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INFLUENZA A VIRUS: ORIGIN AND ITS SUBTYPES

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ABSTRACT

Introduction: It is known that influenza epidemics arise quite frequently, but there are no regular intervals between these events. Epidemics may differ in their consequences, but they usually cause an increase in mortality of older people. The great flu epidemic of the last century claimed millions of human lives. Scientist Richard E. Shope, who investigated swine flu in the 1920s, suspected that the cause of the disease was a virus. As early as 1933, scientists at the National Institute of Medical Research in London isolated the virus for the first time. Thus, the present study seeks to understand how the influenza A virus emerged and was identified. **Method:** Approach used is a literature review, where searches were made through scientific articles, published in the MEDLINE and SciELO databases, where 4 were selected for fitting the inclusion method. **Results and Discussion:** The viral etiology of influenza was proven in 1933, and the three serotypes that infected humans were only identified in 1950. In that same year, it was evident that the strain responsible for the 1918-1919 episode belonged to the particular antigenic variety of subtype A. In 1957, with the emergence of subtype A, influenza reached China and, in 1968, in Hong Kong, subtype A appeared, causing a moderately severe pandemic. Even after almost a century after the recognition of this strain, the influenza virus remains one of the greatest challenges in health control due to its easy antigenic variability and contagiousness. **Final Considerations:** In order for the formation of new subtypes, recombination occurs, which corresponds to the mixture of, for example, genes from a virus that infects humans with genes from viruses that infect other animals, such as birds, thus explaining how the Influenza A retrovirus can acquire greater aggressiveness due to mutations derived from the mixture of animal virus genes, especially poultry and pigs.

Keywords: Viruses. Influenza. Influenza.

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INTRODUCTION

The first description of influenza, also known as Influenza, the Italian word for "influence", in the context of medicine and epidemiology, before the Microbial Theory, was made by Hippocrates, in the fifth century, in the year 412 BC, who described the disease among the inhabitants of the island of Crete, Greece; and, attributed the disease to environmental causes and climatic variations, within the miasmatic theory, influence of the stars and the air.

However, the first medical description with interesting observations is attributed to the physician Molineux, in Ireland and England, between 1688 and 1693. References to flu epidemics in the seventeenth century are found in North America and Europe. From the beginning of the eighteenth century, data on the disease increased in quantity and quality, as chroniclers and doctors recorded information and comments on the number of people infected, whether epidemic or pandemic, the countries involved, and the possible origins of the viral strains.

From the genus *Mixovirus influenzae*, it belongs to the family *Orthomixoviridae*, which contains a single-stranded, segmented RNA genome. It is classified into 03 types: A, B, and C and its isolations occurred in the years 1933, 1940 and 1947, respectively. Type A virus, the most important, can infect humans and animals and is implicated in epidemic and pandemic episodes; the type B virus, which infects only humans, is linked to moderate outbreaks; and the C virus, more stable, affects humans and pigs, causes subclinical disease, without epidemic potential. According to FORLEO NETO et al (2003), pandemics occur irregularly, usually 30 to 40 years apart. Since the century. At least 30 pandemic episodes were described.

Due to its ability to penetrate the body through the mucous membranes of the respiratory tract and eyes, disseminating it through the bloodstream and reaching cells, subtype A presents mutations and rearrangements with higher frequencies in relation to subtypes B and C. That subtype has two surface glycoproteins: hemagglutinin (HA) and neuraminidase (NA) that enable the transport of the virus in host cells. HA has the function of fixing and fusing the virus in the host cell, and is divided into 18 different subtypes, of which 16 circulate in waterfowl and two have been isolated from bats. AN subtypes play a relevant role in the release of viral particles after virus replication, as well as the spread of the virus from one host to another. These proteins are responsible for viral classification and its morbidity, mortality, lethality, and pathogenicity.

The present work aims to carry out a historical approach to the origin and knowledge of the influenza A virus as well as its subtypes, in order to highlight its main occurrences in the world.

METHOD

The study is characterized as a bibliographic study of a systematic review of the specialized literature, carried out through scientific research available in the MEDLINE (Medical Literature Analysis and Retrieval System Online) and SciELO (Scientific Electronic Library Online) databases, using the keywords: Virus, influenza and flu. Articles or theses published between the years 2000 and 2016 were used as inclusion methods, since these were the most recent containing relevant information for the study, with texts available in complete form in the aforementioned databases.

RESULTS AND DISCUSSION

In 2009, the world faced its first flu pandemic of the 21st century, caused by the influenza A/H1N1/California/2009 strain that contains swine, poultry and human genes. Popularly known as "swine flu", swine influenza A had its first cases in Mexico in March 2009 and due to its high contagiousness and virulence it spread quickly to Europe, Canada, Southeast Asia, Africa and Latin America. In June 2009, the World Health Organization officially declared an influenza pandemic. In the post-pandemic period that lasted until August 2010, it had reached 214 infected countries, causing the death of 18,500 people and infection of 575,400. (The Lancet Infectious Diseases, 2012).

In March 2013, a new strain of influenza A virus was described in Asian countries. This strain has the proteins hemagglutinin serotype 7 and neuraminidase serotype 9, and is therefore called influenza A (H7N9). This new variant is a recombination of circulating strains among birds that has shown the ability to infect humans and, as cases outside the Asian continent have not yet been described, classifying the epidemic as geographically restricted.

Among the communities, influenza epidemics and pandemics begin abruptly and peak in two or three weeks, with a total duration of 5 to 8 weeks. The impact of influenza epidemics is a reflection of the interaction between viral antigenic variation, the level of protection of the population against circulating strains, and the degree of virulence of the viruses. Minor antigenic variations occur every two to three years for virus A subtypes and every 5 to 6 years for type B viruses. Such variations are due to point mutations in viral genome segments that result in changes in the amino acids that make up surface

glycoproteins, particularly hemagglutinin. The major antigenic variations are those associated with the complete replacement of one or both segments of the viral genome, which control the production of surface glycoproteins.

> The challenge is, for WHO tracking, to correctly predict or detect emerging lineages at an early stage, as due to the 6 or more months required to prepare a vaccine, there is a possibility that to date a vaccine is manufactured to support a global campaign, it is no longer compatible with circulating viruses. Any vaccination approach that targets the classic neutralizing responses to HA and/or NA must address antigenic drift effectively. (KIM et al., 2018)

The worst epidemic of the flu virus occurred at the beginning of the twentieth century, between the years 1918 and 1920, still with dubious origin, it began in Asia or in the military camps in the interior of the United States of America, due to the intense movement of troops from allied nations and had as a biological agent causing the disease was identified as the virus type A (H1-N1). The Spanish designation is due to the fact that Spain, neutral in World War I, made official notification to the World Health Organization about the disease that devastated lives in the country with great contagion, morbidity and lethality power. In Brazil, for example, although the number of infected and dead are variable, it is estimated that 35,240 people were fatal victims of the virus, among them the 5th president of Brazil, the lawyer and Counselor of the Empire, Mr. Francisco de Paula Rodrigues Alves. This disease was introduced into the country by crew members of the English ship "*Demerara*" that left Liverpool, England, docked and disembarked passengers in the ports of Recife, Salvador and Rio de Janeiro.

> This pandemic was marked by extreme scope, aggressiveness and contagiousness, believed to have victimized 38 million people in Europe and America. Although in many parts of the world there are no data, it is estimated that it has infected 50% of the world's population, 25% have suffered a clinical infection and total mortality has been between 40 and 50 million. The number of 20 million deaths, frequently cited, is visibly very low (Costa, L et al., Influenza Pandemics).

Again on the Asian continent, this time originating in China during the 50s, the Influenza A/Singapore/1/57 (H2N2) virus, with the HA and NA glycoproteins different from all previous types, led to the death of 4 million people, affecting about 25% to 50% of the world's population. The virus was first isolated in Japan in 1957, followed by the United States and England in the same year. Years later, during 1968 and 1969, a genetic variation of H2N2, H3N2, gave rise to the Hong Kong Flu, whose virus was identified and isolated in this Chinese city in 1968, with a higher incidence of 40% in the population aged 10 to 14 years, and hospitalization and mortality among the elderly, young people and individuals with defined risks in chronic and cardiopulmonary diseases.

In 1930, researchers began the development of the flu vaccine in order to find a solution containing the damage caused by the influenza virus. After 10 years, in 1940, the first influenza vaccine was approved in the northern hemisphere, while in Brazil, applications began 40 years later, in 1980, being composed of different strains of the Myxovirus influenza virus and inactivated, fragmented and purified, and generally containing elements of the surface of the virus, such as hemagglutinin and neuraminidase, being an inactivated vaccine, which does not cause the disease and provides protection based on the induction of the production of neutralizing antibodies to the virus, especially against the viral hemagglutinin contained in the vaccine. The immunity conferred by the vaccine develops after 15 days of vaccination and its duration is about 6 months to 1 year. Such as the maximum antibody titers, obtained within 1 to 2 months after vaccination. Currently, there are four brands of the tetravalent influenza vaccine available: Fluarix Tetra (GSK), Fluquadri (Sanofi-Pasteur), Influvac Tetra (Abbott) and Vaxitetra (Sanofi-Pasteur).

CONCLUSIONS/FINAL CONSIDERATIONS

The Influenza A retrovirus can acquire greater aggressiveness due to mutations derived from the mixture of virus genes from animals, especially birds and pigs. For the formation of new subtypes, recombination occurs, which corresponds to the mixture of, for example, genes from a virus that infects humans with genes from viruses that infect other animals, such as birds. The severity of the infection is attenuated as the population is immunized, either by vaccines or by the flu-like clinical condition itself.

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