The Risk of Measles, Mumps, and Varicella among Young Adults: A Serosurvey of US Navy and Marine Corps Recruits

ABSTRACT

Objectives. To assess the risk of epidemic transmission and to guide immunization policy, the seroprevalence of antibody to measles, mumps, and varicella was determined in a group of young adults.

Methods. A cross-sectional study of 1533 US Navy and Marine Corps recruits was conducted in June 1989. Antibody status was determined with commercially available enzyme-linked immunosorbent assays.

Results. Direct sex and race adjustment to the 15- to 29-year-old US population resulted in seronegativity rates of 17.8% for measles, 12.3% for mumps, and 6.7% for varicella. Measles and mumps seronegativity rates were higher among Whites whereas varicella seronegativity was higher among non-Whites. Recruits enlisting from outside the 50 US states, especially those from island territories, were more likely to lack varicella antibody. The sensitivity of a positive history of vaccination or disease in predicting antibody status was less than 90% for all diseases.

Conclusions. These results suggest a continued potential for epidemics, especially of measles, and the need for mandatory immunization policies. Immigrants to the United States, especially those from island territories, may be a high-risk group that could benefit from varicella vaccination. (*Am J Public Health.* 1993; 83:1717–1720)

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Introduction

Despite great progress in the United States over the last several decades in controlling vaccine-preventable illnesses,[1,2] recent increases in the incidence of measles and mumps—including epidemics—have occurred,[3,4] especially among inner-city children and young adult populations.[5–13] These viral illnesses also continue to have considerable military importance.[14–18] In addition, varicella, a serious illness in adults,[19–21] may also be increasing in incidence, particularly in military populations.[22]

Recruits enter the service from all areas of the country and most are between 17 and 19 years old, an age group at high risk in the civilian setting for measles, mumps, and varicella. Because these viral illnesses may have a great impact on health, training time, and overall military readiness, especially in the recruit setting, and because their importance is increasing in the civilian population, a serosurvey was conducted to guide immunization policy. In addition, demographic factors and other information related to individuals' previous disease and vaccination history were evaluated as potential predictors of antibody status.

Methods

This study was conducted in June 1989 at the three US Navy (Great Lakes, Ill; Orlando, Fla; San Diego, Calif) and the two US Marine Corps (Parris Island, SC; San Diego, Calif) recruit training centers. Four consecutive companies/platoons at each location were enrolled in the study. Those recruits who gave informed consent completed a short questionnaire and donated an extra tube of blood.

Blood samples were obtained 1 to 4 days after the recruits' arrival at the training center and before the administration of immunizations. Serum samples were tested for measles, mumps, and varicella antibodies using commercially available enzyme-linked immunosorbent assay (ELISA) tests (MEASLESTAT, MUMPSTAT, and VARICELISA II from Whittaker Bioproducts, Walkersville, Md). To assess interrater reliability, 150 randomly selected samples were retested by the manufacturer. The kappa value for varicella retesting was 0.96, and no further retesting was performed. Because the kappa values for measles and mumps were lower (0.83 and 0.77, respectively), the manufacturer retested all samples for these two antibodies in the laboratory, and the manufacturer's results were used in the analysis. Samples were initially tested for rubella antibody as well, but extremely high seronegativity rates suggested technical difficulties with the procedure, and insufficient serum was available to allow retesting of samples. Therefore, no rubella results are presented. All testing was done without knowledge of the subjects' prior disease or vaccination history.

The self-completed questionnaire included demographic variables and information on state of birth, elementary

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TABLE 1—Sample's Seronegativity to Measles, Mumps, and Varicella, by Demographic Variables

	Men				Women			
	No. Tested	% Seronegative (95% Confidence Intervals)			No. Tested	% Seronegative (95% Confidence Intervals)		
		Measles	Mumps	Varicella		Measles	Mumps	Varicella
Total sample	1392	19.2 (17.1, 21.3)	12.2 (10.5, 13.9)	9.2 (7.7, 10.7)	141	14.2 (8.4, 20.0)	7.1 (2.9, 11.3)	7.1 (2.9, 11.3)
Enlistees from 50 US states	1303	19.5 (17.3, 21.7)	12.2 (10.4, 14.0)	8.3 (6.8, 9.8)	139	14.4 (8.6, 20.2)	7.2 (2.9, 11.5)	7.2 (2.9, 11.5)
Age group, y								
17–19	983	20.3 (17.8, 22.8)	13.2 (11.1, 15.3)	8.2 (6.5, 9.9)	86	15.1 (7.5, 22.7)	5.8 (0.9, 10.7)	4.7 (0.2, 9.2)
20–24	269	16.7 (12.2, 21.2)	9.7 (16.2, 13.2)	8.2 (4.9, 11.5)	40	12.5 (2.3, 22.7)	5.0 (0, 11.8)	15.0 (3.9, 26.1)
25+	42	14.3 (3.7, 24.9)	2.4 (0.0, 7.0)	11.9 (2.1, 21.7)	12	16.7 (0, 37.8)	25.0 (0.5, 49.5)	0.0 (0, 22.1)
Education								
< High school	74	24.3 (14.5, 34.1)	20.3 (11.1, 29.5)	13.5 (5.7, 21.3)	0	...	...	...
High school graduate	976	18.9 (16.4, 21.4)	13.0 (10.9, 15.1)	7.3 (5.7, 8.9)	98	16.3 (9.0, 23.6)	7.1 (2.0, 12.2)	7.1 (2.0, 12.2)
> High school graduate	251	20.7 (15.7, 25.7)	6.8 (3.7, 9.9)	10.8 (7.0, 14.6)	41	9.8 (0.7, 18.9)	7.3 (0, 15.3)	7.3 (0, 15.3)
Race								
White	928	22.4 (19.7, 25.1)	13.8 (11.6, 16.0)	6.5 (4.9, 8.1)	87	17.2 (9.3, 25.1)	10.3 (3.9, 16.7)	4.6 (0.2, 9.0)
Black	221	9.5 (5.6, 13.4)	8.1 (4.5, 11.7)	13.6 (9.1, 18.1)	32	15.6 (3.0, 28.2)	3.1 (0, 9.1)	9.4 (0, 19.5)
Hispanic	121	19.0 (12.0, 26.0)	8.3 (3.4, 13.2)	10.7 (5.2, 16.2)	12	0.0 (0, 22.1)	0.0 (0, 22.1)	25.0 (0.5, 49.5)
Other	33	6.1 (0, 14.3)	9.1 (0, 18.9)	15.2 (3.0, 27.4)	8	0.0 (0, 31.2)	0.0 (0, 31.2)	0.0 (0, 31.2)

Note. Age was missing for 9 males and 1 female, education for 2 males, and area of enlistment for 5 subjects.

school entry, and military enlistment. Subjects were asked to recall their history of having had each of the individual diseases and vaccinations, with four possible responses: (1) yes, definitely; (2) yes, probably; (3) no, definitely not; and (4) I don't know.

The Centers for Disease Control and Prevention reports of school entry immunization laws for each state were available for 1970 to 1977, 1979 to 1980, 1983, and 1985 to 1990. These reports were used to determine the year-specific state school entry immunization laws for each recruit.

Statistical analyses were conducted with EGRET statistical software (SERC, Inc, Seattle, Wash) on a microcomputer. To compare the proportion of recruits who were seronegative, logistic regression for the continuous variable of age, the Mantel-Haenszel chi-square test for trend in education, and the likelihood ratio chi-square for other variables were used. Adjustment for potential confounders in the association between race and seronegativity was performed using logistic regression models.

The proportion of seropositive recruits who reported a positive history of disease or vaccination was defined as the sensitivity of the historical information, and the proportion of seronegative recruits who did not report prior disease or vaccination was defined as the specificity. Positive predictive value was defined as the proportion of history-positive recruits who were seropositive, and the negative predictive value was defined as the proportion of history-negative recruits who were seronegative.

Results

Of the 1568 recruits assigned to the selected companies, 1533 (98%) gave informed consent and participated in the study. Among the 1442 subjects enlisting from one of 48 US states, 90% were male, 74% were aged 17 to 19, 70% were White, 18% were Black, and 9% were Hispanic. Seronegativity rates and 95% confidence intervals were as follows: measles, 19.0% (17.0, 21.0); mumps, 11.7% (9.6, 13.8); and varicella, 8.2% (6.8, 9.6). Direct sex and race adjustment to the 1980 US 15- to 29-year-old population resulted in estimated national seronegativity rates of 17.8% for measles, 12.3% for mumps, and 6.7% for varicella. Seronegativity to measles and mumps was not highly correlated, with only 2.8% seronegative for both.

Men were more likely to be seronegative for all three viruses, and results are presented separately for men and women (Table 1). Younger male recruits were more likely than older ones to be seronegative for measles and mumps ($P > .05$), but older female recruits were more likely than younger ones to be seronegative for mumps ($P < .05$). Age was not associated with varicella antibody status for either men or women. Higher educational level was associated only with lower mumps seronegativity in men ($P < .01$). Among both men and women, Whites were more likely to be seronegative for measles and mumps while non-Whites were much more likely to be seronegative for varicella antibody ($P < .05$ for men). The association between race and antibody status for all three viruses persisted after controlling for age, sex, and educational level.

Recruits in this study had enlisted from 48 of the 50 states, and although there was wide variation in seronegativity between states, no clear geographic trends were evident. Recruits whose state of enlistment had full mumps immunization entry laws (kindergarten through grade 12) were slightly less likely to be seronegative for mumps (9.8%) compared with other subjects (13%). No other associations between state immunization laws and measles or mumps antibody status were present, even when those recruits who reported the same state of birth, elementary school entry, and military enlistment were analyzed separately.

Eighty-four recruits (5%) enlisted from outside the United States. Except for those recruits enlisting directly from the Republic of the Philippines, most of whom receive measles/rubella immunization as part of their processing before arrival in the United States, their rates of measles

and mumps seronegativity were similar to those of US enlistees. However, more than 20% of recruits enlisting from outside the United States, including 3 of 3 from the Canal Zone, 2 of 3 from Puerto Rico, and 6 of 23 enlisting from the Republic of the Philippines, were varicella seronegative.

Combining recruits who reported a positive history of disease *or* vaccination, the sensitivity of a "definite" history in identifying seropositive recruits was less than 35% for both measles and mumps (Table 2), whereas the sensitivity of a definite history of varicella disease was 75%. Definite *or* "probable" histories of disease or vaccination doubled the sensitivity for measles and mumps, and increased the sensitivity of varicella disease history to 86%. Corresponding specificities were similar, ranging from 35% to 72% for measles and mumps, to 66% to 75% for varicella. The sensitivity of vaccine history was generally better than the disease history.

The negative predictive value was lower for mumps than for measles or varicella. On the other hand, the positive predictive value of a history of varicella was over 95%. However, almost all recruits gave a positive history of varicella, including more than 20% of those lacking the varicella antibody.

TABLE 2—The Ability of Undocumented History of Disease or Vaccination to Predict Serum Antibody Status to Measles, Mumps, and Varicella

Self-Reported Historical Information	No. with Positive History/Total	Sensitivity[a]	Specificity[b]	PV +[c]	PV −[d]
Definitely had measles disease or vaccine	470/1434	33.5	70.4	82.8	20.0
Definitely or probably had measles disease or vaccine	935/1434	65.2	35.0	81.0	19.2
Definitely had mumps disease or vaccine	472/1436	33.5	72.1	90.0	12.7
Definitely or probably had mumps disease or vaccine	959/1436	67.5	38.5	89.2	13.6
Definitely had varicella disease	421/1437	74.8	75.2	97.1	20.9
Definitely or probably had varicella disease	1171/1437	85.7	65.8	96.6	28.9

Note. Individual disease/vaccine totals fall below sample total because of missing values.
[a]Sensitivity is the proportion of antibody-positive subjects who gave a positive history.
[b]Specificity is the proportion of antibody-negative subjects who gave a negative history.
[c]PV+ is the positive predictive value, or the proportion of history-positive subjects who were antibody positive.
[d]PV− is the negative predictive value, or the proportion of history-negative subjects who were antibody negative.

Discussion

Based on commercially available ELISA tests, nearly one fifth of the 1533 recruits in this study lacked antibody to measles, 12% lacked antibody to mumps, and 9% were seronegative for varicella antibody. Direct adjustment to the 1980 US 15- to 29-year-old population yielded similar results. If seronegativity correlates with susceptibility, these results suggest the potential for continued epidemic transmission of measles in young adult populations. However, a routine two-dose schedule of the measles/mumps/rubella vaccination, as has been recommended,[23,24] should considerably reduce this potential.

The direct US adjusted measles seronegativity rate (17.8%) observed in this study was higher than expected, based on several serosurveys in the past 2 decades,[15,25,26] but was comparable to the rate of 20.7% in a recent study of US Army recruits.[27] Fewer previous mumps serosurveys have been reported,[28] but the adjusted mumps seronegativity rate of 12.3% in this study was comparable to that found in the most recent US Army recruit survey.[27] The 6.7% adjusted varicella seronegativity rate was similar to that found in two recent studies[27,29] but lower than that found in another.[26]

The lower seronegativity rate for measles and mumps among older male subjects in this study probably reflects increased natural infection during childhood. Among the group born before 1964, vaccination was not widespread when most subjects entered elementary school. The lack of association between age and varicella seronegativity rates observed in this study suggests no decrease in natural infection rates in recent years.

Whites were more likely to be seronegative to both measles and mumps and less likely to be seronegative to varicella, even after adjustment for age, sex, and education. This finding may reflect lower rates of natural measles and mumps infection among Whites or higher rates of waning vaccine-induced antibody levels. The associations between race and varicella seronegativity and between sex and seronegativity to all three viruses may reflect unknown sociocultural differences in patterns of natural infection or vaccination. Recruits enlisting from outside the 50 US states, especially those from island nations or territories, were much more likely to be seronegative for varicella antibody. This supports the previous epidemiological observations of an island phenomenon.[21,30] Especially in the health care and military recruit environments, foreign-born individuals may represent a high-risk group that could benefit from a varicella vaccine.[31]

The specificity of historical information of measles disease or vaccination was higher in this study than in a prior study of medical students.[26] However, using this historical information to determine which recruits should be vaccinated or receive antibody tests would not effectively reduce the proportion remaining seronegative to below 8%. Both the sensitivity and specificity of a history of varicella in this study were generally higher than in a previous study.[26] Most recruits, however, reported a positive history of disease, and more than 20% of seronegative recruits would be missed if such a screening question were used to determine who would receive varicella immunization. The lower negative predictive value for mumps compared with that for measles and varicella is probably owing to the fact that mumps infection is often subclinical.

Several factors need to be considered when interpreting the results of this serosurvey. Although the ELISA tests used here appear to be as good as previous antibody tests when compared to a gold standard,[32–38] they may not correlate with true susceptibility to these illnesses. However, given the evidence for the role of waning vaccine-induced antibody levels in recent outbreaks of measles,[39,40] a less sensitive test may be desirable if it is being used to decide who gets immunized in the recruit setting. Although the true number of young adults currently susceptible to these illnesses may be considerably lower than this serosurvey suggests, these results may be predictive of the future potential for epidemics, especially if the intensity of exposure increases, because

vaccine-induced antibody titers may continue to wane.

Subjects in this study came from most areas of the United States, but whether they are representative of the civilian population with respect to their infection and vaccination experiences and associated risk factors is unknown. This was a cross-sectional study done over a short period, and further studies of these subjects and cross-sectional studies over time will be important in monitoring seroprevalence trends.

The high rates of seronegativity among US recruits suggest the continued potential for epidemics of these illnesses and the need for continued effective immunization programs in both the civilian and military setting. In the recruit training center environment, historical information on previous disease and vaccination history would not be an effective guide in determining who should be immunized upon entry into the US military. □

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