Influenza news from the frontline: what's happening?

Anita K. Simonds

Royal Brompton and Harefield NHS Foundation Trust, London, UK.

Correspondence: Anita K. Simonds, Royal Brompton and Harefield NHS Foundation Trust, London SW3 6NP, UK. E-mail: A.Simonds@rbht.nhs.uk

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Three times more people dying from flu in UK than last winter

The Guardian; January 25, 2018 [1]

Flu patients arrive in droves, and a hospital rolls out the "Surge tent"

The New York Times; February 2, 2018 [2]

French health chiefs on alert as Paris region hit by flu epidemic

The Local; December 14, 2017 [3]

Flu epidemic rages in Japan with record-high cases in one week reported

Kyodo News; January 26, 2018 [4]

Throughout December 2017 and January/February 2018, there have been widespread alarming media reports of escalating cases of seasonal influenza. Yet, the European Union research initiative PREPARE (the Platform for Preparedness Against (Re-)Emerging Epidemics), which monitors the response to outbreaks, reports that the current influenza threat to Europe is limited and concludes that based on available information, there is no evidence for an overall increase in severity in this flu season compared to previous years [5]. Is that the case globally, and how can we reconcile these views, including the personal experiences of frontline respiratory teams managing high numbers of cases?

There is no doubt seasonal flu cases in the temperate zone of the northern hemisphere have increased rapidly this season from December 2017 onwards. European Centre for Disease Prevention and Control surveillance data published in Flu News (February 2, 2018 [6]) show that of individuals sampled presenting with an influenza-like illness (ILI) or acute respiratory infection to reference (sentinel) sites, ~52% tested positive for influenza.

In January 2018, there was a high intensity of influenza cases recorded in Italy, Switzerland, Iceland, Ireland and Wales, and medium intensity in the UK, France, Spain and Germany. In North America, the World Health Organization reports that virus activity remains high, with rising cases of ILI and outpatient visits for ILI at virtually the highest level since a previous peak in 2011 [7].

Worldwide this season, influenza A predominates (62%). In the European Union overall, a higher than usual proportion of type B virus compared to type A viruses has been detected in sentinel sources. The

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type B/Yamagata lineage virus has greatly outnumbered the B/Victoria lineage. For influenza A, A(H1N1) isolation outnumbers A(H3N2) from sentinel sources. The majority of severe cases in Europe are in adults affected by A(H1N1) and type B virus. Predominance, however, varies from country to country: in France, A(H1N1) and B virus are most common, but in the UK, A(H3N2) and B Yamagata predominate. In Canada and the USA, adults aged ⩾65 years account for majority of cases, with A(H3N2) the dominant virus. In northern Africa, detection of B virus is high in Egypt, with A(H1N1) in Morocco, Algeria and Tunisia. Particular hotspots for influenza B include London, UK.

So is this flu season any different? Our advance warning comes from Australia and the Southern hemisphere where the flu season precedes that in the north. Here, the 2017 influenza season was the worst since the 2009 A(H1N1) pandemic year [8]. It is important to note that a pandemic occurs when a *new* virus strain arises and spreads across several continents. The current episode we are experiencing is not a pandemic as circulating viral strains are seasonal, and not new. An epidemic is defined by activity that exceeds usual expected activity. So what we are seeing is activity at the severe end of the expected spectrum (and probably epidemic in some regions), though the extent of increased activity is not well clarified, and undoubtedly, surveillance techniques are improving, resulting in increased case detection.

While labelled "Aussie flu", the influenza A(H3N2) virus that predominated in Australia probably originated in east-southeast Asia. Flu strains tend to move globally from east to west. The Australian 2017 seasonal peak was longer than usual, with activity higher on the eastern seaboard and in the south rather than in Western Australia [8]. It had a major impact on staff absenteeism with significant pressures placed on hospitals and primary care. General practice consultations for ILI were higher than the 5-year average but did not exceed 2009 levels. Deaths were mainly in the elderly but the severity of infection in all those admitted to hospital was towards the low end of the expected range, and admissions to intensive care units and overall mortality were consistent with previous years. Influenza B occurred in 37% of confirmed cases, with a greater frequency in school-age children. The effectiveness of the 2017 vaccine against presentations to primary care was relatively low, at 33%, and lower still against hospitalisation (16%) [8].

This picture seen in Australia turned out to be not too different from that then experienced in the northern hemisphere this winter, with some national variations such as differences between prevalence of A(H1N1) and A(H3N2), as indicated above. There are some new features, including a more rapid climb in B strains seen earlier in the season. What is clear is that even when cases are at the severe end of the normal spectrum, this is likely to put a severe strain on healthcare systems that, in winter, are usually already functioning near full capacity. The situation is exacerbated by flu infections among healthcare staff. Influenza becomes the final straw and precipitates the alarmist media reports.

Hand washing and measures to prevent viral spread are unexciting and make poor news copy, but remain key. Vaccines are the best line of prevention and although they do not give full protection, they should be offered as long as influenza is circulating. Further interim data on vaccine effectiveness from Canada [9] suggest a relatively low efficiency (<20%) against A(H3N2) and ~55% against flu B (indicating cross B lineage protection). The quadrivalent vaccination given to children in England, UK, offers better protection to virus B compared to the trivalent vaccine given to adults. These efficacy reports may contribute to reduced uptake of vaccination by healthcare staff. Vaccination of healthcare teams should be encouraged, however, and there is some evidence of improved uptake this year. Reassuringly, there are no reports of resistance of circulating strains to oseltamivir and zanamivir [6].

It is now 100 years since the 1918 "Spanish Flu" pandemic. We are better able to prevent and manage seasonal flu, but healthcare systems are stressed by relatively small seasonal surges of cases (let alone a pandemic). The holy grail of a universal influenza vaccine that would protect against all strains is perhaps closer, as trials are underway, but the likelihood of success against continually evolving strains is unclear. And as Anthony Fauci, director of the US National Institute of Allergy and Infectious Diseases, has noted, we need to move away from production of vaccine in eggs (CNN report; February 3, 2018 [10]). Molecular biological techniques may allow vaccine manufacture on a far greater scale.

On a positive note, the PREPARE project includes ongoing trials on the efficacy of oseltamivir in primary care [11], pathology studies identifying genotypes and high-risk cases [12], and an adaptive platform design trial of intensive care unit management of pneumonia [13], and much further research is in progress. In the meantime, although seasonal cases will inevitably fall as spring approaches, it is evident that influenza remains a major challenge for our current century.

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