

ACIP/AAP RECOMMENDATIONS FOR HEPATITIS A IMMUNIZATION

THE INCIDENCE OF hepatitis A in Oregon and elsewhere follows a strongly cyclic pattern, with peaks every 5-7 years (see graph). The reported incidence fell 70% from 1995 to 1996, and will probably fall sharply again in 1997. The present interregnum is the first where we can face the future with more than a dread of the inevitable resurgence. Now, new vaccines allow us to shape our own destinies. Here's how.*

THE NEW WEAPONS

In the past two years, two inactivated hepatitis A vaccines have been licensed in the United States: Havrix® (SmithKline Beecham) and VAQTA® (Merck). Both vaccines are highly immunogenic (able to induce antibodies) and efficacious (able to prevent disease). Studies of Havrix indicate that protective levels of antibodies develop in 88% of adults within 15 days of the first dose, rising to 99-100% within a month; after administration of both doses of VAQTA, 95% and 100% of adults had protective levels of antibody at 1 and 7 months, respectively. Similar high rates of seroconversion are seen in children 2 years old and up (few data are available about younger children).

Although apparently perfectly adequate, postvaccination IgG titers are typically 10-100 fold lower than those produced by natural infection—and usually below the detection limits of most commercial lab assays. IgM responses are rarely detectable, either.

In a double-blind, placebo-controlled, randomized, peer-reviewed, IRB-approved, government-sanctioned clinical trial (DBPCRPRIRBAGSCT) among 40,000 children in Thailand, Havrix was 94% effective in protecting against clinical hepatitis A after two doses of vaccine given 1 month apart. Another DBPCRPR-

IRBAGSCT conducted among 1000 children in a New York community with a high incidence of hepatitis A showed VAQTA to be 100% effective after one dose of vaccine.

When used in communities with super-high incidence rates (>700/100,000), e.g., some Alaskan Native and American Indian communities), vaccination programs have resulted in substantial declines in disease rates. In merely epidemic rate communities (50-200/100,000), e.g., much of Oregon in 1995, immediate benefits have been harder to demonstrate.

ABOUT THE VACCINES

Both vaccines are made from HAV grown in human fibroblasts, formalin-inactivated, and adsorbed to an aluminum hydroxide adjuvant. Vaccine must be stored at 2-8°C; freezing will destroy its potency. Shots are given IM in the victim's deltoid (see table, verso).

Either vaccine can be given concurrently with immune globulin, if necessary (e.g., for a traveler with anticipated exposures in <30 days), but if so should be administered at separate sites. Resulting levels of antibody are lower than when vaccine is given alone, albeit much higher than levels considered protective.

Although obviously desirable, combination vaccines that include hepatitis A antigens are not currently available. Unpublished studies among adults show that simultaneous administration with DTP, oral typhoid, and cholera (and some other rather rarely used vaccines) are just as safe and immunogenic as when given separately.

Adverse reactions

No serious adverse reactions have been attributed to Havrix or VAQTA. The most common side effects are soreness at the injection site (56% for adults and 15% for children), and headache (14% and 4%, respectively). As with any vaccine, temporally associated untoward events should be reported to the Vaccine Adverse Events Reporting System (VAERS) at

800/822-7967.

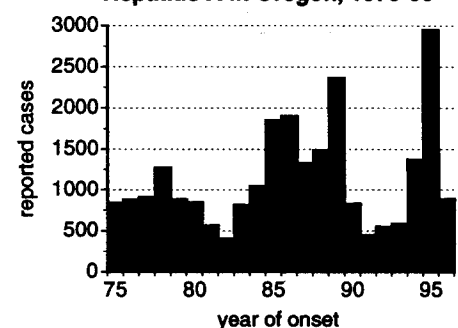
Neither vaccine should be given to persons who are allergic to alum; Havrix should not be given to those allergic to the preservative 2-phenoxyethanol. While the risk of these vaccinations on pregnant women has not been evaluated, as a killed vaccine it should be extremely low (or less). Hepatitis A during pregnancy is no fun, either; vaccinators should use their best judgment. No special precautions are recommended for immunocompromised patients.

WHO SHOULD GET IT?

The ACIP recommends vaccination for the following groups, who historically are at increased risk for infections. Vaccination is also appropriate for anyone wishing to spend the money and obtain immunity.

- **Travelers.** Immunization is recommended for persons ≥2 years old who travel to countries of high or intermediate endemicity of hepatitis A (basically, countries other than Canada, US, Australia, Japan, New Zealand, Western Europe). Although risk varies according to destination, length of stay, and extent of *joie de vivre* exposure, the risk of acquiring infection for U.S. residents travelling abroad averages ~3 per 1000 travelers per month of stay. There is little correlation between degree of risk and number of hotel stars. Ideally, travelers should receive the first dose at least 4 weeks prior to leaving; if traveling sooner, IG may be given concurrently at another site.

Hepatitis A in Oregon, 1975-96



*In other words, here are the newly released and somewhat redacted recommendations for hepatitis A vaccine use promulgated by the Advisory Committee on Immunization Practices (ACIP)¹ and the American Academy of Pediatrics.²

— **Children in high rate communities.**

Children who live in Alaskan Native villages, American Indian reservations, and selected Hispanic or religious communities should be routinely vaccinated beginning at age two.

— **Men who have sex with men.** 'nuf sed.

— **Users of illicit drugs.** Although modes of transmission are probably multifactorial in this group, vaccine is recommended for all members (both injecting and non-injecting) of this "community."

— **Occupationally challenged.** The only occupational groups shown to be at increased risk for infection are those who work with HAV-infected primates or HAV in the research lab. No studies support the routine vaccination of day care, health care, or sewage workers, or those who work with the developmentally disabled.

— **Persons with chronic liver disease.**

While not at increased risk for hepatitis A per se, this group is more likely to develop fulminant hepatitis if infected. Those who are awaiting or have received liver transplants should also be vaccinated.

— **Persons with clotting-factor disorders.** Those who receive solvent-detergent-treated factors VIII and IX are at an

elevated risk.

— **Residents of selected communities with very high incidence rates.** Catch-up vaccination of children ≥ 2 years old should be pursued until about 70% of the herd is immune.

— **Residents of communities with intermediate incidence rates.** Widespread vaccination is not typically feasible in these communities. Targeting subgroups with the highest rate of disease may be considered but the effectiveness of this effort has not been determined.

What about food handlers?

An often asked question is "should we require food handlers to be vaccinated?" Popular misconceptions notwithstanding, professional food handlers are not at increased risk for HAV infection, nor are people who eat out. Many people, including the media, often confuse public alerts about possible restaurant-associated *exposures* with actual restaurant-associated *outbreaks*, which are quite rare. Although the ACIP does not recommend that food handlers be vaccinated qua food handlers, there is a wishy-washy acknowledgment that "consideration may be given to vaccinations [of food handlers at their employers' expense] ...where...such vaccination is

cost effective." In any event, even immunized food handlers should not be given carte blanche to serve fecally contaminated food. Traditional recommendations about personal hygiene and proper food handling remain the best way to reduce the transmission of hepatitis A and other pathogens spread by the fecal-oral route.

REDUCING COSTS

A casual survey of Portland pharmacies found the retail cost of a single dose of Havrix to vary from \$54-\$72 for adults and \$32-\$33 for children. Prices for VAQTA were unavailable. Many Americans are immune to hepatitis A because of past exposure; most have no history of infection. About one-third of U.S. residents >40 years old are immune, and pre-vaccination screening of older individuals may be cost-effective. Postvaccination testing is not indicated.

VFC HIGHLIGHTS

Hepatitis A vaccines are not currently part of the routine childhood immunization schedule and thus are not generally covered by VFC funds. However, coverage is authorized in Oregon for two groups: 1) Native American children; and 2) outbreak control in *selected* communities where a well-defined high-risk population is identified, where other outbreak control measures are in place, and where resources are available to provide vaccine to non-VFC eligible children. For more information, contact your VFC representative.

REFERENCES

This article was adapted (rather liberally, in fact) from reference 1.
 1. CDC. Prevention of hepatitis A through active or passive immunization—recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR. 1996;45(No. RR-15):1-25.
 2. American Academy of Pediatrics. Prevention of hepatitis A infections: guidelines for use of hepatitis A vaccine and immune globulin. Pediatrics 1996;98:1207-1215.

Recommended Doses and Schedules for Hepatitis A Vaccines

Vaccine	Age (y)	Dose	Volume	# Doses	Schedule
Havrix	2-18	360 EL.U.*	0.5 ml	3*	0, 1, 6-12 months
	2-18	720 EL.U.	0.5 ml	2	0, 6-12 months
	≥ 19	1440 EL.U.	1.0 ml	2	0, 6-12 months
VAQTA	2-17	25 U	0.5 ml	2	0, 6-18 months
	≥ 18	50 U	1.0 ml	2	0, 6 months [sic]

* Havrix initially was released in a formulation for a 3-dose pediatric schedule. This formulation is being discontinued.