Recommendations from a National Conference on Universal Vaccination Against Hepatitis B and Hepatitis A in Adults

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ABSTRACT

The Centers for Disease Control and Prevention (CDC) estimate that, in the United States, 78,000 people became infected with hepatitis B in 2001 and that 93,000 cases of hepatitis A occurred in 2002. Current recommendations of the CDC's Advisory Committee on Immunization Practices (ACIP) for hepatitis B and hepatitis A vaccination in adults are based on a daunting list of risk groups, many of which overlap. Simplifying vaccination recommendations and using the term "vaccine-preventable hepatitis" (VPH) may encourage practitioners to administer hepatitis B and hepatitis A vaccines to adults. A group of experts in the fields of primary care, gastroenterology, hepatology, infectious and sexually transmitted diseases, human immunodeficiency virus, travel medicine, and public health convened to discuss prevention of hepatitis B and hepatitis A and to develop recommendations for VPH based on available evidence. They concluded that a universal, age-based vaccination strategy would help to increase vaccination rates among adults, thereby decreasing the incidence of hepatitis B and hepatitis A, and that government funding of hepatitis B and hepatitis A vaccination in adults is needed.

INTRODUCTION

The Centers for Disease Control and Prevention (CDC) estimate that, in the

Table 1. Hepatitis B and Hepatitis A Vaccines Available in the United States

Antigen	Vaccine	Indicated age group (yr)	Dose and schedule*
Hepatitis B	Engerix-B†	≤19	10 µg at 0, 1, and 6 mo
		≥20	20 µg at 0, 1, and 6 mo
	Recombivax-HB‡	≤19	5 µg at 0, 1, and 6 mo
		≥20	10 µg at 0, 1, and 6 mo
Hepatitis A and hepatitis B	Twinrix†	>18	720 ELU hepatitis A Ag/20 µg HBsAg at 0, 1, and 6 mo
Hepatitis A	Havrix†	2-18	720 ELU at 0 and 6-12 mo
		≥19	1440 ELU at 0 and 6-12 mo
	Vaqta‡	1-18	25 U at 0 and 6-18 mo
		≥19	50 U at 0 and 6-12 mo

*Schedules are FDA approved. The text of this article describes other nonapproved dosing schedules.
†Havrix, Engerix-B, and Twinrix are registered trademarks of GlaxoSmithKline Biologicals, Rixensart, Belgium.
‡Vaqta and Recombivax-HB are registered trademarks of Merck & Co., Inc., Whitehouse Station, New Jersey.
Ag=antigen; ELU=enzyme-linked immunosorbent assay units; HBsAg=hepatitis B surface antigen; U=units.

United States, 78,000 people became infected with hepatitis B in 2001,[1] and that 93,000 cases of hepatitis A occurred in 2002.[2] Hepatitis B and hepatitis A vaccines were introduced in the United States in 1981[1] and 1995,[2] respectively (Table 1). Both vaccines are safe and highly immunogenic. Hepatitis B vaccine is universally recommended for infants, children, and adolescents; hepatitis A vaccine now is recommended for all children 1 year (12-23 months) of age.[3]

In contrast, current recommendations by the Advisory Committee on Immunization Practices (ACIP) for vaccination against hepatitis B and hepatitis A in adults are based on a long list of risk groups (Table 2),[4] which makes evaluation of an adult patient a cumbersome process.[5,6] Because people who become infected with hepatitis B and hepatitis A may have risk factors in common, simplifying hepatitis B and hepatitis A vaccine recommendations and using the term "vaccine-preventable hepatitis" (VPH) to refer to hepatitis B and hepatitis A collectively may encourage practitioners to administer hepatitis B and hepatitis A vaccines to adults.

A group of experts in the fields of primary care, gastroenterology, hepatology, infectious and sexually transmitted diseases (STDs), human immunodeficiency virus (HIV), travel medicine, and public health convened to discuss prevention of hepatitis B and hepatitis A. Respected leaders in each field developed summary statements regarding prevention of hepatitis B and hepatitis A as they relate to each expert's respective area of practice. They then presented the rationale for their statements to the other participants.

Following a detailed discussion, the experts came to an agreement on summary statements (Table 3). The conference attendees' main conclusion was that hepatitis B and hepatitis A vaccination should be universally recommended for adults on the basis of age, rather than on presence of risk factors. They acknowledged that, although the incidence of VPH is decreasing, a substantial disease burden remains, and a major obstacle for implementation of a universal vaccination strategy is lack of funding for purchase and administration of vaccines. Regardless of the approach implemented for adult vaccination

Table 2. ACIP Recommendations for Hepatitis B and Hepatitis A Vaccine Use in Adults[4]

Hepatitis B vaccine	Hepatitis A vaccine
• Injection drug users	• Users of illegal drugs
• Men who have sex with men	• Men who have sex with men
• Healthcare and public safety workers who have exposure to blood in the workplace; persons in training for healthcare professions	• Persons working with HAV-infected primates or with HAV in a research laboratory setting
• Travelers who will be in countries with high or intermediate prevalence of chronic HBV infection	• Travelers to countries that have high or intermediate endemicity of HAV
• Patients who receive clotting factor concentrates	• Persons with clotting factor disorders
• Hemodialysis patients	• Persons with chronic liver disease
• Persons with >1 sex partner during the previous 6 months	• Persons who would like to obtain immunity to HAV
• Household contacts and sex partners of persons with chronic HBV infection	
• Clients and staff members of institutions for the developmentally disabled	
• All clients in STD clinics	
• Inmates of long-term correctional facilities	
• Persons seeking protection from HBV infection	

ACIP=Advisory Committee on Immunization Practices; HAV=hepatitis A virus; HBV=hepatitis B virus; STD=sexually transmitted disease.

against hepatitis, the conference attendees agreed that physician, patient, public, and payer education on VPH is necessary. This article summarizes the evidence presented that supports the agreed-on summary statements related to prevention of hepatitis B and hepatitis A.

PRIMARY CARE PERSPECTIVE

Current Hepatitis Vaccination Recommendations

Although safe and effective vaccines to prevent hepatitis B and hepatitis A have been available for many years and the incidence of these diseases has declined since the introduction of the vaccines, hepatitis B and hepatitis A still account for notable morbidity and mortality in the United States (Figure 1).[7] Symptoms of hepatitis A generally do not last longer than 2 months, but they may last up to 6 months in 10% to 15% of patients.[2] Fulminant hepatitis A causes approximately 100 deaths per year in the United States. Chronic infection with hepatitis B virus, however, can result in cirrhosis, chronic liver failure, and hepatocellular carcinoma. As a consequence of increasing hepatitis B vaccine coverage of children and adolescents, the incidence of new infections and acute hepatitis B now is highest in adults.[8] Men experience more infections than women, with the highest rates occurring across the broad age range of 25 to 49 years (Figure 2).

Office-Based Approach to Hepatitis Vaccination

Obstacles to immunization for hepatitis B and hepatitis A in the clinic include cost and lack of reimbursement,[6] inconsistent recommendations for immunization, lack of provider education, and logistical problems such as patient com-

Table 3. National Conference to Reevaluate Prevention of Hepatitis B and A: Summary of Recommendations on Vaccine-Preventable Hepatitis

- Although the incidence of vaccine-preventable hepatitis (VPH) (ie, hepatitis B and hepatitis A virus) is decreasing, a substantial disease burden remains
- The most practical approach to VPH control is universal vaccination among adults aged 19-50 years of age, in addition to continued universal childhood hepatitis B vaccination
- Funding (reimbursement, federal support, etc) represents a major obstacle to implementing universal adult vaccination
- Regardless of the approach to implement adult vaccination against hepatitis, physician, patient, public, and payer education on VPH is necessary

pliance, lack of physician assessment time,[9,10] and lack of standardized documentation forms. Standing orders and consistent recommendations from professional organizations and government agencies may help overcome some of these obstacles, as they have for childhood vaccination. Many excellent resources for implementation of adult vaccination in ambulatory practice exist,[11,12] but most providers are not familiar with them. For instance, the Immunization Action Coalition (IAC) has developed a publication titled *Adults Only Vaccination: A Step by Step Guide*, which contains information that will help healthcare providers implement adult vaccination services. Additional tools and programs to help physicians initiate vaccine services are needed; ideal programs would provide in-office assistance and training on coding and payment of fees for vaccine services.

GASTROENTEROLOGY AND HEPATOLOGY PERSPECTIVE

Prevention of Hepatitis B and Hepatitis A in Chronic Liver Disease

Hepatitis B and hepatitis A may lead to worse outcomes in patients with chronic liver disease than in otherwise healthy patients.[13,14] Chronic hepatitis B and hepatitis C co-infection is associated with more severe laboratory abnormalities, worse histologic disease, more complications of cirrhosis, and higher incidence of hepatocellular carcinoma.[15-18] In a study of 86 patients with chronic hepatitis C, cirrhosis was found more frequently in patients with both hepatitis B and hepatitis C (56.2%) than in patients with only hepatitis B (12.9%).[16] In another study, Sagnelli and colleagues[19] evaluated 44 patients with hepatitis B. Six (28.6%) of the 21 patients with underlying hepatitis C had a severe clinical presentation; 1 patient developed fulminant hepatitis and died. A severe clinical presentation was not observed in any of the 20 patients who did not have hepatitis C ($P<0.05$).

Hepatitis A superimposed on chronic liver disease also is associated with more severe liver disease and a higher fatality rate.[20-23] During the large 1988 outbreak in Shanghai, China, 310,746 cases of hepatitis A occurred after consumption of contaminated shellfish.[23] Fifteen (32%) of the 47 patients who died had underlying hepatitis B or cirrhosis. The case fatality rates of hepatitis A in the United States among patients with chronic hepatitis B and other preexisting liver diseases were calculated to be 11.7% and 28%, respectively, compared with an overall fatality rate of 0.3%.[21]

Based on available evidence, a reasonable approach for protecting patients

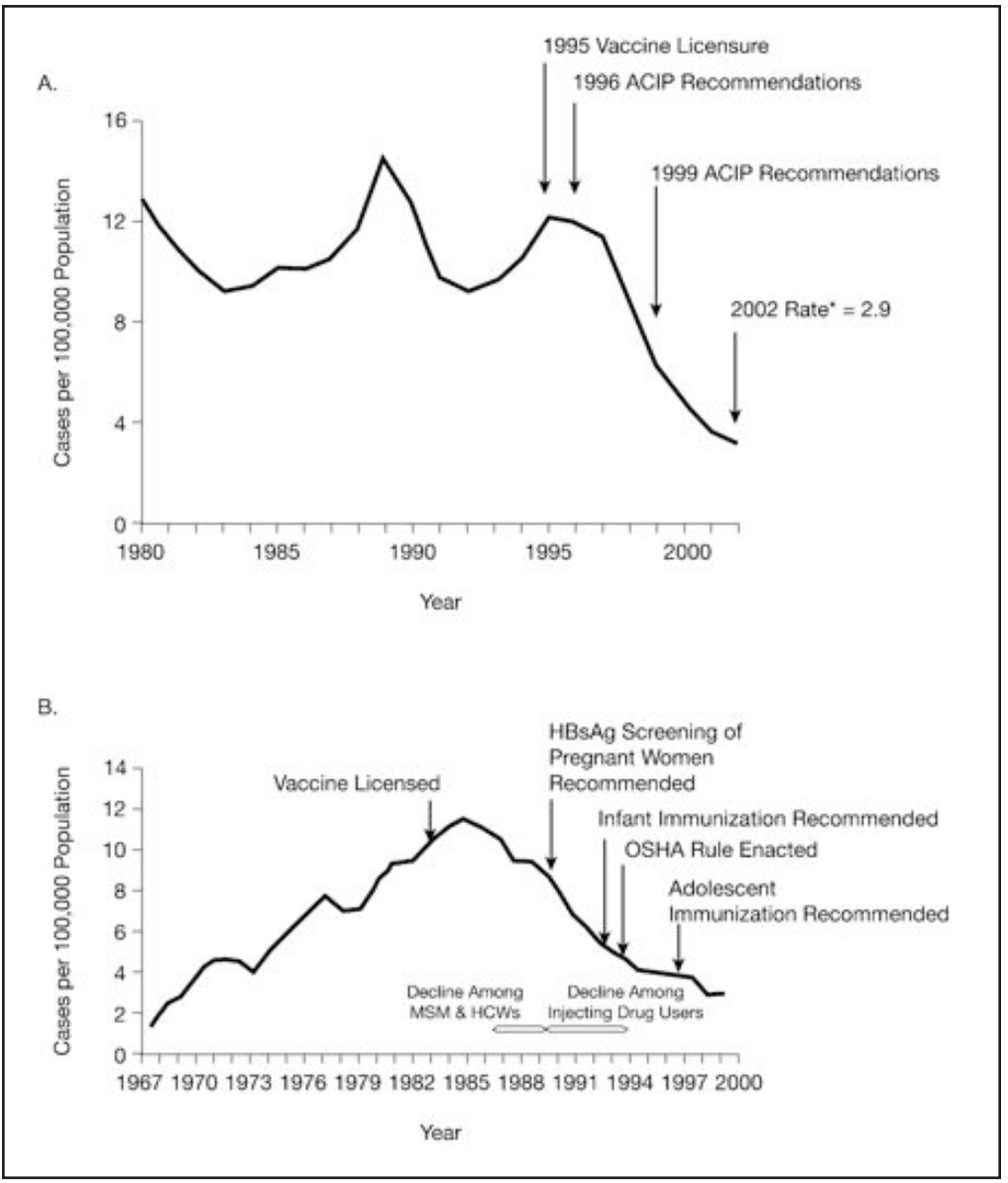

Figure 1. A. Hepatitis A incidence, United States, 1980-2002. The incidence of hepatitis A has declined since the introduction of the first hepatitis A vaccine in 1995. **B**. Hepatitis B incidence, United States, 1966-2000. The institution of hepatitis B vaccination recommendations has coincided with the decline of hepatitis B incidence during the past 2 decades.[8]
*2002 rate provisional.
ACIP=Advisory Committee on Immunization Practices; HBsAg=hepatitis B surface antigen; HCWs=healthcare workers; MSM=men who have sex with men; OSHA=Occupational Safety and Health Administration.

with chronic liver disease is to administer hepatitis B and hepatitis A vaccines as early as possible in the course of disease.[13] However, in a study of 693 patients with chronic liver disease, only 29% and 28% of patients seeing specialists, and 14% and 5% of patients in primary care offices received hepatitis B and hepatitis A vaccine, respectively.[24] A recommendation for universal vaccination of adults against hepatitis B and hepatitis A would help to ensure that

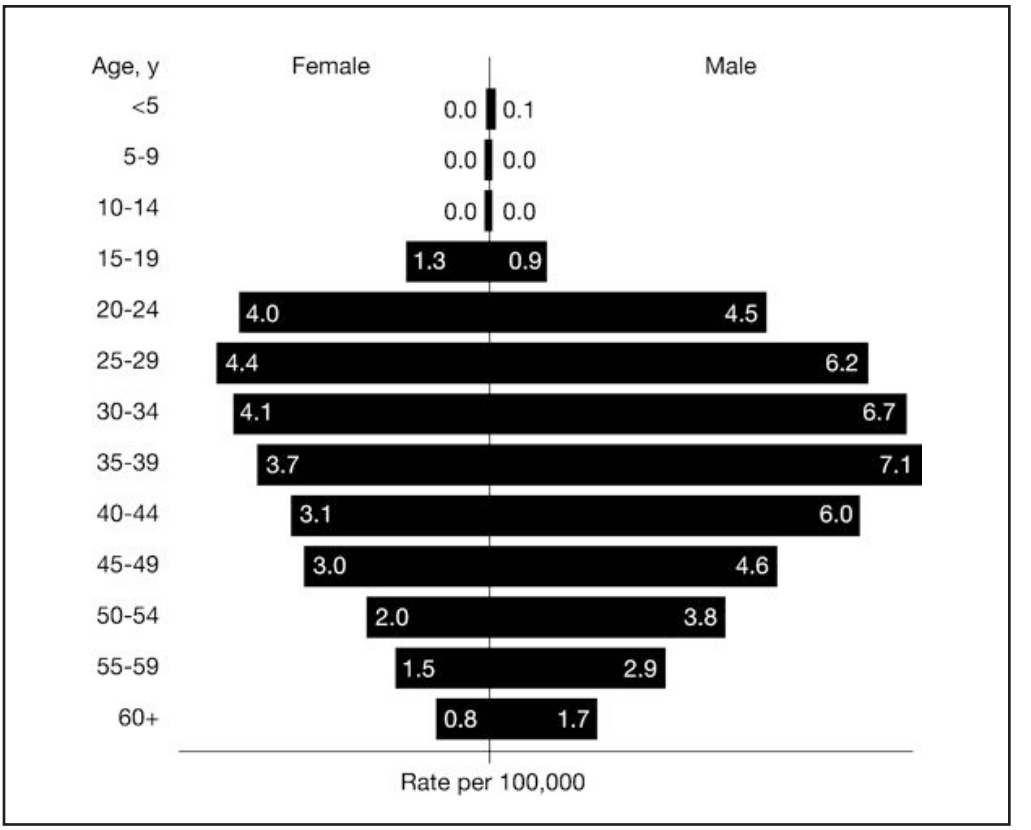

Figure 2. Incidence of reported acute hepatitis B, by age and sex, United States, 2002.[8]

patients with chronic liver disease are appropriately vaccinated. Hepatitis B and hepatitis A vaccines are safe, well tolerated, and have high seroconversion rates in adults with mild-to-moderate chronic liver disease,[14,25-28] although variable efficacy results have been documented in patients with advanced liver disease or after liver transplantation.[25,29-32]

Screening for Hepatitis B and Hepatitis A Antibodies

Because patients with chronic liver disease have a higher prevalence of hepatitis B and hepatitis A antibodies than the general population, prevaccination antibody screening has been demonstrated to be cost effective.[33,34] Patients negative for hepatitis B and hepatitis A antibodies should be vaccinated.

STD AND HIV PERSPECTIVE

Considerations for Hepatitis B and Hepatitis A Vaccination in Patients Being Evaluated for STDs

Substantial overlap of hepatitis B and hepatitis A infection risk exists, especially in persons with or at risk for STDs, in men who have sex with men, and in illicit drug users.[35] Hepatitis B vaccination, but not hepatitis A vaccination, is recommended for all patients being evaluated in STD clinics. Because persons at high risk for VPH as a result of sexual behavior may not make their risk factors known to their physicians,[36-39] protection of these individuals would be maximized by a universal, age-based vaccination strategy.

Several barriers exist to hepatitis immunization in STD clinic settings,

Table 4. Healthy People 2010 Objectives for Reduction in Hepatitis B and Hepatitis A Incidence[71]

Objective	Age group (yr)	Cases/100,000 population		Target reduction (%)
		1997 baseline	2010 target	
Reduction in hepatitis B	19-24	24.0	2.4	90
	25-39	20.2	5.1	75
	≥40	15.0	3.8	75
Reduction in hepatitis A	All ages	11.3	4.5	60

with or without use of a combination vaccine. One of the most cogent barriers is lack of funding for vaccination services. In addition, patients may not consider themselves at risk for infection or they may not return to the clinic after vaccination is recommended, and clinics may not have systems in place to ensure vaccination of patients at risk for infection.[40] Promotion of hepatitis B and hepatitis A prevention by use of the term "VPH" may address some of these barriers. Additionally, implementing a universal vaccination policy for adults may help to decrease the stigma associated with vaccination, as well as increase the likelihood that persons without identifiable risk factors are protected.

Hepatitis Immunization for Patients with HIV

Development of hepatitis B or hepatitis A in HIV-positive patients may be more serious than in HIV-negative patients.[41-44] The incidence of hepatitis B is higher in HIV-infected patients than in the general population.[45,46] The liver-related mortality rate among 5293 men who have sex with men was determined to be higher in men co-infected with HIV and hepatitis B (14.2 deaths/1000 person-years) than in those with HIV only (1.7 deaths/1000 person-years; $P<0.001$).[44] In addition, the duration of hepatitis A viremia was longer in 15 HIV-infected homosexual men (median, 53 days) than in 15 HIV-negative, age-matched controls (median, 22 days; $P<0.05$).[41]

Hepatitis B and hepatitis A vaccines have been demonstrated to be safe in HIV-infected adults.[47-50] Postel and colleagues[51] presented evidence at the First International Workshop on HIV and Hepatitis Co-Infection in 2004 that response to hepatitis B vaccine is lower when the CD4 cell count is low or viral load is high. Similarly, HIV-infected adults with a CD4 cell count of 200 cells/mm^3 or higher are more likely to respond to hepatitis A vaccine than patients with a CD4 cell count below 200 cells/mm^3.[49] As a means to reduce liver-related complications in HIV-infected patients, hepatitis B and hepatitis A vaccines should be administered to all HIV-infected patients as early as possible in the course of infection as part of a policy of universal vaccination against hepatitis B and hepatitis A in adults.

TRAVEL MEDICINE PERSPECTIVE

Hepatitis B and Travel

The ACIP recommends that travelers who will be in countries with high or intermediate prevalence of hepatitis B and who will have close contact with the local population should receive hepatitis B vaccine.[4] Frequently documented potential risk factors for hepatitis B related to travel are casual sexual activity, medical and dental care, and household exposure to carriers in expatriate communities.[52-54]

Because many travelers do not seek

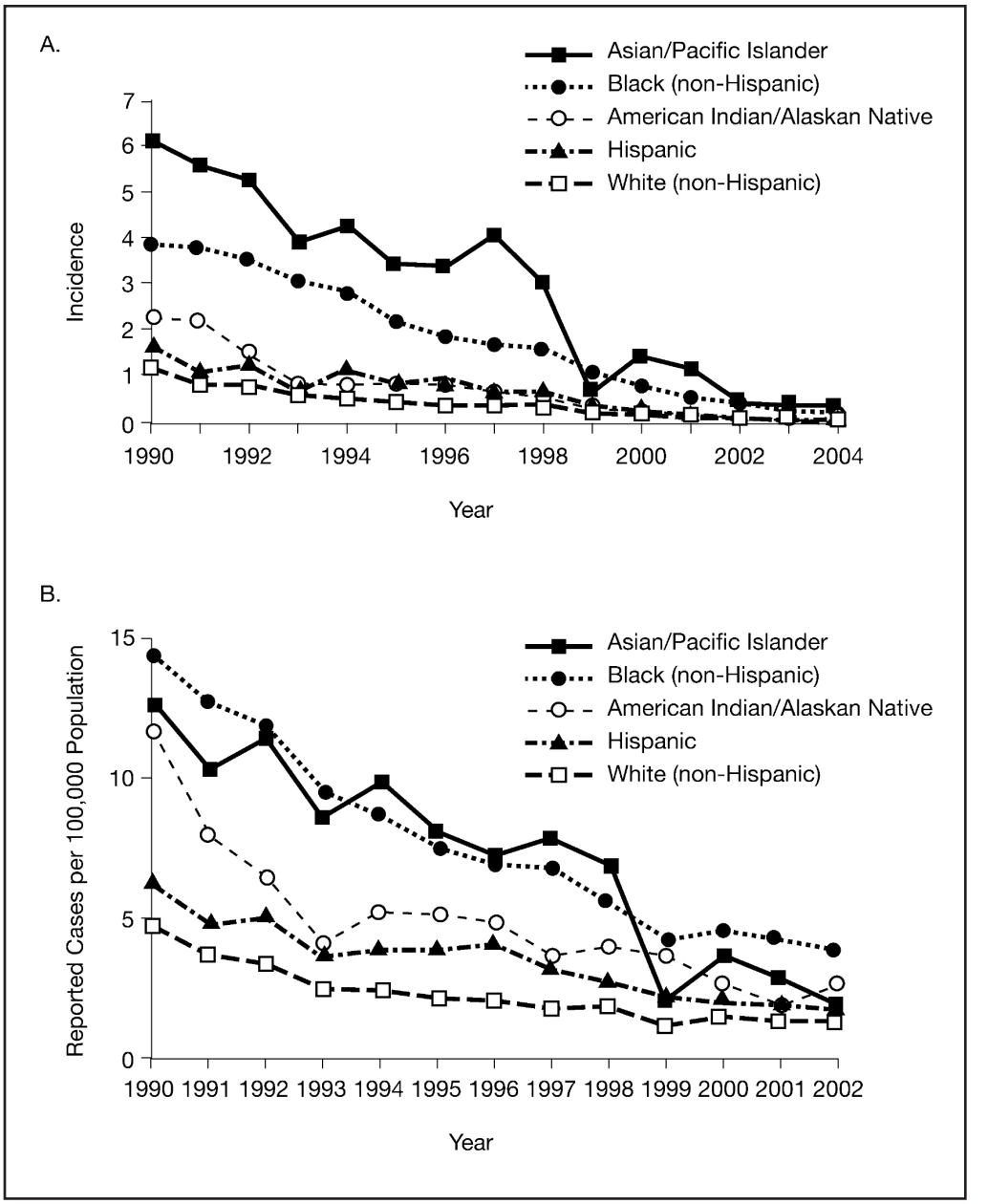

Figure 3. A. Rate per 100,000 population of acute hepatitis B in persons aged ≤19 years, by race and year, United States, 1990-2004.[78]
B. Incidence of reported acute hepatitis B in all age groups, by race and ethnicity, United States, 1990–2002.[79]

pre-travel medical evaluation early enough before departure, they are unable to receive hepatitis B vaccine according to the recommended vaccination schedule. Fortunately for these travelers, results of immunogenicity studies suggest that accelerated hepatitis B immunization schedules are effective and result in sustainable immunity.[55,56] In one study, a hepatitis B seroprotection

rate of 85% was observed 2 months after administration of combination hepatitis A and hepatitis B vaccine to healthy adults at days 0, 7, and 21.[56] A fourth dose of vaccine was given at month 12. Seroprotection rates in both groups increased to 100% by month 13.

Travel-Related Global Epidemiology of Hepatitis A

Various surveys indicate that in the past few decades, the monthly incidence rate for hepatitis A has decreased from 3 to between 0.1 and 1 per 1000 among travelers to developing countries.[57,58] The use of hepatitis A vaccine in the United States since its licensure in 1995 may have contributed to this decrease.[59] Nevertheless, despite recommendations that all travelers to developing countries be immunized against hepatitis A, a recent survey revealed that only 14% of travelers at high risk for hepatitis A departing from John F. Kennedy International Airport in New York were vaccinated.[60]

Because travel may occur unexpectedly, or travelers may be unaware of their risk, universal immunization should be considered to decrease travel-associated hepatitis A. Early vaccination is preferred because of anticipated lifetime risk of exposure.[61]

US Epidemiology of Hepatitis A and Travel by Immigrants Visiting Friends and Relatives

Immigrants and refugees who return to their native countries to visit friends and relatives, as well as migrant workers and orphans adopted from abroad, constitute a high proportion of international travelers.[52] They are at high risk for hepatitis A because many do not consult a physician prior to travel and are likely to have extended stays and close contact with inhabitants of the countries they are visiting. When these travelers return to the United States, they contribute to hepatitis A transmission. Pediatric travelers with undiagnosed hepatitis A pose a particular risk for transmission of the virus among family, caretakers, and playmates.[62] Incorporating hepatitis A vaccine into the adult immunization schedule on a universal basis would decrease the risk of hepatitis A being imported into the United States by such persons.

Hepatitis A Vaccination in the Last-Minute Traveler

The mean incubation period of hepatitis A is 28 days.[2] At the Third European Conference on Travel Medicine in 2002, Van Damme and colleagues[63] reported that most vaccinees develop antibodies within 2 weeks of vaccination. Therefore, it is reasonable to give the first dose of hepatitis A vaccine to travelers shortly before their departure. The second injection should still be given at 6 months to confer long-term immunity. Further support for administering vaccine shortly before travel is provided by demonstration of postexposure protection from hepatitis A vaccine in outbreak situations[64-68] and in reducing household transmission.[69] Despite recommendations that the vaccine be administered 2 to 4 weeks prior to anticipated exposure,[59] current evidence supports efficacy of hepatitis A vaccine in the imminently departing traveler.

PUBLIC HEALTH PERSPECTIVE

The Healthy People 2010 objectives include goals for reducing the incidence of hepatitis B and hepatitis A in the United States.[70] The goals for decreasing hepatitis B incidence in adults aged 19 to 24 years, 25 to 39 years, and 40 years and older are 90% to 2.4 cases per 100,000, 75% to 5.1 cases per 100,000, and 75% to 3.8 cases per 100,000, respectively. The target incidence rate for hepatitis A is 4.5 cases per 100,000 population, a 60% reduction (Table 4).

Increasing public awareness of hepatitis B and hepatitis A as vaccine-preventable diseases should be a part of state and local public health departments' infectious-disease control and prevention programs. Models of effective community-based interventions that raise awareness and increase the number of persons vaccinated should be emulated. A universal, age-based vaccination strategy among adults may help to achieve the national Healthy People 2010 objectives. Routine hepatitis vaccination should be integrated into healthcare settings that serve adults, such as STD and HIV testing and treatment facilities, drug treatment centers, travel clinics, needle exchange programs, criminal justice settings, settings serving men who have sex with men, chronic hemodialysis and end-stage renal disease programs, and facilities for developmentally disabled persons. This integration can be accomplished by educating providers, improving communication skills and consumer awareness, creating office systems and immunization registries, providing payment and coverage for vaccination services through sustainable local and federal funding, and routinely assessing performance and quality.

Inmates and staff in correctional systems, especially prisons and jails, have high burdens of risk for and incidence of hepatitis B,[71-74] but the disease burden of hepatitis A remains unmeasured in this setting. Criminal justice systems present an opportunity to immunize high-risk groups against VPH.[75] The CDC recommend hepatitis B vaccine for all adults in prisons, jails, and community corrections settings (including probation, parole, and re-entry programs), and hepatitis A vaccine for adults with risk factors for hepatitis A or those who are likely to experience complications if infected.[71,76] Despite CDC recommendations, barriers to prevention of hepatitis B and hepatitis A in the criminal justice setting exist and include lack of knowledge, funding, and documentation, and insufficient public health collaboration. Implementation of adult vaccination services in criminal justice settings will require both local and federal funding.

Use of the term "VPH" and a universal age-based hepatitis B and hepatitis A vaccination strategy among adults may help expand funding sources, simplify messages, and advance preventive strategies. Providers should be better informed about mechanisms for reimbursement of VPH vaccines and related services. Stronger and consistent guidelines for universal provision of hepatitis vaccines are necessary to obtain coverage from Medicaid and Medicare, and to influence insurance companies to include vaccine purchase and administration in benefits packages. The federal government, through partnerships with agencies such as the Health Resources and Services Administration (HRSA), CDC, Substance Abuse and Mental Health Services Administration (SAMHSA), Office of Minority Health (OMH), and Centers for Medicare and Medicaid Services (CMS) should cover the cost of hepatitis vaccines and related services. For the federal government to provide this funding, restrictions on federal funding must be lifted and collaborative strategies must be implemented. Additional national, state, and local policies should be adopted or mandated to enable communities to exceed the Healthy People 2010 objectives for prevention of hepatitis B and hepatitis A, and specific goals for prevention should be set for high-risk and minority populations to address disparities in access to health care.

DISCUSSION

Existing recommendations for prevention of hepatitis B and hepatitis A in adults are insufficient to substantially

reduce their burden of disease, and thus need to be broadened. Current recommendations are risk based.[4] Before the introduction of universal childhood and adolescent hepatitis B immunization recommendations, overall incidence of hepatitis B was high, especially among African Americans. In recent years, however, rates of disease for all races in children and adolescents have converged at a low rate (Figure 3A).[77] This success was most likely produced by the universal vaccination strategy employed in these age groups. Currently, most of the new cases of hepatitis B occur in adults aged 19 years and older (Figure 2),[78] and the rates among African Americans are almost 3 times those of other racial groups (Figure 3B). This disparity shows no signs of improving under the risk-based vaccination strategy, but this could change with a recommendation for universal vaccination of adults against hepatitis B.

Many persons who become infected with VPH do not have clearly identifiable risk factors for infection[8,59,72,78,79] or may not confide in their physicians. Furthermore, many physicians remain uncomfortable asking patients about their risk-associated behaviors, particularly those involving sexual expression and illicit drug use.[80-82]

A recent cost-effectiveness study predicted that use of both hepatitis B and hepatitis A vaccines instead of hepatitis B vaccine alone would prevent 2263 cases of hepatitis A, resulting in a 20% decrease in hepatitis A-related hospitalizations, a 19% decrease in liver transplants, and a 17% decrease in death caused by complications of hepatitis A.[83] Costs for treatment of hepatitis A would decline by $2.5 million. The substitution would cost $20,892 per life-year saved, or $13,397 per quality-adjusted life-year (QALY) gained. In comparison, an intervention typically is considered to be cost effective if it costs less than $50,000 per life-year saved or QALY gained. Universally administering hepatitis A vaccine to adults along with hepatitis B vaccine would protect those persons with unidentified risk factors for infection.

CONCLUSIONS

Even though the incidence of hepatitis B and hepatitis A is decreasing, a substantial disease burden remains. Experts in the fields of primary care, gastroenterology, hepatology, infectious diseases, STDs, HIV, travel medicine, and public health who convened to discuss prevention of hepatitis B and hepatitis A agreed that the most practical approach to disease control, in addition to universal childhood vaccination, is universal vaccination among adults.

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REFERENCES

1. Centers for Disease Control and Prevention. Hepatitis B. In: Atkinson W, Hamborsky J, Wolfe C, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 8th ed. Washington, DC: Public Health Foundation. 2005:191-212.
2. Centers for Disease Control and Prevention. Hepatitis A. In: Atkinson W, Hamborsky J, Wolfe C, eds. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 8th ed. Waldorf, MD: Public Health Foundation; 2005:177-189.
3. Centers for Disease Control and Prevention. Recommended childhood and adolescent immunization schedule – United States, 2006. *MMWR*.2006;54:Q1-4.
4. Centers for Disease Control and Prevention. Recommended adult immunization schedule – United States, October 2006–September 2007. *MMWR* 2006;55:Q1-4.
5. Gilbert LK, Bulger J, Scanlon K, Ford K, et al. Integrating hepatitis B prevention into sexually transmitted disease services: US sexually transmitted disease program and clinic trends – 1997 and 2001. *Sex Transm Dis*. 2005;32:346-350.
6. Sharfstein J, Wise PH. Inadequate hepatitis B vaccination of adolescents and adults at an urban community health center. *J Natl Med Assoc*. 1997;89:86-92.
7. National Center for Infectious Diseases. *Viral hepatitis*. Available at: http://www.cdc.gov/ncidod/diseases/hepatitis/slideset. Accessed July 19, 2006.
8. Centers for Disease Control and Prevention. Incidence of acute hepatitis B – United States, 1990-2002. *MMWR*. 2004;52:1252-1254.
9. Crabtree BF, Miller WL, Aita VA, Flocke SA, et al. Primary care practice organization and preventive services delivery: a qualitative analysis. *J Fam Pract*. 1998;46:404-409.
10. Jaén CR, Stange KC, Nutting PA. Competing demands of primary care: a model for the delivery of clinical preventive services. *J Fam Pract*. 1994;38:166-171.
11. Centers for Disease Control and Prevention. Improving influenza, pneumococcal polysaccharide, and hepatitis B vaccination coverage among adults aged <65 years at high risk: a report on recommendations of the Task Force on Community Preventive Services. *MMWR*. 2005;54(RR-5):1-12.
12. Immunization Action Coalition. Adults only vaccination: a stepbystep guide. St Paul, MN: Immunization Action Coalition. 2004.
13. Keeffe EB. Acute hepatitis A and B in patients with chronic liver disease: prevention through vaccination. *Am J Med*. 2005;118:21S-7S.
14. Koff RS. Risks associated with hepatitis A and hepatitis B in patients with hepatitis C. *J Clin Gastroenterol*. 2001;33:20-26.
15. Benvegnù L, Fattovich G, Noventa F, et al. Concurrent hepatitis B and C virus infection and risk of hepatocellular carcinoma in cirrhosis: a prospective study. *Cancer*. 1994;74:2442-2448.
16. Fuiano B, Pannullo A, Annovazzi G, et al. Risk factors and association with HBV infection in chronic C hepatitis. *Ital J Gastroenterol*. 1992;24:409-411.
17. Ilan Y, Ashur Y, Tur-Kaspa R, Shouval D. Chronic hepatitis C virus infection with exposure to hepatitis B virus. *Isr J Med Sci*. 1994;30:259-263.
18. Kew MC, Yu MC, Kedda MA, Coppin A, et al. The relative roles of hepatitis B and C viruses in the etiology of hepatocellular carcinoma in Southern African blacks. *Gastroenterology*. 1997;112:184-187.
19. Sagnelli E, Coppola N, Messina V, Di Caprio D, et al. HBV superinfection in hepatitis C virus chronic carriers, viral interaction, and clinical course. *Hepatology*. 2002;36:1285-1291.
20. Hadler SC. Global impact of hepatitis A virus infection changing patterns. In: Hollinger FB, Lemon SM, Margolis H, eds. *Viral Hepatitis and Liver Disease: Proceedings of the 1990 International Symposium on Viral Hepatitis and Liver Disease: Contemporary Issues and Future Prospects*. Baltimore: Williams and Wilkins. 1991:14-20.
21. Keeffe E. Hepatitis A in patients with chronic liver disease – severity of illness and prevention with vaccination. *J Viral Hepat*. 2000;7(suppl 1):15-17.
22. Vento S, Garofano T, Renzini C, Cainelli F. Fulminant hepatitis associated with hepatitis A virus superinfection in patients with chronic hepatitis C. *N Engl J Med*. 1998;338:286-290.
23. Yao G. Clinical spectrum and natural history of viral hepatitis A in a 1988 Shanghai epidemic. In: Hollinger FB, Lemon SM, Margolis H, eds. *Viral Hepatitis and Liver Disease: Proceedings of the 1990 International Symposium on Viral Hepatitis and Liver Disease: Contemporary Issues and Future Prospects*. Baltimore: Williams and Wilkins. 1991:76-78.
24. Jacobs RJ, Meyerhoff AS, Saab S. Immunization needs of chronic liver disease patients seen in primary care versus specialist settings. *Dig Dis Sci*. 2005;50:1525-1531.
25. Arguedas MR, Johnson A, Eloubeidi MA, Fallon MB. Immunogenicity of hepatitis A vaccination in decompensated cirrhotic patients. *Hepatology*. 2001;34:28-31.
26. Keeffe EB, Krause DS. Hepatitis B vaccination of patients with chronic liver disease. *Liver Transpl Surg*. 1998;4:437-439. Letter.
27. Keeffe EB, Iwarson S, McMahon BJ, Lindsay KL. Safety and immunogenicity of hepatitis A vaccine in patients with chronic liver disease. *Hepatology*. 1998;27:881-886.
28. Lee SD, Chan CY, Yu MI, Lu RH, et al.

Hepatitis B vaccination in patients with chronic hepatitis C. *J Med Virol*. 1999;59:463-468.
29. Arslan M, Wiesner RH, Poterucha JJ, Zein NN. Safety and efficacy of hepatitis A vaccination in liver transplantation recipients. *Transplantation*. 2001;72:272-276.
30. Dumot JA, Barnes DS, Younossi Z, Gordon SM, et al. Immunogenicity of hepatitis A vaccine in decompensated liver disease. *Am J Gastroenterol*. 1999;94:1601-1604.
31. Loinaz C, de Juanes JR, Gonzalez EM, Lopez A, et al. Hepatitis B vaccination results in 140 liver transplant recipients. *Hepatogastroenterology*. 1997;44:235-238.
32. Wiedmann M, Liebert UG, Oesen U, Porst H, et al. Decreased immunogenicity of recombinant hepatitis B vaccine in chronic hepatitis C. *Hepatology*. 2000;31:230-234.
33. Duncan M, Hirota WK, Tsuchida A. Prescreening versus empirical immunization for hepatitis A in patients with chronic liver disease: a prospective cost analysis. *Am J Gastroenterol*. 2002;97:1792-1795.
34. Siddiqui F, Mutchnick M, Kinzie J, Peleman R, et al. Prevalence of hepatitis A virus and hepatitis B virus immunity in patients with polymerase chain reactionconfirmed hepatitis C: implications for vaccination strategy. *Am J Gastroenterol*. 2001;96:858-863.
35. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines 2002. *MMWR*. 2002;51(RR-6):1-80.
36. Gates GJ, Sonenstein FL. Heterosexual genital sexual activity among adolescent males: 1988 and 1995. *Fam Plann Perspect*. 2000;32:295-297,304.
37. Gross M, Holte SE, Marmor M, Mwatha A, et al. Anal sex among HIVseronegative women at high risk of HIV exposure. The HIVNET Vaccine Preparedness Study 2 Protocol Team. *J Acquir Immune Defic Syndr*. 2000;24:393-398.
38. St Lawrence JS, Montaño DE, Kasprzyk D, Phillips WR, et al. STD screening, testing, case reporting, and clinical and partner notification practices: a national survey of US physicians. *Am J Public Health*. 2002;92:1784-1788.
39. Wohl AR, Johnson DF, Lu S, Jordan W, et al. HIV risk behaviors among African American men in Los Angeles County who selfidentify as heterosexual. *J Acquir Immune Defic Syndr*. 2002;31:354-360.
40. Tedaldi EM, Baker RK, Moorman AC, Wood KC, et al and the HIV Outpatient Study (HOPS) Investigators. Hepatitis A and B vaccination practices for ambulatory patients infected with HIV. *Clin Infect Dis*. 2004;38:1478-1484.
41. Ida S, Tachikawa N, Nakajima A, Daikoku M, et al. Influence of human immunodeficiency virus type 1 infection on acute hepatitis A virus infection. *Clin Infect Dis*. 2002;34:379-385.
42. Ridolfo AL, Rusconi S, Antinori S, Balotta C, et al. Persisting HIV1 replication triggered by acute hepatitis A virus infection. *Antivir Ther*. 2000;5:15-18.
43. Sulkowski MS, Thomas DL, Chaisson RE, Moore RD. Hepatotoxicity associated with antiretroviral therapy in adults infected with human immunodeficiency virus and the role of hepatitis C or B virus infection. *JAMA*. 2000;283:74-80.
44. Thio CL, Seaberg EC, Skolasky R Jr, Phair J, et al. HIV1, hepatitis B virus, and risk of liverrelated mortality in the Multicenter Cohort Study (MACS). *Lancet*. 2002;360:1921-1926.
45. Kellerman SE, Hanson DL, McNaghten AD, Fleming PL. Prevalence of chronic hepatitis B and incidence of acute hepatitis B infection in human immunodeficiency virusinfected subjects. *J Infect Dis*. 2003;188:571-577.
46. McQuillan GM, Coleman PJ, Kruszon-Moran D, Moyer LA, et al. Prevalence of hepatitis B virus infection in the United States: the National Health and Nutrition Examination Surveys, 1976 through 1994. *Am J Public Health*. 1999;89:14-18.
47. Bodsworth NJ, Neilsen GA, Donovan B. The effect of immunization with inactivated hepatitis A vaccine on the clinical course of HIV1 infection: 1year followup. *AIDS*. 1997;11:747-749.
48. Keet IPM, van Doornum G, Safary A, Coutinho RA. Insufficient response to hepatitis B vaccination in HIVpositive homosexual men. *AIDS*. 1992;6:509-510.
49. Kemper CA, Haubrich R, Frank I, et al, for the California Collaborative Treatment Group. Safety and immunogenicity of hepatitis A vaccine in human immunodeficiency virusinfected patients: a doubleblind, randomized, placebocontrolled trial. *J Infect Dis*. 2003;187:1327-1331.
50. Wong EKL, Bodsworth NJ, Slade MA, Mulhall BP, et al. Response to hepatitis B vaccination in a primary care setting: influence of HIV infection, CD4+ lymphocyte count and vaccination schedule. *Int J STD AIDS*. 1996;7:490-494.
51. Postel N, Wolf E, Buchberger A, et al. Anti-HBV vaccination in HIV-infection: successful only with CD4 cell count >500 mL combined with a viral load below 1,000 cps/mL [abstract CI25]. Presented at the 1st International Workshop on HIV and Hepatitis Co-Infection; December 2-4, 2006; Amsterdam, The Netherlands.
52. Bacaner N, Stauffer B, Boulware DR, Walker PF, et al. Travel medicine considerations for North American immigrants visiting friends and relatives. *JAMA*. 2004;291:2856-2864.
53. Khuroo MS. Viral hepatitis in international travellers: risks and prevention. *Int J Antimicrob Agents*. 2003;21:143-152.
54. Zuckerman JN, Steffen R. Risks of hepatitis B in travelers as compared to immunization

status. *J Travel Med*. 2000;7:170-174.
55. Bock HL, Löscher T, Scheiermann N, Baumgarten R, et al. Accelerated schedule for hepatitis B immunization. *J Travel Med*. 1995;2:213-217.
56. Nothdurft HD, Dietrich M, Zuckerman JN, Knobloch J , et al. A new accelerated vaccination schedule for rapid protection against hepatitis A and B. *Vaccine*. 2002;20:1157-1162.
57. Steffen R, Rickenbach M, Wilhelm U, Helminger A, et al. Health problems after travel to developing countries. *J Infect Dis*. 1987;156:84-91.
58. Teitelbaum P. An estimate of the incidence of hepatitis A in unimmunized Canadian travelers to developing countries. *J Travel Med*. 2004;11:102-106.
59. Centers for Disease Control and Prevention. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR*. 1999;48(RR-12):1-38.
60. Hamer DH, Connor BA. Travel health knowledge, attitudes and practices among United States travelers. *J Travel Med*. 2004;11:23-26.
61. Jacobs RJ, Meyerhoff AS, Zink T. Hepatitis A immunization strategies: universal versus targeted approaches. *Clin Pediatr (Phila)*. 2005;44:705-709.
62. Chen LH, Barnett ED, Wilson ME. Preventing infectious diseases during and after international adoption. *Ann Intern Med*. 2003;139:371-378.
63. Van Damme P, Lievens M, Stoffel M, Nguyen C. Rapid seroconversion rates after first dose of an inactivated hepatitis A vaccine (Havrix 1440%): results of a retrospective analysis [abstract P60]. Presented at the 3rd European Conference on Travel Medicine; May 15-18, 2002; Florence, Italy.
64. Bonanni P, Franzin A, Staderini C, Pitta M, et al. Vaccination against hepatitis A during outbreaks starting in schools: what can we learn from experiences in central Italy? *Vaccine*. 2005;23:2176-2180.
65. Craig AS, Sockwell DC, Schaffner W, Moore WL, Jr, et al. Use of hepatitis A vaccine in a communitywide outbreak of hepatitis A. *Clin Infect Dis*. 1998;27:531-535.
66. Kaic B, Borcic B, Ljubicic M, Brkic I, et al. Hepatitis A control in a refugee camp by active immunization. *Vaccine*. 2001;19:3615-3619.
67. McMahon BJ, Beller M, Williams J, Schloss M, et al. A program to control an outbreak of hepatitis A in Alaska by using an inactivated hepatitis A vaccine. *Arch Pediatr Adolesc Med*. 1996;150:733-739.
68. Príkazsk? V, Oleár V, Cernoch A, Safary A, et al. Interruption of an outbreak of hepatitis A in two villages by vaccination. *J Med Virol*. 1994;44:457-459.
69. Sagliocca L, Amoroso P, Stroffolini T, Adamo B, et al. Efficacy of hepatitis A vaccine in prevention of secondary hepatitis A infection: a randomised trial. *Lancet*. 1999;353:1136-1139.
70. US Department of Health and Human Services. *Healthy People 2010: Understanding and Improving Health*. 2nd ed. Washington, DC: Government Printing Office, November 2000.
71. Centers for Disease Control and Prevention. Prevention and control of infections with hepatitis viruses in correctional settings. *MMWR*. 2003;52(RR-1):1-36.
72. Centers for Disease Control and Prevention. Hepatitis B outbreak in a state correctional facility, 2000. *MMWR*. 2001;50:529-532.
73. Glaser JB, Greifinger RB. Correctional health care: a public health opportunity. *Ann Intern Med*. 1993;118:139-145.
74. Macalino GE, Vlahov D, Dickinson BP, Schwartzapfel B, et al. Community incidence of hepatitis B and C among reincarcerated women. *Clin Infect Dis*. 2005;41:998-1002.
75. Sosman JM, MacGowan RJ, Margolis AD, Eldridge E, et al; Project START Study Group. Screening for sexually transmitted diseases and hepatitis in 18-29-year-old men recently released from prison: feasibility and acceptability. *Int J STD AIDS*. 2005;16:117-122.
76. Devasia RA, Jones TF, Kainer MA, Halford S, et al. Two community hepatitis B outbreaks: an argument for vaccinating incarcerated persons. *Vaccine*. 2006;24:1354-1358.
77. Centers for Disease Control and Prevention. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States. *MMWR*. 2005;54(RR-16):1-33.
78. Centers for Disease Control and Prevention. *Hepatitis Surveillance Report Number 59*. Atlanta, GA: US Dept of Health and Human Services, Centers for Disease Control and Prevention; 2004.
79. Berge JJ, Drennan DP, Jacobs RJ, Jakins A, et al. The cost of hepatitis A infections in American adolescents and adults in 1997. *Hepatology*. 2000;31:469-473.
80. Centers for Disease Control and Prevention. HIV prevention practices of primary-care physicians – United States, 1992. *MMWR*. 1994;42:988-992.
81. Schwartz JS, Lewis CE, Clancy C, Kinosian MS, et al. Internists' practices in health promotion and disease prevention: a survey. *Ann Intern Med*. 1991;114:46-53.
82. Tao G, Irwin KL, Kassler WJ. Missed opportunities to assess sexually transmitted diseases in U.S. adults during routine medical checkups. *Am J Prev Med*. 2000;18:109-114.
83. Jacobs RJ, Meyerhoff AS. Costeffectiveness of hepatitis A/B vaccine versus hepatitis B vaccine in public sexually transmitted disease clinics. *Sex Transm Dis*. 2003;30:859-865.