Use of Hepatitis B Vaccination for Adults with Diabetes Mellitus: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

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Hepatitis B virus (HBV) causes acute and chronic infection of the liver leading to substantial morbidity and mortality. In the United States, since 1996, a total of 29 outbreaks of HBV infection in one or multiple long-term–care (LTC) facilities, including nursing homes and assisted-living facilities, were reported to CDC; of these, 25 involved adults with diabetes receiving assisted blood glucose monitoring (*1*; CDC, unpublished data, 2011). These outbreaks prompted the Hepatitis Vaccines Work Group of the Advisory Committee on Immunization Practices (ACIP) to evaluate the risk for HBV infection among all adults with diagnosed diabetes. The Work Group reviewed HBV infection–related morbidity and mortality and the effectiveness of implementing infection prevention and control measures. The strength of scientific evidence regarding protection was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology,* and safety, values, and cost-effectiveness were incorporated into a recommendation using the GRADE system. Based on the Work Group findings, on October 25, 2011, ACIP recommended that all previously unvaccinated adults aged 19 through 59 years with diabetes mellitus (type 1 and type 2) be vaccinated against hepatitis B as soon as possible after a diagnosis of diabetes is made (recommendation category A). Data on the risk for hepatitis B among adults aged ≥60 years are less robust. Therefore, ACIP recommended that unvaccinated adults aged ≥60 years with diabetes may be vaccinated at the discretion of the treating clinician after assessing their risk and the likelihood of an adequate immune response to vaccination (recommendation category B). This report summarizes these recommendations and provides the rationale used by ACIP to inform their decision making.

Risk for HBV Infection

An estimate of the risk for HBV infection for adults with diabetes living in LTC facilities was not available; continuing outbreaks suggest that it might be substantial. The population risk for HBV infection among adults with diagnosed diabetes was estimated from 865 confirmed cases of acute HBV infection reported during 2009–2010 from eight Emerging Infections Program (EIP) sites constituting approximately 17% of the U.S. population. The analysis was restricted to persons aged ≥23 years because of high rates of vaccination among younger persons. In multivariate analyses that considered persons without hepatitis B–related risk behaviors (i.e., injection-drug use, male sex with a male, and sex with multiple partners), persons aged 23 through 59 years with diabetes had 2.1 (95% confidence interval [CI] = 1.6–2.8) times the odds of developing acute hepatitis B as those without diabetes; the odds were 1.5 (CI = 0.9–2.5) times as likely for persons aged ≥60 years. The annual incidence of reported cases of acute HBV infection among adults with diabetes was 1.8 per 100,000 (CI = 1.5–2.2) (*2*). Acute HBV infection incidence is underestimated; an additional 10.5 new cases of infection likely occurred for each reported, confirmed case (*3*).

Data for the period 1999–2010 from the National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of the noninstitutionalized U.S. population, indicated a 60% ($p<0.001$) higher seroprevalence of antibody to hepatitis B core antigen (indicative of past or present HBV infection) overall among persons aged ≥18 years with diagnosed diabetes compared with those without diabetes. Stratified by age, the estimated prevalence ratios were 1.7 (CI = 1.3–2.2) for persons aged 18 through 59 years and 1.3 (CI = 1.0–1.6) for those aged ≥60 years (CDC, unpublished data, 2011).

Morbidity and Mortality

The severity of acute HBV infection among adults ranges from asymptomatic to fulminant hepatitis. National viral

hepatitis surveillance data indicate that of the 3,371 acute HBV infections reported in 2009, 47% of the 2,126 infections for which information was available resulted in hospitalization, and 1% of the 1,900 infections for which information was available were fatal (*3*). Data from EIP for the period 2009–2010 indicated a higher case-fatality rate among acute HBV–infected persons with diagnosed diabetes compared with those without diabetes, although the difference was not statistically significant (5% versus 2%, p=0.127) (*2*). Acute HBV infection progresses to chronic infection in approximately 5% of otherwise healthy adults (*4*), but is believed to be greater among older adults with diabetes (*5*). In the United States, an estimated 700,000 to 1.4 million persons are infected with HBV (*3*). Because chronic HBV infection can persist for decades, persons with chronic HBV infection are the reservoir for continuing HBV transmission. Chronic HBV infection is associated with high morbidity and mortality, leading to cirrhosis and liver cancer in ≥15% of affected adults (*5*).

Diabetes is associated with nonalcoholic fatty liver disease, including its most severe form, nonalcoholic steatohepatitis. A study of veterans without HBV infection indicated that adults with diabetes have approximately twice the risk for chronic nonalcoholic liver disease and hepatocellular carcinoma as those without diabetes (*6*).

Infection Control

HBV is highly infectious and environmentally stable (*5*); HBV can be transmitted by medical equipment that is contaminated with blood that is not visible to the unaided eye. Percutaneous exposures to HBV occur as a result of assisted monitoring of blood glucose (*7*) and other procedures involving instruments or parenteral treatments shared between persons. Lapses in infection control during assisted blood glucose monitoring that have led to HBV transmission include multipatient use of finger stick devices designed for single-patient use and inadequate disinfection and cleaning of blood glucose monitors between patients. Breaches have been documented in various settings, including LTC facilities, hospitals, community health centers, ambulatory surgical centers, private offices, homes, and health fairs (*7*; CDC, unpublished data, 2011). Initiatives are ongoing to encourage improvement in the design and labeling of devices used in diabetes monitoring and care, and for greater oversight and training of staff responsible for providing diabetes care.†

Infection control guidelines for safe blood glucose monitoring have been available since 1990, and guidelines targeting LTC settings were published in 2005 (*8*). Since 1982, hepatitis B vaccination has been recommended for health-care personnel, including personnel exposed to blood in LTC settings, in conjunction with meticulous attention to infection control practice (*5,8*). In addition, a recommendation for hepatitis B vaccination exists for persons beginning hemodialysis (*5*).

Hepatitis B Vaccine

Two single-antigen recombinant hepatitis B vaccines, Recombivax HB (Merck & Co., Inc.) and Engerix-B (GlaxoSmithKline Biologicals), and one combination hepatitis A and hepatitis B vaccine, Twinrix (GlaxoSmithKline Biologicals), are available in the United States. Hepatitis B vaccines have been used in the United States since 1982. Extensive data support their safety in all age groups (*5*).

Hepatitis B vaccination usually consists of 3 doses of vaccine administered intramuscularly at 0, 1, and 6 months; other schedules are available. At younger ages, the immune response to vaccine is similar among adults with and without diabetes. The proportion of adults who achieve seroprotection (≥10 mIU/mL antibody to hepatitis B surface antigen [anti-HBs]) after receipt of the 3-dose vaccine series decreases with age, obesity, smoking, immunosuppression, and comorbid conditions including diabetes. When the antibody responses among older adults with and without diabetes are compared, the response might be reduced among those with diabetes. A synthesis of available literature suggests a protective response is achieved after completion of the hepatitis B vaccine series in ≥90%, 80%, 65%, and <40% of adults with diabetes lacking comorbid conditions aged ≤40 years, 41 through 59 years, 60 through 69 years, and ≥70 years, respectively (CDC, unpublished data, 2011). Revaccination with 1–3 additional doses of hepatitis B vaccine safely increases the proportion of adults who achieve a protective level of anti-HBs (≥10 mIU/mL) (*5*). The duration of protection against symptomatic and chronic HBV infection lasts >22 years among healthy vaccine responders (*9*); duration of immunity among persons with diabetes is unknown.

Cost-Effectiveness

The Hepatitis Vaccines Work Group developed economic models that yielded age-stratified calculations (base case) of the incremental cost per quality-adjusted life-year (QALY) saved based on vaccinating adults with diabetes against hepatitis B.§ The estimated cost per QALY saved was $75,100 for persons aged 20 through 59 years but increased substantially with increasing age. From a lifetime perspective, a one-time vaccination program consisting of a 3-dose series of hepatitis B vaccine, covering 10% of unvaccinated U.S. adults with diagnosed diabetes aged 20 through 59 years (or approximately 528,047 persons) would be expected to prevent 4271 HBV infections, 467 hospitalizations, 256 chronic cases, 33 cases of hepatocellular carcinoma, 13 liver transplants, and 130 deaths. Postvaccination serologic testing and revaccination would add considerable cost, with limited increase in disease protection (CDC, unpublished data, 2011).

ACIP Recommendations

On the basis of available information about HBV risk, morbidity and mortality, available vaccines, age at diagnosis of diabetes, and cost-effectiveness, ACIP recommends the following:

- Hepatitis B vaccination should be administered to unvaccinated adults with diabetes mellitus who are aged 19 through 59 years (recommendation category A; evidence type 2).
- Hepatitis B vaccination may be administered at the discretion of the treating clinician to unvaccinated adults with diabetes mellitus who are aged ≥60 years (recommendation category B; evidence type 2).

Remarks

Continued efforts are needed to increase adherence to recommended infection control practice. Shared use of blood-contaminated equipment increases the risk for exposure to bloodborne pathogens, including hepatitis C virus, human immunodeficiency virus, and HBV, which is highly infectious.

Administration of the hepatitis B vaccine series should be completed as soon as feasible after diabetes is diagnosed. Available data do not confirm an advantage to any specific hepatitis B vaccine, dosage, or approved schedule for adults with diabetes. No serologic testing or additional hepatitis B vaccination is recommended for adults who received a complete series of hepatitis B vaccinations at any time in the past.

The hepatitis B vaccination series can be given safely to persons of any age, but current hepatitis B vaccines are less efficacious and less cost-effective among older adults. Evidence for the extent of increased risk for acute HBV infection among persons with diabetes who are aged ≥60 years is less strong than for younger persons with diabetes. In 2008, the median age of diabetes diagnosis was 53 years; two thirds of adult diabetes diagnoses were made before age 60 years.¶

Decisions to vaccinate adults with diabetes who are aged ≥60 years of age should incorporate consideration of the patient's likelihood of acquiring HBV infection, including the risk posed by an increased need for assisted blood-glucose monitoring in LTC facilities, the likelihood of experiencing chronic sequelae if infected with HBV, and the declining immunologic responses to vaccines that are associated with frailty, a geriatric syndrome characterized by decreased physiologic reserve and increased vulnerability, leading to early mortality in older adults (*10*).

Hepatitis B vaccine may be administered during health-care visits scheduled for other purposes as long as minimum intervals between doses are observed; there is no maximum interval between doses that makes the hepatitis B vaccination series ineffective.

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