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# A PERSPECTIVE ON THE 2009 A/H1N1 INFLUENZA PANDEMIC IN MEXICO

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Abstract. In this article, we provide a chronological description of the 2009 H1N1 influenza pandemic in Mexico from the detection of severe respiratory disease among young adults in central Mexico and the identification of the novel swine-origin influenza virus to the response of Mexican public health authorities with the swift implementation of the National Preparedness and Response Plan for Pandemic Influenza. Furthermore, we review some features of the 2009 H1N1 influenza pandemic in Mexico in relation to the devastating 1918-1920 influenza pandemic and discuss opportunities for the application of mathematical modeling in the transmission dynamics of pandemic influenza. The value of historical data in increasing our understanding of past pandemic events is highlighted.

## 1. Introduction.

Seasonal influenza epidemics generate substantial morbidity and mortality rates every year around the world [1]. Novel influenza viruses represent a challenge to public health as they have the potential to trigger influenza pandemics, which are defined as global epidemics associated with substantial morbidity and mortality impact relative to seasonal epidemics. The impact of the 20th century influenza pandemics in 1918-1920 (Spanish influenza), 1957-1959 (Asian influenza) and 1968-1970 (Hong Kong influenza) is not well understood. In particular, the 1918 (H1N1) influenza pandemic has been by far the most devastating of recent history with an estimated global death toll of 20-50 million [2], yet our understanding of its impact in the American continent is still limited although it has been improved by a few quantitative reports from the US [3], Canada [4] and Mexico [5, 6, 7].

Mexico, the epicenter of the 2009 A/H1N1pdm influenza pandemic, is a geographically and climatologically diverse country with a wide variety of ecological systems ranging from coastal plains, temperate highlands, humid tropical forests, and deserts. Mexico is divided into 31 states and a Federal District (Figure 1).

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Mexico comprises a surface of 2 million $km^2$ and a population of about 107 million people heterogeneously distributed across the country.

2. **Parallels and differences between the 1918 and the 2009 influenza pandemics in Mexico.** The 1918-1920 influenza pandemic found a fragmented and disorganized Mexican population in the middle of an economic crisis and revolutionary process [6, 7]. Telegraph communications represented an advantage for public health authorities to maintain daily contact with all states. Information on the status of the 1918 influenza pandemic was continuous and up to date. Before the 1918 influenza pandemic, a typhus epidemic struck the central part of Mexico during 1915 and 1916. To systematically mitigate the effects of the epidemic, the President of the Superior Council of Hygiene organized the largest control campaign at that time. These were the sanitary conditions that existed when the 1918 influenza pandemic hit Mexico [8].

The novel 1918 influenza pandemic virus most likely arrived to Mexico from the United States where an early spring pandemic wave had been reported to occur sometime between February and April of 1918 [3, 6]. The 1918 influenza pandemic swept the Mexican population in a series of waves, a characteristic feature of past influenza pandemics [10]. The first wave during April-May has been identified from mortality records for Toluca, Mexico City and Puebla [5, 7], the second wave during October-December of the same year has been identified in many Mexican states from quantitative studies (Toluca and Mexico City [5], Tlaxcala [6], and Puebla[7]) and newspaper articles (Table 1) and the third wave during January and February of 1920 has been recently reported in Toluca and Mexico City by Chowell et al. [5]. The first news of the presence of the pandemic virus arrived in Mexico via telegrams sent from the United States starting in March of 1918. From the start of the pandemic, there was a constant flow of information to the Office of the Superior Council of Hygiene. However, the situation was different from the typhus epidemic that occurred during 1915 and 1916. The support from the Mexican President Venustiano Carranza diminished due to multiple confrontations with political and military enemies and his popularity declined as a result.

In April of 1918, the first epidemic wave started in the northern Mexican states neighboring the United States, but it did not cause significant mortality [6, 7, 5]. The second more devastating wave started during the first days of September [5, 6, 7]. Table 1 compiles news reports retrieved from national newspapers in chronological order on the devastating fall pandemic wave (October 9th to November 27th, 1918) across Mexican states. These accounts of the fall pandemic wave in Mexico suggest that the virus started to spread among northern populations and swept the country traveling from north to south, probably arriving in Mexico City by train from the north, and quickly spread to central and southern Mexican regions [8]. In fact, northern states were first to report the end of the outbreak in early November while it was still running its course through central and southern states (Table 1). According to reports from the Superior Council of Hygiene, the first two pandemic waves generated an approximate death toll of 436,200 people in Mexico (Table 2) [9]. Thus, the pandemic mortality rate was about 3387.4 per $100,000$. However, recent reports based on individual mortality records have revealed mortality rates greater than 5000 per $100,000$ in some states such as Tlaxcala [6], a mortality rate substantially higher than that reported by the Superior Council of Hygiene (Table 2).

Past pandemics have exhibited signature features [10], and the ongoing 2009 H1N1 influenza pandemic is not an exception. These signature features include an "age shift" in the proportion of influenza-related mortality towards younger age groups compared to seasonal influenza epidemics. Overall, the age-specific mortality profile can be explained as the result of population immunity patterns arising from prior exposure to related influenza viruses during the population life history [1]. The 1918 influenza pandemic in Mexico produced a W-shaped age-specific excess mortality rate curve which highlighted elevated mortality among young adults and senior populations [5]. In contrast, early data of the 2009 H1N1 influenza pandemic in Mexico suggested relative protection for persons who were $\sim 60$ years of age or older, the age group at risk of exposure to H1N1 strains during childhood before the 1957 pandemic [11], a pattern found to be consistent in other countries (e.g., [15, 12, 13, 14]).

Another signature feature of influenza pandemics is the multiple wave profile of morbidity and mortality over short periods of time often occurring unexpectedly during spring/summer seasons in temperate regions. For instance, the 1918 influenza pandemic was characterized by a multiple wave profile (e.g., New York [3], Geneva, Switzerland [16], England and Wales [17], Copenhagen [18], and Sydney, Australia [19]). Similarly, the recent 2009 H1N1 influenza pandemic also exhibited multiple waves in some countries including Mexico [21], the US, and Japan [37]. However, most reports from the southern hemisphere have exhibited a single winter wave (e.g., Chile [23] and Argentina [24], Australia [25], and New Zealand [26]). The wave-like patterns in the temporal distribution of cases are most likely associated with the timing of introduction of the novel virus to different nations relative to school activity periods [27, 28, 29], climatic conditions [30, 31], the strength of the connectivity within countries [32] as well as temporary effects of interventions [33]. Significant changes in the virus composition (increasing antigenic drift) could also explain the emergence of multiple pandemic waves.

The ability of a novel influenza virus to spread in a population can be measured by the basic reproduction number ($R_0$), a transmissibility measure defined as the average number of secondary cases generated by a primary infectious individual in a completely susceptible population [34]. The transmissibility of the 1918 influenza pandemic has been reported to lie in the range 1.5 to 5.4, depending on the serial interval, location, and pandemic wave considered [35, 16, 18]. Compared to the 1918 influenza pandemic, transmissibility estimates of the early spring wave of the 2009 influenza pandemic in Mexico were relatively low ($R_0 \sim 1.6$) [39] within the variability observed for transmissibility levels of inter-pandemic influenza in temperate countries [40], in agreement with a previous estimate for the summer wave of the 1918 influenza pandemic in Geneva [16] and in the lower range for Copenhagen [18]. The basic reproduction number of pandemics can be expected to be influenced by the time of the year when the novel virus is introduced in the population with lower effective transmissibility levels when the virus is introduced during school vacation periods due to reduced contact rates. Furthermore, experimental studies suggest that survival and aerosol transmission of the influenza virus improves substantially as absolute humidity levels decrease [30, 31]. These factors could partially explain the lower disease impact associated with the Spring 2009 H1N1 influenza pandemic wave in Mexico compared to that of the fall wave.

3. **The 2009 H1N1 influenza pandemic in Mexico.** Early pieces of epidemiological indicators suggested an unexpected rebound of the inter-epidemic influenza season in early March 2008-2009. Several signs alerted Mexican Health Officials about the circulation of atypical respiratory infections in the population when influenza epidemics are not expected to occur. In particular, there were reports of severe respiratory disease during late March and early April in Mexico City and the states of Mexico, San Luis Potosi, Tlaxcala and Oaxaca [41, 42]. The fact that young adults were being disproportionately affected in the population (Figure 2) was perhaps the most concerning sign to Mexican public health authorities, which is in stark contrast with the typical age-specific risk pattern of seasonal influenza epidemics [11].

An outbreak investigation initially suggested that the beginning of the 2009 influenza pandemic could potentially be traced back to the Town of La Gloria, Perote, in the state of Veracruz, where a large number of pig farms are located. An outbreak of respiratory disease was suspected to have spread through the population of La Gloria from early March through April 6th with an associated attack rate of about 25% [43]. However, hospitalizations or deaths were not notified during this epidemic. On March 5th, 2009 health officials of the state of Oaxaca reported the death of a diabetic woman who developed severe pneumonia and initially thought to be infected with Severe Acute Respiratory Syndrome (SARS). This fatal case was later confirmed to be positive for novel H1N1 influenza on April 23rd. On March 27th, the National Institute of Respiratory Diseases (INER) reported the first fatal case of influenza in Mexico City. From March 24th through April 24th a total of 98 people were hospitalized for acute respiratory illness in the INER in Mexico City. It was particularly relevant that most of these hospitalizations at INER were previously healthy young persons [41].

Increases in acute respiratory disease in several states of central Mexico together with the unexpected elevation in severe respiratory disease rates among previously healthy young adults triggered an epidemiologic alert on April 17th, 2009 by the Mexico Ministry of Health [11]. From this point on, the Mexican public health authorities maintained a communication channel not only with the Mexican people but also with the world through daily press releases led by the Secretary of Health on the current state of the pandemic and preliminary findings of ongoing research activities. Mexico's efforts were praised by disjoint groups such as the World Health Organization for the transparency and responsibility in responding to the 2009 H1N1 influenza pandemic [44].

On April 18th, the media spread the news about Mexico's epidemiologic contingency and special field work was carried out in search for cases of severe pneumonia in the country. On April 20th, preventive measures for health care workers were issued and laboratory tests initially revealed non-typeable infuenza A virus from samples of Veracruz and Oaxaca raising concerns for the circulation of a novel infectious disease. Specimens were immediately sent to the National Microbiology Laboratory in Canada and soon after Canadian researchers informed Mexican authorities about the detection of a novel influenza virus A/H1N1 of swine origin on April 23rd [20]. These important international cooperation activities with Canada and the United States led the Mexico Ministry of Health to issue a pre-pandemic alert and activate a National Preparedness and Response plan [45].

On April 24th, Mexican President Felipe Calderon Hinojosa empowered the Federal Ministry of Health to coordinate all the national activities of prevention and control of the unfolding epidemic. Education activities were cancelled in the Federal District and the metropolitan area including the state of Mexico on April 24th. School closings were extended to the rest of the country three days later until May 11th when schools were re-opened. Other temporary measures to curb the spread of the epidemic in Mexico City included the closure of movie theaters and restaurants as well as the cancellation of mass-gathering events including soccer games and church services [45].

As of January 20th, 2010, a total of 69,607 confirmed novel H1N1 influenza cases and 944 deaths had been reported by the Mexico Ministry of Health [46]. The temporal course of the pandemic closely resembled that of the 1918 influenza pandemic in Mexico [5]. Roughly, three spatial waves of influenza morbidity and mortality have been documented during this pandemic in Mexico: the initial spring wave during the months of April and May mainly confined to the greater Mexico City area; a second summer pandemic wave during June and July localized in the southern states including the Yucatan Peninsula and a third fall wave that followed the return of students from the summer vacation period to classrooms, with higher morbidity and mortality than the earlier outbreaks. This third wave did not show a unique spatial pattern with outbreaks occurring in central states and northern states. There is a need for studies that carefully address the spatio-temporal characteristics of the 2009 influenza pandemic in Mexico in relation to demographic characteristics, school cycles, influenza seasonality and other geographic information relevant for Mexico. These analyses could suggest improvements to current influenza preparedness plans.

4. **Opportunities for modeling transmission dynamics of pandemic influenza.** Understanding local risk factors and mechanisms that drive the spread of pandemic influenza is essential in the development of novel effective intervention strategies. Mathematical models provide a unique way to analyze influenza transmission patterns. It is worth mentioning that the history of the mathematical modeling of infectious diseases goes back to the work of Sir Ronald Ross in 1911 [47] who discovered the vector mechanism of transmission of the malaria parasite and explored the effects of controlling the mosquito population using simple mathematical models. Also relevant is the well-known work of Kermack and Mckendrick in 1927 [48] who introduced the classical SIR (susceptible-infectious-removed) epidemic model.

A crucial problem faced by decision-makers responsible for epidemic control is to monitor whether interventions are effective or, if not, to devise alternative measures. In particular, for infectious diseases characterized by rapid dissemination (such as pandemic influenza), it is important to identify its implicit profile of propagation. The profile of propagation is defined as the number and sites of cases characterized by random or non-random spatial distributions and, if non-random distribution is suggested by the data, whether cases are uniformly distributed over space or they constitute "clusters." Once the epidemic profile is determined, it is then relevant to identify whether all cases possess an equal influence on epidemic spread or, alternatively, whether some cases may contribute more to epidemic spread (and, therefore, should be prioritized in control measures). If differences in epidemic spread contributions are observed among cases, that would imply the importance of incorporating spatial information into transmission models rather than assuming that all cases are equal in their effects.

Since spatial features (e.g., human mobility patterns, roads, mountains, and weather patterns) are rarely uniformly distributed over space, determining the specific spatial scale(s) within which epidemic dynamic events develop, is crucial. Pandemic influenza spread, like the spread of forest fires, may be influenced by spatial attributes such as local demographic differences and topographic features. Other factors, like winds, human traffic, and seasonal attributes may also influence epidemic spread. Consequently, epidemics tend to be unique. That is, even when the biologic knowledge of the causative agent is known, the role of spatial factors (unique to a specific site and time) will greatly shape the transmission dynamics of infectious diseases. In this regard, a significant amount of prior work has addressed spatio-temporal propagation aspects of influenza (e.g., [49, 50, 51, 52, 53, 32]). In this special issue, Herrera-Valdez and colleagues use a spatial transmission model to underscore the role of social distancing and school closures in shaping the temporal patterns of pandemic influenza in the context of the 2009 H1N1 influenza pandemic in Mexico.

5. **Conclusion.** Overall, the 2009 influenza pandemic in Mexico shares a number of characteristic features with the 1918 influenza pandemic in the same country including 1) the timing of the pandemic onset in the Spring season [5, 39], 2) a multiple wave profile of spread [5, 21], 3) a relatively higher mortality rate among young adults compared to seasonal influenza epidemics [5, 11], and 4)similar transmissibility levels in Mexico City [39, 5]. Yet, these two pandemics also differ in a number of aspects including the speed of propagation across countries with the 1918 influenza pandemic reaching most regions of the world in the order of months while the 2009 influenza pandemic reached most countries in the order of only a few weeks [54]. Also, the mortality burden of the 1918 influenza pandemic was much higher than that of the 2009 influenza pandemic with some Mexican states experiencing mortality rates, circa 5000 per $100,000$ [6]. By contrast, the overall mortality burden and case fatality rate of the 2009 influenza pandemic has not been found to be significantly higher than that of seasonal influenza epidemics [55, 56, 57]. There are other clear differences in certain social and political components between the 2009 and the 1918 influenza pandemic. For example, the 1918 influenza pandemic took place in the middle of the Mexican revolution at relatively low sanitary conditions. In contrast, hygienic and sanitary conditions have significantly improved since then; antibiotics to treat bacterial complications of influenza are now available and influenza preparedness plans have been put together to consider the implementation of social distancing measures including temporary school closures and basic public health measures.

There is potential for vaccination to play a major role during future severe influenza pandemics. Current vaccine technologies are inadequate for the rapid deployment of vaccines that is required to control a fast propagating pandemic influenza virus. This and other issues related to vaccines and vaccination against influenza and other infectious pathogens are discussed by Curtiss in this same issue. Furthermore, several articles in this special issue use mathematical modeling to address aspects associated with vaccination strategies against pandemic influenza including the role of limited vaccine resources and delays in vaccine development.

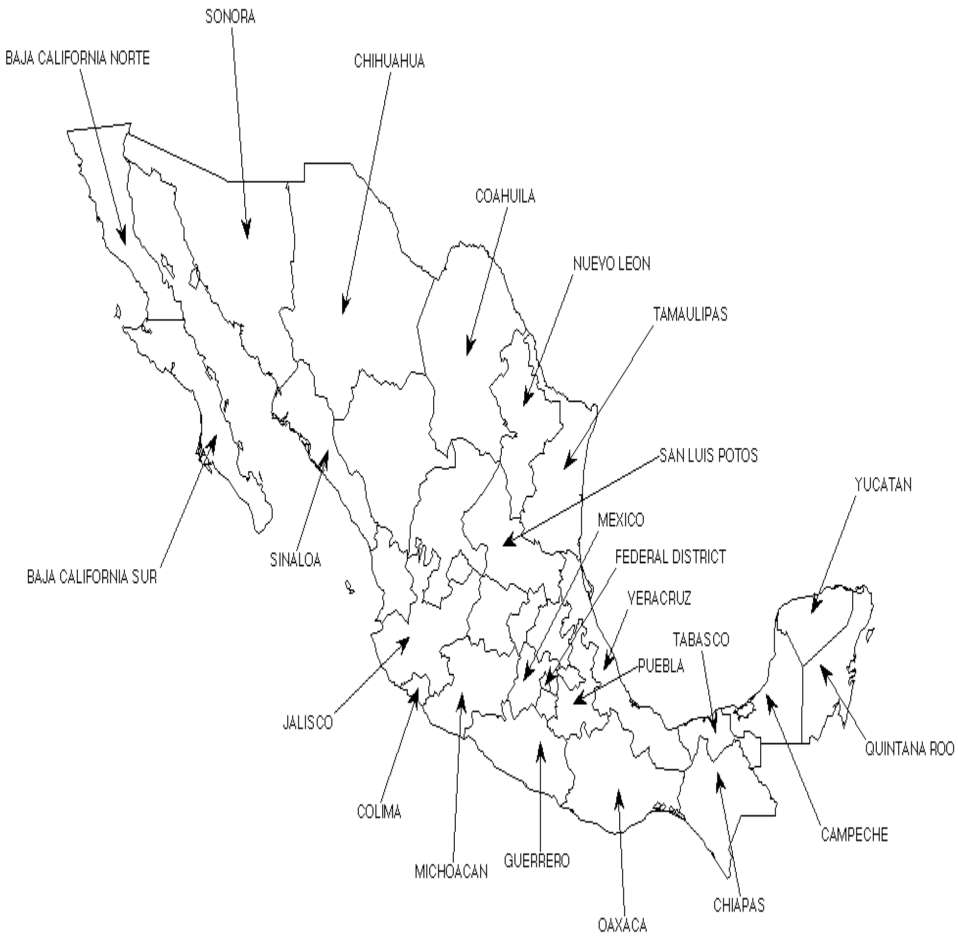


FIGURE 1. Map of Mexico with state divisions.

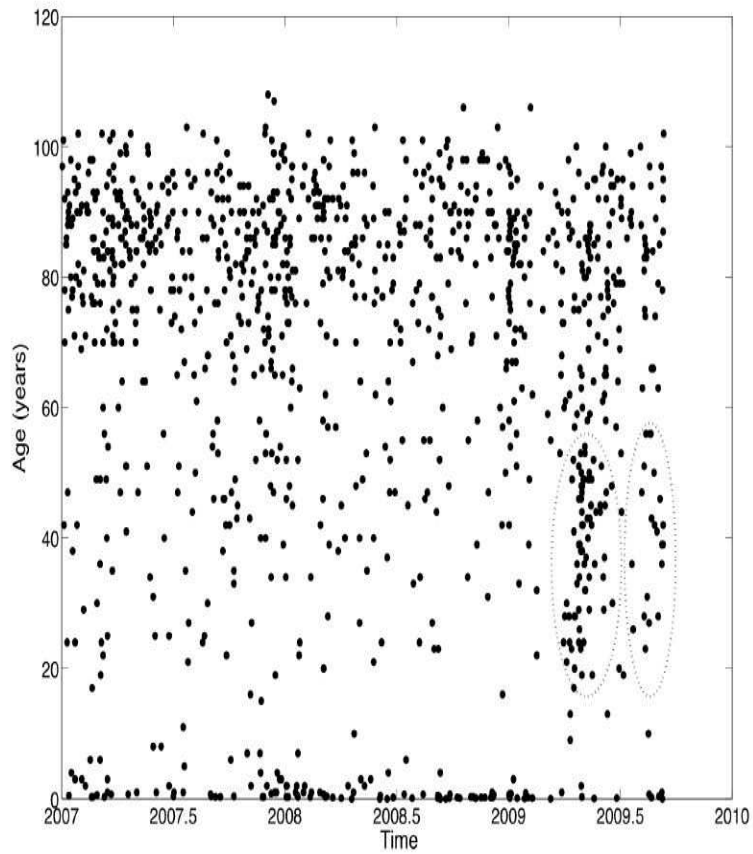


FIGURE 2. The age-specific weekly mortality of all respiratory deaths in the Federal District as recorded by the Civil Registry, Jan-2007 to Sep-2009. The clusters of deaths among young adults in 2009 can be readily identified.

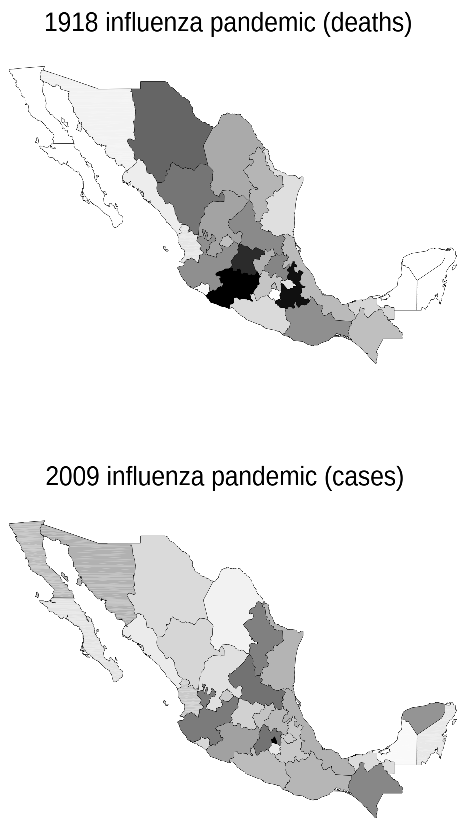


FIGURE 3. Geographic distribution of deaths and influenza specific infections for the 1918 (Spring and fall waves) and 2009 (as of 04-Jan, 2010 [21]) influenza pandemics in Mexico, respectively. For each pandemic wave, the grayscale range was set relative to the highest number of cases across states so that the state(s) with the highest number of cases/deaths are indicated in black.

Table 1. Events in chronological order relevant to the fall wave of the 1918 influenza pandemic in Mexico retrieved from national newspapers (October 09-November 27, 1918).

| Date | Place | Event |
|---|---|---|
| 09 October 1918 | Torreon, Coahuila | In the last 24 hrs. 300 people have died from influenza particularly individuals at low socioeconomic levels |
| 25 October 1918 | Queretaro | 20 daily deaths with 90 to 100 new daily cases |
| 31 October 1918 | Mexico City | President of the Superior Council of Hygiene declares that the number of physicians will not be enough in the Capital City |
| 01 November 1918 | Chihuahua | Epidemic is still causing significant burden and the medical resources are scarce |
| 01 November | Tlaxcala | Governor of the State of Tlaxcala declares that there are over 1000 ill people and medical resources are lacking |
| 01 November 1918 | Veracruz | 5 people have been found dead in the streets |
| 02 November 1918 | Mexico City | Funds granted to the Superior Council of Hygiene are pending |
| 02 November 1918 | Mexico City | Cemeteries in Mexico City were closed for the day of the death. In spite of this, a significant number of people got together in the surroundings of cemeteries |
| 02 November 1918 | Mexico City | Bull fighting events were cancelled |
| 02 November 1918 | Coahuila | Epidemic trend is decreasing. The number of deaths has significantly decreased |
| 02 November 1918 | Coahuila | The influenza epidemic has decreased significantly in the northern region of Mexico particularly in Monclova and Torreon where hygiene campaigns have been implemented with rigor and efficacy. Pubic places are keeping outstanding hygienic levels |
| 02 November 1918 | Mexico City | Red Cross health posts are being established in a number of places of Mexico City |
| 02 November 1918 | Mexico City | According to the Bulletin of Statistics of the City, the number of deaths has reached 319 in October |
| 02 November 1918 | San Luis Potosi | Many people arrived to San Luis Potosi escaping the epidemic in Tampico and surroundings. Many people are found severely ill in the train and died in transit |

| Date | Place | Event |
|---|---|---|
| 02 November 1918 | Guanajuato | The influenza epidemic seems to be slowing down |
| 02 November 1918 | Yucatan | Authorities order the train "Tousian" transporting several sick individuals to halt its journey |
| 02 November 1918 | Tampico | A total of 1981 cases and 389 deaths associated with the influenza pandemic have been recorded |
| 02 November 1918 | Mexico City | Cleaning of streets is declared mandatory. Public dances were cancelled. |
| 03 November 1918 | Michoacan | The epidemic is still causing significant impact in the population |
| 03 November | Puebla | The disease is still affecting a great number of people among all social classes particularly among those at higher risk of exposure to the virus |
| 03 November 1918 | Puebla | There were 97 deaths verified today. This is a low figure compared to the 160 deaths recorded yesterday |
| 03 November 1918 | Tlaxcala | Over 12,000 people have died from the influenza pandemic. There was not enough time to write individual death certificates and give appropriate sepulture |
| 03 November | Veracruz | There are fatal cases from influenza. Public gatherings should be cancelled |
| 03 November | Mexico City | Dr. Maximo Oliva publishes an article on the elimination of "kisses" to stop transmission of repugnant diseases |
| 03 November 1918 | Chihuahua | Yesterday a total of 67 new cases and 26 deaths were recorded |
| 03 November 1918 | Mexico City | 6 inmates succumbed to the disease |
| 04 November | Oaxaca | The virus is causing significant impact while trends are slowing down in several northern regions of the country |
| 05 November 1918 | Monterrey | The epidemic is slowing down |
| 05 November 1918 | Monclova, Coahuila | The epidemic is slowing down |
| 05 November 1918 | Mexico City | Several people are working on developing a vaccine |
| 05 November 1918 | Laredo | The epidemic is essentially over |
| 07 November | Monterrey | The epidemic is over |
| 07 November 1918 | Tuxtla Gutierrez, Chiapas | There are cases among the military and starts to be disseminated among the general population |
| 07 November 1918 | Tapachula, Hidalgo | The epidemic is spreading |
| 07 November | San Luis Potosi | 15 new deaths were recorded, but the epidemic tends to decrease |

| Date | Place | Event |
|---|---|---|
| 07 November 1918 | Chiapas | The epidemic starts in Chiapas and there are estimates that 65% of the population has been affected |
| 09 November 1918 | Mexico City | The number of deaths from influenza have started to decrease ostensibly |
| 09 November 1918 | Tampico, Tamaulipas | A total of 3578 cases and 782 deaths since the epidemic started |
| 11 November 1918 | San Luis Potosi | The City is starting to acquire a normal aspect with the disappearance of the influenza epidemic |
| 14 November 1918 | Mexico City | The epidemic is essentially over in the northern part of the country |
| 15 November 1918 | Yucatan | The influenza virus invades the states of Yucatan, Campeche and Tabasco |
| 18 November 1918 | Mexico State | Greatest impact in the municipalities of El Oro, Valle de Bravo, Tenancingo y Jilotepec |
| 20 November 1918 | Guadalajara | There has been a steady increase of influenza cases in several municipalities |
| 27 November | Guerrero | The epidemic is over |
| 27 November 1918 | Tabasco, Chiapas, Oaxaca, Yucatan, Campeche | The epidemic impact is alarming in these states |
| 27 November 1918 | Colima | There have been 227 deaths since the beginning of the epidemic |

TABLE 2. Mortality attributed to the Spring and fall waves of the 1918 influenza pandemic across Mexican states according to reports of the General Council of Hygiene [9].

| State | Total deaths | Mortality rate per 100,000 |
|---|---|---|
| Aguascalientes | 12000 | 11154.38 |
| Baja California | N.D. | |
| Baja California Sur | N.D. | |
| Campeche | N.D. | |
| Coahuila | 16000 | 4066.28 |
| Colima | 900 | 980.93 |
| Chiapas | 12000 | 2845.32 |
| Chihuahua | 29000 | 7220.72 |
| Distrito Federal | 12000 | 1324.36 |
| Durango | 26000 | 7720.49 |
| Guanajuato | 40000 | 4649.19 |
| Guerrero | 7000 | 1234.92 |
| Hidalgo | 23000 | 3696.31 |
| Jalisco | 21000 | 1761.8 |
| Mexico | 11000 | 1243.47 |
| Michoacan | 48000 | 5007.2 |
| Morelos | N.D. | |
| Nayarit | 5000 | 3064.04 |
| Nuevo Leon | 14000 | 4161.56 |
| Oaxaca | 21000 | 2151.62 |
| Puebla | 45000 | 4390.43 |
| Quertaro | 15000 | 7265.09 |
| Quintana Roo | N.D. | |
| San Luis Potosi | 22000 | 4936.26 |
| Sinaloa | 3500 | 1025.59 |
| Sonora | 2500 | 908.67 |
| Tabasco | 8000 | 3801.61 |
| Tamaulipas | 6000 | 2091.29 |
| Tlaxcala | 5000 | 2800.02 |
| Veracruz | 13000 | 1120.75 |
| Yucatan | N.D. | |
| Zacatecas | 17300 | 4560.68 |
| TOTAL | 436200 | 3387.4 |

N.D. = no datum

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