The New Influenza A (H1N1) Pandemic

Rienk E. Jeeninga,* Menno D. de Jong, Ben Berkhout

Introduction

The latest World Health Organization (WHO) figures (June 17, 2009) show that 88 countries have officially reported 39,620 cases of influenza A (H1N1) infection, including 167 deaths. The rapid worldwide spread and the apparent lack of preexisting immunity in humans qualify this as a pandemic virus. The identification of this novel virus in the beginning of April 2009 and subsequent international screening programs have demonstrated that the virus is able to spread from human to human. These data are sufficient to state that we are currently experiencing an influenza pandemic. WHO raised the pandemic influenza alert to phase 6 on June 10, 2009.

2009 H1N1 Virus

The last influenza pandemic was in 1968; H1N1 is therefore the first opportunity to study a pandemic outbreak in real time with all the modern analytical methods that have been developed in recent decades. Indeed, data have been generated with astonishing rapidity. Full-length viral genome sequences from around the world have been published in public-access databases. The internet has been extensively used to keep track of the spread of the virus. Large community efforts have been made to restrict the spread of the virus right from the start of the pandemic. In this issue of the Journal of the Formosan Medical Association, Chang et al present one of the first reviews about this novel virus. The 2009 H1N1 virus is currently presenting itself as a relatively mild form of influenza, with common symptoms such as cough, sore throat, and headache. A characteristic of the 2009 H1N1 infection is the frequent occurrence of diarrhea and vomiting, which is unusual for seasonal influenza. Also, present data seem to show that younger people are more susceptible to infection. However, more data are needed to determine the cause of this, as it may very well be the result of a bias in sampling or a bias in the spread of the virus among the human population. An initial study reported that hospitalization was needed in almost 10% of cases, and the mortality rate was about 0.4%. Based on the officially reported cases, the current mortality rate is approximately 0.4%. Because of the mild pathogenicity, most infected persons will not be reported, and therefore these numbers are certainly a huge overestimation. One possible exception, reported by WHO on June 10, 2009, is that the infection might be more severe in some isolated groups of the Inuit population in Canada. Obviously, more surveys and further analysis are needed to determine the underlying mechanisms.

Surprising Sequence Data

Sequence data for the new virus became quickly available in public-access databases and showed remarkable characteristics. The H1N1 virus has
a genome derived mostly from North American swine influenza A, but with the NA and M proteins from the Eurasian swine lineage. This particular organization is unique and is especially interesting since it combines a Eurasian and American line. This combination has not been found previously in pigs, only in humans and a small isolated swine herd in Alberta that was likely to have been infected by humans. However, Smith et al very recently demonstrated that it is likely that the virus has been in pigs for several years. Fortunately, the current spread in humans has been detected relatively early, indicating that the surveillance of the human population is adequate to pick up pandemic influenza.

Another surprise from the sequence data is that the virus seems unusually stable in terms of genome evolution. In the context of vaccine development, this is obviously good news. The currently produced vaccines are based on the original viruses and are therefore more likely to be effective. However, it is not clear what this means for the virus-host interaction. It is still possible that this is merely a founder effect. Similar viral sequences from around the world do not mean a lot if it requires only one airplane to transport the virus to another location. But, if this lack of viral evolution remains during the pandemic, then there is apparently little selection pressure on the H1N1 virus to change. This may be related to the limited preexisting immunity. People are infected by this virus, and before the host can mount an appropriate immune response, the virus has propagated sufficiently to reach high enough viral loads to facilitate transmission and spreading in the population. This is in contrast to seasonal influenza, which needs to escape from preexisting immunity in the host.

In this respect, it is interesting that the virus has truncated versions of PB1-F2 and NS1 (see the review of Chang et al for more details). These two proteins are associated with high virulence because of their suppressive effect on the host immune system. The PB1-F2 protein has been shown to specifically target and destroy alveolar macrophages (reviewed by Coleman); the NS1 protein inhibits type 1 interferon production, and may play a role in the suppression of innate immunity by acting as an RNAi suppressor.

### 2009 Influenza A H1N1 and Avian H5N1

With all the focus on the new H1N1 virus, we should not forget about the highly pathogenic influenza A H5N1 virus. The H5N1 picture is quite different from that of H1N1. The avian influenza (H5N1) virus incidentally infects humans but with high mortality. Fortunately, the H5N1 virus has not developed into a variant that can spread from human to human. However, with the worldwide spread and high infection rate of H1N1, the risk exists of reassortment between the H5N1 and H1N1 viruses, which could result in a deadly and infectious virus. An alternative and perhaps more likely reassortment between the pandemic and seasonal H1N1 viruses is another worrying possibility, as the current seasonal H1N1 virus is resistant to oseltamivir (reviewed by the Novel Swine-Origin Influenza A (H1N1) Virus investigation Team). The new 2009 influenza A (H1N1) virus is already resistant to adamantane and a novel reassortment virus could be multidrug-resistant.

In conclusion, we are currently in a phase 6 pandemic with a novel, relatively mild influenza virus (H1N1). Although we have not been able to stop this pandemic, worldwide efforts have resulted in the rapid identification and characterization of the virus. Continual monitoring and surveillance of the H1N1 virus is required to enable us to respond to any change in the virus that could influence its pathogenicity, resistance to antiviral drugs, or sensitivity to the vaccines that are currently being developed.

### References


