Eurosurveillance

Volume 14, Issue 6 - 12 February 2009

Rapid communications

Review articles

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

A fatal case of Lassa fever in London, January 2009

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In January 2009, the eleventh* case of Lassa fever imported to the United Kingdom was diagnosed in London. Risk assessment of 328 healthcare contacts with potential direct exposure to Lassa virus - through contact with the case or exposure to bodily fluids - was undertaken. No contacts were assessed to be at high risk of infection and no secondary clinical cases identified.

Background

Lassa fever is an acute viral haemorrhagic fever (VHF) caused by Lassa virus, a member of the Arenavirus family. It is a zoonosis acquired from the multimammate rat (Mastomys species), which sheds the virus in its urine and droppings. The disease is endemic in many West African countries.

Person-to-person transmission of Lassa fever occurs once symptoms have developed or in the period of convalescence, and then only through direct contact with infected bodily fluids such as blood, urine, faeces, saliva or semen. The incubation period for Lassa fever is usually 7-10 days, although a range of 3-21 days has been reported. Approximately 15-20% of people hospitalised with Lassa fever will die, but overall only about 1% of infections result in death [1, 2].

While Lassa fever does not pose a significant public health risk in Europe [3], occasional travel-associated cases do occur. To date, all imported infections to the United Kingdom (UK) - ten cases between 1971 and 2003, with one fatality in 2000 - have derived from either Sierra Leone or Nigeria. None of these have resulted in further clinical cases in health staff or other contacts [1].

The incident

On 8 January 2009, a 66-year-old man was admitted to the Homerton University Hospital (HUH) in London with symptoms of fever, diarrhoea and confusion.

He had travelled on a flight from Abuja in Nigeria (where he had travelled south to Anambra state) to London on 6 January. He experienced fever, malaise, loss of appetite, and abdominal pain during the flight. He travelled from Heathrow airport by public transport to his home in east London, and was described by a neighbour as being confused and feverish on arrival.

On 8 January, he was taken to HUH by ambulance, where he presented with a three-day history of fever, rigors, lethargy and mild diarrhoea. During his hospital stay, he was initially cared for in two open wards. He attended the radiology department on six occasions and an operating theatre once for lumbar puncture. Tests for a range of travel-associated infections (e.g. malaria, leptospirosis, dengue, yellow fever) were negative, and the case was managed in isolation at HUH as a possible typhoid case from 16 January. He was incontinent of urine and faeces at this time.

On 22 January, he was transferred to the Infectious Diseases Unit (Hospital for Tropical Diseases), University College Hospital, for further management, and on the same evening to the high-security infectious diseases unit (HSIDU), at the Royal Free Hospital, in a category 3 ambulance. The North East and North Central London (NENCL) Health Protection Unit (HPU) were alerted to the incident at this time.

A diagnosis of Lassa fever was confirmed by RT-PCR on 23 January, by the Novel and Dangerous Pathogens Laboratory (NaDP) laboratory at the Health Protection Agency (HPA) Centre for Emergency Preparedness and Response (CEPR), Porton Down. Lassa virus IgG antibodies were also detected in serum, and Lassa virus was subsequently isolated from blood and urine specimens.

The patient was commenced on ribavirin, and remained in isolation for the duration of his admission. He improved initially, but had a degree of nerve deafness - a feature consistent with Lassa fever [2,4]. Despite intensive nursing and medical care, the patient died on 29 January from complications exacerbated by pre-existing medical conditions. No post-mortem examination was undertaken.

Communication with agencies and the media

A series of immediate actions were implemented by an Incident Control Team (ICT). The incident was reported to the World Health Organization (WHO) under the International Health Regulations and followed up with the Federal Ministry of Health, Nigeria through the

WHO Country Office. The European Centre for Disease Prevention and Control (ECDC) was also notified.

A HPA press release was issued, confirming that there was no risk to the general public resulting from the case [5]. Information was cascaded to all general practitioners in the area (via the Primary Care Trust), to NHS Direct, and to all Emergency Departments in London. The incident was subsequently reported in national and local (online and print) media.

Risk assessment

All individuals with potential direct exposure to Lassa virus through contact with the case or exposure to bodily fluids required risk assessment. These contacts fell into a number of different professional and geographical groups:

- Other passengers on the flight
- The neighbour of the patient
- Ambulance staff involved in transporting the patient
- Medical, nursing and allied health professionals at the three hospitals
- Pathology staff handling specimens in several laboratories
- Radiology staff at HUH
- Domestic staff and porters at HUH

Each contact's risk of infection was assessed, and assigned into one of three categories (Table 1). Factsheets were produced on Lassa fever and the monitoring process (including advice for contacts going on holiday) according to risk category. These were available for dissemination to all contacts, most of whom were at HUH. The general factsheet (Category 1) was disseminated to HUH staff via the hospital intranet on 23 - 24 January.

From 23 January onward, members of staff were contacted either in person (at the hospital) or by telephone, asked about their contact with the patient, assigned to a category according to level of risk, and advised according to assigned category. No restriction was placed on work or movement for asymptomatic adults in any of the risk categories. A designated senior nurse was available 24 hours per day at the HUH to answer any queries.

Table 1

Level of risk related to exposure to a patient with Lassa fever, and action, by category

Risk Category	Description	Action
No risk (Category 1)	No contact with the case Casual contact (e.g. sharing a room with the case, without direct contact with a potentially infectious material	Inform of absence of risk Give Category 1 (general) factsheet
Low risk (Category 2)	Close direct contact with the case (e.g. routine medical/nursing care, handling of clinical/ laboratory specimens), but did not handle body fluids or wore personal protective equipment (PPE) appropriately	Self-monitor* for fever and other symptoms compatible with Lassa fever Report to the senior nurse if temperature ≥38°C, with further evaluation as necessary Give Category 2 factsheet
High risk** (Category 3)	Unprotected exposure of skin or mucous membranes (e.g. mucosal exposure to splashes, needlestick injury) to potentially infectious blood or body fluids, or unprotected handling of clinical/laboratory specimens	Record own temperature daily* and report this temperature to the senior nurse by 12 noon each day, with further evaluation as necessary Give Category 3 factsheet

* Contacts to be monitored for 21 days from last possible exposure to case
** Within this group, consideration for ribavirin prophylaxis, if any extreme exposure e.g. percutaneous injury

Table 2

Categorisation of contacts of a patient with Lassa fever at Homerton University Hospital, January 2009

Professional group	Risk category assigned				
	No risk (Category 1)	Low risk (Category 2)	High risk (Category 3)	Not contactable	Total
Medical	17	17	0	4	**38**
Nursing/ AHP[1]	49	71	0	16	**136**
Pathology	0	72	0	0	**72**
Domestic staff	12	0	0	5	**17**
Porters/ transport staff	32	4	0	3	**39**
Phlebotomy	4	8	0	2	**14**
Radiology/ other investigations	7	1	0	4	**12**
Total	**121**	**173**	**0**	**34**	**328**

[1]Allied Health Professionals

Since the airline reported that there was no record of passenger illness or seeking assistance on the flight, the risk to other passengers on the flight was deemed negligible. The ECDC independently assessed the risk to other passengers on the flight and also concluded the case did not pose a significant risk to the citizens of the European Union.

Laboratories holding clinical specimens were contacted and asked to safely destroy these or transfer them for further testing or destruction as appropriate. Risk assessment of laboratory staff was carried out and there were no incidents reported at any of the laboratories involved in handling specimens. The neighbour of the patient was assessed and considered to be at low risk.

The funeral director was advised regarding the infectious state of the deceased who had already been placed in a sealed metal-lined coffin. It was advised that the coffin remain sealed and no viewing of the body take place.

Outcome of monitoring contacts

In total, 328 people at HUH were identified as possible contacts of the case. Thirty-four (10%) could not be contacted but attempts to do so are ongoing. The 21-day surveillance period (from date of last possible exposure) for HUH staff ends on 12 February.

To date, no contacts have reported any illness compatible with Lassa fever, and no high risk (Category 3) contacts have been identified (Table 2).

Discussion and conclusion

The risk for human-to-human transmission of Lassa fever is low. However, healthcare-associated transmission has occurred in areas where Lassa fever is endemic [6], and an instance of asymptomatic seroconversion was reported in a German physician in 2000 [7].

Clinical diagnosis of Lassa fever is difficult, and it is often confused with other more common infections such as severe malaria or typhoid fever [1]. A range of travel-associated infections was requested in this case. However, the diagnosis was only established two weeks after admission. Such a delay is not uncommon in imported Lassa cases [8]. In persons arriving from Africa, clinical histories should include careful assessment of travel to regions where uncommon diseases are endemic [6], including Nigeria, Sierra Leone, Liberia and Guinea for Lassa fever [9]. Early suspicion and diagnosis are vital to the successful management of these patients.

While ribavirin has been shown to be effective in early-stage arenavirus infections, particularly Lassa virus [2], in the absence of proven effectiveness for prophylaxis [3], oral ribavirin was not recommended for persons who might have been exposed to the case described here. Current advice would suggest restricting its use to contacts at highest risk [3].

Meticulous adherence to appropriate infection control practices to prevent unprotected exposure to blood or other body fluids is essential for the safe management of patients with possible Lassa fever [6], and the prevention of onward transmission, particularly given the non-specific presentation of Lassa fever and related VHF syndromes. In this incident, it is commendable that, even without knowing the diagnosis and the risks they were exposed to, all healthcare and other workers at the HUH who had contact with the patient before confirmation of Lassa fever diagnosis had worn appropriate personal protective equipment (PPE), and thus we did not identify any Category 3 risk persons.

* Authors correction
In the Abstract, the sentence "In January 2009, the seventh case of Lassa fever imported to the United Kingdom was diagnosed in London" was replaced by: "In January 2009, the eleventh case of Lassa fever imported to the United Kingdom was diagnosed in London". This was corrected on 13 March 2009.

Aknowledgements

All staff involved in the contact tracing exercise at the Homerton University Hospital and the HPA, and Dr Helen Maguire for comments on the article.

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This article was published on 12 February 2009.

Citation style for this article: Kitching A, Addiman S, Cathcart S, Bischop L, Krahé D, Nicholas M, Coakley J, Lloyd G, Brooks T, Morgan D, Turbitt D. A fatal case of Lassa fever in London, January 2009 . Euro Surveill. 2009;14(6):pii=19117. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19117

Measles resurgence in France in 2008, a preliminary report

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Since the beginning of 2008, France has been experiencing a resurgence of measles. It started in a religious traditionalist group with low coverage and secondarily spread to the general population. This situation is the consequence of the insufficient vaccine coverage (less than 90 % at 24 months of age) which had led to the accumulation of susceptibles over the last years. More than 550 cases have been notified in 2008, the vast majority being unvaccinated. One measles-related death has occurred early 2009. Efforts to enhance communication to the general public and the health professionals on measles vaccination and control measures around cases are ongoing.

Introduction

Since the beginning of 2008, France has been facing an increase of measles incidence. To date, 579 cases were reported in 2008 through mandatory notification, whereas in 2006 and 2007 the numbers of reported cases were 40 and 44 respectively.

Mandatory notification of measles was reintroduced in July 2005, as part of the National Plan for Elimination of Measles and Congenital Rubella. Physicians and microbiologists have to report suspected measles cases without delay to the local Public Health Officer [1]. Laboratory confirmation is strongly recommended for sporadic cases, either through serum or salivary testing. Oral fluid samples (for IgM detection and PCR) are sent to the National Reference Laboratory which also performs genotyping of the circulating viruses (5-10 cases should be sampled when a localised outbreak is investigated). Notification forms are collected and analysed centrally at the InVS.

The current measles vaccination strategy consists of two doses of measles-mumps-rubella vaccine (MMR) to be administered before the age of two years, the first one at 12 months of age and the second one between 13 and 24 months of age. A catch-up with two doses is recommended for children born after 1991 and with one dose for subjects born between 1980 and 1991.

Outbreak description

The ongoing outbreak began in spring 2008 with several clusters. The more important were reported in Burgundy and northern regions of France. A total of 110 cases were identified among elementary and secondary students of two private religious schools and their siblings. The index case was a 10 year-old Swiss girl who had been in contact with a measles case in Austria in mid-April [2,3,4]. Since summer 2008, other clusters and outbreaks have been reported with an upsurge of measles cases in October and a peak in November (131 cases). The virus transmission is still ongoing with 80 cases reported in January 2009 (Figure 1).

Despite the fact that most of the outbreaks were initially linked to schools affiliated with the same religious group as in Burgundy, in several regions the virus is currently circulating in the community and outbreaks in both private and public schools have been reported (Figure 2). The most affected regions are in north-west and south-east.

More than half (55%) of the cases reported in 2008 have been confirmed, either by detecting measles IgM antibodies or viral RNA by RT-PCR (265 cases) or by an epidemiological link with a laboratory-confirmed cases (54 cases). However, the proportion of laboratory-confirmed cases decreased from an average of 71% between January and July to an average of 38% between August and December 2008. Preliminary results from the National Reference Laboratory showed that three main genotypes were co-circulating: D5, D8 and D4, the predominant one being D5.

The median age of the 579 cases reported in 2008 was 12 years (range: 0-56 years). One third of the cases were aged 15 years or above (Table). Amongst the 26 cases less than one year old, 13 were aged between three and nine months (eight were laboratory-confirmed).

Vaccination status was known for 548 cases (95%). Among these, the proportion of unvaccinated cases was 88.5%

Figure 1

Number of reported measles cases, by month, France, January 2008 - January 2009, preliminary data (n=659)

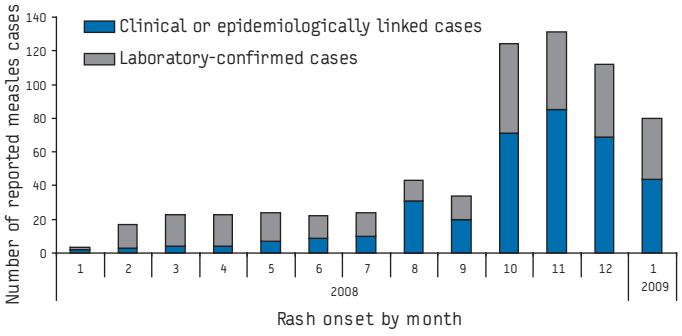
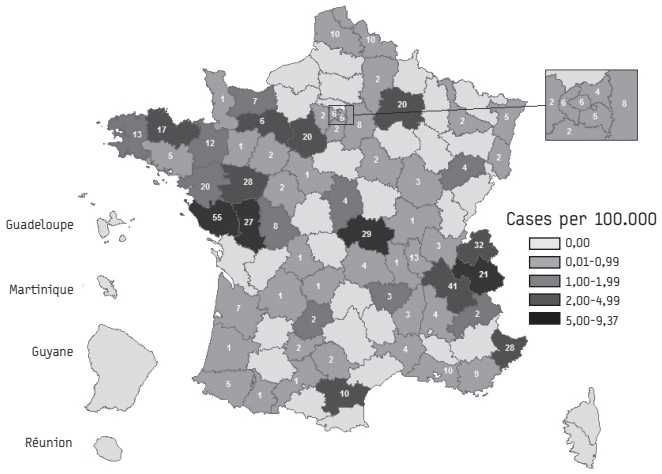


FIGURE 2

Number of reported measles cases and incidence per 100,000 inhabitants, by districts, France, 2008



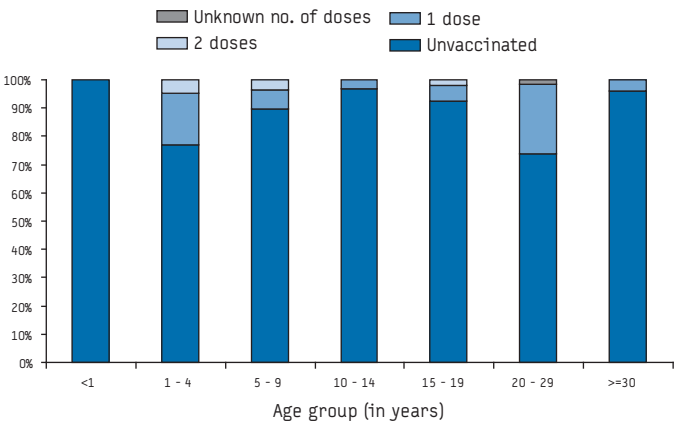
TABLE

Reported cases of measles and incidence rates per 100,000 population, by age group, France, 2008

Age groups (years)	Number of cases	Proportion of total number of cases (%)	Incidence rates (per 100,000)
<1	26	4	3,2
1 - 4	108	19	3,4
5 - 9	116	20	2,9
10 - 14	130	22	3,4
15 - 19	99	17	2,4
20 - 29	67	12	0,8
>=30	33	6	0,1
Total	579	100	0,9

FIGURE 3

Vaccination status of measles cases by age group, France, 2008 (n=548)



(Figure 3). Of the 63 vaccinated cases, 51 were vaccinated with one dose (9%), 11 with two doses (2%) and for one case the number of doses was unknown.

Complications

Hospitalisation was required for 110 patients (19%) according to the notification forms received in 2008. Among these cases, 18 were diagnosed with pneumonia but no encephalitis was reported. Unfortunately, one unvaccinated French 12-year-old girl died in January 2009 in Geneva University Hospital from acute measles encephalitis.

Control measures

Several control measures were implemented by local health authorities, according to national guidelines. They include general information to the public, targeted information to the health professionals covering the affected area, and specific recommendations to pupils' parents, the schools and the involved religious community administration where clusters are identified. The main recommendations are to undergo vaccination according to the national immunisation schedule and to propose post-exposure vaccination or immunoglobulin, depending on age, time since exposure and existence of risk factors of severe measles [1].

Discussion

Although measles incidence rates in 2006 and 2007 were below 0.1 per 100,000 inhabitants, suggesting near elimination, the current measles resurgence is not unexpected in the context of the still insufficient measles vaccination coverage allowing for silent accumulation of susceptibles. Current coverage at 24 months of age with at least one dose is estimated between 87 % and 90 % [InVS, unpublished data]. A survey carried out in 2005 has shown a coverage at 11 years of age of 96% for at least one dose of MMR, through catch-up vaccination beyond two years and a coverage for the second dose of 74% [5].

The data available through the routine notification system underestimate the actual measles incidence. During outbreak investigations, up to 10 times more cases have been identified than those notified to the local health authorities. This is the consequence of both the absence of medical consultation for a large proportion of the cases (especially when several cases occur within the same family) and the insufficient knowledge or motivation of some doctors regarding the notification procedure.

The current measles virus circulation in the community has been triggered by the clustered measles susceptibility in children belonging to traditionalist religious groups where measles vaccination coverage is low. The fact that these children often share the same schools and leisure activities such as summer camps have lead to several outbreaks in this group and to the secondary spread of the virus outside of this community. Efforts have been undertaken by the Ministry of Health to dialogue with representatives of the religious community regarding this specific measles vaccination issue.

The contribution of groups with low vaccination coverage due either to geographical or financial difficulties in accessing vaccination services or reluctance to measles vaccination for religious or philosophical reasons has been identified as one of the major impediments to achieve measles elimination in Europe [6,7,8].

In France, there are virtually no geographical or financial impediments in receiving the vaccine. The network of both private practitioners and public health clinics ensures optimal geographical access to measles vaccination. Furthermore, measles-containing vaccines are the only vaccines offered totally free of charge for children up to 13 years of age. If elimination in France is to be reached, the priority therefore lies in maintaining the efforts to persuade as many parents and health professionals reluctant to measles vaccination as possible. In the context of the current measles situation, communication to the general public and the health professionals has therefore been strengthened, amplified by the media attention drawn by the recent measles-related death case.

Aknowledgements

Vivamus tempor mi quis quam. Fusce tempus, ante sed tincidunt ornare, nisi urna viverra enim, eget venenatis dui ante ut eros.

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This article was published on 12 February 2009.

Citation style for this article: Parent du Châtelet I, Floret D, Antona D, Lévy-Bruhl D. Measles resurgence in France in 2008, a preliminary report. Euro Surveill. 2009;14(6):pii=19118. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19118

Introduction of human papillomavirus (HPV) vaccination in Sweden

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The Swedish National Board of Health and Welfare (NBH) decided that a vaccine that protects against cervical cancer caused by human papillomavirus (HPV) should be included in the childhood vaccination directive as a nationwide-programme targeting 12-year-old girls from 2010 as a part of the school-health programme. Currently, vaccination of girls 13-18 years of age is covered by the public insurance. In this paper we describe the decision-making process behind the introduction of HPV vaccination in Sweden.

Sweden, as many other countries, has a fairly complicated system for decision-making on introduction and financing of new vaccines in the national vaccination-programme. The programme is currently regulated by directives and recommendations from the National Board of Health and Welfare (NBH). The programme is implemented and financed by the counties through child health clinics (for children aged up to to five years) and by the communities through the school-health system (for children from the age of six years).

In response to the number of candidate vaccines that have become available on the market in recent years, the NBH has established a ten-point list of factors to be evaluated for new vaccines [1]. The NBH then appoints an expert-group for a vaccine that is considered a possible candidate for introduction, to collect the knowledge about the vaccine following this general outline. This is further analysed by the NBH in a dialogue with responsible stakeholders in the field before a final decision on the inclusion of the vaccine in the directive on childhood vaccinations can be taken.

For the vaccination against human papillomavirus (HPV), this work started in 2007. The expert group concluded that HPV infection was established as a cause of cervical cancer, condylomas, vulvar cancer, vaginal cancer, anal cancer and tonsillar cancer and that HPV16/18 infection annually contributed to about 500 cases of cancer and about 200 cancer deaths per year in Sweden [2]. Approximately 38,000 annual cases of condyloma were estimated to be caused by HPV6/11 [2]. Modelling of the infection based on Swedish serosurveys and sexual behaviour data indicated that the largest health gains would be seen by vaccination of girls aged 12-18 years [2,3].

Based on the report from the expert-group, the NBH decided that a vaccine that protects against cervical cancer caused by HPV should be included in the childhood vaccination directive as a nationwide-programme targeting 12-year-old girls from 2010 as a part of the school-health programme. The directive specifies for which diseases vaccines should be offered but not what vaccines should be used. The NBH also decided that an introduction could only be recommended if an extensive follow-up programme was implemented. This is in line with the World Health Organization (WHO) recommendations of follow-up for coverage, safety and population effectiveness and its aim is also to ensure that the screening programme continues to be at least as effective as today [4].

In the meantime, both available vaccines have already been included in the national pharmaceutical products insurance programme, meaning that all girls 13-18 years of age can get the vaccine covered by the public insurance, which ensures that any family will not pay more than 180 euros for medicines prescribed by a physician for their children during a year. This coverage starts at the age of 13 years not to interfere with the vaccination programme but rather to complement it.

The follow-up programme is currently being developed as a project by NBH. The vaccination-coverage needs to be followed and the current system can be used for the vaccinations given in schools. To follow the effect on an individual level, an HPV vaccination registry was launched concomitantly with the first licensure of HPV vaccines in Sweden in 2007. The registry has used the legal basis for research projects (informed consent and internation review board (IRB) approval) with informed consent brochures enclosed with the vaccine dose packages. Consent includes permission to follow with registry linkages and to do HPV testing of biospecimens that may later be taken during routine healthcare.

An early effectiveness at population level is obtained by laboratory-based surveillance of incidence of specific virus types. To do this, laboratory capacity and quality needs to be in place. For the quality assurance the WHO HPV LabNet Global Reference Laboratory which is located in Sweden plays an important role. It performs international collaborative studies and proficiency panels for quality assurance and international standardisation of HPV DNA typing and HPV serology [5,6]. The collection of viral samples in

Sweden will be further strengthened by a directive for HPV typing of samples from all women with CIN2-3 changes.

Finally and most importantly, coordination between vaccine monitoring and quality assurance of the cervical screening will be vital to assess the overall impact of the cervical cancer preventive strategies. The nationwide registration of all cervical smears is an essential part of a coherent evaluation strategy [7].

Conclusion

Sweden has pursued implementation of HPV vaccination with high ambitions in providing a solid evidence base for decisions, logistics likely to favour very high population coverage as well as extensive and careful HPV surveillance programmes for monitoring of HPV vaccine programme effectiveness as a part of the cervical cancer prevention programme.

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This article was published on 12 February 2009.

Citation style for this article: Tegnell A, Dillner J, Andrae B. Introduction of human papillomavirus (HPV) vaccination in Sweden. Euro Surveill. 2009;14(6):pii=19119. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19119

International travels and fever screening during epidemics: a literature review on the effectiveness and potential use of non-contact infrared thermometers

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Several countries plan to introduce non-contact infrared thermometers (NCIT) at international airports in order to detect febrile passengers, thus to delay the introduction of a novel influenza strain. We reviewed the existing studies on fever screening by NCIT to estimate their efficacy under the hypothesis of pandemic influenza. Three Severe Acute Respiratory Syndrome (SARS) or dengue fever interventions in airports were excluded because of insufficient information. Six fever screening studies in other gathering areas, mainly hospitals, were included (N= 176 to 72,327 persons; fever prevalence= 1.2% to 16.9%). Sensitivity varied from 4.0% to 89.6%, specificity from 75.4% to 99.6%, positive predictive value (PPV) from 0.9% to 76.0% and negative predictive value (NPV) from 86.1% to 99.7%. When we fixed fever prevalence at 1% in all studies to allow comparisons, the derived PPV varied from 3.5% to 65.4% and NPV was =>99%. The low PPV suggests limited efficacy of NCIT to detect symptomatic passengers at the early stages of a pandemic influenza, when fever prevalence among passengers would be =<1%. External factors can also impair the screening strategy: passengers can hide their symptoms or cross borders before symptoms occur. These limits should be considered when setting up border control measures to delay the pandemic progression.

Introduction

The emergence of Severe Acute Respiratory Syndrome (SARS) in 2003 underlined the role of international travels in the rapid spread of infectious diseases and prompted countries to set up border control strategies, in order to reduce the risk of introduction of an infection. Traditional measures such as information for travellers, self-completion of health cards or visual inspection of passengers were implemented by most countries. In addition, non-contact infrared thermometers (NCIT) were introduced in some international airports or other gathering areas such as bus or railway stations. The principle of NCIT is that heat emitted by any organic body can be detected in the infrared radiation spectrum through a remote sensor and transformed into colour images on a monitor. The clinical applications of non-contact infrared thermography include the diagnostic of inflammatory disorders or cancers, or the surveillance of body temperature in neonatology wards through the monitoring of changes in the skin perfusion over time [1,2]. Yet, the extension of these non-invasive diagnostic tools to a public health application, for instance mass screening of breast cancers or fever, has not been thoroughly assessed. Early reports from the SARS experience suggested a low efficacy of NCIT at international airports [3-5] and some authors stressed that NCIT were not currently manufactured for a fever screening purpose [6]. Nevertheless, given the increasing threat of pandemic influenza, some countries envisage to introduce thermal screening at their borders [7]. Their objective is to delay the introduction of the infection through the early detection and isolation of the first infected cases, thus allowing for more time to organise the response.

In this review we summarise the available information on the sensitivity, specificity and predictive values of NCIT used with the objective of fever screening, in airports or other gathering areas. We discuss their potential benefits under the hypothesis of pandemic influenza.

Materials and methods

We performed a systematic MEDLINE search on the literature from 1975 to August 2008. We used the following key words: fever; screening; non-contact, infrared thermography or thermometers; thermal imagers or scanners or pyrometers; thermal screening. The apparent redundancy for some words was necessary because there did not seem to be a standardised vocabulary for the subject. Among the abstracts identified through these key words, we selected the publications which provided the sensitivity and specificity values of NCIT used in a fever screening objective, whatever the cause of the fever.

For international airports, we found partial data from three mass screening interventions using NCIT: two aimed at detecting SARS among international passengers in Canada [4] and in Singapore [8] and one aimed at detecting dengue fever in Taiwan [9]. The numbers of passengers screened and those subsequently confirmed as SARS or dengue cases were provided in these publications but the numbers of passengers who presented with fever due to another cause, i.e. the total numbers of true positive cases, were not available. We therefore discarded these publications which did not allow to derive the sensitivity, specificity and predictive values of NCIT to screen a fever of any origin.

Our search also focused on fever screening interventions in other settings than airports. We selected those which were carried out under conditions considered to be close to a mass screening at international airports, for instance studies implemented in gathering areas, with no preliminary selection or preparation of the tested subjects. We found six studies, performed mainly in hospitals, in which all subjects who were present and accepted to participate were tested. These selected studies summarised in Table 1, included: one in Singapore [10], two in Hong Kong [11,12], two in Taiwan [13,14] and finally one in France [15]. In all, temperatures measured by NCIT were compared to reference values measured by tympanic thermometers i.e. contact thermometers. The authors considered that tympanic thermometers reflected the actual core body temperature with enough confidence, were easy to use because they were routinely used in many hospitals and were more acceptable for the tested subjects than rectal thermometers. The positive and negative predictive values (PPV and NPV) were reported in three of the selected studies. For the others, we derived these values from the available sensitivity, specificity and prevalence data. Finally, because the prevalence of fever in the study populations varied and in order to allow comparisons, we assumed a fixed fever prevalence of 1% in all studies and derived predictive values based upon the sensitivity and specificity as reported in each study. We considered that 1% prevalence was a plausible assumption of the proportion of febrile subjects among international passengers, based on findings from a review of interventions to control SARS [3].

Through our search, we also identified other studies on NCIT with sensitivity and specificity values but these were discarded because they were carried out under strict surrounding conditions which did not fit with our specific objective which was to assess the performances of NCIT under mass screening conditions, in crowded/gathering areas. For instance, participating subjects were asked to refrain from drinking caffeine-based beverages or from exercising the day before. Elsewhere, the device was scanned across the forehead in order to identify specific skin areas where the physiological variations of the skin temperature were reduced. Finally, we also excluded a large number of reports identified through Internet searches, other than Medline, in which information was too scarce.

Results

The study populations ranged from 176 to 72,327 persons (Table 1). They were composed of either hospitalised patients, or persons presenting for emergency or for outpatient consultations, or supposedly healthy persons selected among hospital visitors or sports clubs. Information on age or gender was mostly unavailable. The fever thresholds varied between 37.5°C and 38°C (these were mainly based on the thresholds which were used in the respective countries during the SARS outbreak). The body areas targeted by NCIT systematically included the forehead; the inner eye corner or the external auricular meatus were other skin areas occasionally targeted by the devices. Different types of devices were tested. In four studies, hand-held thermometers were assessed. This implied a shorter distance between the device and tested subjects (=<50cm) than in the two other studies which used remote sensors linked to a monitor (>=50cm). The devices were calibrated according to the respective producers' recommendations. Two studies were carried out in stable external environments consisting of a single dedicated room with stable ambient temperature and ventilation system [12,14].

The prevalence of fever measured by reference contact tympanic thermometers varied from 1.2% to 20.7% in the respective samples, with variable fever thresholds (Table 2). This prevalence was either based on the entire study population or was estimated from a sub-sample. The sensitivity, specificity and predictive values of NCIT targeting the forehead area largely differed between studies. The sensitivity varied from 4.0% to 89.6%, the specificity from 75.4% to 99.6%, the PPV from 0.9% to 76.0% and the NPV from 86.1% to 99.7%. The lowest PPV was found in the study by Chiu

Table 1

Summary of studies on fever screening by non-contact infrared thermometers, 2004-2008

First author, reference	Country, area	Study population (N)	Settings	Sample size *	Temperature threshold	Target area(s)	Device	Environmental conditions
Ng E [10] *Microvasc Res 2004*	Singapore	502	Hospital	310	37.7° C	Forehead	Flir ® S60 Hand held	na
				310		Inner eye corner		
Liu CC [14] *Infect Control Hosp Epidemiol 2004*	Taiwan	500	Outpatient consultation	500	37.5° C	Forehead	Thermofocus ® Hand held	Stable
				500		Auricular meatus		
Chan LS [11] *Travel Med 2004*	Hong Kong	176	Hospital, consultations and sports club	188	37.5°C & 38°C	Forehead	Flir ® -3 models Remote sensors	na
				116		Auricular meatus		
Ng DK [12] *Ann Trop Paed 2005*	Hong Kong	500	Inpatients (Age:1 month-18 years)	500	38° C	Forehead	Standard ST ® Hand held	Stable
Chiu WT [13] *Asia Pac J Public Health 2005*	Taiwan	993	Hospital visitors	993	37.5° C	Forehead	Telesis ® Remote sensors	na
		72.327	Patients + visitors	72.327	37.5° C	Forehead		na
Hausfater P [15] *Emerg Inf Dis 2008*	France	2026	Emergency department (Age 6 – 103 years)	2.026	38° C	Forehead	Raynger ® ** Hand held	Dedicated nurse

* Number of measurements done in each population
na: Information not available

et al. [13] in their second series of measures conducted among 72,327 patients and hospital visitors, in which fever prevalence was not given.

Receiver operating characteristic (ROC) curves were assessed by three teams; the values of the area under the curve reached 0.96, 0.92 and 0.86 in the studies of E. Ng et al. [10], Hausfater et al. [15] and D. Ng et al. [12], respectively. The correlation coefficient between the forehead and reference tympanic temperatures varied from 0.25 to 0.51 in the two studies where it was quantified [11,14] and was 0.71 when we derived it from the available data in E. Ng [10].

The external auricular meatus area was tested in two studies. This target area yielded higher sensitivity results than the forehead: 82.7% vs. 17.3% [14] and 67.0% vs. 4.0% [11], respectively. Specificity remained high: 98.7% and 96.0%, respectively.

When we fixed the fever prevalence at 1% in all studies and used the sensitivity and specificity values as reported by the respective authors, the derived PPV for the forehead area varied from 3.5% to 65.4% and the derived NPV was =>99% (Table 3).

Discussion

Interpretation and comparison of findings were made difficult by the limited number of selected studies and their wide heterogeneity in terms of methods, study design and environmental conditions. Also, the level of available details in the published papers varied regarding the different study populations which included either healthy or sick persons, and the different types of tested NCIT which included hand-held or remote sensors. The relevance of tympanic (contact) thermometers as reference measurements might also be discussed, but the authors selected feasible and acceptable methods. Another important bias resides in the devices themselves: under operational conditions, the detection of fever by NCIT can be affected by three types of factors [10]. Individual factors such as the consumption of hot beverages or alcohol, pregnancy, menstrual period or hormonal treatments can increase the external skin temperature. Inversely, intense perspiration or heavy face make-up can have a cooling effect on the cutaneous temperature without a parallel decrease of the actual body temperature. The targeted body area scanned by the detector also plays a role, because of physiological differences in vascularisation and consequently in heat distribution. The forehead is subject to important physiological variations but is preferred in screening programmes for feasibility reasons. Inversely, the inner eye corner or the auricular area are less subject to variations but are less accessible: targeting the external auricular area yields better results but travellers would have to be asked to remove their scarves, etc. from around the ear, generating a longer preparation time. Finally, environmental factors can also affect the measurements [2,10], such as the subject-sensor distance, the ambient temperature or humidity and the surrounding ventilation systems, as well as the fact that the person tested should remain immobile for a few seconds in front of the detector.

Despite these constraints, there are several advantages in using NCIT to screen fever at international airports. NCIT save time (temperature is displayed within a few seconds) and reduce close contacts with infected individuals. But, although NCIT appear suitable for entry screening because of high specificity and NPV, the low sensitivity values reported in the studies suggest that the risk of missing febrile individuals (1-sensitivity) would reach 83 to 85% [11,14]. In addition, given the low PPV, hostile reactions may arise among a high proportion of passengers mistakenly classified as febrile by the sensors and subsequently referred for medical examination. Because of these limitations, most authors were extremely cautious in their respective conclusions, stating for instance that NCIT may serve as a proxy tool [11] or that surveillance and contact tracing would be more beneficial [14].

Table 2

Fever screening by non-contact infrared thermometers, 2004-2008: sensitivity, specificity and predictive values according to the body area targeted

First author, country, publication year	Sample size	Target area(s)	Temperature threshold	Fever prevalence %	Sensitivity %	Specificity %	PPV %	NPV %
Ng E Singapore 2004	310	Forehead	37.7°C	16.9	89.6	94.3	***76.0****	***97.8****
	310	Inner eye corner	37.7°C	16.9	85.4	95	***77.7****	***97.0****
Liu CC Taiwan 2004	500	Forehead	37.5°C	-	17.3	98.2		
	500	Auricular meatus	37.5°C	-	82.7	98.7		
Chan LS Hong Kong 2004	188	Forehead	38°C	14.3	4	99	***40.1****	***86.1****
	-	Forehead	37.5°C	Na	15	98		
	116	Auricular meatus	38°C	20.7	67	96	***81.4****	***91.8****
Ng DK Hong Kong 2005	500	Forehead	37.5°C †	12.3 †	89.4	75.4	33.7	98.1
Chiu W Taiwan 2005	993	Forehead	37.5°C	1.2	75	99.6	***69.9****	***99.7****
	72.327	Forehead	37.5°C	-	-	-	***0.9****	
Hausfater P France 2008	2.026	Forehead	38.0°C	3.0	82	77	10	99

* Values derived from the available information are in ***bold italic***
† The 37.5°C cut-off corresponds to the optimal sensitivity and specificity values reported by the authors whereas the prevalence (12.3%) is based on a 38°C threshold.
PPV: Positive predictive values; NPV: Negative predictive values

Under a pandemic influenza scenario, one could expect a higher PPV, because of a higher prevalence of fever (>1%). But it is in the very early stages of the pandemic that NCITs would be considered as a way to delay the introduction of infection in a given area. In these early stages, the number of infected cases would be very low and the overall prevalence of fever among international passengers would remain below the 1% rate which we set in our analysis.

Finally, even if better-performing devices were manufactured and implementation costs were affordable for national authorities, the overall efficiency of the screening intervention would still need to be examined. As stated by an international experts committee [16], the overall sensitivity of border control is likely to be limited. Modelling works show that border control strategies aimed at reducing the risk of introduction of SARS or influenza in a country have poor sensitivity [17] and limited impact [18-21]. The epidemiological characteristics of the infection play a major role, as illustrated by the differences between SARS and influenza. For SARS, infectiousness peaks after the onset of symptoms, therefore early detection of patients may indeed contribute to their early isolation and thus reduce transmission. For pandemic influenza, because it is assumed that infectiousness starts a few hours before the onset of symptoms, some cases would be missed and would generate secondary cases after their entry in the country. Sociological factors can also affect the efficacy of border control measures. Knowing that thermal screening is organised in international airports may motivate some symptomatic passengers to delay their travel, but inversely, others may try to hide their symptoms or by-pass border control [22;23]. The psychological reassuring effect on the public can influence the decision to implement such screening, as was the case in Singapore and Canada [24-26], but these countries also recognised that the public may loose confidence in this measure if an undetected case had entered the country and generated secondary cases. Because public perceptions are important, policy makers may feel some pressure to use NCIT but the decision making process should not ignore the poor scientific evidence on NCIT's efficacy to delay the introduction of a novel influenza strain. For transparency reasons, the surrounding sociological, demographic, epidemiological and environmental factors which can influence the screening strategy must also be taken into consideration.

Table 3

Fever screening by non-contact infrared thermometers (NCIT), 2004-2008: positive and negative predictive values of NCIT for forehead temperature screening, assuming a fever prevalence of 1%

First author, country	Sample	Fever threshold	Sensitivity %	Specificity %	PPV %	NPV %
Ng E. Singapore	310	37.7°C	89.6	94.3	13.7	99.9
Liu CC Taiwan	500	37.5°C	17.3	98.2	8.8	99.2
Chan LS Hong Kong	188	38°C	4	99	3.9	99.0
	188	37.5°C	15	98	7.0	99.1
Ng DK Hong Kong	1.000	37.5°C	89.4	75.4	3.5	99.9
Chiu W Taiwan	993	37.5°C	75	99.6	65.4	99.7
Hausfater P France	2.026	38°C	82	77	9.9	99.3

PPV: Positive predictive values; NPV: Negative predictive values

Aknowledgements

We thank Isabelle Bonmarin, Didier Che, Dennis Falzon and Veronique Vaillant for their helpful comments.

This work was done as part of SARSControl : Effective and Acceptable Strategies for the Control of SARS and New Emerging Infections in China and Europe, a European Commission project funded within the Sixth Framework Programme, Thematic Priority Scientific Support to policies, Contract no. SP22-CT-2004-003824.

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This article was published on 12 February 2009.

Citation style for this article: Bitar D, Goubar A, Desenclos JC. International travels and fever screening during epidemics: a literature review on the effectiveness and potential use of non-contact infrared thermometers. Euro Surveill. 2009;14(6):pii=19115. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19115