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Critically Ill Patients with H7N9: New Virus, Old Challenges

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The emergence of human infections with novel influenza viruses reminds us that the landscape of influenza epidemiology is constantly evolving, and the avian H7N9 infections first identified in March of 2013¹ are just another example. Similar to the re-emergence of avian H5N1 in 2003 and the emergence of the novel pandemic H1N1 in 2009, it is difficult to predict disease severity, extent of transmission, and future incidence of infections when a new virus is recognized. It often takes years to collect enough epidemiologic data before we can make reasonable predictions, and even then influenza viruses can still surprise us. Often the initial focus of clinical reports are on those who suffer from the most severe disease and complications, and while not providing a clear picture of the true epidemiology of a novel virus such as H7N9, these reports appropriately focus our attention on why we must continue to be vigilant and diligently pursue methods to mitigate the morbidity and mortality caused by influenza viruses. In this issue of Critical Care Medicine, Yang et al.² describe 27 hospitalized cases of H7N9, 26 who suffered from severe disease. Their description highlights the challenges critical care medicine physicians face when caring for patients with complicated influenza-induced disease, and why prevention of severe disease is so important.

Severe disease and complications due to an influenza virus infection is not a unique feature of avian or pandemic influenza. All influenza virus infections can lead to severe disease, including seasonal influenza and influenza B³. It is clear that some differences exist between strains in pathogenesis and incidence of severe disease, but commonalities also exist putting these viruses on a spectrum of sorts. For example, in these reported cases of H7N9², similar to H5N1 and 1918 H1N1 infections, a strong immune response occurs in these patients leading to damage to the airways that set these patients up for severe complications. Also similar to H5N1, H7N9 is not fully human adapted and only low levels of limited human-to-human transmission have been observed^{4,5}. It is unclear if susceptibility to H7N9 and other avian viruses like H5N1 are linked, and susceptibility factors, genetic or not, are still a

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mystery. What is clear is that although those who are susceptible are at risk of severe disease, not all who are susceptible develop severe disease⁶, and that there are likely many more infections than have been identified in the H7N9 outbreaks.

The high mortality of those who are hospitalized with H7N9 highlights the importance of disease in these patients, but the disease seems more akin to that of complicated human influenza than H5N1⁷. Hospitalization and severe disease in H7N9 has been observed to be far more common in those who are older and have comorbidities, just as in seasonal influenza⁸. Yang et al described bacterial pneumonia playing a role in the severe disease in a majority² of patients in this cohort, similar to what was seen during the 1918 and 2009 pandemics^{9,10}. In both cases the significance of bacterial secondary and co-infection is likely even higher given that almost all patients were treated with broad spectrum antibiotics at admission and the yield of sputum culture has been reported to be as low as 15% for the diagnosis of community acquired pneumonia¹¹.

Yang et al. report an ICU mortality of approximately 30%, similar to that of 2009 H1N1 pandemic and post-pandemic ICU mortality¹². Critical care physicians face a challenging set of circumstances treating these patients. The aforementioned bacterial pneumonias and worsening of common underlying cardiac and pulmonary comorbidities can lead to SIRS, sepsis, multi-organ dysfunction, and ultimately death. As Yang et al. point out, treatment with antivirals must be undertaken very early to have an effect², but typically by the time a patient has reached the critical care setting it is often too late for the patient to benefit. Once in the ICU, viral replication is not the primary problem, it is rather the consequences and complications of the infection that should be focused on with specifically tailored supportive care and interventions based on each individual case.

Complicated and severe influenza-induced disease from all strains of influenza, whether seasonal, pandemic or even highly pathogenic avian viruses, poses a challenge to critical care physicians worldwide. Clearly prevention is better than any of the available treatment modalities and improving overall population health, reducing spread, and availability of true universal vaccines could make a large impact in reducing the number of patients who present to the critical care setting due to influenza infection. For the critically ill with influenza, whether it is a novel avian strain like H7N9 or a common seasonal one, the same old challenges of critical care medicine exist and improvements in supportive care, modes of ventilation, and treatment of SIRS, sepsis, and multi-organ dysfunction will likely have the greatest impact on reducing ICU morbidity and mortality.

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