

## Rapid communications

# NEW INFLUENZA A(H1N1) VIRUS INFECTIONS IN SPAIN, APRIL-MAY 2009

Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain (psantaolalla@msc.es)<sup>1,2,3,4</sup>

1. Coordinating Centre for Health Alerts and Emergencies, Spanish Ministry of Health and Social Policy, Madrid, Spain
2. National Centre for Epidemiology and National Centre for Microbiology, Instituto de Salud Carlos III, Madrid, Spain
3. Regional Surveillance and Alert Teams from the Autonomous Communities in Spain
4. National Influenza Laboratory Network, Spain

An outbreak of infections with a new influenza A(H1N1) virus that was first detected in the United States and Mexico is currently ongoing worldwide. This report describes the initial epidemiological actions and outbreak investigation of the first 98 laboratory confirmed cases of infection with this new virus in Spain.

### Background

On 25 April 2009, the World Health Organization (WHO) declared the outbreak of swine-origin influenza A(H1N1) virus infections, first reported by the United States (US) [1] and Mexico [2], as a 'Public Health Event of International Concern' (PHEIC) under the International Health Regulations (2005) [3]. The pandemic alert level was raised from level 3 to level 4 on 27 April, and to level 5 on 29 April, after verification of sustained community-level outbreaks in at least two countries from the same WHO region.

On 26 April, epidemiological and laboratory investigations on three persons returning from Mexico were initiated in Spain. On 27 April, Spain reported the first laboratory-confirmed case of the new influenza A(H1N1) virus infection in Europe, in a traveller returning from Mexico. Since then, the number of confirmed cases in Spain has risen continuously and reached a total of 98 as of 11 May 2009.

### Enhanced surveillance

On 24 April, in response to alarming reports from the US of swine-origin influenza A(H1N1) virus infection in several patients [1,4] and media news of a possibly related outbreak of severe respiratory illness in Mexico, the Coordinating Centre for Health Alerts and Emergencies (CCAES) at the Spanish Ministry of Health and Social Policy, issued a national epidemiologic alert. The alert asked public health authorities at national and regional level to enhance surveillance and to report urgently any case of fever and severe respiratory illness among people with history of travel to Mexico or history of previous contact with a confirmed case of influenza virus A(H1N1) infection (Table 1).

On 25 April, following WHO's declaration of a PHEIC, the National Pandemic Influenza Preparedness and Response Plan was activated. A case definition as well as protocols for case and contact management and for infection control were developed and distributed to the National Health Service through regional health authorities and other involved institutions (Table 2).

No increase in seasonal influenza activity has been reported so far. Routine seasonal influenza surveillance will continue beyond week 20. Data analysis of mortality for all causes since 1 May has not shown an increase or change of patterns in mortality.

Since 24 April, the outbreak of new influenza A(H1N1) has been monitored by the Ministry of Health and Social Policy (Centro de Coordinación de Alertas y Emergencias Sanitarias, CCAES) jointly with the National Centre for Epidemiology (Instituto de Salud Carlos

TABLE 1

Timeline of key events in detection and response to the new influenza A(H1N1) virus outbreak, Spain, 24 April-11 May 2009

Date	Event
24 April	Alert issued to enhance surveillance at the public health services and national health system
24 April	Information for the public and recommendations for travellers going to and returning from Mexico published on the website of the Spanish Ministry of Health and Social Policy
25 April	National pandemic influenza preparedness and response plan activated.
25 April	Case definition, case and contact management, and infection control protocols distributed
26 April	Notification of the first three cases under investigation
27 April	First laboratory-confirmed case of new influenza A(H1N1) virus infection reported.
27 April	Ministry of Health recommends avoiding non-essential travel to Mexico
27 April	World Health Organization raises pandemic alert to phase 4
29 April	World Health Organization raises pandemic alert to phase 5
29 April	First secondary case of new influenza A(H1N1) virus reported
1 May	Regional influenza laboratories to start initial testing; National reference laboratory to confirm
7 May	New case definition approved, including the United States as an affected area, reducing incubation period (seven days) and establishing fever cut off at 38°C
11 May	First laboratory-confirmed tertiary case
11 May	Status: 98 laboratory confirmed cases of new Influenza virus A(H1N1) infection

III) and in coordination with all the Regional Surveillance and Alert Teams from the Autonomous Communities in Spain. This new influenza A(H1N1) investigation and control group also discusses and recommends prevention and control measures.

**TABLE 2**

**Case definition and case classification, new influenza A(H1N1) infection, Spain, 25 April-7 May, 2009**

	Incubation period 10 days
Clinical criteria	Any person with ONE of the following: <ul style="list-style-type: none"> <li>• Fever (<math>\geq 37.5</math> °C)* AND signs or symptoms of acute respiratory infection</li> <li>• Pneumonia</li> <li>• Death from an unexplained acute respiratory illness</li> </ul>
Epidemiological criteria	At least ONE of the following in the 10 days* prior to disease onset: <ul style="list-style-type: none"> <li>• Travel to an area where there are confirmed cases of new influenza A(H1N1) (Mexico*)</li> <li>• Close contact to a confirmed case of new influenza A(H1N1) virus infection</li> <li>• Recent history of contact with an animal with confirmed or suspected swine influenza A(H1N1) virus infection (This criterion was substituted on 27 April for: "A person employed at a laboratory and manipulating potentially contaminated samples").</li> </ul>
Laboratory criteria	At least ONE of the following tests: <ul style="list-style-type: none"> <li>• RT-PCR</li> <li>• Four-fold rise in new influenza A(H1N1) virus-specific neutralizing antibodies (implies the need for paired sera, at least from acute phase illness and then at convalescent stage 10-14 days later)</li> <li>• Viral culture</li> </ul>
Case classification	A. Case under investigation Any person meeting clinical AND epidemiological criteria B. Probable case Any person meeting clinical AND epidemiological criteria AND with a positive influenza A infection of an unsubtypable type C. Confirmed case Any person with laboratory confirmation*

\* Differences to proposed case from the European Centre for Disease Prevention and Control.

**FIGURE 1**

**Geographical distribution of cases of laboratory-confirmed new influenza virus A(H1N1) infection, Spain, as of 11 May 2009**



**Confirmed cases of new influenza virus A(H1N1)**

As of 11 May, 98 laboratory-confirmed cases of infection with the new influenza virus A(H1N1) have been reported in Spain out of 640 possible cases investigated. The geographical distribution of reported cases by region is shown in Figure 1.

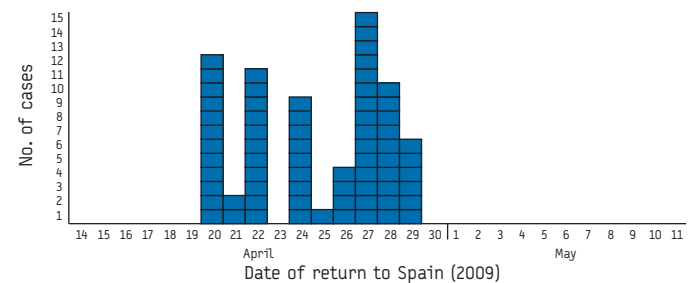
Seventy-six confirmed cases (78%) acquired the infection abroad; all these cases had a history of travel to Mexico. Of the 45 cases for whom this information was available, 16 (36%) were symptomatic during the inbound flight from Mexico. Dates of return from affected areas were available for 70 confirmed cases and ranged from 20 to 29 April (Figure 2).

Information on disease onset was available for 93 cases. The first of the 93 cases reported onset of illness (any symptom) on 19 April, and the most recent case reported onset on 4 May (Figure 3).

More than 2,000 contacts have been traced and followed. Of these, 39% were household members of cases and 45% friends of cases. Twenty-one confirmed secondary cases and one tertiary case have been reported. Secondary cases were family or close contacts of cases with history of travel to Mexico. Five secondary cases were infected by primary cases that did not meet clinical criteria. The

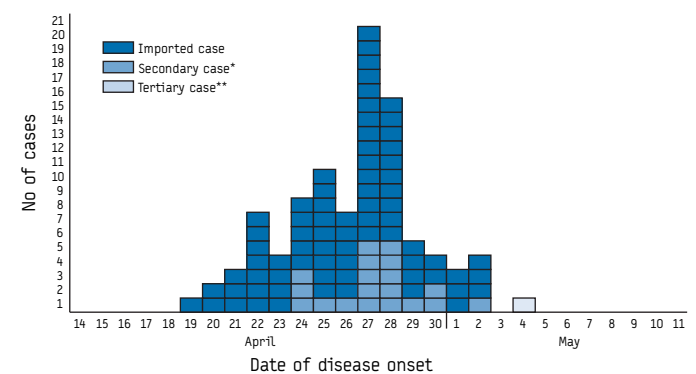
**FIGURE 2**

**Cases of laboratory-confirmed new influenza virus A(H1N1) infection, by date of travel return to Spain, as of 11 May, 2009 (n=70)**



**FIGURE 3**

**Cases of laboratory-confirmed new Influenza virus A(H1N1) infection, by date of disease onset, Spain, as of 11 May 2009 (n=93)**



\* contact of a confirmed imported case  
\*\* contact of a confirmed secondary case

tertiary case was a family contact of a secondary case. Analysis of secondary transmission is ongoing.

Four secondary cases had received prophylaxis with oseltamivir before being diagnosed as cases.

From the analysis of disease onset for primary and secondary cases, the median of the serial interval was estimated to be 3.5 days, ranging from one to six days. The estimation for the maximum incubation period ranged from one to seven days, with a median of three days.

### Demographic and clinical features

Cases ranged in age from 14 to 55 years, with an average of 24 years (standard deviation (SD) 6.3) and a median of 22; 50 (51%) cases were male.

The most frequently reported symptoms were fever (96%) and cough (95%). Four cases did not have fever. Among 41 cases for whom this information was available, 17 (41%) reported diarrhoea (Table 3).

No deaths have been reported. Disease presentation has been described as a mild influenza-like illness with full recovery in all cases. Some cases were hospitalised at the beginning of the outbreak for respiratory isolation following the national pandemic preparedness plan, this procedure having no association with illness severity.

No differences in disease presentation have been described for secondary cases. No pregnancies among confirmed cases have been reported.

Information on seasonal influenza 2008-9 vaccine status is available for 52 cases (53%); of these, only five cases had history of vaccination.

### Laboratory confirmation

Nose and throat swabs from cases who met clinical and epidemiological criteria were taken and referred to the national influenza reference laboratory (WHO National Influenza Centre) at the Instituto de Salud Carlos III for confirmation. Two independent

assays have been used for diagnosis; a reverse transcription (RT)-nested PCR designed for typing the nucleoprotein gene and another one for subtyping the haemagglutinin gene. An alternative RT-PCR was done in case the first two PCR gave contradictory results. Amplified products were sequenced and a phylogenetic analysis was done to identify the new A (H1N1) virus. The strain identified in all cases was confirmed as genetically similar to viruses previously isolated from cases in California (A/California/04/2009).

Detailed information on co-infection with other respiratory viruses is pending. Virological studies on antiviral sensitivity and on molecular-level indicators of severity are ongoing.

### Discussion

Spain was the first country in Europe to report a laboratory-confirmed case of new influenza A(H1N1) virus infection. Several factors may have contributed: intense air traffic and contacts with Mexico [5] but also a timely alert with high media coverage that raised early awareness among public health and healthcare professionals, as well as among the public.

An extremely efficient surveillance system and a sensitive case definition that was distributed early in the event made it possible to detect cases at the very beginning of the outbreak and to trace more than 2,000 close contacts. Secondary cases have been identified among close contacts of the first reported cases. However, they are still only a minor percentage of all reported cases and further spread of this new influenza virus into the community has not been documented. The last imported case had disease onset on 2 May, but the change in the case definition on 7 May including the US as an affected area may lead to notification of new imported cases.

The preliminary findings from the analysis of the first 98 laboratory-confirmed cases of the new influenza A(H1N1) virus infection in Spain indicate that symptoms in these cases appear to be similar to those of seasonal influenza. Cases observed are mainly distributed among young adults, reflecting the age structure of returning travellers from Mexico. This group has no risk factors for influenza complications and is difficult at this stage to assess the potential severity of this virus. For the time being, the impact of this outbreak on the healthcare services has been negligible.

### Conclusion

The evolution of this outbreak of influenza A(H1N1) in Spain is difficult to predict. Though notification of new confirmed cases has decreased and the disease seems mild, we will continue monitoring changes in the epidemiology and/or clinical severity of new influenza A(H1N1) virus infections in Spain in order to implement appropriate prevention and control measures.

### References

- Centers for Disease Control and Prevention (CDC). Swine Influenza A(H1N1) infections— California and Texas, April 2009. *MMWR Morb Mortal Wkly Rep.* 2009;58(16):435-7. Available from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5816a7.htm>
- Centers for Disease Control and Prevention (CDC). Outbreak of swine-origin influenza A(H1N1) virus infection—Mexico, March–April 2009. *MMWR Morb Mortal Wkly Rep.* 2009;58(Dispatch):1-3. Available from: [www.cdc.gov/mmwr/preview/mmwrhtml/mm58d0430a2.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm58d0430a2.htm)
- World Health Organization. International health regulations (2005). 2nd ed. Geneva: World Health organization; 2008. Available from: <http://www.who.int/ihr/9789241596664/en/index.html>

TABLE 3

### Clinical features of confirmed cases for new influenza virus A(H1N1) infection, Spain, as of 11 May 2009

Symptom	Cases with symptom/ cases for whom information is available	Percentage
Fever ( $\geq 37.5$ °C)	87 / 91	96%
Cough	83 / 87	95%
Headache	27 / 44	61%
Coryza	24 / 41	59%
Sore throat	29 / 48	60%
Myalgia	29 / 49	59%
Shortness of breath	18 / 70	26%
Malaise	23 / 38	61%
Diarrhoea	17 / 41	41%
Vomiting	4 / 32	13%

4. Centers for Disease Control and Prevention (CDC). Swine Influenza A(H1N1) infection in two children—Southern California, March–April 2009. *MMWR Morb Mortal Wkly Rep.* 2009; 58(15):400-2. Available from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5815a5.htm>
5. Fraser C, Donnelly CA, Cauchemez S, Hanage WP, Van Kerkhove MD, D’Aquila R, et al. Pandemic Potential of a Strain of Influenza A (H1N1): Early Findings *Science Express* 11 May 2009. DOI: 10.1126/science.1176062. Available from: <http://www.sciencemag.org/cgi/content/abstract/1176062v1>

This article was published on 14 May 2009.

Citation style for this article: Surveillance Group for New Influenza A(H1N1) Virus Investigation and Control in Spain. New influenza A(H1N1) virus infections in Spain, April–May 2009. *Euro Surveill.* 2009;14(19):pii=19209. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19209>