

EDITORIAL



Truly Emerging — A New Disease Caused by a Novel Virus

Heinz Feldmann, M.D.

Contrary to predictions of the mid-20th century, infectious diseases are on the rise, threatening human and animal health on both local and global scales. Multiple factors are contributing to the emergence or reemergence of infectious diseases, including increasing human intrusion into the natural environment, with behavioral changes associated with expanding economic development.¹ In addition to the global viral killers (e.g., human immunodeficiency virus and influenza virus), which are huge regional and global public health burdens, viral zoonoses in particular have become more prominent worldwide. A multidisciplinary approach to addressing zoonotic diseases is being promoted, and the “one world, one health” concept was recently reemphasized with the organization of the First International One Health Congress.²

Our front-line defense against emerging infectious diseases continues to be clinical observation, heightened surveillance, and rapid detection, as shown when an infectious disease emerged in 2009 in rural areas of Hubei and Henan provinces in central China, as reported by Yu et al. in this issue of the *Journal*.³ The disease, with an initial case fatality rate of approximately 30%, was termed the severe fever with thrombocytopenia syndrome (SFTS) and was characterized by fever, gastrointestinal symptoms, thrombocytopenia, and leukocytopenia. Human anaplasmosis, leptospirosis, and hemorrhagic fever with renal syndrome were included in the differential diagnosis but could not be confirmed on laboratory testing. Instead, a virus, designated SFTSV, was isolated from patients' blood. Molecular characterization identified SFTSV as a novel phlebovirus in the Bunyaviridae family, most closely related to Uuku-

niemi virus. After the initial outbreak, surveillance was expanded into neighboring provinces of central and northeast China with the use of a newly designed case definition and advanced laboratory testing. SFTSV was found in patients in all surveyed provinces, indicating a fairly broad distribution in China but no evidence to date of human-to-human transmission. In the Bunyaviridae family, hantaviruses are predominantly transmitted by rodents, whereas other bunyaviruses are transmitted by arthropods. Therefore, molecular screening of mosquitoes and ticks was initiated to identify the bunyavirus vector. *Haemaphysalis longicornis*, a tick with a broad host range, was found to carry SFTSV, suggesting that it was the vector of this newly emerged zoonosis.

Overall, the identification of SFTSV is a prime example of the rapid discovery of a truly emerging infectious disease and its cause.³ Koch's postulates for establishing a causal relationship between a disease and its pathogen are largely fulfilled, with the exception of the most difficult postulate: an animal model to reiterate that relationship. A recent example of the successful fulfillment of this particular postulate in record time was the identification of the coronavirus causing the severe acute respiratory syndrome (SARS).⁴

A refined case definition and specific diagnostics for SFTSV infection are now available, which should allow Chinese physicians and public health officials to quickly identify new cases. The potential vector, *H. longicornis*, needs to be confirmed and potential reservoir species involved in its maintenance cycle need to be identified, but initial strategies for prevention can be designed on the basis of the preliminary infor-

mation.³ Further surveillance work is needed to identify areas in which the disease is endemic and thus to rate the risk of human exposure. An animal model would be helpful for drug and vaccine development.

With approximately one quarter of the world's population and a vast diversity of wild and domestic animals living in close proximity to humans, it is likely that China has the greatest potential for the emergence or reemergence of infectious diseases worldwide.⁵ In particular, Chinese animal markets are considered unique places for the transmission of pathogens from animals to humans.⁵ SARS and influenza have been prominent examples, respectively causing the first pandemic of this century⁶ and still posing a threat of a future avian influenza pandemic with human-to-human transmission.⁷ Similar problems exist in regions of Southeast Asia, as exemplified by the recent avian influenza outbreak^{5,7} and the emergence of Nipah virus in Malaysia in 1999.⁸ As the world was preparing for an avian influenza pandemic, we were blindsided by the 2009 influenza A (H1N1) outbreak.⁹ This history clearly emphasizes the need for vigilance, awareness, and preparedness with respect to infectious diseases and the mind-set for expecting the unexpected. Surveillance systems for notorious pathogens such as influenza have been established, but future systems that are based on clinical syndromes (e.g., respiratory, gastrointestinal, hemorrhagic, hepatic, or encephalitic) should be strengthened. Collected data should be shared with national, regional, and global reference networks.

To date, we still have an alarming number of cases of infectious disease without a laboratory diagnosis. Even clusters of cases or outbreaks sometimes go undiagnosed for long periods, such as the recent outbreak in northern Uganda of what is now reported as yellow fever, a well-known and relatively easy to diagnose human pathogen.¹⁰ This lapse is particularly unfortunate, since the early diagnosis of yellow fever can save lives through immediate vaccination. Such a scenario is not unusual and occurs more often in countries with weak public health infrastructures.

Nowadays, diagnostic capacity in developed countries should not (but sometimes still does) pose a real problem in the context of an outbreak investigation for routine organisms, but

pathogen discovery still largely relies on traditional isolation attempts. However, such efforts often do not detect pathogens that are neither cytolitic in cell culture nor virulent in animals. There is a boom in the development of promising high-tech diagnostic approaches that have increased sensitivity and specificity, as well as being faster and more successful. For example, metagenomics can provide complete molecular characterization of a virus in a certain microenvironment, such as blood, within a day's time.¹¹ This process does not fulfill Koch's postulates but will have a rapid effect on the treatment of patients, intervention therapy, and public health response.

Such opportunities are unlikely to become available in developing countries that have the largest burden of infectious diseases. In order to overcome this dilemma, strategies for rapid communication of case clusters and outbreaks need to be implemented. Other serious problems include the need for rapid collection, storage, and transport of specimens from the bedside or field site to reliable diagnostic laboratories and for the coordination of equitable relationships among investigative groups. The current regulations for the transportation of diagnostic specimens should be amended to better integrate this critical component of the public health response to infectious diseases, which needs to be realistic and not burdened by unnecessary bureaucracy while still maintaining biosecurity and biosafety. The response has to be secure and safe but also rapid and targeted, with the primary goal of immediately supporting public health while providing the best treatment for the affected patient. Early detection and immediate response will save lives and may prevent the next epidemic or pandemic.

The views expressed in this editorial are those of the author and do not necessarily reflect those of the Division of Intramural Research at the National Institute of Allergy and Infectious Diseases of the National Institutes of Health or the Department of Medical Microbiology at the University of Manitoba.

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From the Laboratory of Virology, Division of Intramural Research, National Institute for Allergy and Infectious Diseases, National Institutes of Health, Hamilton, MT, and the Department of Medical Microbiology, University of Manitoba, Winnipeg, MB, Canada.

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