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Identifying Risk Factors for Rubella Susceptibility in a Population at Risk in the United States

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Since the early 1990s, rubella disproportionately affected non-US-born Hispanic persons in the United States. In 2000, 149 (78%) of the 192 rubella cases were among Hispanics, and 23 (77%) of the 30 infants with congenital rubella syndrome reported between 1997 and 2000 were born to non-US-born Hispanic mothers.^{1–5}

The US childhood rubella vaccination program was started in 1969¹; however, many other countries do not have, or have recently implemented, rubella vaccination programs.⁶ Foreign-born workers in certain US industries (e.g., meat- and poultry-processing plants) appear to be at increased risk for rubella, suggesting higher susceptibility rates.^{7–9} In 2000, a varicella outbreak occurring among Mexican-born adults, most of whom worked in a poultry-processing plant in southern Alabama, provided an opportunity to test for rubella susceptibility.¹⁰ Vaccine was offered to susceptible persons. We describe risk factors for susceptibility among these workers.

METHODS

After obtaining informed consent, we collected blood on filter papers¹¹ and administered a questionnaire (in English and Spanish) to obtain information about age, sex, race/ ethnicity, country of birth, length of stay in the United States, length of employment at the plant, and whether the respondent had a health care provider. Persons with negative rubella immunoglobulin G (IgG) test results were offered measles-mumps-rubella (MMR) vaccine. Because of recent rubella activity in northern Alabama, rubella immunoglobulin M (IgM) testing was done to rule out recent rubella cases.

Testing was done at the Centers for Disease Control and Prevention with Wampole (Cranbury, NJ) IgG enzyme-linked immunosorbent assay and Trinity Biotech (Dublin, Ireland) IgM capture enzyme immunoassay. An IgG antibody index of less than 0.91 (6.5 IU) was considered negative (i.e., rubella susceptible).

Double-entered data were analyzed with SAS, Version 8 (SAS Institute Inc, Cary, NC). To determine susceptibility risk factors, prevalence ratios with 95% confidence intervals (CIs) were obtained. For variables initially found to be significant (P<.05), confounding was assessed with logistic regression.

RESULTS

Of the estimated 800 workers at the plant, 343 (43%) were tested for rubella IgG, and 267 (78%) of the 343 were tested for rubella IgM. Table 1 shows the characteristics of the study population. Six persons born in 4 other countries were excluded from the analysis. Of the 135 US-born workers, 95% were African American and 58% were born in Alabama. Most of the 162 Mexican-born workers were from Veracruz (52%) or Chiapas (23%). Of the 337 persons studied, 48 (14%) were susceptible. There were no positive IgM

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TABLE 1—Characteristics of the Poultry-Processing Plant Workers, by Country of Birth: Alabama, June 2000^a

| | Country of Birth | | | |
|---|------------------------------------|-----------------------------|-------------------------------|----------------------------|
| | United States (n = 135) No. (%) | Mexico (n = 162) No. (%) | Guatemala (n = 40) No. (%) | Total (N = 337) No. (%) |
| Age, y ^b | | | | |
| ≤20 | 12 (9) | 33 (21) | 9 (24) | 54 (16) |
| 21-30 | 45 (33) | 82 (52) | 22 (58) | 149 (45) |
| > 30 | 78 (58) | 44 (28) | 7 (18) | 129 (39) |
| Median (range) | 33 (18-65) | 25 (17-60) | 25 (18-57) | 27 (17-65) |
| Sex | | | | |
| Male | 25 (19) | 125 (77) | 33 (83) | 183 (54) |
| Length of stay in the US, $^{\scriptscriptstyle \rm b}$ mo | | | | |
| Median (range) | | 8 (<1-84) | 7 (<1-60) | |
| Length of employment, ^b mo | | | | |
| Median (range) | 12.5 (0-130) | 2.1 (0-21) | 2.6 (0-11) | 3.7 (0-130) |
| Adults in the household $^{\mbox{\tiny b}}$ | | | | |
| Median (range) | 2 (1-5) | 6 (2-12) | 5 (2-9) | 4 (1-12) |
| Children in the household | | | | |
| Median (range) | 2 (0-9) | 0 (0-5) | 0 (0-5) | 0 (0-9) |
| Has a health care provider $^{\scriptscriptstyle \mathrm{b}}$ | 87 (73) | 12 (8) | 0 (0) | 99 (31) |

^aAll these characteristics were statistically different for US-born persons compared with non-US-born persons ($P \le .002$). Percentages may not add to 100% because of rounding.

^bAge not available for 5 persons, length of stay in the United States not available for 4, length of employment not available for 12, number of adults in the household not available for 3, and health care provider information not available for 21 persons.

results. Susceptibility was almost twice as high for workers born in Mexico (Table 2), even after adjusting for age and sex. Mexican-born women were 3 times more susceptible than US-born women: 27% vs 9%, respectively (prevalence ratio=3.12; 95% CI=1.38, 7.08); this remained significant after adjusting for age. No other risk factors were identified.

Documentation of rubella vaccination was not available for any worker tested.

Two weeks after the serotesting, only 19 (34%) of the 56 workers who had negative or equivocal IgG test results could be located to be offered MMR vaccine.

DISCUSSION

Our findings, the first to our knowledge in the postvaccine era in the United States, documented significantly higher susceptibility among Mexican-born workers compared with US-born workers, which is consistent with the recent epidemiology of rubella in the United States. As indicated by recent outbreaks in several similar work settings,^{7–9} susceptibility among Mexican-born workers permits sustained rubella transmission. Additional factors likely contribute to the introduction and spread of the disease among these persons. Non-US-born workers often travel to or receive newcomers and visitors from rubellaendemic areas and tend to live in crowded conditions.

In Mexico, the number of rubella cases has decreased substantially since the MMR vaccine was introduced into the childhood program in 1998; however, rubella is still endemic, with 21 173 cases reported in 1999.² In a serosurvey conducted in 1988, the state of Veracruz was among the 5 Mexican states with the highest rubella susceptibility for women aged 10 to 44 years (31.4%).¹²

The 13% susceptibility observed for USborn workers aged 20–39 years is consistent with previous studies.¹³ Despite this level of susceptibility, US-born persons are hardly affected when rubella outbreaks occur.^{7–9} Possibly, vaccine-induced antibodies remain protective, even if they wane to levels below the test threshold for IgG positivity.^{14–20} The following limitations should be considered when interpreting our data. We tested a convenience sample, which may limit the representativeness of our results, and selection bias may have been present. However, biases according to disease history or vaccination status seem unlikely. Most rubella cases are not recognized clinically, US-born workers did not know their vaccination status, and Mexican-born workers were not offered the vaccine in Mexico. Because reliable information was not available, we were unable to correlate vaccination history with susceptibility.

Our findings reinforce recommendations to vaccinate all individuals at risk for rubella without evidence of immunity¹ and illustrate some of the problems faced when attempting to vaccinate those at risk—mobility and lack of access to health care. Most susceptible workers had left the plant when the MMR vaccine was offered 2 weeks after serotesting.

To protect these populations at risk for rubella and prevent future outbreaks, new vaccination strategies need to be developed. To ensure control and eventually eliminate rubella and congenital rubella syndrome from the United States, health care workers and public health workers should be aware that certain groups of non-US-born persons are more likely to be susceptible to rubella than are US-born adults. Vaccine should be offered to persons who cannot prove rubella immunity whenever they make contact with the health care system, without serotesting.

About the Authors

At the time of the study, M. Carolina Danovaro-Holliday and Susan E. Reef were with the National Immunization Program, Centers for Disease Control and Prevention, Atlanta, Ga. Ely R. Gordon is with Brundidge Medical, Brundidge, Ala. Charles Woernle and Randa H. Judy are with the Alabama Department of Public Health, Montgomery; at the time of the study, Gary H. Higginbotham was also with the Alabama Department of Public Health. Joseph P. Icenogle is with the National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Ga.

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Contributors

M.C. Danovaro-Holliday was the primary writer of the brief and participated in its design and conception and the acquisition, statistical analysis, and interpretation of

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TABLE 2—Risk Factors for Rubella Susceptibility Among Poultry-Processing Plant Workers: Alabama, June 2000^a

| | Susceptibility Status | | Univariate Risk Factor Analysis | |
|---|-----------------------------|---------------------------------|---|-------|
| | Immune (n = 281) No. (%) | Susceptible (n = 48) No. (%) | Prevalence Ratio (95% Confidence Interval) | Р |
| Age, y | | | | |
| ≤20 | 44 (83) | 9 (17) | 1.33 (0.63, 2.81) | .463 |
| 21-30 | 123 (84) | 23 (16) | 1.23 (0.68, 2.22) | .490 |
| > 30 | 109 (87) | 16 (13) | Referent | |
| Sex | | | | |
| Male | 152 (84) | 29 (16) | 1.25 (0.73, 2.13) | .416 |
| Female | 129 (87) | 19 (13) | Referent | |
| Country of birth | | | | |
| US | 115 (90) | 13 (10) | Referent | |
| Mexico | 129 (80) | 32 (20) | 1.96 (1.07, 3.57) | .024* |
| Guatemala | 37 (93) | 3 (8) | 0.74 (0.22, 2.46) | .442 |
| Length of stay in the US, ^b mo | | | | |
| Median (range) | 8 (<1-84) | 6 (<1-36) | | .174 |
| Length of employment, mo | | | | |
| Median (range) | 3 (<1-130) | 2 (<1-25) | | .071 |

^aPersons with equivocal rubella immunoglobulin G results not included (n = 8). Denominators may change because of missing data (age not available for 5 persons, length of stay in the United States not available for 4, and length of employment not available for 12).

^bLength of stay in the United States is only for non-US-born persons.

*Significant at P<.05.

data. E.R. Gordon was key in conception and design, provided logistic support for conducting the study and acquiring data, and provided critical revision. C. Woernle participated in conception and design, facilitated acquisition of data, contributed to the analysis and interpretation of data, and provided critical revision. G.H. Higginbotham participated in conception and design, provided logistic support for conducting the study, participated in acquisition of data, and provided critical revision. R.H. Judy participated in conception and design, participated in acquisition of data, provided technical support, and provided critical revision. J.P. Icenogle participated in acquisition and analysis of data, provided technical support, and provided critical revision. S.E. Reef participated in design and conception, contributed to analysis and interpretation of data, participated in drafting the brief, and provided supervision.

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Human Participant Protection

No IRB approval was needed for this study.

References

1. Centers for Disease Control and Prevention. Measles, mumps, and rubella–vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep.* 1998;47(RR-8):1–57.

2. Centers for Disease Control and Prevention. Measles, rubella, and congenital rubella syndrome— United States and Mexico, 1997–1999. *MMWR Morb Mortal Wkly Rep.* 2000;49(46):1048–1050, 1059.

3. Reef SE, Plotkin S, Cordero JF, et al. Preparing for elimination of congenital rubella syndrome (CRS): summary of a workshop on CRS elimination in the United States. *Clin Infect Dis.* 2000;31:85–95.

4. Centers for Disease Control and Prevention. Control and prevention of rubella: evaluation and management of suspected outbreaks, rubella in pregnant women, and surveillance for congenital rubella syndrome. *MMWR Morb Mortal Wkly Rep.* 2001; 50(RR-12):1–23.

5. Danovaro-Holliday MC, Zimmerman L, Reef SE. Observations from the CDC: preventing congenital rubella syndrome (CRS) through vaccination of susceptible women of childbearing age. J Womens Health Gender-Based Med. 2001;10:617-619.

6. World Health Organization. Preventing congenital rubella syndrome. *Weekly Epidemiol Rec.* 2000;75: 290–296.

 Rangel MC, Sales RM, Valeriano EN. Rubella outbreaks among Hispanics in North Carolina: lessons learned from a field investigation. *Ethn Dis.* 1999;9: 230–236.

8. Centers for Disease Control and Prevention. Rubella among Hispanic adults–Kansas, 1998, and Nebraska, 1999. *MMWR Morb Mortal Wkly Rep.* 1999; 48(RR-8):1–15.

9. Danovaro-Holliday MC, LeBaron CW, Allensworth C, et al. A large rubella outbreak with spread from the workplace to the community. *JAMA*. 2000;284:2733–2739.

10. Centers for Disease Control and Prevention. Public health dispatch: varicella outbreaks among Mexican adults–Alabama, 2000. *MMWR Morb Mortal Wkly Rep.* 2000;49(32):735–736.

11. Helfand RF, Keyserling HL, Williams I, et al. Comparative detection of measles and rubella IgM and IgG derived from filter paper blood and serum samples. *J Med Virol.* 2001;65:751–757.

12. Gutierrez-Trujillo G, Muñoz O, Tapia-Conyer R, et al. Seroepidemiología de la rubeóla en mujeres Mexicanas: encuesta nacional probabilística [The seroepidemiology of rubella in Mexican women: a national probability survey]. Salud Publica Mex. 1990;32:623–631.

13. Dykewicz CA, Kruszon-Moran D, McQuillan G, Williams WW, Hadler S. Rubella immunity in U.S. adolescents and young adults, 1988–1994. In: Abstracts of the 37th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC); September 28–October 1, 1997; Toronto, Ontario, Canada. Abstract H-147.

14. Johnson CE, Kumar ML, Whitwell JK, et al. Antibody persistence after primary measles-mumps-rubella vaccine and response to a second dose given at four to six vs. eleven to thirteen years. *Pediatr Infect Dis J.* 1996;15:687–692.

15. LeBaron CW, Forghani B, Reef SE, et al. Immunogenicity and adverse events of a 2nd dose of rubella vaccine. In: Abstracts of the 37th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC); September 28–October 1, 1997; Toronto, Ontario, Canada. Abstract H-148.

16. Orenstein WA, Herrmann KL, Holmgreen P, et al. Prevalence of rubella antibodies in Massachusetts schoolchildren. *Am J Epidemiol.* 1986;124:290–298.

17. Matter L, Kogelschatz K, Germann D. Serum levels of rubella virus antibodies indicating immunity: response to vaccination of subjects with low or undetectable antibody concentrations. *J Infect Dis.* 1997;175: 749–755.

 Skendzel LP. Rubella immunity: defining the level of protective antibody. *Am J Clin Pathol.* 1996;106: 170–174.

19. Serdula MK, Halstead SB, Wiebenga NH, Herrmann KL. Serological response to rubella revaccination. *JAMA*. 1984;251:1974–1977.

20. Robinson RG, Dudenhoeffer FE, Holroyd HJ, Baker LR, Bernstein DI, Cherry JD. Rubella immunity in older children, teenagers, and young adults: a comparison of immunity in those previously immunized with those unimmunized. *J Pediatr.* 1982;101:188–191.