SWINE FLU: FROM CONTAINMENT TO TREATMENT

SCIENTIFIC ISSUES

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SUMMARY

The antiviral strategy aims to provide prompt treatment for all those with symptoms of A(H1N1) (pandemic swine flu) infection. As well as minimising symptoms and shortening the period for which people are ill, the strategy aims to minimise the risks of people developing complications or dying from A(H1N1) infection.

A(H1N1) is a novel virus; although pandemic swine flu infection has been mild in most people, in some cases it has been severe. Although some of those with severe illness have had risk factors that would make serious illness more likely, others have not.

The strategy will be kept under review. Antiviral medication is associated with side-effects, and widespread use of antivirals may promote the development of antiviral resistance.

BACKGROUND

A(H1N1) emerged in spring 2009, initially in Mexico and then spreading to North America. Recognition of the novel nature of the virus and the extent of its spread led to progressive increases in the World Health Organization (WHO) Pandemic Alert Level, culminating in the declaration of phase 6 on 11 June 2009.

The first cases of A(H1N1) in the UK were confirmed on 27 April 2009. Following the approach set out in *A national framework for responding to an influenza pandemic*, enhanced surveillance of cases and their contacts was instituted and actions were taken to contain the spread of the virus by using antiviral prophylaxis for contacts of known cases in addition to antiviral treatment of those cases. The UK has also been working with the WHO and other international partners to share information about A(H1N1) and its effects.

Worldwide, as of 29 June, more than 70,000 cases have now been laboratory confirmed as having A(H1N1) infection in over 100 countries or territories. This is likely to be a large under-estimate of the number of people infected, as when numbers of cases expand significantly in a country, it is usual to move away from an approach based on laboratory confirmation of all cases.

For most people, the illness appears to be mild and self-limiting. Cases have been confirmed in all age groups, but children and younger people seem to be much more likely to be affected, whereas fewer cases have been confirmed to date in older adults. For a minority of people, A(H1N1) has caused severe illness. In many, but not all, of these cases underlying risk factors have been identified that are likely to have contributed to the severity of the condition.

Worldwide, just over 0.4% of the laboratory confirmed cases reported to WHO have died, which would be a rate consistent with that normally observed with seasonal influenza. However, as noted above, the true number of cases of A(H1N1) is likely to be significantly higher than that reported to WHO and therefore the figure of 0.4% is likely to be an over-estimate of the case fatality rate of A(H1N1).

ANTIVIRAL STRATEGY

The UK's pandemic planning emphasised that it would not be possible completely to contain a pandemic influenza virus. A(H1N1) has now started to spread more rapidly in hot spots in the UK. However, information gained in the containment phase can now be used to review the antiviral strategy going forward.

The WHO, and some countries, have recommended that for mild disease caused by A(H1N1), the use of antiviral treatment should be focussed on those who are at higher risk. The amount of antivirals that WHO's member states have at their disposal varies widely.

The Scientific Advisory Group for Emergencies (SAGE), working with the Pandemic Influenza Clinical and Operational Group (PICO), was asked to advise, based on the present state of knowledge, whether particular groups that were at risk from A(H1N1) could be identified. The Government has taken into account SAGE's advice in developing the antiviral strategy.

This document summarises the available evidence on risk groups at the time of the SAGE meeting on 22 June. Published recommendations from other large countries and WHO are also noted.

DEFINITION OF AN "AT RISK" GROUP

For the purposes of the A(H1N1) antiviral strategy, following the definition used by the Joint Committee on Vaccination and Immunisation in the context of seasonal influenza, SAGE recommended that the definition of an "at risk" group should be: *"Members of an at risk group are defined as those who are at higher risk of serious illness or death should they develop influenza."*

UNDERLYING MEDICAL CONDITIONS THAT MAY INCREASE RISK

It is recognised that a number of underlying medical conditions can increase a person's risk from seasonal influenza. In the UK, those clinical risk groups consist of people aged 6 months or over with:

- chronic respiratory disease (including asthma that requires continuous or repeated use of inhaled or systemic steroids or with previous exacerbations requiring hospitalisation)
- chronic heart disease
- chronic renal disease
- chronic liver disease
- chronic neurological disease
- immunosuppression
- diabetes mellitus.

References to "underlying medical conditions" in this document refers to these conditions.

EXPERIENCE IN THE UK

By 19 June, 48 patients had been hospitalised in the UK, which represented a rate of 2.5% of the laboratory confirmed cases identified by that time. If the additional 850 patients clinically diagnosed by that date were taken into account the rate would be 1.8%.

About 40% of hospitalised patients had a comorbidity of the type recognised to increase risk from seasonal influenza, with asthma being the most common (4 patients). Other comorbidities included liver disease, chronic respiratory disease, recurrent chest infections, cardiac disease and diabetes.

WORLDWIDE EXPERIENCE

An early report from the USA on 642 patients found[1] that of the 399 patients for whom hospitalisation status was known, 36 (9%) required hospitalisation. Of 22 hospitalised patients with available data, 12 had characteristics that conferred an increased risk from severe seasonal influenza, 11 had pneumonia, 8 required admission to an intensive care unit, 4 had respiratory failure, and 2 died.

A report on 30 hospitalised cases from California[2] found that 19 patients (64%) had underlying medical conditions; the most common were chronic lung disease (e.g., asthma and chronic obstructive pulmonary disease), conditions associated with immunosuppression, chronic cardiac disease (e.g., congenital heart disease and coronary artery disease), diabetes, and obesity. Of 5 pregnant women, 2 developed serious sequelae; however, the role that preceding infection with A(H1N1) played in these outcomes is unclear.

As of 17 June, there were 2,026 confirmed A(H1N1) pandemic influenza cases in Australia of which 53 had been hospitalised (2.6%). A report (Sydney Morning Herald) states that "Most people who have been hospitalised have had existing conditions or complications." On the same date, the Australian

Government announced, as part of a new pandemic phase PROTECT, that there would be a focus on early treatment of people who may be vulnerable to severe disease who were listed as including (i.e. the list may not be exclusive): pregnant women, those with respiratory disease (including asthma), heart disease, diabetes, renal disease, morbid obesity, and immunosuppression.

In Canada, as of 15 June, 4,049 laboratory confirmed cases had been reported of which 212 had been hospitalised (5.2%) and 7 had died (0.17%). Publicly available information refers to people with "underlying conditions" as being at increased risk.

According to a WHO report, 46% of 45 fatal cases in Mexico had underlying conditions including pregnancy, asthma, other lung diseases, diabetes, morbid obesity, conditions giving rise to immunosuppression, neurological disorders, and cardiovascular disease.

In conclusion, the data available to date suggest that underlying medical conditions recognised as conferring increased risk from seasonal influenza also confer increased risk of more serious illness from A(H1N1) pandemic influenza.

ASTHMA

With regard to asthma, the UK seasonal influenza at risk group is a sub-set of all patients with asthma, reflecting persons with a more severe form of the condition. Asthma has emerged as a relevant underlying risk factor for hospitalisation in UK, US and Mexican data but there is insufficient information to determine whether the patients would have fitted the specific definition used for seasonal influenza.

The US approach to asthma in terms of at risk groups for A(H1N1), following their approach on seasonal influenza vaccination, is less restrictive than the UK approach to seasonal influenza vaccination. Asthma is identified as a risk group without specification of severity.

A significant proportion of the UK population (up to 25%) might be said to have asthma if the term is defined broadly; not all of those will have received medical treatment for the condition. Some children may be diagnosed as having asthma but not be affected by the disease in adult life. Therefore, SAGE considered that people who have received any medical treatment for asthma in the last three years should be regarded

as being at higher risk, rather than using the more restrictive definition used in the context of seasonal influenza vaccination, whilst further information is gained on the interactions between A(H1N1) and asthma.

PREGNANCY

International data, and the very limited UK experience to date, suggest that pregnancy may also be a risk factor associated with serious illness or death, which would accord with previous experience both in seasonal influenza and in previous pandemics, particularly 1918 and 1957. WHO has highlighted that antivirals may be of benefit to pregnant women.

CHILDREN UNDER THE AGE OF 5

There is very limited experience in the UK, or reported worldwide, with regard to infection with A(H1N1) in children under the age of 5. Attack rates for seasonal influenza are often highest in young children and more severe illness leading to hospitalisation occurs more commonly in this group than in older children or adults (under 65 years). High mortality rates have been seen in very young children (less than one year) in previous pandemics.

In the US, the Centers for Disease Control interim guidance on A(H1N1) antiviral use, based on its guidance on seasonal flu, is that children younger than 5 years old should be considered as a high risk group for A(H1N1), noting that children younger than 2 years have the greater risk for severe complications from seasonal flu. It appears that that this experience is being reflected with A(H1N1), with about 9% of US hospitalisations having been said to be in patients under the age of 2.

Other countries, and WHO, have not so far included young children in at risk groups for A(H1N1) pandemic influenza. However, experience with seasonal influenza suggests that on a precautionary basis, and in accordance with experience in the US, such children should be considered at increased risk until further information makes clear that this is inappropriate.

PEOPLE OVER THE AGE OF 65

People aged 65 years and older are included in the at risk groups for seasonal influenza. The available UK data suggest that attack rates for A(H1N1) for those aged 65 and over have been very low. Mexican data[3] shows that the attack rate in those aged 60 and over has been low but the death rate has been high. It appears that there is a similar picture of a low attack rate but a higher case fatality rate in persons over the age of 65 emerging in the US. The US include the over 65s in their at risk groups for A(H1N1), although over 65s with mild disease have not been recommended as a target group for antiviral treatment by WHO. Although at present the risk of becoming infected in this age group appears to be lower than in other age groups, the risk of more serious illness once infected appears to be higher and therefore at present it is appropriate to consider people over the age of 65 as at risk on a precautionary basis.

PERSONS NOT IN RISK GROUPS

On the basis of the available data, SAGE did not consider that there were other groups that could be recognised as being at higher risk. However, there have been a number of hospitalisations of people not obviously falling within the identified higher risk groups, and it was important to recognise that others may become severely ill as a result of bring infected with A(H1N1).

SAGE noted the importance of antiviral treatment in such situations as those where a person is not in a defined risk group but is severely ill, or where the person is not recovering as expected, or where the person has a medical condition that may be exacerbated by influenza.

IMPORTANCE OF EARLY TREATMENT

Antivirals are most effective if started close to the onset of symptoms. SAGE emphasised the importance of prompt treatment, especially of higher risk groups.

1. NEJM.org 10.1056/NEJMoa0903810

2. MMWR 2009; 58: 536-541

3. WHO Weekly epidemiological record, 22 May 2009, vol. 84, 21 (pp 185–196) http://www.who.int/wer/2009/wer8421/en/index.html

Useful contacts

Call **0800 1 513 513** to hear the latest information on swine flu.

England:
www.nhs.uk
www.direct.gov.uk/swineflu

Scotland:
www.nhs24.com

Wales:
www.nhsdirect.wales.nhs.uk
www.wales.gov.uk/health

Northern Ireland:
www.dhsspsni.gov.uk
www.nidirect.gov.uk

Calls to 0800 numbers are free from UK landlines. Mobile and other providers' charges may vary.

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