ONE MINUTE CONSULT

BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: Do patients who received only two doses of hepatitis B vaccine need a booster?

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A two-dose regimen may provide adequate seroprotection for healthy younger adults

A: The Advisory Committee on Immunization Practices (ACIP) currently recommends that people who have not completed the three-dose vaccination series against hepatitis B virus (HBV) should receive the missed doses: ie, the three-dose regimen does not need to be restarted.[1] However, evidence suggests that a two-dose regimen may provide adequate seroprotection for healthy young adults.

As the three-dose regimen has been shown to protect 90% to 100% of adults,[2] it has gained widespread acceptance and is now standard clinical practice.[2] However, deviating from the three-dose regimen may not leave healthy young adults vulnerable to HBV infection.

RECOMMENDED DOSES AND SCHEDULES

Widespread use of the three-dose regimen for HBV stemmed from the first clinical evaluation of the recombinant vaccine, in which three 10-µg doses were given at 0, 1, and 6 months to healthy, low-risk adult volunteers.[3] This regimen was shown to provide seroprotection in over 95% of adolescents and 90% of healthy adults.[2]

Currently, three HBV vaccines for adults are approved in the United States: Recombivax HB, Engerix-B, and Twinrix (TABLE 1). While Recombivax has a seroprotection rate of 89% in healthy adults over age 40, it has higher seroprotection rates in younger people: eg, two doses of Recombivax given 4 to 6 months apart provide seroprotection to 99% of children aged 11 to 15.[4] On the other hand, patients on hemodialysis require three 40-µg doses of Recombivax or four 40-µg doses of Engerix-B.

TABLE 1

Standard vaccination regimens for hepatitis B virus

For adults over age 20	
Recombivax HB	10 µg at 0, 1, and 6 months
Engerix-B	20 µg at 0, 1, and 6 months
Twinrix	20 µg at 0, 1, and 6 months
For patients on hemodialysis or with compromised immunity	
Recombivax HB	40 µg at 0, 1, and 6 months
Engerix-B	40 µg at 0, 1, 2, and 6 months

Evidence for a two-dose regimen

Since the development of the recombinant HBV vaccine used today, studies have shown that a two-dose regimen offers seroprotection comparable with, if not better than, the three-dose regimen in adolescents and healthy young adults. Marsano et al[5] found that with a two-dose regimen, 96% to 99% of young adults attained seroprotection, with immune memory persisting for up to 2 years.[5] Moreover, Cassidy et al[6] randomized adolescents to a two-dose or a three-dose regimen and found the two regimens to be equally effective in conferring immunogenicity and immunologic memory.[6]

Other studies in adolescents have confirmed these findings and offered new evidence in support of the two-dose regimen.[7,8] For example,

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studies found that the two-dose regimen conferred seroprotection at even lower doses than previously studied, and that it conferred immune memory lasting at least 5 years.[6,7]

However, because these studies were conducted in adolescents and healthy young adults, the findings may not hold true for other populations. Studies suggest that the three-dose regimen is best for those over age 40. Moreover, it is advisable to adhere to a three-dose regimen when treating people at high risk of contracting HBV, such as health care workers; people with chronic liver disease, diabetes mellitus, or end-stage renal disease on hemodialysis; people who have multiple sex partners; and men who have sex with men.

The impact of long intervals between doses

Although the aforementioned studies focused on a two-dose regimen with a 6-month interval, longer intervals between doses do not impair seroprotection and in some cases may even prove beneficial. Heron et al[9] demonstrated that a two-dose regimen with a 12-month interval induces seroprotection as effectively as a standard three-dose or two-dose regimen with a 6-month interval.[9] Moreover, studies of the impact of deviating from a three-dose regimen found that intervals of longer than 1 year did not impede seroprotection. Not only may seroprotection be attained with intervals of 5 to 10 years before the final dose, but final antibody levels tend to increase with increasing time between doses.[10]

Nevertheless, even though an extended interval between doses may prove beneficial after the final dose is received, delaying doses may leave patients unprotected. Indeed, alternative three-dose and even four-dose schedules with shorter intervals between doses exist for certain high-risk populations, such as those recently exposed to HBV and travelers to areas of high prevalence. Therefore, intentionally extending intervals between doses may be inappropriate.

SEROPROTECTION AND PROTECTION AGAINST INFECTION

Legitimate concerns exist about the final antibody level attained with a two-dose regimen, which is typically lower than that attained with a three-dose regimen. As HBV antibody levels decline with time, lower final antibody levels theoretically increase the risk of losing seroprotection. Study of vaccine efficacy has defined seroprotection as antibody levels greater than or equal to 10 mIU/mL.[11] Yet evidence suggests that even when antibody levels drop below this level, the risk of symptomatic HBV infection does not increase. Evidence also suggests that immune memory outlasts the presence of seroprotective antibody levels, indicating that true protection against significant infection does not necessarily correlate with, and may even exceed, seroprotection.[2] This may relate to HBV's long incubation period, which allows memory cells time to generate an effective immune response.[10] For example, Floreani et al[12] showed that even though 15% of adults lost seroprotective antibody levels 10 years after vaccination, none demonstrated hepatitis B antigen reactivity or seroconversion.

POSTVACCINATION TESTING AND ADDITIONAL DOSES

At times, it may be wise to measure antibody levels after the final dose to confirm seroprotection. Seroprotection should be documented when knowledge of the patient's immune status will affect subsequent management. As recommended by the US Centers for Disease Control and Prevention, health care workers, hemodialysis patients, immunocompromised patients, and sexual partners of patients with chronic HBV infection should undergo antibody testing 1 to 2 months after the completion of a three-dose vaccination regimen. Hemodialysis patients require annual confirmation of seroprotection and should receive booster doses of HBV vaccine if necessary.

Postvaccination testing (quantitative HBV surface antibody testing) costs about the same as a single dose of HBV vaccine. Therefore, if postvaccination testing is considered because of missed vaccine doses, it may be more cost-efficient to simply administer the missed dose. ■

An extended interval between doses may be beneficial, but delaying doses may leave patients unprotected

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