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Spotlight on measles 2010: Ongoing measles outbreak in Greece, January–July 2010

D Pervanidou (pervanidou@gmail.com)[1], E Horefti[2], S Patrinos[1], T Lytras[1], E Triantafillou[1], A Mentis[2], S Bonovas[1], T Panagiotopoulos[1,3]
1. Department of Surveillance and Intervention, Hellenic Centre for Disease Control and Prevention, Athens, Greece
2. National Measles Reference Laboratory, Hellenic Pasteur Institute, Athens, Greece
3. Department of Child Health, National School of Public Health, Athens, Greece

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A measles outbreak (126 reported cases to date) has been ongoing in Greece, since January 2010, originally related to the recent outbreak in Bulgaria. Cases are mostly unvaccinated, and mainly belong to three groups: Roma population of Bulgarian nationality, Greek Roma population, and Greek non-minority population. In these population groups, 67%, 95%, and 25% of cases respectively were children aged 0-14 years. Measures were taken to raise clinical awareness, and vaccination of specific population groups was undertaken. Policies are necessary to increase routine vaccination uptake of hard-to-reach groups.

Background

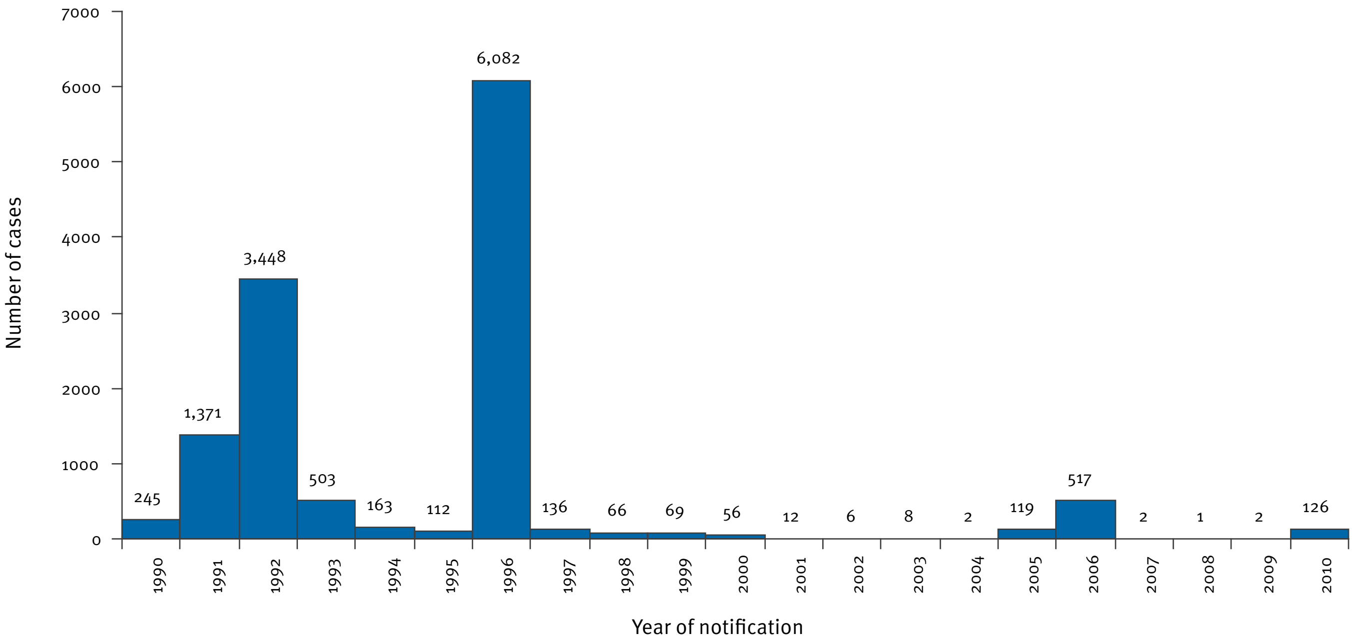
Measles is still present in Europe, causing severe complications and deaths in children [1,2]. Despite a large decline in measles incidence in the past decade in Europe, the World Health Organization (WHO) target to eliminate measles in Europe by 2010 does not seem feasible [2]. A measles outbreak with more than 20,000 reported cases has been taking place in Bulgaria since April 2009 [3,4], and clusters of cases have been reported from several countries in Europe in 2009 and 2010 [5-9].

Measles is a notifiable disease in Greece; the European Union (EU) case definition of 2008 is used [10]. Overall, measles incidence has been steadily declining in Greece during the past 25 years. The last measles outbreaks occurred in Greece in 1996 and in 2005 and 2006 (Figure 1).

The 2-5-year measles epidemic cycles previously observed ended after the 1996 measles outbreak. The last outbreak, in 2005-2006, had mainly affected unvaccinated Roma children aged 0-14 years, older

FIGURE 1

Reported measles cases by year of notification, Greece, 1 January 1990–25 July 2010



teenagers and young adults from the non-minority general population who were either unvaccinated or had had one dose of measles-containing vaccine, and unvaccinated or incompletely vaccinated immigrants [11].

Ongoing measles outbreak in Greece

A total of 126 measles cases have been reported to the Hellenic Centre for Disease Control and Prevention through the mandatory notification system by 25 July 2010 (rate 1.1 cases per 100,000 population). The first case was notified on 29 January 2010.

Case classification

Seventy-seven (61%) of 126 reported cases were laboratory-confirmed (by serology and/or by PCR). Thirty-one cases (25%) were classified as probable (cases meeting the clinical criteria with an epidemiological link). Eighteen cases (14%) were classified as possible (cases meeting the clinical criteria).

Laboratory investigation

So far, measles virus genotype D4 was identified in all 19 cases genotyped by the National Measles Reference Laboratory (Hellenic Pasteur Institute). Nine of these cases are of Bulgarian nationality (Roma), nine are of Greek nationality (six of them are Roma) and one case is of Albanian nationality. Genotyping is in process for more cases.

Nationality / high-risk populations

Thirty-six (29%) of 126 reported cases belonged to Roma communities of Bulgarian nationality, mostly families of seasonal workers in Greece (usually living in poor conditions). Eighty-seven cases (69%) were persons of Greek nationality, 43 (34%) of whom belonged to the Greek Roma community. Seven cases (6%) were health-care workers. Three (2%) cases were persons of other nationalities (one immigrant from Albania, one tourist from Denmark and one from France).

Progress of the outbreak over time

As indicated in the epidemic curve (Figure 2), during the first seven weeks of the outbreak, the majority of cases were of Bulgarian nationality. In the following weeks cases of Greek nationality were reported as well, and after week 21/2010 the majority of cases belonged to Greek Roma communities.

Age distribution

Seventy-eight (62%) of 126 reported cases were children aged 0-14 years, with the largest number of cases (n=34, 27%) in the age group of 1-4 years. Ten cases (8%) were younger than 1 year.

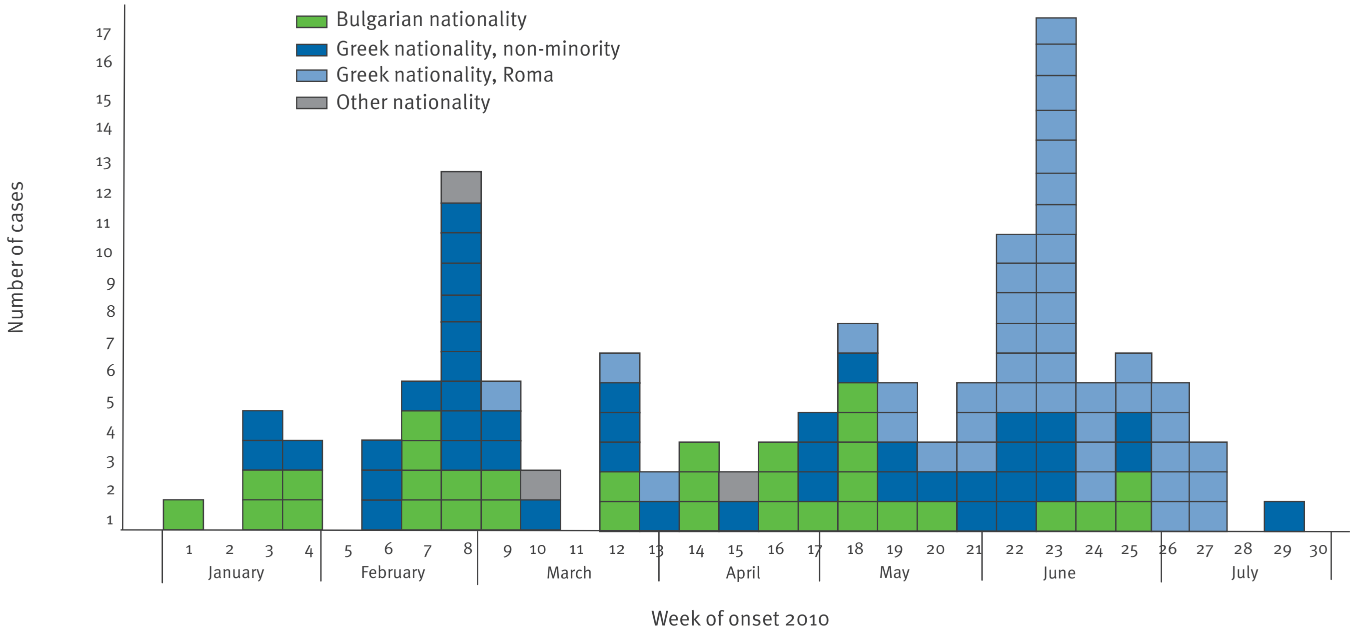
As indicated in the Table, the majority of measles cases of Bulgarian nationality were children 0-14 years (67%), mainly children aged 0-4 years (42%). Almost all cases in the Greek Roma population were children aged 0-14 years (95%), half of whom were 0-4 years-old. The majority of cases from the non-minority Greek population were young adults older than 20 years (66%).

Vaccination status

Information on vaccination status was reported by physicians who got this information from children's health booklets, or by parents or patients themselves. Of the 106 measles cases with known vaccination status, 93 cases (88%) were reported as unvaccinated. Thirteen cases (12%) were vaccinated for measles, all of them

Figure 2

Reported measles cases by week of symptoms' onset and by population group, Greece, 1 January–25 July 2010 (n=122[a])



[a] Date of onset of symptoms was known only for 122 cases.

of Greek nationality (12 cases from the non-minority general population and one from the Roma community). Nine cases were reported to have had one dose of measles vaccine (the case from the Roma community was vaccinated seven days before disease onset) and four cases were vaccinated with an unspecified number of doses.

History of recent travel abroad

Information on recent travel abroad (within three weeks before onset of symptoms) was available for 114 of the 126 cases. One hundred and four cases (91%) had no history of recent travel abroad, including 22 cases of Bulgarian nationality. Ten cases (9%) had a history of recent travel: eight cases had recently travelled to Bulgaria (six persons of Bulgarian nationality, one Roma person of Greek nationality and one of Danish nationality), one case to France (person of French nationality) and another one had an unknown travel itinerary.

Hospitalisation, complications and outcome

Of the 125 cases with known hospitalisation status, 83 (66%) were hospitalised. Of 125 measles cases with known complication status, complications were reported in 31 (25%) of the cases. Complications included pneumonia (18 cases), otitis media (seven cases), laryngitis and/or bronchitis (six cases). Measles was complicated by meningitis in one male aged 29 years, whose vaccination status was unknown. No death has been reported.

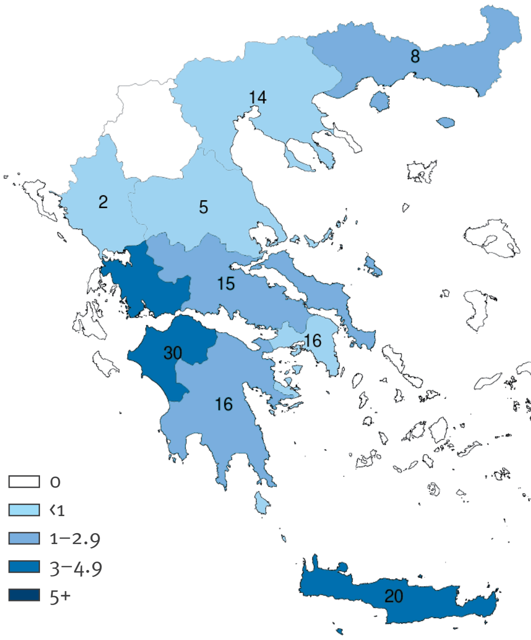
Geographical distribution

The first measles clusters were reported from the district of Ilia in southwestern Greece (a total of 30 cases, most of them in three villages) and from the island of Crete (six cases from the district of Chania and 13 cases from the district of Heraklion, 10 of them from one village). No connection was identified between the clusters in Ilia, Chania and Heraklion.

As of 25 July 2010 measles cases have been reported from 21 of the 52 districts of the country, without any apparent geographical pattern. Clusters have been reported in Greek Roma camps (33 cases from eight clusters in Greek Roma camps) and in villages where Roma of Bulgarian nationality stay (26 cases from five villages). The largest reported cluster had thirteen cases (12 cases from one village, most of them relatives, and one healthcare worker) all belonging to the Greek non-minority population. Only two of the clusters were directly related to imported cases with recent travel history abroad. Of infants under 1 year, half (5/10) were part of family clusters, and one was part of a community cluster.

Figure 3

Notified measles cases and incidence rate per 100,000 population in the 13 administrative regions, Greece, 1 January–25 July 2010



Numbers in the regions represent cases.

Numbers and colours in the legend represent incidence per 100,000 population.

Table

Reported measles cases by age group and nationality/population group, Greece, 1 January–25 July 2010 (N=126)

Age group (years)	Bulgarian nationality, Roma	Greek nationality, non-minority	Greek nationality, Roma	Other nationality	Total
<1	4	1	5	0	**10**
1-4	11	5	16	2	**34**
5-9	4	3	9	0	**16**
10-14	5	2	11	0	**18**
15-19	3	4	0	0	**7**
20-24	3	8	1	0	**12**
25-29	2	7	1	0	**10**
≥30	4	14	0	1	**19**
Total	36	44	43	3	**126**

Control measures

The following public health measures were implemented. All regional and local public health authorities, physicians and other healthcare workers in the public and private sector in Greece were informed about this outbreak and the outbreak in Bulgaria, and about the appropriate investigation and management of measles cases and their contacts (isolation of cases, contact tracing and vaccination of susceptible contacts). Guidelines for measles control were distributed to healthcare staff and are available on the website of the Hellenic Centre for Disease Control and Prevention (www.keelpno.gr). Furthermore, physicians were alerted to increase their awareness for measles cases and to strengthen surveillance and to complete routine immunisation of children, adolescents and young adults in the wider community, according to the national immunisation schedule. In addition, vaccination campaigns of population groups with low vaccine coverage were organised in the country, with priority to high risk communities (mainly Roma) in affected areas.

Discussion and conclusions

This is a preliminary report of an ongoing measles outbreak in Greece, based on national surveillance data. The first cases and clusters were among persons of Bulgarian nationality, probably related to the measles outbreak in Bulgaria which started in April 2009 [3]. However, the high proportion of Greek nationals, mainly from Roma communities, underlines that despite the high national immunisation coverage with measles-mumps-rubella (MMR) vaccine, pockets of unvaccinated populations still exist.

Vaccination with two doses of MMR vaccine has been included in the national immunisation schedule in Greece since 1991. According to the national immunisation schedule, vaccination with the first dose of MMR is recommended at the age of 12-15 months and with the second dose at the age of 4-6 years. Immunisation coverage with MMR is high in children in Greece, but less than optimal in adolescents and young adults. In some population groups (e.g. Greek Roma) vaccination coverage is low. According to the last national study on vaccination coverage, carried out in 2006, about 99% of first grade school children (about 6 years-old) were immunised with one dose of a measles-containing vaccine, and 77% with two doses. In Roma children, coverage was 82% and 45% respectively, but this refers to Roma children going to school and may represent an overestimation of the coverage of all Roma children. In ninth grade school children (about 14 years-old), coverage with one dose of a measles-containing vaccine was 92%, and 80% with two doses [12].

It is of concern that the age distribution of cases in the Greek Roma population (95% of cases under 15 years) is similar to the one observed in many countries in the pre-vaccination era [13]. Children under the age of one year represented 8% of all cases (rate 9.1 per 100,000 population). In some recent outbreaks, the incidence of measles in this age group was found increased compared to previous years [14]. The hospitalisation rate we found (66%) is similar to that reported in some recent outbreaks in Europe [3,5] but higher than in others [6,14], possibly reflecting a greater extent of underreporting of mild cases.

The occurrence of this outbreak highlights the need to achieve high vaccination coverage with two doses of MMR vaccine through routine immunisation in the general population (not only among children, but also among adolescents and young adults) and the need to increase immunisation coverage in hard-to-reach populations. It is equally important to have systematic policies that ensure good access to vaccination services for children in Roma communities in Greece.

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References

1. EUVAC NET. Measles surveillance annual report 2009. Copenhagen: EUVAC NET. Available from: http://www.euvac.net/graphics/euvac/pdf/annual_2009.pdf
2. Lopalco PL, Martin R. Measles still spreads in Europe: who is responsible for the failure to vaccinate?. Euro Surveill. 2010;15(17):pii=19557. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19557
3. Marinova L, Muscat M, Mihneva Z, Kojouharova M. An update on an ongoing measles outbreak in Bulgaria, April-November 2009. Euro Surveill. 2009;14(50):pii=19442. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19442
4. EUVAC NET. Measles outbreak in Bulgaria: update as of week 28, 2010. Copenhagen: EUVAC NET. Available from: http://www.euvac.net/graphics/euvac/outbreak/bulgaria28.html
5. Orlikova H, Rogalska J, Kazanowska-Zielinska E, Jankowski T, Slodzinski J, Kess B, et al. Spotlight on measles 2010: A measles outbreak in a Roma population in Pulawy, eastern Poland, June to August 2009. Euro Surveill. 2010;15(17):pii=19550. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19550
6. Gee S, Cotter S, O'Flanagan D, on behalf of the national incident management team. Spotlight on measles 2010: Measles outbreak in Ireland 2009-2010. Euro Surveill. 2010;15(9):pii=19500. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19500
7. Bätzing-Feigenbaum J, Pruckner U, Beyer A, Sinn G, Dinter A, Mankertz A, et al. Spotlight on measles 2010: Preliminary report of an ongoing measles outbreak in a subpopulation with low vaccination coverage in Berlin, Germany, January-March 2010. Euro Surveill. 2010;15(13):pii=19527. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19527
8. Grgic-Vitek M, Frelih T, Ucakar V, Prosenc K, Tomažič J, Petrovec M, et al. Spotlight on measles 2010: A cluster of measles in a hospital setting in Slovenia, March 2010. Euro Surveill. 2010;15(20):pii=19573. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19573
9. EUVAC NET. Measles outbreaks in Piemonte, Italy between 1 January 2010 and 13 May 2010. Copenhagen: EUVAC NET. Available from: http://www.euvac.net/graphics/euvac/outbreak/italy5.html
10. European Commission. Commission Decision of 28 April 2008 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council. 18.06.2008:L 159. Available from: http://ec.europa.eu/health/ph_threats/com/docs/1589_2008_en.pdf
11. Georgakopoulou T, Grylli C, Kalamara E, Katerelos P, Spala G, Panagiotopoulos T. Current measles outbreak in Greece. Euro

Surveill. 2006;11(8):pii=2906. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=2906

12. Panagiotopoulos T, Georgakopoulou T, Stavrou D, Danis K, Laggas D, Georgiadou L, et al. Greek national study on vaccination coverage and occurrence of tuberculosis infection in children, 2006. Athens: National School of Public Health. 2009 [in Greek]. Available from: http://www.nsph.gr/files/011_Ygeias_Paidiou/Ereunes/emvolia_tblimoxi_2006_ekthesi.pdf
13. Miller E, Nokes DJ, Anderson RM. Measles, mumps and rubella vaccination. BMJ. 1992;304(6839):1440-1.
14. Stein-Zamir C, Abramson N, Shoob H, Zentner G. An outbreak of measles in an ultra-orthodox Jewish community in Jerusalem, Israel, 2007 - an in-depth report. Euro Surveill. 2008;13(8):pii=8045. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=8045

Event-based biosurveillance of respiratory disease in Mexico, 2007–2009: connection to the 2009 influenza A(H1N1) pandemic?

N P Nelson (nelson@isis.georgetown.edu)[1], J S Brownstein[2], D M Hartley[3]
1. Georgetown University School of Medicine, Department of Paediatrics, Washington, DC, United States
2. Children's Hospital Boston and Harvard University Medical School, Boston, MA, United States
3. Georgetown University School of Medicine, Department of Microbiology and Immunology and Department of Radiology, Washington, DC, United States

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The emergence of the 2009 pandemic influenza A(H1N1) virus in North America and its subsequent global spread highlights the public health need for early warning of infectious disease outbreaks. Event-based biosurveillance, based on local- and regional-level Internet media reports, is one approach to early warning as well as to situational awareness. This study analyses media reports in Mexico collected by the Argus biosurveillance system between 1 October 2007 and 31 May 2009. Results from Mexico are compared with the United States and Canadian media reports obtained from the HealthMap system. A significant increase in reporting frequency of respiratory disease in Mexico during the 2008–9 influenza season relative to that of 2007–8 was observed ($p<0.0001$). The timing of events, based on media reports, suggests that respiratory disease was prevalent in parts of Mexico, and was reported as unusual, much earlier than the microbiological identification of the pandemic virus. Such observations suggest that abnormal respiratory disease frequency and severity was occurring in Mexico throughout the winter of 2008–2009, though its connection to the emergence of the 2009 pandemic influenza A(H1N1) virus remains unclear.

Introduction

The emergence in North America and global spread of the novel 2009 pandemic influenza A(H1N1) virus of swine origin was unanticipated in the spring of 2009 by governments and health agencies around the world. Many nations have limited ability to detect outbreaks or maintain situational awareness of them within their borders, making reporting and early warning of emerging influenza viruses with pandemic potential problematic. Event-based biosurveillance, based on local- and regional-level Internet media reports, is an internationally recognised and considered approach to early warning and situational awareness [1,2]. In this study we present the observations of the Argus biosurveillance system on respiratory disease in Mexico between 1 October 2007 and 31 May 2009. These results are compared with observations of the HealthMap system [3, 4] on respiratory disease in the United States and Canada, just before widespread media coverage of the 2009 pandemic influenza A(H1N1), then called 'swine flu', in 21–23 April 2009. In the United States and Canada, media reporting related to swine flu was not observed before that time.

Argus biosurveillance system

The Argus system, a web-based global biosurveillance system hosted at the Georgetown University Medical Center (Washington, DC, United States) and funded by the United States Government, is designed to report and track the evolution of biological events threatening human, plant and animal health globally, excluding the United States [5]. It collects, in an automated process, local, native-language Internet media reports, including blogs and official sources, e.g. World Health Organization (WHO) and World Organisation for Animal Health (OIE), and interprets their relevance according to a specific set of concepts and keywords relevant to infectious disease surveillance (i.e. a taxonomy of media reporting of infectious disease). Argus does not use scientific journals as a primary source for identifying emerging events. Elements of the taxonomy define direct indicators (i.e. reports of disease) and six categories of indirect indicators of disease (Table 1).

Project analysts – about 40 regional specialists who collectively are fluent in approximately 40 languages – monitor several thousand Internet sources daily. They use Boolean keyword searching and Bayesian model tools [6] to select reports from a dynamic database of media reports collected from Internet sources six times daily. A complete archive is maintained for retrospective analyses and refinement of biosurveillance methodology [7]. The project analysts write event reports, which are based on relevant media reports, and a stage is assigned to the report based on observed event progression according to a previously described heuristic model [8], ranging from preparatory (e.g. prevention activities and conditions conducive to disease emergence and transmission) to degree of disease spread to degrees of social disruption to recovery (Table 2) [9,10]. The reports are posted on a secure Internet portal for the diverse set of Argus users [5,11] to view.

HealthMap system

HealthMap is an automated multilingual real-time disease outbreak detection, tracking and visualization system, which, like Argus, relies on publically available information, including social media and official sources, from the Internet for its data [2]. It provides global media coverage, which, unlike Argus, includes the United States. HealthMap data on 2009 pandemic influenza A(H1N1) is therefore used to describe the emergence and evolution of swine-origin influenza in the United States and Canada [3,4].

Aims of this study

Event-based surveillance, as conducted by the Argus and HealthMap systems, has been shown to be able to identify emerging outbreaks [1,5] from information in publically available media sources. This information can be used by public health professionals to investigate an emerging or changing pathogen earlier than they would otherwise. This study was conducted to demonstrate quantitatively how event-based surveillance is a useful tool complementary to traditional public health surveillance methods for providing early warning and tracking of an emerging outbreak.

Methods

Selection of Argus reports

We retrieved from the Argus archive reports written by project analysts based on Spanish- and English-language Internet media reports of respiratory disease, including the 2009 pandemic influenza A(H1N1), in Mexico between 1 October 2007 and 31 May 2009 (thus covering the 2007–8 and 2008–9 respiratory disease seasons). We reviewed the Argus reports and identified the geographical locations of the events described in them. The number of sources and media reports archived did not vary substantially between the 2007–8 and 2008–9 respiratory disease seasons.

Determining frequency of reporting of respiratory disease in Mexico

As Argus does not categorise articles by topic as they are archived, the total number of reports written on respiratory disease by the project analysts was used as the numerator. Each Argus report is based on one or more media reports. The rate of reporting was defined as the ratio of the number of written reports meeting the inclusion criteria to the total number of media reports in the archive from Mexican sources, which were computed as a function of time (in days) for the study period.

Descriptive statistics, including reporting frequency and mean reporting rate, were also computed. Argus heuristic report staging [8] was also analysed for the study period and descriptive statistics computed, including the frequency of each stage and mean stage.

The Shapiro–Wilk test was used to assess the normality of the data. The reporting rate and stage data for

Table 2

Argus staging system

Stage	Description of events
A	Potential antecedent to a biological event
1	Unifocal biological event
2	Multifocal biological event
3	Infrastructure strain
4	Infrastructure collapse
R	Recovery (event no longer present)[a]

[a] Recovery is defined as six weeks of non-reporting on an event or declaration by the World Health Organization (WHO) or the World Organisation for Animal Health (OIE) that the event is no longer present.

Table 1

Argus taxonomy elements of media reporting of infectious disease

Taxonomy element	Content of media reports
Direct indicators of disease	
Reports of human disease	Illness at one or more geographical location
Indirect indicators of disease	
Official acknowledgement	Acceptance or denial of disease presence by a government official
Official action	Implementation of countermeasures, biosurveillance, health alerts, official investigations and changes to current policies and procedures by authorities at local, national and/or international level
Integrity of infrastructure	Compromise or collapse of a society
Local perception of threat	Periods of heightened anxiety and public concern within a society
Demand for medical services	Shifts in supply and demand of medical care, pharmaceuticals (e.g. drugs, vaccines), supplies (e.g. face masks, gloves), etc. and mobilisation of those resources
Business practice changes	Changes in economic markets

each season, 1 October 2007 to 31 May 2008 and 1 October 2008 to 31 May 2009, were not normally distributed (2007–8 rate: W=0.7067, p<0.0001; 2008–9 rate: W=0.647, p<0.0001; 2007–8 stage: W=0.5679, p<0.0001; 2008–9 stage: W=0.6879, p<0.0001). Thus the non-parametric Wilcoxon rank-sum test was used to assess the difference in mean rate of respiratory disease reporting and mean stage between the 2007–8 and 2008–9 seasons. All statistics were computed using R Version 2.9-0 [12].

A sample of Argus reports (n=133) classified as stage 2 or greater from 1 January 2009 to 23 April 2009, was randomly selected using an R-random number generator and assembled into a table of events, before widespread media reporting of the pandemic influenza in the international media. The sample was reviewed and compared with reports not selected by randomisation from the time period and was determined to be representative of the larger dataset.

Selection of HealthMap reports

A table of events from HealthMap, based on English- and Spanish-language sources covering the United States and Canada, was also assembled. HealthMap uses automated crawling and filtering tools to identify relevant media reports, which are posted to the HealthMap website [2, 4, 13]. At least one of eight analysts employed by HealthMap reviews all information posted to the site for accuracy, relevance and correct categorisation. Any report from 21–23 April 2009 referring to swine influenza was included in the table of events.

Results

Frequency of Argus reports on respiratory disease in Mexico

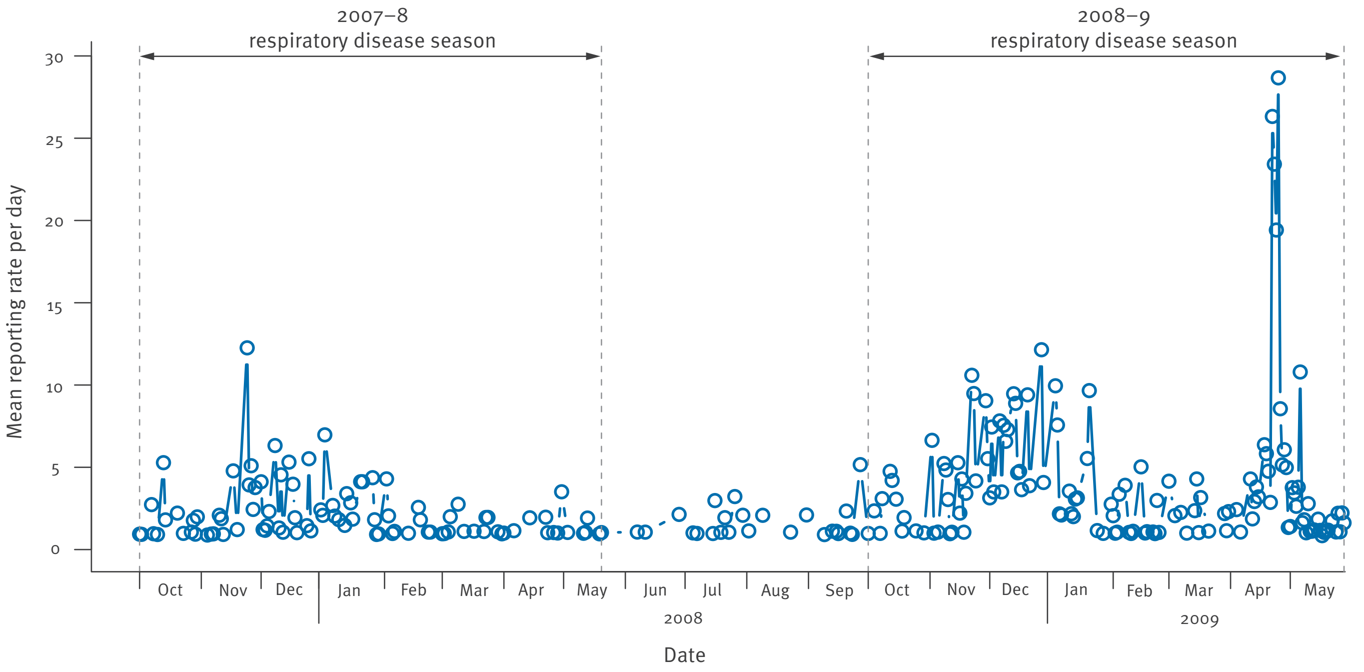
From an archive of 2.1 million Internet media reports collected in 2007–2008 and 2.0 million articles in 2008–2009, 722 Argus reports were identified, 684 of which met the inclusion criteria. Figure 1 shows an increase in reporting frequency during the 2008–9 respiratory disease season relative to that of 2007–8.

Between 1 October 2007 and 31 May 2008, the mean rate of reporting per day was 2.19, whereas in the same period in 2008–2009, the mean rate per day was significantly higher (4.08) (W=3,985, p<0.0001). In 2008, the reporting rate declined by almost twofold from January to February and decreased further in April, whereas in 2009, the reporting rate also decreased from January to February by about twofold, though it remained higher than in the same period in 2008. The reporting rate started to increase in March 2009 and continued to rise in April, spiking more than fivefold by the end of the month. This higher rate of reporting from 1 January to 30 April 2009, compared with the same period in 2008, was also significant (W=780, p<0.001).

The increase in the number of Argus reports in the 2008–9 season (n=491) compared with those in the

Figure 1

Mean rate per day of Argus reporting of respiratory disease in Mexico, based on Internet media reports, 1 October 2007 – 31 May 2009



The number of Argus reports is divided by the number of media reports archived for the day, multiplied by 10,000 for plotting. Days when there was no reporting are not plotted.

Note the increased prominence of reporting on respiratory disease in the first quarter of 2009 relative to that of 2008.

FIGURE 2

Argus respiratory disease reports by Mexican state, based on Internet media reports, for the 2007–8 and 2008–9 respiratory disease seasons

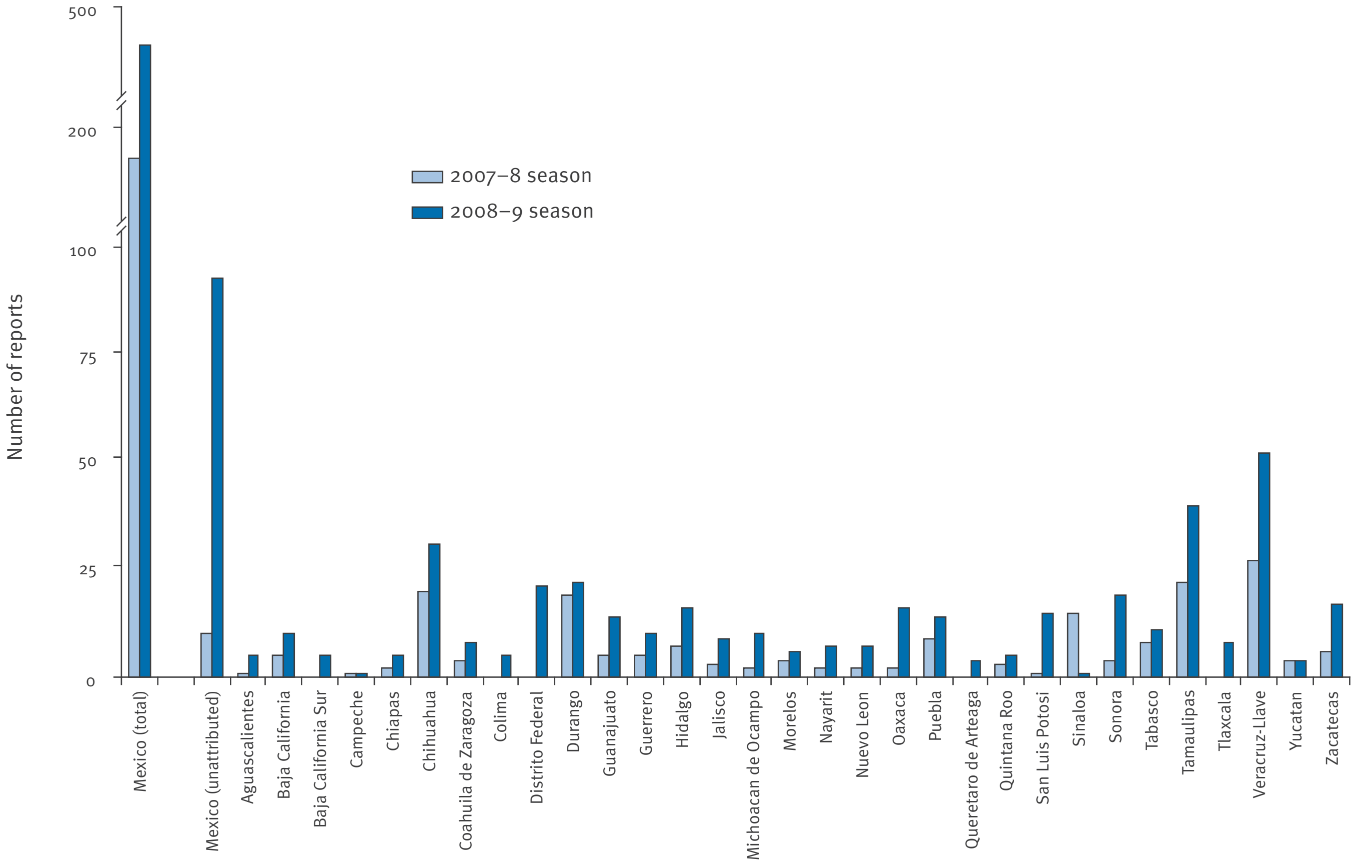
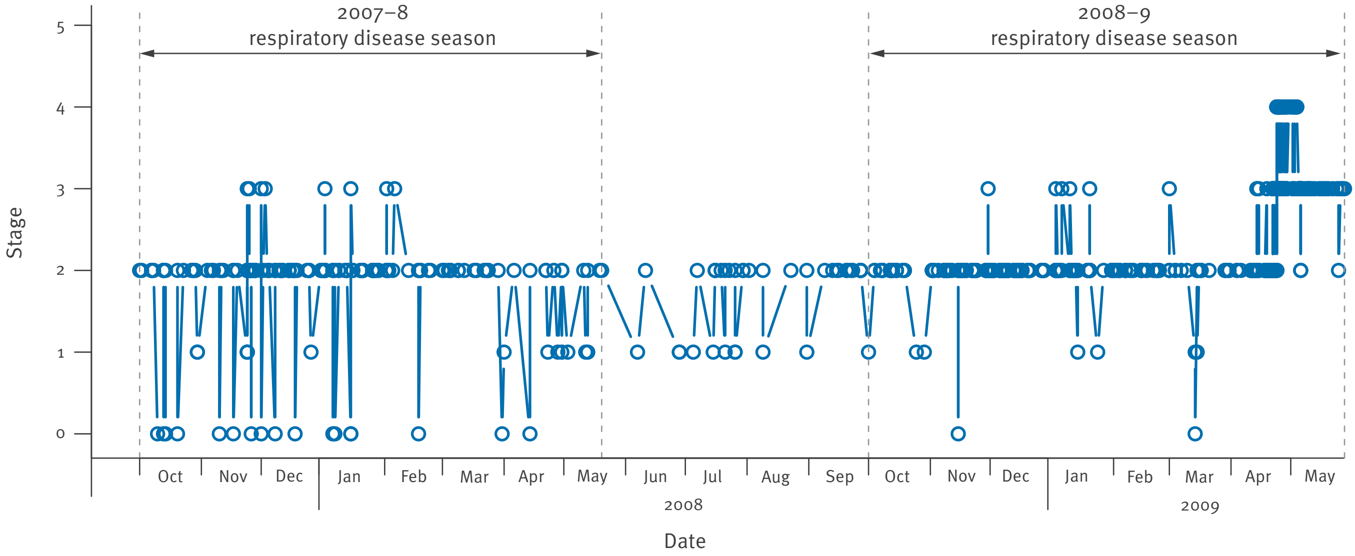


FIGURE 3

Mean stage of Argus reports of respiratory disease, based on Mexican Internet media reports, 1 October 2007 – 31 May 2009



Stage A = 0; Stage 1 = 1; Stage 2 = 2; Stage 3 = 3; Stage 4 = 4; Stage R = 5.
Note the higher mean stage in the 2008–9 respiratory disease season relative to the 2007–8 season.

2007–8 season (n=193) is illustrated by Mexico total, Mexico unattributed and Mexican state in Figure 2.

Geographical focus of respiratory disease reporting in Mexico

No clear geographical focus of respiratory disease reporting during the 2007–8 respiratory disease season was discernable (Figure 2). Potential clusters of increased reporting in the 2008–9 season compared with the 2007–8 season were evident in the states of Chihuahua, Distrito Federal, Guanajuato, Hidalgo, Oaxaca, San Luis Potosi, Sonora, Tamaulipas, Tlaxacala, Veracruz-Llave and Zacatecas. Argus reports based on media reports from these states in the 2008–9 season represented a greater than 60% increase in reporting frequency compared with that in the 2007–8 season. Statistical significance of state trends was not determined.

Outbreak severity

An assessment of outbreak severity via media reports provides context for interpreting the events. As described above, Argus does this by staging reports according to a heuristic model of societal disruption (Table 2) [8]. As depicted in Figure 3, reports on respiratory disease outbreaks in Mexico were predominately stage 2 and occasionally stage 3 (mean=2.35) throughout the 2008–9 season, whereas in the corresponding period the previous year, reports were consistently staged at 2 or less (mean=1.80). Thus, using this staging system, the mean stage of the reports in the 2008–9 season was significantly higher than that of the reports in the 2007–8 season (W=30,184.5, $p<0.0001$), indicating higher social disruption in the later season.

Unusual timing and extent of respiratory disease reporting in Mexico

We reviewed the Argus reports to estimate when respiratory illness reporting frequency became prominent and anomalous in the Mexican media in the 2008–9 respiratory disease season. Table 3 illustrates the timing of events, based on a random selection of reports classed as stage 2 and greater from 1 January to 23 April 2009, before widespread reporting of 2009 pandemic influenza A(H1N1) in the international media. It illustrates that respiratory disease was prevalent in parts of Mexico, and reported as unusual, much earlier than the microbiological identification of the pandemic virus in late April 2009 [14].

Emergence of pandemic influenza A(H1N1) in the United States and Canada

In the United States, two cases developed symptoms of swine influenza A(H1N1) in late March 2009 in California and were reported in mid-April [15]. The timing of the emergence and evolution of the pandemic influenza in the United States and Canada, based on data collected by the HealthMap system from 21 to 23 April 2009, before recognition of the novel virus and reporting by the international media, is depicted in Table 4. As can be seen, the United States media began reporting on the two cases on 21 April [2 and sources cited therein, 15]. This was followed by the reporting of three

TABLE 3

Emergence and evolution of respiratory disease in Mexico, 1 January – 23 April 2009[a]

Date 2009	Mexican state	Report summary	Report stage
5 Jan	Durango	Demand for emergency services at El Salto Hospital increases 100%	2
6 Jan	Veracruz-Llave	Respiratory diseases account for 30% of consultations at Panuco Clinic	2
8 Jan	Chihuahua	Delicias pharmacy runs out of respiratory medicines	2
12 Jan	Chihuahua	Number of respiratory disease cases increases in Juarez; children are most affected	2
16 Jan	Nayarit	Acute respiratory infections increase daily during winter	2
9 Feb	Queretaro de Arteaga	Number of respiratory disease cases increased in San Juan del Rio	2
26 Feb	Chiapas	Acute respiratory diseases are primary cause for consultations in South Chiapas	2
9 Mar	Tlaxcala	Classes suspended at secondary school due to 25 influenza cases in Ixtacuixtla, Tlaxcala	2
18 Mar	Veracruz-Llave	106 acute respiratory infections treated at Tantoyuca Hospital in last month	2
1 Apr	Baja California Sur	Number of respiratory disease cases increased recently in Loreto; hundreds of cases of respiratory disease in recent weeks	2
2 Apr	Veracruz-Llave	60% of La Gloria community affected by ‘strange outbreak’	2
6 Apr	Durango	Demand due to respiratory diseases remains high at El Salto Hospital	2
8 Apr	Veracruz-Llave	30% of La Gloria affected by respiratory disease; influenza ruled out; cannot scientifically implicate hog farm in the respiratory disease cases	2
21 Apr	No state (Mexico in general)	International pharmaceutical company moves forward in plans to manufacture influenza vaccine	3
22 Apr	Distrito Federal	120 clinical cases of influenza at hospitals in Distrito Federal; at least two nurses affected; hospital staff report lack of personal protection	2

[a] Based on randomly selected Argus reports Stage 2 or higher.

Note that the data in these reports are consistent with HealthMap’s coverage of respiratory disease in Mexico (data not shown).

additional cases in California and two in Texas on 23 April. The following day, there were 75 suspected cases in Queens, New York. By 27 April, widespread informal reporting across the United States was observed by HealthMap. Canadian reporting had significant overlap with United States reporting on this event from 21 to 23 April 2009. Thus the recognition of the novel virus in the United States and Canadian media occurred only days before widespread recognition in the international media, in contrast to indications of emergence of the event much earlier in the Mexican media.

Discussion and conclusion

Increased Argus event reporting frequency, longer duration of the respiratory disease season and significantly increased stage (social disruption) of Argus event reports together provide evidence of an anomalous respiratory disease season in 2009. The timing of events, based on media reports, suggests that respiratory disease was prevalent in parts of Mexico, and was reported as unusual, much earlier than the microbiological identification of the pandemic virus. While it is impossible to estimate the earliest date of emergence of the 2009 pandemic influenza A(H1N1) virus in the absence of historical serological collections and microbiological test results, Figure 1 illustrates the significantly higher frequency of respiratory disease reporting in January to April in the 2008–9 influenza season than in the 2007–8 season. Likewise, Figure 2 shows the significantly higher mean stage in the 2008–9 season than in the 2007–8 season. These observations suggest a connection between the anomalous respiratory disease season in Mexico in 2008–9, detected through event-based biosurveillance, and the 2009 pandemic influenza A(H1N1). The connection remains unclear, however, without laboratory confirmation of the cases described in the media reports and without more historical laboratory data on the time frame of the pandemic emergence. Nonetheless, event-based biosurveillance provides a tool for early detection of emerging outbreaks complementary to traditional public health approaches, though quantitative analysis of such data is in the early stages. To the best of our knowledge, this is the first study to attempt to quantitatively analyse event-based biosurveillance data over time.

Event-based biosurveillance systems function as cueing and alerting systems to government officials and public health professionals by disseminating reports of potentially emerging biological events. Public health professionals can act on these surveillance reports mainly when they are considered within the context of societal, epidemiological and immunological factors. Biosurveillance reports, such as those analysed in this study, provide information on these factors. Such event-based surveillance data can cue public health professionals to investigate an emerging or changing pathogen earlier than they otherwise would, as well as provide a means for monitoring the spread of disease and its severity in a population or region. Examples of early public health response include directed sample collection for laboratory confirmation, deployment of diagnostic test kits to affected regions, and initiation of preventive measures, such as border closings, wearing of face masks and limiting public events.

Event-based biosurveillance, such as that described in this study, is a tool complementary to traditional public health surveillance methods used to identify an outbreak and track its progression. Media reports can sometimes be difficult to confirm, highlighting the need for clinic-based syndromic surveillance in conjunction with microbiological surveillance for verification and diagnosis of disease(s) present in suspected outbreaks. In nations where traditional public health surveillance is not possible, event-based biosurveillance data may be helpful in situational awareness until other methods are deployed.

TABLE 4

Emergence and evolution of swine-origin influenza in the United States and Canada, 21–23 April 2009[a]

Date 2009	Location of event	Report title
21 Apr	San Diego and Imperial County, California, USA	The Canadian Press: Unrelated cases of swine flu in Calif. children have US officials on alert
23 Apr	San Diego and Imperial County, California, USA; San Antonio, Texas, USA	More US swine flu cases, Mexico illnesses raise pandemic questions
23 Apr	Canada; California and Texas, USA	Canadian health officials eye Mexican outbreak
23 Apr	Canada	Canadians returning from Mexico urged to be on alert for flu-like symptoms
23 Apr	Cornwall, Ontario, Canada	Health officials on watch after mystery Mexican outbreak
23 Apr	San Diego, California, USA; San Antonio, Texas, USA	CDC confirms 7 cases of swine flu in humans
23 Apr	California and Texas, USA	Doctors warned to watch for mystery illness in tourists returning from Mexico

Calif.: Californian; CDC: United States Centers for Disease Control and Prevention; US: United States; USA: United States of America.

[a] Before recognition of the novel virus and reporting by the international media.

Source: HealthMap.

The value added by event-based biosurveillance is that media reports encompass both direct indicators of disease occurrence and indirect indicators based on societal response to an emerging event, and they are produced in real time. Indirect indicators may allow identification of media signals of anomalous disease activity, and tracking such anomalous events in the media may provide clues to emerging events. In July 2009, WHO recommended that countries monitor unexpected, unusual or notable changes in patterns of influenza transmission or severity of the disease, including spikes in rates of absenteeism from schools or workplaces, or increases in the number of emergency department visits [16]. This type of monitoring became more crucial as the 2009 influenza pandemic evolved, particularly as global diagnostic capabilities became overwhelmed and monitoring of case counts became increasingly problematic. Regional, cultural and linguistic expertise is key to tracking anomalous events through recognising local signatures of social disruption, identifying indirect indicators and assigning the appropriate event staging.

Our study made use of historical data available in the Argus archive from 2007 and for HealthMap from 2006. Though not presented in this study, HealthMap reports from the Spanish media during the 2006–7 season, including but not limited to Mexican sources, show a high frequency of reporting in March similar to that observed in March 2009. This highlights the need for improved baseline data in order to distinguish more precisely anomalous signal from background reporting. Such baseline data, which can be generated from quantitative studies evaluating archival multiyear surveillance data from Argus, HealthMap and other event-based surveillance systems, would provide a means for better understanding of media signatures, enabling more specific signal generation and the establishment of signal thresholds. Consequently, a more robust cueing and alerting capability would be available for officials responsible for determining when to trigger an investigation of a pertinent emerging event. Spatial and temporal modelling have been investigated as methods of distinguishing abnormal from normal patterns in syndromic surveillance data [17], and may be applicable to event-based biosurveillance. Such algorithms will become more applicable as additional biosurveillance records are collected from continuing global media coverage.

This retrospective study highlights a number of factors that are important for developing an actionable event-based biosurveillance prospective methodology. Clearly defined inclusion criteria, validated on past outbreaks such as the 2009 influenza pandemic, are a basic component of such an approach. An established multiyear geospatial baseline of disease reporting will form the basis for quantifying anomaly. Lastly, continual quantification and assessment of the impact of different types of biosurveillance data and data sources upon system sensitivity, specificity and timeliness must be undertaken [18]. An important goal is to make it possible to identify needed improvements in the operation of event-based biosurveillance systems, enabling desired performance targets to be achieved. The results of retrospective studies of event-based biosurveillance systems, in conjunction with lessons learnt from event detection and response, can be used to establish thresholds for early alerting of future pandemics, facilitating more timely official intervention and public health response.

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References

1. Wilson K, Brownstein JS. Early detection of disease outbreaks using the Internet. CMAJ. 2009;180(8):829-31.
2. Brownstein JS, Freifeld CC, Madoff LC. Influenza A (H1N1) virus, 2009--online monitoring. N Engl J Med. 2009;360(21):2156.
3. Freifeld CC, Mandl KD, Reis BY, Brownstein JS. HealthMap: global infectious disease monitoring through automated classification and visualization of Internet media reports. J Am Med Inform Assoc. 2008;15(2):150-7.
4. Brownstein JS, Freifeld CC, Reis BY, Mandl KD. Surveillance Sans Frontière: Internet-based emerging infectious disease intelligence and the HealthMap project. PLoS Med. 2008;5(7):e151.
5. Hartley D. One year later: implementing the bio-surveillance requirements of the 9/11 Act. Statement by Dr David Hartley, Georgetown University Medical Center. Hearing before the Subcomm. on Emerging Threats, Cybersecurity, and Science and Technology of the House Comm. on Homeland Security, 110th Cong., 2nd Sess. (July 16, 2008). [Accessed 19 Jul 2010]. Available from: http://www.fas.org/irp/congress/2008_hr/biosurv.pdf
6. McCallum A, Nigam K. A comparison of event models for naive Bayes text classification. In: AAAI/ICML-98 Workshop on learning for text categorization: 26–27 July, 1998, Madison, Wisconsin. p. 41-8. [Accessed 19 Jul, 2010]. Available from: http://www.cs.cmu.edu/~knigam/papers/multinomial-aaaiws98.pdf
7. Collmann J, Robinson A. Designing ethical practice in biosurveillance: the project Argus doctrine. In: Castillo-Chavez C, Chen H, Lober WB, Thurmond M, Zeng D, editors. Infectious disease informatics and biosurveillance: research, systems and case studies. Springer. Forthcoming 2011.
8. Wilson JM 5th, Polyak MG, Blake JW, Collmann J. A heuristic indication and warning staging model for detection and assessment of biological events. J Am Med Inform Assoc. 2008;15(2):158-71.
9. McGrath JW. Biological impact of social disruption resulting from epidemic disease. Am J Phys Anthropol. 1991;84(4):407-19.
10. Walters R, Harlan P, Nelson NP, Hartley DM. Data sources for biosurveillance. In: Voeller J, editor. Wiley handbook of science and technology for homeland security. New York: John Wiley & Sons; 2010. p. 1-17.
11. Centers for Disease Prevention and Control (CDC). CDC global health e-brief, building USG interagency collaboration through global health engagement. First quarter 2008. [Accessed 27 Jul 2010]. Available from: http://www.cdc.gov/washington/EGlobalHealthEditions/E-brief_first_quarter_2008.pdf
12. R Development Core Team. A language and environment for statistical computing. Vienna: Foundation for Statistical Computing; 2010.

13. Brownstein JS, Freifeld CC. HealthMap: the development of automated real-time internet surveillance for epidemic intelligence. Euro Surveill. 2007; 12(48). pii=3322. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=3322
14. Jon Cohen. Swine flu outbreak. Out of Mexico? Scientists ponder swine flu's origins. Science. 2009;324(5928):700-2.
15. Centers for Disease Control and Prevention (CDC). Swine influenza A (H1N1) infection in two children--southern California, March-April 2009. MMWR Morb Mortal Wkly Rep. 2009;58(15):400-2. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5815a5.htm
16. World Health Organization (WHO). Changes in reporting requirements for pandemic (H1N1) 2009 virus infection. Pandemic (H1N1) 2009 briefing note 3 (revised), 16 July 2009. [Accessed 24 Jul 2009]. Available from: http://www.who.int/csr/disease/swineflu/notes/h1n1_surveillance_20090710/en/index.html
17. Mandl KD, Overhage JM, Wagner MM, Lober WB, Sebastiani P, Mostashari F, et al. Implementing syndromic surveillance: a practical guide informed by the early experience. J Am Med Inform Assoc. 2004;11(2):141-50.
18. Hartley DM, Nelson NP, Walters R, Arthur R, Yangarber R, Madoff L, et al. The landscape of international event-based biosurveillance. Emerging Health Threats Journal 2009, 3:e3 doi: 10.3134/ehtj.10.003. [Accessed 19 Jul 2010]. Available from: http://www.eht-forum.org/JournalStore/Journal

Regional and age-specific patterns of pandemic H1N1 influenza virus seroprevalence inferred from vaccine clinical trials, August-October 2009

T F Tsai (theodore.tsai@novartis.com)[1], P Pedotti[2], A Hilbert[3], K Lindert[1], M Hohenboken[1], A Borkowski[3], N Groth[4], L J da Silva[1], M H Kyaw[1]
1. Novartis Vaccines and Diagnostics, Cambridge, Massachusetts, United States
2. Novartis Vaccines and Diagnostics, Amsterdam, the Netherlands
3. Novartis Vaccines and Diagnostics, Marburg, Germany
4. Novartis Vaccines and Diagnostics, Siena, Italy

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The extent of the H1N1 pandemic has been estimated from case counts and deaths but the proportion of exposed populations with inapparent infections has not been described in detail. We analysed haemagglutination-inhibition (HI) antibody titres of pre-vaccination sera from pandemic vaccine trials conducted in six countries on four continents to provide an indication of A/CA/07/2009(H1N1)-like influenza seroprevalence in those populations. Among 7,962 subjects, ranging in age from 12 months to over 60 years, the proportions with HI antibody titres ≥40 to the H1N1pnd virus in the period from August to October 2009 were, by country: Costa Rica 26.4%, United States (US) 22.5%, Switzerland 16.9%, Germany 12.6%, Belgium 10.1%, and Japan 5.9%. Age-specific seropositivity rates in the samples were higher in children and adolescents in Costa Rica and in the US than in Europe and in Japan. The low proportion of seropositive children in Europe and Japan suggests that little local viral transmission had occurred in those regions even as late as September and October 2009, while in the US and Costa Rica, the greater proportion of previously infected children and young adults suggested that a significant number of asymptomatic infections had occurred during the first pandemic wave. Nevertheless, in all locations, the majority of the population remained susceptible to the pandemic virus at the beginning of the influenza season in the northern hemisphere, justifying the implementation of public health interventions.

Introduction

Influenza A/CA/07/2009(H1N1)-like (abbreviated H1N1pnd in this paper) viruses spread globally within several months after their recognition in April 2009, resulting in the declaration of a pandemic just two months later [1-3]. The extent of the global outbreak has been gauged principally by counting reports of laboratory-confirmed clinical cases, hospitalisations and deaths, and by monitoring clinical visits for influenza-like illness. The former underestimates the number of clinical cases and the latter is compromised by a lack of specificity. Neither approach measures the extent of inapparent infection. In the wake of widespread epidemics in both the northern and southern hemisphere, population seroprevalence rates were not reported systematically. Data on the overall and age-specific prevalence of antibodies to the H1N1pnd virus provide a perspective on the timing of recent public health vaccination programmes and the pandemic's spread.

We examined pre-vaccination serum samples from pandemic vaccine trials conducted in four continents to provide a crude indication of the proportion of those populations with immunity to the H1N1pnd virus and, conversely, the proportion that potentially remained susceptible to infection.

Methods

We analysed baseline (pre-vaccination) antibodies to the H1N1pnd virus among persons participating in vaccine clinical trials at 54 sites in the United States (US), seven in Germany, two in Belgium, one in Switzerland, and one each in Costa Rica and Japan. The clinical trials were conducted during the period from August to October 2009 and enrolled 7,962 persons, ranging in age from 12 months to over 60 years. All studies excluded from participation individuals who reported having had a confirmed influenza illness within the past 3 to 12 months (intervals varied by protocol). Studies in children were initiated after an independent safety monitoring committee had reviewed interim safety of the vaccine in adult subjects (Europe) or after a separate government decision (Japan), so their initial blood samples were taken several weeks after those in adult subjects. In the US and Costa Rica, adults and children were enrolled into their respective trials in parallel.

Prevaccination serum samples were tested for haemagglutination-inhibition (HI) antibodies against influenza A/CA/07/2009(H1N1) according to established protocols in a single laboratory (Novartis Vaccines serology laboratory) [4]. All sera were tested in duplicate in two separate runs and the final titre was the geometric mean of two readings.

Prevalence rates of HI antibodies with a titre ≥40 were analysed by country and by age group. Data for individual European countries were similar and were combined. Crude country- and region-specific rates were not adjusted to standard populations. We chose an HI titre ≥40 as a cut-off to represent H1N1pnd virus-specific antibodies and to reduce the likelihood of misclassifying cross-reactive antibodies (≥10) [5].

Results

The numbers and proportion of subjects with H1N1pnd HI antibodies are shown by country and age group in Figures 1 and 2. The estimated prevalence of HI antibodies to H1N1pnd varied substantially by geographical location and age group (studies in the US were not designed to include children 9-17 years old). Overall, seropositivity rates (proportion with HI titres ≥40) were higher in cohorts from Costa Rica (26.4%, enrolled during August 18-August 31) and from the US (22.5%, enrolled 11–25 September) compared with those in Switzerland (16.9%, enrolled 8–26 August), Germany (12.6%, enrolled 8 August–29 September), Belgium (10.1% enrolled 8 August–2 October) and Japan (5.9%, enrolled 16 September–2 October). The age-specific seropositivity rate in the Costa Rica sample was highest in older children, while in Europe and Japan, rates were higher in adults and were low in children. In the US sample, the proportion of seropositives was two- to three-fold lower in children between three and eight years of age (11.2%) compared with adults (24.9%) and the elderly (31.2%).

The regional and age-specific patterns of subjects with an HI titre ≥10 were similar but were proportionately higher, except in Costa Rica (Figures 1 and 2).

Discussion and conclusions

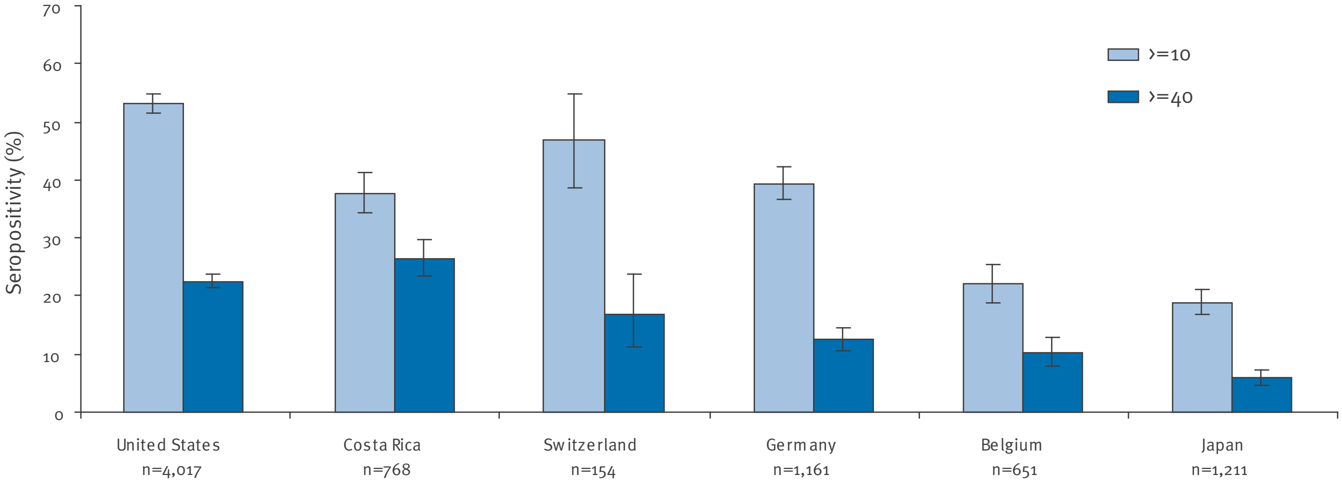
We observed regional differences in overall and age-specific H1N1pnd seropositivity rates (defined as an HI titre of ≥ 40) in the period from August through October 2009 that may have reflected the manner of introduction of the pandemic virus to the respective areas and subsequent patterns of local transmission. While the virus was introduced by infected travellers from North America to distant points, including Europe, Asia, and Oceania, within weeks of its emergence, the extent to which the virus was seeded into those populations and the rapidity of local spread appears to have differed. In Costa Rica, the virus may have been introduced with contiguous expansion of the regional epidemic through Central America from Mexico, as well as directly, by travellers.

Reported surveillance data on influenza like illness (ILI) indicate that baseline serum specimens were taken during the peak of ILI activity in Costa Rica and during the early upswing of renewed epidemic transmission in the US, but that the vaccine trials in Europe and in Japan largely preceded the onset of respective local epidemics [6-8]. The high overall seropositivity rate in Costa Rica and the peak rate occurring in older children are consistent with the epidemiology of the pandemic. In the US, our trial and another conducted in the same time-frame [9] did not study 9-17 year-olds, thus, the overall proportion of seropositive subjects, 22.5% in this study, is likely to underestimate the proportion of the US population that was asymptomatically infected.

In Europe and in Japan, lower overall antibody prevalence rates prevailed at the time that the serum samples were taken, suggesting that local transmission

Figure 1

Proportion of clinical trial subjects with H1N1pnd haemagglutination inhibition antibody titres ≥10 and ≥40, by country, August-October 2009

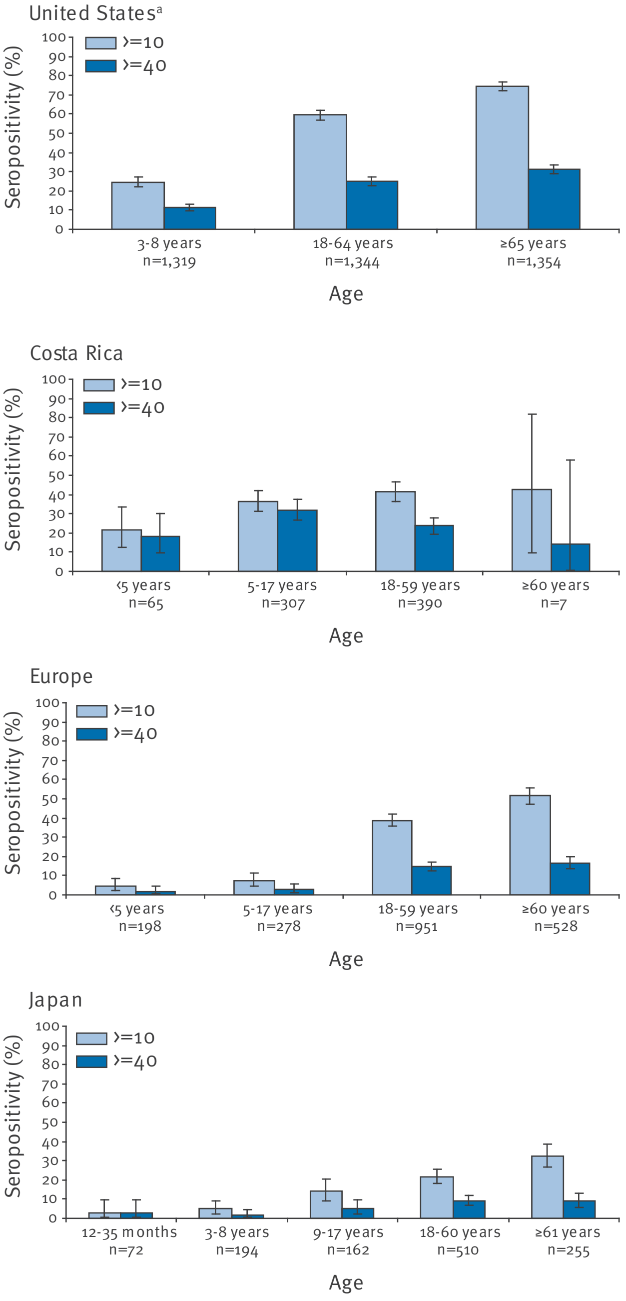


H1N1pnd: Influenza A/CA/07/2009(H1N1)-like virus; n: total number of subjects.

still was limited in Europe in September, and as late as October in Japan. These low seroprevalence rates were consistent with reports from vaccine studies conducted before 18 September in Europe and China that reported, respectively, 0-8% and 4% of subjects had baseline HI titres ≥40 [9-13]. In contrast, approximately one third of adult and older paediatric subjects who were vaccinated in the midst of the epidemic in the southern hemisphere in July and August 2009 had baseline antibody titres ≥40 [14,15]. The low proportion of seropositives in the oldest Japanese age group, approximately one third lower than the 34% prevalence previously reported in the elderly in the US [5] and in our US sample is notable, potentially reflecting the absence of routine seasonal influenza vaccination of the elderly in Japan and perhaps, even a residual effect of the US 1976 swine influenza vaccination campaign.

FIGURE 2

Proportion of clinical trial subjects with H1N1pnd haemagglutination inhibition antibody titres ≥10 and ≥40, by country or region and by age group, August-October 2009



H1N1pnd: Influenza A/CA/07/2009(H1N1)-like virus; n: total number of subjects.

[a] A separate cohort of 9-17 year-olds was not evaluated in US trials.

The last two weeks of August, when the European trials were initiated, is a period when many Europeans return from holidays but before schools reopen. Despite the fact that baseline serum samples were obtained later from children than from adults, the infection rate in children was remarkably low, suggesting that even through September, relatively little local transmission had occurred. At that point in time, it appears that antibodies among adults in Europe (and also in Japan) still were more likely to reflect a combination of recent pandemic infections in returned travellers and past infections with older, related H1N1 viruses rather than local transmission. Of interest, a more systematic and detailed analysis of the population of the United Kingdom (UK) showed that by August, a higher proportion of serum samples submitted for testing were seropositive (HI titres ≥32) than among our samples from continental Europe which were closer to the 2008 UK baseline rates [16]. That discrepancy and differences within the UK itself during the outbreak [16] further underscore the non-uniform dispersion of the pandemic virus even within a continent.

Serological studies of US and European serum samples obtained prior to the pandemic showed that fewer than 7% of persons under 65 years of age and none of the young children were seropositive for the H1N1pnd virus [5]. In these same age groups, we saw a substantially higher proportion of seropositives (e.g. >20% in Costa Rica) by late August and September, suggesting that a significant fraction of the populations of some countries had been asymptomatically infected with the pandemic virus towards the end of the epidemic's first wave, and just four to five months after the index cases were reported. Unfortunately, data were not collected from the US for the age group of 9-17 year-olds, in whom a greater proportion of infections might have been expected, so the overall seroprevalence estimate for the US is likely to be understated. Nevertheless, the great majority of subjects had HI antibodies titres <40 and potentially were susceptible to infection even at this point in early autumn.

The seropositivity proportions reported here derive from convenience samples of healthy persons willing to participate in vaccine clinical trials and who did not report a history of recent influenza illness and, therefore may not be representative of their respective national populations. The proportions provide some indication of age-specific seroprevalence rates in the respective countries in the period from August to October 2009 at various stages of their local epidemic but, in general, before the major resurgence of autumn transmission in the northern hemisphere. Clinical trial subjects were enrolled from a variable number of sites in each country and local infection rates may not have reflected national trends, although the more than 4,000 samples and 54 sites dispersed in the US provide for a more robust estimate for that country than in the other countries.

Minimal antigenic cross-reactivity between H1N1pnd and recently circulating seasonal H1N1 strains has been demonstrated and, in the absence of specific clinical data correlating with protection, we used an HI titre of ≥40 previously to define H1N1pnd-specific immunity in order to exclude antibodies cross-reactive with previously circulating seasonal influenza A(H1N1) viruses [5].

Although our point estimates of seropositivity indicate that a significant proportion of the US and Costa Rica populations sampled may have been asymptomatically infected with the H1N1pnd virus, it is important to note that at the start of the usual northern hemisphere influenza season, a majority of people in all regions and in particular in Europe, did not have antibodies to the pandemic virus at putatively protective levels. Large scale vaccination programmes were therefore in order to protect individuals at risk for acquiring influenza illness and its complications, and to further limit transmission.

The seropositivity rates reported here also are important to guide the interpretation of vaccine clinical trials. Responses to the H1N1pnd vaccine vary significantly between seronegative and seropositive persons (Novartis, unpublished data). Because most pandemic vaccine clinical trials have been undertaken during periods of active viral transmission, the results should be interpreted in the context of the level of pre-vaccination antibodies.

Conflicts of interest

All authors are full time employees of Novartis Vaccines, a manufacturer of pandemic influenza virus vaccines.

References

1. Centers for Disease Control and Prevention (CDC). Swine influenza A (H1N1) infection in two children---Southern California, March-April 2009. MMWR Morb Mortal Wkly Rep. 2009;58(15):400-2.
2. World now at the start of 2009 influenza pandemic Statement to the press by WHO Director-General Dr Margaret Chan. Geneva: World Health Organization; 11 June 2009. [Accessed 21 Dec 2009]. Available from: http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/index.html
3. Khan K, Arino J, Hu W, Raposo P, Sears J, Calderon F, et al. Spread of a novel influenza A (H1N1) virus via global airline transportation. New Eng J Med. 2009;361(2):212-4.
4. Vesikari T, Pellegrini M, Karvonen A, Groth N, Borkowski A, O'Hagan DT, et al. Enhanced immunogenicity of seasonal influenza vaccines in young children using MF59 adjuvant. Pediatr Infect Dis J. 2009;28(7):563-71.
5. Hancock K, Veguilla V, Lu X, Zhong W, Butler EN, Sun H, et al. Cross-reactive antibody responses to the 2009 pandemic H1N1 influenza virus.N Engl J Med. 2009;361(20):1945-52.
6. Regional Update. Pandemic (H1N1) 2009. Washington D.C.: Pan American Health Organization (PAHO); 22 December 2009. [Accessed 23 December 2009. Available from: http://new.paho.org/hq/index.php?option=com_content&task=blogcategory&id=1845&Itemid=2336
7. WHO/Europe influenza surveillance (EuroFlu.org). Copenhagen: World Health Organization European Region. [Accessed 21 Dec 2009]. Available from: http://www.euroflu.org
8. Pandemic (H1N1)2009. Current Situation update. Pandemic influenza A (H1N1) situation report of Japan, update 26. 18 December 2009. Tokyo: Infectious Disease Surveillance Center (IDSC). [Accessed 21 Dec 2009]. Available from: http://idsc.nih.go.jp/disease/swine_influenza_e/idsc_e2009/09idsc26e.html
9. Plennevaux E, Sheldon E, Blatter M, Reeves-Hoche MK, Denis M. Immune response after a single vaccination against 2009 influenza a H1N1 in USA: a preliminary report of two randomised controlled phase 2 trials. Lancet. 2009;375(9708):41-8.
10. Vajo Z, Tamas F, Sinka L, Jankovics I. Safety and immuinogenicity of a 2009 pandemic influenza A H1N1 vaccine when adminsitered alone or simultaneously with the seasonal influenza vaccine for the 2009-10 influenza season: a multicentre, randomised controlled trial. Lancet 2009;375(9708):49-55.
11. Lian XF, Wang HQ, Wang JZ, Fang HH, Wu J, Zhu FC, et al. Safety and immunogenicity of 2009 pandemic influenza A H1N1 vaccines in China: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet. 2010;375(9708):56-66.
12. Clark TW, Pareek M, Hoschler K, Dillon H, Nicholson KG, Groth N, et al. Trial of 2009 influenza A (H1N1) monovalent MF59-adjuvanted vaccine. New Eng J Med. 2009;361(25):2424-35.
13. Ikonen N, Strengell M, Kinnunen L, Österlund P, Pirhonen J, Broman M, et al. High frequency of cross-reacting antibodies against 2009 pandemic influenza A(H1N1) virus among the elderly in Finland. Euro Surveill. 2010;15(5):pii=19478. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19478
14. Greenberg ME, Lai MH, Hartel GF, Wichems CH, Gittleson C, Bennet J, et al. Response to a monovalent 2009 influenza A (H1N1) vaccine. New Eng J Med. 2009;361(25):2405-13.
15. Nolan T, McVernon J, Skeljo, Richmond P, Wadia U, Lambert S, et al. Immunogenicity of a monovalent 2009 inflouenza A(H1N1) vaccine in infants and children: a randomized trial. JAMA. 2010;303(1):37-46.
16. Miller E, Hoschler K, Hardelid P, Stanford E, Andrews N, Zambon M. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. Lancet. 2010;375(9720):1100-8.

Seroprevalence of brucellosis in animals and human populations in the western mountains region in Libya, December 2006–January 2008

M O Ahmed (mhmd73@lttnet.net)[1,2], S E Elmeshri[2], A R Abuzweda[2], M Blauo[2], Y M Abouzeed[1], A Ibrahim[2], H Salem[2], F Alzwam[2], S Abid[2], A Elfahem[2], A Elrais[2]
1. Department of Microbiology and Parasitology, Faculty of Veterinary Medicine, Al Fateh University, Tripoli, Libya
2. Department of Microbiology, Biotechnology Research Centre, Tripoli, Libya

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Brucellosis is a global zoonotic disease, endemic in North African countries and around the Mediterranean. A prospective study of *Brucella* seroprevalence was conducted in north-western Libya (western mountains region). Blood samples collected over 13 months in the period December 2006 to January 2008 from 561 animals (goats, sheep, cattle and camels) and 546 human volunteers were tested for *Brucella* using the Rose Bengal test, tube agglutination test and ELISA assays. Amongst livestock, 31% of goats and 42% of cattle were seropositive. Human samples showed a high seropositivity of 40%, with 95 (43%) of the 221 positive samples positive for IgM, indicating active or recent infection. Control measures are needed to reduce this high prevalence of brucellosis in Libya.

Introduction

Brucellosis is a global zoonotic disease associated with significant morbidity that can lead to increased rates of spontaneous abortions in livestock and also in humans [1-6]. The disease is widely distributed throughout the developing world, considered to be a serious problem in at least 86 countries [7]. Brucellosis is a severe zoonosis in North African countries [8] and the Near East [9,10] causing economic and livestock losses and affecting industrial production [3,11]. In these regions *Brucella melitensis*, the predominant species in goats and sheep, has spread to other animals such as cattle and camels. *B. melitensis* is also the dominant type in humans [9]. Consumption of unpasteurised milk and milk products from cows, small ruminants or camels is considered to be the main route of infection as well as an occupational hazard [12]. In the North African region, as in sub-Saharan countries, social and economic factors play a major role in the spread of brucellosis [13]. Libya is considered to be endemic for brucellosis [2], although little information is available; previous studies are limited to food-producing animals such as cattle and goats [14-16] and reports of human brucellosis in Libya are limited to a few cases [9,17].

We investigated the seroprevalence of brucellosis in humans and several livestock species around eight cities in the Yafran municipality, Al Jabal al Gharbi district (Western mountains region), north-west Libya. This region is 9,310 km2, with a population of 153,000, and dependent on livestock production, mainly goats (750,000 sheep and goats and around 8,000 camels). The Yafran is well-known for its rural culture and traditional lifestyle, where different livestock species are kept together and people live in close proximity to their livestock. Brucellosis is the likely cause of economic losses for owners and companies through abortions in pregnant animals especially in goats.

Methods and materials

Study design

We investigated the seroprevalence of *Brucella* in the Yafran, both in livestock and in humans, from samples collected over a period of 13 months from December 2006 to January 2008. A total of 561 blood samples were collected from different animals (a convenience sample of 340 goats, 188 sheep, 19 cattle, 14 camels). Human blood samples were also collected from 546 selected individuals (332 male and 214 female) from the populations in the area surrounding the farms, who worked and/or had contact with the studied animals. Both human and animal populations are widely dispersed in this large area in Libya, and due to the socio-economic factors of the involved region a few small towns could not be included in this study.

Diagnostic methods

Animal and human samples were processed in various laboratories in Libya, as described [18,19] using the Rose Bengal test and ELISA for the detection of *Brucella* in serum (DRG *Brucella* IgM-ELISA and *Brucella* IgG ELISA). Whole blood samples of 5 ml were collected aseptically. Serum was stored at 2-8 °C until testing could be performed. Statistical analysis was performed using the two-proportion z-test. Lifestyle data on milk consumption and animal contact were collected using a simple questionnaire.

Results and discussion

The prevalence of *Brucella* in different livestock species is summarised in Table 1. Rates of seropositivity were 1.6 times higher ($p=0.05$,) in goats (31%) than in sheep (24%). A local serological survey at the Al Jabal al Gharbi University in the western mountains region in 1997 found that 8.5% of sheep, 28.4% of goats, and 3.5% of camels were positive for brucellosis [20]. Our data indicate a substantial increase over the past ten years, with 24% of sheep, 31% of goats and 14% of camels testing positive for *Brucella* in our study. The increased prevalence in different animal species may be attributable to husbandry methods. Previous research has shown that controlling this disease in goats and sheep can be effective in reducing infection in other livestock [11]. The role of goats in perpetuating brucellosis and in disseminating the disease among humans has also been highlighted [4].

The overall prevalence of *Brucella* seropositivity among humans in the Yafran municipality was 40%, with Jado (47%) and Yifrin (46%) having the highest proportion of brucellosis brucellosis-positive people (Table 2). The prevalence of IgG and IgM antibodies in seropositive individuals was 57% (126/221) and 43% (95/221), respectively, suggesting that a substantial proportion of the population in this region were actively or recently infected. This compares with 8% seropositivity in Egypt [11] where control measures have been introduced.

We observed that significantly more seropositive humans had a history of raw milk consumption than had direct contact with livestock (71% and 58%, respectively, $p<0.02$). Similarly, a study of female brucellosis patients in Egypt found that more than 87% had a history of raw milk consumption [5], which has been identified as a risk factor also by other authors [10,12]. We noticed that seropositivity in the Yafran municipality, Libya, was higher among males than females, with 66% of samples from males and 34% of samples from females positive for *Brucella* infection in our study. This could be explained by the fact that in the culture and tradition of that region raw milk is consumed more frequently by men.

Effective eradication campaigns in the European Union have significantly reduced the incidence of brucellosis, with many countries being given brucellosis-free status [2]. Programmes and control measures have been undertaken in many countries in North Africa and the

TABLE 1

Prevalence of *Brucella* in domestic animal species assayed by the Rose Bengal test, Libya, December 2006–January 2008

Animal species	Animals tested	Seropositive animals	Proportion of positive animals
Goats	340	104	31%
Sheep	188	45	24%
Cattle	19	8	42%
Camel	14	2	14%
Total	**561**	**159**	**28%**

All animals were apparently healthy at sampling; those with a history of any recent disease or vaccination were excluded.

TABLE 2

Brucella prevalence in humans, immunoglobulin analysis, and possible risk factors among seropositive volunteers from eight cities in the Yafran municipality, Libya, December 2006–January 2008

Locality	Number of samples n	Positive samples n (%)	Analysis of *Brucella*-positive individuals			
			Drinking of raw milk n (%)	Direct contact with animals n (%)	IgG-positive n	IgM-positive n
Zentan	128	48 (38)	40 (83)	35 (73)	34	22
Jado	196	93 (47)	61 (66)	52 (56)	44	36
Rujban	29	11 (38)	8 (73)	6 (55)	8	4
Rehibat	50	15 (30)	11 (73)	7 (47)	8	7
Qasr Alhaj	12	4 (33)	3 (75)	2 (50)	1	3
Chkoke	15	2 (13)	2 (100)	2 (100)	1	1
Morgan	32	9 (28)	6 (67)	4 (44)	6	4
Yifrin	84	39 (46)	25 (64)	20 (51)	24	18
Total	**546**	**221 (40)**	**156 (71)**	**128 (58)**	**126**	**95**

Samples were assayed initially using the Rose Bengal test, then seropositive samples were further analysed by ELISA, in duplicate, for IgG and IgM.

Near East (e.g. Egypt and Kuwait) [11,21,22]. However, underreporting and underdiagnosis of other food-borne pathogens is a problem around the Mediterranean [23], particularly in North African countries, where communication with local authorities is problematic and most of the available information is unpublished or limited to seminars and workshops [9]. The high prevalence of *Brucella* seropositivity in the Yafran municipality in Libya might suggests that the size of the problem has been underestimated by the authorities and that action needs to be taken to control brucellosis in this region.

Conclusion

We conclude that in the north-western region of Libya, Brucellosis seroprevalence is high in animals and human populations. Our data highlights the need for further research, including the isolation and characterisation of the causative agents, reliable epidemiological studies and the need to implement a transparency policy and effective control measures in Libya.

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References

1. Boschiroli ML, Foulongne V, O'Callaghan D. Brucellosis: A worldwide zoonosis. Curr Opin Microbiol. 2001;4(1):58-64.
2. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. Lancet Infect Dis. 2006;6(2):91-9.
3. Corbel MJ. Brucellosis: An overview. Emerg Infect Dis. 1997;3(2):213-21.
4. Banai M. Control of small ruminant brucellosis by use of Brucella melitensis rev.1 vaccine: Laboratory aspects and field observations. Vet Microbiol. 2002;90(1-4):497-519.
5. Sabah AA, Aly AM, Tawab AH, Arafa WA. Brucellosis in Egyptian female patients. J Egypt Soc Parasitol. 2008;38(2):671-8.
6. Corbel MJ, Food and Agriculture Organization of the United Nations, World Health Organization, World Organisation for Animal Health. Brucellosis in humans and animals. Geneva: World Health Organization; 2006.
7. World Health Organization, Office of World Health Reporting. The world health report 1996: Fighting disease, fostering development: Executive summary. Geneva: World Health Organization; 1996.
8. Aggad H, Boukraa L. Prevalence of bovine and human brucellosis in western Algeria: Comparison of screening tests. East Mediterr Health J. 2006;12(1-2):119-28.
9. Refai M. Incidence and control of brucellosis in the near east region. Vet Microbiol. 2002;90(1-4):81-110.
10. Jennings GJ, Hajjeh RA, Girgis FY, Fadeel MA, Maksoud MA, Wasfy MO, et al. Brucellosis as a cause of acute febrile illness in Egypt. Trans R Soc Trop Med Hyg. 2007;101(7):707-13.
11. Samaha H, Al-Rowaily M, Khoudair RM, Ashour HM. Multicenter study of brucellosis in Egypt. Emerg Infect Dis. 2008;14(12):1916-8.
12. Almuneef MA, Memish ZA, Balkhy HH, Alotaibi B, Algoda S, Abbas M, et al. Importance of screening household members of acute brucellosis cases in endemic areas. Epidemiol Infect. 2004;132(3):533-40.
13. Makita K, Fèvre EM, Waiswa C, Kaboyo W, De Clare Bronsvoort BM, Eisler MC, et al. Human brucellosis in urban and peri-urban areas of Kampala, Uganda. Ann N Y Acad Sci. 2008;1149:309-11.
14. el Sanousi SM, Omer EE. Serological survey of brucellosis in Benghazi cow project (Libya). Int J Zoonoses. 1985;12(3):207-10.
15. Aboudaya MA. An evaluation of diagnostic methods for bovine brucellosis in Libya. Int J Zoonoses. 1986;13(4):282-5.
16. Gameel SE, Mohamed SO, Mustafa AA, Azwai SM. Prevalence of camel brucellosis in Libya. Trop Anim Health Prod. 1993;25(2):91-3.
17. Tiller RV, De BK, Boshra M, Huynh LY, Van Ert MN, Wagner DM, et al. Comparison of two multiple-locus variable-number tandem-repeat analysis methods for molecular strain typing of human Brucella melitensis isolates from the Middle East. J Clin Microbiol. 2009;47(7):2226-31.
18. Alton GG, Maw J, Rogerson BA, McPherson GG. The serological diagnosis of bovine brucellosis: An evaluation of the complement fixation, serum agglutination and rose bengal tests. Aust Vet J. 1975;51(2):57-63.
19. Al Dahouk S, Tomaso H, Nockler K, Neubauer H, Frangoulidis D. Laboratory-based diagnosis of brucellosis--a review of the literature. Part II: Serological tests for brucellosis. Clin Lab. 2003;49(11-12):577-89.
20. Elarbi A. [Serological study on brucellosis in farm animals in the Yafran municipality]. Al Jabal: al Gharbi University; 1997. [In Arabic].
21. al-Khalaf SA, Mohamad BT, Nicoletti P. Control of brucellosis in Kuwait by vaccination of cattle, sheep and goats with Brucella abortus strain 19 or Brucella melitensis strain rev. 1. Trop Anim Health Prod. 1992;24(1):45-9.
22. Alton GG. Control of Brucella melitensis infection in sheep and goats--a review. Trop Anim Health Prod. 1987;19(2):65-74.
23. Gargouri N, Walke H, Belbeisi A, Hadadin A, Salah S, Ellis A, et al. Estimated burden of human Salmonella, Shigella, and Brucella infections in Jordan, 2003-2004. Foodborne Pathog Dis. 2009;6(4):481-6.

Meteorological and climate change themes at the 2010 International Conference on Emerging Infectious Diseases

N Wilson (nick.wilson@otago.ac.nz)[1], D Lush[2], M G Baker[1]
1. Department of Public Health, University of Otago, Wellington, New Zealand
2. MAF Biosecurity, Ministry of Agriculture and Forestry (MAF), Wellington, New Zealand

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This report outlines selected highlights of presentations that took place at the 2010 International Conference on Emerging Infectious Diseases (ICEID) [1], held between 11 and 14 July 2010 at the Hyatt Regency Atlanta in Atlanta, Georgia, United States (US). The conference was organised by five national and international bodies and was attended by over 1,600 participants from a wide range of professional backgrounds. Abstracts for the posters and slide sessions have been published [2].

This year's conference marked its seventh occurrence and it had a number of prominent themes with the strongest being the A(H1N1) influenza pandemic that emerged in 2009. Another theme was around the drivers for the emergence of infectious diseases including human demographics (e.g. growth of megacities), international movements of people (of travellers and refugees), trade in animals and the smuggling of wildlife, and various other aspects of globalisation. Meteorological and climate change drivers, of growing international and European-focused interest [3,4], were also well covered at this conference. Considering this growing interest, we outlined the latter drivers in this brief conference report.

Mosquito-borne diseases

Wilson (Session G1) discussed the issue of warmer cities favouring mosquito breeding. This was referred to along with higher temperatures shortening extrinsic incubation periods, e.g. in the urban vector Aedes aegypti. Nevertheless, although climate change may be influencing diseases such as dengue virus infection, other human-driven activities may be dominant drivers of risk.

Various speakers mentioned the problem of dengue fever with its expanded global distribution and rising case burden, including increased risk for travellers (e.g. Barnett *et al.*, Poster 418). Although the pattern of dengue outbreaks in China has been variable over the past two decades, researchers suggested that an 'increasing threat of imported dengue will continuously increase the risk of dengue epidemics in China' (Xu *et al.*, Poster 60). Blackmore (Session O1) gave a presentation on an outbreak of locally transmitted dengue virus infection in the city of Key West Florida in 2009, the first such local transmission in 70 years. Blackmore *et al.* concluded that in terms of dengue fever, this was 'the outbreak with the largest disease incidence identified in the continental United States in 60 years'. Subsequent to the initial 2009 outbreak, the occurrence of recent cases during 2010 may suggest that dengue virus continues to be present in this area. In addition to this outbreak, it was reported that there has been an increase in imported cases in Florida in the last decade (Blackmore, Session O1).

Work on West Nile virus (WNV) was reported in the Northern Great Plains region of the US where this virus invaded in 2002. Since then, the incidence of human cases has remained relatively high (Chuang *et al.*, Poster 259). Data on mosquitoes and meteorological factors indicated that higher mosquito populations in a given month were associated with higher temperature and precipitation in the preceding month. Similarly, a study in British Colombia, Canada examined the emergence of WNV in 2009 (after a spread westward across the continent) (Roth *et al.*, Poster 61). This work suggested that 'above average temperatures, low snow pack and resulting reduced stream flows may have caused the observed increase in *Culex tarsalis* numbers in 2009 that facilitated viral amplification and spillover into human and equine populations'.

Other mosquito-borne diseases described at the conference included the following

- Murphree presented on La Crosse encephalitis which appears to have emerged in East Tennessee, US (Session O1), but this pattern may reflect changes in surveillance as opposed to climatic or other factors.
- The re-emergence of chikungunya virus was referred to by Lieberman and Prince (i.e. in the Indian Ocean islands in 2005, spread to the Indian subcontinent

in 2006 and it caused a localised outbreak in Italy in 2007) (Poster 241). This work presented results of newly developed immunofluorescence assays for detecting the virus.
- Pogosta disease is a mosquito-transmitted viral infection caused by Sindbis virus. Work from Finland (Jalava *et al.*, Poster 192) reported that rainfall was a predictor for the occurrence of this disease in humans (with time lags of one, two and three months) and with the rainfall probably influencing the risk of mosquitoes transmitting the disease. However, the data for Finland show no long term increasing trend and the disease appears to have a seven-year cycle which may be related to a role of tetraonid birds (grouse) [5].

The overall pattern of the studies presented on mosquito-borne diseases at the conference was of expanded ranges for disease incidence. Meteorological and climate change factors were identified for some of these patterns but clearly many other factors are involved and may be more important drivers.

Tick-borne diseases

One of the most impressive presentations at the conference was on tick-borne encephalitis (TBE) in central and eastern Europe by Randolph (Session D3). Very detailed work suggested an overall pattern of increased TBE associated with climate change (i.e. increased TBE associated with increased temperature in spring). However, many other factors were described as contributing to the heterogeneous patterns of TBE incidence and trends including changes in: vegetation cover (e.g. favouring deer); land tenure (impacting on human access to land); and human use of the land (e.g. for leisure activities and for collecting firewood and food from forests).

Data from Ukraine presented by Biletska *et al.* (Poster 506) indicated an increase in Lyme disease from 2000 to 2008. Discussion with the author indicated that warmer weather in Ukraine may be playing a role but that other factors are also plausible (e.g. increased human exposure in forested areas).

Various presentations described tick-borne diseases in the US and Kemperman (Session O1) noted the nationwide increase in Lyme disease and human anaplasmosis (previously known as human granulocytic ehrlichiosis) in recent years. An increase in Powassan virus disease in North America was also reported by McQuiston (Session O1) along with the emergence of Rocky Mountain spotted fever in Arizona. The risk for the latter was possibly linked to weather (the 'monsoon season' in Arizona). Others described the evidence for the spread of babesiosis to new states (Lutz *et al.*, Poster 57; and Mosites *et al.*, Poster 310). In a study from Minnesota, Kemperman presented evidence for an increase in the number of counties reporting cases of three tick-borne diseases: Lyme disease, human anaplasmosis, and babesiosis (Session O1). In a study by Rockwell *et al.* on an apparent increase in reporting of human monocytic ehrlichiosis, there were also data to suggest an expansion of the geographic range (northward) of the implicated 'Lone Star tick' (Poster 26). Nevertheless, the role of meteorological and climate factors in these various tick-borne disease studies in the US was not considered in detail by the presenters, and it is plausible that improvements in laboratory tests and in surveillance are playing a role for the apparent increase in these diseases.

Food and water-borne diseases

The threat that climate change poses to water supply quality (e.g. via droughts or flooding) was raised at the conference. A presentation by Chen (Session E3) dealt with an outbreak of leptospirosis associated with a typhoon-related flooding event in Taiwan. Another presentation by Nichols (Session D3) described the relationship between excess cumulative rainfall in the previous seven days and drinking water related outbreaks in the United Kingdom. Furthermore, this study concluded that low rainfall levels (for the three weeks before an outbreak) were significantly associated with increased outbreak risks.

Henao (Session O4) presented a study on foodborne disease trends in the US for the 1996 to 2009 period using FoodNet surveillance data which indicated a decline in salmonellosis. This would suggest that climate change is not a substantive driver for salmonellosis in the US setting, even though higher ambient temperatures appear to increase the risk according to the literature [6] and to other data presented at this conference (Wilson *et al.*, Poster 59). By contrast, *Vibrio* infections increased substantially over this 1996 to 2009 period in the US (Henao, Session O4). This increase in *Vibrio* infections was seen for both FoodNet and the 'Cholera and Other *Vibrio* Illness Surveillance System (COVIS)' in a presentation by Vugia (Session M4). While it was speculated that the increase in sea surface temperature may account for some of the increase in *Vibrio* infections, other factors that are likely to be contributing include trends in shellfish consumption patterns and recreational contact with contaminated water.

In a presentation on *Naegleria fowleri* and primary amoebic meningoencephalitis in the US, Yoder (Session J6) reported no clear trend in incidence since 1978. Nevertheless, given that the occurrence of this organism is associated with warmer water temperatures, it was noted that there was 'potential' for increased risk with climate change.

Airborne diseases

Soebiyanto and Kiang presented a study of forecasting of seasonal influenza using climatic data from satellites and ground-based meteorological stations (Poster 503). This work considered that the resulting model was able to identify the timing of influenza peak activity 'reasonably well'. A study from Brazil by Alonso *et al.* on influenza and respiratory syncytial virus found that both these infections in children were positively correlated to rainfall even after adjusting for seasonality (Poster 492). However, they were only negatively correlated to air temperature when seasonality was not controlled for in the model.

Garrison *et al.* reported in a review of legionellosis outbreaks globally that cooling towers were the environmental source for 41% of outbreaks and 'decorative pools or fountains' as the source of 5% of outbreaks (Poster 183). These findings are of note given that if the use of cooling towers and urban fountains become more prevalent in some countries as a result of climate change, then this may impact on legionellosis risk.

Other infectious diseases

A detailed historical study in Mexico by Acuña-Soto identified that typhus and haemorrhagic fevers of unknown aetiology were strongly associated with drought (Poster 186 and Session K1). Climatic factors were also suggested as contributing to the historical patterns of yellow fever, influenza and cholera in Mexico.

Other work of note included:

- a study on Q fever in the Netherlands by van der Hoek *et al.*, which reported that low ground water levels were associated with increased risk and wet soil with decreased risk (Poster 200);
- a study on Crimean-Congo haemorrhagic fever in Pakistan from 1991 to 2007 by Tariq which reported an association with drought among a range of other risk factors (Poster 51);
- a review of a decade of emerging and re-emerging outbreaks of arboviral disease in livestock in Israel by Brenner which raised the potential role of climate change as a contributing factor (Poster 326);
- a review by Wilson *et al.* on climate change and infectious diseases in New Zealand which reported the results of modelling work and evidence for a temperature gradient for risk of salmonellosis (Poster 59);
- a review of climate change and wildlife health by Sleeman *et al.*, who reported that there was convincing evidence for climate change impacts on animal life cycles and on the geographic range and distribution of diseases and disease vectors (Poster 258). These authors also described a research agenda around studying this topic further.

Discussion and conclusions

This conference included a wide range of data of relevance to considering meteorological and climate change related impacts on infectious diseases. Some of the studies presented have recently been published in the journal literature, but many of the studies appear to have been presented for the first time at this conference. The overall impression was one of concern around how climate change may be currently impacting on various diseases (particularly vector-borne diseases), and how any such effects may increase in the future.

Nevertheless, for many of these diseases, other risk factors relating to human activities may be more important and uncertainties are often large, especially for rarer diseases where there have been improvements in diagnostic tests and surveillance methods. A form of 'publication bias' may also play a role in determining which presentations and posters get offered and selected for such conferences.

Given the growing international concern around climate change, including in a recent US National Research Council Report [7], there is a need for more intensive climate change mitigation and adaptation strategies globally. In the infectious diseases area, a key adaptation strategy will be improved control of vector-borne diseases. But improvements in surveillance and research on whether and how various infectious diseases are influenced by meteorological patterns and climate change are also needed, especially research that considers interactions with other risk factors. Conference organisers can also play a role in designing session themes that allow this topic area to be explored in a coherent way and with panel sessions that attempt to integrate overall pictures of emerging evidence and appropriate research agendas.

References

1. 2010 International Conference on Emerging Infectious Diseases (ICEID). Atlanta: ICEID Conference Organizers; 2010. Available from: http://www.iceid.org/.
2. 2010 International Conference on Emerging Infectious Diseases: Program and abstracts book. Atlanta: ICEID Conference Organizers; 2010.
3. Semenza JC, Menne B. Climate change and infectious diseases in Europe. Lancet Infect Dis. 2009;9(6):365-75.
4. European Centre for Disease Prevention and Control (ECDC). Meeting Report: First meeting of ECDC Expert Group on Climate Change. Stockholm: ECDC; 2009. Available from: http://www.ecdc.europa.eu/en/publications/Publications/0910_MER_First_Meeting_of_ECDC_Expert_Group_on_Climate_Change.pdf
5. Sane J, Guedes S, Kurkela S, Lyytikainen O, Vapalahti O. Epidemiological analysis of mosquito-borne Pogosta disease in Finland, 2009. Euro Surveill. 2010;15(2):pii=19462. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19462
6. Kovats RS, Edwards SJ, Hajat S, Armstrong BG, Ebi KL, Menne B. The effect of temperature on food poisoning: a time-series analysis of salmonellosis in ten European countries. Epidemiol Infect. 2004;132(3):443-53.
7. Committee on Stabilization Targets for Atmospheric Greenhouse Gas Concentrations; National Research Council. Climate stabilization targets: Emissions, concentrations, and impacts over decades to millennia. Washington, DC: National Academies Press; 2010. Available from: http://www.nap.edu/openbook.php?record_id=12877&page=R1.