VOL.11

Issues 10-12
Oct-Dec 2006

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Eurosurveillance

EUROPEAN COMMUNICABLE DISEASE JOURNAL

Early warning and response in Europe

European regulation

- Implementing the International Health Regulations (2005) in Europe

Outbreak report

- A pseudo-outbreak of human A/H5N1 infections in Greece

Surveillance report

- Improvement of a national public health surveillance system through quality circle

FUNDED BY DG HEALTH AND CONSUMER PROTECTION OF THE COMMISSION OF THE EUROPEAN COMMUNITIES

Eurosurveillance VOL.11

Issues 10-12
Oct-Dec 2006

Peer-reviewed European information on communicable disease surveillance and control

Eurosurveillance

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Editorial offices

France
Institut de Veille Sanitaire (InVS)
12, rue du Val d'Osne
94415 Saint-Maurice, France
Tel + 33 (0) 1 41 79 68 33
Fax + 33 (0) 1 55 12 53 35

UK
Health Protection Agency
Centre for Infections
61 Colindale Avenue
London NW9 5EQ, UK
Tel + 44 (0) 20 8327 7417
Fax + 44 (0) 20 8200 7868

RESPONSIBLE EDITOR
Gilles Brücker (InVS, France)

MANAGING EDITORS
Hélène Therre (InVS, France)
h.therre@invs.sante.fr
Elizabeth Hoile (HPA CfI, UK)
elizabeth.hoile@hpa.org.uk

PROJECT LEADERS
Philippe Bossi (InVS, France)
Noel Gill (HPA CfI, UK))

ASSISTANT EDITORS
Anneli Goldschmidt (InVS, France)
a.goldschmidt@invs.sante.fr
Farida Mihoub (InVS, France)
f.mihoub@invs.sante.fr
Candice Pettifer (ECDC, Sweden)
candice.pettifer@ecdc.eu.int

ASSOCIATE EDITORS
Noel Gill (HPA CfI, UK)
Stefania Salmaso (Istituto Superiore di Sanità, Italy)
Henriette de Valk (InVS, France)
Norman Noah (London School of Hygiene and Tropical Medicine, UK)
Richard Pebody (HPA CfI, UK)
Kate Soldan (HPA CfI, UK)
Karl Ekdahl (ECDC, Sweden)

EDITORIAL ADVISORS
(see back cover)

www.eurosurveillance.org

Articles published in Eurosurveillance are indexed by Medline/Index Medicus

Contents

The Eurosurveillance print edition is a compilation of weekly and monthly electronic releases published on the Eurosurveillance website. Only a representative selection of Eurosurveillance's weekly release articles from each three month period are printed here, and the full listing of all Eurosurveillance articles can be found in the Archives section of the website.

EDITORIAL

MEASLES ELIMINATION 2010 TARGET: THE NEED TO MEET THE SPECIFIC RISK GROUP

John S Spika
WHO Regional Office for Europe, Copenhagen, Denmark

Substantial progress has been made within the World Health Organization European Region in recent years towards the measles and rubella elimination targets for 2010. These 2010 targets were set in 2005 by the WHO European Regional Office for Europe, following the approval of the Resolution EUR/RC55/R7 [1,2]. In 2005, 28 (54%) of 52 WHO member states reported a measles incidence of < 1 per million population (one indicator for measuring measles elimination status) and by 2006, 50 (96%) had introduced rubella vaccine into their national programmes. In 2002, member states began reporting measles cases by age and vaccination status to WHO on a monthly basis [3] and case-based reporting was implemented in 2003. Since that time, the number of countries reporting case-based data has increased from one in 2003 to 23 in 2006. In 2006, countries have been asked to report rubella cases monthly (either aggregate or case-based). The WHO European Region measles/rubella laboratory network has also been strengthened through regular laboratory assessments and proficiency testing and by having subregional meetings.

The ability to epidemiologically and virologically link measles cases with a source is critical for assessing the interruption of endemic transmission within and between countries in the European Region.

The past two years have been challenging, with several large outbreaks in the European Region. The outbreaks in Romania and the Ukraine [4] were the source of measles outbreaks in a number of EU countries, including Estonia, Germany, Lithuania, Portugal, Poland and Spain. These primary and secondary outbreaks have identified susceptible people in some countries which had already achieved very good levels of measles control. The outbreaks have also demonstrated the current capacity for investigation at the local level, including the collection of laboratory specimens for virus isolation/ detection, and the capabilities of the measles/rubella laboratory network for tracking specific measles virus genotypes and subtypes.

The paper in this issue of *Eurosurveillance* [5] describing the measles outbreak in La Rioja identifies some of the challenges faced by countries in the European Region as we move towards measles elimination. All countries need to have strong epidemiological surveillance in place to detect importations rapidly and allow quick response to outbreaks when they occur. The ability to epidemiologically and virologically link measles cases with a source is critical for assessing the interruption of endemic transmission within and between countries in the European Region. The D6 measles virus genotype causing disease in La Rioja was genetically identical to the strain causing disease in the Ukraine, based on the sequence of the 450 nucleotides of the C-terminus of the N (nucleoprotein) gene, the single most variable part of the measles genome.

The importance of healthcare workers being immune to measles is demonstrated in the La Rioja outbreak. Many healthcare workers may have received none or only one dose of measles vaccine, yet they have not been exposed to measles because virus circulation has diminished with vaccine use. Ensuring that all healthcare workers are adequately protected is key to preventing healthcare-associated infections. Immunisation records of healthcare workers should be reviewed and careful consideration given to ensuring that all have received two doses of measles vaccine, unless they were born well before measles vaccine was introduced.

The high proportion of measles cases observed in children aged 15 months or younger is noteworthy, given this is younger than the recommended age in La Rioja for the first dose of measles vaccine. The most effective primary prevention strategies for measles among those younger than the age of first dose are to ensure high levels of immunity among older siblings and caregivers. Outbreaks such as the one in La Rioja require that public health officials develop interventions customised to meet the specific risk group based on a thorough epidemiological investigation. Once the decision has been taken to immunise infants at an age younger than the routine first dose, it is also necessary to decide when the practice should be discontinued. Outbreaks such as this could justify the decision for countries where the first dose of measles vaccine is currently given at 12 months not to further postpone the age of first dose, at least until measles has been eliminated in the European Region.

References

1. Resolution EUR/RC55/R7: Strengthening national immunization systems through measles and rubella elimination and prevention of congenital rubella infection in WHO's European Region [http://www.euro.who.int/Governance/resolutions/2005/20050920_3]
2. *Eliminating measles and rubella and prevention congenital rubella infection, WHO European Region strategic plan 2005-2010* [Available from: http://www.euro.who.int/vaccine/20030808_4 in English, French, German and Russian]
3. Hanon FX, J. Spika JS, Wassilak Steven S, Emiroglu N. WHO European Region's strategy for elimination of measles and congenital rubella infection. Euro Surveill 2003;8(6):129-130. Available from: http://www.eurosurveillance.org/em/v08n06/0806-222.asp?langue=02&
4. Spika JS, Aidyralieva C, L Mukharskaya L, Kostyuchenko NN, Mulders M, Lipskaya G, Emiroglu N. Measles outbreak in the Ukraine, 2005-2006. Euro Surveill. 2006;11(3):E060309.1 Available from: http://www.eurosurveillance.org/ew/2006/060309.asp#1
5. Perucha M, Ramalle-Gómara E, Lezaun ME, Blanco A, Quiñones C, Blasco M et al. A measles outbreak in children under 15 months of age in La Rioja, Spain, 2005-2006. Euro Surveill. 2006;11(9). Available from: http://www.eurosurveillance.org/ew/2006

EDITORIAL

A/H5N1 in the European Union: current levels of risk to humans, and responding to human cases and outbreaks

Sarah De Martin, Angus Nicoll and Denis Coulombier
European Centre for Disease Prevention and Control. Stockholm, Sweden

This issue of Eurosurveillance includes a report by Spala *et al.* of the investigation of a suspected outbreak in Greece of humans with avian influenza A/H5N1 virus [1]. This took place in the early spring of 2006 when infected wild birds appeared in many European Union (EU) countries. There were confirmed infections in birds in Greece, but after careful investigation, no human infections were found. However, the massive investigation and control that had to take place around the infections and deaths in the outbreak in Turkey in December 2005 and January 2006 [2] is a reminder of what could have been in Greece or other EU countries.

Worldwide, between the end of 2003 and 31 October 2006 [3], 256 laboratory confirmed cases of human infection (152 of which are known to have died) have been reported by the World Health Organization (WHO). One hundred and nine cases and 74 deaths have been reported to date in 2006. This compares with 97 cases (42 deaths) in all of 2005 and 46 cases (32 deaths) in 2004. Cases have been reported from ten countries: Azerbaijan (8), Cambodia (6), China (21), Djibouti (1), Egypt (15), Indonesia (72), Iraq (3), Thailand (25), Turkey (12) and Vietnam (93). Most of these infections have arisen from exposure to sick infected domestic poultry.

Confirmed A/H5N1 infections in birds have been detected in the majority of EU countries since early 2006, mostly in wild birds [4], but some extended to poultry. Many were associated with a wave of wild bird infections that appeared in late winter and early spring [5]. It must be assumed that while A/H5N1 is found in other continents, the risk of infection in wild birds in Europe will continue. Indeed, during the summer of 2006, there were outbreaks in Hungary, as well as sporadic cases in other EU countries, and there is the imponderable risk of fresh waves of infected migratory birds [6]. There are also other highly pathogenic avian influenzas, like A/H7N7, that pose risks to humans, albeit at a much lower level than A/H5N1 [7].

What are the risks to human health from A/H5N1 in Europe? Putting aside the unquantifiable risk of the emergence of a pandemic H5 strain, the risks are low, but not zero. Essentially, the avian influenza A/H5N1 viruses remain for humans '*a group of influenza viruses of birds, poorly adapted to humans whom they find hard to infect except at high doses. They are dangerous as they are highly pathogenic in those few humans that do become infected, but then they generally do not transmit on to other humans*' [8]. Though the viruses continue to change genetically and extend their geographic range, their pandemic potential remains uncertain there has been no change in its considerable potential threat to humans [9]. The direct risk from wild birds is close to zero (the only people ever known to have been infected worldwide from wild birds acquired the infection while slaughtering wild swans in Azerbaijan) [10]. The risk to humans in Europe is almost entirely among people owning small numbers of domestic or 'backyard' poultry (referred to as Sector 4 poultry by FAO) [11]. Such domestic poultry are to be found in all EU countries, and in many of these countries, they sometimes live in close proximity to humans. The risk to human health from poultry in industrialised farms is considerably lower, both because biosecurity levels can be kept at higher levels, and as a result of the successful EU policy of separating poultry away from wild birds on larger farms.

While A/H5N1 is prevalent in birds, EU member states will need to continue investigating people who present with respiratory illness and who are thought to have had contact, in Europe or elsewhere, with infected domestic birds or, occasionally, with human cases. There will be a steady trickle of such people coming forward with febrile respiratory illness and needing evaluation. Fortunately there are a number of well-tested algorithms developed for this purpose on EU member states' websites (for example, the Health Protection Agency [12] and Institut de veille sanitaire [13] websites).

When making an initial assessment of patients who present with febrile respiratory illness to a health care centre, and in whom infection with avian influenza A/H5N1 has to be considered, it is important for physicians to start by determining the clinical history and epidemiological (exposure) link. Other differential diagnoses are much more likely and so need to be considered. Treatment has to be based on clinical judgment and not on surveillance case definitions. Appropriate samples should be taken. The initial diagnosis will be based on clinical and exposure history, and on laboratory results when received.

There is currently no formal obligation for notification of a person in whom infection with avian influenza A/H5N1 is considered. The European Centre for Disease Prevention and Control (ECDC) has an interim surveillance case definition for influenza A/H5N1 in humans in the EU. This case definition is not intended to be used for clinical diagnosis or management of cases [14]; its purpose is for surveillance of human cases of influenza A/H5N1 infections in humans in the EU.

A number of procedures and protocols need to be in place for the eventuality of an in-country suspected or confirmed outbreak of H5N1 human infection

However, what is much more serious is a situation, such as those seen in Greece or Turkey, where an in-country outbreak of human infection is suspected or confirmed. A number of procedures and protocols need to be in place for this eventuality. These include standard operating procedures for persons under investigation for avian influenza, case definitions and data collection forms, arrangements for public health and animal health collaboration, materials for health education and risk communication, etc.

Some member states have produced guidance for the eventuality of a human A/H5N1 infection in their countries, and in June 2006 ECDC published an avian influenza portfolio with a number of the necessary components [15]. Now, in response to events like that in Greece, and based on experience in Turkey and other countries, ECDC has developed a 'Human Avian Influenza Tool Kit', a set of documents and forms that can by used by countries for the public health assessment and management of human avian influenza outbreaks in Europe.

References

1. Spala G, Panagiotopoulos T, Mavroidi N, Dedoukou X, Baka A, Tsonou P *et al.*. An outbreak of people requiring evaluation for A/H5N1 infection in Greece: A pseudo-outbreak and its public health implications. Euro Surveill. 2006; 11(11). Available from: http://www.eurosurveillance.org/em/v11n11/1111-223.asp
2. WHO international response team. Human cases of influenza A(H5N1) infection in eastern Turkey, December 2005–January 2006. Wkly Epidemiol Rec. 2006;81(43):410-16. Available from: http://www.who.int/wer/2006/wer8143.pdf
3. Epidemic and Pandemic Alert and Response (EPR). Cumulative Number of Confirmed Human Cases of Avian Influenza A/(H5N1) Reported to WHO. 31 October 2006. Available from: http://www.who.int/csr/disease/avian_influenza/country/cases_table_2006_10_31/en/index.html

→→→

4. European Commission. DG Health and Consumer Protection. Animal Health and Welfare. Avian Influenza in wild birds from 1 january 2006 to 2 August 2006. Available from: http://ec.europa.eu/food/animal/diseases/adns/map/20060802/europe.htm

5. European Commission. DG Health and Consumer Protection. Animal Health and Welfare. HPAI cases in wild birds in the MSs. 2006;0911. Available from: http://ec.europa.eu/food/animal/diseases/adns/adns_wildbirds_09112006.pdf

6. World Organisation for Animal Health. Update on Avian Influenza in Animals (Type H5). 16 November 2006. Available from: http://www.oie.int/downld/AVIAN%20INFLUENZA/A_AI-Asia.htm

7. Fouchier RA, Schneeberger PM, Rozendaal FW, Broekman JM, Kemink SA, Munster V, Kuiken T, Rimmelzwaan GF, Schutten M, Van Doornum GJ, Koch G, Bosman A, Koopmans M, Osterhaus AD. Avian influenza A virus (H7N7) associated with human conjunctivitis and a fatal case of acute respiratory distress syndrome. Proc Natl Acad Sci U S A. 2004 Feb 3;101(5):1356-61

8. European Centre for Disease Prevention and Control (ECDC). The public health risk from highly pathogenic avian influenza viruses emerging in Europe with specific reference to type A/H5N1. Technical report. 1 June 2006. Available from: http://www.ecdc.europa.eu/Health_topics/Avian_Influenza/pdf/060601_public_health_risk_HPAI.pdf

9. Webster RG & Govorkova EA H5N1 Influenza – Continuing evolution and spread New England Journal of Medicine. 2006; 355: 2174-7 http://content.nejm.org/cgi/content/short/355/21/2174

10. No authors listed. Human avian influenza in Azerbaijan, February–March 2006. Wkly Epidemiol Rec. 2006;81:183-8. Available from: http://www.who.int/wer/2006/wer8118.pdf

11. European Centre for Disease Prevention and Control (ECDC). ECDC Scientific Advice. Who is at Risk of getting HPAI? Technical Report | Version May 20th 2006. Available from: http://www.ecdc.europa.eu/Health_topics/Avian_Influenza/pdf/Table_Who_is_at_risk_H5N1.pdf

12. Health Protection Agency. WHO Pandemic Alert Phase 3 Algorithms. Reviewed 13 October 2006. Available from: http://www.hpa.org.uk/infections/topics_az/influenza/avian/guidelines.htm

13. Institut de Veille Sanitaire. Conduite à tenir devant des cas possibles de grippe à nouvelle souche de virus grippal sans transmission inter humaine. [Adapted behaviour face to possible influenza cases with new influenza strains and without any human-to-human transmission]. 25 November 2005. In French. Available from: http://www.invs.sante.fr/surveillance/grippe_dossier/conduite.pdf

14. European Centre for Disease Prevention and Control (ECDC). Interim surveillance case definition for influenza A/H5N1 in humans in the EU Version April 2006. Available from: http://www.ecdc.europa.eu/Health_topics/Avian_Influenza/pdf/H5N1_Case_definition.pdf

15. European Centre for Disease Prevention and Control (ECDC). Avian Influenza - Scientific and Technical Guidance. Available from: http://www.ecdc.europa.eu/Health_topics/Avian_Influenza/Guidance.html

EDITORIAL

FROM EVALUATION TO CONTINUOUS QUALITY ASSURANCE OF SURVEILLANCE SYSTEMS

Gérard Krause
Robert Koch-Institut, Berlin, Germany

Surveillance systems have been described as the nerve cells of public health with afferent arms receiving information, cell bodies analysing the information and efferent arms initiating appropriate action or further distribution of information [1]. Increasing numbers of scientific publications on the methodology and evaluation of surveillance systems seem to underline the importance of surveillance systems in public health. The most often cited references in these publications appear to be the definition of public health surveillance by Thacker and Berkelman [2] and variations thereof, and the recommendations for evaluating surveillance systems from 1988 [3] and its update from 2002 written by working groups at the Centers for Disease Control and Prevention (CDC) in the United States [4].

While surveillance certainly does need to be approached systematically, the evaluation of surveillance systems needs to be part of a broader strategy. One example of such a systematic evaluation strategy is the current evaluation process of all European Union Disease Surveillance Networks (DSN) coordinated by the European Centre for Disease Prevention and Control (ECDC) [5].

Do such evaluations have a lasting and positive effect on the quality of the system? If public health surveillance needs to be continuous, should not evaluation of a surveillance system also be continuous? How do these evaluations fit into the concept of continuous quality assurance?

Quality assurance is generally described as a continuous process to improve quality of a system; Decker called this the plan-do-check-act cycle [6]. In such a system, evaluation is only one component of quality assurance, typically followed by problem identification, problem analysis and intervention [6-8]. In hospital epidemiology in particular, it is acknowledged that surveillance is an effective component of quality assurance, yet little has been published about the role of quality assurance as a component of a surveillance system. In one of the few publications on this subject, Salman et al describe surveillance system evaluations as part of quality assurance in animal disease surveillance systems [9]. It is intriguing that most medical disciplines have adopted the principles of quality assurance as a continuous process, while epidemiology appears to maintain a static concept of quality control in surveillance management. On the other hand, one might argue that procedures such as the cleaning of databases, application of case definitions, standard operating procedures, and algorithms to detect statistical deviations are to be seen as part of an integrated quality assurance process. While this is undoubtedly true, there are multiple additional activities that could or should be part of a quality assurance effort.

If public health surveillance needs to be continuous, should not evaluation of a surveillance system also be continuous?

When Germany enacted a new law on infectious disease control in 2001, the national surveillance system for notifiable infectious diseases was significantly restructured and expanded [10]. Simultaneously with the implementation of the system the Robert Koch-Institut (RKI) has applied a variety of activities to accompany and to influence the implementation by actively gathering feedback from participants or other interested parties of the surveillance system. Before implementation of the new system, surveys carried out in local health departments (LHD) provided baseline data for the design of the new system. A few months after the implementation of the new system, the RKI conducted focused group discussions among LHD officers to identify key challenges in the practical implementation of the new system [11]. These led to the instalment of technical info-mails and influenced the design and frequency of data feedback to LHD. Some of the hypotheses generated on the basis of these focused group discussions were then systematically assessed in a survey of all 430 local health departments [12]. The results of this survey had a major impact on the development and design of a number of tools such as SurvStat@RKI, a web-based interactive query system for surveillance data [13]. Additional information was gained through an interdisciplinary quality circle, as described in the report published in this Eurosurveillance issue [14], which was also complemented by larger surveys among general practitioners [15], laboratories [16] and recipients of the yearly epidemiological report. An example for a very specific aspect of evaluation was the application of a round robin methodology including all local health departments to assess the unambiguity and clarity of the national case definitions [17]. This resulted in a new structure and a thorough revision of the national case definitions [18], and has also contributed to the

revised version of the EU case definitions currently being finalised by ECDC. A number of capture-recapture analyses have provided a framework for estimating the completeness of reporting and thus an important aspect of the epidemiological interpretation [19]. All these activities are components of an ongoing effort to further improve the national surveillance systems for notifiable infectious diseases and have resulted in very practical consequences in the surveillance system. Admittedly, these components have not yet been scheduled for a systematic, intermittent reassessment of the progress, and therefore cannot be considered proof of an existing quality assurance system. One module which is, however, designed to contribute to continuous quality assurance is a direct result of the quality circle described in this issue. In 2004 the RKI established a special network of 45 representatively selected local health departments (LHD) (approximately 10% of the total number of LHD) to conduct regular workshops on technical issues of the surveillance system using a quality circle approach. This network, which has been working almost continuously, has enabled the RKI to better assess the needs of LHD and to pre-test various surveillance instruments such as questionnaires and reporting software. Similar approaches certainly exist in other countries. However, as far as can be seen from the current literature, continuous quality assurance is not well established in surveillance systems. If evaluations are integrated into such a quality assurance system they are likely to have more impact on the improvement of the system. It therefore seems worthwhile to assess how the concept of continuous quality assessment should and could be established in the design of surveillance systems. The current evaluation of DSN may be a good opportunity to start this process.

References

1. Thacker SB. Surveillance. In: Field Epidemiology. Gregg MB, Dicker RC, Goodman RA, editors. Oxford University Press, USA; 1996: 17.
2. Thacker SB, Berkelman RL. Public health surveillance in the United States. Epidemiol Rev. 1988;10:164-90.
3. Klaucke DN, Buehler JW, Thacker SB, Parrish RG, Trowbridge FL, Berkelman RL et al. Guidelines for evaluating surveillance systems. MMWR Morb Mortal Wkly Rep. 1988;37 Suppl 5:1-18.
4. Centres For Disease Control. Updated guidelines for evaluating public health surveillance systems: recommendations from the guidelines working group. MMWR Morb Mortal Wkly Rep. 2002; 50 (RR-13):1-35.
5. ECDC. Evaluation of Networks. In: Minutes of the Sixth meeting of the Advisory Forum, Stockholm, 10-11 May 2006 [Accessed 13 Nov. 2006] Available from: http://www.ecdc.eu.int/about_us/governance/AF/Minutes/Minutes_%20AF6.pdf
6. Decker MD. Continuous quality improvement. Infect Control Hosp Epidemiol. 1992; 13(3):165-9.
7. Krause G. [Quality management in hospital epidemiology] In: Hygieneleitfaden (Rüden H, Daschner F, editors). Springer Verlag, Heidelberg; 1998.
8. Donabedian A. The definition of quality and approaches to its assessment. Vol 1 of Explorations in Quality Assessment and Monitoring. Health Administration Press, Ann Arbor, Michigan, 1980
9. Salman, Stark KD, Zepeda C. Quality assurance applied to animal disease surveillance systems. Rev Sci Tech. 2003;22(2):689-96.
10. Krause G, Altmann D, Claus H, Hellenbrand W, Buchholz U, Hamouda O et al. [First evaluation of the surveillance systems of notifiable diseases under the infectious disease control law in Germany]. Gesundheitswesen. 2003; 65 Suppl 1:S8-12. In German.
11. Krause G. [Experiences of the German public health service with the implementation of a new infections disease control act -- results of focus group discussions]. Gesundheitswesen 2004; 66(8-9):522-7. In German.
12. Brodhun B, Kramer MH, Krause G. [Survey among local health departments concerning the implementation of the new infectious disease reporting system]. Bundesgesundheitsbl - Gesundheitsforsch – Gesundheitsschutz. 2004;47(8):755-61. In German.
13. Faensen D, Krause G. SurvStat@RKI – a web-based solution to query surveillance data in Germany. Eurosurveillance Weekly. 2004;5(22) 040527. Available from: http://www.eurosurveillance.org/ew/2004/040527.asp#4
14. Krause G, Benzler J, Reiprich G, Görgen R. Improvement of a national public health surveillance system through use of a quality circle. Euro Surveill. 2006;11(11). Available from: http://eurosurveillance.org/em/v11n11/11-224.asp?langue=02&
15. Krause G, Ropers G, Stark K. Notifiable disease surveillance and practicing physicians. Emerg Infect Dis. 2005;11(3):442-5.
16. Zucs P, Benzler J, Krause G. [Survey among German laboratories regarding practical implications of the Infectious Disease Protection Law, 2003]. Poster at the 11th meeting of the German Association of Epidemiology in Heidelberg, 16-219 March 2004.
17. Krause G, Brodhun B, Altmann D, Claus H, Benzler J. Reliability of case definitions for public health surveillance assessed by Round-Robin test methodology. BMC Public Health. 2006;6:129.
18. Benzler J, Krause G, Mitarbeiter der Abt. für Infektionsepidemiologie. [On the 2004 edition of case definitions for the surveillance of notifiable diseases in Germany]. Bundesgesundheitsbl - Gesundheitsforsch – Gesundheitsschutz. 2004; 47:141-146. In German.
19. Schrauder A, Claus H, Elias J, Vogel U, Haas W, Hellenbrand W. Capture-recapture analysis to estimate the incidence of invasive meningococcal disease in Germany, 2003. Epidemiol Infect. 2006:1-8.

EDITORIAL

ARE THERE 'NEW' AND 'OLD' WAYS TO TRACK INFECTIOUS DISEASES HAZARDS AND OUTBREAKS?

Jean-Claude Desenclos
Institut de Veille Sanitaire, Saint-Maurice, France

In May 2005 the World Health Assembly approved an innovative and ambitious revision of the International Health Regulations, known as IHR(2005), in order to detect and control, in a timely manner, all public health events that may have a serious international impact. It represents a dramatic move from administrative notification by Member States (MS) to the World Health Organization (WHO) of cases of a limited list of diseases to a systematic analysis of health events of international concern, infectious or not [1]. The analysis of the public health events will take into account severity, unexpectedness, potential for international spread, and interference with international movement of people and goods. National focal points are to be identified in each MS to interact with WHO. The philosophy behind the new IHR is to promote early dialogue between MS and WHO, leading early mutual risk assessment of events which may not necessarily have to be notified, depending on the results of the assessment and measures taken. WHO can also use informal sources to detect earlier events of international concern and then, together with the national focal point, conduct verification, risk assessment and implement appropriate measures.

To be successful, IHR(2005) will need to rely on sufficient public health capacity at all levels within the MS, with a strong core surveillance function that can be summarised as the efficient management of health data and response from the first line health practitioner (eg, clinician, biologist) to local, regional and national public health structures. The key issues are the capacity and performance of the public health system and its ability to communicate and interact within its different sectors and with decision makers in a timely, authoritative and transparent way [1]. IHR(2005) add challenges and responsibilities for MS that may need to adjust their national public health infrastructure, often without the help of extra resources. Several events in recent years, such as SARS, avian influenza and the threat of bioterrorism, have served as an early introduction to the concept of IHR(2005). The experience of implementing a weekly early warning committee at the National Institute for Public Health and the Environment in the Netherlands [2] illustrates how some MS are already organised in this respect. The European Early Warning and Response System (EWRS) which has linked MS and the European Commission through an electronic real time secured system since 1998 (and the European Centre for Disease Prevention and Control since 2005) has shown added European value for sharing early validated information on health threats between national public health institutes and authorities and is certainly an experience that can and will be built on [3].

While IHR(2005) were being developed, there was growing interest and investment in real time monitoring of health 'signals' from every possible source, including symptoms, syndromes, crude mortality, drug sales, rumours and media reports. The assumption, which has probably not been sufficiently challenged from a research perspective, is that by using rapidly available but less specific information through automated systems, health threats of the future will (or may) be detected earlier [4]. Although the debate on 'non-specific surveillance' is not new, there are at least two reasons for this development: the information technology now available allows real time technical access to health related databases; and fears about emerging infections and bioterrorism have created social and political demand for faster and more sensitive health information systems.

There is a need for more evidence-based research on the performance, management, effectiveness, cost-effectiveness and added value of non-specific surveillance and new sources of health signals

Indeed, media reports have proven helpful for bringing to light undetected and/or uncontrolled serious outbreaks of international potential, such as SARS [4]. But can we be sure that media reports will detect a future emerging epidemic as effectively, and should we consider media reports as important as the signals generated by surveillance systems? We should recognise that many large or diffuse outbreaks in the recent past have not been detected more quickly because of media reports. However, the way in which the media report a health event or outbreak does give other important and useful information, particularly on its social and political perception. This added social dimension is argument enough for the integration of media monitoring into surveillance schemes.

Three papers [5-7] in this issue of Eurosurveillance report the recent implementation of non-specific surveillance schemes designed for the early detection of health threats. All conclude that the systems were helpful because they were able either to accurately reproduce data generated by existing specific systems or to document excess mortality following an already identified risk. However, none demonstrated a real added capacity to detect events that would otherwise have been missed! In France, real time syndromic surveillance by emergency departments was able to track seasonal influenza as successfully as a network of sentinel general practitioners. It also provided early estimates of the health impact of the July 2006 heat wave [5]. Real time monitoring of the number of deaths also documented a moderate increase of crude mortality during the April 2005 flu outbreak, and of the 2006 heat wave [5]. In order to detect bioterrorist attacks early in the United Kingdom, data on 11 key symptoms/syndromes are received electronically from all National Health System direct call centres covering England and Wales and analysed using automated detection statistical algorithms [6]. The system has indicated many sudden rises in syndromes but their careful analysis has found no evidence of a biological or chemical attack. The system is most suited to detect widespread rises in syndromes in the community, but is currently unlikely to detect more localised outbreaks, such as a cryptosporidiosis outbreak [8]. As shown in France, the benefits were early tracking of rises of community morbidity of already identified risks (eg, influenza-like illness, heat-related deaths following the July 2006 heat wave). It also provided a social added value by reassuring decision makers that widespread disease was not occurring, despite a perceived high health risk [6]. Denmark, with similar goals to the UK, applies a detection algorithm on ambulance dispatch data [7]. The system can implement reactive symptom surveillance in case of an alert. Its evaluation found that decreasing the outbreak detection sensitivity reduced the time to detection moderately, but diminished the number of false alerts considerably. Although the system was able to detect an increased activity related to seasonal influenza in a timely fashion, the authors recognised that small outbreaks occurring over a number of weeks, like the American anthrax outbreak in 2001, would be difficult to detect with ambulance dispatch surveillance.

Enhanced surveillance at mass gatherings has previously been conducted on many occasions [9,10]. Although syndrome based surveillance has been undertaken at several previous mass gatherings, it is not clear whether, for regions with a well-functioning surveillance system, it actually provides more information than that identified through the strengthening of routine surveillance [9]. After

careful consideration of the available evidence and consultation with state health departments, the Robert Koch-Institute concluded that enhancing the German mandatory notification surveillance system would be sufficient for the 2006 World Cup in Germany [9] and decided not to implement syndrome based surveillance. Their experience shows that enhancing the existing system accelerated data transmission and intensified communication and action-orientated cooperation between players of the German public health system. Enhancing surveillance at mass gatherings is, certainly a valuable and cost effective communication and networking exercise of public health structures to face future critical health-related events [8]. An enhanced, but more intensive system than the German example given above was set up in the French region of Hautes-Alpes near the Italian border for the 2006 Olympic Winter Games in Torino [10]. As in Italy, and in most similar experiences previously, it detected no particular health events of high public health concern.

Notification of unusual health events from daily healthcare practice (eg, clinicians, microbiologists, emergency services, hospitals) to public health structures is a valid source of hazard or outbreak detection if the capacity for verification and analysis of the public health system is timely and efficient. Event notification that complements surveillance activities in an effective way is much more likely to work if there is a proactive networking activity of health professionals by those who run the surveillance and public health system. Without a mutual understanding of the usefulness and public health added value of notification and interactive communication between healthcare professionals (in particular clinicians and microbiologists) and public health structures, the challenges and the high social expectations of health security will not easily be met and no automated data collection system will be able to replace it. In this context, the paper by Paquet et al [4] presents an integrated management model of sources of information with a filtering process, with risk assessment linked to decision making and action.

Based on the recent scientific literature and the papers published in this issue, there is a need for more evidence-based research on the performance, management, effectiveness, cost-effectiveness and added value of non-specific surveillance and new sources of health signals. This is important given the cost of implementation and the concurrent needs for disease specific surveillance and other, equally important, public health programmes such as prevention or health promotion. Recent experience has shown that a strong laboratory capacity is necessary at all stages of diagnosis, surveillance and signal assessment and should, therefore, be more clearly integrated and supported. Modelling the spread of a new or epidemic infectious disease, based on available data and reasonable scenarios, is another key element of risk assessment, particularly at national and supranational levels, and should be developed further. Some generic activities such as epidemic intelligence that searches for international health signals would gain in cost-effectiveness if developed and pooled at European level. All of the 'emerging' tools discussed in this issue are of potential interest and may be considered by national authorities to complement gaps in existing national systems based on priority, public health needs and the requirements of IHR(2005). However, their effectiveness cannot be assumed without thorough analysis.

References

1. Rodier G, Hardiman M, Plotkin B, Ganter B. Implementing the International Health Regulations (2005) in Europe. Euro Surveill. 2006;11(12). Available from: http://www.eurosurveillance.org/em/v11n12/1112-222.asp
2. Rahamat-Langendoen JC, van Vliet JA, Suijkerbuijk AWM. Recognition of threats caused by infectious diseases in the Netherlands: the early warning committee. Euro Surveill. 2006;11(12). Available from: http://www.eurosurveillance.org/em/v11n12/1112-230.asp
3. Guglielmetti P, Coulombier D, Thinus G, Van Loock F, Schreck S. The Early Warning and Response System for communicable diseases in the EU: an overview from 1999 to 2005. Euro Surveill. 2006;11(12). Available from: http://www.eurosurveillance.org/em/v11n12/1112-224.asp
4. Paquet C, Coulombier D, Kaiser R, Ciotti M. Epidemic intelligence: a new framework for strengthening disease surveillance in Europe. Euro Surveill. 2006;11(12). Available from: http://www.eurosurveillance.org/em/v11n12/1112-223.asp
5. Josseran L, Nicolau J, Caillère N, Astagneau P, Brücker G. Syndromic surveillance based on emergency department activity and crude mortality: two examples. Euro Surveill. 2006;11(12). Available from: http://www.eurosurveillance.org/em/v11n12/1112-226.asp
6. Smith GE, Cooper DL, Loveridge P, Chinemana F, Gerard E, Verlander N. A national syndromic surveillance system for England and Wales using calls to a telephone helpline. Euro Surveill. 2006;11(12). Available from: http://www.eurosurveillance.org/em/v11n12/1112-225.asp
7. Bork KH, Klein BM, Mølbak K, Trautner S, Pedersen UB, Heegaard E. Surveillance of ambulance dispatch data as a tool for early warning. Euro Surveill. 2006;11(12). Available from: http://www.eurosurveillance.org/em/v11n12/1112-227.asp
8. Cooper D.L., Verlander N.Q., Smith G.E. et al Can syndromic surveillance data detect local outbreaks of communicable disease? A model using a historical cryptosporidiosis outbreak. Epidemiol. Infect. 2006: 134:13-20
9. Schenkel K, Williams C, Eckmanns T, Poggensee G, Benzler J, Josephsen J, Krause G. Enhanced Surveillance of Infectious Diseases : the 2006 FIFA World Cup experience, Germany. Euro Surveill. 2006;11(12). Available from: http://www.eurosurveillance.org/em/v11n12/1112-228.asp
10. Franke F, Coulon L, Renaudat C, Euillot B, Kessalis N, Malfait P. Epidemiologic surveillance system implemented in the Hautes-Alpes district, France, during the Winter Olympic Games, Torino 2006. Euro Surveill. 2006;11(12). Available from: http://www.eurosurveillance.org/em/v11n12/1112-229.asp

Implementing the International Health Regulations (2005) in Europe

G Rodier[1], M Hardiman[1], B Plotkin[1], B Ganter[2]

The adoption of the International Health Regulations (2005) (also referred to as IHR(2005) or the revised Regulations) provides a remarkable new legal tool for the protection of international public health. Upon entry into force on 15 June 2007, Article 2 ('Purpose and scope') provides that the overall focus of the efforts of States Parties (and World Health Organization's efforts under the revised Regulations will be to prevent, protect against, control and provide a public health response to the international spread of disease in ways that are commensurate with the public health risks and which avoid unnecessary interference with international traffic. Health measures under the revised Regulations will be implemented with respect for travellers' human rights, with several specific new requirements in this area. To comply with the IHR(2005), States Parties (WHO member states that will be bound by the IHR(2005)) will have to have core public health capacities in disease surveillance and response, as well as additional capacities at designated international ports, airports and land crossings. This unique collective commitment will require close collaboration between WHO and the States Parties, but also intersectoral collaboration within the States themselves, including collaboration among different administrative or governmental levels, a particular issue for federal states, and horizontally across ministries and disciplines. Collaboration among States Parties is a key aspect of the revised Regulations, whether among neighbours, or with trading partners, members of regional economic integration organisations or other regional groups, or simply members of the international community. This collaboration is particularly relevant for the Member States of the European Union.

Euro Surveill. 2006;11(12): 208-11 Published online December 2006
Key words: health security, health regulations, health emergencies, surveillance, emerging infections, health systems, epidemics, international public health, disease control

Introduction to the IHR(2005)

On 23 May 2005, the World Health Assembly (WHA) adopted the revised IHR(2005) in resolution WHA58.3 [1]. The new text was the conclusion of intensive negotiations of an Intergovernmental Working Group (IGWG) which first met in Geneva in November 2004. The second session of the IGWG was split between deliberations in February and May 2005, with the new public health legal instrument finalised in the early hours of 14 May 2005. These negotiations were preceded by extensive input to the World Health Organization (WHO) from a series of regional consultations, including a consultation of Member States of the WHO Regional Office for Europe in June 2004, as well as a large number of written comments submitted to WHO. Under the new IHR(2005), WHO Member States have until 15 December 2006 to officially notify the WHO Director General of rejection of, or reservations about the IHR(2005), or they will become bound by the revised Regulations on 15 June 2007.

Although the IHR(2005) build in part upon the text of current IHR(1969)[2], they are primarily based on the most recent experiences of WHO and Member States in national surveillance systems, epidemic intelligence, verification, risk assessment, outbreak alert, and coordination of international response, all of which are part of WHO's ongoing work on global health security [3].

More than simply an updated text, the IHR(2005) introduce a range of innovative approaches in global surveillance and response [4,5]. For the first time, states across the globe have agreed on a set of legal rules and procedures to collectively deal with potential public health emergencies of international concern and other international public health risks. The revised Regulations move away from the automatic notification to WHO of a single case of cholera, plague or yellow fever to the notification of all events that may constitute a 'public health emergency of international concern' (PHEIC), taking into account the context in which an event occurs. In addition to assessment and notification requirements, the new Regulations contemplate ongoing communications between WHO and the State Party involved (State Party is the name given to WHO member states that will be bound by the IHR(2005)), and provide specifically for consultation with WHO on appropriate health measures for events which may not need to be notified (at least initially) depending upon evolution of the particular event. A new Emergency Committee will provide its views to the Director-General on whether an event constitutes a PHEIC, in those cases where an affected State Party does not agree that a PHEIC is occurring, and in all cases in which a PHEIC has been declared, on temporary recommendations of the most appropriate and necessary public health measures to respond to the emergency. WHO will play a central role in surveillance, public health response, information sharing, and coordination of international response efforts.

In order to be able to notify, or respond to potential PHEICs, states will have to be able to detect such events through improved national surveillance and response infrastructure that meet at least minimum core capacity requirements. Regarding detection, assessment and reporting of events, for example, Annex 1 of the revised Regulations outlines necessary core capacities for the local (community), intermediate and national levels, culminating at the national level in assessment of all reports of urgent events within 48 hours and reporting to WHO immediately through the National IHR Focal Point if required. Public health response capacity requirements are also indicated for each level; at the national level, for example, States Parties must have the capacities to determine rapidly the control

1. World Health Organization, Epidemic and Pandemic Alert and Response, Geneva, Switzerland
2. World Health Organization, Regional Office for Europe, Copenhagen, Denmark

measures required to prevent disease spread and provide on-site assistance to local investigations. More specifically, States will have to provide response support through specialised staff, laboratory analysis and logistical assistance; direct operational links with senior health and other officials and direct liaison with other relevant government ministries; communications links with hospitals, clinics, ports, airports, laboratories and other key operational areas for dissemination of information; and a national public health emergency response plan, all on a 24-hour basis. For certain international ports, airports and ground crossings designated by the State under IHR(2005), there are additional requirements, including access to appropriate medical service (with diagnostic facilities), services for the transport of ill persons, and trained personnel to inspect ships, aircraft and other conveyances. When health measures are being implemented with regard to travellers, they must be treated with courtesy and respect, taking into consideration their gender, sociocultural, ethnic and religious concerns, and supplied with appropriate food, water, accommodations and medical treatment if quarantined, isolated or otherwise subject to medical or public health measures. Additional provisions establish rules for treatment of personal data and other protections for individuals on international journeys.

Implementing IHR(2005)

Implementing the IHR(2005) will be a challenge for both WHO and the States Parties. It is a challenge for WHO in light of the broad scope of obligations and diseases under IHR(2005), which involve many technical areas and require consistency across a global organisation. WHO's existing alert and response operations [6] will play a key role. For the Member States of WHO, it is also a challenge in many ways. The new rights and obligations for States Parties are extensive. It may be an organisational, administrative or legislative challenge for some states to bring these kinds of infrastructure in line with the requirements of the revised Regulations. It may also present financial challenges for resource-poor countries implementing obligations to strengthen national surveillance and response systems. A WHO strategic implementation plan for IHR(2005) is being developed building on strategies already in place for epidemic-prone diseases in these critical implementation areas, including on-going preparedness efforts related to the threat of avian and pandemic influenza. Implementing IHR(2005) will require sustained national commitment, including budgetary measures, and international cooperation, bilateral and multilateral.

There is a deadline of five years, from entry into force, for States Parties to develop, strengthen and maintain their capacities to detect, assess, notify and report events in accordance with the Regulations, as specified in Annex 1. The same deadline applies to the establishment of capacities to respond promptly and effectively to public health risks and public health emergencies of international concern. More generally, each State Party, within two years of entry into force, must assess the abilities of their national structures and resources to meet the minimum capacity requirements specified in the Annex; based upon these assessments, they must then develop and implement a national implementation plan to achieve the capacities throughout their territories. On the basis of a justified need reported to WHO and the implementation plan, a two-year extension can be obtained by a State Party unable to complete the implementation within the initial 5 years; in exceptional circumstances, a further extension, not exceeding two years, can also be requested by a State Party. In brief, States Parties must establish such core capacities under the IHR(2005) as soon as possible, but have an initial, specific deadline of 15 June 2012 and at most, until 15 June 2016. In some cases, potential small variations may exist.

WHO's six Regional Offices and the recently established WHO IHR Coordination Programme, including its Office in Lyon, will support countries to meet the IHR core capacity requirements.

Focal and contact points

Effective communications between WHO and the States Parties will be central to the rapid management of a possible public health emergency of international concern. Important innovations under the IHR(2005) are the requirements that notification and reporting by States Parties, as well as other urgent IHR communications, generally be transmitted through specific National IHR Focal Points (for States Parties) and IHR Contact Points (for WHO), which must be available at all times for these communications. The primary functions for National IHR Focal Points, which are national centres to be designated or established by each State Party, include sending to WHO IHR Contact Points these urgent communications, and disseminating information to, and consolidating input from, relevant administrative sectors of the State Party, such as those responsible for surveillance and reporting, points of entry (e.g. airports, ports), public health services, clinics, and hospitals. States Parties may also assign additional responsibilities to their focal points. Guidance on IHR national focal points is available on the WHO website; see http://www.who.int/csr/ihr/nfp/en/index.html.

Notification and reporting

While the IHR(2005) contain multiple provisions for event-based reporting by States Parties to WHO, the primary obligation is to *assess* events occurring within their territories according to a specific algorithm contained in the *Decision Instrument* and additional provisions provided in Annex 2 of the revised Regulations, and then to *notify* WHO of all such 'events which may constitute a public health emergency of international concern', within 24 hours of assessment through its National IHR Focal Point. Essentially, the events which must be notified are those that fulfil at least any two of the four criteria in the Decision Instrument: whether the event has or is likely to have a serious public health impact, is unusual or unexpected, creates a risk of international disease spread, or creates a risk that travel or trade restrictions will be imposed by other countries [FIGURE]. There are also further questions and examples for guidance in applying the Decision Instrument.

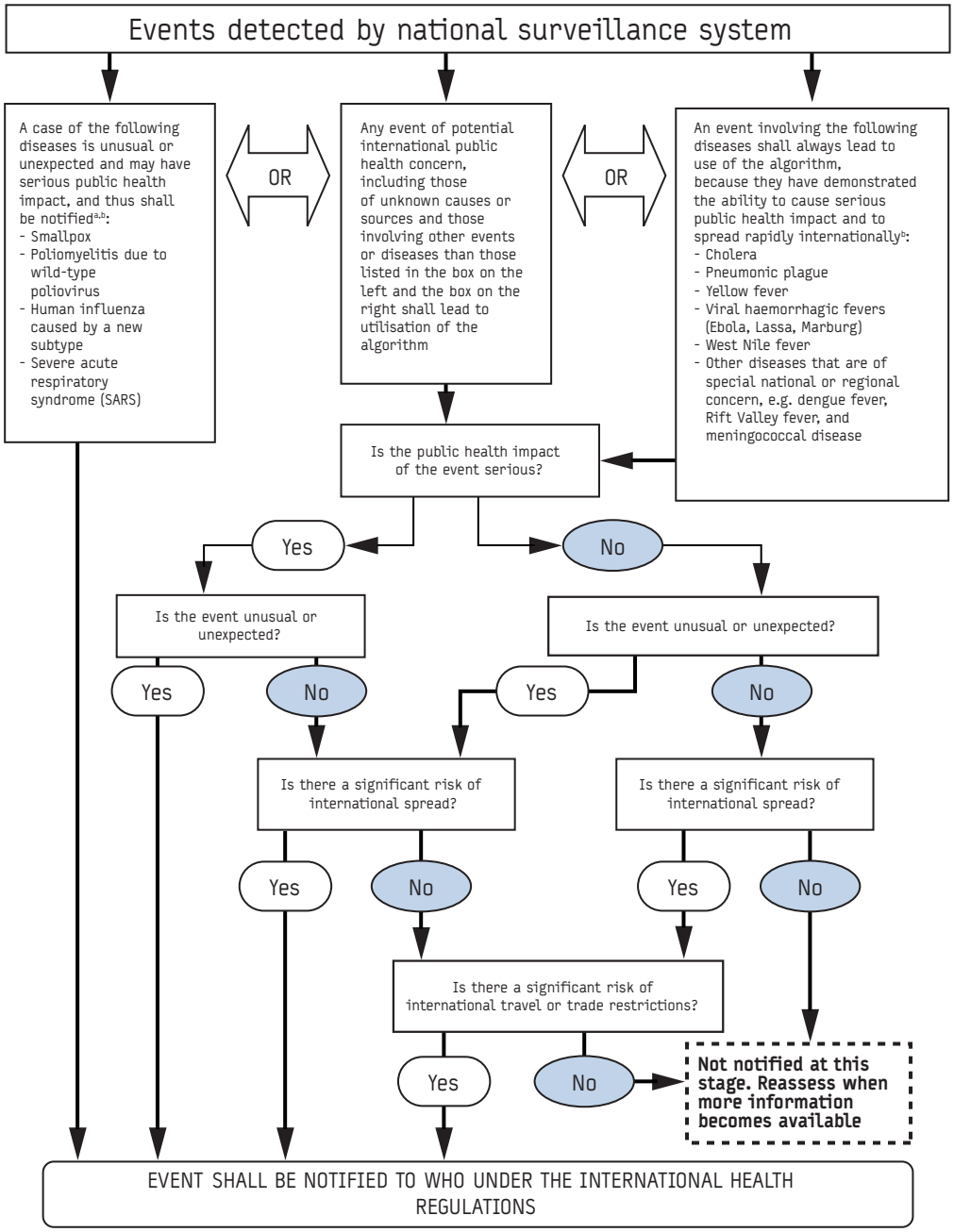
In addition to this broad scope for notification, two groups of diseases are deemed to raise particular concerns as potential international health emergencies of international concern:

1) For four critical diseases even one case, must be notified at all times independent of the context in which it occurs. These diseases are smallpox, poliomyelitis due to wild type poliovirus, human influenza caused by a new subtype and severe acute respiratory syndrome (SARS)
2) Several further epidemic-prone diseases, although not always notifiable, 'have demonstrated the ability to cause serious public health impact and to spread rapidly internationally'. Events involving these diseases must always been assessed using the Decision Instrument but only notified when fulfilling the requirements of the algorithm. Such diseases include cholera, pneumonic plague, yellow fever, viral haemorrhagic fevers, West Nile fever and other diseases that are of special national or regional concern.

Notification is one part of a consultation and assessment process involving the State Party and WHO to determine the appropriate response to an event. As noted, the IHR(2005) specifically provide for optional "consultations" between WHO and a State Party prior to any notification. States must also report to WHO evidence of public health risks occurring outside the State's territory such as, for instance, imported or exported human cases, or the identification of infected or contaminated vectors or contaminated goods.

FIGURE

Decision instrument for the assessment and notification of events that may constitute a public health emergency of international concern



a. As per WHO case definitions

b. The disease list shall be used only for the purposes of these Regulations

Surveillance and verification

WHO has both general surveillance obligations, as well as ongoing responsibilities to receive, assess and respond as required to notifications, reports and requests for consultations from States Parties. A complement to the obligation to notify is the express mandate for WHO to seek *verification* from States Parties of unofficial reports or communications (e.g. the media) of potential events within their territories which may constitute a public health emergency of international concern. States have reciprocal obligations to respond to WHO, within 24 hours, with an initial reply or acknowledgement, and the available public health information on the status of the referenced events, and must also communicate the detailed assessment information required for *notifications* of such events including, for examples, case definitions, laboratory results, number of cases and deaths.

IHR(2005) in Europe

In the European Union (EU), the implementation obligations under the IHR(2005) will apply to each of the EU Member States, and will therefore have some relation to the relevant EU institutions. As all EU Member States are also WHO Member States, the two organisations' respective roles and activities will have to be closely analysed in order to maximise synergies and avoid unnecessary duplication of work, consistent with the requirements of the revised Regulations. The revised Regulations contemplate that generally WHO coordinates and cooperates, as appropriate, with other

competent intergovernmental organisations and international bodies. More specific to the context of the EU, Article 57.3 of the IHR(2005) provides that States Parties that are members of a regional economic integration organisation shall apply in their mutual relations the common rules in force in that regional organisation; the article also specifies however that this provision does not prejudice the obligations of the States Parties under the IHR(2005).

In this context a number of areas may be considered for possible collaboration in support of EU Member States in fulfilling their individual obligations as (future) States Parties under the IHR(2005):

1) The European Commission could play an active role in supporting EU Member States in meeting their IHR(2005) obligations in surveillance and response as well as at their designated ports, airports and ground crossings. The European Community, through its technical EU agencies such as the European Centre for Disease Prevention and Control (ECDC) [7], may provide technical guidance. For instance, taking advantage of a number of well-established disease-specific surveillance networks, the ECDC can play a central role in European data collection and analysis, with a focus on communicable diseases. Within its own resources, or through its European networks of technical institutions, the ECDC can provide EU Member States with access to the best European technical expertise in disease surveillance and response.
2) The EU already has a network mechanism for reporting unusual events that may constitute a public health emergency. Community reportable events are reported to the Early Warning and Response System (EWRS) operated by ECDC and the information automatically shared with all other EU Member States. As noted, the IHR(2005) obligate all States Parties to notify WHO of 'any event that may constitute a public health emergency of international concern'. Although the related IHR(2005) include a range of specific limitations and requirements, the potential for establishing an appropriate technical arrangement between the two reporting mechanisms, again consistent with the States' IHR(2005) requirements, is worth exploring.
3) The national focal points for communicating to WHO or the Community EWRS share some similar requirements. For purposes of efficiency, and to avoid potential confusion arising from parallel channels of information during risk assessment and epidemic response, it may be desirable that the national institutes nominated as National IHR(2005) Focal Points, coordinate closely with, or be the same as, the EWRS Focal Points.
4) A further area for support of the IHR is the potential appointment of relevant scientists from regional economic integration organisations, such as scientists from EU technical agencies, to the IHR Roster of Experts, as described in Article 47.
5) Last but not least, the EU could play a key role in supporting the implementation of IHR(2005) globally, in countries outside of its borders.

Immediate voluntary implementation

On 26 May 2006, the World Health Assembly, concerned about the potential emergence of an influenza pandemic, called upon Member States to comply immediately, on a voluntary basis, with provisions of the IHR(2005) relevant to the risks posed by avian and pandemic influenza [8]. One practical implication of the resolution, for European States as well as others, is the Health Assembly's urging of each WHO Member State to designate immediately its National IHR Focal Point. WHO is also to designate its IHR Contact Points.

Another implication of the resolution has been the endorsement by the Health Assembly of the WHO Influenza Pandemic Task Force which met for the first time on 25 September 2006 in Geneva. This Task Force, with members from all WHO regions, is tasked with advising, upon request, on key international public health issues related to avian and pandemic influenza. Such issues include, for instance, the appropriate phase of pandemic alert and recommended response, the declaration of an influenza pandemic, and the appropriate international response measures to a pandemic. The Task Force can also advise on other technical questions involving avian or pandemic influenza related to WHO influenza activities. The members of the Task Force act as independent international experts in an advisory capacity to the Director General. Under the mandate from the Health Assembly, the Task Force is temporary until the entry into force of the IHR(2005).

References

1. World Health Organization. Fifty-eighth World Health Assembly, Resolution WHA58.3: revision of the International Health Regulations, (2005).
2. World Health Organization. International Health Regulations (1969). Third annotated edition, WHO (1983).
3. World Health Organization. Fifty-fourth World Health Assembly, Resolution WHA54.14: Global health security: epidemic alert and response, (2005).
4. Michael G. Baker, David P. Fidler. Global public health surveillance under the new international health regulations. Emerg Infect Dis. 2006(7):1058-65.
5. World Health Organization. WHO/CDS/CSR/2000.3: Global outbreak alert and response: report of a WHO meeting. Geneva, Switzerland, April 26–28, 2000.
6. World Health Organization. Epidemic alert and verification: summary report 2005. Wkly Epidemiol Rec. 2006;81(38):357-62. (http://www.who.int/wer)
7. F. Van Loock, Gill ON, Wallyn S, Nicoll A, Desenclos JC, Leinikki P. Roles and functions of a European Union Public Health Centre for Communicable Diseases and other threats to health. Euro Surveill 2002;7(5):78-84. Available from: http://www.eurosurveillance.org/em/v07n05/0705-225.asp
8. World Health Organization. Fifty-ninth World Health Assembly, Resolution WHA59.2: Application of the International Health regulations (2005).

Epidemic intelligence: a new framework for strengthening disease surveillance in Europe

C. Paquet[1], D. Coulombier[2], R. Kaiser[2], M. Ciotti[2]

In a rapidly changing environment, national institutions in charge of health security can no longer rely only on traditional disease reporting mechanisms that are not designed to recognise emergence of new hazards. Epidemic intelligence provides a conceptual framework within which countries may adapt their public health surveillance system to meet new challenges.

Epidemic intelligence (EI) encompasses all activities related to early identification of potential health hazards, their verification, assessment and investigation in order to recommend public health control measures. EI integrates both an indicator-based and an event-based component. 'Indicator-based component' refers to structured data collected through routine surveillance systems. 'Event-based component' refers to unstructured data gathered from sources of intelligence of any nature.

All EU member states have long-established disease surveillance systems that provide proper indicator-based surveillance. For most countries, the challenge lies now in developing and structuring the event-based component of EI within national institution in charge of public health surveillance.

In May 2006, the European Union member states committed to comply with provisions of the revised International Health Regulations (IHR(2005)) considered relevant to the risk posed by avian and potential human pandemic influenza. This provides for the European Centre for Disease Prevention and Control (ECDC) with an opportunity to guide member states in developing and/or strengthening their national EI, in addition to the ECDC's task of developing an EI system for the EU.

Euro Surveill. 2006;11(12): 212-4 Published online December 2006
Key words: epidemic intelligence, disease surveillance, Europe, health indicators, health events

Justification

Population movements, behavioural changes, food production and many other factors linked to globalisation and economic development are responsible for the continuous emergence of infectious hazards [1]. Diseases such as SARS or avian influenza, not to mention deliberate release of biological agents, represent new challenges for outbreak alert and response in Europe and elsewhere.

Modern technologies, mainly related to development of the internet, are rapidly changing the way we access health information. Online media, scientific forums and direct electronic communication now allow us to shortcut traditional reporting mechanisms that travel through the various levels of public health administration [2]. Health authorities are no longer in full control of an environment that puts journalists, politicians and the general public in direct contact with raw data.

These phenomena contributed to the revision of the International Health Regulations (IHR(2005)) approved during the 2005 World Health Assembly [3]. Member states of the World Health Organization (WHO) will soon be legally bound to notify both case on a preset list of diseases and all 'public health events of international concern'.

In such a new and rapidly changing environment, national institutions in charge of health security can no longer rely only on traditional disease reporting mechanisms such as mandatory notification of diseases. While these systems can ensure appropriate public health response to identified risks, they cannot recognise the emergence of new threats such as SARS, human cases of avian influenza or potential bioterrorist-initiated outbreaks. In order to overcome the limitations of traditional surveillance for the detection of previously unknown threats, new approaches have been developed, including the monitoring of syndromes, death rates, health services admissions or drug prescriptions [4]. These new approaches represent an attempt to enhance the performance of traditional surveillance system.

At the same time, the media and other informal sources of information are increasingly recognised as valuable sources of public health alerts. Epidemic intelligence provides a conceptual framework into which countries may complete their public health surveillance system to meet new challenges [5]. This approach represents a new paradigm aiming at complementing traditional surveillance systems.

In January 2006, the European Centre for Disease Prevention and Control (ECDC) convened a meeting in Stockholm with representatives from the 25 EU member states to agree on the role of EI in Europe [6]. Basic terminology and methods framework were agreed upon and further developed within a smaller working group. We present here the state of this project as of October 2006.

Definition and principles

Epidemic intelligence (EI) encompasses all activities related to the early identification of potential health hazards that may represent a risk to health, and their verification, assessment and investigation so that appropriate public health control measures can be recommended. The scope of EI includes risk monitoring and risk assessment and does not include risk management [FIGURE 1]

EI integrates indicator-based and event-based components. 'Indicator-based component' refers to structured data collected through routine surveillance systems. 'Event-based component' refers to unstructured data gathered from sources of intelligence of any nature. As a basic principle of EI, both components are given equal attention and processed in the same way, since a signal leading to a public health alert can originate from either one [FIGURE 2].

1. Institut de Veille Sanitaire, Saint-Maurice, France
2. European Centre for Disease Prevention and Control, Stockholm, Sweden

Figure 1

Functions of early warning and response related to epidemic intelligence

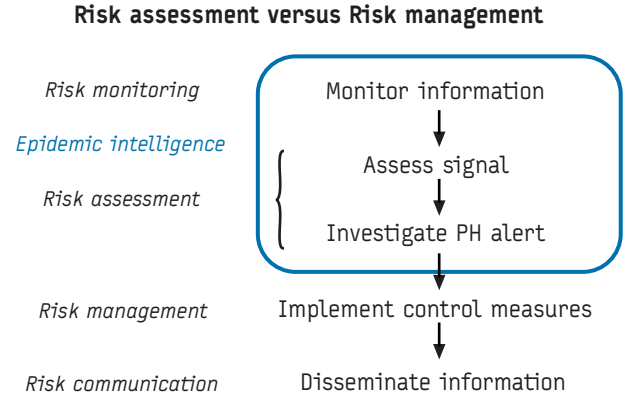


Figure 2

Epidemic intelligence framework

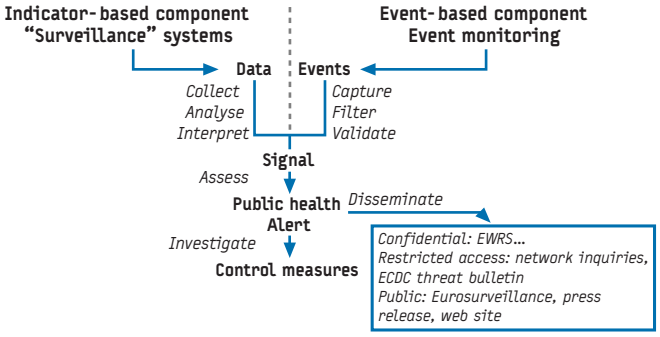


Table 1

Indicator-based component – Example of EI sources

EI Sources	Rationale	Method
Mandatory notification	Some rare but serious diseases need prompt and targeted action	Legal framework
Surveillance on a sample of sources (sentinel)	Trends of some common diseases can be obtained from a representative network of health care professionals	Sentinel network
Syndromic surveillance	Emerging diseases may not fit into disease-specific definitions. Early detection of cluster of syndromes may trigger an alert before cases appear in traditional surveillance systems	Lists of syndromes
Mortality	Serious emerging threats may initially be recognised by an increase of deaths	Real time death reporting
Health services activities	Serious emerging situation may initially present with increased admissions to health services such as emergency rooms	Real time activity reporting
Drug consumption	Increase in specific drug consumption may indicate emerging disease	Pharmacy networks

Table 2

Event-based component – Example of EI sources

EI Sources	Rationale	Method
Scientific watch	Scientific findings related to new organisms, drug resistance, etc. may trigger public health action	Literature review
Direct notifications	Clinicians or public health personnel may come across abnormal health events	On-call numbers
Media watch	Outbreaks and other unusual health events are often picked up early by local media	Media review Web scanning
International watch	A country may be affected secondarily by an health event emerging abroad	WHO reports ProMED, GPHIN
Inter-sectoral events	Agriculture, environment, industry and other sectors collect information on health related risks and exposure	Communication channels

Epidemic intelligence framework

The EI framework is made up of five standard steps. It applies to any situation considered from any level of the public health system. Within a single situation (for example, an outbreak), these different steps may be covered several times as an iterative process allowing new developments to be integrated, and progressively improving the decision making process. There are two ways of entering the framework, corresponding to indicator-based and event-based components of EI, respectively.

The first step is data collection (indicator-based component) and the detection/capture of events (event-based component). Data collection refers to quantitative indicators (number of cases, rates, etc.) routinely obtained from established surveillance systems [TABLE 1]. Capture of events potentially encompasses a much broader scope, as shown in Table 2.

As a consequence of gathering large amount of information from a variety of different sources, EI requires strong filter and validation capacities to avoid an overflow of information. Indicator-based data must be checked for relevance in order to rule out surveillance biases, artefacts or reporting errors (step 2). The significance of the data should then be established (step 3), usually through statistical comparison with baseline rates or thresholds. As far as events are concerned, these steps correspond to evaluating their relevance (step 2: 'is the event within the scope of public health?'), which is usually straightforward; and their reality (step 3: did the event really happen?), which may require a few phone calls to verify.

Indicators and events that have gone through steps 2 and 3 of the framework without being discarded are considered to be signals. A signal is a verified health-related issue. Whatever its origin (indicator or event), a signal has the same value for EI purposes and is processed in the same way.

Many signals have few or no public health consequences and only a few represent genuine public health alerts. Initial signal assessment is thus a key component of EI framework (step 4). Depending on the nature of the signal, the scope of the problem, the type(s) of disease(s) potentially involved and the population of concern, initial assessment may require different methods, of varying degrees of sophistication. It is very often necessary to go back to the source of the signal at this stage, and field investigation is sometimes required (step 5).

Once ascertained, the alert is classified according to its scope; that is, the level of the health system which will have to deal with it. As a simplified scheme, local, national and international levels can be considered. The IHR(2005) contain a decision instrument to help assess whether or not an alert is of international concern [3].

Implementing epidemic intelligence at country level

All EU member states have long-established disease surveillance systems that provide proper indicator-based surveillance to meet early warning objectives. The detection of non-specific events or health events of unknown origin could, in some cases, be improved by building up the sources of indicators with some of the one listed in table 1,

However, for most countries, the challenge lies in developing and structuring the event-based component of EI. Paying the same degree of attention to a local newspaper article as to a statistical analysis may represent a paradigm shift for most national institutions in charge

of surveillance. Examples presented in Table 2 provide suggestions based on which each country can progressively develop systems based on its own objectives: a country with overseas territories and large numbers of people travelling in and out of the country on a regular basis may decide to concentrate on watching international factors, and develop sophisticated methods, using tools such as the Global Public Health Intelligence Network (GPHIN) [7], while another country with fewer overseas interactions may decide to rely on WHO postings in this regard [8].

EI must be seen as a consistent system and there is mutual benefit from implementing each of its two components: clinicians engaged in notifying disease under traditional surveillance will be keen to notify abnormal events while clinicians approached for notification of abnormal events will better understand the need for traditional surveillance. Good scientific principles of surveillance represent a perfect incentive for facilitating notification of events that may not be covered by a surveillance scheme.

Signal processing must be organised in an integrated way, allowing intelligence from different sources to be cross-checked and assessed together: a journal article reporting sewage problems along with an increase in admissions to the local hospital emergency department may lead to the recognition of an outbreak.

For the reasons given above, EI must be developed within the national institution in charge of public health surveillance as an extension of their current scope.,. Furthermore, all processes related to signal management should be carried out from a transversal structure within the institution, allowing experts from the various surveillance systems, as well as media officers, international health specialists and "epidemic intelligence managers" to jointly perform the risk assessment related to threats being detected.

EU perspectives

The founding regulation of ECDC specifies its mandate regarding risk identification and risk assessment. The Centre's tasks under this regulation include identifying and assessing emerging threats to human health from communicable diseases, and establishing, in cooperation with the Member States' (MS) procedures for systematically searching for, collecting, collating and analysing information and data with a view to the identification of emerging health threats which may have mental as well as physical health consequences and which could affect the European Community.

In order to fulfil its mandate, ECDC has begun to monitor potential public health threats from a European perspective [9], under the principle of subsidiarity and building on the experience acquired by the health threat unit of the European Commission. ECDC has developed a threat tracking tool to facilitate the capture, verification and assessment of public health events of relevance. The main output of the tool is a weekly bulletin, for restricted distribution to MS health authorities and to the European Commission. Another EI source is the weekly release of the journal Eurosurveillance, with which ECDC has collaborated since September 2005 [10]. The Eurosurveillance weekly release includes an 'e-alert' capacity used by MS epidemiologists to widely and rapidly share information about ongoing threats.

While ECDC has a mandate to further develop EI at European level, it remains the prerogative of health authorities to implement these activities in their countries. ECDC added value may include facilitating exchange of information among MS and supporting assessments and standardisation of EI systems in MS. ECDC's activities in filtering, processing and summarising information from international sources may also allow MS to reduce their activities in this area and focus on regional threats, or on countries with which they have heavy travel and trade relations.

ECDC will evaluate its EI activities in 2007, after 18 months of operation. This evaluation will focus on finding evidence of the added value of a structured approach to event-based surveillance in complement to indicator-based surveillance. A similar process is encouraged at MS level.

Further operational research on EI is needed in order to optimise the detection of events using keywords and algorithms, filtering of events and other processes involved. It should be carried out in consistence with WHO's activities in this area in order to promote global EI tools.

In May 2006, Members States of the European Community voluntarily committed to complying with provisions of the IHR(2005) considered relevant to the risk posed by avian and potential human pandemic influenza. This provides an opportunity for ECDC to guide MS in developing and/or strengthening their national EI, in addition to the ECDC's task to develop an EI system for the EU. A guideline on EI implementation is currently being prepared.

References

1. King DA, Peckham C, Waage JK, Brownlie J, Woolhouse ME. Infectious diseases: preparing for the future. Science. 2006;313(5792):1392-3.
2. Grein TW, Kamara KB, Rodier G, Plant AJ, Bovier P, Ryan MJ, Ohyama T, Heymann DL. Rumors of disease in the global village: outbreak verification. Emerg Infect Dis. 2000;6(2):97-102
3. World Health Assembly. Revision of the International Health Regulations. World Health Assembly Resolution 58.3. 23 May 2005. Available from: http://www.who.int/gb/ebwha/pdf_files/WHA58/WHA58_3-en.pdf
4. Green MS and Kaufman Z. Surveillance for early detection and monitoring of infectious disease outbreaks associated with bioterrorism. Isr Med Assoc J. 2002;4(7):503-6.
5. Kaiser R, Coulombier D, Baldari M, Morgan D, Paquet C. What is epidemic intelligence, and how is it being improved in Europe? Euro Surveill. 2006;11(2):E060202.4. Available from: http://www.eurosurveillance.org/ew/2006/060202.asp#4
6. European centre for Disease Prevention and Control. Meeting report: Epidemic intelligence in the EU. Stockholm, 18 – 19 January 2006. Available from: http://www.ecdc.eu.int/documents/pdf/Report_Epidemic_intelligence_consultation_060118.pdf
7. Mykhalovskiy E, Weir L. The Global Public Health Intelligence Network and early warning outbreak detection: a Canadian contribution to global public health. Can J Public Health. 2006;97(1):42-4. Can J Public Health. 2006;97[1]:42-4.
8. Heymann DL, Rodier G. Hot spots in a wired world: WHO surveillance of emerging and re-emerging infectious diseases. Lancet Infect Dis. 2001;1(5):345-53.
9. Kaiser R, Coulombier D. Different approaches to gathering epidemic intelligence in Europe. Euro Surveill. 2006;11(4):E060427.1. Available from: http://www.eurosurveillance.org/ew/2006/060427.asp#1
10. Editorial team. Production of Eurosurveillance to be shared with the ECDC. Euro Surveill. 2005;10[9]:E050901.1. Available from: http://www.eurosurveillance.org/ew/2005/050901.asp#1

Original Articles

Surveillance report

The early warning and response system for communicable diseases in the EU: an overview from 1999 to 2005

P Guglielmetti[1], D Coulombier[2], G Thinus[1], F Van Loock[1], S Schreck[1]

Abstract

Under Decision 2119/98/EC of the European Parliament and of the Council, a network for epidemiological surveillance and control of communicable diseases in the Community was set up in 1998. One pillar of Decision 2119/98/EC is the early warning and response system (EWRS). The main objective of the network is to establish permanent communication between European Union (EU) Member States' public health authorities, which are responsible for determining the measures required to control communicable disease-related events. Since 1998, a web based informatics tool has been developed in order to allow information to be shared between the relevant public health authorities. Between 1998 and December 2005, a total of 583 messages were circulated through the EWRS, notifying 396 events. The information shared through the system helped to coordinate public health measures in the EU. However, only few events prompted specific measures at Community level and most of them were controlled with public health measures applied at national level. Major events (such as the Severe Acute Respiratory Syndrome) and the results of simulation exercises prompted the Commission to upgrade the informatics system on the basis of user needs. Since 1 May 2004 the 10 newest Member States have provided information under the current legislation and since April 2005 the European Centre for Disease Prevention and Control (ECDC) is part of the system. Future developments will include a link between the existing EWRS and the communication platform currently developed by the ECDC.

Euro Surveill 2006;11(12): 215-20 Published online December 2006

Key words: EWRS, European Union, Communicable diseases, Legislation

Introduction

The emergence of SARS in 2003 clearly demonstrated how a previously unknown disease could spread rapidly, causing high mortality and morbidity. Fast travel and global trade facilitated transmission in the absence of relevant vaccines and drugs. Effective counter-measures were applied, but the event underlines the need for worldwide cooperation to control such contingencies. Early detection of cases and efficient international communication and coordination was an advantage to tackle the epidemic. Public health measures undertaken not only by the affected countries but by the entire international community, with the support and guidance of the World Health Organization (WHO), helped to prevent catastrophic developments. Coordination in the European Union based on the EWRS contributed to Member States' knowledge of the situation and their readiness to stem any potential spread of the disease.

The threat of a pandemic influenza is currently prompting governments and international bodies with responsibilities in public health protection to address preparedness plans that could mitigate the potential effects of a pandemic, and to reinforce policies, contingency plans and resources, including the alert systems and their networks (1, 2).

The tools for European coordination to tackle communicable disease health threats must enable the key players to obtain and share key information on public health measures, both quickly and securely. The key players engaged in this process are the national health authorities, the national public health agencies, the Ministries for Health in Member States, and the European Commission and its agencies, in particular the ECDC.

The main objective of the paper is to outline the interactions of the EWRS key players and to describe the alert system for communicable diseases currently in place in the EU. It refers to the existing legal basis, the functioning of the system, the main players concerned with operations since its introduction, and the most recent upgrade undertaken on the basis of lessons learned from the past experience.

The legal basis

Decision 2119/98/EC established the early warning and response system as one of the two pillars of the Community network for the epidemiological surveillance and control of communicable diseases. The other pillar of the Community network is the base for the epidemiological surveillance in the EU and is made up by establishing permanent communication between the Commission and those structures which, at Member State level and under the responsibility of each Member State, are competent at national level and are charged with collecting information relating to the epidemiological surveillance of communicable diseases. The early warning and response function allows information exchange, consultation and coordination at Community level, should an event due to communicable diseases endanger public health at Community level. The network brings into communication the European Commission and the competent public health authorities in Member States responsible for determining the measures which may be required to protect public health against communicable disease threats. The system links the European Commission, the 25 Member States, Bulgaria and Romania and the European Economic Area (EEA) countries (Iceland, Liechtenstein and Norway). The ECDC has had access to EWRS since its establishment in May 2005 (3).

1. European Commission – SANCO C3 – Health Threat Unit, Luxembourg
2. European Centre for Disease Prevention and Control – Preparedness and Response Unit, Stockholm, Sweden

Under Decision 2119/98/EC, authorities communicate i) information regarding the appearance or resurgence of cases of communicable diseases, together with information on control measures applied; ii) any relevant information concerning progression of epidemic situations; iii) information on unusual epidemic phenomena or new communicable diseases of unknown origin, including in non-member countries; iv) information concerning existing and proposed mechanisms and procedures for the prevention and control of communicable diseases, in particular in emergency situations; and v) any information which could help Member States to coordinate their efforts for the prevention and control of communicable diseases, including any counter measures implemented (Art. 4, Decision 2119/98/EC)(3). This kind of information is provided through an informatics tool developed expressly for this purpose.

Decision 2000/57/EC states that the EWRS is reserved for events that have 'Community relevance'. These events are: i) outbreaks of communicable diseases extending to more than one Member State of the Community; ii) spatial or temporal clustering of cases of disease of a similar type, if pathogenic agents are a possible cause and there is a risk of propagation between Member States within the Community; iii) spatial or temporal clustering of cases of disease of a similar type outside the Community, if pathogenic agents are a possible cause and there is a risk of propagation to the Community; and iv) the appearance or resurgence of a communicable disease or an infectious agent which may require timely, coordinated Community action to contain it (Art 1 and annex I, Decision 2000/57/EC) (4). The procedures for information, consultation and cooperation under the EWRS are described in article 2 of Decision 2000/57/EC. Three levels of consultation are defined: level 1 for information exchange, level 2 for notification of a potential threat and level 3 for definite threat (Annex II, Section 1,2,3, Decision 2000/57/EC)(2). A specific procedure for information to the general public and concerned professional is reported in section 4 of annex II of Decision 2000/57/EC and states that Member States shall provide suitable information to concerned professional and the general public and shall inform them of the measures adopted and that the Commission and Member States shall inform of any guidance agreed at Community level and when the public health is over (4).

Should one or more of the previously mentioned circumstances occur, Member States shall, on the basis of the information available, consult each other in liaison with the Commission with a view to coordinate their actions. In particular, where a Member State intends to adopt, as a matter of urgency, control measures in response to the appearance of a communicable disease, it shall, as soon as possible, inform the Commission and the other Member States. On the basis of this consultation and of the information provided Member States shall coordinate in liaison with the Commission the measures which they have adopted or intend to adopt at national level (Art 6 Decision 2119/98/EC)(3).

Each Member State designates the structure and/or the authorities referred to the early warning and response function and notifies the Commission and the other Member States (Art 9, 2119/98/EC). The public health authorities which have been formally designated represent the network of the contact points of the EWRS (3).

Description of the informatics tool currently available to implement the early warning and response under Decisions 2119/98/EC and 2000/57/EC

Since Decision 2119/98/EC entered into force, an informatics tool has provided the platform for communicating information. The tool currently linking the EWRS contact points is a web-based system. The access to the system is secured and is limited to the formally appointed contact points. As previously mentioned, following notification from Member States, the contact point receives a login and a password from the Commission to access the system, and full authorisation to write and read messages. When a message is posted on the system, it is automatically circulated to all EWRS contact points, and the network (Commission, Member States, acceding and the EEA countries, and ECDC) is informed at the same time of how the situation is progressing and of the measures planned or undertaken at national level to respond to the specific event.

On the basis of lessons learnt from past events, mainly from the SARS epidemic, and on the basis of the recommendations made in the report of the EWRS activities for the years 2002 and 2003 (3), there has been a complete technological overhaul of the system. The new EWRS application was launched in May 2004 and it is currently in use. Additional modifications of specific functions were introduced after the 2005 simulation exercises (6).

In the current application, a single message can contain a text of up to 3999 characters, and additional comments up to 1999 characters may be added. There is no limit to the number of comments that can be made following a single message. Additional documents, for a maximum of 9 Megabytes, can be attached to messages and comments. Readability and classification of the comments has been also improved. A few 'simple search' features were also added to the 'threat listing' page to select important flags (message content, syndrome/disease, pathogen, reporting reason, and country of occurrence). After rebuilding the core of the application, a calendar function was added to create a meeting agenda and to facilitate the sharing of working documents among users without overloading the core messages. To prevent the risk of overload of messages, should a specific event require a large number of notifications, a 'follow up' section was added. A new messaging system was also introduced in May 2005 (selective messaging) that allows participants to send a message to selected recipients. The European Commission is always notified of 'selective' messages. The user levels were expanded to give access both to the ECDC and the WHO. The WHO has, with the agreement of Member States, a read-only access to the system. Other security enhancements were also added.

A short message service (SMS) messaging function has been activated in order to transmit to the European Commission Officer on duty real time notification that a message has been posted on the system.

In addition to these function the system is linked to the Medical Intelligence System (MedISys) (7). MedISys is a piece of software that browses the web every 20 minutes in order to find articles, documents and latest news about health matters. About 350 keywords are currently used and 1200 websites are visited. Access to the system has been granted to Ministries of Health, national surveillance institutes, specific EU supported projects, ECDC and WHO. Graphs, statistics and world maps allow a quick identification of threats and localisation of the events. The system is based on the European Media Monitor, which is freely accessible to all (8).

The ECDC was officially established in May 2005, but started activities in March 2005. As the assistance of Commission by the ECDC in operating the EWRS is stated in the ECDC founding regulation, the agency was rapidly integrated into all EWRS related activities (9). The ECDC has been connected to the EWRS since April 2005. ECDC has implemented its threat monitoring mandate using the EWRS messages as a source of information on threats in Europe, complemented by an active search of additional formal and informal sources.

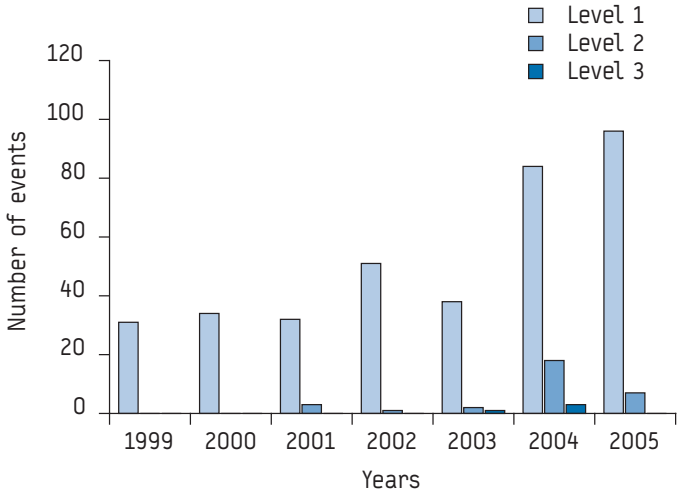
The EWRS operations

Since Decision 2119/98 entered into force at the end of December 2005, a total of 583 messages have been circulated through the

EWRS. These messages notified a total of 396 events. The first message (about legionellosis) was posted on 30 November 1998 and no further messages were posted in 1998. Figure 1 reports the number of the events notified through the EWRS from January 1999 to December 2005, including the level of activation as defined by procedures reported in annex II of Decision 2000/57/EC (4).

Figure 1

Number of events notified to EWRS (1999-2005) under activation level 1, level 2 and level 3



The nature of the events (diseases and/or syndromes) notified during the same period 1999-2005 is reported in Table 1. The trend of the diseases and syndromes which have been reported at least five times in one year (haemorrhagic fever, salmonellosis, meningitis, influenza, SARS and measles) is reported in Figure 2. Only a few events have prompted specific measures at Community level; most were controlled by applying public health measures at national level. Events which required a more complex response, involving coordination of measures and contacts between health authorities in Member States, are summarised in Table 2. Comments were added to the majority (around two thirds) of these events. Details concerning the specific events reported in the Table are available in the annual reports of the EWRS (5, 10).

The SARS epidemic dominated the EWRS activity from March to June 2003. Figures on EWRS activities during this period are reported in Table 3 and Figure 3. The system provided a unique tool to circulate reliable information quickly to the Commission and to the Member States. During the first phase of the event in particular, the EWRS was able to pick up a notification posted by France on 11 March 2003 about a real and serious threat in Vietnam. The content of messages circulated during the SARS outbreak can mostly be put under two categories. The first category is reports of measures undertaken by Member States to control the spread of SARS, and it provided very useful information which helped to coordinate the response to SARS at national and at EU level [Table 3]. The second category is case and update reports, which provided useful and additional information to Member States when weighing the impact of imported cases in the EU. This second set of information was consistent with the WHO notifications. The nature and magnitude of the event caused a huge and rapid flow of messages. Starting from the second week of the outbreak, this situation caused an overload of the EWRS mailbox and had a negative impact on processing and interpreting data and on control activities (5). The problem was solved by creating a specifically dedicated mailbox for selected messages (case and update reports, official communications, call for meetings and consultation teleconferences, etc.). These elements provided the basis for the upgrading of the system (5, 10).

Table 1

Events notified by diseases and/or syndromes (1999-2005)

Events, diseases and/or syndromes reported	Numbers
1999 (Total events: 27)	
Legionellosis	5
Salmonella	3
Cholera, diphtheria, haemorrhagic fever, malaria, yellow fever	2
Acute diarrhoea, Coca Cola event, haemolytic uremic syndrome, influenza, measles, meningitis, plague, rickettsiosis, vCJD	1
2000 (Total events: 36)	
Meningitis	8
Legionellosis	7
Haemorrhagic fever	5
Listeriose	3
Recall of medicinal products, Salmonellosis	2
Cholera, diphtheria, hepatitis A, HIV/AIDS, severe infections in drug users, necrotising fasciitis, syphilis, tuberculosis, West Nile virus	1
2001 (Total events: 32)	
Meningitis	8
Salmonella	4
Haemorrhagic fever	3
Legionellosis	2
Avian influenza, coccidioidomycosis, diphtheria, hepatitis A, severe infection in drug users, legionellosis, measles, shigellosis, tuberculosis, recall of contaminated milk baby powder, vCJD	1
Other information/events related to communicable diseases	4
2002 (Total events: 52)	
Legionellosis, meningitis, salmonellosis	5
Diphtheria, trichinellosis, tularaemia, vCJD	3
Influenza, listeriosis, tuberculosis	2
Acute gastroenteritis, botulism, cholera, fasciola infestation, haemolytic uremic syndrome, measles, peri-myocarditis, plague, *Pseudomonas aeruginosa* infections, rickettsiosis, recall of hepatitis A vaccine, severe infection in transplanted patients, shigellosis, whooping cough, yellow fever	1
Other information/events related to communicable diseases	4
2003 (Total events: 41)	
SARS	5
Legionellosis	4
Acute gastroenteritis, meningitis, salmonellosis, influenza	3
Haemorrhagic fever	2
Acinetobacter spp. infections, avian influenza, botulism, cryptosporidium, diphtheria, haemolytic uremic syndrome, heat wave, HIV/AIDS and STD, listeriosis, measles, monkeypox in humans, other information/events related to communicable diseases, plague, shigellosis, Tetanus, West Nile virus, yellow fever, vCJD	1
2004 (Total events: 105)	
Influenza	21
Legionellosis	8
vCJD, salmonellosis	6
Acute diarrhoea	5
Tuberculosis, meningitis	4
Cholera, hepatitis	3
Anthrax, encephalitis, malaria, rabies, haemorrhagic fever, dengue fever, measles, fever	2
Diphteria, shigellosis, mumps	1
Other information/events related to communicable diseases	26
2005 (Total events: 103)	
Salmonellosis	15
Influenza	13
Acute diarrhoea	10
Legionellosis, measles	5
vCJD	4
Cholera, meningitis, fever	3
Haemorrhagic fever, haemolytic uraemic syndrome, malaria, shigellosis, rabies	2
Anthrax, hepatitis, food intoxication, melioidisis, STD, rubella, plague, encephalitis, diphteria, botulism	1
Other information/events related to communicable diseases	22

Figure 2

Diseases and/or syndromes notified during the period 1999-2005 at least 5 times in one year

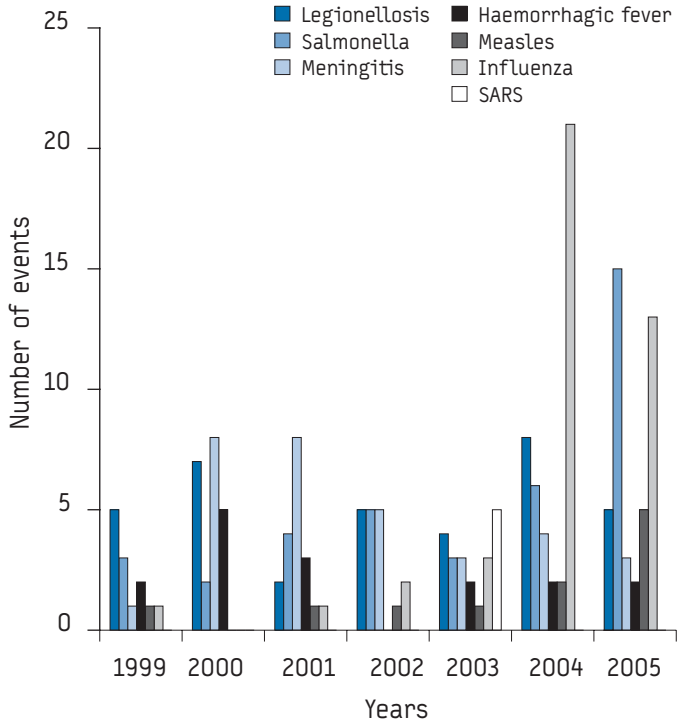


Figure 3

Trend of messages and comments circulated through the EWRS during the SARS epidemic

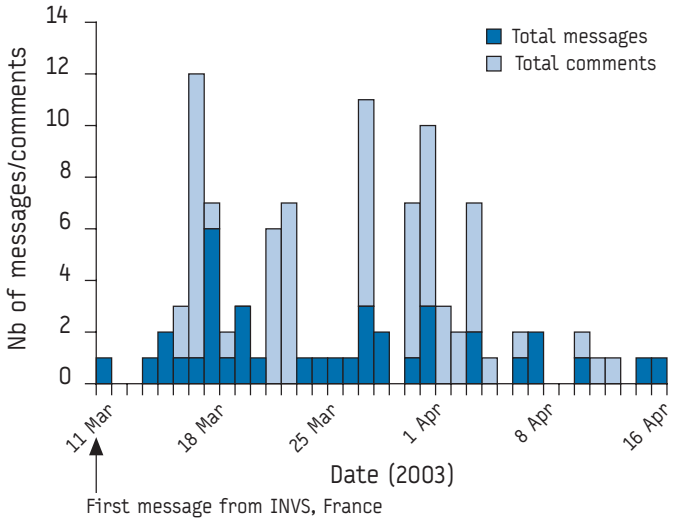


Table 2

Relevant events notified through the EWRS (1999-2005)

1999	• Haemorrhagic fever
2000	• Meningococcal infection • Serious infections among injecting drug users
2001	• Meningococcal infection • Legionellosis
2002	• Pericarditis-myocarditis in Greece • Norovirus outbreaks • Salmonellosis
2003	• Severe acute respiratory syndrome (SARS) • Acute gastroenteritis outbreak (norovirus) in a cruise ship
2004	• Two outbreaks of legionellosis associated with cruise ships • First human cases of the highly pathogenic avian influenza virus type A/H5N1 in Vietnam • Two events associated with West Nile virus infection • Rabid dog illegally introduced in the EU • Outbreak of hepatitis A that clustered in a tourist resort outside the EU • Birds of pray smuggled in the EU from Thailand • Four SARS related events after 5/7/2003
2005	• A/H5N1 events in Russia • A/H5N1 events in Romania and Turkey • Outbreak of Marburg haemorrhagic fever in Angola • A/H2N2 mistakenly distributed in proficiency testing

Table 3

EWRS and SARS epidemic : content of messages (March-June 2003)

Case reports	22
Update on SARS cases	11
Specific requests by MS, EEA Countries and EC	10
Comments	58*
WHO communications	2
Meeting/teleconferences	2
Messages by EC Delegations in affected countries	1
Flight information	1
Technical guidance documents	1
Measures	1
TOTAL	109**

* To 10 specific requests of information by MS, EEA Countries and EC

** 11 messages had more than one content

Discussion

The European collaboration on communicable diseases only started recently, within the context of the public health framework set out in the Commission Communication of 24 November 1993 on the framework for action in the field of public health. The network for the epidemiological surveillance and control of communicable diseases in the Community with its early warning and response function operating under Decisions 2119/98/EC and 2000/57/EC has been one of the most successful public health instruments.

The EWRS is being used more and more frequently to share relevant information between the Member States, the Commission and the ECDC. The system currently available is a unique tool that helps to coordinate public health measures intended to control communicable diseases threats in the EU. The increased number of messages circulated through the EWRS mirrors the efforts done in implementing the current EU legislation on communicable diseases, and also shows the value of such an instrument for appropriate communication between partners.

Although the EWRS is not intended to be a tool to monitor communicable diseases in the EU, analysis of events notified since 1999 tells us about the nature and frequency of the threats which required a response at Community level. The knowledge of these figures can help Member States, the Commission and the ECDC to strengthen mechanisms and actions and thereby to be better prepared to respond to specific events and to predict, at least in part, what we can expect at short and medium term.

A/H5N1 related events were the most frequent cause of notification in 2004 (21 events) and the second most frequent in 2005 (13 events). Sharing information encouraged a tangible effort to coordinate measures for strengthening preparedness to respond to the potential progression of the pandemic alert phases. The Member States were regularly informed through the EWRS about

the measures undertaken at national level and a consistent response was reached at Community level (for the most part, monitoring the situation, implementing active surveillance, advising EU citizens travelling to and from affected areas, strengthening synergies with veterinary services, and finalising pandemic plans).

Unpredictable incidents represent a significant proportion of notified events. The system proved to be a unique tool to circulate reliable information, not only during the unforeseen SARS epidemic, which dominated the EWRS activities from March to May 2003, but also during one-off incidents which required the rapid implementation of public health measures, such as, the event related to the rabid dog illegally imported into the EU that bit or had close contact with several EU citizens, and the incident linked to erroneously distributed samples of live influenza virus A/H2N2 to carry out proficiency testing (Table 2).

Further analysis by the Commission, Member States and the ECDC of the reported events through the EWRS and of the public health responses in term of measures planned and undertaken in response to the notified threats will be essential to better understand and to strengthen the capacity to efficiently tackle communicable diseases in the EU.

All events that required urgent notifications and a more complex response and coordination of measures (Table 2) were notified without delay, demonstrating a clear improvement after 2003 (5). These events were a significant test of the usefulness of the EWRS. The system fulfilled its institutional role by circulating messages in a timely fashion among the EWRS contact points in Member States, by providing shared positions among the national public health authorities, and by facilitating the exchange of information on specific issues. The consultation platform provided by EWRS was very much appreciated by the authorities of the Member States and resulted in consistent national decision making for the control of these events.

The analysis of the content of activation level 1 messages (which include information messages) demonstrates that a number of them still remain focused on risk assessment issues and that a large part deals with requests for information about similar events identified in other Member States. The integration of specific functions of the current EWRS informatics tool in the communication platform that ECDC is developing will be instrumental to focus the use of the system to cover those circumstances as laid down in Decisions 2119/98/EC and 2000/57/EC.

The integration of the 10 new Member States in the EWRS was a special challenge. New Member States made efficient use of the EWRS, demonstrating a level of activity comparable to that of the old Member States. Since accession in May 2004 the 10 new Member States have had full access to the EWRS and have made active use of the system both to notify new events and to follow up with comments events been notified by other Member States or by the Commission. A recent analysis prepared by the ECDC, covering the period from June until December 2005, demonstrates that the amount of threats notified through EWRS is comparable for old and new MS (after adjustment for population), showing good integration of new MS in the EU alert system for communicable diseases (11).

EWRS was the communication tool used during the simulation exercise 'Common Ground' that was conducted by the UK's Health Protection Agency (HPA) as a command post exercise on 23 to 24 November 2005. This exercise was the second of two EU exercises commissioned by the European Commission to evaluate the ability and capabilities of Member States to respond to a health-related crisis, in this case an influenza pandemic. EWRS was made available for the exercise to all 25 Member States plus Norway, Iceland and Switzerland. Despite heavy use during the exercise (437 messages circulated, an average of nearly 10 messages per hour, and 3672 responses), the system performed efficiently and no breakdown was registered. Nevertheless, given the nature of the simulation, there was considerable overload and heavy traffic, and users rapidly became overwhelmed by the huge number of messages. As the EWRS was the only system for simultaneous European communication available, participants used it for all sorts of information exchange, although the system was only developed, as laid down in Community legislation, for official notification of measures and their coordination. As previously mentioned, the future communication platform developed by the ECDC will be also important for strengthening information sharing during emergency situations like those simulated during EU-wide exercises.

The EWRS should also be considered in the perspective of the future implementation of the revised International Health Regulations (IHR) (12, 13). IHR will enter into force on 15 June 2007, and require gradual implementation, to be completed by 2016 at the latest. Close coordination between the Commission and Member States will help to optimise their implementation, and better protect EU citizens from public health emergencies due to communicable diseases. In particular the ECDC and the EWRS will be instrumental to help the implementation process of IHR in a stronger and more coherent way (12, 13).

EWRS contact points (As of 14 September 2006)

Austria: H. Hrabcik and R. Strauss (Bundesministerium für Gesundheit und Frauen); Belgium: D. Reynders (Federal Public Health Service); Cyprus: O.Kalakuta (Ministry of Health Medical and Public Health Services); Czech Republic: M.Vit (Public Health Officer); Denmark: K.Molbak (Statens Serum Institut) and S.Poulsen (National Board of Health); Estonia: M.Muzotsin (Health Protection Inspectorate); Finland: P.Ruutu (Kansanterveyslaitos); France: S.Veyrat (Ministère de la Santé et des Solidarités) and J.C.Desenclos (Institut de Veille Sanitaire); Germany: G.Krause (Robert Koch Institute) and M.Kramer (Federal Ministry for Health); Greece: A.Hatzakis and O.Adrami (Centre for Infectious Diseases Control); Hungary: A.John (Föoszaltályvezetö Népegészségügyi Minisztérium Népegészségügyi Föoszaltályvezetö); Ireland: K.Kelleher (Health Service Executive) and D.O'Flanagan (Health Protection Surveillance Centre); Italy: M.G.Pompa (Ministero della Salute); Latvia: O. Kravcenko and Jurijs Perevoscikovs (Public Health Agency); Lithuania: V. Gailius (Ministry of Health) and R.Liausediene (Centre for Communicable Diseases Prevention and Control); Luxembourg: P.Huberty-Krau (Direction de la Santé); Malta: M.Micallef and C.Gauci (Dipartiment Tas-Sahha Publika); Netherlands: RIVM-Centre for Infectious Disease Control; Poland: A.Trybusz (Sanitary Inspectorate); Portugal: M.Da Graca Freitas (Direccão-Geral da Saúde) and M.T.Paixão (Instituto Nacional de Saúde); Slovakia: Ministry of Health - Public Health Authority of the Slovak Republic; Slovenia: A.Kraigher (Institut za varovanje zdravja); Spain: Dirección General de Salud Pública Ministerio de Sanidad y Consumo; Sweden: A.Tegnell (The National Board of Health and Welfare); United Kingdom: A.Wight (Department of Health); Bulgaria: R.Filipova (Ministry of Health); Romania: R.P.Costinea (Ministry of Health); Iceland: H.Briem (Directorate of Health); Liechtenstein: E.M.Hiebl (Amt für Gesundheitsdienste); Norway: P. Aavitsland (Norwegian Institute of Public Health). ECDC: D. Coulombier (Preparedness and Response Unit, ECDC); European Commission: S.Schreck and P.Guglielmetti (SANCO Health Threats Unit – C3).

Acknowledgements

We would like to thank Celine Verkaeren for the assistance and the preparation of the tables and figures.

References

1. Communication from the Commission to the Council, the European Parliament, the European Economic and Social Committee and the Committee of the Regions on pandemic influenza preparedness and response planning in the European Community. Bruxelles, 28.11.2005, COM (2005) 607 Final. http://eur-lex.europa.eu/LexUriServ/site/en/com/2005/com2005_0607en01.pdf

→→→

2. Communication from the Commission to the Council, the European Parliament, the European Economic and Social Committee and the Committee of the Regions on strengthening coordination on generic preparedness planning for public health emergencies at EU level. Bruxelles, 28.11.2005, COM (2005) 605 Final. http://eur-lex.europa.eu/LexUriServ/site/en/com/2005/com2005_0605en01.pdf
3. Decision no 2119/98/EC of the European Parliament and of the Council of 24 September 1998 setting up a network for the epidemiological surveillance and control of communicable diseases in the Community. Official Journal of the European Communities 3. 10. 98 L 268. http://eur-lex.europa.eu/pri/en/oj/dat/1998/l_268/l_26819981003en00010006.pdf
4. Commission Decision of 22 December 1999 on the early warning and response system for the prevention and control of communicable diseases under Decision No 2119/98/EC of the European Parliament and of the Council. (*Notified under document number C(1999) 4016)(2000/57/EC*). Official Journal of the European Communities 26.01.2000 L 21. http://eur-lex.europa.eu/pri/en/oj/dat/2000/l_021/l_02120000126en00320035.pdf
5. Report from the Commission to the Council and the European Parliament. Report on the operation of the Early Warning and Response System of the Community Network for the Epidemiological Surveillance and Control of Communicable Diseases (Decision 2000/57/EC) during 2002 and 2003. Bruxelles, 29.03.2005 SEC (2005) 394. http://eur-lex.europa.eu/LexUriServ/site/en/com/2005/com2005_0104en01.pdf
6. A pandemic influenza exercise for the European Union. Exercise 'Common Ground'. http://ec.europa.eu/health/ph_threats/com/common.pdf
7. Medical Information System. https://medisys.jrc.it/ and http://medusa.jrc.it
8. Europe Media Monitor. http://press.jrc.it/NewsBrief/worldedition/en/en.html
9. Regulation (EC) no 851/2004 of the European Parliament and of the Council of 21 April 2004 establishing a European centre for disease prevention and control. Official Journal of the European Union 30.04.2004 L 142. http://eur-lex.europa.eu/pri/en/oj/dat/2004/l_142/l_14220040430en00010011.pdf
10. Report from the Commission to the Council and the European Parliament. Report on the operation of the Early Warning and Response System of the Community Network for the Epidemiological Surveillance and Control of Communicable Diseases (Decision 2000/57/EC) during 2004 and 2005. In press.
11. Different approaches to gathering epidemic intelligence in Europe. Eurosurveillance Weekly. Vol 11, 4, 27 April 2006. Available from: http://www.eurosurveillance.org/ew/2006/060427.asp#1
12. Communication from the Commission to the European Parliament and the Council on the International Health Regulations com (2006) 552. http://ec.europa.eu/health/ph_international/documents/comm_ihr_552_2006_en.pdf
13. Fifty-Eighth World Health Assembly - WHA 58.3 agenda item 13.1 - 23 may 2005 revision of the International Health Regulations. http://www.who.int/csr/ihr/IHRWHA58_3-en.pdf

ORIGINAL ARTICLES

Surveillance report

A NATIONAL SYNDROMIC SURVEILLANCE SYSTEM FOR ENGLAND AND WALES USING CALLS TO A TELEPHONE HELPLINE

GE Smith[1], DL Cooper[1], P Loveridge[1], F Chinemana[2], E Gerard[3], N Verlander[4]

Routine primary care data provide the means to monitor a variety of syndromes which could give early warning of health protection issues. In the United Kingdom, a national syndromic surveillance system, operated jointly by the UK Health Protection Agency (HPA) and NHS Direct (a national telephone health helpline), examines symptoms reported to NHS Direct. The aim of the system is to identify an increase in syndromes indicative of common infections and diseases, or the early stages of illness caused by the deliberate release of a biological or chemical agent. Data relating to 11 key symptoms/syndromes are received electronically from all 22 NHS Direct call centres covering England and Wales and analysed by the HPA on a daily basis. Statistically significant excesses in calls are automatically highlighted and assessed by a multi-disciplinary team. Although the surveillance system has characterised many sudden rises in syndromes reported to NHS Direct, no evidence of a biological or chemical attack has been detected. Benefits of this work, however, are early warning and tracking of rises in community morbidity (e.g. influenza-like illness, heatstroke); providing reassurance during times of perceived high risk (e.g. after the 7 July 2005 London bombs and December 2005 Buncefield oil depot fire); and timely surveillance data for influenza pandemic planning and epidemic modeling.

Euro Surveill. 2006;11(12): 220-4 Published online December 2006

Key words: NHS Direct, syndromic, surveillance, influenza

1. Health protection Agency West Midlands, Birmingham, United Kingdom
2. NHS Direct Health Protection and Access Project Manager, NHS Direct Hampshire and the Isle of Wight, Southampton, United Kingdom
3. NHS Direct, London, United Kingdom
4. Health Protection Agency Centre for Infections, London, United Kingdom

Introduction

Routine primary care data provide the means to monitor a variety of syndromes which could give early warning of health protection issues (microbiological, chemical, or radiological). Milder illnesses which patients may not present with at hospitals (e.g. conjunctivitis) or illnesses for which laboratory specimens are not routinely taken (e.g. influenza-like illness (ILI)) can be tracked. Real time data are needed to respond to major health protection incidents. In recent years there has been a growth in the number of telephone triage systems that provide the public with health advice and information. This article describes a real time national syndromic surveillance system covering England and Wales, using data about symptoms reported to a national telephone helpline (NHS Direct [1]).

NHS Direct

NHS Direct is a nurse-led health helpline that provides the population of England and Wales with rapid access to health advice

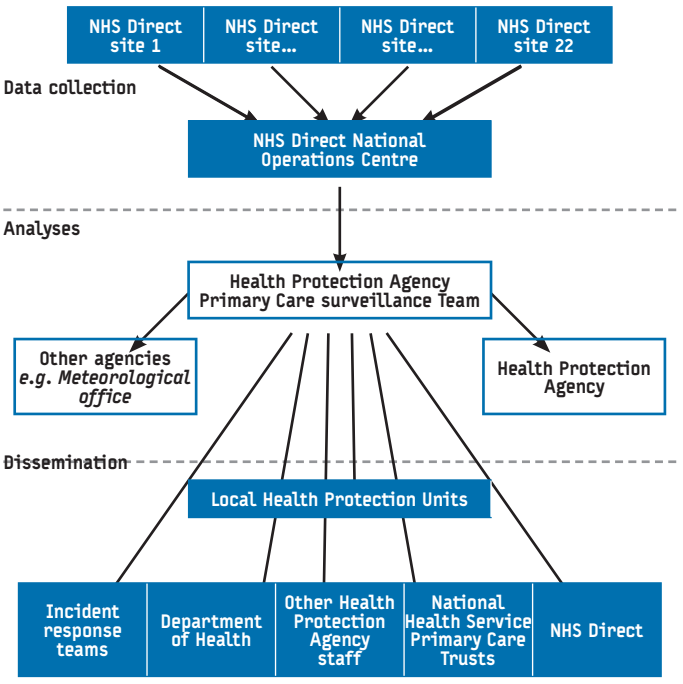
and information about health, illness, and the National Health Service (NHS). The service operates 365 days per year from a network of 21 sites in England and a single site covering all of Wales, is the world's largest online provider of healthcare advice, and answers nearly 7 million calls per year. NHS Direct nurses use clinical decision support software (the NHS Clinical Assessment System (NHS CAS)) to respond to callers. The NHS CAS is structured around 230 computerised clinical algorithms (such as diarrhoea, fever and back pain). Approximately 30% of NHS Direct calls are requests for health information, and 70% of calls are to report symptoms. The nature and severity of the reported symptoms dictate which algorithm is selected by the nurse and, ultimately, which outcome is recommended (these include advice for self care (19% of total calls); family doctor referral (51%); referral to accident and emergency department of a hospital (8%); '999' emergency call (either made by the caller or from NHS Direct) both depending on the seriousness (5%); or other services (17%). Abdominal pain, vomiting, toothache, fever, chest pain, diarrhoea, headache and sore throat collectively account for 30% of total symptomatic calls made to NHS Direct.

Who use NHS Direct?

Approximately 25% of the population of England have used NHS Direct [2], although the total call rate is approximately 3% of the total consultation rate for primary care doctors [3]. The highest NHS Direct call rates are for young children (calls about symptoms: <1 year: 358 calls per 1000 per year; 1-4 years: 173 per 1000 during 2005; 15-44 years: 76 per 1000), and the lowest for those over 65 years. Women are more likely than men to use the service: the ratio of female to male calls is 1.3:1. This age-sex distribution is largely comparable to consultations for primary care doctors, with the exception of the low NHS Direct call rate from those over 65 years. With respect to sociodemographic background of NHS Direct callers, ecological studies suggest call rates rise with increasing social deprivation before falling in the most deprived areas [4, 5]. The proportion of callers from different ethnic groups mirrors the census population, with the exception of under representation from the Chinese population sub-group [personal communication, Frances Chinemana, NHS].

FIGURE 1

NHS Direct / Health protection agency syndromic surveillance flow chart



NHS Direct/HPA syndromic surveillance system

The Health Protection Agency (HPA) is an independent body that protects the health and wellbeing of the population. The Agency plays a critical role in protecting people from infectious diseases and in preventing harm when hazards involving chemicals, poisons or radiation occur [6]. In recent years there has been an increase in syndromic surveillance systems that analyse non-specific or pre-diagnostic data to detect changes or trends in the health of a population, particularly in the United States [7, 8]. NHS Direct and the HPA run a syndromic surveillance system to enable country-wide monitoring and identification of an increase in calls about 'key symptoms' reported to NHS Direct. The aim of the system is to identify an increase in syndromes indicative of common infections and diseases, or the early stages of illness caused by the deliberate release of a biological or chemical agent [9].

Method

Transfer of data

Daily call data relating to 11 algorithm groupings (syndromes) and numbers of total calls, are received electronically by the HPA for all 22 NHS Direct sites in England and Wales each weekday [FIGURE 1]. Syndromes were selected [TABLE] which may be indicative of infections or illnesses resulting from chemical exposure, or the early stages of a range of illnesses caused by the deliberate release of biological or chemical agents. Data are broken down by NHS Direct site, syndrome, age group and call outcome.

Statistical analysis

Upper confidence limits (99.5% level) of calls for each syndrome, as a proportion of daily total calls, are constructed each weekday for each NHS Direct site. These confidence limits are derived from standard formula for proportions [10] with the baseline numbers of total calls and symptom calls adjusted for seasonal effects (monthly adjustment).

In addition to the confidence interval analyses, control charts are constructed for six of the eleven syndromes (cold/flu, cough, fever, difficulty breathing, diarrhoea, and vomiting) at the 10 NHS Direct sites covering major conurbations in England. Baselines for the control charts are calculated by assuming the number of syndromic calls follow a Poisson distribution. Total calls are used as an offset. A model is fitted

TABLE

Eleven syndromes monitored by the NHS Direct syndromic surveillance system; number of calls and proportion of total calls recorded by the surveillance system, England and Wales, 2005

Syndrome	Calls	Calls as a proportion of total calls
Cold/flu	32 462	0.8%
Cough	105 740	2.5%
Diarrhoea	119 399	2.8%
Difficulty breathing	49 205	1.2%
Double vision	371	0.01%
Eye problems	42 613	1.0
Fever	133 761	3.2%
Heat/sunstroke [only monitored June-September]	947	0.03%
Lumps	31 754	0.8%
Rash	170 202	4.1%
Vomiting	164 742	3.9%
Total	**851 196**	**20.3%**

to each site and syndrome separately using data from December 2001 onwards. These models always contain a public holiday and seasonal term, and if shown to be necessary, a day of the week (weekday, Saturday or Sunday) and a linear long term trend factor. Scaling is performed to account for over-dispersion when present.

Investigating rises in calls ('exceedances' and 'alerts')

Statistically significant excesses (termed 'stage 1 exceedances') in calls for any of the eleven syndromes are automatically highlighted and investigated further if the on-call project scientist considers they represent a potential threat. The scientist considers issues including: obvious data errors; single or multiple day 'exceedances'; and the proportion of calls where emergency care has been recommended by NHS Direct nurses.

If no reasonable explanation can be found for the 'exceedance', additional call details are requested, and this is termed a 'stage 2 investigation'. Factors that influence whether to progress from a stage 1 exceedance at an NHS Direct site to a stage 2 exceedance are:

- Call activity at adjacent NHS Direct sites
- Call activity in other syndromes
- The degree of statistical excess
- Call outcomes ('dispositions')
- Whether it is a 1 day or >1day exceedance
- Intelligence from other surveillance systems, colleagues, or the media

The current day's data, if available, are used to determine whether the high level of calls has persisted for a particular syndrome. A geographical information system (GIS) may be used to map calls for obvious clustering. When the scientist considers that the information provided by the 'stage 2 investigation' necessitates further action (potentially due to geographical clustering or persistently high level of calls), this is discussed with the on-call project consultant epidemiologist and NHS Direct medical advisor.

If it is considered to be warranted, a 'stage 3 alert' is issued and may result in reports being disseminated to local public health teams (e.g. HPA Health Protection Units) and national coordinators (e.g. for influenza surveillance), or the NHS Direct on-call medical adviser contacting callers to obtain further clinical information. When this type of action is taken, local or national agencies are normally informed within 24-48 hours of the NHS Direct calls being made. Although a mechanism to provide self-testing kits to NHS Direct callers in order to obtain diagnostic specimens for influenza testing has been developed [11], this procedure is not routine.

Routine outputs

As well as the ad hoc stage 3 alerts, weekly bulletins that summarise NHS Direct call activity for all 11 syndromes are emailed to local and national health protection teams, NHS Direct sites, and the NHS every Wednesday. These bulletins and additional surveillance data are also published on the HPA website [12].

Results

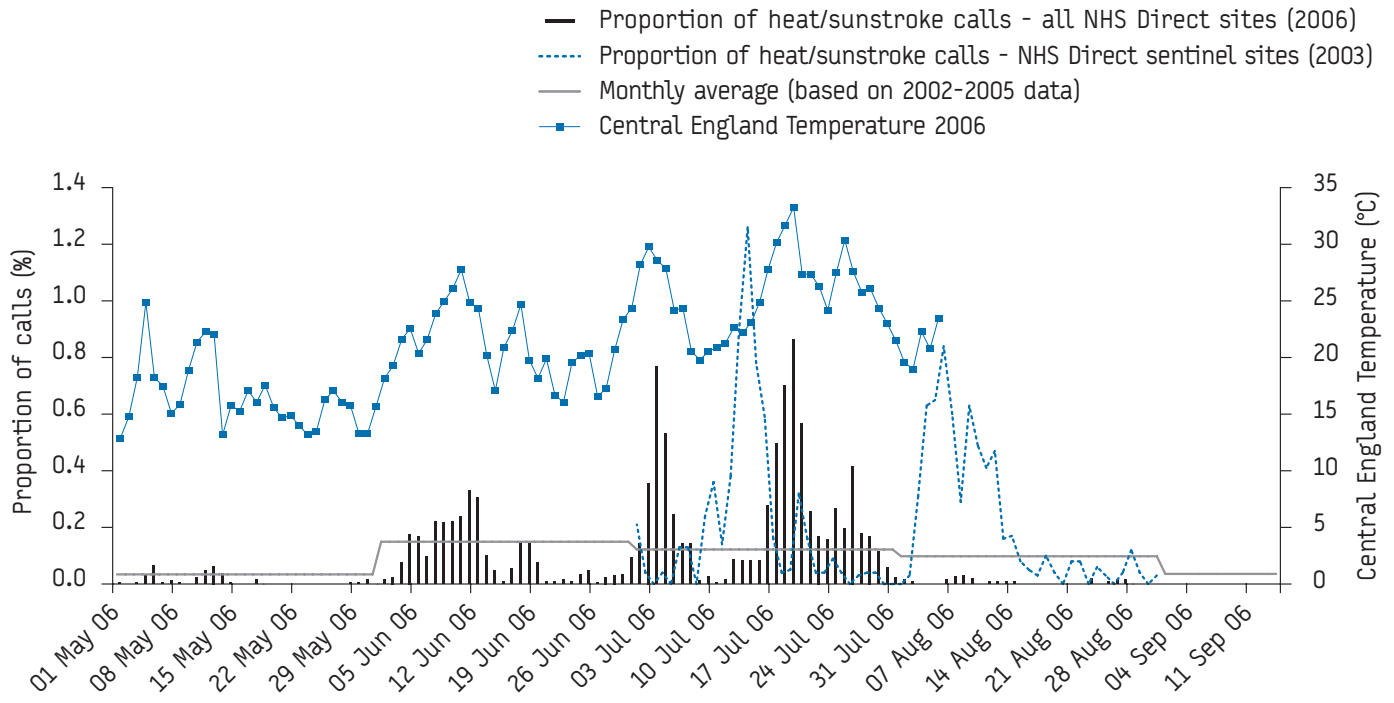
Obtaining precise measures of sensitivity for our system is difficult as there is no agreed 'gold standard' against which to compare our results. It has been shown retrospectively that NHS Direct cold/flu calls show a weak correlation with consultations for ILI recorded by the Royal College of General Practitioners Weekly Returns Service [13]. Prospectively, the NHS Direct syndromic surveillance system generates many stage 1 exceedances, of which most are not investigated. For example, during March 2004 to February 2005, there were 158 single site control chart exceedances. Twenty three (14.6%) of these progressed to a stage 2 investigation and 3 (1.9%) to a stage 3 alert. The alerts highlighted separate rises in calls about diarrhoea and difficulty breathing, of which no cause could be found, and no further action was taken. The third alert was a rise in cold/flu calls during December 2004, occurring concurrently at separate NHS Direct sites, which heralded a seasonal rise in influenza and ILI detected by other surveillance systems over the following weeks.

How has the syndromic surveillance system helped?

Although established as an incident / outbreak detection system, as the work has evolved further utilities of the surveillance outputs have emerged. Examples of how the data have been used are given below.

Figure 2

Daily NHS Direct 'heat/sunstroke' calls as a proportion of total calls summer 2006 and 2003, monthly average (2003-2005), and Central England temperature (summer 2006)



Early warning of rises in disease

NHS Direct syndromic data are used as part of the national influenza surveillance programme. For example, during January 2006 there was a sudden increase in school outbreaks of influenza B [14] and media concern that schools in the West Midlands were particularly affected. The reporting of school outbreaks is not consistent across the country, however, so it was necessary to carefully examine the various sources of available surveillance data.

On 25 January 2006 the weekly NHS Direct syndromic surveillance bulletin reported a significant national rise in the proportion of NHS Direct 'fever' calls for the 5-14 year age group. At the same time clinical and laboratory indicators of influenza remained relatively low. Regional trends indicated that fever calls in the West Midlands were high (peaking at 14.4% of total calls), but not significantly higher than the rest of the country (national peak 13.5%).

In this instance NHS Direct syndromic surveillance data were able to provide an early indication of a community rise of fever in school aged children (a proxy for ILI), confirmation that this rise was not specific to the West Midlands (quelling media fears), and ongoing regional specific surveillance data (along with other primary care surveillance systems) for the remainder of the national outbreak.

Verification of community morbidity

NHS Direct calls about 'heat and sunstroke' have been used as part of the Department of Health Heat Health watch plan for England [15] in order to monitor the health impact of heatwaves, for example during July 2006 when a heatwave affected large parts of Europe.

Between 1 May and 15 September 2006 the daily numbers of heat/sunstroke calls were monitored, broken down by NHS Direct site (22 in total), age group (0-4, 5-74, ≥ 75 years) and call outcome (999 call out, A&E referral, GP referral, home care advice, other). During this time 1474 heat/sunstroke calls were received by NHS Direct in England and Wales out of 1 739 768 total symptomatic calls (0.08%). There were four distinct peaks in heat/sunstroke calls, as a proportion of total calls, on 11 June (52 calls, 0.3%), 3 July (109 calls, 0.8%), 19 July (115 calls, 0.9%) and 26 July (26 calls, 0.4%). These four peaks occurred on the same day or one day after peaks in the Central England Temperature [FIGURE 2]. Over the summer all NHS Direct sites handled heat/sunstroke calls, with the highest proportions of calls being received in Wales (80 calls, 0.11%), the West Midlands (162 calls, 0.11%) and the South East (297 calls, 0.10) regions. The 5-74 year age group accounted for 1299 heat/sunstroke calls (89% of total).

Throughout the summer trends in heat/sunstroke calls were summarised in the weekly NHS Direct syndromic surveillance bulletin. During the two periods in which high temperatures triggered 'heat-health' response levels 'Alert' and 'Heatwave', *daily* NHS Direct heat/sunstroke bulletins (4-5 July, 17-28 July) were issued to the Department of Health and other agencies involved in implementing the heatwave plan.

NHS Direct call data were the only real time health data available during the heatwave and a timely measure of increased community morbidity due to heat. The relatively low numbers of heat/sunstroke calls (1 74 during the summer) may indicate that these data were important as a prompt signal for detecting health effects, rather than as a mechanism for quantifying such effects.

Reassurance

'Real time' data have been used to provide reassurance about the lack of health impact following major incidents (e.g after the traces of ricin were found in a London flat in January 2003; after the London bombs of 7 July 2005). This was helped by ability to report on data more frequently than daily (for special circumstances), and by mapping NHS Direct calls.

Most recently, on 11 December 2005 there was a huge explosion at the Buncefield fuel depot in southern England [16]. Twenty oil tanks were destroyed in one of the largest blasts in peacetime Europe. In the immediate aftermath of the blast, and for the following six weeks, total NHS Direct calls, calls about 'breathing problems' and 'cough' and the outcomes of NHS Direct respiratory calls were monitored for the eight NHS Direct sites covering the potentially effected area. Although increases in respiratory calls were detected at local NHS Direct sites during December/January 2006, these rises were considered normal for the winter period and no increases in calls thought to be due to the blast were observed. The data, with accompanying interpretation, were used to provide reassurance to the incident team about a lack of an unusual increase in clinical illness and to provide reassurance for the public.

Emergency planning and exercises

The systematic collection of almost five years worth of daily national call data, with well established statistical baselines, means the surveillance database is now a well used resource, providing data extracts for emergency planning exercises and modeling work, particularly around pandemic influenza.

Evaluation

A preliminary evaluation of the NHS Direct syndromic surveillance system in 2004 using the 'Framework for Evaluating Public Health Surveillance Systems for Early Detection of Outbreaks' [17] concluded that the system was timely, representative and useful [13]. The direct annual operating cost of the system (£150 000 per annum or around €224 000) was considered to be low for a national surveillance system. This value did not include data costs, however, as the surveillance requirements of the system are embedded into the core operations of NHS Direct.

Discussion

The NHS Direct syndromic surveillance system has been used several times to reassure public health teams and the public about the lack of major impact of a health protection incident. We are still not sure, however, (for differing syndromes) what increase in calls would occur for unexpected health protection incidents. The evaluation [13] found that the system was more likely to detect large scale events or generalised rise in syndromes than localised outbreaks of communicable disease. This is supported by the early warning of ILI detected during January 2006 and rapid detection of heat related illness during July 2006. The opportunity to detect very localised rises in illness (potential outbreaks) may improve as NHS Direct call rates rise over time and the statistical methodology used to flag local data anomalies is refined (e.g. using integrated spatio-temporal analysis tools).

The total NHS Direct call rate is low when compared to the total consultation rate for family doctors (approximately one thirtieth the rate). Therefore, even though NHS Direct has national coverage, the system captures only a small proportion of illness reported to primary care in England and Wales. Our system is designed to monitor acute symptoms which may be indicative of a health protection incident, and are mainly respiratory and gastrointestinal in nature. The system uses routinely generated data and does not require the NHS Direct nurses to enter additional information, thus causing minimal disruption to the work patterns of the data providers. The algorithms used are those collected routinely for telephone triage purposes and the surveillance team have been 'pragmatic' about lack of clear case definitions. However, although there was initial scepticism about what, for example, the 'cold/flu' algorithm may be measuring, good accordance with generalised ILI activity has been noted [17, 18].

The surveillance team (NHS Direct and HPA) that operate the

surveillance system believe it is helpful to have a clear and working link between themselves, and those conducting any resulting public health response (e.g. local HPA Health Protection Units). Future challenges for are the provision of local surveillance data to a newly defined network of Primary Care Trusts in England and Wales, integrating routine spatio-temporal analyses into the surveillance system, and further evaluation of the usefulness of the surveillance system for public health practitioners.

Conclusions

Although syndromic surveillance systems based on data from regional *telephone* triage systems exist, the use of data from a national telephone health help line (NHS Direct) is unique in the field of syndromic surveillance. The NHS Direct syndromic surveillance system is also the only national daily surveillance system in UK and provides a timely national snapshot of community morbidity for selected symptoms. To date, no deliberate release of either chemical or biological agents has been detected. The main benefits of using NHS Direct telephone triage data for public health surveillance have been in providing early warning of rises in infectious disease and disease caused by environmental factors, tracking and verification of trends in community morbidity, and reassurance that widespread disease is not occurring when there is a perceived high public health risk.

Acknowledgements

We thank the NHS Direct National Operations Centre and all NHS Direct sites for continuing supply and use of call data.

References

1. NHS Direct Online website. http://www.nhsdirect.nhs.uk/.
2. Knowles E, Munro J, O'cathain A, Nicholl J. Equity of access to health care. Evidence from NHS Direct in the UK. J Telemed Telecare. 2006;12(5):262-5.
3. Rowlands S, Moser K. Consultation rates from the general practice research database. Br J Gen Pract. 2002;52(481):658-60.
4. Burt J, Hooper R, Jessopp L. The relationship between the use of NHS Direct and deprivation in southeast London: an ecological analysis. J Public Health Med. 2003;25(2):174-6..
5. Cooper DL, Arnold E, Smith GE, Hollyoak VA, Chinemana F, Baker M, O'Brien SJ. The effect of deprivation, age and gender on NHS Direct call rates. Br J Gen Pract. 2005;5:287-1.
6. Health Protection Agency. http://www.hpa.org.uk/default.htm.
7. Micheal D, Pavlin JA, Mansfield LJ et al. Disease outbreak detection system using syndromic data in the greater Washington DC area. Am J Prev Med. 2002; 23:180-6.
8. Heffernan R, Mostashari F, Das D, Karpati A, Kulldorff M, Weiss D. Syndromic surveillance in public health practice, New York City. Emerg Infect Dis. 2004; 10(5):858-64.
9. Baker M, Smith GE, Cooper DL, Verlander NQ, Chinemana F, Cotterill S et al. Early Warning and NHS Direct: a role in community surveillance? J Public Health. 2003; 25:362-8.
10. Armitage P, Berry G. Statistical method in medical research (2nd Edition). Blackwell Scientific Productions, Oxford 1987.
11. Cooper DL, Smith GE, Loveridge P, Chinemana F, Gerard E, Joseph C et al. Using self-testing to augment syndromic surveillance? A pilot study using *influenza*. MMWR Morb Mortal Wkly Rep. 2005; 54(Suppl):186.
12. CDR Weekly: Primary Care. Available from: http://www.hpa.org.uk/cdr/pages/primarycarewr.htm
13. Doroshenko A, Cooper D, Smith GE, Gerard E, Chinemana F, Verlander NQ et al. Evaluation of Syndromic Surveillance Based on NHS Direct Derived Data in England and Wales. MMWR Morb Mortal Wkly Rep. 2005 Aug 26;54 Suppl:117-22.
14. HPA National Influenza season summary. Influenza/ Respiratory Virus Team, HPA Centre of infections. May 2006. Available from: http://www.hpa.org.uk/infections/topics_az/influenza/seasonal/activity0506/reports/Season_Summary0506.pdf.
15. Heatwave plan for England. Protecting health and reducing harm from extreme heat and heatwaves. Department of Health, 2006. http://www.dh.gov.uk/NewsHome/NewsArticle/fs/en?CONTENT_ID=4135379&chk=V6LqCf.
16. Buncefield Major Incident Investigation Board. Buncefield major incident investigation. Health and Safety Executive, Sudbury 2006. http://www.buncefieldinvestigation.gov.uk/reports/initialreport.pdf
17. Buehler JW, Hopkins RS, Overhage JM, Sosin DM, Tong V. CDC Working Group. Framework for evaluating public health surveillance systems for early detection of outbreaks : recommendations from the CDC Working Group. MMWR Morb Mortal Wkly Rep.2004;53(No.RR-5).
18. Cooper DL, Smith GE, Hollyoak VA, Joseph CA, Johnson L, Chaloner R. Use of NHS Direct calls for the surveillance of influenza – a second year's experience. Commun Dis Public Health. 2002;5(2):127-31.

Original Articles

Surveillance report

Syndromic surveillance based on emergency department activity and crude mortality: two examples

L Josseran[1], J Nicolau[1], N Caillère[1], P Astagneau[2], G Brücker[1]

Recent public health crises have shown the need for readily available information allowing proper management by decision-makers. One way of obtaining early information is to involve data providers who already record routine data for their own use.

We describe here the results of a pilot network carried out by the InVS (Institut national de veille sanitaire) which gathered data available in real time from hospital emergency departments and register offices.

Emergency departments data were registered from patients' computerised medical files. Mortality data were received from the national institute of statistics (Insee). Data were transmitted automatically on a daily basis. Influenza data from outbreaks in 2004/05 and 2005/06 were compared with data from the sentinel network for the same periods. Environmental health data were compared with meteorological temperatures recorded in Paris between June and August 2006. A mortality analysis was conducted on a weekly basis.

Correlation between influenza data from emergency departments and data from Sentiweb (sentinel network) was significant ($p<0.001$) for both outbreaks. In 2005 and 2006, the outbreaks were described similarly by both sources with identification of the start of the outbreaks by both systems during the same weeks. As for data related to heat, a significant correlation was observed between some diagnoses and temperature increases. For both types of phenomena, mortality increased significantly with one to two weeks lag.

To our knowledge, this is the first time that a study using real time morbidity and mortality data is conducted. These initial results show how these data complement each other and how their simultaneous analysis in real time makes it possible to quickly measure the impact of a phenomenon.

Euro Surveill. 2006;11(12): 225-29 Published online December 2006

Key words: Syndromic surveillance, emergency department, mortality

Introduction

The social and political impacts of health events are essential parameters to take into account in health surveillance [1]. Recent health events such as the European heat wave of 2003 and widespread outbreaks of chikungunya, emphasise the need to provide information to health authorities to help with decision making [2]. One of the possibilities for obtaining early information is to involve physicians and others relevant data providers who record routine data for their own use, which can be transmitted automatically and daily [3, 4]. The French national institute for public health surveillance (Institut de Veille Sanitaire, InVS) initiated a pilot network in July 2004, gathering different sources of data available in real time from hospital emergency departments, registry offices, emergency general practitioners (a service known in France as 'SOS médecins'). This article presents an evaluation of this surveillance based on emergency departments and mortality recording from registry offices for influenza outbreaks (2005 and 2006) and health impact of the 2006 heat wave.

Material and method

Description of the network

Emergency Departments (ED)

Data were collected directly from patients' computerised medical files filled in during medical consultations. Selected hospitals use appropriate software. Two architectures for gathering data were used. The first was based on a regional server in Ile-de-France (Paris area) developed by regional health authorities. This server centralises data from hospitals in the area, which are then transferred to InVS. The second data gathering method consists of a direct connection between hospitals and the central server at InVS.

Mortality recordings

The national institute for statistics (Institut National de la Statistique et des Études Économiques, Insee) is responsible for the administrative recording of deaths from all causes in France. For several years, Insee has managed a system for recording and centralising daily mortality. Data processing was near real time. Data from 1152 cities were transmitted daily to InVS.

Variables

Items collected included the diagnosis coded according to ICD-10, with a score of severity ranked from 1 to 5 after medical examination, the date of admission to hospital, age, sex, post code, and the chief complaint. For mortality, only data on age, sex, and date and city of death were available.

Each patient or death corresponded to a single recording, including all variables.

Data transmission and processing

Data were transmitted encrypted to InVS over the internet using file transfer protocol (FTP), seven days a week. Computer assisted extraction and transmission were performed using specific programmes. These data were then included in a database, using SAS programmes.

For hospitals, each file transmitted to InVS included all patient visits to the emergency department logged during the previous 24-hour period (midnight to midnight). Data were sent according to the hospitals between 4 am and 6 am. They were transmitted twice, at day +1 (temporary file) and day +2. This double sending allowed the files already transmitted to be supplemented; the second file automatically superseded the first one.

1. Institut de Veille Sanitaire, Saint-Maurice, France
2. Service de santé publique, Hôpital de la Pitié Salpétrière, Paris, France

Mortality data were transmitted daily and the file included deaths recorded for the last 30 days.

Data analysis

The study covered the period from July 2004 to the end of July 2006.

Hospitals

We analysed data categorised by week, for the Paris area, in relation to influenza outbreaks (2005 and 2006), measured through emergency departments (ICD-10:J10 / J11) compared to data from the Réseau Sentinelles (sentinel network) which is the reference for studying influenza in France [5]. A correlation coefficient was performed between the two datasets. We completed a daily analysis of a number of influenza diagnoses done in emergency departments with the Cusum method developed by the United States Centers for Disease Control and Prevention (CDC) within the framework of the EARS" programme (Early Aberration Reporting System) (6). This allowed us to define the first days of alert for influenza compared to onsets published by SentiWeb.

To monitor the health impact of hot weather, we defined an indicator as follows: total number of daily cases of three pathologies linked to high temperatures (hyperthermia, dehydratation and hyponatraemia). The study was focused on the Paris area and data were correlated to daily temperatures measured in Paris from June to August 2006 by Météo France® (the French meterological office). Results were compared with the official periods of alert launched by the French Ministry of Health (MoH).

Mortality

All-causes mortality analyses were conducted on a weekly basis. The analysis was based on the method of historical means, adapted from the CDC and used to monitor infectious diseases [7,8]. For each week, the expected number (historical mean) of deaths corresponded to the mean of 3 weeks (comparable, previous, and next weeks) for the past 5 years. The ratios were computed as 1, plus or minus 2(SD/X), (SD=standard deviation and X=mean of the 15 considered weeks). When the ratio is outside the thresholds, the elevated (or diminished) portion of the ratio is significant.

An alert was defined as a threshold-crossing by ratio. The EARS® programme was run on a daily basis for the whole period.

Results

Hospitals

Overall, 46 emergency departments participated in the study. Thirty one were within Paris area and 15 in other regions, including one overseas territory in the Indian Ocean (Saint Denis-Reunion Island). Over the monitoring period, 3.2 million visits were recorded with an average of 4024 visits per day including 980 paediatric visits (< 15) (+/- 25.3%), 2668 adult visits (+/- 15.1%), and 377 visits (+/- 16.7%) to people above 75 years. The medical diagnosis was missing from 26% of records, and the chief complaint from 12% of records. The severity score was missing in 17% of cases, and data on sex and age were missing in less than 1%. Fifty four percent of patients were male and 46% female (P<0.001).

Figure 1 shows the relationship between data from emergency departments and the Réseau Sentinelles. The two curves were similar, with a coefficient of correlation of 0.94 (P<0.001). The scales were different but data from both sources followed a similar kinetic. The outbreak started in week 3 of 2005, followed by a dramatic increase 3 weeks later. Peaks were reached in week 7 of 2005 and then decreased for 4 weeks. In the 2006 influenza outbreak, although curves were very similar, there were some differences. The emergency department influenza visit curve was above the Réseau Sentinelles from week 45 of 2005 to week 5 of 2006. A gap was observed in week 7 of 2006 with Réseau Sentinelles data and appeared a week later with emergency department data. A peak was shown by the Réseau Sentinelles in week 9 of 2006 but not by emergency departments. Subsequently, an abrupt fall was described by both sources.

For both outbreaks, EARS® programme was run on a daily basis. In 2005, the first alerts were detected on 16 January 2005 (positive for C1, C2 and C3 methods), which corresponded to week 3, the first week of the influenza outbreak onset this season (9). During the following outbreak, alerts were detected on 29 and 30 January and on 1, 2 and 3 February (positive for C2 and C3) which corresponded to week 5, the first week of the 2006 outbreak [10].

Regarding the health impact of the 2006 heat wave, the indicator showed three peaks [FIGURE 2]. The first one was on 19 June, the second on 3 and 4 July. The first two peaks were correlated with increased temperatures. The third peak lasted longer (starting 18 July

Figure 1

Weekly evolution of number of influenza diagnosis in emergency departments (ED) and number of influenza diagnosis (extrapolated) from the Réseau Sentinelles – Paris area, seasons 2004/05 – 2005/06

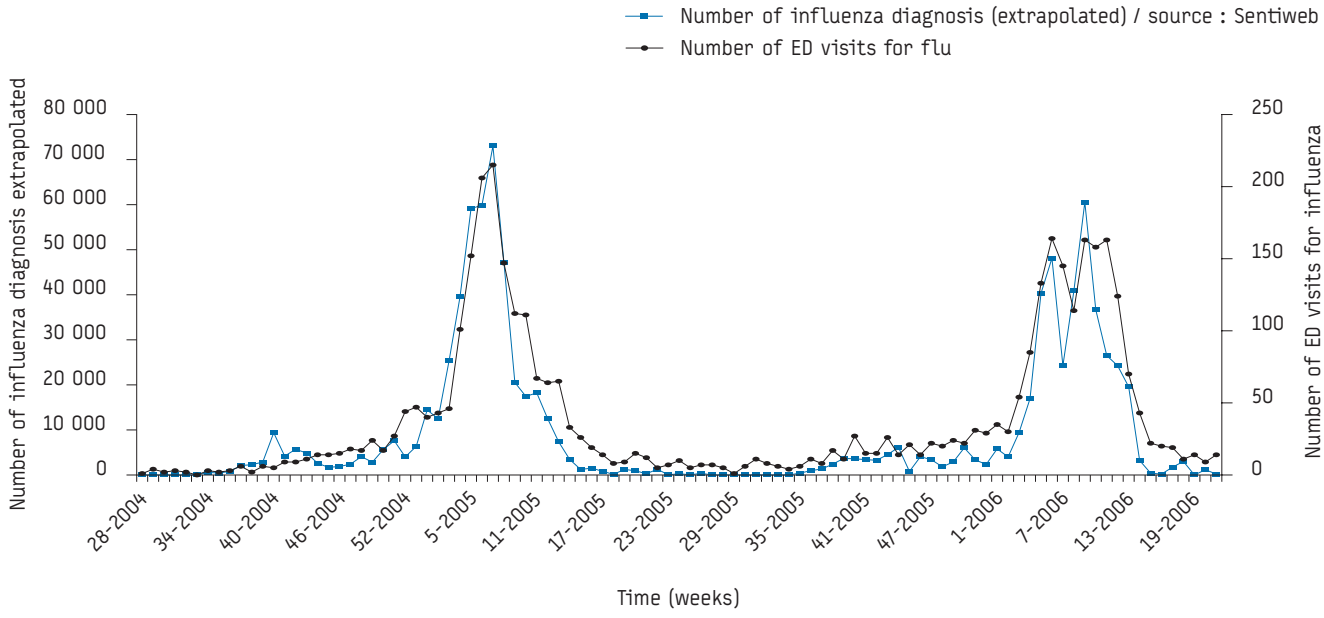


Figure 2

Daily evolution of the health impact hot weather indicator, temperature and days of alert (MoH and EARS) – Paris area, June to August 2006

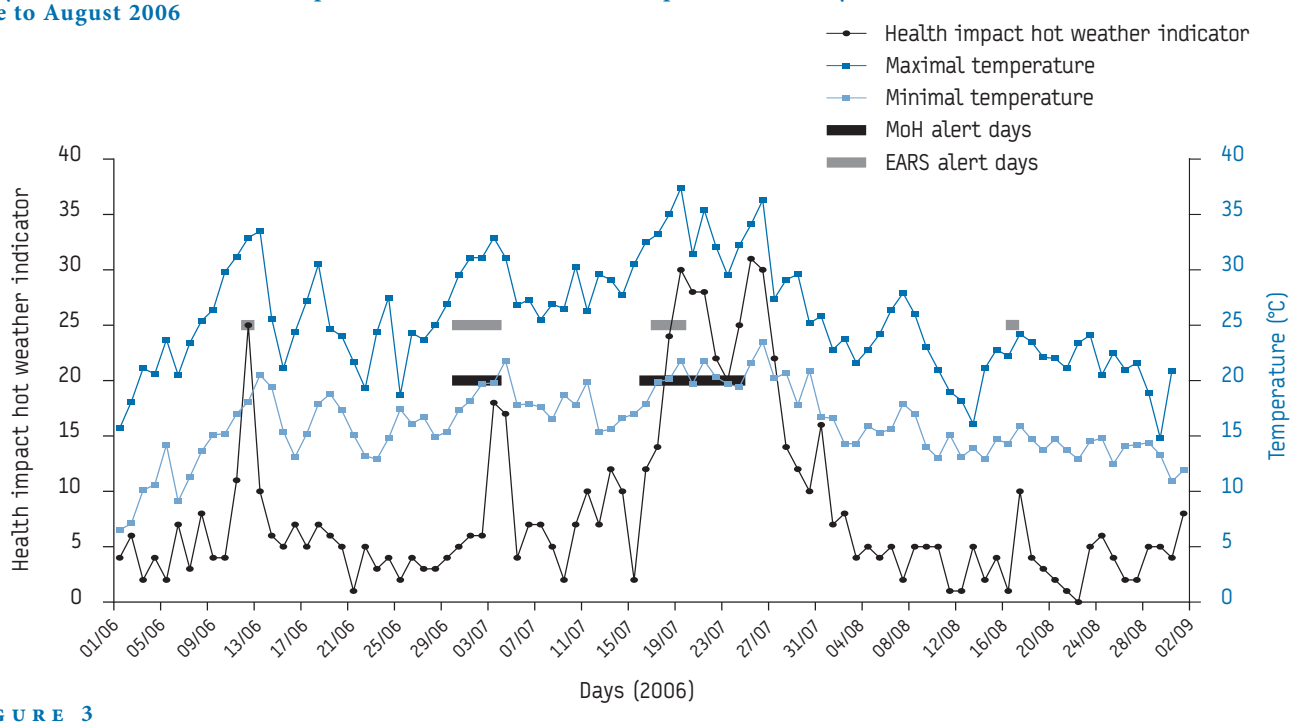
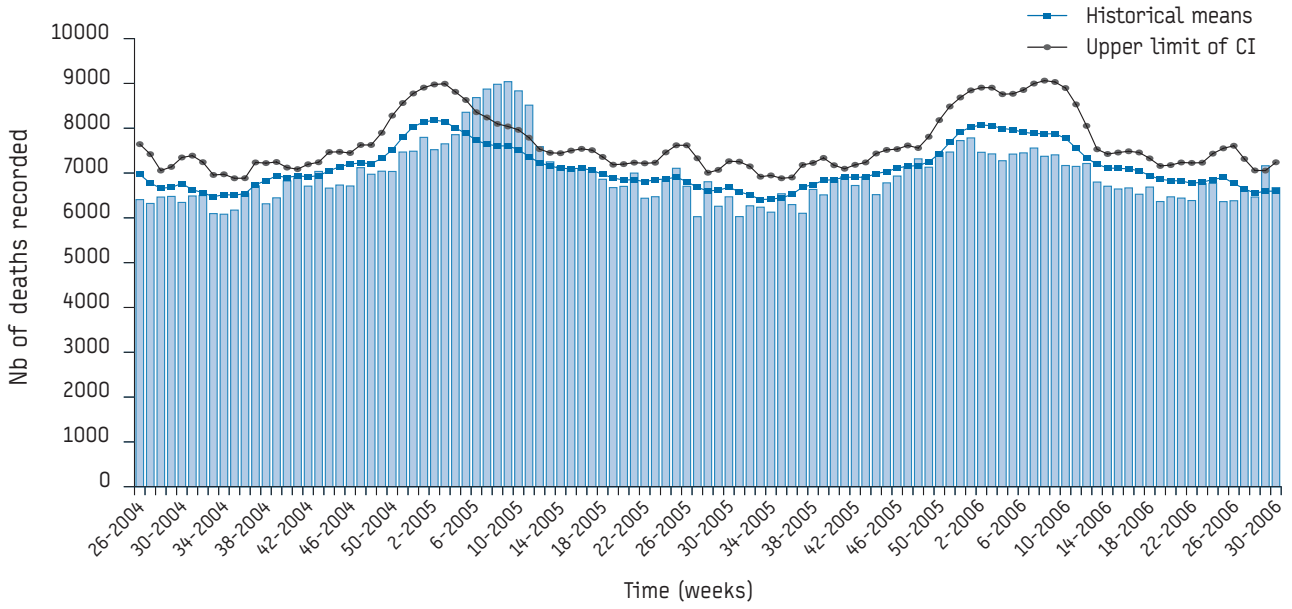


Figure 3

National mortality surveillance - weekly evolution of deaths recorded, France, June 2004-July 2006



and continuing for nearly 10 days) and was on a large scale. Between 21 and 23 July, the indicator fell by 35.7%, while temperature rapidly decreased. Coefficients of correlation between indicator and daily temperatures were significant (0.67 (P<0.001) for maximal and 0.72 (P<0.001) for minimal). The EARS® analysis showed one alert in June (11 and 12 June), two in July (1 to 4 and 18 to 20 July) and one in August (17 August). During this period, the MoH launched two alerts: 1-4 and 17-25 July.

Mortality

Since the beginning of the study more than 560 000 deaths were recorded. Out of these deaths, 53% were male and 47% were female (P< 0.001), representing nearly 1000 deaths per day and two thirds of the French daily mortality. For any given day, 50% of data were recovered within a period of 3 days, 90% within a period of 7 days and 95% within a period of 10 days.

At the national level, the mortality exceeded the alarm threshold during a 7 weeks time interval (week 6 to week 12 in 2005) and week 29 in July 2006 for the entire period. No other threshold-crossing was identified [FIGURES 3, 4].

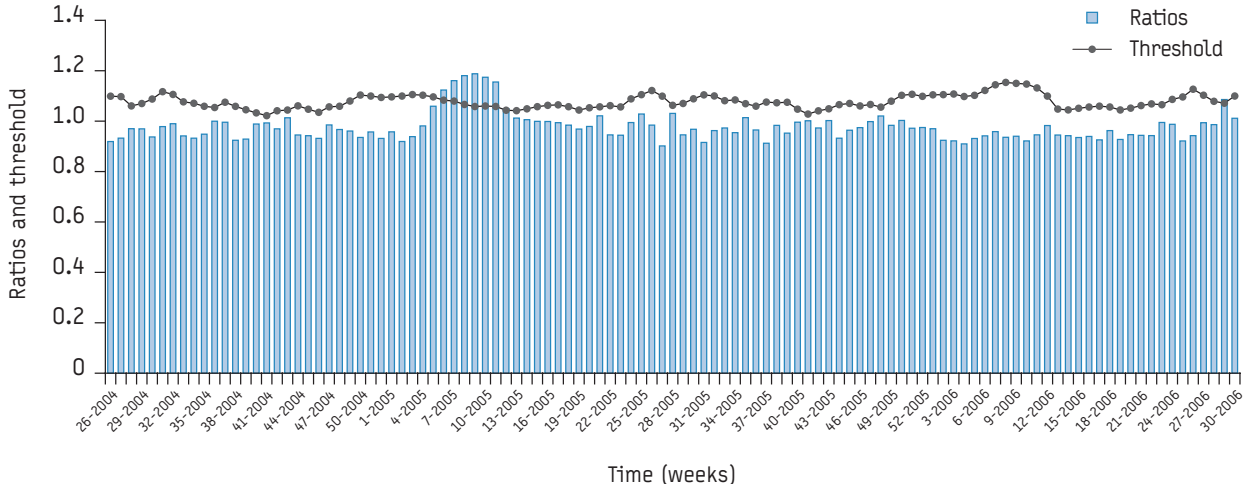
Discussion

At this point, networks represent nearly 10% of emergency department visits in France, and around 66% of the daily mortality.

Among various syndromic surveillance systems tested, none was associated to two matched data sources in real time (emergency department visits, crude mortality) [11]. Our first results illustrate the sensitivity of the system for evaluating the health impact of

Figure 4

National mortality surveillance - Method of historical means. Two years of follow up, 2004-06, France



known events or detecting a public health threat by its health impact [12]. Consequently, each emergency department or registry office can be used to capture information, each patient or death being a source of information [13]. For example, our system contributed to measure the crude mortality during the chikungunya outbreak in Reunion in 2005, with no effort expended by the data providers [14]. In 2003. the monitoring and analysis of the impact of the heat wave was made possible thanks to the efforts of both data providers and epidemiologists, and the situation could be understood only after several weeks [15].

Moreover, the processing for data collection in real time frees the data collection from one of the major difficulties for health surveillance: the reporting delay, which can distort the true picture [16].

The lack of 26% of key information (medical diagnosis) can be explained in two ways: some patients leave emergency departments before a diagnosis is made (discharge without medical staff authorisation), and others, for whom no diagnosis was established, are kept in hospitals for further medical examination; and two hospitals consistently failed to fill in the diagnosis section of the forms provided. A positive trend of this percentage has been observed compared to July 2004, when around 40% of this information was missing, Whatever the rate of missing information, the medical diagnosis coded in ICD-10 is preferably used than the one based on chief complaint because of its greater reliability.

Similarity between influenza data based on ED and data from the Réseau Sentinelle on a weekly basis was confirmed by the EARS® results. For both outbreaks, the first alerts detected corresponded to the week of the official onset of these outbreaks.

The correlation between our 'health impact hot weather' indicator and temperatures showed that emergency departments are a very relevant source of information for environmental health impact surveillance. We identified a period of alert in June whereas the MoH did not. In July, two alert periods were identified: the first one on the same day as the MoH did (1 July 2006) and the second one on 18 July i.e. one day after the MoH. It is more likely that the August alert detected only by EARS® analysis was an artefact considering that temperatures were very low.

These validations with two different kinds of disease (infectious and environmental) allow us to use this data to monitor other infectious diseases and health impacts of environmental conditions. Furthermore, its non-specific character made it interesting as a routine surveillance tool, because it detects less common or emerging diseases [17].

As for mortality, each different threshold-crossing detected corresponded to widely recognised phenomena (2005 influenza outbreak, 2006 heat wave).

Interestingly, no mortality increase appeared to correspond with the very small influenza outbreak in the winter of 2005/2006, and during the period monitored, no health threat with potential impact (infectious or environmental) on mortality was identified [18].

These three facts demonstrate the interest of this mortality surveillance.

With the implementation of this new surveillance system of all-cause mortality, we have demonstrated the availability of mortality data in real time and thus that health impacts of events are becoming quantifiable in real time. Few systems currently use crude mortality data for health surveillance in real time, which makes our approach original [19, 20].

This is the first experiment of its kind with syndromic surveillance in France. The usefulness of emergency departments data for surveillance had previously been validated by other international experiences. Here, we corroborate those previous findings in the context of the French healthcare system and also demonstrate the interest of ongoing surveillance of crude mortality. The complementarity of the two data sources, emergency departments and registry offices, is relevant. In the case of influenza and hot weather, we first observed an effect on morbidity, followed the week after by an effect on mortality. Progress is now needed to develop national coverage of the system, so that it can be efficient in all regions.

Acknowledgments

Ms. Amandine Rodrigues from Insee and all emergency departments are acknowledged for their contribution.

References

1. Broome CV. Federal role in early detection preparedness systems. In: Syndromic surveillance: reports from a national conference, 2004. MMWR Morb Mortal Wkly Rep. 2005; 54 Suppl:7-9.
2. Butler D. Disease surveillance needs a revolution. Nature. 2006;440(7080):6-7.
3. Peterson D, Prencevich E, Harris A, et al. Using existing electronic hospital data for syndromic surveillance. J Urban Health. 2003;80(2-Suppl 1):i122-3.
4. Sartorius B, Jacobsen H, Törner A, Giesecke J. Description of a new all cause mortality surveillance system in Sweden as a warning system using threshold detection algorithms. Eur J Epidemiol. 2006;21(3):181-9.
5. Flahault A, Boussard E, Vibert JF, Valleron AJ. Sentiweb remains efficient tool for nationwide surveillance of disease. BMJ. 1997;314(7091):1418.
6. Hutwagner L, Browne T, Seeman GM, Fleischauer AT. Comparing aberration detection methods with simulated data. Emerg Infect Dis. 2005;11(2):314-6 Emerg Infect Dis 2005;11(2):314-316. (http://www.cdc.gov/ncidod/EID/vol11no02/04-0587.htm).

7. Centers for Disease Control (CDC). Proposed changes in format for presentation of notifiable disease report data. MMWR Morb Mortal Wkly Rep. 1989;38(47):805-9.
8. Centers for Disease Control (CDC). Graphic method for presentation of notifiable disease dante-United States, 1990. MMWR Morb Mortal Wkly Rep. 1991;40(7):124-5.
9. SentiWeb hebdo N° 2005-3. http://rhone.b3e.jussieu.fr/senti/ressources/fr/hebdo/hebdo_2005s03.pdf (last visit 11/21/06).
10. SentiWeb hebdo N°2006-5. http://rhone.b3e.jussieu.fr/senti/ressources/fr/hebdo/hebdo_2006s05.pdf (last visit 11/21/06).
11. Bravata DM, McDonald KM, Smith WM, Rydzak C, Szeto H, Buckeridge DL, Haberland C, Owens DK. Systematic Review: surveillance systems for early detection of bioterrorism-related diseases. Ann Intern Med. 2004;140(11):910-22.
12. Pavlin JA. Investigation of disease outbreaks detected by syndromic surveillance systems. J Urban Health. 2003 Jun;80(2 Suppl 1):i107-14.
13. Josseran L, Gailhard I, Nicolau J,et al. Organisation expérimentale d'un nouveau système de veille sanitaire, France, 2004-2005. Bulletin Epidémiologique Hebdomadaire. 2005;27-28:134-137. (http://www.invs.sante.fr/beh/2005/27_28/beh_27_28_2005.pdf) (last visit 11/21/06).
14. Josseran L, Paquet C, Zeghnoun A, et al. Mortality and chikungunya disease outbreak in Reunion Island. Emerg Infect Dis. Under press.
15. P Pirard, S Vandentorren, M Pascal, K Laaidi, A Le Tertre, S Cassadou, M Ledrans. Summary of the mortality impact assessment of the 2003 heat wave in France. Euro Surveill 2005;10(7):153-6. Available from: http://www.eurosurveillance.org/em/v10n07/1007-224.asp.
16. Farrington CP, Andrews NJ, Beale AD, Catchpole MA. A Statistical Algorithm for the Early Detection of Outbreaks of Infectious Disease. Journal of the Royal Statistical Society. Series A (Statistics in Society). 1996;159;3:547-563.
17. Fleischauer AT, Silk BJ, Schumacher M, Komatsu K, Santana S, Vaz V, Wolfe M et al. The validity of chief complaint and discharge diagnosis in emergency department based syndromic surveillance. Acad Emerg Med. 2004;11(12):1262-7.
18. Heffernan R, Mostashari F, Das D, et al. Syndromic Surveillance in public health practice, New York City. Emerg Infect Dis. 2004 May;10(5):858-64.
19. Brammer TL, Murray EL, Fukuda K, Hall HE, Klimov A, Cox NJ. Surveillance for influenza – United States 1997-98, 1998-99 and 1999-00 seasons. MMWR Surveill Summ. 2002;51(7):1-10.
20. Connolly MA, Gayer M, Ryan MJ, Salama P, Spiegel P, Heymann DL. Communicable diseases in complex emergencies: impact and challenges. Lancet. 2004;364(9449):1974-83.

ORIGINAL ARTICLES

Surveillance report

SURVEILLANCE OF AMBULANCE DISPATCH DATA AS A TOOL FOR EARLY WARNING

KH Bork[1], BM Klein[2], K Mølbak[3], S Trautner[4], UB Pedersen[1], E Heegaard[1]

Early detection of disease outbreaks is essential for authorities to initiate and conduct an appropriate response. A need for an outbreak detection that monitored data predating laboratory confirmations was identified, which prompted the establishment of a novel symptom surveillance system.

The surveillance system monitors approximately 80% of the Danish population by applying an outbreak detection algorithm to ambulance dispatch data. The system also monitors both regional and national activity and has a built-in, switch-on capacity for implementing symptom surveillance reporting in case of an alert.

In an evaluation with outbreak scenarios it was found that decreasing the outbreak detection sensitivity from a prediction limit of 95% to one of 99% moderately reduced the time to detection, but considerably diminished the number of false alerts.

The system was able to detect an increased activity of influenza-like illness in December 2003 in a timely fashion. The system has now been implemented in the national disease surveillance programme.

Euro Surveill. 2006;11(12): 229-33 Published online December 2006

Key words: Ambulance, bioterrorism, outbreak surveillance, statistical data analysis.

1. National Centre for Biological Defence, Statens Serum Institut, Copenhagen, Denmark.
2. Biostatistics Department, Statens Serum Institut, Copenhagen, Denmark.
3. Department of Epidemiology, Statens Serum Institut, Copenhagen, Denmark.
4. Falck A/S, Copenhagen, Denmark.

Introduction

New infectious threats such as SARS and human H5N1 infections have necessitated detection systems that respond in a timely way to emerging epidemics, allowing authorities to respond at the earliest possible stage. Worldwide developments concerning biological weapons and terrorism were an additional driving force for improving public health surveillance and outbreak response. In case of a covert attack with biological agents the impact is likely to be multinational due to extensive land, sea and air transport. Several terrorist organisations have publicly stated their intent to use unconventional weapons including biological and chemical agents and the risk of an attack therefore is generally considered as credible.

A number of diagnostic-based disease surveillance systems already operate in Denmark, including a sentinel surveillance scheme for influenza and influenza-like illness and a detection system for outbreaks of gastrointestinal illness such as salmonellosis. These surveillance systems are disease specific and do not serve as indicators of disease of unknown origin, including emerging diseases. Furthermore, the delays between outbreak, confirmed laboratory diagnosis, collection and analysis of results, and, eventually, notification of the authorities have in the past resulted in impediments for implementing countermeasures. Unfortunately only a minority of the established disease surveillance systems in Denmark had a capability for regional surveillance. If implemented, it could improve sensitivity in symptoms surveillance and direct diagnostic investigation to a predefined area.

Given this background, our aim was to develop a disease detection system that had the capacity to react promptly following an outbreak

or attack, thereby reducing the median outbreak detection time (MOD-Time) and allowing authorities sufficient time to start outbreak investigation and implement medical countermeasures such as quarantine, mass vaccination or administration of antibiotics. Specifically, the goal was to detect outbreaks of severe illness at an earlier stage than is possible when using traditional sources of information such as clinical reports and laboratory results. Ambulance transport data has previously been found to be useful as an early indicator of increased disease activity unrelated to origin [1], but a thorough testing with scenarios had not been done. The present paper reports results from validation and implementation of the system, which has been termed Bioalarm.

Material and methods

In brief, the surveillance system monitored the activity of ambulance dispatch data by daily applications of an outbreak detection algorithm (Level I). In case of an alert due to an increase in the demand for ambulance transport, a built-in reporting system could be activated (Level II). The second level served as a switch-on capacity for online recording of epidemiological data (selected patient symptoms, geographical data and onset of symptoms) in order to collect information for a preliminary case definition before patients arrived at the hospital.

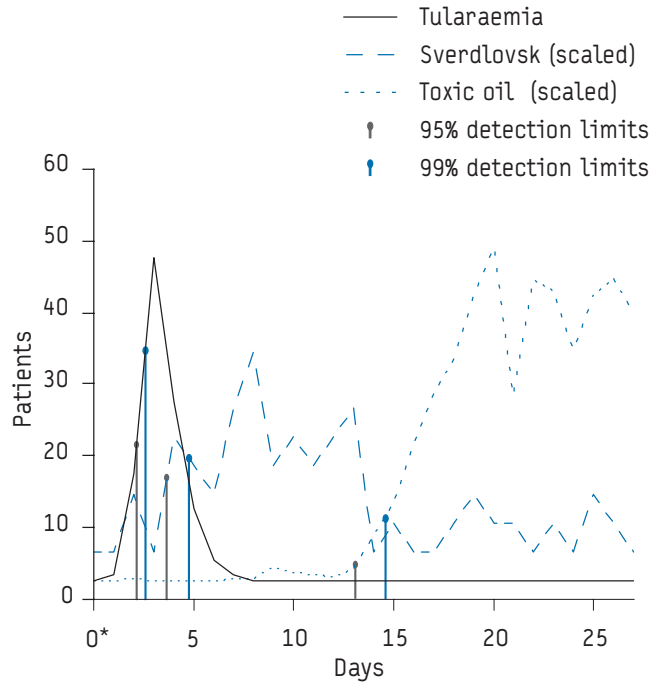
Level I

Ambulance dispatch data

In Denmark, ambulance transport data has been recorded for more than a decade. We collected data on dispatch for emergency medical conditions from January 2000 to August 2005 from six regions in Denmark and evaluated regional as well as national activity simultaneously. Data was recorded at a central registration unit operated by a primary ambulance transport contractor (Falck A/S). This dataset covered more than 80% of the total Danish population of approximately 5.4 million people. The data demonstrated significant variation and included a period with several minor and one major influenza epidemic.

Figure 1

Median outbreak detection time of the three scenarios, Denmark, January 2000-August 2005



* Time = 0 denotes the time of exposure in scenarios I and II, whereas it denotes the beginning of the sale of toxic oil in scenario III

Incidence data from outbreaks

Three scenarios were developed to test and optimise the outbreak detection algorithm. The amplitude (new cases/day) of some of the scenarios was scaled to fit the regional background transport level of the region where the scenarios were applied. The epidemiological profiles of the outbreaks were unaffected.

Scenario I: Outbreak of tularaemia with 100 persons displaying symptoms due to *Francisella tularensis*. The incidence curve resulted from standardised epidemiological calculations [2]. Scenario II: From the Sverdlovsk outbreak of anthrax in 1979 [3,4] incidence data was collected and the amplitude of the outbreak was up scaled to a total number of 420 persons contracting the disease. Scenario III: Incidence data from Madrid in 1981 concerning an outbreak of symptoms later revealed to be due to the illegal sale of toxin-laced cooking oil causing toxic oil syndrome (TOS) [5]. The amplitude of the extensive outbreak was downscaled to a total number of 448 displaying symptoms [FIGURES 1, 2].

Statistical methods

We developed a model in which previous observations were primarily used to determine the variations, while deviations from the baseline were evaluated based upon the observations of the most recent day. The model predicted short term level of transport frequencies one day ahead and calculated prediction intervals with 95% and 99% limits. The upper limits were the focus for analysis and defined the alert thresholds. Whenever transport frequencies increased to above the threshold level of either 95% or 99%, an automatic notification was generated. The statistical engine consisted of a state space dynamic model with local level combined with a Kalman smoother [6,7]. The model was calibrated to fit regional transport frequencies in each region. A user-friendly interface was designed for day-to-day operation and graphic presentation of events.

Testing

The system was first tested in a dry run on background data alone, defining the baseline number of alerts and overall stability. Subsequently, background data for one region with approximately 640 000 inhabitants were spiked with incidence data from outbreaks. This process created a simulated data-material that was used to estimate the response times of the system. The starting point (Day 0)

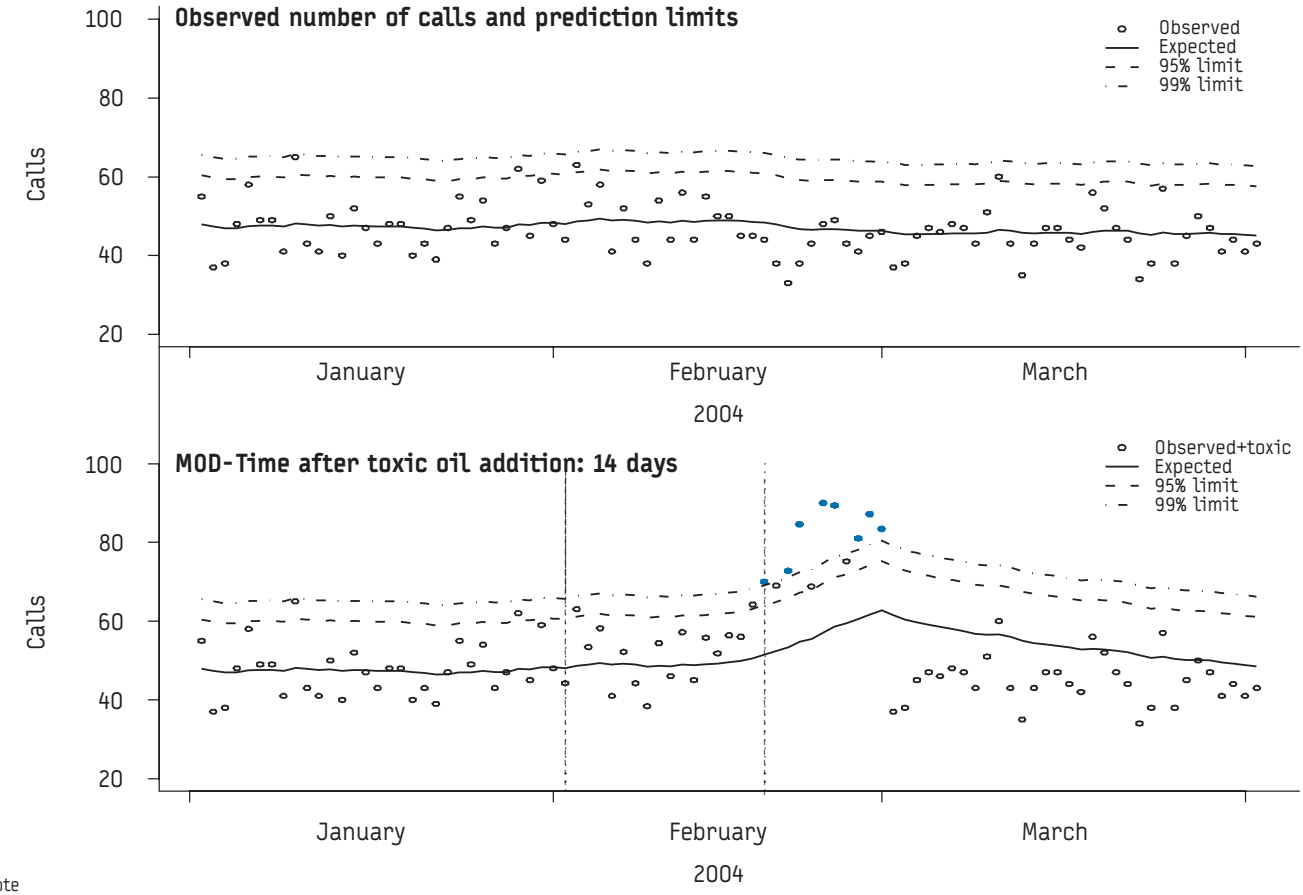
Table 1

Content of the forms distributed to paramedics

Transport data
Pickup-time
Pickup-place
Patient data
Sex
Age
Duration of symptoms
Similar symptoms among relatives or friends
Symptoms
Fever
Vomiting
Speech impairment
Blurred vision
Paralysis
Paresis
Rash
Blisters
Respiratory problems
Cough
Expectorations
Haemorrhage

Figure 2

Addition of scenario (toxic oil syndrome) to background data



Note

The smoothed activity of alerts before and after addition of data from the toxic oil syndrome scenario, Madrid 1981. The dotted vertical lines on the lower illustration denote time from the sale of toxic oil to system alert. The MOD-Time of the 99% detection limit was 14 days. The blue dots mark the calculated daily dispatch intensities above the 99% threshold limit

of the epidemiological profiles in the three scenarios were added to the background data, beginning with the first day of January 2004, then the second day of January 2004 and so forth until the end of July 2004 (three scenarios on 182 days, the equivalent of 546 runs) ([FIGURE 2]. The average, median and maximum outbreak detection time in days were then recorded after each new starting point for all three scenarios.

Level II

For eight days in March 2006, epidemiological data from patients with emergency medical illnesses in one region with approximately 640 000 inhabitants were collected online, following a command from the Danish National Centre for Biological Defence (NCBD) (*Nationalt Center for Biologisk Beredskab*) Data contained selected patient symptoms, patient characteristics and geographical information, [TABLE 1]. Paramedics recorded the data on forms prepared for this purpose and forms were sent by fax to the NCBD for estimation of baseline values (incidences of symptoms, geographical distribution, etc.). Subsequently, the data was spiked with epidemiological symptom data before analysis, in order to simulate a geographically located, symptom-specific disease outbreak.

Results

Ambulance dispatch data:

The data was collected from six regional dispatch centres which had median dispatches ranging from 45 to 130 per day. There were no significant simultaneous seasonal variations on the six dispatch centrals. At a 95% detection limit, we expected 109.5 alerts per year,

Table 2

Scenario outbreak detection time (day)

Scenario	Delay	95% Limit	99% Limit
		Days	
I	Mean	2.36	2.70
	Minimum	1.00	1.00
	Maximum	3.00	3.00
II	Mean	3.08	4.80
	Minimum	1.00	1.00
	Maximum	8.00	8.00
III	Mean	12.68	14.23
	Minimum	10.00	10.00
	Maximum	16.00	16.00

while a 99% limit resulted in an expected number of 21.9 alerts per year (95%: 5 alerts every 100 days per region or 18.25 alerts per year per region, 18.25 _ 6 = 109.5 alerts/year), (99%: 1 alert every 100 days per region or 3.65 alerts per year per region, 3.65 _ 6 = 21.9 alerts/year).

During an influenza epidemic in 2003 the ambulance reporting system issued 13 alerts at the 99% level. Immediately prior to this, one alert had been issued at the 99% level detection limit. During the period when the observed numbers of influenza cases were below the National Influenza Sentinel Registration's threshold level, the system

issued two alerts. Ambulance dispatch activity, compared with the Sentinel Registration, is illustrated in Figure 3.

Scenario detection

When the ambulance dispatch data were spiked with data on the outbreak scenarios, we were able to detect all outbreaks both at a 95% and 99% detection limit [FIGURE 1]. Based on daily applications of the algorithm, a change from a 95% to a 99% detection limit increased the MOD-Time by 1 (scenario I) or 2 days (scenario II and III) [TABLE 2].

Operational issues

One minor system breakdown occurred during the period of automatic prospective ambulance transport frequency monitoring, but overall, the system was operative above 99% of the time. The system updated automatically once every 24 hours. Running costs were limited; the operating officer checked the status of the system and the transport level daily and the procedure required no special skills or training. There was good compliance by operating officers.

Collection of early epidemiological data, Level II

During eight days a total of 553 patients were transported as critically ill medical patients in the selected region. During the same period 243 patients were registered at the NCBD by online faxing of completed ambulance forms which indicated underreporting (243/553 = 44%). Of the 243 patients, 186 were uniquely identifiable in the ambulance statistics. The remaining 57 patients had erroneous or missing patient identification numbers.

Discussion

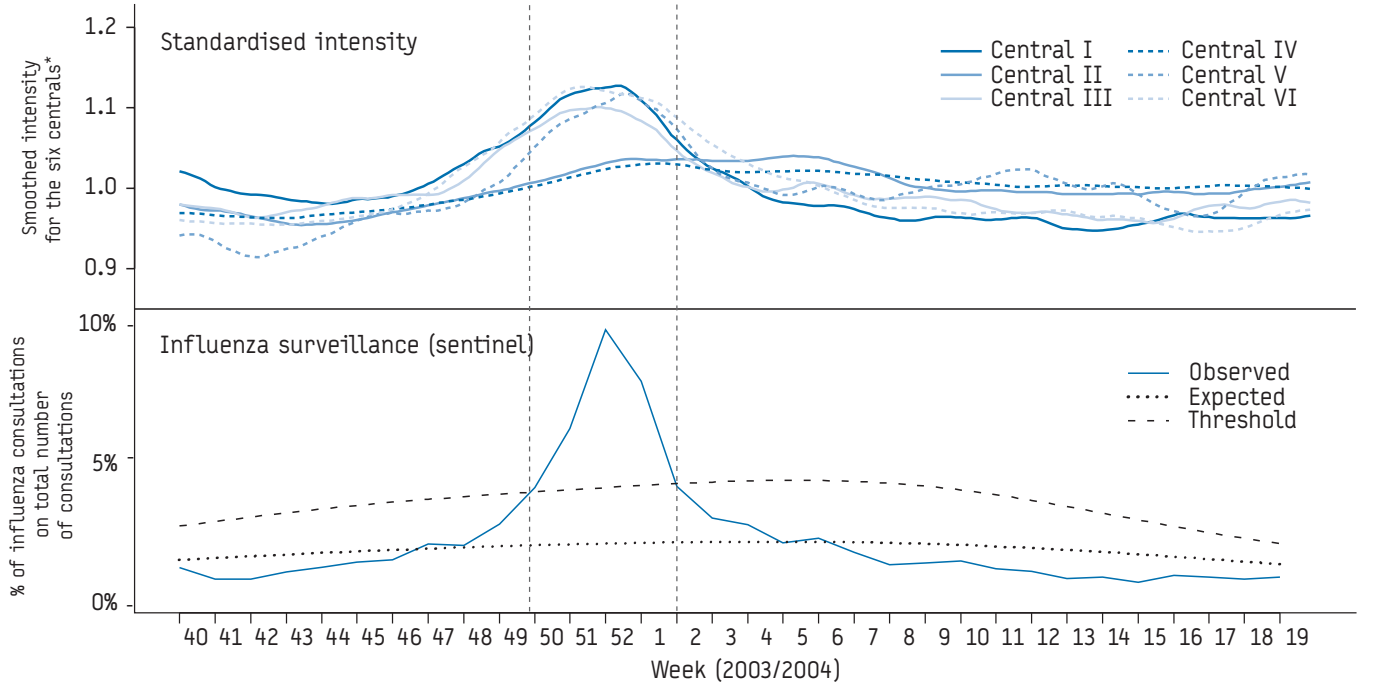
Data to monitor early increased disease activity can be obtained from several sources, including work/school absenteeism and 'over the counter' pharmaceutical sales. We chose to develop a symptom surveillance system that used ambulance transport data and operated on two levels. One advantage was that we could make use of existing high-quality ambulance transport data for achieving a reduction in MOD-Time. The need for an early unspecified alert in case of abnormal ambulance transport frequency was accomplished with this model. Our requirements for operational success were few false alerts, high sensitivity and the ability to adapt in case of minor regional changes over time. An increased number of patients, for whatever reason, will, to a variable degree, influence transport statistics as well as other parameters, such as physician calls and emergency centre statistics. With increased severity of an outbreak, the degree of patients requiring ambulance transport will invariably be high, thereby increasing the likelihood of a system alert. However, the system has limitations in case of a larger mild disease outbreak where only a smaller fraction of patients require transport by ambulance. Overall, the system responds rapidly to differences in epidemiological profiles for instance as a result of a massive patient influx or geo-clusters.

Level I

The results from initial testing indicated that the system had a low degree of false alerts. On two consecutive days in December 2003 the system reported increased activity. This episode heralded the beginning of a subsequently well-documented influenza epidemic in Denmark [8]. This suggests that the system was able to trace and report this outbreak from an early stage, in a timely fashion compared with existing monitoring systems which rely on manual reporting and compiling of results. By adding scenarios to background transport activity we were able to determine the MOD-Time of the system from a precise event. Balancing sensitivity and number of false alerts was a key issue. By the use of a 99% detection limit we achieved sensitivity almost as high as with the 95% detection limit, but significantly reduced the number of false alerts. This was essential for the performance and acceptability of the system. The scaling of some scenarios influenced only the amplitude of the outbreak, but maintained the unique epidemiological profile of the outbreak curve which best simulated a real event. The system responded rapidly

FIGURE 3

Ambulance dispatch activity compared to National influenza Surveillance Reporting Systems, Denmark, October 2003 – May 2004



* In order to compare the data from the centrals the intensities have been scaled by dividing with the average number of transports for each central during the period 1 January 2002 to 31 March 2006

The vertical lines indicate the period where the observed number of influenza cases exceeded the threshold, i.e. the Sentinel system indicated an influenza epidemic

in all cases and would, with regards to scenario III, have notified authorities at an earlier stage than documented by the historical facts. The prospective testing of the system demonstrated reliability, few false alerts and good compliance with operating officers.

The Kalman filter is a recursive estimator. This means that the only estimated state from the previous time step and the current measurement are needed to compute the estimate for the current state. Thus, the chosen method was robust against 'noise' generated from previous spikes of ambulance dispatches and changes in the baseline by, for example, organisational changes or other artefacts. On the other hand, the system would not respond to a slow increase in the number of ambulances. Hence, the system may have limited sensitivity to detect an outbreak from a continuous source or an outbreak of a disease with a long and variable incubation time.

Level II

In case of an alert at level I, the responsible officer at the regional ambulance dispatch centre has to determine the credibility and severity of the alert and to a certain degree what caused it. In most cases the alert is easily explained by known events and local conditions leading to an increased demand, but ultimately the duty officer might choose to upgrade monitoring to second level preliminary epidemiological investigation after consulting with the NCBD, epidemiologists and public health officials. In case further investigation is needed, the completed ambulance reporting forms containing information such as patient data, patient symptoms and pickup time/place, will be the object of a further centrally guided investigational process and cluster analysis. Reporting of symptoms by faxed forms during testing supplied the basis for further investigation. However, this proved to be a bottleneck, since forms were not completed for a large proportion of patients transported on the days of the exercise, while other forms were difficult to match with actual patients in the database of the ambulance contractor. This illustrates the need for the automatic collection of epidemiologically relevant data and the development of a standardised data collection procedure for further improvement of the system. Testing of automatic online distribution and transferral of patient data, such as temperature and ECG from ambulances to emergency wards, is being conducted by the ambulance contractor.

Small outbreaks with a limited number of exposed persons over a number of weeks, such as the American anthrax outbreak in 2001, would be difficult to detect with ambulance dispatch surveillance. However, medium to large sized outbreaks with a disease with or without potential epidemic can be difficult to recognise in the very early stages unless statistical real time evaluation is available, as demonstrated by an outbreak of salmonellosis in Oregon in 1984 [9]. The outbreak detection system presented in this study serves as a tool for reducing the essential MOD-Time, through limited investments, using existing databases and the implementation of specific reporting procedures.

Acknowledgements

The authors would like to thank the European Union Directorate General for Health and Consumer Affairs (DG SANCO) for financial support.

References

1. Mostashari F, Fine A, Das D, Adams J, Layton M. Use of ambulance dispatch data as an early warning system for communitywide influenzalike illness, New York City. J Urban Health. 2003;80(2 Suppl 1):i43-i49.
2. Giovachino M, Carey N. Modeling the consequences of bioterrorism response. Mil Med. 2001;166(11):925-30.
3. Brookmeyer R, Blades N, Hugh-Jones M, Henderson DA. The statistical analysis of truncated data: application to the Sverdlovsk anthrax outbreak. Biostatistics. 2001; (2):233-47.
4. Meselson M, Guillemin J, Hugh-Jones M, Langmuir A, Popova I, Shelokov A, et al. The Sverdlovsk anthrax outbreak of 1979. Science. 1994;266(5188):1202-8.
5. Grandjean P, Tarkowski S. Toxic oil syndrome - Mass food poisoning in Spain. Report on WHO meeting, Madrid, 21-25 March 1983. Copenhagen: World Health Organization, Regional Office for Europe; 1984.
6. Harvey AC. Forecasting, structural time series models and the Kalman filter. Cambridge University Press; 1989.
7. West M, Harrison PJ. Bayesian Forecasting and Dynamic Models. 2nd ed. New York: Springer-Verlag; 1997.
8. Sentinel surveillance of the influenza activity. Epidemiological Department SSI. EPI-NEWS. 2004(9).
9. Torok TJ, Tauxe RV, Wise RP, Livengood JR, Sokolow R, Mauvais S, et al. A large community outbreak of salmonellosis caused by intentional contamination of restaurant salad bars. JAMA. 1997;278(5):389-95.

ENHANCED SURVEILLANCE OF INFECTIOUS DISEASES: THE 2006 FIFA WORLD CUP EXPERIENCE, GERMANY

K Schenkel[1], C Williams[1,2], T Eckmanns[1], G Poggensee[1], J Benzler[1], J Josephsen[1], G Krause[1]

The 2006 FIFA World Cup was held in 12 German cities between 9 June and 9 July 2006. We identified a need to accelerate and sensitise the pre-existing surveillance system for infectious diseases in order to timely detect adverse health events during the World Cup. Enhanced surveillance, based on Germany's pre-existing system of mandatory notifications was conducted between 7 June and 11July 2006 in the 12 World Cup cities by: accelerating frequency of electronic data transmission of case-definition based notifiable diseases from weekly to daily transmission, additional reporting of non-case definition-based infectious disease events, lay and expert press screening and intensifying communication between all stakeholders of the surveillance system. Median delay of notification data transmission from the community to the federal level was reduced from three days to one day. The enhanced reporting system detected a norovirus outbreak in the International Broadcast Centre in Munich with 61 epidemiologically linked cases within the first week after onset, as well as four single cases related to the World Cup, two of them with relevance for the International Health Regulations. After the World Cup, all surveillance stakeholders agreed that communication between local, state and federal levels had improved considerably. Unlike the majority of health planners of previous mass gatherings in the last decade we did not introduce syndromic surveillance. Nevertheless, enhancement of infectious disease surveillance successfully detected adverse health events in a timely manner during the FIFA World Cup. Additionally, it provided a valuable communication and networking exercise for potentially critical health-related events. We recommend continuing daily notification data transmission for routine infectious disease surveillance in Germany.

Euro Surveill. 2006;11(12): 234-8 Published online December 2006
Key words: 2006 FIFA World Cup, Germany, surveillance, mass gatherings

Introduction

The FIFA World Cup was held between 9 June and 9 July 9 2006 in 12 cities within nine federal states of Germany. According to preliminary reports of the Federal Office for Statistics, this international sporting event resulted in 2 million additional overnight stays from abroad.

Although serious medical illness during mass gatherings is uncommon [1] and recent mass gatherings such as the Olympic Games and previous World Cups have not been associated with an increased number of infectious disease outbreaks [2-9], security threats and the recent emergence of avian influenza in Europe have heightened the profile of and need for a good surveillance strategy during such events.

1. Department of Infectious Disease Epidemiology, Robert Koch-Institut, Berlin, Germany
2. European Programme for Interventional Epidemiology Training (EPIET)

The two main rationales for enhanced infectious disease surveillance at mass events include a perceived increased risk of infectious disease events, and a need to detect and respond to events more quickly, due to the short-lived nature of infectious diseases. Moreover, the requirements of the International Health Regulations (IHR) issued by the World Health Organization (WHO), which take effect in mid-2007, define the need for timely reporting of infectious diseases during international mass events [10].

Methods

An enhanced surveillance system for infectious diseases based on the existing German system of mandatory notifications and reporting was conducted between 7 June and 11 July. In brief, the enhanced surveillance system for the World Cup consisted of four major branches:

1) Acceleration of data transmission in the pre-existing, electronic notifiable-disease reporting system using existing case definitions.
2) Introduction of an additional free-text reporting system for relevant public health events, with 'relevant events' being defined individually by local and state health departments, and not necessarily based on case definitions.
3) Monitoring of domestic and international media sources for epidemiological events that could be relevant to the World Cup
4) Strengthening communication and interaction between the different public health stakeholders within Germany and internationally.

The system was designed to detect adverse health events of public health relevance in a timely fashion during the 2006 FIFA World Cup in the area under surveillance (the 12 World Cup cities).

The first branch of enhanced surveillance, acceleration of the data transmission process was accomplished by increasing the usual weekly transmission frequency of mandatory notification data to daily transmission (Monday to Saturday, excluding holidays) within the 12 World Cup cities and a few other cities that had been identified as relevant focal points by the State Health Department (SHD). Such relevant focal points could be cities neighbouring the World Cup cities, where World Cup-related mass gatherings such as public televised screenings took place. Mandatory notifications were transmitted from the local health department to their respective state health department and from there to the Robert Koch-Institut (RKI) on the same working day. In accordance to the pre-existing weekly procedure, data transmission was electronic and anonymous. Underlying case definitions for transmission of data (and therewith the underlying specificities) were not altered for the purpose of accelerated transmission. Cases not investigated and confirmed according to the pre-existing case definitions were not transmitted until they met the standard case-definitions for inclusion in the data.

Two additional modifications were made to the existing electronic notification system. The data included disease notifications of non-

residents of Germany, which are not routinely reported. Also, a 'World Cup-related' flag was created in the electronic data systems. Any case related to a World Cup event (such as spending time in a stadium, at public screening, or in the 'fan mile' areas set up within the World Cup cities) was flagged at the sole discretion of the local health departments based on their intimate knowledge of local events.

In the second branch of our enhanced strategy, a new reporting system was introduced. Information on outbreaks, clusters or any type of 'relevant' public health event was sent from the local and state health departments to the RKI in a standardised, free-text written report. Relevancy to the World Cup was determined by the sole and subjective judgement of the local health departments. In an effort to increase the sensitivity of the surveillance system, the information contained in these daily reports was not based on case definitions for mandatory notifications.

In the third branch of surveillance, international and German lay press and expert sources (ProMED-mail, the European Centre for Disease Prevention and Control (ECDC), the United States Centers for Disease Control and Prevention (CDC), the World Health Organization, etc.) were screened daily by the World Cup surveillance team at the RKI for infectious disease issues of public health relevance. Lay press sources were pre-screened daily with the help of an automatic press screening service after applying sensitive search terms relevant for infectious disease issues.

Regular telephone conferences were held in order to strengthen communication and outcome-orientated interaction between the stakeholders of the enhanced World Cup surveillance (local and state health departments and RKI). These telephone conferences also served as a tool for quality management, where questions and suggestions for process optimisation were discussed and documented. Also, information of international public health concern was exchanged in a daily telephone conference with the ECDC's Unit for Preparedness and Response. Discrepancies between different information sources (for example, between local health department reports and press sources) were clarified in these discussions. This strengthened communication system represented our fourth branch of surveillance.

Surveillance activities were coordinated by the RKI in cooperation with the 12 local health departments and nine state health departments affiliated with World Cup cities.

The RKI produced a daily report on the status of infectious disease epidemiology. Sources of information included all four branches of our strategy as well as weather data (daily temperatures) provided by the Deutscher Wetterdienst (German Meteorological Office) to provide prospective for outbreaks and other public health situations, in light of the European heat wave of 2003 [11]. In a final, summarised RKI daily report, the domestic and international infectious disease situation was assessed for eventual public health threats with relevance for the World Cup. The RKI daily report was distributed on the same afternoon to the local and state health departments, the German Ministries of Health and the Nationales Informations- und Kooperationszentrum (National Information and Cooperation Centre), which was the national security communication hub for the World Cup. An extended version was uploaded daily onto a restricted-access web-based communication and information forum for German public health institutions, and a short version was published daily on the public webpage of the RKI in both English and German.

All components of the enhanced World Cup surveillance were tested during a trial week in May 2006, involving all World Cup surveillance stakeholders.

After the World Cup, a preliminary analysis of aggregated mandatory notification data was undertaken in order to assess whether daily versus weekly data transmission actually influenced the mean data transmission delay from the LDH in the World Cup cities to RKI.

We compared transmission delay in days (25th, 50th and 75th percentiles) for all data transmitted between notification weeks 23 and 29, 2006 (the notification weeks of the World Cup period) with the transmission delay for the same time period in 2005, when weekly transmission was in place.

Results

Daily transmission of mandatory notification data

Table 1 gives comparative data for transmission delay in days (25th, 50th and 75th percentiles) for data transmitted between notification weeks 23 and 29, in the years 2005 and 2006.

Table 1

Mandatory notification data transmission delay (in days) for years 2005 and 2006 in World Cup cities

Percentile (days)	2005	2006
25%	2	0
50%	3	1
75%	7	1

In the period of enhanced surveillance, RKI received 69 World Cup-associated, electronically transmitted cases of gastroenteritis. Of those, 62 were norovirus infections (61 with an epidemiological link to a norovirus outbreak in Munich), 4 salmonella infections cases and 3 were cases of campylobacter infections.

One event (not associated to the World Cup) was detected neither by daily transmission of mandatory notification data nor by the written reports submitted to RKI. A single case of meningococcal disease in Bavaria was identified through daily routine screening of press sources for infectious-disease related events. The local health department had detected the case early and immediately began contact tracing and postexposure prophylaxis, but reported the case electronically to the SHD and the RKI with delay. Since this case was not connected with the World Cup, and was not relevant for IHR, the local health department did not include it in their daily reports or flag it as World Cup-related in the electronic data transmission system.

World Cup related infectious disease events: norovirus outbreak in the Munich International Broadcast Centre (IBC)

On 15 June the local health department in Munich was informed of a cluster of patients with gastrointestinal symptoms. That evening, the local health department took initial hygiene measures (see below), and the following day, within the first week after onset of the first case, the outbreak was reported via the additional, non-case definition-bound reporting system to the RKI. Patients came from several countries, including Mexico and the United States. All patients were temporarily employed at the IBC. Hygiene precautions, such as disinfecting surfaces and providing hand disinfection liquids in sanitary areas, were immediately implemented, and multilingual information leaflets giving hygiene advice were distributed within the IBC. Large-scale stool diagnostics were performed. The first five stool samples were proven to be positive for norovirus. Later, a sequential analysis detected genotype GGII.4-2006a. Altogether, 61 cases of gastroenteritis were epidemiologically linked to the norovirus outbreak in Munich. By the end of the second week of June 2006, the outbreak had come to an end.

Other infectious disease events during the World Cup

The World Cup coincided with the largest measles outbreak ever reported in Germany. This had raised concerns by the Pan American Health Organisation (PAHO) and various European national public health institutes which issued travel warnings for visitors to the World Cup events in Germany. Between 1 January and 7 June 2006 (the date when the enhanced World Cup surveillance began), a total

Table 2

Major public health relevant infectious disease events during FIFA World Cup 2006, Germany, in chronological order

Event: Date of onset/ duration, cases involved, history	Disease/ pathogen	Number of cases	World-Cup related?	IHR relevant?	Media attention?	Mode of detection (source)
June 4: Indonesian journalist with varicella virus infection (chicken pox) lands at Munich airport and reports immediately to local PH authorities	Varicella virus	1	Yes	Yes	Yes	LHD daily report
June 9: eight members of Croatian football team with gastrointestinal symptoms, subfebrile temperature; no diagnostic samples taken; suspicion of viral gastroenteritis	Unknown; suspected viral gastro-enteritis	8	Yes	No	Yes	Lay press screening, ECDC teleconference
June 15: Laboratory confirmed case of mumps in a 23 year old man from the UK who had visited World Cup match in Frankfurt on June 10	Mumps virus	1	Yes	Yes	No	LHD daily report
June 16 - 29: 22 persons from different countries working at the International Broadcasting Centre (IBC) in Munich with gastroenteritic symptoms; altogether, 61 persons with epidemiological link; stool samples show norovirus in majority of cases; sequencing detects genotype GGII.4-2006a	Norovirus	61	Yes	Yes	Yes	LHD daily report
June 25: Australian fan hospitalised with acute *Salmonella* Enteritidis gastroenteritis; visits World Cup match on June 26 against medical advice	*Salmonella* Enteritidis	1	Yes	No	No	LHD daily report, mandatory notification transmission

of 1406 measles cases were reported in North Rhine-Westphalia, primarily from cities of the Ruhr region and from the Lower Rhine region which borders the Netherlands. Genotyping revealed D6 as the predominant measles genotype in this region. During the World Cup period, the total number of measles cases since January 2006 rose to 1625, but no case of measles associated with the World Cup was observed during the enhanced World Cup surveillance.

Another coincidental event during the World Cup was an outbreak of haemolytic uraemic syndrome (HUS) in the federal states of North Rhine-Westphalia, Lower Saxony, Hamburg and Schleswig-Holstein in Northern Germany. Between 4 April and 6 July 2006, 15 cases of HUS were notified. Of these, only two occurred during the World Cup period. None was epidemiologically linked to the World Cup. Table 2 summarises the major public health relevant infectious disease events during the World Cup.

Communication

Participation in non case-definition based daily reporting by the affected local and state health departments was 100%. Telephone conferences were held at the beginning and ending of the trial week for the World Cup surveillance, and immediately before, during and after the World Cup period. After the World Cup, the majority of World Cup surveillance stakeholders agreed that communication and interaction between the local and state health departments and RKI has been considerably strengthened during the enhanced surveillance period.

Weather monitoring

The World Cup weather was pleasant and warm, with a temperature range in between 14 and 34 degrees Celsius (maximum day temperature). A heat wave comparable to that of 2003 was not observed during the tournament. Analysis of daily weather data did not find any temperature-related correlation to any public health relevant events in the World Cup cities.

Discussion

'Public health surveillance should be implemented at mass gatherings to facilitate rapid detection of outbreaks and other health-related events and enable public health teams to respond with timely control measures….' This was recommended in a recent CDC-published journal article [12]. Infectious disease surveillance is an important subset of public health surveillance, but why and how should it be increased at mass events?

It is worth considering which characteristics of mass events might increase the risk of infectious diseases. Table 3 summarises these characteristics, along with examples of different types of event.

Of the published results of surveillance at mass events, it is interesting to note that few identified any significant increase in infectious disease occurrences during the period studied. No increase in usage of healthcare services was found during the 1998 World Cup in France [5]. The evaluation of surveillance during the Euro 2004 football tournament in Portugal found no effect on numbers of infections in either visitors or the local population [22]. Two positive examples found were norovirus cases in a Virginia camping event [12], and the change in profile of sexually transmitted infection clinic attendances during the Sydney Olympic Games. During the millennium year in Rome, with 26 million visitors to the city, an increase in *Legionella* cases and foodborne outbreaks in foreign tourists was observed, but no increase was seen in overall cases or in cases in the local population [23].

Enhanced surveillance at mass gatherings has previously been conducted by a number of public health specialists organising preparations for such events. Syndrome-based surveillance has been undertaken at several previous mass gatherings [2-6]. However, at the current time, it is not clear whether, in regions with a well-functioning surveillance system in place, a syndrome-based system provides more than minimal additional information that is not identifiable through routine surveillance. Poor specificity and difficulties in determining epidemic thresholds are the most important limitations of syndromic surveillance [24,25]. In a study from the United Kingdom, syndromic surveillance data gained by National Health Service (NHS) direct calls using diarrhoea as a proxy for cryptosporidiosis were unable to detect a large scale local cryptosporidiosis outbreak [26]. During the 2006 Winter Olympic Games in Italy, syndromic surveillance did not provide any additional information that could not be identified through the pre-existing routine surveillance system [2].

More evidence-based research on the effectiveness and cost-effectiveness of syndromic surveillance at mass gatherings is needed, especially given the high cost of implementation. After careful consideration in consultation with the local and state health departments and in the light of a lack of documented outbreaks detected by syndrome surveillance that would not have been detected by routine surveillance alone, it was assumed that the enhanced mandatory notification surveillance system would be sufficient, and a syndrome-based surveillance system was not implemented for the 2006 World Cup in Germany.

Table 3

Aspects of (international) mass events with implications for infectious disease risks

Aspect of mass event		Potential effect on infectious disease occurrences	Example
Primary aspects	Absolute increase in population and increase in population density	Increase in absolute numbers of cases, frequency of person to person contacts, proximity of interpersonal contacts	Visitor numbers: 300 000 at the Sydney Olympics [13], 2 million to the Hajj [14], "hundreds of thousands" at the 1998 World Cup in France[5]; 430 000 at the 2002 World Cup in Korea and Japan [15], Increase in meningococcal carriage during Hajj [16]
	Population movement: exposure to "foreign" diseases	Visitors affected by locally endemic diseases Local population exposed to "imported" infections	Concern at World Cup about measles outbreak [17], and cholera in Angola [18], Malaria cases in travellers to endemic areas [19]
Secondary aspects	Target for bioterrorism	Deliberate release of pathogens	CDC scenario of anthrax release [20]
	Strain on infrastructure	Breakdown in public health safeguards e.g. water quality, accommodation standards	Refugee camps
	Changes in services/behaviour	Increase in numbers and turnover of food outlets may lead to a fall in hygiene standards	Environmental health inspections prior to Athens Olympic Games [21]
		Increased prevalence of risky sexual behaviour	Change in epidemiology of sexually transmitted infections at Sydney Olympic Games [13]

Our aim was to monitor all public health relevant events in order to distribute timely information to all stakeholders and thus to be able to respond immediately to events of public health concern. The enhanced surveillance system allowed us to timely detect a World Cup related norovirus outbreak with consequences for IHR. It seems quite likely that due to the improved alertness and communication conditions during enhanced surveillance (daily local health department reports, immediate telephone contacts) this outbreak was detected more quickly on the federal level than it would have been without enhanced surveillance in place.

The implementation of daily instead of weekly notification data transmission proved to be a successful strategy of accelerating transmission [Table 1] and was well-accepted by the participating local health departments of the World Cup cities. The state of North Rhine-Westphalia, the most heavily populated state in Germany, has continued daily transmission of notification data since the World Cup, with the majority of local health departments participating. Maintaining daily data transmission frequency could be problematic in small, resource-poor rural local health departments. Nevertheless, daily rather than weekly data transmission for all local and state health departments - routinely, not only during mass events - should be recommended as a future goal.

Introducing an additional, sensitive, non-case definition-based additional written report system was overall beneficial. Additional information which complemented daily transmission of notifiable data reached RKI in a timely manner. Daily reporting was practicable for local and state health departments and RKI and served as a method of increasing less formal, but nonetheless valuable, communication between the different levels of public health. We therefore recommend additional reporting systems that are flexible and not bound to case-definitions, provided that at least one case-definition system or syndrome-based system is in place.

Analysing the benefits of enhancing a pre-existing system of notification data surveillance versus introducing a syndromic surveillance system is difficult, since we lack comprehensive data from syndromic surveillance. Nevertheless, enhanced World Cup surveillance was found to accelerate data transmission and was clearly able to intensify communication and action-orientated cooperation between different players in the German public health system; therefore, it also benefited the routine infectious disease surveillance in Germany and provided a valuable communication and networking exercise for potential critical health-related events.

Acknowledgements

The authors would like to thank Dr. Petra Graf from the City of Munich Health department and Dr. Ulrich Van Treek from the Institute of Public Health, North Rhine-Westphalia in Münster. Also, we would like to thank all colleagues involved in the enhanced World Cup surveillance, namely from the following institutions of Public Health: the Local Health Departments in Berlin, Dortmund, Frankfurt, Gelsenkirchen, Hamburg, Hanover, Kaiserslautern, Cologne, Leipzig, Nuremberg, Munich and Stuttgart, and the State Health Institutions in Baden-Wurttemberg, Bavaria, Berlin, Hamburg, Hesse, Lower Saxony, North Rhine-Westphalia, Rhineland-Palatine and Saxony. We would also like to thank our colleagues in the department of Infectious Disease Epidemiology and the department of molecular Epidemiology at the Robert Koch Institute in Berlin, especially Doris Altmann for analysing notification data.

References

1. Varon J et al. Critical illness at mass gatherings is uncommon. J Emerg Med. 2003 Nov;25(4):409-13.
2. Epidemiological Consultation Team. Results from the integrated surveillance system for the 2006 Winter Olympic and Paralympic Games in Italy. Euro Surveill 2006;11(8):E060817.5. Available from: http://www.eurosurveillance.org/ew/2006/060817.asp#5.
3. Gesteland PH, Wagner MM, Chapman WW, Espino JU, Tsui FC, Gardner RM et al. Rapid deployment of an electronic disease surveillance system in the state of Utah for the 2002 Olympic Winter Games. Proc AMIA Symp. 2002:285-9.
4. Hadjichristodoulou C, Mouchtouri V, Soteriades ES, Vaitsi V, Kolonia V, Vasilogiannacopoulos AP, Kremastinou J. Mass gathering preparedness: the experience of the Athens 2004 Olympic and Para-Olympic Games. J Environ Health. 2005;67(9):52-7.
5. Hanslik T, Espinoza P, Boelle PY, Cantin-Bertaux D, Gallichon B, Quendez S, Sentinel monitoring of general community health during the 1998 World Football Cup. Rev.Epidemiol. Sante Publique. 2001.49(2):135-45.
6. Jorm LR, Thackway SV, Churches TR, Hills MW. Watching the Games: public health surveillance for the Sydney 2000 Olympic Games. J Epidemiol Community Health. 2003;57(2):102-8.
7. Meehan P, Toomey KE, Drinnon J, Cunningham S, Anderson N, Baker E. Public health response for the 1996 Olympic Games. JAMA. 1998 May 13;279(18):1469-73.
8. Panella H, Plasencia A, Sanz M, Cayla JA. [An evaluation of the epidemiological surveillance system for infectious diseases in the Barcelona Olympic Games of 1992]. Gac Sanit. 1995;9(47):84-90.

➔➔➔

9. Weiss BP, Mascola L, Fannin SL. Public health at the 1984 Summer Olympics: the Los Angeles County experience. Am J Public Health. 1988 Jun;78(6):686-8.
10. World Health organisation. Current International Health Regulations. 2005.
11. Kosatsky T. The 2003 European heat waves. Euro Surveill 2005;10(7):148-9. Available from: http://www.eurosurveillance.org/em/v10n07/1007-222.asp
12. Centers for Disease Control and Prevention (CDC). Surveillance for early detection of disease outbreaks at an outdoor mass gathering--Virginia, 2005. MMWR Morb Mortal Wkly Rep. 2006;55(3):71-4.
13. McNulty AM, Rohrsheim R, Donovan B. Demand for sexual health services during the Olympic Games: both sides of the Sherman effect. Int J STD AIDS. 2003 May;14(5):307-8. .
14. Balkhy HH, Memish ZA, Bafaqeer S, Almuneef MA. Influenza a common viral infection among Hajj pilgrims: time for routine surveillance and vaccination. J Travel Med. 2004 Mar-Apr;11(2):82-6.
15. Takahashi H, Kaku K, Tanaka T, Matsui T, Osaka K, Ohyama T, Okabe N. [An estimation of imported infections concerning 2002 FIFA world cup Korea/Japan]. Kansenshogaku Zasshi. 2002;76(2):102-8.
16. Ahmed QA, Arabi YM, Memish ZA. Health risks at the Hajj. Lancet. 2006;367(9515):1008-15.
17. Centres for Disease Control, CDC. Media Advisory: CDC Urges Awareness of Measles in Americans Returning from Germany. CDC Division of media relations. 2006.
18. World Health Organization. Cholera in Angola- Update 4. World Health Organisation: Epidemic and Pandemic Alert and Response (EPR). 2006.
19. Williams CJ, Jones J. E-alert 9 December: Malaria cases and deaths in UK travellers returning from The Gambia. Euro Surveill. 2005;10(12):E051215.6. Available from: http://www.eurosurveillance.org/ew/2005/051215.asp#6
20. Inglesby TV. Anthrax: A possible case history. Emerg Infect Dis. 1999;5(4):556-60.
21. Hadjichristodoulou C, Soteriades ES, Kolonia V, Falagas ME, Pantelopoulos E, Panagakos G, et al. Methodological aspects of a GIS-based environmental health inspection program used in the Athens 2004 Olympic and Para Olympic Games. BMC Public Health. 2005;5:93.
22. Goncalves G, Castro L, Correia AM, Queiros L. Infectious diseases surveillance activities in the north of Portugal, during the EURO 2004 football tournament. Euro Surveill. 2005;10(4):86-9. Available from: http://www.eurosurveillance.org/em/v10n04/1004-224.asp.
23. Giorgi Rossi P, Sangalli M, Faustini A, Forestiere F, Perucci CA Infectious diseases in Rome during the Millennium Year. Euro Surveill. 2003;8(9):181-5. Available from: http://www.eurosurveillance.org/em/v08n09/0809-223.asp.
24. Centers for Disease Control and Prevention (CDC). Syndromic surveillance for bioterrorism following the attacks on the World Trade Center-New York City, 2001. MMWR Morb Mortal Wkly Rep. 2002;51 Spec No:13-5.
25. Osaka K, Takahashi H, Ohyama T. Testing a symptom-based surveillance system at high-profile gatherings as a preparatory measure for bioterrorism. Epidemiol Infect. 2002;129(3):429-34.
26. Cooper DL, Verlander NQ, Smith GE, Charlett A, Gerard E, Willocks L, O'Brien S. Can syndromic surveillance data detect local outbreaks of communicable disease? A model using a historical cryptosporidiosis outbreak. Epidemiol Infect. 2006;134(1):13-20.

Original Articles

Surveillance report

Epidemiologic surveillance system implemented in the Hautes-Alpes district, France, during the Winter Olympic Games, Torino 2006

F Franke[1], L Coulon[2], C Renaudat[1,3], B Euillot[2], N Kessalis[2], P Malfait[1]

Some of the competitions of the Olympic Winter Games in Torino, 10 to 26 February 2006, were organised in France near the city of Briançon, in the department of Hautes-Alpes.
An epidemiologic surveillance system was set up by the local health authorities. The goals were to detect in a timely fashion any phenomenon which could justify prevention or sanitary control action, and to guide interventions in the case of outbreak or environmental pollution.
Surveillance was implemented from 30 January to15 March 2006 in the Briançon area.
Mortality was tracked using by analysing the number and cause of deaths.
A sentinel network of general practitioners was set up and reported the frequency of acute gastroenteritis, influenza-like illness and measles. Medical laboratories provided data about the analyses they undertook. Hospital emergency department and emergency ambulance service activities were followed up. Statutory notification diseases and toxic effects of carbon monoxide surveillances were reinforced.
Analysed data were transmitted daily to the health authorities. A French/English report was sent weekly to all participants.
The participation rate was close to 100%, and data transmission deadlines were respected. No adverse health event was identified. The strong acceptability of this surveillance system comes from its good understanding by the participants. This surveillance, structured around routine and ad-hoc systems, allowed the establishment of the foundations of a network to be used in case of outbreak or environmental pollution.

Euro Surveill. 2006;11(12): 239-42 Published online December 2006
Key words: Mass gathering, early warning system, syndrome-based surveillance, Europe

Background

The Olympic Winter Games 2006 took place from 10 to 26 February 2006 in Torino, Piemonte, Italy. This event was followed by the Paralympic Games, held from 10 to 19 March. An integrated epidemiological surveillance and response system, set up by the regional and national Italian health authorities during the Games, had as its goal the early detection of any adverse health events (particularly clusters of communicable diseases) [1].

As some of the competitions were held at Sestriere, close to the French-Italian border, with the nearest French city being Briançon, in the Hautes-Alpes department, it was judged that many spectators would choose to find accommodation on the French side, particularly in and around Briançon. The French health authorities considered that there was a possibility of health hazards related to such mass gatherings, because of [2]:

- large numbers of people gathering in the same place, which could increase the risk of disease transmission;
- possible saturation of healthcare structures;
- installation of temporary restaurants with potentially precarious hygiene conditions despite reinforcement of hygiene inspetions;
- mobility of the population concerned.

Only a small number of adverse health events, such as diseases or outbreaks, had been detected during previous mass gatherings [3-5], but the large concentration of people expected in a very limited area heightened the necessity of developing a surveillance strategy.

An epidemic intelligence mass gathering system was set up by the local public health authorities: the Direction départementale des affaires sanitaires et sociales (Ddass) des Hautes-Alpes, and the Cellule interrégionale d'épidémiologie Sud (Cire Sud). The aim was the early detection of any event that could justify prevention or sanitary control measures, and to guide interventions in the case of outbreak or environmental pollution.

Methods

Surveillance was implemented from 30 January to 15 March 2006, a period of time which covered the Games and the French school holidays in the Briançon area [FIGURE 1].

The system aimed to complement to the Italian system; surveillance targeted diseases with strong infectious epidemic potential (such as meningitis, legionellosis and gastroenteritis) or events which could represent a specific risk in the area under surveillance (such as very low environmental temperatures or carbon monoxide poisoning). Reinforcement of the carbon monoxide poisoning monitoring was carried out, because private residences with poor quality heating equipment were known to be available to rent during the Games.

Surveillance was based partly on existing surveillance systems that were enhanced during the Games and partly on systems set up for the occasion. Surveillance allowed indicators of mortality, morbidity and activity to be tracked.

The system collected the following information:

- Mortality was monitored daily through deaths recorded by the Town Hall in Briançon, and the analysis of the causes reported on the death certificates sent to the Ddass.
- Acute gastroenteritis, influenza-like illness, and measles surveillance was carried out through a sentinel network of general practitioners (GPs) set up especially for this period.

1. Cellule inter régionale d'épidémiologie Sud, Marseille, France
2. Direction départementale des affaires sanitaires et sociales des Hautes-Alpes, Gap, France.
3. Programme de formation à l'épidémiologie de terrain PROFET

FIGURE 1

Area under surveillance, Winter Olympic Games, Hautes-Alpes, France, 30 January - 15 March 2006

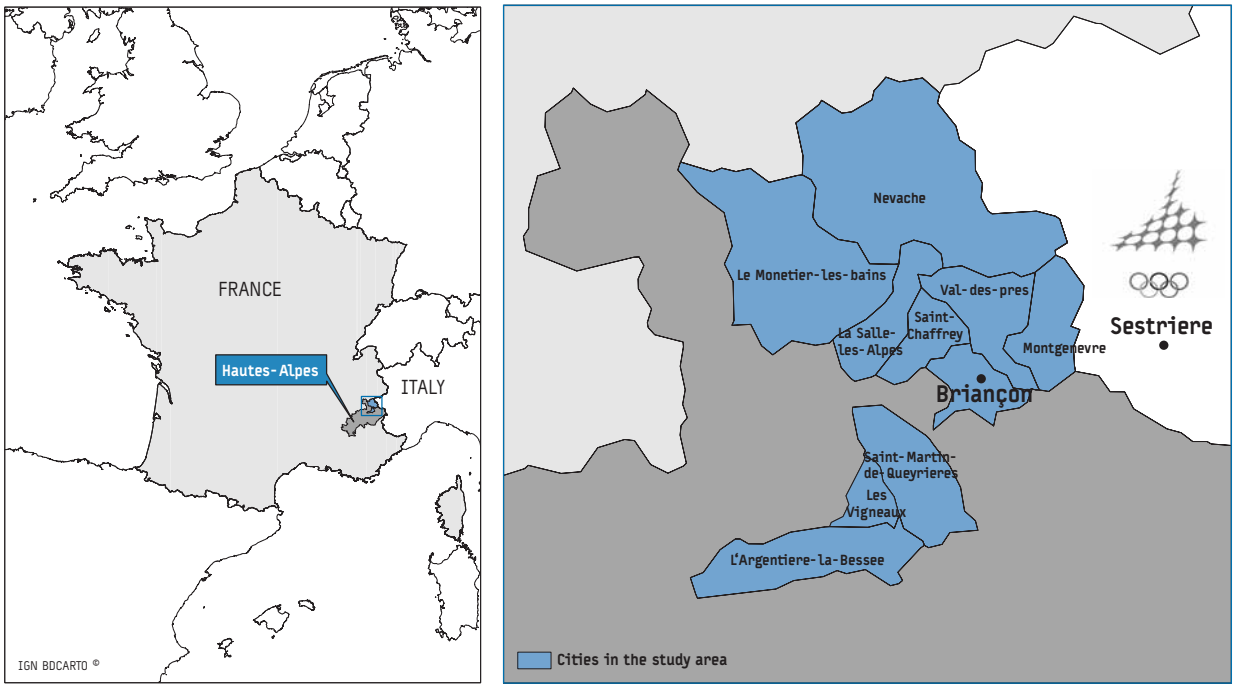
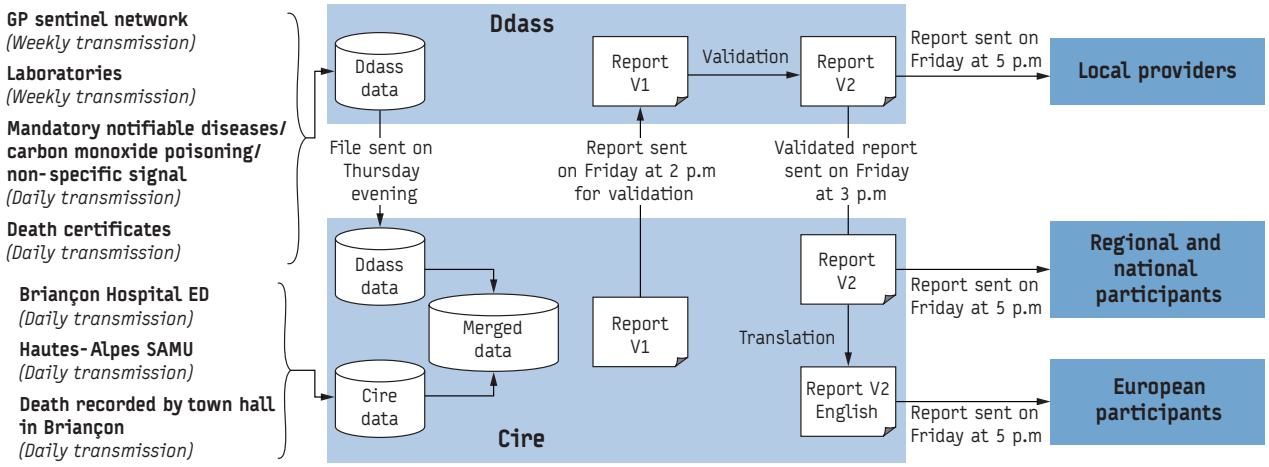


FIGURE 2

Organisation of data collection, redaction and transmission of the weekly report, Winter Olympic Games, Hautes-Alpes, France, 30 January - 15 March 2006



The two private and public microbiology laboratories in Briançon provided test result data for stool cultures, hepatitis A serology and methaemoglobinaemia. Daily data were collected and reported once a week.

- The activities of Briançon Hospital's Emergency Department and the Hautes-Alpes Emergency Ambulance Service (SAMU) were followed daily through the routine non-specific surveillance system implemented by Cire Sud.
- Selected complaints (acute gastroenteritis, carbon monoxide poisoning and illness related to low environmental temperatures) recorded in Briançon Hospital's Emergency Department were followed up via the French national surveillance network of hospital emergency departments. Data collection began on 9 February; the delay was due to logistical problems.
- Surveillance data for mandatory notifiable diseases [6] and carbon monoxide poisoning were reported daily, as usual, and communication channels were reinforced.
- Preventive measures were also taken in and around Briançon: monitoring the quality of food and accommodation services, in accordance with statutory food hygiene standards, intensification of routine water quality checks and adjusted and reinforced water treatment, public information campaigns about legionellosis and carbon monoxide poisoning, and enhanced controls of quality standards for personal skiing equipment.

Ad hoc tools were created: computerised data collection sheets for Ddass and Cire, standardised forms for GPs and laboratories. Some data were collected by the Ddass and some by the Cire Sud [FIGURE 2].

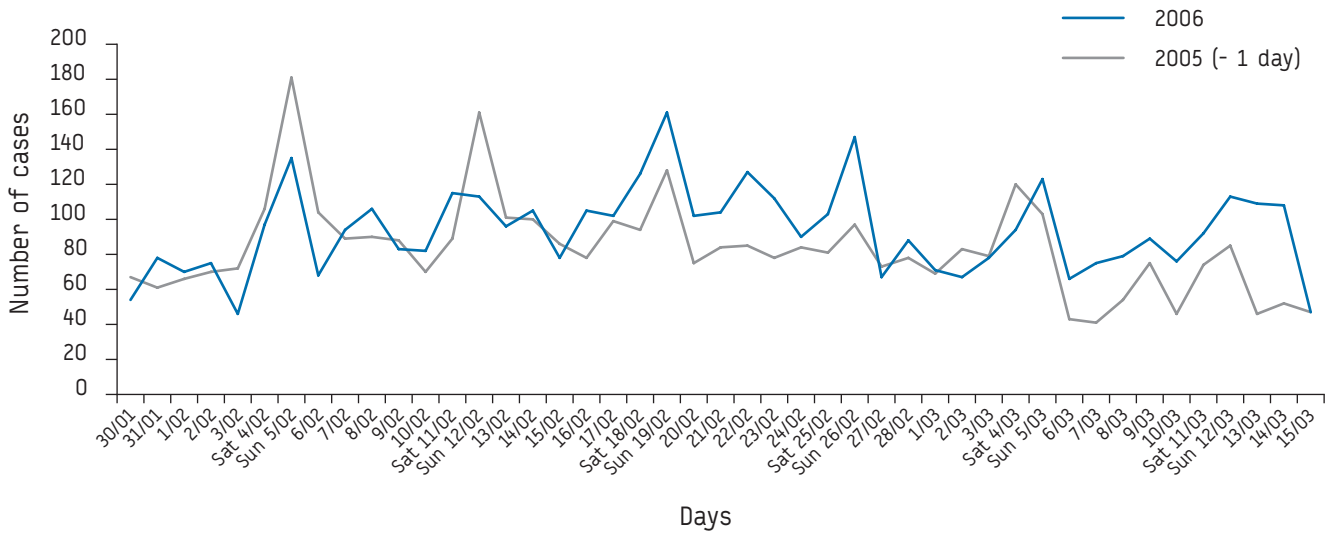
Two analysis systems were implemented: one based on historical data (not available for all the indicators) – threshold built on the upper limit of the 95% confidence interval – and one based on the method of the control charts for individual measurements [7].

Every day, data collected were analysed jointly by the Cire Sud and the Ddass. In addition, the Cire Sud consulted the daily report published by the Italian Epidemiological Consultation Team [1].

In case of unexpected events, the concerned Italian regional

FIGURE 3

Daily number of recorded cases per day by the SAMU – 30 January to 15 March 2006 – compared with the same period in 2005



(Piemonte) and national health authorities, the European Centre for Disease Control and Prevention (ECDC), and the French National Institute for Public Health Surveillance (InVS) would have been alerted.

Once a week, all the data were merged by the Cire Sud [FIGURE 2].

A weekly report in both French and English was sent every Friday to the data providers, the regional and national Italian health authorities, the ECDC, and the InVS [FIGURE 2]. It was made available on the internet [8].

The surveillance system was evaluated through a satisfaction survey of the Gs sentinel network and the completeness of data and transmission deadlines.

Results

Twenty nine deaths were registered by the town hall in Briançon. There was no excess of deaths compared with the previous year. Two deaths due to mountain accidents in the area under surveillance, but not related to the Games, were identified by the analysis of the causes of death reported on death certificates.

During the period of surveillance, the daily average number of cases recorded by the SAMU was 94 (range: 46 – 161). The overall volume of activity was 12% higher than during the same period in the previous year [Figure 3]. However, the activity recorded in 2006 was more specifically higher than 2005 after 16 February.

The daily average number of cases recorded by the emergency department at Briançon Hospital was 58 (range: 36 – 85), with an overall volume of activity 7% lower than the previous year at the same period. There was a daily average of 16 admissions to hospital after a consultation at the emergency department (range: 9-27), 18% lower than the number registered during the same period in 2005. On average, one patient in three was admitted to hospital after a consultation at the emergency department. Among the 2024 consultations for which selected complaints were recorded, only 24 acute viral gastroenteritis, 11 influenza-like illnesses and three cases of illness related to low environmental temperatures were reported. Most admissions were related to trauma.

Of the consultations of the GP Sentinel network, 6% were for acute gastroenteritis and 12% for influenza-like illness. Only one consultation for measles was recorded. Peak of visits for influenza-like illness were observed during weekends.

No cluster of cases was detected by the two public and private microbiology laboratories in Briançon during the period of surveillance. Among the 91 stool cultures and the 31 hepatitis A serologies recorded, 6 and 2, respectively. were positive. No methaemoglobinaemia tests were requested.

No mandatory notifiable diseases and no carbon monoxide poisoning were reported in the area. An outbreak of severe gastroenteritis due to *Mycobacterium avium paratuberculosis* in a ski resort was recorded, but this diagnosis was refuted after investigation.

Data transmission deadlines were met. The satisfaction survey of the GP sentinel network showed that GPs were satisfied with the organisation of the system, because of the simplicity of the procedures, the limited number of collected variables, the modes of data transmission and the content of weekly reports. Completeness of data transmitted by the GP's was 89%. For other systems, completeness was 100%, mostly because of automatic computerised data transmission.

Discussion

The 2006 Olympic Winter Games had a very limited impact on illness and adverse events in the neighbouring French department of Hautes-Alpes. No alert was issued by the French epidemiological surveillance system. In Italy, no increase was seen during the Games in visits to healthcare facilities in the area where the games were held [9].

Surveillance was based on the mandatory diseases system and the routine non-specific surveillance system used by the Cire Sud, collecting data from hospitals, emergency ambulance services and mortality statistics collected by the local municipal authority, completed by GPs and medical laboratories. In this limited geographical area under surveillance, the high number of participants involved in the system, covering all different sectors of medical activities, would probably have detected any health event which could reveal a potential risk for the population.

The surveillance system was found to have been adapted successfully to its assigned objectives by both data providers and decision makers. The system implemented was a good complement to inspection and control measures, and allowed the establishment of the foundations of a network to be used in case of outbreak or environmental pollution.

Acknowledgements

The Cire Sud and the Ddass acknowledge all participants for their cooperation and time devoted to this surveillance.

References

1. Epidemiological Consultation Team. Surveillance system in place for the 2006 Winter Olympic Games, Torino, Italy, 2006. Euro Surveill 2006;11(2):E060209.4. Available from: http://www.eurosurveillance.org/ew/2006/060209.asp#4
2. Coulombier D, Malfait P, Ballereau M. Dispositif de veille sanitaire pour la coupe du monde de football, 1998. Bulletin Epidémiologique Hebdomadaire. 1998;22:95.
3. Jorm LR, Thackway SV, Churches TR, Hills MW. Watching the Games: public health surveillance for the Sydney 2000 Olympic Games. J. Epidemiol. Community Health. 2003;57;102-8. Available from: http://jech.bmj.com/cgi/content/full/57/2/102
4. Wetterhall SF, Coulombier DM, Herndon JM, Zaza S, Cantwell JD. Medical care delivery at the 1996 Olympic Games. Centers for Disease Control and Prevention Olympics Surveillance Unit. JAMA. 1998;279:1463-8.
5. Allen T, Jolley S, Cooley V, Winn R, Harrison J, Price R, Rich J. The epidemiology of illness and injury at the alpine venues during the Salt Lake City 2002 Winter Olympic Games. J Emerg Med. 2006;30(2):197-202.
6. Institut de veille sanitaire. Le dispositif de surveillance des maladies à déclaration obligatoire. Updated 21 July 2006. Accessed 14 August 2006. Available from: http://www.invs.sante.fr/surveillance/mdo/index.htm
7. NIST/SEMATECH e-Handbook of Statistical Methods. Accessed on 29 November 2006. Available from: http://www.itl.nist.gov/div898/handbook/pmc/section3/pmc322.htm
8. Cellule interrégionale d'épidémiologie Sud. Dispositif de veille sanitaire dans le département des Hautes-Alpes durant les Jeux Olympiques d'hiver de Turin, 2006. Accessed on 29 November 2006. Available from: http://www.invs.sante.fr/surveillance/jo_turin/index.htm
9. Epidemiological Consultation Team. Results from the integrated surveillance system for the 2006 Winter Olympic and Paralympic Games in Italy. Euro Surveill. 2006;11(8):E060817.5. Available from: http://www.eurosurveillance.org/ew/2006/060817.asp#5

ORIGINAL ARTICLES

Surveillance report

RECOGNITION OF THREATS CAUSED BY INFECTIOUS DISEASES IN THE NETHERLANDS: THE EARLY WARNING COMMITTEE

JC Rahamat-Langendoen, JA van Vliet, AWM Suijkerbuijk

The early warning committee was established in order to recognise threats to public health caused by infectious diseases in the Netherlands in a timely and complete fashion. This article describes the outcome of a retrospective and descriptive evaluation into the completeness of the recognitions made by the early warning committee.

Information about outbreaks of infectious disease in the Netherlands in 2002 and 2003, as reported in the *Nederlands Tijdschrift voor Geneeskunde (Dutch Journal of Medicine)*, and about infectious disease events in other countries, was compared with reports of the regular weekly meetings of the Dutch early warning committee. If an outbreak or a foreign event was not mentioned in the meetings of the early warning committee, the cause for this was established. For events in other countries, it was established on the basis of whether or not the event could have been a threat to public health in the Netherlands.

All outbreaks of infectious disease in the Netherlands, published or mentioned in the *Nederlands Tijdschrift voor Geneeskunde* were discussed by the early warning committee. Three of the events occurring in other countries in 2002 had not been discussed by the committee although, based on the criteria for a potential threat to the Netherlands, they should have been: the outbreak of avian influenza A/H5N1 in domestic fowl in Hong Kong, the increase among hospitalised patients of carriers of extended-spectrum _-lactamase producing micro-organisms in Scotland, and outbreaks of measles in several countries. In 2003, all events in other countries that could have posed a threat to the Netherlands were discussed by the early warning committee.

In 2002 and 2003, the early warning committee recognised nearly all threats due to infectious diseases and outbreaks of infectious diseases which were of national importance and published in various sources of literature.

Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, The Netherlands.

Euro Surveill. 2006;11(12): 242-5 Published online December 2006

Key words: early warning, threats, public health, infectious diseases

Introduction

Threats to public health caused by infectious diseases usually appear without warning, but can have major consequences within a very short period of time. Recognition of these threats is essential [1]. The early warning committee was established in the Netherlands in 1999 under the authority of the Inspectie voor de Gezondheidszorg (Health Care Inspectorate). Its main task is to assess information from various sources, both foreign and national, in order to recognise threats to public health caused by infectious diseases in a timely fasion. If necessary, further outbreak investigation can be done, or measurements to control the outbreak can be taken [2, 3].

The weekly meeting of the early warning committee takes place at the Rijksinstituut voor Volksgezondheid en Milieu (RIVM, National Institute for Public Health and the Environment). The participants are microbiologists and epidemiologists from various departments of the RIVM, including the Landelijke Coördinatiestructuur Infectieziektebestrijding (LCI, National Coordination Centre for Outbreak Management), as well as representatives from the Voedsel en Waren Autoriteit (VWA, Food Safety Authority). Prior to the meeting, each participant selects, from various sources of information, items

(known an 'signals') which in his or her opinion are important to discuss at the meeting [TABLE 1] [4]. There can be several reasons for selecting a signal. These are outlined in a protocol and are based on previous experience gathered by the RIVM.. A sudden change in the incidence or prevalence of an infectious disease (e.g. the upsurge of West Nile virus infections), the appearance of an infectious disease among certain groups of people or in certain places (e.g. the lymphogranuloma venereum outbreak among men who have sex with men), or the emergence of a completely new or unknown disease (e.g. SARS) are some of the reasons mentioned [3]. During the meeting, the various signals are discussed and interpreted by the participants in order to estimate the threat for public health in the Netherlands.

On the same day, the RIVM sends a report of the meeting to about 500 people engaged in the control of infectious diseases in the Netherlands. They include physicians and nurses of the municipal health services, microbiologists, specialists in infectious disease, infection control practitioners, the Ministry of Health and the Inspectorate of Health. The report is formulated in such a way that signals are not reducible to persons, institutions or locations.

To fulfill its task properly, the early warning committee must recognise all important threats caused by infectious diseases. This article describes the outcome of a study into the completeness of the recognitions made by the early warning committee.

Methods

Information from other sources than those used by the early warning committee, were compared with the reports of the meetings of the early warning committee in order to assess how completely the committee had performed its task. The sources used for this study were different from the sources of information used regularly by the early warning committee. We focused on the years 2002 and 2003, because they saw a greater mix of minor, major, foreign and national threats caused by infectious diseases than the years immediately preceding or following [5-7].

Infectious disease events in the Netherlands

Using articles and news items published in the Nederlands Tijdschrift voor Geneeskunde (Dutch Journal of Medicine, *NTvG*) between January 2002 and June 2005, we gathered information about outbreaks of infectious diseases in the Netherlands that constituted a potential threat to public health. This is the only peer-reviewed general medical journal published in the Netherlands that has a wide distribution nationally. All outbreaks of national importance are published in this journal, either as an article or as a news item. We compared the information with the reports of the meeting of the early warning committee. If an outbreak had not been mentioned during the meeting, we tried to determine the reason for this.

Infectious disease events in other countries

Information about infectious disease events in other countries was gathered from the following sources:

- weekly bulletins from Belgium, England and Wales, Scotland, Norway and Germany, in which reports about infectious diseases were given. These bulletins are similar to the report of the early warning committee and are available on the internet (http://www.eurosurveillance.org/links).
- The 'Infectious diseases surveillance update' section in *The Lancet Infectious Diseases*. This is the only international journal with such a section, and is not one of the sources used by the early warning committee. The *International Journal of Infectious Diseases* has a similar section, but uses information based on ProMED-mail. ProMED-mail is one of the regular sources for the early warning committee, and therefore we did not use this journal for our investigation.

Information about events in other countries gathered from these sources was compared with the reports of the early warning committee. Subsequently, we determined whether those events that were not discussed during the meeting of the early warning committee could have been a threat for public health in the Netherlands, by answering two questions:

1) was there a possibility of importation and further dissemination in the Netherlands of the micro-organism mentioned?
and/or
2) was there a possibility that the (potential) source of the infection mentioned was present in the Netherlands?

Table 1

Sources of information used by the early warning committee*

Domestic sources of information	ISIS (Infectious disease Surveillance Information System, an electronic system for notifiable diseases reported by Municipal Health Services, and for laboratory surveillance)
	Weekly Virological Surveillance reports
	Surveillance of influenza
	National Reference Laboratory for Bacterial Meningitis (NRBM)
	Laboratories of the RIVM
	National Coordination Centre for Outbreak Management (LCI)
	Electronic reporting system inf@ct (confidential)
	Food Safety Authority (VWA)
Foreign sources of information	WHO Weekly Epidemiological Record
	WHO Disease Outbreak News
	WHO Outbreak Verification List (confidential)
	Eurosurveillance weekly release
	European Early Warning and Response System (confidential)
	ECDC Weekly Communicable Disease Threats Report (confidential)
	Morbidity and Mortality Weekly Report (MMWR)
	Other scientific literature (since February 2005)

* Besides these formal sources, people engaged in infection control in the Netherlands themselves can put forward signals to be discussed during the meeting of the early warning committee

Results

Infectious disease events in the Netherlands

An overview of the outbreaks of infectious diseases which occurred in the Netherlands in the years 2002 and 2003, based on the information in the *NTvG*, and which constituted a potential threat to public health, is given in table 2. All outbreaks were also discussed in the meetings of the early warning committee.

Infectious disease events in other countries

Based on information from various sources as described above, for the year 2002 we found 122 infectious disease events in other countries. We compared these 122 events with the information from the reports of the early warning committee. Forty eight of these events were discussed during the meetings of the early warning committee. For the remaining 74, we tried to determine whether or not they represented a threat to pubic health in the Netherlands, defined by the two questions mentioned above. For three events, the answer to one or both questions was 'yes'. These events thus represented a threat

Table 2

Overview of the outbreaks of infectious diseases which occurred in the Netherlands in 2002 and 2003, based on the information in the Dutch Journal of Medicine

2002	Outbreak of methicillin-resistant *Staphylococcus aureus* (MRSA) in two hospitals in the Rijnmond region [8]
	Increase of infections due to *Neisseria meningitidis* serogroup C [6,9]
	Increase in the amount of outbreaks of gastro-enteritis (mainly caused by norovirus infection) [10]
	Rise in sexually transmitted diseases (STD) [11,12]
	Shigellosis as an STD among men having sex with men (MSM) [13]
	Increase of pertussis [14]
	Increase in the amount of cases of tick bites and Lyme borreliosis seen by general practitioners [15]
2003	Outbreak of avian influenza A/H7N7 [5]
	Outbreak of lymphogranuloma venereum among MSM [16]

to public health in the Netherlands and ought to have been discussed by the early warning committee. The events were:

a) the outbreak of avian influenza A/H5N1 among poultry in Hong Kong;
b) the outbreak of extended-spectrum-β-lactamase (ESBL)-producers among hospitalised patients in Scotland;
c) outbreaks of measles in various countries (Republic of Ireland, Denmark, United Kingdom, Lithuania).

Seventy one of the 74 events not mentioned during the meetings of the early warning committee did not meet the criteria for a threat to public health in the Netherlands.

For the year 2003, 106 infectious disease events were identified in the various sources of information. Forty six of these 106 were discussed by the early warning committee. None of the remaining 60 events met the criteria for a threat to public health in the Netherlands as defined by the two questions mentioned above.

As an illustration, a few events in the area of infectious diseases in foreign countries in the years 2002 and 2003 are listed in table 3. The events listed were discussed by the early warning committee, and were also found in various sources of information different from the sources used by the early warning committee.

Discussion

This study shows that, in 2002 and 2003, the early warning committee was capable of recognising outbreaks of infectious diseases in the Netherlands, published or mentioned in the *NTvG*, which constituted a potential threat to public health. In addition to the regular sources used by the committee, each committee member represents a scientific network. These networks, and other people engaged in the control of infectious diseases in the Netherlands who regularly receive reports from the early warning committee, all contributed to the completeness of the information discussed during the meetings.

Our study into infectious disease events in other countries found that during the year 2002, three events that met the criteria for threat to public health in the Netherlands were not discussed by the early warning committee. Together with the committee members who participated during 2002, we tried to reconstruct the reasons why these events were not discussed. The outbreak of avian influenza A/H5N1 among poultry in Hong Kong was probably not discussed

Table 3

Examples of foreign events in the area of infectious diseases discussed at the meeting of the early warning committee and mentioned in several other sources of information, 2002 and 2003

• West Nile virus infections, United States (2002, 2003)
• Outbreak of respiratory tract infections combined with myocarditis/ pericarditis caused by Coxsackie B virus, Greece (2002)
• Outbreak of measles, southern part of Italy (2002)
• First documented case of vancomycin resistant *Staphylococcus aureus*, United States (2002)
• Outbreak of legionellosis, with a cooling tower as source of infection, United Kingdom (2002)
• Outbreak of Q fever among 28 persons living in Chamonix and its surroundings, France (2002)
• Outbreak of monkeypox related to the import of prairie dogs, United States (2003)
• SARS coronavirus infection caused by a laboratory incident, Singapore (2003)
• Two human cases of infection with avian influenza A/H5N1, Hong Kong (2003)
• Outbreak of meningitis caused by *Neisseria meningitidis* serogroup A, Moscow (2003)
• Outbreak of MRSA among men having sex with men, due to strains with the Panton-Valentin-Leucocidin gene, United States (2003)
• Five cases of tetanus among injecting drug users, United Kingdom (2003)

because at the time there were no human cases. Today, with advanced understanding of the impact of avian influenza, such an event would most probably be discussed.

Another event that was not discussed during by the early warning committee were the problems with ESBL-producing organisms in Scotland. ESBL is an enzyme capable of inactivating a broad spectrum of antibiotics. It is mainly produced by Gram negative bacteria, especially nosocomial *Klebsiella* spp [17,18]. This specific event was important, because ESBL production had spread among species, including *E. coli* and *Enterobacter* spp, as well as klebsiellas. Because of the restrictive usage of antibiotics, ESBL is not yet of major concern in the Netherlands, where incidence is low. However, it is an emerging problem, and in that sense, it should have been discussed during by the early warning committee. The results of this study were discussed with the participants of the early warning committee. During this discussion it was mentioned that, besides a lack of attention for emerging resistance to antibiotics, the early warning committee also does not give enough attention to hospital acquired infections.

A third event that met the criteria of a threat to public health in the Netherlands, but was not discussed by the committee, were various outbreaks of measles in different countries. These events were not discussed because they were limited in size, with only regional spread. Information about the outbreaks appeared most of the time at a fairly late stage of the outbreak, so that it was not useful any more to take any measures related to these outbreaks in the Netherlands.

Our study has some limitations. A threat to public health is not a well defined concept. We compared the signals mentioned in the reports of the early warning committee with published data in order to make completeness plausible. However, only major or unusual outbreaks or events are likely to be published. Events that were not published in the sources of information used in this study were not taken into account, nor was information about events that were not published at all. We cannot know whether or not such events could have been of national importance. However, health threats other than those mentioned in this study may have existed.

In order to make an early warning system more sensitive, additional sources of information, formal (e.g information from surveillancesystems) as well as informal (e.g. information based on media reports), may be necessary [19, 20]. We included scientific literature as a source of information, partly because of the lack of attention paid to antibiotic resistance and hospital acquired infections by the early warning committee. However, more signals do not automatically make a better early warning system. More study into the methodology of early warning and into defining threats to public health, both in the Netherlands and abroad, is needed.

This study was undertaken during a period in which there were many developments, both nationally and internationally. At a national level, the Centre for Infectious Disease Control was recently established to prevent and control infectious diseases through effective prevention, greater vigilance, and rapid response to potential outbreaks (http://www.rivm.nl/en/aboutrivm/organization/cib/index.jsp). One of the main tasks is clear and reliable communication with professionals engaged in the control of infectious diseases. The reports of the early warning committee play an important role in this.

At the international level, several developments should be mentioned. The European Centre for Disease Prevention and Control (ECDC) in Stockholm, Sweden, has been established to help strengthen Europe's defences against infectious diseases. Surveillance of communicable disease and keeping track of emerging health threats inside and outside Europe are a few of its main tasks [21]. The ECDC could itself become a major source of information for countries in Europe. As for the early warning committee in the Netherlands, it will be necessary to identify criteria to be used for selecting source information [22].

The implementation of the revised International Health Regulations (IHR) is another relevant international development [23]. In 1995, the World Health Assembly decided that the IHR should be thoroughly revised. One major change is that a member state must report all events that possibly could endanger public health in other countries, regardless of the cause of the event. For this, timely and complete recognition of health threats at a national level is of importance.

The conclusion of this study is that, in 2002 and 2003, the early warning committee in the Netherlands recognised nearly all threats due to infectious diseases and outbreaks of infectious diseases which were of national importance and published in various sources of literature. The early warning committee can serve as an example to other countries or organisations in recognising threats to public health caused by infectious diseases.

Acknowlegdements

We thank Dr. M.A.E. Conyn-van Spaendonck, MD PhD, head of the Center for Infectious Diseases Epidemiology of the RIVM, J.K. van Wijngaarden, MD, Chief Inspector of Public Health at the Health Care Inspectorate, and A. Timen, MD, consultant in communicable disease control at the National Coordinator Center for Outbreak Management of the RIVM, for their useful remarks on former versions of this article. We thank S. Hahné, MD, for carefully reading the final version.

This article is based on a study first reported in the Nederlands Tijdschrift voor Geneeskunde (Dutch Journal of Medicin) [Recognition of the threats caused by infectious diseases in the Netherlands in 2002 and 2003 by the weekly meetings of the early warning committee] Ned Tijdschr Geneeskd. 2005;149:2238-42. Dutch

References

1. Wijngaarden van JK. [Pro-active government]. In: Dissel JT van, red. Refresher course Infectious diseases 2004. Leiden: Leiden Universiy Medical Centre (Boerhaave Commissie); 2004, p. 131-145. In Dutch.
2. Suijkerbuijk AWM, Vliet JA van. [The early warning committee]. Infectieziekten Bulletin. 2001;10;368-70. In Dutch
3. Bosman A, Vliet JA van. [Surveillance of and recognizing threats caused by infecious diseases]. In: Helsloot I, Steenbergen J.E van. Control of Infectious Diseases. Studies into organisation and practices. Den Haag: Boom; 2005. In Dutch.
4. Melker HE de, Conyn-van Spaendonck MAE, Sprenger MJW (red). [Infectious Diseases in the Netherlands. Epidemiology, diagnostics and control]. RIVM 1997. Den Haag: Sdu;1997. In Dutch.
5. Bosman A, Mulder YM, Leeuw JRJ de, Meijer A, Ry van Beest Holle M du, Kamst RA, et al.[Avian flu epidemic 2003: public health consequences]. RIVM report 630940001. 2004. In Dutch.
6. Furth AM van, Zaaijer HL. [Meningococcal disease in the Netherlands: media hype, but not an epidemic]. Ned Tijdschr Geneeskd. 2001;145(36):1716-8. In Dutch.
7. Christian MD, Poutanen SM, Loutfy MR, Muller MP, Low DE. Severe acute respiratory syndrome. Clin Infect Dis. 2004;38(10):1420-7.
8. Melles DC, Hendriks WD, Ott A, Verbrugh HA. [Outbreak of methicillin-resistant *Staphylococcus aureus* (MRSA) in the Rijnmond region: the largest outbreak in the Netherlands]. Ned Tijdschr Geneeskd. 2004; 22;148(21):1038-43. In Dutch.
9. [Universal vaccination against meningococcal serogroup C and pneumococcal disease]. Den Haag: Health Council of the Netherlands, 2001; publication number 2001/27. In Dutch.
10. Lopman B ea. Increase in viral gastroenteritis outbreaks in Europe and epidemic spread of new norovirus variant. Lancet. 2004;363:682-88.
11. Haks K, Schout C, Cremer WS, Sigurdsson V, Ameijden EJC van. [Increased consultations and numbers of sexually transmitted diseases at the STD clinic of Utrecht, 1994-2002]. Ned Tijdschr Geneesk. 2004;148(33):1632-5. In Dutch.
12. Kievits F, Adriaanse MT. [Large increase in sexually transmitted diseases [news round up]]. Ned Tijdschr Geneesk. 2003;147:1380. In Dutch.
13. Bovée LPMJ, Peerbooms PGH, Hoek JAR van den. [Shigellosis, a sexually transmitted disease in homosexual men]. Ned Tijdschr Geneesk. 2003;147:2438-9. In Dutch.
14. Greeff SC de, Schellekens JFP, Mooi FR, Melker HE de. Pertussis in the Netherlands, 2001-2002. RIVM report 128507010/2003.
15. Boon S den, Schellekens JFP, Schouls LM, Suijkerbuijk AWM, Docters van Leeuwen B, Pelt W van. [Doubling of the number of cases of tick bites and Lyme borreliosis seen by general practitioners in the Netherlands]. Ned Tijdschr Geneesk. 2004; 148(14):665-9. In Dutch.
16. Gotz HM, Ossewaarde JM, Nieuwenhuis RF, Meijden WI van der, Dees J, Thio B, Zwart O de, Laar MJ van der. [A cluster of lymphogranuloma venereum among homosexual men in Rotterdam with implications for other countries in Western Europe]. Ned Tijdschr Geneeskd. 2004;148(9):441-2. In Dutch.
17. Neeling AJ de.[ESBL: superbug or troublemaker].Infectieziekten bulletin. 2002;7: 273-4. In Dutch.
18. Stürenburg E, Mack D. Extended-spectrum β-lactamases: implications for the clinical microbiology laboratory, therapy, and infection control. J Infect. 2003;47(4):273-95.
19. Heymann DL, Rodier GR. Hot spots in a wired world: WHO surveillance of emerging and re-emerging infectious diseases. Lancet Infect Dis. 2001;1(5):345-53.
20. Grein TW, Kamara KO, Rodier G, Plant AJ, Bovier P, Ryan MJ, Ohyama T, Heymann DL. Rumors of Disease in the Global Village: outbreak verification. Emerg Infect Dis. 2000;6(2):97-102.
21. Commission publishes proposal for establishing a European Centre for Disease Prevention and Control (ECDC). Can Commun Dis Rep. 2004;30(5):50-2.
22. Kaiser R, Coulombier D, Baldari M, Morgan D, Paquet C. What is epidemic intelligence, and how is it being improved in Europe? Euro Surveill. 2006;11(2):E060202.4. Available from: http://www.eurosurveillance.org/ew/2006/060202.asp#4
23. Nicoll A, Jones J, Aavitsland P, Giesecke J. Proposed new International Health Regulations. BMJ. 2005;330(7487):321-2.

IMPROVEMENT OF A NATIONAL PUBLIC HEALTH SURVEILLANCE SYSTEM THROUGH USE OF A QUALITY CIRCLE

G Krause[1], J Benzler[1], G Reiprich[2], R Görgen[3]

Surveillance systems for infectious diseases build the basis for effective public health measures in the prevention and control of infectious diseases. Assessing and improving the quality of such national surveillance systems is a challenge, as many different administrations and professions contribute to a complex system in which sensitive information must be exchanged in a reliable and timely fashion. We conducted a multidisciplinary quality circle on the national public health surveillance system in Germany which included clinicians, laboratory physicians, and staff from local and state health departments as well as from the Robert Koch-Institut. The recommendations resulting from the quality circle included proposals to change the federal law for the control of infectious diseases as well as practical activities such as the change of notification forms and the mailing of faxed information letters to clinicians. A number of recommendations have since been implemented, and some have resulted in measurable improvements. This demonstrates that the applied method of quality circle is a useful tool to improve the quality of national public health surveillance systems.

Euro Surveill. 2006;11(10): 246-8 Published online November 2006
Key words: public health, quality circle, quality management, surveillance systems, recommendations

Introduction

In 2001 the infectious disease control act (IfSG) in Germany resulted in the implementation of a completely restructured and technically modernised national surveillance system for notifiable infectious diseases. The most important changes were:

a) The number of diseases to be notified by physicians was reduced from 52 to 17, while the number of pathogens to be notified by laboratories was increased from 52 to 53.
b) Case definitions were introduced whereby local health departments must verify notifications before reporting them to the next level.
c) The federal surveillance institute (Robert Koch-Institut, RKI) became the agency responsible for defining the technical standards by which data is to be reported to the national level, which has resulted in the implementation of a complex electronic database network. Local health departments (LHD) receive paper based case notifications from physicians or laboratories. LHDs forward the case reports electronically using software either produced by the RKI and offered free of charge or one of five commercially available software packages tailored for health department administration [1-3].

The Federal Ministry of Health in Germany formally asked all 16 state health administrations and the RKI to report their experiences with the new infectious disease control law in order to collect suggestions for a future revision of the law. By 2003 the RKI had conducted a focus group discussion of public health physicians, a survey among general practitioners and a survey among local health departments as part of our comprehensive quality management efforts [4-6]. On the basis of these studies we intended to assess the experiences with the new surveillance system by taking into account the different perspectives of the various professions and institutions contributing to this system. We decided to conduct a quality circle, which is an instrument of quality management, generally consisting in a group of stakeholders or other affected persons of a specific process who discuss, in a structured way, needs and ways to improve specific processes. The aim of this quality circle was to identify possibilities for technical or organisational improvements of the system and to recommend changes to be made in a potential revision of the legal framework.

Methods

The quality circle (QC) took place on 4-5 March 2003 in Berlin. Members of the different professions and institutions were invited and grouped by structural level of the surveillance system:

1) Notifiers: hospital clinicians (2 persons), general practitioners (2), and laboratory physicians (2)
2) Local public health level: public health nurses (2) and public health physicians (2)
3) State public health level: representative of state health department (1), medical epidemiologists in state surveillance institute (2)
4) Federal public health level: data management personnel at RKI (3), epidemiologists at RKI (3).

We selected the 19 participants according to the following criteria: the greatest possible number of states and geographic areas should be represented; groups representing the different levels should be of a similar size; only one participant could take part from any one employer or institution (with exception of RKI staff); and no participants with direct hierarchical relationships between each other could participate (so, for example, participants from local public health level must come from different states than participants from state public health level). Participation was voluntary. The participants came from the following eight of the 16 German states: Berlin, Brandenburg, Sachsen, Sachsen-Anhalt, Niedersachsen, Nordrheinwestphalen, Hessen, Baden-Wurttemberg.

The QC was moderated by two external public health scientists. Both moderators were trained and experienced in moderating focus groups and in health system research and had no conflict of interest for the issue to be discussed. The QC was structured in two main phases:

The first phase was dedicated to problem identification. This phase was executed simultaneously in four homogenous groups (groups 1 to 4, as described above). Each group had 2 hours to describe their experiences with the surveillance system and to compile issues for improvement. The groups were asked to present their results on a flip chart without presenting any suggestions on how improvement might be done. These presentations were then discussed in plenary.

Between the two phases, the study results of the focus group discussions, the survey among general practitioners, the survey among LHD and statistical evaluations of the surveillance system were presented to the participants [5-8].

The second phase was dedicated to identifying possible solutions to the identified problems. In contrast to the first phase, participants were regrouped into three heterogeneous groups (A, B, C) with members of

1. Department of Infectious Disease Epidemiology, Robert Koch-Institut, Berlin, Germany
2. Health Focus GmbH, Potsdam, Germany
3. Evaplan GmbH at the University of Heidelberg, Germany

all structural levels. In this phase, participants were asked to identify possible solutions to the problems previously discussed. The following three questions served as a guide for this process:

1) What can be done at each level to improve the quality of the system?
2) How can cooperation be improved at the different interfaces?
3) What should be taken into account during a revision of the infectious disease control act (IfSG)?

The proposed solutions were discussed in plenary. The moderators collected the presented suggestions and new ideas that have come up during the discussion applying a card based (metaplan) Delphi technique [9]. The recommendations were clustered according to two categories: The first category contained recommendations that can be implemented under the current legal framework of the IfSG, while the second category consisted of recommendations that required changes of the IfSG. Recommendations of the first category were further sorted by the four different levels of implementation.

Results

First phase: problem identification

1. Problems identified by clinical and laboratory level (group 1):

1.1 Laboratory work for a notifiable disease is not always medically indicated but represents a burden on the clinician's laboratory budget.

1.2 The notification form is not always readily available and the list of notifiable disease is not known to all clinicians.

1.3 The notification form is complicated.

1.4 Clinicians do not see the benefit of reporting, they are not reimbursed for the time involved in completing and sending the notification.

1.5 Clinicians are reluctant to notify, as they want to prevent their patients from being approached by the public health department. Laboratory notification often reach the LHD before the clinician has informed the patient about the result, which may lead to the situation that the patient first learns about his diagnosis from the LHD and not from his physician.

1.6 Laboratories are uncertain which laboratory results are to be notified and the respective case definitions do not always take newly introduced laboratory methods into account.

2. Problems identified by local public health level (group 2):

2.1 Notification of rotavirus results in a high workload without any public health consequences.

2.2 Clinicians refuse to provide patient data to LHD upon request if the LHD has received a laboratory notification (currently a strict interpretation of the law does not allow this).

2.3 Notifications by kindergartens and similar institutions often lack diagnostic precision as the kindergarten administrators have no medical training.

2.4 The evaluation of vaccination programs and recommendations has become difficult as various vaccine-preventable diseases are not longer notifiable under the IfSG.

2.5 Reporting of institutional outbreaks (such as nursing homes) require a high work load from the LHD.

2.6 Epidemiological data on some diseases of high public health importance are not notifiable according to the current law.

3. Problems identified by state public health level (group 3):

3.1 The role of surveillance centers at state level (often not identical with the public health administration of a state) is not legally defined, resulting in unclear responsibilities towards LHD and RKI.

3.2 Interfaces between commercial software and RKI software do not function well, resulting in data transmission or coding errors

3.3 Clinicians' refusal to provide clinical patient data to LHD may hamper the application of case definitions.

4. Problems identified by federal public health level (group 4):

4.1 Data transfer discontinuity: Information already digitally formatted (e.g. by the laboratory IT system) is transferred to a paper-based text format in order to complete the notification form, sent to the LHD where it must be converted back to a digital format.

4.2 The IfSG is a federal law but the implementation of the law is the responsibility of the states, resulting in numerous problems of standardisation. (For example, some states have additional diseases or slightly different or complementary conditions, notifiable only in their states, causing confusion and lack of comparability.)

4.3 Insufficient user friendliness of various software packages causes incomplete or false data transmission.

4.4 The large quantity of surveillance data is not analysed and evaluated sufficiently.

Second phase: problem solution

The following recommendations were identified. They are not necessarily all supported by the authors of this paper:

First category: Recommendations that can be implemented without revision of the law.

Recommendations to clinicians and laboratories:

- If a notifiable disease is diagnosed by a laboratory, the laboratory report to the clinician should contain a reminder that this disease is notifiable (in response to problem formulated under 1.2).
- The association of laboratory physicians and other relevant associations should define (based on the national case definitions) the specific laboratory methods and findings that constitute a notifiable condition (1.6).

Recommendations to local health departments (LHD):

- Define clear contact details for disease notification within the LHD (1.2).
- Improve availability of notification forms by sending sample forms to clinicians (1.2).
- Produce mouse pads, plasticised memos, posters or other reminders that contain the list of notifiable diseases and distribute them to clinicians (1.2).
- Simplify notification forms (1.3).
- Improve visibility of LHDs by presenting the work of LHDs at scientific conferences in order to demonstrate the public health relevance of notification (1.4).
- Improve communication with clinicians (e.g. by distributing information letters, bulletins, and reports via fax or email and by personally welcoming new general practitioners in the county) (1.5).
- Develop a notification form for outbreaks (2.5).

Recommendations to state health departments (SHD):

- Improve availability of notification forms by publishing it in the journal of the state medical association (which implies, however, that a statewide uniform reporting form is established) (1.2).
- Offer training on reportable diseases at medical schools (1.2).
- Distribute epidemiological reports to LHDs (4.4).
- Provide more training opportunities for LHD personnel (4.4).

Recommendations to RKI:

- Develop a proposal for simplified notification form (1.3).
- Provide feedback on surveillance data, also through the journal of the national medical association (1.4, 4.4).
- Revise case definitions (1.6).
- Reduce the amount of data to be reported by LHDs (2.5).
- Improve software tool that facilitates identification of the appropriate LHD to notifying laboratories (4.1).
- Develop a national standard for an interface between software used in laboratories and software used by LHDs (4.1).
- Provide more training opportunities for LHD personnel (4.4).

Recommendations for revision of infectious disease control law

- Detailed provision of patient data by clinicians should be financially compensated (1.2).
- The law should request a national standard which defines which laboratory results are to be notified (1.6).
- If more than one laboratory is involved in identification of specification of a pathogen, there must be a clear rule, defining which one of the laboratories has to notify the result (1.6).
- Sporadic infections with rotavirus should be removed from the lists of notifiable diseases (2.1).
- Clinicians must be obliged and allowed to provide patient data upon request of the LHD if the data is relevant for public health measures (2.2).

- Borelliosis and connatal cytomegaly virus infection should be considered for inclusion (2.4).
- Vaccine preventable diseases not yet included (such as pertussis and tetanus) and infectious meningitis of unknown origin should be included in the list of notifiable diseases (2.4).
- Notification of hepatitis B and C virus infections should also include first diagnosed chronic illness and not be limited to acute infections (2.6).
- Syphilis should no longer be notified anonymously, in order to allow LHDs to conduct investigations (2.6).
- Surveillance units at state level must be given a clearly defined function within the law (3.1).
- Data standards must be uniform and nationally standardised, including the LHD level (and not at state level as it is in the current version) (3.2).

Discussion

This quality circle generated a number of valuable suggestions and recommendations on how the current surveillance system could be further improved. A methodological variation to most quality circles was that we intentionally invited participants from all affected structural and administrative levels [10]. The two phase approach, in which homogenous grouping was followed by heterogeneous grouping, proved to be successful: Homogenous grouping in the phase of problem identification allowed the participants to express their worries and frustrations without having to worry about hierarchical relationships and conflicting interests that may arise when representatives of different administrative levels come together. The following phase of developing possible solutions then required an interhierarchical and interdisciplinary approach in order to avoid each structural level projecting the need for improvement to another level. The re-grouping also forced the participants to search for solutions to problems which they have not necessarily identified themselves, which supports a pragmatic approach to the process. The presentation of results from previous studies between the two phases allowed the participants to compare their individual experience with data resulting form more quantitative assessments.

We support the majority of the recommendations presented in the result section, but cannot comment on all of them in detail in this report. However, the most important issues supported by our experience and by results of other studies are certainly those that deal with standardisation of information technology and with measures to improve notification compliance.

A number of recommendations have meanwhile been implemented, as can be seen in the following examples:

- Delegates of the RKI have been called as external advisors by the Ministry of Health for the revision process of the IfSG, which provided the opportunity to feed the recommendations of this quality circle into the discussion process. It remains to be seen how far the revision will take into account technical and scientific necessities of the system and practical experiences of those who implement the law on a daily basis.
- A number of laboratories are already providing physicians with complementary information on notification of infectious diseases.
- In a pilot study with 44 representatively selected LHDs, mouse pads and information letters were distributed by fax to general practitioners. Preliminary analyses suggest that these measures have resulted in a significant increase of notifications [11;12].
- In January 2004, a completely revised new edition of case definitions was published by the RKI [13;14].
- RKI was actively involved in a federal initiative to foster e-government (Bund online 2005) which provided a feasibility study on how to design a system for electronic laboratory notifications. This process has, however, recently come to a temporary stop, as resources to progress to the implementation stage are not available [15].
- RKI has released a simplified notification form, developed in cooperation with pilot LHDs and state health departments [12], which has generated a lively and positive response among state and local health departments.

The recommendations formulated in this quality circle have therefore already led to practical interventions and some of these have in turn had a measurable effect. This is a good indication that a quality circle, conducted in the above described manner, is an effective tool for quality improvement of public health surveillance systems.

Acknowledgements

We would like to acknowledge the valuable contributions of all participants of the quality circle and we would also like to thank Inge Mücke and Irene Schöneberg for editorial support to this manuscript.

References

1. Pfaff GM. [The protection against infection act - counties and states have to adjust their reportable disease notification systems]. Bundesgesundheitsblatt - Gesundheitsforsch – Gesundheitsschutz. 2000;43 (11): 900-4. [In German].
2. Forßbohm M. [The regulations of the protection against infection act on the reportable disease notification systems: the view of the local health department]. Bundesgesundheitsblatt - Gesundheitsforsch – Gesundheitsschutz. 2000;43(11):905-9. [In German].
3. Faensen D, Claus H, Benzler J, Ammon A, Pfoch T, Breuer T et al. SurvNet@ RKI - a multistate electronic reporting system for communicable diseases. Euro Surveill. 2006;11(4): 100-3.. Available from: http://www.eurosurveillance.org/em/v11n04/1104-224.asp
4. Framework for program evaluation in public health. MMWR Morb Mortal Wkly Rep. 1999;48,(RR-11):1-40.
5. Krause G, Ropers G, Stark K. Notifiable disease surveillance and practicing physicians. Emerg Infect Dis. 2005;11(3):442-5.
6. Brodhun B, Kramer MH, Krause G. [Survey among local health departments concerning the implementation of the new infectious disease reporting system]. Bundesgesundheitsblatt - Gesundheitsforsch – Gesundheitsschutz. 2004;47(8):755-61. [In German].
7. Krause G. [Experiences of the German public health service with the implementation of a new infections disease control act -- results of focus group discussions]. Gesundheitswesen. 2004;66(8-9):522-7.
8. Krause G, Altmann D, Claus H, Hellenbrand W, Buchholz U, Hamouda O, et al. [First evaluation of the surveillance systems of notifiable diseases under the infectious disease control law in Germany]. Gesundheitswesen. 2003;65 Suppl 1:S8-12.
9. Mira JJ, Perez-Jover V, Lorenzo S, Aranaz J, Vitaller J. [Qualitative research: a valid alternative]. Aten Primaria. 2004;34(4):161-6. Spanish Aten
10. Tausch BD, Harter MC. Perceived effectiveness of diagnostic and therapeutic guidelines in primary care quality circles. Int J Qual Health Care. 2001; 13(3):239-46.
11. Linnig S, Altmann D, Benzler J, Krause G. [Fax information letters to enhance the completeness of physicians' notifications]. 12. Jahrestagung der Deutschen Arbeitsgemeinschaft für Epidemiologie. Freiburg im Breisgau. 2005;(9):12.
12. RKI. [RKI-study 'pilot local health departments': accomplished projects and interventions]. Epidemiologisches Bulletin. 2005; 36:332-4.
13. Benzler J, Krause G, staff of the Dept. for Infectious Disease Epidemiology. [The 2004 edition of case definitions for the surveillance of notifiable infectious diseases in Germany]. Bundesgesundheitsblatt - Gesundheitsforsch - Gesundheitsschutz. 2004;47:141-6. [In German].
14. RKI. [Case definitions for transmission of infectious diseases and their detected pathogens – edition 2004]. http://www.rki.de/cln_006/nn_229194/DE/Content/Infekt/IfSG/Falldefinition/IfSG/ifsg__node.html__nnn=true. Accessed 20 December 2005.
15. BundOnline. [Notification of infectious diseases and their detected pathogens - data exchange within the public health system]: http://www.wms.bundonline.bund.de/cln_007/lang_de/nn_100986/Content/99__shareddocs/Publikationen/CC__VBPO/10__beratungs__auftraege/datenaustausch__gesundheitsdienst.html__nnn=true Accessed 15 December 2005

SURVEILLANCE OF INFLUENZA-LIKE ILLNESS IN ENGLAND AND WALES DURING 1966-2006

AJ Elliot, DM Fleming

We report surveillance data collected since 1966 from a general practice database in England and Wales. Incidence rates of influenza-like illness (ILI) peaked during the winter of 1969/70, and were then followed by a decade of heightened activity. There has since been a gradual downward trend of ILI, interspersed with winters of heightened activity; since 1999/2000, the incidence of ILI has been at its lowest for 40 years. We argue that the decade following the herald waves of the pandemic could be equally important for the planning of healthcare services in the community.

Euro Surveill. 2006;11(10): 249-50 Published online October 2006
Key words: Influenza, influenza-like illness, sentinel surveillance, pandemic, general practitioner

Introduction

Despite decades of research and recent advances in the fields of influenza vaccines and antivirals, the influenza viruses continue to cause high levels of morbidity and mortality in the community during each winter season. Although current attention is focused on the impending challenge of the introduction of a novel pandemic strain (H5N1) into the human population [1,2], it has long been recognised that the cumulative effect of 'inter-pandemic' periods of influenza are more significant in respect of mortality [3]. In this surveillance report, we aimed to investigate the long term trends of influenza-like illness (ILI) collected from a sentinel general practice network over the last 40 years in England and Wales and to assess its changing burden on primary care.

Methods

The Royal College of General Practitioners Weekly Returns Service (WRS) is a clinical information system based on a national network of sentinel general practices throughout England and Wales and is best known for its routine surveillance of respiratory illnesses [4]. Clinical diagnostic data are recorded by general practitioners (GPs) and stored as Read codes [5], which are mapped to the International Classification of Diseases (version 9; ICD-9) for analytical purposes. New episodes of illness are distinguished from ongoing consultations; new episodes of recurring or chronic conditions such as asthma are deemed to occur when exacerbations occur or when the condition is out of control. Currently (winter 2005/06), the network consists of 94 practices, comprising approximately 427 GPs, who continually record data on a twice-weekly basis, covering a patient population of approximately 940 000 (1.6% of the population of the United Kingdom). The network is representative of the national population in terms of both urban/rural and socioeconomic demographic spread [6]. A virological sampling scheme runs concurrently during the winter season: GPs take a combined nose and throat swab from a proportion of patients presenting with ILI or an acute respiratory infection. In collaboration with the Health Protection Agency, swabs undergo a molecular analysis for currently circulating influenza A viruses (subtypes H3 and H1), influenza B and respiratory syncytial virus [7]. This scheme is unique in providing virological validation of the clinical incidence data and timely information relating to the antigenicity and genetic composition of the influenza viruses circulating the community [8]. Swabs taken from this scheme have also been tested retrospectively to assess the clinical burden of newly discovered pathogens, e.g., human metapneumovirus, and their contribution to respiratory morbidity in different age groups [9].

Weekly episode incidence rates of ILI (ICD-9 487) were calculated for combined male and female and all-ages. GPs in the WRS do not adhere to strict clinical case definitions of ILI as used in some other European influenza surveillance systems [10]. It is routinely accepted, however, that symptoms of ILI are recognised by the sudden onset of one or more prominent systemic symptoms including fever, headache, myalgia and malaise, and one or more respiratory symptoms including cough, coryza, sore throat and shortness of breath.

Influenza seasons were defined as weeks 40 to 20, that is, a period from approximately October through to May the following year. Thresholds used to define levels of ILI activity in the community are based upon analyses of clinical and virological data [8,11]. The differing threshold levels of ILI are defined as: baseline activity (rates of <30 per 100 000); normal seasonal activity (30-200 per 100 000); above average seasonal activity (200-400 per 100 000); and epidemic activity (>400 per 100 000).

Results

During the forty years of influenza surveillance, there have been four discernable winters of high ILI rates [FIGURE]. The highest rates of ILI were recorded during the winter of 1969/70, peaking at 1252 per 100 000 during week 01. This was followed by a season of low activity where the peak rate was 144 per 100 000 during week 11 of 1971. During 1972/73 ILI peaked in week 52 (707 per 100 000) but the second highest seasonal rates were recorded during 1975/76 (789 per 100 000, week 08 1976); this was followed by a season of relatively low activity. After the 1975/76 season, there were 13 years of moderate activity until the last substantial epidemic of influenza, which occurred in 1989/90; rates reached a peak of 584 per 100 000 during week 49 of 1989. During the decade following the 1989/90 epidemic, there was moderate activity, except for the season of 1997/98, when there was an unusually low season of ILI activity. Following the winter of 1999/2000 there was low ILI activity; rates did not exceed 81 per 100 000 during any week within this period. There was evidence of a reducing trend of ILI which started from the early 1980s and continued through to the 2005/06 season. The last six winters have seen such low activity that the baseline threshold was reduced accordingly in 2003, from an incidence rate of 50 to 30 per 100 000 [11].

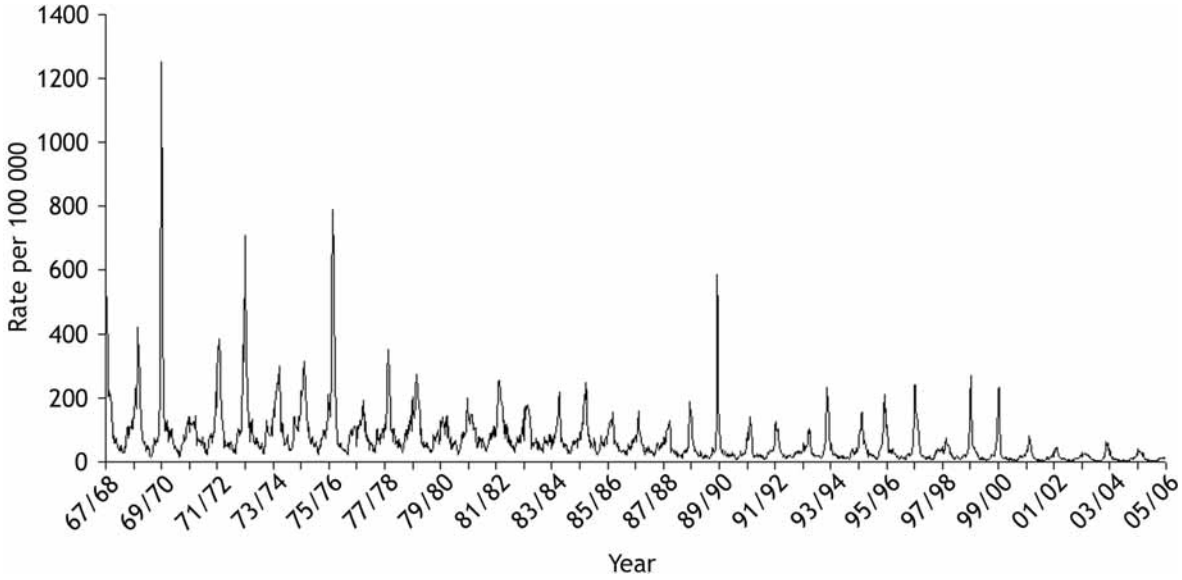
Discussion

The WRS was established in 1964 and has archived all data since 1966/67, providing an unrivalled opportunity to look at long-term trends of a variety of diseases. In this report we investigated the long term trends of ILI in England and Wales over a forty year period. The clinical impact of the 1968/69 pandemic was felt in the UK during the winter of 1969/70 when the WRS recorded higher rates of ILI than during any subsequent winter. Although there was much reduced morbidity in the following season, the next ten years saw sustained high levels of ILI. It is interesting to note that during the last years of H2N2 circulation (1966/67 to 1968/69) rates of ILI were relatively high compared to the rest of the time series. It is important to remember that the H2N2 subtype was introduced into the population during the

Birmingham Research Unit of the Royal College of General Practitioners, Birmingham, United Kingdom

FIGURE

Clinical incidence of influenza-like illness in England and Wales: weekly episode incidence rates from 1967 to 2006



1957/58 pandemic and therefore had been circulating for fewer than ten years when the WRS first began recording ILI morbidity statistics. The time series also incorporates the 1977/78 pandemic, when the influenza A H1N1 subtype was re-introduced and co-circulated with the H3N2 subtype. The clinical impact of this pandemic was not as great; rates peaked at 351 per 100 000, less than one third of rates recorded during 1969/70, and were not discernibly higher than any other winter during that decade. During this pandemic, H1N1 infection was limited to young people; this might explain why the impact of this pandemic was so clinically understated.

The introduction of a novel influenza subtype into a mainly immunologically naive population (with the possible exception of the elderly population who might have had previous exposure to similar antigenic strains [12]) provides the influenza virus with the optimal conditions to infect, transmit and thus inflict high levels of morbidity on the community. Analysis of the figure reveals that over the years following the winter season of 1980/81, there was a general reducing trend of ILI, with the exception of intermittent periods of heightened activity, for example 1989/90. This may reflect the declining ability of the H3N2 virus to efficiently infect susceptible hosts. Factors influencing this might include mutational changes to the virus structure (especially in domains of the haemagglutinin associated with receptor binding), forced by decades of immunological pressure from the population. This could result in a gradual decrease in viral fitness and thus a virus that is not able to infect and transmit as efficiently as when first introduced to the population.

If this scenario were true, then we would predict that the H3N2 subtype is making way for another pandemic strain, whether H5N1, or possibly another subtype from a yet unknown source. From analysis of our data, we would expect that following the introduction of a novel pandemic strain, incidence rates of ILI would peak at extremely high levels during the initial waves of the pandemic, but would then be sustained for a period of approximately 10 years following its introduction. Potentially, it is this ten year period that presents more problems to healthcare systems than the original pandemic waves, as both primary and secondary healthcare resources would be stretched over much longer periods of time. This, in combination with an increasingly ageing population, may present serious problems in the post-pandemic decade. Current debate revolving around pandemic planning has only considered the initial herald waves of the pandemic, and not the subsequent years in the post-pandemic era, which we argue could be equally important. This report does not advocate changing current pandemic plans, its aim is rather to raise awareness of the challenges we face in the post-pandemic decade.

The WRS currently reports incidence rates of ILI in the community that are very close to baseline threshold levels. The reduction may also reflect changes in social behaviour: family sizes are smaller; levels of hygiene have increased; air quality has improved; smoking has decreased; all might have played a part in reducing the transmissibility of influenza viruses and thus have contributed to the reduction of ILI. However, we must not be complacent in the face of the apparent decline of ILI in recent years, it is most likely that this is not a result of our attempts to control the spread of the influenza virus through treatment and prophylaxis; we must remember that this may simply be the calm before the storm.

Acknowledgments

We gratefully acknowledge the contribution of the WRS sentinel practices and their staff to providing the general practitioner episode data. Dr AJ Elliot is jointly funded by the Royal College of General Practitioners and Health Protection Agency.

References

1. Webby RJ, Webster RG. Are we ready for pandemic influenza? Science. 2003;302(5650):1519-22.
2. World Health Organisation. Confirmed human cases of avian influenza A(H5N1); [cited 2006 Aug 8]. Available from: http://www.who.int/csr/disease/avian_influenza/country/en/.
3. Simonsen L, Clarke MJ, Williamson GD, Stroup DF, Arden NH, Schonberger LB. The impact of influenza epidemics on mortality: introducing a severity index. Am J Public Health. 1997;87(12):1944-50.
4. Fleming DM. Weekly Returns Service of the Royal College of General Practitioners. Commun Dis Public Health. 1999;2(2):96-100.
5. Booth N. What are the Read Codes? Health Libr Rev. 1994;11(3):177-82.
6. Harcourt SE, Edwards DE, Fleming DM, Smith RL, Smith GE. How representative is the population covered by the RCGP spotter practice scheme? Using Geographical Information Systems to assess. J Public Health (Oxf). 2004;26(1):88-94.
7. Stockton J, Ellis JS, Saville M, Clewley JP, Zambon MC. Multiplex PCR for typing and subtyping influenza and respiratory syncytial viruses. J Clin Microbiol. 1998;36(10):2990-5.
8. Fleming DM, Zambon M, Bartelds AI, de Jong JC. The duration and magnitude of influenza epidemics: a study of surveillance data from sentinel general practices in England, Wales and the Netherlands. Eur J Epidemiol. 1999;15(5):467-73.
9. Stockton J, Stephenson I, Fleming D, Zambon M. Human metapneumovirus as a cause of community-acquired respiratory illness. Emerg Infect Dis. 2002;8(9):897-901.
10. Aguilera JF, Paget WJ, Mosnier A, Heijnen ML, Uphoff H, van der Velden J, et al. Heterogeneous case definitions used for the surveillance of influenza in Europe. Eur J Epidemiol. 2003;18(8):751-4.
11. Goddard NL, Kyncl J, Watson JM. Appropriateness of thresholds currently used to describe influenza activity in England. Commun Dis Public Health. 2003;6(3):238-45.
12. Tumpey TM, Garcia-Sastre A, Taubenberger JK, Palese P, Swayne DE, Basler CF. Pathogenicity and immunogenicity of influenza viruses with genes from the 1918 pandemic virus. Proc Natl Acad Sci U S A. 2004;101(9):3166-71.

RESPIRATORY VIRUSES AND INFLUENZA-LIKE ILLNESS: A SURVEY IN THE AREA OF ROME, WINTER 2004-2005

G Rezza[1], C Valdarchi[1], S Puzelli[1], M Ciotti[2], F Farchi[1], C Fabiani[1], L Calzoletti[1], I Donatelli[1], CF Perno[2]

Limited information is available on the viral aetiology of influenza-like illness (ILI) in Southern European countries. Hereby we report the main findings of a survey conducted in the area of Rome during the 2004-2005 winter season.

ILI cases were defined as individuals with fever >37.5°C and at least one constitutional symptom and one respiratory symptom, recruited during the survey period. Influenza and other respiratory viruses were identified using polymerase chain reaction (PCR) on throat swabs. Basic individual information was collected through a standard form.

Of 173 ILI cases enrolled, 74 tested positive for one virus, and two tested positive for two viruses. Overall, 33.5% of the cases were positive for influenza viruses, 5.2% for adenoviruses, 3.5% for parainfluenza viruses, 1.7% for coronaviruses, and 1.2% for the respiratory syncitial virus. The proportion of influenza virus detection was higher in the 'high influenza activity' period. The distribution of viral agents varied across age groups, influenza viruses being more likely to be detected in younger patients.

Viral pathogens were identified in less than 50% of ILI cases occurred during a high activity influenza season. The detection of other than influenza viruses was sporadic, without evidence of large outbreaks due to specific agents.

Euro Surveill. 2006;11(10): 251-3 Published online October 2006
Key words: Survey, PCR, ILI, respiratory viruses, influenza, Italy.

Introduction

Respiratory infections are common in both adults and children. Most of them are fairly mild, self-limiting, and confined to the upper respiratory tract, but severe illness may sometimes occur.

Most respiratory infections occurring during the winter in industrialised countries are attributable to viral agents [1, 2]. The incidence of acute respiratory illness is highest in young children and decreases with increasing age [3].

The frequency of detection of specific viral agents varies between different studies, depending on case definition, diagnostic techniques, and seasonality [1]. When all respiratory illnesses are considered, rhinoviruses and influenza viruses are the most represented agents, followed by parainfluenza viruses (PIV), respiratory syncytial virus (RSV), and adenoviruses [1,4]. However, the findings may differ depending on the case definition used: as far as influenza-like illness (ILI) is concerned, influenza viruses are most commonly detected, whereas rhinoviruses may rank first when a more generic definition of acute respiratory tract infection is used [5]. High detection rates of RSV in ILI have also been reported [6].

Most of the above mentioned studies have been conducted in the United States or in central or northern Europe, while limited information is available from the Mediterranean area. The objectives of the present study were: (i) to identify viruses responsible for ILI, (ii) to determine their proportion, and (iii) to identify virus-specific clinical syndromes in an Italian population during a winter season.

1. Department of Infectious, Parasitic and Immunomediated Diseases, Istituto Superiore di Sanità, Rome, Italy
2. Department of Molecular Virology, Policlinico Tor Vergata, Rome, Italy

Material and methods

The survey was conducted in the area of Rome. Nine general practitioners, including two paediatricians, were recruited (seven in urban or suburban areas and two from rural villages in the province of Rome). At the beginning of November and January, each doctor was provided with 20 virocult swabs and was asked to enrol all patients fulfilling the recruitment criteria (that is, the case definition, and maximum time interval between onset of symptoms and sample collection). All patients with ILI, as defined by the presence of fever >37.5°C and at least one other symptom (headache, malaise, myalgia, chills or sweats, retrosternal pain, asthenia) and one respiratory symptom (cough, sore throat, nasal congestion or runny nose), between November 2004 and March 2005, were eligible for the study. Our case definition was different from that provided by the Italian Ministry of Health for ILI surveillance [7], so that we could include milder febrile cases. A throat swab was collected from patients who received home visits from their doctor within four days after the onset of symptoms.

Sample collection

Throat swabs were taken from individuals presenting with ILI, using 'Virocult swabs' (Medical Wire and Equipment, United Kingdom). Essential information (such as date of sample collection, patient's initials, sex, age, clinical symptoms, vaccination status) was collected for each specimen. On arrival in the laboratory, separate aliquots of each clinical samples were prepared and used for RT-PCR analysis.

RNA and DNA Extraction and RT-PCR

A multiplex RT-PCR was performed to identify influenza A or B viruses. In this case, viral RNA were extracted either directly from clinical samples or from virus-infected MDCK culture fluid using an RNA extraction kit (RNeasy; Qiagen, Santa Clara, California, USA). cDNA synthesis and amplification procedures were carried out as described elsewhere (8). PCR was performed using specific primers which amplified regions within the genes for: (i) the influenza A nucleoprotein and the influenza A/H1- and A/H3-subtype haemagglutinins; (ii) the influenza B haemagglutinin and neuraminidase. Primers used in PCR reactions are available from the authors upon request.

In order to identify other respiratory viruses, total DNA and RNA was extracted from a separate aliquot of the clinical sample, by Ultrasens kit (Qiagen, Hilden, Germany), in accordand with the manufacturer's instructions. To verify the acid nucleic extraction (DNA and RNA), we amplified the nucleic acid with the b-actin gene (9): all the samples tested positive. Thus, the samples were screened for the presence of adenovirus, RSV, PIV type 1, 2, 3 and 4, enteroviruses, and coronaviruses, using primers sequences as reported [10-13].

Statistical analysis

The association between demographic variables or preventive measures (that is, vaccination) and specific viral infections was evaluated by using odds ratios (OR) and their 95% confidence intervals (95% CI). The statistical significance of other associations was assessed through the chi square test. Based on the number of ILI cases notified to FLU-ISS in the province of Rome, we identified a 'high' and a 'low/medium' influenza activity period, using a threshold

of 850 cases, which was about 60% of the maximum weekly number of cases (1436 cases reported during week 5). The distribution of specific viruses in the two periods was then compared. With regard to the association between each symptom and specific viral infections (that is, influenza versus other viruses), the Bonferroni correction was used to test the statistical significance of the associations, in order to minimise the risk of a Type I error in the presence of multiple outcome measures of importance [14].

Results

Overall, 173 patients with available samples were recruited during the study period. Of the participants, 96 (55.5%) were female and 77 (44.5%) male. The median age was 27 years (range: 0.5-82 years); 57 patients (32.4%) were children (13 years or younger), and 14 were under three years old. Most of the study participants (164, 94.8%) were of Italian nationality. One hundred and thirty seven patients were recruited in urban areas and 39 in rural villages located in the province of Rome.

Of the 173 samples tested, 74 were positive for one virus and two were positive for two viruses, totalling in 78 viruses detected. The numbers of samples positive for influenza and/or other viruses, and negative samples, is shown in the figure. The most commonly detected agent was influenza virus, which was found in 58 samples (74.4% of all isolates), followed by adenoviruses (11.5%), PIV (7.7%), coronaviruses (3.8%), and RSV (2.6%). Of the influenza isolates, 56 were influenza A (23 of these were typed: 22 were H3N2 and one H1N1), and only two were influenza B strains. With regard to PIV isolates, three were PIV type 3, two were type 4, and one was type 1. Of the samples positive for two viruses, one was positive for influenza and coronavirus, the other for RSV and adenovirus.

Of the 173 samples, 66 were collected during the low-medium influenza activity period (that is, from weeks 46 to 53 and weeks 10 to 17), and 107 during high influenza activity (between weeks 1 and 9). As shown in Table 1, the distribution of the different viral agents differed between the two periods (P = 0.01), due to increased influenza activity in early 2005. The proportion of negative samples was higher in the 'low' activity compared with the 'high' activity period: negative samples were 43 (65.1%) and 54 (48.6%), respectively (P = 0.01).

As shown in Table 2, the proportion of samples positive for influenza viruses was higher in the youngest age group and tended to decrease with increasing age (chi square for trend, P<0.01). Children (≤13 years of age) were more than twice as likely than adolescents over 13 years and adults to be infected with influenza viruses (OR: 2.2, 95% CI: 1.08-4.50). None of the 13 patients aged 65 years or over was positive for influenza viruses.

Overall, 40 of the 173 participants (23.1%) had been vaccinated for influenza: 12 of them (30%) were infected by influenza viruses versus 46 of 133 (34.6%) of non-vaccinated participants; the difference was not statistically significant (OR: 0.81, 95% CI: 0.35-1.85). Among participants younger than 65 years old, 12 of the 30 vaccinated (40%) and 46 of 130 unvaccinated (35.4%) were found to be infected with influenza viruses (OR: 0.82, 95% CI: 0.34-2.00), while none of the 10 vaccinated and the 3 unvaccinated participants aged 65 years or older was positive.

The distribution of symptoms among ILI patients with laboratory confirmed influenza and among the other cases is shown in Table 3: muscle pain (P=0.028) and productive cough (P=0.046) were more likely, and nausea (P=0.045) less likely to be reported in cases positive for influenza viruses; however, no statistical significance remained after applying the Bonferroni correction.

Discussion

In our study, about 44% of the samples were positive for at least one virus. This is fairly consistent with the results of other studies where viruses were detected in a range between 36%-38% (6, 15) and 58% (5). In another study of community-acquired respiratory infections, including also *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* in addiction to viral agents (4), at least one potentially pathogenic microorganism was detected in 52% of the swabs.

During the study period, a major influenza epidemic occurred. Thus, in accordance with other studies (4, 6, 15), influenza was the most commonly detected virus. The lack of a protective effect from influenza vaccination was probably due to viral drift leading to the mismatch between wild and vaccine strains [16]. RSV, which was reported to be almost as common as influenza viruses in one of the abovementioned studies, with the highest impact in the youngest age

Table 1

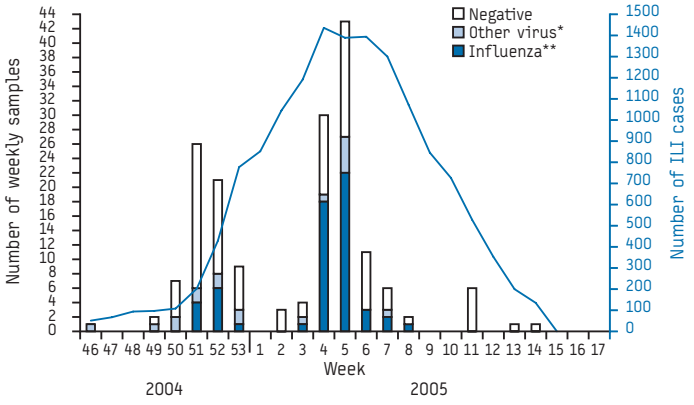
Frequency distribution of specific viral agents by period of sample collection, Rome, 2004-2005

	Weeks 46-53 (2004) and 10-17 (2005)		Weeks 1 to 9 (2005)		Total	
Virus	No.	%	No.	%	No.	%
Influenza	11	47.8	47	85.5	58	74.4
Adenovirus	5	21.7	4	7.3	9	11.5
PIV	4	17.4	2	3.6	6	7.7
Coronavirus	2	8.7	1	1.8	3	3.8
RSV	1	4.4	1	1.8	2	2.6
Total	23	100.0	55	100.0	78	100.0

Note: The percentages are calculated from the total number in each column.

Figure

Cumulative number of positive and negative samples for influenza and other viruses, and number of ILI cases in the province of Rome, winter season 2004-2005



Notes:

* Only one sample is considered for the sample positive for two 'other viruses' (weeks 52 and 53).

** The sample positive for both influenza and another virus is included among influenza positive samples.

Source: FLU – ISS (National Surveillance System)

Table 2

Proportion of samples with laboratory confirmed influenza viruses and samples with other pathogen or no pathogen identified by age class, Rome, 2004-2005

	Samples with laboratory confirmed influenza		Samples with other or no pathogen identified		Total	
Age (years)	No.	%	No.	%	No.	%
0 - 2	7	50.0	7	50.0	14	100.0
3 - 13	19	44.2	24	55.8	43	100.0
14 - 64	32	31.1	71	68.9	103	100.0
>65	0	0	13	100.0	13	100.0
Total	58	33.5	115	66.5	173	100.0

Note: The percentages are calculated from the total number in each row

Table 3

Distribution of signs and symptoms of ILI patients with laboratory confirmed influenza versus ILI patients with other pathogen or no pathogen identified, Rome, 2004-2005

Symptoms	Influenza (n=58*) %	Other (n=115) %	Total (n=173) %
Sore throat	67.2	72.0	70.5
Nasal congestion	67.2	60.0	62.4
Muscle pain	63.8	46.1	52.0
Headache	50.0	39.1	42.8
Dry cough	50.0	53.9	52.6
Productive cough	44.8	29.6	34.7
Chills	37.9	38.3	38.2
Joint pain	29.3	33.9	32.4
Retrosternal pain	29.3	22.6	24.9
Sweating	20.7	25.2	23.7
Short breath	15.5	18.3	17.3
Abdominal pain	8.6	10.4	9.8
Diarrhoea	3.4	6.1	5.2
Nausea	3.4	13.0	9.8
Vomiting	3.4	9.6	7.5

*One patient was positive for both influenza and coronavirus

groups [6], was rarely detected in our survey: this might be due to the low proportion of children recruited, which was itself a result of the low number of paediatricians involved in the survey. Other viral agents, such as adenoviruses, PIV, and coronaviruses were detected in sporadic cases in our study population.

The virological pattern tended to be consistent with the trend of ILI cases reported to FLU-NET in the province of Rome: as expected, influenza viruses were more likely to be detected in the 'high' influenza activity period, whereas the other viruses were only sporadically detected both in the 'high' and in the 'low/medium' influenza activity period. The distribution of the different viral agents varied across age groups, with influenza viruses being more likely to be detected in younger patients.

Before drawing conclusions limits and biases of this study should be mentioned. Firstly, recruitment bias could have affected the results of our study in several ways: i) the consultation pattern of the doctors included in our study was not completely consistent with that of the national surveillance system (FLU-ISS) in the area of Rome; ii) the proportion of children enrolled in our study was relatively low, due to limited participation of paediatricians; iii) irregular sampling, including the lack of recruitments during the Christmas holidays, may have biased the overall distribution of specific viruses during the study period. Thus, to what extent our study population was representative of ILI cases occurred in Rome in the winter 2004/05 remains undefined. Secondly, some viruses, such as rhinoviruses and metapneumoviruses, and bacteria, such as *M. pneumoniae* or *C. pneumoniae*, were not studied. In particular, the inclusion of rhinoviruses might greatly increase virus detection frequency, as indicated by studies reporting a higher proportion of these viruses compared to influenza virus [1], and explain the relatively high proportion of unidentified aetiologies in our study. Nevertheless, our findings do not differ significantly from those of other studies conducted up to now. Thirdly, the potential occurrence of false negative results due to the variable sensitivity of the laboratory techniques, and to the type of biological samples, should not be completely ruled out. Furthermore, timing of collection may have decreased the rate of detection, since some swabs were taken up to 4 days after the onset of symptoms (when viruses may have been cleared, at least in part, by the immune response). The maximum sample delay was set at four days because most patients are not visited before the third day after onset. Finally, the extent to which the case-definition we used was unspecific compared with that provided by the Italian Ministry of Health remains undefined. In particular, we cannot exclude the possibility that the inclusion of patients with milder symptoms may have 'diluted' the frequency of detection of influenza viruses.

In conclusion, we were able to identify the aetiology of about half of the ILI that were reported during the 2004-2005 winter season. Influenza was the most commonly identified agent, while cases attributable to other viruses were sporadic. Although surveillance of respiratory viruses associated with ILI is not sustainable, due to high costs and lack of preventive tools, limited aetiological surveys may provide useful information on the effect of specific agents affecting human populations in the winter season.

Acknowledgements

We thank Claudio D'Anna and Stefania Mariani for their excellent technical work, and the following GPs for sample and data collection: G. Nati, V. Calzini, G. Grasso, A. Filabozzi, M. Mocci, A. Verginelli, M. Corongiu, A. Palma, and C. Colistra. We also thank A. Di Bella (CNEPS, ISS) for providing FLU-ISS data on ILI reported in the province of Rome in winter 2004-05.

The surveillance activity, which is currently sponsored by the CCM (Centro Controllo Malattie), Ministry of Health, ha been funded in part by the Programma Nazionale Ricerca Finalizzata (Project entitled 'SARS and other Coronaviruses').

References

1. Monto AS. Viral respiratory infections in the community: epidemiology, agents, and interventions. Am J Med. 1995; 99(6B):24S-27S)
2. Gwaltney JM. Clinical significance and pathogenesis of viral respiratory infections. Am J Med. 2002:112 (Suppl 6A):13S-18S.
3. Badger GF, Dingle JH, Feller AE, Hodges RD, Jordan WS, Rammelkamp CH Jr. A study of illness in a group of Cleveland families. II. Incidence of common respiratory disease. Am J Hyg. 1953;58:31-40.
4. Heijnen MLA, Dorigo-Zetsma JW, Bartelds AIM, Wilbrink B, Sprenger MJW. Surveillance of respiratory pathogens and influenza-like illness in general practices – The Netherlands, winter 1997-98. Euro Surveill. 1999;4(7):81-4. Available from: http://www.eurosurveillance.org/em/v04n08/0408-223.asp
5. van Gageldong-Lafeber AB, Haijnen M-LA, Bartelds AIM, Peters MF, van der Plas SM, Wilbrink B. A case-control study of acute respiratory tract infection in general practice patients in The Netherlands. Clin Infect Dis. 2005;41: 490-7.
6. Lina B, Valette M, Foray S, et al. Surveillance of community-acquired viral infections due to respiratory viruses in Rhone-Alpes (France) during winter 1994 to 1995. J Clin Microbiol. 1996; 34: 3007-11.
7. Gabutti G, Guido M, Quattrocchi M, et al. Surveillance of influenza in Apulia, Italy, 1999-2000, 2000-2001, 2001-2002, and 2002-2003 seasons. Med Mal Infect. 2004;34: 469-76.
8. Puzelli S, Frezza F, Fabiani C, et al. 2004. Changes in the hemagglutinins and neuraminidases of human influenza B viruses isolated in Italy during the 2001-02, 2002-03, and 2003-04 seasons. J Med Virol. 2004;74(4):629-40.
9. Strassburg CP, Strassburg A, Nguyen N, Li Q, Manns MP, Tukey RH. Regulation and function of family 1 and family 2 UDP-glucuronosyltransferase genes (UGT1A, UGT2B) in human oesophagus. Biochem J. 1999;338:489-98.
10. Heim A, Ebnet C, Harste G, and Pring-Akerblom. Rapid and quantitative detection of human adenovirus DNA by real-time PCR. J Med Virol. 2003; 70:228-39.
11. Templeton KE, Scheltinga SA, Beersma MFC, Kroes ACM, and Claas ECJ. Rapid and sensitive method using multiplex real-time PCR for diagnosis of infections by Influenza A and Influenza B viruses, Respiratory Syncitial virus and Parainfluenza viruses 1, 2, 3, and 4. J Clin Microbiol 2004, 42(4): 1564-9.
12. Verstrepen WA, Bruynseels P, Mertens AH. Evaluation of a rapid real-time RT-PCR assay for detection of enterovirus RNA in cerobrospinal fluid specimens. J Clin Virol. 2002; 25: S39-S43.
13. Adachi D, Johnson G, Draker R, Ayers M, Mazzulli T, Talbot PJ, Tellier R. Comprehensive detection and identification of human coronaviruses, including the SARS-associated coronavirus, with a single RT-PCR assay. J Virol Methods. 2004; 122: 29-36,
14. Altman DG. Practical statistics for medical research. Chapman and Hall. London, 1991.
15. Vabret A, Mourez T, Gouarin S, Petitjean J, Freymuth F. A outbreak of coronavirus OC43 respiratory infection in Normandy, France. Clin Infect Dis. 2003;36: 985-89.
16. Ansaldi F, Icardi G, Gasparini R, et al. New A/H3N2 influenza variant: a small genetic evolution but a heavy burden on the Italian population durino the 2004-2005 season. J Clin Microbiol. 2005;43 027-29.

USING SENTINEL SURVEILLANCE TO MONITOR EFFECTIVENESS OF INFLUENZA VACCINE IS FEASIBLE: A PILOT STUDY IN DENMARK

A Mazick[1,2], AH Christiansen[2], S Samuelsson[2], K Mølbak[2]

The influenza vaccine for the season 2003/04 did not contain the circulating A(H3N2)/Fujian virus strain. Vaccine effectiveness (VE) estimates were needed but unavailable. We explored whether or not laboratory based influenza surveillance can be used to estimate VE. We carried out a case-control study nested within Danish sentinel surveillance. A case was defined as a person aged 25 or above with A(H3N2)/Fujian/411/02 influenza. Four controls per case, matched on age groups and time, were selected from clients of sentinel practitioners (SP) who reported cases. SPs collected the following data in structured one-page questionnaires: vaccination status, chronic illness and previous pneumococcal vaccination. We sent postal survey questionnaires to participating SPs to assess acceptability and simplicity of data collection.

Twenty four cases were identified. Data from 19 case-control sets were analysed. One control was excluded because information on vaccination status was missing. Two of the 19 cases and 11 of 75 controls had been vaccinated against influenza. The VE adjusted for chronic illness was 33% (95% CI 0%–88%) and 37% (95% CI 0%–89%) when excluding 5 controls with influenza-like illness. Twenty two SPs returned survey questionnaires. Fifteen of 17 SPs reported that it was easy to find controls. SPs collected data through interviews and clinical notes, spending 1 to 5 minutes per case and 5 to 15 minutes for all four controls. Nineteen of 22 SPs considered the amount of time they spent on the study to be acceptable, 17 said that they would like to participate again, and none ruled out further participation.

Monitoring VE within sentinel surveillance systems is feasible. The small numbers in our study limit interpretation of VE. Expansion to a European multicountry study could overcome this limitation and provide VE estimates earlier in the season, for different age groups and emerging virus strains, including new and pandemic subtypes.

Euro Surveill. 2006;11(10): 254-6 Published online October 2006
Key words: Influenza vaccine, drug evaluation, case control studies, surveillance, pandemic

Introduction

Influenza is a major cause of morbidity and mortality in Europe[1]. Surveillance of influenza, usually designed as sentinel surveillance, is crucial to early detect epidemics and changes in circulating virus strains. With this objective in mind, Danish sentinel surveillance for influenza was implemented in 1994. The system is based on voluntary participation of up to 150 general practitioners, distributed nationwide. Between week 40 and week 20 of the following year, sentinel practitioners (SP) report weekly the number of consultations for influenza-like illness (ILI, defined as acute onset of fever, myalgia and respiratory symptoms) by age group and the number of total consultations in their practice. For surveillance of circulating virus strains, 50 SPs collect throat swabs from the first five ILI patients seen on three occasions during the influenza season (beginning, peak and end). These swabs are analysed and typed by PCR, virus isolation and haemagglutination inhibition assay at the National Influenza Reference Laboratory at the Statens Serum Institut (SSI). In Denmark, annual influenza vaccination is recommended for people aged 65 years or over and for people with chronic medical conditions.

During the 2003/04 season, the influenza vaccine recommended by the World Health Organization did not contain the circulating A(H3N2)/Fujian virus strain, and reports of severe illness and paediatric deaths associated with Fujian alarmed the public [2-4]. Vaccine effectiveness (VE) estimates were needed, but were unavailable.

The objective of the study reported here was to explore whether it is feasible to use sentinel surveillance to monitor the effectiveness of seasonal influenza vaccination, with the perspective of using a similar methodology to rapidly estimate effectiveness of a vaccine against pandemic influenza.

Methods

The study was designed as a case-control study nested within the Danish sentinel surveillance, in order to estimate effectiveness of the seasonal influenza vaccine during the influenza season 2003/04. A case was defined as a person aged 25 years or older, from whom a specimen taken by the SP was found to be positive for influenza A/Fujian/411/02 (H3N2). Younger patients were initially included in the study but were later excluded after preliminary analysis showed low vaccination coverage in this population. Cases were identified based on test results received from the National Influenza Laboratory. SPs who reported a case selected as controls four patients attending the clinic two weeks afterwards a particular case. Controls were matched to cases by age groups that corresponded to those used in ILI surveillance (25 – 64 years and ≥ 65 years).

SPs used one-page questionnaires to collect information on influenza vaccination, severity of illness, underlying chronic illness (cardiovascular and chronic pulmonary disease, diabetes mellitus, immunodeficiency and other chronic diseases), previous pneumococcal vaccination, residence and presence of ILI in controls at the time of selection. Case questionnaires were sent to SPs together with the laboratory sampling kits, and were completed by SPs when they collected specimens from ILI patients. As soon as a case was identified, we sent four control questionnaires to the SP reporting the case. Cases who had received influenza vaccine more than one week before specimen collection were coded as vaccinated. Controls were considered vaccinated if they had received vaccine more than one week before selection. To estimate vaccine effectiveness, case-control sets were analysed by conditional logistic regression using two different control groups: Control group 1 included all controls regardless of whether or not they had symptoms of ILI at the time of selection (case–cohort approach) [5,6]. In control group 2, people reporting ILI at the time of selection were excluded.

To assess workload and acceptability of the VE study we sent anonymous questionnaires to all SPs, who had cases, at the end of the influenza season. Information collected included time spent participating in the study, ease of control selection and data collection, reasons for non-response and willingness to participate again.

1. European Programme for Intervention Epidemiology Training (EPIET)
2. Department of Epidemiology, Statens Serum Institut, Denmark

Results

In the 2003/04 influenza season, 79 SPs submitted a total of 219 specimens from ILI patients; of these, 55 specimens (submitted by 34 SPs) tested influenza virus positive [TABLE 1].

Table 1

Number of throat swab specimens submitted by sentinel practitioners by laboratory result and age group, influenza season 2003/2004, Denmark

Age group (years)	Sentinel specimens			
	A(H3N2)[a]	B[b]	Negative	Total
0-24	30		33	63
25-64	21	1	117	139
65+	3		14	17
Total	**54**	**1**	**164**	**219**

a A(H3N2): Influenza virus A(H3N2), all with Fujian/411/02 characteristics.

b B: Influenza B virus

Among 54 patients with A/Fujian positive influenza, 24 were in the relevant age groups for this study. Control data was obtained for 19 of these cases (79%) and consequently 19 case-control sets were analysed. One control was excluded because information on influenza vaccination status was missing. Cases and controls did not significantly differ with regards to age, sex and presence of underlying chronic illness [TABLE 2]. None of the cases or controls lived in a residential home. Of all cases and controls with underlying chronic illness 31.3% (10/32) had been vaccinated with seasonal influenza vaccine.

Table 2

Characteristics of A(H3N2)/Fujian influenza infected study cases and controls, influenza season 2003/04, Denmark

Characteristics	Cases (n =19) (%)	Control group 1 (n=75) (%)	P value*
Age in years: median (range)	36 (25-68)	46 (25-82)	0.14†
Female	13/19 (68.4)	46/73 (63)	0.66
Underlying chronic illness	6/18 (33.3)	26/75 (34.7)	0.92
Previous pneumococcal vaccination	0/15	3/72 (4.2)	0.42
Living in institution	0/19	0/75	
ILI at time of selection	19/19	4/75 (5.3)	

* Pearson χ^2

† Kruskal-Wallis rank test

Of 75 controls, four (5.3%) had symptoms of ILI and were excluded from analysis in control group 2.

Factors related to A(H3N2)/Fujian influenza were analysed in a conditional logistic regression model. Chronic disease was introduced as confounding variable; other variables did not alter the model [TABLE 3]. The vaccine effectiveness (1-OR) adjusted for chronic illness was 33% (95% CI 0%–88%) in the model including control group 1 and 37% (95% CI 0%–89%) in the model including control group 2.

Twenty two of 30 SPs returned survey questionnaires, and of these, 17 had returned control questionnaires and 15 of these 17 reported that they had found it easy to find controls. SPs collected data through interviews and clinical notes, spending 1 to 5 minutes per case and 5 to 15 minutes for all four controls. Nineteen of 22 SPs considered the amount of time they spent on the study to be acceptable, 17 of 22 said that they would like to participate again, and none ruled out further participation. Inadequate briefing was mentioned a reason for non-participation

The additional costs for the national coordination of the VE study were calculated based on direct and indirect costs shown in table 4, and totalled approximately 2000 Euro.

Table 4

Operational costs of influenza vaccine effectiveness study at national level, 2003/04, Denmark

Indirect costs (at SSI*)	Hours	Euro
Epidemiologist	32	1176
Nurse	12	364
Laboratory technician, secretary	20	558
Total	**64**	**2098**

Direct costs	Euro
Postage	94
Stationary	13
Telephone	13
Total	**120**

* SSI: Statens Serum Institute

Discussion

The results suggest that monitoring the effectiveness of influenza vaccines within sentinel surveillance systems is generally feasible. However, the small numbers of positive specimens collected by the Danish sentinel system limit the interpretation of the vaccine effectiveness estimate and therefore the value of the method for ongoing monitoring of VE in Denmark. Expansion to a European multicountry study could overcome this limitation and provide VE estimates earlier in the season, for different age groups and for emerging virus strains.

Monitoring of seasonal influenza vaccine effectiveness within surveillance systems is, in addition to the Danish pilot study presented here, also carried out in France [7,8] and in Canada[9]. All three approaches use a case-control method, and identify cases from sentinel surveillance (study outcome either ILI (France) or laboratory confirmed influenza (Canada, Denmark)), but they differ in the selection of the control group [FIGURE]. The Canadian controls are sentinel patients with ILI that test negative for influenza, while in France, the control group is the study population of an annual vaccine uptake survey of the preceding influenza season.

Table 3

Factors related to A(H3N2)/Fujian influenza among study cases and controls, influenza season 2003/04, Denmark

		Control group 1			Control group 2		
		n/total	Crude OR*	Adjusted matched OR[a] (95% CI[b])	*n*/total	Crude OR	Adjusted matched OR (95% CI)
Influenza vaccination	Cases	2/19	0.7	0.67 (0.1-3.7)	2/19	0.64	0.63 (0.1-3.4)
	Controls	11/75			11/71		
Chronic disease	Cases	6/18	0.98	1.11 (0.3-4.1)	6/18	0.92	1.08 (0.3-4.0)
	Controls	26/75			25/71		

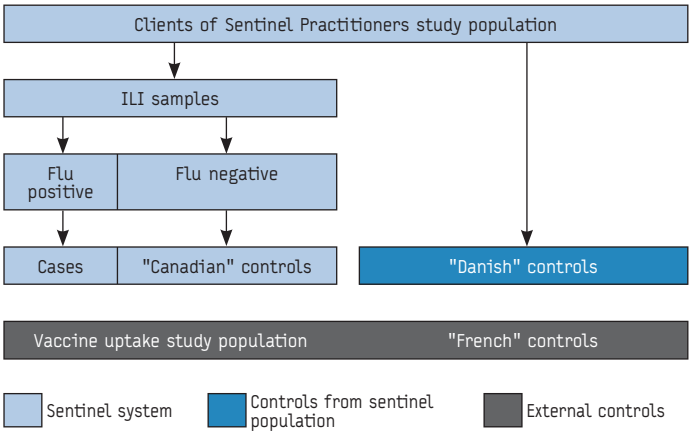
* Crude OR were estimated on matched sets by Mantel Hænszel method

a Odds ratio,

b Confidence interval

FIGURE

Framework for case-control studies to monitor influenza vaccine effectiveness within surveillance systems: three different control groups as used in the Danish, French and Canadian study designs



As observational studies with rather simple designs, all three approaches are subject to potential bias and confounding. Particular methodological limitations include: in Canada, the limiting or the study population to patients with ILI who consult sentinel practitioners, and it is not known how far these VE estimates can be generalised to the general population. Furthermore, the approach is very sensitive to misclassification of outcome, as demonstrated in the Canadian study and in a simulation with German data [10]. The screening method used in France is limited its adjustability for confounding, for example for underlying chronic illness, and the validity of the VE estimate depends on a valid external vaccine uptake estimate for relevant age groups in a comparable population [10,11]. Both the Danish and the Canadian approaches use laboratory confirmed influenza as an outcome measure, allowing the study to distinguish between co-circulating virus (sub-)types and to estimate VE for the different influenza vaccine components. An operational limitation of both approaches is, however, the requirement that SPs collect a limited set of additional information.

A further weakness of all approaches is the inability to ensure susceptibility of controls such as would be required to derive a valid estimate on the strength of an association when the outcome is common [5].

In spite of these limitations, the approaches may well be suitable for monitoring changes over time by comparing VE estimates between influenza seasons, as the estimates will be comparable. The validity of the seasonal estimates may be studied by triangulating the results of the three methods by additional registry (i.e. population or GP) based VE studies in countries where these are feasible or by rigorous focused studies in particular risk groups as required.

Integrating VE monitoring into existing sentinel surveillance has a number of advantages. It builds on already well established networks and capitalises on routinely collected information. It further means that most European Influenza Surveillance Scheme (EISS) member countries already have the minimum capability requirements for participation already in place, although one particular method may be more suitable for some countries than for others. In Denmark the study was considered a surveillance project and did not require ethical approval. However, requirements for scientific ethical clearance and for financial issues may vary from country to country. These aspects would need to be considered in a European study.

Timeliness is a priority consideration in choosing a suitable methodology, so that a first VE estimate can be obtained early in the influenza season, with precision continuing to increase as the season progresses

In the Danish VE study, data on controls were available already 14 days after the occurrence of the case, and an external vaccine uptake, which may only be available later in the influenza season, is not required.

In a pandemic there will be an urgent need to determine the effectiveness of the pandemic vaccine, as only limited or no trial data on the protective vaccine efficacy will be available prior to licensure of a pandemic vaccine [12,13]. The present designs offer an attractive and feasible approach for a rough estimate of the effectiveness of a pandemic vaccine but the methods must be trialled and be in place prior to the pandemic.

Acknowledgements

We thank all sentinel practitioners for their participation. We thank Bente Andersen and Per Grauballe (SSI) for laboratory collaboration and Andrea Gervelmeyer (EPIET/SSI), Steffen Glismann (SSI) for their contribution. Special thanks go to Alain Moren (Chief EPIET coordinator) for his valuable support.

References

1. Fleming DM, Elliot AJ. The impact of influenza on the health and health care utilisation of elderly people. Vaccine. 2005;23 Suppl 1:S1-9.
2. Crofts C. Current influenza activity in the United Kingdom: A/Fujian/411/2002 (H3N2)-like strains circulating in the community, week 44. Eurosurveillance Weekly. 2003;11(45) 031106. Available from: http://www.eurosurveillance.org/ew/2003/031106.asp#2
3. Fitzgerald M, Conlon M, Murphy P, Connell JCS, Danis C. Early Arrival of Influenza A in Secondary School Children in the Eastern Regional Health Authority. Epi-Insight. 2003;4(9).
4. Paget WJ, Meerhoff TJ, Meijer A. Epidemiological and virological assessment of influenza activity in Europe during the 2003-2004 season. Euro Surveill. 2005;10(4):107-11. Available from; http://www.eurosurveillance.org/em/v10n04/1004-221.asp
5. Rodrigues L, Kirkwood BR. Case-control designs in the study of common diseases: updates on the demise of the rare disease assumption and the choice of sampling scheme for controls. Int J Epidemiol. 1990;19(1):205-13.
6. Smith PG, Rodrigues LC, Fine PE. Assessment of the protective efficacy of vaccines against common diseases using case-control and cohort studies. Int J Epidemiol. 1984;13(1):87-93.
7. Carrat F, Flahault A, Boussard E, Farran N, Dangoumau L, Valleron AJ. Surveillance of influenza-like illness in France. The example of the 1995/1996 epidemic. J Epidemiol Community Health. 1998;52 Suppl 1:32S-38S.
8. Legrand J, Vergu E, Flahault A. Real-time monitoring of the influenza vaccine field effectiveness. Vaccine. 2006; 9. [Epub ahead of print].
9. Effectiveness of vaccine against medical consultation due to laboratory-confirmed influenza: Results from a sentinel physician pilot project in British Columbia, 2004-2005. CCDR. 2005;31(18):181-91.
10. Uphoff H, Hauri AM, Schweiger B, Heckler R, Haas W, Grueber A, et al. [Zur Schaetzung der Schutzwirkung der Influenzaimpfung aus Surveillance-Daten]. Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz 2006;2006(Feb).
11. Farrington CP. Estimation of vaccine effectiveness using the screening method. Int J Epidemiol. 1993;22(4):742-6.
12. Guideline on Dossier Structure and Content for Pandemic Influenza Vaccine Marketing Authorisation Application, EMEA/CPMP/4717/03, European Agency for the Evaluation of Medicinal Products, (2004).
13. Guideline on Submission of Marketing Authorisation Applications for Pandemic Influenza Vaccines through the Centralised Procedure, EMEA/CPMP/4986/03, European Agency for the Evaluation of Medicinal Products, (2004).

LABORATORY DIAGNOSIS OF LYME BORRELIOSIS AT THE PORTUGUESE NATIONAL INSTITUTE OF HEALTH (1990-2004)

I Lopes de Carvalho, MS Núncio

Lyme borreliosis is considered to be an emerging infection in some regions of the world, including Portugal. The first Portuguese human case of Lyme borreliosis was identified in 1989. Since 1999, this disease is considered a notifiable disease (DDO) in Portugal, but only a few cases are reported each year, which does not allow consistent analysis of risk factors and the impact on public health. In this study the authors analyse the data available at the Centre for Vectors and Infectious Diseases Research (CEVDI) laboratory, at the Instituto Nacional de Saúde Dr. Ricardo Jorge (National Institute of Health, INSA) during the past 15 years (1990-2004) and evaluate them against the registry of national reported cases (1999-2004). Serological tests were the basis for laboratory diagnosis. Data on year of diagnosis, sex, age, geographical origin and clinical signs are available for 628 well documented Portuguese positive cases. The number of cases per year varied between 2 and 78, with the highest number of cases reported in 1997. Of the positive cases, 53.5% were female and the age group most affected was 35-44 years old. Neuroborreliosis was the most common clinical manifestation (37.3%). Human cases were detected in 17 of the 20 regions of Portugal, and the highest number of laboratory confirmed cases were from the Lisbon district. The comparison of the number of notified cases and the number of positive cases confirmed by our laboratory show that Lyme borreliosis is clearly an underreported disease. Due to the scattered distribution of the positive cases and the low prevalence of the tick species *Ixodes ricinus*, the most effective prevention measure for Lyme borreliosis in Portugal is education of the risk groups on how to prevent tick bites.

Euro Surveill. 2006;11(10): 257-60 Published online October 2006
Key words: laboratory diagnosis, Lyme borreliosis, Portugal.

Introduction

Lyme borreliosis has been reported throughout Europe where it is the most common tickborne infection, as it is in the United States [1].

Clinically, it shows up as a multisystemic disease, presenting dermatological, rheumatic, neurological and cardiac manifestations.

The first reported human case of Lyme disease in Portugal was identified in 1989 [2]. Diagnosis is preformed by the Centre for Vectors and Infectious Diseases Research (CEVDI) at the Instituto Nacional de Saúde Dr. Ricardo Jorge (National Institute of Health, INSA), using several techniques including culture, PCR, and antibody detection. The first strains of *Borrelia burgdorferi* sensu lato were isolated from ticks captured in the south of Portugal [3] and the study showed that they belong to a new species, *B. lusitaniae* [4]. Subsequent studies confirm the presence of several *B. burgdorferi* s.l. species (*B. lusitaniae*, *B. afzelii*, *B. garinii* and *B. valaisiana*) in ticks and the infection prevalence could vary between: studies have found prevalences of 11.9% (n= 234, collected in several regions), 11.8% (n= 2806, Mafra region), 34.7% (n=206, Grandola region); and 31.2% (n=285, the island of Madeira) [5, 6, 7, 8]. In all the studies made so far, *B. lusitaniae* is the most prevalent borrelia species. Recently, a strain of this species was isolated from a human sample, indicating that it could cause disease in humans [9]. Other species of borrelia, *B. garinii*, *B. afzelii B. burgdorferi* sensu stricto and *B. valaisiana* have already been detected in mainland Portugal and/or the island of Madeira [5, 10]. Since 1999, Lyme borreliosis has been a mandatorily notifiable disease in Portugal, but only a few cases are reported each year, which does not allow consistent analysis of risk factors and the impact on public health. The aim of this study was to contribute to a more precise evaluation of the epidemiological situation of Lyme borreliosis in Portugal, analysing the data available at the CEVDI's laboratory concerning the serological diagnosis of this disease and data available on the statutory notifiable disease register.

Centre for Vectors and Infectious Diseases Research, Instituto Nacional de Saúde Dr. Ricardo Jorge (National Institute of Health), Águas de Moura, Portugal

Material and methods

The results of previous testing of all the sera and/or cerebrospinal fluid (CSF) of patients with clinical suspicion of Lyme borreliosis received at CEVDI's laboratory between 1990 and 2004 were analysed retrospectively. The antibodies were detected by indirect immunofluorescence in-house assay using a strain of *B. garinii* and a cut-off of 1:256 for IgG in sera and 1:4 in CSF were adopted. All borderline and positive samples were confirmed by immunoblot assay also an in-house test, using a strain of *B. garinii*. The interpretation was done according to the European group recommendations [11].

All the positive sera were tested to *Treponema* spp. and rheumatoid factor and all sera with a positive result were considered to be false positives for Lyme borreliosis. The laboratory definition of a positive case is when we detected a seroconversion (significant change in levels of the specific antibodies IgG and/or IgM in two samples), or when we detected a positive titres of specific antibodies in one sample, in patiens with clinical suspicion of Lyme borreliosis [12].

The data from the laboratory confirmed positive cases were compared with the available data from the cases of Lyme borreliosis notified during the period of 1999-2004. The notification of human cases of Lyme borreliosis was done directly by the clinician to the competent health authority, the Direcção Geral de Saúde (DGS), at the health Ministry. The case definition establish to the clinicians by the health authority must fit the following criteria. Confirmed case: Erythema migrans confirmed by laboratory findings or at least one of the late manifestations of Lyme borreliosis with laboratory confirmation.

Results

Among 12 535 biological samples taken for analysis from patients with clinical suspicion of Lyme borreliosis, 628 (5%) tested positive using the EUCALB diagnostic criteria.

In patients with neurological symptoms, CSF was sometimes sent for analysis (21%). Data is available describing the 628 Portuguese patients, 129 of whom tested positive for both CSF and sera. The remaining 499 patients were diagnosed based in the result of sera analysis, with the observation of seroconversion. The number of cases per year varied between 2 and 78, with the highest number of cases in 1997 [FIGURE 1].

The geographical distribution of the positive cases, based in the patients' home addresses, shows that Lyme borreliosis infection has been seen in 17 of the 20 districts of Portugal [FIGURE 2].

There were slightly more female patients (53.5%) than male patients (46.5%).

FIGURE 1

Number of samples received at CEVDI/INSA, and percentage of Lyme borreliosis cases found to be positive, Portugal, 1990-2004

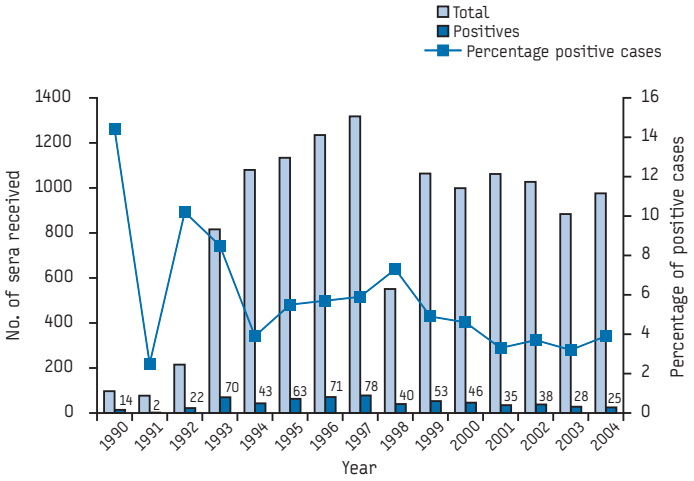
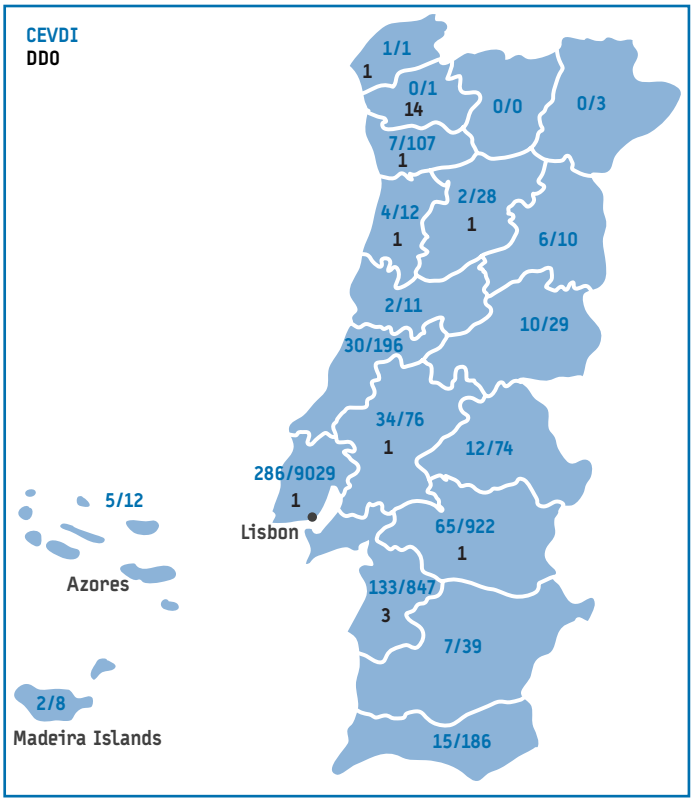


FIGURE 2

Geographical distribution of the positive cases by cases studied at CEVDI (1990-2004) and number of notified cases, Portugal, 1999-2004



The notification forms were frequently not filled in completely, which may have caused some distortion in the data analysis of age and clinical manifestations. Information on patient age was available on only 62.3% of the forms. Analysing the available data, the mean age was 44 years old (range: 2 months to85 years) and the age group most affected was 35-44 years old (21.3%) [FIGURE 3].

No clinical symptoms were reported in 237 (37.7%) of the 628 positive cases [FIGURE 4]. Analysis of the information provided by the physician in the remaining 391 cases showed that the most frequently reported manifestations were neurological, reported in 146 patients (37.3%), followed by nonspecific symptoms in 109 cases (27.8%). Five of the cases with nonspecific symptoms had hepatic symptoms (4.5%), nine had myalgia (8.3%), 19 had optical symptoms (17.4 %) and 76 reported only fever (69.7%).

The evaluation of the number of cases reported nationally between

FIGURE 3

Number of Lyme borreliosis cases by age group, Portugal, 1999-2004

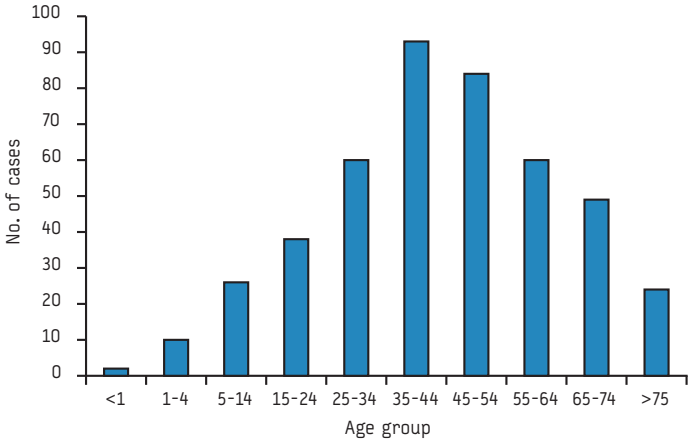
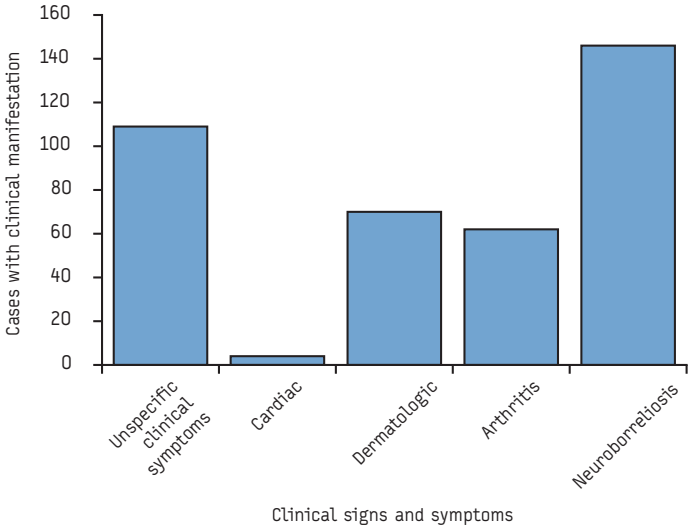


FIGURE 4

Distribution of positive Lyme borreliosis cases, by clinical signs and symptoms, Portugal, 1999-2004



1999 and 2004 (n=24) [13] and the number of positive cases confirmed by our laboratory (n=225) during the same period, show that is clearly an underreported disease. The annual incidence, estimated on the basis of the statutory notifiable disease is 0.04 per 100 000 inhabitants. However, when laboratory data are taken into account, we assume that this rate could be on average 10 times higher, 0.4 per 100 000 inhabitants [FIGURE 5].

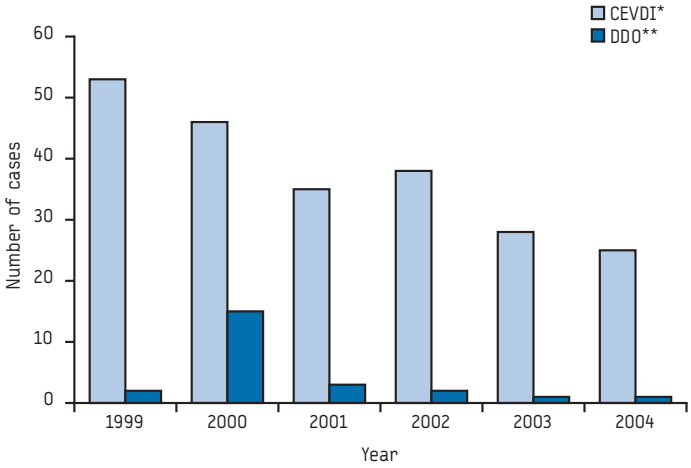
Discussion/Conclusion

Although Lyme borreliosis is a mandatorily notifiable disease in Portugal, the evaluation of CEVDI data concerning human cases of Lyme borreliosis and the number of notified cases during the same period (1999-2004) shows that this disease, like other vector borne diseases, such as boutonneuse fever (the most prevalent tick borne disease in Portugal), is clearly underreported in our country [14]. According to our data, between 1999-2004 we detected an average of 35 new cases of Lyme borreliosis each year. Other diseases such as AIDS and tuberculosis have a bigger impact on public health and the general impression gained is that Lyme borreliosis cases are not considered important enough to notify and to publish.

The major problem of underreporting is the impossibility of realise an epidemiological analysis of Lyme borreliosis in Portugal. For example, according to the notification data, Lyme borreliosis is more common in the Braga district (n=14) in northern Portugal, but when the results are analysed, the only sample from this district to be sent for analysis was negative and the districts showing higher number of confirmed cases are Lisbon (n=286), Setubal (n=133) and Evora (n=65)

FIGURE 5

Number of notified Lyme borreliosis cases and number of cases diagnosed at CEVDI during the period 1999-2004, Portugal



* CEVDI : Centro de Estudos de vectores e doenças infecciosas

** DDO : Doença de Declaração Obrigatória (Mandatory notification of disease)

districts located in central and southern Portugal. It is also possible that the results have been influenced by the proximity of the CEVDI's facilities to these regions, and the hospitals and physicians located at Northern regions of Portugal may usually send their samples to other regional laboratories that also perform these tests. For example, if sufficient samples from Braga district and other northern regions were sent to our laboratory, perhaps the proportion of positive cases in these regions would increase. Also, if we analyse not only the number of positive cases but also the proportion of it, the district of Lisbon is simultaneously the district with a higher number of positive cases and one of the districts with a lower proportion of positive cases.

As the laboratory data are not cross-checked with the official data, it is impossible to know which cases detected at CEVDI were reported to the health authorities, which laboratories performed the laboratory testing and why the clinicians did not notify the positive cases that they diagnose. Also, the fact that some of the positive cases may have been in patients who acquired their infections in districts or countries other than their area of residence should be considered, although patients in Portugal usually use the health facilities in their area of residence. In our experience, fewer than 10 patients during the time period considered (1999-2004) mentioned the possibility that they may have acquired their infection outside of their area of residence. However, the number of positive cases of Lyme borreliosis detected is undoubtedly higher than the number of cases reported. The reported incidence of Lyme borreliosis in Portugal is among the lowest reported in Europe. However, if we analyse the proportion of positive cases detected during this study (5%), we can see that this value is similar to the detected in other studies of seroprevalence in risk populations performed in several European countries [15]. After 15 years performing laboratory diagnosis, even knowing the limitations of laboratory results and being aware that the diagnosis of Lyme borreliosis should be always established by the clinician, these data, could contribute to the better understanding of the epidemiology of Lyme borreliosis in our country. To improve the notification of this disease, a network should be established to link all laboratories performing Lyme borreliosis diagnosis, aggregating all laboratory detected cases. This would allow the competent health authority to compare this information with the cases notified by clinicians and to make a more accurate analysis.

The distribution of positive cases is influenced by clinicians' awareness of vector borne diseases, but the size of the *I. ricinus* population and the prevalence of infected ticks are also contributory factors to the incidence of the disease. The estimated annual incidence for Lyme borreliosis in Portugal is 0.04 per 100 000 inhabitants. A higher estimated can be obtained if we take laboratory data into consideration (0.4 per 100 000 inhabitants). However, as other laboratories also perform this test, it seems likely that underreporting is even higher, and consequently the true incidence of Lyme borreliosis in Portugal should be similar to the published values detected in other countries such as Scotland (0.6 per 100 000 inhabitants), United Kingdom (0. 3 per 100 000 inhabitants) and much lower than that detected in countries such as France (16 per 100 000 inhabitants), Germany (17.8-25 per 100 000 inhabitants), Bulgaria (55 per 100 000 inhabitants), Slovenia (120 per 100 000 inhabitants) and Austria (130 per 100 000 inhabitants) [1, 16, 17]. It would be interesting to compare the incidence detected in Portugal with geographical areas such as southern Spain, Morocco, Tunisia and Algeria but, to our knowledge, there are no available data published concerning the incidence of the disease in the these regions. All these areas share with Portugal some eco-epidemiological aspects such as vector population abundance and prevalence of infection, lack of information about the vertebrate reservoirs and the presence of the different *Borrelia burgdorferi s.l.* strains with particular relevance to *B. lusitaniae*., During the past five years, the number of human cases detected each year at CEVDI seems to have stabilised at approximately thirty five cases per year. This reduction may perhaps be explained by the increased number of other laboratories performing this diagnosis. Also, due to the diversity of the possible clinical presentations of Lyme borreliosis that may be confused with other aetiologies, the benign course of the majority of clinical cases, and the usually very positive response to the timely application of antibiotics, a large percentage of cases are never sent to the laboratory to confirm a clinical diagnosis. In this study, the positive cases which mention erythema migrans are very rare, probably because many clinicians are aware that this stage frequently does not evoke an antibody response and that laboratory confirmation cannot be expected, and therefore do not request a laboratory confirmation of their clinical diagnosis. Considering that the incidence of Lyme borreliosis is directly linked to the density of the tick vector *I. ricinus*, and knowing that this species is not found in high tick population densities, we would expect the incidence of Lyme borreliosis to also be low. However, we should also consider the *I. ricinus* **has been found to exist** all over the country, but due to differing environmental characteristics, especially climate, distribution is not uniform throughout Portugal but focused in some regions where conditions are more suited to the survival of this tick species, and where this species predominates, achieving high population density.

In the absence of publications describing clinical cases, the information available in the clinical forms is very useful because the analysis allows us to clarify some epidemiological aspects such as risk factors concerning age, sex and geographic localisation.

Other information that would help laboratory diagnosis, such as symptom onset date, information about occurrence of recent tick bites, and recent trips, are frequently unavailable. This is why collaboration and exchange of information between clinicians and laboratories are so important.

Research concerning the eco-epidemiology of Lyme borreliosis in Portugal has so far been slow to advance, and it is difficult to study the impact and risk factors. However this knowledge is essential if we are to implement adequate prevention programmes, which are currently considered the best approach to solving the problem of vectorborne diseases. Sixteen years after the report of the first human case of Lyme borreliosis in Portugal this is still a poorly understood disease in Portugal. Due to the scattered distribution of the positive human cases and the scattered nature of the tick vector distribution throughout Portugal, the most effective prevention measure for Lyme borreliosis in Portugal is probably educating risk groups about how to avoid tick bites.

Acknowledgements

The authors wish to thank to Dr. Joseph Piesman, CDC, USA, and Dr. Teresa Paixão, INSA, Portugal, for helpful editing on this manuscript.

References

1. O'Connell S, Granstrom M, Gray JS, Stanek G. Epidemiology of European Lyme Borreliosis. Zent bl Baketeriol. 1998; 287: 229-240.
2. David de Morais JA, Filipe AR, Núncio MS. Doença de Lyme em Portugal. Caso clínico. Rev Port Doenç Infec.1989;12:261-76.

→→→

3. Núncio MS, Péter O, Alves, MJ, Bacellar F, Filipe AR. Isolamento e caracterização de borrélias de *Ixodes ricinus* em Portugal. Rev Port Doenç Infec. 1993;16:175-9.
4. Le Flèche A, Postic D, Girardet K, Péter O, Baranton, G. Characterization of *Borrelia lusitaniae* sp. nov. by 16S ribosomal DNA sequence analysis. Int J Syst Bacteriol. 1997; 47:921-925.
5. Núncio MS, Schouls L, van de Pool I, Almeida V, Filipe AR. "Ecoepidemiology of Borrelia spp. in Madeira Island, Portugal". Proceedings of the VIth International Potsdam Symposium on Tick-borne diseases; 2001 Apr 26 – 27; Berlin, Germany.
6. Núncio MS. Contribuição para o estudo de borrélias e borreliose de Lyme em Portugal. [dissertation]. Lisbon: Lisbon University; 2002.
7. Baptista S, Henriques G, Aires T, Nicholson M, Walker H, Kurtenbach K, et al.. *Ixodes ricinus* in Portugal-a five-year study on seasonal dynamics and infection of *Borrelia burgdorferi* sensu lato in a suitable habitat. Proceedings of the 10th International Conference on Lyme borreliosis and Other Tick.-Borne Diseases; 2005 Sep 11-15; Vienna, Austria.
8. Quaresma A, Baptista S, Santos-Reis M, Vitorino L, Collares-Pereira M. *Borrelia lusitaniae* infection in Grândola region (Portugal): new eco-epidemiological data in potencial vectors and sylvatic reservoirs. Proceedings of the 10th International Conference on Lyme borreliosis and Other Tick.-Borne Diseases; 2005 Sep 11-15; Vienna, Austria.
9. Collares-Pereira M, Couceiro S, Franca I, Kurtenbach K, Schafer SM, Vitorino L, et al. First Isolation of *Borrelia lusitaniae* from a Human Patient. J Clin Microbiol. 2004;42(3):1316-8.
10. Baptista S, Quaresma A, Aires T, Kurtenbach K, Santos- Reis M, Nicholson M, et al. Lyme borreliosis spirochetes in questing ticks from mainland Portugal. Int J Med Microbiol. 2004; 293 Suppl 37:109-16.
11. Robertson J, Guy E, Andrews N. et al. A European multicenter study of immunoblotting in serodiagnosis of Lyme borreliosis. J Clin Microbiol. 2000;38:2097-102.
12. European Union Concerted Action on Lyme Borreliosis [updated 2006 Apr; cited 2006 March]. Available from: http://www.oeghmp.at/eucalb/diagnosis_clinical-features-ds.html.
13. Direcção Geral de Saúde [updated 2006 April; cited 2006 March]. Available from: http://www.dgsaude.pt.
14. Sousa R, Nobrega SD, Bacellar F, Torgal J. Sobre a realidade da febre escaro-nodular em Portugal. Acta Med Port. 2003;16:429-436.
15. World Health Organization (WHO). [updated 2006 April; cited 2006 March]. The vector-borne human infections of Europe. Their distribution and burden on Public Health. 2004. Available from: http://www.euro.who.int/document/e82481.
16. World Health Organization (WHO). Report of WHO workshop on Lyme Borreliosis Diagnosis and Surveillance, Warsaw, Poland. 1995 June. Report No.: WHO/CDS/VPH/95.141-1.
17. Mehnert WH, Krause G. Surveillance of Lyme borreliosis in Germany, 2002 and 2003. Euro Surveill. 2005;10(4):83-5. Available from: www.eurosurveillance.org/em/v10n04/1004-223.asp. 2005.

ORIGINAL ARTICLES

Surveillance report

CASE-CONTROL STUDY FOR RISK FACTORS FOR Q FEVER IN SOUTHWEST ENGLAND AND NORTHERN IRELAND

HJ Orr[1], H Christensen[1], B Smyth[2], DAB Dance[1], D Carrington[3], Ian Paul[3]
JM Stuart[1] on behalf of the South West Q Fever Project Group*

Q fever (*Coxiella burnetti*) is thought to account for 1% (700 cases) of community acquired pneumonia in the United Kingdom each year, and can result in serious complications such as endocarditis. Although outbreaks have frequently been reported worldwide, the causes are often not clearly identified and there have been few studies of risk factors in sporadic cases.

We conducted a matched case-control study. Cases of acute Q fever in people aged over 15 years in southwest England and Northern Ireland were identified from January 2002 to December 2004. Controls were matched for age, sex and the general practice at which they were registered. Questionnaires asking about contact with animals, and leisure and work activities, were posted to cases and controls.

Questionnaires were completed by 39/50 (78%) of the cases and 90/180 (50%) of the controls. In the single variable analysis, occupational exposure to animals or animal products was the only risk factor associated with cases at the 5% level (P=0.05, odds ratio (OR) 3.4). Long term illness appeared to be significantly protective (P=0.03, OR 0.3). In multivariable analysis the strength of association between occupational exposure and illness remained high (OR 3.6, 95% confidence interval (CI) 0.9 to 14.8) and smoking emerged as a possible risk factor.

This is the first case-control study to identify occupational exposure to animals or animal products as the most likely route of infection in sporadic cases as opposed to outbreaks.

1. Health Protection Agency South West, Stonehouse, Gloucestershire, England, United Kingdom
2. Communicable Disease Surveillance Centre Northern Ireland, Belfast, Northern Ireland, United Kingdom
3. Health Protection Agency South West Regional Laboratory, Bristol, England, United Kingdom

Euro Surveill. 2006;11(10): 260-2 Published online October 2006

Key words: Coxiella, Q fever, occupational exposure, case-control studies.

Introduction

Q fever is a zoonotic infection caused by the rickettsial organism *Coxiella burnetii*. In the United Kingdom it is most commonly carried, often asymptomatically, in sheep, cattle and goats, and is transmitted to humans by inhalation of aerosols. High concentrations of the organism are found in the placenta/placental fluids. Coxiellae can remain viable for months in the environment. The disease occurs most frequently in humans exposed to farm animals or in areas where animal products are handled [1]. Retrospective serological studies have shown evidence of high rates of past infection in farm workers, which suggests that many cases are often not identified at the time of illness [2].

The major clinical manifestations of Q fever are respiratory, cardiac and hepatic, although symptoms are often non-specific. *C. burnetii* is thought to account for 1% (700 cases) of community-acquired pneumonia in the UK each year, and although more serious complications such as endocarditis are rare, they do represent a significant burden of disease [3].

Although outbreaks have frequently been reported worldwide, the causes have often not been identified [4] and we have only been able to

find one previous case-control study in the literature determining risk factors in sporadic cases [5]. The highest incidence of cases in England is consistently reported from the southwest and in an epidemiological review this rural region reported one third of all cases in England and Wales [3]. Northern Ireland reports even higher rates of Q fever per 100 000 population, with between 21 and 75 cases per year since 1990 [6].

Methods

We collaborated with laboratories in southwest England and Northern Ireland to identify cases of Q fever for a matched case-control study to determine risk factors for sporadic infection. A required sample size of 43 cases was estimated using Epi Info. This size was based on a case-control ratio of 1:3, with 95% confidence and 80% power to detect an OR of 3.

Cases in patients resident in southwest England and Northern Ireland aged 16 years and over between 1 January 2002 and 31 December 2004 were identified by local laboratories and confirmed as acute by the Health Protection Agency Regional Laboratory in Bristol on the basis of a history of acute illness and the detection of specific immunoglobulins to *C. burnetii* phase 2 antigens in human sera (Coxiella burneti-Spot IF, bioMerieux® sa, France, using sheep anti-human IgG and IgM conjugates supplied by The Binding Site Ltd,UK), to detect either a fourfold rise in IgM and/or IgG on paired sera, or IgM and IgG titres ≥ 640.

Initially, three controls of the nearest age, same sex and registered with the same general practice were selected for each case (general practices in the UK cover an average population of 6000 people in the same geographical area). In 2003, the study duration was extended from two to three years and the number of controls per case increased to five, because case numbers had been lower than expected and there had been poor response rates, especially from controls.

Postal questionnaires, including questions about contact with animals, consumption of pasteurised/unpasteurised milk, and leisure and work activities within the four weeks before illness (past four weeks for controls), were sent to cases and controls. Non-responders were sent one reminder after four weeks. Data were entered onto a Microsoft Access database. Where responses were not received and there was evidence of individuals only responding where the answer was 'yes', a 'no' response was entered for data that were missing. 'Don't know' responses were excluded from the analysis. Single variable conditional logistic regression was carried out using Stata (v8.2). Variables with P<0.2 in the single variable analysis were then included in a multivariable conditional logistic regression analysis. The study received approval from the appropriate local ethics committees.

Results

Questionnaires were returned by 39/50 (78%) of the cases identified with acute Q fever and 90/180 (50%) of the controls. After excluding records without case or control matches, data from 34 cases and 77 controls were available for analysis, a ratio of 1:2.3. The age range for both cases and controls was 20-73 years (mean 47 and 48 years respectively). Twenty five (73.5%) of the case patients were men, and 9 (26.5%) were women. Over the three year study period, the majority of cases (63.6%) were reported between the months of March and June and were from a rural location (29/34 cases lived on a farm or within 3 miles of farmland). There was a clustering of four cases within a 10 mile (16 km) radius in one rural area. Further investigation did not identify any specific exposure common to these cases.

All cases reported sweating and/or a fever, 28 (82.4%) had a headache, 27 (79.4%) had respiratory symptoms (shortness of breath and/or cough), 27 (79.4%) experienced weight loss, 23 (67.7%) had joint pain and 20 (58.8%) had chest pain. Three (8.8%) had jaundice and 8 (28.6%) patients experienced other symptoms including vomiting, blurred vision, dizziness, extreme thirst, 'sore kidneys' and increased sensitivity of senses (taste and smell). The median duration of illness was 21 days. Twelve patients (35.2%) said they were still unwell at the time of completing the questionnaire.

In the single variable analysis, occupational exposure to animals or animal products was the only risk factor associated with cases at the 5% level (P=0.05, OR 3.4, 95%CI 1.0 to 11.8) [TABLE 1]. Long term illness

Table 1

Single variable analysis of risk factors for Q fever, southwest England and Northern Ireland, January 2002 - December 2004

Risk factor		Cases exposed (%) (n=34)	Controls exposed (%) (n=77)	Matched OR (95% CI)	P value
Close contact with sheep		4 (11.8)	10 (13.0)	0.8 (0.2 to 2.7)	0.66
Close contact with cows[1]		2 (6.1)	4 (5.3)	1.5 (0.3 to 8.4)	0.63
Close contact with pigs		3 (8.8)	1 (1.3)	6.9 (0.7 to 70.9)	0.11
Close contact with goats		2 (5.9)	2 (2.6)	2.8 (0.4 to 20.4)	0.32
Contact with pets (Cats, dogs, birds and other animals)		31 (91.2)	65 (84.4)	1.6 (0.4 to 6.1)	0.50
Occupational exposure to animals/animal products (e.g. veterinarian, butcher, arable farmer)		9 (26.5)	8 (10.4)	3.4 (1.0 to 11.8)	0.05
Consumption of unpasteurised dairy products (milk or cheese)		1 (2.9)	5 (6.5)	0.5 (0.1 to 4.2)	0.51
Proximity to nearest farmland[2]	0	5 (17.2)	5 (7.9)	0.6 (0.2 to 1.7)*	0.38
	0 – 1.6 km	18 (62.1)	49 (77.8)		
	1.6 – 5 km	6 (20.7)	9 (14.3)		
Handling/use of organic matter (Straw, hay, manure and/or compost)		15 (44.1)	24 (31.2)	1.8 (0.8 to 4.1)	0.18
All river/lake water contact (Swimming, water sport and other contact in a river/lake water)		9 (26.5)	15 (19.5)	1.6 (0.6 to 4.7)	0.36
Other outdoors activities (Country walking, horseriding, gardening and other outdoors activities)		27 (79.4)	56 (72.7)	1.4 (0.6 to 3.7)	0.46
Long-standing illness/medical condition[3]		8 (24.2)	34 (46.6)	0.3 (0.1 to 0.9)	0.03
Smoking status	Never smoked	7 (20.6)	35 (45.5)	1	0.11
	Ex-smoker	17 (50.0)	27 (35.1)	2.6 (1.0 to 7.1)	
	Smoker	10 (29.4)	15 (19.5)	2.4 (0.7 to 7.7)	

* For each additional increase in category

1 Case n = 33; Control n = 76 2 Case n = 29; Control n = 63 3 Case n = 33; Control n = 73

Table 2

Multivariable analysis of risk factors for Q fever, southwest England and Northern Ireland, January 2002 – December 2004

Risk factor		Matched OR (95% CI)	P value
Long-standing illness/ medical condition		0.2 (0.05 to 0.7)	0.006
Smoking status	Never smoked	1	0.03
	Ex-smoker	4.5 (1.3 to 15.2)	
	Smoker	2.5 (0.7 to 9.6)	
Occupational exposure		3.6 (0.9 to 14.8)	0.06

appeared to be significantly protective (P=0.03, OR 0.3, CI 0.1 to 0.9). In the multivariable analysis, long term illness remained significantly protective, and smoking emerged as a possible risk factor [TABLE 2]. Although the P value increased from 0.05 to 0.06 when added to the multivariable model, the strength of association between occupational exposure and illness remained high (OR 3.6, 95% CI 0.9 to 14.8).

Discussion

Occupational exposure has been documented as a risk for Q fever in case series and outbreaks since the organism was first discovered in 1937 [7]. As far as we are aware, this is the first case-control study to identify it as the most likely route of exposure in sporadic cases. The temporal distribution of Q fever cases between March and June is similar to that seen in other studies in the UK and Spain, consistent with increased exposure to *C. burnetii* after animal births in spring [3, 8].

As expected, the majority of cases reported non-specific symptoms such as fever and sweating. However, cough and shortness of breath were consistent with respiratory tract involvement, the most common manifestation of Q fever in the UK. The low proportion of cases with jaundice supports the observation that hepatitis is not a common presentation in the UK [3], although patients with mild or granulomatous hepatitis would not necessarily have been jaundiced. Other countries have reported a higher proportion of cases with hepatitis, up to 40% of acute cases in one study in France [9].

The incidence of Q fever in the study regions fell almost as soon as the study started. It is possible that this was due to the effects of foot and mouth disease that occurred in England in 2001, just before the study commenced. Also, a low response rate, especially among controls, resulted in some variables being dropped from the analysis, and misclassification bias may have been introduced into the analysis by assigning missing values to 'no'. It is also possible that other risk factors were not included in the study, such as exposure to rats, which have been identified as an important reservoir for *C. burnetii* in the UK [10].

The apparent protective effect of long term illness was surprising, but could reflect lower outdoor exposure to rural environments in people with long term illness. Apart from occupational exposure and a possible link with smoking, other risk factors studied did not reach statistical significance at the 5% level. Occupational exposure could explain at most a quarter of cases, but we did not expect to have sufficient statistical power to identify risk factors below an odds ratio of 3. Further studies to elucidate risk factors for sporadic Q fever should plan for a larger sample size. In the meantime, prevention and control measures should be directed at reducing the risk of occupational exposure [11].

* **Members of the South West Q Fever Project Group:**
David Dance (chairman), David Carrington, John Hartley, Simon Hill, Graham Lloyd, Conall McCaughey, Marina Morgan, Isabel Oliver, Hilary Orr, Mike Smith, Robert Smith, Brian Smyth, James Stuart

References

1. Sawyer LA, Fishbein DB, McDade JE. Q fever: current concepts. Rev Infect Dis. 1987;9(5):935-46.
2. Thomas DR, Treweek L, Salmon RL, Kench SM, Coleman TJ, Meadows D, et al. The risk of acquiring Q fever on farms: a seroepidemiological study. Occup Environ Med. 1995;52(10):644-7.
3. Pebody RG, Wall PG, Ryan MJ, Fairley C. Epidemiological features of Coxiella burnetii infection in England and Wales: 1984 to 1994. Commun Dis Rep CDR Rev. 1996;16;6(9):R128-32.
4. Cutler SJ, Paiba GA, Howells J, Morgan KL. Q Fever – a forgotten disease? Lancet Infect Dis. 2002;2(12):717-8.
5. Gardon J, Heraud J, Laventure S, Ladam A, Capot P, Fouquet E, et al. Suburban Transmission of Q Fever in French Guiana: Evidence of a Wild Reservoir. J Infect Dis. 2001;184(3):278-84.
6. 2000 Review of Communicable Diseases. Communicable Disease Surveillance Centre (Northern Ireland). Available from: http://www.cdscni.org.uk/publications/AnnualReports/pdf/Review%20of%20Communicable%20Diseases%202000.pdf.
7. Derrick EH. «Q» fever, a new fever entity: clinical features, diagnosis and laboratory investigation. Med J Aust. 1937; 2:281-99. Reprinted in Rev Infect Dis. 1983;5(4):790-800.
8. de Alarcon A, Villanueva JL, Viciana P, Lopez-Cortes L, Torronteras R, Bernabeu M, et al. Q fever: epidemiology, clinical features and prognosis. A study from 1983 to 1999 in the South of Spain. J Infect. 2003;47:110-6.
9. Raoult D, Tissot-Dupont H, Foucault C, Gouvernet J, Fournier PE, Bernit E, et al. Q Fever 1985-1998 Clinical and Epidemiologic Features of 1,383 infections. Medicine (Baltimore). 2000; 79:109-23.
10. Webster JP, Lloyd G, Macdonald DW. Q fever (Coxiella burnetii) in wild brown rat (Rattus norvegicus) populations in the UK. Parasitology. 1995;110 (Pt 1):31-5.
11. Centers for Disease Control and Prevention [homepage on the Internet], Atlanta. Q fever [last reviewed 2003 Feb 13; cited 2006 Jul 7]. Available from: http://www.cdc.gov/ncidod/dvrd/qfever/

A PSEUDO-OUTBREAK OF HUMAN A/H5N1 INFECTIONS IN GREECE AND ITS PUBLIC HEALTH IMPLICATIONS

G Spala[1], T Panagiotopoulos[1,2], N Mavroidi[1], X Dedoukou[1], A Baka[1], P Tsonou[1], P Triantafyllou[3], A Mentis[4], V Kyriazopoulou[4], A Melidou[4], S Tsiodras[1,5]

The recent wide geographic spread of the highly pathogenic avian influenza A/H5N1 virus has important public health implications. Several wild migratory birds were confirmed to be infected with avian influenza A/H5N1 in Greece in February and March 2006. The aim of this paper is to report data from potential H5N1 human cases that presented to local hospitals during this period with a respiratory infection and expressing concern about exposure to avian influenza.

A case-control investigation was conducted that included case identification with the use of a structured definition, review of epidemiological and clinical characteristics and molecular testing for avian influenza A/H5N1. The setting was the entire country of Greece during February and March 2006. The main outcomes were rates of possible cases (meeting both a clinical and an epidemiological criterion) and clinical or epidemiological characteristics differentiating them from potential cases that met either one of the criteria of a possible case, but not both.

Twenty six potential patients (81% of whom met a clinical criterion, and 39% of whom met an epidemiological criterion) presented and most (85%) were admitted in local hospitals during the period of interest. The majority of cases (85%) were observed in northern Greece where most of the confirmed A/H5N1 avian cases were documented. Five of the 26 evaluated patients met the definition of a possible case. These clustered within the early period of confirmed A/H5N1 cases in wild migratory birds (P=0.05). Molecular testing was negative for all possible cases. Application of a revised case definition constructed according to newer European Union guidance resulted in the exclusion of two possible cases.

Several potential A/H5N1 human cases were recently identified in Greece. Both the timing of identification and the geographical location of potential cases suggest an increased awareness on the part of the general public, as well as poor interpretation of the case definition by the clinicians.

Euro Surveill. 2006;11(11): 263-7 Published online November 2006
Key words: Avian influenza, H5N1, suspect cases, possible cases, case definition, surveillance.

Introduction

The recent wide geographic spread of the highly pathogenic avian influenza A/H5N1 virus in the avian population has important public health implications. This spread has been currently attributed to the long distance carriage of the virus by migratory birds from Asia to Europe; however, this is still an issue of scientific debate [1]. The virus has affected birds in several European countries [(2,3] and was identified in other hosts besides avian species, including cats, dogs and stone martens [3-8]. An increased risk has been recognised for humans involved in commercial poultry farming [9-12]. Data on suspect human cases in European countries are scarce [13,14]. In this report we describe data on potential A/H5N1 human cases examined in Greek hospitals during the recent epizootic of confirmed migratory bird cases found infected in Greece (February-March 2006), according to an initial and a revised definition for a possible case.

1. Department of Epidemiological Surveillance and Intervention, Hellenic Center for Disease Control and Prevention, Athens, Greece
2. National School of Public Health, Athens, Greece
3. Department of Avian Pathology, Ministry of Rural Development and Food, Athens, Greece
4. National Reference Laboratories for Influenza, Greece
5. 4th Academic Department of Internal Medicine, University of Athens Medical School, Athens, Greece

Methods

Initial case definition

A specific standard operating procedure was in place for all suspect bird or human cases during the period from 1 February 2006 to 27 March 2006 (this period includes 14 days that were added after the date of last identification of dead migratory birds in Greece i.e. 13 March; the two weeks equal two times the incubation period). These procedures were put in place by the Hellenic Center for Diseases Control and Prevention (HCDCP -also known as KEELPNO), the Ministry of Health, and the Department of Avian Pathology in the Ministry of Rural Development and Food, Greece. All cases fulfilling a clinical or an epidemiological criterion were considered potential cases, whereas cases meeting both criteria met the case definition of a possible case [TABLE 1]. The whole country of Greece was considered an affected area, despite lack of confirmed human or poultry cases.

Revised case definition

The definition of a possible case was revised [TABLE 1] after the publication of the 30 March 2006 guidance document from the European Centre for Disease Prevention and Control (ECDC) [15]. Greek prefectures with suspect or confirmed A/H5N1 cases in birds and their neighbouring prefectures were considered to be affected areas [TABLE 1].

Standard operating procedure

All human cases were reported to the HCDCP's Department of Epidemiological Surveillance and Intervention. The HCDCP prepared notification forms for each case with all relevant epidemiological and clinical information. Laboratory investigation for both seasonal influenza (types A and B) and the highly pathogenic avian influenza A/H5N1 virus was conducted for all potential cases by RT-PCR and/or real time PCR in the National Influenza Reference Centres. If antiviral medications were deemed necessary, they were prescribed immediately by the treating physician from the local or national stockpile. Antivirals were discontinued if the laboratory investigation was negative. The patients admitted for observation were admitted to hospital isolation rooms specifically reserved for such cases in each hospital. Most tertiary care hospitals in Greece have had suitable negative pressure rooms since the time of the SARS global epidemic in 2003 or the Athens 2004 Olympic Games. Specific guidance documents were issued by the HCDCP for handling and admission of potential cases in such isolation rooms, to prevent transmission. However if the local hospital did not have negative pressure wards, the guidelines were to admit potential cases to single bed isolation rooms with appropriate precautions. For suspect bird cases, a standard operating procedure was enforced by the Ministry of Rural

Table

Comparison between initial and revised case definitions for possible influenza A/H5N1 human cases in Greece, February-March 2006

INITIAL CASE DEFINITION FOR A POSSIBLE INFLUENZA A/H5N1 HUMAN CASE[1]		
Clinical criteria		**Epidemiological criteria**
Temperature ≥38 °C **AND** respiratory symptoms including cough or shortness of breath **OR** death from unexplained respiratory illness	**AND**	Travel or residence 7 days before onset of symptoms to one of the areas affected by avian influenza A/H5N1 **AND** close contact (≤1 metre) with live or dead domestic fowl or wild birds or swine in any place, including bird markets. **OR** a) close contact with another case of serious respiratory disease or unexplained death coming from the affected areas, b) the case was part of cluster of cases of unexplained serious respiratory disease in a healthcare worker, c) the case is a laboratory worker with potential exposure to influenza A/H5N1 virus.
REVISED CASE DEFINITION FOR A POSSIBLE INFLUENZA A/H5N1 HUMAN CASE[1,2]		
Temperature ≥38 °C **AND** acute respiratory infection **OR** death from acute unexplained respiratory illness		At least one of the following exposures (a, b, c) within 7 days prior to onset of symptoms: a) *Human contact*: Having been in close contact (within one metre) of a person reported as probable or confirmed case of influenza A/H5N1 b) *Laboratory contact*: Having worked in a laboratory where there is potential exposure to influenza A/H5N1 c) *Contact with poultry or wild birds* (not game birds): Resides in or has visited an area of Greece or another country where influenza A/H5N1 is currently suspected or confirmed **AND** has been in contact with sick or dead domestic poultry or wild birds (not game birds) in the affected area **OR** has been in an environment (residential or systematic breeding) where sick or dead domestic poultry have been reported in the previous six weeks in the affected area The affected area in Greece was defined as a prefecture with suspect or confirmed cases of A/H5N1 in birds (domestic or wild) and their neighbouring prefectures

1. HCDCP : Hellenic Centre for Diseases Control and Prevention
2. Major differences are underlined in the revised case definition (see text for details)

Development and Food's Department of Avian Pathology. Laboratory testing of the bird cases was performed at the National Veterinary Reference Laboratory and confirmatory testing was performed at the Weybridge World Health Organization and European Community Reference Laboratory in the United Kingdom.

Greece has a standard sentinel surveillance system collecting data for influenza-like illness (ILI) and laboratory confirmed influenza from primary care centers and private physicians (approximately 200 physicians). Data from this system were compared for the entire country and between prefectures affected and not affected by confirmed H5N1 bird cases.

Statistical analysis

Data on subjects meeting the definition of a possible case were compared to data from potential cases meeting either of the criteria of a possible case but not both. Data compared included dates of presentation (before or after 15 February), rates of admission, and variances in geographical characteristics. The cases were classified according to which of the 51 prefectures and the 13 geographical regions of Greece was affected and furthermore if they were from northern or southern Greece. The Mann-Whitney procedure was used to compare non-parametric data between the two groups. The entire dataset was re-examined with the application of the revised HCDCP definition.

Results

During the period from 1 February to 27 March, 2006, 33 migratory birds were identified as being infected with highly pathogenic avian influenza A/H5N1 virus [FIGURE 1]. During the same period, 26 potential patients [48.7% male, median age 30 years, range 17.5-45.8 years] presented to local hospitals throughout Greece [FIGURES 1, 2] with respiratory tract infection symptoms and expressing concern about possible exposure to highly pathogenic avian influenza. Nineteen potential cases (73.1%) reported exposure to birds but only 10 of these 19 cases (52.6%) met the epidemiological criterion regarding the time of exposure (7 day interval). Thirteen potential cases (50%) reported exposure to wild migratory birds and 6 (23.1%) contact with domestic live or dead poultry while 7/26 (26.9%) had no exposure to birds. Only one patient was exposed to a bird (a dead swan) that was later confirmed to be A/H5N1 positive. Six of the 26 patients (23.1%) were hunters or were otherwise exposed to game meat. Seven patients had no exposure to birds. Four had travelled from A/H5N1 affected areas (two from Turkey and two from Nigeria), but did not report of exposure to local fowl or wild birds. Three reported exposure to surfaces potentially contaminated with bird droppings. Twenty two of the 26 potential cases (84.6%) were admitted to isolation units in regional hospitals for observation. All potential cases were submitted to molecular testing that disclosed negative results for influenza A/H5N1 and positive results for influenza B in 3 cases. One patient (3.8%) received treatment with oseltamivir that was discontinued after the results of the molecular testing.

Twenty one of the 26 potential H5N1 patients (80.8%) met the clinical criterion (the remaining five did not have fever but had other respiratory infection symptoms) and 10/26 (38.5%) the epidemiological criterion for a possible case [FIGURE 3]. Five of the 26 cases (19.2%) met both criteria and were classified as possible cases according to the definition [FIGURE 3]. The rest 21/26 (80.8%) cases were potential cases meeting either of the criteria of a possible case but not both [FIGURE 3]. Sixteen from these 21 (76.2%) cases met the clinical criterion and 5/21 (23.8%) met the epidemiological criterion. Subjects meeting the criteria of a possible case differed from the rest only for the epidemiological criterion [5/5 (100%) versus 5/21 (23.8%), P=0.004] whereas for the clinical criterion the difference was not significant (P=0.5). There was no difference between the two groups regarding age (P=0.5), sex (P=0.6), exposure to wild migratory avian species (3/5 (60%) versus 10/14 (71.4%) respectively) or involvement in hunting activities (P=0.6). All five patients meeting the definition for a possible case and the majority (17/21, 81%) of the rest were admitted to the local hospital for observation (P=0.54 for between group comparison). The median duration of stay was short (2 days, IQR: 1.5-3). Most (14/21, 66.7%) of the potential cases that met only one criterion occurred after 15 February 2006, whereas patients meeting the possible case definition clustered before 15 February 2006 (P= 0.05 for between group comparison).

FIGURE 1

Avian influenza A/H5N1 cases in birds and potential human cases in Greece, February-March 2006

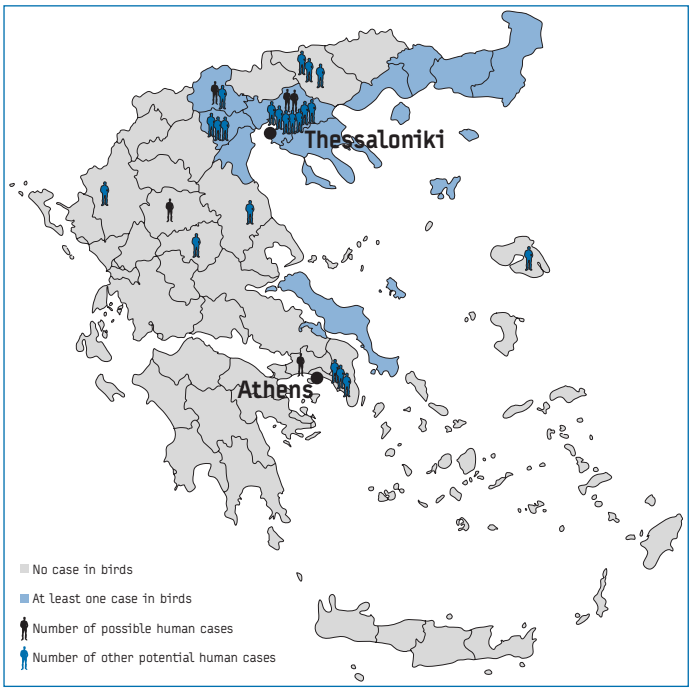
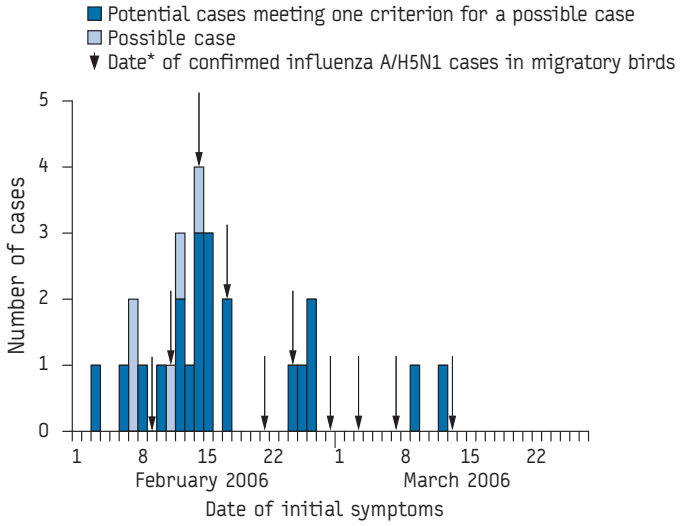


FIGURE 2

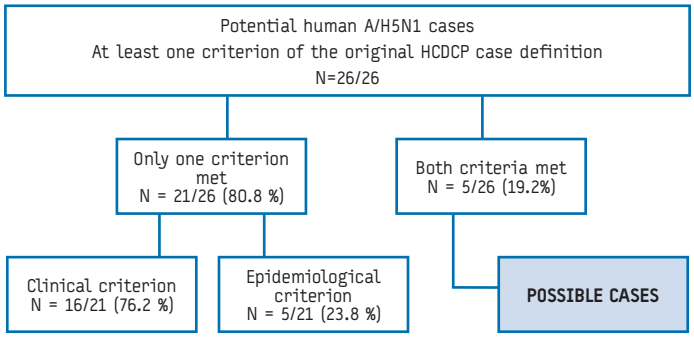
Potential human A/H5N1 cases over time and dates of A/H5N1 in birds, Greece, February-March 2006



* Date of H5 testing completion (all later confirmed to be H5N1 positive)

FIGURE 3

A flow chart showing evaluated cases and their classification according to the original definition of a possible case, Greece



Note : The original definition is the one from the Hellenic Centre for Diseases Control and Prevention (HCDCP)

Human A/H5N1 cases were suspected in 9 of the 51 (17.6%) prefectures of Greece. Most of them (84.6%) presented in northern Greece [FIGURE 1]. Confirmed A/H5N1 cases in migratory birds were detected in 10 of the 51 (19.6%) prefectures of Greece, mostly in northern Greece [FIGURE 1]. In 3 of the 51 prefectures, both confirmed A/H5N1 cases in birds [12/33 (36.4%)] and potential human cases were identified. The majority of potential human cases (61.5%) clustered in these three prefectures [3/5 (60%) met the possible case definition versus 11/21 (52.4%) meeting one criterion only, P=NS]. Four of the five patients meeting the possible case definition were seen from the northern geographical prefectures [FIGURE 1] with confirmed A/H5N1 cases in wild migratory birds [FIGURE 1].

The application of the revised HCDCP definition in the dataset resulted in the exclusion of two of the five patients who met the definition of a possible case. Both had exposure to birds relating to hunting activities and one of them was not living in a prefecture with confirmed A/H5N1 cases or in a neighbouring prefecture.

In Greece the 2005-2006 influenza activity increased from between the fifth and thirteenth week of 2006, but it was lower than that observed during the influenza season of 2004-2005. During the period February-March 2006, 3080 ILI cases over 123 921 visits (2.5%) were reported for the entire country (482 ILI cases over 30 296 (1.6%) visits for any cause in the districts affected by A/H5N1 in migratory fowl versus 2598 cases of ILI over 93 625 (2.8%) visits for the rest of the country).

Discussion

Several potential human cases were identified after the recently confirmed highly pathogenic avian influenza A/H5N1 cases in migratory birds in Greece. These cases were more likely to present in areas with confirmed cases in migratory birds. A case definition that combined clinical and epidemiological criteria assisted in identifying patients more likely to exhibit a true infection (possible cases according to the definition). Possible cases clustered around early February 2006, which was when the first avian influenza cases in dead wild migratory birds were identified in Greece. The case definition, together with molecular testing, assisted in excluding real H5N1 human infection.

In the initial phase of the epizootic in wild birds, a more sensitive approach in defining a possible case was considered appropriate by the Greek public health authorities. However this approach may be associated with several practical problems. The application of a crude epidemiological criterion by physicians in the emergency departments could lead to over-diagnosis and unnecessary admissions. Most of the potential cases evaluated were admitted to hospital for observation in isolation. In addition, molecular testing was performed for all potential cases, regardless of whether or not they met the definition of a possible case. Despite the fact that these cases were quickly discharged after the results of molecular testing, this rate of admissions indicates anxiety and fear on the part of both healthcare workers and the patients asking for extra attention. Other organisations, such as the Health Protection Agency (HPA) in England and Wales, have devised a structured algorithm including in the clinical criterion defining a possible case the decision to hospitalise or not [16]. In the HPA case definition it is implied that only seriously ill cases in need of hospital care will be admitted. Obviously, using such a criterion in a case definition requires good training of physicians and would not have worked well in Greece during this particular period of time. However, all case detection and surveillance systems based on detecting people with moderate to severe respiratory symptoms must be expected to detect cases continuously. In Thailand, a country heavily hit by outbreaks of A/H5N1 in poultry all people with severe respiratory problems are investigated. Between 1 January and 31 August 2006, 4500 cases of clinical influenza or pneumonia cases were evaluated in Thailand, and only 2 positive A/H5N1 cases were detected [17]. It would be more worrying if a surveillance system was not detecting suspect H5N1 cases coming through it continuously such as the ones

presented here. A detailed textual guidance document on handling such cases, such as the one proposed by the French public health authorities [18], may be more appropriate. As more experience is gathered, more detailed documents, harmonised at a European level, on, for example, clinical criteria for hospital admission, may accompany the formal definitions, in order to avoid multiple variants of case definitions in each country. In Greece, it seemed that the question of whether or not the epidemiological criteria was met, was as important as the severity of the clinical picture in deciding to admit them. A contributing factor was the anxiety experienced by the evaluating physicians.

An interim case definition for human avian influenza possible cases was proposed by the ECDC almost two months after the initial cases in migratory birds in Greece. The revised HCDCP definition followed the ECDC guidance and differs from the initial HCDCP definition in several regards. The clinical criteria of symptoms are broader and include not just cough or shortness of breath but acute respiratory infection as a syndrome [TABLE 1]. Death is attributed to an acute unexplained respiratory illness, not simply any respiratory illness. In the epidemiological criteria [TABLE 1]. the contact must be with sick or dead avian species (not simply any live species of wild birds, as was the case with the initial HCDCP definition). This definition further excludes contact related to hunted birds. Moreover, the term 'affected area' includes only prefectures with suspect or confirmed cases of A/H5N1 in birds and their neighbouring prefectures rather than the entire country. This definition, when applied to the initial observations, excluded two of the five cases that met the original definition of a possible case.

The revised case definition was applied to the original data some time after the initial case evaluation (April-May 2006). Since only two cases meeting the definition of a possible case were excluded, one can speculate that these patients might have avoided admission to hospital. However the majority of the other cases (17/21 potential cases not meeting the case definition of a possible case) were also admitted. If the reaction of the evaluating physicians was appropriate, no patients except for those meeting the definition of a possible case should have been admitted. In addition, the admitted patients should have been discharged when the laboratory tests results were found to be negative, since the clinical picture was not severe.

The revised definition opted for more specificity with the addition of several epidemiological parameters. The geographical criterion for surveillance was reduced to include the local and the neighbouring prefectures with H5N1 cases in avian species, rather than the entire country. The area of 10 km around a confirmed H5N1 bird case was still much wider than the zone used for biosecurity measures, to ascertain that no human cases would be missed. The geographical criterion for surveillance can be treated in a more specific manner depending on the level of animal surveillance as well as the level of communication between human and veterinarian public health authorities. Communication between central and local public health authorities is of great importance in this respect, in addition to educational activities and specific exercise testing with active participation of the local public health personnel. As these are enhanced, the affected area definition can be modified to include smaller geographical areas, further increasing specificity in identifying possible cases. The revised case definition also takes viral characteristics into consideration. The current low transmissibility of avian influenza A/H5N1 virus from avian species to humans [9] justifies stricter approaches in defining a possible case. Although no predictions can be made about the future transmission potential of the A/H5N1 virus, several genetic barriers need to be surpassed for such a major event to occur [19]. If this happens, the possibility of a virus that is associated with milder clinical features cannot be excluded [10]. Nevertheless, defining a possible case is a continuously evolving process and should be modified according to the specific clinical and epidemiological characteristics of the circulating virus.

With regards to the cost of admissions no specific data were available. The cost was low since no patient was hospitalised in an intensive care unit, and the length of stay was short. However, if many similar cases had presented to local hospitals the cost would have dramatically increased.

These observations highlight the need for immediate and direct education that should target first healthcare workers and then the general public. In a more serious scenario, actions like the ones observed in this study could rapidly lead to a depletion of healthcare resources. Nevertheless the Greek authorities including the HCDCP and the Ministries of Health and Rural Development and Food made every possible effort to educate, protect and inform both healthcare workers and the public. Healthcare worker training included 'training the trainers' sessions (committees on infectious diseases in each hospital), seminars delivered locally by HCDCP personnel, guidance on standard operating procedures and formal exercise testing in the hospitals. In addition a 24/7 on-call duty system operates in the HCDCP, with a command centre evaluating urgent phone calls relating to communicable diseases from the entire country. However, the decision to admit in all these cases was always left with the treating physician. The authors believe that this system during the specific period did not lead to the avoidance of unnecessary admissions, because of the anxiety experienced by the physicians and the pressure to admit from patients and their families. During this period, a discharge from hospital that felt 'safe' for physicians could only come about after negative laboratory results.

The intense media attention both in Greece and elsewhere likely contributed to some of the observations, along with genuine concern following fatal cases in other countries. The public needs to be completely and accurately informed about the risks from avian influenza. In Greece, public information activities during that period and afterwards included: a) participation in press conferences, television shows and video spots on national television b) issuing oral and written statements to the press, c) publication of educational leaflets for the public and travellers, both on paper and on the official web sites of the authorities d) local visits in the affected areas and high-risk prefectures, ('for example' those with confirmed H5N1 cases in wild fowl and affected neighbouring countries) and e) special educational activities and printed materials for farmers and poultry workers. These activities will be continued in autumn and winter 2006-2007, but should be accompanied by a quality control procedure.

It has previously been shown that media campaigns have helped to convey appropriate preventive healthcare messages, especially when targeting specific high-risk groups [20]. However, this is not always an easy task. Just before the 2005-2006 influenza season in the United States, there was a surge in the purchasing of influenza antivirals as evidenced by a surveillance system targeting syndromic data [21]. Nevertheless, this increase was not associated with true epidemiological markers of influenza activity and it was simultaneously observed with the media coverage of avian influenza A/H5N1 and the possibility of an influenza pandemic [21]. The role of the media in the conveyance of appropriate messages to the public as we prepare for pandemic influenza is of critical importance. Accurate information should be aimed particularly at carefully selected high-risk groups. In Europe the ECDC has issued a scientific guidance document to be used by national authorities in drafting public messages for at risk populations [22]. Such clear messages are essential in future attempts by local governments to control the anxiety associated with the continuous flow of data about the disease, especially when avian and/or animal cases are observed locally.

The findings of the current work have important implications for public health systems dealing with confirmed cases in wild migratory birds and suspect potential cases in humans. Well-organised surveillance systems with the assistance of expert molecular testing can effectively handle these cases. Continuous healthcare worker training is necessary. Collaboration of local authorities with media experts is essential in conveying the appropriate messages to help decreasing unspecific fear in the public so that the health system does not get overwhelmed.

Acknowledgements

The authors would like to acknowledge Stefanos Bonovas, Georgios Dougas, Stratos Fantopoulos, Margarita Prokofieva, Eleni Triantafyllou, and the staff of the Department of Epidemiological Surveillance and Intervention at the Hellenic Center for Disease Control and Prevention for assistance with the collection of information during this study. In addition they thank the members of the National Influenza Reference Centers Antonios Kalliaropoulos and Athanassios Kossivakis for the laboratory work, Eleni Kalamara and Ioannis Karagiannis for assistance with the graph work, and the members of the Department of Avian Pathology of the Hellenic Ministry of Rural Development and Food for their collaboration.

References

1. No authors listed. Avian influenza goes global, but don't blame the birds. Lancet Infect Dis. 2006;6(4):185
2. No authors listed. Highly pathogenic H5N1 avian influenza virus confirmed in a dead swan in Great Britain. Vet Rec. 2006;158(15):494.
3. Editorial team, Avian influenza H5N1 detected in German poultry and a United Kingdom wild bird. Euro Surveill 2006; 11(4):E060406.1. Available from: http://www.eurosurveillance.org/ew/2006/060406.asp#1.
4. European Centre for Disease Prevention and Control. May 26th 2006. Influenza update. H5N1 Avian Influenza update. Available at http://www.ecdc.eu.int/influenza/update_Influenza_060526.php.
5. Rimmelzwaan GF, van Riel D, Baars M, Bestebroer TM, van Amerongen G, Fouchier RA et al. Influenza A virus (H5N1) infection in cats causes systemic disease with potential novel routes of virus spread within and between hosts. Am J Pathol. 2006 ;168(1):176-83.
6. Kuiken T, Fouchier R, Rimmelzwaan G, Osterhaus A, Roeder P. Feline friend or potential foe? Nature. 2006;440(7085):741-2.
7. Duke K. Germany says people in areas with bird flu should keep cats indoors. BMJ. 2006;332(7541):568.Bmj 2006; 332(7541):568.
8. Butler D. Thai dogs carry bird-flu virus, but will they spread it? Nature. 2006;439(7078):773.
9. European Centre for Disease Prevention and Control. Who is at risk of getting "Bird Flu" – Type A/H5N1 influenza? Version April 6th 2006. Available at: http://www.ecdc.eu.int/avian_influenza/Human_H5N1_Bird_Flu_Risk.pdf.
10. Thorson A, Petzold M, Nguyen TK, Ekdahl K. Is exposure to sick or dead poultry associated with flulike illness?: a population-based study from a rural area in Vietnam with outbreaks of highly pathogenic avian influenza. Arch Intern Med. 2006;166(1):119-23.
11. Yu H, Shu Y, Hu S, Zhang H, Gao Z, Chen H et al. The first confirmed human case of avian influenza A (H5N1) in Mainland China. Lancet. 2006;367(9504):84.
12. Swayne DE. Occupational and consumer risks from avian influenza viruses. Dev Biol (Basel). 2006;124:85-90.
13. Quoilin S, Thomas I, Gérard C, Maes S, Haucotte G, Gerard M, Van Laethem Y, Snacken R, Hanquet G, Brochier B, Robesyn E. Management of potential human cases of influenza A/H5N1: lessons from Belgium. Euro Surveill 2006;11(1): E060126.1. Available from: http://www.eurosurveillance.org/ew/2006/060126.asp.
14. Mølbak K, Trykker H, Mellergaard S, Glismann S. Avian Influenza in Denmark, March-June 2006: public health aspects. Euro Surveill 2006;11(6):E060615.3. Available at http://www.eurosurveillance.org/ew/2006/060615.asp#3.
15. European Centre for Disease Prevention and Control. Interim surveillance case definition for influenza A/H5N1 in humans in the EU. 30/03/2006. Available at: http://www.ecdc.eu.int/avian_influenza/EU_case_definition_AH5N1.pdf.
16. Health Protection Agency revised interim guidelines for investigation and reporting of suspected human cases of avian influenza Available at http://www.hpa.org.uk/infections/topics_az/influenza/avian/case_definition.htm.
17. European Centre for Disease Prevention and Control. August 31st 2006. Influenza Update. Available at : http://www.ecdc.eu.int/Influenza/update_Influenza_060817.php.
18. No authors listed. Conduite à tenir devant des cas possibles de grippe à nouvelle souche de virus grippal sans transmission inter humaine. Actualisation au 25/11/2005. Available from http://www.invs.sante.fr/surveillance/grippe_dossier/conduite.pdf. 2006.
19. Kuiken T, Holmes EC, McCauley J, Rimmelzwaan GF, Williams CS, Grenfell BT. Host species barriers to influenza virus infections. Science. 2006;312(5772):394-7.
20. Schade CP, McCombs M. Do mass media affect Medicare beneficiaries' use of diabetes services? Am J Prev Med. 2005;29(1):51-3.
21. Centers for Disease Control and Prevention (CDC). Increased antiviral medication sales before the 2005-06 influenza season--New York City. MMWR Morb Mortal Wkly Rep. 2006; 55(10):277-9.
22. European Centre for Disease Prevention and Control. Avian influenza: Interim guidance for national authorities to produce messages for the public concerning the protection of vulnerable groups. 16 February 2006. Available at: http://www.ecdc.eu.int/press/press_releases/PDF/060216_press_release.pdf.

ORIGINAL ARTICLES

Outbreak report

A MEASLES OUTBREAK IN CHILDREN UNDER 15 MONTHS OF AGE IN LA RIOJA, SPAIN, 2005-2006

M Perucha[1], E Ramalle-Gómara[1], ME Lezaun[1], A Blanco[1], C Quiñones[1], M Blasco[2], MA González[1], C Cuesta[1], J E. Echevarrría[3], MM Mosquera[3], F de Ory[3].

This paper describes a measles outbreak in La Rioja, Spain, which began in December 2005 and mainly affected children under 15 months of age who were not yet immunised with MMR vaccine. The measles cases were detected by the mandatory reporting system, under which laboratories must report every confirmed measles case. Cases were classified in accordance with the National Measles Elimination Plan: suspected and laboratory-confirmed. In the period 14 December 2005 to 19 February 2006, 29 suspected cases of measles were investigated, and 18 were confirmed. The mean incubation period was 13.8 days (range: 9 to 18). Of the 18 confirmed cases, only two were in adults. MMR vaccination was recommended fpr all household contacts, as well as for children aged 6 to 14 months who attended the daycare centres where the cases had appeared. At these centres, the second dose of MMR was administered ahead of schedule for children under three years of age. It was recommended that the first dose of MMR vaccine be administered ahead of schedule for all children aged 9 to 14 months. During an outbreak of measles, children aged 6 months or older, who have not previously been vaccinated against measles, mumps and rubella, should receive a first dose as soon as possible, and those who have had a first dose should receive a second dose as soon as possible, provided that a minimum of one month has elapsed between the two doses.

1. Department for Epidemiology and Health Prevention. La Rioja Regional Authority, Spain
2. Virology Laboratory. Rioja Health Foundation. La Rioja, Spain.
3. Diagnostic Microbiology Department. National Centre for Microbiology, Carlos III Institute of Public Health, Madrid, Spain

Euro Surveill. 2006;11(10): 267-70 Published online October 2006
Key words: disease outbreaks, measles, children, communicable diseases, epidemiology, vaccination

Introduction

The Autonomous Community of La Rioja is situated in northern Spain and has a population of 301084. To comply with the World Health Organization (WHO) objectives, Spain has adopted a policy of interruption of indigenous measles transmission since 2000 [1]. The Strategic Plan for Measles and Congenital Rubella Infection in the European Region of WHO identifies key strategies to meet the targets for the European Region of interrupting indigenous measles transmission by 2010 [2]. Measles vaccination began in La Rioja in 1977 [3] and was replaced by combined measles, mumps and rubella (MMR) vaccine in 1984. In 1990, a second dose of MMR vaccine was introduced at the age of 10-11 years for both boys and girls. Since then, the number of cases has declined markedly, although there was a measles outbreak in La Rioja in 1992 which affected children and young adults aged 12 to 20 years, with an attack rate of 22.2 per 1000 population [4].

The most recent measles case to be reported in La Rioja occurred in 1999 [5]. In Spain, the incidence in 2004 was 0.06 cases per 100 000 population [6]. Measles is no longer an endemic disease in La Rioja, yet it is evident that there is a risk of the appearance of cases of disease linked to imported cases, as has been described in other areas [7].

In La Rioja the first dose of measles, mumps, and rubella vaccination is given to children at age 15 months and the second at 3 years of age. In 2005, childhood vaccine coverage against measles in La Rioja was estimated to be 96.3% at 15 months of age [8]. Children below this age are particularly at risk for measles after the disappearance of maternal measles antibodies [9]. Young adults who have not had a measles infection and have not been vaccinated are also at risk [10].

This paper describes a measles outbreak in La Rioja, which began in December 2005 and mainly affected children under 15 months of age and therefore not yet immunised with MMR vaccine.

Methods

The measles cases were detected by the mandatory reporting system. According to this system, physicians must report every suspected measles case, and laboratories must report every confirmed measles case.

Cases were classified as per the National Measles Elimination Plan, as follows [1,11]:

- Suspected case, that is, any case with maculopapular rash, high fever and one or more of the following symptoms: cough, coryza or conjunctivitis;
- Laboratory-confirmed case, that is., any case with virological diagnosis of the infection, with the diagnostic criterion of choice being indirect detection through presence of serum IgM-specific antibodies and/or detection of measles virus genome by RT-PCR; and,
- Confirmed case with epidemiological link, that is, any suspected case that could not be studied by a laboratory for serological confirmation and that had been in contact with a serologically-confirmed case of measles in which onset of rash took place 7-18 days before the current case.

Serodiagnosis of measles was based on detection by IgM-specific indirect enzyme-linked immunosorbent assay (ELISA) (Enzygnost, Dade Behring, Germany). The polymerase chain reaction (PCR) technique, performed on two different aliquots of specimen of urine, serum and/or nasopharyngeal exudate, also contributed to diagnosis [12]. For genotyping purposes, a different PCR test, designed to detect the variable fragment of the C terminal domain of the measles virus nucleoprotein (456 pb), was used on the specimens above, followed by sequencing of the fragment and phylogenetic analysis.13 A positive result with the two different PCR techniques [12,13] confirmed cases in which there was no specimen for serological study.

We consider that an outbreak is over when there has been at least 21 days without any new cases [14].

Results

On 10 January 2006, a paediatrician reported suspected measles in two children aged 9 and 14 months. The index case was identified as a 32 year old female physician who had been working during the period of disease transmissibility and had seen these two children for consultation on 26 December 2005. On 14 December 2005, this physician had been present by chance at a health centre at the same time as a 28 year old woman who presented with rash that same day. The 28 year old woman is considered to be the primary case in the outbreak.

In the period from 14 December 2005 to 19 February 2006, 29 suspected cases of measles were investigated. Of these, 18 were confirmed (62.1%), 17 by laboratory and one by epidemiological link. The latter case involved a child, aged 18 month, who was the son of the primary case. This child was the second case. All suspected but unconfirmed cases were excluded from analysis. All the cases lived in Logroño, the capital city of La Rioja.

The last case to be documented presented with rash on 28 January 2006, and the outbreak came to an end 21 days later on 19 February. Three clinically compatible cases without any epidemiological link were reported after this date, but were subsequently ruled out by the laboratory.

The mean incubation period was 13.8 days (range: 9-8 days). The epidemic curve of the confirmed cases is shown in the figure. Two incidence peaks can be seen: the first corresponds to secondary cases related with the cases that took place in December 2005, and the second to secondary cases related with the cases that occurred in January 2006.

Distribution by age and sex

Of the 18 confirmed cases, only 2 (11.1%) were in adults; both were women (see results) aged 28 and 32 years. Children's ages ranged from one and half months to three years (see results), with thirteen children aged under 15 months (72.2%). A breakdown of this total by sex yielded 12 cases in females (66.7%) and 6 in males (33.7%) [TABLE]. Fourteen of the children attended two daycare centres (thirteen attended the same one). We do not know the epidemiological link between these two daycare centres. There was a case in an unvaccinated three year old child who was born outside Spain and had recently migrated to La Rioja, and whose vaccination status had not yet been updated.

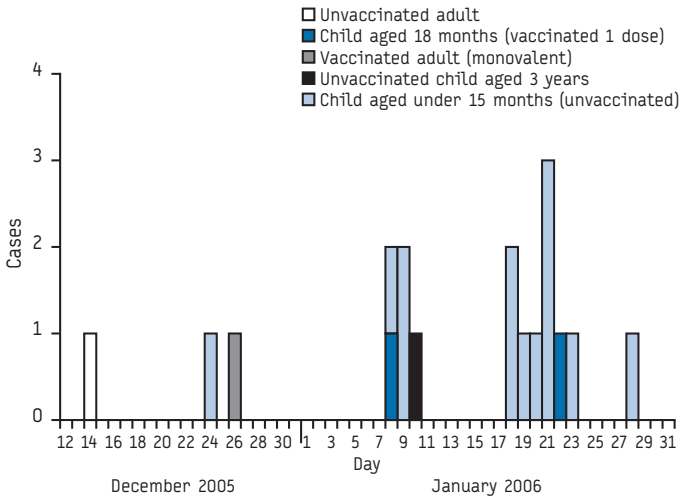
Clinical characteristics

All cases presented with maculopapular rash and high fever. The remaining symptoms were: cough, 16 cases (88.9%); coryza, 15 cases (83%); conjunctivitis, 12 cases (66.7%). Six cases (33.3%) presented with adenopathies.

Complications were as follows: earache, three cases (16.7%); bronchitis, three cases (16.7%); laryngitis, one case (5.6%); and laryngotracheitis, one case (5.6%). No case required hospital admission. There were no deaths.

FIGURE

Epidemic curve for laboratory confirmed cases from date of onset of rash. La Rioja, Spain, December 2005 to January 2006



Table

Age and sex distribution of patients with laboratory-confirmed cases of measles. La Rioja, Spain, December 2005 to January 2006

Age	Sex		Laboratory results	
	Male	Female	PCR +	IgM
0-6 months	0	1	0	1
7-15 months	5	7	12	8
16 months-3 years	1	2	2	3
4 years-24 years	0	0	0	0
> 24 years	0	2	1	2
All	6	12	15	14

PCR: Polymerase chain reaction

Laboratory results

Fourteen confirmed cases presented with anti-measles IgM antibodies (77.8%). In 14 of the confirmed cases (77.8 %) genotype D6 virus was identified by PCR. One case (5.6%) could not be genotyped. In three cases, PCR proved negative in serum, urine and pharyngeal exudate and IgM was positive and considered as laboratory confirmed.

Measures adopted

MMR vaccination was recommended for all family contacts, and for children aged 6 to 14 months who attended the two daycare centres where there had been cases. At these centres, the second dose of MMR was administered ahead of schedule to children under three years of age. Work colleagues who were previously unvaccinated were also vaccinated in one case (only unvaccinated). It was recommended that the first dose of MMR vaccine be administered ahead of schedule for all children aged 9 to 14 months in La Rioja.

Discussion

In the post-vaccination era, incidence of measles cases is very low in western countries with very high vaccination coverage. Outbreaks occur with a certain frequency, generally among adolescents or young adults who have neither been vaccinated nor exposed to the circulating virus [15,16]. In Spain, this group coincides with the 1975-1982 birth cohort [17]. Cases are seen less frequently in children and infants than in older children, though outbreaks have been reported in children who have not yet been vaccinated [18,20]. In a recent outbreak in London, 40% of subjects affected were infants under 12 months of age [21]. In Spain, 9% of measles cases reported in 1997 involved children aged under 1 year, and over 50% were in ages ranging from 10 to 19 years [22].

Recently, there have been reports of outbreaks in infants [21,23,24]. In Spain, children aged under 15 months, that is, those who have not yet been vaccinated against measles, constitute an important risk group. The risk is higher in non-vaccinated children aged 6 months old or older [25], because from the age of 7 months onwards, 65% of children no longer have titres of protective maternal antibodies [26]. Children aged under 15 months are currently at greater risk of measles infection than children and adolescent, and at greater risk of serious sequelae.

This outbreak underscores the need for an epidemiological surveillance system which enables rapid detection of virus circulation in the population, early identification of outbreaks and immediate adoption of control measures, since vaccination is not routinely recommended in children under the age of 12 months [27].

These results support the recommendation that, during an outbreak of measles, children aged 6 months or older who have not been vaccinated against measles, mumps and rubella should receive a first dose of MMR vaccine as soon as possible, and that those who have already had a first dose should receive a second dose as soon as possible, provided that a minimum of one month has elapsed since the first dose [28]. Children of vaccinated mothers lose measles antibodies quicker than children of mothers who have been naturally infected with measles [29].

In this outbreak, there were no cases in children who had been vaccinated with two doses of MMR, and this highlights the need to maintain two-dose vaccination coverage above 95%, since this interrupts viral circulation [30] in the population. In La Rioja, these coverages have been maintained since 1995 [31].

D6 genotype identification coincides with a genotype that circulated in Spain in the period 1993-1997 but has not been identified in Spain since [13]. The D6 measles virus identified was genetically identical to the outbreak strain circulating in the Ukraine at this time [32].

The appearance of outbreaks and the evidence of measles virus circulation in countries or regions that have previously been virus-free have led the WHO Regional Office for Europe to postpone the goal of eradicating measles by the year 2010 [6].

Acknowledgements

We should like to thank the following for their collaboration: the National Centre for Epidemiology; paediatricians and emergency services attached to the La Rioja Public Health System; and the heads of all day-care centres.

References

1. Centro Nacional de Epidemiología. Plan de eliminación del sarampión en España. Madrid: Ministerio de sanidad y Consumo, 2000.
2. Strategic plan for measles and congenital rubella infection in the European Region of WHO. Copenhagen, WHO Regional Office For Europe, 2003 (http://www.euro.who.int/document/e81567.pdf, accessed 4 September 2006)
3. Ministerio de Sanidad y Consumo. Vacunación en adultos. Recomendaciones. Madrid: Ministerio de Sanidad y Consumo, 2004.
4. Lezaun Larumbe ME, Perucha González J, Ramalle Gómara E. Descripción de una situación epidemica de sarampión en La Rioja, año 1992. Boletín Epidemiológico de La Rioja. 1992;(57):307-312.
5. Quiñones Rubio C. Enfermedades de declaración obligatoria y brotes epidemiológicos.La Rioja 2004. Boletín Epidemiológico de La Rioja 2005;(206):1495-9.
6. Martínez de Aragón MV, Castellanos T, Cortés M. Eliminación del sarampión en España. Plan Nacional de Eliminación del Sarampión. Evaluación año 2004. Bol Epidemiol Semanal. 2005;13(5):49-56.
7. Centers for Disease Control and Prevention (CDC). Measles--United States, 2004. MMWR Morb Mortal Wkly Rep. 2005; 54(48):1229-31.
8. Ministerio de Sanidad y Consumo. Coberturas de Vacunación. http://www msc es/profesionales/saludPublica/prevPromocion/vacunaciones/coberturas htm 2005; Access 5/6/2006.
9. Johnson CE, Darbari A, Darbari DS, Nalin D, Whitwell J, Chui LW et al. Measles vaccine immunogenicity and antibody persistence in 12 vs 15-month old infants. Vaccine 2000;18(22):2411-2415.
10. Zandotti C, Jeantet D, Lambert F, Waku-Kouomou D, Wild F, Freymuth F et al. Re-emergence of measles among young adults in Marseilles, France. Eur J Epidemiol. 2004;19(9):891-3.
11. Lezaun Larumbe ME. Plan de eliminación del sarampión en La Rioja (II). Boletín Epidemiológico de La Rioja. 2001;(160):1127-31.
12. Mosquera MM, de Ory F, Moreno M, Echevarria JE. Simultaneous detection of measles virus, rubella virus, and parvovirus B19 by using multiplex PCR. J Clin Microbiol. 2002; 40(1):111-6.
13. Mosquera MM, Ory F, Echevarria JE. Measles virus genotype circulation in Spain after implementation of the national measles elimination plan 2001-2003. J Med Virol 2005; 75(1):137-146.
14. World Health Organization. Guidelines for Measles Surveillance. Revised December 2004. Geneva: World Health Organization, 2004.
15. De Schrijver K. Outbreak of measles among adolescents, Belgium, 1996. Euro Surveill. 1996;1(6):46-47.
16. Mantzios G, Mastora M, Liapis E, Giannakakis I, Akritidis NK. Outbreak of measles in adults in the north west of Greece. Euro Surveill. 1997;2(7):57-8.
17. Lardinois R, Carrasco JL, Arroyo M. Estimación de la población infantil con susceptibilidad conjunta a sarampión, rubeola y parotiditis, 1975-1984. Rev Esp Ped. 1985; 41:343-359.
18. Muscat M, Glismann S, Bang H. Measles in Europe in 2001-2002. Euro Surveill. 2003;8(6):123-9.
19. Papania M, Baughman AL, Lee S, Cheek JE, Atkinson W, Redd SC et al. Increased susceptibility to measles in infants in the United States. Pediatrics. 1999; 104(5):e59.
20. Yip FY, Papania MJ, Redd SB. Measles outbreak epidemiology in the United States, 1993-2001. J Infect Dis. 2004; 189 Suppl 1:S54-S60.
21. Atkinson P, Cullinan C, Jones J, Fraser G, Maguire H. Large outbreak of measles in London: reversal of health inequalities. Arch Dis Child. 2005; 90(4):424-5.
22. Pachon I. Situación del sarampión en España. Estudio seroepidemiológico. Rev Esp Salud Publica. 1999; 73(5):609-616.

23. Ohsaki M, Tsutsumi H, Takeuchi R, Seki K, Chiba S. Recent increase in the frequency of infant measles in Japan. Pediatr Int. 2000; 42(3):233-5.
24. Bilkis MD, Barrero PR, Mistchenko AS. Measles resurgence in Argentina: 1997-8 outbreak. Epidemiol Infect. 2000; 124(2):289-293.
25. Gans HA, Arvin AM, Galinus J, Logan L, DeHovitz R, Maldonado Y. Deficiency of the humoral response to measles vaccine in infants inmunized at age 6 months. JAMA. 1998; 280:527-533.
26. Szenborn L, Tischer A, Pejcz J, Rudkowski Z, Wojcik M. Passive acquired immunity against measles in infants born to naturally infected and vaccinated mothers. Med Sci Monit 2003; 9(12):CR541-6.
27. Zanetta RA, Amaku M, Azevedo RS, Zanetta DM, Burattini MN, Massad E. Optimal age for vaccination against measles in the State of Sao Paulo, Brazil, taking into account the mother's serostatus. Vaccine. 2001; 20(1-2):26-234.
28. Morgan OW, Meltzer M, Muir D, Hogan H, Seng C, Hill J et al. Specialist vaccination advice and pockets of resistance to MMR vaccination: lessons from an outbreak of measles. Commun Dis Public Health. 2003; 6(4):330-3.
29. Maldonado YA, Lawrence EC, DeHovitz R, Hartzell H, Albrecht P. Early loss of passive measles antibody in infants of mothers with vaccine-induced immunity. Pediatrics 1995; 96(3 Pt 1):447-50.
30. Cilla G, Basterretxea M, Artieda J, Vicente D, Perez-Trallero E. Interruption of measles transmission in Gipuzkoa (Basque Country), Spain. Euro Surveill. 2004; 9(5):29-31.
31. Lezaun Larumbe ME. Plan de eliminación del sarampión en La Rioja (I). Boletín Epidemiológico de La Rioja 2001;(159):1119-1121.
32. van Treeck U. Measles outbreak in Germany: over 1000 cases now reported in Nordrhein Westfalen. Euro Surveill 2006; 11(5):E060511.1.

ORIGINAL ARTICLES

Outbreak report

OUTBREAK OF *SALMONELLA ENTERICA* SEROTYPE MANHATTAN INFECTION ASSOCIATED WITH MEAT PRODUCTS, FRANCE, 2005

H Noël[1], M Dominguez[1], FX Weill[2], A Brisabois[3], C Duchazeaubeneix[4], A Kerouanton[3], G Delmas[1], N Pihier[4], E Couturier[1]

Between August 2005 and March 2006 in France, 69 cases of *Salmonella enterica* serotype Manhattan (*Salmonella* Manhattan) were reported, 51 (74%) of them from southeastern France.
At the time of the alert (November 2005), 13 cases and 33 controls were interviewed. Cases were more likely than controls to have eaten pork sausages (OR=5.9, confidence interval CI [1.3; 26.9]) and beef (OR=9.3, CI [1.3; 68.6]). At the same time, 19 strains of *Salmonella* Manhattan isolated from meat products in southeastern France, reported to Afssa (the French Food Safety Agency) in September and November 2005, had an indistinguishable PFGE profile to the 7 human isolates of *Salmonella* Manhattan from the outbreak in southeastern France. Trace-back investigations revealed that pork samples came from one wholesaler whose pork products had tested positive for *S.* Manhattan during routine food testing in August 2005. This wholesaler supplied retail outlets in southeastern France. Additionally, a slaughterhouse supplying the wholesaler was inspected and widespread contamination with *Salmonella* spp. and *S.* Manhattan was found. Cooperation between the national agencies in charge of human health (InVS) and food safety (Afssa) allowed us to determine the most probable source of contamination and to take appropriate control measures.

Euro Surveill. 2006;11(11): 270-3 Published online November 2006
Key words: *Salmonella enterica* serotype Manhattan, France, outbreak, meat products

Introduction

In France, the National Reference Centre for *Salmonella* (NRC) collects human isolates through a voluntary network of medical laboratories and Afssa (the French Food Safety Agency) also collects salmonella strains isolated from animals, foods or the environment.

On 25 November 2005, the NRC for Salmonella identified an unusual increase of isolates of *Salmonella enterica* serotype Manhattan (*Salmonella* Manhattan). Thirty cases had been reported since August 2005, of which 26 were from several districts in southeastern France.

Although salmonellosis is the largest documented cause of foodborne infections [1], *S.* Manhattan is rarely isolated from humans, foods or animal*S.* The NRC identified an annual average of 7 cases in the previous five years and no isolate of *S.* Manhattan was reported in 2004 in food (A. Brisabois, personal communication, 2005).

An investigation was conducted to determine the extent of the outbreak, the source of infection and to implement control and prevention measures.

Methods

Epidemiological investigation

Basic epidemiological data (age, sex, district of residence, address of the medical laboratory) for all isolates of *S.* Manhattan identified through the NRC were transmitted for investigation. A case was defined as a person living in France, with diarrhoea (at least 3 watery stools a day) or fever, and *S.* Manhattan isolated from a stool or blood specimen, since August 2005. At the time of the alert, the most recently identified cases were retrospectively interviewed by telephone using a trawling questionnaire that collected food consumption and purchase in the 7 days before onset of symptoms. The questionnaire also enquired about symptoms, other possible exposures such as contact with other cases of diarrhoea in the household, pets or wild animals, recent travel, etc. A case-control study was carried out. Three controls per case were matched by district and by age group (child, adult if older than 15 years). Controls were sourced from the medical laboratory or general practitioner that had identified the case, from among the cases' family or friends, or at random from the telephone directory. Controls had no reported gastrointestinal illness in the two weeks before the interview.

1. Institut de Veille Sanitaire, Saint-Maurice, France
2. Centre National de Référence des Salmonella, Paris, France
3. Afssa-LERQAP, Maisons-Alfort, France
4. Direction générale de l'alimentation, Paris, France

They were asked detailed questions about food consumption and purchase in the 7 days before the interview. For analysis, meat products were grouped according to type and preparation (e.g. dried sausages, cooked sausages, raw sausages, cooked pork pieces). Analysis was performed using EpiData®, and frequencies were compared using Pearson's χ^2 or 2-tailed Fisher's exact test. Confidence intervals of the odds ratios were calculated using the Mantel-Haenszel method, stratified by district of exposure.

European investigation

Enter-net (the international network for surveillance of human gastrointestinal infections) was informed of the ongoing French outbreak and its members were requested to report any increase in number of cases of *S.* Manhattan or any cases possibly linked to the French outbreak.

Veterinary investigation

Food isolates of *S.* Manhattan recorded by Afssa since August 2005 were traced back by the district veterinary services.

Microbiological investigation

Human and food isolates of *S.* Manhattan linked to the outbreak and unrelated *S.* Manhattan isolates were characterised by pulsed field gel electrophoresis (PFGE) [2]. DNA was digested by the enzyme *Xba*1. Each profile that differed by at least one clear band >100 kbp was considered as a distinct profile. The software BioNumerics® was used to analyse and compare the genomic profiles obtained.

Results

Epidemiological investigation

Between August 2005 and March 2006, 69 cases were reported, 51 (74%) of which were from 10 districts located in southeastern France [FIGURE 1, FIGURE 2]. Among the 69 cases, 38 were female. All age groups were affected; 74% were adults and among them, 27 (55 %) were aged 65 years or older.

At the time of the alert (week 47/48), 13 cases were interviewed. Twelve lived or had spent a few days in one of the districts in southeastern France during the week before the onset of symptoms. Among the 13 cases, 9 were adults (3 more than 65 years old). The dates of onset of symptoms were from 2 September to 11 November 2005. The most frequently reported symptoms were diarrhoea (12/13, of which 4 cases reported bloody diarrhoea) and abdominal pain (10/13). Three patients were admitted to hospital, and there were no deaths.

FIGURE 1

Cases of *Salmonella* Manhattan infection by district, August 2005-March 2006, France

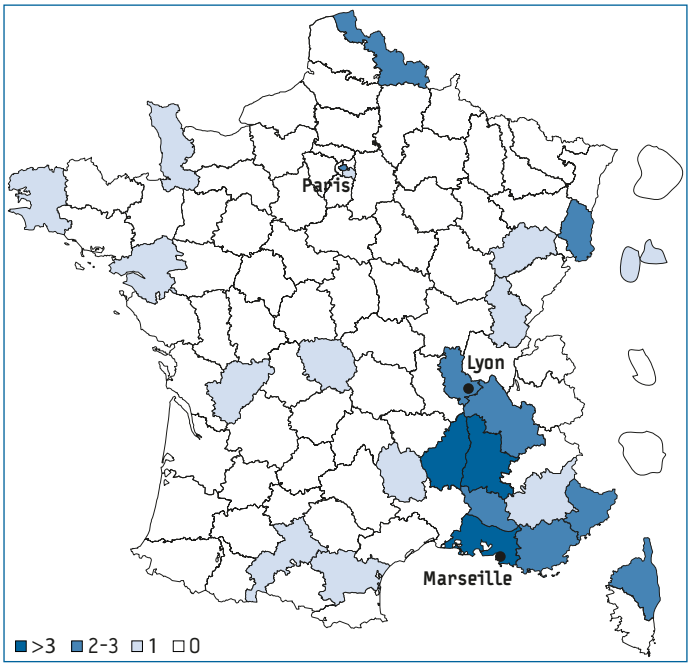
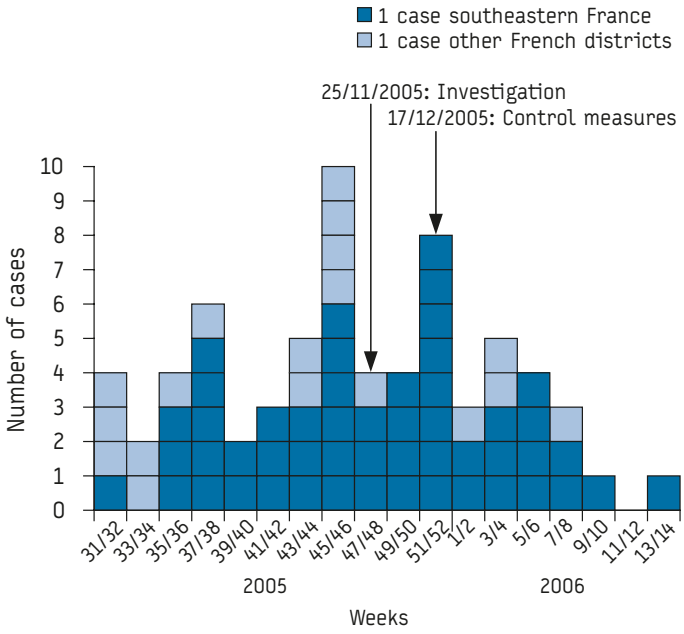


FIGURE 2

Epidemic curve by fortnight of isolation, *Salmonella* Manhattan, France, 2005-2006



The most frequently reported food products were cooked pork (boiled ham, 12/13), beef (12/13), dried pork sausages (11/13) and pork sausages (9/13), goat cheese (11/13), minced beef (10/13) and surimi (10/13) (minced, processed fish used in the preparation of imitation shellfish) [TABLE].

TABLE

Food consumption among cases and controls, *Salmonella* Manhattan, southeastern France, 2005

Food consumption	Cases N=13 n[1] exposed (%)	Controls N=33 n[1] exposed (%)	OR[2] CI 95%	p value
Beef	12 (92)	16 (48)	9.3 [1.3-68.6]	0.02
Pork sausages	9 (69)	10 (30)	5.9 [1.3-26.9]	0.05
Goat cheese	11 (85)	18 (55)	5.4 [0.9-32.0]	0.14
Cooked pork pieces	12 (92)	29 (88)	1.8 [0.2-19.2]	0.93
Dried sausages	11 (85)	21 (64)	5.8 [0.5-30.0]	0.20
Rare minced beef	6 (46)	11 (33)	1.4 [0.3-6.0]	0.65
Minced beef	10 (77)	21 (64)	1.7 [0.4-7.2]	0.47
Surimi[3]	10 (77)	5 (15)	9.5 [2.0-45.1]	0.001

1. Number exposed
2. Mantel-Haentzel estimate controlling for district
3. Minced, processed fish used in the preparation of imitation shellfish

Cases were more likely than controls to have eaten pork sausages (OR=5.9, confidence interval CI [1.3; 26.9]), beef (OR=9.3, CI [1.3; 68.6]) and surimi (OR=9.5, CI [2.0; 45.1]) [TABLE]. Because of the small number of cases, no multivariable analysis could be performed.

Veterinary investigation

Between September and November 2005, *S.* Manhattan was isolated from 19 food samples from 2 districts in southeastern France: 12 from pork, 6 from minced beef and 1 from veal [FIGURE 3].

Trace-back investigations revealed that 8 out the 12 pork samples originated from one wholesaler (establishment Y) [FIGURE 4]. It was noted that in August 2005, routine food controls on merguez sausages, Italian sausages and chipolatas manufactured in establishment Y were positive for *S.* Manhattan. Establishment Y supplied retail outlets in southeastern France. Slaughterhouse X, producing mainly pork (80%) but also beef (20%), was the supplier for establishment Y. The

Figure 3

Number of food strains of *Salmonella* Manhattan isolated by month, southeastern France, 2005

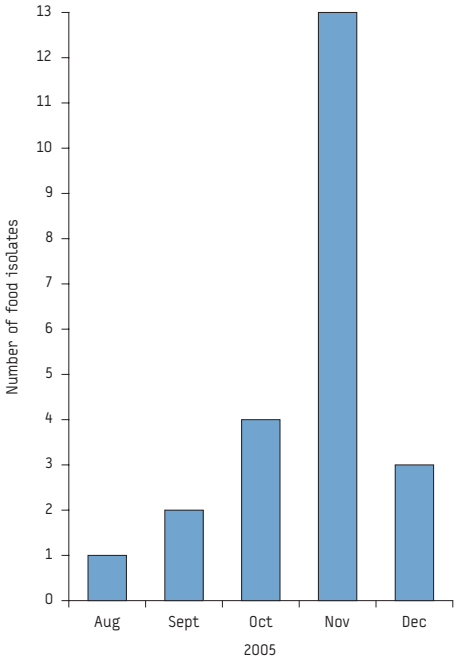
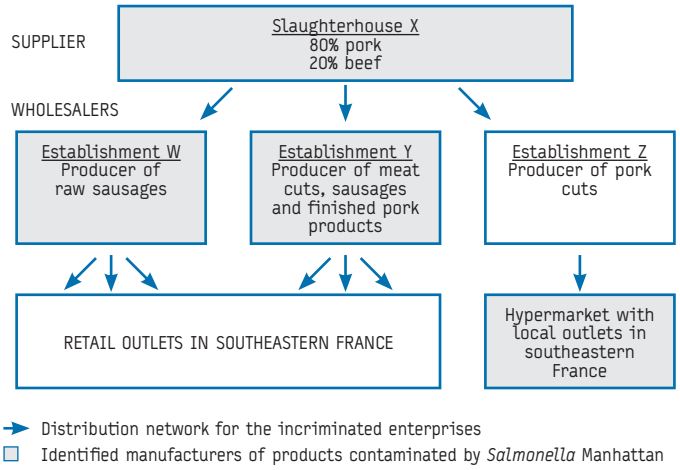


Figure 4

Traceback investigation, *Salmonella* Manhattan, southeastern France, 2005



slaughterhouse's facilities were inspected and revealed a widespread contamination with *Salmonella* spp. and *S.* Manhattan, as well as poor operational hygiene control practices.

Slaughterhouse X also supplied two other wholesalers (establishment W and establishment Z) and further investigations showed that since October 2005, pork products purchased by these wholesalers had been contaminated with *Salmonella* spp. Furthermore, 9 *S.* Manhattan isolates were obtained in slaughterhouse X products distributed in retail outlet*S.* These four establishments (X, W, Y and Z) distributed their products in the districts where 75% of the interviewed patients lived.

Microbiological investigation

Seven human isolates of *S.* Manhattan received by the NRC in October and November 2005 from southeastern France had an indistinguishable PFGE profile to the 19 strains of *S.* Manhattan isolated from meat products reported in September and November 2005. The PFGE profile of 2 human isolates received in March and September 2005, and not linked to the outbreak, was different.

European investigation

In European countries, *S.* Manhattan is a rare serotype and only five European countries (Austria, Belgium, Denmark, Finland and Scotland) had reported human, animal or food isolates of *S.* Manhattan in the previous two years. However none of these cases could be epidemiologically related to the French outbreak. Moreover, distribution of products from the incriminated slaughterhouse X was restricted to France.

Preventive and control measures

Production was suspended in establishment Y and its supplier, slaughterhouse X (on 6 and 15 December 2005, respectively) and X's facilities were cleaned and disinfected on 17 and 18 December. After those control measures were taken, products were routinely analysed for *Salmonella* spp. before being released for sale or used in the manufacture of other product*S.* No more *S.* Manhattan positive isolates in meat products occurred after implementation of these measures.

Discussion

From August 2005 to February 2006, a community-wide outbreak of *S.* Manhattan infections occurred in France. The investigation incriminated pork products from slaughterhouse X as being the most likely source of this outbreak. There is a concordance between the temporal (October-December 2005) and the geographical (southeastern France) occurrence of the majority of cases and the distribution of products from the slaughterhouse X. Furthermore, *S.* Manhattan, a rare serotype, was isolated from cases and from pork products, and seven human cases had the same PFGE profile as isolates from the pork products. Additionally, the consumption of pork sausages was associated with illness in the case-control study, and could explain the majority of cases.

There was no sampling frame for cases or controls. At the time of the alert, the most recently identified cases were retrospectively interviewed in order to lessen recall bias on food consumption and purchase. Controls were selected from different sources in order to recruit adequate numbers within a short timeframe. This enabled us to identify the incriminated food item(s) and rapidly implement control and prevention measures.

Decreasing numbers of cases and the absence of positive food isolates in early 2006 indicate the efficacy of the control measure*S.* However, cases were reported from mid-December 2005 to March 2006, and could be explained by the shelf life of pork products (at least 2 months) distributed before implementation of control measures.

The main production of slaughterhouse X was pork, but beef was also produced (20% of production). The outbreak could be due in part to the distribution of contaminated beef. In the case-control study, there was an association between beef consumption and illness. Although beef and pork production were carried out in different units, cross-contamination of the beef unit could not be ruled out. Therefore, the beef production unit was cleaned and disinfected as well as the pork unit.

Among the cases, 77% reported surimi consumption, and its consumption was associated with illness. However, the hypothesis of surimi as a source of contamination was highly unlikely. First, surimi consumption by case was from a wide range of brands. Second, these brands had no raw material or processing plants in common. In addition, the production process includes a double pasteurisation, so surimi contamination by *Salmonella* spp. was considered unlikely. As far as we know, no salmonella outbreak due to contaminated surimi has been reported in the scientific literature.

Despite the wide contamination of products from slaughterhouse X, relatively few cases were identified. Consumption of food contaminated with salmonella that has been properly cooked does not imply disease. Furthermore, it is likely that not all cases were reported through the surveillance system. In France in 2003, there were only 2 *S.* Manhattan food isolates, accounting for 0.2% of the salmonella isolates from pork and 0.1% from poultry. A recent British study showed that *S.* Manhattan accounted for 51.9% of all salmonella isolates in slurry in a commercial pig farm [3]. However, few human outbreaks due to

S. Manhattan have been described in Europe [4]. To our knowledge, the most recent *S.* Manhattan outbreak before this one occurred in France in 1982 in a hospital nursery, but the source of contamination was not identified [5].

In France, cooperation between the national agencies in charge of human health and food safety allowed us to determine the most probable source of contamination and to take appropriate control measures. To prevent community acquired salmonella infections, the greatest care should be taken in animal husbandry, to prevent contamination, and in slaughterhouses, to prevent cross contamination. Cooking meat and dairy products thoroughly before consumption should be recommended. This advice may prevent not only salmonellosis but also other potentially serious foodborne infections.

References

1. Vaillant V, De Valk H, Baron E, Ancelle T, Colin P and al. Foodborne Infections in France. Foodborne Pathog Dis. 2005;2(3):221-32.
2. Ribot EM, Fair MA, Gautom R, Cameron DN, Hunter SB, Swaminathan B, Barett TJ. Standardization of pulsed-field gel electrophoresis protocols for the subtyping of Escherichia coli O157:H7, Salmonella, and Shigella for PulseNet. Foodborne Pathog Dis. 2006;3(1):59-67.
3. Watabe M, Rao JR, Stewart TA, Xu J, Millar BC and al. Prevalence of bacterial faecal pathogens in separated and unseparated stored pig slurry. Lett Appl Microbiol. 2003;36(4):208-12 .
4. Fisher I, Hald T, Mølbak K, Riewerts Eriksen N. Outbreak of *Salmonella* manhattan infection in Denmark with international implications . Eurosurveillance Weekly. 1998;2(9) 980226. Available from: http://www.eurosurveillance.org/ew/1998/980226.asp#2 .
5. Sarlangue J, Billeaud C, Mégraud F, Martin C. [Neonatal epidemic caused by *Salmonella* Manhattan. Protective role of maternal milk]. Pediatrie. 1982;37(6):461-6. [In French]

ORIGINAL ARTICLES

Outbreak report

INVESTIGATION OF A TUBERCULOSIS CLUSTER AT A JOB CENTRE IN MANCHESTER, UK

A Kirkpatrick[1], C Bell[2], M Petrovic[1], M Woodhead[1], A Barrett[3], E Duffel[1], A Verma[4], F Reynolds[1]

During the summer of 2005, four cases of active tuberculosis from the same occupational setting were investigated in Manchester, UK. The index case had been diagnosed in December of the previous year. At that stage the closest occupational contacts had been screened, all of whom were assessed as being free from active disease, and none had met nationally recommended criteria for chemoprophylaxis for latent tuberculosis infection (LTBI).

In June 2005, two work contacts developed progressive primary extrapulmonary (pleural) TB. Following a detailed risk assessment, the screening programme was widened to include 137 staff who worked at the job centre (employment agency) where the first four cases had been found. This screening programme was based on tuberculin Mantoux testing, CXR and gamma-interferon testing. Of these 137 contacts screened, one additional person was found to have active disease and six others were offered chemoprophylaxis for LTBI. The isolates from the index case and the first two secondary cases were indistinguishable on VNTR-MIRU (variable number tandem repeat - mycobacterial interspersed repetitive unit) typing at 15 loci. No samples were available for testing from the fourth case of active disease.

Management of this incident has benefited from the evolving fields of both genotyping and diagnostic testing for LTBI. However, further research into the epidemiological inferences made through genotyping, as well as the significance of a positive gamma-interferon test in assessing the risk of development of active disease, is still required.

Euro Surveill. 2006;11(11): 273-5 Published online November 2006

Key Words: Tuberculosis, cluster, epidemiology, latent infection, gamma-interferon testing, genotyping

1. Greater Manchester Health Protection Unit, Manchester, United Kingdom
2. Central Manchester and Manchester Children's University Hospitals NHS Trust, Manchester, United Kingdom
3. HPA Regional Centres for Mycobacteriology, Newcastle, United Kingdom
4. Evidence for Population Health Unit, University of Manchester, Manchester, United Kingdom

Introduction

In December 2004 a case of sputum smear positive tuberculosis (TB) was diagnosed in an employee of a job centre (a branch of the United Kingdom government funded employment agency) in North Manchester. The isolate was confirmed to be fully sensitive *Mycobacterium tuberculosis*. In accordance with pre-existing national guidance [1] all household and close occupational contacts were screened. None of the three household contacts had active disease but two were offered chemoprophylaxis on the basis of their tuberculin Heaf test result, age and BCG status [1]. Ten close occupational contacts were all assessed as being free from active disease and none of them met the recommended criteria [1] for chemoprophylaxis for latent tuberculosis infection (LTBI).

In June 2005, however, two of these occupational contacts developed progressive primary extrapulmonary (pleural) TB. Initial screening had revealed Grade II and IV Heaf tests (neither had had BCG vaccination) and normal chest x rays (CXRs). Gamma interferon (GIF) testing was not performed, since at this time it was not available for routine use within Greater Manchester. Given the ages of these contacts, both of whom were adults in their late fifties and early sixties, neither were offered chemoprophylaxis: this was in accordance with national guidance. An incident management team (IMT) was subsequently convened to assess the need to expand screening in the workplace setting.

Methods

In order to guide the extent of further screening, a risk assessment was undertaken. This took into account the presumed infectious period of the index case, the duration of exposure for both staff and clients, the layout of the job centre, social activities, and use of canteens and smoking rooms. The two new cases were carefully assessed and were judged to be at low risk of being infectious, on the basis of their clinical presentation and the absence of any evidence that they were smear positive on sputum microscopy.

The centre was divided into three floors. The index case worked almost exclusively on the ground floor. The exact onset of symptoms

in the index case was uncertain and it was therefore decided to assume a maximum infectious period of three months before the diagnosis.

Given the change in availability of the Heaf test and that the National Institute of Clinical Excellence (NICE)'s draft national guidance on tuberculosis [1] had just been published, a screening programme was undertaken based on tuberculin Mantoux testing, CXR and gamma interferon testing (QuantiFERON-TB Gold In Tube Method). GIF testing was offered to anyone who had a Mantoux positive result, defined as either an induration of 6 mm or more without prior BCG vaccination or an induration of 15 mm or greater with prior BCG vaccination. In turn, a GIF test was considered positive for M. tuberculosis infection if it had a GIF response to either of the TB specific antigens early secretory antigenic target (ESAT) 6 or culture filtrate protein (CFP) 10 that were significantly above the control value obtained using the QuantiFERON-TB Gold In Tube Method. Contacts with a positive GIF test were offered CXR. Those with radiological signs suggestive of TB were clinically assessed to exclude active disease. Those with no radiological signs of TB were diagnosed as having LTBI. The criteria for chemoprophylaxis were diagnosis of latent infection where the benefit was felt to outweigh the risks as judged by the treating physician.

At least six months elapsed between the last known exposure to the index case and further investigations being undertaken after the two secondary cases coming to light. Screening investigations were completed for all contacts over the following three-month period with the condition that anybody eligible for GIF testing was fast-tracked, so that this was undertaken within a fortnight of the tuberculin skin test (TST) being performed.

Screening was initially limited to staff on the ground floor, including repeat screening of the eight initial close contacts who remained disease free. As positive results, on the basis of the GIF tests, were subsequently found in both close and more distant ground floor contacts, screening was extended to all staff in the centre, in accordance with the 'stone in the pond' principle [3]. This principle means that those with the closest, most prolonged contact are screened first and if there is a high rate of infection in these contacts, screening is then extended to those who had a lesser degree of contact. Although it was initially judged necessary to screen only those employees who worked at the job centre during the three months before the diagnosis in the index case, because of the high degree of anxiety being expressed by staff within the centre, the pragmatic decision was taken to extend the screening period up to the time when the two subsequent (non-infective) cases were diagnosed.

All available isolates from cases in this cluster were genotyped by VNTR-MIRU (variable number tandem repeat - mycobacterial interspersed repetitive unit) at the Northern Regional Centre for Mycobacteriology, Newcastle.

Results

Following the methodology outlined above, a total of 137 staff members from all areas of the job centre were screened. Their distribution throughout the job centre is shown in the table together with the distribution of those who were subsequently found to have a positive GIF test.

All of the 30 contacts eligible for GIF testing all were offered it, and an uptake rate of 93% (28/30) was achieved. Two people did not attend for testing, despite repeated attempts to facilitate this, and their general practitioners were informed accordingly. Those testing negative for GIF were given advice about the symptoms of TB, as were the remaining 107 people who had a negative TST.

The actions taken for the eight people who had a positive GIF test are shown in the figure. One of these eight had not been present in the occupational setting during the three month infectious period and furthermore had a previous history of a positive Heaf test before receiving BCG as part of the routine childhood immunisation schedule, and was considered unlikely to benefit from chemoprophylaxis. The other seven positive GIF tests were all in workers who had no other known risk factors and who had either worked on the ground floor of the job centre or had close contact with the index case in the smoking room. One was assessed to have active disease. This person had also been investigated as part of the initial screening earlier in the year. These previous investigations had revealed a Grade II Heaf Test (in the context of no previous BCG) together with a normal CXR and therefore had not been offered chemoprophylaxis, which was at that time in line with national guidance [1]. The remaining six had not previously been investigated, were all asymptomatic and were offered chemoprophylaxis for LTBI.

The isolates from the index case and the first two secondary cases were indistinguishable on VNTR-MIRU typing at 15 loci. No samples were available for testing from the fourth case of active disease.

TABLE

Distribution of staff members screened and results, Manchester, United Kingdom, 2005

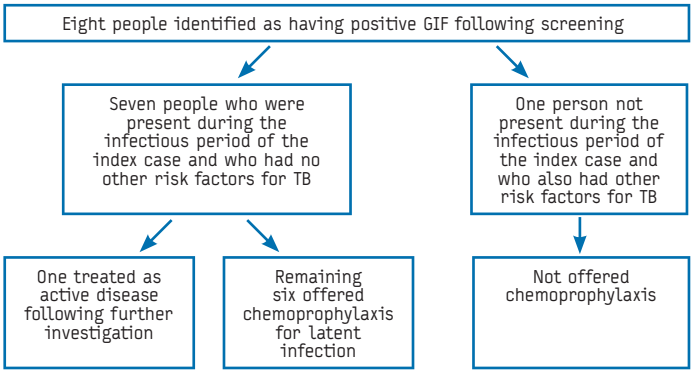
Category of contacts	Ground floor (Close contact with index case)	Ground floor (Distant contact with index case)	Other floors	Total
THOSE SCREENED USING TST				
Number screened with tuberculin Mantoux test	8	15	114	137
Number with positive tuberculin Mantoux test*	2	4	24	30
THOSE SCRENED USING GIF				
Number offered GIF testing**	2	4	24	30
Number who accepted GIF testing	2	4	22	28
Number with positive GIF test result	2	3	3	8
THOSE SCREENED USING CXR				
Number offered CXR	2	3	3	8
Number who accepted CXR	2	3	3	8
Number with abnormal CXR suggestive of active TB	1	0	0	1
FINAL RESULTS OF SCREENING				
Number diagnosed with active TB	1	0	0	1
Number diagnosed with LTBI	1	3	3	7
Number offered chemoprophylaxis	1	3	2	6

* Mantoux positive result is defined as either an induration of 6mm or greater without prior BCG vaccination or an induration of 15mm or greater with prior BCG vaccination

** GIF Testing was offered to all people with a positive Mantoux test defined as either an induration of 6mm or greater without prior BCG vaccination or an induration of 15mm or greater with prior BCG vaccination

FIGURE

Actions taken after identification of positive GIF test following screening, Manchester, United Kingdom, 2005



Discussion

Management of this incident has benefited from new technology in the evolving fields of both genotyping and diagnostic testing for LTBI.

The use of VNTR-MIRU genotyping, in preference to RFLP (restriction fragment length polymorphism), has provided more rapid laboratory evidence [4] of linkage between the cases, therefore offering the potential for real-time epidemiological investigation. However it should be remembered that studies have identified significant limitations in the operating characteristics of these newer techniques, which are likely to compromise the epidemiological inferences so derived [5] and further research is still needed in this area. Furthermore, although in this case the most likely explanation is that the three secondary cases all contracted their disease form the identified index case, it is possible that an unidentified alternative source existed.

Although tuberculin skin tests are the mainstay of the diagnosis of LTBI, they have recently been supplemented by the advent of GIF technology. The GIF test is based on short-term incubation with TB specific antigen and is therefore designed to detect cytokine secretion by primed effector T cells which are present only in true latent infection. This has resulted in improved specificity [4] in the diagnosis of LTBI. The improved specificity of these assays is based on the fact that the genes encoding the secretory proteins' early secretory antigenic target (ESAT) 6 / culture filtrate protein (CFP)10 are absent in the BCG vaccine strain and most environmental mycobacteria [6] .

GIF assays have been shown to have higher sensitivities than TSTs [6,7]. However recognising that the GIF assay is not 100% sensitive it must be recognised that even in the presence of a negative GIF test, the possibility of later developing active disease cannot be excluded. For this reason, all such patients were counselled accordingly told to should contact their general practitioner if at any stage in the future they developed symptoms suggestive of TB.

It is also important to consider the various issues that affect the optimum timing of screening investigations using GIF technology. National guidance indicates that there shold be at least six weeks between exposure and testing with GIF for TST negative contacts of smear positive pulmonary disease [2], since levels of GIF may not appear for at least two weeks after exposure. Although this would not have been an issue in this investigation, the time interval from exposure to taking the specimen for GIF may have influenced the result in another way, since GIF levels may start to wane for people who subsequently progress to active TB [8].

Nevertheless, the improvements in diagnosis of LTBI that results from the use of GIF assays offer the potential for a reduction in the number of cases inappropriately offered chemoprophylaxis, and the potentially serious side effects that this sometimes entails. It meant that chemoprophylaxis could be offered to people older than had been advocated by pre-existing guidance [1], taking into account the age-dependent hepatotoxicity profile of drugs used for chemoprophylaxis. This resulted in an additional five people being offered chemoprophylaxis in this outbreak.

However, the improved confidence that GIF technology offers needs to be treated with caution, given the absence of a gold standard for the diagnosis of LTBI. While GIF testing offers a significant step forward in terms of considering the possibility of a diagnosis of true latent infection, the evidence base for the significance of a positive GIF test in assessing the risk of development of active disease is currently lacking [9].

References

1. Joint Tuberculosis Committee of the British Thoracic Society. Control and prevention of tuberculosis in the United Kingdom: Code of Practice 2000. Thorax. 2000;55(11):887-901.
2. National Institute of Clinical Excellence. Clinical diagnosis and management of tuberculosis, and measures for its prevention and control - second consultation, June 2005. Available from http://www.nice.org.uk/page.aspx?o=271279
3. Veen J. Microepidemics of tuberculosis: the stone-in-the-pond principle. Tuber Lung Dis. 1992;73(2):73-6.
4. National TB Controllers Association/CDC Advisory Group on Tuberculosis Genotyping. Guide to the application of genotyping to tuberculosis prevention and control. Atlanta, GA: US Department of Health and Human Services, CDC; 2004. Available from http://www.cdc.gov/nchstp/tb/genotyping/toc.htm.
5. Allison N. Scott, Dick Menzies, Terry-Nan Tannenbaum, Louise Thibert, Robert Kozak, Lawrence Joseph, Kevin Schwartzman, and Marcel A. Behr. Sensitivities and Specificities of Spoligotyping and Mycobacterial Interspersed Repetitive Unit-Variable-Number Tandem Repeat Typing Methods for Studying Molecular Epidemiology of Tuberculosis. J Clin Microbiol. 2005;43(1):89-94.
6. Davies P.D.O and Drobniewski. Editorial. The use of interferon-gamma-based blood tests for the detection of latent tuberculosis infection. Eur Respir J. 2006; 28:1-3.
7. Richeldi Luca. An update on the diagnosis of tuberculosis infection. Am J Respir Crit Care Med. 2006;174(7):736-42.
8. Rothel JS, Andersen P. Diagnosis of latent *Mycobacterium tuberculosis* infection: is the demise of the Mantoux test imminent? Expert Rev Anti Infect Ther. 2005;3(6):981-93.
9. National Institute for Health and Clinical Excellence. Clinical diagnosis and management of tuberculosis, and measures for its prevention and control, March 2006. Available from http://www.nice.org.uk/page.aspx?o=CG033

Current outbreak of hepatitis A in Bulgaria, 2006

M Kojouharova[1], Editorial team[2]

1 National Center of Infectious and Parasitic Diseases, Sofia, Bulgaria
2 Eurosurveillance editorial office

Published online 5 October 2006.
Citation: Euro Surveill 2006;11(10):E061005.1.
Available from:
http://www.eurosurveillance.org/ew/2006/061005.asp#1

Hepatitis A is the most common type of viral hepatitis in Bulgaria, and accounts for more than 75% of all cases of viral hepatitis. Bulgaria is a country with intermediate endemicity of hepatitis A viral (HAV) infection. Between 1984 and 2005, incidence has varied between 27 – 80 cases per 100 000 population during non-epidemic periods, but has reached 234 cases / 100 000 during epidemic periods. Since 1983, all acute cases of jaundice due to hepatitis A virus have been subject to mandatory notification in Bulgaria. Since 2005, the European Union case definition and case classification have been adopted.

Since the beginning of 2006, 4793 viral hepatitis cases have been reported in Bulgaria (1498 cases more than the same period in 2005, when a total of 3295 cases occurred) (Figure 1). The increase of viral hepatitis incidence in 2006 is related mainly to two hepatitis A outbreaks in the regions of Sofia and Plovdiv.

Outbreak in Sofia Region, 2006: probably waterborne

The first outbreak occurred in Svoge municipality (Sofia region) in July – August 2006, and was probably associated with contamination of the drinking water supply. The incidence in the area has now returned to pre-outbreak levels (Figure 2).

Outbreak in Plovdiv, 2006

The second hepatitis A outbreak began at the end of June 2006 in Plovdiv, a city in southern central Bulgaria. Since the beginning of the year, 1727 cases of acute jaundice due to hepatitis A virus have been reported in the Plovdiv region, including 1393 cases notified between 23 June and 26 September 2006. This compares with 179 cases reported during the same period in 2005 (Fig. 3)

Figure 1

Weekly number of cases of acute viral hepatitis in Bulgaria, 2005 and 2006

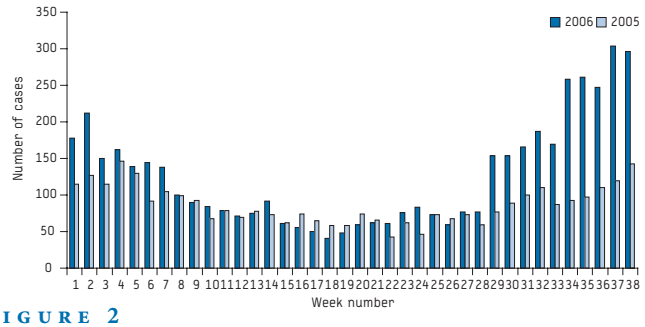


Figure 2

Number of cases of acute hepatitis in Sofia region, 2005 and 2006

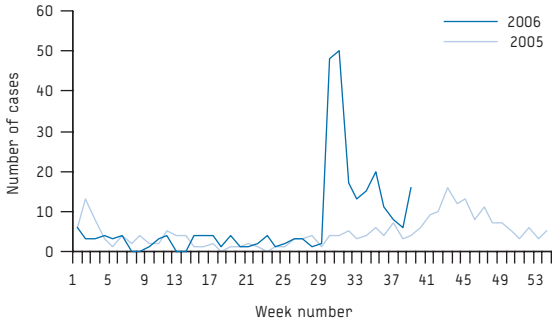


Figure 3

Number of cases of acute hepatitis in Plovdiv region, weeks 1 - 37, 2005 and 2006

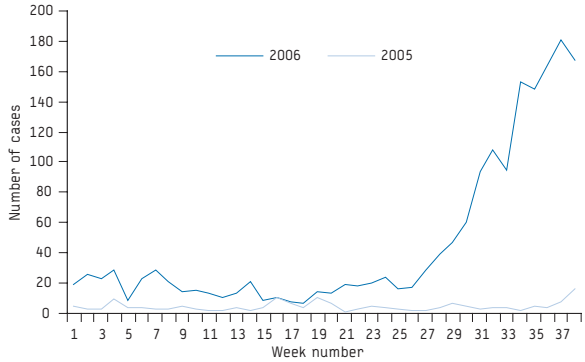
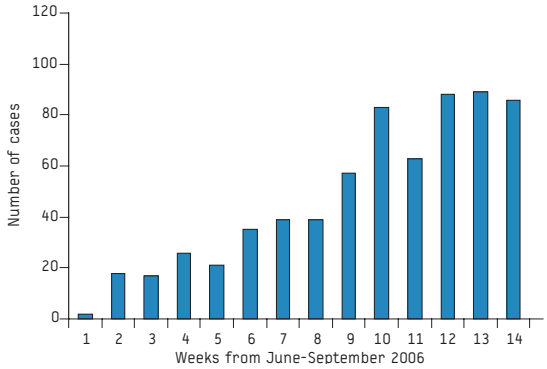


Figure 4

Weekly number of cases of acute viral hepatitis in Stolipinovo, Plovdiv, June – September 2006



The majority of the recent cases (975) occurred in Plovdiv, and 794 (81%) of these occurred in two neighbourhoods where people belonging to the Roma ethnic minority live: Stolipinovo (701 cases) and Sheker Mahala (93 cases). In Stolipinovo, 75% of cases were in children aged 1-9 years, and since the beginning of September, an average of over 80 cases has been notified each week (Figure 4). One hundred and ninety patients are currently admitted to hospital. Hepatitis A virus infection has been confirmed by serological tests on samples from the majority of patients admitted.

Sanitation and hygiene conditions in the Plovdiv area are poor, and include illegal dung hills, a substandard sewage system, and an irregular water supply. In response to the outbreak, the Bulgarian government is releasing emergency funds to help improve sanitation and food safety [1].

The Bulgarian Ministry of Health, in collaboration with Roma non-governmental organisations, launched an immunisation campaign against hepatitis A in Plovdiv on 13 September 2006. The immunisation campaign is targeting all children 2 to 18 years of age, living in Stolipinovo neighbourhoods.

Hepatitis A viral infections occur worldwide. In highly endemic regions (such as Africa, Asia, and Central and South America) outbreaks of disease are uncommon because infection occurs during early childhood, when it is mostly asymptomatic. Outbreaks of symptomatic disease are more common in countries where the economy is in transition, as a decrease in hepatitis A circulation increases the susceptibility of the population, and increases the proportion of symptomatic cases [2]. This is currently being seen in some eastern European countries such as Bulgaria, and in some regions of southern Europe.

References:

1. WHO Regional Office for Europe. Hepatitis A in Bulgaria, Plovdiv City. 5 September 2006 (http://www.euro.who.int/surveillance/outbreaks/20060905_1)
2. WHO. Hepatitis A factsheet. (http://www.who.int/csr/disease/hepatitis/HepatitisA_whocdscsredc2000_7.pdf)

TRICHINELLA IN PORK: CURRENT KNOWLEDGE ON THE SUITABILITY OF FREEZING AS A PUBLIC HEALTH MEASURE

E Pozio[1], CMO Kapel[2], AA Gajadhar[3], P Boireau[4], J Dupouy-Camet[5], HR Gamble[6]

1. Department of Infectious, Parasitic and Immunomediated Diseases, Istituto Superiore di Sanita, Rome, Italy
2. Lab. of Zoology, Department of Ecology, The Royal Veterinary and Agricultural University, Frederiksberg, Denmark
3. Centre for Food-borne and Animal Parasitology, Canadian Food Inspection Agency, Saskatoon, Canada
4. UMR BIPAR INRA AFSSA ENVA UPVM, Maisons-Alfort, France
5. Parasitologie, Hopital Cochin, Universite Descartes, Paris, France
6. National Research Council, Washington, USA

Published online 16 November 2006
Citation: Euro Surveill 2006;11(11):E061116.1.
Available from:
http://www.eurosurveillance.org/ew/2006/061116.asp#1

Nematodes of the genus *Trichinella* are the causative agents of trichinellosis, a potentially severe disease in humans. Raw or undercooked pork, horse and game meat (predominantly wild boar and bear) poses a health risk to consumers. Various European and international regulations and guidelines have been developed to protect consumers from exposure to this parasite [1-3]; these regulations and guidelines cover both slaughter inspection and post-slaughter processing (e.g., freezing, cooking). Scientific studies have been conducted to validate these methods in pork, including an international study, which described the time and temperature requirements for the freezing process to inactivate *Trichinella spiralis*, the species of *Trichinella* most commonly associated with pork [4]. Results of this study have been widely used to develop regulations governing the commercial freezing of pork and pork products [1, 3]. However, recent scientific information on the geographical distribution of species of *Trichinella*, other than *T. spiralis*, which can infect pigs, and the ability of some of these species to tolerate freezing, have raised doubts about the effectiveness of commercial freezing methods to kill *Trichinella* larvae in pork intended for human consumption [5].

Freeze resistant species of Trichinella

More than 50 years ago, it was discovered that *Trichinella* larvae (at that time all *Trichinella* larvae were considered to be *T. spiralis*), present in the muscles of animals living in arctic and subarctic regions of the world (e.g., Greenland, Canada, Russia, Siberia), were able to survive freezing for months or even years. We now recognize eight species and three genotypes of the genus *Trichinella* [5]. Of these, only muscle larvae of *Trichinella* nativa, its related genotype *Trichinella* T6, and *Trichinella* britovi are known to survive extended periods of freezing in the muscles of some of their natural hosts, including pigs [5].

From the perspective of food safety, freeze tolerant species of *Trichinella* are a potential concern as they might remain infective in pork following commercial freezing treatments. However, a number of experimental studies have demonstrated that T. nativa and *Trichinella* T6 larvae are only able to establish in very low numbers in the domestic pig [6, 7]. In general, the infectivity of T. nativa and *Trichinella* T6 for pigs is 10^4 lower than the infectivity of *T. spiralis*, and neither T. nativa nor *Trichinella* T6 has ever been found in a domestic pig in nature. These *Trichinella* species pose a very low or negligible risk to consumers of pork from domestically reared pigs and therefore may not need to be considered in regulations governing freezing of pork and pork products.

Potential risks associated with freezing pork in areas where *T. britovi* is endemic

T. britovi is found across Europe, Asia, Northern and Western Africa and has been shown in experimental studies to have moderate infectivity for the domestic pig [5,6]. According to the database of the International *Trichinella* Reference Centre (http://www.iss.it/site/Trichinella/index.asp), 36 of 200 (18%) of *Trichinella* species isolated from domestic pigs in Europe were identified as *T. britovi*.

Freeze tolerance of *T. britovi* in pork is influenced by the age of the infection as well as the conditions of freezing and thawing (i.e. temperature and time) [8]. Data shown in Table 1 [9-11], demonstrate the high variability of survival of *T. britovi* larvae in frozen meat of domestic pigs and wild boar (Sus scrofa).

Recommendations

Considering the moderate infectivity of *T. britovi* for pigs, the regular isolation of this species from the domestic pig in Europe, and the uncertainty of freezing as a method to inactivate this species, pork from areas where *T. britovi* is endemic should not be treated by freezing alone as a method to protect human health until further research has been conducted. In the interim, pork from areas where *T. britovi* is endemic should be inspected using reliable detection methods [2].

Research on freezing pork as a method to inactivate *T. britovi* should account for all the factors which may influence the susceptibility of this parasite, such as intra-specific variation of isolates from and within different geographic regions. Furthermore, studies investigating the susceptibility of *T. britovi*, or other *Trichinella* species in different hosts to various freezing conditions should be conducted with the same rigour as applied in earlier studies [4], as these results will influence future regulations on meat safety.

Note: The authors are members of the International Commission on Trichinellosis (http://monsite.wanadoo.fr/intcomtrichinellosis) and provide information and recommendations based on recent recognition of gaps in knowledge on this parasite which may impact regulatory decisions. Additional information on the subject of freeze tolerant Trichinella *can be found in an opinion paper from the European Food Safety Authority [12].*

TABLE 1

Infectivity of *T. britovi* larvae after freezing of pork of naturally or experimentally infected swine

Origin of infected pork	Age of larvae	Temperature °C	Week/s of freezing	Infectivity of larvae after thawing	Reference
Naturally infected wild boar	unknown	-20	3	yes	9
Naturally infected wild boar	unknown	-20	4	no	9
Experimentally infected pigs	5 - 10 weeks	-18	1 - 4	no	10
Experimentally infected pigs	5 - 10 weeks	-5	1 - 4	yes	10
Experimentally infected wild boar	5 - 10 weeks	-18	1 - 4	no	10
Experimentally infected wild boar	5 - 10 weeks	-5	1 - 4	yes	10
Naturally infected pigs	unknown	-18	1	no	a
Naturally infected wild boar	unknown	-35	1	yes	11

References:

1. Commission Regulation (2075/2005) laying down specific rules on official controls for *Trichinella* in meat. Official Journal of the European Union, 2005, 338:60-82.
2. Gamble HR, Bessonov AS, Cuperlovic K, Gajadhar AA, Knapen F van, Noeckler K, Schenone H, Zhu X. International Commission on Trichinellosis: Recommendations on methods for the control of *Trichinella* in domestic and wild animals intended for human consumption. Vet. Parasitol. 2000, 93:393-408.
3. U.S. Code of Federal Regulations, § 318.10. Prescribed treatment of pork and products containing pork to destroy trichinae. (http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=f9361ee66063187dffee4c083c24b6a7&rgn=div5&view=text&node=9:2.0.2.1.19&idno=9#9:2.0.2.1.19.1.21.9)
4. Kotula AW, Sharar A, Paroczay E, Gamble HR, Murrell KD, Douglas L. Infectivity of *Trichinella* from frozen pork. J. Food Prot. 1990, 53:571 573.
5. Pozio E, Murrell KD. Systematics and epidemiology of *Trichinella*. Advances in Parasitology, 2006, 63:367-439.
6. Kapel CMO, Gamble HR. Infectivity, persistence, and antibody response to domestic and sylvatic *Trichinella* spp. in experimentally infected pigs. Int. J. Parasitol. 2000, 30:215-221.
7. Nockler K, Serrano FJ, Boireau P, Kapel CMO, Pozio E. Experimental studies in pigs on *Trichinella* detection in different diagnostic matrices. Vet. Parasitol. 2005, 132:85-90.
8. Pozio E, La Rosa G, Amati M. Factors influencing the resistance of *Trichinella* muscle larvae to freezing. In, Trichinellosis (Eds C.W. Campbell, E. Pozio, F. Bruschi), ISS Press, Rome, Italy, 1994, pp. 173-178.
9. Pozio E, La Rosa G, Mignone W, Amati M, Ercolini C. Sopravvivenza delle larve muscolari di *Trichinella* britovi nei muscoli congelati di cinghiale. Arch. Veterin. Italiano 1992, 43:28-31.
10. Kapel CMO, Webster P, Malakauskas A, Hurnikova Z, Gamble HR. Freeze tolerance of nine *Trichinella* genotypes in muscle tissue of experimentally infected pigs, horses, wild boars, mice, cats, and foxes. Abstracts, XIth International Conference on Trichinellosis, August 8-12, San Diego, California, 2004, p. 28.
11. Gari-Toussaint M, Tieulie N, Baldin J, Dupouy-Camet J, Delaunay P, Fuzibet J et al. Human trichinellosis due to *Trichinella* britovi in southern France after consumption of frozen wild boar meat. Euro Surveill 2005;10(6):117-8 (http://www.eurosurveillance.org/em/v10n06/1006-226.asp)
12. European Food Safety Authority. Opinion of the BIOHAZ Panel on the suitability and details of freezing methods to allow human consumption of meat infected with *Trichinella* or Cysticercus. Adopted on 1 December 2004 in Parma. (http://www.efsa.europa.eu/en/science/biohaz/biohaz_opinions/777.html)

Impact of a genetic variant of *Chlamydia trachomatis* on national detection rates in Sweden

T Söderblom[1], A Blaxhult[1], H Fredlund[2], B Herrmann[3]

1. Swedish Institute for Infectious Disease Control, Solna, Sweden
2. Department of Clinical Microbiology, University Hospital, Örebro, Sweden
3. Department of Clinical Microbiology, Uppsala University Hospital, Uppsala, Sweden

Published online 7 December 2006
Citation: Euro Surveill 2006;11(12):E061207.1.
Available from:
http://www.eurosurveillance.org/ew/2006/061207.asp#1

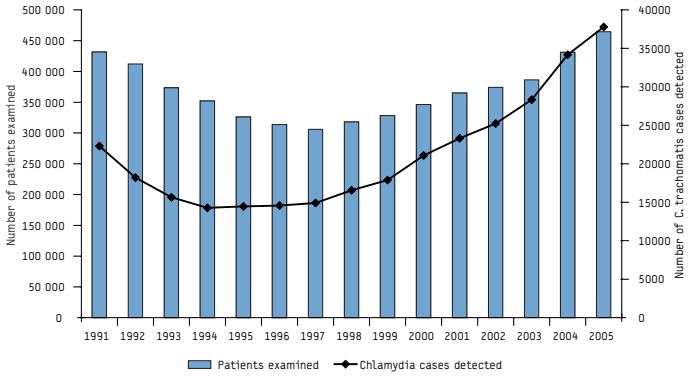
In the Swedish county of Halland, it was recently reported that a proportion of sexually transmitted *Chlamydia trachomatis* infections could not be detected using standard laboratory tests manufactured by Abbott and Roche [1]. Chlamydia bacteria with a variation in a genomic region targeted by PCR primers have been identified. A subsequent investigation to see whether the presence of genetic varients could be inferred from the basic epidemiological data reported from all 21 counties in Sweden has recently been completed.

In Sweden, four commercially available nucleic acid amplification assays are used for chlamydia routine diagnostics, although in most counties, only one assay is used. Three of the detection systems (two from Roche and one from Abbott) use the same PCR primer target region. The chlamydia genetic variant recently identified has a deletion in this region, therefore these tests cannot detect it [1]. The diagnostic test by BectonDickinson uses a different primer target region and can therefore detect this variant.

Chlamydia trachomatis infection is one of the 60 notifiable diseases under surveillance at a national level in Sweden. Chlamydia infections are reported both as individual clinical cases and as the number of people with detected chlamydia infections. The annual number of people in Sweden testing positive for chlamydia has consistently increased since 1994 (Figure 1).

Figure 1

Number of people with detected chlamydia infections, and number of people tested for chlamydia, 1991 - 2005*



* Even though the overall number of patients tested for chlamydia in 2006 is not yet available, on the basis of preliminary data, it is assumed to be the same as in 2005.

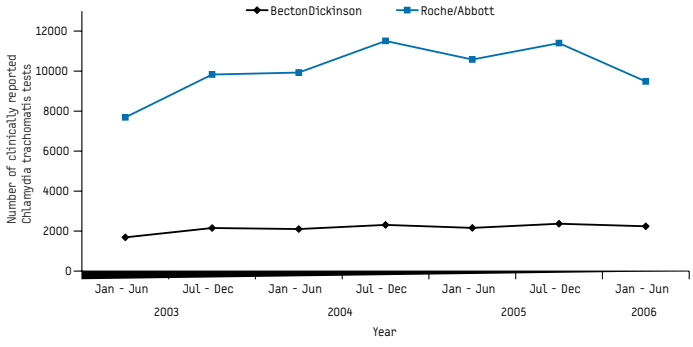
Detection of chlamydia infections by different methods

Data showing clinically reported cases reported between January 2003 and June 2006 according to diagnostic test used is presented in Figure 2. The data was provided by 20 laboratories covering the whole of Sweden, except three counties where laboratories either changed the detection method during the observed period or used both Roche and BectonDickinson systems. The data accounts for approximately 80% of all reported chlamydia cases in Sweden during the period from January 2003 to June 2006. In 2003 and 2004, the number of reported cases increased or stayed at a similar level regardless of the test used.

Due to seasonal variations in chlamydia infections, the incidence is higher in the second half of the year. However, the counties where laboratories used BectonDickinson tests reported a similar number of chlamydia cases in the first and second half of 2005, while the counties using Roche or Abbott tests reported fewer cases in the second half of the year.

Figure 2

Number of clinically reported chlamydia cases in Sweden from January 2003 to June 2006, by diagnostic method



This trend is even more visible when the first half of 2006 is compared with the same period in 2005. A 10% decline in number of chlamydia cases diagnosed with Roche or Abbott tests can be seen, compared with a 1% increase in cases detected with the BectonDickinson test. This could be caused by a nationwide distribution of a genetic variant of *Chlamydia trachomatis* being undiagnosed.

Discussion

At present, it is still unclear when the variant appeared (it still also not determined whether there are several clones), and how far it has spread in Sweden. There are considerable variations in case numbers from month to month between counties which use the same test and there is a lack of information about prevention and control measures (such as chlamydia prevention programmes) for each individual county.

We can assume that this genetic variant, because it is not being detected and treated, is spreading more easily than other strains. In counties that have used Roche/Abbott technology for several years, genetic variants may be more prevalent than in counties using alternative test systems. Due to the presence of chlamydia cases caused by a genetic variant, one laboratory (Örebro University Hospital) recently changed over from the Roche test system to diagnostics by cell culture.

Although data are still based on low numbers, the proportion of cases caused by the chlamydia genetic variant (negative by Roche PCR and a fraction confirmed by sequence analysis) accounted for 39% of all chlamydia cases during one month from unselected patients examined at primary health care/STI-/youth clinics. If this was a representative figure, the failure to detect this genetic variant would also have an effect on the complication rates of genital chlamydia infections. However, since complication risks are difficult to estimate and the rates of complication or infections are low in Sweden, it would be even more difficult to measure the impact of this chlamydia variant on public health [2].

Regardless of the exact proportion of chlamydia cases caused by the variant, it is evident that the failing diagnostic methods must urgently be modified to enable detection of all prevalent *C. trachomatis* strains. It appears that the present findings are an example of bacterial evolution driven by diagnostic methods. This could have been prevented by using double target genes of the infectious agent in the same test reaction, as has been applied for other pathogens [3].

Assuming that the recently discovered chlamydia variant is evenly spread throughout Sweden, using the data from Halland county as a basis, it can be estimated how much this would affect the nationally reported numbers. From January to September 2006, the number of clinically reported chlamydia cases in Sweden decreased by 6%, compared with the same period in 2005. If the case numbers from laboratories using Roche/Abbott test are compensated with a 13% 'loss in detectability' (13% was the proportion of missed cases in Halland county) a 4% national increase in chlamydia cases would have been expected compared with the same period in 2005. Assuming that the prevalence is increasing, as has been the trend since 1997, this 6% decrease could more easily be explained by a drop in detection rather than an actual decrease. Further data are still needed to determine the size of the problem of this chlamydia variant and failing detection systems. The results obtained so far highlight the importance of active monitoring of test accuracy and epidemiological surveillance.

References:

1. Ripa T, Nilsson P. A variant of *Chlamydia trachomatis* with deletion in cryptic plasmid: implications for use of PCR diagnostic tests. Euro Surveill 2006;11(11): E061109.2. (http://www.eurosurveillance.org/ew/2006/061109.asp#2)
2. Low, N, Egger M, Sterne J, Harbord R, Ibrahim F, Lindblom B, Herrmann B. Incidence of severe reproductive tract complications associated with diagnosed genital chlamydial infection: the Uppsala Women's Cohort Study. Sex Transm Inf 2006; 82: 212-8
3. Herrmann B, Cavaglia-Larsson V, Rubin C-J, Sund F, Eriksson B-M, Yun Z, Bondeson K, Blomberg J. Comparison of a duplex quantitative real time PCR and COBAS Amplicor CMV Monitor for detection of cytomegalovirus. J Clin Microbiol 2004, 42:1909-14.

Other Online-only content

Other weekly release items from the past 3 months, available online only at www.eurosurveillance.org

Outbreak of enteroviral meningitis in Latvia, August – October 2006
5 October 2006

Personal (non-pharmaceutical) protective measures for reducing transmission of influenza – ECDC interim recommendations
12 October 2006

Cluster of measles cases in the Roma/Sinti population, Italy, June-September 2006
12 October 2006

Outbreak of legionellosis suspected to be related to a whirlpool spa display, September 2006, Lorquin, France
12 October 2006

Unexplained summer increase in non-travel related legionellosis in the UK and Netherlands
18 October 2006

Coordinated European actions to prevent and control norovirus outbreaks on cruise ships
18 October 2006

Hepatitis A cases in a travelling community in southeast England
18 October 2006

Analysis of 721 Chlamydia trachomatis-positive urogenital specimens from men and women using LGV L2-specific real-time PCR assay, Switzerland, 2006
18 October 2006

No link established between deaths in elderly patients in Israel and influenza vaccination
26 October 2006

An outbreak of Salmonella Enteritidis infections linked to a restaurant in Riga, August 2006
26 October 2006

Surveillance methods and case definition for extensively drug resistant TB (XDR-TB) and relevance to Europe: summary update
3 November 2006

Potential rabies exposure after a bat bite, Denmark, June 2006
3 November 2006

Increase in viral meningitis cases reported in the Autonomous Region of Madrid, Spain, 2006
3 November 2006

Dr Margaret Chan appointed WHO Director-General
9 November 2006

A variant of Chlamydia trachomatis with deletion in cryptic plasmid: implications for use of PCR diagnostic tests
9 November 2006

Vibrio alginolyticus infections in the Netherlands after swimming in the North Sea
9 November 2006

Mumps outbreak in young adults following a village festival in the Navarra region, Spain, August 2006
9 November 2006

Unexplained increase in Paecilomyces variotii blood culture isolates in the UK
16 November 2006

A case of autochtonous Plasmodium vivax malaria, Corsica, August 2006
16 November 2006

Pneumococcal conjugate vaccine is efficacious against invasive disease with fewer doses than currently recommended
16 November 2006

Ongoing HIV and viral hepatitis infections in IDUs across the EU, 2001-2005
23 November 2006

Salmonella contamination in non-UK produced shell eggs on retail sale in some regions of England
23 November 2006

Hajj 2007: vaccination requirements and travel advice issued Two unrelated cases of septicaemia due to Vibrio cholerae non-01, non-0139 in Poland, July and August 2006
30 November 2006

Legionnaires' disease: when an 'outbreak' is not an outbreak
30 November 2006

Third case of vCJD reported in the United States
7 December 2006

Use of 7-valent pneumococcal conjugate vaccine in EU
7 December 2006

Increase in norovirus circulation in Hungary in October - November 2006
14 December 2006

Plasmodium falciparum malaria in Jamaica, October – December 2006
14 December 2006

Outbreak of foodborne botulism linked to barbecue, Austria, 2006
14 December 2006

Highly Pathogenic Avian Influenza A/H5N1 – update and overview of 2006
21 December 2006

Soft tissue infections in Belgian rugby players due to Streptococcus pyogenes emm type 81
21 December 2006

Epidemic intelligence during mass gatherings
21 December 2006

Cooperation between animal and human health sectors is key to the detection, surveillance, and control of emerging disease: IMED 2007 meeting in Vienna, February 2007
21 December 2006

Contributions to Eurosurveillance are welcomed. Full instructions to authors are available at our website, http://www.eurosurveillance.org

National Bulletins

Austria
Mitteilungen der Sanitätsverwaltung
Bundesministerium für Gesundheit und Frauen
Stabsstelle I/A/4
Radetzkystrasse 2
A-1031 Wien
Monthly, print only. In German.
Ministry Website: http://www.bmgf.gv.at

Belgium
Vlaams Infectieziektebulletin
Gezondheidsinspectie Antwerpen
Copernicuslaan 1, bus 5
2018 Antwerpen
Quarterly, print and online versions available. In Dutch.
http://www.vlaanderen.be/epibul/

Infectious Diseases in the Spotlights
Institut Scientifique de la santé Publique Louis Pasteur
14, rue Juliette Wytsman
B-1050 Bruxelles
Weekly, online only. In English.
http://www.iph.fgov.be/epidemio/epien/plaben/idnews/index_en.htm

Bulgaria
Epidemiological Surveillance
National Centre of Infectious and Parasitic Diseases
26 Yanko Sakazov blvd.
Sofia 1504
Print version available, online version available soon. In Bulgarian, titles translated into English.
http://www.ncipd.org/bulletin.php

Cyprus
Newsletter of the Network for Surveillance and Control of Communicable Diseases in Cyprus
Medical and Public Health Services
Ministry of Health
Markou Drakou 10
1449 Nicosia
Biannual, print and online versions available. In Greek.

Czech Republic
Zpravy CEM
(Monthly Bulletin of Centre Epidemiology and Microbiology)
Centrum epidemiologie a mikrobiologie Státního zdravotního ústavu (Centre of Epidemiology and Microbiology, National Institute of Public Health)
Srobarova 48
100 42 Praha 10
Monthly, print and online versions available, in Czech with some important notifications in English.
http://www.szu.cz/cema/adefaultt.htm

EPIDAT
Notifications of infectious diseases in the Czech Republic
http://www.szu.cz/cema/epidat/epidat.htm

Denmark
EPI-NEWS
Department of Epidemiology
Statens Serum Institut
Artillerivej 5
DK-2300 København S
Weekly, print and online versions available. In Danish and English.
http://www.ssi.dk

England and Wales
Communicable Disease Report Weekly (CDR)
Health Protection Agency
61 Colindale Avenue
London NW9 5EQ
Weekly, online only. In English.
http://www.hpa.org.uk/cdr

Finland
Kansanterveys
Department of Infectious Disease Epidemiology
National Public Health Institute
Mannerheimintie 166
00300 Helsinki
Monthly, print and online versions available. In Finnish.
http://www.ktl.fi/portal/suomi/julkaisut/kansanterveyslehti/

France
Bulletin epidémiologique hebdomadaire
Institut de veille sanitaire
12, rue du Val d'Osne
94415 Saint-Maurice Cedex
Weekly, print and online versions available. In French.
http://www.invs.sante.fr/beh/default.htm

Germany
Epidemiologisches Bulletin
Robert Koch-Institut
Presse, Oeffentlichkeitsarbeit, Bibliotheken
Nordufer 20
D-13353 Berlin
Weekly, print and online versions available. In German.
http://www.rki.de/DE/Content/Infekt/EpidBull/epid__bull__node.html

Hungary
Epinfo (Epidemiológiai Információs Hetilap)
National Center For Epidemiology
Gyali ut 2-6
1097 Budapest
Weekly, online version available. In Hungarian.
http://www.antsz.hu/oek/epinfo/szoveg/Heti2004/hetiindit04.htm

Ireland
EPI-INSIGHT
Health Protection Surveillance Centre (HPSC)
25-27 Middle Gardiner Street
Dublin 1
Monthly, print and online versions available. In English.
http://www.ndsc.ie/EPI-Insight/

Italy
Notiziario dell'Istituto Superiore di Sanità
Istituto Superiore di Sanità
Reparto di Malattie Infettive
Viale Regina Elena 299
I-00161 Roma
Monthly, online only. In Italian and English.
http://www.iss.it/publ/serie.php?id=4

Bolletino Epidemiologico Nazionale (BEN)
Istituto Superiore di Sanità
Reparto di Malattie Infettive
Viale Regina Elena 299
I-00161 Roma
Monthly, online only. In Italian and English.
http://www.epicentro.iss.it/ben/

Latvia
Epidemiologijas Bileteni
State Public Health Agency
7 Klijanu Street
1012 Riga
Online. In Latvian.
http://www.sva.lv/epidemiologija/bileteni/

Netherlands
Infectieziekten Bulletin
Rijksinstituut voor Volksgezondheid en Milieu
PO Box 1
NL-3720 Bilthoven
Monthly, print and online versions available. In Dutch, some summaries in English.
http://www.rivm.nl/infectieziektenbulletin/

Northern Ireland
Communicable Disease Monthly Report
Communicable Disease Surveillance Centre (Northern Ireland)
McBrien Building, Belfast City Hospital,
Lisburn Road
Belfast BT9 7AB
Monthly, print and online versions available. In English.
http://www.cdscni.org.uk/publications/

Norway
MSIS-rapport
Folkehelseinstituttet
Postboks 4404 Nydalen
N-0403 Oslo
Weekly, print and online versions available. In Norwegian.
http://www.fhi.no

Poland
Reports on cases of infectious disease and poisonings in Poland
Instytut Naukowo-Badawczy (National Institute of Hygiene)
ul. Chocimska 24
00-791 Warsawa
Fortnightly. In Polish and English.

Portugal
Saúde em Números
Direcção-Geral da Saúde
Alameda D. Afonso Henriques 45
1049-005 Lisboa
Sporadic, print only. In Portuguese.
Ministry website: http://www.dgsaude.pt/

Romania
Info Epidemiologia
Bulletin of the National Center for Surveillance and Control of Communicable Diseases, Institute of Public Health of Bucharest
1-3 Dr Leonte Street (Strada Dr.Leonte 1-3)
Sector 5 Bucharest Romania
Sporadic, print only.

Scotland
Health Protection Scotland Weekly Report
Health Protection Scotland
Clifton House, Clifton Place
Glasgow, G3 7LN
Scotland
Weekly, print and online versions available. In English.
http://www.show.scot.nhs.uk/scieh/wrhome.html

Slovenia
CNB Novice
Institut za varovanje zdravja Republike Slovenije
Center za nalezljive bolezni
Trubarjeva 2
Ljubljana
Monthly, online only. In Slovene.
http://www.ivz.si/ivz/aktualno/

Spain
Boletín Epidemiológico Semanal
Centro Nacional de Epidemiología - Instituto de Salud Carlos III
C/ Sinesio Delgado 6 - 28029 Madrid
Bi-weekly, print and online versions available. In Spanish.
http://www.isciii.es/jsps/centros/epidemiologia/boletinesSemanal.jsp

Sweden
EPI-aktuellt
Smittskyddsinstitutet
171 82 Solna
Weekly, online only. In Swedish.
http://www.smittskyddsinstitutet.se/SMItemplates/Article____2414.aspx

Smittskydd
Smittskyddsinstitutet
171 82 Solna
Monthly, print only. In Swedish.

A selection of report titles from the national epidemiological bulletins in the European Union and Norway are translated and published online each month in the Eurosurveillance Monthly release section of our website, http://www.eurosurveillance.org

Eurosurveillance Editorial Advisors

ISSN 1025 496X
6000 copies
Graphic Design © Françoise Parraud, Paris
Réalisation : Labrador 00 33 1 53 06 30 80
Registered July 2004

Eurosurveillance

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Visit our website at
www.eurosurveillance.org

The **Eurosurveillance** print edition is a compilation of **weekly** and **monthly electronic releases** published on the Eurosurveillance website.

All the articles in this issue are available on our website: you can print each page separately or download the whole quarterly in pdf format.

The website archives all articles since 1995, and offers a search facility.

To receive Eurosurveillance free **electronic releases** and e-alerts by e-mail, please subscribe on our website.

European Commission
InVS INSTITUT DE VEILLE SANITAIRE
Health Protection Agency