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TO THE HISTORY OF PANDEMICS: STATISTICS AND FORECAST

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Abstract. The article is devoted to the study of human experience related to fight against a viral disease known as influenza infection. The outbreaks of the disease occurred over several millennia and described in the surviving documentary sources are considered. The main attention is paid to investigations of native epidemiologists on this problem. In particular, an analysis of works published more than 80 years ago is shown. It is emphasized that some elements of the influenza epidemic described in this publication are in many respects similar to the features of the modern coronavirus pandemic. History of studies devoted to mechanism of infection transmission is described. Significant attention is paid to the developments of scientists associated with the problem of identifying the causative agent of the disease. The contribution of native scientists in revealing the features of the pathogenesis of infection diseases is highlighted. It is noted that important factors in the spread of infection nowadays are globalization and migration processes. It is emphasized that the speed of infectious diseases spread is considerably caused by the capabilities of modern transport too. The history of studies related to the prevention of influenza by immunization and vaccination is reviewed. A comparative analysis of the application of these prophylactic arrangements in a historical retrospective is given. The possibility of preventing the spread of a viral infection by taking appropriate measures was emphasized. The important role of the mass media is indicated, which consists in timely and truthful information of the population. The position of leading modern scientists on this issue, in particular, M. Honigsbaum, K. G. Vasiliev, S. V. Komisarenko etc. is cited. It is summarized, that the works of native epidemiologists L. V. Hromashevskiy, N. F. Gamaleya, D. S. Samoilovych and others has not lost its relevance and can be the basis for the searching effective methods to combat influenza infection in future.

Key words: influenza, epidemic, infection transmission, coronavirus, immunization, vaccination.

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ДО ІСТОРІЇ ПАНДЕМІЙ: СТАТИСТИКА ТА ПРОГНОЗУВАННЯ

Анотація. Стаття присвячена вивченню людського досвіду боротьби з вірусним захворюванням, відомим як грип. Розглянуто спалахи захворювання, що відбувалися протягом кількох

тисячоліть й описані в документальних джерелах, що збереглися. Основну увагу приділено дослідженням вітчизняних епідеміологів з цієї проблеми. Зокрема, подано аналіз праць, виданих понад 80 років тому. Наголошується, що деякі елементи описаної в цій публікації епідемії грипу багато в чому схожі з особливостями сучасної пандемії коронавірусу. Описано історію досліджень, присвячених механізму передачі інфекції. Значна увага приділяється розробкам вчених, пов'язаних з проблемою ідентифікації збудника захворювання. Висвітлено внесок вітчизняних учених у розкриття особливостей патогенезу інфекційних хвороб. Зазначається, що важливими чинниками поширення інфекції сьогодні є глобалізація та міграційні процеси. Підкреслюється, що швидкість розповсюдження інфекційних захворювань сьогодні значною мірою викликає можливість сучасних транспортних засобів. Оглядається історія досліджень, пов'язаних із профілактикою грипу шляхом імунізації та вакцинації. Подано порівняльний аналіз застосування цих профілактичних заходів в історичній ретроспективі. Наголошено на можливості запобігти поширенню вірусної інфекції шляхом вжиття відповідних заходів. Вказано на важливу роль засобів масової інформації, яка полягає у своєчасному та правдивому інформуванні населення. Наводиться позиція з цього питання провідних сучасних науковців, а саме: М. Хонінгбаума, К. Г. Васильєва, С. В. Комісаренка та ін. Робиться висновок, що праці вітчизняних епідеміологів Л. В. Громашевського, М. Ф. Гамалії, Д. С. Самойловича та інших не втратили своєї актуальності і можуть бути основою для пошуку ефективних методів боротьби з грипоною інфекцією в майбутньому.

Ключові слова: грип, епідемія, передача інфекції, коронавірус, імунізація, вакцинація.

Introduction. In December 2019, an outbreak of a cruel disease began in China, in the city of Wuhan. This illness quickly spread to various regions of the planet and was recognized by the World Health Organization as a pandemic on March 11, 2020. At the beginning of 2020, there were no vaccines or specific antiviral drugs against it, and the only way to prevent it was to stop physical contact and strict quarantine, which led to serious global socio-economic consequences. Due to the restriction of movement, many people could not get the help they needed in time. The supply shortage led to panic purchases and destocking in shopping centres. Mass cultural and scientific events were cancelled, work and study were conducted mostly online, and people received information only through the Internet. Unfortunately, not all the information spread over mass media was relevant. Fake information increased the threat of danger, which itself was significant; apocalyptic prophecies gave rise to eschatological ideas; common provocative scarecrows caused stress, which contributed to the deterioration of health, especially in hypertensive and cardiac patients.

Analysis of recent research and publications. After the appearance of COVID-19, Dean Koontz's book "Eyes of Darkness", first published in 1981, has found its supporters again [10]. In this tense thriller, the author described the fictional virus "Wuhan-400", which was characterized by 100% mortality at the absence of any medicine against it. In addition to scaring people with predictions of inevitable death, Koontz's book focused on the origin of the pathogen in China, which contributed to manifestations of xenophobia against the Chinese. Some modern researchers also tend to emphasize the danger of this disease [8, p. 10; 9, p. 35].

The 2002–2004 outbreak of severe acute respiratory syndrome began in rural Foshan, Guangdong Province, southern China, on November 16, 2002. The previously unknown form of atypical pneumonia was called severe respiratory syndrome SARS. Its causative agent turned out to be a virus from the SARS-CoV family of coronaviruses, and its carriers from bats to humans became civets, which are sometimes kept as pets in that region [8, p. 10]. In 2012, Saudi Arabia experienced a SARS-like disease called Middle East Respiratory Syndrome (MERS). Its causative agent turned out to be MERS-CoV, which was transferred from bats to humans through camels [8, p. 11].

The 2019 pandemic also has a "Chinese" origin. However, there is no reliable evidence about the experimental origin of this virus in the Wuhan laboratory. Thus, such a version can be considered more as political than scientifically confirmed [8, p. 16]. Among known human coronaviruses, four periodically cause acute respiratory diseases, and three are fatal for humans (SARS-CoV-1, MERS-CoV, SARS-CoV-2) [9, pp. 13–14]. According to the English historian of medicine Mark Honigsbaum, this happens not only because microbes are very changeable. It has been known since the time of Pasteur. The problem is that we

repeatedly help them to occupy new ecological niches and spread to new places in the world. It usually becomes evident only after the outbreak of another disease [8].

At the same time, there is a certain number of publications devoted to the history of the fight against epidemics of various etiologies. Among them we can mark the works of recent years [6; 7].

Sources and methods. The study is based on the fundamental principles of historicism, objectivity and comprehensiveness, which determine the research methods, including comparative-historical, subject-logical, system-functional methods. Special techniques, such as problem-chronological, comparative, biographical methods are also engaged. We used the origin and archival approaches for analysis of the source base. The method of generalization and systematization of facts is employed in the preparation of conclusions.

Thus, **the aim of the article** to analyze the history of native scientists developments dedicated to the problem of combating viral infections, in particular, influenza. Also the purpose of this work is to show the importance of these studies in the conditions of the spreading modern pandemics, in particular, COVID-19.

Basic material and results. Indeed, a number of viral pandemics with symptoms of influenza originated in China. The pandemic of the disease of 1781–1782, known as “epidemic catarrhal fever” and first named “influenza”, arose in the autumn of 1781 in China, as it was written by N. Gamaleya [3]. Of course, identification of the causative agent was not discussed in those distant times. The pandemic (“Spanish disease”) of the First World War (1918–1919) appeared in 1917 also in China.

So, it happened that bat colonies in China, where natural source of coronavirus is located, became the historical reservoir for the existence of this type in the biosphere. This situation confirms the doctrine concerning the “mechanism of infection transmission”, which was developed 60 years ago by L. Hromashevskiy, a student of D. Zabolotny. The mechanism of transmission in his interpretation is moving the pathogen from one organism to another, which was formed in the process of evolution and ensures the existence of this species in nature. In substantiating the theory of transmission mechanism L. Hromashevskiy noted three successive stages:

- 1) isolation of the pathogen from the infected organism;
- 2) its stay in the environment;
- 3) penetration into a susceptible organism [11].

Urbanization and globalization are the key factors in the rapid spread of infection today. Another important factor, of course, is the greatly increased global interconnection via international travel and trade. In the sixteenth century, it took weeks for smallpox, measles, and other Old-World pathogens to reach the New World. It took even more time for carriers of diseases such as yellow fever to take root in the Americas. A significant contribution to the epidemiology and epizootology of infection diseases was made by N. Gamaleya [12]. According to his investigations, in 1830, it took 11 months for the flu to travel from Moscow to America, and in 1889, the flu travelled the same distance within 3 months. The more accessible was rail travel, the faster disease was transmitted. Although, according to the scientist, “it is not the linear distance that is important for the spread of influenza, but the active communication” [3, p. 8].

Today, international flights on jet aircraft contribute to the fact that the virus can be transferred to any country or continent within 72 hours. Wuhan is the seventh largest city in China, with more than 11 million people. It is the main transport hub in central China, connected by direct flights to Europe. It is not surprising that after becoming active in a natural reservoir in China, the coronavirus was able to spread very quickly around the globe. And it is quite clear that Wuhan was considered as a place to create the world’s largest Centre for the Control of Disease Prevention, which is engaged in the study of coronaviruses.

In the first half of the 19th century, the level of scientific knowledge did not allow us to clearly define the characteristics of viruses that cause influenza diseases and the mechanism of their transmission. However, some features of the influenza epidemic, highlighted 80 years ago in the work of N. Gamaleya, are similar to certain elements of the coronavirus pandemic noted by modern scientists.

The flu virus visits us every year and can cause epidemics that sometimes take the form of a pandemic. Epidemic influenza has been known to mankind since ancient times. In the 5th century BC this contagious disease raged in Thrace, in the north of Greece. It was described by Hippocrates in his 6th book “Epidemic” [7]. Plague, cholera, and influenza epidemics caused a huge number of victims. Suffice it to say that more than 690,000 people died from cholera alone in 1848 [16, p. 217]. But the worst of such pandemics was the Spanish flu (1918–1919), which affected the course of World War I. During 1.5 years (18 months), it went around the entire globe and caused 20 million victims, three times more than in 51 months of the war [3, p. 11].

“Especially characteristic of the flu is in its epidemic form,” – wrote N. Gamaleya, – “it is the extreme contagiousness, the speed of its movement, the huge number of the population affected by it. Nothing could be compared to the ability of an epidemic flu to capture all the countries of the globe in a short period of time” [3, p. 4]. Today’s pandemic, which was named COVID-19, turned out to be even more active: its causative agent, SARS-CoV-2, is transmitted more easily than the flu virus. In the case of influenza, according to N. Gamaleya: “Contamination by droplet infection is the main way of spreading the disease. But there is another possibility – the using shared utensils” [3, p. 33]. The most efficient path of COVID-19 transmission is airborne, but it is also possible through infected surfaces. “A characteristic (and extremely dangerous) feature of SARS-CoV-2 is the ability to spread from infected people to those who do not have symptoms of the disease yet [9, p. 24]. Similar information can be found in N. Gamaleya’s work: “Recently, the existence of healthy carriers with influenza has been experimentally confirmed” [3, p. 26].

During the flu, high fever, headache and muscle aches are combined with serious pulmonary disorder, bronchitis, bronchopneumonia and pneumonia, which can often cause death [3, p. 7]. The three main symptoms of COVID-19 are fever, high temperature, dry cough and difficulty breathing [9, p. 35]. The final phase is acute respiratory distress syndrome and possible death [9, p. 22].

Influenza affects the entire system of the body. Localizing initially in the respiratory organs, the flu infection affects the heart and its vessels, the digestive organs, the nervous and the endocrine systems, and the sense organs [3, p. 46]. The SARS-CoV-2 virus can cause significant damage to the kidneys, liver, heart and, in general, almost every human organ system [9, p. 35].

In 1890, the medical academy in Paris reported: “The influenza epidemic is becoming more and more malignant and recovered people do not acquire immunity; there are many examples of 2- or 3-times repeating disease of the same person” [3, p. 7]. In the monograph of N. Gamaleya it is stated that “Immunity to influenza in humans is short-lived, and repeated diseases in humans are very frequent. This is a characteristic exception to the general rule, since usually viral infections leave persistent immunity” [3, p. 18]. Research over the next ten years proved that the possibility of re-infection cannot be excluded [9, p. 43].

In various parts of the world until the middle of the 20th century, many strains of the influenza virus were isolated, which have certain qualitative and quantitative differences. They differ in serological and antigenic properties, which are important in the development of vaccines [3, p. 49]. According to S. Komisarenko, the natural reservoir that has existed in China for more than 65 million years has created unique opportunities for the evolution of viruses [9, p. 16].

Until the beginning of the 40s of the 20th century, according to N. Gamaleya, attempts to actively immunize people against the influenza virus were made. But certain results were not achieved. As S. Komisarenko said, referencing to foreign source [14]: “Despite the efforts of the best laboratories and pharmaceutical companies in the world, specific and effective drugs against COVID-19 have not yet been invented” [9, p. 47]. And in spite of the world’s leading scientists have developed a number of antiviral vaccines and drugs (Pfizer-BioNTech, Moderna, Paxlovid), the final victory over infectious diseases is still far away.

According to the modern researchers, the spread of the Chinese COVID-19 virus can still be limited by certain means, unlike the seasonal flu epidemic, which is transmitted from person to person very quickly. This is exactly what N. Gamaleya’s monograph is about. He notes that it is possible to restrain the spread of a pandemic or seasonal epidemic, but it is very difficult to prevent their appearance: “Terrible pandemics and large epidemics appear

after an indefinite period of time, and it is not easy to prevent them with a vaccine. It is irrational to vaccinate the population in advance, as was done against smallpox due to the instability of influenza immunity. For the same reasons, it is also impractical to fight endemic influenza with vaccination, which is common and often recurring” [3, p. 58].

For thousands of years, mankind has constantly suffered from both influenza viruses and the causative agents of plague, cholera, tuberculosis, etc. At the end of the 19th century, the prospects of a successful fight against an invisible enemy appeared. In the 1880s, the German bacteriologist Robert Koch and his French colleague Louis Pasteur discovered the “germ theory” of disease, showing that tuberculosis was a bacterial infection, and proposed vaccination against anthrax and rabies. In the 1950s, during the period of euphoria caused by the discovery of antibiotics, the American microbiologist René Dubos opposed the expediency of overly optimistic illusions in solving serious medical problems [2]. That time the most of his colleagues considered the fight against infectious diseases quite successful. They believed that the eradication of the common causes of infection would come in a short time. But R. Dubos argued that medical science caused “essentially destructive forces” that could one day destroy the medical utopia. In his opinion, complete freedom from disease was a “mirage”, it was almost incompatible with the life process, and at some unpredictable time and in some irresistible way nature would strike back. “Modern humans believe that they have achieved almost complete domination over the natural forces that shaped his evolution in the past, and that he can now direct his own biological and cultural destiny. But this may be an illusion. Like all other living beings, it is part of an extremely complex ecological system and is connected to all its components by countless connecting links” [2, pp. 266–267].

All the advances in science and technology, R. Dubos argued, do not actualize the utopian dream of general well-being because they ignore the dynamic process of adaptation to the ever-changing environment with which every living organism inevitably comes into contact. Organized species such as ants have established a satisfactory equilibrium with their environment and do not suffer from large waves of disease or changes in their social structure. But humans are essentially dynamic; their way of life constantly changes from century to century. They experiment with synthetic products and change their diet; construct cities where rats and infections spread; build cars and factories that pollute the air; create radioactive bombs. Life becomes more comfortable, technology becomes more complex, and new factors create new dangers.

An assessment of pandemics and epidemics development that have already occurred allows us to conclude that this process is accelerating. “Despite our limited understanding of how the novel coronavirus works and what it does to the human body, many are putting what I consider a disproportionate amount of faith in the possibility of a COVID-19 vaccine by 2021” [6]. The cruel COVID-19 pandemic should be a useful lesson for us. “Further development of the situation,” as S. Komisarenko notes, “depends, on the one hand, from the evolution of this virus, and on the other hand, from the success of humanity’s efforts to contain the spread of the virus, compliance with a set of anti-epidemiological measures, and the creation of effective antiviral drugs, diagnostics, and vaccines. With a high probability, SARS-CoV-2 (or its derivatives) can become companions of our lives for many years, and humanity needs to adapt to the corresponding changes in everyday life” [9, p. 89].

Conclusion. The discussion started by R. Dubos a quarter of a century ago is gaining relevance today. His disappointing forecast is not hopeless: we must recognize the inevitability of our coexistence on the same planet with representatives of the microcosm and learn to create conditions for preserving our own health. Medical researchers should not be blinded by the threats posed by known and unknown pathogens, and depend of uncertain paradigms and causation theories, both apocalyptic and exorbitantly optimistic. The ecological postulate of R. Dubos: “Think globally, act locally” can help scientists determine the real trends of the harmonious development for all existing forms of living matter in the biosphere, without departing from the requirements of the ecological imperative.

The means of mass communication should not intimidate people by outbreaks of epidemic diseases. They should, as recommended by one of the founders of epidemiological science, our compatriot Danylo Samoilovych, “...raise people’s courage by showing them with simple and clear examples that we have possibility to fight cruel disease and there are

ways to prevent its spread” [13, p. 48]. A century and a half later, the French novelist and philosopher Albert Camus expressed a similar opinion regarding the task of the press during the epidemic. Printed editions, he believes, should inform citizens with maximum objectivity about the progression or fading of the disease; to give them the most authoritative information about the further course of the plague; maintain the spirit of the population, distribute the necessary medical recommendations; in a word, to consolidate the good will of all and everyone in order to successfully overcome a natural disaster together [1]. Remember appeal of epidemiologist and writer Yuriy Shcherbak, which is actual today. It proclaims that pandemic is still ongoing. And the fight against a dangerous infection is in at its peak [15].

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