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Rising Hepatitis A Immunity in U.S. Military Recruits

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Background: The U.S. military immunizes new recruits against hepatitis A. Since 2001, immunization with the hepatitis A vaccine has been recommended for civilian adolescents in higher risk areas. Recently, the Armed Forces Epidemiological Board recommended serologic screening where feasible to reduce redundant recruit immunizations. Objectives: The purpose of this study was to determine hepatitis A seroprevalence in recruit populations to inform screening policy. Methods: Banked serum from a sample of military recruits (n = 2,592) in 2004 was tested for total antibody to hepatitis A (anti-hepatitis A virus (HAV)). Results: The overall anti-HAV seroprevalence was 12.0% (95% confidence interval, 10.8%–13.3%). Adjusted to the age distribution of the 18- to 34-year-old population, the seroprevalence was 11.9% (10.5%–13.4%). The lowest seroprevalence was noted in the 1984 birth cohort, with significantly higher seroprevalence among younger recruits. Conclusions: Rising hepatitis A immunity among successive birth cohorts suggests increasing compliance with immunization recommendations. In anticipation of rising population immunity, universal screening of military recruits for anti-HAV is recommended.

Introduction

In 2004, the Armed Forces Epidemiological Board (AFEB), which serves as a continuing scientific advisory body to the Assistant Secretary of Defense for Health Affairs and the military Surgeons General, recommended that the military implement serologic screening of recruits where feasible to reduce unnecessary or redundant immunizations.[1] To inform implementation of this recommendation, a detailed economic analysis of various serologic screening policy options has been performed by Army investigators.[2] In conjunction with hepatitis B immunization, hepatitis A immunization is now required at accession for all U.S. military recruits.[3] To maximize potential reductions in unnecessary immunizations in accordance with the AFEB recommendation, this analysis considered the addition of screening for total hepatitis A antibody (anti-hepatitis A virus (HAV)) as a marker of pre-existing immunity.[4] This analysis found that adding universal hepatitis A screening to existing hepatitis B screening programs would be incrementally cost-beneficial at a population seroprevalence of 17% or more.[5]

In 1999, the Advisory Committee on Immunization Practices (ACIP) recommended routine immunization with hepatitis A vaccine for children residing in states where the annual rate of hepatitis A in 1987 to 1997 was ≥20 cases per 100,000 population[6] (ACIP region 1). Immunization was to be considered for children living in states where the historic rate was ≥10 cases per 100,000 population (ACIP region 2). No immunization recommendations were made for the remaining states and the U.S. territories (ACIP region 3). The published 2000 Recommended Childhood Immunization Schedule[7] limited its region-specific recommendations to immunization of children up to age 12, although by 2001 the schedule[8] expanded the region-specific recommendations to include routine immunization of adolescents through age 18.

Prior to the era of vaccination, rates of hepatitis A immunity among the U.S. population varied significantly by ethnicity, birthplace, and age. The linear association of increasing age with rising immunity across all demographic groups indicates the cumulative incidence of naturally occurring disease and the effect of periodic nationwide epidemics which occurred every 10 to 15 years. African-American and Hispanic race ethnicity and residence in the Southwest were also associated with higher hepatitis A seroprevalence.[9]

Comprehensive estimates of rates of hepatitis A immunity among the young adult population reflecting the effects of active immunization have not been assessed to date. Our study was conducted to determine rates of immunity among military recruit cohorts, to estimate the effects of the ACIP immunization recommendations on current and future rates of immunity, and to inform accurate economic analyses of service-specific serologic screening policy options.

Subjects and Methods

Serum Specimens

For the purposes of routine human immunodeficiency virus surveillance, all applicants for enlistment in the U.S. military have serum drawn during the application process. The serum that remains (approximately 2.5 ml) is sent for permanent storage at the Department of Defense Serum Repository (DoDSR). The DoDSR contains surveillance specimens collected from civilian applicants and from members of the Armed Forces at subsequent intervals of approximately 2 years or less.[10] Stored specimens are predominantly in their second freeze and are maintained at −30°C pending retrieval for study.

Source of Data

The source of data for this study is the Defense Medical Surveillance System (DMSS), an integrated public health surveillance database that includes information on all health care

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visits among military personnel, as well as demographic data (e.g., age, gender) and service-related data (e.g., date of entry into service, date of separation from service, rank, service component, occupation, and deployment history). Serum specimens are linked to complete medical outcomes and demographic and service-related data contained in the DMSS, which is maintained by the Army Medical Surveillance Activity, facilitating their later identification and use in military seroepidemiologic and surveillance studies.[10]

Study Population

The study population included enlisted recruits from all 50 states, the District of Columbia and U.S. territories, first entering military service in 2004. Exclusion criteria included age <18 at time of serum collection, age >34 at day of entry to military service, previous military service, or the absence of a serum specimen obtained within 6 months before the date of entry. Individuals with previous military service were excluded from analysis since previous service may have exposed the subjects to hepatitis A[11] immunization from mandatory vaccination policies dating from the mid-1990s. Restrictions were placed on date of serum collection to improve the study's ability to detect cohort effects in seroprevalence.

Study Approval

This research was conducted under a protocol approved by the Walter Reed Army Institute of Research Institutional Review Board, exempt from Human Use Committee review. Only existing data sources and serum specimens specifically collected and banked for surveillance purposes were used. The principal investigators were blinded to all subject personal identifiers during the conduct of the study.

Sample Size

Sample size was determined primarily by available funding. A random sample and two additional specified oversamples (defined by age and home of record at application to military service) were extracted. Based on existing seroprevalence studies and the estimated demographics of the 2004 recruit cohort, the rate of hepatitis A seroprevalence among all recruits was predicted to be no >20%. To facilitate service-specific policy implementation, a 95% confidence interval (CI), at most ±2.5%, was desired for the seroprevalence approximation for Army recruits. Based on preliminary queries of available DMSS data, Army enlisted accessions were expected to comprise 48.6% of all nonprevious service-enlisted accessions, necessitating a random sample size of 2,023 recruits. Preliminary DMSS data queries further suggested a minimum of 6.7% of recruits would be 25 years of age or older; previously published figures revealed recruits with home of record in ACIP region 1 comprised 22.1% of the active duty recruit cohort in 2002.[12] To ensure CI of ±3.5% for these two specific groups at a maximum expected seroprevalence of 25%, a total oversample of 588 recruits was required for each group. A random sample of 2,023 enlisted accessions was projected to result in sampling 453 enlisted accessions from ACIP region 1 and a minimum of 136 enlisted accessions age 25 years of age and older. Oversampling 135 accessions from ACIP region 1 and 452 enlisted accessions age 25 years of age and older would produce sufficient collective sample sizes. Remaining funding permitted an additional 5% sampling in all groups.

Subject Sampling

Using DMSS, a random sample of 2,124 recruits age 34 or younger were selected. Additionally, random oversamples of 452 eligible recruits age 25 and older and 142 eligible recruits from ACIP region 1 were selected to improve the precision of the seroprevalence estimate in those that were less likely to be represented in the original random sample.

The earliest serum specimen available in the DoDSR within the 6 months preceding accession was identified for each subject, generally corresponding to the serum specimen obtained at first application to military service. A list of unique specimen identifiers were used to link to selected subjects' military service and demographic data.

Specimen Handling and Laboratory Testing

The DoDSR retrieved, thawed, and aliquotted each identified specimen, labeling each aliquot with its corresponding unique specimen identifier. Aliquots were then refrozen and shipped on dry ice to the Immunology Laboratory at Brooke Army Medical Center for processing. Qualitative testing for the presence of total IgG and IgM antibody to hepatitis A antigen was performed in a College of American Pathologists-certified laboratory through the use of the ETI-AB-HAVK PLUS total anti-HAV EIA assay (DiaSorin, Inc., Stillwater, Minnesota). Equivocal results (optical densities >0.8 of the cutoff value) were reported as negative results. Laboratory personnel were blinded to personnel identifiers and results were reported by unique specimen identifier.

Statistical Analysis

Evaluation of overall seroprevalence of anti-HAV was performed by generating point estimates and corresponding 95% binomial CI for various strata. Age adjustment of crude seroprevalence results to the age distribution of the 2004 U.S. general population was performed using population figures available from the U.S. Census Bureau.[13,14] Pearson's χ^2 tests of significance and two-sample proportion tests were performed to assess differences in crude seroprevalence across strata. All analyses were performed using Stata 8.0 (Stata Corporation, College Station, Texas).

Results

Sample Characteristics

A total of 2,718 samples were aliquotted and shipped for testing and qualitative laboratory results were available on 2,717 specimens. Before final analysis, 102 specimens were found to be from individuals age 17 years at the time of serum collection; laboratory results from these specimens were discarded and excluded from further analysis. Complete laboratory results and demographic data were available for 2,026 random samples, 452 age-specific oversamples, and 137 ACIP region 1 oversamples. Of the random sample, 215 were from recruits age 25 and older and 444 were from ACIP region 1 (Table I). Our random sample was similar to the nonprevious service 2004 recruit population age 18 to 34 in gender and home of record, but differed significantly in service ($p < 0.001$, $\chi^2 = 46.6$, $df = 3$), age ($p < 0.001$, $\chi^2 = 41.9$, $df = 2$), and race ethnicity ($p = 0.032$, $\chi^2 = 8.8$, $df = 3$). Differences in the age proportion of study

TABLE I

STUDY POPULATIONS COMPARED WITH TOTAL ELIGIBLE YEAR 2004 ENLISTED RECRUIT POPULATION ENTERING THE ARMY, NAVY, AIR FORCE, AND MARINE CORPS

Variable	No. (%) in							
	Random Sample		Age 25–34 Oversample		ACIP Region 1 Oversample		2004 Recruit Population[a]	
Overall	2,026	(100)	452	(100)	137	(100)	174,867	(100)
Military service[b]								
Army	1,076	(53)	306	(68)	76	(55)	82,671	(47)
Navy	290	(14)	57	(13)	16	(12)	33,804	(19)
Air Force	368	(18)	61	(14)	32	(23)	29,747	(17)
Marine Corps	292	(14)	28	(6)	13	(9)	28,645	(16)
Sex								
Male	1,674	(83)	358	(79)	120	(88)	145,271	(83)
Female	352	(17)	94	(21)	17	(12)	29,596	(17)
Age[b,c] (years)								
18–19	981	(48)	0	(0)	72	(53)	97,234	(56)
20–24	830	(41)	0	(0)	51	(37)	61,618	(35)
25–34	215	(11)	429	(100)	14	(10)	16,015	(9)
Home of record[d]								
ACIP region 1	444	(22)	85	(18)	137	(100)	37,426	(21)
ACIP region 2	306	(15)	65	(14)	0	(0)	26,960	(15)
ACIP region 3	1,276	(63)	303	(67)	0	(0)	109,843	(62)
Race Ethnicity[e]								
African American	325	(16)	68	(15)	11	(8)	25,066	(14)
Hispanic	163	(8)	41	(9)	19	(14)	12,346	(7)
Caucasian	1,368	(68)	300	(66)	89	(65)	121,801	(70)
Other/unknown	170	(8)	43	(10)	18	(13)	15,654	(9)

[a] Total 174,867 nonprior service recruits aged 18–34 identified by the DMSS. Home of record at accession was unknown for 638 eligible subjects.
[b] Value of $p < 0.001$, χ^2 eligible recruit population vs. random sample.
[c] Age at date of serum collection (within 6 months of date of accession) for sample populations.
[d] ACIP region 1 includes Alaska, Arizona, California, Idaho, New Mexico, Nevada, Oklahoma, Oregon, South Dakota, Utah, and Washington where adolescent immunization has been recommended since 2001. ACIP region 2 includes AR, CO, MO, MT, TX, and WY, where adolescent immunization has been recommended for consideration. Region 3 includes the remaining states and the U.S. territories not specifically referenced in the recommendations.
[e] Value of $p = 0.032$, χ^2 eligible recruit population vs. random sample.

subjects were attributed both to the exclusion of serum collected on applicants age 17 years and to age-specific recruiting practices and serum collection timelines resulting in differential rates of study exclusion. The consequential confounding of military service and race ethnicity and the expected differences in service characteristics, gender, and race ethnicity of both oversamples were consistent with previously published military demographic data.[12]

Total Anti-HAV Seroprevalence

The overall total anti-HAV seroprevalence among the random sample was 12.0% (95% CI, 10.7%–13.5%). When adjusted to the U.S. population 18 to 34 age distribution (using age categories 18–19, 20–24, 25–29, and 30–34 years),[13,14] the anti-HAV seroprevalence was 11.9% (10.5%–13.4%). When crude seroprevalence among subjects in the random sample was stratified by demographic characteristics (Table II), a significant difference in seroprevalence was found across age groups ($p = 0.015$, $\chi^2 = 10.4$, $df = 3$) and home-of-record ACIP region ($p = 0.005$, $\chi^2 = 10.7$, $df = 2$). By strata, crude seroprevalence was highest among recruits with homes of record in ACIP regions 1 and 2 where immunization was recommended or recommended for consideration, and among recruits <20 years of age. There were no significant differences in seroprevalence noted by race ethnicity, gender, or service.

Regional Variations in Seroprevalence

The age and racial-ethnic distributions of recruits were similar between the random sample and the ACIP region 1 oversample (data not shown); data were pooled to increase power in further analyses. When the results were stratified by the presence or absence of regional ACIP immunization recommendation (Table III), a significantly higher seropositivity ($p = 0.002$, $\chi^2 = 10.0$, $df = 1$) was noted among recruits from ACIP regions 1 and 2 (14.8%,;95% CI, 12.5%–17.3%) than from ACIP region 3 (10.3%; 95% CI, 8.7%–12.1%).

Birth Cohort Effects

The magnitude of age-specific differences in seroprevalence among young adults differed by presence of the regional ACIP recommendation. Although point estimates of seroprevalence were higher among recruits age 18 to 19 than those age 20 to 24 across the ACIP region, nonoverlapping CI were found between age groups only in ACIP region 3 ($p = 0.03$ by two-sample

TABLE II

TOTAL HEPATITS A ANTIBODY SEROPREVALENCE IN THE RANDOM SAMPLE STUDY POPULATION, BY DEMOGRAPHIC VARIABLE

Variable	Subjects in Random Sample No.	Total Anti-HAV Seroprevalence	
		%	(95% CI, %)
Overall			
Unadjusted	2,026	12.0	(10.7–13.5)
Age adjusted[a]	2,026	11.9	(10.5–13.4)
Service Branch			
Army	1,076	12.5	(10.5–14.6)
Navy	290	13.4	(9.7–17.9)
Air Force	368	10.3	(7.4–13.9)
Marine Corps	292	11.3	(7.9–15.5)
Sex			
Male	1,674	12.3	(10.8–14.0)
Female	352	10.8	(7.8–14.5)
Age[b,c]			
18–19	981	14.1	(12.0–16.4)
20–24	830	9.3	(7.4–11.5)
25–29	164	14.0	(9.1–20.3)
30–34	51	11.8	(4.4–23.9)
Home of record[d,e]			
ACIP region 1	444	14.4	(11.3–18.0)
ACIP region 2	306	16.0	(12.1–20.6)
ACIP region 3	1,276	10.3	(8.7–12.1)
Race ethnicity			
African American	325	15.1	(11.4–19.4)
Hispanic	163	14.1	(9.2–20.4)
Caucasian	1,368	11.0	(9.4–12.7)
Other	170	12.4	(7.4–17.3)

[a] Age adjusted to the distribution of the 2004 U.S. population aged 18–34 using the age categories listed; 95% CI uses the normal approximation to the binomial distribution.

[b] Age at date of serum collection (within 6 months of date of accession).

[c] Value of $p = 0.015$, χ^2.

[d] ACIP region 1 includes Alaska, Arizona, California, Idaho, New Mexico, Nevada, Oklahoma, Oregon, South Dakota, Utah, and Washington where adolescent immunization has been recommended since 2001. ACIP region 2 includes Arkansas, Colorado, Missouri, Montana, Texas, and Wyoming where adolescent immunization has been recommended for consideration. Region 3 includes the remaining states and the U.S. territories not specifically referenced in the recommendations.

[e] Value of $p = 0.005$, χ^2.

proportion test), reflecting a significant rise of 5.2% between recruits age 20 to 24 and younger recruits age 18 to 19. Similarly, when tabulated by specific age and birth cohort (Table IV) for subjects age 18 to 24, a nadir in the point estimate of seroprevalence was observed in the cohort age 20 across the ACIP regions.

Discussion

To our knowledge, this is the first cross-sectional study to demonstrate evidence of increasing hepatitis A seroprevalence among successive birth cohorts exposed to the availability and recommended use of hepatitis A vaccine. Tabulated by birth cohort among subjects age 18 to 24, the lowest seroprevalence was observed among members of the 1984 birth cohort, age 20 in the year 2004 and age 17 upon release of the 2001 adolescent ACIP recommendations.

Among recruits age 18 to 20, each subsequent birth cohort demonstrated an increase in seroprevalence. Assuming a stable background rate of natural infection, the net annual increase in seroprevalence above the background rate represents excess population immunity acquired coincident with the availability and recommended use of hepatitis A vaccine.

We believe the elevated immunity observed among members of this cohort is consistent with active immunization commencing within a year of the first adolescent immunization recommendation in the year 2001. The nadir in seroprevalence among the 1984 birth cohort argues against significant rates of active immunization among young adults age 18 years and older, suggesting that active immunization against hepatitis A in our study population may be principally associated with high school attendance.

We believe our results may reflect in part the adoption of concurrent hepatitis A and B vaccination among older adolescents receiving catch-up hepatitis B immunization as a result of high school enforcement of hepatitis B immunization mandates. Recent work by investigators has demonstrated rates of immunity to hepatitis B among military recruits rising by approximately 5% per year,[15,16] comparable to the rise in hepatitis A immunity observed in our study across the ACIP regions.

Unlike hepatitis B requirements, few states have mandated catch-up immunization of adolescents with hepatitis A vaccine.

TABLE III

TOTAL HEPATITS A ANTIBODY SEROPREVALENCE IN THE POOLED RANDOM AND REGIONAL OVERSAMPLE BY HOME OF RECORD ACIP RECOMMENDATION STATUS

	ACIP Regions 1 and 2[a]				ACIP Region 3[a]			
	Subjects in Pooled Sample		Total Anti-HAV Seroprevalence		Subjects in Pooled Sample		Total Anti-HAV Seroprevalence	
Variable	No.	(%)	%	(95% CI, %)	No.	(%)	%	(95% CI, %)
Overall[b] (n = 2,163)	887	(100)	14.8	(12.5–17.3)	1,276	(100)	10.3	(8.7–12.1)
Age[c] (years)								
18–19	453	(51)	16.1	(12.8–19.8)	600	(47)	12.3	(9.8–15.2)
20–24	343	(39)	13.4	(10.0–17.5)	538	(42)	7.1	(5.0–9.6)
25–29	72	(8)	11.1	(4.9–20.7)	105	(8)	15.2	(9.0–23.6)
30–34	19	(2)	21.1	(6.1–45.6)	33	(3)	9.1	(1.9–24.3)
Race ethnicity								
African American	81	(9)	13.6	(7.0–23.0)	255	(20)	15.3	(11.1–20.3)
Hispanic	96	(11)	17.7	(10.7–26.8)	86	(7)	10.5	(4.9–18.9)
Caucasian	598	(67)	13.9	(11.2–16.9)	859	(67)	9.1	(7.2–11.2)
Other/unknown	112	(13)	17.9	(11.3–26.2)	76	(6)	6.6	(2.2–14.7)

[a] ACIP region 1 includes Alaska, Arizona, California, Idaho, New Mexico, Nevada, Oklahoma, Oregon, South Dakota, Utah, and Washington where adolescent immunization has been recommended since 2001. ACIP region 2 includes Arkansas, Colorado, Missouri, Montana, Texas, and Wyoming where adolescent immunization has been recommended for consideration. Region 3 includes the remaining states and the U.S. territories not specifically referenced in the recommendations.

[b] Value of $p = 0.002$ by χ^2.

[c] Age at date of serum collection (within 6 months of date of accession).

TABLE IV

AGE-SPECIFIC TOTAL HEPATITIS A ANTIBODY SEROPREVALENCE IN THE POOLED RANDOM AND REGIONAL OVERSAMPLE BY HOME OF RECORD ACIP RECOMMENDATION STATUS, AGES 18–24

	ACIP Regions 1 and 2[a]				ACIP Region 3[a]			
	Subjects in Pooled Sample		Total Anti-HAV Seroprevalence		Subjects in Pooled Sample		Total Anti-HAV Seroprevalence	
Variable	No.	(%)	%	(95% CI, %)	No.	(%)	%	(95% CI, %)
Overall[b] (n = 1,934)	796	(100)	14.9	(12.5–17.6)	1,138	(100)	9.8	(8.1–11.7)
Age[c] (years) (Birth cohort)								
18 (1986)	277	(35)	16.6	(12.2–21.0)	320	(28)	13.1	(9.4–16.8)
19 (1985)	176	(22)	15.3	(10.0–20.7)	280	(25)	11.4	(7.7–15.2)
20 (1984)	119	(15)	10.9	(5.2–16.6)	183	(16)	4.4	(1.4–7.4)
21 (1983)	91	(11)	12.1	(5.3–18.9)	137	(12)	6.6	(2.4–10.8)
22 (1982)	64	(8)	18.8	(8.9–28.6)	88	(8)	8.0	(2.2–13.7)
23 (1981)	47	(6)	14.9	(6.2–28.3)	64	(6)	12.5	(5.6–23.2)
24 (1980)	22	(3)	13.6	(2.9–34.9)	66	(6)	9.1	(3.4–18.7)

[a] ACIP region 1 includes Alaska, Arizona, California, Idaho, New Mexico, Nevada, Oklahoma, Oregon, South Dakota, Utah, and Washington where adolescent immunization has been recommended since 2001. ACIP region 2 includes Arkansas, Colorado, Missouri, Montana, Texas, and Wyoming where adolescent immunization has been recommended for consideration. Region 3 includes the remaining states and the U.S. territories not specifically referenced in the recommendations.

[b] Value of $p < 0.001$ by χ^2.

[c] Age at date of serum collection (within 6 months of date of accession).

Alaska, Nevada, Oklahoma, and some Texas counties have mandates requiring new high school enrollees to provide proof of immunity.[17] Due to the brief time these mandates have been in effect, they alone would not have been the cause of the increased seroprevalence we observed among adolescent recruits in ACIP regions 1 and 2, and these mandates would not have explained the significant rise in immunity noted in ACIP region 3.

Our findings suggesting broad use of hepatitis A vaccine are supported by a recent survey of hepatitis A immunization status among matriculating college students. A 2003 study using review of immunization records found that 9.8% of 448 matriculating college students with immunization records were completely immunized for hepatitis A and an additional 10.0% were partially immunized.[18] This surprisingly high rate of vaccine coverage within 2 years of the release of the ACIP adolescent immunization recommendation lends support to our hypothesis that active immunization, rather than naturally acquired infection, are the cause of the increased seroprevalence observed within the 1985 and 1986 birth cohorts.

These findings of widespread adolescent hepatitis A vaccination practices differ markedly from the highly region-specific vaccination practices observed among younger children. For

example, a recent study of children age 24 to 35 months found 50.9% of children in the ACIP region 1, 25.0% of children in the ACIP region 2, and only 1.4% of children in the ACIP region 3 received at least one dose of hepatitis A vaccine[19] in 2003. Similarly, using public and private sector vaccine distribution data, another study[20] estimated rates of childhood vaccine coverage in 2001 of 30% in ACIP region 1, 19% in ACIP region 2, and only 1% in ACIP region 3. These data predate the year that widespread adoption of adolescent immunization was demonstrated from the results of our study and therefore these results may not generalize to the population we studied.

Our study has a number of limitations. The key limitation is that we could not definitively assess the potential impact of natural infection on the elevated seroprevalence we observed among the 1985 and 1986 birth cohorts. The vaccination histories of study subjects were not available to provide confirmation of the active immunization that we postulate has occurred in these birth cohorts. These cohorts were born during a period of relatively low hepatitis A incidence, between peak epidemics of infection.[21] In the absence of a clear explanation by which natural infection would have affected these isolated birth cohorts disproportionately, and in a manner inconsistent with the established epidemiology of hepatitis A infection, we believe it is reasonable to infer active immunization as the source of the increased immunity observed.

Another limitation of this study is that our performing regional seroprevalence analysis on the basis of reported home of record may have resulted in ACIP region misclassification, as the ACIP region where a subject's exposure to most risk of naturally acquired disease and to active immunization may have differed from that reported. In the absence of evidence that directional migration of the military recruit population occurs before enlistment, we believe that this misclassification, if any, would be primarily nondifferential and would tend only to diminish the magnitude of any measured regional differences.

This study was conducted principally to assess seroprevalence among military recruit populations. Among nonprevious service recruits from our random sample, we found an unadjusted total anti-HAV seroprevalence of 12.0%. Our general seroprevalence results can be compared with two previous studies performed in U.S. military populations before the widespread availability of hepatitis A vaccine. One prospective seroprevalence study performed in 1999 at Madigan Army Medical Center among 1,332 Army Reserve Officer Training Corps cadets found an overall seroprevalence of 13.7% (95% CI, 11.9%–15.7%), with non-Caucasians demonstrating a higher rate of 17.1% (95% CI, 12.0%–20.3%).[22] As in our study, no statistically significant difference in seroprevalence between men and women was found. Another prospective seroprevalence study performed a decade earlier among 1,538 Navy and Marine Corps recruits found a seroprevalence of 8.4% (95% CI, 7.0%–9.8%), although a rate of 5.5% was demonstrated for those born within the United States and a rate of 44.9% was found for those born outside the United States.[23]

Based upon previous studies demonstrating screening cost benefit in populations where hepatitis A seroprevalence exceeds 17%, our results suggest selective serologic screening of recruits age 18 and younger from ACIP regions 1and 2 might be expected to produce cost savings soon after adoption. However, on the basis of our finding of rising hepatitis A immunity among successive birth cohorts and across ACIP regions, we believe that implementing a policy of universal screening will be preferable over the long-term to policies that attempt to target screening to specific ages or regional homes of record. The excess marginal costs incurred through universal screening at current rates of immunity are approximately $1 per recruit,[8] and this cost is expected to decrease with further reductions in the costs of serology reagent, such as might be achieved through high-volume contracts. In its April 2004 memorandum on the subject of multiple concurrent vaccinations, the AFEB recommended the use of serologic screening, where feasible, to reduce vaccination of those immune from previous infection or routine vaccination. We believe that universal screening of military recruits for preexisting immunity to hepatitis A is feasible and should be implemented across all military services that currently perform serologic screening on the grounds of affordably reducing unnecessary immunizations, while also promising future cost savings. Indeed, on the basis of the findings presented here, the U.S. Army has recently adopted a policy of universal recruit screening for hepatitis A,[24] and serologic surveillance data emerging from early implementation of this program have confirmed the rising rates of immunity observed in our study.[25]

In implementing serologic screening, we believe the U.S. Army's use of total anti-HAV to assess immune status is acceptable in healthy populations. Assays specific to IgG are more expensive than total anti-HAV assays and the use of two-stage, confirmatory IgM testing to rule out active infection is cost-prohibitive.[22] Due to the lower specificity of total anti-HAV screening, careful implementation of screening policies is necessary to avoid falsely assuming immune status among those with potential IgM fractions. Transient hepatitis A IgM responses may be observed in as many as 1% of those immunized up to a month after active hepatitis A immunization.[26] In the event a recruit receives their first dose of hepatitis A vaccine within the month before screening, full immunity may be falsely assumed on the basis of the resultant positive total anti-HAV result. Therefore, a thorough clinical preimmunization assessment, under the direction of a credentialed medical provider, is necessary to rule out hepatitis A immunization within the previous month. A similar screening process has been previously recommended in mass immunization campaigns to rule out recent history of live virus vaccination.[27] Such medical assessment should also be expected to detect clinical cases of active hepatitis A infection that would also induce an IgM response, although the rate of symptomatic acute hepatitis A infection in the military recruit-age populations is exceedingly low, and active infection nonetheless confers lifelong immunity.

Our findings of widespread compliance with adolescent hepatitis A vaccination recommendations herald the beginnings of a new era in the epidemiology of hepatitis A. With the recent decision by the ACIP to expand its hepatitis A immunization recommendations to include the universal vaccination of children age 12 to 18 months,[28] and continued compliance with adolescent catch-up immunizations, we anticipate increased demand for hepatitis A vaccine for use among pediatric and adolescent populations. The availability and licensure of a pediatric and adolescent bivalent hepatitis A and B vaccine,[29,30] on either a two- or three-dose schedule, would facilitate both rou-

tine and catch-up immunization for those desiring both vaccines. Additional serologic studies examining the relationship between hepatitis A immunity and hepatitis B immunity among successive birth cohorts and across ACIP regions in young adult populations would help to further define the success of adolescent immunization recommendations.

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