Viktor Mikhailovich Zhdanov and the eradication of smallpox

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Abstract. Considering current epidemiological and social phenomena such as CoVid-19 pandemic, re-occurrence of monkeypox and vaccine hesitancy, the authors chose to delineate an historical, human, and scientific profile of Dr. Viktor Mikhailovich Zhdanov, as a key figure related not only to smallpox eradication, but also to the building up of worldwide vaccination strategies. The authors present some of Zhdanov main life and scientific experiences and awards in virology, epidemiology, and public health. The authors highlight the need for international commitment to cooperate in the fields of vaccine research and vaccine hesitancy.

Key words: Smallpox Eradication, Zhdanov, Vaccination campaigns, History of Public Health.

Introduction

In 2020, Viktor Mikhailovich Zhdanov was awarded the "Future of Life Award", alongside William Foege, for his determinant contribution to smallpox eradication. In an online ceremony, Bill Gates, Anthony Fauci and Nobel Laureate Jennifer Doudna praised the role of the Soviet virologist and epidemiologist (1). Prof. Will MacAskill, from Oxford University (United Kingdom), defined Zhdanov "the best person who ever lived" (1) "for successfully persuading the World Health Assembly to initiate an eradication campaign where the USA and the Soviet Union collaborated despite the Cold War" (1). In present times, the authors consider extremely worthy to dedicate a paper to commemorate the figure of Dr. Zhdanov, for four main reasons:

1. The occurrence of a global pandemic caused by a "new" virus.
2. The re-occurrence of monkeypox in humans.
3. The recent 40th anniversary of human smallpox eradication.
4. The need for international cooperation in the fields of vaccine research and vaccine hesitancy.

Smallpox is an airborne disease, caused by a *poxvirus*, with a very high fatality-rate (15-40%) and possible severe and irreversible consequences (scars, ulcers on the body, encephalitis, and loss of vision). The infection spreads rapidly and claimed a huge number of lives around the world (2, 3). Epidemics and pandemics occurred worldwide during centuries, American native population were decimated by smallpox in the XVI century, over 60 million people died in Europe only during the XVIII century and over 400 million people died of smallpox in its last century (4, 5, 6).

For as long as this infectious disease existed, scientists from all over the world have carefully studied its course, clinical manifestations, consequences, and causes. As a result of the huge work on the study of this pathology, it was noted that people who often encountered animals and were infected with cowpox were much less likely to suffer from smallpox (5, 6). From this empiric evidence, Dr. Edward Jenner developed a first vaccination, and tested it on the young James Phips, opening the era of vaccination (3, 7).

After the worldwide eradication campaign lead by the WHO, a laboratory accident with cases and deaths occurred in the United Kingdom, and laboratories retaining smallpox virus decreased first to 4 and after to

only 2, CDC (Center for Diseases Control) in Atlanta (U.S.A.) and VECTOR (Государственный научный центр вирусологии и биотехнологии - State Research Center of Virology and Biotechnology) in Koltsovo (Russian Federation) (8, 9). An intense debate on the real scientific meaning and sanitary of such a storage is today opened also for the fear of military use of them (10, 11).

We consider Viktor Zhdanov as a pioneer in the field of the prevention of infectious diseases, and our paper aims at putting him in the spotlight to set an example for current and future generations of researchers and public health operators in light of the four previously mentioned reasons.

Early life and education

Viktor Mikhailovich Zhdanov (Віктор Михайлович Жданов) was born on February 1st (February 14th in N.S. dating), 1914 in the village of Shtepino, Bakhmut district, Yekaterinoslav province, from the family of a rural physician. At age twelve, young Zhdanov proved his competence, and his desire to continue his father's work, as he made a wound dressing for a peasant who had hurt his leg while mowing grass. In the end, he was able to save the man's lower limb and life.

It should be noted that since his school years, he had always shown leadership skills, a natural desire to understand issues to come to the right conclusions and make the right decisions. While still studying at school, intending to enter a university, Zhdanov began writing a textbook for admission to a higher educational institution, "Fundamentals of Physics" (12, 13).

In 1930, he became a student of the Kharkiv Medical University, from which he graduated with honors in 1936. During his studies, to earn a living, he worked as an accompanist in a cinema. In his second year, he wrote his own opera "The Ballad of the Cossack Opanas", acting simultaneously as the author, director, and producer. Already in his first year, Zhdanov actively showed interest in scientific activities. His first scientific work, written at the age of 19 - "The effect of tissue autolysates on the sugar content in blood serum and red blood cells", was highly appreciated by university professors, who spotted the promising student (12, 13). After his graduation from the University, Zhdanov chose to keep engaging in scientific research, and between 1937 and 1941 he studied by correspondence at the Physics Faculty of the Leningrad State University.

At that time, Zhdanov's scientific activity was mainly devoted to the study of infectious pathology and regional epidemiology of infectious diseases in the south of Soviet Union. He took an active part in the fight against malaria, dysentery, worked on quarantine measures to prevent the spread of infections from abroad into USSR. Thus, Zhdanov highly contributed to the creation and organization of the sanitary and epidemiological service. It was at that time that the scientist first focused on the need to eradicate deadly epidemic and pandemic infections that claim a huge number of lives.

After the end of the Great Patriotic War (World War II), Zhdanov returned to Kharkiv, to continue his scientific activity. In 1946, Zhdanov gained his PhD, with a doctoral dissertation on "Infectious hepatitis (Botkin's disease). Etiology and epidemiology", which was later published as a monograph.

Zhdanov's further activity is linked to the Institute of Epidemiology and Microbiology. In 1948, he became its headmaster, while also holding the position of Professor at the Department of Epidemiology of the Kharkiv Institute of Advanced Medical Training. In 1950, Zhdanov was elected a corresponding member of the Academy of Medical Sciences of the USSR. In the same year, Zhdanov accepted a position as Chief of the Epidemiology Department in the USSR Ministry of Health and was then promoted Deputy Minister of Health (14). In 1953, he wrote a book - "Infectious human diseases. Systematics and evolution" (15) and in 1955 he authored a three-volume publication "Sanitary and Epidemiological station" ("Organization and methods of work", "Preliminary and current sanitary supervision", "Prevention of infectious diseases"). A year later, he founded the medical scientific journal "Problems of Virology", and in the same year he gave a lecture on "Problems of prevention and elimination of infectious diseases in the USSR" at the XVIII All-Union Congress of hygienists, epidemiologists, microbiologists, and infectious disease specialists in Leningrad. In 1961, he began his activity at the Moscow Institute

of Virology named after D. I. Ivanovsky, which, under his leadership, became the leading virological institute of the country dealing with problems of general and molecular virology. In 1961, Zhdanov, having received the title of the Academician of the USSR Academy of Medical Sciences, continued to study epidemiology, offering measures for the state protection and treatment of infectious diseases: dysentery, diphtheria, pertussis, childhood viral infections, measles, epidemic hepatitis, typhoid fever, influenza, infectious mononucleosis.

Later he studied the variability of influenza viruses, and the research results were the basis for the international development of influenza knowledge and effective vaccines (12, 16). In the fall of 1977, he isolated an unusual influenza virus strain, that eventually caused the 1977 pandemic, and that he immediately made available to the other WHO Collaborating Centers, where vaccines were developed (14).

His part in the global fight against Smallpox

At the age of thirty, Zhdanov actively began to thoroughly study viral human diseases, in particular viral hepatitis A, B, D and E (14). A little later, the scientist focused on another infectious pathology, smallpox. Zhdanov and his colleagues concluded that only universal vaccination could defeat and eradicate smallpox. In 1958, at the XI session of the World Health Assembly, a program for the global elimination of smallpox was announced, which became the first experience in trying to eradicate this infection worldwide. Zhdanov understood the importance of this work, as he nurtured the idea of a global organized fight against smallpox (17). He considered the most important part of the program to be the universal vaccination of the entire world population. According to the scientist, only combining the efforts of all countries, it might be possible for mankind to cope with this particularly dangerous viral infection. In confirmation, Zhdanov cited the example of the USSR, where smallpox was defeated in the 1930s after the implementation of the decree of the Council of People's Commissars on mandatory smallpox vaccination (18).

Unfortunately, Zhdanov's program required large financial investments and a huge number of vaccines doses that were not available with disposable resources (18, 19). In 1959, after the death of one of the Soviet delegates who had returned from India (Alexey Kokorekin) and was diagnosed with smallpox at the Institute of virology, it became clear that the need to stop the spread of smallpox was imperative. In this regard, an operation was carried out in Moscow with the participation of Moscow sanitary and law enforcement agencies. A quarantine was declared, and the general vaccination of the population began. According to statistics, a total of 46 people contracted smallpox in Moscow in January 1960, and three died. Smallpox was identified at the Institute directed by Zhdanov, who, just a year before, had defended the Program for the Global Elimination of Smallpox at the WHO assembly (20, 21). Terrible conclusions were made: smallpox is able to return to where it has not been for 30 years and therefore here is no doubt that the vaccine is vital.

WHO fully supported the program only in 1966, until that time, most of the vaccine (25 million doses in the first year) had been supplied by the USSR (22). The elimination of smallpox has acquired a global character (18, 21). The program was implemented despite the Cold War. Healthcare professionals from different countries successfully worked together and in an organized manner in places where unsanitary conditions flourished and contributed to the spread of smallpox, and where people refused to be vaccinated (18).

It took 20 years of hard work by heath workers all over the world for smallpox to be finally defeated with the help of Zhdanov's program, including Africa and the Indian sub-continent. The last case of the disease worldwide was recorded in 1978 (18, 23, 24).

For his great contribution to science and scientific achievements in the elimination of a particularly dangerous viral infection, WHO awarded Zhdanov with the "Bifurcation Needle" badge and the diploma "For Outstanding Services in the elimination of smallpox worldwide".

Later life

The world managed to defeat one of the deadliest human diseases, also thanks to Zhdanov's efforts. The scientist, despite such a great success, continued

to conduce new research, together with academicians of the Russian Academy of Sciences such as Valentin Ivanovich Pokrovsky and Rėm Viktorovich Petrov, with whom he studied the HIV infection, highlighting this problem as global and extremely important for all mankind. A very innovative and one of Zhdanov's favorite speculations was to contemplate the evolution of cells and viruses as life forms. He believed that the viruses could enrich the gene pool of the cells, as they possess the unique mechanism of penetration and exit (14).

Zhdanov would often say: "Fastidium est quies" - "Boredom is peace" (25). Colleagues and students of the great scientist loved and respected their teacher for his simplicity in communication, for trust, for the ability to admit mistakes.

Zhdanov engaged not only in scientific, but also in political activities, always trying to improve the scientific work of his institute and never forgetting to pay attention to cultural life.

He regularly traveled abroad and encouraged his colleagues to do the same. Zhdanov considered the achievements of science as an international treasure. Academician of the Russian Academy of Sciences Nikolai Fedotovich Izmerov in his memoirs pointed out "how high the authority of V. M. Zhdanov among the famous virologists of the world actually was. He was highly appreciated and deeply revered by the WHO Director-General, Dr. Marcolino Gomes Candau, who often listened to the advice of the Soviet scientist and recommended him as a member of the WHO Advisory Council on Medical Research" (25).

Viktor Mikhailovich Zhdanov passed away in 1987. He was awarded two Orders of the October Revolution, two Orders of the Red Banner of Labor, the Order of the Red Star and many medals.

He was an honorary member of several foreign medical associations, including the American Association of Preventive Medicine, the Belgium Society of Tropical Medicine, the Hungarian Scientific Medical Society, and the Polish Society of Microbiologists (14). He made a very significant contribution to science, leaving behind a huge scientific legacy of more than 20 monographs and a very large number of scientific articles.

His last words in his personal diary read: "I failed to do what I should have and could have done in my life" (26).

Conclusions

This paper does not only report the personal history of a man, but also highlights his commitment for an idea and a global health goal. The long-lasting and strong effort was full of dismay and frustration for the slow progress of the project and the conviction that vaccines could be able to eradicate smallpox in a foreseeable future (22). The project had been carried out during the Cold War with the involvement of scientists and healthcare professionals of countries from all over the world. Key lessons include firstly the ability to overcome political and ideological differences and cooperate for protection and improvement of public health (22), as much as a strong involvement in vaccine research and against vaccine hesitancy in a period of wide anti-vaccine attitude spread (27, 28). The theme of Human Sciences in medical education should be a central topic (29, 30), history of Medicine ought to take into account also medical biographies as they set real life examples and allow both students and practitioners to gain a mixture of knowledge that can benefit their daily work.

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