

VACCINE-PREVENTABLE DISEASE SUSCEPTIBILITY IN A YOUNG ADULT MICRONESIAN POPULATION

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Abstract. Current US military recruit vaccination policy presumes that recruits have had a complete childhood immunization series. This assumption may not be appropriate for recruits from Micronesia, who may have had limited access to modern health care, including immunization programs. During 1988 and 1990, a cross-sectional serosurvey was conducted among 66 US military recruits, 56 from the Federated States of Micronesia and 10 from the Republic of the Marshall Islands, collectively referred to as Micronesia. Antibody seronegativity levels for 12 vaccine-preventable (or potentially so) diseases were: measles (52%), mumps (14%), rubella (21%), varicella (38%), diphtheria (39%) tetanus (0%), polio type 1 (4%), polio type 2 (0%), polio type 3 (14%), hepatitis A (9%), hepatitis B (17%), and hepatitis C (98%). Compared with Army recruits in general, Micronesian recruits were significantly more likely to be seronegative for measles and varicella and seropositive for hepatitis types A and B. Personal histories of disease were felt to be inadequate in predicting antibody status.

INTRODUCTION

The US Army currently inducts approximately 100,000 active and reserve component soldiers per year. Immunization policy calls for all recruits to undergo immunization to 16 diseases: measles, rubella, diphtheria, tetanus, three types of influenza, three types of polio, four groups of meningococci, and adenovirus types 4 and 7. The current policy presupposes that the recruit has received a full primary series of many of these immunizations. For logistic reasons, recruits usually receive the complete battery of vaccines, regardless of their pre-existing immune status (US Army Regulation 40-562, 1988). Vaccination rates among soldiers must be kept high to prevent occurrence of specific infectious disease (Takafuji and Russell, 1990). The benefits of immunization far outweigh the rare, serious sequelae in otherwise healthy patients (Gillum *et al*, 1989). The Army's recruit immunization program costs roughly \$5M per

year and is periodically reassessed in light of surveillance. The current policy may direct insufficient or unnecessary doses for certain sub-populations of recruits such as American Indians, Puerto Ricans, or Micronesians.

Young men and women from present and former US-related jurisdictions in the southwest Pacific are eligible to enlist in the US armed forces. The Federated States of Micronesia and the Republic of the Marshall Islands, collectively referred to as Micronesia, are two such sovereign groups of islands. Each year, several hundred Micronesian recruit applicants begin the process for entry into the service. Further testing includes a physical examination, normally administered on the islands by the Honolulu Military Entrance Processing Station (MEPS). Fully qualified recruits enter the service, most passing through the Honolulu MEPS for a day of administrative and medical processing.

The Micronesian islands maintain a third world lifestyle. While western-style medicine is available in the larger towns, many islanders have limited access to modern care, including immunization programs. As a result, antibody to vaccine-preventable diseases may be lacking. While the immune status of

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Micronesian children and young adults has not been definitively studied, it may be similar to some other third world countries where vaccine coverage, program monitoring, and sufficient protective antibody are often suboptimal (Ijsselmuiden *et al*, 1987). There is evidence that persons from the Pacific Islands are more likely to be susceptible to varicella (Gray *et al*, 1990).

The purpose of this study was to collect data to form the basis for a recommendation to the US Army Surgeon General regarding the adequacy of immunizing Micronesian recruits with the same schedule used for recruits from the US. Specific objectives were: 1) to determine the serologic status of Micronesian military recruits, as a group, with regard to 12 infectious diseases: measles, mumps, rubella, varicella, diphtheria, tetanus, polio types 1, 2, and 3, and hepatitis types A, B, and C, 2) to compare the serologic status of Micronesian recruits to the 1989 sample of all Army recruits (Kelly *et al*, 1991), 3) to test the usefulness of personal medical histories in predicting antibody status, 4) to determine associations between immune status and demographic and historical data, and 5) to establish an ongoing sero-surveillance system for Micronesian recruits.

MATERIALS AND METHODS

During 1988 and 1990, a cross-sectional serosurvey was conducted among Micronesian military recruits as they processed through the Honolulu MEPS. After providing written informed consent, each subject anonymously completed a questionnaire and donated a 13 ml blood sample. All data were collected before any recruit immunizations were given.

The sera were frozen and shipped to the Walter Reed Army Institute of Research (WRAIR), where they were aliquoted and distributed for analysis. Measles, mumps, rubella, and varicella antibody testing was performed by Walter Reed Army Medical Center, Washington, DC, by enzyme immunoassay (EIA) using Measlestat[®], Mumpstat[®], Rubestat[®], and Varicella Stat[®] kits (Whittaker Bioproducts, Walkersville, MD) (Deforest *et al*, 1989; Demmler *et al*, 1988). St Christopher's Hospital for Children, Philadelphia, PA, tested for diphtheria antitoxin by toxin neutralization and tetanus antitoxin by modified passive hemagglutination (Miyamura *et al*, 1974; Hardegree *et al*, 1970; Ipsen, 1946; MacLennan *et al*, 1965).

Polio types 1, 2, and 3 antibody testing was performed by the Centers for Disease Control, Atlanta, GA, by micro-neutralization (Melnick *et al*, 1979). WRAIR, Washington, DC, tested for hepatitis A total antibody by radioimmunoassay (RIA) using HAVAB[®] (Abbott Laboratories, North Chicago, IL), hepatitis B surface antigen by RIA using AUSRIA II-125[®] (Abbott Laboratories) hepatitis B core antibody by RIA using CORAB[®] (Abbott Laboratories) and hepatitis C total antibody by EIA using ORTHO HCV[®] (Ortho Diagnostic Systems, Raritan, NJ) (Hollinger *et al*, 1975; Decker *et al*, 1979; Overby *et al*, 1973; Bradley *et al*, 1991). Each result was dichotomized as seronegative or seropositive, based on standard cut-points for each test. (Orenstein *et al*, 1983) For hepatitis B, those who were seronegative for both surface antigen and core antibody were classified as negative.

The brief questionnaire covered information such as demographics and infectious disease history. Because the 1990 questionnaire was updated to seek additional information such as race, education, place of birth, and hometown size, these data are available only for those sampled that year. All data were compiled in DBASE IV[®] (Ashton-Tate, Torrance, CA) and analyzed using True Epistat[®] (Epistat Services, Richardson, TX) and SAS[®] (SAS Institute, Cary, NC). For point estimates of seronegativity, 95% confidence intervals were calculated based on the binomial distribution. Risk ratios (RRs) and their (Taylor series) confidence intervals were calculated to assess correlates of seronegativity. Significance levels were calculated using Fisher's exact test.

The 1989 US Army recruit serosurvey, conducted by the Division of Preventive Medicine, WRAIR, studied the immune status of 1,504 non-prior service recruits. Measles, mumps, rubella, varicella, polio types 1, 2, and 3 and hepatitis types A and B were studied using the same laboratory techniques and test kits.

RESULTS

Data were collected from 35 subjects during 1988 and 31 subjects during 1990, for a total of 66. Fig 1 shows the distribution of subjects by age and sex. The mean age of the group was 23.5 years (SD = 4.8). Of the 64 that reported their sex, 58 (91%) were males (mean age = 23.8 years, SD = 4.9) and 6 (9%) were females (mean age = 19.8 years, SD = 2.5).

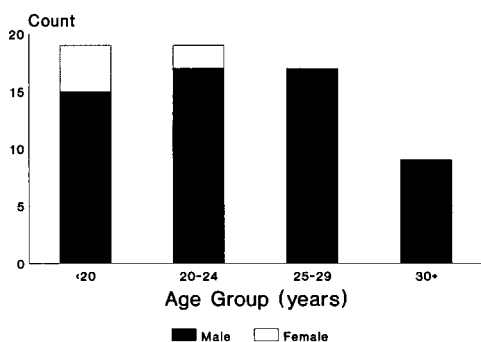


Fig 1—Population distribution by age and sex for Micronesian military recruits.

All subjects responded that they were Micronesian. Eighty-three percent reported being born in the Federated States of Micronesia, 14% in the Marshall Islands, and 3% in the Mariana Islands. Twenty-one percent said they were raised in towns (over 1,000 people), 65% said they were raised in villages (under 1,000 people), and 14% said they were raised in rural settings. Nearly half the group (41%) reported having lived outside their hometown for more than 2 years. While most of these had lived on other Micronesian or Pacific islands (excluding Hawaii), 14% of the entire group had lived in the US (including Hawaii). Concerning education, 48% reported being high school graduates (only), 16% reported having some

college, and 36% reported being college graduates.

Antibody seronegativity results are shown in Table 1. For comparison, results from the 1989 Army recruit serosurvey are shown (Kelley *et al*, 1991; Kadlec, unpublished data).

Varicella seronegativity correlated with age and having always lived in Micronesia. Recruits under 20 years old were more likely to be seronegative than those over 20 (RR = 2.7, p = 0.002). Only 26% of the older group were seronegative. Recruits who had lived in Micronesia all their lives were more likely to be seronegative than those who had lived outside for over 2 years (RR = 2.2, p = 0.04).

While hepatitis A and B seronegativity rates were low, all recruits but one were found to be seronegative for hepatitis C. The correlations between hepatitis A and B seronegativity and female sex approached significance. For hepatitis A, the RR for female vs male was 4.8 (p = 0.09); for hepatitis B the RR was 3.6 (p = 0.06). The measured seronegativity for hepatitis B core antibody (30%) was significantly lower (p < 0.001) than the 59% measured during a 1979 survey on the Micronesian island of Ponape; (Wong *et al*, 1979) however, the two populations were not necessarily demographically comparable.

Compared with all Army recruits, Micronesian recruits were significantly more likely to be seronegative for measles and varicella and significantly less likely to be seronegative for hepatitis types A and B (p < 0.001) (Kadlec, unpublished data). Unlike Army male recruits, who were more likely to lack measles antibody than female recruits, Micronesian

Table 1

Seronegativity rates for Micronesian recruit applicants and a sample of Army recruits.

Disease	Micronesians (n=66)	Army (n=1,504)
Measles	*52 (39-65)	17 (15-19)
Mumps	14 (6-25)	14 (12-15)
Rubella	21 (11-33)	16 (14-18)
Varicella	*38 (26-51)	9 (7-1)
Diphtheria	39 (27-52)	
Tetanus	0	
Polio type 1	4 (1-14)	3 (2-4)
Polio type 2	0	1 (0.4-1.3)
Polio type 3	14 (6-25)	13 (11-15)
Hepatitis A	*9 (3-19)	91 (90-93)
Hepatitis B	*17 (8-20)	97 (96-98)
Hepatitis C	98 (91-100)	

*p < 0.001 (95% confidence intervals)

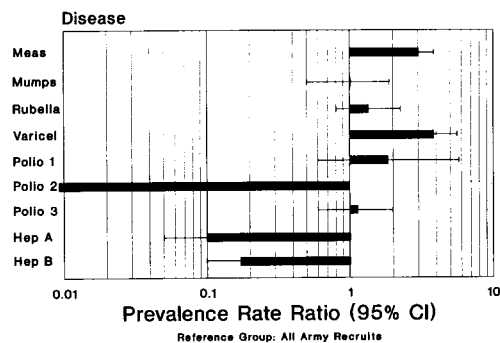


Fig 2—Seronegativity prevalence (Pr) rate ratios (RR) and 95% confidence intervals for 9 infectious diseases, comparing Micronesian and a sample of all Army recruits.

$$RR = Pr_{\text{Micronesian}} / Pr_{\text{Army}}$$

male recruits were less likely to lack measles antibody than female recruits, but this relation was not statistically significant (RR = 1.7, $p = 0.20$).

Prevalence rate ratios for seronegativity, comparing Micronesian recruits to the 1989 sample of all Army recruits, are shown in Fig 2 for those diseases studied in both surveys.

Subjects were queried about their history of having had five communicable diseases. The percentage that reported having had each disease was: measles (3%), mumps (21%), chickenpox (24%), polio (0%), and hepatitis (type unspecified) (4%). Of subjects who gave a history of measles, 50% had protective levels of measles antibody. Similarly, 86% of those with a history of mumps and 81% with a history of varicella had antibody.

DISCUSSION

Measles seronegativity was surprisingly high at 52% and significantly more than the 17% found during the 1989 Army recruit study ($p < 0.001$). Generally, in less developed countries, measles susceptibility in the population is low, perhaps less than 10% (Black, 1989). The relative isolation of tropical island life, with possibly fewer imported cases of measles, may account for the high proportion of Micronesians that reach adulthood who are seronegative. It is unknown what proportion of this seronegativity is due to primary vaccine failure, secondary vaccine failure, or lack of vaccination. If a lower cutoff were chosen, one which considers 'equivocal' results as positive, 44% of the group would still be classified seronegative (Whittaker Bioproducts, 1990). The number of Micronesian recruits that would remain unprotected after one dose of measles vaccine during induction is likely to be very small; after integration with the general recruit population, herd immunity would likely be sufficient to block transmission. It does not appear that measles epidemics affecting these young adult Micronesians have been widespread. Most current epidemics in the islands occur preponderantly in grade school children (Bice, personal communication).

Varicella seronegativity (38%) was significantly greater than that found in all Army recruits (9%), but several authors have found high varicella susceptibility in adults from tropical regions (Gray *et al*, 1990; Venkitaraman *et al*, 1984; Weller, 1983; Maretic and Cooray, 1963). Tropical environmental factors may

operate to reduce overall varicella infection. The strong tendency of Micronesian recruits under age 20 to varicella seronegativity suggests that this disease may have been more common on the islands before 1970.

Concerning diphtheria antibody, 39% of the subjects had titers less than 0.1 IU/ml. This is a conservative cut-off, chosen purposefully to maximize specificity at the expense of sensitivity, in order to minimize false positive results. Many authorities consider titers of 0.01 IU/ml and greater to be minimally protective (Orenstein *et al*, 1983). No Micronesian recruits had titers below this lower level. In light of this, both the diphtheria and the striking tetanus results evidence solid coverage by childhood immunization programs. Polio seronegativity results were similar to those from the 199 sample of all Army recruits. While confidence intervals overlapped, the seronegativity relationship for the three polio types ($3 > 1 > 2$) is classically found in American populations. It appears that primary polio vaccination coverage is high.

Hepatitis seronegativity was strikingly low for both types A and B and consistent with rates from many underdeveloped areas. Susceptibility to both is significantly less than that of all Army recruits. Vertical transmission at birth and casual household transmission underlie much of the hepatitis B endemicity in the Pacific islands (West, 1981). The hepatitis C assay has been improved since this analysis; hepatitis C seronegativity may have been overestimated.

Immunization policies in Micronesia have mirrored USPHS policy for over 40 years. Program coverage has been spotty in the past, but is improving steadily. In the Federated States of Micronesia, recent emphasis on infant hepatitis B immunization has greatly enhanced overall immunization coverage (Bice, personal communication).

The results support the conclusion that immunization programs are generally in place, but the high measles seronegativity indicates that some program aspects may need improvement. These results may not be generalizable to all Micronesian children. The study population was more highly educated than most young adult Micronesians, suggesting higher socio-economic status and possibly better access to medical care.

This study succeeded in determining the serologic

status of recent Micronesian military recruits with regard to several diseases, comparing these recruits with the 1989 sample of all Army recruits, and noting some correlates of serologic status. Personal histories of disease were felt to be inadequate in predicting antibody status.

The results warrant no policy change for immunizing Micronesian military recruits. It is important, however, that all recruits receive their measles vaccination within the first few days of reporting to basic training camp, as the seronegativity rate of all incoming recruits is high enough to allow transmission. When licensed, varicella vaccine should be strongly considered. This might be particularly helpful for young adults from the tropics, who generally suffer increased morbidity from varicella.

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