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The Global Prevalence of Hepatitis A Virus Infection and Susceptibility: A Systematic Review

Immunization, Vaccines and Biologicals

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BACKGROUND

HEPATITIS A VIRUS

Hepatitis A virus (HAV) is a member of the *Hepatovirus* genus of the family *Picornaviridae*, and is a nonenveloped single-stranded RNA virus [Cuthbert, 2001; Koff, 1998]. HAV replicates in hepatocytes (liver cells) and interferes with liver function, sparking an immune response that causes liver inflammation. Four of the seven genotypes of HAV affect humans (genotypes I and III are the most common), but only one serotype exists. Infection with any of the genotypes usually results in lifelong immunity against all strains of hepatitis A virus.

TRANSMISSION

HAV is transmitted via the fecal-oral route either by direct contact with an infectious person or by ingestion of contaminated food or water. (Persons with hepatitis A can shed the virus in their stool beginning several weeks before the onset of symptoms. The viral concentration in stool is highest in the prodromal phase. For those who develop symptoms, the viral concentration is usually very low by the time jaundice appears and undetectable before symptoms resolve.)

RISK FACTORS

Predictors of past or recent infection with hepatitis A virus include low household socioeconomic status (low income, wealth, and/or educational level), a larger household size and crowding, residence in a rural area, membership in certain ethnic groups, limited access to improved water sources, and limited access sanitation facilities [Jacobsen, 2004]. Several additional high-risk population groups have been identified, including those who travel or immigrate from a non-endemic region to an endemic region and those who work in certain high-risk occupations (such as some day-care employees) [Franco, 2003].

CLINICAL CHARACTERISTICS

Hepatitis A infection has four clinical phases, although these do not occur in all patients. The first stage is an incubation period of 15 to 50 days (mean 28 to 30 days). This stage is asymptomatic, but the infected person may be actively shedding the virus in the stool. The second stage is a pre-icteric period of several days to weeks that may precede the onset of jaundice. This prodromal period is characterized by nonspecific symptoms followed by gastrointestinal symptoms such as anorexia (loss of appetite), nausea, vomiting, abdominal pain, fatigue, malaise, and fever. Other symptoms at this stage may include myalgia (muscle pain), arthralgia (joint pain), cough, pharyngitis, constipation, diarrhea, pruritus (itchiness), and urticaria (hives). Dark urine caused by elevated bilirubin levels usually occurs prior the onset of jaundice. In the third stage, the characteristic yellowing of the skin and eyes of jaundice appear and most symptoms subside, although clinical signs such as hepatomegaly and hepatic tenderness are found in about half of patients. There is no treatment for HAV infection. Jaundice usually resolves within a few weeks. The final stage is a convalescent period during which the patient recovers.

AGE

The course of HAV infection varies by age. Young children with an acute hepatitis A viral infection are usually asymptomatic or non-specific and not diagnosed as hepatitis A because of the lack of jaundice. Adults with acute infections may have mild disease or may develop serious complications. (An estimated 80 to 95% of children less than 5 years old have asymptomatic infections, compared to 10 to 25% of adults [Hollinger, 1996].) The risk of disease increases with age.

COMPLICATIONS

The vast majority of hepatitis A patients make a full recovery, and the case fatality rate is low. The estimated mortality rate is 0.1% for children less than 15 years old, 0.3% for adults ages 15 to 39, and 2.1% for adults ages 40 and old [Hollinger, 1996]. Several complications may occur. About 15% of patients experience prolonged jaundice and/or relapses over several months. Some develop cholestatic hepatitis, in which the bile duct leading from the liver to the intestine becomes blocked. A few suffer from fulminant (acute) liver failure that may require a transplant or cause death. Although liver failure is more likely to occur in patients suffering from chronic liver disease prior to the onset of hepatitis A, it can occur in anyone with HAV infection. Hepatitis A does not cause chronic liver disease.

COST

The low mortality associated with hepatitis A does not mean that disease is not severe: infection may require several days or weeks of hospitalization and may cause absenteeism from work or school for several weeks or months. Thus, infection can be expensive in terms of both direct medical costs and lost productivity.

SEROLOGY

Current or recent infection can be determined by the presence of anti-HAV IgM antibodies in serum, which are detectable soon after infection and can remain detectable for about 6 months (or longer, in some cases). Past infection can be determined by the presence of anti-HAV IgG antibodies in serum, which appear shortly after the onset of symptoms and confer long-term (usually lifelong) immunity. In this report, the prevalence of anti-HAV antibodies in serologic (blood) samples taken from population-based samples will be the primary measure of population seroprevalence rates. (These assays measure total anti-HAV and assume that IgM anti-HAV, found only in those with recent infection, is rare and as a result IgG anti-HAV is the only contributor to the total anti-HAV.) The laboratory