

Selected references

WHO Position Paper Hepatitis A vaccines

(WER 4 Feb 2000)

Epidemiology

Tufenkeji H. Hepatitis A shifting epidemiology in the Middle East and Africa. Vaccine. 2000 Feb 18;18 Suppl 1:S65-7.

Data on the endemicity of hepatitis A virus (HAV) infection in Africa and the Middle East are scant, but most of Africa appears to remain a high endemicity region, with the exception of subpopulations in some areas, e.g. White people in South Africa. Saudi Arabia is a model for the Middle East, and is a country in which shifting HAV epidemiology has been documented in recent years, concurrent with the social and economic development that has occurred over the last two decades. Earlier studies generally showed very high prevalence rates, with most people becoming infected in early childhood. Between 1989 and 1995, however, there was a significant fall in the seroprevalence of antibodies to HAV in children up to 12 years old throughout the country except in one region bordering the Yemen. The highest seroprevalence is found in children from rural backgrounds, while the seroprevalences in Bedouin and urban children are similar. Seroprevalence is related to socioeconomic status, being highest in the lowest groups. Similar findings have been reported from other countries in the Middle East. The existence of pockets of high endemicity for HAV infection with surrounding areas shifting towards intermediate endemicity may lead to outbreaks, and widespread vaccination should be considered.

Barzaga BN. Hepatitis A shifting epidemiology in South-East Asia and China. Vaccine. 2000 Feb 18;18 Suppl 1:S61-4.

A review of the epidemiology of hepatitis A virus (HAV) infection over the last 20 years shows shifting patterns in the prevalence of antibodies to HAV (anti-HAV) throughout South-East Asia and China. A number of countries have shifted from high to moderate and from moderate to low endemicity, with a corresponding increase in the age of exposure from childhood to early adulthood. The changes have resulted from improvements in hygiene, sanitation and the quality of drinking water, reflecting improvements in living standards and socioeconomic progress. In general in the late 1970s and early 1980s, 85-95% of the population of developing countries like the Philippines, Korea, China and Thailand were anti-HAV-positive by age 10-15 years, compared with only about 50% in the more affluent countries like Malaysia and Singapore. In the early 1990s, 85-95% of the population were immune by age 30-40 years in the Philippines, Korea, China and Thailand, and by 50 years of age and above in Malaysia and Singapore. Similar trends were noted in Hong Kong, Taiwan and Japan.

Exposure to HAV at a later age may be associated with an increase in hepatitis A morbidity and a greater propensity for outbreaks.

Cianciara J. Hepatitis A shifting epidemiology in Poland and Eastern Europe. Vaccine. 2000 Feb 18;18 Suppl 1:S68-70.

The clinical morbidity of hepatitis A probably only represents 20% of cases of hepatitis A virus (HAV) infection. When it became possible to determine specific antibodies, a seroepidemiological survey of anti-HAV was undertaken in Poland, which showed that between 1979 and 1997 there was a shift in the peak age of infection from childhood to adulthood, concomitant with a substantial decline in the incidence of HAV infection. Data from the World Health Organization also indicate that there has also been a decline in the incidence of hepatitis A in Eastern European countries in general, over the 3 years from 1994 to 1996. The potential risk of epidemics still exists, however, when appropriate conditions are created. The available data show that fewer young people are becoming infected with HAV, and general preventive measures, including vaccination of children and high-risk groups (e.g. healthcare and childcare personnel and those living in 'closed communities') are needed to deal with HAV infections in Eastern Europe.

Tanaka J. Hepatitis A shifting epidemiology in Latin America. Vaccine. 2000 Feb 18;18 Suppl 1:S57-60

In the past, Latin America was considered to be an area of high endemicity for hepatitis A virus (HAV) infection, with most people infected in early childhood. A seroepidemiological study was recently undertaken in six countries to determine whether this pattern has changed. The highest seroprevalence of antibodies to HAV (anti-HAV) was found in Mexico and the Dominican Republic. Analysis of the different age groups showed that at age 6-10 years, 30% of children in Chile and 54-55% in Brazil, Venezuela and Argentina had been infected, compared with almost 70% in Mexico and 80% in the Dominican Republic. At age 11-15 years, nearly 90% in Mexico and 91% in the Dominican Republic had been infected, compared with 54% in Argentina, 62% in Venezuela, 60% in Brazil and 70% in Chile. By age 31-40 years, over 80% of the populations in all six countries had been exposed to HAV. In all of the countries except Brazil and Venezuela, the seroprevalence of anti-HAV was significantly higher in females than in males. In Mexico, Argentina and Brazil, anti-HAV seroprevalence was significantly higher in the low socioeconomic groups than in the middle/high socioeconomic groups. The results show that there has been a shift from high to medium endemicity of HAV infection throughout Latin America, which may result in more clinical cases in adolescents and adults and a greater potential for outbreaks. The vaccination strategy for hepatitis A should thus be reviewed.

The virus and the disease

Tong MJ, el-Farra NS, Grew MI. Clinical manifestations of hepatitis A: recent experience in a community teaching hospital. J Infect Dis. 1995 Mar;171 Suppl 1:S15-8

A study of the clinical profile of 59 patients who presented with hepatitis A virus infection showed that dark urine, fatigue, gastrointestinal complaints, and fever were the most common presenting symptoms. The most frequent physical findings were hepatomegaly and jaundice. The mean presenting laboratory tests included total bilirubin of 5 mg/dL, alkaline phosphatase of 269 units/L, and serum aspartate aminotransferase and alanine aminotransferase levels of 1442 mIU/mL and 1952 mIU/mL, respectively. Atypical manifestations included relapse, cholestasis, rash, and arthralgia. Two patients presented with hepatitis A and concomitant type I autoimmune chronic hepatitis, and both required immunosuppressive therapy. Five patients who presented with hepatitis A were pregnant, and during follow-up, none of their infants developed elevated serum transaminase values or had detectable IgM anti-HAV antibody. All 59 patients experienced complete clinical and biochemical recovery within 6 months after onset of illness.

Schiff ER. Atypical clinical manifestations of hepatitis A. Vaccine. 1992;10 Suppl 1:S18-20.

Viral A hepatitis is a self-limited infection occurring predominantly among children usually as an anicteric often subclinical illness. Adults afflicted with this virus are more likely to develop icteric hepatitis. This is exemplified in developed countries when a common source outbreak occurs among non-immune adults. Fulminant hepatitis is uncommon in the USA and hepatitis A has never been documented to evolve into chronic hepatitis. However, prolonged cholestasis and relapsing hepatitis are well described. The usual features of cholestatic viral hepatitis A are pruritus, fever, diarrhoea, and weight loss. Serum bilirubin levels are > 10 mg/dl and the clinical course lasts at least 12 weeks. Cholestasis will spontaneously resolve, although corticosteroids will hasten the resolution but may predispose the patient to develop a relapse of the hepatitis. A biphasic or relapsing form of viral hepatitis A occurs in 6 to 10% of cases. The initial episode lasts 3 to 5 weeks and is followed by a period of remission characterized by normal liver chemistries lasting 4 to 5 weeks. Relapse may mimic the initial episode of the acute hepatitis. The full duration of the illness ranges from 16 to 40 weeks from the onset and immunoglobulin M antibody to hepatitis A virus persists throughout the clinical course. Hepatitis A virus has been recovered from stools during the relapse. Extrahepatic manifestations of hepatitis A include evanescent skin rash and transient arthralgias. Documented cases of arthritis and cutaneous vasculitis have been associated with cryoglobulinaemia and are rare.

Melnick JL. Properties and classification of hepatitis A virus. Vaccine. 1992;10 Suppl 1:S24-6

Hepatitis A virus (HAV) is a member of the picornavirus family. It was first provisionally classified as enterovirus 72, but subsequent determinations of its nucleotide and amino acid sequences showed them to be sufficiently distinct to assign the virus to a new genus. Heparna-virus (Hep-A-RNA-virus) has been suggested as the genus name. HAV shares the key properties of the picornavirus family: an icosahedral particle 28 nm in diameter with cubic symmetry, composed of 30% RNA and 70% protein. The genome is single-stranded 7.48 kb RNA, linear and positive-sense. Like other picornaviruses, HAV possesses four major polypeptides cleaved from a large precursor polyprotein. The surface proteins VP1 and VP3 are major antibody-binding sites. The internal protein VP4 is much smaller than the VP4s of other picornaviruses. As other picornaviruses, HAV has no envelope and replicates in the cytoplasm. HAV is stable to treatment with either and acid, and is much more heat-resistant than other picornaviruses. It withstands 60 degrees C for 1 h. MgCl₂ stabilizes the virus to withstand temperatures up to 80 degrees C. The relative resistance of HAV to disinfection indicates a need for extra precautions in dealing with hepatitis patients and their products. Only one serotype is known. There is no antigenic cross-reactivity with other hepatitis viruses. HAV initially was identified in stool and liver preparations by employing immune electron microscopy as the detection system. Chimpanzees and marmoset monkeys are susceptible to HAV. HAV has been cultivated serially in primary explant cultures of adult marmoset livers and in cell lines of primate origin.(ABSTRACT TRUNCATED AT 250 WORDS)

Lemon SM, Jansen RW, Brown EA. Genetic, antigenic and biological differences between strains of hepatitis A virus. Vaccine. 1992;10 Suppl 1:S40-4.

Recent studies have documented a considerable degree of genetic divergence among wild-type hepatitis A virus (HAV) strains recovered from different geographical locations. Human HAV strains can be grouped into four genotypes (I, II, III and VII) and unique simian strains belong to three additional genotypes (IV, V and VI). Between each of these genotypes, the nucleotide sequence varies at 15-25% of base positions in the P1 region. Despite this, there is good evidence that most, if not all, human strains of HAV are closely related antigenically. In contrast, although simian strains recovered from Old World monkeys are cross-reactive in immunoassays employing polyclonal antibodies, these strains have significant antigenic differences from human HAV strains. Nonetheless, because biological differences in the host range of these strains apparently preclude significant human infection, this is unlikely to pose a problem in controlling HAV infections with active immunization. Inactivated and attenuated vaccines produced from genotype I human strains (HM175 or CR326) are likely to provide protection against all relevant human HAV strains.

Evaluations of inactivated hepatitis A-vaccines

Innis BL, Snitbhan R, Kunasol P, Laorakpongse T, Poopatanakool W, Kozik CA,

Suntayakorn S, Suknuntapong T, Safary A, Tang DB, et al. Protection against hepatitis A by an inactivated vaccine. JAMA. 1994 May 4;271(17):1328-34.

OBJECTIVE--To evaluate the safety and efficacy of a new inactivated hepatitis A vaccine. **DESIGN**--Double-blind randomized controlled trial stratified by community. **SETTING**--Community-based in Thailand. **STUDY PARTICIPANTS**--A total of 40,119 children, aged 1 to 16 years, attending 148 primary schools: 38,157 (95%) entered surveillance a mean of 138 days after receiving vaccine dose 1; 33,586 (84%) completed the controlled trial of 532 days; and 31,075 (81%) received crossover vaccine and remained under surveillance until day 844. **INTERVENTION**--Participants received hepatitis A vaccine or control hepatitis B vaccine starting January 7, 1991 (doses in months 0, 1, and 12), and crossed over to the alternate vaccine 18 months later. **MAIN OUTCOME MEASURE**--Cases of hepatitis A (symptoms, alanine aminotransferase levels of 45 U/L or higher, and IgM to hepatitis A virus) were identified by evaluating school absences of 2 or more days. **RESULTS**--There were no serious adverse reactions despite administration of more than 109,000 doses of hepatitis A vaccine. Among initially seronegative recipients of two doses of hepatitis A vaccine, the proportion with 20 mIU/mL or more of antibody to hepatitis A virus before and 5 months after a 1-year booster was 94% and 99%, respectively. Of 6976 episodes of illness during the controlled trial, there were 40 cases of hepatitis A; 38 were in the control group. Of the 40 cases, six, all in controls, occurred after the 1-year booster dose. Following two doses of hepatitis A vaccine (days 138 through 386), protective efficacy was 94% (95% confidence interval, 79% to 99%); cumulative efficacy including the postbooster period (days 138 to 532) was 95% (95% confidence interval, 82% to 99%). The two hepatitis A vaccine recipients who had symptomatic infections (257 and 267 days after dose 1) appeared to have been partially protected since their illnesses were brief and associated with only slight increases in alanine aminotransferase. **CONCLUSIONS**--Inactivated hepatitis A vaccine is safe; when administered in two doses, it protects against hepatitis A for at least 1 year.

André FE. Approaches to a vaccine against hepatitis A: development and manufacture of an inactivated vaccine. J Infect Dis. 1995 Mar;171 Suppl 1:S33-9.

The basis for the development of a vaccine against hepatitis A was laid in the 1970s, when virus was replicated in cell culture. Adaptation to growth in cell culture resulted in attenuation and sufficient quantities of virus particles, allowing the development of both live attenuated and inactivated vaccines. Testing of candidate vaccines in volunteers began in the early 1980s. Recently, a formaldehyde-inactivated whole-virion hepatitis A vaccine, the first licensed vaccine against hepatitis A, was introduced in many countries worldwide, and a live attenuated vaccine became available in the People's Republic of China. Other possible avenues for vaccine development include the use of either conventional or recombinant DNA techniques to obtain subunit vaccines, empty capsids, live viral or bacterial vectors, genetic immunization, synthetic peptides, and anti-idiotypes.

Clemens R, Safary A, Hepburn A, Roche C, Stanbury WJ, Andre FE. Clinical experience with an inactivated hepatitis A vaccine. J Infect Dis. 1995 Mar;171 Suppl 1:S44-9.

Clinical trials of an inactivated hepatitis A vaccine have encompassed 104 studies completed by December 1993 in 27 countries. Studies involved 50,677 subjects and administration of > 120,000 vaccine doses. Results show that the vaccine is safe, clinically well-tolerated, and highly immunogenic in all age groups. A seroconversion rate of 100% is achieved 1 month after primary vaccination. Vaccine-induced antibody titers persist after a primary vaccination course for > or = 1 year with a single dose of 1440 ELISA units (EL.U.) in adults and after two doses of 360 EL.U. in children. A booster dose 6-12 months after the first vaccine dose induces very high antibody titers, which according to a mathematical model, are expected to protect against hepatitis A for > 20 years. The vaccine is equally immunogenic when administered simultaneously with other traveler vaccines, therefore enabling flexible and convenient vaccination against hepatitis A.

Vidor E, Xueref C, Blondeau C, Bajard A, Francon A, Goudeau A, Peyron F, Brasseur P, Zuckerman A. Analysis of the antibody response in humans with a new inactivated hepatitis A vaccine. Biologicals. 1996 Sep;24(3):235-42.

Sera from subjects vaccinated with the Pasteur Merieux (PM) inactivated hepatitis A vaccine (AVAXIM) have been analysed in order: (1) to assess comparability of the results provided by a modified radio-immunoassay (mRIA) in the different laboratories involved in testings of sera during clinical trials and by enzyme-linked immunoabsorbent assay (ELISA) used during development of other inactivated hepatitis A vaccines; (2) to describe the IgM responses elicited by this vaccine compared with one control vaccine [HAVRIX, 720 ELISA antigens units; Smithkline Beecham (SB), Rixensart, Belgium]; (3) to provide comparative data between the PM vaccine and the SB vaccine on neutralizing activities of vaccine-induced antibodies. Vaccine-induced antibody titres evaluated by a mRIA in different laboratories correlated well and validated the comparability of the results obtained in various vaccine trials conducted by PM. Geometric mean titres (GMTs) expressed as milli-international units (mIU/ml) were higher with ELISA especially after the first dose, but seroconversion rates were similar and a good correlation was found between the two assays. IgM vaccine-induced antibodies were detectable in nearly all vaccinated subjects from week 2 after vaccination, with a peak titre between weeks 2 and 4 after the first dose. Comparison of GMTs by the Student Fisher t-test was statistically significant ($P < 0.05$) only at week 2 with higher titres in PM vaccinees. Neutralizing antibodies were detected after vaccination with the PM inactivated hepatitis A vaccine. The titres gradually increased between the second week after the first dose and the booster dose (week 24). A strong booster effect of the second dose on neutralizing titres was observed. Seroneutralizing titres induced at week 2 in subjects vaccinated with the PM inactivated hepatitis A vaccine were statistically significantly higher ($P < 0.05$) from those induced by the SB vaccine.

Mao JS, Chai SA, Xie RY, Chen NL, Jiang Q, Zhu XZ, Zhang SY, Huang HY, Mao HW, Bao XN, Liu CJ. Further evaluation of the safety and protective efficacy of live attenuated hepatitis A vaccine (H2-strain) in humans. Vaccine. 1997 Jun;15(9):944-7.

A study on the possibility of transmission of live hepatitis A vaccine (H2-strain) from vaccinees to nonvaccinees was conducted. As a result, no seroconversion was found among 87 seronegative nonvaccinees, who had a close contact with their 141 subcutaneously vaccinated classmates nor was it found among 101 seronegative children administered the vaccine orally. The above findings suggest that by losing the ability to be transmitted orally the vaccine virus may result in a decreasing possibility of dissemination among contacts. A 4-year study on the protective efficacy of the H2-strain vaccine was done at 11 primary schools starting at 1991 in Shaoxing County. Since then, there has been no hepatitis A reported among 18102 cumulative person-years in the vaccination group, while 495 cases occurred among 242168 cumulative person-years in the control groups. A large scale vaccination with a cumulative vaccination coverage of 89.45% was carried out in Jiaojiang City among children 1-15 years old. Hepatitis A in this age group in the city, which had 12-87 cases per annum with an average of 32 for 8 years before vaccination, decreased drastically to 0-1 cases after vaccination. The protective efficacy of H2-strain vaccine proved to be satisfactory.

Ambrosch F, Wiedermann G, Jonas S, Althaus B, Finkel B, Gluck R, Herzog C. Immunogenicity and protectivity of a new liposomal hepatitis A vaccine. Vaccine. 1997 Aug;15(11):1209-13

In this study we investigated a new liposomal hepatitis A vaccine (Epaxal) developed by the Swiss Serum and Vaccine Institute clinically and immunologically using a one dose priming schedule and a booster injection after 1 year. This vaccine contains formalin inactivated hepatitis A virus particles attached to phospholipid vesicles together with influenza virus haemagglutinin. Two doses of the vaccine were administered at months 0 and 12 in 117 volunteers. Blood samples were drawn at days-7, 14 and 28 and after 6, 12 and 13 months, local and systemic reactions were monitored by means of questionnaires. Immunogenicity was evaluated as usual by the determination of anti-HAV from the collected sera using the ELISA technique. In order to evaluate the protective efficacy of the vaccine induced antibodies a sample of 25 sera mainly from vaccinees showing low ELISA titres was additionally analysed by means of a virus NT. The vaccine was excellently tolerable and highly immunogenic. Seroconversion evaluated by ELISA was 97 and 99%, respectively, 14 and 28 days after the first dose and 100% after the second dose. NT titres were well correlated with ELISA titres and showed similar seroconversion rates even in the early phase of immunization. The results of this study show that with two doses of the liposomal hepatitis A vaccine administered at months 0 and 12 early protection within 14 days and long lasting immunity can be achieved.

Czeschinski PA, Binding N, Witting U. Hepatitis A and hepatitis B vaccinations: immunogenicity of combined vaccine and of simultaneously or separately applied single vaccines. Vaccine. 2000 Jan 6;18(11-12):1074-80

The vaccination success and side effects of hepatitis A and hepatitis B immunisation of health care employees when using a combined vaccine were compared to those observed with simultaneous or single immunisations. The immunological response of two groups of healthy participants (75 each) receiving either single HAV or HBV vaccination was compared with that of two groups (75 each) vaccinated either simultaneously with both vaccines or with the combined vaccine. There were no non or low responders with respect to hepatitis A vaccination. Only one participant failed to build up an anti-HBs titer after combined vaccination. The good tolerance of separate, simultaneous and combined vaccinations was confirmed. Both combined and simultaneous vaccination led to significantly higher anti-HAV titers than single immunisation, while markedly but not significantly higher anti-HBs titers were found only with simultaneous vaccination. Considering the additional advantage of the higher acceptance of only one injection with the combined vaccine, this vaccination should be recommended for employees at risk for both hepatitis A and hepatitis B.

Duration of protection

Wiedermann G, Kundi M, Ambrosch F, Safary A, D'Hondt E, Delem A. Inactivated hepatitis A vaccine: long-term antibody persistence. Vaccine. 1997 Apr-May;15(6-7):612-5.

During the clinical development of safe, well tolerated and immunogenic vaccines against hepatitis A the persistence of protective antibodies was estimated, based on relatively short observation periods of 18 months to 3 years. We report here on longterm persistence of antibodies in volunteers who participated in one of the early clinical trials on inactivated hepatitis A candidate vaccines. In a randomized trial three groups of altogether 110 healthy adults, initially hepatitis A virus (HAV) seronegative persons were vaccinated with an inactivated hepatitis A vaccine according to the schedule 0-1-2-12 months. One group received 180 ELISA units, one group 360, and one 720 ELISA units per dose. Blood samples were taken prior to the first vaccination and at months 1, 2, 3, 4, 6, 12, 13, 18, 24, 36 and 84. The decrease of antibodies was characterized by two disappearance rates: a rapidly decreasing component and a slower decreasing one becoming predominant ca 12 months after booster vaccination. The disappearance of antibodies could be described by a two-component model which holds for $t \geq 13$ months. The estimated disappearance rates for the slow component (annual decrease) was found to be 11 and 13% for the 180 and 360 El. U groups, respectively (the 720 El. U group showed no decline, which was probably due to the small sample size). The estimated persistence of antibodies within protective range varied between 24 and 47 years depending on individual titres reached at month 13 and vaccination dose.

Maiwald H, Jilg W, Bock HL, Loscher T, Sonnenburg F. Long-term persistence of anti-HAV antibodies following active immunization with hepatitis A vaccine. Vaccine. 1997 Mar;15(4):346-8.

Seventy-one anti-hepatitis A virus (HAV) negative volunteers were immunized against hepatitis A. An inactivated hepatitis A vaccine (HAVRIX, SmithKline Beecham), derived from tissue cell cultures, at single doses of 720 ELISA units was used following a schedule of vaccinations at month 0.1 and 6. The vaccines were tested for the presence of HAV antibodies 1 month after each vaccination and then after 2, 3, 4 and 5 years. The annual decrease of anti-HAV titres was 25%. Five years after vaccination a protective antibody titre, varying between 20 and 5200 mIU ml⁻¹, could be demonstrated in all 47 retested volunteers with a geometric mean titre (GMT) of 442 mIU ml⁻¹. Levels of anti-HAV-antibodies following active immunization were significantly higher in female volunteers. This could be consistently demonstrated throughout the observation period. Based on these data the antibody persistence was calculated over time. GMTs at protective levels higher than 20 mIU ml⁻¹ can be expected to persist for at least 15 years.

Immunization of travellers

Steffen R, Kane MA, Shapiro CN, Billo N, Schoellhorn KJ, van Damme P. Epidemiology and prevention of hepatitis A in travelers. JAMA. 1994 Sep 21;272(11):885-9

OBJECTIVE--To assess the risk of hepatitis A in international travelers and to recommend preventive measures. **DATA SOURCES**--Index Medicus, 1974 through 1983; MEDLINE, 1984 through 1993; and unpublished data of the Centers for Disease Control and Prevention. **STUDY SELECTION**--Review of all retrospective and cohort studies on hepatitis A and other vaccine-preventable diseases in travelers, of seroepidemiologic surveys of hepatitis A virus (HAV) antibodies in travelers, of data on the various hepatitis A vaccines, of economic analyses, and of recommendations of recognized organizations. **DATA EXTRACTION**--Independent analysis by multiple observers. **DATA SYNTHESIS**--The incidence rate for unprotected travelers, including those staying in luxury hotels, is estimated to be three per 1000 travelers per month of stay in a developing country. Persons eating and drinking under poor hygienic conditions have a rate of 20/1000 per month. This makes hepatitis A the most frequent infection in travelers that may be prevented by immunization. In many industrialized countries persons born after 1945 have an HAV antibody seroprevalence (immunity) of less than 20%. New inactivated HAV vaccines induce protective antibodies in more than 95% of recipients and offer protection estimated to last for 10 years or more, whereas protection by immune globulin lasts only 3 to 5 months. **CONCLUSIONS**--Hepatitis A vaccine, or immune globulin where HAV vaccine is not available, is recommended for all nonimmune travelers visiting developing countries. Prescreening for antibodies to HAV in travelers living in countries with low prevalence is usually not necessary in persons born after 1945.

Bienzle U, Bock HL, Kruppenbacher JP, Hofmann F, Vogel GE, Clemens R. Immunogenicity of an inactivated hepatitis A vaccine administered according to two different schedules and the interference of other "travellers" vaccines with the immune response. Vaccine. 1996 Apr;14(6):501-5

A total of 2036 persons consulting vaccination centers in Germany were vaccinated with an inactivated hepatitis A vaccine (containing 720 ELISA units of antigen) either according to the standard schedule (two vaccinations given 4 weeks apart) or to an abbreviated schedule (two vaccinations given 2 weeks apart) in a controlled clinical study. The abbreviated schedule induced a similar rate of seroconversion and geometric mean antibody titre as compared to the standard schedule. The incidence of reactions reported after vaccination was similar in both groups. When other "travellers" vaccines were given simultaneously neither the immunogenicity nor the reactogenicity of the hepatitis A vaccine were influenced. These findings have considerable practical importance in the prevention of hepatitis A in travellers.

Cost-effectiveness

Tormans G, Van Damme P, Van Doorslaer E. Cost-effectiveness analysis of hepatitis A prevention in travellers. Vaccine. 1992;10 Suppl 1:S88-92.

The advent of new vaccines and the changing epidemiology of hepatitis A call for an update of the economic evaluation of costs and benefits associated with the various alternative preventative strategies. A decision-tree-based model has been developed which enables the calculation of expected costs and expected numbers of hepatitis A virus HAV infections based on different intervention strategies. The model is sufficiently generic to allow for the evaluation of both population-wide strategies and strategies targeted at particular risk groups. An economic analysis focusing on travellers from Europe to high-endemic countries compared a non-intervention strategy to the following three strategies: active immunization with HAV vaccine; screening for HAV antibodies and vaccinating only susceptibles; passive immunization by means of immunoglobulin. The net cost per HAV infection prevented proved very sensitive to a number of important input parameters of the model. These included epidemiological characteristics such as HAV attack rate and prevalence of immunity, behavioural characteristics such as compliance with the vaccination scheme and vaccine characteristics such as rate and duration of protection. Our estimated expected cost per HAV infection prevented among Belgian travellers to high-endemic countries for three weeks per year over ten years amounts to approximately US\$4880 for active immunization, US\$5621 for screening followed by vaccination of susceptibles and US\$29932 for passive immunization. Although these estimates are clearly sensitive to a number of crucial assumptions pertaining to the input parameters of the model, it seems safe to conclude that vaccination is more cost-effective than the currently recommended passive immunization with immunoglobulin. (ABSTRACT TRUNCATED AT 250 WORDS)

Relevant WHO documents

Hepatitis A. World Health Organization Department of Communicable Diseases surveillance and Response. WHO/CDS/CRS/EDC/2000.7