

## Influenza at the beginning of the 21st century

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As if nature had intentionally paved the way, the first influenza pandemic of the 21st century was preceded by two disease outbreaks of global importance: highly pathogenic avian influenza (HPAI) H5N1 virus infection appeared in humans in 1997 and was followed in 2003 by severe acute respiratory syndrome (SARS). In 2004, HPAI re-emerged and spread west from south-eastern Asia until it reached Europe and Africa in 2005. The clinical syndromes caused by these viruses were severe enough to trigger pandemic and epidemic preparedness efforts by the global public health community.

Heightened political interest has led to substantial investment in influenza surveillance and response activities, particularly the expansion of laboratory surveillance to nearly all parts of the world. The National Influenza Centres of the Global Influenza Surveillance and Response System (GISRS), which exist in 106 of the 193 Member States of the World Health Organization (WHO),<sup>1</sup> diagnose influenza and report influenza activity to the GISRS. This enables WHO to map the circulation of influenza viruses and to select the best viruses for the production of seasonal and pandemic influenza vaccines.

The impact of influenza on society has been amply studied in high-income economies, where seasonal influenza vaccination policy seeks to protect high-risk groups from the complications of severe disease. However, how influenza viruses behave in tropical climates and how people living in lower-income countries with complex health problems are affected by influenza need further exploration. Efforts to probe these questions have been made, as shown by Steffen et al. in this issue,<sup>2</sup> and studies by researchers like Feikin et al.<sup>3</sup> and Homaira et al.,<sup>4</sup> also in this issue, have contributed important new data. It is encouraging that more and more influenza research is being carried out in countries that cover a broad geographical and economic spectrum.

The polymerase chain reaction (PCR), a laboratory diagnostic method

with high sensitivity and specificity, is the technology behind these studies. The technique makes it possible to identify the etiologic agent causing influenza-like illness, including influenza viruses, in an extremely short time. This and other advanced technologies have resulted in the development of rapid on-site diagnostic systems that will greatly contribute to the clinical management of severe acute respiratory infections and epidemic control.

Two major pharmaceutical interventions for influenza control and prevention are currently in use: vaccination and antiviral treatment. Neither is perfect. Influenza vaccines, which have been in use a long time, are safe but need to be administered annually and their immunogenicity in high-risk groups, such as very young children, the elderly and severely immunocompromised patients, is lower than in the rest of the population.<sup>5,6</sup> Antiviral drugs are in very limited supply and the choices are few, a clear disadvantage if drug resistance develops. Furthermore, their effectiveness when initiated late in severely ill patients has not been clearly established.<sup>7</sup> The effectiveness of vaccines and antivirals against influenza B viruses has been less clearly established than their effectiveness against A viruses.<sup>8</sup> Studies published recently, including one in this issue by Feng et al.,<sup>9</sup> highlight the importance of influenza B virus infection in severe influenza disease.<sup>10</sup>

Because of the aforementioned limitations and the shortage of resources in some settings, influenza control has to often rely on or be backed up by non-pharmaceutical interventions and syndromic case management of severe acute respiratory infection (SARI). In this issue, Bolton et al.<sup>11</sup> and Cohen et al.<sup>12</sup> propose potential approaches to influenza control. Improved diagnostic technologies have shown that influenza is a much more important component of SARI than formerly thought, although to different degrees from year to year.<sup>13</sup> Integrated pneumonia prevention and treatment interventions are clearly the way forward.

The world has just experienced the century's first influenza pandemic. The two outstanding characteristics of the 2009 A(H1N1) influenza pandemic were its ability to cause major out-of-season epidemics in temperate countries and to cause unusually severe disease and death among the young and in healthy people. It was the first influenza pandemic for which both antiviral drugs and vaccines were deployed and for which national pandemic preparedness plans were put in effect in developed countries and many lower-income countries. Nonetheless, it is thought that the pandemic has claimed hundreds of thousands of lives in one year. When compared with the death toll during an average influenza year, this figure may seem insignificant, yet the years of life lost in the pandemic were higher, considering that during normal influenza season at least 90% of deaths occur in people over 65 years of age.<sup>14</sup>

Several years are expected to transpire before the 2009 influenza pandemic virus acquires the full characteristics of a seasonal influenza virus. In 2010, the global response to the A(H1N1) pandemic was assessed by the International Health Regulations Review Committee, an external body of experts with a broad mix of scientific expertise and practical experience in public health. In its final report, the Committee recommended that WHO amend its pandemic preparedness guidance to include measures for assessing disease severity.<sup>15</sup>

The challenge ahead is to ensure the resources and momentum needed to continue the important work under way in spite of the current global economic recession. Integrating international efforts to reduce pneumonia mortality, increasing global capacity to respond to health emergencies and improving basic health systems can help us overcome the challenge. ■

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