Hepatitis A

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resuscitation guidelines recommend administration of supplementary oxygen to infants needing positive-pressure ventilation and to cyanotic infants needing free-flow oxygen. However, there are no firm guidelines for the most effective oxygen concentration to use. Recent literature has suggested that resuscitation with room air may be as effective as 100% oxygen for term infants. If an oxygen concentration less than 100% is used during assisted ventilation, the AHA recommends that 100% oxygen be available for use if there is no clinical improvement within 90 seconds. The use of pulse oximetry may be more useful than assessment of an infant's color to guide administration of appropriate oxygen concentration during resuscitation.

Evidence-based guidelines for neonatal resuscitation, including newborn ventilation, are limited. Experts continue to convene every 5 years to evaluate the literature and optimize the standard of care for neonatal resuscitation. Clinicians must recognize the need for, and be able to ensure, adequate ventilation as a keystone to effective resuscitation of a newborn.

Comment: Prompt interventions in the delivery room are essential for the best outcomes for compromised neonates. Clinicians need to differentiate between infants who need minimal respiratory assistance and those needing maximal resuscitation. Although earlier recommendations had suggested that an Apgar score of 3 or less at 1 minute should prompt immediate positive-pressure ventilation, recent evidence suggests that this intervention should be initiated earlier. Brief positive-pressure ventilation may be all that an infant requires, and an increase in heart rate demonstrates an adequate response. Another recommendation had been to initiate increased pressure for the first breath, but current recommendations suggest an individualized approach based on chest movement of the infant. This *In Brief* reinforces the importance of lifelong learning for clinicians and the need to change behavior when new recommendations are available based on up-to-date research findings. Research is examining the use of pulse oximetry in the delivery room and whether room air may be preferable to 100% oxygen in some circumstances during neonatal resuscitation. Regardless of the resuscitation strategies used, timely communication with the family is essential when their infant needs respiratory assistance.

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Author Disclosure

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Hepatitis A virus (HAV) is the most common cause of viral hepatitis worldwide, and in highly endemic developing countries, infection is universal during childhood. By adulthood, about 50% of the population of the United States has been infected. A member of the *Picornaviridae* family, HAV has only one serotype and, except for the possibility of primates, has no known animal reservoir. Unlike hepatitis B (HBV) and C (HCV) viruses, HAV is spread primarily through the fecal-oral route. HAV is carried via the bloodstream to its primary target, the hepatocyte, where it

replicates robustly but without causing much damage to the cells. Newly made virus is released via the bile ducts into the intestines and out in the stool.

While adaptive immune responses are being activated, which takes about 2 to 3 weeks, the virus multiplies and is released into stool unchecked. Until that activation, the initial phase of HAV infection is asymptomatic because the virus itself is not cytolytic to hepatocytes; activated CD8+ T cells are responsible for the destruction of infected liver cells. In many cases, especially in children younger than 6 years of age, the number of HAV-infected hepatocytes is small enough that their destruction does not compromise liver function, and infection remains asymptomatic.

When damage to the liver is more extensive, infection leads to the classic symptoms of hepatitis: malaise, anorexia, fever, nausea, vomiting, and eventually, jaundice. Whereas 40% to 70% of patients older than 15 years become jaundiced, fewer than 10% of children younger than 4 years develop jaundice, making diagnosis of HAV difficult in a patient presenting with a flulike illness, which generally resolves without sequelae within a few weeks. HAV is effectively eliminated by the immune system, and unlike HBV and HCV, does not carry the risk of chronic infection. Immunity after infection is life-long. Although rare, HAV infection can result in sufficient liver damage to produce fulminant hepatic failure (FHF). Up to 30% of pediatric cases of FHF are seen in highly endemic areas in Latin America compared with fewer than in 5% the United States. FHF carries a significant risk of mortality, and survival may depend on liver transplantation.

Unchecked fecal viral shedding in the weeks following initial infection makes HAV highly transmissible, as does the virus's ability to survive for weeks in dried feces, unaffected by freezing or heating. HAV is killed by hypochlorite (bleach). Risk factors for HAV infection are ingestion of food or water contaminated with feces harboring HAV virus, household and child care center contact with infected individuals, international travel, illicit drug use, and being a man who has sex with men. Raw shellfish, which concentrate HAV-contaminated water, are a particularly common source of infection in the United States.

Because most cases are asymptomatic, estimates are that 10 times more people are infected each year in the United States than are reported, with the highest incidence among children in diapers. Historically, a very high incidence rate was reported among American Indian/Alaskan Natives (AIANs). Since the introduction of vaccine against HAV in the United States in 1995, combined with improved water supplies, sewage disposal, and food safety, the number of cases reported to the Centers for Disease Control and Prevention has declined considerably. The most significant decline was among AIANs, with vaccination programs reducing infection from 120 to 0.8 cases per 100,000 people from 1994 to 2003. The 2006 national incidence of 1.2 cases per 100,000 people is the lowest ever recorded.

Although targeted vaccination in the United States has led to an overall 85% decrease in the rate of infection, the burden of HAV illness has shifted to untargeted populations (eastern states, adults). Infants and children have remained the primary reservoir of HAV (being mostly asymptomatic and having longer fecal shedding of virus) and are a source of infection for vulnerable adults. Hence, the Advisory Committee on Immunization Practices recommended in 2006 routine vaccination against HAV of all children, starting at 12 to 23 months of age.

Until 2005, concern that passively acquired maternal antibody would result in a diminished response to HAV vaccine led to the recommendation that children not be immunized before their second birthday. Now both available HAV vaccines (Havrix® and Vaqta®, GlaxoSmithKline, Philadelphia, Pa.) have been approved for children starting at 12 months of age, with excellent immunologic response no matter the maternal HAV antibody status. Both are inactivated whole-virus vaccines that require a booster at least 6 months after the initial dose. Vaccine-induced protective immunity appears to be long term, with kinetics-based estimates indicating at least 20 years. The vaccines are safe, are interchangeable, and can be administered at the same time as other vaccines. The dose doubles for individuals older than 18 years. Both vaccines are classified in pregnancy category C. There also is a combined HAV-HBV vaccine approved for patients 18 years and older.

HAV infection is more likely to result in significant liver disease in individuals coinfected with HBV or HCV, patients waiting for or having undergone liver transplantation, pregnant women, and people infected with human immunodeficiency virus (HIV). With HIV coinfection, HAV disease may be prolonged for months. HAV infection has a particularly high mortality rate in the presence of chronic liver disease from HCV. For these high-risk populations, not only is the acute infection more severe, but the immune response to HAV vaccination is relatively poor. Hence, it is imperative to vaccinate patients at special risk early, before they have suffered significant hepatic damage from their underlying disease.

HAV grows very slowly in cell culture. Acute HAV infection is diagnosed by detection of antibody. Anti-HAV immune globulin M (IgM) in a single serum sample is a good test for current or recent infection, with sensitivity and specificity reaching 98%. IgM initially can be detected about 1 week before the onset of symptoms; it per-

sists throughout the illness and usually declines slowly over 3 to 6 months. IgG appears shortly after IgM and indicates past infection or vaccine-induced immunity.

Treatment is supportive, but because antipyretics/analgesics such as acetaminophen have the potential to exacerbate damage to liver cells, they should be avoided.

Prevention of HAV infection can be promoted by enforcing good hygiene in child care centers, with conscientious handwashing after changing diapers and before handling food. Food should be heated to 85.0°C for more than 1 minute to inactivate HAV. Immunization against HAV is indicated as prophylaxis for international travelers to endemic areas. Immunity is active within 1 week after vaccination, and otherwise healthy children are protected even by one dose of vaccine. If travel is imminent or the patient is immunocompromised, immune globulin (IG) can be administered simultaneously with vaccine (in different muscles). A dose of 0.02 mL/kg provides protection for about 3 months and a dose of 0.06 mL/kg for approximately 6 months. Because the vaccine is not approved for children younger than 1 year of age, IG is the preferred preexposure prophylaxis in this age group. Families adopting a child from a country where HAV is endemic should check their own HAV serostatus and, if necessary, be immunized before the arrival of the child. Although hospital outbreaks are uncommon, contact precautions should be implemented for children in diapers who are admitted with or are suspected of having HAV infection.

Although community-wide epidemics have decreased significantly in the United States, most disease currently occurs in the setting of common-source foodborne outbreaks as well as outbreaks in child care centers. In these situations, the local health department should be notified and postexposure prophylaxis (PEP) instituted. For people younger than 40 years of age, vaccine given within 2 weeks of exposure to HAV is as effective as IG. Further, because vaccine is less expensive, is more available, and provides prolonged immunity, it is preferred for PEP. IG is indicated for PEP for infants younger than 1 year of age, for individuals who have chronic liver disease, and for immunocompromised patients, but vaccine should be administered simultaneously to these individuals if there is no contraindication. Among child care centers' nondiapered children, vaccine (or IG) only needs to be administered to classroom contacts of the index case. When a case, usually an adult, is identified in a center that has diapered toddlers, all attendees should receive PEP. If HAV infection has been identified in two or more families, PEP should be considered for household members of all diapered children at the center. Although the index case as well as others who have identified disease should not return to the center or school for 1 week after onset of illness (when shedding of virus in stool has diminished), those who have received PEP may return immediately thereafter.

Comment: The two most important public health interventions over the past century or so surely have been the development of vaccines and, probably even more importantly, the widespread construction of sewage systems. Although we now have effective vaccines against HAV, we should not forget the importance of cleanliness. The virus, excreted in feces, often is spread through raw shellfish from contaminated waters, but food in restaurant and child care center kitchens handled by infected workers who have not washed properly also is a common source of outbreaks. Fruits and vegetables, salads, cold cuts and sandwiches, milk, and juices all have been implicated in HAV infection. Handwashing really is cost effective!

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