Respiratory Syncytial Virus Prevalence and Risk Factors among Healthy Term Infants, United States

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DOI: http://doi.org/10.3201/eid3010.240609

In a population-based birth cohort study of respiratory syncytial virus surveillance in the United States, 897/1,680 (53.4%) children were infected during infancy; 25/897 (2.8%) of those were hospitalized. Among symptomatic infants, 143/324 (44.1%) had lower respiratory tract infections. These data provide benchmarks to monitor effects of maternal vaccines and extended half-life monoclonal antibodies.

Respiratory syncytial virus (RSV) is a leading cause of illness in infants (*1*). Previous epidemiologic studies of RSV infection during infancy have focused on symptomatic illness, predominantly lower respiratory tract infections (LRTI) and hospitalizations (*2*). However, population-based surveillance studies to determine prevalence of and risk factors for RSV infection among healthy infants in the United States are lacking.

We determined prevalence of RSV infection by 1 year of age in a population-based birth cohort of healthy term infants in the United States. We excluded infants from the parent study, Infant Susceptibility to Pulmonary Infections and Asthma Following RSV Exposure (INSPIRE) (*3*,*4*), if they were not enrolled during well-child visits from 1 of 11 participating regional pediatric practices. We ascertained RSV infections by active surveillance using quantitative reverse transcription PCR (qRT-PCR) testing of nasal samples collected based on symptom surveys every 2 weeks and by passive surveillance by serum RSV antibody testing of all infants at 1 year of age during 2 RSV seasons, 2012–13 and 2013–14. If an infant met specified criteria for an acute respiratory infection, we conducted an in-person respiratory illness assessment and collected a nasal wash sample, which we used for the molecular detection of RSV by qRT-PCR. We also collected blood samples from all participating infants at 1 year of age and measured RSV serum antibody titers by ELISA using published protocols (*5*). We calculated 1-year prevalence of RSV infections, upper respiratory tract infections, LRTI, and healthcare utilization. We estimated the adjusted association and relative

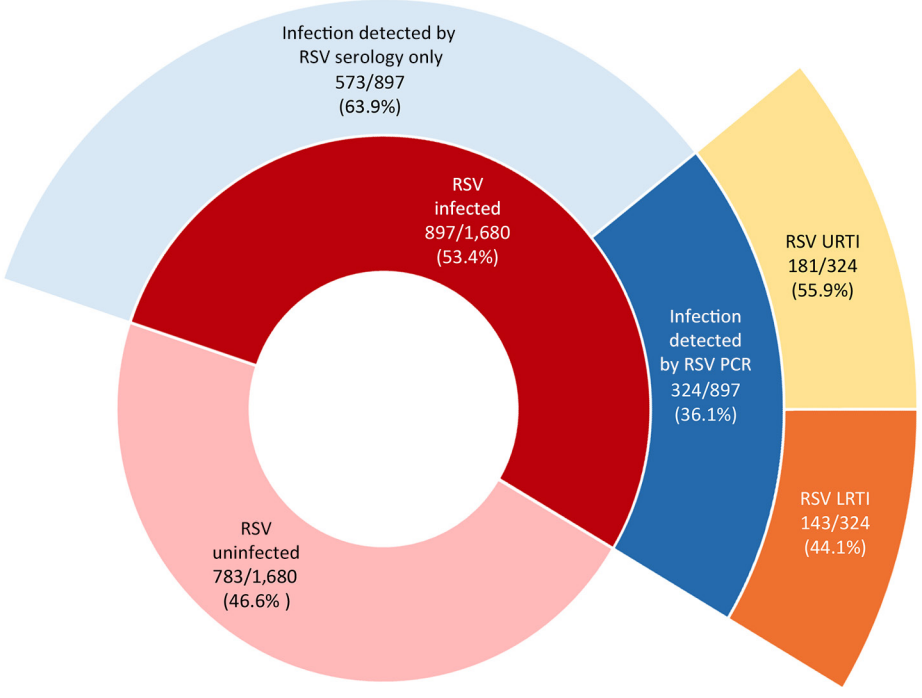

Figure 1. Percentages of RSV infection, symptomatic disease, LRTI, and URTI in the first year of life among healthy term infants, United States. Each ring represents the subset of the inner ring and adds to 100%. LRTI, lower respiratory tract infection; RSV, respiratory syncytial virus; URTI, upper respiratory tract infections.

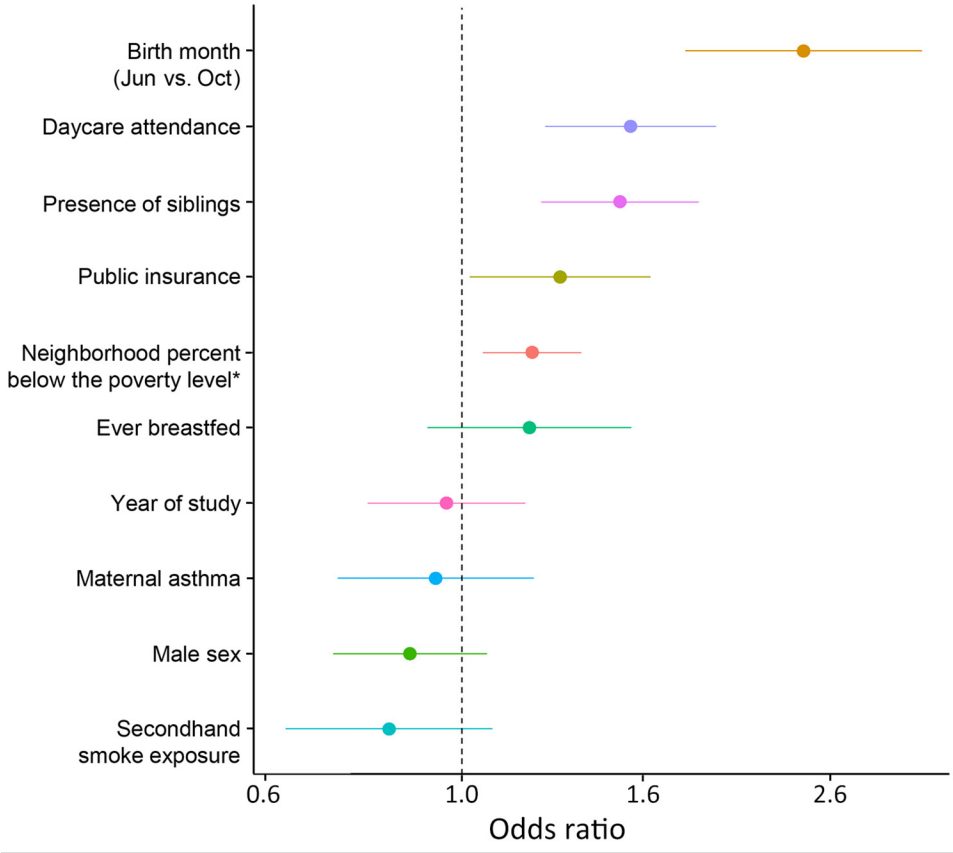

Figure 2. Respiratory syncytial virus infection risk factors in the first year of life in study of RSV among healthy term infants, United States. Adjusted odds ratios were estimated using multivariable logistic regression, referent is October birth month. Dots indicate odds ratio and horizontal line 95% CI. Dashed vertical line indicates the null effect. Asterisk indicates residence in a census tract with increasing percentage of people below the poverty level (interquartile range difference).

contribution of risk factors for RSV infection in the first year of life using multivariable logistic regression. The Institutional Review Board of Vanderbilt University approved INSPIRE, and 1 parent of each child provided written informed consent. INSPIRE methods have been published, and full study methods are available (*3*,*4*) (Appendix, https://wwwnc.cdc.gov/EID/article/30/10/24-0609-App1.pdf).

Among 1,680 infants who met inclusion criteria for our study, 897 (53.4%) were infected with RSV in the first year of life and 783 (46.6%) were not (Figure 1; Appendix Figure). Active surveillance detected 36.1% of RSV infections in symptomatic infants, whereas 63.9% were ascertained by serology alone. In all study infants, 1.5% (95% CI 0.96%–2.1%; n = 25) were hospitalized for RSV and 8.5% (95% CI 7.2%–9.9%; n = 143) had RSV LRTI. Among the subset with RSV infection, 2.8% (95% CI 1.9%–4.1%; n = 25) were hospitalized for RSV and 15.9% (95% CI 13.6%–18.4%; n = 143) had RSV LRTI. Restricted to the subset with symptomatic RSV infections meeting study criteria for a respiratory illness visit (n = 324), 55.9% had upper respiratory tract infections and 44.1% LRTIs. There were no infant deaths from RSV infection. We found that more than half of infants were RSV-infected in the first year of life. The rates of symptomatic disease, LRTI, and healthcare utilization demonstrate the considerable burden of respiratory illness in otherwise healthy infants; 1.5% of the cohort, or 2.8% of those infected, experienced RSV-associated hospitalizations.

Risk factors for RSV infection during infancy in order of contribution were infant birth month (June vs. referent October, OR 2.42 [95% CI 1.78–3.29]), presence of siblings (OR 1.50 [95% CI 1.22–1.84]), daycare attendance (OR 1.54 [95% CI 1.24–1.93]), increasing percentage below the poverty level in the residential neighborhood (21% vs. 8%; OR 1.19 [95% CI 1.05–1.36]), and public insurance (OR 1.28, 95% CI 1.02–1.62) (Figure 2). Secondhand smoke exposure, sex, ever being breastfed, maternal asthma, and study year were not significantly associated with likelihood of infant RSV infection.

The risk factors we identified increase viral exposure and underscore the potential for nonpharmacologic interventions to prevent infection (*6*). Earlier birth month was the strongest risk factor; we speculate that parental behaviors based on infant age affect exposure intensity (e.g., age at which infants are started in daycare). The risk factors of neighborhood percentage poverty and public insurance indicate the need to address socioeconomic determinants of RSV prevention.

The first limitation of our study is that eligibility criteria and sociodemographic characteristics might not be generalizable to other populations. In addition, our cohort represents a population that may be healthier, because they were term infants; however, this group represents half of RSV hospitalizations who are eligible for RSV prevention products. There is also potential for misclassification of infants categorized as uninfected with RSV in infancy (*4*). However, the proportions of both those with symptomatic respiratory illness and overall RSV serologic positivity are very similar to estimates from other studies (*7*–*9*). Although this cohort represents 2 RSV seasons during 2012–2014, we do not expect that time period to significantly affect the rates or risk factors for infection, which were similar across both RSV seasons.

In conclusion, our data are important estimates of the burden of RSV disease and risk factors for infection in healthy term infants. Our findings provide a benchmark to monitor the effects in the United States of recently available maternal vaccines and extended half-life monoclonal antibodies for severe RSV illness prevention in early life (*10*).

Acknowledgments

We thank the middle Tennessee pediatric practice sites and all the INSPIRE participants and their families for their involvement in and dedication to this study.

This work was supported with funds from the US National Institute of Allergy and Infectious Diseases (award nos. U19AI095227, UG3OD023282, and K24AI77930); the Vanderbilt Institute for Clinical and Translational Research (grant support from the National Center for Advancing Translational Sciences, award no. UL1TR000445); the US National Heart, Lung, and Blood Institute (award no. K23HL148638); the Department of Pediatrics at Vanderbilt University Medical Center (grant support from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, award no. K12HD087023); and the Vanderbilt University Training Program in Environmental Toxicology (NIH T32 ES007028). The content is solely the responsibility of the authors and does not necessarily represent the official views of the funding agencies. The National Institutes of Health had no role in the design and conduct of the study.

Author contributions: F.C. conceptualized and designed the study, created the figures, drafted the initial manuscript, and critically reviewed and revised the manuscript. T.G. performed the statistical analysis, created the figures, and critically reviewed and revised the manuscript. L.J.A. and J.D.C. contributed to acquisition of data and biospecimen analysis and critically reviewed and revised the manuscript. C.R.-S. and J.R.O. contributed to analysis and interpretation of data and critically reviewed and revised the manuscript. T.H. designed the cohort and acquired study funding, coordinated and supervised study conduct, conceptualized and designed the current analysis, and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

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Prosthetic Valve Endocarditis Caused by *Pasteurella dagmatis*, Germany

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DOI: https://doi.org/10.3201/eid3010.240727

An 81-year-old male patient in Germany had prosthetic valve endocarditis caused by *Pasteurella dagmatis* after a domestic cat bite. We surgically treated a paravalvular abscess and administered definitive antibiotic therapy consisting of penicillin G and levofloxacin. The patient was discharged from the intensive care unit in good condition 21 days after the surgery.

Pasteurella spp. are gram-negative, facultative anaerobic bacteria. They are part of the oral flora of domestic animals, including cats and dogs. In cases of animal bites, *Pasteurella* spp. bacteria can be detected culturally in 50%–75% of cases (*1*). Infections are typically caused by *Pasteurella multocida*, whereas *P. dagmatis* are rarely isolated from wounds, and severe *P. dagmatis* infections are exceedingly uncommon or unreported. Few cases of infective endocarditis (IE) attributable to *P. dagmatis* bacteria have been reported in the English-language literature (*2*–*5*). We report an additional case in a man in Germany. Given the rarity of gram-negative non-HACEK endocarditis (i.e., caused by species other than *Haemophilus* species, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, or *Kingella*) and the unfavorable prognosis associated with it, the contribution of case reports is essential to improve the management of affected patients (*6*).

An 81-year-old male patient was admitted to the hospital with a fever of up to 39.3°C. He reported weight loss of 10 kg during the preceding month. Vital signs and physical examination revealed no relevant pathologies. A domestic cat bite on the foot 2 months before admission was the only potential source of infection, but the wound had already healed weeks before. Underlying medical conditions included a mechanical aortic valve implanted 20 years previously because of a combined vitium.

After obtaining a set of blood cultures, we administered empiric antibiotic therapy with piperacillin/tazobactam. Results of chest radiograph, urine dipstick, and venous blood gas analyses were unremarkable. Results of point-of-care respiratory PCR testing for influenza and SARS-CoV-2 were negative. Blood testing showed mild anemia (hemoglobin 10.2 g/dL [reference range 11.6–15.5 g/dL]) but unremarkable leukocyte and platelet levels. C-reactive protein was moderately elevated at 47 mg/L (reference range <5 mg/L). Creatinine, urea, and liver function test results were unremarkable except for an international normalized ratio of 2.3 as a result of phenprocoumon therapy.

A set of blood cultures showed bacterial growth after 5 hours (anaerobic) and 10 hours (aerobic). We identified *P. dagmatis* bacteria by using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI Biotyper Sirius System; Bruker, https://www.bruker.com). The antibiogram demonstrated susceptibility to penicillin G, doxycycline, cotrimoxazole, and levofloxacin. Transthoracic echocardiography revealed a paravalvular abscess. We diagnosed prosthetic valve IE on the basis of modified Duke criteria (1 major clinical criterion, imaging; 3 minor clinical criteria, predisposition, fever, and microbiologic evidence falling short of a major criterion) (*7*).

The abscess measured at 24 ×14 × 31 mm on the subsequent computed tomography scan (Figure) and was communicating with the left ventricular outflow tract. The cardiac surgery department recommended