

Hepatitis A and B Booster Recommendations: Implications for Travelers

Jane N. Zuckerman,^{1,2} Bradley A. Connor,^{3,4} and Frank von Sonnenburg⁵

¹Academic Centre for Travel Medicine and Vaccines and Royal Free Travel Health Centre, and ²World Health Organization Collaborating Centre for Travel Medicine, Royal Free and University College Medical School, London, United Kingdom; ³Division of Gastroenterology and Hepatology, Weill Medical College of Cornell University, and ⁴The New York Center for Travel and Tropical Medicine, New York, New York; and ⁵Department of Infectious Diseases and Tropical Medicine, University of Munich, Munich, Germany

Hepatitis A and B are serious vaccine-preventable diseases with a predominantly overlapping epidemiological distribution. Travelers, a term encompassing a range of individuals, are at risk of contracting these diseases if they are unvaccinated. Although the benefits of the primary vaccination course of hepatitis A and B vaccines are clear, the administration of hepatitis A and B boosters varies worldwide. Recommendations on the need for booster vaccinations have recently been published, and the implications of these recommendations for travelers are discussed in this review. Until a greater understanding is reached on the immunogenicity of hepatitis A and B vaccines in certain special groups (e.g., immunocompromised persons), there will be a need to monitor antibody levels to assess whether booster vaccinations are required. However, for the majority of immunocompetent travelers, the full primary vaccination course will provide protection from both hepatitis A and B infection in the long term, without the need for boosters.

Hepatitis A and B are serious diseases with a widespread and predominantly overlapping epidemiological distribution (figure 1) [1, 2]. Hepatitis B is a major global health problem and is the tenth-leading cause of mortality in the world, responsible for 500,000–1.2 million deaths per year. Deaths occur as a result of complications of acute hepatitis, such as fulminant liver failure, as well as a result of sequelae of chronic liver disease, including hepatocellular carcinoma [3]. Infection with hepatitis A virus (HAV) is also of considerable concern, with ~1.5 million clinical cases reported annually [4]. Although usually self-limiting, hepatitis A can be a life-threatening disease. For example, in the United Kingdom, it is responsible for 10%–20% of cases of liver failure and has an overall mortality rate of 0.1% [5]. In the United States, 72% of patients with hepatitis A described in 2002 developed jaundice, and 25% required hospitalization, with an associated mortality of 0.5%, as re-

ported similarly for previous years [6]. The case-fatality rate was highest among persons aged ≥ 60 years (1.2%).

Nonimmune travelers are at risk of contracting hepatitis A and B: 40%–50% of reported cases in some northern European countries are acquired while traveling [7]. In September 2004, a total of 219 cases of hepatitis A were reported among German tourists who had stayed at 1 hotel in Egypt, with an additional 49 cases identified in other countries [8]. In a European survey of 9008 individuals, 6.6%–11.2% of travelers were classified as being at high risk of infection with hepatitis B virus (HBV), depending on the destination of travel, with 60.8%–75.8% classified as being at potential risk of exposure to infection [9].

RISK ASSESSMENT FOR TRAVELERS

The level of risk of infection with HAV or HBV for travelers depends on several factors, including the disease endemicity in the travel destination, the duration and frequency of travel, the activities to be undertaken, and the purpose of the travel [10]. Travelers who remain in an area of high endemicity for extended periods (>1 month) are likely to be at higher risk of exposure to hepatitis A and/or hepatitis B than are those who take short trips. This is also true for those who travel frequently, but for shorter periods, to countries of endemicity, who may be at a cumulative lifetime risk.

Received 4 March 2005; accepted 1 June 2005; electronically published 29 August 2005.

Reprints or correspondence: Dr. Jane N. Zuckerman, Academic Centre for Travel Medicine & Vaccines, Royal Free and University College Medical School, WHO Collaborating Centre for Travel Medicine, Rowland Hill St., London NW3 2PF, England (j.zuckerman@medsch.ucl.ac.uk).

Clinical Infectious Diseases 2005;41:1020–6

© 2005 by the Infectious Diseases Society of America. All rights reserved.
1058-4838/2005/4107-0016\$15.00

Hepatitis A



Hepatitis B



■ Countries/areas with moderate to high risk of infection

Figure 1. Worldwide geographical distribution of hepatitis A and B in 2003 [1, 2]. (Reproduced with permission from the World Health Organization.)

The type of traveler is also an important factor, with backpackers generally having a higher probability of exposure to infection with HAV and/or HBV than business travelers and, thus, being at increased risk. The risk behavior profile of the traveler should be considered, with sexual promiscuity, [11], acupuncture, body piercing, tattooing, and adventure sports considered to be high-risk activities in terms of potential exposure to infection.

The health and age of the traveler are other factors to be taken into account when assessing the risk of infection. If a traveler has an underlying medical condition that might necessitate medical care while traveling, then subsequent exposure to bloodborne viruses, such as HBV, is a possibility. This is also true for older travelers, for whom the likelihood of requiring medical attention (e.g., because of cardiac disease) is higher. The risk applies similarly for those who may undergo dental treatment while traveling and for individuals traveling to undergo specialized medical procedures in other countries.

The importance of preventing hepatitis A and B in traveling children should be emphasized. Although HAV infection is usually asymptomatic in younger children, this population plays an important role in the transmission of HAV through importation of disease and subsequent transmission in nursery settings [12]. For hepatitis B, the risk of developing chronic infection is higher for children who are infected at birth (90%) than for those who are infected at an older age (for 1–5 years of age, 30%; for >5 years of age, 6%) [13].

Although it is often difficult to assess whether an individual has natural immunity to HAV or HBV when relying on clinical history alone, it is not practical to evaluate immunity prior to vaccination. Therefore, judgement on whether to test for immunity should be based on observations relating to the age of the individual, the epidemiology of the infection, and the cost of both the vaccine and the test.

HEPATITIS A AND B VACCINATION

Effective and well-tolerated hepatitis A and B vaccines are available either as monovalent formulations or in various combinations. Although the benefits of a full primary vaccination course are clear—protection against potentially life-threatening diseases—the requirement for a booster (i.e., vaccination administered after the full primary course) varies in different countries. Recommendations for the administration of hepatitis boosters in the United States, the United Kingdom, and Germany illustrate this. In the United States, a hepatitis B booster is not recommended for children and adults with a normal immune status [14], whereas in the United Kingdom, administration of a single booster dose 5 years after completion of the primary course is deemed necessary [15]. In Germany, for example, Empfehlungen der Ständigen Impfkommission recommendations published in July 2004 [16] state that immune

response should be checked for persons who are immunodeficient and suggest the same for persons aged >40 years. For persons with anti-hepatitis B surface antigen (anti-HBs) titers of <100 mIU/mL, 1 extra dose is recommended, followed by an additional antibody test. In vaccinees with anti-HBs titers of >100 mIU/mL, a booster is recommended after 10 years when the potential for risk continues (e.g., risk associated with needlestick injuries, blood exposure, and hemodialysis). The World Health Organization has recognized that almost all children are protected against hepatitis B after vaccination, without a requirement for boosters, and that the protection is most likely lifelong [17].

The disparity in use of hepatitis A and B boosters worldwide has led vaccination experts to reassess the need for such immunizations on the basis of clinical experience and the available scientific evidence. This review discusses the implications of the recent hepatitis A and B booster recommendations for travelers and provides guidance and practical advice to assist in the clinical decisions involved in the administration of hepatitis A and/or B booster vaccinations.

Search Strategy and Selection Criteria

The recommendations for the administration of booster doses of hepatitis A [18] and hepatitis B [19] formed the basis of the search. The literature cited in these articles was updated and expanded to include articles relevant to hepatitis A and B and travel. The following were searched: the PubMed database, World Health Organization and Centers for Disease Control and Prevention Web sites, current hepatitis recommendations, and relevant publications (*Eurosurveillance Weekly*, *Viral Hepatitis*, and *Travel Medicine and Infectious Disease*). Only articles written in English were included.

Booster Recommendations

Hepatitis A. The schedule for completing a primary course of hepatitis A vaccination varies between countries and depends on the vaccine product licence, as determined by the regulatory authorities. A recommended schedule consists of 2 doses, with the second dose administered 6–18 months after the first. The booster recommendations state that there is no evidence to support the need for a booster dose of hepatitis A vaccine in healthy (i.e., immunocompetent) individuals who have received the complete primary course of vaccination [18].

Pertinent to last-minute travelers, immunity against hepatitis A can be provided in a single dose immediately before departure, when travelers may be at subsequent risk of exposure to hepatitis A at their destination [20]. In a retrospective analysis of 9 clinical trials of GlaxoSmithKline's inactivated hepatitis A vaccine, Havrix (Havrix 1440 EL.U [ELISA Units]), 79% of vaccinated healthy adults who received 1 dose had seroconversion by day 13 after vaccination, and all had seroconversion

by day 19 [20, 21]. Similar seroconversion rates of 78%–98% have been reported 14 days after administration of a single dose of Sanofi Pasteur's hepatitis A vaccine, Avaxim [22]. It is still important for the individual to receive the second dose, preferably within the specified period, to ensure a robust anamnestic response and subsequent long-term protection [18], and this is a continuing challenge. Although studies involving travelers that have compared different intervals between administration of the 2 hepatitis A vaccine doses (24–66 months apart vs. 6–14 months apart [23], and up to 8 years after the first dose [24]) revealed similar anamnestic responses, irrespective of the delay, the best clinical practice is to ensure that the travelers' immunity—and, therefore, level of protection against infection—is maintained at all times.

Hepatitis B. The administration of a primary course of hepatitis B vaccination can be completed by several schedules, thereby providing flexibility to aid compliance and subsequent completion of the full primary course. The standard primary course of hepatitis B vaccination consists of 3 doses, with doses administered at 0, 1, and 6 months. A short 0-, 1-, and 2-month schedule and an accelerated 0-, 7-, and 21-day schedule also exist, with a fourth dose recommended at 12 months in both schedules. Other accelerated schedules—0, 14, and 28 days and 0, 10, and 21 days—have been investigated [25–27], and a 2-dose schedule that involves adult vaccine doses is also available in some countries for adolescents aged 11–15 years. Administration of a 2-dose schedule of GSK Biological's hepatitis B vaccine (Engerix B) in adolescents aged 12–14 years was found to be well-tolerated, and seroprotection was achieved in 97.9% of subjects [28]. These schedules are particularly valuable for those travelers who seek travel health advice just prior to departure and who, therefore, may be exposed to hepatitis B in the immediate future [29].

Theoretical concerns that the protection afforded by short/accelerated hepatitis B vaccination schedules may not persist have proven to be unfounded in a number of studies, with comparably high seroprotection rates and geometric mean titers reported in individuals who have completed standard and shortened schedules [26, 27]. Effective immunological boosting is also evident for each of the schedules following administration of a fourth dose. Moreover, immunological memory was shown to persist for up to 5 years following a short schedule (with doses at birth and the first and third months of life) [30]. The recent hepatitis B immunity recommendations state that no data exist to support the need for the administration of hepatitis B booster doses in immunocompetent individuals who have responded to a full standard primary course [19].

IMPLICATIONS FOR TRAVELERS

Because many travelers continue to be at risk of contracting both hepatitis A and B, practical recommendations for the

administration of boosters in different groups of travelers are given in table 1.

Immunocompetent travelers. Hepatitis A and B boosters are not recommended for immunocompetent travelers, provided they have received a full standard primary vaccination course [18, 19].

Immunocompromised travelers. No recommendations have yet been published for hepatitis A booster vaccination in immunocompromised individuals. Although seroconversion rates and antibody titers for this group (e.g., patients with chronic liver disease, renal disease, and/or HIV infection) are lower than those reported for immunocompetent individuals, protection can be achieved with the full course of 2 doses of hepatitis A vaccine [31–34]. However, attainment of protective levels of anti-HAV antibodies (sometimes defined as anti-HAV titers of ≥ 33 mIU/mL, according to the assay used) [35] cannot be guaranteed in immunosuppressed patients. Therefore, until additional studies on antibody persistence have been performed, immunocompromised travelers should have their hepatitis A antibody titers monitored, and additional vaccine doses should be administered when necessary.

Although it may be considered advisable to monitor anti-HBs titers in all adult travelers after they receive a complete vaccination course, a more targeted monitoring approach would be more practical. Travelers who may not achieve seroprotection against hepatitis B following a complete primary course and whose anti-HBs level may need monitoring include immunocompromised individuals, those with underlying chronic disease, and elderly travelers. It has been recommended that anti-HBs titers should be monitored for immunocompromised travelers, with additional doses of vaccine administered when the level decreases to less than what is generally considered to be seroprotective (i.e., 10 mIU/mL) [18]. Indeed, the administration of an additional dose of vaccine to people with a low response to primary vaccination and, on occasion, to people with no response (i.e., those individuals with no detectable anti-HBs antibodies after receipt of the full primary course) has been reported to effect an antibody response and immunological priming [36]. For elderly travelers, age-related decreases in immune response may also necessitate monitoring of anti-HBs levels, with administration of additional doses as appropriate.

In some instances, it would be prudent to perform serological tests for levels of anti-HBs to confirm adequate protection. This would apply, in particular, to persons who are at occupational risk of exposure to hepatitis B and for long-term business travelers and emergency relief workers, among others.

Frequent travelers and those with an uncertain vaccination history. An additional dose of hepatitis A vaccine can be administered to travelers who are unsure of their vaccination status/history and who wish to ensure that they are protected.

Table 1. Hepatitis A and hepatitis B vaccine booster recommendations for travelers.

Vaccine, traveler type	Recommendation
Hepatitis A	
Healthy infants up to 1 year of age, children, adolescents, adults, and elderly persons, as well as specific groups (i.e., air crews, asylum seekers, backpackers, businessmen, civil servants, immigrants, migrants, military personnel, nongovernmental organization personnel, refugees, seamen, tourists, and truck drivers)	No booster after completion of the primary course of vaccine
Immunocompromised persons	Additional research is required before a clear recommendation can be made; the current guidance is to determine anti-HAV titers and to administer additional doses of vaccine when necessary (i.e., titers of <33 mIU/mL)
Healthy persons who are unsure of vaccination status	An additional dose may be given to ensure protection
Healthy persons aged >40 years who have lived abroad in areas of endemicity	Immunity (anti-HAV titers) can be determined to avoid unnecessary administration of vaccine
Hepatitis B	
Healthy children, adolescents, and adults	No booster after completion of the primary course of vaccination
Specific groups (i.e., aircrews, businessmen, civil servants, health care workers, nongovernmental organization personnel, seamen, and truck drivers)	No booster after completion of the primary course of vaccination, although serological testing (for anti-HBs titers) to confirm immunity may be considered for those who at occupational risk of exposure to hepatitis B, with additional doses given as appropriate
Immunocompromised persons	Monitor anti-HBs levels and administer additional doses when the level is <10 mIU/mL
Elderly persons and those with underlying chronic disease	Following a risk assessment, monitoring of anti-HBs levels may be needed, with additional doses given as appropriate

NOTE. HAV, hepatitis A virus; anti-HBs, anti-hepatitis B surface antigen.

However, travelers aged >40 years who have lived abroad or have traveled frequently may have naturally acquired immunity to hepatitis A. In such circumstances, an assessment of their anti-HAV titers can be undertaken initially [37], to avoid unnecessary administration of hepatitis A vaccine.

Combined vaccination against hepatitis A and B. Hepatitis A and B vaccines can be administered to travelers as part of various combination vaccines (e.g., hepatitis A/B and hepatitis A/typhoid). The combined hepatitis A and B vaccine provides effective and convenient dual protection for travelers and can be administered with the standard 0-, 1-, and 6-month 3-dose schedule and with an accelerated 0-, 7-, and 21-day schedule. Seroconversion rates of 99.6%–100% for hepatitis A and 92.3%–100% for hepatitis B have been reported for the standard schedule, with the accelerated schedule giving comparable seroprotection rates of 100% for hepatitis A and 98.5% for hepatitis B [38, 39]. No formal guidance has yet been given on the need for hepatitis B boosters after administration of a combined hepatitis A and B vaccine, but evidence suggests that booster doses will not be required for immunocompetent individuals. Specifically, the immunogenicity of a combined hepatitis A and B vaccine has been shown to be at least comparable to that of the monovalent vaccines [38], with a similar decrease in antibody titers observed over time [40]. Moreover, the anti-HAV and anti-HBs titers in adults elicited by a combined hep-

atitis A and B vaccine have been shown to remain high for up to 6 years after vaccination [41].

A hepatitis A booster is not recommended when a full course of combined hepatitis A and B or combined hepatitis A and typhoid vaccine is given [18], as long as a second dose of hepatitis A vaccine has been administered within 6–12 months, either as a monovalent or combination vaccine. When the combined hepatitis A and B vaccine is administered with the accelerated 0-, 7-, and 21-day schedule, a fourth dose given at 12 months is required to guarantee the same results as the 0-, 1-, and 6-month schedule.

CONCLUSIONS

Vaccination against hepatitis A and B is an important preventive travel health measure in travelers. The term “travelers” encompasses a range of individuals (e.g., tourists, backpackers, students, military personnel, migrants, asylum seekers and refugees, immigrants, nongovernmental organization personnel, aid workers, expatriates, civil servants, businessmen, air crews, seamen, and truck drivers) of all age groups (from infants to elderly persons) [42]. Despite this diversity, the majority of immunocompetent travelers can be advised and reassured that, following the completion of a primary course of vaccination with hepatitis A and hepatitis B monovalent or combined vaccine, they will be afforded long-term protection against these

serious infectious diseases, without the requirement of a booster dose. Mathematical models predict that the duration of protection against hepatitis A is likely to be 20–25 years, and possibly lifelong [4, 43]. The duration of protection against hepatitis B is at least 15 years, with current scientific evidence also suggesting lifelong protection [17].

This advice is based on the caveat that, when appropriate, anti-HBs levels should have been reviewed in travelers in whom seroconversion to hepatitis B vaccine cannot be assured (e.g., those who are immunocompromised, elderly persons, persons with underlying chronic disease, or those who are at occupational risk). Similarly, anti-HAV levels should be checked in immunocompromised travelers.

The current and predicted trend for increased travel to regions outside of northwestern Europe, North America, Australia, and New Zealand is set to continue, with the result that many more people are likely to travel and to be exposed to the risk of infection with either HAV or HBV. It is important that travelers receive appropriate and up-to-date travel health advice, as well as appropriate and timely vaccination, to reduce this risk. Additional research is needed to understand the immunogenicity of hepatitis A and B vaccines, particularly in relation to the necessity of hepatitis A boosters in special groups (e.g., immunocompromised persons) and in those who are considered to be nonresponders to the currently licensed hepatitis B vaccines, all of whom contribute to the group “travelers.” However, current evidence and recommendations suggest that, after completion of a primary vaccination course, the vast majority of travelers are protected for many years from both hepatitis A and B, with this protection most likely being lifelong.

Acknowledgments

Potential conflicts of interest. J.N.Z. has been reimbursed by several manufacturers of vaccines, including Baxter AG, GlaxoSmithKline, Sanofi Pasteur, Chiron Evans, and Wyeth, for attending conferences, conducting vaccine studies, and running educational programs; has received unrestricted educational grants; and is a consultant in travel medicine to the British Airways Travel Clinics. B.A.C. serves as a consultant to and is member of speaker’s bureaus for several pharmaceutical companies and vaccine manufacturers, including GlaxoSmithKline and Sanofi Pasteur, and has received compensation for conducting vaccine clinical trials. F.v.S. has been reimbursed by several manufacturers of vaccines, including GlaxoSmithKline and Sanofi Pasteur, for conducting vaccine studies, attending conferences, and running educational programs and has received unrestricted educational grants.

References

1. World Health Organization (WHO). International travel and health: hepatitis A, 2003. Available at: <http://www.who.int/ith/en/>. Accessed August 2004.
2. World Health Organization (WHO). International travel and health: hepatitis B, 2003. Available at: <http://www.who.int/ith/en/>. Accessed August 2004.
3. Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *J Viral Hepat* **2004**; *11*:97–107.
4. World Health Organization (WHO). Hepatitis A vaccines. *Wkly Epidemiol Rec* **2000**; *75*:38–44.
5. O’Grady JG. Fulminant hepatitis in patients with chronic liver disease. *J Viral Hepat* **2000**; *7*(Suppl 1):9–10.
6. Centers for Disease Control and Prevention. Hepatitis disease surveillance report no. 59. Atlanta, GA: US Department of Health and Human Services. Available at: <http://www.cdc.gov/ncidod/diseases/hepatitis/index.htm>. Accessed 26 May 2005.
7. Loscher T, Keystone JS, Steffen R. Vaccination of travelers against hepatitis A and B. *J Travel Med* **1999**; *6*:107–14.
8. Frank C, Stark K. Cases of travel-associated hepatitis A in Germany: update. *Eurosurveillance Weekly* **2004**; *8*:2.
9. Zuckerman JN, Steffen R. Risks of hepatitis B in travelers as compared to immunization status. *J Travel Med* **2000**; *7*:170–4.
10. Steffen R, Banos A, deBernardis C. Vaccination priorities. *Int J Antimicrob Agents* **2003**; *21*:175–80.
11. Rogstad KE. Sex, sun, sea, and STIs: sexually transmitted infections acquired on holiday. *BMJ* **2004**; *329*:214–7.
12. Staes CJ, Schlenker TL, Risk I, et al. Sources of infection among persons with acute hepatitis A and no identified risk factors during a sustained community-wide outbreak. *Pediatrics* **2000**; *106*:E54.
13. Centers for Disease Control and Prevention. Hepatitis B fact sheet. Available at: <http://www.cdc.gov/ncidod/diseases/hepatitis/b/fact.pdf>. Accessed September 2004.
14. Hepatitis B virus: a comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination. recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR Recomm Rep* **1991**; *40*:1–25.
15. Salisbury DM Begg NT. Immunisation against infectious disease. London: HMSO, **1996**.
16. STIKO Committee. *Epidemiologisches Bulletin* **2004**; *4*:235–50.
17. World Health Organization (WHO). Hepatitis B vaccines. *Wkly Epidemiol Rec* **2004**; *79*:255–63.
18. Van Damme P, Banatvala J, Fay O, et al. Hepatitis A booster vaccination: is there a need? *Lancet* **2003**; *362*:1065–71.
19. European Consensus Group on Hepatitis B Immunity. Are booster immunisations needed for lifelong hepatitis B immunity? *Lancet* **2000**; *355*:561–5.
20. Connor BA, Van Herck K, Van Damme P. Rapid protection and vaccination against hepatitis A for travellers. *BioDrugs* **2003**; *17*(Suppl 1): 19–21.
21. Van Damme P, Lievens M, Soffel M, et al. Rapid seroconversion rates after first dose of an inactivated hepatitis A vaccine (Havrix 1440): results of a retrospective analysis [abstract 60]. In: Program and abstracts of the 3rd European Conference on Travel Medicine (Florence, Italy). WHO Collaborating Centre for Tourist Health and Travel Medicine, **2002**:210.
22. Vidor E, Fritzell B, Plotkin S. Clinical development of a new inactivated hepatitis A vaccine. *Infection* **1996**; *24*:447–58.
23. Landry P, Tremblay S, Darioli R, et al. Inactivated hepatitis A vaccine booster given ≥ 24 months after the primary dose. *Vaccine* **2001**; *19*: 399–402.
24. Iwarson S, Lindh M, Widerstrom L. Excellent booster response 4 to 8 years after a single primary dose of an inactivated hepatitis A vaccine. *J Travel Med* **2004**; *11*:120–1.
25. Marchou B, Excler JL, Bourderiou C, et al. A 3-week hepatitis B vaccination schedule provides rapid and persistent protective immunity: a multicenter, randomized trial comparing accelerated and classic vaccination schedules. *J Infect Dis* **1995**; *172*:258–60.
26. Bock HL, Loscher T, Scheiermann N, et al. Accelerated schedule for hepatitis B immunization. *J Travel Med* **1995**; *2*:213–7.
27. Bock HL. Rapid hepatitis B immunisation for the traveller: comparison of two accelerated schedules with a 2-month schedule. *BioDrugs* **2003**; *17*(Suppl 1):11–3.
28. Heron LG, Chant KG, Jalaludin BB. A novel hepatitis B vaccination regimen for adolescents: two doses 12 months apart. *Vaccine* **2002**; *20*: 3472–6.

29. Zuckerman JN, Van Damme P, Van Herck K, et al. Vaccination options for last-minute travellers in need of travel-related prophylaxis against hepatitis A & B and typhoid fever: a practical guide. *Travel Med Infect Dis* **2003**; 1:219–26.
30. Belloni C, Pistorio A, Tinelli C, et al. Early immunisation with hepatitis B vaccine: a five-year study. *Vaccine* **2000**; 18:1307–11.
31. Stark K, Gunther M, Neuhaus R, et al. Immunogenicity and safety of hepatitis A vaccine in liver and renal transplant recipients. *J Infect Dis* **1999**; 180:2014–7.
32. Reiss G, Keeffe EB. Review article: hepatitis vaccination in patients with chronic liver disease. *Aliment Pharmacol Ther* **2004**; 19:715–27.
33. Neilsen GA, Bodsworth NJ, Watts N. Response to hepatitis A vaccination in human immunodeficiency virus–infected and –uninfected homosexual men. *J Infect Dis* **1997**; 176:1064–7.
34. Keeffe EB, Krause DS. Hepatitis B vaccination of patients with chronic liver disease. *Liver Transpl Surg* **1998**; 4:437–9.
35. Keeffe EB, Iwarson S, McMahon BJ, et al. Safety and immunogenicity of hepatitis A vaccine in patients with chronic liver disease. *Hepatology* **1998**; 27:881–6.
36. Chiamonte M, Ngatchu T, Majori S, et al. Response to an extra dose of hepatitis B vaccine and specific antibody persistence in non-responders to primary immunization. *Scand J Gastroenterol* **1995**; 30: 601–3.
37. Zuckerman JN, Powell L, Lequin RM, et al. Determination of hepatitis A antibody response to vaccination by an enzyme immunoassay. *J Virol Methods* **1996**; 56:27–31.
38. Van Damme P, Van Herck K. A review of the efficacy, immunogenicity and tolerability of a combined hepatitis A and B vaccine. *Expert Rev Vaccines* **2004**; 3:249–67.
39. Nothdurft HD, Dietrich M, Zuckerman JN, et al. A new accelerated vaccination schedule for rapid protection against hepatitis A and B. *Vaccine* **2002**; 20:1157–62.
40. Thoelen S, Van Damme P, Leentvaar-Kuypers A, et al. The first combined vaccine against hepatitis A and B: an overview. *Vaccine* **1999**; 17: 1657–62.
41. Van Damme P, Leroux-Roels G, Law B, et al. Long-term persistence of antibodies induced by vaccination and safety follow-up, with the first combined vaccine against hepatitis A and B in children and adults. *J Med Virol* **2001**; 65:6–13.
42. Viral Hepatitis Prevention Board. Prevention and control of hepatitis B in migrant populations. *Viral Hepatitis* **2003**; 12:6–8.
43. Van Herck K, Van Damme P. Inactivated hepatitis A vaccine-induced antibodies: follow-up and estimates of long-term persistence. *J Med Virol* **2001**; 63:1–7.

Copyright of *Clinical Infectious Diseases* is the property of Infectious Diseases Society of America and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.