

antimicrobial therapy is not required and the long-term outcome for the patient is favorable.

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HEPATITIS A VACCINE

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Hepatitis A is one of the most frequently reported vaccine-preventable diseases in the US.¹ The ability to propagate hepatitis A virus (HAV) in cell culture allowed for the development of hepatitis A vaccines.

HAV infection

HAV infection is acquired primarily by the fecal-oral route. After an average incubation period of 28 days, HAV produces either asymptomatic or symptomatic infection. The likelihood of having symptoms is related to age. In children <6 years old, most infections (70%) are asymptomatic or characterized by nonspecific symptoms.² Among older children and adults, infection is usually symptomatic, with jaundice occurring in >70% of adult patients.³ Chronic infection does not occur.

Among reported cases in the US, the highest disease incidence rates occur among children 5-14 years old, and almost 30% of cases occur among children <15 years old.¹ Higher disease incidence rates occur in the West and Southwest compared to other regions of the country.¹ The most common source for infection is

household or sexual contact with a person who has hepatitis A. However, 40-50% of reported cases do not have an identified source.¹

Most hepatitis A occurs in the context of community-wide epidemics, by person-to-person transmission in households and extended family settings. Children likely play an important role in transmission during these outbreaks. In studies in which household contacts of adult cases without an identified infection source were tested, 25-40% of their contacts <6 years old had serologic evidence of acute HAV infection.⁴

Hepatitis A vaccines

Both inactivated and live, attenuated hepatitis A vaccines have been developed using defined isolates from infected cell lines, but only inactivated vaccines have been evaluated for efficacy in controlled clinical trials.^{5,6} The two inactivated vaccines currently licensed in the US are HAVRIX (SmithKline Beecham Biologicals) and VAQTA (Merck & Co., Inc.). Both vaccines are licensed for children ≥ 2 years old and for adults, and are available in pediatric and adult formulations given intramuscularly in a two dose schedule. The pediatric formulation of HAVRIX is licensed for persons <19 years old, and that of VAQTA for persons <18 years old.

Immunogenicity

In extensive studies among children and adults, both vaccines were highly immunogenic when administered according to a variety of schedules. In general, >97% of children ≥ 2 years old develop levels of antibody considered to be protective by four weeks after one dose. Large boosts in antibody levels occur after a second dose given at least 6 months later.^{7,8} This second dose is felt to be necessary for long term protection. Studies among children <2 years old indicate a favorable safety profile and high rates of seroconversion. However, among infants with passively transferred maternal antibody, fi-

nal antibody concentrations have been one-third to one-tenth those of vaccine recipients without maternal antibody.^{9,10} Studies to determine the optimum dosage and schedule to overcome this interference are underway.

Efficacy

Inactivated hepatitis A vaccines have been shown to be highly efficacious. In large studies conducted among children 2-16 years old, hepatitis A vaccines were 94-100% efficacious in preventing clinically apparent disease when administered before exposure.^{5,6} Hepatitis A vaccines are not recommended for postexposure prophylaxis because no trials have been conducted comparing vaccine to immune globulin (IG). IG, administered within two weeks of exposure, is highly efficacious and continues to be recommended to prevent hepatitis A in this setting.¹

Levels of antibody considered protective have been shown to persist for at least 6 years in adults vaccinated according to the recommended schedule.¹¹ Estimates based on kinetic models of antibody decline suggest that the duration of protection could be longer than 20 years.¹²

Limited data from studies conducted among adults indicate that hepatitis A vaccine can be administered with other vaccines commonly given to international travelers¹³ and concurrently with IG.¹⁴

Safety

In total, >65 million doses of hepatitis A vaccine have been administered worldwide.¹ In prelicensure trials, soreness at the injection site was reported for 9-15% of vaccinated children. Reviews of data regarding adverse events have not identified any serious adverse events among children or adults that could be attributed to the vaccine.¹

Recommendations

Recommendations for the use of hepatitis A vaccine have been developed by the ACIP and AAP.^{1,15} Because of the marked geographic

TABLE. Recommendations for Routine Preexposure Vaccination with Hepatitis A Vaccine*^{1, 15}

Group	Comments
Children living in communities with consistently elevated rates	Includes Alaska, Arizona, California, Idaho, Nevada, New Mexico, Oklahoma, Oregon, South Dakota, Utah, Washington, and selected areas in other states†‡ Immune globulin may be given in addition to or instead of vaccine; children <2 years old should receive immune globulin Increased risk of fulminant hepatitis A with HAV infection
International travelers§	
Men who have sex with men¶	
Illicit drug users¶	
Persons with chronic liver disease	
Persons receiving clotting factor concentrates	
Persons who work with HAV in research laboratory settings	

* Hepatitis A vaccine is not licensed for children <2 years old.
† Where the average reported hepatitis A incidence during 1987 to 1997 was $\geq 20/100,000$ population (approximately twice the national average).
‡ Routine vaccination can also be considered for children living in Arkansas, Colorado, Missouri, Montana, Texas, Wyoming, and selected areas in other states where the average reported incidence during 1987–1997 was $\geq 10/100,000$ population.
§ Persons traveling to Canada, western Europe, Japan, Australia, or New Zealand are at no greater risk than in the United States.
¶ Includes adolescents and adults; prevaccination serologic testing may be cost-effective for older persons.

variation in hepatitis A rates, areas can be identified in which rates have been consistently elevated and that contribute the majority of cases to the national disease burden. Routine vaccination is recommended for children living in states, counties and communities where the average annual reported hepatitis A incidence during 1987–1997 was at least twice the national average of approximately 10 cases/100,000 population (Table).^{1, 15} In these areas, routine vaccination of children is being implemented using a variety of strategies, including vaccination of single age cohorts and vaccination of children in settings such as child care centers. In addition, consideration of routine vaccination is recommended for children living in states, counties and communities where reported hepatitis A rates were less than twice, but at least the national average during this time (Table).

In populations that have high rates of HAV infection, prevaccination testing may be considered to reduce costs. However, in most instances testing of children is not necessary, because of their expected low prevalence of infection. Postvaccination testing is not indicated because of the high rate of vaccine response. In addition, response to vaccination cannot be determined using the commercially available assay because it is not sensitive enough to detect the low, but protective, anti-HAV concentrations induced by vaccination.

Persons from developed countries who travel to developing countries are at substantial risk for acquiring hepatitis A (Table).¹ Children account for approximately 36% of reported hepatitis A cases among returning international travelers. Children visiting in their parents' country of origin may be at particular risk because their need for preexposure prophylaxis often is not recognized. Hepatitis A vaccine is also recommended for other persons in identified groups at increased risk of infection or its adverse consequences (Table).

There has been considerable interest in using hepatitis A vaccine to control ongoing community-wide epidemics. Although individuals who received a single dose of vaccine during outbreaks did not develop hepatitis A, the success of vaccination programs in interrupting an epidemic has been variable. Efforts are probably better focused on sustained, routine childhood vaccination to prevent future epidemics.

Outbreaks in childcare centers have been recognized since the 1970s, often only when adult contacts become ill.⁴ Outbreaks rarely occur in childcare centers that do not include diapered children. Until more data become available, IG, which has proven effective in limiting transmission, should continue to be used in this setting. In communities where vaccination of childcare attendees is being used as a way to implement routine hepatitis A vaccination, previously un-

vaccinated children receiving IG can also receive hepatitis A vaccine.

Summary

Inactivated hepatitis A vaccines are highly immunogenic and efficacious. Because of their high disease rates and importance as a reservoir of transmission to others, children should be the primary focus of vaccination. A long-term strategy of sustained routine vaccination of children living in areas with consistently elevated hepatitis A rates has been adopted. Ultimately, elimination of HAV transmission will require vaccination of all children in the US. This effort would be facilitated by the availability of vaccine formulations or schedules for use in infants or children in the second year of life, and combination vaccines that include hepatitis A.

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