

The 2009 pandemic in Mexico: Experience and lessons regarding national preparedness policies for seasonal and epidemic influenza

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Abstract

Influenza is a viral respiratory disease capable of causing epidemics that represent a threat for global security. Mexico was the first country to notify the WHO of an outbreak of what later became the first influenza pandemic of the 21st Century, caused by the virus A(H1N1)2009. Before this event Mexico had a national pandemic influenza preparedness plan, which included seasonal influenza vaccination, stockpiles of personal protection equipment and strategic drugs, and risk communication strategies. During the epidemic, the national public health laboratory network and case surveillance systems were strengthened together with surge capacities for intensive care and delivery of antiviral drugs. Risk communication was conducted for people to comply with implemented measures regarding social distancing (workplace and school closures, household quarantine). This report describes the Mexican experience during the 2009 influenza pandemic and the lessons that this experience provides to public health preparedness for future pandemics. (Gac Med Mex. 2017;153:102-10)

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Resumen

La influenza es una enfermedad viral respiratoria capaz de ocasionar epidemias que representan una amenaza para la seguridad mundial. México fue el primer país que notificó a la Organización Mundial de la Salud un brote que habría de convertirse en pandemia, que fue la primera del siglo XXI causada por el virus A(H1N1)2009. Antes de este evento, México contaba con un plan de preparación nacional que incluía vacunación estacional, reservas de equipo para protección personal y fármacos antivirales, así como estrategias de comunicación. Durante la epidemia se fortaleció la red nacional de laboratorios de salud pública, así como las capacidades de crecimiento de las unidades de terapia intensiva y el sistema de distribución de medicamentos antivirales. Se condujo una comunicación de riesgos para que la población tuviera apego con las medidas implementadas, tales como el distanciamiento social (cierre de escuelas y centros de trabajo, cuarentena en domicilio). Esta revisión describe la experiencia mexicana durante la pandemia de influenza de 2009 y las lecciones aprendidas, que son de utilidad para la preparación contra epidemias futuras.

PALABRAS CLAVE: Influenza. Pandemia. Preparación.

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Background

Type A influenza viruses cause large pandemics that may threaten national and global security by overwhelming public health capacities and healthcare facilities. Pandemic influenza A(H1N1) 2009 was the first public health emergency of international concern (PHEIC) declared by the World Health Organization under the International Health Regulations (IHR) of 2005.

Clinical presentation of influenza is characterized by sudden onset of fever greater than 37.9 °C (although some patients may not be feverish), cough, sore throat, headache, muscle and joint pain, runny nose, and often, intense malaise. The predominance of high fever and cough over nasal symptoms helps differentiate influenza from the common cold, but the illness caused by many viruses may have symptoms similar to those of the “influenza like illness “. In fact, in most countries, the definition of influenza like illness is simple: fever > 37.9 °C together with cough or sore throat. Most people recover without medical attention; however, vulnerable populations (e.g. pregnant women and people with chronic conditions or morbid obesity) comprise key high-risk groups for severe pneumonia, complications, and death. The deregulated release of cytokines (“cytokine storm”) has been proposed as a major biological underpinning of acute lung injury and multiorgan failure in individuals infected by influenza¹. Anti-influenza vaccination is a widely accepted public health intervention for preventing severe influenza, reducing hospitalizations and mortality. Other preventive measures include social distancing, frequent hand washing, respiratory etiquette (i.e. covering mouth and nose when coughing or sneezing, and avoiding touching the face)².

Seasonal influenza

Influenza viruses are notable for their adaptability. They accumulate small changes in their genetic constitution, resulting in the yearly seasonal appearance of viral variants. In the Northern hemisphere, the influenza season typically starts in early October, peaks in January and February, and tapers in late March. In the Southern hemisphere, the winter seasonal influenza peak occurs between June and August.

The World Health Organization (WHO) estimates that about 1,000 million cases of seasonal influenza occur in the world each year (~15% of the population), leading to 300,000 to 500,000 deaths³. In the USA,

influenza claims the lives of about 36,000 people and the hospitalization of another 200,000, with medical costs of about 10 billion USD⁴. In Mexico, information on influenza morbidity is limited; Charu, et al estimated that seasonal influenza epidemics from 2000 through 2008 were responsible for an average of about 19,200 all-cause excess mortality per year⁵.

Pandemic influenza

Pandemic influenza originates in at least two mechanisms: re-assortment between an animal influenza virus and a human influenza virus that yields a new virus, and direct spread and adaptation of a virus from animals to humans⁶. Against those new viruses, people have no immunity and a pandemic that affects millions around the world then arises, which can become very serious if the new variants are particularly virulent and easily transmitted.

Three major pandemics of influenza occurred in the 20th century: the 1918 Spanish influenza A(H1N1) virus, the 1957 Asian influenza H2N2 virus, and the 1968 Hong Kong influenza H3N2 virus. The pandemic 1918 influenza killed at least 50 million people worldwide, with adults aged 20-50 years suffering the highest rates of morbidity⁷; incidentally, this mortality pattern was observed again for the new variant A(H1N1)pdm in 2009^{8,9}.

Antiviral drugs and vaccines are key tools to forestall influenza pandemics. The effectiveness of these measures heavily depends on the ability of the surveillance system to detect a pandemic influenza strain quickly; once the strain is identified, the potential use of antiviral drugs may be assessed. Specifically targeted vaccines cannot be produced until a pandemic strain is identified; vaccines will be available 20-23 weeks after the strain is identified. Therefore, vaccines are likely to play little or no role in efforts to forestall a pandemic in its initial phases.

Countries that experience earlier outbreaks of a pandemic are more likely to experience healthcare saturation than countries distant to the origin, as the latter have a vital time lag to activate public health responses and to decide how many doses of the new vaccine they may acquire (if available), identify and protect the groups with high risk to become infected, mitigate the threats to governance, implement risk communication strategies to prepare the community response and avoid panic, and finally, to lobbying with representatives (community leaders, parliamentarians, and heads of state) for the immediate release of emergency resources and supplies to better prepare and to help the affected areas.

The pandemic of 2009 and the Mexican reaction

On April 21, 2009, the Centers for Disease Control and Prevention (CDC) in the USA reported the identification of a novel influenza A (H1N1) virus¹⁰. At that time, the report expressed concern that the new strain could infect a large proportion of the population and that the seasonal influenza vaccine might not provide adequate protection. The virus was reported to have resistance to the adamantane antiviral drugs and be sensitive to oseltamivir and zanamivir; it was a chimeric strain with genetic material originated from four different influenza A viruses circulating in birds, pigs, and humans^{11,12}. In Mexico, the circulation of this strain concurred with increased rates of severe pneumonia, predominantly in young adults, in March and April 2009¹³. Such unusual age switch in the distribution of pneumonia was reported to the WHO as compatible with a PHEIC, as defined by the IHR of 2005. A subset of samples from cases of influenza-like illness were shared with the CDC and the Public Agency of Canada, the first as part of Mexico's participation in the Global Influenza Surveillance and Response System, and facilitated by the North American Plan for Avian and Pandemic Influenza. On April 23, cases were confirmed by the Public Health Agency of Canada as influenza A(H1N1)pdm2009 and hours later by the CDC Influenza Division, which led to the immediate declaration of a national health emergency and triggered the response contemplated by the National Influenza Plan. On April 25, the WHO stated that the outbreak in Mexico and the USA was an international emergency¹⁴; finally, the existence of the pandemic was declared on June 11^{15,16}. In August 2010, the WHO officially declared the end of the pandemic and the beginning of a post-pandemic phase.

The fact that the pandemic began in the Mexican-USA border left important lessons: influenza pandemics can start in any place and the risk of another one has not diminished. Looking back, we now know that the virus lacked the virulence that was anticipated; it was simply chance that allowed that the new virus was no more lethal and had no wider resistance against available drugs. In economic terms, however, the 2009 pandemic in Mexico had an estimated cost of about 0.7% of GDP^{17,18}. It is estimated that in the first year after the emergence of the A(H1N1)pdm2009, between 20 and 50% of the Mexican population was infected with the new virus, disproportionately affecting individuals aged 5-59 years. The pandemic in Mexico was associated with 11.1 excess of all-cause deaths

per 100,000 population and 445,000 years of life lost during the three waves of virus activity from April to December 2009⁵.

Regarding global mortality, the WHO reported 18,631 laboratory-confirmed pandemic deaths, but it is clear that the total pandemic mortality burden was higher. Mexico alone, with about 2% of the world's population, reported 1,316 laboratory-confirmed deaths, which means that real global mortality was substantially higher if, as expected, even Mexico's report underestimates the final count. In fact, new analyses estimate that the 2009 global pandemic mortality was ~10-fold higher than the WHO's laboratory-confirmed mortality tally; for Mexico, it is estimated that laboratory-confirmed deaths represent 1/7 pandemic excess deaths overall, and 1/41 deaths in persons less than 60 years of age in 2009^{5,19}.

Preparedness of Mexico and response to the 2009 pandemic

As a result of the SARS/coronavirus crisis and the re-emergence and continuing spread of the highly pathogenic H5N1 virus in Asia, Mexico initiated in 2003 its National Influenza Preparedness Plan (NIPP), which was completed in 2005, with a national full-scale exercise in 2006. The NIPP was further complemented and reviewed in accordance with the North American Plan for Avian and Pandemic Influenza developed by the Mexican, United States, and Canadian governments. The NIPP delineated activities for local preparedness and inter-sectorial work to ensure the continuity of social operations.

The strategic actions for the health sector included: development of risk communications strategies and pre-tested education material, seasonal influenza vaccination campaigns, preparedness plans for hospitals and primary care centers, strategic stockpiling, strengthening of epidemiological and laboratory surveillance, and supporting influenza research. In 2007, an independent evaluation ranked the Mexican NIPP with a completeness score of 60%²⁰. By 2008, the health services activities included an annual seasonal flu vaccine (20 million doses for about 110 million inhabitants), which prepared the system for the distribution and dispensation of influenza vaccines. In addition, Mexico signed a collaborative agreement with Sanofi-Pasteur to develop self-sufficiency for influenza vaccine manufacturing, which was regarded as a national security issue. The agreement included the obligation to provide vaccine if a pandemic happened before the plant was finished.

Stockpiling included oseltamivir in bulk powder to produce 1.2 million treatment packages, as well as antibiotics to treat secondary bacterial lung infection and personal protective equipment (gloves, gowns, goggles, face shields). In addition, a pre-tested risk communication campaign was designed to communicate influenza information, risks, possible effects, and practices to mitigate the risks. All these anticipatory actions were useful when Mexico had to face the unusual situation of being the epicenter of a pandemic (not considered in the NIPP). Once the pandemic was recognized, Mexico's response was timely and transparent, allowing an early international warning and the possibility to develop preparation measures in distant countries. Actions were promptly implemented, such as social distancing procedures (closing of schools and some economic activities in the metropolitan area of Mexico City and its surroundings), which gave a period to delineate actions and gather resources. Internally, the distribution of antiviral drugs and vaccines was performed by the company responsible for the production and distribution of vaccines at a national level (Birmex).

Vaccines

The reason to have an influenza vaccine manufacturing capacity is fundamental for any country's sovereignty. During pandemics, producing countries may enact production embargos, canceling commercial trade for vaccines, until their own populations are covered. For such reasons, the WHO is developing a project to increase the production of influenza vaccine by domestic producers in order to improve regional availability during pandemics²¹. Additionally, governments may choose to sign agreements for advance purchase, without a guarantee for timely delivery. In the USA, local vaccine production was planned to cover the highest risk groups as soon as the vaccine became available (people involved in the pandemic response and who provide care for persons who are ill, those who maintain essential community services, pregnant women, children, and those involved in national security.) People in these groups were calculated to be 159 million, and from those, a subset of 42 million was identified to be the first recipients; however, at that time only 16.5 million doses of vaccine were available²². The combination of slow vaccine production and the evolution of the pandemic resulted in a lower number of people vaccinated by the spring of 2010. Only about 90 million from a total of 229 million produced vaccines were administered; even with such a low coverage, the

vaccination has been calculated by the CDC to prevent between 700,000 to 1,500,000 clinical cases, 4,000 to 10,000 hospitalizations, and 200 to 500 deaths²³.

Mexico, despite international agreements, received their first 600,000 A(H1N1)pdm2009 vaccines in November 2009²⁴; once that they became available in 2010, the uptake was excellent (Fig. 1) and the vaccination campaign went fast, focused on priority groups: (i) healthcare workers, (ii) young adults with underlying chronic conditions, (iii) pregnant women, and (iv) children aged six months to six years. At the end of 2010, 28.5 million doses were administered free of charge, with few reported cases of severe adverse effects, and notably, no cases of Guillain-Barre syndrome found. During the pandemic, vaccination against A(H1N1)pdm2009 was subject to intense media discussions that resulted in misinformation to the public. As a result, compliance with the national recommendations for pandemic vaccination among certain groups (pregnant women and healthcare workers) was low. According to the results of one national survey, one year after the emergence of the pandemic, over half of the Mexican population had anti-influenza antibody titers below the threshold of immunity, either by natural infection or vaccination with monovalent vaccine.

Antiviral drugs

Clinical trials have established the efficacy of oseltamivir and zanamivir as compared with placebo for early treatment of non-complicated influenza A²⁵. As antiviral drugs seem to work only if used early in the course of disease, public health authorities and physicians should encourage high-risk patients to seek early medical attention. Non-randomized trials, however, suggest that there may be some benefit of oseltamivir treatment started more than two days after illness²⁶.

In Mexico, having stocks of antiviral drugs helped to respond immediately. Some of the problematic situations have been described in detail by Gutierrez-Mendoza, et al.²⁷. In 2006, Mexico stockpiled oseltamivir in powder enough to produce 1.3 million treatment courses. After the emergency was declared, Mexico purchased 900,000 additional treatments (tablets) from Roche and received 700,000 treatment courses (tablets) in donation. Buying oseltamivir in bulk helps to avoid problems of expiration dates, but the reconstitution faces many difficulties because of the lack of facilities equipped or authorized to prepare pharmaceuticals. During the first weeks of the epidemic, powder was reconstituted in liquid by a private

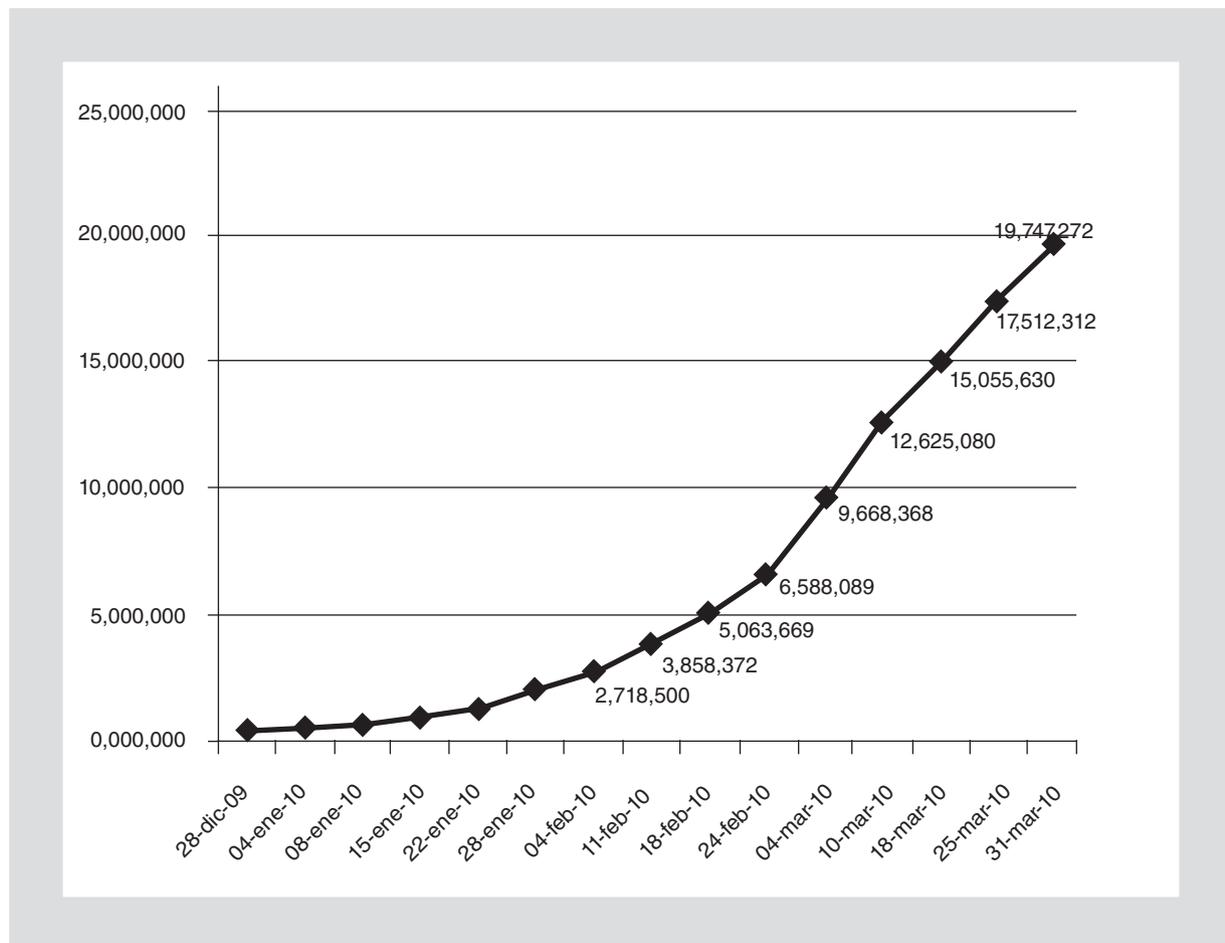


Figure 1. Uptake of pandemic influenza vaccine during the first months of its availability in Mexico.

laboratory and thereafter in tablets by the original provider (Roche). The lessons learned included that the regulatory agency needs to work in order to certify the shelf life of reconstituted drugs or the mechanisms to urgently reconstitute those bought in bulk. For Mexico, it took three weeks for distant regions to receive adequate numbers of treatment courses.

National preparedness plans against influenza

Preparing for a pandemic requires leadership and coordination from the highest levels of government. Influenza pandemics threaten countries' institutions because they create social disturbances and remove essential personnel from their workplace. This makes a pandemic a threat that requires multi-sector actions well beyond the health sector. Every country must have a well developed and updated preparedness plan against influenza, whose components have been well described by the WHO in essential documents

easily accessible (Table 1)²⁸; as seen, the vaccination program is an essential component, but not the only one. From the Mexican experience, we describe below in more detail six aspects that we consider of current major importance regarding surveillance, vaccination, communication, primary care, strategic reserves, and intensive care preparedness.

Surveillance and reporting of influenza infections

Every country must have a system to continuously monitor influenza, both clinically and epidemiologically. These systems should not count every case, but rather infer a wider scenario from sentinel units that indicate the number and proportion of influenza-like illness and severe acute respiratory diseases attended, as well as the proportion of those diagnosed with influenza by a laboratory test. Having efficient surveillance and laboratory reports, the beginning and the end of the season can be reported to the clinicians that will use

Table 1. Main aspects to consider for a national preparedness plan against influenza, according to the World Health Organization

1. Preparing for an emergency
Includes command, communication, and legal issues
2. Surveillance
Includes interpandemic and pandemic periods
3. Case investigation and treatment
Includes diagnostic capacity, epidemiological investigation, clinical management, and infection control in healthcare settings
4. Preventing spread of the disease in the community
Includes public health measures, personal hygiene, community infection control, social distance, quarantine, vaccine programs, and antiviral use
5. Maintaining essential services
Includes health services and other essential services
6. Research and evaluation
7. Implementation, testing and revision of the national plan

Table 2. Respiratory infection surveillance data from a system of six specialized hospitals in Mexico City during the 2009 peak and the 2010 end of the pandemic influenza A H1N1

Date	Patients hospitalized for acute respiratory infection	Patients in mechanical ventilation for acute respiratory infection
October 14, 2009	163	89
June 28, 2010	22	9

such information to make clinical decisions. Also, influenza monitoring allows for detecting drug-resistant or unusual viruses, which could be the cause of treatment failure in pandemics.

The Mexican experience indicates the importance of paying attention to complementary surveillance systems such as the one of reports from clinicians working at regional hospitals. Physicians attending an unusual number of severe respiratory diseases must have a direct channel of communication with health authorities because, as said, they may well be the first to infer that an outbreak is in course. In fact, crowding of emergency and intensive care units with acutely sick patients is typical of ongoing epidemics. Table 2 shows data from the daily report of a group of six reference hospitals from the Mexican National Institutes of Health in Mexico City during the A(H1N1)pdm2009 pandemic. A clinical report like this can be a good index of the overcrowding of emergency and critical services of a healthcare system. The advantage of surveillance systems built on direct clinical reports is the early outbreak detection because they do not require waiting for the information to be collated by epidemiology departments.

Vaccination

Rational for vaccination

The influenza vaccine can be administered as an injection or as a nasal spray. As influenza viruses A and B are slowly changing, vaccination against seasonal influenza is prepared annually²⁹. Thus, the currently

available seasonal influenza vaccine contains antigens representing three or four strains of influenza virus, one influenza A(H1N1)pdm2009, one influenza A subtype H3N2, and one or two strains of virus influenza type B (lineages Victoria or Yamagata, or both); in order to have a better coverage, there is a current trend to use tetravalent vaccines because, as we said, influenza B is not a minor disease³⁰.

Vaccination campaigns against seasonal influenza tend to focus on groups at high risk of complications, such as children aged under five years, the elderly, pregnant women, immunodeficient patients, healthcare workers, and people with chronic degenerative diseases. However, the U.S. Advisory Committee on Immunization Practices recommends universal vaccination for everyone aged over six months³¹. Recently, the Mexican Academy of Pediatrics recommended the universal vaccination of everyone aged from six months to 18 years. Prevention for infants aged less than six months includes vaccinating pregnant women and all household members and caregivers, the so-called “cocooning” strategy.

Importantly, in the event of a pandemic, vaccine will need to target particular groups in addition to those of high medical risk or healthcare workers, such as members of the security (army, police, firemen) as well as people of high hierarchy in the government or the financial system. It is important to consider the potential benefit of previous vaccination against the risk of being infected in a pandemic; we found a certain level of protection in people vaccinated during the season preceding the 2009 pandemic³².

Seasonal vaccination in the context of pandemic preparation

The best preparation to build effective vaccination campaigns for epidemic influenza is the conditioning

of national systems through efficient annual vaccination programs against seasonal influenza. As the 2013-2014 season showed all over North America, the concept of "high-risk persons" may well be obsolete as the intense circulation of the influenza A(H1N1)pdm2009 affected particularly young adults²⁷. The new lesson of the 2013-14 season is for favoring universal vaccination, including intense vaccination drills during the October-December period to avoid having highly vulnerable populations by January-February, the usual peak phase for influenza activity in the northern hemisphere.

The goal of achieving wide seasonal vaccine coverage, which allows for pandemic preparation, requires a complex plan. Collaboration agreements with the private sector are essential to establish national or regional centers for vaccine production (*vide retro*). These partnerships offer economic benefits and allow achieving sovereignty for the vaccine production, which is essential to maintain facilities with sufficient capacity, not only for seasonal influenza, but also for scaling their capabilities quickly if an epidemic arises. The progressive refinement of the annual vaccination program allows also for having a distribution strategy of permanent application, without which it is impossible to effectively face the complex logistics required during epidemics.

Concerns on vaccine safety and anticipation to the anti-vaccine groups

The production technology of egg-based influenza vaccine, still in use, is more than 60 years old, with an excellent safety record. One of the biggest blows to the prestige of the vaccine occurred in the USA in 1976 when a possible swine flu pandemic urged a vaccination program plagued by technical problems, while maximum containment efforts succeeded unexpectedly in confining the new strain on the sole army base where it originated. The national vaccination program was canceled when about 25% of the USA population had been vaccinated. Further analysis showed an excess of cases and hospitalizations of Guillain-Barre syndrome, illustrating that the vaccine itself is not without risks. Although this phenomenon never occurred again, it has been cited to add fuel to lingering doubts about vaccination. Despite the many attacks of tabloids and conspiracy theorists, however, the demonstrated safety of flu vaccines is reassuring³³. To anticipate anti-vaccine groups, all countries must have programs for the detection and transparent reporting of adverse events temporally associated with

vaccination, which helps to prevent rumors remaining unanswered in the mass media.

Strategies for risk communication

Disease outbreaks frequently trigger uncertainty and social unrest in the affected communities. Effective risk communication is a key part of the preparedness and control efforts. During a public health emergency, it is important to raise awareness of the health risks, to decrease social anxiety, and to enable behavioral changes that will help control the outbreak. Health authorities should be prepared to communicate information about the health risks and practices to control them. It is important to recognize that the public has the right to know the actual and potential risks.

According to our experience during the 2009 pandemic in Mexico, effective risk communication, transparency, and timing are critical for public information. This is particularly true if the country is the epicenter of the pandemic because the panic spreads easily, which can cause as much damage as the disease. Obviously, the information should not be exaggerated and health authorities must train and designate, beforehand, spokespersons that understand the art of reporting the truth without falling into alarmism. In press statements, people perceive if the government is telling the truth, allowing health officials to maintain the credibility required to lead the critical situations of an outbreak of influenza.

For seasonal influenza, the authorities have the advantage of knowing that there will surely be cases of influenza during the usual months, allowing them to communicate with transparency and reassurance about hygiene measures, vaccination, and the need for early medical attention. The campaign should be started as soon as the surveillance systems indicate that the influenza season has begun; a bad strategy is to start press statements once rumors about excessive numbers of cases or deaths of influenza are spreading among clinicians, the media, or the public; when that happens, authorities lose credibility, which will be difficult to restore. If every year health authorities inform about the prevention and early treatment of influenza, the task to report transparently will be much easier during pandemics.

Primary healthcare of infectious respiratory diseases

It is essential to maintain continuous surveillance and training in primary care to make sure that acute

respiratory infections are appropriately handled, avoiding the indiscriminate use of antibiotics and promoting, by contrast, the use of antiviral drugs for patients with influenza-like illness during the influenza season. Prescription is further supported with surveillance data regarding the susceptibility of influenza strains to antivirals. As many patients with acute respiratory diseases are treated in private practice, the use of antiviral drugs in this setting reduces the pressure on government reserves.

These provisions not only allow mitigation of seasonal influenza, but also help in the preparation of an efficient structure for pandemic mitigation. When these strategies are successful, pressure on hospitals is reduced because early intervention prevents complications that saturate intensive care units. During the 2013-2014 influenza season, Mexican health authorities faced the highest increased activity of influenza since the pandemic of 2009. A report by the Ministry of Health showed that patients who were in intensive care for influenza complications had, again, the story of being prescribed with antibiotics, not with antiviral drugs and, by the time when respiratory failure started, more than five valuable days had been lost.

Strategic reserve

Having a strategic stockpile of antiviral drugs such as oseltamivir and zanamivir, antibiotics, anesthetics, and relaxing agents, as well as protective equipment for health personnel, allowed dealing immediately with the health contingency during the pandemic in Mexico in 2009; it was also important to reassure the population.

During a global influenza emergency, the governments' ability to negotiate the acquisition of drugs and materials in the international market, in a time of high demand, is severely limited. The strategic reserve then becomes a matter of national security that requires continuous reviewing of drugs and materials that will be in high demand in pandemic situations. In Mexico, before the 2009 pandemic, we had a strategic reserve of antiviral drugs for about 1% of the population. Since antiviral drugs have expiry dates for only a few years, it is essential to have a "revolving" program that includes the public and private sectors to help bring to the market the antiviral drugs closest to their expiry date. Apart from the aforementioned supplies, it is desirable to have a functional reserve of ventilators to increase the surge capacity of some hospitals to offer mechanical ventilation.

Intensive care preparedness and surge capacity in hospitals

During the 2009 pandemic and during seasonal peaks of influenza, it was evident that most countries do not have enough intensive care beds to provide safe mechanical ventilation when there is an unusual demand³⁴, and Mexico was not an exception. Hospitals' reaction ability was limited by the lack of proficiency to care for patients on mechanical ventilation, not only within the specialized units, but also by a lack of preparedness to expand these capacities in reference hospitals. There are few medical specialists and technicians with the skills to handle mechanical ventilation; improvisation of care with untrained personnel often causes more harm than good.

In 2009 in Mexico, the National Center for Health Technology Excellence estimated that we had a total of only 2,349 intensive care beds, with 1,984 ventilators in a total of 311 general hospitals, 88 specialty hospitals, and 204 community centers. We acquired emergently ventilators and conducted parallel training courses for the management of critically ill patients with influenza; these courses were offered either for attendance or for taking online at the different states of the republic, together with the study of a procedure manual. The attention of critically ill patients was a challenge because the intensive care units of the reference centers were quickly saturated. Then, the capacity of intensive care services was expanded using general wards or units of short stay, which in some cases tripled the capacities for mechanical ventilation. It is expedient to stress the fact that Mexico was the first place of implementation of many of the theoretical recommendations from international organizations for the care of critically ill patients during pandemics. Having units staffed became a challenge, given that absenteeism existed, which was solved with the will of the majority of the staff to do double shifts.

An interesting aspect resulted from the formation of "command" teams composed of medical specialists, residents, and nurses that were sent to different states to educate on service and to assist in the surge capacity implementation for mechanical ventilation. In all cases, such teams helped to reduce mortality in the hospitals visited.

Conclusions

Influenza represents a persistent threat for humanity, and in case of strains with a high transmission and

lethality such as Influenza A(H5N1), the risk could be a social crisis because of the impossibility to attend the huge demand for services; thus, preparedness against influenza must be considered a national priority for all countries because there is a lot that governments, the public, health authorities, and healthcare workers can do to reduce its impact. It is important to increase vaccination coverage, starting with timely seasonal campaigns to be completed before the expected seasonal incidence peak (October to December for the northern hemisphere, April to June for the southern one). Influenza vaccines have been used for decades with an excellent safety record.

Pandemic preparedness in Mexico was helpful to contend against the 2009 crisis. There was an early warning system that detected and communicated the epidemic according to the International Health Regulation, viral samples were shared opportunely, antiviral stockpiles and protection equipment were mobilized, and effective risk communication was conducted, which supported the implementation of public health measures related to social distancing. Vaccines were available, but they arrived late and in limited amounts, which signals a need for improvement.

Countries that are better prepared to contend with seasonal influenza through programs for surveillance, sentinel diagnosis centers, early detection of emergent problems, production and distribution of vaccines, effective and transparent communication strategies, stockpiling of antiviral drugs and other medications and materials, as well as hospital preparation for mechanical ventilation and intensive care, will face the next pandemic more effectively.

References

- Writing Committee of the WHO Consultation on Clinical Aspects of Pandemic (H1N1) 2009 Influenza. Clinical aspects of pandemic 2009 influenza A (H1N1) virus infection. *N Engl J Med.* 2010;362:1708-19.
- Macias AE, de la Torre A, Moreno-Espinosa S, Leal PE, Bourlon MT, Ruiz-Palacios GM. Controlling the novel A (H1N1) influenza virus: don't touch your face! *J Hosp Infect.* 2009;73:280-1.
- Influenza (Seasonal). World Health Organization, Fact sheet No. 211, April 2009. Available from: <http://www.who.int/mediacentre/factsheets/fs211/en/>.
- USA National Strategy for Pandemic Influenza, November 2005. Available from: <http://www.flu.gov/professional/federal/pandemic-influenza.pdf>.
- Charu V, Chowell G, Palacio Mejia LS, et al. Mortality burden of the A/H1N1 pandemic in Mexico: a comparison of deaths and years of life lost to seasonal influenza. *Clin Infect Dis.* 2011;53:985-93.
- Belshe RB. The Origins of Pandemic Influenza – Lessons from the 1918 Virus. *N Engl J Med.* 2005;353:2209-11.
- Taubenberger JK, Morens DM. 1918 Influenza: The Mother of All Pandemics. *Emerg Infect Dis.* 2006;12:15-22.
- Dominguez-Cherit G, Lapinsky SE, Macias A, et al. Critically ill patients with 2009 influenza A(H1N1) in Mexico. *JAMA.* 2009;302:1880-7.
- Perez-Padilla R, de la Rosa-Zamboni D, Ponce de Leon S, et al. Pneumonia and respiratory failure from swine-origin influenza A (H1N1) in Mexico. *N Engl J Med.* 2009;361:680-9.
- Centers for Disease Control (CDC). Swine influenza A (H1N1) infection in two children—Southern California, March–April 2009. *MMWR Morb Mortal Wkly Rep.* 2009;58:400-2.
- Garten RJ, Davis CT, Russell CA, et al. Antigenic and genetic characteristics of swine-origin 2009 A(H1N1) influenza viruses circulating in humans. *Science.* 2009;325:197-201.
- Dawood FS, Jain S, Finelli L, et al. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. *N Engl J Med.* 2009;360:2605-15.
- Chowell G, Bertozzi SM, Colchero MA, et al. Severe respiratory disease concurrent with the circulation of H1N1 influenza. *N Engl J Med.* 2009;361:674-9.
- The 2009 H1N1 Pandemic: Summary Highlights, April 2009–April 2010. Available from: <http://www.cdc.gov/h1n1flu/cdcreponse.htm>.
- Swine Influenza. Statement by WHO Director General, Dr Margaret Chan, WHO 25 April 2009. Available from: http://www.who.int/mediacentre/news/statements/2009/h1n1_20090425/en/index.html.
- World now at the start of 2009 influenza pandemic. Statement to the press by WHO Director General Dr Margaret Chan, WHO 11 June 2009. Available from: http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/index.html.
- Cepal. Evaluación preliminar del impacto en México de la influenza AH1N1. Available from: http://www.eclac.cl/publicaciones/xml/4/38894/2010-011_Influenza-L958w.pdf.
- Organización Panamericana de la Salud. CEPAL/OPS-OMS. Evaluación preliminar del impacto en México de la influenza A H1N1. LC/MEX/L.958/23 March 2010.
- Simonsen L, Spreeuwenberg P, Lustig R, et al. Global mortality estimates for the 2009 Influenza Pandemic from the GLAMOR project: a modeling study. *PLoS Med.* 2013;10:e1001558.
- Mensua A, Mounier-Jack S, Coker R. Pandemic influenza preparedness in Latin America: analysis of national strategic plans. *Health Policy Plan.* 2009;24:253-60.
- WHO Guidelines on the use of vaccines and antivirals during influenza pandemics. Available from: http://www.who.int/csr/resources/publications/influenza/11_29_01_A.pdf.
- Guidance on allocating and targeting pandemic influenza. Available from: http://www.flu.gov/images/reports/pi_vaccine_allocation_guidance.pdf.
- Borse RH, Shrestha SS, Fiore AE, et al. Effects of vaccine program against pandemic influenza A(H1N1) virus, United States, 2009-2010. *Emerg Infect Dis.* 2013;19:439-48.
- Vacuna contra A H1N1 llega a Mexico. Available from: <http://www.eluniversal.com.mx/notas/641548.html>.
- Harper SA, Bradley JS, Englund JA, et al. Seasonal influenza in adults and children – diagnosis, treatment, chemoprophylaxis, and institutional outbreak management: clinical practice guidelines of the Infectious Diseases Society of America. *Clin Infect Dis.* 2009;48:1003-32.
- Muthuri SG, Myles PR, Venkatesan S, Leonardi-Bee J, Nguyen-Van-Tam JS. Impact of neuraminidase inhibitor treatment on outcomes of public health importance during the 2009-2010 influenza A(H1N1) pandemic: a systematic review and meta-analysis in hospitalized patients. *J Infect Dis.* 2013;207:553-63.
- Gutiérrez-Mendoza LM, Schwartz B, Méndez de Lira JJ, Wirtz VJ. Oseltamivir storage, distribution and dispensing following the 2009 H1N1 influenza outbreak in Mexico. *Bull World Health Organ.* 2012;90:782-7.
- World Health Organization. WHO checklist for influenza pandemic preparedness planning. Available from: <http://www.who.int/influenza/resources/documents/FluCheck6web.pdf>
- Couch RB. Seasonal Inactivated Influenza Virus Vaccines. *Vaccine.* 2008;26(Suppl 4):D5-9.
- McKeage K. Inactivated quadrivalent split-virus seasonal influenza vaccine (Fluarix® quadrivalent): a review of its use in the prevention of disease caused by influenza A and B. *Drugs.* 2013;73:1587-94.
- Centers for Disease Control and Prevention (CDC). Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices – United States, 2013-2014. *MMWR Recomm Rep.* 2013;62:1-43.
- García-García L, Valdespino-Gómez JL, Lazcano-Ponce E, et al. Partial protection of seasonal trivalent inactivated vaccine against novel pandemic influenza A/H1N1 2009: case-control study in Mexico City. *BMJ.* 2009;339:b3928.
- Manzoli L, Ioannidis JP, Flacco ME, De Vito C, Villari P. Effectiveness and harms of seasonal and pandemic influenza vaccines in children, adults and elderly: a critical review and re-analysis of 15 meta-analyses. *Hum Vaccine Immunother.* 2012;8:851-62.
- Devereaux AV, Dichter JR, Christian MD, et al. Definitive care for the critically ill during a disaster: A framework for allocation of scarce resources in mass critical care from a task force for mass critical care summit meeting, January 26-27, 2007, Chicago, IL. *Chest.* 2008;133:51-66S.