Correspondence

Necrotizing Bronchiolitis in Influenza A of Swine Origin (H1N1)

To the Editor:

To reduce mortality from swine-origin influenza A (H1N1) infection is one of the most important tasks of pulmonary physicians. Mauad and colleagues found that necrotizing bronchiolitis was a characteristic finding of fatal novel human influenza A (H1N1) infection in their autopsied cases (1). We encountered two patients with bronchiolitis caused by pandemic influenza A (H1N1) 2009 (2). Despite the absence of pathological confirmation, these patients were thought to have necrotizing bronchiolitis without diffuse alveolar damage, since high-resolution computed tomography chest scanning revealed only characteristic findings of bronchiolar diseases. Also, they were treated successfully with oral oseltamivir phosphate. Cells in bronchioles and alveoli can become infected with pandemic A (H1N1) 2009 influenza virus (3). Without adequate treatment, necrotizing bronchiolitis might become complicated by diffuse alveolar damage. Early intervention for swine-origin influenza A (H1N1) infection with antiviral agents will be required to prevent necrotizing bronchiolitis from becoming complicated with diffuse alveolar damage and reduce mortality from infection with influenza (H1N1).

Author Disclosure: None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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References

1. Mauad T, Hajjar LA, Callegari GD, da Silva LF, Schout D, Galas FR, Alves VA, Malheiros DM, Auler JO Jr, Ferreira AF, *et al.* Lung pathology in fatal novel human influenza A (H1N1) infection. *Am J Respir Crit Care Med* 2010;181:72–79.
2. Toyoshima M, Chida K, Suda T, Sato M. Bronchiolitis caused by pandemic influenza A (H1N1) 2009. *Intern Med* 2011;50:167–168.
3. Liu Y, Childs RA, Matrosovich T, Wharton S, Palma AS, Chai W, Daniels R, Gregory V, Uhlenendorff J, Kiso M, *et al.* Altered receptor specificity and cell tropism of D222G hemagglutinin mutants isolated from fatal cases of pandemic A(H1N1) 2009 influenza virus. *J Virol* 2010;84:12069–12074.

From the Authors:

We thank Toyoshima and colleagues for the comments on our paper reporting the pathology of 21 fatal cases of H1N1 during the 2009 pandemics (1). Necrotizing bronchiolitis was indeed one of the major findings in these patients, associated with extensive diffuse alveolar damage and lung hemorrhage (1).

Toyoshima and colleagues reported two adult patients who presented with a predominant clinical and tomographic picture of bronchiolitis without diffuse alveolar damage due to H1N1 infection. These patients recovered completely with oseltamivir treatment (2). Their report of an acute isolated bronchiolitis pathology resulting from H1N1 infection is very interesting. It is tempting to speculate that either an improved host immune response in these patients or a decreased affinity of the infecting virus for alveolar epithelial cells resulted in the lesions being confined to the airways.

The authors suggest that prompt treatment with oseltamivir prevented the evolution of the disease to a more life-threatening condition such as diffuse alveolar damage. However, in our series, we observed a rapid progression from the time of development of flu symptoms to the development of acute lung injury and death without interval clinical manifestations of bronchiolitis. Our results are consistent with a recent report by Sasbón and coworkers, who described 30 patients admitted to a Pediatric Intensive Care in Buenos Aires, Argentina with H1N1 infection in 2009 (3). They found that 40% presented with bilateral pneumonia and 50% had acute respiratory distress. None of the children presented with bronchiolitis. We believe that in severe cases, infection by the virus and an exacerbated inflammatory response are likely to be widespread in the lungs at the onset of symptoms.

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References

1. Mauad T, Hajjar LA, Callegari GD, da Silva LF, Schout D, Galas FR, Alves VA, Malheiros DM, Auler JO Jr, Ferreira AF, *et al.* Lung pathology in fatal novel human influenza A (H1N1) infection. *Am J Respir Crit Care Med* 2010;181:72–79.
2. Toyoshima M, Chida K, Suda T, Sato M. Bronchiolitis caused by pandemic influenza A (H1N1) 2009. *Intern Med* 2011;50:167–168.
3. Sasbón JS, Centeno MA, García MD, Boada NB, Lattini BE, Motto EA, Zuázaga MA, Acebedo VV, Truszkowski ME, Filippini S. Influenza A (pH1N1) infection in children admitted to a pediatric intensive care unit: Differences with other respiratory viruses. *Pediatr Crit Care Med* 2011;12:e136–e140.

Risk and Incidence of Pulmonary Diseases among HIV-infected Patients in the Era of Combination Antiretroviral Therapy

To the Editor:

We read with great interest the article by Crothers and colleagues (1) that determined the incidence and risk of pulmonary diseases in HIV-infected patients compared with matched HIV-uninfected patients in the era of combination antiretroviral therapy (ART) by analyzing the data from the Veterans Aging

Cohort Study Virtual Cohort. The findings of this study further emphasize the role of bacterial pneumonia along with chronic obstructive pulmonary disease as important causes of morbidity among HIV-infected patients. While the message that behavioral interventions to enhance adherence to smoking cessation (2, 3) and combination ART (4) are important, surprisingly, the authors did not analyze the impact of pneumococcal vaccination on the incidence of bacterial pneumonia. Among the HIV-infected veterans of the same cohort, a previous study by Rodriguez-Barradas and colleagues (3) has shown that, although less than 50% of the veterans received pneumococcal polysaccharide vaccination, pneumococcal vaccination offered protection against pneumonia in this cohort. Furthermore, a recent double-blind, randomized, placebo-controlled clinical trial (5) has demonstrated that the 7-valent pneumococcal conjugate vaccine protected HIV-infected adults from recurrent pneumococcal infection caused by vaccine serotypes or serotype 6A. Although the cost-effectiveness of pneumococcal conjugate vaccine versus polysaccharide vaccine remains debatable in these aging populations (6), further analyses using the data from this large cohort will be worthwhile and informative.

Author Disclosure: None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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References

1. Crothers K, Huang L, Goulet JL, Goetz MB, Brown ST, Rodriguez-Barradas MC, Oursler KK, Rimland D, Gibert CL, Butt AA, *et al.* HIV infection and risk for incident pulmonary diseases in the combination antiretroviral therapy era. *Am J Respir Crit Care Med* 2011;183:388–395.
2. Crothers K, Goulet JL, Rodriguez-Barradas MC, Gibert CL, Oursler KA, Goetz MB, Crystal S, Leaf DA, Butt AA, Braithwaite RS, *et al.* Impact of cigarette smoking on mortality in HIV-positive and HIV-negative veterans. *AIDS Educ Prev* 2009;21:40–53.
3. Rodriguez-Barradas MC, Goulet J, Brown S, Goetz MB, Rimland D, Simberkoff MS, Crothers K, Justice AC. Impact of pneumococcal vaccination on the incidence of pneumonia by HIV infection status among patients enrolled in the Veterans Aging Cohort 5-Site Study. *Clin Infect Dis* 2008;46:1093–1100.
4. Gordin FM, Roediger MP, Girard PM, Lundgren JD, Miro JM, Palfreman A, Rodriguez-Barradas MC, Wolff MJ, Easterbrook PJ, Clezy K, *et al.* Pneumonia in HIV-infected persons: increased risk with cigarette smoking and treatment interruption. *Am J Respir Crit Care Med* 2008;178:630–636.
5. French N, Gordon SB, Mwalukomo T, White SA, Mwafurirwa G, Longwe H, Mwaiponya M, Zijlstra EE, Molyneux ME, Gilks CF. A trial of a 7-valent pneumococcal conjugate vaccine in HIV-infected adults. *N Engl J Med* 2010;362:812–822.
6. Musher D, Sympath R, Rodriguez-Barradas MC. The potential role for protein-conjugate pneumococcal vaccine in adults: what is the supporting evidence? *Clin Infect Dis* 2011;52:633–640.

From the Authors:

We appreciate the comments by Dr. Hung and colleagues, and their interest in our article (1). We agree that pneumococcal

vaccination status is an important factor to consider in assessing the risk for bacterial pneumonia in HIV-infected, as well as HIV-uninfected, persons. Unfortunately, vaccination status was not readily available nationally within the administrative Veterans Affairs (VA) databases at the time that we were conducting analyses for this article. In our prior work analyzing the impact of pneumococcal vaccination status on risk for pneumonia in subjects enrolled in the Veterans Aging Cohort 5 Site Study (VACS 5), we established receipt of pneumococcal vaccine by a combination of retrospective review of VA electronic administrative data and direct medical record review (2). In VACS 5, subjects gave informed consent to permit medical record review; however, direct review of medical records has not been feasible within the 100,260-member Veterans Aging Cohort Study Virtual Cohort (VACS VC), as it has included only administratively available electronic data sources. We have only recently been able to access data within the VA immunization files, and are currently using this data along with a combination of other sources to determine immunization status among subjects in the VACS VC.

We agree that further studies to examine risk factors for bacterial pneumonia among HIV-infected compared with HIV-uninfected patients are warranted, including the impact of vaccination status on risk for bacterial pneumonia. These analyses will also need to consider type and timing of vaccination as well as duration of protection in a series of models with time-varying covariates, expanding substantially beyond the scope of the work presented in our article (1).

Author Disclosure: K.C. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. L.H. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. A.A.B. has received industry-sponsored grants from Valeant Pharma.

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References

1. Crothers K, Huang L, Goulet JL, Goetz MB, Brown ST, Rodriguez-Barradas MC, Oursler KK, Rimland D, Gibert CL, Butt AA, *et al.* HIV infection and risk for incident pulmonary diseases in the combination antiretroviral therapy era. *Am J Respir Crit Care Med* 2011;183:388–395.
2. Rodriguez-Barradas MC, Goulet J, Brown S, Goetz MB, Rimland D, Simberkoff MS, Crothers K, Justice AC. Impact of pneumococcal vaccination on the incidence of pneumonia by HIV infection status among patients enrolled in the Veterans Aging Cohort 5-Site Study. *Clin Infect Dis* 2008;46:1093–1100.

Low Bone Mineral Density in Emphysema: Epiphenomenon of a Wasting Phenotype?

To the Editor:

Progressive wasting of muscle tissue and bone minerals are serious extrapulmonary impairments of chronic obstructive pulmonary disease (COPD), and both appear to be more prevalent in patients with emphysema. However, it remains unclear if emphysema is a predictor of a low bone mineral density (BMD) as