THE 1918/19 SPANISH FLU IN PISA (TUSCANY, ITALY): CLINICAL, EPIDEMIOLOGICAL AND AUTOPTIC CONSIDERATIONS

ŠPANJOLSKA GRIPA (1918./1919.) U PISI (TOSKANA, ITALIJA): KLINIČKA, EPIDEMILOŠKA I AUTOPTIČKA RAZMATRANJA

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SUMMARY

The Spanish flu pandemic spread in 1918-19 and infected about 500 million people, killing 50 to 100 million of them. People were suffering from severe poverty and malnutrition, especially in Europe, due to the First World War, and this contributed to the diffusion of the disease. In Italy, Spanish flu appeared in April 1918 with several cases of pulmonary congestion and bronchopneumonia; at the end of the epidemic, about 450,000 people died, causing one of the highest mortality rates in Europe.

From the archive documents and the autopic registers of the Hospital of Pisa, we can express some considerations on the impact of the pandemic on the population of the city and obtain some information about the deceased. In the original necroscopic registers, 43 autopsies were reported with the diagnosis of grippe (i.e. Spanish flu), of which the most occurred from September to December 1918. Most of the dead were young individuals, more than half were soldiers, and all of them showed confluent hemorrhagic lung bronchopneumonia, which was the typical feature of the pandemic flu.

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We believe that the study of the autopsy registers represents an incomparable instrument for the History of Medicine and a useful resource to understand the origin and the evolution of the diseases.

**Keywords:** Spanish flu, pandemic, Pisa, autopsy

# Introduction

The Spanish flu pandemic spread in 1918/19 is considered one of the greatest health tragedies in history. It infected about 500 million people across the world and killed 50 to 100 million of them, which corresponds to 3 to 5 percent of the world’s population.¹

In May 1918, the Agencia Fabra of Madrid sent to the Reuters in London a cable about a new epidemic emerged in the Spanish capital. Spain was not involved in the First World War, and therefore there was no military censorship, and the newspapers could freely mention this new disease, which was then called the ‘Spanish flu’, just because Spain was the first country to report it.²

This pandemic spread in three distinct waves within an interval of about 9 months.³ The first wave occurred in late spring 1918 and was associated with high morbidity but low mortality. The second wave manifested in late summer-fall 1918 with high morbidity and an extremely high mortality rate. The last wave occurred in winter 1918–1919 also with high mortality but causing fewer deaths because many subjects had already died during the previous waves or had contracted the disease and overcome it, thus resulting immunized.⁴ The presentation in different waves and the mortality trend are certainly anomalous. For example, contagion (and subsequent healing) during the second wave created protection against the third one, while contagion during the first wave created only minimal and negligible protection against the second and third one. Different theories on the three waves have been hypothesized.⁵ The scarce information about the first arrival of the disease does not allow to exclude that the virus was not the same one that caused the

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pandemic in the other two waves, or it is possible that a major mutation of the virus occurred during mid-1918, leading to greater pathogenicity. However, the presentation of the pandemic in three waves remains unexplained.

Where the 1918 pandemic originated is still an unresolved question. The first hypothesis argues that it originated in the United States since, already in March 1918, several cases appeared in the prison of Sing-Sing (New York, USA), in some factories and among the soldiers herded in training camps waiting to leave for Europe. The first known victim, the so-called ‘Patient Zero’, was an American soldier assigned for food preparation at his army training camp, Camp Funston, who may have unintentionally started the contagion.

Another hypothesis claims that the infection came from China, introduced by 200,000 “coolie” (i.e. labourers) transported to France in 1917 in wartime. In fact, from 1910 to 1918 in China, several cases of pneumonic plague are reported, whose differential diagnosis with haemorrhagic influenza pneumonia is problematic, especially at that time.

Finally, it was also suggested that the origin of the disease might be in France due to the poor conditions of European population that was exhausted from the war.

The nature and the origin of the disease have been much investigated, and there was great confusion about its aetiology, which was initially attributed to the Pfeiffer’s bacillus.

About 20 years ago, in 1997, RNA was isolated from a formalin-fixed, paraffin-embedded lung tissue sample of a 1918 pandemic victim. Viral RNA fragments were sequenced from the coding regions of hemagglutinin, neuraminidase, nucleoprotein, matrix protein 1, and matrix protein 2. These investigations characterized the pathogen as the H1N1 influenza A virus, even though it was not possible to sequence the entire genetic pool of the

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pathogen.\textsuperscript{11} Only in 2005, the researchers were able to describe the genetic sequences of the last three genes that were missing for the completion of the genome of the Spanish flu virus.\textsuperscript{12}

Based on these studies, it is currently suggested that the severity of Spanish influenza can be attributed to viral pneumonia with superimposition of bacterial pneumonia (mainly caused by \textit{Streptococcus pneumoniae} and \textit{Streptococcus pyogenes}). Moreover, the high mortality rate among the young adults may be ascribed to a vigorous immune response mediated by cytokine storm, which is a deleterious overexuberant release of proinflammatory cytokines.\textsuperscript{13}

\textbf{The 1918 Spanish flu in Italy}

In Italy, in March-April 1918, several cases of flu with pulmonary congestion and bronchopneumonia appeared; in early September, Italian newspapers started to talk about the disease.\textsuperscript{14} Censorship, established at the beginning of the war, was particularly severe and contributed to concealing the problem. As in the rest of the world, the “Spanish flu” debuted in Italy in the late spring (April-June) 1918, but with bland characteristics. Instead, the lethal second wave occurred in fall. The first official report of the disease was in Sossano, in the province of Vicenza (northeast of Italy) in mid-September, and in Turin in October.\textsuperscript{15} The “Spanish flu” killed more than 400 people a day, but the report should not circulate so as not to condition the public opinion and demoralise the army involved in the war. In the Austro-Hungarian army, the incidence of mortality was almost triple compared to the Italian soldiers because it was engaged in multiple fronts (Italy in the South and France in the West) and was therefore exposed to multiple sources of infection.\textsuperscript{16}

In mid-December, with the homecoming of the troops, even the second wave ran out. There was also the third wave, from February to April 1919, equally deadly, but, at this point, the number of immune people due to the previous contagion was high enough to contain the epidemic extension.

At the end of all epidemic waves, Italy recorded the highest number of deaths in Europe, even if the final amount is debatable. According to the first epidemiological study on the Spanish flu in Italy\textsuperscript{17}, the estimated amount of deaths is around 600,000. Recently, a more detailed study based on several registers concluded that the Spanish flu in Italy caused approximately 466,000 deaths.\textsuperscript{18} Considering that the Italian population in 1917 was about 38 million,\textsuperscript{19} we can estimate that Spanish flu, summing all the waves, caused the death of more than 1.2% of Italians.

**The 1918 Spanish flu in Pisa**

In Pisa, as in the rest of Europe and Italy, the “Spanish flu” arrived and spread with the same clinical characteristics described above. The first wave probably also reached Pisa but was not recognised and passed unobserved. In fact, the first patients were registered in mid-September 1918. This is the timeline of the so-called ‘second wave’ of the disease in autumn.\textsuperscript{20} The course of the disease in Pisa can be reconstructed through the correspondence between the health and political authorities.

9 September – The President of the Hospital of Pisa writes to the Mayor to obtain more drinking water for the hospitalised patients (about 200 people, including civilians and soldiers) housed in the churches of San Iacopo in Orticaia and S. Croce in Fossabanda.

10 September – The Mayor of the municipality of Collesalvetti (near Livorno) writes to the directorate of the Hospital in Pisa to ask the admission of its own citizens.

12 September – The directorate of the Hospital claims to procrastinate the admissions because the hospital had already admitted 220 infirm.

\textsuperscript{17} Mortara, G. (1925). La salute pubblica in Italia durante e dopo la Guerra. Laterza, Bari, Yale University Press, New Haven.


\textsuperscript{19} Istat (2018) Ricostruzione della popolazione residente e del bilancio demografico, Rilevazione del movimento e calcolo della popolazione residente (dal 2012). Roma

\textsuperscript{20} Fornaciari, G. (2009), 14-28.
20 September – The prefect congratulates for the agreement between the Hospital of Pisa and other neighbouring towns for the extension of the hospitalisations.

22 September – A Health Department memo reports that in the hospital 550 military personnel are hospitalized. The rooms are full, and the staff is scarce, so more doctors and health assistants are necessary.

23 September – The Mayor of Montopoli Valdarno (a little town between Pisa and Florence) asks for help; there is an urgent need for beds in the hospital to care for their own patients.

25 September – The hospital’s President responds, urging him to turn to his own province, Florence, because the hospital in Pisa lacks additional resources and beds.

7 October – Due to a lack of staff, the Director of the hospital, Dr. Dello Sbarba, sends a letter directly to the Minister of the Interior, Mr. Orlando, asking for help.

9 October – King Vittorio Emanuele III scheduled to arrive in Pisa. Specific room with twelve beds for him and his entourage are arranged in the church of San Iacopo in Orticaia if symptoms of influenza should appear. The ward is exposed at the sunny side and fully separated from the rest of the hospital and is fitted with a vast courtyard in which the access is forbidden for other sick persons. Despite the shortage of staff, one doctor is assigned to the King.

10 October – The Hospital asks for 100 doses of anti-pneumococcal serum from the Sierotherapic Institute of Milan.

15 October – The President of the hospital, given the high number of inpatients, asks the Minister of War, Orlando, to use the premises of the Institute of St. Catherine. The Minister responds, inviting him to take all the appropriate measures.

18 October – A telegram from the Military Health Management and the Army Corps of Florence communicates the impossibility to get the anti-pneumococcal serum.

20 October – Minister Orlando issues instructions on influenza epidemic.

21 October – The President of the hospital calls for the urgent dispatch of soldiers to provide for the patients.
21 October – Dr. Dello Sbarba, Dr. Toscanelli and other doctors ask Minister Orlando for new doctors and military nurses, in fact there is a growing awareness among the population about the lack of any assistance.

At this point, the spread of the disease becomes worrying. At 12 p.m. on October 21, hospitalised patients for Spanish influenza among the various medical facilities (many of whom improvised) amounted to 704, of which 557 were soldiers (Table 1). Considering that about 60,000 people lived in Pisa at that time (data from ISTAT, the National Institute of Statistic), the hospitalised patients represented almost 1.2% of the city’s population on that day.

Table 1. Hospitalised patients for Spanish flu among the various medical facilities at 12 p.m. on October 21, 1918, in Pisa (from the Archives of the Azienda Ospedaliero-Università Pisana).

<table>
<thead>
<tr>
<th>Medical Facility</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinica Medica ground floor</td>
<td>111</td>
</tr>
<tr>
<td>Clinica Medica 1st floor</td>
<td>89</td>
</tr>
<tr>
<td>Clinica Medica 2nd floor</td>
<td>99</td>
</tr>
<tr>
<td>Annex</td>
<td>48 women</td>
</tr>
<tr>
<td>San Jacopo</td>
<td>123</td>
</tr>
<tr>
<td>Porta Nuova</td>
<td>26</td>
</tr>
<tr>
<td>Porta Nuova</td>
<td>43 women</td>
</tr>
<tr>
<td>Bagni di San Giuliano</td>
<td>165</td>
</tr>
<tr>
<td><strong>TOTAL AMOUNT</strong></td>
<td><strong>704 (of which 557 soldiers)</strong></td>
</tr>
</tbody>
</table>

22 October – New beds and cots are added in the premises of Bagni di San Giuliano and S. Caterina for new patients. The Health Director of the Hospital of Pisa writes to the Colonel that “the militaries suffering from grippe, hospitalized today, reach the number of 600. Given the current exceptional circumstances, this number is subject to increase dramatically. The daily average of infected by flu and parotitis is around 50 soldiers”.

23 October – The Hospital Healthcare Management asks the Military Health Directorate to relocate 400 soldiers to free rooms for civilians. The Minister of the Interior says to the Prefect that he could not send reinforcements, so to turn to the Red Cross.

24 October – Members of the Provinces of Pisa and Lucca go to the President of the Council of Ministers to expose the serious conditions of the population because of the outbreak of Spanish flu. They mention the
measures he arranged for Pisa (sending 8 military doctors and 20 soldiers of the Red Cross) and prove that these measures were insufficient. They also deliver the list of municipalities in which medical care is missing or inadequate. In the same day, the General Directorate of Logistics Services of the Ministry of War asks the Central Military Pharmacy of Turin to send 2 kg of salicylate quinine.

27 October – The President of the hospital, Dr. Dello Sbarba, writes to the General Directorate of Public Health pointing out the need not only for medical staff and nursing personnel but also for pharmacists.

30 October to 5 November – Broad correspondence between the Military Management and the Hospital Management; the tone of the conversation is elevated, and the request to move the military in order to make places for civilians is rejected.

5 November – The President of the Hospital writes to the prefect that, due to the significant reduction of cases of flu and the decreased use of beds, there is no need to assign other premises. The sick hospitalized in the “Great Hall” are transferred to various departments of the medical clinic.

12 November – The President of the Hospital writes to military physician, Dr. Colombini, in order to complete the collaboration concerning the Hospital in S. Iacopo church by 15 November. In the following days, the wards in Porta Nuova and other hospitals are closed, and the personnel is dismissed. The second “Spanish flu” epidemic wave is ended.

The 1918 Spanish flu in Pisa: clinical data

The Spanish flu ‘first wave’ arrived in Pisa in March-April 1918, but there are no precise data. In fact, the disease was not yet known, and the deaths were almost all caused by superinfection of tuberculosis or bronchopneumonia, both catarrhal and fibrinous, so in the autopsy registries the causes of death are generally attributed to pneumonia or TBC, which were not rare at the time. The symptoms were cough, pain in the eyes and ears, soreness in the lumbar region, and then numbness, fever chills even up to forty degrees. Incubation lasts two days, with sore throats and headaches. However, the virulence of the disease during the first wave was so mild that usually by the third day, the symptoms had almost completely disappeared.

The ‘second wave’ of the epidemic showed greater severity of the symptoms, longer course of the disease, and an increased frequency of
complications, and morbid sequences. In September 1918, this second wave made its way into the Hospital of Pisa. The first death reported in the Clinica Medica was of an 18-year-old civilian male, and the diagnosis was “grippe”. This term probably derives from the German word ‘grippen’ that means ‘to grasp abruptly’, or from the French ‘agripper’ with the meaning of ‘snatch’.21 The pathologist that performed the autopsy reported that the lungs showed patterns of “confluent haemorrhagic pneumonia”. From that day on, several corpses were sent at the Pathology Unit in order to be analysed. The list reports that the victims were always young adults. The disease struck with particular violence the young soldiers because of the promiscuous life in the barracks and trenches and because of a more vigorous immune response that led to intense haemorrhagic pneumonia that caused the death. Another theory that may partially explain these findings is that “the 1918 virus had an intrinsically high virulence, tempered only in those patients who had been born before 1889 because of exposure to a then-circulating virus capable of providing partial immunoprotection against the 1918 virus strain”.22

The infirms felt continuous chills that marked the beginning of the disease. “The chills occur without warning, in full health and determined not by general sensation of intense cold, which occurs for the malaric fever or pneumonia, but by a cold wave rising from the limbs through the back until it reaches the head”.23

After the first chills, the temperature began to rise slowly until it reached its peak (about 39°-40°) in 5-6 hours. The fever was always accompanied by strong oppressing-type headache and rheumatic-type pains in the knees, loins (similar to common lumbago), or the orbits in the distribution of the supraorbital nerve (especially in the movement of the eyeballs upwards). Slight catarrhal inflammation of all mucosae generally accompanied the onset of the disease, characterized by conjunctival, nasal and faringo–laryngeal inflammation spread to the bronchi. Patients turned up red in the face, with intense red conjunctiva and persistent cough without excreted. Another feature was the speed with which a severely debilitating condition appeared, with a clinical appearance similar to that of serious intoxication. These symptoms were often associated with diarrhoea, vomiting, and nausea.

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21 Petrin, I. (1931), Per la storia dell’influenza e la sua denominazione, Bollettino dell’Istituto Storico Italiano dell’Arte Sanitaria XI (5), 223-234.
Many people suffered from severe and uncontrollable nosebleeds. Doctors and nurses learnt to recognize the clinical signs: the face turned purple, cyanotic, and the sputum was tinged with blood. The lungs of the victims filled with fluids and blood, causing a lack of oxygen. As a result, cyanosis started to spread from their extremities, including fingers, toes, nose, ears, and mouth.\textsuperscript{24}

Medical treatment consisted of very few medications, administered orally or via hypodermic.

This was a medical prescription: “ten grams of sodium salicylate and one gram of bismuth magisterium. During the night, three pills of iodoform and quinine, with a two-hour interval. The drugs were dissolved in castor oil, which could also be drunk alone. The diet must be soft and liquid”.\textsuperscript{25}

\textbf{The 1918 Spanish flu in Pisa: autoptic data}

A valuable collection of autopsy registers from 1880 to the present day is conserved in the Archive of the Museum of Anatomical Pathology of the University of Pisa. They represent an essential source to understand the trend of diseases; in fact, through the study of the autopsy records, we can analyse the impact of the Spanish flu on the population of Pisa.

From March 1918 to March 1919, a total of 184 autopsies were performed in the Pathology Unit in Pisa; among them, for 43 of the patients the final cause of death is the Spanish flu. The first autopsy of a deceased patient due to “grippe” was recorded on September 17, 1918. Most of the autopsies (35 out of 43) occur from September 17 to December 31, 1918 (fig. 1).

In the peak of deaths from September 1918 to January 1919, we noticed that the majority of the deceased were young adults between 16 and 30 years (26 out of 38 deaths), while fewer autopsies were performed on patients over 35 years (fig. 2). Moreover, 8 of 38 deaths were females.

The reported diagnosis is always of ‘confluent haemorrhagic bronchopneumonia’, often synthesized with the word ‘grippe’. In all the deceased, large scattered globular clusters, partially merging, with haemorrhagic exudate, were found. In particular, for all the deceased, these anatomical features are reported:

\begin{itemize}
  \item hyperaemia of the brain;
\end{itemize}

\textsuperscript{24} Fornaciari, G. (2009), 26.
\textsuperscript{25} Ibid, 27.
• renal and hepatic degeneration;
• confluent haemorrhagic bronchopneumonia.

In addition, the physical strength of the subjects is directly proportional to the severity and extension of the pulmonary lesion. In fact, the more the

Figure 1. The number of autopsies performed on patients deceased from 'confluent haemorrhagic bronchopneumonia' from August 1918 to March 1919 in Pisa (from the Archives of the Museum of Anatomical Pathology of the Hospital of Pisa).

Figure 2. The age of the deceased submitted to an autopsy at the peak of the Spanish flu from September 1918 to January 1919 in Pisa (from the Archives of the Museum of Anatomical Pathology of the Hospital of Pisa).
health, nutritional status and physical condition of the subject were good, the more the disease manifested itself with aggressiveness and severity. As mentioned above, this data is related to the fact that in young people, the immune response is more intense, paradoxically causing more damage. Moreover, individuals over 40 years were probably ‘immunized’ by a virus similar to the ‘Spanish flu’, but less aggressive, which circulated years before the lethal pandemic. Finally, the young male population was enlisted in the war where the poor hygienic-nutritional conditions favoured the contagion and the mortality. If, in fact, we analyse from the autopsy registers the occupation of the deceased from August 1918 to March 1919, we will note that more than half of the total of number of casualties (43) are soldiers (23). As a result, male sex is also the most represented (34 males vs 9 females).

The last autopsy recorded with the diagnosis of grippe was in March 1919, when even in the rest of the world the epidemic was slowly dwindling.

This data must necessarily be considered partial. In fact, during the ‘second wave’ of the Spanish flu, many deaths are not included among the cases of grippe but are reported as generic pneumonia, pulmonary tuberculosis, septicaemia, nephritis, and pericarditis. Therefore, we cannot certainly exclude that these deaths were caused by the pandemic. Moreover, many patients died at home without being registered in the hospital.

The Pisan pathologists, in the autopsy records, constantly describe the detection of the presence of the Pfeiffer’s bacillus (Haemophilus influenzae), which was the major suspect as the etiological agent of the “confluent haemorrhagic pneumonia” (or grippe). In fact, the majority of the Italian scientists at that time supported the theory of Richard F.J. Pfeiffer. After all, knowledge in virology in the second decade of the 20th century was in its infancy, and doctors were obstinately searching for a bacillus as the cause of the disease.

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26 Tognotti, E. (2015), 76.
Conclusions

Even though there has been a gradual increase in interest recently, the Spanish influenza remains a little-known and underestimated topic. The ‘Spanish flu’, even if people really ‘feared for the end of the world’, was soon forgotten mainly for three reasons. First, during the pandemic the First World War, which devastated the world, caught the attention of the press and people. In addition, censorship prevented the real data of the pandemic from being transmitted and communicated. Finally, immediately after the war, the population wished to overcome the tremendous period of hardship and suffering.

Nowadays, the study of this disease plays a central and masterful role in the history of medicine. Since the virus has been identified and completely sequenced, for the first time, we have been able to compare the biology of an ancient pathogen (albeit ‘recent’) with the historical data reported in the chronicles of the time. The interest is not only historical, but it also has a crucial impact on contemporary and future medicine. In fact, the virus shows genetic characteristics similar to those of influenza viruses that come to Europe mainly from Asia every winter. It is not surprising that when the periodic flu presents with more aggressive characteristics than usual, we begin to talk about the threat of a new “Spanish pandemic”. However, with the information obtained by studying the genetic “heritage” of the 1918/19 virus, we can be ready to face a new virus with the same aggressive characteristics, by creating, for example, a vaccine. Instead, by studying historical data, we can compare the hygienic-sanitary precautions adopted in the past to be able to deal with a serious health emergency today. Lastly, we want to emphasise the importance of the past autopsy registers stored in various archives. Nowadays, non-medicolegal autopsies are in progressive decline, mainly due to the introduction and improvement of imaging techniques. In the past, on the contrary, autopsies had a central role as they were the only occasion in which the doctor could have a direct observation of the disease that he could only suspect. We, therefore, believe that the study of autopsy registers should be encouraged since it represents an incomparable tool for the history of medicine and a useful resource to understand the origin and the evolution of the diseases in the contemporary age.

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References


Sažetak

Pandemija španjolska gripe širila se od 1918. do 1919. i zarazila oko 500 milijuna ljudi, smrtno 50 do 100 milijuna. Ljudi su zbog Prvoga svjetskog rata patili od teškog siromaštva i pothranjenosti, posebno u Europi, što je pridonijelo širenju bolesti. U Italiji se španjolska gripa pojavila u travnju 1918. s nekoliko slučajeva plućne kongestije i bronhopneumonije. Do kraja epidemije umrlo je oko 450 tisuća ljudi, što je uzrokovalo jednu od najviših stopa smrtnosti u Europi.

Iz arhivskih dokumenata i autoptičkih registara bolnice u Pisi možemo doći do nekih zaključaka o utjecaju pandemije na stanovništvo grada i dobiti određene podatke o pokojnicima. U izvornim nekroskopskim registrima zabilježene su 43 obdukcije s dijagnozom gripe (tj. španjolske gripe), od kojih se većina dogadala od rujna do prosinca 1918. Većina umrlih bili su mlade osobe, a više od polovice njih vojnici, i svi su pokazivali simptome konfluentne hemoragične bronhopneumonije pluća, što je bilo tipično obilježje pandemijanske gripe.

Vjerujemo da je proučavanje obduksijskih zapisa neusporediv instrument za povijest medicine i koristan izvor za razumijevanje podrijetla i razvoja bolesti.

Ključne riječi: španjolska gripa, pandemija, Pisa, obdukcija