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■ EDITORIAL ■

# Novel Influenza A (H1N1): Where Are We?

In late March and early April, 2009, an outbreak of H1N1 influenza A virus infection was detected in Mexico, with subsequent cases observed in several other countries including the United States (1, 2). Though limited information was available on the early pre-pandemic situation in Mexico, subsequent cases in the U.S. and Canada had a common travel history of returning from Mexico, the epicenter of the current outbreak. After that, however, secondary cases without a travel history developed in the U.S. and Canada, which spread to the United Kingdom and Spain over several weeks with increasing local community-wide transmission. As the days go by, the number of infected patients and countries with laboratory-confirmed cases is increasing. As of May 19, 2009, there have been over 9,830 laboratory-confirmed cases in 40 countries (3).

## Characteristics of Novel A/H1N1

Current novel A/H1N1 virus has been found to contain a unique combination of genes from pig, bird, and human flu viruses. This peculiar recombinant influenza virus is entirely new, and has not been seen before elsewhere (3). This creates an almost universal vulnerability to infection in nearly all people. Therefore, the emergence of novel A/H1N1 infection among humans presents the greatest pandemic threat since the 1968 pandemic caused by A/H3N2 (4). The current pandemic alert level still remains at phase 5-just one level short of a full pandemic. However, considering the situation in Japan and other countries these days, raising the pandemic level to 6 is imminent.

Given that novel A/H1N1 influenza viruses nearly met the three prerequisites for pandemic; emergence of a novel virus with little or no pre-existing immunity in the world's population, the potential to infect humans causing clinically apparent illness, and efficient transmissibility from one human to another. Therefore, it may be quite difficult to predict how the pandemic situation will evolve as time goes on.

## Vulnerable populations

That 60% of patients were 18 yr of age or younger suggests that children and young adults have a higher susceptibilty to novel A/H1N1 infection than elderly groups. Likewise, in the early periods of the previous pandemics, young adults were more likely to acquire A/H1N1 infection through frequent social activities. In turn, there is a concern that those infected young adults transmit the influenza virus to elderly of local communities. On the other hand, it is also possible that elderly may show partial protectivity against novel A/H1N1 influenza with preexisting antibodies, as proposed by 1976 swine influenza vaccine studies (5, 6). There is a possibility of bias in case-diagnosis may also exist, with more of the young people being tested as part of outbreaks in schools (7) and fewer of the elderly persons being tested for influenza. However, the epidemic is evolving rapidly and spreading worldwide, and the number of confirmed cases is an underestimate of the number of cases that have really occurred.

## Clinical features

To date, most confirmed cases of novel A/H1N1 influenza have been characterized by mild influenza like illness (fever, chills, headache, upper respiratory infection symptoms, myalgias, arthralgias and fatigue) similar to those of typical seasonal influenza; the incubation period is known to range from 2 to 7 days. Gastrointestinal symptoms such as vomiting and diarrhea have also been common (38%), both of which are atypical of seasonal influenza (8). However, we should pay attention to certain groups, such as infants, elderly persons, and immunocompromised hosts, because they may present atypical clinical manifestations. Although the full range of complications of current A/H1N1 influenza is not yet known, it seems to be similar to that of seasonal typical influenza: respiratory complications and exacerbation of underlying chronic medical conditions. Several cases of respiratory failure due to rapidly progressive pneumonia have been reported in Mexico (9). In comparison, according to U.S. data, most described infected patients have been mild, 36 (9%) required hospitalization and a 6% (2/36) death rate was observed among hospitalized patients (8). Among 22 hospitalized U.S. patients with available data, >50% of complicated cases have risk factors for influenza complications (8). Young children (e.g., <5 yr of age), pregnant women, and people with comorbidities are at increased risk of influenza complications.

## Mortality

There have been 79 deaths over 9,830 laboratory-confirmed

novel A/H1N1 cases, and overall mortality is 0.8% so far (2). This rate is not much higher than seasonal influenza mortality. In Mexico, 72 of 3,648 laboratory-confirmed cases of A/H1N1 influenza have been fatal (2). Most of these deaths were related to respiratory failure. Among 5,123 cases in the United States, there have been five deaths (8). Among 496 cases in Canada, one patient has died, while one patient has died among nine cases in Costa Rica (2). All of the deaths except in Mexico occurred in persons with chronic health problems (3, 8), and one death in a pregnant woman was observed (10).

## Antivirals for novel A/H1N1

Novel H1N1 viruses isolated from patients in Mexico and the United States have shown that those viruses are sensitive to neuraminidase inhibitors, but resistant to the adamantanes (11). However, considering current clinical features of novel A/H1N1 infection, treatment with neuraminidase inhibitor may not be absolutely indicated for all cases of infection. Antiviral treatment is recommended for all hospitalized patients with confirmed, probable, or suspected novel H1N1 influenza, and patients who are at higher risk for seasonal influenza complications. Furthermore, in the use of antiviral drugs for prophylactic purposes, judicious decisions are necessary according to national pandemic influenza preparedness plans.

## Perspective

Many questions still remain unresolved. Will novel A/H1N1 virus replace the human A/H1N1 virus as the seasonal influenza virus this year? Will the virus reassort with A/H3N2 or A/H5N1 influenza virus to make another variant? When will a new vaccine be available?

Most of all, we should note that the novel A/H1N1 influenza viruses were rapidly transmitted across the continents to multiple countries within merely one month of time. Of note is the fact that the viruses are still spreading; therefore they may not easily eradicable soon. Though the novel A/H1N1 influenza viruses have shown low virulence so far, there is a chance that they might become better adapted to humans and become more drastic, causing a large second wave of influenza during this fall-winter season in the Northern hemisphere with higher mortality. At this time, without available vaccine seed virus, there is no consensus on how much A/novel H1N1 virus vaccine we should plan to produce. We do not know if this vaccine will be effective for the A/H1N1 mutant of next season. Moreover, no one knows what detrimental effects a subsequent shortage of seasonal influenza vaccine will have.

In conclusion, we stand enveloped in a heavy cloud now. We should prepare for the upcoming second wave, waiting until the clouds are cleared away. The potential damage varies according to the degree of pandemic preparedness; thus, such damage may be more serious in socio-economically deficient countries. In addition to maximal preparedness in each country, worldwide collaboration is required.

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