# **Q:** Who should receive hepatitis A vaccine?

STEVEN D. MAWHORTER, MD\* Department of Infectious Diseases, Cleveland Clinic

A: THE FOOD AND DRUG ADMINISTRATION (FDA) and the Advisory Committee on Immunization Practices (ACIP) recommend vaccination for anyone at high risk of acquiring the hepatitis A virus, including overseas travelers.<sup>1</sup> The ACIP also recommends the vaccine for children, older adults, and recipients of solid organ and bone marrow transplants. People with chronic liver disease are also high-priority candidates.

### WHY VACCINATION IS NECESSARY

Hepatitis A infection is highly contagious, and although it is typically self-limited and moderately symptomatic, acute infection can be fulminant and even fatal.<sup>2</sup> Furthermore, the virus is relatively resistant to heat and chemicals<sup>3</sup> and is spread via the fecal-oral route through close personal contact, contact with contaminated food and water, and, rarely, parenterally. Because infected persons begin to shed the infectious virus as early as 2 weeks before the onset of symptoms, the infection is difficult to contain in its early stages.

### VACCINATION IS EFFECTIVE

The hepatitis A vaccine became available in the mid-1990s and has an efficacy rate of 95% to 100%.<sup>4</sup> It is effective only against hepatitis A virus and not other hepatitis agents.

The vaccine induces a rapid and protective antibody response after a single injection, though the FDA calls for a two-shot series. The booster dose is given 6 to 12 months after the first dose and appears to facilitate longterm immunity (estimated at 10 to 20 years or longer) in all vaccine recipients.

\*This paper discusses treatments that are "off label," ie, not approved by the Food and Drug Administration for the use under discussion.

## TABLE 1

## Doses of the two hepatitis A vaccines

VACCINE	DOSE (UNITS)*	
	2-18 YEARS OLD <sup>†</sup>	> 18 YEARS OLD
Havrix	720‡	1,440
Vaqta	25	50

\*Given intramuscularly; doses listed are the same for both initial and booster vaccination

<sup>†</sup>Limited data for use in children below 2 years of age <sup>‡</sup>Alternatively give two doses of 360 units 1 month apart

The vaccine causes few serious adverse effects. Injection-site soreness and headache occur in some recipients but are short-lived.<sup>5</sup>

Single-dose efficacy has nearly eliminated the need for passive immunization with immune globulin for people exposed to the virus and travelers leaving within 2 weeks of vaccination. However, when necessary, immune globulin and hepatitis A vaccine can be given on the same day without significantly reducing the efficacy of the vaccine; give the injections at different body sites.<sup>6</sup>

Two companies make very similar vaccine products (TABLE 1), which has helped to hold down their cost. Their efficacy is nearly identical. Although the products can be used interchangeably, it is preferable to use the same agent for the initial and booster dose.<sup>5</sup>

It has been suggested that persons older than age 55 be screened for hepatitis A antibodies before vaccination. Screening may also be helpful for persons born in or living for extended times in areas with a high prevalence of hepatitis A before vaccination. However, vaccinating someone who is already immune does not increase adverse events. The decision can be based on the cost of serologic testing vs the cost of vaccine.<sup>7</sup> Vaccinate people at risk of hepatitis A, especially international travelers





QUESTIONS

## ■ FDA-APPROVED INDICATIONS: HIGH-RISK POPULATIONS

The vaccine is indicated for persons who are likely to acquire the disease, including the following:

International travelers. The hepatitis A vaccine is predominantly used in people traveling abroad to areas where hepatitis A is common. It is recommended for almost all overseas travelers except those going to low-risk areas such as Scandinavia. Among nonimmune travelers, hepatitis A is the most common vaccinepreventable disease, being 1,000 times more common than cholera and 100 times more common than typhoid.<sup>8</sup> Because the hepatitis A virus is shed in stool and is transmitted enterically, support staff and food preparers can unintentionally spread hepatitis A even at the most exclusive vacation destinations.

Military personnel should be vaccinated because they often must travel abroad on short notice.

**Homosexual men.** According to the Centers of Disease Control and Prevention, the incidence of hepatitis A among men having sex with men has increased.<sup>9</sup> Oral-anal sexual contact appears to be a particular risk factor for hepatitis A infection. However, male homosexual activity in general seems to facilitate disease transmission.

**Intravenous drug users** are at risk because hepatitis A virus is found in the blood in early infection and can be passed on to those who share contaminated needles.

Recipients of blood products and clotting factor supplementation.<sup>10</sup>

**People with chronic liver disease** are high-priority candidates for hepatitis A vaccination, partly because fulminant hepatitis A can develop in those who already have chronic hepatitis C.<sup>11</sup> In addition, patients with chronic hepatitis B or C, alcoholic cirrhosis, autoimmune hepatitis, and primary biliary cirrhosis should be vaccinated to minimize the potential for further hepatic insult.<sup>11,12</sup>

Unfortunately, advanced liver disease reduces the vaccine's effectiveness. In one study, only 7 of 14 patients with liver failure and none of 8 liver transplant recipients sero-converted after receiving two standard doses of the vaccine.<sup>13</sup> Another study found that

immunogenicity was better early in the course of chronic liver disease, suggesting that early vaccination is beneficial.<sup>14</sup>

**Employees of daycare centers and institutions for the developmentally challenged.** Daycare centers have occasionally been efficient sites for epidemic spread.<sup>15</sup>

**Laboratory personnel** who handle hepatitis A virus or work with primate animals should receive vaccination.

**Residents of outbreak communities.** When hepatitis A vaccination is used in large community outbreaks, it is almost 100% effective in preventing the development of symptomatic disease among exposed individuals.<sup>16</sup> The vaccine also helps prevent the disease from spreading any further.

#### OTHER TARGET POPULATIONS

**Children.** A 1999 report by the ACIP<sup>17</sup> stated: "Another phase of hepatitis A immunization strategy is now needed to achieve widespread routine vaccination of children and to reduce the overall incidence of hepatitis A over time."

**Older adults.** Although many adults over the age of 55 have naturally acquired hepatitis A, which confers lifelong immunity, seronegative persons in this age group are at greatest risk for increased morbidity and mortality. Fulminant hepatic involvement is rare but it can lead to a fatal infection. The rate of fatal infections increases dramatically after age 49.<sup>18</sup> Minimizing exposure to potentially infectious children is another reason to consider childhood vaccination as a means to reduce severe complications associated with hepatitis A in older people.

Solid organ and bone marrow transplant candidates and recipients. Immunizing for any preventable medical illness before transplantation will always result in higher antibody levels compared with vaccinating after transplantation. Given the lifelong suppression of immunity necessary to maintain solid organ transplants, it is important to consider vaccinating this population.

**Bone marrow donors.** In the case of allogeneic bone marrow transplantation, in which transplant recipients acquire the immune system of the donor, it makes sense to consider

Give a booster dose 6–12 months after the first dose H

vaccinating a seronegative donor before transplantation. However, no clinical studies have assessed the efficacy of this strategy.

## REFERENCES

- Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1996; 45:1–30.
- Jelinek T, Northdurft HD. Changing epidemiology of hepatitis A: time for vaccination in childhood. J Travel Med 2000; 7:142–148.
- Terrault N, Wright TL. Viral hepatitis A through G. In: Feldmann M; Scharschmidt B, Sleisenger M, editors. Gastrointestinal and Liver Disease. 6th ed. Vol 2. Philadelphia: WB Saunders, 1998: 1123–1129.
- Werzberger A, Mensch B, Kuter B, et al. A controlled trial of formalin-inactivated hepatitis A vaccine in healthy children. N Engl J Med 1992; 327:453–457.
- Zuckerman J, Kirkpatrick C, huang M. Immunogenicity and reactogenicity of Avaxim (160 UA) as compared with Havrix (1440 EL.U) as a booster following primary immunization with Havrix (1440 EL.U) against hepatitis A. J Travel Med 1998; 5:18–22.
- Prevention of hepatitis A infections: guidelines for use of hepatitis A vaccine and immune globulin. American Academy of Pediatrics Committee on Infectious Diseases. Pediatrics 1996; 98:1207–1215.
- Thompson RF. Travel and routine immunizations. A practical guide for the medical office. Shoreland, Inc: Milwaukee, WI; 2000:34–42.
- Steffen R. Risk of hepatitis A in travellers. Vaccine 1992; 10(suppl 1):S69–S72.
- 9. Hepatitis A among homosexual men—United States, Canada, and Australia. MMWR 1992; 41:155–164.
- Shapiro CN, Coleman PJ, McQuillan GM, et al. Epidemiology of hepatitis A: seroepidemiology and risk groups in the USA. Vaccine 1992; 10(suppl 1):S59–S62.
- Vento S, Garofano T, Renzini C, et al. Fulminant hepatitis associated with hepatitis A virus superinfection in patients with chronic hepatitis C. N Engl J Med 1998; 338:286–290.
- Helbling B, Renner EL, Kammerlander R. Acute hepatitis A in patients with chronic hepatitis C [letter]. Ann Intern Med 1999; 131:314.
- Dumont JA, Barnes DS, Younossi Z, et al. Immunogenicity of hepatitis A vaccine in decompensated liver disease. Am J Gastroenterol 1999; 94:1601–1604.
- 14. Keeffe EB, Ewarson S, McMahon BJ, et al. Safety and immunogenicity of hepatitis A vaccine in patients with chronic liver disease. Hepatology 1998; 17:881–886.
- Smith PF, Grabau JC, Werzberger A, et al. The role of young children in a community-wide outbreak of hepatitis A. Epidemiol Infect 1997; 118:243–252.
- Bulkow LR, Wainwright RB, McMahon BJ, et al. Secular trends in hepatitis A virus infection among Alaska natives. J Infect Dis 1993; 168:1017–1029.
- Prevention of hepatitis A through active or passive immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1999; 48(RR-12):1–37.
- Hadler SC. Global impact of hepatitis A virus infection: changing patterns. In: Hollinger FB, Lemon SM, Margolis HS, editors. Viral Hepatitis and Liver Disease. Baltimore, MD: Williams & Wilkins; 1991:14–20.

ADDRESS: Steven D. Mawhorter, MD, Department of Infectious Diseases, S32, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail mawhors@ccf.org.