Respiratory Syncytial Virus: A Global Pathogen in an Aging World

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(See the Major Article by Lee et al on pages 1069–77.)

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Respiratory syncytial virus (RSV) was identified in 1957 as a cause of infant bronchiolitis and is now recognized as the major cause of hospitalizations for respiratory infection in young children [1]. Shortly after its discovery, mild illness in adults with RSV reinfection was observed and since the 1980s evidence has been slowly mounting that the burden of adult RSV disease is substantial [2, 3]. Groups at highest risk for severe infection include the elderly, persons with chronic cardiopulmonary diseases, and those with immunosuppression [4, 5]. Despite the currently available epidemiologic data, RSV infection is rarely considered by internists evaluating patients with respiratory illness in their offices or in the hospital. In addition, health agencies and industry remain uncertain as to whether adult RSV disease warrants programs to develop therapeutics and vaccines. The reason for the adult RSV “identity crisis” is in large part because physicians rarely make a specific viral diagnosis in an individual patient and thus, they are unable to personalize the disease.Insensitive point-of-care diagnostics, the lack of a distinct clinical syndrome, and a broad epidemic curve that overlaps with influenza and other respiratory viruses all contribute to this lack of recognition of the problem. The development of new sensitive molecular diagnostics have dramatically altered epidemiologic research involving respiratory viruses, and recent studies now provide a more accurate picture of the burden of RSV disease [6, 7]. Yet, here too, the global community cannot personalize the problem to their own region or countries as most studies to date are from Europe and North America. Unless a disease is demonstrated in one’s own backyard, there is a natural tendency to ignore or minimize the problem.

In this issue of *Clinical Infectious Diseases*, Lee and colleagues [8] present data from a large, 3-year study of adults hospitalized with respiratory illness in Hong Kong, China. In this study, the clinical and radiologic features of 607 adults with confirmed RSV infection are compared and contrasted to patients with seasonal influenza infection. The findings clearly demonstrate significant morbidity and mortality in older persons associated with RSV infection, which is comparable to influenza. RSV accounted for 6%–9% of respiratory illnesses during seasonal peaks; 72% of those admitted with RSV had lower respiratory tract complications, 11% required ventilatory support, and 9% died within 30 days. Similar to previous reports, infected patients were elderly (mean age, 75 years), and most had underlying medical conditions with chronic lung disease reported in 36%. Of note, although substantial proportions of both RSV and influenza patients had underlying medical conditions, RSV patients had significantly more lung disease and major systemic comorbidities. This observation may reflect the very large sample size of the current study allowing detection of more subtle differences in patient groups than previous reports. Importantly, there was no significant difference in the overall outcomes of survival and duration of hospitalization of RSV- and influenza-infected patients.

Although a number of the observations in this study are confirmatory, this confirmation is critical. The study by Lee et al was conducted in Asia, a region previously with little data on the incidence and impact of adult RSV disease. In a part of the world widely recognized as an epicenter for novel influenza and other respiratory viruses, the authors clearly show the importance of a well-known virus in a new age group. Although less likely to generate media frenzy than a new highly lethal...
Several features of this study are unique and deserve further comment. The observed rates of fever (75%) and pneumonia (42%) in the current study by Lee and colleagues are higher than similar studies of hospitalized patients where rates of fever and pneumonia were 54%–61% and 20%–31%, respectively [4, 11, 12]. It is likely that different definitions of fever and pneumonia account for these observations. It is also possible that secondary bacterial infections may have been higher, yet, given the short period of symptoms prior to admission, this explanation seems unlikely. As noted previously, the use of immunofluorescence testing may have skewed detection to patients with higher viral loads either due to severity of illness or evaluation earlier in the course of illness. Future studies to determine if there are true regional differences in clinical features using polymerase chain reaction for detection should be considered.

The use of steroids was not associated with improvement in survival and was associated with longer hospital stays compared to those who did not receive steroids in the current study. Conclusions regarding the value of steroids should be cautious as this investigation was not a randomized clinical trial. However, these observations raise appropriate questions about the use of corticosteroids during acute viral infection. Animal models of RSV infection suggest that neither the use of antiviral agents nor the use of corticosteroids alone produces an optimal clinical outcome. Rather, the combination to reduce viral load plus an anti-inflammatory agent may be the best approach [13]. Thus, if effective antiviral agents for RSV can be developed, it may be worth revisiting the question of corticosteroid use in the context of effective control of the virus.

Last, the observation that bacterial infections occurred in 12.5% of patients deserves further reflection. It is important to point out that establishing a bacterial diagnosis for respiratory infections is difficult under ideal circumstances and it is not clear how aggressively bacterial diagnosis was pursued in the current study. Despite these limitations, it is notable that 95% of RSV-infected patients received antibiotics, highlighting the global issue of antibiotic overuse. Given the current state of bacterial diagnostics, the best way to prevent antibiotic misuse with RSV infection may be development of an effective RSV vaccine.

In summary, the study by Lee and colleagues is one more important step toward convincingly establishing RSV as an important global adult pathogen. The data from this comprehensive study confirm age and chronic lung disease as major risk factors for severe RSV disease and provide useful information for future research targeting groups that would most benefit from vaccines and therapeutics.

Note

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