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Dear Colleague

NEW H1N1v INFLUENZA: CURRENT SITUATION AND NEXT STEPS

This letter gives doctors:

- a synopsis of the epidemiology of the new H1N1v (Swine 'flu) virus so far
- some pointers as to what might happen next
- the rationale for the public health and clinical response so far
- information and guidance on steps that now need to be taken
- an outline of further planning and policy decisions

The first illness caused by a new influenza A virus was confirmed in the United Kingdom on 27 April 2009.

Since then the virus has become much more common in this country and globally with the World Health Organization declaring the situation a pandemic on 11 June 2009. This is the first influenza pandemic since the 1968-1970 period.

For the first four weeks most new cases in the United Kingdom were in travellers returning from affected areas and their contacts. In the last four to six weeks, the majority of new cases are unrelated to travel. In some parts of the country there have been large outbreaks with sustained community spread.

Overview of spread internationally

The latest reports from WHO show that cases of the new virus have occurred in 120 countries including the UK. There have been more than 77,000 laboratory confirmed cases and 332 deaths globally. The countries with the highest numbers of cases include USA (27,700 cases, 127 deaths), Mexico (8680 cases, 116 deaths) and Canada (7983 cases, 25 deaths).

The actual number of cases of people infected with the new virus is likely to be much higher than these numbers suggest, as most cases are not tested. For example, CDC in the USA estimates that there have been approximately 1 million cases there.

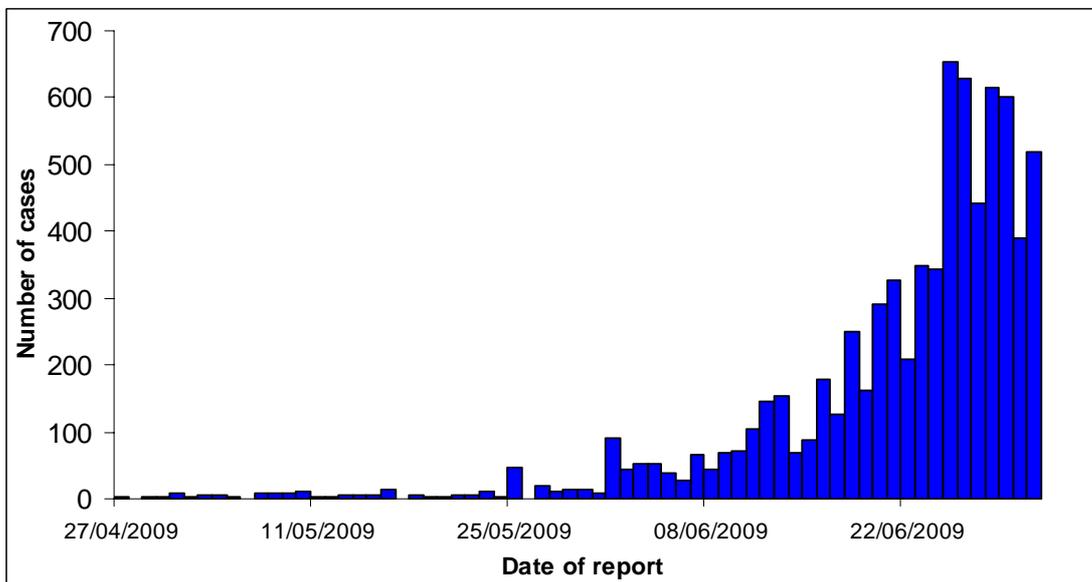
Earlier this week, one influenza A(H1N1v) virus strain showing oseltamivir resistance was reported in a patient from Denmark who had received treatment.

Detection of oseltamivir resistance in individual patients does occur in a low percentage of treated cases and is of limited public health significance, although it is important to monitor whether such viruses are being transmitted from person to person.

Overview of Spread in the United Kingdom

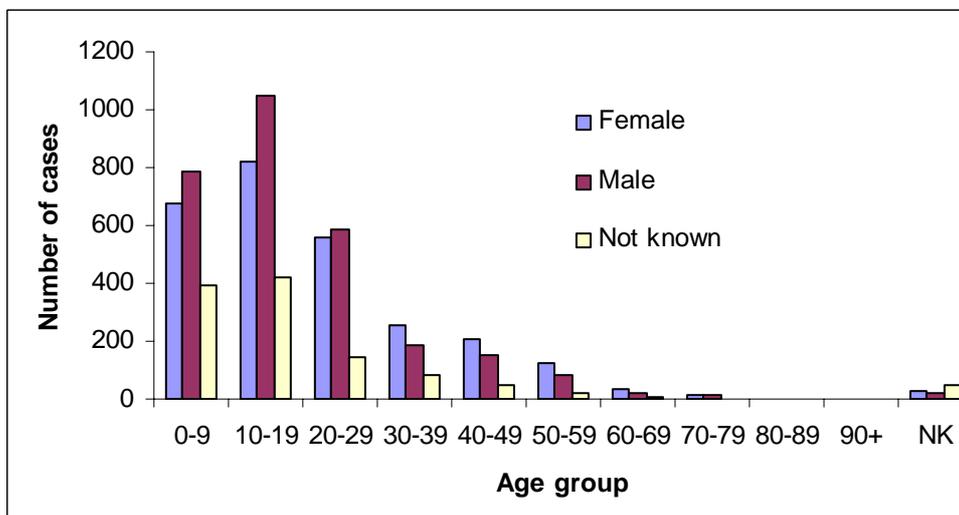
As of 2 July 2009, there have been 7447 laboratory confirmed cases of new influenza A H1N1v in the United Kingdom. The virus is becoming increasingly widespread. Over the last two weeks a significant increase has occurred in the number of new cases each day (figure 1).

Figure 1: New cases of new H1N1 in the UK by day



The vast majority of cases so far have been in those less 60 years (figure 2)

Figure 2: Age distribution of cases of new H1N1 (as of 1st July)



So far, at least 111 cases in the UK have been hospitalised over the course of the outbreak, including 83 in England, 25 in Scotland, 2 in Wales and 1 in Northern Ireland.

Previous and present pandemics: some pointers

There were three influenza pandemics in the 20th Century. Compared to seasonal 'flu all have shown:

- A shift of mortality to the younger age groups.
- Excess mortality from the pandemic virus for up to 5 years after its first emergence.

The behaviour of the present pandemic virus so far is consistent with this: deaths are occurring at younger ages than in seasonal 'flu.

While the scientists cannot yet predict the future spread of the virus with much precision, the pandemics of 1957-58 and 1968-70 demonstrate that there will be more than one wave of infection.

The 1958 epidemic arrived in Britain in the month of June, but the number of cases did not start to increase rapidly until September when schools returned after their summer holidays. The initial autumn peak was then followed by a second peak over Christmas and New Year, which was associated with a higher mortality rate.

In 1968, the first cases arrived in this country in the month of August, but infection rates remained at a relatively low level until an initial peak in March 1969. It was not until Christmas 1969/1970 that a second, much larger peak occurred.

These features of previous pandemics suggest a much larger wave of infection (with more illness and death) in autumn or winter this year. It remains possible that the virus could change increasing its virulence.

The Public health and clinical response so far

As the H1N1 virus has spread, the response has been matched to the circumstances.

The pre-existing pandemic plans had three key features:

- Widespread use of antivirals to protect people until a vaccine was available.
- Obtaining a safe, effective vaccine as quickly as possible (bearing in mind the considerable lead times involved).
- Creating alternative routes of access to assessment and antiviral treatment to reduce pressure on primary care and hospital services.

The early response to the pandemic has gone according to planning. The approach of containment allowed detailed investigation of cases (including swabbing to confirm the diagnosis), tracing and the use of prophylaxis for contacts and selective closure of schools. Children have been "super spreaders" in previous pandemics.

The containment measures were sustained when there were worrying reports of deaths from other parts of the world. It enabled maximum protection to be offered to people in the face of uncertainty about the virus's behaviour. It may have also slowed spread, buying time for the arrival of a vaccine.

With the advent of large outbreaks in some parts of the country (West Midlands and London in particular), there was evidence of much more non-travel related illness and sustained community spread. As a result, containment was no longer appropriate and the outbreaks are now being managed with relaxation of the need for swabbing, detailed investigation of cases and prophylactic use of antivirals.

The number and size of outbreaks around England means that the approach needs to move to treatment only, with public health investigation only being necessary in special circumstances.

Risk

There has been much speculation that the illnesses caused by the current influenza virus are "mild" and "like seasonal 'flu". Whilst it is true that most infections so far have not been severe, there have been hospitalisations and deaths. These have generally been in younger people and not all have had significant underlying illness. Moreover, the epidemiology is not like seasonal 'flu in that it is occurring out of the normal 'flu season and different age groups are being most affected.

There is still considerable uncertainty about the behaviour of the virus. It remains the case that for a doctor, faced with a previously healthy adult with symptoms strongly suggestive of H1N1v, there is no way to predict whether the course of their illness will be mild or very serious. That is why a precautionary approach of offering antivirals to such patients has been recommended so far.

Information which has so far emerged (internationally as well as in the UK) suggests that the following groups are at higher risk of serious illness or death. They are: people with underlying chronic disease, with asthma requiring drug treatment, immunosuppressed (whether caused by disease or treatment), pregnant women, people aged 65 years or over and children under 5 years old.

Summary of actions for doctors

>Clinical diagnosis

Doctors should make the diagnosis of H1N1v by clinical diagnosis alone; there is no need for swabbing in primary care unless there are special reasons to do so (e.g. control of infection in hospitals) or as part of 'spotter' surveillance schemes. The exception to this is that if there are unusual syndromes which are considered to have an infectious basis, it may be important to swab then.

>Treatment of Priority Groups

Doctors should give priority to early treatment with antivirals of people in higher risk groups (see **Annex A**): those with underlying illness, those who are immunosuppressed, pregnant women, the over 65 year olds and the 0-5 year olds (but see **Annex B** on advice on the under 1s).

>Treatment of other age groups

In considering treatment of people aged 5-64 years with no underlying illness, doctors are advised to take a precautionary approach and offer antivirals to patients with symptoms strongly suggestive of H1N1v. It is acknowledged that doctors must use their clinical judgement and will not usually choose to offer antivirals in circumstances where there are minor or unrelated respiratory symptoms.

>Prophylaxis

Doctors should not usually offer prophylaxis to contacts of cases unless for example, a household member has serious underlying health problems or there are other special circumstances.

>Next steps in pandemic 'flu plans

Doctors are asked to note that in line with pre-existing pandemic influenza plans, in the near future, alternative routes of access to antivirals (so called 'Flu-Line') will be made available to the public. This is to reduce anticipated massive demand on primary care and hospital services when the number of cases becomes more extensive. Further information will be sent to out when the arrangements are implemented.

>Further information

A number of further sources of information may be useful:

1. HPA Swine Flu – Information for Health Professionals

<http://www.hpa.org.uk/web/HPAweb&Page&HPAwebAutoListName/Page/1240812234677>

2. Department of Health – Swine Flu

<http://www.dh.gov.uk/en/Publichealth/Flu/Swineflu/index.htm>

3. British Medical Association

<http://www.bma.org.uk/>

4. Royal College of General Practitioners

<http://www.rcgp.org.uk/>

From the Chief Medical Officer, Sir Liam Donaldson



Thank you for all the excellent work you are doing to combat this new disease.

Yours sincerely

A handwritten signature in black ink that reads 'Liam Donaldson'. The signature is written in a cursive, slightly slanted style.

**SIR LIAM DONALDSON
CHIEF MEDICAL OFFICER**

ANNEX A

Pandemic influenza - Who are the high risk groups?

Some people will be at greater risk of becoming more seriously ill from swine flu than others. As advised by the Scientific Advisory Group for Emergencies (SAGE) these high risk groups are:

- People with:
 - Chronic lung disease
 - Chronic heart disease
 - Chronic kidney disease
 - Chronic liver disease
 - Chronic neurological disease
 - Immunosuppression (whether caused by disease or treatment)
 - Diabetes mellitus

- Patients who have had drug treatment for their asthma within the past three years
- Pregnant women
- People aged 65 years and older
- Young children under 5 years old.

ANNEX B

ADVICE ON USE OF OSELTAMIVIR IN CHILDREN AGED UNDER 1 YEAR

Oseltamivir (Tamiflu) is currently licensed only for use in those aged 1 year and over.

In the context of the current pandemic of H1N1v, the European Medicines Agency (EMA – which oversees the Tamiflu licence across Europe) has evaluated whether oseltamivir could be recommended for use in those aged under 1 year.

This evaluation included review of available evidence, including data from clinical trials and other studies, on the possible risks and benefits of use of oseltamivir in those aged under 1 year.

Considering the urgent need for recommendations on use in this age group for treatment and prevention of H1N1v, the EMA has advised that:

- children below 1 year of age may be treated with oseltamivir
- the appropriate dosage to treat children below 1 year of age is 2 to 3 mg/kg twice daily for 5 days
- post-exposure prophylaxis of children below 1 year of age should be very carefully considered
 - the appropriate dose for prevention should be 2 to 3 mg/kg once a day for 10 days (but should not exceed 10 days)
- such use should preferably be undertaken under medical supervision as deemed appropriate depending on the local situation
- the paediatric suspension or dilution of the capsule content can be used to prepare the dose in children below 1 year of age

This advice is endorsed by the UK's Medicines and Healthcare products Regulatory Agency and UK paediatric experts.

A precautionary approach should be taken by general practitioners to seek paediatric advice if they are worried about a child under 1 with presumed H1N1 swine flu.

This advice is intended as guidance to EU public health authorities in dealing with the pandemic threat and does not represent a change to the licence for oseltamivir. The recommendations are specific to the H1N1v outbreak and are not applicable to use in seasonal influenza.