EDITORIAL

A/H1N1v influenza pandemic in Italy: an update

P. CROVARI, M. ALBERTI, R. GASPARINI
Department of Health Sciences, University of Genoa, Italy

At the end of March/beginning of April 2009, a new type A influenza virus, subtype H1N1 (A/H1N1v), appeared on the world epidemiological scene. This subtype emerged from the re-assortment of two viruses that had long been present in swine in Americas and Eurasia respectively [1]. The first human cases of illness were reported in Mexico and the United States, and within a few weeks the virus had spread worldwide with unprecedented speed through direct person-to-person transmission. On account of this rapid evolution, attention regarding preparation and the response to the influenza pandemic was raised by the World Health Organization (WHO) to the maximum level of alert, level 6 (on 11th June 2009), corresponding to an increased and prolonged transmission of the virus in the populations of numerous countries in the world [2].

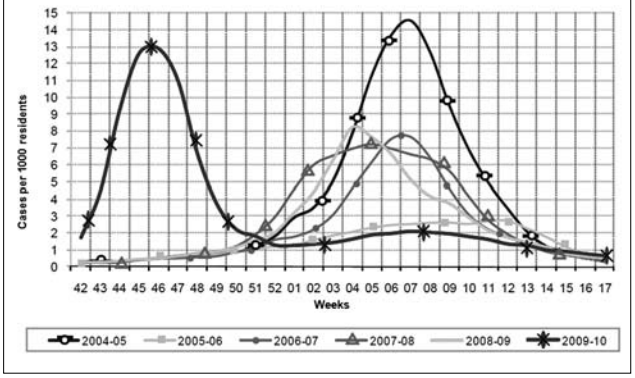
With regard to the susceptibility of the world population to the new virus, studies carried out by the Centers for Disease Control and Prevention (CDC) on serum samples gathered before the beginning of the pandemic revealed that a high percentage of subjects aged > 60 years possessed antibodies against the new virus; a considerable proportion of subjects with antibodies against A/H1N1v was also detected in the 18-60-year age-group, while cross-reactive antibodies were not found in children or adolescents (< 18 years) [3]. These findings suggest that some degree of pre-existing immunity towards the new virus was present in adults and, especially, the elderly. The most probable explanation for this is that these two age-groups had already been exposed to the virus either through infection or vaccination with an A/H1N1virus that was partially related, genetically and antigenically, to the new A/H1N1v.

This background situation influenced the course of the pandemic. Indeed, the new virus spread easily among children and adolescents, causing an important pre-seasonal (October-November) epidemic peak both in Italy and in the temperate zones of the northern hemisphere, while the incidence in adults and elderly subjects was low [4].

The rapidity of the spread of the virus and the risks of serious public health consequences prompted activation of the pandemic plan [5] which had previously been drawn up following the alarm caused by the H5N1 virus (avian flu). In Italy, various monitoring systems, some already operating and some newly implemented, enabled the course of the pandemic and its consequences to be controlled. Epidemiological surveillance, based on a network of sentinel physicians recruited by the various Italian Regions, revealed that the epidemic reached its peak in the 46th week, with an incidence of about 13 cases per 1000 residents assisted by the National Health Service: a higher value than that reached in the four previous influenza seasons, though lower than in 2004-2005 (Fig. 1). Moreover, the curve of the epidemic displayed a narrower base than the previous epidemics, owing to the rapid decline in incidence. From the 43rd week of 2009 to the first week of May 2010, it was estimated that 5,582.000 new cases of influenza syndrome occurred [6].

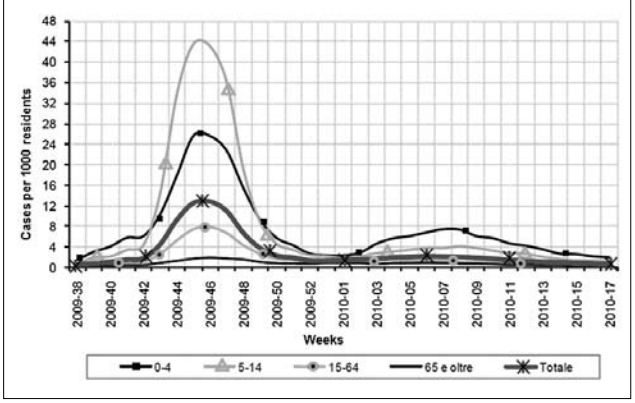
In comparison with previous years, the 2009-10 season displayed two substantial differences due to the unforeseen circulation of the new virus. Indeed, a sharp rise in the epidemic curve occurred several weeks earlier than in the typical influenza season, followed by an equally rapid decline a few weeks later. Moreover, the peak of morbidity chiefly involved the 5-14-year age-group (Fig. 2), with the virus spreading rapidly among schoolchildren; by contrast, intra-family transmission proved to be lower than expected.

Fig. 1. Incidence of influenza epidemics from the 2004-05 season to the 2009-10 season.



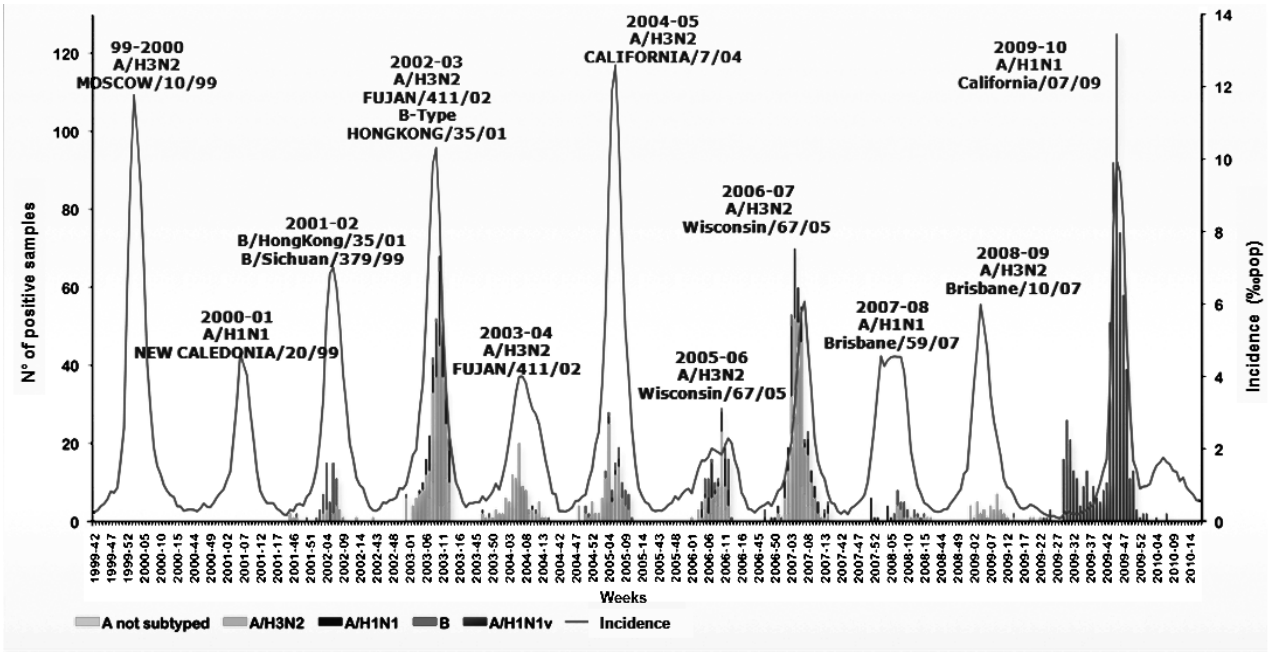
Source: Ministry of Health, Influnet.

Fig. 2. Incidence of influenza by age-class in the seasons 2008-09 and 2009-10.



Source: Ministry of Health, Influnet.

Fig. 3. Virological surveillance from the 1999-2000 season to the 2009-10 season.



Source: Inter-University Centre for Research on Influenza and Viral Infections.

Another representative finding was provided by the virological surveillance. Analyzing the data of the Inter-University Centre for Research on Influenza and Viral Infections, based on a network of laboratories which carry out surveillance through samples collected both by sentinel physicians and by hospitals, it showed that the A/H1N1v has clearly dominated the virological scene; only a few type B strains were isolated from children in January-February 2010 (Fig. 3).

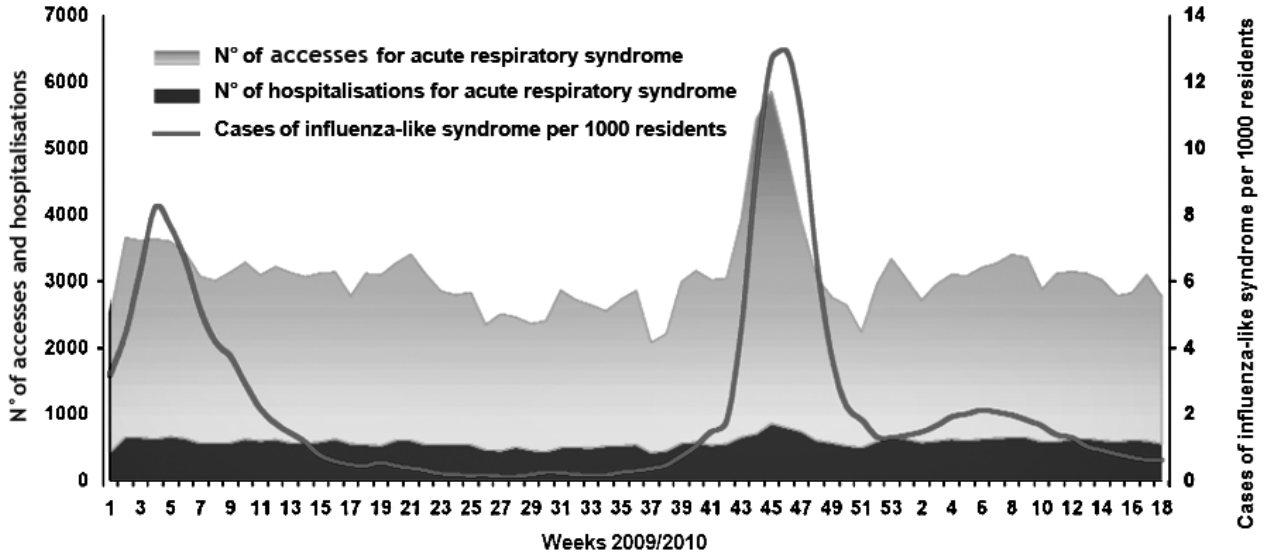
In addition, the number of accesses to emergency departments for acute respiratory syndrome (principal diagnosis based at least on one of these ICD IXCM codes: 462, 466, 480, 487, 786, 793, 780) was monitored in several Italian Regions, as this is an indirect indicator of the activity of influenza viruses. The number of admissions began to rise in the 41st week and peaked in the 44th week, when the epidemic alert threshold was exceeded in all age-groups except for persons over 65 years old (Fig. 4) [7, 8]. The alert threshold has been estimated using a statistical model of cyclical regression based on historical data sent to emergency room. Weekly data collected were compared with the baseline calculated by the model.

A special surveillance programme was also activated to monitor deaths linked to the new A/H1N1v. A total of 259 deaths were recorded from the beginning of the epidemic. Of these, 41.7% were of women; the age-groups most affected were those of subjects from 15 to 44 years of age (32.4% of deaths) and from 45 to 64 years (34%). The most severely affected Regions were Campania, with 52 deaths, followed by Puglia (36), Lazio (29), Piedmont (26), Sicily (24) and Calabria (16). Two Regions (Valle d'Aosta and Sardinia) did not register any deaths [5]. As pointed out by the WHO, virologically ascertained deaths are to be distinguished from those calculated statistically each year as excess mortality [9, 10].

The initial data provided by national and international surveillance programmes indicated the trend in A/H1N1v infections and revealed a significant incidence of respiratory complications, especially of pneumonia rapidly evolving to Acute Respiratory Distress Syndrome (ARDS), particularly in young adults. Accordingly, in November 2009, the national network for the management of ARDS caused by pneumonia due to A/H1N1v and the possible use of ECMO (Extra Corporeal Membrane Oxygenation) therapy was set up [11]. Although most A/H1N1v infections were clinically mild or moderate, in some cases major pulmonary complications arose. The high quality of clinical management of patients with severe complications in intensive care units undoubtedly saved many lives and avoided the need for prolonged hospitalisation.

Containment measures (diagnostic tests, voluntary isolation, personal hygiene, anti-viral prophylaxis) proved effective from May to September 2009. Nevertheless, considering that the most efficacious means of containing a pandemic is vaccination, a specific vaccine was speedily produced, in accordance with the indications of the WHO and the regulations of the European Medicines Agency (EMA), and the preparation Focetria® (Novartis) became available in Italy in the second half of October 2009 [12]. A campaign of immunisation with the pandemic monovalent vaccine was then launched. Initially, this was aimed at Health Care Workers, workers in essential public services and those subjects aged < 65 years who were at risk of complications in the event of infection (Ministry of Health ordinances of 11th and 30th September 2009; Ministry of Health ordinance of 3rd December 2009) [13-15].

Fig. 4. Emergency Department accesses and hospitalisations for acute respiratory syndrome and weekly incidence of influenza-like syndromes.



Source: Higher Institute of Health, Flunews.

Unfortunately, however, as a result both of the fact that the vaccine became available when the epidemic had already started and of misinformation regarding the safety and efficacy of the vaccine with respect to a pathology that was regarded as mild, overall compliance with vaccination was low in comparison with the level predicted by the previously constructed models.

By contrast, in other European countries broader approaches were adopted; a large portion of the population was vaccinated without distinction in terms of individual characteristics or age-group. In Italy, a total of 871,277 first doses and 52,782 second doses were administered [5]. The category which registered the highest rate of vaccine coverage (15%) was that of Health Care Workers, while among at-risk subjects aged between 6 months and 65 years and among women in the second and third trimesters of pregnancy, coverage rates were 12.7% and 12.1%, respectively. Babies born preterm received 1595 doses (vaccine coverage 7.7%), while at-risk subjects aged > 65 years registered a coverage rate of 1.9%. This low value can be ascribed to the fact that the vaccination of this group of subjects became possible only in December, when the curve of the epidemic was declining and the pandemic risk was less acutely perceived.

Tab. I. Vaccine coverage by subject category.

Category	Doses administered	Population eligible	Vaccine coverage (%)
Health Care Workers	160,659	1,069,264	15.03
Subjects aged from 6 months to 65 years with at least one risk condition	549,167	4,309,466	12.74
Women in the second or third trimester of pregnancy	23,016	189,915	12.12
Minors living in communities or institutions (not included in the above categories)	1,120	10,155	11.03
Subjects aged < 24 months born seriously preterm	1,595	20,657	7.72
Security forces and Civil Protection staff Firefighters and Interior Ministry staff Armed Forces Essential public services	72,181	1,228,155	5.88
Children aged > 6 months attending nurseries (not included in the above categories)	4,618	89,394	5.17
Women who had given birth within the previous 6 months or the person caring for the baby	8,170	237,594	3.44
Subjects aged > 65 years with at least one risk condition	13,562	710,862	1.91
Periodic blood donors	6,329	742,349	0.85
Healthy subjects aged from 6 months to 17 years	20,307	7,671,581	0.26
Healthy subjects aged from 18 to 27 years	5,650	4,642,188	0.12
Subtotal	866,374	20,921,580	4.14
Subjects not included in the above categories	4,903		
Total	871,277		

Source: Higher Institute of Health, Flunews.

Overall vaccine coverage proved to be 4.1% (Tab. I). On the whole, the damage caused by the first wave of the new influenza pandemic in the 2009-2010 season was reasonably contained even though the liaison between central and regional authorities was not always optimal and the level of preparation for the pandemic differed from one region to another. Nevertheless, influenza was again confirmed as a socially serious illness that can cause hospitalisation and death. Its unpredictable nature, which fascinates researchers, requires continuous and thorough surveillance on the part of healthcare authorities. Moreover, surveillance should not be restricted to the human population, but extended to animal species, particularly swine and birds.

References

[1] Crovari P, Gasparini R. *Influenza Pandemic AH1N1v/2009 – early experience and autumn perspectives.* J Prev Med Hyg 2009;50:77-8.

[2] World Health Organization (WHO). *Statement to the press by WHO Director-General Dr Margaret Chan.* June 11, 2009. http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/index.html. Last accessed on 11 August 2010.

[3] Centers for Disease Control and Prevention (CDC). *Serum cross-reactive antibody response to a novel influenza A (H1N1) virus after vaccination with seasonal influenza vaccine.* MMWR 2009;58:521-4.

[4] Crovari P, Gasparini R. *Influenza (AH1N1v) Pandeimc 2009: an update.* J Prev Med Hyg 2009;50:129-30.

[5] Ministry of Health. *National influenza pandemic plan.* http://www.nuovainfluenza.salute.gov.it/imgs/C_17_pubblicazioni_501_allegato.pdf. Last accessed on 11 August 2010.

[6] Ministry of Health. *Influnet, report of 17th week 2010.* http://www.salute.gov.it/influenza/documenti/epidemiologica/Italia2010_17.pdf. Last accessed on 11 August 2010.

[7] Higher Institute of Health. *Flunews, report of 18th week 2010.* http://www.epicentro.iss.it/focus/h1n1/pdf/flunews/FluNews_28.pdf. Last accessed on 11 August 2010.

[8] Higher Institute of Health. *Flunews, report of 45th week 2009.* http://www.epicentro.iss.it/focus/h1n1/pdf/flunews/FluNews_28.pdf. Last accessed on 11 August 2010.

[9] Rizzo C, Bella A, Viboud C, et al. *Trends for influenza-related deaths during pandemic and epidemic seasons, Italy, 1969-2001.* Emerg Infect Dis 2007;13:694-9.

[10] World Health Organization (WHO). *Considerations for assessing the severity of an influenza pandemic.* Weekly Epidemiological Record, 2009;84:197-212.

[11] Ministry of Health. *Permanent Conference for relations between State, Regions and autonomous provinces of Trento and Bolzano. November 05, 2009.* http://www.normativasanitaria.it/jsp/dettaglio.jsp?id=31445. Last accessed on 11 August 2010.

[12] European Medicines Agency (EMA). C*HMP Assessment report for Focetria.* http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/000710/WC500023755.pdf Last accessed on 11 August 2010.

[13] Ministry of Health. *Ordinance 11th September 2009.* http://www.normativasanitaria.it/jsp/dettaglio.jsp.aggiornamenti=&attoCompleto=si&id=30255. Last accessed on 11 August 2010.

[14] Ministry of Health. *Ordinance 30th September 2009.* http://www.normativasanitaria.it/jsp/dettaglio.jsp?id=30406. Last accessed on 11 August 2010.

[15] Ministry of Health. *Ordinance 3rd December 2009.* http://www.normativasanitaria.it/jsp/dettaglio.jsp?id=31555. Last accessed on 11 August 2010.

■ Received on August 11, 2010. Accepted on September 29, 2010.

■ Correspondence: Marisa Alberti, Department of Health Sciences, University of Genoa, via Pastore 1, 16132 Genoa, Italy - E-mail: marisa.alberti@unige.it