Vaccine diplomacy during the Cold War (i), heads or tails. Heads: Mikhail Chumakov and the oral poliomyelitis vaccine of Albert Sabin

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This study was presented at the 75th Annual Meeting of the Spanish Society of Neurology.

ABSTRACT

Medicine and public healthcare have been used as a means of collaboration between politically opposed countries within the framework of the so-called soft diplomacy. One of the clearest examples of this type of diplomacy is vaccines, peaking in the 1950s with the cooperation between American and Soviet scientists to eradicate poliomyelitis. This task was led by the iron will of Albert Sabin and Mikhail Chumakov. This process was not free of difficulties, but the triumph over this severe disease was one of the greatest public healthcare achievements of the 20th century, saving countless lives and preventing the paralysis it caused. This article analyses the figure of Chumakov and his relationship with Sabin within the framework of the development of Soviet virology, which had already shown its potential by the late 1930s with the discovery of tick-borne encephalitis. A second article will address the vaccine born in the USSR at the same time that the poliomyelitis vaccine was developed, with the aim of treating acute encephalomyelitis and multiple sclerosis. This second vaccine, which was also assessed by Western scientists, did not meet the expectations of its developers.

KEYWORDS

Cold War, vaccine diplomacy, Mikhail Chumakov, Albert Sabin, oral poliomyelitis vaccine, Soviet virology

Introduction

The Cold War defined international relations from the mid-20th century, with the participation of two blocs of countries divided into the American and the Soviet spheres of influence. This period was marked by confrontation, with key examples being the nuclear arms race, the Korean War, and the Cuban Missile Crisis. However, not all the ties between the blocs were cut, and after Stalin's death in 1953, there was cooperation in various different fields including culture, technology, and medicine and public healthcare. The latter two fields witnessed significant events, especially in the field of infectious diseases, with the development of vaccines to fight them, the so-called vaccine diplomacy.[1]

In this first article, we will address the success represented by the American-Soviet cooperation in the development of the oral poliomyelitis vaccine and its benefits for humankind, focusing on the two main protagonists: Albert Sabin (1906-1993) and Mikhail Chumakov (1909-1993). To do this, we must introduce the history of Soviet virology and the legendary medical expeditions to the Russian Far East that discovered tick-borne encephalitis.

A second article will address another vaccine, this time developed in the Soviet Union, which was used to treat

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Received: 6 March 2023 / Accepted: 12 July 2023

acute encephalitis and multiple sclerosis, but which fell short of expectations. The main proponent was the virologist Antonina Shubladze (1909-1993), and in this case Albert Sabin also played an important role in its study from a Western perspective.

Material and methods

An extensive literature search was performed on the history of the poliomyelitis vaccine and its protagonists, especially focusing on relations between the United States and the Soviet Union during the Cold War, and the history of Soviet virology and its most remarkable protagonists, in particular Mikhail Chumakov and his colleagues. The article also examines Albert Sabin's relationship with Soviet scientists, reflected in documents in his archives, which are preserved at the University of Cincinnati and freely accessible online. The search was performed in different languages, including Russian.

Results

Soft diplomacy in medicine and public healthcare

Soft diplomacy and soft power are means used by governments to influence the actions of other states through cooperation in cultural and scientific projects, without coercion. Medicine and public healthcare are common tools in this endeavour, especially in the field of contagious diseases, which have no borders. Healthcare challenges are shared by ideologically opposed countries, with no effect on national security.[2]

Despite isolation from the international medical community by the late 1940s, during the critical moments of the Cold War, the bonds of Soviet medicine and public healthcare with the Western world were not fully broken, and were strengthened during the de-Stalinisation that occurred during the second half of the 1950s, with a wide range of strategies and hopes to establish relationships with other countries, especially the United States. Thus, in 1957, the Soviet Union rejoined the World Health Organization (WHO), which it had left in 1949.[2] This climate of cooperation flourished not only because of the rational desire of scientists, but also because of the will of politicians, who were interested in the success of these relationships.[3]

From 1955, meetings were held between American and Soviet healthcare officials and medical researchers, who participated in international exchanges, missions, and congresses, which further expanded after the Lacy-Zarubin agreement was signed in October 1957. The content of these activities also expanded in 1972 with the incorporation of the US-USSR Committee for Health Cooperation, which remained active until the dissolution of the Soviet Union in 1991. In the field of medicine, remarkable protagonists included specialists in infectious diseases and public healthcare, surgeons, haematologists, cardiologists, and oncologists, creating an atmosphere of curiosity and mutual respect. With this new cooperation, Soviet scientists had the chance to access Western advances and show their own achievements.[2]

This was the context to the development of a new chapter of the so-called vaccine diplomacy, a branch of international healthcare diplomacy in which cooperation, independently of political models, saved numerous lives from the threat of such destructive infectious diseases as poliomyelitis, also known as infantile paralysis or polio.[1]

The problem of poliomyelitis

According to current data, one in four individuals infected with the poliovirus presents flu-like symptoms, and one in five develops meningeal symptoms. However, one in every 200-1000 infected individuals will present weakness, which preferentially affects the limbs and respiratory muscles. Paralysis is the most severe symptom, as it can cause permanent disability and death, which is caused by respiratory failure in 2%-10% of patients showing motor symptoms.[4]

In the early 1950s, the world, and especially more developed countries, was shaken by the fear of poliomyelitis, a disease mainly affecting children and young adults. Among patients presenting motor symptoms, half would suffer from lifelong paralytic sequelae.[5]

The global effort to put an end to poliomyelitis outbreaks led to the creation of a community of scientists that transcended the borders imposed by the Cold War, resulting in an unprecedented medical cooperation represented by the iconic figures of Albert Sabin and Mikhail Chumakov, who endeavoured to develop efficacious vaccines to control the disease.[6] In this case, the scientists' ability to convince politicians of the need to prioritise this task over political beliefs was decisive, achieving one of the greatest challenges of 20th-century medicine.[1,7]

Live virus vaccines had existed for more than a century, in the case of smallpox, and almost two centuries, in the case of yellow fever; they were not a novel concept, and many scientists were convinced of their superiority over killed vaccines, as they acted faster and for longer. Furthermore, the attenuated virus persisted in the faeces of vaccinated patients, with the potential to indirectly immunise other individuals.[6]

In the case of polio, Max Theiler (1899-1972) reported in 1946 that after several passes in mice he had obtained innocuous strains of poliovirus. The first experiments with attenuated poliovirus vaccines were performed in 1948 by Hilary Koprowski (1916-2013). In 1949, John Enders (1897-1986), Thomas Weller (1897-1985), and Frederick Robins (1916-2002) succeeded in cultivating this neurotrophic virus in other tissues, especially in the monkey kidney; this procedure was used in the development of vaccines. The awarding of the 1954 Nobel Prize in Physiology and Medicine to these three scientists meant that Jonas Salk (1914-1955) and Albert Sabin, the main developers of the vaccines, were not eligible for this prize, as it had already been awarded in relation to this disease.[6,8]

The killed poliovirus vaccine developed by Jonas Salk was authorised in the United States in April 1955 after a randomised double-bind trial in 1.3 million children, sponsored by the National Foundation for Infantile Paralysis (NFIP).[7,8] By that time, Albert Sabin was working to develop an attenuated poliovirus vaccine with higher potential to immunise the entire population. In 1957, he presented a series of successful trials, reaching the stage in which he needed to perform the large trials recommended months earlier by the WHO during his meeting with the Poliomyelitis Expert Committee. However, Salk's vaccine was already available, which decreased the incidence of polio to a few thousand cases per year. The leaders of the NFIP and the US Public Health Service were satisfied and showed no interest in supporting trials with other vaccines.[9] Furthermore, the United States had forbidden trials with live virus vaccines since the "Cutter Incident": in the spring of 1955, a trial with Salk's vaccine manufactured by Cutter Laboratories caused more than 200 cases of paralytic poliomyelitis, as some strains had not been sufficiently inactivated.[6]

The research groups led by the three scientists Albert Sabin, Hilary Koprowski, and Herald Cox (1907-1986) tested three different attenuated poliovirus vaccines around the world. In 1956, Koprowski trialled his vaccine in Belfast, but this was troublesome as it became virulent. An outbreak that occurred in 1958 in Singapore represented the first opportunity to use Sabin's vaccine in 200 000 children, yielding positive results. In early 1958, Koprowski conducted mass vaccination in the Belgian Congo, obtaining inconclusive results. In 1959, field tests with the Cox vaccine were performed in Central America, with negative results, but a trial performed in Minnesota obtained excellent results. Koprowski's strains were later administered in Finland and Poland. By 1959, at least 15 countries had performed field trials with the live poliovirus vaccine, although on a small scale. Finally, Albert Sabin's vaccine prevailed.

Soviet Russian virology

Russian virology began in 1892, when the plant physiologist Dmitri Ivanovsky (1864-1920) discovered the tobacco mosaic virus, the first virus ever discovered. Another remarkable event, now in the Soviet era, was the eradication of smallpox in the country in 1929. But the most significant milestone was the discovery of tick-borne encephalitis, an event that had a decisive influence on the progression of Soviet virology. This disease and the virus causing it were studied during three legendary medical expeditions to the Russian Far East in 1937-1939.[10] This achievement merits further discussion.

During the spring and summer of 1930, an unknown sudden-onset disease was observed in some regions of the Siberian taiga; the disease caused severe neurological symptoms and high mortality rates.[10] In 1935, a neurologist from Vladivostok, Aleksandr Panov (1905-1978), suggested that it could be a viral encephalitis. Clinical symptoms included flaccid paralysis, shoulder girdle involvement, and bulbar manifestations. It was suggested that the disease may be Japanese encephalitis, a viral disease transmitted by mosquitoes, discovered in 1922.[11]

In March 1937, a medical expedition was sent to the area, led by Lev Zilber (1894-1966), considered the founder of Soviet virology. Zilber directed the Central Virus Laboratory in Moscow, created in 1935. He created a group of 20 members, the majority enthusiastic young scientists, including the virologists Elizaveta Levkovich (1900-1982), Mikhail Chumakov, Alexandra Sheboldaeva (1900-?), Antonina Shubladze, and Valentin Soloviev (1907-1986). These scientists, many of them younger than 30 years, have been called the "first

Figure 1. From left to right: Anatoly Smorodintsev, Elizaveta Levkovich, and Mikhail Chumakov in the 1930s.[14]

generation of virologists"; they later created the scientific schools that dominated Soviet virology for several decades.[10-12]

The expedition performed its research between May and August 1937. They determined that the disease was caused by a virus transmitted by tick bites. Zilber named the disease Russian spring-summer encephalitis or tick-borne encephalitis. In only three months, they had discovered a new virus; isolated 29 strains; identified the vector (the tick *Ixodes persulcatus*); described the epidemiology, clinical symptoms, and histology of the disease; and demonstrated the effectiveness of serum therapy.[10-12]

Three members of the expedition contracted encephalitis, although with differing fortunes. Valentin Soloviev presented optic nerve involvement with impaired vision, recovering after a few months; the laboratory assistant Gnevysheva presented acute psychosis; and Mikhail Chumakov developed severe neurological damage that left permanent sequelae.[10,11]

A few days after the end of the expedition, Lev Zilber, Alexandra Sheboldaeva, and the epidemiologist Tamara Safonova were arrested, falsely accused of attempting to propagate a dangerous viral infection. Zilber was released in June 1939, but was arrested again in 1940 and sent to a Gulag labour camp; he was not released until 1944.[11,12] Despite this, from 1939 until his death in 1966, with the exception of the time he spent imprisoned, he was head of the virology department at the Gamaleya Research Institute of Epidemiology and Microbiology in Moscow, where he dedicated a large part of his scientific career to researching the relationship between viruses and cancer.[13]

In 1938, a second expedition to the Russian Far East took place under the leadership of the entomologist Evgeny Pavlovsky (1884-1965) and the virologist Anatoly Smorodintsev (1901-1986), both from Leningrad. They confirmed the role of *I. persulcatus* in the transmission of the infection, the pathways of virus circulation, and the natural reservoirs in wild animals and goats. They

selected the strains used to create the vaccine that was approved in April 1939. Elizaveta Levkovich and Valentin Soloviev also participated in this expedition.[10,11]

In 1939, a third expedition took place, this time led by the epidemiologist Isaak Rogozin (1900-1973) of Leningrad, with the aim of testing the effectiveness of the vaccine, which was trialled in prisoners. They succeeded in artificially immunising the population and obtained authorisation for the prophylactic use of the vaccine. Two members of the second expedition and one member of the third died due to encephalitis (Figure 1).[10,11,14]

In March 1941, several members of the expeditions, including Smorodintsev, Chumakov, Soloviev, and Shubladze, received the Stalin prize for the discovery of the disease and the development of its treatment. The three members who were imprisoned were excluded from the prize. Antonina Shubladze and Valentin Soloviev married soon after the end of the expeditions.[10]

The main promoters of the research into the effectiveness of the oral poliomyelitis vaccine

Mikhail Chumakov was born in 1909 in Yepifan, in the Tula Oblast, on the left bank of the Don River. He was the son of a veterinary assistant and an agricultural worker. He moved to Moscow in 1927 to study law and medicine, eventually choosing this latter discipline and graduating from the First Moscow State Medical University in 1931. He later studied microbiology and worked as an assistant at the Vaccine-Serum Laboratory of the Red Army Bacteriology Institute in Vlasikha, north-west of Moscow. At that time, he married Nadezhda Saprykina; the couple had a daughter in 1936, whom they named Dolores in honour of the Spanish communist leader Dolores Ibárruri, "La Pasionaria."[15]

Chumakov was one of the most remarkable members of the first expedition to the Russian Far East that discovered tick-borne encephalitis. During an autopsy study of a patient who died due to encephalitis, in which he lacked the necessary tools, he injured his right hand with a piece of bone while sawing the skull, and contracted the disease, developing a severe neurological disorder. After his admission to the Hospital of Khabarovsk, his wife travelled there to meet him and they both returned to Moscow, where he was examined at the neurological clinic of Mikhail Margulis (1879-1951), and later transferred to the I.M. Sechenov Institute of Physical Methods of Treatment at Sevastopol. He recovered but remained permanently deaf; he could only perceive 5% of sounds and had to use hearing aids for the rest of his life. He could only move one finger of his right hand, which he always kept inside his jacket pocket, but regained mobility of his left hand and learned to write with it.[10,15]

During the 1940s, he worked as head of the viral diseases section of the Institute of Neurology.[9] In 1944, he presented his doctoral thesis "Tick-borne encephalitis."[15] In 1950, he was also designated director of the Ivanovsky Institute of Virology of the Academy of Medical Sciences, which had been created in 1946, and in 1955 was named director of the recently created Institute of Poliomyelitis and Viral Encephalitis of the Russian Academy of Medical Sciences.[3]

Marina Voroshilova (1922-1986) was born in Simferopol. Her parents were a lawyer and a bacteriologist. Her father died when she was seven years old, and the family moved to Moscow, where they were neighbours of Mikhail Chumakov. In 1941, Marina was admitted to the First Moscow State Medical University and enrolled in a course completely made up of women, as her male colleagues were all enlisted in the army. In 1946, she was sent to the Baltics and later to East Germany, areas affected by polio outbreaks. During the course of this expedition, which was led by Chumakov, they started a relationship and eventually had four children, who were cared for by their maternal grandmother and a nanny. The couple lived in a time of economic hardship, as they had to pay for the nanny as well as child support for the son and two daughters Mikhail had had with Nadezhda Saprykina.[15]

In the summer of 1952, they went on holiday with the grandmother and the children to Sukhumi, in Abkhazia. During their experiments with poliovirus in monkeys, Marina and her son Kostya, whom she was breastfeeding, contracted poliomyelitis. The child developed mild symptoms, but Marina's symptoms were more severe, even preventing her from walking. Thanks to physiotherapy, she slowly recovered, but needed a stick to walk for three years.[15]

In January 1943, with Marina still sick, Mikhail Chumakov lost his position as director of the Ivanovsky Institute. During the "doctors' plot," he was accused of having employed a large number of Jewish workers and ordered to dismiss them; he refused, and was immediately deposed and expelled from the Communist Party of the Soviet Union (CPSU). He became a lowly head of

department at the Institute of Neurology. He spent several months drying cookies and stocking winter clothes in preparation for an arrest that never happened. This was common practice among people who feared being sent to the Gulag.[5,15]

Anatoly Smorodintsev was the son of a rural physician. He was born in 1901 in Askino, a town in the Bashkir Autonomous Soviet Socialist Republic, in the Urals, and graduated in medicine at the University of Tomsk in 1923. He worked at the Pasteur Institute of Epidemiology and Microbiology in Leningrad (1933-1937), the All-Union Institute of Experimental Medicine in Moscow (1938-1945), and the Leningrad Institute of Experimental Medicine (1946-1967), where he directed the virology department. He was the scientific director of the second expedition to the Russian Far East that discovered tick-borne encephalitis.[16]

Albert Sabin was born in 1906 in the Polish city of Bialystok, then part of the Russian Empire. His father was a Jewish weaver. The family emigrated in 1921 to the United States, and Sabin took American citizenship in 1930, changing his name from Abraham Saperstein to Albert Bruce Sabin. He studied medicine at New York University, graduating in 1931, and completed his internship at Bellevue Hospital. Led by his interest in infectious diseases, he was awarded a travel grant to work at the Lister Institute of Preventive Medicine in London. After his return to New York, he dedicated his work to research at the Rockefeller Institute. In 1939, he founded his own laboratory at Cincinnati Children's Hospital, where he created his oral poliomyelitis vaccine and continued working until 1969. During the Second World War, he was an army physician in the Pacific, developing vaccines against dengue and Japanese encephalitis.

Poliomyelitis in the Soviet Union

Polio struck the Soviet Union late, and it was the European country with the lowest incidence until 1930, but with industrialisation and improvement of the healthcare system, the disease expanded and healthcare authorities began to grow concerned.[17]

During the Second World War, information on infectious diseases was being shared with Western countries. In January 1944, a British-American scientific mission visited the USSR; a few months later, the Soviet virologists Anatoly Smorodintsev and Valentin Soloviev travelled to the United States. For two months, they met with their American colleagues, bought laboratory equipment, and visited several research centres on the East Coast. Contact persisted until 1947 but was suspended with the exacerbation of the Cold War.[3]

In 1945, Mikhail Chumakov started his experimental studies with poliovirus, and succeeded with the help of A.P. Belyaeva and Marina Voroshilova in isolating a first strain in the brain of a child who died due to poliomyelitis. Up to 1955, 224 strains were obtained from other patients. The Institute of Neurology sent teams of virologists and epidemiologists to study polio epidemics in the three Baltic republics in 1946 and 1947 and in Western Siberia in 1949. Despite this, professor Konstantin Vinokurov, of the Institute of Neurology, asserted in the Second International Conference on Poliomyelitis, held in Copenhagen in 1951, that the USSR was free of epidemics, a smokescreen that was dispelled after the death of Stalin in 1953. At that time, the country was struck by severe epidemics, such as the Karaganda outbreak in 1952 and the Moscow outbreak in the summer of 1955.[3,18]

That year, due to the recent epidemics, the Institute of Poliomyelitis and Viral Encephalitis of the Russian Academy of Medical Sciences was created in Moscow. The Soviet government wished to start large vaccine trials as soon as possible, although it was uncertain as to which vaccine to use.[17] Chumakov was summoned by the Central Committee of the CPSU and appointed director of the new institute to address the problem of polio. He was requested to marry Marina Voroshilova to legalise their relationship and so that the children may take his surname. He also insisted on being readmitted to the CPSU.[13]

In 1955, the Soviet authorities asked the authorities in the United States to send a medical mission to gather researchers from both countries to address the problem of polio. A mission of American microbiologists and epidemiologists visited the Soviet Union during the month of March 1956,[19] but before this, on 18 January, a group of Soviet experts on poliomyelitis travelled to the United States; the group included the virologists Mikhail Chumakov, Anatoly Smorodintsev, Marina Voroshilova, and the young epidemiologist Lev Lukin. For a month, they examined the state of the research and the production problems with Salk's vaccine, working alongside researchers from the National Institute of Health and the NFIP. They visited the laboratories of John Enders, Jonas Salk, Albert Sabin, and other experts. Chumakov paid

Figure 2. From left to right: Marina Voroshilova, Albert Sabin, Mikhail Chumakov, and Anatoly Smorodintsev. Cincinnati, February 1956 (Hauck Center for the Albert B. Sabin Archives. University of Cincinnati).

special attention to the production of Salk's vaccine, and to obtaining the latest laboratory equipment developed in the United States.[3,6]

From 5 to 17 February, they visited Sabin at his laboratory at Cincinnati Children's Hospital (Figure 2). By that time, Salk's vaccine, which used killed virus, had already been developed, approved, and distributed in the United States and other countries. Meanwhile, Sabin was beginning his studies on the stability of the attenuated strains selected from the three types of polioviruses, and preparing the first trial with 53 volunteers. During the visit with Sabin, they also exchanged information on the development of Soviet research on the haemorrhagic fevers of Crimea and Omsk, the sandfly fever vaccine, Smorodintsev's new influenza vaccine, Antonina Shubladze's vaccine against multiple sclerosis and, particularly, the discovery by Chumakov and Voroshilova of a suspected fourth type of poliovirus that they had discovered in 1952 during the Karaganda outbreak. This virus caused a disease indistinguishable from poliomyelitis in monkeys. It was later studied by Americans, who concluded that it was a coxsackievirus A7. It was a significant finding that established that, in addition to the poliovirus, coxsackie and echovirus could also cause paralytic diseases.[3,18] Sabin was encouraged by the American military medical and intelligence authorities to travel to the Soviet Union. By February 1956, he had already informed the Office of the Surgeon General of the content of his conversations with Chumakov and Smorodintsev.[20] Together with other American scientists, he attended a congress on infectious diseases in Leningrad in June 1956 (Figure 3), and subsequently visited Moscow to participate in a series of

Figure 3. From left to right: Mikhail Chumakov, Albert Sabin, and Marina Voroshilova. Leningrad, June 1956 (Albert B. Sabin Collection. University of Cincinnati Libraries).

meetings to address problems related to bacteriology and virology, organised by Chumakov and Viktor Zhdanov (1914-1987), the deputy minister of health. He delivered two lectures on the genetic variations of poliovirus and resistance to viral infections. This successful trip established or consolidated his friendship with the Chumakov-Voroshilova and Soloviev-Shubladze couples, Zhdanov, and the neurologist Nikolai Grashchenkov (1898-1965), a former collaborator of Edgar Adrian (1889-1977) and John Fulton (1899-1960).[3,21] In particular, the link established between Chumakov and Sabin progressed to a long-term friendship, despite the former not speaking English and Sabin barely speaking any Russian.[17] Both had strong personalities; Sabin was more meticulous and Chumakov had great organisational skills. This new entente with Soviet scientists influenced Sabin's decision to test his vaccine in the USSR, given the difficulties of testing in the United States, which was immersed in the Salk vaccination campaign.[3]

When in October 1956 Sabin selected the most attenuated strains of each of the three types of polioviruses he needed to test in humans, he wrote to Grashchenkov and Zhdanov to stress that, if they were successful, he would distribute part of the batches produced to Soviet virologists. He kept his word, sending vaccine strains to Smorodintsev for testing at orphanages in Leningrad. Between 1956 and 1959, Sabin distributed samples not only to Soviet scientists, but also to colleagues in the United States, the Netherlands, Mexico, Malaysia, South Africa, Italy, France, and Singapore to perfect and test the vaccine he was developing.[3,6]

Chumakov was not involved in the initial agreement to trial Sabin's vaccine, as he had been charged with setting up the production of Salk's vaccine in the Soviet Union. In the spring of 1957, Sabin wrote to Chumakov on his latest experiences with the vaccine in hundreds of volunteers, family members, and friends, who had shown immunity against all three types of viruses.[3] He later delivered strains to Chumakov and Voroshilova, who self-administered the vaccine and used it on their family members.[22]

Sabin returned to Moscow in May 1957 to visit Chumakov's institute and specifically analyse the progress of the research on the attenuated poliovirus vaccine. From his two trips to the Soviet Union in 1956 and 1957, Sabin brought home information on Soviet medical achievements, batches of viruses that they used, and vaccines, including a vaccine with attenuated mumps and measles viruses, as well as strains of the virus used in the multiple sclerosis vaccine developed by Antonina Shubladze.[3]

In the spring of 1958, Chumakov, busy with his work with Salk's vaccine, became sceptical about its usefulness in achieving rapid immunisation of the Soviet population. His scepticism arose from the continuous epidemics occurring in the United States, despite the use of the vaccine, and his personal conviction that the vaccine was inferior to Sabin's. He discovered that Salk's vaccine decreased the incidence of paralytic polio among vaccinated subjects, but not in the remaining population, as it did not reduce circulation of the virus. He also observed such other disadvantages as the high production costs and administration by injection. Chumakov invited Salk to the USSR to examine his trials with the vaccine, but the latter, being less friendly than Sabin, declined.[3,17]

In June 1958, Chumakov requested that Sabin send him as many attenuated poliovirus strains as possible to conduct a testing programme in the Soviet Union. However, he did not mention the type of study he had in mind. It was not until 26 December of that year that he explained his intentions. Resistance from government bureaucrats forced him to postpone his plans. This situation was further complicated by the unusual position of Anatoly Smorodintsev, who declared that he had created his own vaccine in Leningrad, which was superior to Sabin's vaccine. The Ministry of Health authorised its use in 20 000 children, having tested it previously in another 1200 children from the city. In parallel to this, it requested that Chumakov use Sabin's vaccine in another 20 000 children. Therefore, a resolution from the ministry supposedly affected two vaccines, Sabin's vaccine, used by Chumakov, and Smorodintsev's vaccine, probably developed using the old strains that Sabin delivered him in 1956. After obtaining satisfactory results in his trial, Chumakov proposed that the vaccine be used to immunise another two or three million citizens, and later the rest of the Soviet population. Chumakov's plans were important to Sabin, as success in the USSR would favour the authorisation of his vaccine in the United States.[3]

When Chumakov wanted to start mass trials with Sabin's vaccine, officials from the Ministry of Health outright refused him permission to use it, as they had Salk's vaccine and did not need to test another one. Chumakov went over the head of a high-level civil servant and called Anastas Mikoyan, vice-president of the Council of Ministers and responsible for public healthcare issues, to complain about the bureaucrats and request authorisation to start clinical trials with the vaccine. Mikoyan granted him this authorisation, a source of irritation for the minister of health.[5,7]

The great vaccination campaigns in the Soviet Union

Mikhail Chumakov directed the work on the live poliovirus vaccine from the Institute of Poliomyelitis and Viral Encephalitis in Moscow, where the main research was being conducted. In 1957, the institute had also created the first Salk-type vaccine in the Soviet Union (Figure 4).[9,15]

During 1959, a mass immunisation campaign was run in 14 republics of the Soviet Union. By the end of the year, 15.2 million children and young adults had been vaccinated: 1.67 million were immunised under the direct supervision of Smorodintsev, with vaccines prepared at the Leningrad Institute of Experimental Medicine, and the other 13.5 million were immunised with vaccines from the Institute of Poliomyelitis and Viral Encephalitis in Moscow.[23]

Given the success of the campaign, the USSR Ministry of Health issued an order on 16 December 1959 for mass immunisation before 1 July 1960 of the Soviet population aged between 2 months and 20 years, a total of 77.4 million children and young adults (74.25 million with Sabin's vaccine and three million with Salk's vaccine, representing 35% of the total population of the Soviet Union). Only five million individuals vaccinated in 1960

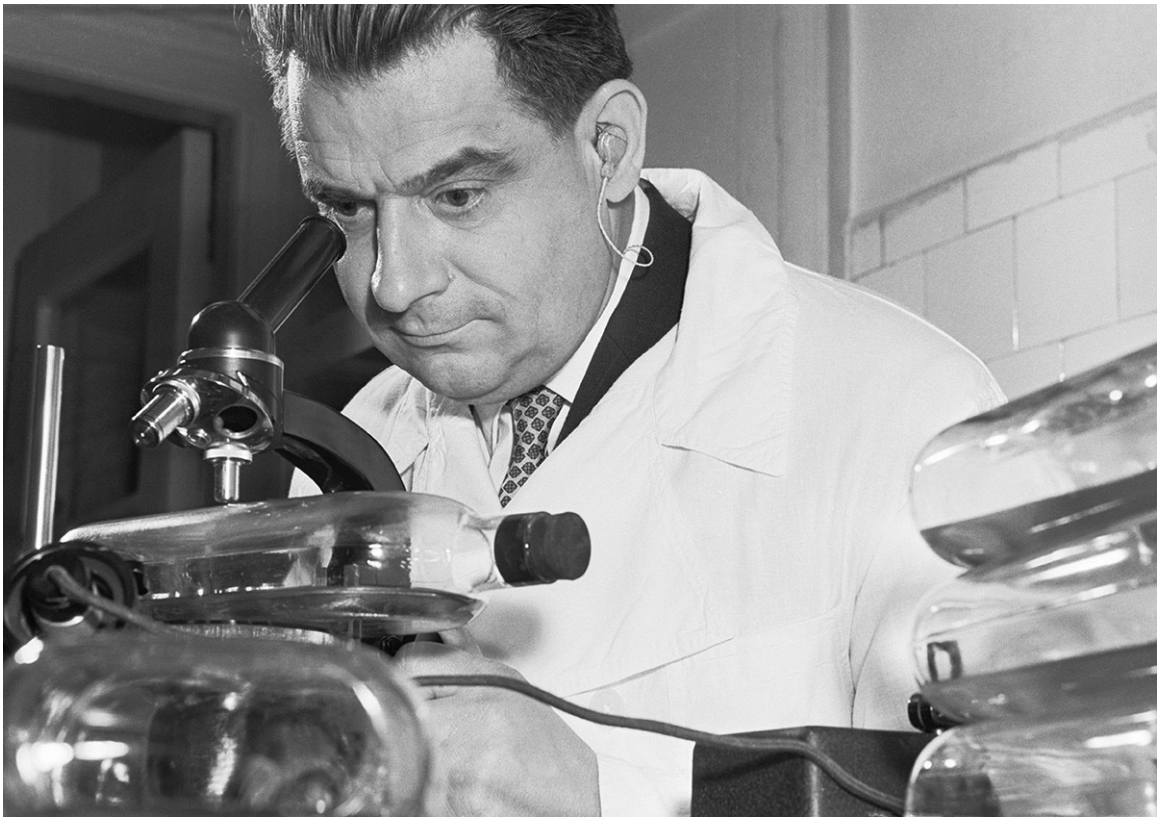

Figure 4. Mikhail Chumakov in 1959.[15]

were older than 20 years. The remaining 72 million represented 92% of the population younger than that age. In September 1960, Sabin's vaccine was used to immunise individuals who had previously received Salk's vaccine.[23]

The Institute of Poliomyelitis and Viral Encephalitis in Moscow, in collaboration with the confectionery industry, developed a new presentation in the form of sweets and candies that provided good immunisation. The majority of those vaccinated in 1960 received this presentation, and drops were reserved for children who could not suck hard sweets.[23]

Deliberately, there was no vaccine selection or control group. The campaign was based on humanitarian principles to eradicate poliomyelitis, something that Sabin had wanted but had been denied in the United States. It was not a controlled trial but a mass vaccination programme that led to faster general immunisation of families and communities. Comparing polio incidence between 1960 and 1958-1960 against the areas where Salk's vaccine had been used, it was clear that this vaccine had no influence on the epidemic process, whereas Sabin's caused an abrupt decrease in the incidence of the disease and prevented the typical increase of cases in summer and autumn.[9,23]

Chumakov proposed vaccinating the entire population with four doses: three initial monovalent doses using the sequence of types 1, 3, and 2 virus, at intervals of four to six weeks, followed by a trivalent dose between three and 18 months. When comparing this schedule with the exclusive use of the trivalent formula, no differences were found and therefore many republics only used the trivalent vaccine.[9,23]

Vaccination centres were set up in nurseries and playschools, schools, clinics, factories, and other places. Parents were informed about when and where to go. Local officials ensured that everybody attended the centres, and paediatricians were responsible for the medical side. Meticulous record-keeping included all the essential data. The plan was well executed thanks to the organisational skills of Chumakov and the coercive power of the state police.[17]

The follow-up process to identify suspected cases was very appropriate, especially among vaccinated children, and used local paediatricians and epidemiologists, who indicated the hospitalisation of suspected cases. Numerous serological tests and stool cultures were performed.[9]

In Estonia, mass vaccination was started in May 1959 as the republic presented one of the highest polio incidence rates, despite Salk's vaccine having been used there in previous years, as was also the case in Latvia. Both republics showed similar incidence rates to that observed in Scandinavian countries. A mass vaccination campaign was performed in Tashkent in the months of July and August, in the midst of a severe epidemic. Smorodintsev led the vaccination campaign in Latvia, Moldavia, and Belarus, which took place between March and June.[9]

In Sabin's words, Russians waged a blitzkrieg against poliomyelitis, winning the battle. This process was slower in the United States as it was not led by General Chumakov, who was victorious even using his left hand and with hearing aids.[3,5]

Given the reluctance of some American scientists to accept the data provided by Soviets, the WHO, which was greatly interested in the attenuated poliovirus vaccine, sent the Yale expert Dorothy Horstmann (1911-2001) to Eastern Europe in August 1959 with the aim of analysing the safety of the live virus vaccines used. Between August and October 1959, she travelled around the USSR, the Czech Republic, and Poland, conducting a detailed assessment of the work carried out at the laboratories and the precautions taken to ensure the quality and safety of vaccines, which were excellent. It was unlikely that paralytic cases would have escaped her assessment. Although the data were not definitive, a positive report was issued that helped spark a resurgence of interest in the oral vaccine, paving the way for extensive trials to be conducted in the United States.[3,9]

Controversies around Sabin's vaccine

In late June 1959, the First International Conference on Live Poliovirus Vaccines was held in Washington; the event was organised by the Pan American Health Organization to assess the results of the immunisation campaigns in Eastern Europe. A Soviet delegation led by Chumakov reported that trials with Sabin's vaccine had been a success. Despite the Soviet enthusiasm, many American virologists and epidemiologists were not willing to acknowledge it.[3,9]

A week before the conference, the newspaper *Izvestia* reported that Smorodintsev had developed a live virus vaccine that was being used in Soviet trials. The article compared the achievements of this virologist with those made in the United States, where the laws of capitalism had prevented the use of Sabin's vaccine, and blamed the pharmaceutical industry manufacturing Salk's vaccines and the physicians performing vaccinations, who received vast incomes. Parents paid 15-30 dollars per vaccine, and also had to renew them periodically. When the *New York Times* reprinted the article from *Izvestia*, Sabin exploded with rage and sent a telegraph to Chumakov demanding that it be retracted. The latter, also surprised by the article, sent a telegraph with his apologies, and attributed the publication to an initiative of Smorodintsev. A few days later, the TASS agency transmitted Chumakov's opinion that the basis of the work performed by Soviet virologists had been the result of collaboration with Sabin in the study of the properties of his vaccine. Sabin already had concerns about Smorodintsev in 1944, when the latter visited him at the laboratories of the Rockefeller Foundation in Princeton, where Sabin was working as an army physician.[3]

Despite the positive report from Dorothy Horstmann, American scientists were again sceptical about the results of the Soviet trials presented in June 1960 by a delegation led by Viktor Zhdanov at the Second International Conference on Live Poliovirus Vaccines, held once more in Washington. The origin of the threat was again Smorodintsev, who was envious of Chumakov. Smorodintsev led the trials with Sabin's vaccine in the Soviet Union from 1956 until December 1958, when the Ministry of Health entrusted the task to Chumakov, who did not share the leadership with his colleague. Obviously, this loss of control led Smorodintsev to claim that he developed his own attenuated poliovirus strains.[3]

When Chumakov used sweets in an effort to make the vaccine more appealing to children, Smorodintsev immediately criticised him, stating that this change would reduce its effectiveness and put the vaccination campaign at risk. In the late summer of 1960, he privately informed Sabin of these changes to the vaccine and asked him for help to forbid them. In response, Chumakov sent Sabin randomised samples of the new vaccine in which these innovations were shown not to reduce its effectiveness, demonstrating that Smorodintsev's complaints were unjustified.[3]

After Sabin's lectures in the USSR, he was criticised by some attendees, who condemned his ignorance of the principles of Lysenko and Michurin, with which a perfect vaccine may be manufactured, as Soviet genetic principles would enable better selection of virus strains.[3,17]

Chumakov's victory helped to eradicate poliomyelitis in the Soviet Union and added a new political and social dimension to the vaccine. In the 1960s, the country was the largest manufacturer of Sabin's vaccine worldwide, and exported it to other countries. It was known as the "communist vaccine," a Soviet achievement that should be legitimised. Boris Petrovsky (1908-2004), in his book *Public health in the USSR*, asserted that Chumakov and Smorodintsev had developed the live poliovirus vaccine. In the summer of 1968, a physician from Cincinnati who had visited the Soviet Union presented Sabin with a copy of the book. He had already read similar information in a leaflet from Intourist, the Russian tourism agency, but had paid it little attention. However, Petrovsky's story was different, as he was the minister of health and a member of the Academy of Sciences and the Academy of Medical Sciences of the USSR, and Sabin complained bitterly about this distortion of events to Chumakov, Smorodintsev, and Vladimir Timakov (1905-1977), president of the Academy of Medical Sciences. The latter wrote him a letter apologising for the mistake, which he attributed to a mistake in the English translation. In a meeting held the following year at the WHO headquarters in Geneva, Sabin publicly confronted the Soviet representatives, and asked them to acknowledge whether they had developed new attenuated poliovirus strains in their vaccines or if it was a mistranslation. Despite a public apology from the Soviet delegate, Petrovsky's assertion was not officially amended.[3]

Sabin's vaccine in the world

In parallel to the Soviet Union, important trials with the vaccine were performed in the late 1950s in other Eastern European countries, especially the Czech Republic and Hungary, which had suffered severe epidemics in the previous years. They used strains sent by Sabin and Chumakov, with excellent results. In Poland and the Belgian Congo, vaccines were manufactured using strains of Koprowski's vaccine.[5] By the end of 1960, the oral vaccine had been used to immunise 92.6 million people in the Soviet Union, and another 23 million in other Eastern European countries.[8,23]

The introduction of Sabin's vaccine in the United Sates was hampered by controversies, rivalries, and delays. Whereas the authorities needed only two hours to authorise Salk's vaccine, it took them several years for Sabin's.[5] Between 1955 and 1960, with Salk's vaccine, between 3000-5000 cases of poliomyelitis were recorded annually in the United States. Sabin's vaccine was approved in August 1960, and was administered to 100 million children of all ages in 1961-1962. In 1964, for the first time, there were no new cases in summer or poliomyelitis outbreaks in the country.[8,24]

A mass vaccination campaign was also conducted in Belgium, where the disease practically disappeared from 1963. The effects of the vaccine were also fast and pronounced in Spain and Italy, although it was not able to eradicate some foci. Japan, Israel, and Cuba almost completely eliminated the disease. In less developed countries in South America, Africa, and Asia, collective oral vaccination campaigns were performed that spectacularly reduced the number of cases within a matter of weeks in non-epidemic periods, but transmission was only partially interrupted.[24] In the USSR, 42 million doses of Sabin's vaccine were prepared and sent to another 40 countries, mainly those within the socialist sphere of influence.[13,20] This success served to show that Eastern European countries took better care of their citizens in healthcare terms. They used it to underscore their cultural, economic, and moral superiority over the West, and especially the United States, with its convoluted market economy and racial segregation. Why was the United States not using Sabin's vaccine by 1959? The response from Albert Sabin was that, since 1954, Salk's vaccine had been in private hands of those who expected to obtain great financial benefits from it.

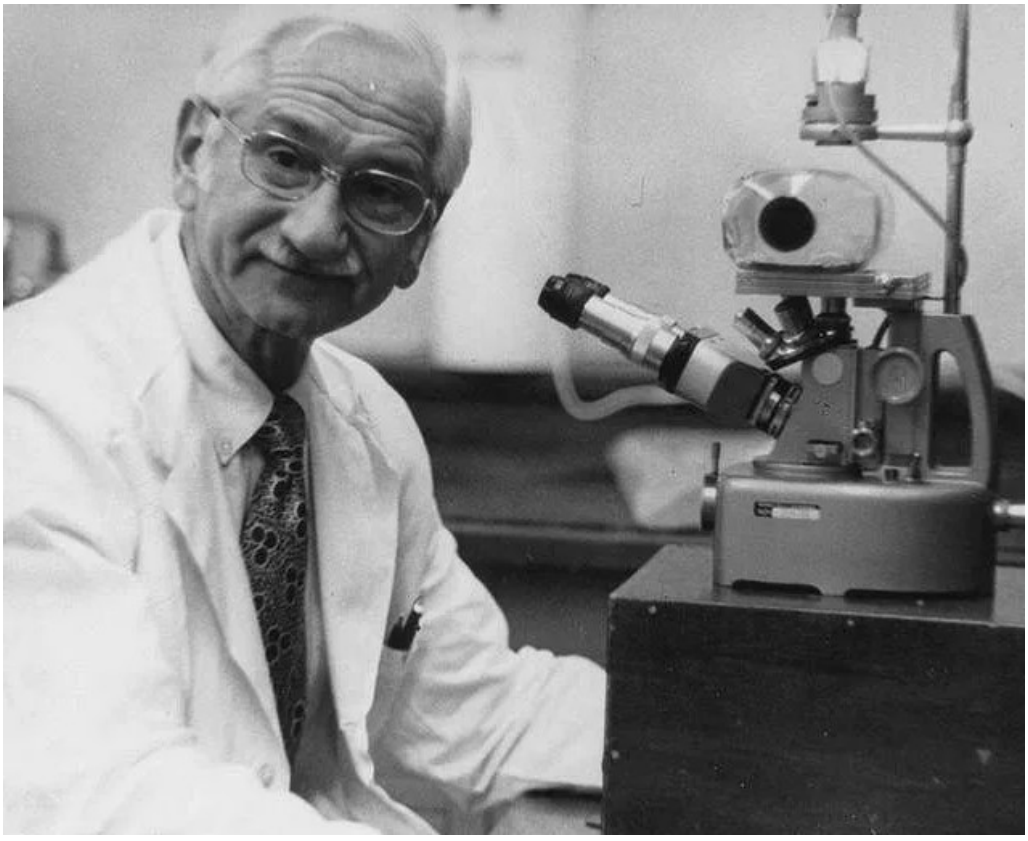

Figure 5. Albert Sabin.[26]

Although Sabin's vaccine was superior, it was not manufactured while supplies of Salk's vaccine lasted.

After the mass vaccination campaigns conducted in many countries, Sabin calculated that by 1966, more than 350 million people worldwide had received his vaccine.[15] In 1972, he donated his poliovirus strains to the WHO to increase their availability in developing countries (Figure 5).[25,26]

Another success of the Soviet virology of the time was the development in 1962-1966 of the lyophilisation techniques that enabled the country to provide 450 million units of the smallpox vaccine with the financial support of the United States, thanks to which the disease was globally eradicated in 1977, a process led by Donald Henderson (1928-2016).[1]

Life goes on

In 1963, Chumakov and Smorodintsev were jointly awarded the Lenin prize for their work with Sabin's vaccine. In a letter to Sabin, Chumakov stated that the prize should have been awarded to Sabin alone. In 1960, he had already succeeded in securing his American colleague's acceptance as an honorary member of the Academy of the Medical Sciences of the USSR, and in the 1970s he unsuccessfully fought for Sabin to be awarded the Nobel Prize in Physiology or Medicine.[3,17]

The grudge held by officials at the Ministry of Health against Mikhail Chumakov surfaced in the early 1970s, when they refused to authorise the smallpox vaccine manufactured at his institute and destroyed 13 million doses in autoclaves, in the midst of a severe epidemic of

the disease that was hitting Ukraine. In a meeting at the Ministry of Health, Chumakov confronted the minister, his former classmate Boris Petrovsky. In 1975, the virologist was dismissed from his position as director of the Institute of Poliomyelitis and Viral Encephalitis, becoming deputy scientific director, and was later sent to the department of haemorrhagic fevers. In the last 15 years of his life, he dedicated his work to researching an influenza vaccine. His wife Marina, who studied the non-specific effects of live virus vaccines and worked in the field of oncology, was denied access to her own laboratory.[5,15]

Despite adversities, Chumakov remained loyal to communism, although he helped some of his employees to emigrate. His sons Konstantin and Alexei moved to the United States, where they were protected by their father's friends.[15] All four of his children with Marina Voroshilova became scientists, as did his son and two daughters from his first marriage.[5,22] He also tried to convert Sabin to his ideology, and vice versa. Both failed, but it did not affect their friendship.[3]

Marina Voroshilova secretly brought from the United States a photocopier, which she installed in her laboratory; in the 1960s, she distributed copies of *samizdat*, the clandestine publications of political dissidents. In 1966, after the trial of Andrei Sinyavsky (1925-1997) and Yuli Daniel (1925-1988), she bought a book in France by Abram Tertz (the pseudonym of Sinyavsky), keeping it secret from her husband and making her children read it. She had a first myocardial infarction at the age of 54, but continued working at the same rate. She was a member of the Academy of Medical Sciences since 1969, and created the concept of beneficial human viruses. She died in November 1968 while seated in front of her typewriter, finishing an article on these viruses. Her children translated it into English and it was published in the United States.[15] She established that the poliomyelitis vaccine had an unexpected benefit, as vaccinated children did not present other viral conditions during the months following immunisation, and children receiving a booster dose in the autumn were protected against influenza. In 1968-1975, she supervised an extensive study including 320 000 participants from the Soviet Union, which revealed a decrease in mortality due to influenza among subjects who had recently received other vaccines, including polio vaccines, due to stimulation of the immune system.[22]

Mikhail Chumakov died in June 1993 at the Kremlin hospital, due to pneumonia. He donated his brain to the institute, and the tick-borne encephalitis virus, with which he was infected 50 years earlier, was found still to be present.[5]

After the success of his oral vaccine, Albert Sabin continued directing his laboratory in Cincinnati until 1969. In 1970, he was awarded the National Medal of Science of his country. Between 1970 and 1972, he was president of the Weizmann Institute of Science in Israel, and subsequently continued working as a consultant for several organisations until his definitive retirement in 1986. He died in 1993 following a heart attack.[25]

Smorodintsev directed the Research Institute of Influenza of the USSR between 1967 and 1972. He had been the first in the world to create a vaccine against influenza in 1937, and later created vaccines against tick-borne encephalitis, smallpox, and parotiditis. He studied antiviral immunity and vaccine protection mechanisms. He described haemorrhagic nephrosonephritis (haemorrhagic fever with renal syndrome) in 1944, and biphasic meningoencephalitis in 1953. He was a member of the Academy of Medical Sciences of the USSR from 1945 and of the CPSU from 1967. As previously mentioned, he was granted the Stalin Prize together with other virologists in 1941, and the Lenin Prize in 1963, in this case only shared with Chumakov. He died in 1986.[16]

Conclusions

Vaccine diplomacy was an important element of the détente and cooperation between the opposing blocs of East and West during the Cold War. The most notable achievement was the development of the oral poliomyelitis vaccine, which saved countless lives worldwide. The architects of this achievement were Albert Sabin, the creator of the vaccine, and Mikhail Chumakov, who in 1959-1960 led a mass immunisation campaign for children and young adults in the Soviet Union, demonstrating its effectiveness. Sabin was not allowed to trial the vaccine in the United States, where Salk's killed virus vaccine was already in use, and Chumakov had to convince political leaders in his country to carry out this task. This was a great achievement of Soviet virology, which was exploited politically to show the superiority of socialised healthcare over the capitalist healthcare

system of North America, which took several years to adopt Sabin's vaccine and become convinced of its superiority over Salk's vaccine.

As a young man, Chumakov had already participated in one of the legendary medical expeditions to the Russian Far East in 1937-1939, which resulted in the discovery of tick-borne encephalitis, a disease that he himself contracted and left him with severe neurological sequelae, although these did not prevent him from developing a fruitful scientific career together with his wife Marina Voroshilova, also a virologist.

Conflicts of interest

The author has no conflicts of interest to declare. The author has received no public or private funding for this study.

References

1. Hotez PJ. "Vaccine diplomacy": historical perspectives and future directions. PLoS Negl Trop Dis. 2014;8(6):e2808.
2. Michaels PA. Soviet medical internationalism amid destalinization, 1953-1958. The Soviet and Post-Soviet Review. 2022;50:40-63.
3. Benison S. International medical cooperation: Dr. Albert Sabin, live poliovirus vaccine and the Soviets. Bull Hist Med. 1982;56:460-83.
4. CDC [Internet]. Atlanta (USA): CDC; [s.d.]. ¿Qué es la poliomielitis?; Aug 2022 [cited 12 Jul 2023]. Available from: https://www.cdc.gov/polio/es/que-es-polio/index.htm
5. Chetverikova A. Virusolog Mikhail Chumakov: Pobedivshiy smert' odnoy levoy on vyzhil, obezvrediv entsefalitnogo kleshcha, i spas chelovechestvo ot poliomiyelita [Virologist Mikhail Chumakov: having defeated death with one hand, he survived, neutralising the encephalitis tick and saving humankind from polio] [Internet]. Rodina; 1 May 2021 [cited 9 Nov 2022]. Available from: https://rg.ru/2021/05/01/kak-virusolog-mihail-chumakov-spas-chelovechestvo-ot-poliomielita.html
6. Vargha D. Polio across the Iron Curtain: Hungary's Cold War with an epidemic. Cambridge (GB): Cambridge University Press; 2018.
7. Swanson W. Birth of a Cold War vaccine. Sci Am. 2012;306:66-9.
8. Franklin JL. A Cold War vaccine: Albert Sabin, Russia, and the oral polio vaccine. Hektoen Int. [Internet]; 2020 [cited 25 Jan 2023];12(3). Available from: https://hekint.org/2020/05/11/a-cold-war-vaccine-albert-sabin-russia-and-the-oral-polio-vaccine/
9. Horstmann DM. The Sabin live poliovirus vaccination trials in the URSS, 1959. Yale J Biol Med. 1991;64:499-512.
10. Karpova MR. Legendarnaya ekspeditsiya (K 75-letiyu otkrytiya virusa kleshchevogo entsefalita) [A legendary expedition (on the 75th anniversary of the discovery of the tick-borne encephalitis virus)]. Sibirskiy Meditsinskiy Zhurnal. 2012;3:20-7.
11. Kolyasnikova NM, Zlobin VI, Ishmukhametov AA, Maleev VV. Istoriya otkrytiya i izucheniya kleshchevogo entsefalita v Rossii: tri dal'nevostochnyye ekspeditsii (1937–1939 gg.) [History of the discovery and study of tick-borne encephalitis in Russia: three expeditions to the Russian Far East (1937-1939)]. Terapevticheskii Arkhiv. 2021;93(11):1407-12.12.
12. Voyna s nevidimym vragom. Izucheniye virusov – delo vsey zhizni [War against an invisible enemy. The study of viruses: a lifelong endeavour]. Vestnik Ferona. 2016;1:44-7.
13. Kisselev LL, Abelev GI, Kisseljov F. Lev Zilber, the personality and the scientist. Adv Cancer Res. 1992;59:1-39.
14. Interesno vnezapnoye poyavleniye zabolevaniya... [Interesting, sudden onset…] [Internet]. El Tolstyh, 10 Nov 2022 [cited 27 Jan 2023]. Available from: https://el-tolstyh.livejournal.com/11885635.html
15. Mikulina M. Konfeta — ot bol'shoy bedy [Sweetness comes from great trouble] [Internet]. Takie Dela; 23 Oct 2020 [cited 8 Nov 2022]. Available from: https://takiedela.ru/2020/10/konfeta-ot-bolshoy-bedy/
16. The Great Soviet Encyclopedia, 3rd ed. [Internet]. The Gale Group Inc.; ©2010. Smorodintsev, Anatolii Aleksandrovich; [cited 21 Jan 2023]. Available from: https://encyclopedia2.thefreedictionary.com/_/mdict.h=1&word=Anatolii+Aleksandrovich+Smorodintsev
17. Oshinsky DM. Polio: an American history. New York: Oxford University Press; 2005.
18. United States-USSR Medical Exchange Mission 1956. Part I. Visit of the Soviet Poliomyelitis Team to the United States, January 18 – February 22, 1956. Public Health Monograph No. 50. Washington (DC): U.S. Department of Health and Welfare; 1957; p. 1-40.
19. United States-USSR Medical Exchange Mission 1956. Part II. American Medical Mission on Microbiology and Epidemiology to the Soviet Union, February 27 - March 28, 1956. Public Health Monograph No. 50. Washington (DC): U.S. Department of Health and Welfare; 1957; p. 41-91.
20. Bayne-Jones S. Letter to Albert B. Sabin, 26 Feb 1956. Albert B. Sabin Archives; University of Cincinnati Libraries.
21. Grashchenkov NI. Letter to Albert B. Sabin. 11 Oct 1956. Albert B. Sabin Archives; University of Cincinnati Libraries.

22. Kramer AE. Decades-old Soviet studies hint at coronavirus strategy. The New York Times [Internet]. 25 Jun 2020 [cited 28 Aug 2023]. Available from: https://www.nytimes.com/2020/06/24/world/europe/vaccine-repurposing-polio-coronavirus.html
23. Chumakov MP, Voroshilova MK, Drozdov SG, Dzagurov SG, Lashkevich VA, Mironoca LL, et al. Some results on the work on mass immunization in the Soviet Union with live poliovirus vaccine prepared from Sabin strains. Bull Org Mond Santé / Bull Wld Hlth Org. 1961;25:79-91.
24. Sabin AB. Poliomielitis: resultados de la vacunación con virus vivos. Boletín de la Oficina Sanitaria Panamericana. 1968;65:52-61.
25. Biography of Albert B. Sabin, 1906-1993. Albert B. Sabin Papers. Albert B. Sabin Archives; University of Cincinnati Libraries.
26. Agencia AJN. Se cumplen 25 años de la muerte de Albert Sabin, inventor de la vacuna oral [Internet]. AJN; 2 Mar 2018 [cited 30 Jan 2023]. Available from: https://agenciaajn.com/noticia/se-cumplen-25-anos-la-muerte-albert-sabin-inventor-la-vacuna-oral-93217