Rapid communications

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Rapid communications

Description of the early stage of pandemic (H1N1) 2009 in Germany, 27 April-16 June 2009

Novel influenza A(H1N1) investigation team1,2
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We report characteristics of the early stage of the pandemic (H1N1) 2009 in Germany. Until 16 June 2009, 198 confirmed cases were notified. Almost half of the cases (47%) were imported, mostly from Mexico and the United States. About two thirds of indigenous cases were outbreak-related (with two large school-associated outbreaks, n=74). According to our results Germany is still in the early stage of the pandemic with limited domestic transmission.

Introduction

After identification of the first cases in April 2009, the rapid spread of the new influenza A(H1N1)v pandemic is a clear signal that global spread of this new virus is inevitable. Within six weeks the novel influenza A(H1N1)v virus has spread as far as previous pandemic influenza viruses have spread within six months [1].

As of 15 July, the European Centre for Disease Prevention and Control (ECDC) reported 125,993 confirmed human cases worldwide from 129 countries with a total of 667 deaths. Most deaths occurred by far in the United States (n=211), Argentina (n=137) and Mexico (n=124) [2].

The first German case was notified on 27 April 2009. However, the dynamics of the unfolding pandemic in Germany and the rest of Europe differed markedly from that of North America.

We present data reported during the first two months including cases notified until 16 June 2009. The information is therefore focussed on the characteristics of the early stage of the evolving pandemic in Germany.

Methods

Immediately after the first cases in the United States became public the Robert Koch Institute (RKI) established a case-based reporting of influenza A(H1N1)v. Information on possible, probable and confirmed cases was collected in a database.

A possible case was defined as a person with febrile (>=38°C) respiratory illness and with (a) an epidemiological link to a country with domestic transmission or (b) contact to a probable or confirmed case, (c) residence in a county or region with at least five cases that had no epidemiological link to a country with domestic transmission or a confirmed case or (d) laboratory exposure.

A probable case was defined as a person with a laboratory diagnosis of influenza A with a negative test result for seasonal influenza (A/H1 and A/H3).

A confirmed case was defined as a person who had a sample positive for influenza A(H1N1)v virus confirmed by the National Reference Laboratory (NRL) or by a laboratory approved for surveillance by the NRL.

A case was considered as imported if the date of onset of symptoms was within seven days after departure from a country with sustained community-level transmission. By 16 June 2009 according to the definition of the Robert Koch Institute this included: Argentina, Australia, Chile, Costa Rica, El Salvador, Honduras, Israel, Canada, Mexico, New Zealand, Panama, Singapore, Spain, United Kingdom, Uruguay and the United States. If no recent travel history to one of these countries fulfilling the RKI definition at the time of travel was reported, the case was considered as indigenous.

For laboratory-confirmed cases (self-) isolation was recommended (adults: for seven days, children: for 10 days after onset of symptoms)

Contact management in the early phase was as follows:

All contacts of confirmed and probable cases were registered at local health authorities and informed about pandemic influenza (H1N1). Contacts were classified in two categories: 1) close contacts (e.g. household contact or sexual partner or unprotected person involved in patient care or treatment) and 2) repeated casual contacts (including conversation and physical contact).

Measures for close contacts included home quarantine for seven days after the last relevant contact, daily health monitoring by local health authorities and consideration of antiviral prophylaxis for 10 days. Less close contacts were advised to reduce contact to vulnerable persons for seven days.

Results

As of 16 June 2009, 198 laboratory confirmed cases of influenza A(H1N1)v have been detected in Germany (Figure 1).

Of the 190 confirmed cases, for whom the sex was reported, 110 (58%) were female. Cases ranged in age from 1 to 67 years, with an average of 23 years and a median of 18 years (Figure 2). The majority of the female cases in the age-group 10-19 years can be explained by the high number of infected girls associated with a school outbreak, where 70% of students in the two affected classes were female.
The confirmed cases were distributed over 14 districts (Figure 3).

While in the beginning most cases were imported, the proportion of indigenous cases has increased since 2 June 2009 (Figure 1). Overall 93 cases (47%) were imported.

The most frequently involved countries were: United States with 77 cases (83%), Mexico with 10 (11%), Argentina with three (3%) and United Kingdom, Canada and Panama with one case each (total 3%).

105 domestic cases (53%) were notified. Amongst these the source of the infection was known in 96 cases (91%). Out of these 96 cases 73 (76%) were outbreak-related and 23 related to an imported case (20 secondary cases=direct contact to an imported case, and 3 tertiary cases=direct contact to a secondary case). The infections of these 96 cases were most likely acquired in the following settings: school (73 cases), family/household (8), private party (6), healthcare (3), child care centre (3) and unknown (3).

For nine cases notified in June that were not restricted to a certain area the source of infection was unknown, i.e. the case did not report any travel history or contact to a confirmed case and was not part of an outbreak.

Four larger outbreaks (≥ 5 cases) have been identified: one outbreak associated with a child care centre (5 cases), one outbreak following a private party (6 cases) and two recent outbreaks related to two schools in North Rhine-Westphalia (16 and 58 confirmed cases so far).

The clinical features of the confirmed cases are shown in Figure 4. In 29% of all confirmed cases information about symptoms was not (yet) available. Asymptomatic infection occurred in 3% of cases.

Reliable information on comorbidities is only available for a limited number of cases, who have been followed up intensively. Among 18 of these cases four reported underlying medical conditions including metastasising carcinoid, arterial hypertension, hypothyroidism and chronic respiratory disease.

Hospitalisation was reported for 40 cases (20%), the reasons were primarily infection control measures, not disease severity. Detailed information on the severity of the infection is pending, but up to 16 June 2009 no case was known to require mechanical ventilation and no deaths were been reported.

Data on vaccination status was available for 49% of confirmed cases. Of these, 11% (n=11) had a history of vaccination with seasonal influenza vaccine.

In 55% of cases information on contacts ascertained by the local health authorities was available. The mean number of contacts per case was five (range 0-291). The type of contact and applied infection control measures are currently under investigation.

For those cases (n=22) that have been followed up intensively the number of contacts who acquired influenza A(H1N1)v infection was calculated per case. Seven contacts had a PCR-confirmed infection, corresponding to 0.3 infected contacts per case. None of the symptomatic contacts with a confirmed infection had received timely antiviral prophylaxis. This calculation was performed for cases notified before 4 June 2009. With an increasing number of indigenous cases and the occurrence of larger outbreaks this ratio is now expected to increase considerably.

Discussion

The characteristics of cases in the beginning of the pandemic closely resemble the data presented by other European countries (e.g. United Kingdom [3]) and Japan [4] in the early phase of the pandemic.

The majority of cases in the beginning were imported from Mexico and the United States. Strategies for early detection and
Geographical distribution of laboratory-confirmed cases of influenza A(H1N1)v, Germany, as of 16 June 2009 (n=198)
management of these cases seemed to work in this stage as no recommendations for travel restriction were in place. In the time period described Germany did not experience an exploding number of cases, however this might not only be due to the effect of the control measures taken but also due to other factors [5].

According to our results the first two months represented the early stage of the pandemic in Germany characterised by a high proportion of cases being imported, short chain of infections and limited outbreaks within the general population. The number of cases showed a rapid incline since mid-July 2009 with 7,963 confirmed cases notified until 5 August 2009 (of these, 6,259 cases (79%) were imported). However the overall picture has not changed considerably since June since the recent increase is mainly due to travellers, in part German high-school graduates, returning from Spain and UK.

Due to the increasing case numbers the surveillance system has by now been changed from reporting of suspected cases individually by fax to the routine case-based electronic notification to the state and national level of laboratory-confirmed cases and cases with an epidemiological link to a laboratory-confirmed case.

Taking into account the mildness of symptoms in the majority of cases the strategy for contact management has been adapted recently. Only close contacts (definition as above) with either a) an increased risk of severe infection (e.g. immunocompromised or chronic ill patients or pregnant women or infants) or b) with close contacts to vulnerable groups or with a high risk of causing outbreaks (e.g. in schools) are being followed up. The adapted measures are now focused on close contacts.

Furthermore, information on hospitalisation, treatment and risk groups are collected through the electronic notification system as with an increasing number of cases the burden of disease and severity of the clinical presentation becomes the main focus of the monitoring.

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![Figure 4](http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19295)

**Clinical presentation of laboratory-confirmed cases of influenza A(H1N1)v, Germany, as of 16 June 2009 (n=140)**

*Note: Data on symptoms was unavailable for 58 cases*
Between May and September each year, influenza sentinel surveillance is conducted in general practices in Melbourne and the state of Victoria in southern Australia. We describe the first 11 weeks of sentinel surveillance in 2009 (weeks 18–28), during which time pandemic influenza (H1N1) 2009 virus became established, and investigate the protective effect of seasonal influenza vaccine against laboratory-confirmed infection caused by the pandemic virus. At the time of reporting, the peak ILI activity in 2009 had been reached and was similar to the peak recorded in 2007 but below the peak of 2003. The proportion of cases positive for any influenza virus increased from 6% in the first week of surveillance (week 18) to 59% by week 28, during which time the proportion of influenza viruses detected as pandemic influenza increased from zero to 95%, with at least 91% of all influenza viruses confirmed as pandemic influenza by the eighth week of surveillance (week 25). The median age of all 223 patients with pandemic influenza for whom age was known was 21 years (range 2-63 years) compared with the median age of 53 patients with seasonal H1N1 influenza in 2007 or 2008 of 23 years (range 1-75 years). There was no evidence of significant protection from seasonal vaccine against pandemic influenza virus infection in any age group.

**Introduction**

Australia reported its first case of pandemic influenza (H1N1) 2009 on 8 May 2009 in a traveller returned from the United States [1]. Ten days later the state of Victoria in southern Australia reported its first three cases, in three brothers from one family, also recently returned from the United States [2]. Victoria has used an existing sentinel general practice network, established with laboratory support in 1998 [3], to monitor the pandemic. Sentinel monitoring is designed to overcome the potential testing biases that arise from monitoring all diagnosed cases, including those identified from outbreaks and contact tracing. During the current pandemic, sentinel surveillance general practitioners have been encouraged to test those patients who satisfied the case definition of fever (reported or observed), cough and fatigue/malaise [4], as they have done in previous years [5-10].

We have previously demonstrated the feasibility of estimating influenza vaccine effectiveness (VE) using a case control study of patients tested for influenza as a component of sentinel surveillance [11]. We now aim to describe the first 11 weeks, from 27 April to 12 July (weeks 18–28), of sentinel surveillance in Victoria in 2009, during which time pandemic influenza (H1N1) 2009 virus became established. We compare influenza-like illness (ILI) in 2009 with previous seasons and compare our surveillance system with ILI surveillance using the novel Google Flu Trends. We investigate the protective effect of seasonal influenza vaccine against medically attended ILI due to laboratory-confirmed infection caused by the pandemic virus in this period.

**Methods**

**The Victorian sentinel general practice network**

Victoria is a southern Australian state with a temperate climate. The influenza season occurs in winter and often extends into the early months of spring. Between May and September each year, sentinel surveillance is conducted in general practices scattered throughout Melbourne and regional Victoria. Victoria’s population is more than 5 million, with 3.9 million people living in the state capital, Melbourne. For each season, participating general practitioners (GPs) report weekly on the total number of consultations and any patients presenting with ILI, defined as fever (reported or observed), cough and fatigue/malaise [4].

Laboratory-confirmed influenza has been a gazetted notifiable disease in Victoria since 2001. Because of the legal requirement
for the laboratory to notify positive cases, formal ethics approval is not required for the surveillance program. However written consent is obtained from sentinel patients, indicating that aggregate anonymous data will be used for surveillance purposes and influenza positive results will be notified to the state government Department of Human Services, Victoria. After consent is obtained GPs collect data on the age, sex, symptoms and vaccination status (recording the date of administering the vaccine) of the sentinel patients. The swab is couriered to the Victorian Infectious Diseases Reference Laboratory (VIDRL), a WHO National Influenza Centre, for laboratory testing. In 2009 sentinel surveillance commenced on 27 April (week 18), with a network of 87 sentinel GPs, 60 in Melbourne and 27 in regional Victoria. Optional on-line data entry was introduced and we continued to use surveillance data from the Melbourne Medical Deputising Service (MMDS) [12]. We compared publicly available ILI data from the Google website, (http://www.google.org/flutrends/intl/en/au/) expressed as the Google search ratio, with our surveillance data, expressed as ILI consultations per 1,000 consultations.

We used data from all surveillance sources to describe the first 11 weeks of the influenza season and compared features of the 2009 season with previous influenza seasons. Seasonal thresholds were based on the proportion of ILI cases per 1,000 consultations. Baseline activity, normal seasonal and higher than expected seasonal activity were defined as below 2.5, between 2.5 and <15, and between 15 and <35 per 1,000 consultations, respectively. According to these thresholds, 'epidemic influenza activity' was defined by proportions at or above 35 cases per 1,000 consultations [13].

Laboratory testing
Specimens were tested in the Viral Identification Laboratory at the Victorian Infectious Diseases Reference Laboratory (VIDRL). Viral RNA was extracted and tested for all influenza types and specific subtypes using a series of in-house polymerase chain reaction (PCR) assays directed at matrix gene sequences of influenza A and B. Any sample positive for influenza virus A was subtyped as influenza A(H1N1), influenza A(H3N2) or pandemic influenza A(H1N1) using specific PCR assays directed at hemagglutinin gene sequences. Any positive samples were referred to the World Health Organization Collaborating Centre for Influenza Reference and Research where an attempt to culture an isolate was made.

Estimating influenza vaccine effectiveness
Analysis was restricted to patients who presented for medical attention to any of the sentinel surveillance practices and who subsequently had a swab taken for the identification of influenza virus by real-time PCR. Patients whose PCR tests were inhibited were excluded from the analysis, as were patients whose vaccine

![Figure 2](image-url)  
**Figure 2**  
Influenza-like illness (ILI) from GP sentinel surveillance, 2003 to 2009, Victoria, Australia

<table>
<thead>
<tr>
<th>Week number</th>
<th>Date commencing</th>
<th>Patients tested</th>
<th>Number (%) of influenza detections</th>
<th>Patients with subtyping data available (% of patients with influenza)</th>
<th>Number (% of patients with influenza) of influenza detections due to pandemic (H1N1) 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>27 April</td>
<td>16</td>
<td>1 (6%)</td>
<td>0</td>
<td>Not available</td>
</tr>
<tr>
<td>19</td>
<td>4 May</td>
<td>17</td>
<td>2 (12%)</td>
<td>2 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>11 May</td>
<td>23</td>
<td>1 (4%)</td>
<td>1 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>21</td>
<td>18 May</td>
<td>20</td>
<td>3 (15%)</td>
<td>3 (100%)</td>
<td>1 (33%)</td>
</tr>
<tr>
<td>22</td>
<td>25 May</td>
<td>69</td>
<td>11 (16%)</td>
<td>6 (55%)</td>
<td>6 (55%)</td>
</tr>
<tr>
<td>23</td>
<td>1 June</td>
<td>82</td>
<td>20 (24%)</td>
<td>5 (25%)</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>24</td>
<td>8 June</td>
<td>73</td>
<td>32 (44%)</td>
<td>1 (3%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>25</td>
<td>15 June</td>
<td>105</td>
<td>55 (52%)</td>
<td>50 (91%)</td>
<td>50 (91%)</td>
</tr>
<tr>
<td>26</td>
<td>22 June</td>
<td>123</td>
<td>75 (61%)</td>
<td>70 (93%)</td>
<td>70 (93%)</td>
</tr>
<tr>
<td>27</td>
<td>29 June</td>
<td>84</td>
<td>56 (67%)</td>
<td>51 (91%)</td>
<td>51 (91%)</td>
</tr>
<tr>
<td>28</td>
<td>6 July</td>
<td>70</td>
<td>41 (59%)</td>
<td>39 (95%)</td>
<td>39 (95%)</td>
</tr>
<tr>
<td>18-28</td>
<td>27 April - 12 July</td>
<td>682</td>
<td>297 (44%)</td>
<td>228 (77%)</td>
<td>223 (75%)**</td>
</tr>
</tbody>
</table>

* Confirmed as pandemic (H1N1) 2009  
** Per cent underestimated because subtyping is incomplete to date

![Table 1](image-url)  
**Table 1**  
The proportion of influenza detections and the proportion of detections due to pandemic influenza H1N1 2009 from sentinel surveillance patients, Victoria, Australia, 2009
status or age was unknown, and patients for whom subtyping data were not available. We used a case control design to estimate VE, where case and control status were not defined at the time of recruitment. Counting all patients from whose swabs pandemic (H1N1) 2009 influenza virus was detected as cases and all patients whose swabs were negative for influenza as controls, we estimated unadjusted VE (%) = (1-OR) x 100, where OR, the odds ratio, was the odds of being a vaccinated case divided by the odds of being a vaccinated control. We performed age-stratified analyses and adjusted for age by logistic regression using the following age groups: 0-4 years, 5-19 years, 20-49 years, 50-64 years and 65 years and above. The southern hemisphere seasonal vaccine contained A/Brisbane/59/2007-like virus as the H1N1 component.

Results
The 2009 influenza season
The influenza season of 2009 appeared to be already established when surveillance commenced at the end of April, with ILI activity above the threshold designated as normal seasonal activity. ILI activity increased quickly, crossing the threshold designated as higher than normal activity in the week commencing 8 June. Activity appeared to peak in week 26, and decreased again almost to the threshold of normal seasonal activity by the end of week 27 (Figure 1).

At the time of reporting the peak ILI activity in 2009 was similar to the peak recorded in 2007 (in week 34) but below the peak of 2003, also recorded in week 34 (Figure 2).

The proportion of cases positive for any influenza virus increased from 6% in the first week of surveillance to 59% by week 28, by which time the first 223 cases of pandemic H1N1 influenza had been detected. During this same period the proportion of influenza viruses detected as pandemic influenza increased from zero to 95%, with at least 91% of all influenza viruses confirmed.

Table 2
Proportion of detections of seasonal H1N1 influenza 2007 or 2008 and pandemic H1N1 influenza 2009 compared with population proportions by age group, Victoria, Australia, 2009

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Seasonal H1N1 influenza detected 2007 or 2008 N (%)</th>
<th>Pandemic H1N1 influenza detected 2009 N (%)</th>
<th>Per cent Victorian population 2008* N = 5,297,560</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>3 (6%)</td>
<td>7 (3%)</td>
<td>6%</td>
</tr>
<tr>
<td>5-19</td>
<td>14 (27%)</td>
<td>81 (37%)</td>
<td>19%</td>
</tr>
<tr>
<td>20-49</td>
<td>30 (57%)</td>
<td>118 (53%)</td>
<td>43%</td>
</tr>
<tr>
<td>50-64</td>
<td>5 (9%)</td>
<td>15 (7%)</td>
<td>18%</td>
</tr>
<tr>
<td>65+</td>
<td>1 (2%)</td>
<td>0</td>
<td>14%</td>
</tr>
<tr>
<td>All</td>
<td><strong>53</strong></td>
<td><strong>221</strong></td>
<td>100%</td>
</tr>
</tbody>
</table>


Table 3
Vaccine effectiveness of seasonal influenza vaccine against pandemic influenza H1N1 2009 by age group, Victoria, Australia, 2009

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Patients tested (age and vaccine status known)</th>
<th>Number (%) positive for pandemic influenza (cases)</th>
<th>Number (%) negative for influenza (controls)</th>
<th>Number (%) vaccinated</th>
<th>Cases (%) vaccinated</th>
<th>Controls (%) vaccinated</th>
<th>Vaccine effectiveness (%)</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>35</td>
<td>7 (20%)</td>
<td>28 (80%)</td>
<td>7 (20%)</td>
<td>1 (14%)</td>
<td>6 (21%)</td>
<td>39%</td>
<td>-510 to 94</td>
</tr>
<tr>
<td>5-19</td>
<td>158</td>
<td>80 (51%)</td>
<td>78 (49%)</td>
<td>12 (8%)</td>
<td>6 (8%)</td>
<td>6 (8%)</td>
<td>3%</td>
<td>-216 to 70</td>
</tr>
<tr>
<td>20-49</td>
<td>311</td>
<td>111 (36%)</td>
<td>200 (64%)</td>
<td>57 (18%)</td>
<td>19 (17%)</td>
<td>38 (19%)</td>
<td>12%</td>
<td>-62 to 52</td>
</tr>
<tr>
<td>50-64</td>
<td>52</td>
<td>14 (27%)</td>
<td>38 (73%)</td>
<td>25 (48%)</td>
<td>8 (57%)</td>
<td>17 (45%)</td>
<td>-65%</td>
<td>-46% to 52</td>
</tr>
<tr>
<td>65+</td>
<td>21</td>
<td>0 (0%)</td>
<td>21 (100%)</td>
<td>15 (71%)</td>
<td>0</td>
<td>15 (71%)</td>
<td>not defined</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td><strong>577</strong></td>
<td><strong>212</strong> (37%)</td>
<td><strong>365</strong> (63%)</td>
<td><strong>116</strong> (20%)</td>
<td><strong>34</strong> (15%)</td>
<td><strong>82</strong> (22%)</td>
<td><strong>3%</strong></td>
<td><strong>-56 to 40</strong></td>
</tr>
</tbody>
</table>

*Adjusted for age-group as a discrete variable
Comparison of ILI surveillance using sentinel practices and the MMDS with Google Flu Trends showed remarkable correlation between all three systems, with the comparison shown for surveillance extended to week 31, ending 2 August (Figure 3).

Although males comprised 56% of the sample of sentinel patients, pandemic influenza virus was detected in equal proportions of males and females (37.7% vs 36.8%). The median age of infection of all 221 patients with pandemic influenza for whom age was known was 21 years (range 2-63 years) compared with the median age of infection of 53 patients with seasonal H1N1 infection in 2007 or 2008 of 23 years (range 1-75 years). By contrast the median age of infection of patients with seasonal H3N2 was 28 years in 2007 (n=147) and 33 years in 2008 (n=43). Although the proportion of patients in whom pandemic H1N1 influenza was detected was higher in 2009 than the proportion in whom seasonal H1N1 influenza was detected in 2007 or 2008 (37% vs 6%, respectively), there was no significant difference by age group in the proportion of seasonal H1N1 infection detected in 2007 or 2008 compared with the proportion of pandemic H1N1 influenza detected in 2009 (Table 2, Fisher’s exact p=0.17). However the proportion of the 5-19 year old age group with seasonal or pandemic influenza H1N1 was higher than the proportion of this age group in the population (Table 2).

Vaccine effectiveness

By week 28, sentinel practitioners had seen 81,992 patients, had notified 982 (1.2%) of these patients with ILI and taken nose and throat swabs from 682 (69%) of them. Influenza virus was detected in 297/682 (44%) patients, and in 223/297 (75%) patients pandemic influenza (H1N1) 2009 was detected. After exclusion of patients for whom definitive subtyping is pending (n=69), patients for whom age was unknown (n=10), patients with unknown vaccination status (n=22) and patients with influenza due to a non-pandemic subtype (n=6), 577 patients were available for analysis, of whom 212 (37%) had pandemic influenza virus detected and the remainder had no virus detected. These patients were used for the estimates of VE.

Twenty per cent of patients were vaccinated against influenza but, as expected, the proportion of patients differed significantly by age group, with people aged at least 50 years more likely to have been vaccinated (p<0.001, Table 3). Pandemic influenza virus was detected in 37% of all patients, again with significant differences by age group (p<0.001, Table 3). People aged 5-19 years were most likely to have influenza virus detected (80/158, 51%), compared with none of 21 patients aged at least 65 years and 7/35 (20%) patients aged 0-4 years (Table 3).

There was no evidence of significant protection from seasonal vaccine against pandemic influenza virus infection in any age group, with point estimates ranging from 39% in persons aged less than 5 years to -65% (OR = 1.65) in persons aged 50-64 years (Table 3). Age adjusted VE was 3% (95% CI -56 to 40) for all patients, 10% (95% CI -54 to 48) in patients aged 5-49 years and 1% (95% CI -70 to 42) in patients aged 50-64. In patients younger than 50 years, VE was 12% (95% CI -48 to 48) and VE was -65% (95% CI -467 to 52) in patients aged 50 years or older. The latter estimate was based only on patients aged 50-64 years, as pandemic influenza was not detected in the group of patients aged 65 years and older. The oldest patient in whom pandemic influenza was detected was aged 63 years.

We further restricted our analysis to weeks 25-28 inclusive, when pandemic influenza comprised at least 90% of all influenza detections, and the age groups 5-49 years, where most infections occurred. This period accounted for 352 patients with known age and vaccination status (61% of all comparable patients) and 201 cases (95% of all comparable cases). For all ages in this four-week period, age-adjusted VE was 24% (95% CI –37 to 58) and, for ages 5-49 years, VE was 20% (95% CI –52 to 48).

Discussion

The seasonal pattern of ILI in Victoria between 27 April and 12 July 2009 was similar comparing data from sentinel general practices and the Melbourne Medical Deputising Service (MMDS). Both surveillance systems peaked in the same week, although the peak from the MMDS was higher. We have shown these two surveillance systems can be used interchangeably to monitor ILI in the community but, as seen in the first 11 weeks of surveillance in 2009, the correlation between the two systems is better for lower ILI activity [14]. These two systems also showed remarkable concordance with Google Flu Trends, Google used historical data from the Victorian sentinel surveillance system from 2006-2008 to validate its Australian version of Flu Trends (http://blog.google.org/2009/06/google-flu-trends-for-australia-and-new.html) so that retrospective similarity of data is expected. The prospective similarity is interesting. Unfortunately there is no detailed published information on the approach used by Google for ILI surveillance in the southern hemisphere, preventing a more detailed comparison.

With complete subtyping, influenza in sentinel patients was shown to be exclusively due to pandemic influenza in weeks 30 and 31 (not included in Table 1, available from: http://www.vldrl.org.au/surveillance/flu%20reports/flu_idx.html). However, considering only patients for whom subtyping data were complete in previous weeks when these patients comprised at least 90% of all influenza detections, influenza in these sentinel patients was entirely due to pandemic influenza from week 25 (commencing 15 June, Table 1).

We have previously suggested the median age of patients infected with influenza A(H1N1) was similar for patients infected with seasonal and pandemic influenza H1N1 strains [15, 16] and the surveillance data presented here confirm these original observations. Infections with influenza A(H3N2) tend to occur in older people [15, 17] and comparisons of the age of infection with pandemic H1N1 influenza with the age of infection of all seasonal influenza may be misleading if previous seasons were dominated by influenza A(H3N2). A younger median age of infection with pandemic H1N1 influenza is likely to reflect the age of infection with influenza A(H1N1) viruses. We detected no sentinel patients with pandemic influenza over the age of 63 years, consistent with some protection afforded to older people as demonstrated by the detection of cross-reacting antibodies to the pandemic H1N1 virus in people aged 60 years and above [18].

We found no evidence of protection against medically attended laboratory-confirmed pandemic influenza from receipt of the seasonal vaccine in age-stratified or age-adjusted analyses. However, we do not collect data on co-morbidities and could not adjust for potential confounders, other than age. The ILI case control observational study design has limitations, some of which may bias the VE estimate towards the null. Sampling of patients
is not systematic and the sampling proportion increased to 69% in 2009 from 40% in the five influenza seasons from 2003 to 2007 [11]. Seasonal influenza infection may be asymptomatic or febrile [19] and the same is no doubt true for infection with pandemic H1N1 influenza. Sentinel patients therefore represent the mid-range of the influenza morbidity spectrum, although this is likely to be true for both seasonal and pandemic infections. Given the high level of community concern, patients may have been more likely to attend their general practitioner with an ILI in 2009, compared with previous seasons, and GPs may have been more likely to swab patients. However the proportion of 44% of sentinel patients positive for influenza in the first 11 weeks of surveillance in 2009 is not significantly different to the proportion of 42% positive in the five influenza seasons between 2003 and 2007 [11].

Because of the high workload in the early weeks of the pandemic in Victoria, not all influenza positive specimens have been definitively subtyped. However, the distribution of vaccination status and pandemic influenza infection in the weeks where subtyping is incomplete would need to be remarkably different to the distribution in the weeks with almost complete data for this lack of data to bias our estimate of VE. Because of low case numbers in the early weeks, we did not adjust for week of presentation in the interim analysis, but performed an analysis restricted to the four weeks when subtyping data were almost complete and in which pandemic influenza comprised at least 90% of all influenza detections. There was no significant difference in VE estimates comparing these four weeks with the entire period. We did not adjust for time between symptom onset and date of specimen collection since GPs are instructed to collect a specimen only within four days of symptom onset.

While there are potential limitations with interim analyses of VE from observational studies using routinely collected data, the results reported here, showing no protection from seasonal vaccine against laboratory confirmed medically attended infection due to pandemic influenza (H1N1) 2009, are not unexpected.

Acknowledgements
We acknowledge the continued support of Ms Josie Adams for access to data from the Melbourne Medical Deputising Service. We thank all general practitioners involved in sentinel surveillance for IIL in Victoria. We are most grateful for helpful advice on the manuscript from Dr Edward Belongia, Marshfield Clinic, USA; Dr Esther Kissling, EpiConcept, England; Dr Alain Moren, EpiConcept, France; and Dr Ake Ortvist, Karolinska Institute, Sweden. We thank all staff of the Viral Identification Laboratory at VIDRL for influenza testing. The Victorian general practice sentinel surveillance scheme receives funding from the Victorian Department of Human Services.

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**Rapid communications**

A PRELIMINARY ANALYSIS OF THE EPIDEMIOLOGY OF INFECTIOUS A(H1N1)v VIRUS INFECTION IN THAILAND FROM EARLY OUTBREAK DATA, JUNE-JULY 2009

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As the influenza A(H1N1)v pandemic unfolds globally, it is vital to monitor closely for signals of change in the current patterns of transmission. We estimate the basic reproduction ratio for A(H1N1)v virus in Thailand and propose a method to keep track of the actual case count notwithstanding the exponential growth rate.

**Introduction**

The threat of an influenza pandemic posed by a novel re-assortant influenza A virus was identified in late April in Mexico. The influenza A(H1N1)v virus has since spread into five continents infecting at least 134,503 people and causing 816 deaths as reported by World Health Organization (WHO) on 27 July 2009. Further spread of the virus especially within affected countries is considered inevitable at this point. Also, the increasing number of cases in many countries is making it difficult for laboratories to individually test and confirm all suspected cases.

The first two cases of A(H1N1)v in Thailand were reported on 10 May. After a two week lapse and despite intense containment measures, more cases were reported, building up into an exponential growth phase in early June. The basic reproduction ratio ($R_0$), estimated from the daily case reports in the exponential growth phase, is useful in assessing the ultimate course of the epidemic in Thailand. The reproduction ratio as a function of time ($R_t$) generally drops after the primary exponential phase due to a drop in susceptibles as well as due to control measures, and varies individually test and confirm all suspected cases.

We calculate the intrinsic growth rate ($r$) during the exponential growth phase from 1 to 12 June and estimate $R_0$ and the final size [1,2] - the proportion of the population that would be ultimately infected assuming 100% susceptibility at the outset and minimal control measures - of the epidemic. Furthermore, we give a rough estimate for the case fatality ratio (CFR) from early fatality counts and use it to extrapolate the number of infected cases at a later date, after laboratory testing of all suspected cases was abandoned (20 June) paving the way for significant underreporting. All reported deaths up to 14 July are analysed to compare the CFR between age groups.

**Methods**

Our data come from two sources. First, we counted the cases by symptom onset date from the records at the WHO National Influenza Centre, which was used to calculate $r$, $R_0$ and CFR. The age distribution of the infected population up to 14 July was inferred from the daily incidence reports from the Bureau of Emerging Infectious Diseases, Department of Disease Control (DDC), Ministry of Public Health in Thailand (http://beid.ddc.moph.go.th/th/index.php?option=com_content&task=view&id=1784902&Itemid=240) while the disease onset dates and age of the deceased were obtained directly from DDC.

**Estimate of $r$, $R_0$ and final size**

The intrinsic growth rate $r$ is estimated by Poisson regression of the epidemic curve over the exponential growth phase, $R_0$ is derived by $R_0 = 1 + rT_e$ (where is the mean generation interval [GI]) and the final size by a Newton-Raphson numerical solution [1] of $\ln(1 - \chi) + R_0\chi = 0$.

The mean GIs derived in two previous studies ($T_1=2.6$ [2.1-3.0] [3] and $T_2=1.9$ [1.3-2.7] [4]) were used as no information was available for the current epidemic. The equation used to calculate $R_0$ gives the Laplace transform of the GI distribution assuming it is exponentially distributed, whereas the error for non-exponentially distributed GIs are known to be small [3]. Visual inspection of the epidemic curve revealed significant deviations from the exponential curve toward the latter part of the period of 1-12 June, necessitating the choice of a valid combination of points in order to achieve a realistic goodness of fit. Goodness of fit (or lack of it) of the model was assessed by a combination of the R-squared measure and Pearson’s statistic.

**Estimate of CFR and present case count**

We estimated the CFR for cases with symptom onset on or before 18 June using our daily onset data for that period and the number of fatalities subsequently arising from these cases until 15 July. This rough estimate was used to extrapolate the number of infected cases from the number of deaths on later dates. The normalised age-specific CFR was calculated by dividing the age distribution of all deceased patients as of 14 July against the age distribution.
of all reported cases as of 7 July, and further dividing each value by the overall CFR for the total population. Since the seven-day gap is not sufficient to account for the delay from onset to death, there are two implicit assumptions made here: the age distribution of the infected population is constant over time, and the time from onset to death is independent of the patient’s age. Underreporting bias is effectively eliminated by normalising, provided the rate of underreporting was similar across all age groups.

Results

The epidemic curve for the period 1-12 June minus the counts for 8, 10, and 11 June (Figure 1 and Table) yielded the best fit for exponential growth ($R^2 = 0.9802$), giving $r=0.41$ [95% CI: 0.35-0.47]. The corresponding $R_0$ were 2.07 [1.92-2.22] for $T_1$ and 1.78 [1.67-1.89] for $T_2$. The final-size were 81.5% [77.4-84.8]% for $T_1$ and 72.5% [67.7-76.4]% for $T_2$.

A total of 690 confirmed cases with disease onset on or before 18 June gave rise to four deaths (as of 15 July) yielding a CFR of 0.58%. The reported number of deaths arising from patients with disease onset on or before 30 June was 16 (as of 15 July), hence the expected value for the actual number of cases at the same date is 2,760 assuming a constant CFR, which is 87% higher than the number of confirmed cases (1,473) reported on 1 July. The normalised age distribution of the CFR (overall CFR=1) is shown in Figure 2.

Discussion

The basic reproduction ratio gives us a fairly good idea about the infectiousness of the virus within a particular demographical area and the potential effect it would have on the community if no public health intervention or changes in social habits take place. Generally, the reproduction ratio decreases after the initial exponential phase due to intervention and a reduction of the number of susceptibles. Thus, $R_0$ gives us a reasonable upper bound for the reproduction ratio as well.

Making an estimate of $R_0$ is not trivial due to various limitations in the information we have about an epidemic at the beginning. Firstly, it is highly dependent on the generation time interval [5] which is not easy to estimate when the transmission network is not known. We use mean $T_c$ values estimated elsewhere: $T_1$ from a comprehensive analysis of household transmission data [3] found to be consistent with viral shedding data from experimental studies; and $T_2$ from an independent estimate of the influenza A(H1N1)v outbreak in Mexico [4].

Another limitation is the difficulty of fitting the real-life epidemic curve to an exponential growth model. Human errors in reporting as well as stochastic errors arising from the relatively small numbers involved required an arbitrary decision on which data points displayed exponential growth.

<table>
<thead>
<tr>
<th>period</th>
<th>$R^2$</th>
<th>Pearson r</th>
<th>SD</th>
<th>95% CI</th>
<th>$R_0$</th>
<th>95% CI</th>
<th>final size</th>
<th>95% CI</th>
<th>$R_0$</th>
<th>95% CI</th>
<th>final size</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>8, 10, 11 June</td>
<td>0.9802</td>
<td>0.6485</td>
<td>0.41</td>
<td>0.029</td>
<td>0.35-0.47</td>
<td>2.07</td>
<td>1.92-2.22</td>
<td>81.5%</td>
<td>77.4-84.8%</td>
<td>1.78</td>
<td>1.67-1.89</td>
<td>72.5%</td>
</tr>
<tr>
<td>9, 11, 12 June</td>
<td>0.9695</td>
<td>0.3018</td>
<td>0.54</td>
<td>0.041</td>
<td>0.46-0.62</td>
<td>2.60</td>
<td>2.19-2.61</td>
<td>87.9%</td>
<td>84.2-90.6%</td>
<td>2.02</td>
<td>1.87-2.18</td>
<td>80.3%</td>
</tr>
<tr>
<td>8, 12 June</td>
<td>0.968</td>
<td>0.1264</td>
<td>0.43</td>
<td>0.028</td>
<td>0.37-0.48</td>
<td>2.11</td>
<td>1.97-2.25</td>
<td>82.4%</td>
<td>78.7-85.5%</td>
<td>1.81</td>
<td>1.71-1.91</td>
<td>73.6%</td>
</tr>
<tr>
<td>8, 10, 12 June</td>
<td>0.9644</td>
<td>0.2452</td>
<td>0.47</td>
<td>0.036</td>
<td>0.40-0.54</td>
<td>2.22</td>
<td>2.03-2.40</td>
<td>84.7%</td>
<td>80.5-87.9%</td>
<td>1.89</td>
<td>1.75-2.02</td>
<td>76.3%</td>
</tr>
<tr>
<td>10 June</td>
<td>0.9454</td>
<td>0.0082</td>
<td>0.40</td>
<td>0.025</td>
<td>0.35-0.45</td>
<td>2.05</td>
<td>1.92-2.17</td>
<td>80.9%</td>
<td>77.3-83.8%</td>
<td>1.76</td>
<td>1.67-1.86</td>
<td>71.8%</td>
</tr>
<tr>
<td>9 June</td>
<td>0.928</td>
<td>0.001</td>
<td>0.39</td>
<td>0.023</td>
<td>0.35-0.44</td>
<td>2.02</td>
<td>1.90-2.13</td>
<td>80.1%</td>
<td>76.7-83.0%</td>
<td>1.74</td>
<td>1.66-1.83</td>
<td>71.0%</td>
</tr>
<tr>
<td>12 June</td>
<td>0.9258</td>
<td>0.001</td>
<td>0.47</td>
<td>0.031</td>
<td>0.41-0.53</td>
<td>2.22</td>
<td>2.06-2.38</td>
<td>84.7%</td>
<td>81.1-87.5%</td>
<td>1.89</td>
<td>1.77-2.00</td>
<td>76.3%</td>
</tr>
<tr>
<td>8 June</td>
<td>0.9244</td>
<td>0</td>
<td>0.42</td>
<td>0.026</td>
<td>0.37-0.47</td>
<td>2.08</td>
<td>1.95-2.21</td>
<td>81.8%</td>
<td>78.4-84.7%</td>
<td>1.79</td>
<td>1.70-1.89</td>
<td>72.9%</td>
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<tr>
<td>None</td>
<td>0.9131</td>
<td>0</td>
<td>0.40</td>
<td>0.024</td>
<td>0.35-0.45</td>
<td>2.04</td>
<td>1.92-2.16</td>
<td>80.8%</td>
<td>77.4-83.6%</td>
<td>1.76</td>
<td>1.67-1.85</td>
<td>71.7%</td>
</tr>
<tr>
<td>11 June</td>
<td>0.8972</td>
<td>0</td>
<td>0.39</td>
<td>0.024</td>
<td>0.35-0.44</td>
<td>2.03</td>
<td>1.90-2.15</td>
<td>80.4%</td>
<td>76.8-83.3%</td>
<td>1.75</td>
<td>1.66-1.84</td>
<td>71.3%</td>
</tr>
</tbody>
</table>

Note: All plausible combinations of dates that may yield a better fit were tested.
Underreporting at the beginning of an epidemic is also usually a confounding factor [6], but we believe the effect of this was minimal in our data due to a highly vigilant healthcare department which sprang into action just after the first few cases were reported in North America.

Our estimate of $R_0$ for A(H1N1)v in Thailand is higher than one estimate for the Mexican outbreak which used $T_0$ as the GI [4], but it is lower than another estimate for the same outbreak [6]. The results should be interpreted with caution due to the many uncertainties described above. Nevertheless, they may be used to compare the epidemiological factors of the A(H1N1)v outbreak in Thailand with those from other countries, provided the assumptions behind the calculations are kept in mind.

The final size is a good indicator of the potential magnitude of the epidemic, which may be used by public health officials to estimate the level of damage the epidemic would have on the society should there be no control measures. The case fatality ratio is another vital indicator of the effect of the epidemic on society in general and needs to be continually kept track of until the epidemic is over.

Nevertheless, significant underreporting of infected cases expected after the first few weeks of the infection may result in a CFR estimate significantly higher than the actual value, given that fatalities will not be overlooked as easily even in the middle of the epidemic. Thus, it is imperative to estimate the CFR with data from the initial phase. We used this rate to extrapolate the case counts for later dates after the reporting rate has decreased. Also, our normalised CFR for each age group clearly shows a marked increase in fatality risk with age. However, relatively few infections were seen in the elderly, possibly compensating, at least partly, for the higher fatality rate.

Our rough estimate for the CFR in Thailand, though highly prone to stochastic errors considering the low number of deaths, is not so different from the CFR for Mexico estimated previously [4], but a more recent study [7] showed much lower CFRs for developed countries. Their multiplier method essentially assumes 10-30 unreported cases for each diagnosed case, and incorporating this into the calculation brings down the CFR estimate from a value which would have been in the same order as ours into something drastically lower. Considering the largely undefined nature of asymptomatic or mildly symptomatic infections, we refrain from assigning a number to these cases as that may bring some confusion in the interpretation and comparison of CFR estimates from different countries or regions. Nevertheless, this issue is undoubtedly valid for Thailand as well, more so after the initial growth phase. Another reason for this comparatively higher CFR may be attributed to differences in the healthcare infrastructure and awareness levels of the public in general.

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Figure 2
Normalised case fatality ratio (CFR) by age group, influenza A(H1N1)v in Thailand, June 2009 (n=25 deaths)
Preparedness planning for two large mass gatherings events were considered in Serbia in the context of pandemic influenza (H1N1) 2009. Planning included approaches to prevention, detection and response in order to mitigate the situation at this early stage of the epidemic in Serbia. Cases of influenza A(H1N1)v were identified nationally immediately prior to the mass gatherings but also identified in association with both events, as expected in the context of the pandemic situation. This article describes the experiences of planning and the epidemiological situation during the period of the mass gathering events.

Introduction
Mass gatherings present a particular challenge for public health. Unusual population increases, high crowd density, international visitors, temporary catering and accommodation facilities, are some factors that may contribute to increased risk for communicable diseases and consequently demands on local health services [1]. Therefore preparations for mass gatherings may also require public health planning. In the context of the current pandemic influenza (H1N1) 2009, preparedness becomes even more important, especially for a country not affected at the time of planning. In this rapid communication we report on experiences in preparedness planning for two mass gatherings in Serbia.

Background
During July 2009, Serbia hosted two large international mass gatherings. Firstly, the 25th Universiade, an international sporting event for young university athletes, took place from 1 to 12 July, involving 53 sites in nine locations (Belgrade, Indjija, Lazarevac, Novi Sad, Obrenovac, Smederevo, Stara Pazova, Vrsac, Zrenjanin), with 8,600 athletes from 143 countries, 10,000 volunteers, 5,000 staff and an estimated 500,000 spectators [2]. This sporting event included both indoor and outside venues, and a restricted-entry accommodation and hosting facility site ‘Universiade village’ for all the delegations that included a medical clinic. Secondly, the 10th EXIT music festival held at Petrovaradin fortress, Novi Sad, Autonomous Province of Vojvodina. This was held from 9 to 12 July (closing 13 July 05:00), with an estimated 190,000 visitors [3], including 20,000 from abroad. The open-air festival included over 12 stages within the fortress. Visitors were hosted in local hotels, hostels, private accommodation and a dedicated campsite for 6,000 persons.

Risk assessment and considerations for pandemic influenza (H1N1) 2009
Following international reporting of the new influenza virus in April 2009 [4], considerations for preparedness for these mass gathering events were included in the regular meetings of the National Working Group on Pandemic Planning, under the coordination of National Institute of Public Health (IPH) and Ministry of Health of Serbia. Recommendations were then implemented by Military Medical Academy (providing medical support to the Universiade event), Institutes of Public Health and healthcare facilities in the districts where mass gathering sites were located. By early June, when preparedness activities for the two mass gathering events were being finalised, no case of influenza A(H1N1)v had yet been identified in Serbia. However, with global travel to and from affected areas and continuing spread worldwide, cases were anticipated to be detected at any time, irrespective of the mass gathering events.

As the circulating strain was considered mild-moderate at declaration of the pandemic by the World Health Organization (WHO) [5], and containment in Serbia was regarded unfeasible, a mitigation approach was implemented both as national policy and towards the mass gathering events. Overall key objectives were to detect first cases wherever they may appear, reduce possible spread of infection where possible, monitor the epidemiological situation and mitigate morbidity and mortality through timely diagnosis and treatment of cases according to national guidelines.

In addition, further prevention actions were taken for the first mass gathering, Universiade, because no cases had yet been reported in Serbia one month before the event and the delegations were a reachable population. Information was sent on 4 June 2009 to delegations recommending persons to reconsider travel to Serbia if presenting with any influenza-like symptoms. Criteria for recommending cancellation of Universiade were also set in
case of a rapidly evolving situation. These criteria were: 1% of the attending population diagnosed with influenza A(H1N1)v, a case of acute respiratory distress, or a death in a confirmed case.

Detection and management of influenza A(H1N1)v cases

National approach

According to pandemic plans, enhanced national surveillance for influenza A(H1N1)v was implemented with daily reporting of confirmed cases by the national reference laboratory 'Torlak' integrated with information reported from district IPH on individual case assessments. Guidelines were produced by the National IPH on requirements and procedures for reporting cases using case definition for influenza A(H1N1)v according to WHO case definition as of 27 April 2009 [6]. At the national level reported cases were categorised as travel-related or domestic (no travel abroad known during the incubation period, or contact with a confirmed case in Serbia). Influenza-like illness (ILI) surveillance was continued after week 20 in accordance with recommendation of WHO.

Strategies to detect cases included:

- Posters and information leaflets on symptoms and phone numbers for arriving travellers at airports on when and where to seek medical help;
- Communication to the general public through media and posters on prevention measures and when to seek medical help;
- Sensitising medical facilities and health care workers in all districts to the presentation, management and reporting of cases through cascade of training from national IPH to district IPHs and to health facilities;
- 24/7 on duty and epidemiology mobile teams to respond to queries about suspected cases to assess and triage persons to be tested.

On 22 July there was an alteration in the national testing policy, with suspected cases no longer all being laboratory-tested for influenza A(H1N1)v.

Management of cases

Quarantine measures were not implemented. However, suspected cases were provided isolation at medical facilities until diagnosis, with results aimed to be provided within 24 hours. Furthermore, based on individual medical assessment, confirmed cases were subsequently advised on self-isolation or hospitalised if medical care needed. All confirmed cases were provided antiviral treatment. Masks were not widely distributed to the general public, but used by health care workers as standard infection control practices and provided to suspected or confirmed cases to minimise spread. Contact tracing was undertaken where feasible including medical monitoring, but prophylaxis not given as according to national guidelines.

Mass gathering events

Enhanced daily surveillance was implemented for both mass gathering events for the following diseases: influenza A(H1N1)v, haemorrhagic fever, polio/AFP, diphtheria, measles, botulism, meningococcal meningitis, and all diseases which request urgent reporting in accordance with national law for communicable diseases (cholera, plague, smallpox, yellow fever, malaria) and reporting of outbreaks of acute diarrhoeal syndrome or acute haemorrhagic diarrhoeal syndrome.

At Universiade, the Military Medical Academy provided daily further epidemiological information on cases to both the national IPH and IPH of Belgrade. Event-based surveillance for influenza and other abovementioned diseases were supplemented through daily epidemic intelligence [7] activities performed by the European Centre for Disease Prevention and Control (ECDC), as done earlier in other international mass gathering events [8,9]. A special edition threat bulletin was developed by ECDC together with IPH Serbia and circulated daily to all district IPHs (24 districts and the city of Belgrade), Military Medical Academy and Ministry of Health.

Strategies to detect cases included:

- posters at Universiade sites in French, English and Serbian about prevention measures and when to seek medical help;
- obligatory daily zero-reporting for suspected cases by all delegation doctors to the Military Medical Academy, that no influenza-like symptoms had been observed in their teams;
- guidelines by Military Medical Academy for diagnosis and referral of suspected cases at the Universiade village clinic to the Military hospital;
- in Novi Sad (site of the EXIT festival), leaflets in English and Serbian provided in public areas such as taxis, bus stops, restaurants, hotels and other locations about prevention measures, symptoms and phone numbers and locations where to seek medical attention;
- information on disease symptoms, prevention measures and contact numbers printed inside the EXIT festival programme;
- mobile teams on site at festival to respond to any suspected case-presentation;
- contact tracing where feasible for cases who could be reached.

Management of cases

- as national approach;
- in Universiade:
  - an isolation area was available in the clinic at the Universiade village;
  - referral and transfer of confirmed or seriously-ill suspected cases to isolation facilities at Military Medical Academy hospital;
  - recommendation to self-isolate in accommodation for confirmed cases not needing hospitalisation;
- for EXIT festival:
  - basic isolation area in some medical tents at festival site;
  - mobile medical assessment teams on site at festival and camp;
  - contact phone numbers to local epidemiology teams for triage of suspected cases;
  - referral and transfer of suspected cases presenting at festival site or campsite to local health facilities in Novi Sad;
  - treatment of confirmed cases at health facilities in Novi Sad.

Results

Prior to mass gathering events

On 24 June, six days before the start of Universiade, the first imported case of influenza A(H1N1)v in Serbia was detected and laboratory-confirmed in Belgrade in a returning traveller from Argentina (Figure 1). A further 10 travel-associated cases and two domestic cases (contacts with travel-related cases) were detected nationally, until the first mass gathering event officially opened on 30 June. Among these 13 cases, eight were reported from three of the six districts hosting Universiade events (Belgrade city, South Backa and Srem). By 6 July when the EXIT festival campsite opened, a further eight travel-associated cases (returning residents) were reported, all in the district of South Backa.
Universiade sport event
As of 24 July, six athletes and one volunteer had confirmed influenza A(H1N1)v (Figure 2) with 22 other suspected cases presenting at the Universiade clinic but testing negative. According to incubation periods and contact histories, three cases among athletes were considered as travel-related (Argentina, Australia, Uganda), whereas three athletes (one from France and two from Zambia) and one volunteer were suspected to have been infected within Serbia. Cases were aged between 20 and 25 years and all experienced mild symptoms.

EXIT music festival
As of 24 July, a total of 62 confirmed cases were identified associated with EXIT festival, including secondary cases to cases exposed at the festival site (Figure 3). Fifteen cases in total were classified as travel-associated (11 from United Kingdom, two from Canada, one from the Former Yugoslav Republic of Macedonia and one from the Netherlands). Ninety-five percent of all cases were aged between 16 and 30 years and all presented with mild symptoms. Fifty-two of the confirmed cases had been referred from the festival to Novi Sad health facilities. A total of 23 confirmed cases associated with the festival were residents from Novi Sad.

An additional 32 probable cases, of whom four were among staff working at the festival site, were identified in Novi Sad after 15 July as likely associated with the festival, as a primary or secondary contact, but were not confirmed due to the new testing policy.

No complications or deaths were reported among any cases.

Discussion
Cases of influenza A(H1N1)v had been detected in Serbia before the mass gatherings occurred but were also associated with these events, as was expected in the context of the pandemic situation. The choice of an overall mitigation approach was in accordance with WHO recommendations at the stage of the global pandemic in June [10]. Preparedness planning assisted towards detecting and responding to the evolving situation in Serbia.

Outbreaks of ordinary seasonal influenza in populations similar in size and age-group structure have been reported at other mass gatherings worldwide [11] thus transmission under these events is not unexpected. Relatively few influenza A(H1N1)v cases were identified among athletes and staff associated with Universiade. Though further cases may have presented among delegations after departure (as reported in Montenegro [12]), this suggests transmission at Universiade was limited which may have been influenced by both the directed travel information as well as health monitoring by delegations. No cases were passively detected or reported among spectators of the Universiade event.

Cases at EXIT festival were first identified among foreign visitors, suggesting importation of the virus to the festival site, however, travel-related cases had been detected in Novi Sad prior to the festival. Though the age groups involved in the festival were similar to Universiade, many more cases were identified in association with EXIT and within a shorter timeframe. This difference could be partly explained by the active contact-tracing undertaken in the local districts. However it might also reflect the characteristics of this mass gathering event including higher person density in specific areas and differences in social interaction.

The number of probable cases detected in Novi Sad after the festival suggests local spread. However, it is difficult to assess the impact of either of these mass gathering events on the development of the epidemic in Serbia as the virus was already present in the country and cases may have been under detected nationally.

Conclusions
Both mass gathering events went ahead as planned. Transmission of influenza A(H1N1)v at both events was inevitable due to the nature of the infection, but preparations were put in place to
mitigate the situation, including detection, isolation options and treatment of cases, during this early stage of the epidemic in Serbia.

Acknowledgements

We wish to thank the team of the Military Medical Academy (S Lazic, R Cekanac) Institute of public health of Belgrade (N Zakula), Institute of Public Health of Vojvodina (Z Seguljev, M Ristic) and all District Institutes for Public Health for providing data.

References


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On 6 July 2009 the Belgian enhanced surveillance system for influenza-like illness among travellers returning from influenza A(H1N1)v affected areas detected a case linked to a rock festival which took place on 2-5 July. The health authorities implemented communication and control measures leading to the detection of additional cases. This paper describes the outbreak and its impact on the management of the influenza pandemic in Belgium.

**Background**

In response to the ongoing influenza A(H1N1)v pandemic, first detected in North America in April 2009 [1], many European countries developed active surveillance systems for influenza-like illness among travellers returning from affected areas [2,3,4,5]. Amplifying events, like school outbreaks of influenza A (H1N1)v infections reported by the United Kingdom (UK) and France [6,7,8] confirmed sustained community transmission [9] and required the surveillance systems to adapt accordingly [5,10].

In Belgium the enhanced surveillance system for influenza-like illness in travellers returning from affected areas [11] detected an outbreak around the “Rock Werchter” festival that took place from 2 to 5 July 2009.

This communication describes the epidemiology of this outbreak and the control measures taken as well as the impact of this event on the management of the current influenza A(H1N1)v pandemic in Belgium.

**The index case and initial investigation**

The first case found was an Israeli citizen who arrived in Belgium (via London) on 2 July 2009 and visited the festival from 3 to 5 July. He felt sick on 3 July but only sought medical care at the festival, in the Belgian Red Cross facility, on 5 July. The same day respiratory tract swabs were taken from this patient and sent to the National Reference Laboratory for Influenza where influenza A(H1N1)v infection was confirmed by real-time reverse transcription PCR on 6 July. The patient was isolated and treated with oseltamivir. Four of his friends, considered as close contacts, were also isolated and given post-exposure doses of oseltamivir.

**Descriptive epidemiology**

**Setting**

The outbreak occurred at the Rock Werchter festival, one of the four biggest annual rock music festivals in Europe. It lasts four days and can host 80,000 guests at a time. It is estimated that about 69,000 participants attend all four days, which adds up to a total of 113,000 different attendees. Visitors come mainly from Belgium but also from the Netherlands, the UK, and many more countries.

**Case definitions**

The case definitions used for identifying cases of influenza A(H1N1)v at the Rock Werchter festival are summarised in Table 1.

**Outbreak description**

We found 12 confirmed cases of A(H1N1)v infection out of a total of 30 people with influenza-like symptoms who were linked to the festival and were tested for influenza A(H1N1)v virus from 2 to 13 July in Belgium.

These cases are shown in the Figure, together with all confirmed cases reported in Belgium from 12 May to 13 July 2009 by date of onset of symptoms. Note that the Interministerial Influenza Coordination Committee decided to stop the enhanced surveillance system on 13 July, which may explain the smaller number of cases for whom symptoms onset was 11 or 12 July.

The mean age of cases linked to the festival was 23 years (range 18-45) and median 20 years. There were nine men and three women among the cases (ratio male: female = 3).

Taking the index case as the common source, the generation interval for secondary cases ranged from 3 to 7 days (median four days). After a request to the UK, Spain, Germany, France and the Netherlands, an additional case linked to Werchter was notified by the Dutch surveillance system: a 22-year-old man with onset of symptoms on 6 July 2009. Luxembourg reported another laboratory-confirmed case: a 20 year-old man with symptoms onset on 7 July.* These two cases were not included in our analysis.

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2. Department of Epidemiology, Scientific Institute of Public Health, Brussels, Belgium
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On 6 July 2009 the Belgian enhanced surveillance system for influenza-like illness among travellers returning from influenza A(H1N1)v affected areas detected a case linked to a rock festival which took place on 2-5 July. The health authorities implemented communication and control measures leading to the detection of additional cases. This paper describes the outbreak and its impact on the management of the influenza pandemic in Belgium.
Clinical epidemiology
The distribution of symptoms among the cases is illustrated in Table 2. These were typical of influenza-like illnesses. No cases were admitted to hospital.

The public health response
Medical care at the festival was ensured by the Belgian Red Cross in collaboration with the university hospital of the Catholic University of Leuven. No active case finding was set up at the festival site but the abovementioned medical care facilities had procedures in order to diagnose, notify and manage cases in line with the national enhanced surveillance system.

Case finding: Communication through the press, the festival’s website and case definition update
The official daily press releases on the influenza pandemic from the Belgian Interministerial Influenza Coordination Committee reported cases linked to the festival on 6 July and from 8 to 12 July. Mass media (including press, internet, TV and radio) published this information and conducted a careful follow up of the event describing every confirmed case of influenza A(H1N1)v related to the festival [12,13]. On 6 July a separate message for those having visited the festival was published on the official Belgian influenza website [14]. Additionally on 7 July, a communication in Dutch, English and French was displayed on the festival’s website in coordination with the festival organisers. All these messages advised the participants of the festival to visit a physician if fever or respiratory symptoms appeared [15].

As a consequence of this outbreak, the case definition used by the national surveillance system was updated to include participation in the festival and the criterium of travel to an affected area was removed as of 6 July 2009.

Case management and contact tracing
Cases were managed individually, within the regular healthcare system, by general practitioners in coordination with provincial health inspectors. According to the protocols, patients were isolated at home, contact tracing was performed and prophylactic treatment for close contacts recommended [11]. No epidemiological link, apart from attending the same event, was found for any of the cases linked to Werchter festival.

Beside the index case from Israel, three of the cases linked to the festival consulted their physician on 7 July, one on 8 July, five on 9 July, one on 10 July and one on 11 July 2009.

Discussion and conclusions
This outbreak of influenza A(H1N1)v is one of the first associated with a mass gathering event. The index case, detected by the enhanced surveillance system, was imported probably from Israel or, less likely, from the UK, where he was in transit the day before the onset of symptoms.

An initial assessment led to isolation and post-exposure prophylaxis of four close contacts. The fact that the index case had attended the “Rock Werchter festival” for three days while being

<table>
<thead>
<tr>
<th>Table 1</th>
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</thead>
<tbody>
<tr>
<td><strong>Case definition of influenza A(H1N1)v used for investigating cases linked to Rock Werchter festival in Belgium, 2-5 July 2009</strong></td>
</tr>
<tr>
<td><strong>Case linked to Werchter</strong></td>
</tr>
<tr>
<td><strong>Other case</strong></td>
</tr>
</tbody>
</table>

Figure
Distribution of laboratory-confirmed cases of influenza A(H1N1)v by date of onset, including cases with epidemiological link to “Rock Werchter festival”, Belgium, 12 May-28 June 2009 (n=123)*

*Note: The total number of confirmed cases for this period is 131 but for eight cases the date of onset of symptoms was not available. None of these were linked to the festival.
symptomatic prompted the Belgian Interministerial Committee for Influenza to implement further communication and control measures.

The eleven cases found in Belgium as well as the one reported in the Netherlands and one in Luxembourg* might have acquired the infection at the festival. This is plausible because their symptoms started within five days after the end of the festival hence within the incubation period estimated to be from one to seven days for influenza A(H1N1)v [16].

However, given the lack of epidemiological link among the cases and the fact that community transmission existed in neighbouring countries where many attendees came from, we believe that other cases, apart from the index case identified, were present at the festival and could therefore have been seeding cases as well. The average generation interval (number of days between onset of symptoms in the source case and in the secondary case) for secondary cases found in our previous analysis of influenza A(H1N1)v cases in Belgium (not published) was two days compared to three found in the Netherlands [4]. This makes it difficult to believe that all eleven cases were contaminated by the same index case, as for eight cases the generation interval was estimated to be four to seven days, i.e. at least twice as long as expected.

The likelihood of community transmission having occurred independently of the festival can not be ruled out either. If this was the case, increased awareness of physicians and patients, after the public health messages by the press and the authorities, might have contributed to the detection of some of the cases, especially those with latest symptoms onset.

This latter possibility highlights the role of chance in detecting this outbreak: had the index case not been an imported one, it would not have been detected and subsequently cases linked to Werchter would not have been diagnosed either because at that time the case definition included a visit to an affected country.

This outbreak demonstrated that community transmission was taking place in Belgium. The festival itself could have been the seeding event leading to community transmission although other sources must have played a role because the number of cases not linked to Werchter was already rising steeply. The outbreak also challenged the surveillance system at that time forcing us to update the case definition. Furthermore a shift into a mitigation strategy was decided on 13 July 2009, one week after the index case had been diagnosed.

Communication measures raised public awareness; this is shown by the fact that after the information on the first case linked to the festival was published, subsequent cases sought medical attention and were identified.

As pointed out by this investigation, mass gatherings can concentrate infectious diseases and amplify their transmission. Once more, preparedness and communication become essential in order to detect and respond to infectious disease outbreaks in complex situations.

**Acknowledgements**

We would like to acknowledge Belgian general practitioners and staff of the National Reference Laboratory for Influenza for their continuous work and the European Programme for Intervention Epidemiology Training (EPIET) fellows and coordinators for their valuable information and support.

*Authors’ correction

Information on the case detected in Luxembourg was added after the publication of the article, upon the request of authors. This change was made on 10 August 2009.

**References**


**Table 2**

Distribution of symptoms among cases of influenza A(H1N1)v linked to Rock Werchter festival in Belgium, 2-5 July 2009 (n=12)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Number of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>12</td>
<td>100%</td>
</tr>
<tr>
<td>Disconfort</td>
<td>11</td>
<td>92%</td>
</tr>
<tr>
<td>Fever</td>
<td>11</td>
<td>92%</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>2</td>
<td>17%</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>1</td>
<td>8%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1</td>
<td>8%</td>
</tr>
</tbody>
</table>


This article was published on 6 August 2009.

We report here an update on human cases of West Nile virus (WNV) infection in Veneto region, northeastern Italy. In addition to two cases of WNV neuroinvasive disease notified through a surveillance programme started in September 2008, further four cases were retrospectively identified (in May 2009) by investigating patients with aseptic meningoencephalitis of unknown aetiology occurring in Veneto region in June-September 2008. All six patients had symptom onset in August-September 2008 and were resident in a wetland area close to the Po river delta in Rovigo province. Further five cases of asymptomatic WNV infection, including four residents of the same area in Rovigo, were identified in a seroprevalence study in farm workers from Veneto region. To date, no human cases have been notified in 2009.

Introduction

In Italy, the first outbreak of West Nile virus (WNV) infection was reported in the late summer 1998 among horses residing in a wetland area in Tuscany. At that time, 14 horses had neurological illness and six of them died, but no human cases of WNV disease were reported [1]. Subsequently, a national veterinary surveillance plan for WNV was activated in 2002 in Italy, aiming to identify risk areas and to monitor WNV circulation based on observation of wild bird mortality, and on entomological and sentinel chicken surveillance, as well as to check for WNV seroconversion in horses residing in risk areas. Thereafter, sporadic seroconversions have been identified in sentinel chickens and horses [2,3], but no equine or human cases of symptomatic WNV infection had been notified until September 2008, when an outbreak of WNV infection was identified in the northeastern part of Italy [4,5].

The first possible case of WNV neuroinvasive infection in a horse was notified on 8 September 2008 in Emilia-Romagna region, Italy. A special plan for WNV surveillance was subsequently activated in Emilia-Romagna on 16 September, which led to the identification of other horses with WNV neuroinvasive illness [4] and, on 20 September 2008, to the identification of the first human case of meningoencephalitis caused by WNV infection in a female patient who lived in a rural area between Ferrara and Bologna in Emilia-Romagna region, and had symptom onset on 15 September 2008 [5].

In Veneto region, the first WNV-seropositive horse was identified on 24 September 2008 in a stable in Rovigo province, where a horse presented neurological symptoms after being brought back from Emilia-Romagna region. Thereafter, on 29 September 2008, Veneto region activated a special veterinary surveillance plan in horse stables of Rovigo, Venezia and Padova provinces, and started a seroepidemiological investigation of all workers on farms where infected horses were identified, as well as a surveillance programme for possible human cases of WNV infection in Veneto region. To identify cases that might have occurred before the implementation of these surveillance activities, in May 2009, we performed a retrospective investigation of cases of aseptic meningoencephalitis of unknown aetiology occurring in Veneto region in June-September 2008. Here we describe the results of this retrospective study as well as provide an update on cases reported through the surveillance programme and on those identified in the seroepidemiological study of stable workers, and present the results of screening of blood and organ donations from the affected area.

Retrospective study of cases of aseptic meningoencephalitis

Methods

To identify cases of WNV neuroinvasive disease occurring before the activation of the surveillance programme in Veneto region, we retrospectively analysed cerebrospinal fluid (CSF) samples referred to our Regional Reference Centre from hospitals of Veneto region in the period June-September 2008 for the presence of specific immunoglobulin M (IgM) antibodies against WNV. This study was performed in May 2009.

CSF samples from patients aged ≥15 years with suspected viral encephalitis, but with negative viral test results (routine PCR and serology tests for herpes simplex virus (HSV), varicella zoster virus (VZV), enteroviruses, tick-borne encephalitis virus (TBEV), Toscana virus (TOSV) and other neurotropic viruses), were selected for the study, according to definition criteria for possible cases of WNV neuroinvasive disease (Table 1).

WNV IgM testing was done by using WNV IgM capture DxSelect™ ELISA (Focus Diagnostics, Cypress, California) according to the manufacturer instruction, with the exception that CSF was diluted 1:2, as recommended by Prince et al. [6]. CSF samples which were positive at WNV IgM capture ELISA were tested for neutralising antibodies by plaque-reduction neutralisation test (PRNT) for WNV and for tick-borne encephalitis virus (TBEV), a flavivirus commonly found in northeastern Italy, to rule-out cross-reactivity. PRNT was conducted in a biosafety level 3 lab, according to the protocol.
described in the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2008 of the World Organisation for Animal Health (OIE). Briefly, heat-inactivated CSF or serum samples were tested at 1:100 final dilution. Equal volume of serum and medium containing 100 plaque-forming units of WNV were incubated for 75 min at 37 °C before inoculation onto confluent monolayers of Vero E6 cells grown in 25 cm² flasks. After the inoculum was adsorbed for 1 h at 37 °C, cells were overlayed with agarose-containing medium, and then incubated for 72 h at 37 °C. Then, a second agarose overlay containing 0.003% neutral red dye was applied to each flask for plaque visualisation. Following a further overnight incubation at 37 °C, the number of virus plaques per flask was assessed. Endpoint titres were assigned as the greatest dilution in which >90% neutralisation of the challenge virus was achieved. Samples with reciprocal 90% neutralisation titres of >10 were considered positive. WNV IgM-positive CSF samples were also tested by real-time RT-PCR for WNV-RNA detection using the oligonucleotide primers and TaqMan probe targeting the WNV E gene designed by Lanciotti et al. [7]. For real-time RT-PCR, nucleic acids were purified from 200 μl CSF or plasma samples by using an NucliSSENS® easyMAG® system (bioMérieux, Inc., Durham, NC) and eluted in a final volume of 50 μl. Then, 5 μl of RNA was combined with Superscript® One Step RT-PCR System reagents (Invitrogen Ltd, Paisley, UK), primers and probe in a 20-μl total reaction volume and amplified in a LightCycler® 2.0 Real-Time PCR System (Roche Diagnostics S.p.A., Monza, Italy).

**Results**

Of the 74 investigated patients (40 males and 34 females; median age 51.5 years, range 21-94 years) with aseptic meningoencephalitis of unknown aetiology, four (a 69-year-old woman and three men aged 69, 70, and 86 years) had IgM antibodies against WNV in CSF, as demonstrated by IgM capture ELISA (Table 2). The presence of WNV-specific neutralising antibodies in CSF was confirmed in all four cases by PRNT, which showed neutralisation titres >1:40, while WNV-RNA testing gave negative results. The presence of WNV-reactive neutralising antibodies was also demonstrated in a convalescent serum specimen, subsequently provided. For two patients, two consecutive serum samples were available, which showed an increase of WNV-specific antibody titre. All four WNV-positive patients were resident in Rovigo province and were hospitalised in the period from 25 August to 9 September. One of these patients (male, 70 years old), who had encephalitis in early September 2009, was described as a probable case in a previous report, based on the detection of high titre WNV IgG in February 2009 [8].
**WNV infection surveillance in Veneto region, 2008-2009**

**Methods**
A surveillance programme for possible human cases of WNV infection was activated in Veneto region on 29 September 2008, after the notification of the first equine case on 24 September 2008. All infectious disease units of hospitals in Veneto region were asked to report suspected cases of aseptic encephalitis and/or meningitis of unknown aetiology from all provinces of the region and cases of fever and rash from areas where WNV infection had been documented in horses (initially only Rovigo, eventually also Venice and Padua provinces), and to collect blood and CSF samples from these patients. Specimens of blood and CSF were sent to our Regional Reference Centre and investigated for IgM and IgG antibodies against WNV by ELISA testing (Focus Diagnostics), PRNT to confirm ELISA-positive samples, and WNV real-time RT-PCR, as above described.

**Results**
Within this ongoing surveillance programme, to date, 61 patients from Veneto region (33 males and 28 females; median age 47 years, range 19-85 years) were reported with suspected WNV infection and referred for further investigation. Of these, 37 were referred in October-November 2008, and 24 were referred in June-July 2009. Of these, only two cases in 2008 were confirmed for WNV infection, as described in a previous report [8]. The first was an 81-year-old woman from Rovigo hospitalised in the end of August 2008 for suspected viral meningoencephalitis with fever, headache, and altered mental status. On October 16, serology testing demonstrated the presence of IgM and IgG antibodies against WNV, confirmed by PRNT; retrospective analysis of a CSF sample collected on 6 September demonstrated the presence of IgM antibodies against WNV, while WNV RNA testing was negative. The second case was a 48-year-old female patient resident in Rovigo province, who had an episode of fever, severe headache, maculopapular rash, pharyngitis, adenopathy, and arthralgia starting in early August 2008. WNV serology testing, performed in the end of November for persistence of symptoms, was positive for IgM and IgG antibodies, confirmed by PRNT.

To date, no human cases of WNV infection have been identified in 2009.

**Seroepidemiological survey**

**Methods**
A seroepidemiological survey was started in Veneto region on 29 September 2008 involving all workers employed in farms where WNV-positive horses were identified by the veterinary surveillance. The aim of the study was to investigate the prevalence of WNV infection and to promote the awareness of the disease in this at-risk population. In the survey, local Public Health Services conducted interviews with farm workers to ascertain their risk for WNV infection and collected serum samples, which were sent for analysis to our Regional Reference Centre. We tested the samples for IgM and IgG antibodies against WNV by ELISA and used PRNT for confirmation, as above described.

**Results**
Of 321 investigated subjects (178 males and 143 females, median age 45 years; range 4-84 years), two men (71 and 76 years old) and three women (51, 60, and 67 years old), all asymptomatic, were IgM and IgG WNV-reactive (two cases) or only IgG WNV-reactive (three cases) and confirmed by PRNT. Four of these persons were resident in Rovigo province and one in Venice province (Table 2). Four have been previously reported [8].

**Screening of blood and organ donations**

**Methods**
Following the notification of the first human case of WNV infection in Veneto region, in accordance with the European Union blood safety directive [9], a nucleic acid test (NAT) for WNV RNA screening was started on 28 October 2008 in all blood, stem cells, tissue, and organ donations collected in the period from 1 September to 5 December 2008 from donors who were resident in Rovigo province or who stayed for at least one night in Rovigo province during the last 28 days before donation. In 2009, based on estimates of WNV circulation in Italy, WNV-RNA NAT screening will be done on all donations collected from 1 August to 31 October in Rovigo province, as well as in the provinces of Ferrara (Emilia-Romagna region) and Mantova (Lombardia region).

**Results**
During 2008, our Regional Reference Centre individually screened a total of 5,500 donations by using the Procleix WNV Assay (Chiron, Novartis). All donations resulted WNV RNA-negative.

**Discussion**
Surveillance of suspected cases of WNV infection and retrospective investigation of cases of meningoencephalitis of unknown aetiology occurring in Veneto region led to the identification of six patients with WNV neuroinvasive disease. All cases were resident in a wetland area of about 40 km in diameter in Rovigo province and had symptom onset in the period ranging from early August to mid-September 2008. The incidence of WNV disease in this area could be estimated at 12 cases per 100,000 population, but this is probably an underestimation because based in part on retrospective data.

In the neighbouring provinces of Ferrara and Bologna in Emilia-Romagna region, three human cases of WNV neuroinvasive disease were reported, with symptom onset in early, mid-, and late September 2008 [5,8].

The seroprevalence study in farm workers from Veneto region demonstrated a low prevalence (<2%) of WNV infection, but, notably, four of the five cases with asymptomatic infection were resident in the above mentioned wetland area in Rovigo province. Moreover, the veterinary survey in horse stables reported the highest seroprevalence in Rovigo province, where 58% horses had WNV-neutralising antibodies [10]. WNV infection appears to be widespread among horses in northeastern Italy. In fact, in 2008, several equine outbreaks of WNV infection were identified in Veneto, Emilia-Romagna, and Lombardia regions, with a total of 794 seropositive horses out of 2,030 investigated (39.1%), including 32 horses with WNV neuroinvasive disease [10,11]. On 28 July 2009, a case of equine WNV disease was notified in Reggio Emilia province (Emilia-Romagna region), which is located outside the area where WNV circulation was identified [12].

We could not recover and characterise the virus responsible for the human cases described here. It was isolated from birds, a horse, and a donkey by the National Reference Veterinary Laboratory [11,13]. Genome sequencing and phylogenetic analysis showed that the virus isolated in 2008 was closely related to the WNV strain isolated during the equine outbreak, which occurred in Tuscany...
region in 1998, and to other European strains [11,13,14]. So, both 1998 and 2008 Italian outbreaks could be related to a continuous endemic circulation of WNV, although a recent new introduction of WNV by migratory birds cannot be excluded, since the location of the current outbreak is very close to a migratory bird resting area.

To date, no human cases have been notified in 2009, but it is conceivable that new cases will present this year. In fact, the virus has been frequently isolated from local birds and mosquitoes [10] thus indicating it has established an endemic infection cycle.

In conclusion, a relatively high incidence of WNV infection was observed in August-September 2008 in Veneto region, in an area close to the Po river delta. The burden of WNV infection in this area is probably still underestimated. To clarify this issue, Veneto region has recently started a seroepidemiological study in blood donors from Rovigo province. This will be done on samples obtained from 2,550 blood donors (about 1/3 of all donations) from Rovigo province, for 17 weeks, starting on 15 July 2009.

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The authors Luisa Barzon and Laura Squarzon contributed equally to this study.

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Rapid communications

MENINGOCOCCAL DISEASE IN A BACKPACKERS’ HOSTEL IN SCOTLAND: A RISK ASSESSMENT FOR PROPHYLAXIS

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This paper outlines the risk assessment and communication strategy carried out by the Lothian Health Protection Team after notification of a probable case of meningococcal disease (later confirmed as Neisseria meningitidis) in a resident of a city centre backpackers' hostel. Six close contacts were identified from the hostel and given rifampicin prophylaxis. Two days after commencing rifampicin one of these contacts was admitted to hospital with a purpuric/petechial rash and thrombocytopenia. The final diagnosis for this contact was thrombocytopenia, either idiopathic or secondary to rifampicin. This example and the potential side effects of administering rifampicin prophylaxis highlight the importance of a thorough risk assessment of contacts of a case to avoid prescribing prophylaxis to anyone other than those at highest risk of becoming a subsequent case.

Introduction
The Lothian Health Protection Team (HPT) was notified of a probable case of meningococcal disease in a foreign national who was resident in a large city centre backpackers' hostel. The HPT undertook an investigation to identify close contacts requiring prophylaxis.

In the United Kingdom prophylaxis (usually rifampicin) is routinely offered to close contacts of confirmed or probable cases of meningococcal disease to eradicate carriage of the organism in those most at risk [1].

The Health Protection Agency [1] defines a close contact as:

- Someone who has had an overnight stay in the household, or with whom the patient has stayed overnight, during the seven days before onset of illness in the index case.
- Someone who is an intimate kissing contact.

In larger institutions defining close “household” contacts is more challenging [1,2,3]. In this case the Consultant in Public Health Medicine is responsible for deciding who constitutes the “household”.

The administration of rifampicin is not without risk. Adverse effects have been reported to occur in about 4% of patients receiving “usual doses” of rifampicin (for example 10mg/kg/day) [4]. Mild adverse effects include nausea, diarrhoea, abdominal pain, headache, dizziness and skin rash [5]. More severe adverse effects include thrombocytopenia, with or without purpura, and hepatic reactions [6].

If prophylaxis is not prescribed for contacts the absolute risk to a person in the same household of developing meningococcal disease one to 30 days after an index case is about one in 300 [1].

It has been estimated that 200 household contacts need to be treated with prophylaxis in order to prevent a subsequent case of meningococcal disease in the first month [7].

Methods
For this incident a household contact was defined as:

1. Anyone who shared a room with the case in the seven days prior to symptom onset.
2. Anyone who had spent prolonged periods of time socialising with the case in the seven days prior to symptom onset.

To identify close contacts who required prophylaxis the layout of the hostel was inspected. The names of close contacts were identified through hostel records and through discussion with other residents.

Blood samples were sent from the case for confirmation and typing of Neisseria meningitidis.

Results
Contacts
The hostel comprised two separate buildings, a short stay facility with 170 beds and a long-stay facility with 130 beds. The index case was resident in a three bedded room of the long stay facility and had been living there for several months.

On the day of notification (day 1) six close contacts were identified who fitted the definition. All were given rifampicin prophylaxis. These contacts included: two room-mates, three friends and the case’s partner.

Administration of rifampicin
Day 1: Five of the close contacts received rifampicin from the local hospital. Three of these close contacts were foreign nationals, only one of whom spoke English. Communication regarding prophylaxis and its contra-indications was done through translation by this individual. No contraindications were identified.

Day 2: One contact, travelling in Ireland, had prophylaxis arranged by public health colleagues in Ireland.
Day 3: Two days after commencing rifampicin prophylaxis one of the contacts from the hostel was admitted to hospital with a purpuric/petechial rash. This person had taken three doses of rifampicin 600mg. Differential diagnoses included idiopathic thrombocytopenic purpura, thrombocytopenia secondary to rifampicin and possible meningococcal septicaemia.

Communication to hostel residents

Day 4: Following the admission to hospital of the contact (where meningococcal disease was a possibility), information letters, written in English, were placed on each resident's bed in the hostel. These letters informed residents that there had been a confirmed case of meningococcal disease in the hostel and included information on the signs and symptoms of the disease. The HPT also visited the hostel for question and answer sessions.

Microbiology

Day 4: The samples from the index case were confirmed as N. meningitidis serogroup W135. The HPT advised that the previously identified close contacts of this case should be vaccinated against W135.

Day 9: The contact was discharged from hospital with a final diagnosis of thrombocytopenia which was either idiopathic or secondary to rifampicin. A blood sample sent for PCR was negative for N. meningitidis.

No further cases of meningococcal disease were notified from the hostel.

Discussion

Risk assessment for the administration of prophylaxis

Deciding how extensively to give prophylaxis in an institution such as a hostel is not straightforward. In this incident the HPT identified contacts requiring prophylaxis amongst those most closely linked with the case. This totalled six close contacts from the 300 bed hostel. This health protection response was similar to the response in a hall of residence in Southampton in 1997 when the first case in an outbreak was treated as a “single case” and mass prophylaxis was only advised when further cases were notified [8].

A contrasting approach was taken in a 282 bed hostel in Vancouver in 2001 when, after notification of a single case, the entire hostel was considered a “household” and ciprofloxacin prophylaxis was recommended for all staff and residents who had stayed at the hostel for up to a week before the case was admitted. It was estimated that this could have been up to 750 people [9].

The fact we have reported that a close contact who was given rifampicin was discharged from hospital with a final diagnosis of thrombocytopenia, either co-incidental or secondary to rifampicin stresses that all close contacts should be informed of the potential dangerous side effects of rifampicin prophylaxis and that a thorough risk assessment should be undertaken before administering prophylaxis to contacts.

Communications

Contact tracing proved challenging during this incident due to the limited information held about possible contacts in hostel records and by other residents.

Communication to the wider community at the hostel was also difficult due to the multiple nationalities of its residents. The letter given to individuals in the hostel was in English. Consideration was given to preparing letters in a variety of languages however this would have caused a lengthy delay in communicating the risk. Being aware of the signs and symptoms of meningococcal disease is essential to ensure that cases are given medical treatment as soon as possible. Prior preparation of information about meningococcal disease in different languages would be helpful especially in busy European tourist cities with visitors from across the world.

Acknowledgements

Thorn SN, Stevenson J

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6. The electronic Medicines Compendium (eMC). Rifadin 300mg Capsules. Available from: http://emc.medicines.org.uk/medicine/21223/SFC/Rifadin+300mg+Capsules

This article was published on 6 August 2009.


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6. The electronic Medicines Compendium (eMC). Rifadin 300mg Capsules. Available from: http://emc.medicines.org.uk/medicine/21223/SFC/Rifadin+300mg+Capsules

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Salmonella enterica serotype Muenster (hereafter referred to as S. Muenster) is rare in France and in Europe. In France, a nationwide outbreak of gastrointestinal illness due to S. Muenster occurred during March and April 2008. Twenty-five laboratory-confirmed cases of S. Muenster were documented by telephone using a trawling questionnaire. Four patients were admitted to hospital and no death was recorded. Among the 21 interviewed cases, 16 reported consumption of goat’s cheese in the days prior to symptoms. The investigation incriminated goat’s cheese from producer X as being the most likely source of the outbreak. S. Muenster was isolated from both cases and the incriminated batch of cheese, the number of cases decreased to its usual level.

To our knowledge, this is the first published outbreak of S. Muenster associated with food consumption in Europe.

**Methods**

**Epidemiological information**

A case was defined as a person living in France with S. Muenster isolated from a stool or a blood specimen since 25 February of 2008 (week 9). Cases were reported by the NRC for Salmonella and clusters of cases were identified through the mandatory notification of suspected food poisoning. Basic epidemiological data (age, gender, district of residence, address of the medical laboratory) was available. Cases were interviewed by the relevant district health office or the InVS by telephone using a trawling questionnaire, in order to inquire about the onset of illness, type of symptoms, hospitalisation, and exposures during the week before the onset of illness such as contact(s) with other symptomatic individual(s), or with animal(s) or water, recent travel abroad, food consumption and the places where they had purchased food.

**European investigation**

The European Food- and Waterborne Diseases Network of the European Centre for Disease Prevention and Control (ECDC) was informed on 28 March of the ongoing outbreak in France, and the network members were requested to report any recent increase in number of cases of S. Muenster or any cases possibly linked to the French outbreak.

**Microbiological investigation**

Antimicrobial drug susceptibility was determined by disk diffusion as previously described [3]. Human and food isolates of
S. Muenster linked to the outbreak as well as isolates not related to the outbreak (isolates received by the NRC in 2006 and 2007) were characterised by standard pulsed-field gel electrophoresis (PFGE) analysis of XbaI-digested chromosomal DNA [3]. Each profile that differed by at least one clear band >100 kb was considered as a distinct profile. BioNumerics software (Applied Maths) was used to compare the PFGE profiles [4].

Results

Epidemiological information

Between 28 February and 24 April 2008, a total of 25 laboratory-confirmed cases of S. Muenster were reported by the NRC to the InVS, and among them six cases were reported as clusters of food poisoning through the mandatory notification. Four of them were isolated from children (8-12 years-old) and 21 from adults (median age 58 years). Only nine cases were male. The cases lived in 17 different administrative “Départements” spread across the country (Figure 1).

Of the 25 reported cases, 21 could be interviewed. The dates of onset of symptoms were from 27 February (week 9) to 3 April 2008 (week 14) (Figure 2). The most frequently reported symptoms were fever (20/21), diarrhoea (20/21), abdominal pain (17/21) and nausea (12/21). None of the interviewed cases had underlying medical conditions such as chronic illness or immunosuppressive therapy. Four patients were admitted to hospital and no death was recorded.

Among the 21 interviewed cases, 16 reported consumption of goat’s cheese in the days before the onset of symptoms. The place of purchase of the goat’s cheese was known for 10 cases: Seven cases had purchased unpasteurised goat’s cheese at an agriculture exhibition that was held in Paris from 23 February until 2 March, and three cases had purchased this type of cheese at a local market in south-eastern France. Other food products frequently consumed were beef, ham, Emmentaler cheese and chicken (Table).

During the same period, a household cluster of salmonellosis involving three cases was reported through the mandatory notification system. The investigation of this cluster incriminated unpasteurised goat’s cheese (consumed on 8 February 2008) as the source of infection. The isolates of these cases were later shown to be positive for S. Muenster.

In parallel, a routine food control was carried out on 14 March 2008 at a producer X, based in south-eastern France, and was positive for Salmonella for one of the batches of unpasteurised goat’s cheese. This producer had delivered 360 unpasteurised goat’s cheeses to the agriculture exhibition in Paris and supplied several local markets in south-eastern France. Control measures were taken by the producer immediately after this positive routine control: the contaminated batch and, as a precautionary measure, all the other batches on the market were withdrawn and recalled. Following the withdrawal, the number of cases decreased to its usual level, around two isolates per month.

European investigation

A notification was made to the Rapid Alert System for Food and Feed (RASFF) on 20 March 2008 because the product had also been distributed to Belgium, Germany the Netherlands, and Sweden. No cases related to the French outbreak nor an unusual increase of S. Muenster isolates was reported from the ECDC’s Food- and Waterborne Diseases Network.

Microbiological investigation

The human outbreak isolates of S. Muenster were susceptible to all antimicrobials tested. The PFGE profile (XMUES-11) of the 20 isolates related to the outbreak was identical to the one of the food isolates of producer X. Ten different profiles other than XMUES-11 were observed for the 12 isolates found in 2006 and 2007 from cases not related to the outbreak (Figure 3).
Discussion

We describe a nationwide salmonellosis outbreak involving 25 cases of infection with the uncommon serotype Muenster that occurred in France between February and April 2008. The investigation incriminated unpasteurised goat’s cheese from producer X as being the most likely source of the outbreak.

The incrimination of this goat’s cheese was supported by the following findings: Firstly, a high proportion of cases (16 of 21) reported having eaten goat’s cheese from the same small producer X. Secondly, a cluster of cases followed the consumption of goat’s cheese from producer X. Thirdly, there was a concordance between the temporal (March 2008) and the geographical occurrence of salmonellosis infections, including cases of haemolytic-uraemic syndrome. In spite of the large amounts of many different types of raw milk cheeses consumed in France, foodborne outbreaks related to these cheeses remain relatively rare [5-8]. To our knowledge, this is the first published outbreak of S. Muenster associated with food consumption in Europe. This outbreak highlighted also the importance of routine food controls in order to prevent community-wide outbreaks of salmonellosis and other foodborne infections.

This event was picked up by three surveillance systems. The NRC for Salmonella and the mandatory notification of clusters of food poisoning performed well by reporting cases of S. Muenster simultaneously to the InVS. The positive routine food control of producer X allowed early withdrawal of the contaminated batch, resulting in a limited number of cases.

In the literature, unpasteurised dairy products have been shown to cause outbreaks of salmonellosis, campylobacteriosis, listeriosis and Shigatoxin-producing Escherichia coli (STEC) infections, including cases of haemolytic-uraemic syndrome. Food exposures of interviewed cases of S. enterica serotype Muenster, France, February–April 2008 (n=21)

<table>
<thead>
<tr>
<th>Food exposure</th>
<th>Number/total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goat’s cheese</td>
<td>16/21</td>
</tr>
<tr>
<td>Beef</td>
<td>11/21</td>
</tr>
<tr>
<td>Ham</td>
<td>10/21</td>
</tr>
<tr>
<td>Emmentaler cheese</td>
<td>9/21</td>
</tr>
<tr>
<td>Chicken</td>
<td>9/21</td>
</tr>
</tbody>
</table>

Table

Pulsed-field gel electrophoresis profiles of XbaI-digested DNA from S. enterica serotype Muenster isolates, France

Figures

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