

SHORT ARTICLE

The response of the Liguria Region (Italy) to the pandemic influenza virus A/H1N1sv

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summary

Influenza is a cause of acute respiratory disease. It has a typical epidemic nature during the winter season, but may also assume a pandemic pattern when a completely new virus spreads among humans. Influenza places a heavy economic and healthcare burden on both the National Health Service and society.

During the 2009/2010 influenza pandemic season, the Liguria Region drew upon the specific skills of the various sectors of the Department of Health and Social Services. In collaboration with the Department of Health Sciences of the University of Genova, the Regional Health Agency (RHA) and other public organizations, steps were taken to address the issues of technical and sci-

entific updating and the coordination of all the departments of Local Healthcare Units in Liguria.

The main activities conducted at the regional level provided an adequate response to the influenza pandemic. These activities focused on Local and National Influenza Surveillance Systems, the regional Pandemic Plan, vaccination strategies for seasonal and pandemic influenza, and the communication of data from monitoring programs (sentinel physicians – syndromic surveillance).

The prevention of influenza transmission and containment of epidemics and pandemics require effective communication strategies that should target the whole population.

Introduction

Influenza is a highly infectious respiratory disease. It is generally benign, but may cause serious complications, especially in patients with chronic disease, the elderly, young children and pregnant women. The World Health Organisation (WHO) reports 3-5 million cases of influenza annually [1]. Seasonal epidemics typically involve 3 to 5% of the population, with peaks up to 10% depending on the size of the antigenic drift of viruses involved. Not only does influenza cause serious health problems, it also engenders high direct and indirect costs for society as a whole [2]. During the 2009-2010 season, a new influenza virus, A/California/07/09, also called H1N1sv or H1N1v, spread throughout the world. Given the widespread circulation of this virus, its features and the vulnerability of the population (especially children and young people), international organizations (WHO) issued a phase-6 (pandemic) alert on June 11, 2009 [3]. Studies of evolutionary influenza genomics indicated that this new US strain had arisen as a result of reassortment between two viruses present in pigs for some time:

- a pig virus strain H1N1 derived from a triple reassortment, which incorporated RNA segments of human and avian influenza into its genome, this triple-reassortant American strain had circulated in pigs for about 10 years without creating serious problems either for humans or for the animals themselves;
- a strain of the H1N1 swine virus of Eurasian lineage, which had long caused sporadic outbreaks of swine

flu in farms in Europe and Asia, without human involvement [4-6].

Once transmitted to humans, this new virus proved to be capable of causing disease clinically similar to “classical” influenza, and to be transmitted directly from person to person through the air, like the previously known human flu viruses; the outbreak of these new viruses occurred in North America.

Fortunately, the 2009 A/H1N1 influenza pandemic proved to be less deadly than had first been feared. Indeed, in the opinion of many experts, the “severity” of the pandemic was mild, being slightly higher than that of seasonal influenza in the USA and Canada, though markedly higher in Mexico [7, 8].

During both epidemics and pandemics, strategies to mitigate and contain influenza rely on well-known effective non-pharmaceutical and pharmaceutical interventions, such as personal hygiene, wearing face-masks, quarantine, social distancing and the administration of antiviral drugs and vaccines. Today, vaccination is the most effective means of preventing influenza and its potential complications [9, 10]. These strategies of containment and mitigation were described in the 2006 Italian National Pandemic Preparedness and Response and Response Plan prepared by the Directorate General for Public Health in collaboration with the Influenza subgroup of the Centre for Disease Control (CCM). This plan also provided guidance for the preparation of regional plans, which were endorsed by almost all Regions [11]. In 2009, in response to the WHO’s phase-6 pandemic

alert, a National Crisis Management (NCM) Committee, headed by the Minister of Health, was created at the national level to choose the strategies to adopt regarding preparedness, response and communication [12].

During the 2009/2010 influenza pandemic season, the Liguria Region drew upon the specific skills of the various sectors of the Department of Health and Social Services. Specifically, the Sector of Prevention, Hygiene and Public Health, in collaboration with the Regional Health Agency (RHA) and other organizations, worked to address the issues of technical and scientific updating and coordination, with specific reference to the various structures of Hygiene and Public Health Authorities operating in the area and direct calls to action in the event of a pandemic.

The main activities conducted at the regional level in order to provide an adequate response to the influenza pandemic are briefly described in the present article.

Local and National Surveillance Systems

The surveillance network of the Inter-university Centre for Research on Influenza and other Viral Infections (CIRI-IV) is active in Genoa (Liguria, Northern Italy) and coordinates other regions of Italy (Abruzzo, Calabria, Marche, Sicilia, Umbria, Lombardia, Friuli Venezia Giulia, Toscana, Puglia, Campania). Based on sentinel surveillance, it combines clinical and virological information.

It plans, organizes and manages the network of clinical and epidemiological surveillance and assesses the impact of influenza and acute respiratory diseases. It also promotes national and international research on influenza and acute respiratory diseases, particularly with regard to etiology, epidemiology and prevention. Moreover, it monitors the isolation and identification of circulating influenza viruses and their antigenic and genetic features. The centre collaborates with national scientific societies and research institutions that contribute to data collection (the National Institute of Health, the Italian Society of General Medicine, the Centers for Disease Control [CCM], Ministry of Health, Italian Federation of Medical Paediatrics [FIMP]), and is part of the European surveillance system coordinated by the WHO [13].

In particular, the CIRI-IV provides scientific support for the regional Public Health Services. During the 2009/2010 pandemic season, weekly reports by the CIRI-IV were distributed to local stakeholders.

Since July 2007, the Liguria Region has funded a project, proposed by the Department of Health Sciences of the University of Genova, to implement a syndromic surveillance system able to readily detect clusters of Influenza-Like Illness (ILI) and Lower Respiratory Tract Infections (LRTI) through the analysis of data on admissions to the Emergency Department of a regional reference hospital, San Martino Hospital in Genoa [14]. Syndrome coding, data gathering, transmission and processing, statistical analysis to assess indicators of disease activity and alert thresholds, and signal response are systematically registered. The project also seeks to improve the system of communication with relevant institutions, including the Department of Health and Social Services of Liguria,

the prevention departments of Local Health Agencies (LHA), hospitals and other institutions involved.

The system of feed-back includes periodic reports on early warnings sent by e-mail to the representatives and operators of the institutions involved.

During the pandemic, the CIRI-IV and syndromic surveillance constituted an important system that monitored the local setting, providing relevant information on the spread of the influenza virus and morbidity in the population.

Regional Pandemic Plan

The Regional Plan for the organization of a health response in the event of A/H1N1 pandemic influenza was promptly prepared (DGR n. 1255 of 21/09/2009) [15] and was distributed to healthcare managements and professionals directly involved in the field. The Regional Plan provided for joint actions applicable to the entire region and other response actions to be implemented directly by the healthcare facilities on regional management lists. This plan was aimed at strengthening preparedness and response by improving epidemiological and virological surveillance (identification, confirmation and daily reporting of cases), implementing containment measures at an early stage of a pandemic (isolation, border restrictions, probable/confirmed cases, contact tracing), and reducing the impact of the disease by applying pharmaceutical and hygiene measures. To determine an adequate emergency response, four phases of response were drawn up, and indicators for the progressive activation of specific territorial surveillance activities were defined. Furthermore every LHA had prepared its plan.

Other measures applied

Briefly, the following joint actions were carried out at the regional level:

1. VACCINATION STRATEGIES FOR SEASONAL AND PANDEMIC INFLUENZA

During the phase-6 pandemic alert, the active immunization strategies to be adopted in the 2009/2010 season had to be revised in accordance with the possible co-circulation of the seasonal influenza virus and the new H1N1 virus. This eventuality raised the need to administer two vaccines: a trivalent vaccine containing the strains A/Brisbane/59/2007 (H1N1)-like virus, A/Brisbane/10/2007 (H3N2)-like virus and B/Brisbane/60/2008-like virus, and a monovalent vaccine against the new H1N1 variant, obtained by means of a reverse-genetics technique.

Once available, the pandemic vaccine was administered mostly through the vaccination service; the seasonal vaccine was administered by general practitioners, paediatricians and the vaccination service. The Ministry of Health sent ordinances, recommendations and circulars on pandemic vaccination and target groups to the Department of Health and Social Services of Liguria.

2. COMMUNICATION OF DATA OF MONITORING PROGRAMS (SENTINEL PHYSICIANS – SYNDROMIC SURVEILLANCE)

Every region was required to send in weekly reports indicating the total numbers of probable, possible and confirmed cases and deaths due to pandemic influenza. Data communication was coordinated at the regional level, and newsletters dedicated to H1N1 influenza were prepared by RHA that provided updates on the epidemic and the most recent knowledge on the matter through downloads at <http://www.arsliguria.it> [16].

3. HYGIENE MEASURES TO REDUCE THE RISK OF TRANSMISSION, AND INFORMATION ON THE PREVENTION, SURVEILLANCE AND CONTROL OF THE PANDEMIC

Hygiene recommendations were issued to the population, especially schoolchildren, students, teachers, state employees etc. The most frequent advice was: to stay at home if ill, to wash hands often, especially after frequenting public places (public transport, schools, hospitals, etc.), and to muffle coughs and sneezes with a handkerchief or in the fold of the elbow. Self-diagnosis was also encouraged, so as not to overcrowd physicians' offices.

4. AVAILABILITY OF ANTIVIRAL DRUGS

The availability of specific drugs against the influenza virus is recognized as an important element in preparing the response to pandemic influenza [17, 18]. The Scientific Committee of the CCM, in collaboration with the Technical Committee of the Italian Drug Agency (AIFA), issued recommendations and opinions on the usefulness of antiviral drugs in a situation of pandemic influenza.

Antiviral drugs may be used to treat pandemic influenza, as they can mitigate the severity of the disease and reduce the risk of complications and death. They can also be used by people who have had close contact with a flu patient, and who may therefore have been infected. Antiviral drugs are useful in the early stages of a pandemic, or when the person exposed to the infection carries out public tasks, such as health care and assistance; they cannot be used for prophylaxis in general, as they are efficacious only when taken immediately before exposure or within 48 hours after contact.

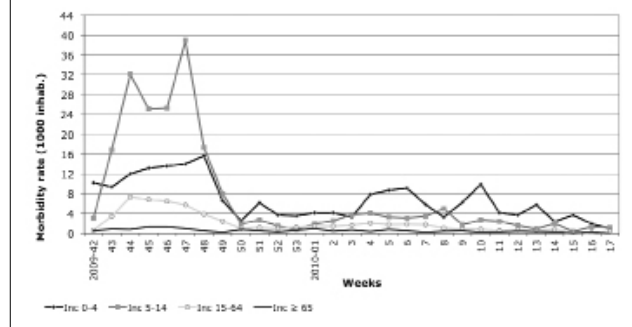
On August 21, 2009, the WHO published guidelines on the use of antivirals for the treatment of patients who contracted the new H1N1 flu virus [19].

Results and discussion

The Regional Commission on Vaccines and Infectious Diseases and the Regional Pandemic Committee made important technical and scientific contributions to the field monitoring and management of the pandemic. The Liguria Region oversaw the vaccination campaign and managed the usability of antiviral drugs.

The pandemic period was characterized by an early epidemic peak (mid-October–mid-November) as reported in Figure 1. The highest incidence was observed in

Fig. 1. Morbidity x 1,000 inhabitants, influenza like illness for age class (data from CIRI-IV).



schoolchildren (38.0% peak in November), while in the elderly, morbidity was very low. The Regional Surveillance System extended its activity to monitoring the incidence of medically attended ILI to identify the extent of the seasonal epidemic and collecting information on circulating viral strains from week 42 of 2009 to week 17 of 2010.

The Regional Plan provided for joint actions applicable to the entire region and other response actions to be taken directly by the healthcare facilities on regional management lists. The Regional Prevention Department applied vaccination strategies for seasonal and pandemic influenza and monitored programs by means of syndromic surveillance and sentinel physicians.

The sector "Prevention, Hygiene and Public Health" worked with other agencies in the field to publicise measures to reduce the risk of transmission. In the future, however, further research will be necessary to educate the public and to inform policy-makers as to what measures should be recommended and how they should be implemented [20]. Vaccination is undoubtedly the most efficacious means of providing protection against influenza infection. Nevertheless, the pandemic vaccines were not widely accepted by the population and health personnel. This could be explained by the manner of European Medicine Agency authorization (mock-up vaccine procedure and use of clinical data supporting the safety and effectiveness of vaccines developed from the influenza A/H5N1 strain) and the presence of adjuvant (MF59-squalene) [11].

Vaccination coverage by the first and second pandemic vaccine doses is shown in Table I. Coverage of 3.17% was achieved in subjects aged < 65 years and of 3.91% in those aged > 65 years in Liguria. Higher coverage rates were achieved in Liguria than in Italy as a whole among blood donors (7% vs. 0.8%) and subjects with at least one chronic underlying condition aged 6 months-65 years (15% vs. 12.7%). By contrast, vaccine coverage was lower in Liguria than in Italy as a whole among chronic patients aged > 65 years (0.3% vs. 1.9%) and children aged < 6 months attending nursery/day care centres (0.4% vs. 5.2%). Vaccination coverage was not registered in the class "subjects younger than 24 months born preterm" in Liguria.

In sum, the Regional Action Plan, which was worked out in collaboration with LHA, was aimed at minimizing

Tab. I. Ligurian coverage of pandemic influenza vaccination by target group in the period October 2009 - April 2010.

| Target groups | Number of first doses administered in Liguria | Number of second doses administered in Liguria | Regional vaccine coverage % | Number of first doses administered in Italy | Italian vaccine coverage % |
|--|---|--|-----------------------------|---|----------------------------|
| Healthcare personnel | 3,750 | | 15 | 165,562 | 15.5 |
| Essential service personnel (armed forced) | 1,219 | | 4 | 72,181 | 5.9 |
| Blood donors | 557 | 6,329 | 7 | 6,329 | 0.8 |
| Pregnant women in second or third trimesters | 688 | | 11 | 23,016 | 12.1 |
| Women who have delivered in the previous 6 months or persons who take care of babies | 196 | | 3.2 | 8,170 | 3.4 |
| Subjects with at least one chronic underlying condition aged 6 months-65 years | 11,775 | 1,148 | 15 | 549,167 | 12.7 |
| Subjects with at least one chronic underlying condition aged > 65 years | 409 | 153 | 0.3 | 13,562 | 1.9 |
| Children aged < 6 months who attend nursery/day care centres | 25 | 19 | 0.4 | 4,618 | 5.2 |
| Children living in communities | 74 | 1 | 12 | 1,120 | 11.0 |
| Subjects younger than 24 months born preterm | 11 | 3 | - | 1,595 | 7.7 |
| Persons 6 months-17 years | 145 | 54 | 0.71 | 20,307 | 0.3 |
| Subjects 18-27 years | 43 | 8 | 0.04 | 5,650 | 0.1 |
| Total | 18,892 | 7,715 | 3.17 | 871,277 | 4.2 |

the consequences of pandemic influenza. A multidisciplinary approach was adopted in order to implement interventions in different phases, and updated information was promptly made available to decision-makers, health professionals, the media and the community. National

and regional preparedness and response were the guiding principles in tackling the influenza pandemic. The prevention of influenza transmission and containment of epidemics and pandemics require efficacious strategies that target the whole population.

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