A Large Rubella Outbreak With Spread From the Workplace to the Community

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Between March 23 and 26, 1999, a 29-year-old man residing in Douglas County, Nebraska, sought treatment in 3 health care facilities for what he thought was a sexually transmitted disease. At his third visit, he was noted to have a maculopapular rash, low-grade fever, and lymphadenopathy. Though no case of rubella had been reported in Douglas County in the previous 9 years, the patient had a positive rubella IgM test result. The patient worked in a meatpacking plant where a second rubella case was identified. Surveillance for rash illness was enhanced, resulting in the detection of more individuals in other meatpacking plants and in the community, almost all of whom were young adults born in Latin American countries, where rubella vaccination only recently has been implemented for children.

Vaccination campaigns in 7 Douglas County meatpacking plants targeted 3000 workers. Physicians and clinics enhanced immunization efforts, and the health department provided other activities that included press, radio, and television coverage, and distribution of information through churches and community organizations. Despite these efforts, the outbreak continued for 4 months. Of the 125 cases reported from this outbreak, 83 occurred in Douglas County (Omaha), 12 in other Nebraska counties, and 30 in neighboring Iowa. Among the 83 cases in Douglas County, 14 were US-born children who attended 2 day care centers, and at least 7 pregnant women were infected. This outbreak ultimately became the largest US rubella outbreak in the past 5 years.
Rubella is one of the most common causes of birth defects in the world, resulting in spontaneous abortions, stillbirths, and congenital rubella syndrome (CRS). The manifestations of CRS include hearing impairment, blindness, heart defects, and mental retardation. According to the World Health Organization, in 1996, two thirds of the world’s population lived in countries where rubella vaccination was not practiced routinely, and the number of infants with CRS born each year worldwide was estimated to be 110,000 in 1999.

In the United States, childhood vaccination strategies have reduced rubella and CRS to record low levels, and in 1990, a goal was established to eliminate indigenous rubella and CRS from the United States by the end of 2000. However, outbreaks have continued to occur. The pattern seen in Douglas County is typical of recent outbreaks: of the 14 rubella outbreaks reported to the Centers for Disease Control and Prevention (CDC) in 1996-1998, 7 were workplace-associated and all disproportionately affected Hispanics (median percent Hispanics, 92.5%).

It has been assumed that high susceptibility levels to rubella in unvaccinated populations play an important role in such outbreaks, but data to support this hypothesis are lacking. Furthermore, the role of vaccine failure in the US-born population has been unclear: serosurveys of school children have suggested that 33% of adolescents were seronegative and might be susceptible to rubella, raising the possibility that they provide a pool for potential outbreak spread. Mathematically models have suggested that poorly implemented childhood vaccination strategies can actually increase CRS rates by increasing the number of susceptible women of childbearing age beyond the 87% thought to provide community-level herd immunity.

We investigated the Douglas County rubella outbreak to help shed light on the following issues: risk factors for disease, susceptibility levels in a population at risk, whether failure to vaccinate children or vaccine failure contributed to the outbreak, and whether additional strategies beyond childhood vaccination are necessary to prevent future US rubella outbreaks.

**METHODS**

**Inclusion Criteria**

We restricted our analysis to cases confirmed by laboratory testing or epidemiological linkage. Laboratory confirmation included a positive IgM result, isolation of rubella virus, or significant increase in serum rubella IgG antibodies (4-fold increase or seroconversion) from paired acute and convalescent samples. An epidemiologically linked case was defined as a person who was exposed to a laboratory confirmed case during the infectious period and who met the standard clinical case definition: (1) acute onset of generalized maculopapular rash; (2) temperature greater than 99°F (37.2°C) if measured; and (3) arthritis/arthralgia or conjunctivitis or lymphadenopathy. We analyzed only cases residing in Douglas County (where 83 of the 95 Nebraska cases occurred) between March 23, 1999 (rash onset of the first case), and August 24, 1999 (2 incubation periods after rash onset of the last reported case).

**Case Finding**

Case-finding efforts during the outbreak included active surveillance for rash illness in all meatpacking and related facilities, weekly calls to physicians and infection control practitioners in high-risk areas, weekly calls to clinical laboratories to report any rubella serological tests requested, and weekly contact with school nurses to investigate reports of rash illness among the county’s 64,463 schoolchildren.

**Data Sources**

**Characteristics of the Cases.** The Douglas County Health Department investigated each case using a form developed in collaboration with the CDC. We obtained the following information: birth date, country of birth, sex, race/ethnicity, vaccination status, place of exposure, and census tract of residence. For comparison, we abstracted census data for the general population of Douglas County.

**Childhood Vaccination Rates.** We used data from the 1998 National Immunization Survey for Nebraska and the 1997 Douglas County school survey.

**Susceptibility Among Selected Pregnant Women.** We identified 2 clinics serving a predominantly immigrant Hispanic population in Douglas County and conducted a chart review for rubella IgG screening results obtained from local laboratories for pregnant women between October 1998 and March 1999 to estimate susceptibility rates before the outbreak. To estimate the susceptibility rates when the outbreak started, serum samples obtained for routine prenatal rubella IgG screening in the larger clinic between April 1 and November 30, 1999, were tested at the CDC. To assess risk factors for susceptibility, women seen between June and November 1999 were given a self-administered questionnaire in English and Spanish that sought information concerning age, race/ethnicity, birth country, length of stay in the United States, US schooling, and previous US deliveries of infants.

**Laboratory Analysis**

The CDC used the Trinity Biotech (Dublin, Ireland) IgM capture enzyme immunoassay and Wampole (Cranbury, NJ) IgG enzyme-linked immunosorbent assay. Following the manufacturer’s standards, for both assays an antibody index of 1.10 and greater (8.2 International Units [IU] for IgG) was considered a positive result, 0.91 to 1.09 (6.6-8.1 IU) equivocal, and 0.90 and less (6.5 IU) a negative result. Rubella susceptibility was defined as either a negative IgG or a positive IgM result.

**Statistical Analysis**

Data were analyzed using SAS 6.12 (SAS Institute, Cary, NC). To determine risk factors for susceptibility among pregnant women, we used the $\chi^2$ and Fisher exact tests (bivariate) and, where more than 1 factor was found significantly associated with susceptibility, we performed multivariate stratified analysis.
and logistic regression. To determine risk factors for rubella attack rate by census tract, we used bivariate and multivariate linear regression analyses.

RESULTS

Outbreak Time Course

During the first 2 months of the outbreak (March 23-May 31, 1999), 75% (46/61) of cases were identified as workers from a meatpacking plant or their household contacts (FIGURE 1). During the last 2 months (June 1-July 27, 1999), 73% (16/22) of cases identified were related to 2 day care centers.

Characteristics of Cases

The 83 confirmed cases (69 laboratory confirmed and 14 epidemiologically linked) fell into 3 groups (TABLE 1).

Meatpacking Plant–Related Cases. Of the 83 cases, the meatpacking plant group included 52 cases (63%): 39 meatpacking plant workers and 13 household contacts. Unlike the general population of Douglas County, these persons were predominantly foreign-born, Hispanic adult males (median age, 26 years). High attack rates (14.4 per 1000; range, 3.3-33.3 per 1000 employees) were found in affected meatpacking plants (TABLE 2), compared with a countywide attack rate of 0.19 per 1000 persons.

Day Care Center–Related Cases. Of the 83 cases, 16 were from 2 day care centers (center A and center B). All individuals were US-born non-Hispanic whites, of whom 14 were children (aged 5-17 months), and 2 were the parents (aged 34 and 35 years) of 2 case children. Prior to the first case, certain children from center A were thought to have been exposed to an asymptomatic individual with ties to the Hispanic community who subsequently tested posi-

![Figure 1. Number of Rubella Cases by Week of Rash Onset](image)

Three cases did not have a rash and are not shown. Data collection occurred from the week of March 21 to the week of August 22.

| Table 1. Characteristics of Rubella Cases Compared With Douglas County Population |
|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| Characteristic                            | Douglas County Population, No. (%)             | Meatpacking Plant–Related (n = 52)             | Day Care–Related (n = 16)                      | Community–Related (n = 15)                     | Total (N = 83)                                 |
| Age, y†                                    | (N = 443 794)                                  |                                                |                                              |                                              |                                             |
| <5                                         | 31 919 (7)                                     | 1 (2)                                         | 14 (88)                                      | 1 (7)                                         | 16 (20)                                      |
| 5-19                                       | 99 183 (22)                                    | 4 (8)                                         | 0                                            | 2 (13)                                        | 6 (7)                                        |
| 20-39                                      | 134 992 (30)                                   | 40 (76)                                       | 2 (12)                                       | 12 (80)                                       | 54 (66)                                      |
| ≥40                                        | 177 700 (40)                                   | 6 (12)                                        | 0                                            | 0                                            | 6 (7)                                        |
| Sex                                        |                                                |                                               |                                              |                                              |                                              |
| Male                                       | 213 975 (48)                                   | 40 (77)                                       | 6 (38)                                       | 10 (67)                                       | 56 (67)                                      |
| Female                                     | 229 816 (52)                                   | 12 (23)                                       | 10 (62)                                      | 5 (33)                                        | 27 (33)                                      |
| Race/ethnicity                             |                                                |                                               |                                              |                                              |                                              |
| White, non-Hispanic                        | 361 324 (81)                                   | 4 (8)                                         | 16 (100)                                     | 1 (7)                                         | 21 (25)                                      |
| Black, non-Hispanic                        | 52 295 (12)                                    | 0                                             | 0                                            | 0                                            | 0                                            |
| Hispanic                                   | 23 003 (5)                                     | 48 (92)                                       | 0                                            | 14 (93)                                       | 62 (75)                                      |
| Other                                      | 7172 (2)                                       | 0                                             | 0                                            | 0                                            | 0                                            |
| Country of birth‡                          |                                                |                                               |                                              |                                              |                                              |
| United States                              | 430 480 (97)                                   | 9 (18)                                        | 16 (100)                                     | 2 (13)                                        | 27 (33)                                      |
| Other                                      | 13 314 (3)                                     | 42 (82)                                       | 0                                            | 13 (87)                                       | 55 (67)                                      |
| Documented vaccination§                     | NA                                             | 0                                             | 0                                            | 0                                            | 0                                            |

*Projections for 1998 by the US Census Bureau. NA indicates data not available.
†The age for 1 case was unknown.
‡The country of birth for 1 case was unknown.
§Before the outbreak period.
Susceptibility and Infection Among Selected Pregnant Women

Rates. In the retrospective chart review (October 1998-March 1999), rubella IgG results were available for 197 (97.5%) of 202 medical charts. Of these, 26 patients (13%) were reported to be susceptible to rubella. In the prospective study (April-November 1999), 216 (96.8%) of the 223 blood samples tested at the CDC provided nonequivocal IgG and IgM results. Of these, 24 (11.1%) showed susceptibility based on a 6.5-IU threshold. When the laboratory threshold was varied, these susceptibility rates changed but were not high: 11% at 5 IU; 13% at 10 IU; and 17% at 15 IU. Susceptibility rates before (13%) and after (11%) the outbreak onset did not differ significantly ($P = .52$).

Risk Factors. Of the 167 pregnant women from whom serum samples were obtained between June and November 1999, 96 (58%) provided complete information on the questionnaire, had nonequivocal laboratory results, and were included in the analysis (Table 3). Of the 96 women analyzed, 95 (99%) were Hispanic, 89 (93%) non–US-born, and their median age was 25 years (range, 15-39 years). They did not differ significantly from the 71 nonincluded ($P = .38$) women in terms of susceptibility, age, ethnicity, US-born status, US school attendance, or delivery of an infant in the United States. Mother's young age and short stay in the United States were risk factors in this population.

Infection. Of the 24 susceptible women tested, 6 (25%) had positive rubella IgM results. None reported symptoms. All women shared the characteristics of the rest of the pregnant women studied (Hispanic 100%, non–US born 100%, age range, 18-23 years), and none had documentation of prior vaccination. In March 2000, an infant with CRS (deafness, thrombocytopenia, and heart defect) was born to one of the surveyed women who had tested IgM equivocal and had had a rash during her first trimester. Ongoing surveillance for CRS in the area should ultimately document the final number of CRS infants born as a result of this outbreak.

Table 2. Attack Rate in Meatpacking Plants and Day Care Centers With Rubella Cases

<table>
<thead>
<tr>
<th>Setting</th>
<th>No. of Cases</th>
<th>Population</th>
<th>Attack Rate (per 1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Douglas County</td>
<td>83</td>
<td>443,794</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>Meatpacking plant</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>5</td>
<td>374</td>
<td>13.4</td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td>580</td>
<td>3.4</td>
</tr>
<tr>
<td>C</td>
<td>16</td>
<td>480</td>
<td>33.3</td>
</tr>
<tr>
<td>D</td>
<td>3</td>
<td>100</td>
<td>30.0</td>
</tr>
<tr>
<td>E</td>
<td>4</td>
<td>280</td>
<td>14.3</td>
</tr>
<tr>
<td>F</td>
<td>1</td>
<td>300</td>
<td>3.3</td>
</tr>
<tr>
<td>G</td>
<td>10</td>
<td>600</td>
<td>16.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>39</strong></td>
<td><strong>2714</strong></td>
<td><strong>14.4</strong></td>
</tr>
<tr>
<td><strong>Day care center</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>5</td>
<td>94</td>
<td>53.2</td>
</tr>
<tr>
<td>B</td>
<td>9</td>
<td>65</td>
<td>138.5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>14</strong></td>
<td><strong>159</strong></td>
<td><strong>88.1</strong></td>
</tr>
</tbody>
</table>

*Only workers (n = 39) and not their household contacts (n = 13) were included. Two person-cases worked in more than 1 meatpacking plant.
†Only children (n = 14) and not adults (n = 2) were included. In each center, all cases occurred in only 1 classroom but attack rates were calculated using a denominator of the entire center’s child population. If the classroom had been used as the denominator, the attack rates would have been 42% and 100%.

Vaccination Status of Cases

Of the 83 cases, none had a documented history of rubella vaccination: 57 (69%) were known not to have received the rubella vaccine, and 26 (31%) had unknown vaccination status. Of the 26 persons with unknown vaccination status, 19 (73%) were born in countries where rubella immunization was not routine, 5 (19%) began school in the United States before the rubella vaccine was licensed, and 2 (8%) began school in the United States before school laws for rubella vaccination were enforced. A state law required rubella vaccination of children in day care centers, but in each center, all cases occurred in 1 classroom where children at or younger than the minimum age of vaccination were grouped. Of the 14 children in the day care group, 9 (64%) were younger than the minimum age of vaccination (<12 months), 3 (21%) were age-eligible but not overdue (12-15 months) for vaccination, and 2 (14%) were overdue (16 and 17 months). Of the 159 children in the 2 day care centers, no vaccinees acquired symptomatic disease.

Childhood Vaccination Rates

Vaccination rates (95% confidence interval) for 1 dose of rubella vaccine were 90.2% (3.5%) for children aged 19 to 35 months in Nebraska, according to the 1998 National Immunization Survey, and 99.8% for the Douglas County school population according to the 1997/1998 Douglas County school survey. Prior to the outbreak, a second dose of rubella vaccine was recommended for all Nebraska seventh graders, but the proportion who received it is unknown (after the outbreak, a second dose was required, although no cases were documented among school children).
Geographic Patterns

Of the 107 census tracts in Douglas County, cases occurred in 35 (33%): meatpacking plant–related cases in 26, community-related cases in 9, and day care center–related in 8 (Figure 2). Tract-specific attack rates ranged from 0 to 6 per 1000 inhabitants.

In bivariate analysis, attack rate by census tract was significantly associated with percent Hispanic ($R^2=0.279; P<.001$), percent non–US born ($R^2=0.187; P<.001$), and population density ($R^2=0.118; P<.001$) but not with percentage below poverty level ($R^2=0.032; P=.06$). In multivariate analysis, percentage non–US born lost significance when paired with percent Hispanic. The fit of a model, including percent Hispanic and population density ($R^2=0.356; P<.001$), improved when the interaction between the 2 terms was included ($R^2=0.505; P<.001$). The pattern for meatpacking plant–related cases followed that of the overall outbreak. Two thirds (10/15) of the community-related cases resided in tracts where meatpacking plant–related cases resided (attack rate, 0.11 per 1000), and a model combining the presence of a meatpacking plant–related cases residing in tracts where the efficiency of rubella transmission was such that a high proportion of susceptible pregnant women attending prenatal clinics in the outbreak area were infected, despite preoutbreak immunity levels among these women (87%) which had been thought to protect against community-based rubella transmission. Ultimately, the disease found its way into day care centers distant from the outbreak, where it infected US–born, non–Hispanic children, most of whom were younger than the minimum age of vaccination. Fortunately, high countywide vaccination levels among children and adults vaccinated as children limited outbreak spread beyond unvaccinated persons at risk, and no cases were documented among vaccinees.

These data suggest that neither vaccine failure nor failure to implement current child-based vaccination strategies was responsible for the outbreak. Rather, the findings imply that to prevent such outbreaks new approaches must be found to achieve high vaccination levels among adults missed by the US school-based strategy, particularly non–US-born adults working and living in crowded conditions where the efficiency of rubella transmission appears to be high.

Workplace-based rubella outbreaks, such as this one in Douglas County, involving persons born in countries where rubella vaccination is not routine, have become increasingly common. Concentration of large numbers of unvaccinated adults indoors may provide a far more favorable environment for the airborne transmission of a disease like rubella than farm fields or other outdoor working conditions. Among military recruits, barracks conditions have been shown to overcome high levels of immunity and produce outbreaks when disease is introduced. Since meatpacking plant employees frequently report that they travel to and from countries, such as Mexico (country of birth of 62% of Douglas County cases) where approximately 40,000 rubella cases annually have been reported between 1994 and 1998, the possibility of introducing disease is increased.

High exposure rates among Hispanics may explain why Hispanic ethnicity, rather than birth outside the United States, was a primary risk factor for disease incidence in our geographical analysis. It also may explain why the proportion of US rubella cases of Hispanic ethnicity has risen to 83% (1998). Additionally, many non–US-born Hispanics may not be counted in census surveys for immigration reasons, and the presence of these persons may facilitate disease transmission through increased population density. High population density has been shown to facilitate community spread of measles but previously has not been identified as a risk factor for community rubella outbreaks.

Table 3. Factors Associated With Susceptibility Among Pregnant Women in the Outbreak Locale Between June and November 1999

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Susceptibility Status, No. (%)</th>
<th>Risk Factor Analysis*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall (&lt;N = 96&gt;)</td>
<td>Susceptible (&lt;n = 11&gt;)</td>
</tr>
<tr>
<td>Hispanic ethnicity</td>
<td>95 (99)</td>
<td>11 (100)</td>
</tr>
<tr>
<td>Non–US born</td>
<td>89 (93)</td>
<td>11 (100)</td>
</tr>
<tr>
<td>Nonattendance to US school</td>
<td>73 (76)</td>
<td>10 (91)</td>
</tr>
<tr>
<td>Age ≤20 y</td>
<td>20 (21)</td>
<td>5 (45.5)</td>
</tr>
<tr>
<td>Length of stay in the US &lt;1 year</td>
<td>23 (24)</td>
<td>6 (54.5)</td>
</tr>
<tr>
<td>Not having delivered an infant in the US</td>
<td>54 (56)</td>
<td>10 (91)</td>
</tr>
</tbody>
</table>

*OR indicates prevalence odds ratio; CI, confidence interval. Blank means nonsignificant at $P<.05$.

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However, it is important to note that the attack rate in the community was 131 times lower than in the workplace (0.11 per 1000 inhabitants vs 14.4 per 1000 workers), suggesting that population immunity levels were sufficient to contain what could have become a far larger outbreak. Moreover, the force of transmission was likely lower outside the Hispanic community. If we impute to Douglas County the age-specific seropositivity patterns found in the US general population, approximately 40,000 persons (13%) were rubella seronegative but fewer than 100 were identified as rubella cases. Disease did spread beyond the Hispanic community but only to 2 day care classrooms where children younger than the minimum age of vaccination were concentrated.

The data from Douglas County do not support the hypothesis that secondary vaccine failure provides a large pool of susceptible individuals that can contribute to outbreak transmission. While proving a negative is inherently difficult, surveillance for rash illness was aggressive for the 64,463 schoolchildren during the outbreak period, so that it seems unlikely that many cases, much less a widespread outbreak, would have been missed. Failure to vaccinate susceptible individuals rather than vaccine failure also was suggested from outbreak investigations in the early 1990s by Lindegren et al. Most Douglas County cases occurred among unvaccinated young adults, suggesting that the school population was spared, not because of their age, but because of protective levels of immunity.

The problem of rubella transmission in US workplaces is likely to grow because certain industries increasingly depend on non–US-born workers, and 67% of the 1996 world’s population lived in countries where rubella vaccination was not routine. To prevent future rubella outbreaks, our data suggest that childhood immunization strategies alone may not be enough, and that workplace vaccination of high-risk adults needs to be considered. The Advisory Committee on Immunization Practices only recommends rubella vaccination in health care settings. However, industries employing many non–US-born individuals, such as meatpacking plants, could help prevent rubella outbreaks—and the disruption of their own operations—by requir-

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**Figure 2. Maps of Douglas County by Census Tract**

A. Rubella Total Incidence

B. Proportion of Hispanics

C. Population Density (Persons/Square Miles)

A, The rubella attack rate was characterized per 1000 persons in each census tract into 4 levels: no cases, low (bottom tercile), intermediate (middle tercile), and high (top tercile). Heavy borders indicate census tracts with only day care center–related cases. B, Ranked distribution of the proportion of Hispanic individuals by census tract divided into quartiles: very low, low, intermediate, and high. C, Ranked distribution of population density by census tract divided into quartiles: very low, low, intermediate, and high.
ing or encouraging rubella vaccination as a condition of employment.

Based on the Douglas County data, work-based strategies are most likely to reach men, which will reduce, but not prevent, disease among women. The Special Supplemental Food Program for Women, Infants and Children (WIC) comprises 44% of the pregnant women in the US, and vaccination initiatives through WIC have been successful in vaccinating children, but greater efforts are needed to include women. The role of missed opportunities in health care settings should not be ignored: it has been estimated that 62% of mothers of children with CRS had at least 1 missed opportunity for rubella vaccination, 81% of which were postpartum.

This is consistent with Douglas County data: 93% of the women in our survey were born outside the US, but almost half (44%) had previous US deliveries. Since containing 1 case of rubella costs about $5000 (P. Kramaz, MD, et al, oral presentation, 33rd National Immunization Conference, Dallas, Tex, June 1999) and the lifetime cost of 1 child with severely disabling CRS may run into millions, the savings to society can be great for routine rubella vaccination of all susceptible women of childbearing age.

As a descriptive investigation, our findings lack the degree of certainty associated with prospective or case-control studies. We were not able to document any vaccine failures, but almost all our cases were adults and most adults lack documentation of childhood vaccination even when it has been received. Susceptibility rates were low among pregnant women and did not differ before and after the outbreak. Antibody levels obtained by chart review may have not been comparable to those determined at the CDC since different tests might have been used. Additionally, these rates may not have been representative of workers in meatpacking plants where most cases occurred. However, equally low susceptibility rates were found among meatpacking workers in Kansas and among pregnant women in a similar outbreak in Arkansas (trip report, P. Kramaz, MD, 1998, and M. Hladik, MD, 1999, written communication). The pregnant women in our serosurvey did acquire rubella disease, suggesting that they were indeed part of the risk population whose susceptibility we wished to survey. Our finding that population density facilitated transmission was based on census tract correlations, and cases were compared ecologically to the general population; thus, these results should be interpreted with caution.

Despite these limitations, we believe that the Douglas County data demonstrate that rubella outbreaks can occur in communities where unvaccinated individuals are concentrated in workplace or other environments where rubella is introduced. New vaccination strategies targeting high-risk adults will be needed if such outbreaks are to be prevented in the future.

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