Virus shedding and environmental deposition of novel A (HINI) pandemic influenza virus: interim findings

B Killingley,[1]* J Greatorex,[2] S Cauchemez,[3] JE Enstone,[1] M Curran,[2] RC Read,[4] WS Lim,[5] A Hayward,[6] KG Nicholson[7] and JS Nguyen-Van-Tam[1]

[1]Division of Public Health and Epidemiology, University of Nottingham, Nottingham, UK
[2]Department of Clinical Microbiology and Public Health, Health Protection Agency, Addenbrooke's Hospital, Cambridge, UK
[3]Department of Infectious Disease Epidemiology, Imperial College, London, UK
[4]Department of Infectious Diseases, University of Sheffield, Sheffield, UK
[5]Department of Respiratory Medicine, Nottingham University Hospitals NHS Trust, Nottingham, UK
[6]Department of Infection and Population Health, University College London, London, UK
[7]Department of Infection, Immunity and Inflammation, University of Leicester, Leicester, UK

*Corresponding author

Executive summary

Health Technology Assessment 2010; Vol. 14: No. 46
DOI: 10.3310/hta14460-04

Health Technology Assessment
NIHR HTA programme
www.hta.ac.uk

Executive summary

Background

The threat posed by pandemic influenza is high on the agenda of health-care organisations and governments around the world. As pandemic mitigation strategies have been developed over recent years it has become very clear that influenza transmission is an area that is poorly understood and hotly debated. The biggest controversy relates to whether influenza is mainly transmitted by touching virus deposited on surfaces, or by droplets or bioaerosols in the air. If touch is important then hand washing offers a major defence. If droplets are important, simple barriers, such as a surgical mask, will stop transmission. But if bioaerosols are important, specialised respirators are needed. Thus, infection control guidance is difficult to formulate and mainly based on weak evidence. Current evidence suggests that infectious virus is not typically released from adults after 5 days of illness (slightly longer in children). However, little is known about the extent to which virus is deposited by infected individuals into the environment and whether deposited virus has the ability to infect new hosts, i.e. whether it remains viable. The generation of information about the deposition of viable influenza virus in the immediate vicinity of patients with pandemic influenza is fundamental to our understanding of the routes and mechanisms of transmission.

Objectives

This study was conducted to collect data on patients who had pandemic H1N1 2009 infection (swine flu). The primary objectives were to correlate the amount of virus detected in a patient's nose with that recovered from his/her immediate environment (on fomites and in the air), and with symptom duration and severity. Secondary objectives were to describe virus shedding and duration according to major patient characteristics: adults versus children, and those with mild illness (community patients) versus those with more severe disease (hospitalised patients).

Methods

Adults and children, both in hospital and from the community, who had symptoms of pandemic H1N1 infection, were enrolled and visited every day during follow-up for a maximum of 12 days. Information about symptoms was collected and samples were taken, including nose swabs and swabs from surfaces and objects (fomites) around patients (e.g. door handles, remote controls). Samples of air were obtained using validated sampling equipment. These samples were tested for the presence of pandemic H1N1 virus, using polymerase chain reaction (PCR) to detect virus genome and an immunofluorescence technique to detect viable (live) virus.

Results

Forty-three subjects were followed up, and 19 of them were subsequently proven to be infected with pandemic H1N1 virus. The median duration of virus shedding from the 19 infected cases was 6 days when detection was performed by PCR, and 3 days when detection was performed by a culture technique. Over 30% of cases remained potentially infectious for at least 5 days. However, contrary to conventional understanding, virus shedding was not always greatest when an individual was most symptomatic. Few fomites were found to be contaminated with virus – in fact only 0.5% of all community and none of the hospital swabs taken revealed virus. Five subjects had samples of the air around them collected and virus was detected by PCR from four. Some of the air particles in which virus was detected were small enough to be inhaled and deposited deep in the lungs.

Conclusions

Despite some limitations caused by the small number of subjects recruited, important observations have been made. The finding that over 30% of infected individuals have infectious

virus in their noses for 5 days or more has infection control implications. The evidence for the significance of both contact and bioaerosol routes of transmission, depends upon demonstrating that viable virus is deposited from an infected patient. This has been shown for touched fomites. Virus has been demonstrated by PCR in air samples, but the results of live virus testing are inconclusive. The data generated suggest that contact transmission of pandemic influenza via fomites may be less important than hitherto emphasised, whereas transmission via bioaerosols at short range may be possible, meaning that high-level personal protective equipment (PPE) might be needed by health-care workers when attending patients with pandemic influenza. Further work is being undertaken to consolidate these findings as they have important potential implications for the protection of health-care workers and the formulation of advice to households, nationally and internationally.

Publication

Killingley B, Greatorex J, Cauchemez S, Enstone JE, Curran M, Read RC, *et al.* Virus shedding and environmental deposition of novel A (H1N1) pandemic influenza virus: preliminary findings. *Health Technol Assess* 2010;**14**(46):237–356.

How to obtain copies of this and other HTA programme reports
An electronic version of this title, in Adobe Acrobat format, is available for downloading free of charge for personal use from the HTA website (www.hta.ac.uk). A fully searchable DVD is also available (see below).

Printed copies of HTA journal series issues cost £20 each (post and packing free in the UK) to both public **and** private sector purchasers from our despatch agents.

Non-UK purchasers will have to pay a small fee for post and packing. For European countries the cost is £2 per issue and for the rest of the world £3 per issue.

How to order:

– fax (with **credit card details**)
– post (with **credit card details** or **cheque**)
– phone during office hours (**credit card** only).

Additionally the HTA website allows you to either print out your order or download a blank order form.

Contact details are as follows:

Synergie UK (HTA Department)
Digital House, The Loddon Centre
Wade Road
Basingstoke
Hants RG24 8QW

Email: orders@hta.ac.uk

Tel: 0845 812 4000 – ask for 'HTA Payment Services' (out-of-hours answer-phone service)

Fax: 0845 812 4001 – put 'HTA Order' on the fax header

Payment methods

Paying by cheque
If you pay by cheque, the cheque must be in **pounds sterling**, made payable to *University of Southampton* and drawn on a bank with a UK address.

Paying by credit card
You can order using your credit card by phone, fax or post.

Subscriptions

NHS libraries can subscribe free of charge. Public libraries can subscribe at a reduced cost of £100 for each volume (normally comprising 40–50 titles). The commercial subscription rate is £400 per volume (addresses within the UK) and £600 per volume (addresses outside the UK). Please see our website for details. Subscriptions can be purchased only for the current or forthcoming volume.

How do I get a copy of *HTA on DVD*?

Please use the form on the HTA website (www.hta.ac.uk/htacd/index.shtml). *HTA on DVD* is currently free of charge worldwide.

The website also provides information about the HTA programme and lists the membership of the various committees.

The National Institute for Health Research

The National Institute for Health Research (NIHR) has been established as a part of the Government's strategy, 'Best Research for Best Health'. It provides the framework through which the research staff and research infrastructure of the NHS in England is positioned, maintained and managed as a national research facility.

The NIHR provides the NHS with the support it needs to conduct first-class research funded by the Government and its partners alongside high-quality patient care, education and training. Its aim is to support outstanding individuals (both leaders and collaborators), working in world-class facilities (both NHS and university), conducting leading-edge research focused on the needs of patients.

This themed issue of the *Health Technology Assessment* journal series contains a collection of research commissioned by the NIHR as part of the Department of Health's (DH) response to the H1N1 swine flu pandemic. The NIHR through the NIHR Evaluation Trials and Studies Coordinating Centre (NETSCC) commissioned a number of research projects looking into the treatment and management of H1N1 influenza.

NETSCC managed the pandemic flu research over a very short timescale in two ways. Firstly, it responded to urgent national research priority areas identified by the Scientific Advisory Group in Emergencies (SAGE). Secondly, a call for research proposals to inform policy and patient care in the current influenza pandemic was issued in June 2009. All research proposals went through a process of academic peer review by clinicians and methodologists as well as being reviewed by a specially convened NIHR Flu Commissioning Board.

The final reports from these projects have been peer reviewed by a number of independent expert referees before publication in this journal series.

Criteria for inclusion in the HTA journal series

Reports are published in the HTA journal series if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reports in this themed issue were funded through the Cochrane Collaboration; the Health Services Research programme (HSR); the Health Technology Assessment programme (HTA); the Policy Research Programme (PRP); the Public Health Research programme (PHR); and the Service Delivery and Organisation Programme (SDO).

The Cochrane Collaboration is an international not-for-profit and independent organisation, dedicated to making up-to-date, accurate information about the effects of health care readily available worldwide. It produces and disseminates systematic reviews of health-care interventions and promotes the search for evidence in the form of clinical trials and other studies of interventions. Cochrane reviews and the Cochrane Central Register of Controlled Trials are published and updated in *The Cochrane Library* (www.cochranelibrary.com).

The HSR programme aims to lead to an increase in service quality and patient safety through better ways of planning and providing health services. It funds both primary research and evidence syntheses, depending on the availability of existing research and the most appropriate way of responding to important knowledge gaps.

The HTA programme produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The PRP provides the evidence base for policy development on public health and social care issues. It funds research in three main ways: 5-year programmes of research in 16 research units, a primary-care research centre, a public health research consortium, and a surveillance unit; programmes of interlinked studies on key policy initiatives; and single projects and literature reviews.

The PHR programme evaluates public health interventions, providing new knowledge on the benefits, costs, acceptability and wider impacts of non-NHS interventions intended to improve the health of the public and reduce inequalities in health. The scope of the programme is multi-disciplinary and broad, covering a range of interventions that improve public health.

The SDO programme commissions research evidence that improves practice in relation to the organisation and delivery of health care. It also builds research capability and capacity amongst those who manage, organise and deliver services – improving their understanding of the research literature and how to use research evidence.

The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report. The views expressed in this publication are those of the authors and not necessarily those of the NIHR or the Department of Health.

ISSN 1366-5278

Published by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk), on behalf of NETSCC, HTA.