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The PHLS response to a pandemic of influenza

*An action plan**

P. Morgan-Capner
For the PHLS Influenza Subcommittee
Public Health Laboratory, Royal Preston Hospital, Preston, UK

Abstract. This document sets out the Public Health Laboratory Service (PHLS) action plan for responding to an influenza pandemic. The plan entails, in phase 0, interpandemic surveillance by the Communicable Disease Surveillance Centre (CDSC) and the Enteric & Respiratory Virus Laboratory (ERVL) of the Central Public Health Laboratory (CPHL), as well as maintenance by Area & Regional (A & R) Public Health Laboratories of updated diagnostic techniques for influenza. In phase 1 (the emergence of a 'shifted' influenza virus strain) a Pandemic Working Group will be convened to consider what action by PHLS is necessary. In phase 2 (pandemic influenza outside UK) the pre-defined roles for PHLS laboratories and CDSC will be adopted. When a pandemic is imminent in the United Kingdom (phase 3) the Working Group will coordinate PHLS activities and the Director of the Service will assess what special studies should be implemented. In phase 4, when the pandemic has reached the UK, the action plan sets out comprehensive measures that will be taken by CDSC, ERVL and A & R Laboratories to gather and collate information, provide DoH with weekly surveillance data and develop recommendations for prophylaxis, clinical management and treatment. When influenza activity has returned to background levels (phase 5) a report will be drafted by the Working Group prior to it being stood down by the Director of the Service. The response is summarised in tabular form in Table 1.

Key words: Influenza virus, Pandemic, Public Health Laboratories

Introduction

Influenza A virus undergoes major antigenic shifts at unpredictable intervals and, as a result, causes worldwide epidemics ('pandemics') with high morbidity and mortality. The principal pandemics this century were in 1918, 1957 and 1968. The largest was in 1918 and caused approximately 20 million deaths.

Typically, new shifted strains of influenza virus emerge in the Far East and spread via Asia or the Antipodes towards Europe. Laboratories, therefore, can be forewarned of the likely arrival of a new strain in the United Kingdom.

The imminence of a pandemic is suggested when there is:

a) An existing strain of human influenza virus exhibiting an antigenic 'shift' to a novel haemagglutinin;
b) A high proportion of the population susceptible to the new virus; and
c) A new virus spreading rapidly and causing disease.

A pandemic exists when the virus has been confirmed as a shifted influenza strain and has been associated with rapid international spread and a high incidence of infection and disease.

To enable the PHLS to respond to a pandemic there must be adequate surveillance of influenza *before* as well as during the pandemic. The principal surveillance role of the PHLS is to provide virological and epidemiological data upon which prompt national decisions, such as the choice and deployment of vaccine and the use of antiviral agents, can be based. This continuing surveillance requires central resources and the maintenance of diagnostic expertise in A & R laboratories. New diagnostic methods and surveillance techniques are being developed and these must be available as necessary in the event of a pandemic.

In addition to the PHLS' major role in the event of a pandemic of influenza, the Department of Health (DoH) and the Welsh Office (WO) will require information and advice. During a pandemic, a second role of the PHLS will be to initiate studies in the UK.

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These may influence the management and treatment of patients and measures taken to protect the community. This paper summarises the PHLS activities required to meet these roles.

Phasing the PHLS response

Six phases can be recognised in the emergence of a pandemic, each covered by the PHLS Action Plan:

Phase 0 The interpandemic period.

Phase 1 The emergence outside the UK of an influenza virus with novel haemagglutinin ('new virus').

In the event of the new virus appearing first in the UK, phases 1 and 2 are bypassed.

Phase 2 An epidemic or pandemic of influenza caused by new influenza virus outside the UK.

Phase 3 New influenza virus isolated in UK: pandemic imminent.

Phase 4 Pandemic influenza in UK

Phase 5 Return to background influenza activity: report of pandemic to be drafted.

The necessary laboratory and epidemiological response to each phase (summarized in Table 1) is set out below in the details of the Action Plan.

Phase 0: Interpandemic period

Surveillance

Early Warning: In an interpandemic period, surveillance will identify an epidemic increase in illness and the spread of a virus can be analysed in the population by time, location and age.

CDSC and the ERVL of the Virus Reference Division of CPHL receive data on influenza activity from many sources in England and Wales. Reports are issued after collating and interpreting the data. Information about influenza in other countries is provided by the World Health Organization (WHO) and other national surveillance programmes. The main surveillance programmes are listed below.

International surveillance. Information on international influenza activity, including data on antigenic drift of the virus, supplied by WHO, Geneva. The information is faxed weekly during the influenza season and as new information appears during the remainder of the year.

Mortality surveillance. The Office of Population Censuses and Surveys (OPCS) provide CDSC with mortality data which are received by CDSC 4–5 days after the week in question. Deaths due to 'all causes', 'influenza', and 'total respiratory deaths' in England and Wales are recorded. Deaths from pneumonia, bronchitis and influenza are combined to give 'total respiratory deaths'.

Morbidity surveillance. Every week the Royal College of General Practitioners (RCGP) Unit, in Birmingham, UK, supplies CDSC with morbidity data on new illnesses diagnosed by approximately 240 general practitioners in about 66 practices in the UK. These serve a population of approximately 650,000. Provisional figures are telephoned to CDSC 3–4 days after the week in question and so provide prompt, if provisional, indices. The diagnoses include 'influenza-like illness' and 'epidemic influenza', and the data are provided by age and by sex. Laboratory confirmation is not required but studies have shown that a higher proportion of cases of 'epidemic influenza' are virus-positive than those of 'influenza-like illness'. Similar data is also supplied from Sentinel Practice Schemes in Wales (CDSC Welsh Unit) and Scotland (Communicable Disease [Scotland] Unit).

'Spotter RCGP Practices' can be designated and are one of the best early warning systems available. Under appropriate conditions, they can be funded to carry out prospective sampling with proper virological back-up.

The Medical Officers of Schools Association (MOSA) provides information on 'influenza and influenza-like illness' in a population of approximately 16,000 boarding school children, aged 5–18 years, in 50 schools. These data are provided weekly for two age groups (5–12 years and 13–18 years) and both sexes, and are available to CDSC within 5 days of the week in question.

The Emergency Bed Service provides monthly data on the number of applications for hospital admission through the service in the London area.

Laboratory data. Most PHLS laboratories provide diagnostic services for influenza together with other non-NHS laboratories in London, Newcastle, North Manchester and in Scotland. They supply CDSC with weekly reports on isolation of influenza viruses A and B, categorizing patients by age and sex. These laboratory reports provide information on circulating strains of influenza virus. Strains of virus are sent to the ERVL for antigenic analysis to monitor seasonal antigenic drift as well as to detect strains showing antigenic shift. Cases of influenza diagnosed serologically are also reported to CDSC.

Population immunity. Serological surveillance is carried out annually by ERVL to estimate antibody levels existing in the population against predominant

Table 1. PHLS action in relation to influenza activity

Phase	CDSC	ERVL	A & R laboratories	Other
0 Interpandemic period.	Data collection (Laboratory, WHO, OPCS, RCGP, MOSA, etc.). Data interpretation and information distribution (CDR and BMJ).	Virus antigenic analysis. Serological surveillance.	Virus isolation, diagnostic serology. Virus isolates to ERVL. Provide summer sera to ERVL.	
1 'New' virus with novel haemagglutinin detected in human infections outside UK.	Prompt notification to Director of PHLS of WHO notification. International liaison. Inform virus labs. Surveillance activities as in Phase 0.	Obtain 'new' virus for antigenic analysis. Test summer sera for susceptibility. Liaise with NIBSC and NIMR.	No additional diagnostic response. Plan special studies to be supported in the event of a pandemic in UK.	Pandemic Working Group convened by Director PHLS.
2 'New' virus outside UK shown to have pandemic potential.	Initiate increased surveillance. Disseminate information by Epinet and weekly CDR.	Obtain new sera for up-to-date serological surveillance. Test virus isolates for antiviral sensitivity.	Increase submission of specimens from suspected influenza. Provide sera from cases for ERVL.	
3 'New' virus identified in UK; pandemic imminent.	Activities as for Phase 0, DoH and WHO to be kept informed. Update all laboratories by Epinet of current situation.	Continue identification and analysis of virus strains submitted from PHLS and virus laboratories in UK.	Continue to encourage increased specimens from influenza suspects to locate distribution of "new virus". All isolates to ERVL. Report outbreaks to CDSC.	Pandemic Working Group organizes additional activities with A & R laboratories.
4 Influenza pandemic in UK.	As for Phase 3.	As for phase 3.	Diagnosis by culture reduced but increase direct immunofluoresence.	
5 Return to background influenza activity.	Preparation of final epidemiological report.	Further analysis of isolates: post pandemic serological studies.		Preparation of final report to Director of Service.

strains of virus circulating both in the UK and elsewhere in the world. This provides background information against which the pandemic potential of new strains of virus can be assessed.

Approximately 500 sera over a wide age range are collected each summer from various laboratories and analysed to give an estimate of the likely susceptibility of the population to influenza viruses currently circulating in the world.

Dissemination of information. Influenza activity is reported each week during the influenza season (weeks 44–25) in the Communicable Disease Report (CDR). In addition, annual and, as necessary, interim reviews of influenza activity are regularly prepared by CDSC and published in the CDR. Bulletins on influenza activity are also transmitted by the Epinet system to microbiologists and public health physicians. Reports of various communicable diseases are published by CDSC and, quarterly, in the British Medical Journal and Community Medicine; influenza is included in these reports when there is increased activity or if unusual or new influenza virus strains are circulating elsewhere.

Additional studies. Other studies which could usefully be undertaken between pandemics by PHLS laboratories include:

a) Inclusion of laboratory investigation in surveillance by 'spotter' general practices to enhance the isolation of influenza virus strains and their antigenic characterization.

b) Monitoring susceptibility to antiviral drugs of recent isolates.
c) Assessment of the immunogenicity of influenza vaccines.
d) Trials of vaccine efficacy.
e) Estimation of vaccine uptake in at-risk groups.
f) Adverse reactions to vaccines.

Phase 1: Emergence of an influenza virus with a novel haemagglutinin (i.e. a 'new' influenza virus) in human infections outside the UK

When a new virus with pandemic potential has been isolated in another country, WHO informs CDSC and ERVL.

Action to be taken

CDSC notifies the Director of the PHLS and all virus diagnostic laboratories. Statement on the front page of the next weekly CDR. DoH and WO alerted.

*The Director of the PHLS convenes a Pandemic Working Group (see Appendix).** Surveillance arrangements already in force are designed to detect the emergence of the new virus in the UK. Until such time as the virus has been demonstrated to have pandemic potential elsewhere in the world, extra surveillance measures in the UK are unnecessary. If there is evidence of pandemic potential, surveillance must be increased in the UK. Should the new virus appear in the UK, phases 1 and 2 are by-passed and the plan goes to phase 3.

ERVL. Obtains new virus for antigenic analysis and for tests with summer sera obtained from inter-pandemic surveillance. Liaises with NIBSC and National Institute for Medical Research.

Phase 2: Pandemic influenza outside the UK

When a pandemic of influenza due to a new virus is reported in another part of the world, the risk of a pandemic in the UK is high. Surveillance must be increased to detect the new virus in the UK at the earliest opportunity.

Action to be taken

Area and regional laboratories

Virus isolation. PHLS laboratories should try to increase the number of nose and throat swabs or pharyngeal aspirates submitted for attempted virus isolation from suspected cases of influenza. Isolates are sent to ERVL.

Serology. Laboratories should arrange to provide recent samples of sera, especially from cases of laboratory-proven influenza.

ERVL

Analyses antigenic structure. Strains of virus referred from UK laboratories.

Examines recent serum samples (from A & R laboratories, see 'serology' above). Determines prevalence of antibody to the new virus. Assesses the age distribution of pre-existing antibody, if any, to the pandemic virus strain.

Determines the sensitivity of new isolates to antiviral drugs.

CDSC

Epidemiological surveillance. During phase 2, indicators of influenza activity (as in Morbidity surveillance of phase 0) must be interpreted cautiously, as increased awareness by clinicians of the possibility of a pandemic can cause spurious rises in reports of influenza activity; cases are often notified on the basis of clinical diagnosis without virus isolation. PHLS/CDSC should initiate systematic surveillance to obtain reliable information on virologically confirmed cases of influenza.

Information dissemination. Information on influenza activity will be circulated weekly in the CDR and through the Epinet system. CDSC, in liaison with the Pandemic Working Group, will produce a Weekly Influenza Supplement to the CDR with information on:

a) Laboratory reports of influenza;
b) Clinical reports of influenza from the RCGP surveillance;
c) Deaths reported to OPCS due to 'all causes', 'influenza', and 'total respiratory deaths';
d) Outbreaks of influenza-like illness in the UK;
e) Data on population susceptibility, i.e. studies on prevalence of antibody to the new virus; and
f) Influenza activity in other parts of the world, including information on the age distribution of infection and severity of illness in different age groups.

* If it subsequently becomes apparent that the new virus is not spreading widely in the world the Pandemic Working Group will be stood down and laboratories notified accordingly.

Phase 3: New virus isolated in the UK – pandemic imminent

When the new virus has been isolated in the UK, surveillance must be increased to monitor its spread into different parts of the country and to record notifications (and rates) of influenza illness. DoH and WO to be kept informed.

Action to be taken

CDSC

CDSC will notify all laboratories of the situation by the fastest means available (e.g. Epinet).

Influenza activity. Monitoring will continue with extra care in interpreting observations because of the possible spurious increases in reporting due to heightened clinical awareness.

Information distribution. Information on influenza activity, virus isolation and morbidity indices will be circulated in the CDR as for phase 2, but with additional data on reports from special studies undertaken at the time of the pandemic.

Area and regional laboratories

Virus isolation. Enhanced virus isolation to identify the virus in different parts of the country is necessary (as in phase 2). A & R laboratories and the Royal College of General Practitioners should appeal to general practitioners for increased numbers of nose and throat swabs and, if possible, nasopharyngeal aspirates. Members of the Medical Officers of Schools Association should be encouraged to submit specimens from boarding school pupils.

Outbreak investigations. It is important, early in the pandemic, to document outbreaks of influenza in different population groups and determine age-specific attack rates, morbidity and mortality and, if possible, the efficacy of vaccination or chemoprophylaxis. This will enable the national impact of the pandemic to be measured reliably.

Additional activities. The Pandemic Working Group will ask A & R Laboratories to support the following activities, and it will be helpful if Directors can decide in advance which activities they would be able to support.

a) Study of prevalence of new strains in general practices.
b) Necropsy study. A study of fatal pneumonia with bacteriological and virus cultures. This study will be initiated by the Laboratory of Hospital Infection, CPHL, with the object of recommending the best antibiotic treatment at the time of an influenza pandemic.
c) Studies on influenza prophylaxis and treatment, particularly to assess the use of amantadine in high risk populations at the time of an influenza pandemic.
d) Surveillance of the effect of influenza in hospitals. To investigate the effect of the pandemic on hospital staffing with possible ward closures and on the clinical management of patients in hospital.

Phase 4: Pandemic influenza in the UK

Once the new virus has been shown to be causing pandemic infection in the UK, surveillance is directed to the monitoring of the pattern and intensity of activity.

Action to be taken

CDSC

Surveillance. The usual indices of influenza activity (as in phase 0) should be supplemented by additional information, e.g. absence of children from school, absence due to sickness in workers, illness in very elderly groups. This additional surveillance may already be taking place (e.g. in phase 2) but will now become of particular value.

Laboratories (area, regional and ERVL)
Enhanced surveillance through virus isolation is of little value at this stage. The number of specimens submitted for isolation is likely to be overwhelming, though direct immunofluorescence may enable diagnostic services to meet demand. Virus isolation should not, of course, cease altogether as it remains important to monitor prevalent strains of virus and detect any change in the pandemic strain or, possibly, the emergence of other strains.

Phase 5: End of pandemic

A pandemic is deemed to have ceased when the epidemiological indices have returned to background levels.

Report. The Pandemic Working Group will prepare a report for the Director of the Service to include an assessment of the measures taken to monitor the pandemic, together with recommendations for the future (it should be noted that pandemics of influenza may recur over successive winters).

Dissolution of Pandemic Working Group. The Director of the PHLS will decide if and when the Pandemic Working Group should stand down.

Appendix

Pandemic Working Group

The Director of the PHLS will convene the Working Group in consultation with the Chairman of the PHLS Influenza Subcommittee (see Phase 1) when notified by CDSC that WHO has identified a new influenza virus with pandemic potential.

Functions

a) *To co-ordinate* PHLS activities in the face of a potential or actual pandemic of influenza in the UK.
b) *To advise* the Director of the PHLS.
c) *To liaise* with the WHO Influenza Centre at the National Institute for Medical Research (NIMR) and DoH.

The Working Group will advise the Director of the PHLS on:

a) The progress of the pandemic and the resources available – or required – within the PHLS so that it can fulfil its role in diagnosis and surveillance.
b) The estimated impact on the population with particular reference to rate of spread, incidence of infection by age and identification of those at greatest risk.
c) Vaccination policy and use of antiviral agents.
d) Research to be implemented at the time of an pandemic.

Suggested membership

- The Director of the PHLS or designated representative – Chairman
- Chairman of the PHLS Virology Committee
- Chairman and Secretary of the PHLS Subcommittee on Influenza
- Director of CDSC or designated representative
- Director of ERVL or designated representative
- Consultant Virologist in A & R virus laboratory
- Director WHO Collaborating Centre for reference and research on influenza, National Institute of Medical Research, Mill Hill
- Representative of DoH
- Such co-opted members as are necessary to carry out the Working Group's tasks

Secretariat

The Secretary of the PHLS Influenza Subcommittee will be responsible for preparing agenda, writing minutes, summarizing individuals' tasks, collecting and distributing documentation/information and arranging meetings. If necessary, temporary clerical help will be made available.

Meetings

It is clear that the Pandemic Working Group may need to be convened at short notice and that frequent meetings may be necessary. Members will be expected to give the Working Group top priority.

Items for consideration at the Inaugural Meeting of Pandemic Working Group:

a) Current worldwide influenza activity – liaison with WHO and DoH to determine the influenza situation elsewhere in the world. Information on the age-specific attack rates, morbidity and mortality of the pandemic strain in other parts of the world will be supplied by WHO to CDSC.
b) Arrangements for increased specimen collection to identify isolates of the new virus. Ensure that isolates are available to ERVL, NIMR and NIBSC if they have not already obtained these.
c) Organization of the collection of sera for testing against the new virus including consideration of the most appropriate sources of the specimens.
d) Investigation of characteristics of the new virus in tissue culture, eggs and by immunofluorescence.
e) Arrangements for the additional resources needed for virus isolation and identification throughout the PHLS. This may require the temporary redeployment of staff to collect specimens and assist in laboratory diagnosis.
f) Assess requirements for, and availability of, diagnostic sera, including those needed for direct immunofluorescence tests.

Minutes of meetings

In addition to members of the Pandemic Working Group, minutes will be sent to each member of the PHLS Influenza Subcommittee.

Communications to the media

These will be arranged through the PHLS Press Officer and with the DoH.

Pandemic report

At the end of the pandemic a report will be prepared for the Director of the Service. This will also be considered by the PHLS Influenza Subcommittee.

Standing down the working group

The decision to stand down the Committee will be taken by the Director of the PHLS when the pandemic has resolved.

Address for correspondence: P. Morgan-Capner, Public Health Laboratory, Royal Preston Hospital, P.O. Box 202, Sharoe Green Lane, Preston PR2 4HG, UK
Phone: (772) 710 114; Fax: (772) 710 166