Incidence of Congenital Rubella Syndrome at a Hospital Serving a Predominantly Hispanic Population, El Paso, Texas

Laura Zimmerman, MPH, and Susan E. Reef, MD

ABSTRACT. Objective. The current epidemiology of rubella reveals an increase in the number of cases among adult Hispanics and an increase in the number of congenital rubella syndrome (CRS) cases among infants of Hispanic mothers. Recent rubella outbreaks have occurred primarily among adult Hispanics, many of whom are foreign-born natives of countries where rubella vaccination is not routine or has only recently been implemented. The objective of this study was to estimate the incidence of CRS in a hospital serving a predominantly Hispanic population.

Methods. Hospital charts of infants <1 year old discharged between January 1, 1994 and December 31, 1996 with International Classification of Diseases, Ninth Revision (ICD-9) discharge codes consistent with CRS were reviewed; we looked for cataracts, deafness, congenital heart defects, dermal erythropoiesis, microcephaly, meningomyelocele, and other defects associated with CRS. We abstracted data on maternal and infant ethnicity, maternal age, gestational age, infants’ birth weight, infants’ clinical characteristics, and laboratory evaluation. Cases were categorized according to the Council of State and Territorial Epidemiologists’ case classification for CRS.

Results. Of the 182 infants with 1 or more ICD-9 codes consistent with CRS, 6 (3.3%) met either the confirmed or probable case definition for CRS. Two infants met the definition for confirmed CRS. Although laboratory tests for rubella immunoglobulin M antibodies were positive for both of these infants, only 1 of the cases had been reported to the state health department. Four other infants had clinical presentations that met the definition for a probable case. One of these had been tested for rubella immunoglobulin M antibodies, and the test was negative. The other 3 had not been tested. The rate of infants meeting the definition of confirmed and probable CRS was 3.1 per 10,000 hospital births. All confirmed and probable cases were among infants born to Hispanic mothers. Maternal country of origin was Mexico for the 2 confirmed cases and 1 of the probable cases, and unknown for the remaining 3 probable cases.

Conclusions. The rate of confirmed and probable CRS among infants in this predominantly Hispanic population is higher than the reported rate in the United States in the vaccine era, which has been reported to range from approximately 0.01–0.08 per 10,000 live births. These findings indicate a need for heightened awareness of CRS among physicians who serve populations at risk for rubella. Physicians should report all confirmed and probable CRS cases to the state health department. The lack of appropriate laboratory testing in 3 infants with probable CRS indicates that physicians should consider a diagnosis of CRS in infants with some signs consistent with CRS, particularly in areas serving high numbers of individuals at risk for rubella. Pediatrics 2001;107(3). URL: http://www.pediatrics.org/cgi/content/full/107/3/e40; congenital rubella syndrome, rubella, Hispanic.

ABBREVIATIONS. CRS, congenital rubella syndrome; ICD-9, International Classification of Diseases, Ninth Revision; IgM, immunoglobulin M; PDA, patent ductus arteriosus.

An effective vaccination program has brought the United States within range of its goal of eliminating indigenous rubella and congenital rubella syndrome (CRS) by year-end 2000. The number of reported rubella cases has declined from 57,600 in 1969, when the vaccine was first available, to a total of 267 cases in 1999. Reported cases of CRS have declined by 99% over the same period, with 6 cases reported in 1999 to the National Congenital Rubella Syndrome Registry of the Centers for Disease Control and Prevention.

Because of the success of the US vaccination program, rubella now disproportionately affects foreign-born residents from countries that have no rubella vaccination program or only recently have instituted programs. In 1991, 4% of reported cases in the United States were among persons of Hispanic ethnicity; by 1999, >70% were Hispanic. Moreover, the age distribution of cases in the United States has shifted. In 1991, 29% of rubella cases were among those 20 years of age and older; in 1999, the proportion was 74%.

Hispanics are also disproportionately affected by CRS. Between 1985 and 1999, 48% of the 140 reported US CRS cases were born to Hispanic women, although Hispanic women accounted for only 15% of the annual births. The proportion of infants with CRS born to Hispanic women increased during this time; in 1999, all 6 infants with confirmed CRS were born to Hispanic mothers.

In 6 of 8 rubella outbreaks in the United States in 1997 and 1998, more than three quarters of the confirmed cases occurred among Hispanics. Most of these persons of Hispanic ethnicity were foreign-born. Country of origin data collected in 4 outbreaks showed that nearly three quarters of the 175 persons with confirmed rubella were born in Mexico (30%), Central America and the Spanish-speaking Carib-
bean (43%), or South America (9%; Centers for Disease Control and Prevention, unpublished data, 1999). Moreover, from 1994 to 1996, Mexico reported >40 000 rubella cases each year, and in some US outbreaks the source case acquired rubella infection in Mexico.

Objectives of this study were to assess clinical and laboratory screening for suspected CRS and to evaluate the completeness of reporting of CRS cases at a US hospital where patients are predominantly Hispanic. A hospital in the El Paso area was selected because 1 case of CRS in an Hispanic infant was reported in 1994. Because El Paso is a border city with a high volume of migration from Mexico, it provides a unique opportunity to examine the incidence of CRS in the United States among persons at high risk for rubella and CRS.

**METHODS**

To identify possible CRS cases we reviewed computerized discharge data of infants <1 year old who were discharged between January 1, 1994 and December 31, 1996 at an El Paso hospital. Charts were selected for review if they contained any of the International Classification of Diseases, Ninth Revision (ICD-9) discharge codes for conditions most commonly associated with CRS (Table 1). We abstracted data on maternal and infant ethnicity, maternal age, gestational age, infants' birth weight, infants' clinical characteristics, and laboratory evaluation. Case definitions approved by the Council of State and Territorial Epidemiologists (CSTE) were used to classify cases of CRS as confirmed or probable. A confirmed CRS case was a clinically compatible case with a positive laboratory test for isolation of rubella virus, demonstration of rubella-specific immunoglobulin M (IgM) antibody, or an infant antibody level that persists at a higher level and for a longer period than expected from passive transfer of maternal antibody (ie, rubella titer that does not drop at the expected rate of a twofold dilution per month). A probable CRS case lacked laboratory confirmation of rubella infection but had a clinical presentation consistent with CRS. According to the case classification of the CSTE, infants with probable CRS must have one of the primary conditions and either one additional primary condition or one secondary condition, without evidence of any other cause. Primary conditions for CRS include: cataracts/congenital glaucoma, congenital heart disease (most commonly patent ductus arteriosus [PDA] or peripheral pulmonary artery stenosis), loss of hearing, or pigmentary retinopathy. Secondary conditions for CRS include: purpura, splenomegaly, jaundice, microcephaly, mental retardation, meningoecephalitis, or radiolucent bone disease.

Incidence rates of infants with probable and confirmed CRS were calculated from the total number of live births registered at the hospital from January 1, 1994 to December 31, 1996. We performed a descriptive analysis of the entire group of infants born between 1994 and 1996 who met the study criteria, as well as those fitting the probable and confirmed case definition, in examining potential risk factors for CRS. Cases meeting the probable and confirmed case definition for CRS were then assessed as to whether each case had been reported to public health authorities in accordance with the reporting requirements of the state of Texas.

**EXCLUSION CRITERIA**

Infants with birth weights of ≤2500 g who had only a PDA and/or microcephaly were excluded as possible CRS cases. Because these conditions are common among low birth weight infants, including these infants could dramatically reduce the specificity of the diagnosis.

We used Epi Info, Version 6.02 (Centers for Disease Control and Prevention, Atlanta, GA) for data entry and analysis. Univariate analysis was performed using $\chi^2$ analysis or Fisher’s exact test.

**RESULTS**

From 1994 to 1996, 294 infant discharges indicated one or more ICD-9 codes consistent with CRS. Of these, 39 charts were not reviewed because they represented repeated hospitalizations and 17 were unavailable for review. Of the 238 charts reviewed, 56 were excluded for the following reasons: 9 were charts of children >1 year old at the time of hospitalization, 8 were charts of infants not born at this hospital, and 39 were charts of infants with low birth weight with only a PDA and/or microcephaly. The study population consisted of the remaining 182 infants.

Of the 182 infants, 4 (2.2%) met the definition of probable CRS and 2 others (1.1%) had confirmed CRS with demonstration of rubella-specific IgM antibodies. When combined, the rate for infants meeting the probable and confirmed definition of CRS was 3.1 per 10 000 births.

There was no marked difference in ethnicity among infants meeting the probable and confirmed definition for CRS and the entire group of infants; 92.9% of entire group of infants were Hispanic and 100% of the infants with probable and confirmed CRS were Hispanic. Of those with known maternal country of origin data in the entire group of infants, 17.6% were from Mexico. Maternal country of origin for one infant with probable CRS and both infants with confirmed CRS was Mexico. Median maternal age for the infants with probable and confirmed CRS was 25 years (range: 19–37 years) and was 26 years (range: 14–43 years) for the entire group of infants. The median gestational age for all groups of infants was 40 weeks; however, the mean birth weight of infants with probable and confirmed CRS was lower, at 2557 g ± 878 g, than the mean birth weight of the entire group of infants, at 2898 g ± 929 g.

The 2 infants with confirmed CRS had multiple clinical findings that were consistent with CRS (Table 2), including ones from both the primary and secondary categories. One infant with confirmed CRS had dermal erythropoiesis and leukopenia, abnormalities also consistent with CRS. In contrast, among the infants with probable CRS, none had >3 clinical findings consistent with CRS (Table 2). The infant with 3 clinical findings consistent with CRS tested negative for rubella IgM antibodies within 1 week after birth; this patient also tested IgM-negative for toxoplasmosis, cytomegalovirus, and herpes. The other 3 infants with probable CRS were not tested for rubella IgM antibodies.

The mother of one infant with confirmed CRS reported receiving no prenatal care during this pregnancy. She reported a rash illness during the second month of pregnancy. Although no record of serology

**TABLE 1.** ICD-9 Condition and Hospital Discharge Code*

<table>
<thead>
<tr>
<th>Condition (Hospital Discharge Code)</th>
</tr>
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<tbody>
<tr>
<td>CRS (771.0)</td>
</tr>
<tr>
<td>Cataracts (bilateral or unilateral; 743.3)</td>
</tr>
<tr>
<td>Deafness/loss of hearing (389.1)</td>
</tr>
<tr>
<td>Congenital heart disease (particularly PDA and peripheral pulmonic stenosis; 745, 747)</td>
</tr>
<tr>
<td>Dermal erythropoiesis (Blueberry muffin syndrome (759.89)</td>
</tr>
<tr>
<td>Microcephaly (742.1)</td>
</tr>
<tr>
<td>Meningoecephalitis (323.9, rubella associated 056.01)</td>
</tr>
</tbody>
</table>

* Includes only defects most commonly associated with CRS.
for rubella-specific IgM or IgG antibodies was noted, rubella was diagnosed and documented by a physician. Mexico was noted as the country of rubella exposure. The mother of the second infant with confirmed CRS reported receiving prenatal care during this pregnancy beginning in the third trimester. She did not report a rash illness during pregnancy. There was no documentation regarding rash illness in the charts of the mothers of the infants with probable CRS.

One infant with confirmed CRS had been reported appropriately to the Immunization Program of the Texas State Health Department; however, the other was not reported until identified in this study. Because none of the infants with probable CRS had been identified as having probable CRS, they had not been reported to the Texas State Health Department.

**DISCUSSION**

The recent epidemiology of rubella in the United States suggests that cases occur disproportionately among foreign-born individuals, particularly Hispanics. Moreover, most infants with CRS are born to Hispanic mothers. Thus, in hospitals serving populations that include many foreign-born persons, physicians should be vigilant to the potential diagnosis of CRS and perform the appropriate diagnostic tests in infants with a clinical presentation consistent with CRS, even if not classical for CRS. In the El Paso hospital we studied, laboratory testing was performed only among infants with 3 or more predictive signs of CRS. In contrast, testing may be most important for those who have 1 or 2 signs consistent with CRS but who lack the classical triad of hearing impairment, heart defects, and cataracts. One study showed that 35% of infants with laboratory-confirmed CRS had hearing impairment only, 11% had cardiac defects only, and 1% had only cataracts. Among the 4 infants meeting the definition for probable CRS, only the infant with cataracts was tested for rubella IgM antibodies. This test, conducted at 1 week, was negative. However, comparisons between results of serologic tests and viral cultures have shown that in ~20% of infants tested for rubella IgM, titers may not be detectable before age 1 month (L. Z. Cooper, MD, personal communication, April 1998). Consequently, infants who test negative shortly after birth should be retested at age 1 month.

The rate of confirmed or probable CRS among infants in this predominantly Hispanic population is higher than reported in the United States in the vaccine era, which has been reported to range from ~0.01 to 0.08 per 10 000 live births. Data from Ghana, Israel, Jamaica, Mexico, Oman, Panama, Singapore, Sri Lanka, and Trinidad and Tobago show an annual incidence of CRS ranging from 6 to 22 per 10 000 live births, usually associated with a documented rubella outbreak; these rates are similar to those found in developed countries before the introduction of rubella vaccine.

Although the rate of infants with probable and confirmed CRS found in this study is higher than would be expected in the US-born population, 2 of the 4 infants who met the definition for probable CRS were diagnosed based solely on the presence of PDA and neonatal jaundice. Because PDA even in term infants is not uncommon and because jaundice is quite common, chance alone would dictate that occasionally they would occur together in an otherwise healthy infant. Therefore, it is uncertain that these 2 findings alone would indicate CRS reliably and results should be interpreted in light of the low specificity of the CRS case classification of this combination of defects. However, even excluding the 2 infants with only PDA and neonatal jaundice, the rate of CRS in this population is 2.1 per 10 000 live births and exceeds the reported CRS rate in the United States in the vaccine era.

Although it remains unclear whether the 4 infants with probable CRS were truly rubella-infected, conversely some infants with CRS could have been missed. During the study, few infants were assessed with hearing screening evaluations and this common clinical sign of CRS easily could have been missed. It is intriguing that all infants identified in this study had PDA; the literature suggests that ~30% of infants with CRS have PDA. This discrepancy might be because of better cardiac diagnostic capabilities in the modern era or an increased likelihood of under-diagnosis of CRS if cardiac pathology is absent. Further studies are needed in hospitals of similar size and care level that serve populations not considered to be high risk for rubella to aid in interpreting the data obtained from the hospital in this study.

To document elimination of indigenous transmission of rubella in the United States, surveillance of

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<table>
<thead>
<tr>
<th>CRS Status</th>
<th>Infant 1 Confirmed</th>
<th>Infant 2 Confirmed</th>
<th>Infant 3 Probable</th>
<th>Infant 4 Probable</th>
<th>Infant 5 Probable</th>
<th>Infant 6 Probable</th>
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<tbody>
<tr>
<td>Cataract</td>
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<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
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<td>X</td>
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</tr>
<tr>
<td>PDA</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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</tr>
<tr>
<td>Microcephaly</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Meningoencephalitis</td>
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<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Purpura</td>
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<td>X</td>
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<td>X</td>
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<td>X</td>
</tr>
<tr>
<td>Long bone radiolucencies</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
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<tr>
<td>Neonatal jaundice</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

*Includes conditions from the ICD-9 review used to select study charts and others associated with CRS identified during the chart review. Other conditions included in the chart review but not identified in any of the infants were mental retardation, ventrical septal defect, and peripheral pulmonic stenosis.
CRS cases must be heightened. By suspecting CRS in infants with conditions consistent with CRS, conducting appropriate laboratory tests at appropriate times, and reporting all suspected cases to health authorities, physicians can improve ascertainment and reporting of CRS in the United States. Because hearing impairment is the most common single defect associated with CRS and because newborn hearing screening is now implemented in more than half of the US states, performing rubella-specific IgM tests on infants who fail hearing screenings, in particular in higher risks groups, may increase CRS ascertainment. Studies are needed to determine the effectiveness and cost-effectiveness of incorporating rubella testing with hearing screening programs. With these comprehensive surveillance measures, CRS trends can be accurately monitored and high-risk groups targeted for intervention strategies.

ACKNOWLEDGMENTS

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