Measles, Mumps, and Rubella Titers in Air Force Recruits

Below Herd Immunity Thresholds?

Paul E. Lewis, MD, MPH,¹ Daniel G. Burnett, MD, MPH,¹ Amy A. Costello, MD, MPH,² Cara H. Olsen, PhD,¹ Juste N. Tchandja, PhD, MPH,³ Bryant J. Webber, MD, MPH³

From the ¹Department of Preventive Medicine and Biometrics, Uniformed Services University of the Health Sciences, Bethesda, Maryland; ²Immunizations Healthcare Branch, Defense Health Agency, Falls Church, Virginia; and ³Trainee Health Surveillance, Joint Base San Antonio–Lackland, Texas

Address correspondence to: Paul E. Lewis, MD, MPH, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bldg A, Room 1040A, Bethesda MD 20814-4799. E-mail: paul.lewisiii@usuhs.edu.

Introduction: Preventable diseases like measles and mumps are occurring with increasing frequency in the U.S. despite the availability of an effective vaccine. Given concern that an outbreak may occur among military recruits, we compared serologic evidence of immunity to measles, mumps, and rubella among military recruits with known herd immunity thresholds and determined whether the current Department of Defense policy of presuming mumps immunity based on measles and rubella titers is reliable.

Methods: Serum antibody levels for measles, mumps, and rubella were obtained from all new recruits upon arrival at Joint Base San Antonio–Lackland, Texas, from 25 April 2013 through 24 April 2014. Seroprevalence of each disease was assessed by age and sex, and concordance between mumps titers and measles and rubella titers was calculated. Data analysis was performed in 2014–2015.

Results: Among 32,502 recruits, seroprevalences for measles, mumps, and rubella antibodies were 81.6, 80.3%, and 82.1%, respectively. Of the 22,878 recruits seropositive for both measles and rubella antibodies, 87.7% were also seropositive for mumps.

Conclusions: Seroprevalences for measles, mumps, and rubella antibodies among a large cohort of recruits entering U.S. Air Force basic training were generally lower than levels required to maintain herd immunity. In order to reduce the incidence of mumps infections, the Department of Defense should consider obtaining antibody titers for measles, mumps, and rubella and vaccinating all individuals susceptible to one or more of the viruses.

Introduction

CDC reported >600 measles cases in 2014, the most in any year since the virus was declared eliminated from the U.S. in 2000. Most cases have been linked to travelers from measles-endemic areas, and the majority occurred in unvaccinated individuals.¹ Mumps is also on the rise, with 1,151 cases reported in 2014. Mumps outbreaks have occurred primarily on college campuses, where congregate settings provide an ideal environment for disease transmission. Unlike measles, mumps cases have occurred primarily in previously vaccinated individuals whose vaccine-mediated immunity appears to have waned.²

Herd immunity is the minimum proportion of a population required to have immunity to prevent sustained disease transmission.³ Based on the sensitivity and specificity of a given serologic test for immunity, an adjusted herd immunity threshold can be derived.⁴ Outbreaks may ensue when seroprevalence levels fail to achieve these thresholds.

Military recruits are at increased risk for communicable diseases given close living and sleeping quarters and weakened immune systems secondary to fatigue and stress.⁵ Many will be sent to overseas locations where the likelihood of exposure is elevated. To decrease this risk, antibody titers for six diseases are obtained on all incoming recruits at the start of U.S. Air Force basic training, followed by vaccination against those diseases for which they are seronegative. Given the lack of monovalent vaccines in the U.S., seronegativity for any one of measles, mumps, or rubella antibodies leads to measles, mumps, and rubella (MMR) vaccine administration.

Department of Defense (DoD) immunization policy recommends presuming mumps immunity if measles and rubella titers are positive.⁶ The mumps component of the MMR vaccine, however, is the least effective and tends to wane the fastest.⁷ This presumption may result in mumps antibody seroprevalence below the herd immunity threshold.

By reporting the serologic status of a large sample of young people entering the military, this study provides a unique window into current measles, mumps, and rubella immunity. In addition, by determining the proportion seropositive for mumps among those seropositive for both measles and rubella (i.e., seroconcordance), this study estimates the prevalence of mumps susceptibility accepted by current DoD policy.

Methods

We obtained demographic and antibody titer data on all recruits who entered U.S. Air Force basic training between April 25, 2013 and April 24, 2014. Seropositivity, which indicates a measurable level of serum antibody against a pathogen due to past infection or immunization, was recorded qualitatively as immune or non-immune. All serum specimens were processed using the BioRad BioPlex 2200 MMRV IgG multiplex flow immunoassay (MFI), which allows for simultaneous detection of measles, mumps, and rubella antibodies and, compared with more traditional testing by enzyme immunoassay (EIA), produces respective sensitivities and specificities of 94.6%/96.4%, 98.1%/82.8%, and 94.9%/100%.⁸ Plans and colleagues⁴ derived EIA-based upper and lower herd immunity threshold estimates for each virus (p_c) by applying the accepted herd immunity threshold (I_c) and sensitivity (Se) and specificity (Sp) of EIA to the equation $p_c = I_c Se + [(1 - I_c)(1 - Sp)]$. Using this equation and the aforementioned MFI test

characteristics, we calculated MFI-adjusted herd immunity thresholds for each virus. The cross-sectional study was approved by the IRB of the Uniformed Services University, Bethesda, Maryland.

Multivariate binomial regression was used to calculate prevalence ratios (PRs) in evaluating immune status by age and by sex, after adjusting for age. All tests were two-sided with $p < 0.05$ indicating statistical significance. Analyses were performed using Stata, version 12.0 in 2014–2015.

Results

Overall seropositivity rates for measles, mumps, and rubella antibodies among the 32,502 recruits were 81.6%, 80.3%, and 82.1%, respectively (Table). Measles seropositivity decreased with age (test for trend $p < 0.001$); those aged 20–24 years and 25–29 years were significantly less likely to be seropositive for measles than those aged 17–19 years (PR=0.97 and 0.96, respectively, $p < 0.001$ for both). Mumps and rubella seropositivity, however, was significantly higher in those aged 30–35 years than those aged 17–19 years (PR=1.06 [$p=0.002$] and PR=1.05 [$p=0.007$], respectively). After adjusting for age, seropositivity among women was 4%–6% higher than that among men for all three antibody titers ($p < 0.001$ for all).

Of the 22,878 recruits seropositive for both measles and rubella antibodies, 20,064 were also seropositive for mumps antibodies, for an overall seroconcordance of 87.7%. Compared with their counterparts, seroconcordance rates were lower among those aged 20–24 years (86.7%) and

men (87.0%). More than 38% ($n=12,433$) of recruits were seronegative for at least one viral antibody and nearly 4% ($n=1,226$) were seronegative for all three.

Discussion

Measles, mumps, and rubella seroprevalence rates among new U.S. Air Force recruits from April 2013 through April 2014 were lower than those reported in a nationally representative sample of the civilian, non-institutionalized U.S. population from a decade earlier. Although not necessarily equivalent to immune status, the decrease in seropositivity is concerning. In the 1999–2004 National Health and Nutrition Examination Survey, the 1977–1986 birth cohort ($N \approx 5,200$) had measles,⁹ mumps,¹⁰ and rubella¹¹ seropositivity rates of 96%, 90%, and 89%, respectively. Among a smaller cohort ($N=3,000$) who entered the U.S. military between 2000 and 2004, Eick et al.¹² found respective seroprevalence rates of 86.1%, 91.6%, and 94.8%. The use of MFI likely contributed to the lower seroprevalence of measles and rubella antibodies in our study. However, after adjusting for the sensitivity and specificity of MFI, measles and mumps seroprevalence remained below the levels required for herd immunity for almost all age groups and both men and women (Figure 1). Waning immunity is possible, though age-related decrements were seen only in measles seropositivity. Poor vaccination uptake prior to joining the military is more likely, although it does not match current civilian data. According to the National Immunization Survey-Teen, 91.8% of all U.S. adolescents sampled in 2013 ($N=18,264$) had received $\geq$ two doses of the MMR vaccine, increasing annually from 88.9% in 2007.¹³

Higher seroprevalence of measles, mumps, and rubella among women has been noted previously. This might be anticipated in the general population, given the emphasis on rubella

vaccination of women after pregnancy,¹¹ but that effect should not be pronounced in our young recruit population. It may also be due to increased immune response in women, as noted after influenza vaccination.¹⁴

The 87.7% overall concordance of positive mumps titers in individuals who were positive for both measles and rubella titers was lower than the 94.2% seroconcordance found by Eick and colleagues¹² in their earlier U.S. military study. Had the U.S. Air Force followed current DoD immunization policy and presumed mumps immunity based on measles and rubella titer status, more than 2,800 new recruits would not have been vaccinated against the mumps virus, perhaps leaving the population vulnerable to a mumps outbreak with sub-herd immunity vaccination levels.

Conclusions

Seroprevalence rates of measles, mumps, and rubella antibodies in a large cohort of young people entering U.S. Air Force basic training were lower than expected based on previous civilian and military studies and generally fell below estimates required for herd immunity (Figure 1).^{3,4} If these rates are generalizable to their counterparts entering college and the workforce across the U.S., outbreaks of vaccine-preventable disease can be anticipated to continue. In order to reduce the incidence of mumps infections, the DoD should consider obtaining antibody titers for measles, mumps, and rubella and vaccinating all individuals susceptible to one or more of the viruses.

Acknowledgments

The opinions expressed in this paper are solely those of the authors and do not represent an endorsement by or the views of the Uniformed Services University, the U.S. Air Force, the Department of Defense, or the U.S. Government.

No financial disclosures were reported by the authors of this paper.

References

1. CDC. Measles Cases and Outbreaks 2014. www.cdc.gov/measles/cases-outbreaks.html.
2. CDC. Mumps Cases and Outbreaks 2014. www.cdc.gov/mumps/outbreaks.html.
3. Fine PE. Herd immunity: history, theory, practice. *Epidemiol Rev.* 1993;15(2):265-302.
4. Plans P. New preventive strategy to eliminate measles, mumps and rubella from Europe based on the serological assessment of herd immunity levels in the population. *Eur J Clin Microbiol Infect Dis.* 2013;32(7):961-966. <http://dx.doi.org/10.1007/s10096-013-1836-6>.
5. Gomez-Merino D, Chennaoui M, Burnat P, Drogou C, Guezennec CY. Immune and hormonal changes following intense military training. *Mil Med.* 2003;168(12):1034-1038.
6. Departments of the Army, the Navy, the Air Force, and the Coast Guard. Immunizations and Chemoprophylaxis for the Prevention of Infectious Diseases 2013. www.vaccines.mil/documents/1682_Joint_Instruction_Immunization_2013.pdf.
7. McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2013;62(RR-04):1-34.
8. Binnicker MJ, Jespersen DJ, Rollins LO. Evaluation of the Bio-Rad BioPlex Measles, Mumps, Rubella, and Varicella-Zoster Virus IgG multiplex bead immunoassay. *Clin Vaccine Immunol.* 2011;18(9):1524-1526. <http://dx.doi.org/10.1128/CVI.05207-11>.

9. McQuillan GM, Kruszon-Moran D, Hyde TB, Forghani B, Bellini W, Dayan GH. Seroprevalence of measles antibody in the U.S. population, 1999-2004. *J Infect Dis.* 2007;196(10):1459-1464. <http://dx.doi.org/10.1086/522866>.
10. Kutty PK, Kruszon-Moran DM, Dayan GH, et al. Seroprevalence of antibody to mumps virus in the U.S. population, 1999-2004. *J Infect Dis.* 2010;202(5):667-674. <http://dx.doi.org/10.1086/655394>.
11. Hyde TB, Kruszon-Moran D, McQuillan GM, et al. Rubella immunity levels in the United States population: has the threshold of viral elimination been reached? *Clin Infect Dis.* 2006;43(Suppl 3):S146-S150. <http://dx.doi.org/10.1086/505947>.
12. Eick AA, Hu Z, Wang Z, Nevin RL. Incidence of mumps and immunity to measles, mumps and rubella among U.S. military recruits, 2000-2004. *Vaccine.* 2008;26(4):494-501. <http://dx.doi.org/10.1016/j.vaccine.2007.11.035>.
13. Elam-Evans LD, Yankey D, Jeyarajah J, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13-17 years--United States, 2013. *MMWR Morb Mortal Wkly Rep.* 2014;63(29):625-633.
14. Engler RJ, Nelson MR, Klote MM, et al. Half- vs full-dose trivalent inactivated influenza vaccine (2004-2005): age, dose, and sex effects on immune responses. *Arch Intern Med.* 2008;168(22):2405-2414. <http://dx.doi.org/10.1001/archinternmed.2008.513>.

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Figure 1. Percent seropositive for measles, mumps, and rubella.

Table 1. Percent Seropositive and Prevalence Ratio of Seropositivity for Measles, Mumps, and Rubella

Characteristics	Measles				Mumps			Rubella		
	n(%)	%(95% CI)	PR	p-value	%(95%CI)	PR	p-value	%(95%CI)	PR	p-value
Total	32502 (100.0)	81.6 (81.2-82.0)	--	--	80.3 (79.9-80.8)	--	--	82.1 (81.7-82.5)	--	--
Age										
17-19	15,275 (47.0)	83.0 (82.4-83.6)	1.00		81.1 (80.4-81.7)	1.00		82.3 (81.6-82.9)	1.00	
20-24	13,927 (42.9)	80.5 (79.8-81.1)	0.97	<0.001	79.0 (78.3-79.7)	0.97	<0.001	81.6 (81.0-82.3)	0.99	0.160
25-29	2,708 (8.3)	80.0 (78.4-81.5)	0.96	<0.001	82.5 (81.0-83.9)	1.02	0.076	82.6 (81.1-84.0)	1.00	0.694
30-35	473 (1.3)	79.7 (75.8-83.2)	0.96	0.082	86.0 (82.6-89.0)	1.06	0.002	86.5 (83.1-89.4)	1.05	0.007
>35	119 (0.5)	78.2 (69.6-85.2)	0.94	0.213	73.1 (64.2-80.8)	0.90	0.064	84.9 (77.2-90.8)	1.03	0.421
Sex										
Male	25,556 (78.6)	81.0 (80.5-81.4)	1.00 ^a		79.4 (78.9-79.9)	1.00 ^a		81.1 (80.6-81.5)	1.00 ^a	
Female	6,946 (21.4)	84.1 (83.2-84.9)	1.04 ^a	<0.001	83.8 (82.9-84.7)	1.06 ^a	<0.001	85.9 (85.0-86.7)	1.06 ^a	<0.001

Note: Boldface indicates statistical significance ($p < 0.05$)

^a Age-adjusted prevalence ratios

--- Area bounded by dashed lines indicates upper and lower estimates of herd immunity thresholds after adjusting for sensitivity and specificity of MFI.

Figure 1