Emerging infectious diseases have been described as a “clear and present danger to humanity” [1, p. 1887]. To protect against this danger, medical care must be advanced through clinical research. The severe acute respiratory syndrome (SARS) outbreak demonstrated the need for clinical research to evaluate medical interventions. For SARS, ribavirin and corticosteroids were frequently used for treatment [2, 3]. Clinicians treating patients who are dying because of a disease with no known treatment should utilize measures that are thought to have potential efficacy. However, definitive data collection should follow the treatment, because the use of medical interventions without supporting clinical studies can have significant implications. During the SARS outbreak, ribavirin was shown to cause hemolytic anemia in 61% of treated subjects, with a mean decrease in hemoglobin levels >2 g/dL [4]. The use of corticosteroids was implicated as a cause of hip pain and osteonecrosis in a significant portion of the treated population [5]. It has subsequently been shown that neither drug has efficacy in the treatment of SARS [6].

The initial outbreak report of H5N1 influenza in humans in Vietnam was issued by the World Health Organization on 13 January 2004 [7]. The initial study that summarized the epidemiology, clinical findings, and outcomes for 10 patients with H5N1 influenza in Vietnam was published in an online report 6 weeks later on 25 February 2004 [8]. Since that time, knowledge regarding H5N1 infections in humans has advanced in marginal increments. Additional case series have provided further details about H5N1 infection [9, 10]. Case series have also been published that detail atypical presentations or provide detailed virologic investigations [11–13]. All of these have served to refine the clinical knowledge of H5N1 infection, but definitive studies have been lacking.

Prospective, controlled trials are the gold standard of clinical research. The implementation of clinical research studies in the midst of an outbreak is fraught with challenges, ranging from identifying subjects in the face of changing case definitions, uncertainty about interventions to be studied, and delays associated with regulatory review and funding [14]. Even with an infrequent and episodic disease, such as H5N1 influenza, developing research networks for study involves a significant investment of time and money [15].

Bridging the gap between case series and controlled trials for avian influenza, the World Health Organization has convened a series of consultations [16, 17]. These meetings involve many of the world’s leading authorities on avian influenza, including clinicians, epidemiologists, researchers, public health authorities, and others. Although they clearly provided invaluable guidance to those who are facing patients with H5N1 infection, the assimilation of pieces of data from many sources clearly has limitations.

In this issue of Clinical Infectious Diseases, Liem et al. [18] demonstrate that another way to improve the granularity of clinical knowledge is to return to the medical record with a structured assessment and perform a new abstraction and analysis of the data. By bringing together multiple key collaborators, they were able to assimilate data for 72% of human H5N1 cases diagnosed in Vietnam through December 2006. This method eliminates some of the sampling and abstraction errors associated with compilations.

Other large retrospective case series involving H5N1 have relied on analysis of previously collected case-investigation reports [19]. However, the medical record will usually contain more clinical data than case investigation reports. The abstraction tool can also be modified to seek data to answer relevant clinical questions. This analysis by Liem and colleagues further defines the clinical features of H5N1 influenza infection. It also reinforces the usefulness of oseltamivir and the detri-
mental effects of corticosteroids in the treatment of infected patients.

There are clear shortcomings with a retrospective review. The data are only as good as what is captured in the medical record. For example, the presence or absence of symptoms and epidemiologic exposures cannot truly be measured. It can only be known if the symptoms and exposures were noted in the medical record. However, in lieu of definitive studies, these retrospective reviews are the most likely source for advancing clinical data in emerging infectious diseases.

How should the capture of clinical data regarding H5N1 and other emerging diseases evolve? The natural immediate evolution is the review and abstraction of defined data sets for particular diseases from multiple countries. Current efforts toward this goal are underway. However, this does not eliminate the limitations of incomplete data recorded in the medical record. Prospectively defining data sets by listing the clinical variables that need to be captured for all patients would allow for more accurate and thorough analysis. Furthermore, there is a critical need for improved mechanisms to centralize data acquisition.

The efforts by Liem et al. [18] demonstrate the need and benefit of cooperation and collaboration across institutions. This collaboration is even more critical when crossing geographic areas, but the greater benefit demands that these efforts be made. Emerging infectious diseases will continue to occur [1], and we must learn how to work toward acquisition of better clinical data to improve outcomes of these diseases.

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**References**