

H5N1 influenza and the implications for Europe

A pandemic is likely, but Europe is getting prepared

In the 20th century, the world experienced three influenza A pandemics: “Spanish flu” claiming 20-40 million lives in 1918-9 and the “Asian flu” of 1957 and “Hong Kong flu” of 1968, each of which claimed 1-4 million lives.¹ It might be about to face another.

Birds are the natural hosts of influenza A, but most avian viruses are not transmitted to humans. However, the current influenza A/H5N1 virus is more virulent in birds than in the past and is associated with human infections.² Since its appearance in Hong Kong in 1997, the H5N1 epizootic, affecting both wild birds and domestic poultry, has spread to most countries in South East Asia and recently to Russia and Kazakhstan, directly threatening Europe.^{3,4} An epidemic of another less virulent virus, A/H7N7, in the Netherlands in 2003 emphasised the potential for emergence of infection in Europe.⁵

There are three prerequisites for a pandemic: a novel virus subtype for which humans are immunologically naive must be transmitted to humans; it must replicate and cause disease; and it must be efficiently transmitted among humans.¹ The present H5N1 avian virus lacks the third step, but sustained human to human transmission could occur through additional mutations in the H5N1 genome, or through “reassortment”—that is, mixing with a virus of human origin in a co-infected host. The risk of such events increases as the avian epizootic continues.

It is hard to assess precisely the risk of a pandemic. The recent situation in South East Asia, with low grade transmission of severe disease to (and between) humans, may remain stable. Alternatively, there might be a pandemic, with a virus of as yet unknown pathogenicity. The start of a pandemic may be controlled by targeted interventions around the first clusters of human cases, provided they are detected promptly.⁶ Should this initial containment fail, however, all countries will eventually be affected because quarantine and border closures would probably be futile.¹

Because of its dependence on sophisticated infrastructures, Europe would be very vulnerable to a pandemic. If 25% or more of the population were affected, vital functions such as food and fuel supplies would be severely threatened, unless appropriate preparations to maintain resilience are made—such as prophylaxis for key staff and plans within organisations for maintaining activities with a reduced workforce.^{7,8}

Guidelines for public health interventions have been produced by the World Health Organization.^{8,9,10} While there is still additional work to be done to refine

them,⁵ there is a general agreement on their nature and their phasing. They cover appropriate surveillance and detection systems, stockpiling of antiviral drugs, timely vaccine development, but also non-medical interventions, such as improved personal hygiene, early self isolation of cases, and cancelling of mass events. Implementing these measures in a major pandemic will be feasible only with good national and international coordination.

Success in controlling the epidemic of SARS (severe acute respiratory syndrome) in 2003 has proved the value of supranational public health governance, supporting country efforts. The 2005 World Health Assembly emphasised the importance of better preparedness at country level and in supporting the International Health Regulations.¹¹ Furthermore, the European Council in June 2005 asked European Union member states to improve the coordination of their national measures.

In the past 10 years, the EU has created technical agencies such as the European Agency for the Evaluation of Medicinal Products (EMEA), the European Food Safety Agency (EFSA), and the European Centre for Disease Prevention and Control (ECDC) to support member states. The various EU bodies and WHO are operating together to improve Europe’s preparedness for major public health crises, including pandemic influenza. An early warning and response systems allows for timely exchange of information between the EU Commission, the European Centre for Disease Prevention and Control, and member states.

A recent WHO-EU workshop revealed that only 18 of the 25 member states had a published preparedness plan, and just one had conducted a simulation exercise.¹² The involvement beyond the health service sector and development of detailed plans subnationally needs strengthening. The European Commission in collaboration with WHO will arrange a follow-up meeting and conduct a European pandemic influenza simulation exercise later in 2005.

Europe produces more influenza vaccine than any other continent. But in a pandemic there will inevitably be shortages. These are strong arguments for making annual influenza vaccination more routine and increasing European production capacity. The European Commission has developed a partnership with European vaccine manufacturers to speed up vaccine production in a pandemic, and the EMEA and the centre for disease prevention will join forces to monitor adverse effects, effectiveness, and vaccine coverage. Antiviral drugs are effective for early treatment of

influenza and play some part in prevention. The EMEA has produced guidance to aid national decisions on procurement and use of antivirals.

The European Centre for Disease Prevention and Control monitors the epidemiological situation and is currently developing a preparedness assessment tool to be field tested in the coming weeks. The centre and the European Commission are also supporting the European influenza surveillance scheme, which is continuously adapting its epidemiological and virological monitoring to the threat of an H5N1 pandemic. On the EU level, links between human and veterinarian medicine exist but need to be further strengthened. More work is especially needed for effective crisis communication.

A pandemic will occur in the future. European institutions are taking this threat seriously, with efforts that will eventually pay off through reduced morbidity and mortality in the next pandemic. Meanwhile, activities to prepare for an influenza pandemic also make Europe better equipped to tackle seasonal influenza and other major public health crises. This is worth the investment and efforts.

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Survival after stroke in south London

Is apparently higher in black patients than in white ones

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Few studies have compared the incidence and outcome of stroke in black and white people from the same population. Two population based stroke registers in US cities^{1,2} and one in the United Kingdom (the south London stroke register)³ found twice the incidence of stroke adjusted for age and sex in black people than in white people. Adjusting for socioeconomic status in the south London register attenuated but did not abolish this excess.³ None of these registers has found a significant difference between black people and white people in survival after stroke, and all have therefore attributed the excess mortality in black people to a higher incidence of stroke.²⁻⁴

The south London register now includes more than 2000 patients with a first ever stroke over seven years and has accrued 6000 person years of follow-up.⁵ Such studies are rare these days even in the UK, whose universal healthcare system makes it an ideal location for population based epidemiological research. The challenges include obtaining ethical approval for observational studies without explicit consent, getting long term grants to support the research, and maintaining the enthusiasm of the research team and its collaborators.

In today's *BMJ*, Wolfe et al present their updated comparison of survival after stroke in black people and white people. On the face of it, the findings are surpris-

ing: black patients seemed to have a survival advantage, with a reduction of about a third in the relative risk of dying, corresponding to an increased median survival time of almost 14 months.⁵

So is this finding real or a methodological artefact, and if artefact what are the possible reasons? One possible methodological explanation is differential under-ascertainment of stroke cases between ethnic groups. The researchers on the south London register have previously assessed completeness of case ascertainment by using capture-recapture methods, implying that it is almost 90% complete for both black people and white people.⁶ However, the validity of these methods for stroke registers has been questioned.^{7,8} Also the proportions of cases in the register that were notified by general practitioners (14%) and not admitted to hospital (15%) were lower than in the UK based Oxfordshire Community Stroke Project and its successor, the Oxford vascular study, in both of which most cases were notified by general practitioners, and over 40% were not admitted to hospital.⁸⁻¹⁰ This may indicate that the register missed a disproportionate number of patients with mild strokes who were not admitted to hospital. If this affected more white patients than black ones (for example, if more black patients sought care directly at hospital rather than at their general practice, and white patients obtained private health care outside the NHS more often, making