



Eurosurveillance

Europe's leading journal on infectious disease epidemiology, prevention and control

Vol. 15 | Weekly issue 21 | 27 May 2010

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Mass psychogenic illness in nationwide in-school vaccination for pandemic influenza A(H1N1) 2009, Taiwan, November 2009–January 2010

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Citation style for this article:

Citation style for this article: Huang WT, Hsu CC, Lee PI, Chuang JH. Mass psychogenic illness in nationwide in-school vaccination for pandemic influenza A(H1N1) 2009, Taiwan, November 2009–January 2010. *Euro Surveill.* 2010;15(21):pii=19575. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19575>

This article has been published on 27 May 2010

From 16 November 2009 to 22 January 2010, Taiwan investigated 23 clusters of mass psychogenic illness after vaccination (MPIV) in the nationwide in-school vaccination programme against the 2009 pandemic influenza A(H1N1). The median age of the 350 ill students (68% female) was 13 years. Intense media coverage of these events has driven public concerns about the safety of the pandemic influenza vaccine. In the future, countries should incorporate surveillance and communication strategies for MPIV in their pandemic preparedness plans.

The 2009 pandemic influenza A(H1N1) virus is highly transmissible in schools, and mathematical modelling suggests that vaccinating 70% of schoolchildren could mitigate a pandemic [1]. In Taiwan, schoolchildren (first to 12th grade) are among the priority groups to receive the pandemic influenza monovalent vaccine. On 16 November 2009, the government began a nationwide in-school influenza vaccination (NISIV) programme against pandemic influenza, using an inactivated vaccine without adjuvant (Adimmune Corporation, Taichung, Taiwan). Children under the age of nine years (first to third grade) received two doses, separated by approximately four weeks; children aged 10 years or older (fourth grade or higher) received one dose.

Mass adverse events following immunisation

On 23 November 2009, the government was notified that within two hours of pandemic influenza vaccination, a cluster of adverse events marked by dizziness, nausea and weakness occurred in 46 (7%) of the 692 schoolchildren aged 12 to 15 years who had received the vaccine at a middle school. Students were transported by ambulance to nearby hospitals and believed the illness was caused by the vaccine. Of the 46 ill students (26 female), physical and laboratory examinations found no organic cause for the reported symptoms. Forty-five patients recovered spontaneously and were discharged from the emergency department

within 12 hours; one patient was hospitalised but discharged the following day. Public health officials reviewed the school vaccination process and found that all recommended procedures had been followed. It was concluded that this incident was a case of mass psychogenic illness after vaccination (MPIV) [2].

In response to safety concerns that might arise as the NISIV programme proceeded, we conducted enhanced surveillance to identify and investigate potential clusters of MPIV. Utilisation data on pandemic influenza vaccines were analysed to assess the impact of MPIV on vaccine coverage among schoolchildren.

Methods

Enhanced surveillance for mass psychogenic illness after vaccination

Each day, starting 23 November 2009, potential clusters of MPIV were retrospectively and prospectively identified through a search of two sources: (i) reports on adverse events following immunisation (AEFI) received by the national passive surveillance system jointly operated by the Taiwan Centers for Disease Control and the Taiwan Food and Drug Administration, and (ii) incident reports received by the Emergency Medical Management System, the Ministry of Health's web-based system coordinating regional medical resources. A cluster of MPIV was defined as a constellation of symptoms suggestive of organic illness, but without an identifiable cause, in two or more children who were vaccinated on the same day, at the same school, and shared the belief that the pandemic influenza vaccine was the cause of the symptoms [3]. We requested that local health authorities provided additional details of illness onset, laboratory data, diagnoses, and treatment of ill students, and reviewed the storage and handling of the pandemic influenza vaccine involved in each cluster. The enhanced surveillance continued until 22 January 2010, the end of the school winter semester.

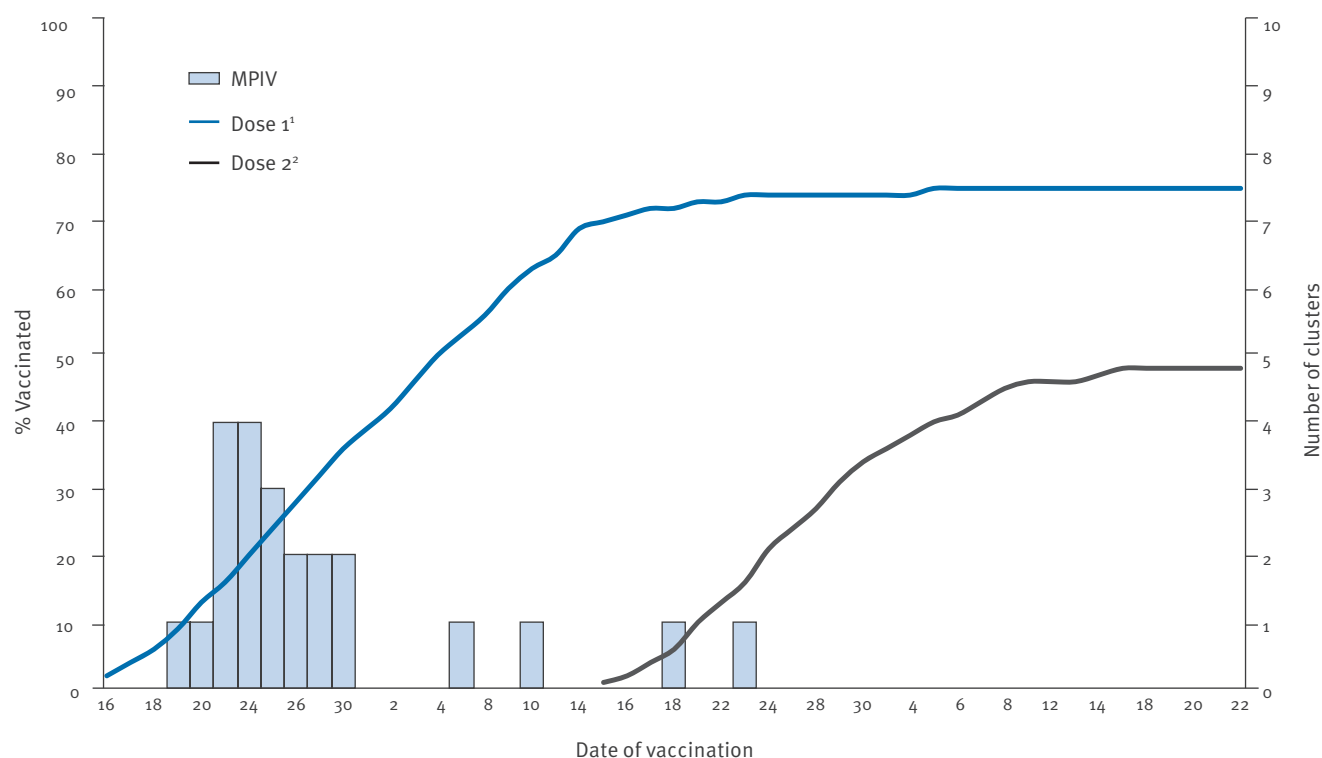
Monitoring pandemic influenza A(H1N1) monovalent vaccine coverage

The National Influenza Vaccine Information System (IVIS) receives daily electronic reports from all vaccination facilities on the pandemic influenza vaccine doses administered. Two measures of pandemic influenza vaccine coverage were calculated for schoolchildren from 16 November 2009 to 22 January 2010: (i) receipt

of one or more doses for all students (dose 1), and (ii) receipt of two doses for students in first to third grade who had received the first dose (dose 2).

FIGURE

Cumulative percentage of schoolchildren receiving pandemic influenza A(H1N1) monovalent vaccine, by date of vaccination and dose received, Taiwan, 16 November 2009–22 January 2010



MPIV: mass psychogenic illness after vaccination.

¹ Among all schoolchildren (n=3,564,831).

² Among first through third grade schoolchildren who received the first dose (n=646,379).

TABLE

Characteristics of mass psychogenic illness to pandemic influenza A(H1N1) vaccination involving 15 or more schoolchildren, Taiwan, 16 November 2009–22 January 2010

Date reported	Number of students vaccinated	Number of ill students (%) ¹	Females (%) ²	Median age in years (range)	Number of ill students hospitalised	Predominant symptoms
23 Nov	692	46 (7)	26 (57)	13 (12–15)	1	Dizziness, nausea, weakness
24 Nov	1,831	19 (1)	15 (79)	14 (13–15)	0	Hyperventilation, nausea, dyspnea
24 Nov	100	17 (17)	15 (88)	12 (12–15)	0	Dizziness, nausea
25 Nov	1,173	24 (2)	15 (63)	13 (12–14)	0	Dizziness, hyperventilation
26 Nov	768	37 (5)	24 (65)	13 (12–16)	0	Dizziness, headache
26 Nov	537	16 (3)	14 (88)	15 (12–15)	0	Dizziness, nausea, headache
27 Nov	266	21 (8)	10 (48)	10 (6–12)	0	Dizziness, headache, nausea
30 Nov	1,760	17 (1)	10 (59)	11 (8–12)	0	Nausea
7 Dec	817	32 (4)	23 (72)	12 (12–15)	0	Dizziness, nausea
10 Dec	1,171	43 (4)	32 (74)	12 (12–14)	0	Dizziness, hyperventilation, headache

¹ Proportion of students vaccinated.

² Proportion of ill students.

Results

Between 16 November 2009 and 22 January 2010, 23 clusters of MPIV in association with the NISIV programme were reported and investigated (Figure), including a total of 350 students. Each cluster involved between two and 46 ill students (median: 11). These clusters shared characteristics of the acute onset, the absence of physical or laboratory findings suggestive of an organic cause, the benign morbidity, the rapid spread and resolution of symptoms, and the absence of unprompted symptoms among students in other schools with exposures to the same batches of the vaccine. The age of the 350 ill students ranged from six to 16 years (median: 13), and 237 (68%) were female. Ten clusters involved 15 or more schoolchildren; the overall rate of illness among the 9,115 vaccinated students was 3% (range: 1–17%) (Table).

As of 22 January 2010, the cumulative percentage of schoolchildren receiving one or more doses of pandemic influenza vaccine was 75%; few schoolchildren received their first dose after mid-December 2009 (Figure). A total of 646,379 schoolchildren in first to third grade who received the first dose required a second dose, but only 313,144 (48%) did receive one by 22 January 2010.

Discussion

Although similar outbreaks of MPIV have been reported in school settings [2,4,5], to the best of our knowledge, this report is the first to describe that MPIV could occur as a result of mass introduction of vaccines to adolescents in a pandemic. Published literature suggests that, once vaccines are identified as a probable cause of mass psychogenic illness, a dismissive approach may actually be harmful [2]. In Taiwan, the government responded with rapidly investigating the school clusters of adverse events, well briefing the press, and reassuring the public with key messages that it was the process of vaccination, instead of the vaccine itself that triggered the occurrence of MPIV. On 1 December 2009, a guidance document was issued to school staff and local immunisation organisers regarding appropriate measures to minimise the risk of MPIV and prevent traumatic injuries related to fainting episodes after vaccination [6]. The recommendations included (i) vaccinating first those students who reported less fear of injections, (ii) providing a supportive group of volunteers or teachers to help relieve anxieties, and (iii) having students sitting down during the 30-minute observation period after vaccination. Through the aforementioned efforts, the number of MPIV reports decreased (four reports since 1 December 2009 compared with 19 reports from 16 to 30 November 2009), and we were able to proceed with the mass vaccination campaign against pandemic influenza.

This series of MPIV, along with the death of a first grade student on 21 December 2009 who died after receiving the vaccine, generated considerable media interest and had driven public concerns about the safety of the pandemic influenza vaccine in Taiwan. With a strengthened

AEFI surveillance system, the government could rapidly detect and distinguish between true vaccine reactions, coincidental events, and injection reactions from the fear or pain of the injection itself rather than the vaccine [7,8]. However, not only were local health authorities unprepared to respond to possible outbreaks of MPIV in adolescents, but the requirement to vaccinate all students within two months limited the time available for education and consultation to healthcare providers and the public. Failure to communicate in advance that there are different causes of AEFI and a background of distrust of the domestically manufactured pandemic influenza vaccine provided the media with an opportunity to blame the vaccine for the mass adverse events. Although the government was able to reach a high vaccine coverage rapidly at the beginning, the subsequent stagnant progress on the first-dose vaccination and the low vaccine coverage for the second dose compared with the first dose coverage suggested a loss of confidence in the safety of the pandemic influenza vaccine, which undermined the impact of the NISIV programme in effectively achieving maximal coverage among schoolchildren.

In the future, public health officials should be aware that mass vaccination campaigns, particularly those targeting adolescents, could generate MPIV. Countries should incorporate surveillance and communication strategies for MPIV in their pandemic preparedness plans.

Acknowledgements

We thank the staff of local health authorities, Yu-Fang Tsai, Shi-Chuan Wang, Su-Ching Yao, Mei-Ling Wu, Yu-Yuan Hu, and Mei-Chu Lee for their support throughout the investigations.

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Travel-associated Legionnaires' disease in Europe in 2008

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Citation style for this article:

Citation style for this article: Ricketts K, Joseph CA, Yadav R, on behalf of the European Working Group for Legionella Infections. Travel-associated Legionnaires' disease in Europe in 2008. Euro Surveill. 2010;15(21):pii=19578. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19578>

This article has been published on 27 May 2010

In 2008, the European Surveillance Scheme for Travel Associated Legionnaires' Disease (EWGLINET) received reports of 866 cases of travel-associated Legionnaires' disease, 42 of whom were reported to have died. 824 of the cases were classified as confirmed and 42 were presumptive. As in previous years, a very low proportion of clinical isolates were obtained (63 cases, 7.3%). Males outnumbered females by 2.8:1 in the 2008 dataset and had a median age of 60 years compared with women, whose median age was 63 years. Travel outside Europe was reported for 12% of the cases. The scheme identified 108 new clusters in 2008. Sixteen were located in countries outside EWGLINET and 38 (35.2%) involved only one case from each reporting country, and would not ordinarily have been detected by national surveillance schemes alone. The largest cluster (six cases) was associated with travel to Spain. The 108 clusters were associated with 144 environmental investigations, 35 of which were at re-offending sites, (sites which had previously been investigated and where additional cases had subsequently occurred). At 61 (42.1%) of the sites *Legionella* species were detected. The names of 12 sites were published on the EWGLINET website.

Introduction

EWGLINET (the European Surveillance Scheme for Travel Associated Legionnaires' Disease) is a disease-specific network which aims to detect clusters of Legionnaires' disease associated with accommodation sites across Europe. It was established in 1987 by EWGLI (the European Working Group for Legionella Infections) in order to better protect the health of travellers by improving the detection and control of sources of infection in European countries.

Travel-associated clusters are unusual in that they often involve residents from more than one country and as such may not be identified by national surveillance systems alone. EWGLINET collates and coordinates the information held by each country, and communicates with the country in order to initiate investigations and control measures at sites of potential exposure.

In 2002, EWGLI introduced The European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease [1]. These guidelines are designed to ensure a common standard of response to single cases and clusters of travel-associated Legionnaires' disease across Europe, and were endorsed by the European Commission in 2003. The history and current activities of EWGLI are described further on its website (www.ewgli.org).

This paper provides results and commentary on cases of travel-associated Legionnaires' disease reported to EWGLINET with onset in 2008.

Methods

National surveillance systems collect data on all cases of Legionnaires' disease that occur within their countries. Cases that have stayed overnight in a public accommodation site during their incubation period, and that meet EWGLINET's case definition [2] are reported to the scheme.

Basic epidemiological, microbiological and exposure information for each reported case is entered into a database held by the coordinating centre at the Health Protection Agency Centre for Infections in London. A database search is performed for each new case, to determine whether it should be classified as a single case or as part of a cluster. These are defined as follows [1]:

- **Single case:** A person who stayed, in the two to 10 days before onset of illness, at a public accommodation site that has not been associated with another case of Legionnaires' disease within two years.
- **Cluster:** Two or more cases who stayed at the same accommodation site in the two to 10 days before onset of illness and whose onset is within the same two-year period.

This classification determines the response that is expected from the country of infection under the

European guidelines [2]. A single case may have contracted Legionnaires' disease at any time during their incubation period of two to 10 days, and as such the accommodation site will often be only one of many potential sources. Therefore, the only required response to single cases is that the collaborator in the country of infection must send the accommodation site a checklist for minimising the risk of Legionella infections, to encourage the site to follow best practice. Further investigations may be conducted locally at the discretion of the national collaborator.

However, if the site is identified as a cluster site, a full investigation is required. Within two weeks a risk assessment must have been conducted and control measures initiated. These actions are reported back to the coordinating centre in London using a 'Form A'. Within a further four weeks, environmental sampling must have been carried out and control measures completed; a 'Form B' report is then submitted to the coordinating centre. If any of these actions are not completed within the time frame allowed, or if the report states that control measures are unsatisfactory, EWGLINET will publish the details of the accommodation site on its website. This is done so that individual travellers and tour operators can determine for themselves whether or not to contract with these sites. The notice is removed once investigations have been completed satisfactorily.

If the investigation of a cluster site has been completed, but the site is subsequently linked to additional cases within a two-year period, these are termed 're-offending sites' and a complete re-investigation is required. If two cases have more than one accommodation site in common during their incubation periods, it is not possible to determine which site was responsible

for the infections and both will be subject to investigation; these are termed 'complex clusters'.

The number of clusters reported in this paper do not include those that were identified in previous years and were associated with a subsequent case in 2008 ('cluster updates'); such clusters are included in the previous years' figures.

Results

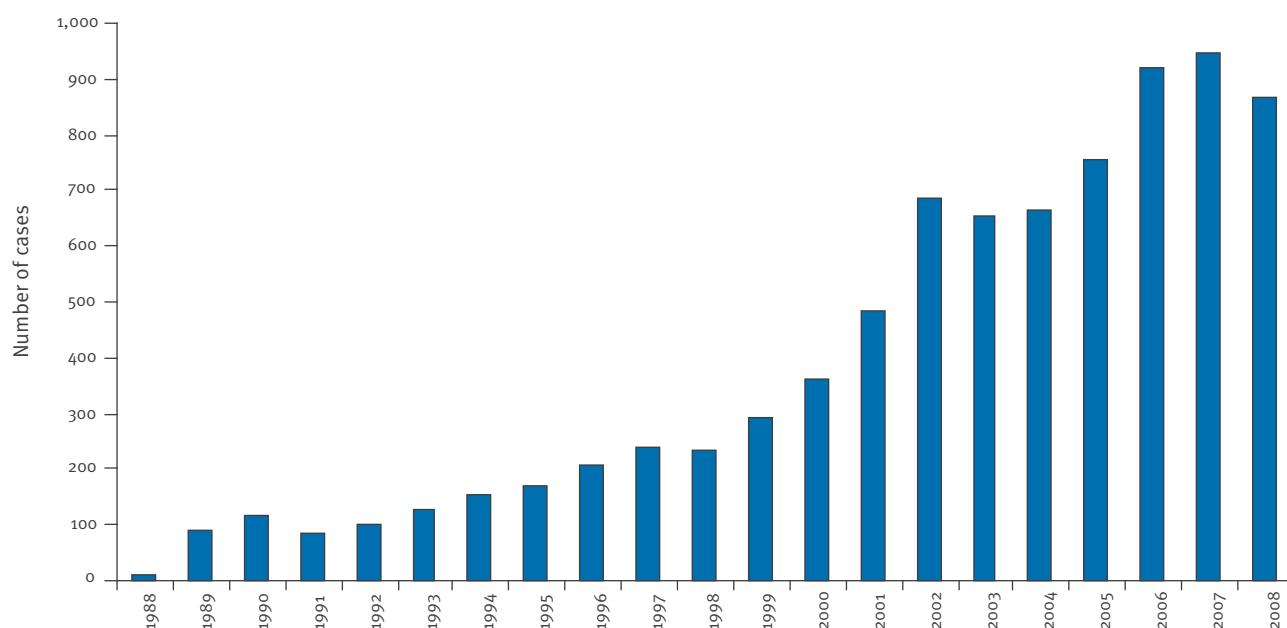
A total of 866 cases were reported to the EWGLINET surveillance scheme with onset during 2008. Among these cases, 853 were reported by 19 of the 35 countries who officially collaborate in the scheme. The remaining 13 cases were reported by Australia and the United States (not part of the official network). The overall number of cases with onset in 2008 was lower than the number with onset in 2007 (946 cases) (Figure 1). The mean interval between onset and report to EWGLINET in 2008 was 27 days (range: 1–300 days).

The highest numbers of cases were reported by France (190 cases), the United Kingdom (UK) (166 cases), Italy (127 cases) and the Netherlands (127 cases), and in total represented 70.4% (610 cases) of case reports (Table 1).

The sex and age distribution reflected the classical distribution for cases of Legionnaires' disease with a ratio of 2.8:1 (641 males and 225 females) and a median age of 60 years for men and 63 years for women. The age group with the most cases for men was 50–59 years and for women 60–69 years. Outcomes were provided for 427 cases (49.3%, the same proportion as in 2007), and 42 were reported to have died (9.8%). Overall, the case fatality for reported cases was 4.8% compared with 3.0% in 2007. The deaths occurred in 36 men and

FIGURE 1

Travel-associated Legionnaires' disease cases reported to EWGLINET since the scheme began in 1987 (n=8,161)



six women aged 26 to 85 years and 15 were associated with clusters (35.7%).

Cases of Legionnaires' disease tend to peak during late summer, and in a travel-associated scheme this seasonality is exaggerated, although cases occurred in all months of the year. September was the peak month for onset for cases reported to EWGLINET in 2008 (136 cases, 16.6%) and similar to the peak in September 2007 (157 cases, 15.7%).

Microbiology

Under the EWGLINET case definition, 824 (95%) of the 866 cases were confirmed and 42 were presumptive [2]. The confirmed cases consisted of 754 cases diagnosed primarily by urinary antigen detection (87.1%, an increase from 85.1% in 2007), 63 cases diagnosed by culture (7.3%, compared with 8.2% in 2007), and seven cases diagnosed by a fourfold rise in serology titre as *L. pneumophila* serogroup 1 (0.8%, compared with 0.7% in 2007). Of the 63 culture-confirmed cases, 57 were identified as *L. pneumophila* serogroup 1, one was serogroup 2, one was serogroup 3, three had unknown serogroups, and one had unknown species. The presumptive cases consisted of a further four cases (0.5%) diagnosed by a fourfold rise in serology titre, 25 cases (2.9%) diagnosed by a single high titre, and 13 diagnosed primarily by PCR (1.5%, an increase from 1.1% in 2007).

In addition to the 13 cases diagnosed primarily by PCR in 2008, 16 of the confirmed cases had a positive PCR test result in conjunction with other tests, to give a total of 29 cases with a positive PCR result. Fourteen of these were reported by Denmark, seven by the Netherlands, five by Sweden, and one each from Belgium, Finland and Scotland. The first PCR-positive cases were reported to EWGLINET in 1994; since then a total of 241 PCR-positive cases have been reported by

fifteen countries. Over half of these (147 cases) were reported by Denmark.

Travel

A total of 60 different travel countries were reported in 2008 (Figure 2), with 104 cases (12.0%) visiting countries outside the EWGLINET scheme. Eleven cases were associated with cruise ships, and 62 cases visited more than one country during their incubation periods. The four countries in this dataset most frequently associated with infection were Italy (182 cases, 21.0%), France (151 cases, 17.4%), Spain (144 cases, 16.6%) and Turkey (62 cases, 7.2%); together they accounted for 62.2% of the total 2008 dataset.

The numbers of cases associated with travel to Italy, France and Spain include a high proportion of persons infected when travelling in their own country, in contrast to cases acquired as a result of travel abroad: 57.7% of the infections associated with Italy occurred among Italian nationals travelling in their own country (105 cases). For France this proportion was higher, at 72.2% (109 cases), and lower for Spain at 44.4% (64 cases). In contrast, there were no Turkish nationals among the cases reported with travel to Turkey.

Clusters

108 new clusters were identified in 2008, occurring in 24 countries and on one cruise ship. The highest numbers of clusters were associated with Italy (n=31), followed by France (n=17), Turkey (n=12), Spain (n=11), Greece (n=5), and Germany (n=3) (Table 2). Sixteen of the remaining clusters (14.8%) occurred in countries outside EWGLINET, a similar proportion to the 14.2% in 2007.

Altogether, 252 (29%) cases were associated with the clusters in 2008. For travel to Italy the proportion was 39.0% (71 cases), for France it was 23.2% (35 cases), and for Spain 20.8% (30 cases). The proportion of cases associated with travel to Turkey that were part of clusters continues to remain high. It was at its highest in 2005 when 53% of cases were part of clusters and at its lowest in 2006 (38%). In 2008 the proportion was 43.5% (27 cases).

The largest new cluster in 2008 involved six cases and occurred in Spain. Thirty-eight of the new clusters (35.2%) consisted of single cases that were reported by two or more countries; these would not ordinarily have been detected by national surveillance systems alone. The proportion of such clusters was higher in 2008 compared with 2007 (29 clusters, 25.9%) ($p=0.13$).

Clusters were detected in every month of the year in 2008 (by date of onset of the second case in the cluster). Following the seasonality seen in cases of Legionnaires' disease, there was also a seasonal pattern in the onset of clusters: 81 (75.0%) occurred between May and October.

TABLE 1

Countries reporting more than 10 cases of travel-associated Legionnaires' disease to EWGLINET in 2008

Reporting country	Number of cases	
	2007	2008
France	181	190
United Kingdom	236	166
Italy	153	127
The Netherlands	137	127
Spain	68	97
Denmark	31	38
Sweden	41	35
Norway	17	21
Austria	21	20
United States	4	12
Belgium	15	11

A further ten countries (including Australia) reported fewer than 10 cases and are not listed here.

Investigations and publication

Some clusters were complex and involved more than one accommodation site. The 108 clusters were associated with 129 accommodation sites. Twenty of these sites (15.5%) were situated in countries that had not signed up to follow the European guidelines, leaving 109 sites that required EWGLINET investigations. In addition, 35 're-offending sites' were reported in 2008 (compared with 40 in 2007), 16 situated in Italy, six in France, four in Spain, four in Turkey, two in Greece, one on a cruise ship and one each in Austria and Malta.

EWGLINET therefore requested a total of 144 environmental investigations in 2008 (109 new cluster sites in Europe and 35 re-offending sites). Four of these Form B reports have not been returned to date: one of the sites is closed and a Form B will be required prior to reopening, and three are published on the EWGLI website for failure to return a Form B report in time. Reports were submitted for the remaining 140 sites, 59 (42.1%) of which reported that *Legionella* spp. had been isolated from water samples taken at the accommodation sites. This positivity rate is lower than that reported in 2007 (54.3%) and in 2006 (66.4%). Seventy-eight (55.8%) of these forms reported that *Legionella* was not detected in samples, and three (2.1%) reported 'unknown', i.e. delayed results due to site closures (in these situations the site investigation would be delayed until immediately prior to the site reopening, in order to ensure optimal protection for travellers). When the investigation results for re-offending sites are considered

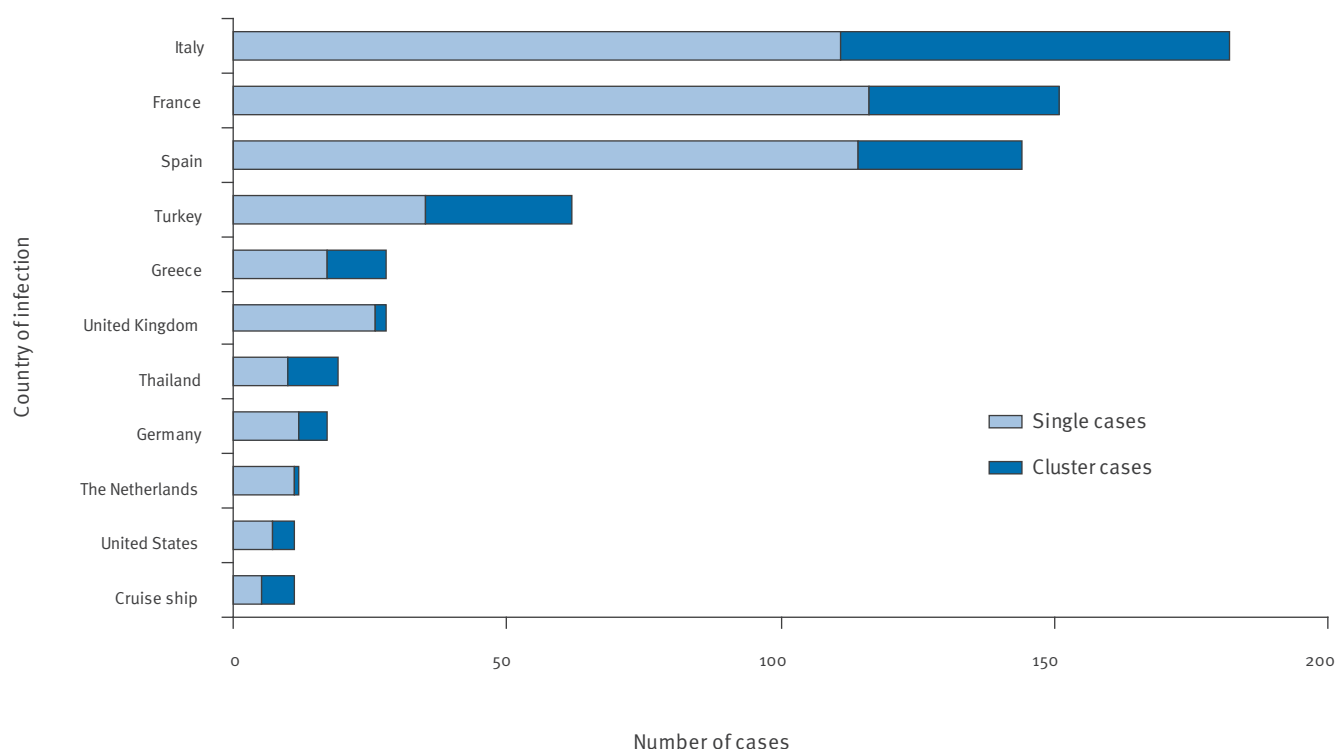
separately, 13 of 35 (37.1%) returned positive samples (compared with 54.8% in 2007).

Of the 59 sites where *Legionella* spp. was isolated from the water, *L. pneumophila* serogroup 1 was isolated from 37 sites (62.7%) and non-serogroup 1 isolates were reported for 12 sites (20.3%) (representing other species or serogroups). The reports for ten sites did not include enough information to categorise the isolates in this way (16.9%).

Since sequence-based typing (SBT) became available [3], EWGLINET aims to match clinical and environmental cultures during cluster investigations, thereby strengthening the evidence that the accommodation site was the probable source of infection. The opportunities to do this are rare due to the low percentage of cases with a positive culture. Of the 140 investigations carried out in 2008, 59 (42%) yielded positive environmental isolates, but only 19 (of 140, 14%) had associated clinical isolates. There were 12 sites that had both clinical and environmental isolates available for comparison, and matching was achieved for three of these, representing only 2% of all investigations. In one instance the clinical and environmental isolates were of different sequence types, and for the remaining eight instances, SBT was not undertaken for both isolates.

FIGURE 2

Countries visited by 10 or more cases of travel associated Legionnaires' disease in 2008, by type of case



A further 49 countries were visited by less than 10 cases and do not feature on this graph. EWGLINET data.

Twelve accommodation sites were published on the EWGLI website during 2008 for failure to return a Form A or Form B report on time, or for failure to implement appropriate control measures within the required period. These sites were located in Turkey (n=6), Italy (n=3), Bulgaria (n=1), France (n=1) and Greece (n=1). In comparison, thirteen site names were published during 2007, four in 2006, nine in 2005, and four in 2004.

The European guidelines do not require an investigation to be carried out at sites associated with a single case report. However some countries do systematically carry out such investigations. In 2008, Italy reported that 150 of their single sites were investigated, of which 61 (40.7%) reported positive sampling results for *Legionella* spp. There was also one instance of sequence matching being undertaken for a single case of travel-associated Legionnaires' disease [4].

Discussion

EWGLINET received reports of 866 cases of travel-associated Legionnaires' disease with onset in 2008, slightly below the number of cases reported in 2007. Prior to 2007 there had been a steady increase in the number of cases reported to the scheme since its inception in 1987, due in part to improved national surveillance and to an increasing number of countries joining the scheme. There is still significant under-ascertainment of Legionnaires' disease within Europe, especially among the newer Member States of the European Union (EU) which include many countries where surveillance for Legionnaires' disease is less well developed. Therefore there is still potential for case numbers to increase.

The small decline in case numbers in 2008 may reflect the early impact of the economic recession on the

tourist industry. As people take fewer holidays abroad, we would expect the proportion of travel-associated cases reported to national surveillance schemes to decrease, and therefore the number of cases reported to EWGLINET to decrease in turn. Whilst data are not available for all European travellers, the UK Office for National Statistics keeps a record of the number of travellers entering or leaving the UK. Between 1999 and 2006, UK travellers increased year on year, but their numbers subsequently declined (2006: 69,536,000; 2007: 69,450,000; 2008: 68,644,000) [5]. With a decrease in foreign travel, it is possible that there may be an increase in domestic travel as people holiday closer to home. EWGLINET does encourage the reporting of domestic travel-associated cases, but historically collaborators have reported these cases with less urgency than cases that travelled abroad. Over the next couple of years, it will be important to ensure that the scheme captures domestic travel as fully as it captures foreign travel.

The use of PCR in the diagnosis of Legionnaires' disease is increasing, although the proportion of travel-associated cases diagnosed by this method is still very low. Where respiratory samples can be obtained, PCR offers a rapid approach to the diagnosis of Legionnaires' disease, and the clinical sensitivity is likely to be higher than that of culture [6].

Over the last three years there has been a decrease in the proportion of cluster sites that yield positive environmental samples. This trend might indicate a change in the range of laboratory services used for investigations across Europe; alternatively it may reflect the high number of cases reported to the EWGLINET database on an annual basis, which inevitably include some cases whose infection was not linked with the accommodation site that they visited during their incubation period.

The number of accommodation sites published on the EWGLI website for failure to meet EWGLI's standards of investigation remained high in 2008, however the number of publications associated with sites in Turkey fell from 11 of 13 in 2007 to six of 12 in 2008. This suggests that there has been improvement in Turkey's response to clusters following discussion of the situation in our last annual report [7].

Also highlighted in Joseph *et al.* [7] were the difficulties faced by EWGLINET when dealing with clusters that occur in countries outside Europe. The proportion of these clusters in 2008 was similar to that in 2007, and there remains a lack of feedback on the environmental investigations carried out as a result of EWGLINET cluster notifications. However, recent discussions with the World Health Organisation have led to renewed efforts to strengthen existing investigation and reporting mechanisms in non-European countries. EWGLINET is continuing to pursue ways to improve the response

TABLE 2

Countries where two or more clusters of travel-associated Legionnaires' disease occurred in 2008

	Country of infection	Number of clusters
Europe		
	Italy	31
	France	17
	Spain	11
	Turkey	12
	Greece	5
	Germany	3
	Russia	2
Outside Europe		
	India	4
	Mexico	3
	Thailand	2
	United States	2

A further fifteen countries and one cruise ship were associated with only one cluster and are not listed here.

EWGLINET data.

to travel-associated clusters of Legionnaires' disease in these countries.

Within Europe, attention has been focused on the newer EU Member States. With funding obtained from the European Centre for Disease Prevention and Control (ECDC) a training course for health professionals and the tourist industry was held in Bulgaria in September 2008. Several travel associated outbreaks of Legionnaires' disease have occurred in Bulgaria, including one in 2008 which was not satisfactorily investigated and which was published on the EWGLI website. The local Ministry of Health has noted the need for Bulgaria to increase its laboratory and microbiological resources for testing both clinical and environmental specimens.

Efforts are also required within EWGLINET to increase the use made of SBT typing data where both clinical and environmental cultures are available for a cluster site. Countries are regularly reminded to report microbiological updates, such as culture results after the case has been reported. When positive cultures are available, countries are encouraged to carry out SBT typing of any isolates that are known to be part of a cluster and to make greater use of the international SBT database managed by EWGLI [3]. Two of the three matching sets of clinical and environmental isolates came from the same country in 2008, a country with a high proportion of cases diagnosed by culture and a large number of domestic travel-associated cases of Legionnaires' disease among their own residents, providing the opportunity to encourage greater use of SBT methods.

On 1 April 2010, the EWGLINET scheme moved from London to Stockholm and is now coordinated by ECDC. Collaborators are encouraged to maintain their commitment to rapid reporting and cluster management under the new arrangements, in order to ensure the continued success of this highly active and responsive surveillance scheme.

Acknowledgements

This work is funded by the European Centre for Disease Prevention and Control. We would like to thank all collaborators for reporting their cases and all people involved in public health control and prevention programmes for travel-associated Legionnaires' disease. The list of EWGLINET collaborators is available at the following URL address: <http://www.ewgli.org/collaborators.htm>

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Influenza A(H1N1) outbreak in a long-term care facility for severely handicapped residents, Slovenia, March–April 2009

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Citation style for this article:

Citation style for this article: Socan M, Prosenc K, Tevž-Cizej N. Influenza A(H1N1) outbreak in a long-term care facility for severely handicapped residents, Slovenia, March–April 2009. *Euro Surveill.* 2010;15(21):pii=19577. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19577>

This article has been published on 27 May 2010

Long-term care facilities are vulnerable to outbreaks of influenza. This report describes the response to such an outbreak in a long-term care facility for severely handicapped children and adults near Ljubljana, Slovenia, in March and April 2009. Of the 23 residents who lived in a unit of the facility, 10 fell ill with fever (≥ 37.5 °C) during a period of nine days. Probable and confirmed cases were residents who developed a fever after 24 March 2009. Respiratory symptoms were not included in the case definitions as some residents were unable to describe their symptoms due to their mental and/or physical impairment. Epidemiological data were collected and throat and nasal swabs taken. Influenza A virus was identified (without subtyping) and treatment with oseltamivir was given to patients with fever of no more than 48 hours' duration. Oseltamivir was also given prophylactically to healthy residents and staff. Rigorous adherence to standard and droplet precautions was recommended by the regional institute of public health. Two days after respiratory and standard precautions have been strengthened, four more residents became ill. Viral subtyping showed that 12 of the 23 residents were infected with influenza virus A(H1N1); one had an influenza B virus infection. Of the 12 confirmed influenza A cases, 10 had been vaccinated with the seasonal influenza vaccine. Follow-up swabs were taken and were found to be still positive for influenza A virus in 6 of the 12 confirmed cases more than a week after illness onset. The virus was resistant to oseltamivir and susceptible to zanamivir. This influenza outbreak demonstrates the need for rapid typing and subtyping of influenza viruses for accurate diagnosis, treatment and chemoprophylaxis in special settings.

Introduction

Outbreaks of influenza in care facilities, such as nursing homes for elderly people and people with special needs, are common, despite good vaccination coverage among the residents [1] and a good match between the vaccine type and the viral strain [2]. According to the clinical practice guidelines of the Infectious Diseases Society of America, an epidemiological investigation

should be carried out for such outbreaks and measures taken to prevent the spread of the influenza virus among the residents, as they often develop severe complications due to primary chronic illnesses or injuries [2]. To limit an outbreak, antiviral drugs need to be prescribed to those who are ill as well as to all (residents and staff) who still show no signs of illness [2]. The development of influenza A viral resistance to rimantadine and amantadine (M2 inhibitors) and the emergence of resistance of the seasonal influenza A(H1N1) virus to oseltamivir (neuraminidase inhibitor) narrow the therapeutic and prophylactic possibilities to control an outbreak [3].

In this report, we describe an influenza outbreak in March–April 2009 caused by the seasonal influenza A(H1N1) virus in a unit of long-term care facility for severely handicapped children and adults near Ljubljana, Slovenia. The facility consisted of five separate low-rise buildings, with 148 residents and 162 staff members (health and pedagogical workers) in total. There were also 21 non-residents who attended day-care services and some residents spent occasional weekends away from the facility. In the unit in which the March–April 2009 outbreak occurred, two to a maximum four residents shared the same bedroom. During the day, the residents were transported in specially adapted wheelchairs from their bedrooms to common rooms in the same unit.

An earlier influenza outbreak occurred on 17 February 2009 in a different unit of the care facility, which was reported to the regional institute of public health. Of the 21 residents, 16 became infected: five of them were hospitalised. The last patient with fever and respiratory symptoms fell ill on 24 February 2009. Throat and nasal swabs from the residents who were hospitalized were positive for influenza A(H3N2) virus. Of the 16 staff members, 10 reported a high fever (>38 °C) with accompanying respiratory infection symptoms. No swabs were taken for virological analysis. Oseltamivir was used to treat the ill residents, while the healthy residents and staff were prescribed it prophylactically.

The outbreak did not spread in the same unit or to other groups of residents in the care facility.

About a month later, a second outbreak occurred, beginning on 24 March 2009. This time, 10 of the 23 residents of a second, spatially separated unit fell ill with fever during a nine-day period; some residents also had respiratory symptoms. The attending physician notified epidemiologists at the regional institute of public health on 2 April 2009 and an epidemiological investigation was started. The evolution of the outbreak was followed: clinical data were collected and repeat swabs taken from all the residents (symptomatic and asymptomatic) to enable the early detection of possible infection among still asymptomatic individuals.

Methods

Case definitions

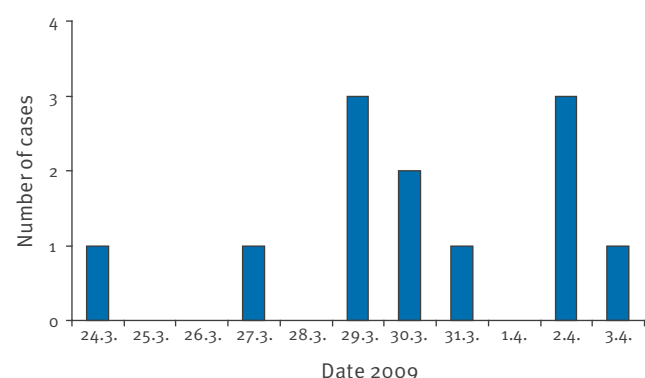
We used the following definitions in our investigations:

- **Confirmed case:** a resident who fell ill with fever ($\geq 37.5^{\circ}\text{C}$) and in whom the presence of influenza viral RNA was confirmed by real-time reverse-transcription polymerase chain reaction (rt-RT-PCR). The European Union definition of influenza requires at least one further symptom, in addition to acute onset of fever, such as a cough, sore throat or breathing difficulties to be present [4]. In this investigation, however, we used a modified definition of influenza, as some of the residents were incapable of describing their symptoms, due to mental and/or physical impairment.
- **Probable case:** a resident from the group who had fever ($\geq 37.5^{\circ}\text{C}$), no virological confirmation of influenza virus infection, but was epidemiologically linked to a confirmed case.

Nursing staff measured the body temperature of residents daily (part of routine care) and recorded the patients' symptoms (when possible), as well as signs of infection observed in patients.

FIGURE

Confirmed influenza A(H1N1) cases in a long-term care facility for severely handicapped residents, Slovenia, March – April 2009 (n=12)



Virological analysis

Throat and nasal swabs were tested for influenza viral RNA from patients with symptoms of influenza-like illness. After influenza A was identified as the causative agent of the illness, repeat swabs were taken from all the residents (symptomatic and asymptomatic). The follow-up swabs were taken on 6, 15 and 22 April 2009, regardless of the results from the preceding sample.

The swabs were tested at the National Influenza Centre (Laboratory for Virology, National Institute of Public Health) by rt-RT-PCR (QIAGEN OneStep RT-PCR Kit, ref. no. 210212), using reagents and oligonucleotide primers and probes as described in the literature [5–7], with some modifications (O. Hungnes, personal communication). Influenza A and B viruses were detected in a single PCR reaction. In samples positive for influenza A, additional PCR reactions were carried out to detect subtypes H1 and H3.

Most of the influenza A (H1) viruses were tested for sensitivity to the antiviral drug oseltamivir at the Health Protection Agency (a WHO influenza reference centre) in London, United Kingdom, by pyrosequencing of the neuraminidase gene [8]. This detects the mutation that causes viral resistance to oseltamivir – a histidine-to-tyrosine substitution at position 275 (H257Y) in the neuraminidase.

Results

Epidemiological information

At the time of the outbreak, there were 23 residents in the care facility unit: their ages ranged from nine to 34 years (mean: 21.7 years, median: 22 years); 12 of the 23 residents were male. All but two of the residents had been vaccinated with the seasonal influenza vaccine. A total of 14 (10 men, four women; mean age: 17.7 years, median: 17 years) fell ill with fever: in 12, body temperature was $\geq 38^{\circ}\text{C}$; in two, it was between 37.5°C and 37.9°C . The first confirmed case fell ill on 24 March 2009 and the last on 3 April 2009 (Figure).

The rise in body temperature persisted from one to a maximum of nine days (mean: 3.5 days, median: 3.5 days). Of the 14 patients, five had a fever only, with no additional signs observed by staff. One or more additional symptoms were recorded in nine patients: six had a cough, four had a runny nose, two had a sore throat and/or myalgia.

A total of 12 patients were confirmed cases, according to the definition chosen for this investigation. Two patients were probable cases: the first was a male resident whose initial swab was negative for influenza A viral RNA, but influenza B viral RNA was detected in the second sample taken 16 days after the beginning of his illness. The second probable case was a female resident with fever lasting for two days, but whose swab (taken shortly after the fever abated) was negative. Further samples could not be obtained as she temporarily left the care facility.

The attack rate was higher for males than females: of the 12 confirmed cases, nine were male, three were female (attack rates of 75% and 27% respectively). We could not find any explanation for the observed difference.

On 3 April 2009, the day after notification of the outbreak, type A influenza virus was confirmed. However, the subtyping results were not available. If not more than 48 hours had passed since the appearance of symptoms, confirmed cases (n=3) were treated twice daily with 75 mg oseltamivir. The nine residents who remained asymptomatic (two men, seven women; mean age: 28.8 years, median: 28 years) were given oseltamivir prophylactically for 12 days. All asymptomatic residents had been vaccinated against influenza in November 2008.

In addition to chemoprophylaxis, adherence to standard and droplet precautions was intensified. A total of 23 staff members cared for the residents daily: none had been vaccinated against influenza. Two nurses fell ill with high fever $>38.0^{\circ}\text{C}$ and cough before the outbreak but no swabs were taken. The other 21 staff

members received oseltamivir prophylactically for 12 days, as for the asymptomatic residents.

Virological data

Throat and nasal swabs were taken from residents on four occasions (in 2009): 2 or 3 April (n=7), 6 April (n=23), 15 April (n=22) and 22 April (n=21) (Table).

In the first swab collection, all seven samples were positive for influenza A(H1) virus, 10 of 23 from the second swab batch and one of 22 from the third. All 21 samples from the fourth batch were confirmed negative.

Influenza A viral RNA was detected in the 12 confirmed cases even after body temperature returned to normal. In six cases, the virus could still be detected seven or more days after illness onset; in one case, even the third sample (taken 18 days after illness onset) was positive (Table). None of the patients was immunocompromised.

All samples that were positive for influenza A were also tested for the H257Y mutation, which causes resistance to oseltamivir. The mutation was detected in samples

TABLE

Residents' data, influenza A (H1N1) outbreak, long-term care facility for severely handicapped residents, Slovenia, March–April 2009 (n=23)

ID no.	Sex/age (years)	Date of illness onset, in 2009	Duration of fever (days)	Treatment or prophylaxis with oseltamivir	Date treatment or prophylaxis started, in 2009	Throat/nasal swab results, in 2009 (number of days from illness onset to taking of swab)				H275Y mutation detected
						2–3 April	6 April	15 April	22 April	
1	F/19	24 March	9	none	–	NA	pos (14)	neg (23)	neg (30)	ND
2	M/17	27 March	3	none	–	NA	pos (11)	neg (20)	neg (27)	ND
3	M/28	29 March	3	none	–	pos (6)	pos (9)	neg (18)	neg (25)	yes
4	M/23	29 March	5	none	–	pos (6)	neg (9)	neg (18)	neg (25)	yes
5	M/29	29 March	4	none	–	pos (5)	pos (9)	pos (18)	neg (25)	yes
6	M/13	30 March	4	none	–	NA	pos (8)	neg (17)	neg (24)	ND
7	M/27	30 March	7	none	–	pos (5)	neg (8)	neg (17)	NA	ND
8	M/30 ^a	31 March	3	none	–	pos (3)	pos (7)	neg (16)	neg (23)	yes
9	M/17	31 March	2	none	–	NA	neg (7)	B (16)	neg (23)	–
10	F/9	1 April	2	none	–	NA	neg (6)	NA	NA	–
11	M/22	2 April	4	treatment	3 April	pos (2)	pos (5)	neg (14)	neg (21)	yes
12	F/17 ^a	2 April	2	treatment	3 April	pos (2)	pos (5)	neg (14)	neg (21)	yes
13	F/29	2 April	1	none	–	NA	pos (5)	neg (14)	neg (21)	yes
14	M/28	3 April	4	treatment	3 April	NA	pos (4)	neg (13)	neg (20)	yes
15	F/25	asymptomatic	–	prophylaxis	3 April	NA	neg	neg	neg	–
16	F/26	asymptomatic	–	prophylaxis	3 April	NA	neg	neg	neg	–
17	M/17	asymptomatic	–	prophylaxis	3 April	NA	neg	neg	neg	–
18	M/12	asymptomatic	–	prophylaxis	3 April	NA	neg	neg	neg	–
19	F/20	asymptomatic	–	prophylaxis	3 April	NA	neg	neg	neg	–
20	F/21	asymptomatic	–	prophylaxis	6 April	NA	neg	neg	neg	–
21	F/15	asymptomatic	–	prophylaxis	5 April	NA	neg	neg	neg	–
22	F/34	asymptomatic	–	prophylaxis	3 April	NA	neg	neg	neg	–
23	F/22	asymptomatic	–	prophylaxis	3 April	NA	neg	neg	neg	–

B: influenza B virus detected; F: female; H: histidine; ID no. identity number; M: male; NA: not available; ND: not determined, due to insufficient viral RNA; neg = negative; pos: positive; Y: tyrosine.

^a Patients not vaccinated against influenza.

from eight confirmed cases. However, in samples from the other four cases, there was insufficient viral RNA for pyrosequencing (Table).

Discussion

In Slovenia, influenza virus infection was confirmed in 556 patients in the 2008–9 season (from week 40 in 2008 to week 20 in 2009), within the virological sentinel and non-sentinel surveillance system network. A total of 493 (88.6%) of these patients were positive for influenza A(H3N2) virus. Only 33 (6%) were positive for influenza B virus and influenza A(H1N1) virus was seen in just two (0.4%); 28 (5%) of influenza A viruses were not subtyped [9].

In the March–April 2009 influenza outbreak in the care facility, an epidemiological investigation of the outbreak was launched 10 days after the first patient started showing symptoms. The main reason why the outbreak had not been reported sooner was the clinical impression that it was not influenza. This arose from the experience of the first outbreak in the same care facility, which was caused by influenza A(H3N2) virus. That outbreak, in February 2009, took place in a different building and affected staff and residents, who had similar intellectual and motor impairments as the residents in the March–April outbreak. The patients in the first outbreak suffered more severe disease: five of the 16 affected residents had to be hospitalised, due to respiratory problems and/or uncontrollable symptomatic epilepsy in their febrile state. In the March–April outbreak, the affected residents, who were infected with influenza A, experienced less severe disease, had shorter febrile illness and suffered no serious complications; none needed hospital care. The clinical findings in the two outbreaks are in agreement with the general experience that influenza A(H3) infection is more severe and causes more complications than influenza A(H1). One of the indicators of illness severity is excess mortality, which is higher during influenza A(H3) seasons [10].

Before we received the influenza A virus subtyping results, we assumed that the March–April outbreak was caused by influenza A(H3N2) virus. This was based on the fact that this was the predominant circulating virus and, moreover, had been the causative agent in the previous outbreak at the same institution. In this second outbreak, influenza A virus was confirmed and was later subtyped as H1N1. Until this second outbreak, there had been only two laboratory-confirmed cases of infection with A(H1N1) virus in the 2008–9 season in Slovenia and there were no data on drug resistance of these viral isolates. As the National Reference Laboratory does not have the necessary equipment to assess influenza virus resistance to antiviral drugs, in the 2007–8 season, the Health Protection Agency in London, UK, analysed 28 Slovenian influenza A virus isolates and detected the H275Y mutation in only one of the isolates.

After obtaining the subtype results of the isolates in the March–April 2009 outbreak, treatment and prophylaxis with oseltamivir could have been suspended, as it was likely that the virus was resistant to it. At that time, data showed that influenza A(H1N1) viral resistance to oseltamivir in countries of the WHO European Region was 90–100% [11]. Result from the Health Protection Agency revealed the presence of the H275Y mutation in viral isolates from eight of the 12 confirmed cases in the March – April 2009 outbreak (Table) and resistance to oseltamivir was confirmed on 22 April 2009. Given these results, and the fact that influenza A(H1N1) viruses circulating in Europe are almost exclusively resistant to oseltamivir [3], we can assume that the resistance of the influenza A(H1N1) viruses in the outbreak was not a result of treatment.

Three influenza A viruses were tested for zanamivir sensitivity at the Health Protection Agency, London, UK, and no resistance was found (data not shown). However, in this outbreak, either treatment or prophylaxis with zanamivir was out of the question as most of the residents would not have been able to use the disk inhaler due to their psychophysical condition. Such problems with zanamivir use have already been described – nursing home residents with decreased functional and mental status had difficulty with zanamivir inhalations [12]. The issue of its use did not arise, however, as the neuraminidase inhibitor sensitivity results were known after the outbreak was over and treatment or prophylaxis with zanamivir was no longer needed.

The outbreak investigation showed that 12 of the 14 ill residents had been vaccinated against influenza. In the 2008–9 season, there was a good match between the vaccine type and the circulating influenza A and B viruses [11]. Nonetheless, a high percentage of influenza vaccine failure was detected in this group of residents. Few data are available on the success of influenza vaccination in mentally and/or physically handicapped children and adults. A recent study showed that the immune response after vaccination depends more on age than on the level and type of physical and mental impairment [13]. Our residents were children and adults, yet they failed to develop protection after vaccination. Although the vaccine was offered free of charge, the nursing and pedagogical staff had not been vaccinated, which does not comply with national recommendations. Two healthcare workers fell ill with fever and cough before the outbreak, but it is not known whether they had influenza. If they did, it is possible that they may have been the source of infection for the residents. It is also possible that a visitor brought the virus into the facility.

Given the resistance of the influenza A(H1N1) viral isolates in this outbreak, it is unlikely that oseltamivir given as treatment and prophylactically had any impact on the course of illness in those affected and the mitigation of the outbreak. It is more likely that confirmation that this was an influenza outbreak contributed to

stricter following of standard and droplet precautions, stopping further the spread of the virus.

According to recommendations from the United States Centres for Disease Prevention and Control for preventing the spread of influenza virus in acute care facilities, standard and droplet isolation should be adopted for patients for five days after the onset of their illness [14]. Studies involving healthy young volunteers showed that secretion of influenza virus lasts approximately five days and ceases when the symptoms start to disappear: after intranasal inoculation of the virus, secretion lasted for seven days at most [15]. The results of such studies are probably an approximation of what happens after natural influenza virus infection. Intranasal virus application is different from natural infection, which can be a consequence of indirect contact with infected respiratory secretions. After natural infection, children and people with immunity impairment secrete influenza virus longer than immunocompetent adults do [16,17]. In our investigation, most of the cases had viral RNA in their swabs after more than five days since the onset of illness, even after the symptoms disappeared. A semiquantitative method (observing cycle threshold values of rt-RT-PCR results) demonstrated that the concentration of the influenza virus reduced with time and, consequently, the possibility of transfer to other people (data not shown). The question remains as to how long the residents who recovered from influenza were still able to spread the virus within their community in their facility. Perhaps we only detected the inactive viral RNA. In addition, there is also the question of whether five days after the onset of symptoms is really an appropriate time interval for standard/droplet isolation in such an institution or longer period should be recommended [2].

In conclusion, rapid detection, reporting of and response to influenza outbreaks in long-term care facilities must be emphasised [18]. Influenza cannot be distinguished from other respiratory infections on a clinical basis: virological diagnosis is required. In our experience, it is insufficient to confirm the influenza A virus with a near patient or another rapid test – it is necessary to carry out subtyping, which serves to guide the selection of the appropriate antiviral drug. Further studies need to be encouraged to determine the duration of influenza virus secretion in special population groups (such as severely mentally and physically handicapped people) and adapt the duration of isolation.

More will have to be done on the implementation of national recommendations regarding influenza vaccination of health workers and populations at risk, as the immunisation coverage in Slovenia is unacceptably low [19].

Acknowledgements

We sincerely thank Angie Lackenby from the Health Protection Agency, London, UK, for carrying out the antiviral susceptibility tests for this study.

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Underreporting of communicable diseases in the prefecture of Achaia, western Greece, 1999-2004 – missed opportunities for early intervention

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Citation style for this article:

Citation style for this article: Jelastopulu E, Merekoulis G, Alexopoulos EC. Underreporting of communicable diseases in the prefecture of Achaia, western Greece, 1999-2004 – missed opportunities for early intervention. *Euro Surveill.* 2010;15(21):pii=19579. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19579>

This article has been published on 27 May 2010

This study investigates the completeness of the reporting of infectious diseases in the prefecture of Achaia, western Greece in the period of 1999-2004. We collected hospital records relating to infectious diseases retrospectively from three major hospitals in the region and compared the records to corresponding records at the prefectural public health department (PHD). After record-linkage and cross-validation a total of 1,143 notifiable cases were identified in the three hospitals, of which 707 were reported to the PHD of Achaia, resulting in an observed underreporting of infectious diseases of 38% during the study period. At prefecture level, a further 259 cases were notified by other sources, mainly by the fourth hospital of the region not included in our study, resulting in a total of 966 cases reported to the PHD; 73% of these were reported from the three hospitals included in our study, 27% were notified by the fourth hospital not included in our study and less than 0.3% by physicians working in a private practice or health centre. Meningitis (51%), tuberculosis (12%) and salmonellosis (8%) were the most frequently reported diseases followed by hospitalised cases of varicella (7%), brucellosis (6%) and hepatitis (6%). During the study period, clustering of specific diseases like brucellosis, meningitis, mumps, and salmonellosis was observed, indicating possible outbreaks. Our results show that notification system needs to be improved, in order to ensure proper health resources allocation and implementation of focused prevention and control strategies.

Introduction

The objectives of epidemiological surveillance by mandatory notification of communicable diseases differ depending on the disease, but in general terms they are (i) to describe the ongoing pattern of disease occurrence and to link it to public health action, (ii) to provide information and baseline data for disease investigation and control as well as public health planning and (iii) to study the history and epidemiology of disease [1].

An increasing awareness of challenges posed by the re-emergence of 'old' communicable diseases [2], together with new threats such as Severe Acute

Respiratory Distress Syndrome (SARS), (multidrug-resistant tuberculosis (MDR TB), intentional release of biological agents [3] which emerge from increasing globalisation, climate change, international trade and population movements (especially migration and displacement), has stimulated the strengthening of communicable disease-related health resources in the European Union (EU) [4-6]. The first European communicable disease epidemiological report, published in 2007, listed several diseases such as chlamydia infections, campylobacteriosis and gonorrhoea as diseases with the highest incidence in the EU (together with salmonellosis, mumps and tuberculosis) [3]. For chlamydia, campylobacteriosis and gonorrhoea the report stated that trends were rising or stable. Infections with human immunodeficiency virus (HIV) and hepatitis C virus (HCV)-associated infections showed rising trends [3]. To be able to use surveillance data as an element of priority setting for health policies, a well organised notification system is crucial.

In Greece, physicians and laboratories use a standardised notification form to report the mandatorily notifiable diseases if certain criteria are met according to the case definition manual of KEELPNO [7]. At prefectural level, public health departments (PHD) are charged with the collection of data for all notifiable diseases. At national level, KEELPNO receives information from all PHDs for the purpose of carrying out epidemiological surveillance and trend analysis.

Table 1 shows the list of mandatorily notifiable diseases. Overall, they are similar to those in most European countries, with the exception of campylobacteriosis, chlamydia infections, cryptosporidiosis, giardiasis, gonorrhoea, *Haemophilus influenzae* infections, yersiniosis (non-pestis) and healthcare associated infections for which notification is voluntary. In 2008, syphilis, gonorrhoea, human papilloma virus infections (HPV), herpes simplex virus infections and chlamydia infections were included in the list of mandatorily notifiable diseases in Greece [7]. Over the last two years efforts have been made by the Hellenic Center for Diseases Control (KEELPNO) to reorganise the notification system by redefining the list of

notifiable diseases and introducing weekly reporting instead of monthly reporting.

International literature has shown that undernotification of communicable diseases, and the resulting underestimation of the disease burden is a major flaw of many surveillance systems, because undernotification limits the efficacy of these systems especially concerning the early identification of possible outbreaks [8-15]. Any surveillance system can only be useful and cost effective if directly linked to the decision-making authorities of the respective country. The linking is needed in order to ensure that public health threats are not only monitored and identified but also contained [1].

The objective of this study was to investigate the completeness of the notification system for communicable diseases in place in western Greece between 1999 and 2004. For the period under study, we also analysed the incidence, seasonality and other characteristics of the communicable diseases in the area.

Methods

The study was carried out in the prefecture of Achaia in western Greece, which covers an area of 3,271 square kilometres (2.4% of the total area of Greece). According to the 2001 census, the population of the region was 322,790 (3% of the total population of Greece). For the study period 1999-2004, all official infectious disease

TABLE 1

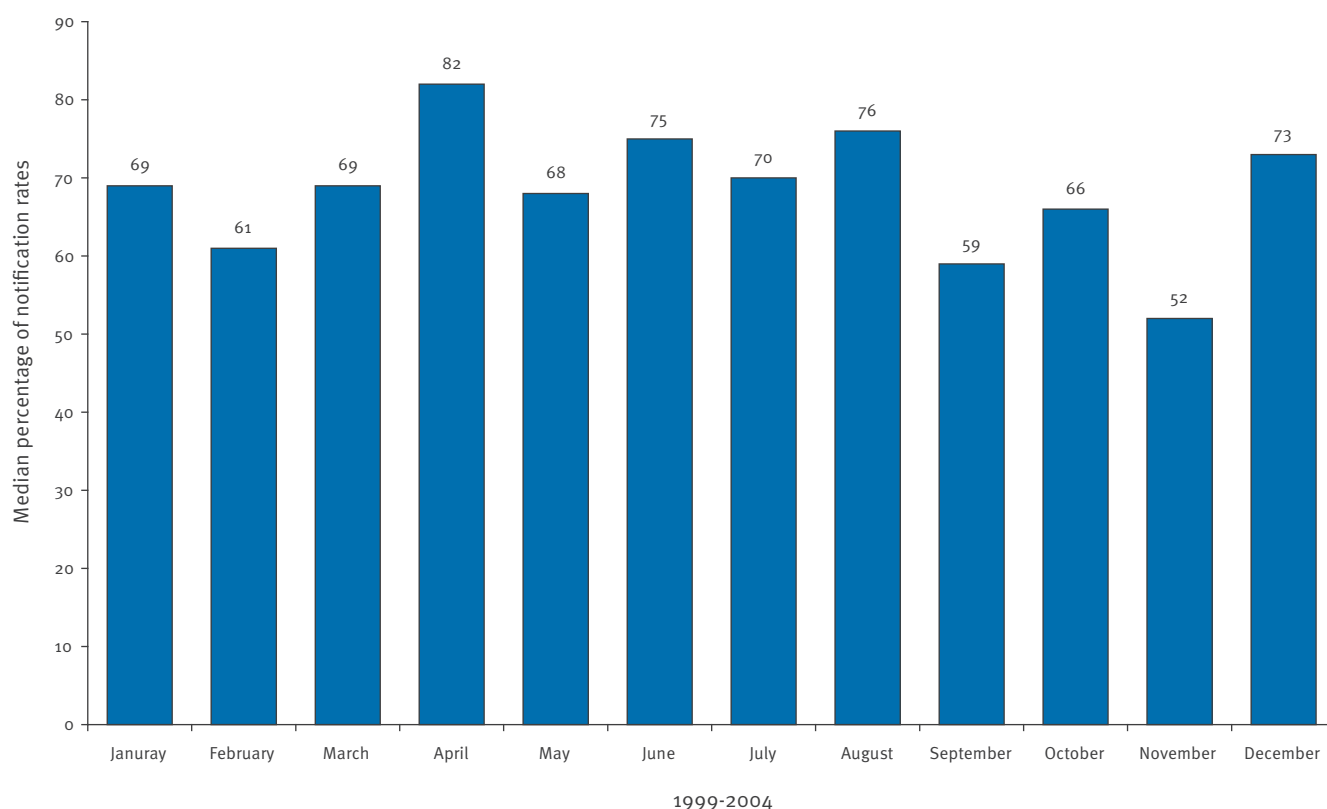
Mandatorily notifiable communicable diseases under epidemiological surveillance in Greece, 2010

Mandatory notification	Diseases under surveillance
Immediate	anthrax ; botulism; cholera; diphtheria; encephalitis from arbo-viruses; melioidosis; plague; rabies; severe acute respiratory syndrome (SARS); tularaemia; smallpox; viral hemorrhagic fevers
Within 24 hours from diagnosis	acute hepatitis A; clusters of food- and water- borne infections; enterohaemorrhagic <i>Escherichia coli</i> ; influenza; invasive meningococcal disease; legionellosis; measles; pertussis; meningitis (bacterial, aseptic); paratyphus; parotitis; rubella; salmonellosis; shigellosis; trichinosis; typhoid fever
Within a week from diagnosis	acute hepatitis B, HbsAg(+) in infants; acute hepatitis C, anti-HCV positive (first diagnosis); AIDS/ HIV; brucellosis; Chlamydia; congenital rubella; congenital syphilis; congenital toxoplasmosis; echinococcosis; gonorrhoea ^a ; herpes simplex virus infections; poliomyelitis; human papilloma virus infections (HPV) ^a ; leishmaniasis; leptospirosis; listeriosis; malaria; Q fever; syphilis ^a ; tetanus; tuberculosis; variant Creutzfeldt-Jakob Disease (vCJD); varicella with complications

^a Syphilis, gonorrhoea, human papilloma virus infections (HPV), herpes simplex virus infections and chlamydia infections are included in the list of mandatorily notifiable diseases in Greece only since 2008, hence outside the period reported in this study.

FIGURE 1

Monthly distribution of notification rates (median percentage of all notifiable diseases) prefecture of Achaia, western Greece, 1999-2004



notifications were obtained from the public health department (PHD) of Achaia.

For the same period, all clinical records of cases with mandatorily notifiable infectious diseases were collected by two researchers, trained nurses attending a masters of science course, from three major hospitals in the area covering 70% of hospital beds in the prefecture of Achaia: the university hospital of Patras (663 beds), the paediatric hospital Karamandaneio, (88 beds) and the general hospital of Aigio (78 beds). Due to access restrictions we did not include the fourth hospital in the area (355 beds). Non-hospital notification is extremely low and is unlikely to cause a bias in our study.

Researchers traced and confirmed notifiable cases by using three sources. Firstly, the records kept by the hospital-based Committee of Infectious Disease Control which is responsible in each hospital by law for the continuous monitoring of all communicable diseases. Secondly we traced additional cases through the lists of patients who were discharged from the departments of internal medicine, pulmonology and paediatrics of each hospital and at last, by the records kept in handwritten form in a corresponding book logging laboratory results in the departments of microbiology and cytology of each hospital. These laboratory records were also used to confirm all the cases traced. For each case traced that fulfilled criteria for notification, a form was filled by the researchers including data on the date of diagnosis or admission, co-morbidities, criteria used for the ascertainment of the case and demographic characteristics (age, sex, residence and prefecture).

Data collected was then compared with official notification data at the PHD to calculate underreporting. The regional results were also compared to the incidence for the corresponding diseases during the same time period, in Greece, by using data from KEELPNO [16]. Incidence rates (per 100,000 population) were calculated using the 2001 census data provided by the National Statistical Service of Greece.

The study was approved by both the Board of Medical School of the University of Patras and the Regional Health Authority of western Greece. The statistical package for social sciences (SPSS) program-version 16.0 was used for data entry and descriptive analysis.

Results

During the six-year study period from 1999 to 2004, 966 cases of communicable diseases were reported to the PHD of Achaia; most of the reported cases were in local inhabitants (76%). Of the 966 reported cases, 707 were notified by the hospitals included in the study, while 259 (27%) additional cases were notified to the PHD by other sources, mostly by the hospital not included in the study and less than 0.3% by private practice and health centre physicians.

For the same time period, 1,143 documented cases of communicable diseases that would have fulfilled notification criteria were identified in the three hospitals; most of these cases (90%) were traced in the official records of the Committee of Infectious Disease Control. The addition of 259 cases that were notified to the PHD by mainly the fourth hospital sums up to 1,402 cases. After record-linkage and cross-validation of the 1,143 hospital-documented cases, we found that only 707 cases (62%) had been reported to the PHD of Achaia, resulting in an observed under notification of 38% during the six-year study period. In particular, only 368 out of 571 cases identified at the university hospital were notified to the PHD, resulting in a notification rate of 64%. In the Karamandaneio hospital, the notification rate was similar, as 324 of 522 total cases (62%) were notified to the local PHD. The notification rate decreased to 30% in the hospital of Aigio, where only 15 of 50 cases were notified. Hence the undernotification rate was 36% for the university hospital, 38% for the Karamandaneio hospital and 70% for the hospital of Aigio. Eighty-eight cases deriving from the hospitals examined and notified to the PHD could not be traced in official hospital archives, indicating incomplete documentation in the archives and unofficial ways of notification.

TABLE 2

Main characteristics of the nine most frequent communicable diseases notified, prefecture of Achaia, western Greece, 1999-2004

	Cases identified	Cases notified	Notification rate in %	Annual incidence per 100,000 population	Male/female ratio	Median age in years
Meningitis (bacterial and viral)	720	550	76	35	1.7	9
Tuberculosis	177	92	52	9	2	36
Salmonellosis	105	60	57	5	1	6
Varicella	96	54	56	5	1	7
Brucellosis	86	64	74	4	1	14
Hepatitis	81	52	64	4	1	12
Leptospirosis	30	17	57	1	6	52
Echinococcosis	26	18	69	1	1	57
Leishmaniasis	23	17	74	1	1	20

Notification rates showed great variation depending on the patients' residence and the season. For local inhabitants rates tended to be rather high, reaching 78% for the hospitals examined, while notification rates were significantly lower, below 40%, when the patient resided in other prefecture. A higher rate of undernotification was observed in autumn (Figure 1).

Sixty per cent of cases were younger than 15 years with a median of 11 years and 63% were males. Almost 50% of the cases were children under the age of 10, both in the PHD and hospital data.

Meningitis, tuberculosis and salmonellosis were the diseases most frequently notified. The nine most frequently identified diseases represent 96% of the total cases (Table 2).

Table 2 also shows the notification rate per disease in per cent as well as the annual incidence per disease (observed cases) per 100,000 population in Achaia during the study period and the sex and age distribution.

Diseases with rising trends during the study period were hospitalised cases of varicella and tuberculosis, while diseases with decreasing trends were brucellosis and meningitis. The incidence peaks of brucellosis occurred in 1999, beginning of study period, (37 cases), of meningitis in 2001 (254 cases), of varicella in 2002 (35 cases), of salmonellosis in 2003 (37 cases), of

tuberculosis in 2004 (54 cases) and of leptospirosis in 2003 and 2004 (14 cases in two years), indicating possible outbreaks (Figure 2; meningitis data not shown).

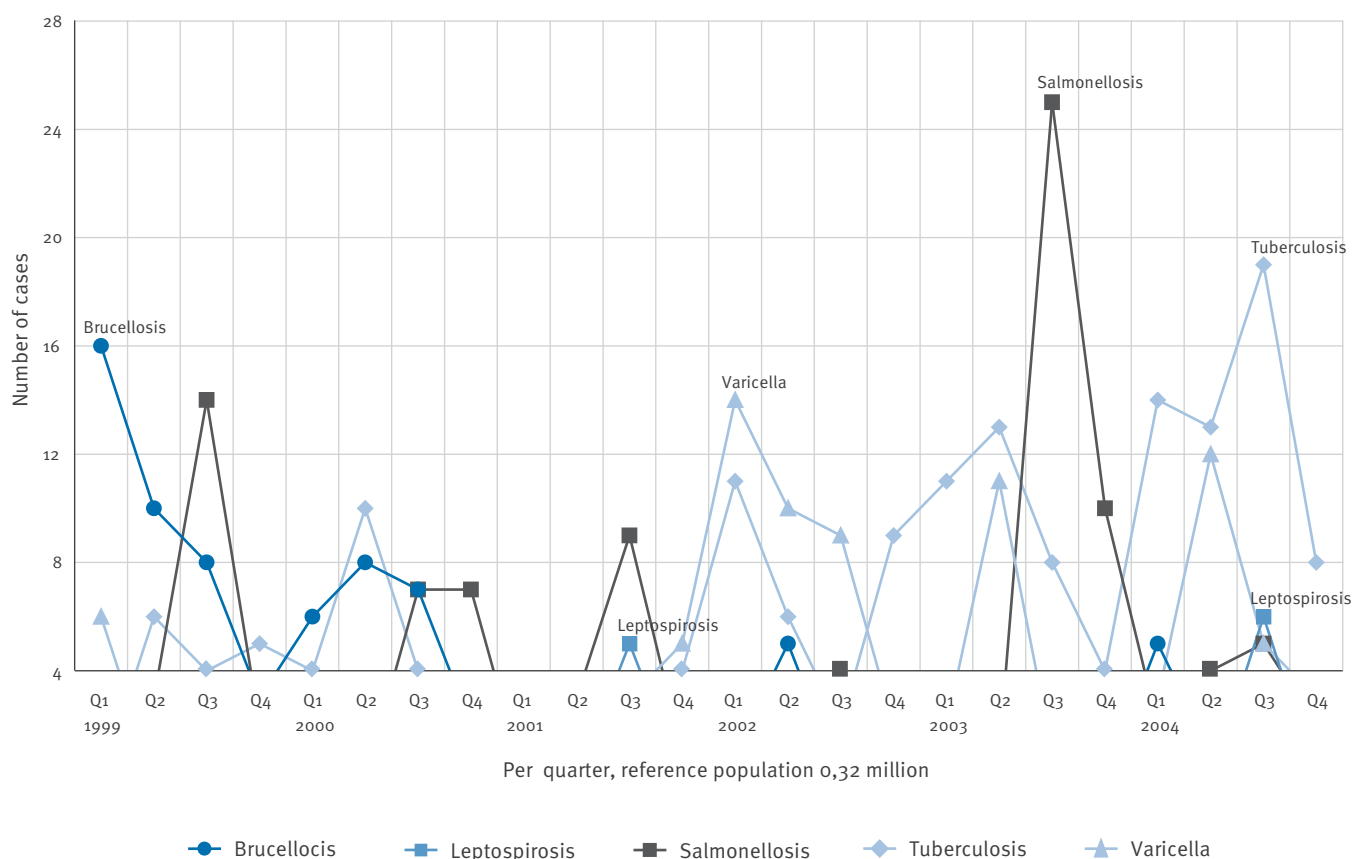
A cluster of five mumps cases was observed in the second half of 2002, with only one additional case reported over the study period.

Salmonellosis and leptospirosis showed a greater incidence during the summer, while brucellosis and varicella peaked in the first half of the year (Figure 2). The incidence for meningitis was greater in summer months (higher temperatures) and occurred mainly in urban populations. Only 20% of cases were identified as having bacterial meningitis. Our data also indicated that viral or aseptic meningitis affects younger people whereas bacterial meningitis affects older patients. Bacterial meningitis was observed more often in winter and viral meningitis more often in summer.

Moreover, our study showed a higher incidence of cases of varicella, salmonellosis, tuberculosis and hepatitis in urban populations than in rural population. In contrast, brucellosis, leptospirosis and leishmaniasis mainly affected rural populations. There was a clear male preponderance, especially for leptospirosis (6.5:1) and tuberculosis (2.5:1) (Table 2).

FIGURE 2

Number of cases of specific notifiable diseases during the study period, prefecture of Achaia, western Greece, 1999-2004



Discussion

The study demonstrates a substantial underestimation of infectious disease incidence and burden in the prefecture of Achaia, western Greece, by present regional surveillance mechanisms, which have not changed significantly during the last years. It is common practice in Greece that cases of infectious diseases are referred from local health centers and private physicians to second and third level hospitals for laboratory verification and treatment. Given the fact that more than one third of the cases (38%) identified in the hospitals included in the study was not reported to the public health authorities, the corresponding incidence of notifiable infectious diseases for the study period would be at least 1.5 times higher. Several studies have shown that undernotification is observed for most of the notifiable diseases in the majority of Member States in the European Union [8-14] and worldwide [15]. According to our findings, the rate of undernotification was higher for patients from outside the prefecture even though every case should have been notified to the local PHD. Also a higher undernotification in autumn was monitored, which could partly be explained by a reduced alertness of the physicians, because of the decrease in the incidence of infectious diseases following the warmer months.

Obviously the participation of physicians, both in primary and hospital care, in the described mandatory reporting system, may not be so efficient compared with a laboratory reporting system or even a web-based surveillance system that exists in other European countries [17]. Over the last decade several electronic national surveillance systems and specific disease networks have been introduced in several EU countries [18]. The benefits of which in terms of improved timeliness and completeness compared with conventional records have been clearly demonstrated [19]. Several countries, including Greece, may need to look at how best to improve their national standards of electronic disease reporting to be able to compare their data with other EU Member States like the United Kingdom, Germany, the Netherlands and Sweden, where such systems are already in use [19-21]. Low penetration of internet usage in the Greek society, even among health professionals, along with ethical considerations made it difficult to impose a web-based surveillance system in the last decade [22]. However, the latest surveys indicate that internet use is rising in Greece, especially among young, well-educated individuals and health professionals [23]. Under these circumstances, efforts like the Integrated Geographical System for Epidemiological and other Medical Information (GEPIMI) may be effective, for building a web based surveillance system [23].

Among the reasons that may have lead to the noticed undernotification, are the complicated notification forms and the procedures required, as well as the fact that the reporting system was not introduced well to health professionals and other related stakeholders [14]. A pilot sentinel system for improving notifications of private physicians across the country was not

successful due to declining participation over the study period [24]. Physicians were discouraged from participating by the number of diseases that they are obliged to report.

At least 50% of cases in our survey were in children indicating that even though each infectious disease has a specific pattern, children are one of the most affected groups [25-27]. However, an over-representation of children in our data cannot be excluded since one of the three hospitals in the study was a paediatric one. There was also a male preponderance in our data which could partly be attributed to social factors in Greece [28]. Urban/rural distribution is a research field that needs attention in order to understand the epidemiology of any infectious disease, however different social structures across countries could make this element difficult to interpret [29].

A finding worth mentioning is the retrospective identification of possible outbreaks for some diseases in the study period. For example, national data and press confirmed the increase of incidence of viral meningitis in the summer of 2001 [16,30]. However, 2001 was the year when the new combined vaccine for meningitis was introduced in Greece, so this may have played a role in notification of the disease becoming more increased. The notification rate for meningitis was nearly 90% that year. In 2004, due to the Olympic Games taking place in Greece, the surveillance system was strengthened, by new personnel and informational campaigns on infectious diseases on health services, leading to improved notification rates at least for tuberculosis cases [16,31].

Communicable diseases may spread through uncontrolled immigration of people coming from endemic regions to Greece [32,33]. In 2004, immigrants in Greece numbered more than one million, accounting for 10% of the population. In the prefecture of Achaia, a continuous influx of immigrants originating from Asia, namely Pakistan, India, Iraq, and Afghanistan, regions with a high incidence of infectious diseases, was observed in the last decade, however, the majority of immigrants still come from neighbouring countries, especially from Albania (55%) [30]. Given that cases among immigrants who do not have an official residence are less likely to be notified [33], targeted services that ensure that also these cases are captured should be available.

We acknowledge that the results of this study cannot be extrapolated to the whole national notification system of Greece but are indicative of the magnitude of undernotification that takes place. Variations in notification rates related to residence, to hospital size, to season and to informal reporting need to be studied further to verify the full extent of undernotification and factors influencing it.

To conclude, we believe that reporting of communicable diseases should be improved in regional level.

The Athens Olympic Games revealed that inadequate training, alertness and limited funding were major drawbacks in system efficacy [31]. Until a more sophisticated system is adopted, simplifying the notification form and KEELPNO providing physicians and PHD personnel with targeted and regular information on trends for specific notifiable diseases and the necessity of completing the notification forms would be measures which could be applied with benefit. In addition, early-warning systems involving for example primary health-care services could be utilised.

Acknowledgements

The authors sincerely thank the nurses Ioanna Kaltsa and Anna Kalouri for collecting the data for the survey, as well as the Director of Public Health Department of Achaia and the Committees for Infectious Diseases at the University Hospital of Patras, the Paediatric Hospital Karamandaneio and the General Hospital of Aigio for their administrative support and provision of the hospital-based notification data.

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