

The end of the pandemic – what will be the pattern of influenza in the 2010-11 European winter and beyond?

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On 10 August 2010 Margaret Chan, the Director-General of the World Health Organization (WHO), announced that the world has moved into the post-pandemic period [1]. Following the advice of the Emergency Committee, which based its assessment on the global situation, WHO declared that there has been a pandemic phase change and that the WHO post-pandemic definition, 'Levels of influenza activity have returned to the levels seen for inter-pandemic influenza in most countries with adequate surveillance', has been met [2]. In order to come to this conclusion it has been important to observe the pattern of influenza in the southern hemisphere temperate countries which are now experiencing their winter. What does this mean for the 2010-11 winter in Europe and winters beyond?

Current influenza activity in the southern hemisphere temperate countries

In their 2010 winter, the five southern hemisphere countries with ongoing surveillance (Argentina, Australia, Chile, New Zealand and South Africa) have experienced levels of influenza-like illness (ILI) or acute respiratory infection (ARI) that are considerably lower than those of the 2009 winter. In these countries the level of illness is looking more like inter-pandemic influenza than the pandemic levels seen in the winter of 2009 [3,4], as documented in a special issue by Eurosurveillance [5]. In 2010 in Chile there have been more cases of acute ARI in children but this is attributable to epidemics of respiratory syncytial virus infections (RSV) rather than influenza [3]. This emphasises the importance of countries being able to test for a suite of respiratory pathogens, not just influenza. In the equatorial countries, the combined epidemiological and virological surveillance needed for routine influenza surveillance was uncommon until the 2009 pandemic. Hence whether what is being seen in 2010 is normal for inter-pandemic influenza is unclear as there are simply no baseline data in many countries. However, in the locations that have consistently delivered good quality surveillance data for a wide range of respiratory pathogens, such as Singapore and southern China, the epidemics of 2010 have shown levels that are more similar to those of 2008 and not that of the 2009 pandemic [4]. Virologically the

2010 southern hemisphere winter epidemics have been mixed: New Zealand has been dominated by pandemic A(H1N1) viruses while Australia, Argentina and Chile have seen more of a mix of the pandemic A(H1N1), A(H3N2) and some B viruses [3,4]. Exceptional among the five, South Africa has experienced A(H3N2) and B viruses with few pandemic viruses resembling the situation reported from eastern Africa [4]. Indeed, it can be seen now that even in the pandemic winter of 2009 the A(H3N2) and B viruses never entirely disappeared in the southern hemisphere [6]. The viruses that are now missing everywhere are the previous inter-pandemic A(H1N1) viruses, whether oseltamivir resistant or not [7]: they have been displaced by the pandemic A(H1N1) virus [4,7]. Thus the WHO recommendation to have trivalent vaccines composed of a pandemic A(H1N1)-like virus, an A(H3N2)-like virus and a B virus for the northern and southern hemisphere seasonal vaccines for 2010 and 2010–11, respectively, is very reasonable [8].

Influenza during the 2010–11 winter in Europe – what is to come ?

Influenza in Europe has been at very low levels in 2010 after the end of the autumn–winter waves of the 2009–10 influenza A(H1N1) pandemic [9]. However, pandemic phases are global, not regional and the activity of influenza in the spring and summer has little predictive value for the subsequent winter. Some observations can be made based on the forward look risk assessment of the European Centre for Disease Prevention and Control (ECDC) and the data that has come forth subsequently which were recently reviewed by an ECDC convened expert group [10]. To date, it seems increasingly unlikely that the 2009-10 pandemic will follow the pattern of the last (1968) pandemic in Europe when transmissibility increased for the second winter [11]. There are two important differences between now and then. First, many people in their late fifties and older currently have natural immunity from exposure to a similar earlier influenza A(H1N1) virus circulating before the 1957 pandemic [12]. Second, there have been unprecedented influenza vaccination campaigns in some European countries, increasing the population protected beyond those who acquired natural

immunity when they became ill during the pandemic [13]. It may also be that in the 2009 pandemic the proportion of asymptomatic or very mild infections was exceptionally high as suggested by some serological surveys, notably the one from New Zealand. However that is speculation as there are few serological data from earlier pandemics [14]. It would therefore seem probable that the European 2010-11 winter epidemic will be similar in its levels to the current epidemics in the southern hemisphere - inter-pandemic influenza with a mix of the 2009 pandemic A(H1N1), A(H3N2) and B viruses [3,4]. However those predictions will need to be checked and confirmed or refuted. This can only be done by networks of laboratories at local, national and international level so that new virus variants can be detected in a timely manner [7, 15].

Beyond that further predictions on the pattern of infection and disease and for subsequent winters would be unwise. What happens in each pandemic changes the composition of the circulating inter-pandemic influenza A viruses, either entirely replacing the previous influenza A viruses or at least introducing a vigorous new competitor [16]. So essentially there is now a 'new' inter-pandemic influenza – a new mix of circulating influenza A and B viruses which may change the pattern of infection, perhaps introducing some features of the 2009 pandemic which differed from the preceding seasonal pattern such as the higher rate of mortality in younger age-groups and the unusual appearance of cases of severe acute respiratory distress syndrome (ARDS) even in healthy adults [17,18]. Many of the previous assumptions and knowledge will need to be revisited and re-evaluated, notably on risk groups for severe course or outcome of infection, on other groups to be offered vaccination and on the effectiveness of antiviral drugs and vaccines. Evidence from the most recent (1970–2008) inter-pandemic influenza mixes provides reasonable information for now but that cannot be entirely relied upon. New evidence will need to be sought scientifically, mostly using observational approaches. For example ECDC-coordinated studies (among others) have found that the 2009-10 pandemic vaccines were effective against the pandemic strain but field effectiveness of the new trivalent seasonal vaccines will need to be monitored regularly [19, 20].

It should not be assumed that the new inter-pandemic influenza will be worse than its predecessor. It could be milder and/or affect different groups, for example continuing to affect pregnant women as the 2009 pandemic did [17]. It is the nature of influenza viruses that they constantly change. Some may adapt to humans to transmit more efficiently and perhaps also become more benign, but drift variants will also appear that may be more pathogenic, as were the variant A(H3N2) viruses that emerged in the 1990s [15]. Risk groups will need to be re-evaluated and ECDC will provide scientific analyses to support those who have to make recommendations in Europe [21,22]. While it is to be hoped that the cases of lethal acute respiratory distress

syndrome (ARDS) that characterised the pandemic A(H1N1) will become very rare, that cannot be guaranteed [16]. If cases of ARDS still occur among fit, healthy younger people that may change thinking about inter-pandemic influenza and the case for who to vaccinate. Equally it may be that the 2009 pandemic A(H1N1) virus may add resistance to neuraminidase inhibitors to its existing adamantane (i.e. amantadine and rimantadine) resistance as its predecessor did in 2007–8 [4,7]. The Ministers of European Union (EU) and European Economic Area Member States have committed to improving the use of seasonal vaccines, and to learning from the many evaluations of the response to the 2009 pandemic [22-24]. Finally, an article by the French public health institute recently published in this journal reminded us that A(H5N1) has not gone away [25]. The main message from ECDC is ensure an appropriate surveillance and analysis capacity for health threats, both during and in between the emergencies, and also ensure immediate sharing of information through the relevant structures. Hence the recent EU Presidency conclusion from the informal Employment, Social Policy, Health and Consumer Affairs Council Health Council (EPSCO) to not just learn from the 2009 pandemic but to strengthen defences for one worse than the 2009 pandemic, and other threats, would be seen to be of the utmost importance [23]. In order to achieve the target that EPSCO set out, it is crucial to safeguard adequate resources and continued support to National Public Health Institutes and networks which are key in ensuring that measures are in place for all threats not just influenza.

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