

# Spanish Flu and Covid-19: Historical Correlations and Bioethical Implications

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## ABSTRACT

This historical review of the Spanish Influenza, better known as Spanish Flu, compared to current scientific knowledge shows many similarities related to the clinical and anatomopathological aspects, and their complications with Covid-19.

Specifically, this study suggests a correct implication of the bioethical criteria aimed at both an early diagnosis of the disease and a correct management of complications. An adequate therapeutic protocol is determined both by clinical evidence and by bioethical guidelines with particular regard to the elderly, the disabled and to those with chronic multisystem diseases.

**Keywords:** Spanish flu; Covid-19; Historical correlations; Bioethical implications

## INTRODUCTION

In December 2019, in Wuhan, a city in China, there were numerous cases of viral infection characterized by severe acute respiratory failure caused by a virus named SARS-CoV2 (Coronavirus 2). The virus, responsible for Covid-19 disease, spread from China to Italy first, then to Europe and the rest of the world to become a serious pandemic. The History of Medicine recalls that our great-grandparents found themselves in similar and even worse conditions a hundred years ago. The famous Spanish influenza, first described by the Spanish press from which it owes its name, actually originated in China as international studies and centres have documented, including the Pasteur Institute [1-4].

China, however, through its researchers, recently denied this provenance in an article in the "Journal of the Chinese Medical Association", vol. 79, written by Dennis Shanks [5]. In 2014, the Canadian Mark Humphries documented the employment of many Chinese as workers in Europe on the French and British fronts of the Great War (1914-1918).

In northern China, towards the end of 1917, there was a flu syndrome identical to the Spanish one, documented by the diagnoses of Chinese health workers, which described an acute respiratory syndrome superimposable on the clinical picture that

appeared later in 1918-1919, with the pandemic called "Spanish", responsible for the death of around 50 million people worldwide. The censorship of the time prevented the spread of news, and the soldiers who fought on the battlefields of the First World War unknowingly favoured the spread of the virus [6-8].

## SPANISH FLU AND COVID-19: HISTORICAL CONSIDERATIONS

Many clinical aspects of Covid-19 are similar to those of the "Spanish" influenza of a century ago. Beside the type of virus, one of the differences, which in the Spanish flu is called H1N1, was the death of mainly young adults in comparison to the elderly who died from Covid-19 [9-10].

In 1997, researchers Taubenberger and Reid, following a previous insight by another Swedish scholar, recovered the Spanish virus in an Alaskan village, in 72 frozen bodies of subjects who had died from this serious pandemic [11-12].

The virus was extracted from the bodies of frozen victims. In subjects affected by the Spanish flu, research described a "chain reaction" that involved cytokines in an exaggerated response from the immune system which, in an attempt to defeat the virus, instead directed itself against its own organism [13-14].

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**Received:** July 15, 2020; **Accepted:** July 29, 2020; **Published:** August 5, 2020

**Citation:** Tornali C, Vecchio FAG, Vecchio I (2020) Spanish Flu and Covid-19: Historical Correlations and Bioethical Implications. J Clin Res Bioeth. 11:352. doi: 10.35248/2155-9627.20.11.352.

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In 1918, many elderly people were "protected" from the pandemic thanks to immunity obtained from a previous exposure that they had had, due to the flu pandemic of 1889-1890, called "Russian Influenza". A relevant datum of the Spanish pandemic regards the exposure to contagion of young adults engaged in war fronts and the lack of information, caused by censorship, on the presence of the virus [15].

Moreover, a hundred years ago, there were no places for "gatherings" of elderly people, as it is the case today in geriatric hospices. It is necessary to underline the fact that 50 percent of coronavirus deaths, in many countries, concerned elderly people hospitalized in geriatric structures. Autopsies, performed in the late 1990, on bodies found in Alaska showed particular inflammation in the lower and bilateral parts of the lungs. Other organs such as the liver, spleen, and kidneys showed damage.

Nerve tissue showed changes in the meninges. In Italy, in 1919, Polettini described the findings of 50 autopsies concerning the military and also pregnant women. They were performed at the University of Pisa between September and October 1918. These autopsies documented the presence in the macroscopic findings of haemorrhagic pictures in many organs [16-17].

An important study on the Spanish flu communicated by Edwin D. Kilbourne, at The Medical College, Valhalla, N.Y. in 1998, and published in 1999, identified the presence of the gene that codes for hemagglutinin in the Spanish virus.

The presence of hemagglutinin seems constant in different types of viruses: influenza A, Swine and now in the Covid virus-19. The researchers found two different types of HA (hemagglutinins) [18-20].

The HA of a 1976 virus subpopulation was similar to that of the swine type A virus and was identified on virus isolates dating back to 1957. Another subpopulation, however, would be similar to that of several other isolated viruses. From 1971 to 1976. These studies also provide evidence that the two subpopulations, antigenically distinguishable, could coexist in the human host. In an article in the journal *Nature* Michael Hopkin reveals that in 1999 and 2000, some researchers recreated part of the pathogenic power of the Spanish virus [21].

From the preservation of this virus in samples taken from victims preserved in Alaska by permfrost, Tumpey, in 2005, managed to reconstruct the Spanish viruses *novo* [22].

Hopkin describes the experiments of the Japanese Yoshihiro Kawaoka, professor of the University of Wisconsin-Madison, in the United States, specialized in the study of influenza and Ebola viruses. Kawaoka's team managed to reconstruct the virus's eight RNA segments, and subsequently inserted some of these genes into a modern flu virus in laboratory mice.

The infected mice developed a lung-like illness of the lung type characterized by severe bleeding, and developed a pathology comparable to that of the Spanish one.

Hopkin reports a sentence from Kawaoka: "What we saw was similar to what we saw in man in 1918" Yoshihiro Kawaoka has

confirmed, in his studies, that one of the fundamental keys to entry into the cells of the victims of the infection is the gene that encodes the Ha protein.

According to Kawaoka, viruses with the gene encoding that special "Ha" protein may still be in circulation among wild birds and both use the Ace2 receptor as the 'gateway' into the cells of the organisms they infect. Thus, in fact, it is expressed:

"One of the key players is hemagglutinin (HA), which is the viral surface glycoprotein that has two functions in the early stage of virus replication: receptor binding and membrane fusion."

In a study published in January 2011, entitled "Pathogenesis of the 1918 pandemic influenza virus", Yoshihiro Kawaoka compares avian influenza with the "Spanish" one and speculates: "... that the 1918 virus could have been of avian origin and transmitted from birds to humans directly or indirectly".

In the process of adaptation to humans through mutations, the 1918 virus is thought to have acquired its high virulence.

According to Kawaoka, wild birds may still be the carriers of the virus that holds that special deleterious protein, the Ha protein.

The Spanish pandemic had a sudden onset characterized by: asthenia, headache, joint pain, neurological symptoms (lethargic encephalitis), dry cough, high fever, bradycardia, haemorrhagic fever, cyanosis, primary flu virus pneumonia and secondary pneumonia bacterial superinfections.

Covid-19 occurs with sudden onset, high fever, cough, fatigue, neurological symptoms, lack of taste and smell, inflammation of the conjunctivae of the eye, gastrointestinal disturbances, bilateral pneumonia. Death caused by Spanish flu occurred after eight days of illness due to secondary bacterial infection [23].

It should also be noted that antibiotics had not yet been discovered at the time of this serious pandemic. The geographical origin of the Spanish remains a topic of controversial discussion. Historian Crosby and writer Barry reported that in the U.S. this pandemic began in the state of Kansas. In 1917, in the USA, in fifteen military camps, there was a first wave of the disease and its high mortality. The war and military hospitals, with their overcrowding, were an ideal place for the spread of the respiratory virus. The Oxford studies concluded that a precursor virus from birds managed to mutate and infect pigs reared in the rear of the war front [24].

One of the most important researchers specialized in the study of the Spanish epidemic, Claude Hannoun, hypothesizing a Chinese origin of the virus and its subsequent mutation in the United States, with further spread of it in France, and in the other battlefields of Europe through the soldiers and sailors.

In 2014, studies carried out in a Canadian university, by historian Mark Humphries, documented with archival evidence, a respiratory disease that would have affected northern China in November 1917, and that the following year was considered identical to the "Spanish" just by the Chinese health authorities.

The spread of the Spanish virus in Europe was caused by thousands of Chinese workers serving on the British and French western front during the First World War [25].

One hundred years ago little was known about viruses, and Spanish flu was thought to be of bacterial origin, and due to *Haemophilus influenzae*, an agent believed to be responsible for the common flu.

In 1918, America hoped to discover a vaccine made from it from *Haemophilus influenzae*, then known as *Bacillus Pfeiffer*. The researchers observed that many flu symptoms were not typical of this bacillus, which had only a small percentage of the victims. Pfeiffer vaccines were irrelevant and aspirin was used on the patients and two serious complications were observed: pulmonary edema and a bacterial over-infection, with subsequent bacterial pneumonia. It is necessary to remember that antibiotics did not yet exist in 1918-19 and therefore people died from bacterial pneumonia, a serious complication.

For the organism was first hit by the virus and later was also attacked by bacteria.

The descriptions of the time reveal that the most surprising complications due to the virus were the appearance of numerous haemorrhages in the mucous membranes, bleeding in the ears and diffuse petechiae, as an effect of the cytokine storm. Today the complications of Covid-19 are always due to cytokines [26].

The virus responsible for the "Spanish" belongs to the family of influenza A viruses, the same that evolves causing the classic seasonal flu. Even today there is no scientific agreement on the origin and pathogenicity of the Spanish virus, also called the H1N1 virus. The 1918 pandemic virus originated earlier from a human H1 virus. This acquired the avian neuraminidase N1 and the genes of internal proteins. The surprising aspect was that this virus, simultaneously with the human pandemic, also spread among pigs previously free from the flu [27-28].

The porcine H1N1 virus, derived from the human Spanish virus, would later return to humans after 1922. Since then many animal experiments have been done. The Spanish pandemic manifested itself in four waves, independent of the seasons, and the second was more lethal than the first due to widespread travels [29].

One hundred years ago, even in the geographic areas least affected by the virus, there were difficulties in everyday life because shops closed and social distancing was implemented, schools were closed and illiteracy ensued, the sick could not be visited, and mass graves were created to bury the dead. In the autumn of 1919, the Spanish flu disappeared without the discovery of a vaccine. Denney in the book "Risk and Society" published in 2005 underlines that many experts had speculated that the world was "on the brink of a flu pandemic" [30].

In Italy, the Experimental Zoo prophylactic Institute of Lombardy and Emilia Romagna "Bruno Ubertini" wrote: "the influenza epidemic in Asia is a crisis of global importance and will continue to demand attention from the international community". The Sars - CoV-2 virus, with its rapid infection, poses a serious danger to the health and life of many people [31-32].

The report of the "Global Preparedness Monitoring Board" (GPMB), published in September 2019 had already focused on the risk. In fact, many countries have organized themselves to discover and isolate people who are the source of contagion and to treat the sick of Covid-19 [33].

## BIOETHICAL IMPLICATIONS

For public health, the SarS-CoV-2 pandemic has determined complex critical issues to be solved, some with profound bioethical implications related to the attempt to protect the lives and health of millions of people. Also, to evaluate the most appropriate priority choices to be made on the sick hospitalized in health facilities.

It is necessary to emphasize that it is always right to protect everyone's health with no exception. To operate without being in a condition of serious shortage of human and bed resources; not to mention medical and protective equipment [34].

The people who need medical assistance are both those infected by the virus alone and those affected by other already existing acute and chronic diseases. A pandemic emergency situation concerns patients hospitalized and undergoing medical treatment and life support in intensive care and in intensive care centres and subjects already clinically evaluated at home. The main priorities to be adopted are the "clinical criterion" and the use of all available, instrumental and professional resources.

The fundamental bioethical implication in the management of various pathologies must not be based on a priori choice or conditioned by the patient's age. It is important to treat chronic, elderly, disabled patients who are most vulnerable to the virus. Furthermore, the criteria used in the health sector must be made clear and official for everyone. Institutional authorities and public opinion must always show a sense of gratitude for all doctors and health professionals who are subject to the risk of infection and extraordinary work rhythms, with added danger for health and life [35-41].

The important bioethical implication concerns the attention and care of the elderly, chronically ill, disabled and terminally ill who slip away without the possibility of having a last farewell from their families.

## CONCLUSIONS

The bioethical implications correlated to the Covid-19 pandemic are based on some parameters: the clinical criteria always need to be correlated to the principles of equality, justice and solidarity, the best possible life expectancy is always to be found using correct bioethical guidelines, the priority exclusion of choices based only on age and past critical issues could avoid serious repercussions for the elderly, the multi-systemic chronically ill and the disabled.

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