EDITORIALS

H1N1 Influenza A Disease — Information for Health Professionals

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A video is available at NEJM.org

In the first 2 weeks in April, cases of infection with an untypable influenza A virus began to be identified in Mexico and southern California.[1] Although the exact sequence of events is uncertain, by the third week of April it was established that the illness resulted from a triple recombination of human, avian, and swine influenza viruses; the virus has been found to be H1N1. This virologic analysis allowed for the development of a polymerase-chain-reaction (PCR) test to determine whether, in any given person, illness with the protean manifestations of cough, fever, sore throat, diarrhea, and nausea could be confirmed as a case. Armed with this critical tool, clinicians and epidemiologists are able to make case assignments to define and track the outbreak and to determine disease severity.

Health authorities from around the world formulated plans for monitoring and controlling this outbreak. On May 7, 2009, just about a month after the first case of this new H1N1 influenza was recognized, we are publishing articles providing background information about novel recombinant forms of H1N1 influenza causing human disease in the United States and a summary of the outbreak cases reported in the United States as of May 6.

Our goal in publishing these articles is to provide clinical descriptions of patients with the condition so that health professionals can use this information in making the difficult decision about whether an individual patient has a suspected case. This decision will depend on the presence of typical, but unfortunately variable and nonspecific, symptoms; an epidemiologic link to other known suspected or established cases (though this may become less useful as the infection becomes widespread throughout the population); and, where appropriate, a positive identification of the H1N1 virus by the PCR test (see video for the correct method of obtaining a nasal sample). Making informed decisions is important for several reasons. First, credible suspected cases should trigger public health measures such as contact tracing and quarantine — which will benefit the community — and consideration for treatment with neuraminidase inhibitors, which will potentially benefit the individual patient. Obviously, if we assign suspected-case status to more people than belong in this category, we alarm the public and create hardship for many who will turn out to be influenza-negative. If we miss suspected cases and the affected people circulate in the community, the illness will spread more rapidly. Finding the right balance will be difficult, but our efforts should be guided by the data as they emerge. The ability to clearly define a confirmed case will also allow for a careful assessment of the associated illness and its severity.

We now have important tools with which to fight this outbreak: a clear case definition, an aware health care system, and an informed public. We await the availability of a vaccine, which will require several months to prepare.

Although it has been just over a month since the first cases were identified, it seems unlikely that this outbreak will lead to widespread, severe illness and deaths. However, this may be just the first wave, and we will carefully monitor this outbreak. To help in this process, we have established the H1N1 Influenza Center at NEJM.org, which is open and available to all. We will post

original research and other articles, as well as *Journal Watch* summary and commentary on important articles that may appear elsewhere. We have also posted historical pieces from our archive on the "swine flu" epidemic of the 1970s and the 1918 influenza epidemic. The H1N1 Influenza Center will also have links to the most up-to-date news on the outbreak, including material from sources such as the World Health Organization and the Centers for Disease Control and Prevention. One highlight is an interactive map from HealthMap showing the location of confirmed and suspected cases of H1N1 influenza in the United States and around the world (http://healthmap.org/nejm). This map, which uses information from many different sources, will be updated regularly. We hope that the H1N1 Influenza Center will be of value to health professionals as they participate in the control of this outbreak. In addition, we will continue to follow this problem after the current outbreak subsides, since illness may recur in the Southern Hemisphere during the coming winter or again in the Northern Hemisphere when the traditional influenza season returns.

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1. Swine influenza A (H1N1) infection in two children — southern California, March–April 2009. MMWR Morb Mortal Wkly Rep 2009;58:400-2.

Implications of the Emergence of a Novel H1 Influenza Virus

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In this issue of the *Journal*, there are two reports of recent transmissions of swine influenza viruses in humans. One group of viruses, described by Shinde et al.,[1] are triple reassortants of viruses from pigs, humans, and birds, called triple-reassortant swine influenza A (H1) viruses, which have circulated in pigs for more than a decade. The other group, described by the Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team,[2] is a recent reassortant of the triple-reassortant swine influenza A (H1) viruses and a Eurasian swine influenza virus, resulting in the swine-origin influenza A (H1N1) virus (S-OIV), currently being transmitted among humans.

The two groups of viruses behave very differently. Triple-reassortant swine influenza A (H1) viruses are found in pigs and may occasionally be transmitted to humans but have not spread efficiently from human to human. S-OIV, in contrast, is not currently known to be epidemic in pigs (although pigs may be infected by exposure to humans), but it is exhibiting human-to-human transmission and has spread to several countries. Both viruses are H1 hemagglutinin viruses, which appeared in humans and swine in 1918 and have subsequently evolved, in both species, into divergent H1 viruses. The current situation is not "1918 again," it is "1918 continued," in that we are still being infected with remnants of the 1918 pandemic influenza virus.

Most adults have substantial immunity to H1 variants that have circulated among humans from 1918 through 1957 and then again from 1977 through the present. Whether cross-reacting antibodies from previous H1 infections will provide protection against S-OIV is not known, but the epidemiologic features of the current S-OIV infections suggest that there may be partial protection from multiple previous influenza infections. The age range of the 642 patients with confirmed cases of S-OIV infection was 3 months to 81 years, but 60% were 18 years of age or younger. This age distribution is typical for seasonal influenza; schoolchildren are the group with the highest rates of influenza, and they spread the virus to household contacts.[3] The clinical manifestations of S-OIV also were typical of seasonal influenza, with fever in 94% of patients, cough in 92%, and sore throat in 66%; in addition, however, vomiting (found in 25%) or diarrhea (found in 25%) was common. A total of 36 patients were hospitalized; of the 22 hospitalized patients for whom data were available, several had risk factors: young age (4 patients) or chronic medical conditions (9 patients) or both, or pregnancy (1 patient). The two deaths occurred in a 22-month-old child with chronic medical conditions and a 33-year-old woman who was pregnant. Several hospitalized patients had evidence of pneumonia on radiography, and some had secondary complications. The spectrum of illnesses seems very much like those of seasonal influenza.

Many questions remain. Will S-OIV virus replace the human H1 virus as the seasonal influ-