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Hepatitis A: The Changing Epidemiology of Hepatitis A

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Hepatitis A is a communicable disease of the liver caused by hepatitis A virus (HAV), which is a single-stranded, linear, nonenveloped RNA virus of the Picornaviridae family. The incubation period is 14 to 28 days (up to 50 days). The diagnosis is made with a positive test for immunoglobulin M antibody to hepatitis A virus (anti-HAV), which is detectable from 2 weeks before the onset of symptoms to 6 months afterward. Children are often asymptomatic; the severity of acute hepatitis A generally increases with age. HAV infection typically causes an acute viral illness with jaundice, is limited to several weeks' duration, and often results in substantial morbidity and associated costs.^{1–5} Although uncommon, severe hepatic and extrahepatic complications, including liver failure, occur.

HAV is shed in the feces. The primary mode of transmission is fecal-oral, and transmission usually occurs through direct contact or person-person contact. HAV's ability to survive for extended periods in the environment facilitates its transmission through the consumption of contaminated food or water. Blood-borne transmission is rare.

Hepatitis A Epidemiology

HAV infection occurs with distinct patterns of geographic distribution and transmission⁶ (Fig. 1). Socioeconomic conditions, standards of hygiene and sanitation, household crowding, and access to clean drinking water are factors strongly associated with the incidence of acute hepatitis A disease and endemicity.^{2–6} In highly endemic areas (i.e., parts of Africa and Asia), almost all infections occur in children, and this results in high rates of population immunity and a low burden of disease. In areas with intermediate endemicity (i.e., Central and South America, Eastern Europe, and parts of Asia), childhood transmission is less frequent, more adolescents and adults are susceptible to infection, and outbreaks are common. In areas with low and very low endemicity (i.e., the United States and Western Europe), most disease occurs among adolescents and adults in defined high-risk groups (e.g., injection drug users and international travelers), during community or cyclic outbreaks facilitated by transmission among children, or through exposure to contaminated food.^{2,3,5–7}

Acute hepatitis A became reportable in the United States in 1966.⁸ Before vaccination, Alaska and Western states and children between the ages of 5 and 14 years had the highest

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rates of reported acute hepatitis A cases; substantial geographic, age, and racial/ethnic disparities existed.^{1,8} Almost 50% of hepatitis A cases in the United States had no identified risk factor. Household or sexual contact with an acute hepatitis A case was the most commonly reported risk for infection, and this was followed by contact with an asymptotically infected child resulting in transmission to adult caretakers and household contacts.^{2,5} Community outbreaks of HAV infection have been linked to transmission among diapered children in daycare settings.²

Hepatitis A Vaccination

HAV was successfully propagated in a cell culture in 1979.³ Since then, inactivated and live attenuated hepatitis A vaccines have been developed worldwide. The World Health Organization recommends vaccination in countries with intermediate to low endemicity.³ National immunization campaigns have been initiated in 11 countries, including the United States; most countries use two-dose schedules.^{4–6} As the socioeconomic status of countries improves and the age-specific patterns of disease shift to include an increasing proportion of susceptible adolescents and adults, a re-evaluation of vaccine strategies may be warranted at either the country or regional level. For example, a delay of the second dose for up to 10 years has provided seroprotection for adult travelers in Switzerland and Sweden.^{3,5} Moreover, a single-dose hepatitis A vaccination regimen has been successful in controlling community-wide outbreaks and has been implemented in Argentina's universal hepatitis childhood vaccination program.^{3,7}

United States

Hepatitis A vaccines were approved for use in the United States in 1995–1996. From 1996 to 1999, hepatitis A vaccine was recommended incrementally, with the initial focus on persons and geographic areas with an increased risk for infection.⁸ In 2006, routine hepatitis A vaccination was added to the childhood immunization schedule. The number of reported acute hepatitis A cases decreased more than 95% from 1996 to 2010⁸ (Fig. 2). In 2010, the reported acute hepatitis A case rates were similar for all age groups and both sexes⁸ (Fig. 3). Geographic variability (Fig. 4) and most disparities in nationally reported acute hepatitis A disease by race/ethnicity have been eliminated.⁵ Travel is the most prevalent reported risk factor, and this is followed by food/water outbreaks and household or sexual contact with an infected person.^{8,9} Current recommendations for hepatitis A vaccination in the United States are included in Table 1.^{1,2,10,11}

A nationally representative serosurvey (2007 – 2010)¹² focusing on the ages of 6 to 19 years in the United States recently reported a 37.6% prevalence of immunity to hepatitis A (as measured by anti-HAV levels); this represented a 13.1% increase in comparison with the prevaccine era (1988 – 1994). The increase primarily reflected increasing childhood vaccination. However, disparities remained in the prevalence of immunity to HAV by race/ethnicity; the lowest prevalence of anti-HAV (25.5%) was among white, non-Hispanic children, and this was consistent with relatively low rates of hepatitis A vaccination coverage.^{12,13}

Conclusion

Hepatitis A vaccine is highly effective and confers long-term protection against HAV infection that is expected to last for at least 25 years.² Some countries with routine childhood hepatitis A vaccination programs have achieved an up to 90% reduction in the incidence of hepatitis A^{5,6} and decreased rates of morbidity and mortality attributable to hepatitis A. However, an estimated 1.4 million cases of hepatitis A occur every year globally, and international travel and food-related exposures remain two of the most frequent causes of HAV infection.⁴

Ongoing monitoring of surveillance data for changes in national and regional disease burden, seropositivity, and longterm immunization protection is critical for informing vaccine policy. Global strategies for sustaining hepatitis A immunity in areas of low endemicity might include improvements in routine childhood vaccination rates, vaccination targeted at groups at risk, and consideration of the expanded use of single-dose vaccination or a delayed second (booster) dose.

Abbreviations

anti-HAV	immunoglobulin M antibody to hepatitis A virus
HAV	hepatitis A virus

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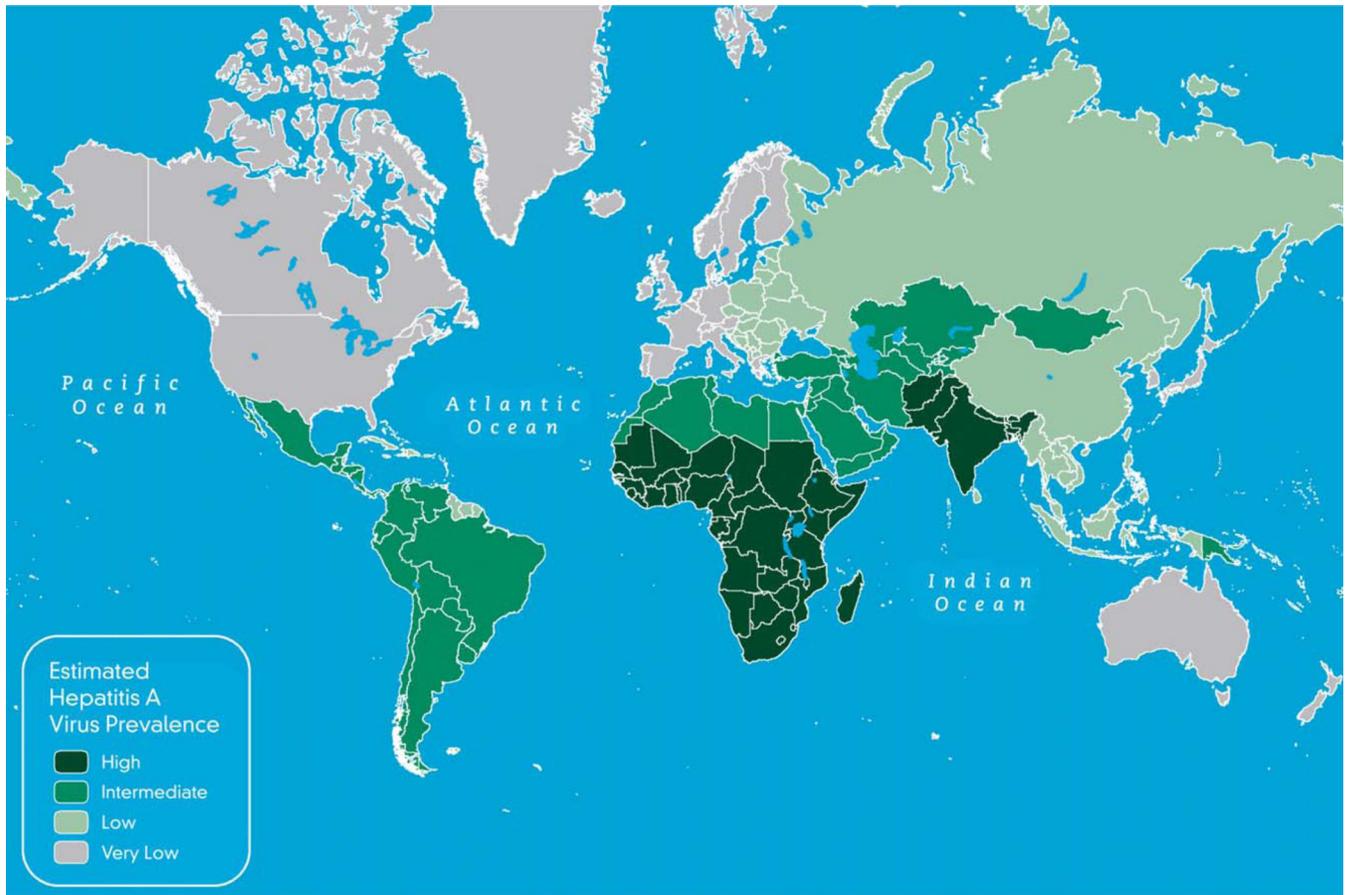


FIGURE 1. HAV global distribution. Reprinted with permission from Jacobsen, 2010.⁶

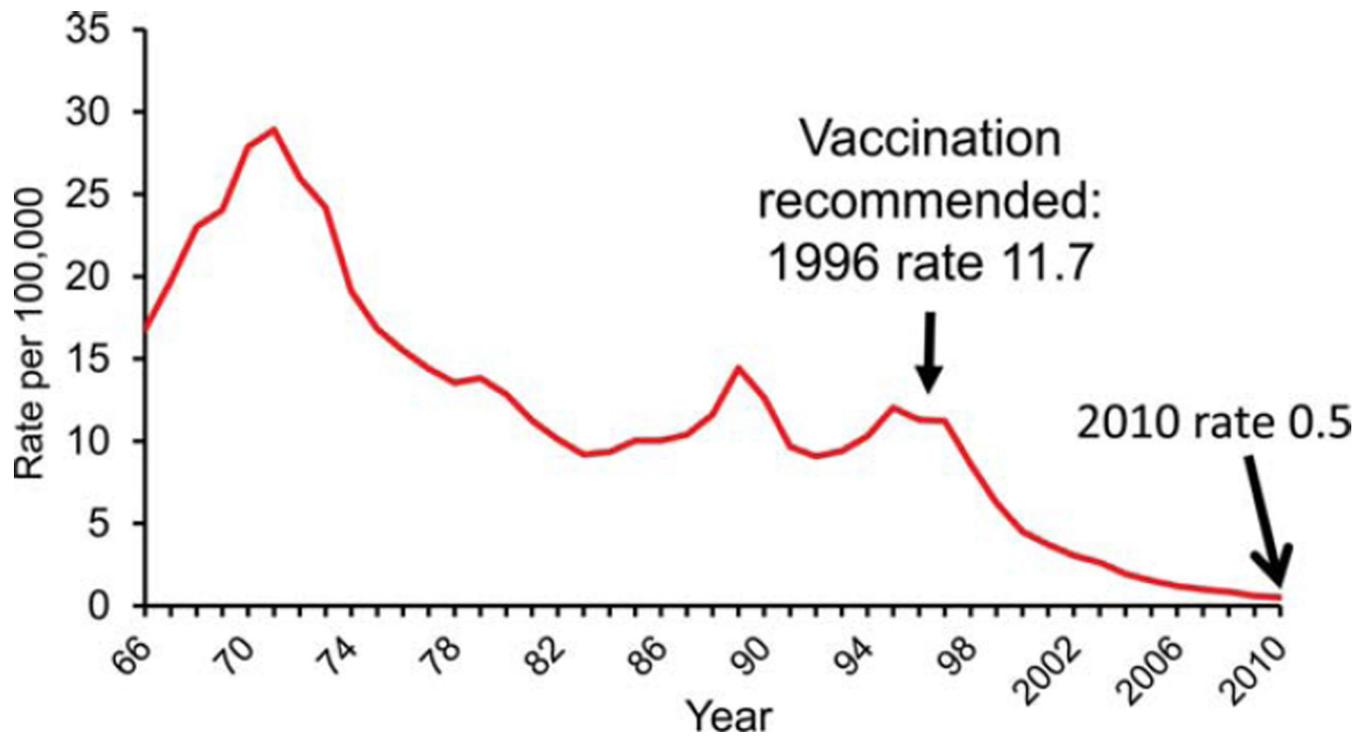


FIGURE 2. Rates of reported acute hepatitis A cases in the United States: 1966–2010. The data come from the National Notifiable Diseases Surveillance System of the Centers for Disease Control and Prevention.

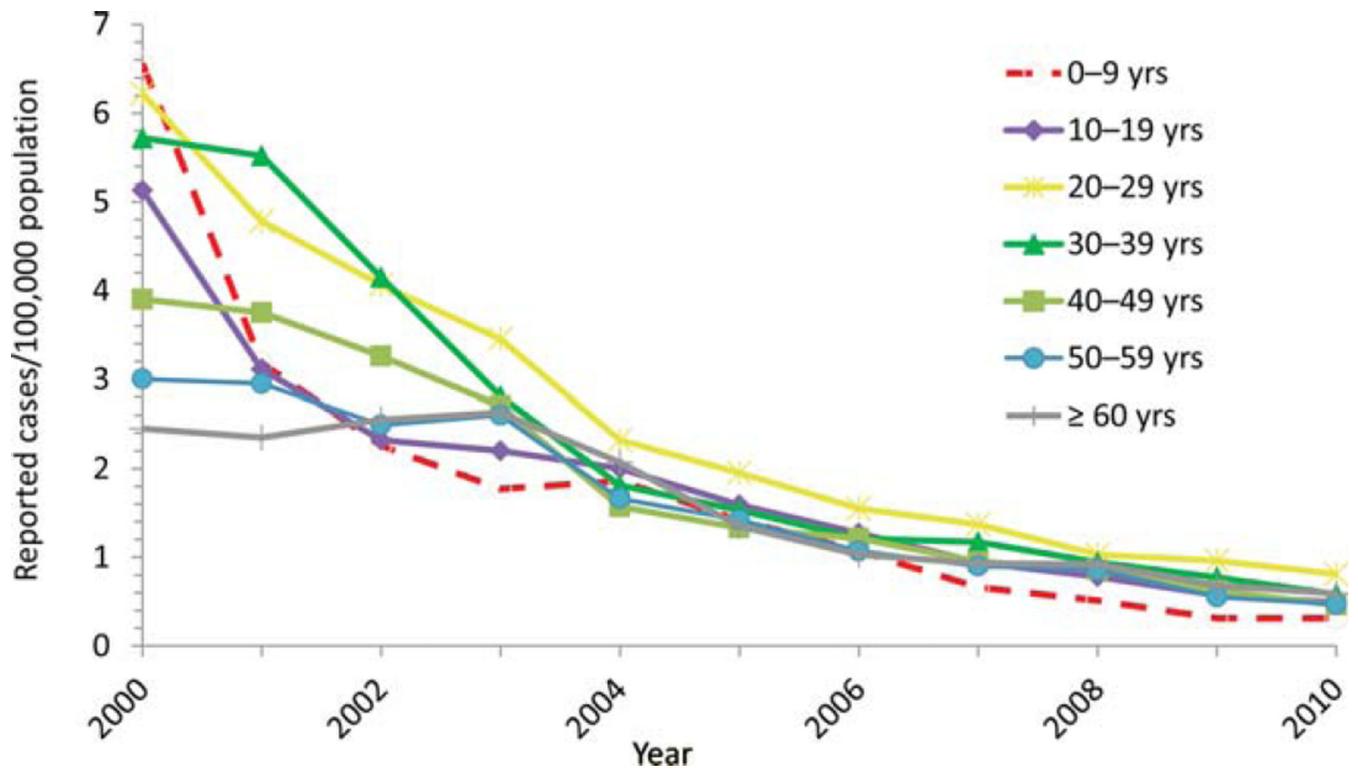


FIGURE 3. Incidence of acute hepatitis A by age group and year in the United States: 2000–2010. The data come from the National Notifiable Diseases Surveillance System of the Centers for Disease Control and Prevention. Reprinted from *Viral Hepatitis Surveillance: United States, 2010*.⁸

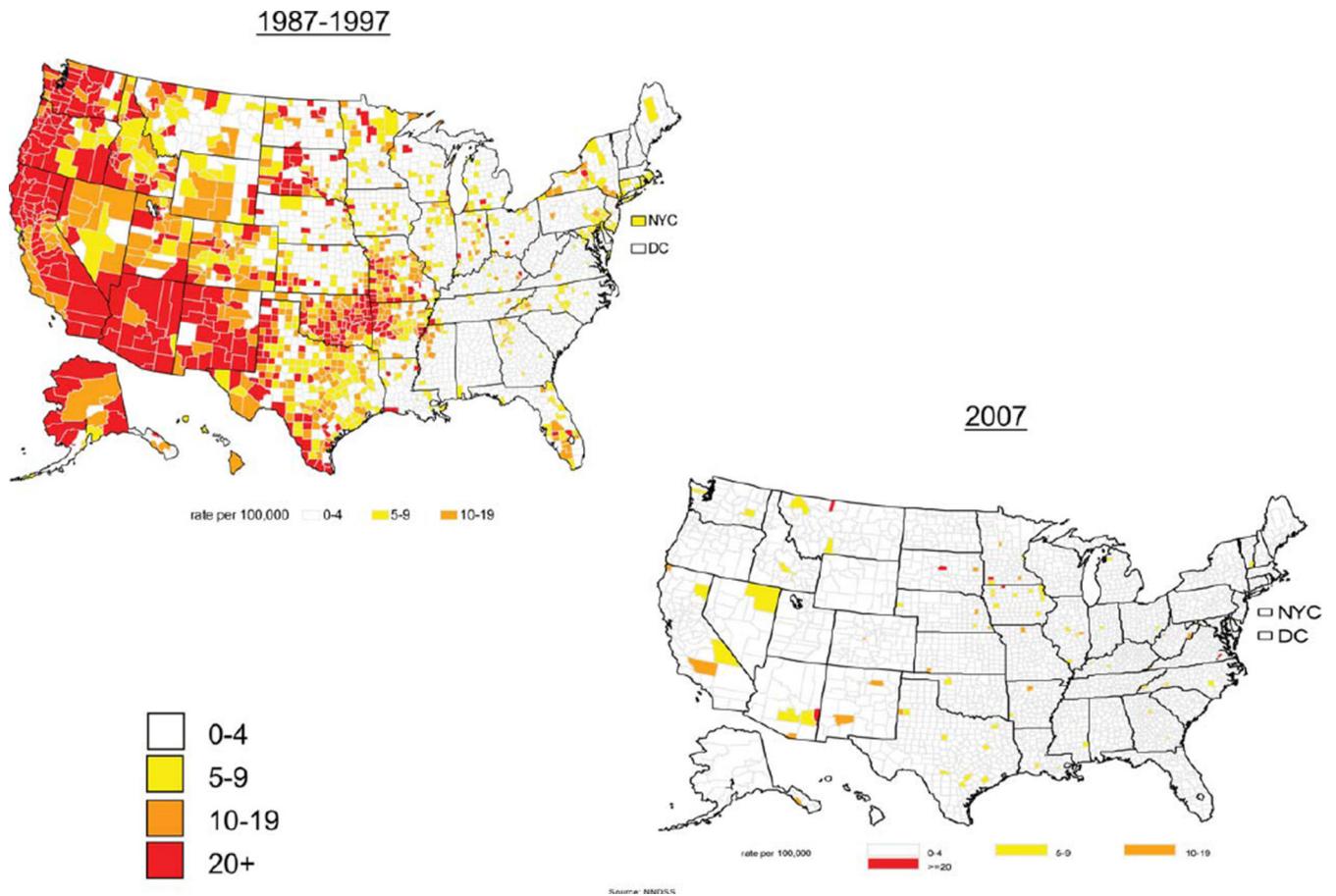


FIGURE 4. Incidence of hepatitis A (cases per 100,000 population) by county in the United States: 1987–1997 and 2007. The data come from the National Notifiable Diseases Surveillance System of the Centers for Disease Control and Prevention. Reprinted with permission from Murphy, 2012.²

TABLE 1

Recommendations of the Advisory Committee on Immunization Practices for the Routine Pre-Exposure Use of the Hepatitis A Vaccine in the United States: Children and Adults^{1,2,10,11}

All children between the ages of 12 and 23 months
Children between the ages of 2 and 18 years in existing programs (catch-up vaccination can be considered in areas without existing programs)
International travelers
Persons who anticipate close contact with an international adoptee
Men who have sex with men
Illicit drug users
Persons with chronic liver disease
Persons receiving clotting factor concentrates
Persons who work with HAV-infected primates or with HAV in research settings
Anyone who wants to obtain immunity

This table was adapted with permission from Murphy, 2012.²

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