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Hepatitis A vaccine should receive priority in National Immunization Schedule in India

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Hepatitis A is an acute, usually self-limiting infection of the liver caused by a virus known as hepatitis A virus (HAV). Humans are the only reservoir of the virus; transmission occurs primarily through the fecal-oral route and is closely associated with poor sanitary conditions. The virus has a worldwide distribution and causes about 1.5 million cases of clinical hepatitis each year. The risk of developing symptomatic illness following HAV infection is directly correlated with age. As many 85% of children below 2 years and 50% of those between 2–5 years infected with HAV are anicteric, and among older children and adults, infection usually causes clinical disease, with jaundice occurring in more than 70% of cases. The infection is usually self-limiting with occasional fulminant hepatic failure and mortality. In most developing countries in Asia and Africa, hepatitis A is highly endemic such that a large proportion of the population acquires immunity through asymptomatic infection early in life. HAV is endemic in India; most of the population is infected asymptomatically in early childhood with life-long immunity. Several outbreaks of hepatitis A in various parts of India have been recorded in the past decade such that anti-HAV positivity varied from 26 to 85%. Almost 50% of children of ages 1–5 years were found to be susceptible to HAV. Any one of the licensed vaccines may be used since all have nearly similar efficacy and safety profiles (except for post-exposure prophylaxis/immunocompromised patients, where only inactivated vaccines may be used). Two doses 6 months apart are recommended for all vaccines. All hepatitis A vaccines are licensed for use in children aged 1 years or older. However in the Indian scenario, it is preferable to administer the vaccines at age 18 months or more when maternal antibodies have completely declined. Vaccination at this age is preferable to later since it is easier to integrate with the existing schedule, protects those who have no antibodies, and protects children by the time they attend day care. In India the vaccine against hepatitis A is available for the people who can afford it, but the government of India should give this vaccine as a priority in the national immunization schedule.

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Hepatitis A is an acute, usually self-limiting infection of the liver caused by HAV. The virus has a worldwide distribution and causes about 1.5 million cases of clinical hepatitis each year. Humans are the only reservoir of the virus. Transmission occurs primarily through the fecal-oral route, and is closely associated with poor sanitary conditions. The most common modes of transmission include ingestion of contaminated food and water. The virus is shed in the feces of persons with both asymptomatic and symptomatic infection. Under favorable conditions HAV may survive in the environment for months. Blood-borne transmission of HAV is not documented to occur. The average incubation period is 28 d, but may vary from 15 to 50 d. The risk of developing symptomatic illness following HAV infection is directly correlated with age. As many 85% of children below

2 years and 50% of those between 2–5 years infected with HAV are anicteric and may just have non-specific symptoms like any other viral infection.[1] Among older children and adults, infection usually causes clinical disease, with jaundice occurring in more than 70% of cases. Therefore, highly HAV-endemic regions are characterized by asymptomatic childhood infection, with only the occasional occurrence of clinical hepatitis A. In areas of high disease endemicity, where the lifetime risk of infection is greater than 90%, most infections occur in early childhood and are asymptomatic.[1] Thus, clinically apparent hepatitis A is rarely seen in these countries. The infection is usually self-limiting with occasional fulminant hepatic failure and mortality, but does not lead to chronicity.

In most developing countries in Asia and Africa, hepatitis A is highly endemic such that a large proportion of the population acquires immunity through asymptomatic infection early in life.[2] However, several recent reports documented changing epidemiology of hepatitis A in these countries from hyper-endemicity to intermediate endemicity.[3-6] An explosive outbreak of hepatitis A reporting over 300,000 cases (47 deaths) and associated with consumption of raw clams in Shanghai, China in 1988 represents an example of the magnitude of HAV infection in a susceptible population.[7]

HAV is endemic in India, such that most of the population is infected asymptomatically in early childhood with lifelong immunity.[8] Several outbreaks of hepatitis A in various parts of India have been recorded in the past decade; children from rural and semi-urban areas of the state of Maharashtra (2002–2004),[9] an explosive outbreak among adults from Kerala involving 1,137 cases (2004). and over 450 cases in children and adults in Shimla (2007).[9] Analysis of 1612 subjects representing 55 cities from different parts of India (Kolkata, Cochin, Indore, Jaipur and Patna) showed that anti-HAV positivity varied from 26 to 85%. Almost 50% of children between the ages of 1–5 years were found to be susceptible to HAV. Interestingly, municipal water supply and not family income were associated with exposure to HAV.[10]

A recent study from Delhi has reported that the frequency of HAV infection among children has increased from 8.4 to 12.3% over a period of five years, with the frequency of HAV infection having increased in adults also from 3.4 to 12.3% during the same period.[11] Similarly, outbreaks of epidemics of hepatitis A have been reported from Kottayam, Kerala State; the infection was traced to the presence of a sewage treatment plant which was overflowing and getting mixed with a canal.[12] Recent reports from India also have shown a variable prevalence in HAV exposure in middle and upper socioeconomic strata.[13,14] A study shows exposure to HAV among the children reached 97% by the age of 12 y.[15] This prevalence is similar to the results reported by Aggarwal et al.[16] and Arankalle et al.[17] where they reported > 95% HAV exposure by late childhood. Improved sanitation and personal hygiene will remain as an effective intervention to control the transmission of HAV. In India, the hepatitis A vaccine is available for the people who can afford it, but the government of India should give this vaccine as a priority in the national immunization schedule. Duration of immunity is an important concern for developing countries. If the policy of childhood immunization is adopted, in the absence of desired long-term immunity, exposure to HAV in adulthood would lead to severe clinical disease, especially because circulation of HAV continues in a substantial proportion of the population.[18]

Vaccine

Inactivated vaccines. Most of the currently available vaccines are derived from HM 175/GBM strains and grown on MRC5 human diploid cell lines. The virus is formalin-inactivated and adjuvanted with aluminum hydroxide.[19] The vaccine is stored at 2–8°C. The vaccines are given intramuscularly in a two-dose schedule, 6 months apart. The adult formulation should be used above the recommended cut-off age of 18 years. Protective antibodies are seen in 95–100% of subjects one month after the first dose and almost 100% after the second dose. The rate of protective efficacy is 90–100% and onset of protection is two weeks to one month after the first dose of the vaccine. The vaccine may be given with other childhood vaccines. Immunity is lifelong due to anamnestic antibody responses, and no boosters are recommended in immunocompetent subjects. Adverse reactions are minor and usually include local pain and swelling.[19]

Live attenuated vaccine. This vaccine is derived from the H2 strain of the virus attenuated after serial passage in human diploid cells (KMB 17 cell line). It has been in use in China since the 1990s in mass vaccination programs. The vaccine meets the requirements of the WHO. It is licensed and available in India. The recommended dose is 1 mL administered subcutaneously in children aged 1–15 years. Immunogenicity studies with a single-dose show seroconversion rates of > 98%, two months after vaccination and persistence of protective antibodies in > 80% of vaccines at 10-year follow-up.[19] Uncontrolled studies show an efficacy of almost 100% sustained over 10 years despite a decline in seroprotection rates and antibody titers. Recent immunogenicity studies from India have shown > 95% seroconversion, 6 weeks following single dose of the vaccine and sustained protection for at least 2 years. Antibody titers are significantly lower than those achieved with inactivated vaccines although still above the protective level. No horizontal transmission or serious adverse effects have been noted. The vaccine is not effective as post-exposure prophylaxis.[9]

Recommended Schedule in India

Any of the licensed vaccines may be used since all have similar efficacy and safety profiles (except for post-exposure prophylaxis/immunocompromised subjects where only inactivated vaccines may be used). Two doses 6 months apart are recommended for all vaccines. All hepatitis A vaccines are licensed for use in children aged 1 year or older. However in the Indian scenario, it is preferable to administer the vaccines at age 18 months or more when maternal antibodies have completely declined. Vaccination at this age is preferable to immunization later since it is easier to integrate with the existing schedule,

protects those who have no antibodies, and protects children by the time children attend day care.[9]

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