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Pandemic Research in the ICU: Always Be Prepared*

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In 2009, a novel H1N1 influenza A virus, a reassortment between two swine influenza lineages containing a hemagglutinin surface protein ultimately derived from the 1918 pandemic virus (1), spread quickly worldwide causing a pandemic. This impacted emergency rooms, physician offices, and ICUs worldwide. Approximately 20%–30% of the patients who required hospitalization required care in an ICU (2–4). These patients suffered from the most severe complications of influenza-induced disease; requiring more resources and adding to the challenge critical care providers face each day in caring for the sickest individuals in the hospital (5, 6). Early during the course of the pandemic, it was difficult to obtain definitive information regarding which patients were at risk of severe disease and what the best options were for treating such patients. Even 3 years postpandemic, many of these questions remain only partially answered, and critical care providers lack important data that could improve the quality care, that can only be generated by well-designed clinical research protocols.

In this issue of *Critical Care Medicine*, Burns et al (7) describe a carefully performed survey that offers some valuable insights into the current infrastructure for performing clinical research in the ICU setting and describe the limitations and barriers that may interfere with performing quality clinical research in response to a pandemic. Worldwide, clinical research in ICUs during the pandemic and in the years that have passed since has been considered an important component of the pandemic response and preparation for future pandemics. Most of the ICU studies published to date have been either retrospective or observational focusing on describing the clinical symptoms and course of illness, identifying risk factors for developing severe disease and death, and recording clinical outcomes (8–13). A smaller number of prospective observational studies in ICUs have attempted to evaluate therapeutic modalities such as early oseltamivir therapy (14) and modes of mechanical ventilation and oxygenation (15, 16). Although many of these published studies have been instructive, due to their limitations and a lack of randomized controlled trials, they have not adequately addressed all the issues necessary to allow critical care providers to significantly reduce morbidity and mortality in the ICU due to pandemic or even postpandemic influenza.

*See also p. 1009.

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The authors here aptly identify a number of interesting factors that play an important role in the success and quality of clinical research in ICUs during pandemics (7). Importantly, the authors describe that the motivation to perform research in response to a pandemic was great, as both ICU administrators and research coordinators overwhelmingly reported feeling that this research was important, impactful, and worth resource allocation. Many of them did, however, often report that the design and approval process of protocols was too slow, resources were often limiting, and balancing patient care and research was a challenge (7). The authors limited their questions in this survey to simply addressing research during the pandemic, but in order to better address the issues of resource availability, slow approval processes, and the balance of patient care; a useful approach would be to ask these same individuals to respond about clinical research protocols designed to study seasonal influenza and other epidemic diseases in the absence of a pandemic.

In interpandemic periods, it is much more difficult to generate the interest and momentum necessary to study diseases such as seasonal influenza, especially in a busy hospital setting. This is important because prospective studies, especially randomized controlled trials, ongoing at the time of a pandemic will have resources, protocols, and procedures already available and approved by Institutional Review Boards and appropriate regulatory bodies. This would allow ICUs to quickly and smoothly respond to a change from an epidemic to a pandemic outbreak. If studies of seasonal influenza or respiratory viruses in general were ongoing in the ICUs surveyed, it seems plausible that a shift to focus on 2009 H1N1 could have occurred more quickly and efficiently. In this scenario, it is likely that a significant number of the ICU administrators and research coordinators surveyed would have felt that responding to the pandemic would have been much faster, easier, and more impactful than they indicated in their responses.

Burns et al (7) reported that research coordinators and ICU administrators feel that pandemic research is an extremely important part of their role in healthcare, and this study clearly demonstrates that they wish to make an impact on reducing the overall burden of pandemics. Their main concern is clearly having the resources, funding, protocols, and approvals needed to quickly implement quality studies during pandemics in the ICU. Thus, the most expedient way to address these issues is to continue to strengthen the infrastructure for more clinical studies of seasonal influenza and other potential pandemic illnesses in our ICUs worldwide.

The authors also describe that international research consortia, such as the International Forum of Acute Care Trialists and the International Severe Acute Respiratory Consortium, as well as hospital networks and databases such as the Spanish Network for Research in Infectious Diseases, Australia and New Zealand Intensive Care Research Center, and Intensive Care National Audit and Research Center, have made great progress towards creating the needed infrastructure during the interpandemic period that will allow for quicker responses during a pandemic (7). Multicenter collaborations and infrastructure augmentation is a good start, and these should be strengthened during interpandemic periods. Research infrastructure in place to study epidemic influenza and other diseases in ICUs is thus extremely important for future pandemic preparedness.

We must retain the momentum and interest sparked by the pandemic in the postpandemic and interpandemic periods to strengthen ICU-based clinical research programs. The importance of studying potentially pandemic diseases such as seasonal influenza in this period must be reinforced with ICU administrators, research coordinators, as well as physician and other ICU staff. Only through a constantly evolving, integrative approach to studies of these diseases that include hospital networks and databases, international consortia, and collaborations between critical care providers and scientists, will we be able to meet one very important goal of ICUs worldwide—to always be prepared.

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