Importance of Global Surveillance for Respiratory Syncytial Virus

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This supplement of the *Journal* provides a compendium of epidemiologic, clinical, and laboratory data to address gaps in knowledge regarding acute respiratory illness associated with respiratory syncytial virus (RSV) in countries participating in the International Emerging Infections Program and the Influenza Program of the Global Disease Detection (GDD) network of the US Centers for Disease Control and Prevention, Center for Global Health. The GDD network is described in the supplement review articles by Breiman et al and Fields et al. Six GDD Centers (in China, Guatemala, Egypt, Kenya, South Africa, and Thailand) present supplement articles about children and adults with community-acquired RSV infection confirmed by sensitive real-time reverse-transcription polymerase chain reaction (RT-PCR) assays during recent years of active, prospective, population-based surveillance for acute respiratory illness and severe lower respiratory tract infections; a seventh GDD Center, in Bangladesh, provided RSV seasonality data. These countries are classified as low- and middle-income economies by the World Bank and include populations considered at high risk for infectious diseases, including urban poor, rural, and human immunodeficiency virus (HIV)–infected persons. The GDD data underscore the need to develop public health and preventive strategies to mitigate the influence of RSV worldwide.

RSV is an enveloped RNA virus with surface proteins that mediate RSV infection of human airway epithelial cells. RSV strains are classified into genotypes within 2 major RSV subgroups, RSV-A and RSV-B. RSV is the leading viral cause of acute lower respiratory tract infections, including bronchiolitis and pneumonia, among infants and young children globally. Resource-constrained populations bear the largest burden of severe RSV disease, accounting for 91% of 2.8–4.3 million hospitalizations and 99% of 66 000–199 000 deaths among children aged <5 years in 2005, based on a global meta-analysis by Nair et al [1]. The study by Nair et al also noted that, although RSV-associated mortality data were scarce, almost all RSV-associated deaths reported from high-income countries occurred among children aged <1 year, whereas RSV deaths in developing countries also occurred among children during their second year of life.

The burden of severe RSV disease is likely underrecognized because of the limited number of population-based studies from developing countries, the challenges in capturing non–medically attended cases of RSV infection in the community, and the scarcity of data on laboratory-confirmed RSV-associated deaths. Our understanding of the etiology of acute respiratory illness will be enhanced by the increasing capacity for multipathogen testing. GDD Center laboratories test specimens for multiple respiratory viruses, thus providing opportunities to assess the impact of real-time RT-PCR–confirmed RSV.

In addition to estimating the age-specific incidence of RSV-associated hospitalization, 2 GDD Centers provided data for this supplement on outpatient visits for RSV-associated illness, and the Kenya site identified cases through household-level community-based surveillance for respiratory disease. Several GDD Centers conducted healthcare utilization surveys to determine patterns of healthcare-seeking behavior for acute
respiratory illness within their surveillance populations. For example, a healthcare utilization survey by the GDD Center in Guatemala found that 67% of residents aged <5 years in one area who were hospitalized for respiratory illnesses were admitted to a surveillance hospital. These surveys allowed a more accurate estimation of population-based RSV hospitalization rates and cases missed by facility-based surveillance.

To avoid underestimating the burden of disease associated with RSV due to missed cases, surveillance systems should consider the appropriateness of case definitions. The clinical presentation of RSV infection may differ from that of other respiratory viruses. For example, RSV infections may be associated with mild fever or an absence of fever particularly in young infants and older persons, whereas influenza is more likely to cause a febrile illness. Also, it may not be possible to differentiate bronchiolitis from pneumonia with or without chest radiographs, particularly in young children. As multipathogen testing is added to more surveillance platforms, it will be important to assess inclusion/exclusion criteria.

RSV infection rates and severity of illness differ by age. Almost all children are infected with RSV by their second birthday, with the highest rates among young infants. Infection does not confer immunity to subsequent RSV infection, however the primary infection is typically the most severe among young infants, with obstruction of their small airways from epithelial necrosis, edema, and mucus production [2].

The contribution of RSV to morbidity and mortality among older children and adults may be underappreciated because of the scarcity of studies with laboratory confirmation of RSV infection in these age groups. In this supplement, all GDD Centers included children aged <5 years, and Centers in Egypt, Guatemala, Kenya, and Thailand also included children aged ≥5 years and adults. The articles contributed by GDD Centers reported a range of population-based annual rates of RSV-positive hospitalizations, depending on the age and risk group. For example, the GDD Centers in Guatemala and Thailand presented rates of RSV-positive hospitalization for acute respiratory illness across age groups and noted that rates were highest among infants, declined with increasing age, and then rose again among older adults aged 50–64 years and ≥65 years.

Although rates of severe RSV illness appear highest among children with high-risk conditions including premature birth, the majority of severe cases in a study from the United States were reported to occur among otherwise healthy young children [3]. RSV has also been associated with moderate-to-severe disease among persons who are elderly, are immunocompromised, or have chronic lung conditions [2, 4, 5]. There are few studies of risk groups for RSV infection in resource-constrained populations. In this supplement, several GDD Centers reported data on underlying medical conditions. For example, among RSV-positive hospitalized patients, the GDD Center in Guatemala reported a higher proportion of underlying conditions in those with more severe clinical outcomes, compared with those with less severe outcomes. The South Africa study reported higher RSV-positive hospitalization rates for acute respiratory illness or neonatal sepsis among HIV-positive children, compared with HIV-negative children.

Currently, there is no treatment for or vaccine to prevent RSV infection. The only available product against RSV infection is palivizumab, a humanized monoclonal antibody licensed for prophylactic use in certain high-risk infants and young children on the basis of its efficacy in preventing RSV-associated hospitalization. The high cost of palivizumab remains a barrier to its use in resource-constrained countries. In this supplement, L. Haynes provides an overview of the status of RSV prophylaxis and vaccine development.

RSV seasonality varies substantially within and across geographic areas. In this supplement, the country-specific articles and the article by A. Haynes et al. describe how RSV circulation varies by area, year, or climate. Although RSV-A and/or RSV-B may circulate in an area, it is unclear how patterns of circulation, repeat infections, and disease severity are related to different RSV genotypes or subgroups. Additional information on RSV strains will be important as vaccine development progresses. In this supplement, Venter et al. report on how circulating RSV genotypes have changed during 1997–2012 in South Africa.

In summary, this supplement contributes important data on RSV in low- and middle-income countries and in high-risk groups, confirming that these populations have a high burden of severe RSV illness. Surveillance for respiratory illness by GDD is ongoing and will provide more years of population-based data. The data will contribute to the knowledge base for designing and conducting RSV vaccine trials and for assessing the impact of future vaccines in resource-constrained populations, which bear the greatest burden of RSV disease.

Notes

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