

# Hepatitis A and B Vaccination in the United States

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## ABSTRACT

Use of hepatitis A vaccine is a main component of travel vaccination practices. In the United States, fluctuations in the number of annual hepatitis A infections have occurred recently due to large outbreaks related to imported foods and urban transmission among homeless individuals, warranting consideration for wider local use of hepatitis A vaccine.

Hepatitis B vaccine is indicated for all adults, and especially healthcare workers. Since 1992, it has been administered at birth. A new novel hepatitis B vaccine given in two doses one month apart is available and has increased efficacy in adults. This article reviews the complete administration of these hepatitis vaccines.

**KEYWORDS:** hepatitis A, hepatitis B, immunizations, healthcare workers, heplisav-B

## HEPATITIS A

Hepatitis A virus (HAV) is a nonenveloped positive strand RNA virus, member of the Picornavirus family, that is mainly transmitted through fecal-oral route and exposure to contaminated food and water sources. It commonly causes a self-limited inflammatory response in the liver that is associated with generalized symptomatology, but in rare cases it may progress to fulminant hepatitis and liver failure.<sup>1</sup> Although the average number of annual HAV infections reported to the Centers for Disease Control (CDC) recently has declined substantially compared to the year 2000, fluctuations have occurred in the last 20 years because of large outbreaks related to imported foods, people who use drugs, experience homelessness and men who have sex with men.<sup>2</sup>

### Vaccines

There are two licensed Hepatitis A antigen vaccines available in the United States for individual 12 months and older, HAVRIX® (manufactured by GlaxoSmithKline) and VAQTA® (manufactured by Merck & Co., Inc). The schedule for HAVRIX® is 0, 6–12 months and for VAQTA® 0, 6–18 months.<sup>3</sup> Both vaccines provide high immunogenicity-inducing protective antibody levels in 94%–100% of adults one month after the first dose, and 100% one month after the second dose. Similar rates of neutralizing antibodies are

found in children and adolescents. Protective antibody levels appear to persist beyond 20 years in healthy individuals.<sup>1</sup>

Twinrix® (manufactured by GlaxoSmithKline), a combined hepatitis A and hepatitis B vaccine, was first licensed by the Food and Drug Administration (FDA) in 2001 on a 3-dose schedule (0, 1, and 6 months) for vaccination of persons aged ≥18 years.<sup>4</sup> The efficacy of Twinrix has been found to be comparable with existing single antigen hepatitis vaccines at 1 month after completion of series. At an alternate 4-dose schedule, Twinrix doses can be administered at 0, 7, and 21 to 30 days, followed by a dose at 12 months. This alternate dosing may be useful when vaccination with Twinrix has been initiated and travel or other potential exposure is anticipated before the second dose.<sup>5</sup>

### Indications

In 1999 the Advisory Committee on Immunization Practices (ACIP) recommended vaccination against hepatitis A routinely to children at age 12 to 23 months living in communities with high rates of disease, which led to a 79% decline of cases in states with prior elevated rates in 2004 compared to 1996.<sup>6</sup> In 2006, ACIP extended the recommendation of routine hepatitis A vaccination to children nationwide.

Other groups advised for HAV vaccination due to increased risk of exposure include: men who have sex with men (MSM), users of injection and non-injection drugs, persons with clotting-factor disorders, persons with occupational risk of infection, persons with chronic liver disease, persons traveling to or working in countries that have high or intermediate hepatitis A endemicity.<sup>1</sup>

Preexposure prophylaxis with hepatitis A vaccine is also indicated for unvaccinated persons who are household members and other close personal contacts of adopted children newly arriving from countries with high or intermediate hepatitis A.<sup>7</sup> The first dose of the HAV vaccine should be given ideally 2 or more weeks before the arrival of the adoptee. For infants 6–11 months of age that are at increased risk for HepA exposure, a single dose of HAV vaccine may be given; this dosage will not be counted toward the routine 2-dose series.

Given the higher risk for HAV infection and severe infection-associated outcomes in persons experiencing homelessness, in October 2018 the ACIP advised that all persons aged 1 year and older in this group be routinely immunized

against HAV.<sup>8</sup> Immunity towards HAV in this population is expected to reduce the risk of large-scale, person-to-person outbreaks, but possible barriers to vaccination include limited access to care and insurance coverage among persons experiencing homelessness.

Post-exposure prophylaxis has been shown to be beneficial for persons exposed to HAV within a 2-week period; it is favored over the immunoglobulin due to induction of active immunity, longer duration of protection, ease of administration, and greater acceptability and availability.<sup>9</sup>

### Adverse Effects

Pain at the injection site (56%–67%), headache (14%–16%), and malaise (7%) are the most common side effects reported in adults. No serious adverse events have been definitively related to the hepatitis A vaccine.<sup>1</sup>

### Contraindications

Hepatitis A vaccine should be avoided in those with a history of severe allergic reaction such as anaphylaxis to any component of the vaccine.

### Pregnancy

The risk to the fetus when the vaccine is given during pregnancy has not been determined; since the vaccine is inactivated, it is suspected to be low.<sup>10</sup>

### Safety

The vaccine may be given to immunocompromised patients, since it is inactivated. In this population, efficacy may be lower depending on the degree of immunosuppression.

### Hepatitis A Immunoglobulin

GamaSTAN S/D is available in the United States, with recommended dosing of 0.1 mL/kg for up to 1 month of planned travel duration and 0.2 mL/kg for up to 2 months has been shown to decrease HAV infection by 90%. It may be given, in conjunction to the HepA vaccine, at separate anatomic sites, within 2 weeks potential exposure to HAV for: adults aged >40 years, immunocompromised persons, those with chronic liver disease, or other chronic medical conditions. Persons may receive the hepatitis A immunoglobulin alone if they are <12 months of age, are allergic to a component of the vaccine or choose not to receive the vaccine.<sup>11</sup> Immunoglobulin cannot be administered simultaneously with MMR.

## HEPATITIS B

Hepatitis B (HepB) is a DNA virus of the Hepadnavirus family that is an important cause of chronic liver disease worldwide, which may lead to liver cirrhosis and hepatocellular carcinoma. It is transmitted through percutaneous or mucosal exposure to infectious blood or body fluids. The liver is the main site of infection, causing asymptomatic

and symptomatic disease. The primary infection is usually self-limited in immunocompetent adults, causing chronic infection in about 5% but it may be as high as 30–90% in children <5 years old. In the US, the rate of reported acute hepatitis B virus infections declined 88.5% since recommendations for HepB vaccination were first issued, from 9.6 cases per 100,000 population in 1982 to 1.1 cases per 100,000 population in 2015.<sup>12,13</sup>

### Vaccines

Two single antigen vaccines against hepatitis B are available in the United States, Recombivax HB® (Merck & Co., Inc., Whitehouse Station, New Jersey) and Engerix-B® (GlaxoSmithKline Biologicals, Rixensart, Belgium). Either should be administered at 0, 1, and 6 months, but alternate schedule of 0, 2 and 4 months or 0, 1 and 4 months will provide similar response. After the first dose, 30–50% of healthy adults will have protective antibody levels, 75% after the second dose and 90% after the third. An accelerated schedule may be given at 0, 7, and 21 days, followed by a booster at 12 months. The hepatitis B virus (HBV) vaccine after the completed vaccination series provides protection for about 20 years and possibly lifelong.

A combined inactivated hepatitis A and hepatitis B vaccine (Twinrix, GlaxoSmithKline) is available for those 18 years and older to be given 0, 1 and 6 months or an accelerated schedule at 0, 7, 21–30 days with a booster at 12 months.

On February 2018, Heplisav-B (HepB-CpG), a single-antigen HepB vaccine with a novel immunostimulatory sequence adjuvant was recommended for the prevention of HBV in persons aged ≥18 years. This vaccine is administered as 2 doses, 1 month apart, and has improved immunogenicity with a similar safety profile to Engerix-B®.<sup>14,15</sup> Seroprotective antibody to hepatitis B surface antigen (anti-HBs) levels were achieved in 90.0%–100.0% of subjects receiving 2 doses of HepB-CpG, compared with 70.5%–90.2% of subjects receiving 3 dose series of Engerix-B.

The same vaccine formulation should be used to complete the series, although vaccination should not be deferred if same vaccine manufacturer is not available or unknown.<sup>16</sup>

### Indications

HepB vaccination is universally indicated within 24 hours of birth for medically stable infants weighing ≥2,000 grams. In addition, routine vaccination is advised for unvaccinated children and adolescents aged <19 years, as well as adults at risk for HBV infection – all healthcare workers, sexual exposure to hepatitis B, history of current or recent injection drug use, risk for infection by percutaneous or mucosal exposure to blood, persons with chronic liver disease, persons with human immunodeficiency virus infection, incarcerated persons – and those requesting protection from HBV without acknowledgment of a specific risk factor.<sup>17</sup>

International travelers to countries with high or

intermediate levels of endemic HBV infection (HBsAg prevalence  $\geq 2\%$ ) should be vaccinated against HBV, particularly healthcare workers, disaster relief personnel, receipt of medical care, sexual activity, intravenous drug use, tattooing, among others.

Postvaccination serologic testing 1–2 months after the final dose of vaccine is recommended for certain persons following vaccination (e.g., hemodialysis patients, HIV-infected and other immunocompromised persons, healthcare personnel, and sex partners of HBsAg-positive persons). Revaccination may consist of administration of a second complete HBV vaccine series using any of the available vaccines. Administration of more than two complete HBV vaccine series is generally not recommended, except for hemodialysis patients.<sup>17</sup>

### Adverse events

Most common reported side effects are pain at the injection site  $>10\%$ . Other reactions such as low-grade fever, myalgia, and headaches are rare ( $<1\%$ ). Mild adverse event, serious adverse event, or cardiovascular event in subjects that received HepB-CpG were 45.6%, 5.4%, and 0.27% compared to subjects receiving Engerix-B, 45.7%, 6.3%, and 0.14%, respectively.<sup>14</sup>

### Contraindications

Hepatitis B vaccine should not be administered to those with a history of severe allergic reaction such as anaphylaxis to yeast or any other component of the vaccine.

### Pregnancy

The vaccine contains a noninfectious hepatitis B surface antigen and the risk to the fetus when the vaccine is given during pregnancy is low. There is limited human data of vaccine-associated risks on HepB-CpG administered to pregnant women.

### Immunoglobulin

HepB immunoglobulin may be administered in conjunction with the hepatitis B vaccines in patients after high-risk exposure with infected blood or body fluids within 24 hours of exposure.

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