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NEWS & VIEWS

Severe fever with thrombocytopenia syndrome virus expands its borders

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The war on emerging pathogens is intensifying in 2013.

The outbreak of avian-origin influenza A (H7N9) virus in eastern China[1,2] has reminded the world of the imminent threat of unexpected pathogens, including an ''old'' virus, influenza. Recent conversation has centered on H5N1, H9N2, H7N3, and H7N7, but never before had we considered H7N9 to be the cause of outbreaks of human infection or the next possible pandemic. Maybe we have to take a closer look at the possibility of reassortment among any of the 16 hemagglutinins and 9 neuraminidases subtypes, and even within the newly identified bat-derived, influenza-like virus H17N10.[3,4]

A new coronavirus, called human coronavirus Erasmus Medical Center (hCoV-EMC) (with a recent proposed new name as Middle East respiratory syndrome coronavirus, or MERS-CoV in abbreviation), has caused alarm in the Middle East, as human infection was first reported in March 2012.[5] In one year, as of May 12, 2013, there have been 34 cases, with 18 fatalities in total (www.who.org). More importantly, human-to-human transmission has been reported, with second-generation infections in France and the UK in those individuals who have had close contact with patients with a history of travel to the Middle East.

Less publicized but equally significant, the recently emerged severe fever with thrombocytopenia syndrome virus (SFTSV) expanded its geographic spectrum in 2012–2013, from China to the USA, and now to Japan.

SFTSV-induced disease was first suspected in China in 2009, and the virus was isolated and confirmed in 2011.[6] SFTSV is a new member of the genus *Phlebovirus*, with over 70 known members in the genus, which is in the family *Bunyaviridae*. Although the phlebovirus has been found in Africa and Europe for many years, SFTSV is the first-ever virus of this type isolated in China.[6–10] The virus is known as the Heartland virus after the name of the place (Heartland, Missouri) where the virus was first isolated in the USA. The Heartland virus is phylogenetically distinct from SFTSV isolated in China, although
similar clinical manifestations have been observed.[9]

Early this year, SFTSV was confirmed in western regions of Japan. Officials referred to the etiological agent of this outbreak as the same that caused disease in China, or SFTSV. However, these two agents are similar but not identical. As Dr. William L. Nicholson from the USA Centers for Disease Control and Prevention (CDC) suggested, these viruses could be considered as ''cousins.''

The viruses from three countries are too different to be linked in their transmission. The viruses are most likely of the same type but with local origins. In fact, both USA Heartland virus- and Japanese SFTSV-infected patients were retrospectively confirmed, and travel by certain patients can be traced back to 2009 for the USA and the summer of 2012 for Japan. Scientists from both countries are now working on several earlier suspected cases. There is no evidence that the patients in the USA or Japan had travelled to China. Therefore, it seems the virus has been in the USA and Japan for some time. The three viruses may not have a common origin but certainly cause similar or even the same symptoms and clinical outcomes.

In China, SFTSV has caused an approximately 12% case fatality rate (CFR), which is an alarming number for this country.[6,11] Retrospective cases in Japan have an even higher CFR, with four deaths out of eight confirmed cases (additional suspected cases still need to be confirmed). The infected areas in China are concentrated in central China, covering six provinces. The major clinical symptoms and signs in the patients from the three countries are the same: high fever, thrombocytopenia, leucopenia, and elevated levels of serum hepatic enzymes. Although this group of viruses is transmitted by ticks, there is evidence in China that person-to-person transmission was highly probable through direct blood contact when the index patients had high viremia.[12–14] Therefore, SFTSV is indeed a dangerous pathogen, and precautionary measures should be implemented in epidemic areas. Although no virus has yet been isolated from ticks, reverse transcription polymerase chain reaction (RT-PCR) tests on tick samples revealed evidence of virus.

To prevent infection and a possible epidemic, a call for vaccine development has been made in China. Scientists from the China CDC are working on this task in collaboration with large pharmaceutical companies. As high-level viremia is observed in acutely infected patients, therapeutic human-origin monoclonal antibodies or even antisera will serve as lifesaving agents that should be developed in the near future. Studies on pathogenesis, tick transmission, and useful animal models should also be pursued. A comparative study of the viruses from China, the USA, and Japan will

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answer many questions about the origins and diversity of these viruses.

Indeed, our war on emerging pathogens may never end.

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