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Impact of the 2009 influenza pandemic

J Dunning, P J M Openshaw

A GENERALLY MILD DISEASE THAT SOMETIMES KILLED

One year on from the start of the 21st century's first influenza pandemic, it is a good time to take stock of how the outbreak evolved and what has been learned. Although we now know that many infections were mild or inapparent, it is important not to forget the severe disease that it sometimes caused, and may still cause, in future winters.

During April 2009, reports from Mexico provided a worrying picture of unusually severe influenza in large numbers of healthy people including healthcare workers.[1] The impact on hospitals was particularly marked with up to one in four specialist beds being occupied by patients with influenza, often needing highly specialised care and mechanical ventilation. Medical resources were exceeded by demand, and elective admissions and surgery halted; transmission to staff and to other patients was common, placing specialised nursing care, consumables, ventilators, drugs and containment facilities under great pressure.

Once cases began to appear in UK schools in May 2009, an intensive cooperative campaign of quarantine and antiviral prophylaxis was mounted by the Heath Protection Agency, the Department of Health and the NHS. Antiviral drugs have not been used in this way in previous pandemics; although it was unlikely that the spread of influenza could be halted, it was important to gather information about the pattern and severity of disease and to slow the spread, buying time for vaccine development and capacity building. Despite the public health campaign, the numbers of cases increased in London and the West Midlands, putting considerable strain on primary care. By 2 July, case numbers were rising sharply in most parts of the UK and containment measures no longer seemed appropriate. Routine antiviral prophylaxis was discontinued and a telephone helpline was launched on 23 July.[2] Call centres took a history according to defined algorithms and authorised antiviral treatment for those with appropriate symptoms. Case numbers declined rapidly soon after schools broke up for the summer holidays in late July, with a second autumn wave occurring after children returned to school in September.

The impact of the outbreak on hospitals was considerable. Pandemic (H1N1) 2009 Influenza (pH1N1) spread predominantly among children and young adults, causing severe disease in some vulnerable adults (particularly patients with asthma, those with various chronic illnesses and pregnant women). In the first week of November there were approximately 850 patients hospitalised with confirmed pH1N1, 20% of whom required critical care. The worst recent daily estimate was at the height of the second wave (4 November) with 172 patients hospitalised in critical care and 848 patients hospitalised overall. Provisional data from a retrospective analysis of hospital admissions in the UK indicated that influenza-associated bed-days increased from 4163 in 2008 to 33 376 in 2009, about a sevenfold rise. In those aged 17–39 years of age the increase was from 169 to 6253 in the October to December period, an extraordinary 37-fold increase.[3] Fortunately, the number of confirmed UK deaths remains at 474, which is fewer than feared.[4]

The report by Fajardo-Dolci *et al* in this issue of *Thorax* describes the characteristics of the first 100 consecutive fatalities due to pH1N1 during Mexico's first wave of the pandemic (***see page 505***).[5] This is a particularly important study since it describes influenza-related deaths occurring close to the source of the pH1N1 outbreak, presumed to be in southern USA or Mexico. This study highlights several important features about pH1N1-related deaths that generally mirror those seen elsewhere across the globe.[6–8] Although the Mexican deaths were often in previously healthy people, metabolic syndrome, cardiovascular disease and chronic respiratory disease were identified as risk factors associated with high mortality. Obesity seems to be an important risk factor for hospital admission, but not necessarily for death.[9]

Although the relative contribution of individual at-risk groups appears to vary from country to country, the overall message so far appears to be that, when pH1N1 does kill, the majority who die are young to middle-aged adults with comorbidities, although 10–20% of those who died were previously healthy. pH1N1 tended to cause viral pneumonitis and acute lung injury, but antibiotic use was frequent in Mexico (as it was in many other countries). While sometimes complicated by bacterial pneumonia, confirmation of bacterial coinfection prior to death remains significantly lower than that described in the limited post-mortem series, although this may reflect how bacterial coinfection is both investigated and defined.[10–12]

It is also notable that almost 60% of cases described by Fajardo-Dolci *et al* received steroids, although it is not clear how many received high-dose corticosteroids, how many received steroids for adrenal support in sepsis and what proportion required continuation of pre-existing steroid treatment. The role of steroids in both the pathogenesis and potential treatment of viral pneumonitis remains unclear, but many authorities advise against routine use of high-dose steroids in viral pneumonitis based on experience with the management of SARS and H5N1 infection.[13]

Notably, Fajardo-Dolci *et al* reported that >80% of patients developed symptoms before a national influenza alert was issued. Local populations and healthcare providers may not therefore have been in

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a position to facilitate an optimal response to the emerging infection. Furthermore, only 56% had access to neuraminidase inhibitors, agents which have increasingly been shown to be useful in treating severe pH1N1 disease and appear to reduce the requirement for increasing levels of medical care when initiated early.[14 15]

In the UK almost one-third of the 474 so far confirmed deaths were in those with minimal or no underlying health problems.[4] The US Center for Disease Control and Prevention estimates that 60 million Americans have been infected to date and that 12,000 deaths have occurred, 11,000 of which were thought to be in those aged <65 years.[16] Since it is likely that pH1N1 will return later this year in the Northern Hemisphere, and many Southern Hemisphere countries anxiously await their expected second waves, missing the opportunity to protect at least those who have been identified as being at high risk of complications and death is unacceptable, especially when safe and efficacious vaccines are available. Vaccine uptake remains low in many countries for a variety of reasons, and it is important for clinicians to take note of evidence from published series to provide leadership and advice to prevent resurgence and to optimise the management of those needing medical care for the uncommon but serious and medically challenging complications of pH1N1.

We are unlikely to have accurate estimates of the true impact of pH1N1 on morbidity and mortality for some time to come. A detailed analysis of trends in records of hospital admission and death will allow more direct comparisons with previous estimates of the impact of seasonal influenza, an illness that almost exclusively hospitalises and kills those of advanced age. Seasonal influenza rarely causes overt viral pneumonitis and acute lung injury in children or in adults. It is important to take such variations in pattern of disease and demographic factors into account when planning future vaccination campaigns and the provision of hospital services.

Although it is fortunate that this pandemic strain did not match the reasonable worst case scenarios that had to be planned for propagating the erroneous message that pH1N1 is 'no worse than seasonal flu' could result in a false sense of security and have a negative effect on planning and response for future pandemic threats. Putting appropriate plans in place is vital but inevitably difficult, given the unpredictability of novel infectious diseases. In addition, communicating risk and uncertainty to non-specialists is a hard task.

While influenza activity in January and February 2010 was lower than in some other years, it is clearly premature to say that pH1N1 has been defeated. In recent weeks the south-eastern region of the USA has seen a gradual but sustained increase in pH1N1 activity, including a recent rise in adult influenza hospitalisations in several states within this region. Although vaccine uptake was relatively low in the south-eastern region, other states which had similar rates of symptomatic pH1N1 during the second wave but higher vaccination rates are not seeing the current increase in case numbers. Although the significance of this report is unclear, the US Center for Disease Control is maintaining active surveillance in anticipation of a possible third wave and encouraging continued vaccination uptake.[16 17]

UK seroprevalence and vaccine uptake data suggest that immunity against evolving H1N1 strains varies widely in different locales and age groups, leaving many (including those without comorbidities) at risk of future infection.[18] Why different population groups and regions had such variable rates of vaccination, infection and severe disease remains an important unsolved puzzle.

Although past performance is not predictive of future behaviour, it is possible that in the coming winter we will again see severe pH1N1 influenza disease in pregnant women, in children and in healthy (or near-healthy) adults. While interpretation of news from countries affected early in a pandemic needs to be cautious, failure to respond with those countermeasures available to us when novel strains of pandemic influenza emerge in the future will put the lives of our patients—and our families—at risk.

Competing interests PJMO has advised the Department of Health as a member of the Scientific Pandemic Influenza panel (SPI) since 2006 and is a member of the Clinical Countermeasures Subgroup; he also serves on the Joint Committee on Vaccination and Immunisation (JCVI) subgroup on influenza and RSV prophylaxis (2009), is a member of the UK Scientific Advisory Group in Emergencies (SAGE), a member of European Scientific Working Group on Influenza (ESWI) and a member of the Department of Health Influenza Clinical Information Network (FluCIN). PJMO leads Mechanisms of Severe Acute Influenza Consortium (MOSAIC), which funds JD.

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