatitis A virus infection. Treatment and management of HAV infection is supportive.

## EPIDEMIOLOGY

### OCCURRENCE

Hepatitis A occurs throughout the world. Some areas are highly endemic, particularly Central and South America, Africa, the Middle East, Asia, and the Western Pacific.

### RESERVOIR

Humans are the only natural reservoir of the virus. There are no insect or animal vectors. A chronic HAV carrier state has not been reported.

### TRANSMISSION

HAV infection is acquired primarily by the fecal-oral route by either person-to-person contact or ingestion of contaminated food or water. Because the virus is present in blood during the illness prodrome, HAV has been transmitted on rare occasions by transfusion. Although HAV may be present in saliva, transmission by saliva has not been demonstrated. Waterborne outbreaks are infrequent and are usually associated with sewage-contaminated or inadequately treated water.

### TEMPORAL PATTERN

There is no appreciable seasonal variation in hepatitis A incidence.

### COMMUNICABILITY

Viral shedding persists for 1 to 3 weeks. Infected persons are most likely to transmit HAV 1 to 2 weeks before the onset of illness, when HAV concentration in stool is highest. The risk then decreases and is minimal the week after the onset of jaundice.

### RISK FACTORS

From 1990 through 2000, the most frequently reported source of infection was personal contact (household or sexual) with an infected person (14%). Two percent of cases involved a child or employee in daycare; 6% of cases were a contact of a child or employee in daycare; 5% of cases reported recent international travel; and 4% of cases reported being part of a recognized foodborne outbreak. Injection drug use was a reported risk factor in 6% of cases; men who have sex with men represented 10% of cases. Forty-five percent of reported hepatitis A cases could not identify a risk factor for their infection.

### Hepatitis A Epidemiology

• Reservoir	Human. Endemic
• Transmission	Fecal-oral
• Temporal pattern	None
• Communicability	2 weeks before to 1 week after onset

Hepatitis A – United States, 1990-2000 Risk Factors



Groups at increased risk of hepatitis A or its complications include international travelers, men who have sex with men, and illegal drug users. Outbreaks of hepatitis A have also been reported among person working with hepatitis A-infected primates. This is the only occupational group known to be at increased risk of hepatitis A.

Persons with chronic liver disease are not at increased risk of infection, but are at increased risk of fulminant hepatitis A. Persons with clotting-factor disorders may be at increased risk of HAV because of administration of solvent-detergent-treated factor VIII and IX concentrates.

Food handlers are not at increased risk for hepatitis A because of their occupation, but are noteworthy because of their critical role in common-source foodborne HAV transmission. Health-care workers do not have an increased prevalence of HAV infections, and nosocomial HAV transmission is rare. Nonetheless, outbreaks have been observed in neonatal intensive care units and in association with adult fecal incontinence. Institutions for persons with developmental disabilities previously were sites of high HAV endemicity. But as fewer children have been institutionalized and conditions within these institutions have improved, HAV incidence and prevalence have decreased. However, sporadic outbreaks can occur. Schools are not common sites for HAV transmission. Multiple cases among children at a school require investigation of a common source. Workers exposed to sewage have not reported any work-related HAV infection in the U.S., but serologic data are not available.

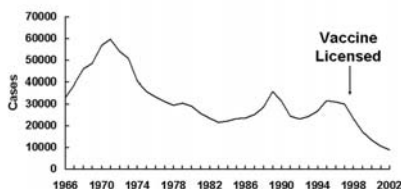
Children play an important role in HAV transmission. Children generally have asymptomatic or unrecognized illnesses, so they may serve as a source of infection, particularly for household or other close contacts.

## SECULAR TRENDS IN THE UNITED STATES

In the United States, hepatitis A has occurred in large nationwide epidemics approximately every 10 years, with the last increase in cases in 1989. However, between epidemics HAV infection continues to occur at relatively high rates. Hepatitis A became nationally reportable as a distinct entity in 1966. The largest number of cases reported in one year (59,606) was in 1971. In 2002, a total of 10,609 cases of hepatitis A were reported. After adjusting for under-reporting, 93,000 infections are estimated to have occurred in 2002, approximately half of which were symptomatic. Hepatitis A rates have been declining since 1995, and since 1998 have been at historically low levels. The wider use of vaccine is probably contributing to this marked decrease in hepatitis A rates in the United States. From 1987 through 1997, the average annual incidence of reported hepatitis A in the U.S. was approximately 10 cases per 100,000 population.

**The highest rates of hepatitis A are among children 5-14**

Hepatitis A – United States, 1966-2002



**years of age** (15–22 cases per 100,000 population in 1987–1997). Approximately one third of reported cases occur among children <15 years of age.

Based on testing from phase 1 of the Third National Health and Nutrition Examination Survey (NHANES III) conducted in 1988–1994, the prevalence of total antibody to HAV (anti-HAV) among the general U.S. population is 33%. Seroprevalence of HAV antibody increases with age, from 9% among 6–11 year olds to 75% among persons 70 years and older. Anti-HAV prevalence is highest among Mexican-Americans (70%), compared with blacks (39%) and whites (23%). Anti-HAV prevalence is inversely related to income.

**During the past several decades, the incidence of reported hepatitis A has been substantially higher in the western United States than in other parts of the country.** From 1987–1997, 11 mostly western states (AZ, AK, OR, NM, UT, WA, OK, SD, ID, NV, CA) accounted for 50% of all reported cases but only 22% of the U.S. population.

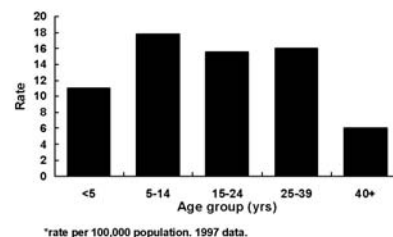
Many hepatitis A cases in the United States occur in the context of community-wide epidemics. Communities which experience such epidemics can be classified as high-rate and intermediate-rate communities. **High-rate communities** typically have epidemics every 5–10 years that may last for several years with substantial rates of disease (as high as 700 cases per 100,000 population annually during outbreaks) and few cases among persons >15 years of age. These communities often are relatively well-defined either geographically or ethnically and include Native American, Alaskan Native, Pacific Islander, selected Hispanic communities, and certain religious communities. Experience with hepatitis A vaccination programs in these high rate communities has shown that when relatively high (65%–80%) first dose vaccination coverage of pre-school and school-age children is achieved and routine vaccination of young children is sustained, ongoing outbreaks of hepatitis A could be interrupted. In these areas, sustained reduction in HAV incidence has been achieved and subsequent outbreaks have been prevented.

In **intermediate-rate communities**, hepatitis A cases occur primarily among children, adolescents, and young adults. Epidemics often occur at regular intervals and persist for several years with rates typically between 50 and 200 cases per 100,000 per year. However, some communities experience sustained elevated rates. Often cases are concentrated in specific census tracts or neighborhoods within a larger community. In these communities, children with asymptomatic HAV infection can be a substantial source of infection for older persons during community-wide outbreaks.

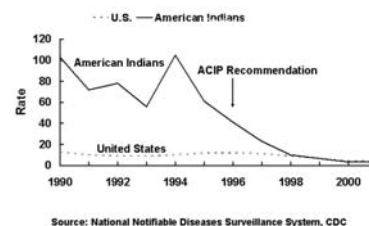
## CASE DEFINITION

The case definition for hepatitis A was approved by the Council of State and Territorial Epidemiologists (CSTE) in 1997. It reflects a

Hepatitis A Incidence\* by Age Group



Hepatitis A Incidence - United States and American Indians, 1990–2001



## Hepatitis A Vaccines

- Inactivated whole virus
- Pediatric and adult formulations
- Licensed for persons  $\geq 2$  years

## Hepatitis A Vaccine Immunogenicity

### Adults

- 95% seropositive after one dose
- 100% seropositive after two doses

### Children ( $\geq 2$ years) and Adolescents

- $>97\%$  seropositive after one
- 100% seropositive after 2 doses

## Hepatitis A Vaccine Efficacy

### GlaxoSmithKline

- 40,000 Thai children 1-16 years
- Vaccine efficacy 94%

### Merck

- 1,000 children 2-16 years
- Vaccine efficacy 100%

clinical diagnosis of hepatitis and, because HAV cannot be differentiated from other types of viral hepatitis on clinical or epidemiologic features alone, serologic evidence of HAV-specific IgM antibody is necessary.

The clinical case definition for hepatitis A is an acute illness with discrete onset of symptoms, and jaundice or elevated serum aminotransferase levels. The laboratory criterion for diagnosis is a positive anti-HAV IgM.

## HEPATITIS A VACCINE

### CHARACTERISTICS

Two inactivated whole virus hepatitis A vaccines is available: Havrix (GlaxoSmithKline) and VAQTA (Merck Vaccine Division). To produce each vaccine, cell culture-adapted virus is propagated in human fibroblasts, purified from cell lysates, inactivated with formalin, and adsorbed to an aluminum hydroxide adjuvant. HAVRIX is prepared with a preservative (2-phenoxyethanol); VAQTA does not contain a preservative. Both vaccines are available in both pediatric and adult formulations. **Neither vaccine is currently licensed for children  $<2$  years of age.**

### IMMUNOGENICITY AND VACCINE EFFICACY

Both vaccines are highly immunogenic. More than 95% of adults will develop protective antibody within 4 weeks of a single dose of either vaccine and nearly 100 percent will seroconvert within a month. Among children and adolescents, more than 97% will be seropositive within a month of the first dose. In clinical trials, all recipients had protective levels of antibody after 2 doses.

Both vaccines are highly effective in the prevention of clinical hepatitis A. The efficacy of HAVRIX in protecting against clinical hepatitis A was 94% among 40,000 Thai children 1-16 years of age who received 2 doses one month apart while living in villages with high HAV disease rates. The efficacy of VAQTA in protecting against clinical hepatitis A was 100% among 1,000 New York children 2-16 years of age who received 1 dose while living in a community with a high HAV disease rate.

Data concerning the long-term persistence of antibody and of immune memory are limited because the currently available vaccines have been being evaluated for  $<10$  years. Estimates of antibody persistence derived from kinetic models of antibody decline indicate that protective levels of anti-HAV could be present for  $\geq 20$  years. Other mechanisms (*e.g.*, cellular) may contribute to long-term protection, but this is unknown. The need for booster doses will be determined by postmarketing surveillance studies.

### VACCINATION SCHEDULE AND USE

Since its introduction in 1995, hepatitis A vaccine has been prima-

rily targeted to individuals at increased risk of HAV infection, particularly international travelers. While this strategy prevented infection in this group, and in other vaccinated individuals, it had little or no impact on the incidence of HAV infection in the United States.

As a result of successful vaccination programs in areas with a high incidence of HAV infection, the Advisory Committee on Immunization Practices in 1999 recommended **routine vaccination of children 2 years of age and older with hepatitis A vaccine be implemented in states, counties or communities where the average annual incidence of hepatitis A during 1987-1997 was 20 cases per 100,000 population or higher** (*i.e.*, at least twice the U.S. average of 10 cases per 100,000 population). ACIP also recommended that **routine vaccination be considered for states, counties or communities where the average annual incidence of hepatitis A during 1987-1997 was 10 cases per 100,000 population or more but less than 20 cases per 100,000 population.**

Determination of age groups recommended for vaccination should take into account community disease patterns. In communities with high rates of hepatitis A, routine vaccination of children beginning at 2 years of age and older and catch-up vaccination of preschool children should receive the highest priority. In other areas where routine childhood vaccination is recommended, possible strategies include vaccination one or more single age cohorts of children or adolescents (*e.g.*, at entry into preschool, elementary school and/or middle school), vaccination of children and adolescents in selected settings (*e.g.*, daycare) or vaccination of children and adolescents with a wide range of ages in a variety of settings, such as when they seek healthcare for other purposes.

**Persons at increase risk for HAV infection, or who are at increased risk of complications of HAV infection, should continue to be routinely vaccinated** (see below).

Havrix is available in 2 formulations - pediatric (720 EL.U. per 0.5 mL dose) and adult (1,440 EL.U. per 1.0 mL dose). Children 2-18 years of age should receive a single primary dose of the pediatric formulation followed by a booster dose 6-12 months later. Adults 19 years and older receive one dose of the adult formulation followed by a booster 6-12 months later. The vaccine should be administered intramuscularly into the deltoid muscle. A needle

Recommended Doses of Havrix® Hepatitis A Vaccine					
Group	Age	Dose (U)	Volume	No. Doses	Schedule*
Children and Adolescents	2-18 years	720	0.5 mL	2	0, 6-12
Adults	>18 years	1,440	1.0 mL	2	0, 6-12

\*Months: 0 months represents timing of the initial dose; subsequent number(s) represent months after the initial dose.

length appropriate for the vaccinee's age and size (minimum of 1 inch) should be used. VAQTA is quantified in units (U) of antigen

### Hepatitis A Vaccine Recommendations

Routine hepatitis A vaccination should be considered for:

- Children >2 years in states, counties, or communities where the average annual hepatitis A rate during 1987-1997 was 10 to 20 per 100,000 population

### Hepatitis A Vaccine Recommendations

Routine hepatitis A vaccination is recommended for:

- Children >2 years in states, counties, or communities where the average annual hepatitis A rate during 1987-1997 was  $\geq 20$  per 100,000 population

### Hepatitis A – High Incidence States

■  $\geq 20/100,000$  population    ■ 10-20/100,000 population



and is available in a pediatric and adult formulation. Children 2-18 years of age should receive one dose of pediatric formulation (25 U per dose) with a booster dose 6-12 months later. Adults 19 years of age and older should receive one dose of adult formulation (50 U per dose) with a booster dose 6-12 months after the first dose. The vaccine should be administered intramuscularly into the deltoid muscle. A needle length appropriate for the vaccinee's age and size should be used (minimum of 1 inch).

Recommended Doses of VAQTA® Hepatitis A Vaccine					
Group	Age	Dose (U)	Volume	No. Doses	Schedule*
Children and Adolescents	2-18 years	25	0.5 mL	2	0, 6-18
Adults	≥18 years	50	1.0 mL	2	0, 6-12

\*Months: 0 months represents timing of the initial dose; subsequent number(s) represent months after the initial dose.

Limited data indicate that vaccines from different manufacturers are interchangeable. Completion of the series with the same product is preferable. However, if the originally-used product is not available or not known, vaccination with either product is acceptable.

For both vaccines, the booster dose given should be based on the person's age at the time of the booster dose, not the age when the first dose was given. For example, if a child received the first dose of the pediatric formulation of VAQTA at 18 years of age, and returns for the booster dose at age 19 years, the booster dose should be the adult formulation, not the pediatric formulation.

The minimum interval between the first and booster doses of hepatitis A vaccine is six calendar months. If the interval between the first and booster doses of hepatitis A vaccine is longer than the recommended interval of 6-18 months, it is not necessary to repeat the first dose.

Studies among adults do not indicate a decrease in immunogenicity or an increase in adverse events when hepatitis A vaccine is administered at the same time as other vaccines. Similar studies among infants are in progress.

### COMBINATION HEPATITIS A AND HEPATITIS B VACCINE

In 2001, the U.S. Food and Drug Administration approved a combination hepatitis A and hepatitis B vaccine (Twinrix, GlaxoSmithKline). Each dose of Twinrix contains 720 EL.U. of hepatitis A vaccine (equivalent to a pediatric dose of Havrix), and 20 mcg of hepatitis B surface antigen protein (equivalent to an adult dose of Engerix-B). The vaccine is administered in a 3 dose series at 0, 1, and 6-12 months. Appropriate spacing of the doses must be maintained to assure long-term protection from both vaccines. The first and third doses of Twinrix should be separated by at least 6 months. The first and second doses should be separated by at least 4 weeks, and the second and third doses should be separated by at least 5 months. It is not necessary to restart the series

#### Twinrix

- Combination hepatitis B (adult dose) and hepatitis A vaccine (pediatric dose)
- Schedule: 0, 1, 6-12 months
- Approved for persons ≥18 years



or add doses if the interval between doses is longer than the recommended interval. Twinrix is approved for persons aged 18 years and older, and can be used in persons in this age group with indications for both hepatitis A and hepatitis B vaccines.

Because the hepatitis B component of Twinrix is equivalent to a standard dose of hepatitis B vaccine, the schedule is the same whether Twinrix or single-antigen hepatitis B vaccine is used.

### PERSONS AT INCREASED RISK FOR HEPATITIS A OR SEVERE OUTCOMES OF INFECTION

Persons at increased risk for hepatitis A should be identified and vaccinated. Hepatitis A vaccine should be strongly considered for persons 2 years of age and older who are **traveling to or working in countries with high- or intermediate-risk of hepatitis A virus infection**. These areas include all areas of the world except Canada, Western Europe and Scandinavia, Japan, New Zealand, and Australia. Vaccinated persons can be assumed to be protected by 4 weeks after receiving the first dose, although the second dose 6 to 12 months later is necessary for long-term protection.

Available data suggest that 40%–45% of vaccinated persons might lack neutralizing antibody at 14 days after receiving the first dose. No data are currently available regarding the risk of hepatitis A among persons vaccinated 2–4 weeks before departure. Because protection might not be complete until 4 weeks after vaccination, persons traveling to a high-risk area less than 4 weeks after the initial dose should also be administered immune globulin (0.02 mL/kg) at a different anatomic injection site. Hepatitis A vaccine is not approved for children less than 2 years of age. Children <2 years of age should receive immune globulin (0.02–0.06 mL/kg, depending on length of stay) prior to travel to high-risk areas. Other groups which should be offered vaccine include **men who have sex with other men, drug users, persons who have clotting-factor disorders, and persons with occupational risk of infection**. Persons with occupational risk include only those who work with hepatitis A-infected primates or with hepatitis A virus in a laboratory setting. No other groups have been shown to be at increased risk of hepatitis A infection due to occupational exposure.

Persons with chronic liver disease are not at increased risk for HAV infection because of their liver disease alone. However, these persons are at increased risk of fulminant hepatitis A should they become infected. **Susceptible persons who have chronic liver disease should be vaccinated**. Available data do not indicate a need for routine vaccination of persons with chronic hepatitis B virus or hepatitis C virus infections without evidence of chronic liver disease. Susceptible persons who either are awaiting or have received liver transplants should be vaccinated.

Hepatitis A vaccination is **not routinely recommended for healthcare workers, persons attending or working in**

#### Hepatitis A Vaccine Recommendations

- Travelers to high- or intermediate-risk countries
- Protected by 4 weeks after dose
- Give concurrent IG for travel in <4 weeks

#### Hepatitis A Vaccine Recommendations

- International travelers
- Men who have sex with men
- Drug users
- Persons with occupational risk
- Persons with chronic liver disease, including hepatitis C

## Hepatitis A Vaccine Recommendations

- **Healthcare workers: not routinely recommended**
- **Daycare centers: not routinely recommended**
- **Food handlers: may be considered based on local circumstances**

## Hepatitis A Serologic Testing

### Prevaccination

- Not indicated for children
- May be considered for some adults and older adolescents

### Postvaccination

- Not indicated

## Hepatitis A Vaccine Adverse Reactions

- Pain at injection site
- Systemic reactions uncommon
- No serious adverse events reported

**daycare centers, or persons who work in liquid or solid waste management** (e.g., sewer workers or plumbers). These groups have not been shown to be at increased risk of hepatitis A infection. **ACIP does not recommend routine hepatitis A vaccination for food service workers**, but vaccination may be considered based on local epidemiology.

## PREVACCINATION SEROLOGIC TESTING

HAV infection produces lifelong immunity to hepatitis A, so there is no benefit of vaccinating someone with serologic evidence of past HAV infection. The risk for adverse events following vaccination of such persons is not higher than the risk for serologically negative populations. As a result, the decision to conduct prevaccination testing should be based chiefly on the prevalence of immunity, the cost of testing and vaccinating (including office visit costs), and the likelihood that testing will interfere with initiating vaccination.

Testing of children is not indicated because of their expected low prevalence of infection. Persons for whom prevaccination serologic testing will likely be most cost effective include adults who were either born in or lived for extensive periods in geographic areas that have a high endemicity of HAV infection (e.g., Central and South America, Africa, Asia); older adolescents and adults in certain populations (i.e., Native Americans, Alaskan Natives, and Hispanics); adults in certain groups that have a high prevalence of infection (see above); and adults >40 years of age.

Commercially available tests for total anti-HAV should be used for prevaccination testing.

## POSTVACCINATION SEROLOGIC TESTING

Postvaccination testing is not indicated because of the high rate of vaccine response among adults and children. Testing methods sufficiently sensitive to detect low anti-HAV concentrations after vaccination are not approved for routine diagnostic use in the U.S.

## ADVERSE REACTIONS FOLLOWING VACCINATION

For both vaccines, the most commonly reported adverse reaction following vaccination is a **local reaction** at the site of injection. Injection site pain, erythema, or swelling is reported in 20% to 50% of recipients. These symptoms are generally mild and self-limited. **Mild systemic complaints** (e.g., malaise, fatigue, low grade fever) are reported in <10% of recipients. No serious adverse reactions have been reported.

## CONTRAINDICATIONS AND PRECAUTIONS TO VACCINATION

Hepatitis A vaccine should not be administered to persons with a history of a **serious allergic reaction to a vaccine component**

**or following a prior dose** of hepatitis A vaccine, hypersensitivity to alum or, in the case of Havrix, to the preservative 2-phenoxyethanol. Vaccination of persons with **moderate or severe acute illnesses** should be deferred until the patient has improved.

The safety of hepatitis A vaccination during pregnancy has not been determined. However, because it is an inactivated vaccine, the theoretical risk to the fetus is low. The risk associated with vaccination should be weighed against the risk for HAV infection. Because hepatitis A vaccine is inactivated, no special precautions are needed when vaccinating immunocompromised persons.

### VACCINE STORAGE AND HANDLING

Hepatitis A vaccine should be stored and shipped at temperatures ranging from 35.6°F (2°C) to 46.4°F (8°C) and should not be frozen. However, the reactogenicity and immunogenicity are not altered by storage for 1 week at 98.6°F (37°C).

### POSTEXPOSURE MANAGEMENT WITH IMMUNE GLOBULIN

Standard immune globulin (IG; formerly called gamma globulin) is a concentrated solution of antibodies prepared from pooled human plasma. In the U.S., only plasma that has tested negative for hepatitis B surface antigen, antibody to hepatitis C virus, and antibody to human immunodeficiency virus is used to manufacture IG. The IG is made with a serial ethanol precipitation procedure that has been shown to inactivate hepatitis B virus (HBV) and human immunodeficiency virus.

Serious adverse reactions from IG are rare. Anaphylaxis has been reported after repeated administration to persons who have known IgA deficiency, thus IG should not be administered to these persons. Pregnancy or lactation is not a contraindication to IG use.

When administered intramuscularly before exposure to HAV, or within 2 weeks after exposure, IG is >85% effective in preventing hepatitis A. Later administration of IG often only attenuates the clinical expression of HAV infection.

An appropriately large muscle mass (*e.g.*, the deltoid or gluteal muscle) should be used as the site of the injection. A single intramuscular dose of 0.02 mL/kg of IG confers protection for <3 months; 0.06 mL/kg protects for 5 months. IG should be given to exposed persons who have not previously received hepatitis A vaccine as soon as possible, but not more than 2 weeks after the exposure.

Recipients may include 1) persons with close contact (household or sexual) to a person with hepatitis A; 2) staff and attendees at child care centers where a hepatitis A case has been recognized; and 3) persons in certain common-source exposure situations (*e.g.*, to patrons of a food establishment with an HAV-infected food han-

#### Hepatitis A Vaccine Contraindications and Precautions

- Severe allergic reaction to a vaccine component or following a prior dose
- Moderate or severe acute illness

dlar, if the risk of transmission is determined to be high). Persons who have received one dose of hepatitis A vaccine at least 1 month before a HAV exposure do not need IG.

IG can interfere with the response to live injected vaccines (*e.g.*, measles, mumps, rubella, and varicella vaccines). Thus, administration of live vaccines should be delayed for at least 3 months after administration of IG (see the chapter on General Recommendations on Immunization, p. 7). Conversely, unless the benefits of IG prophylaxis exceed the benefits of vaccination, IG should not be administered for 2 weeks after measles-, mumps-, and rubella-containing vaccines, and for 3 weeks after vaccination with varicella vaccine. If IG is given during this period, the person should be revaccinated with the live vaccine, but not sooner than 3 months after administration of IG.

## DISEASE SURVEILLANCE AND REPORTING

Hepatitis A is a reportable disease in all states. Disease surveillance should be used to 1) monitor disease incidence in all age groups; 2) determine the epidemiologic characteristics of infected persons, including the source of their infection; 3) identify contacts of cases who require postexposure prophylaxis; 4) detect outbreaks; 5) determine the effectiveness of hepatitis A vaccination; and 6) determine missed opportunities for vaccination. Surveillance for hepatitis A is especially important because determining vaccination strategies to control ongoing outbreaks depends upon the identification of specific groups (*e.g.*, by geographic area, age group, or other characteristics) at increased risk of hepatitis A.

In the United States, case reports of viral hepatitis are classified as hepatitis A, hepatitis B, or hepatitis C/non-A, non-B hepatitis. Serologic testing is necessary to determine the etiology of viral hepatitis. Case reports should be based on laboratory confirmation (see Laboratory Diagnosis section). Each state and territory has regulations and/or laws governing the reporting of diseases and conditions of public health importance. These regulations/laws list the diseases and conditions that are to be reported and describe those persons or groups who are responsible for reporting, such as healthcare providers, hospitals, laboratories, schools, daycare facilities, and other institutions. Contact your state health department for reporting requirements in your state.

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