Serosurveillance of First-Year Military Personnel for Hepatitis A and B

The US military utilizes a number of vaccines as strategic medical countermeasures, mandating immunizations in personnel against common infectious diseases, as well as special immunizations against rare and weaponized agents.[1] Important among the former are the vaccines against hepatitis A and B, which the military requires of all military accessions into service. While the Advisory Committee on Immunization Practices (ACIP) does not explicitly recommend hepatitis A and B vaccination for military personnel, the military's rationale for preexposure prophylaxis is based on the likelihood that active duty military personnel may encounter populations for which ACIP does recommend vaccination, and work in countries that have high or intermediate endemicity of hepatitis.[2]

In the United States, the hepatitis B vaccine is available as a single-antigen vaccine for adults, administered as a three-dose series over six months in various schedules, and hepatitis A vaccine is available as a single-antigen vaccine, administered as a two-dose series at least six months apart.[2,3] A three-dose vaccination regimen with combined hepatitis A and B vaccine (Twinrix; GlaxoSmithKline, Rixensart, Belgium) given at zero, one, and six months is indicated to confer protection against both hepatitis A virus (HAV) and hepatitis B virus (HBV) infections. ACIP recommends universal vaccination of adults at risk for HBV infection.[3] HAV antibody equal to or above the antibody assay cut-off is considered a positive response to the vaccine. The level of protection for HBV infection has been recognized at antibody concentrations of 10 or more milli-international units per milliliter specific to hepatitis B surface antigen (anti-HBs).[4,5]

In the zero-, one-, and six-month regimen, seroprotection to HBV in young adults increased with each dose from 30% to 55% after the first dose of the hepatitis B vaccine given alone, to 75% after the second dose, and greater than 90% after the third dose.[6] Twinrix appears to be an effective preventive measure in persons traveling to endemic areas, even when used under an accelerated schedule; however, limited data are available regarding its benefits to military personnel.

In a retrospective serosurvey of 428 military personnel who entered the military in 2006 to 2010 (284 were White, 54 were Hispanic, 37 were Black, and 11 were Asian; mean age = 20 years; 8% were female), we examined whether Twinrix as part of their vaccination regimen was associated with measurable HAV and HBV antibodies above baseline levels upon entry and throughout their first year of service. Military personnel routinely receive several vaccines as medical countermeasures during their first two weeks of training, of which Twinrix is one. For example, other vaccines coadministered in this cohort were measles, mumps, and rubella (n = 270); tetanus and diphtheria toxoids (adsorbed for adult use, n = 156); poliovirus vaccine (inactivated, n = 144); influenza virus vaccine (purified surface antigen, n = 40); influenza (whole, n = 100); influenza virus vaccine (live, attenuated, intranasal use [FluMist], n = 27); meningococcal polysaccharide vaccine (n = 296); and pneumococcal vaccine (n = 140). This comprehensive vaccination regimen ensures that military personnel are protected against infectious agents that they may encounter during their tour of duty. For hepatitis A and B, the second dose of Twinrix is routinely scheduled for administration at approximately two to five weeks from the first dose, and the third dose is scheduled for administration six months from the original dose. In our study, we did not have records verifying receipt of the second and third doses.

We found at least 55% and 85% of participants evaluated 331 to 360 days after baseline were seroprotected against HAV and HBV, respectively (Table 1). Geometric mean concentrations started to peak two months after entry to service for anti-HBs and three months for anti-HAV. The percentage of personnel protected against HBV was significantly higher across time than the percentage protected against HAV (two-way ANOVA for month and antigen found $P < .001$ for both main effects, with the interaction $P = .239$). Antibody concentrations of HAV and HBV antigens remained at high levels for seven to eight months after entry to service. Although a decline in antibody concentrations was observed over time, the geometric mean concentrations remained above baseline levels at 360 days (Table 1).

This is highly important because military personnel may engage in a variety of activities, from assisting civilian authorities with disaster preparation to assisting first responders, rescuing victims, providing medical care,

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TABLE 1—Geometric Mean Concentrations (GMCs) of Antibodies Specific to Hepatitis A Virus (Anti-HAV) and Hepatitis B Surface Antigen (Anti-HBs,) and Percentage of Personnel Protected Over Time After Entry Into Military Service: United States, 2006–2010

	Anti-HAV			Anti-HBs		
Days[a]	Total No.[b]	GMC[c]	% Protected	Total No.[b]	GMC[c]	% Protected
Baseline	426	2.1	14	407	21.0	57
31–60	91	6.9	37	90	139.4	67
61–90	53	17.8	57	52	1471.6	87
91–120	71	35.0	69	71	1197.7	89
121–150	63	25.8	68	62	1477.4	92
151–180	31	38.0	74	29	1157.0	90
181–210	24	31.0	79	23	642.5	83
211–240	22	23.1	64	22	1055.0	100
241–270	17	20.6	71	17	293.3	82
271–300	13	14.5	54	14	417.2	79
301–330	15	4.7	47	14	489.2	93
331–360	20	14.2	55	20	453.3	85

[a]Days at which serum samples were collected relative to military service entry. Serum samples were obtained from the Department of Defense Serum Repository as part of routine surveillance.

[b]Number may vary from the total number of participants in a group or day range because of the sampling process.

[c]GMC of serum antibodies as measured in mIU/mL at the Centers for Disease Control and Prevention by using the ETI-AB-HAVK PLUS enzyme immunoassay diagnostic kit (DiaSorin, Saluggia, Italy), which includes a high positive control, containing 1200–2000 mIU/mL anti-HAV (World Health Organization second International Standard, 1998) and the VITROS ECi Immunodiagnostic System for anti-HBs (Ortho Clinical Diagnostics, Inc., Raritan, NJ, USA). Anti-HBs levels ≥10 mIU/mL indicated seroprotection and a similar level was considered seroprotective for anti-HAV. SPSS version 23.0 (IBM Corp., Armonk, NY, USA) was used to calculate two-way ANOVA comparisons, GMCs, and percentages at or above seroprotective levels.

delivering supplies, and cleaning up the aftermath. The experience with Hurricane Katrina in the Gulf Coast in 2005 demonstrated the extent of the need for military involvement during an emergency, in which tens of thousands of reserve and active duty personnel were called upon.

PUBLIC HEALTH IMPLICATIONS

The military requires vaccination of all military accessions into service. Vaccines are a medical countermeasure dispensed to military personnel during their first two weeks of training camp to ensure protection of personnel upon deployment to areas of conflict or during response to public health emergencies like Hurricanes Harvey, Irma, and Maria where exposure may happen (e.g., sewage, medical waste, or via direct contact with populations in which hepatitis A and B are endemic). In this report, a large proportion of personnel remained seroprotected against HAV (55%) and HBV (85%) at 360 days after entry to the military. There were relatively more personnel with antibodies below protective levels for HAV than to HBV antigens at all time points measured (Table 1), likely a reflection of the earlier universal infant hepatitis B vaccination recommendation in 1991 compared with the hepatitis A universal childhood vaccination recommendation in 2006.[2,3] Although the third dose of Twinrix would have been scheduled, it is possible some personnel instead received a dose of the hepatitis B vaccine only. Participants' records in this serosurvey did not include whether they had been screened for existing anti-HAV or anti-HBs antibodies. Screening is currently done at most basic training camps but not all. Only military personnel who have antibodies below the protective level of hepatitis A and hepatitis B are immunized with Twinrix. Based on this serosurvey, persons seronegative for hepatitis A only should receive hepatitis A vaccine in two doses separated by approximately six months rather than Twinrix. However, it may be reasonable to administer Twinrix to hepatitis B seronegative personnel because most are seronegative to hepatitis A, and therefore will benefit from dual vaccination. Hepatitis A and B vaccines both afford long-term protection even among those who are seronegative but retain immunological memory. Therefore, review of immunization records instead of antibody screening may be cost-effective because the cost of serologic screening and immunization of seronegative individuals could be avoided. As new formulations emerge, vaccine practices and recommendations may change to meet the demands of populations at risk, like the military. Additional studies may be required to determine if, in the military setting, antibody-level monitoring and revaccination of nonresponders to HAV and HBV should be considered to ensure 100% protection among active duty military personnel, a group at risk for infection because of travel to endemic areas and close personal contacts while on active duty. AJPH

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M. P. Broderick and S. Romero-Steiner were involved in designing, implementing analyses, and writing the report. S. Kamili supervised all laboratory data generation and analysis, contributed and edited the report. T. Le performed serologic testing of samples. N. P. Nelson contributed and edited the report. D. J. Faix took the lead in the original concept for the report and editing the report.

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HUMAN PARTICIPANT PROTECTION

The Naval Health Research Center institutional review board approved the initial study (Protocol NHRC.2011.0015). This report was determined to be as non-engaged in human participant research at CDC.

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14. ABSTRACT

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