Online publication ahead of print, AJMHS Vol 68, 2025

Smallpox in Albania: History, Epidemiology and Prevention

Adriana Manuka[1*], Irsida Mehmeti[1*], Antonia Radaelli[1,2], Eduart Hashorva[3], Carlo Zanotto[2] and Carlo De Giuli Morghen[1]

[1] Faculty of Pharmacy, Catholic University "Our Lady of Good Counsel", Tirana, Albania
[2] Department of Medical Biotechnologies and Translational Medicine, State University of Milano, Italy
[3] Statistics Service, "Queen Geraldine" Obstetrics & Gynecology University Hospital, Tirana, Albania
*These authors contributed equally to this work

Abstract

Background: Smallpox is caused by the variola virus, a member of the Orthopoxvirus genus of the Poxviridae family. It is the only human disease eradicated worldwide, making it the most significant global public health. In May 2022, the Albanian Committee of Vaccination Experts recommended vaccination against smallpox to human subjects in close contact with confirmed monkeypox cases.

Aim: The main aim of this review is to report the history of smallpox in Albania in terms of epidemiological background and vaccination, considering the changes in health policies during the years influenced by political and economic alliances.

Methods: Data were obtained from the Albanian State Archive, focusing on records of the Institute of Public Health and the Ministry of Health, as well as from the Archive Library's Literature. A literature search was also performed in online databases.

Results and conclusions: Vaccination against smallpox became mandatory for all age groups in Albania in 1947. Primary vaccination was carried out at 6 months of age, and three boosting doses were administered at the ages of 6-7, 11-12, and 18-19 years from 1953 to 1964. The elimination of smallpox in Albania was officially reported in 1966. Although the smallpox vaccine was produced in Albania by the Institute of Hygiene

Address for correspondence: Irsida Mehmeti*, Catholic University "Our Lady of Good Counsel", Rr. Dritan Hoxha, 123, Tirana, Albania 1000. E-mail: i.mehmeti@unizkm.al

and Epidemiology in 1954, several other types of smallpox vaccine strains have been imported from other countries.

Keywords: Smallpox; Smallpox vaccines; Albanian vaccines; Epidemiology; Infectious diseases; MPXV, monkeypox virus; MPOX, monkeypox disease.

INTRODUCTION

Smallpox is caused by the Variola virus, a member of the Orthopoxvirus genus of the Poxviridae family. It is the only human disease to have been eradicated, making it the most significant global Public Health milestone (1).

In different countries worldwide, key methods, such as mass vaccination, targeted surveillance strategies, and immunization programs, have been used to achieve the objective of eradication. While a few European countries eliminated the disease in 1900, in most of the countries it was still emerging (2). Vaccination is the greatest achievement of Public Health. There are two recognized variants of the variola virus, variola major and variola minor. Variola major was the predominant endemic strain in Europe, and it was responsible for approximately 400,000 deaths annually in Europe by the end of the 18th century (2). During the first half of the 20th century, variola minor was the causative agent of most outbreaks. Intensive research into vaccine development across multiple countries was conducted with the main aim at producing more resilient and effective vaccines. Advances in production techniques in 1950 led to the development of heat-stable and freeze-dried vaccines, which did not require refrigeration for storage.

Albania is a middle-income country with a population of 2.4 million, located in the Balkan Peninsula of southeastern Europe (3). It is bordered by Montenegro and Kosovo to the North, North Macedonia to the East, and Greece to the Southeast. Since its independence from the Ottoman Empire in 1912, Albania has transitioned from a monarchy to a communist regime, and then to a sovereign Parliamentary Constitutional Republic. During these periods, different political alliances with other countries have also influenced the national policies on controlling infectious diseases and vaccination. The country endured Italian occupation before the 2nd World War (1939–1945) and by Nazi Germany in 1943 (4). At the end of the 2nd World War, in 1944, Albania became a Communist Country until 1991, which led the country to form new political alliances such as the Union of Soviet Socialist Republics (USSR) (1944-1961) and China (1961-1978) (5).

The Institute of Public Health (IPH), established in 1994, represents the national scientific and reference center for infectious disease control and prevention (6). The IPH replaced the Research Institute of Hygiene, Epidemiology, and Immunobiology Products, established in 1969. The Albanian epidemiological surveillance system on infectious diseases dates back to 1950, with a vaccination program implemented in 1960 (7). Due to the improvement of the vaccination programs, vaccine-preventable diseases have decreased dramatically.

The World Health Organization (WHO) launched the Smallpox Eradication Program in 1959, and member States enhanced their support and cooperation for low-income countries (5). The Soviet Union played a significant role in providing freeze-dried vaccines during the

Intensified Smallpox Eradication Program in 1967. First-, second-, and third-generation smallpox vaccines were critical to the successful eradication of smallpox in the 20th century (8), and are now recommended by WHO and the US Centers for Disease Control and Prevention (CDC) for use in high-risk populations, also to mitigate the current monkeypox outbreak (9).

In May 2022, the Albanian Committee of Vaccination Experts adopted official recommendations to enable those in close contact with confirmed monkeypox cases to receive the smallpox vaccine (10). Considering this scenario, the main aim of this review is to report the history of smallpox in Albania in terms of epidemiological background and vaccination, considering the changes in health policies during the years influenced by political and economic alliances.

LITERATURE REVIEW

Databases such as PubMed, Web of Science, and Google Scholar were envisaged to find published material about smallpox in Albania using English keywords such as smallpox, Albania, infectious diseases, vaccines, vaccination, variola minor, variola major, and epidemiology. No published studies resulted.

The presented data were obtained from the Albanian State Archive, focusing on the records of the Institute of Public Health and the Ministry of Health, as well as the literature from the Archive Library.

The archival research was based on the selection of the materials through the official website of the Albanian State Archive (11) using Albanian keywords such as variola vera, lia e vërtetë, vaksina jenneriano, vaksinim antivariolik, prodhim i vaksinës anti-variolike, shartim, laboratori i pordhimit të vaksinave, certifikatë vaksinimi, epidemia në Kosovë. Following these requests, archival materials were accessed and reviewed by in-person visits between September and November 2024.

SMALLPOX VACCINATION COVERAGE

Vaccination against smallpox became mandatory for all age groups in Albania in 1947. WHO requested Albania to introduce mandatory smallpox vaccination certificates in 1951.

In 1953, the Albanian Ministry of Health requested the mandatory vaccination of the entire population. Vaccination was not performed regularly until that year.

Data from the State Archive show that about 30% of the vaccinated population did not have an immune conversion and should be revaccinated.

Every year, the Institute of Hygiene and Epidemiology (IHE) in Albania produced 100,000 vaccine doses against smallpox, and around 70,000 children were vaccinated each year.

Data from the State Archive indicate that from 1953 to 1964, the Southern region of Albania had a higher percentage of vaccinated children, whereas the Northern cities showed a low vaccination coverage. The discrepancies among

the different cities are attributed to a still undeveloped surveillance system rather than a low vaccination coverage. Vaccination was performed correctly, but the record-keeping in the registers was not conducted regularly. Conversely, a document dated 1977 reported a 100% national vaccination coverage.

Prior to 1990, approximately two-thirds of the Albanian population lived in rural areas. In 1984, among the WHO member States, only Albania and France did not cease smallpox vaccination (1). From 1984 to 1987, only the primary vaccination against smallpox was performed in Albania, and it was officially interrupted in 1987 (11).

In the State Archive, data on specific smallpox vaccine strains were not found, and population vaccination coverage before 1970 was poorly recorded, resulting in incomplete data. Also, Albanian published literature does not report information about smallpox history and vaccination in Albania. Smallpox vaccination registers were mainly paper-based. Data were manually entered through handwriting and they were not transferred to electronic databases later on.

Taube et al. (23) describe that vaccination coverage data are available for only 37% of countries and for 14% of the global population, as details of historical vaccination programs were often not documented before the eradication of smallpox.

VACCINATION SCHEDULE

The WHO Expert Committee on Smallpox (1964) recommended that primary vaccination should be carried out as early as possible, preferably in the neonatal period, and repeated about 12 months later. Experts recommended a 5-10-year revaccination interval for non-endemic countries and a 1-3-year interval for endemic countries. However, in some European countries, hospital staff were obliged to be vaccinated every 3 years.

An attesting document of vaccination was requested for children before school registration, but the vaccination schedule changed over the years. In 1947, primary vaccination was administered at the 6th month and revaccination at the 7th year of life. A document released to WHO by Albanian Health Authorities stated that, from 1953 to 1964, primary vaccination was carried out at the 6th month of age, and was followed by three booster doses, given at 6-7, 11-12, and 18-19 years of age.

Vaccination was performed by scarification in the external region of the deltoid muscle of the arm. Before vaccination, the skin was disinfected with alcohol or ether. The space between the two parallel scarified sites was 3 to 4 cm in width. The scars should be at least 0.5 cm in length and should not cause bleeding. The control of children after primary vaccination was performed from the 8th to the 12th day after vaccination. Simple needle, pen, and bifurcated needles were

used, and the appearance of at least one pock was considered a successful vaccination. From 1982 to September 1987, only the primary vaccination was administered at the 6th month of life.

ELIMINATION OF SMALLPOX IN ALBANIA

The first smallpox epidemic reported in the State Archive documents dates back to 1848, when Istanbul was the epicenter of an epidemic, which spread to neighboring countries, including Albania.

Smallpox was present in Albania until the beginning of the 20th century, with the last epidemic recorded in 1913. However, data from the WHO report that during 1920, smallpox was endemic in about 30 countries in Europe, including Albania (1). Archival data show that between 1947 and 1948, five cases were registered in Albania.

The elimination of smallpox in Albania was officially reported in 1966, as documented by the WHO. Forty years after the last registered case, in March 1972, the WHO reported a smallpox epidemic in Yugoslavia with a population of 20.8 million (13). The infection was imported from Iraq. The epicenter of the epidemic was Kosovo, a country bordering Albania, resulting in 175 cases and 35 deaths (Fig. 1). As a precaution, the Albanian Ministry of Health vaccinated or revaccinated the entire population from 6 months to 60 years old.

Mass vaccination was divided into two phases. The first to be vaccinated were the populations of cities bordering Yugoslavia, such as Shkoder, Kukes, Tropoje, Diber, Lezhe, Durres, Vlore, Sarande, Pogradec, and Tirana, using the Chinese vaccine imported into Albania in 1972. Meanwhile, military servants, healthcare professionals, communication personnel, and workers of the Ministry of Interior were vaccinated with the Italian smallpox vaccine (Lancy, lyophilized, strain Elstree). In the second vaccination phase, the population living in the cities distant from Yugoslavia was vaccinated with the smallpox vaccine produced in the IHE.

Other preventive measures included prohibiting Albanian people from traveling to Kosovo and returning to Albania. It also recommended closing land, maritime, and air borders with Yugoslavia.

From 1980 onward, herd immunity against smallpox has waned over time, contributing to the resurgence of the monkeypox virus (MPXV), particularly among individuals who have not been previously vaccinated against smallpox. Given that the genome of the MPXV shares 96.3% similarity with that of vaccinia virus (20), data from studies of humans vaccinated with traditional vaccinia viruses in Africa in the 1980s reported 85% protection during outbreaks of MPXV (21). Moreover, multiple global serologic studies have demonstrated that antibodies induced by smallpox vaccine can cross-neutralize MPXV proteins (22).

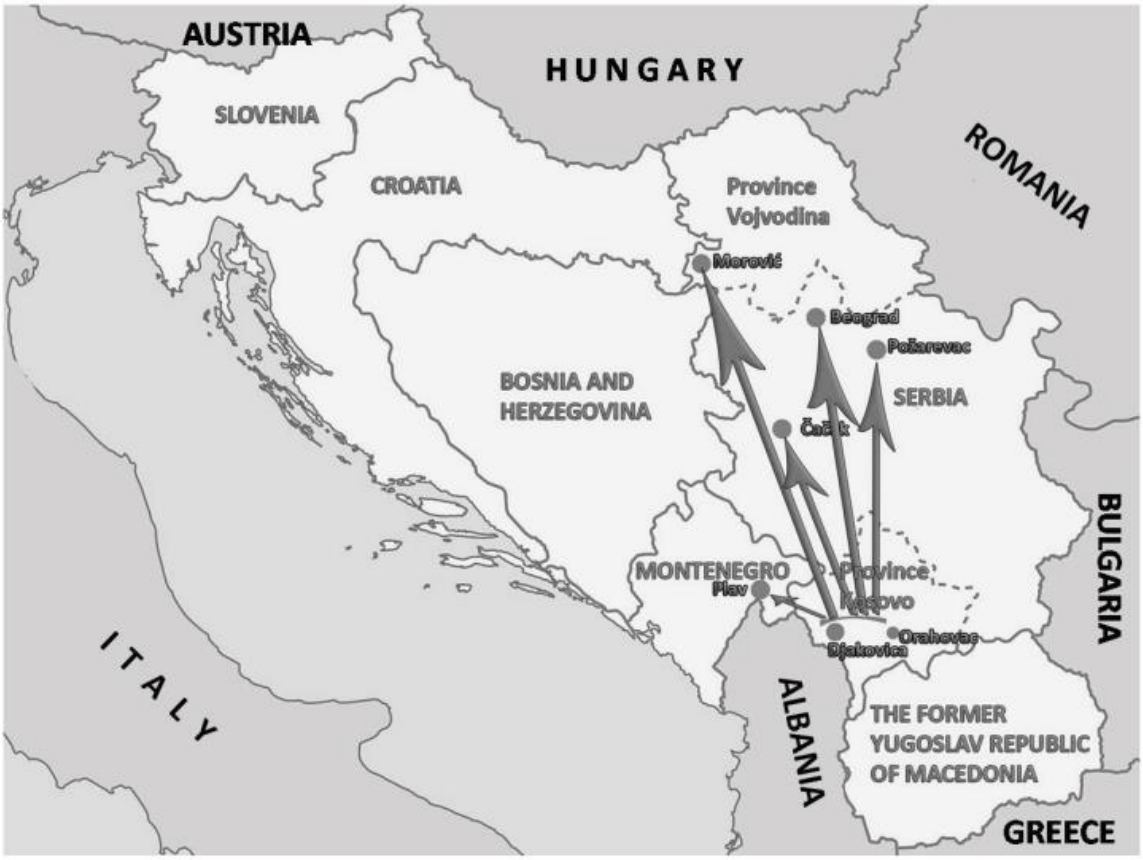

Figure 1. Smallpox outbreak in Yugoslavia in 1972, and spreading of the disease from the primary focal point in Kosovo (Ristanovicet al., 2016)

Considering these results, serological studies measuring the Albanian population's antibodies against smallpox as a protective measure against MPXV can be conducted. Data retrieved from the State Archive reveal that the Albanian population has been vaccinated with different smallpox vaccines since 1924, when 20,000 doses of the Jennerian type were imported from Italy, although continuing with vaccinia vaccines imported from Russia and China. Therefore, different antibody levels are expected in the Albanian population, which might suggest several levels of protection against monkeypox disease (MPOX).

The availability of epidemiological surveillance data from 1947, when the mandatory smallpox vaccination began in Albania, provides a better understanding to combat the current and future MPOX outbreaks.

First-, second-, and third-generation smallpox vaccines were critical in the successful eradication of smallpox in the 20th century (8), and are now recommended by the WHO and the US Centers for Disease Control and Prevention (CDC) for use in high-risk populations to mitigate the current monkeypox outbreak (9, 26). In May 2022, the Albanian Committee of Vaccination Experts decided to issue a

recommendation to enable those who had been in close contact with confirmed cases of monkeypox to receive the smallpox vaccine. In July 2022, the Ministry of Health established the Committee of Experts for the Prevention and Control of Monkeypox.

Currently, as MPOX continues to spread globally, despite Albania being classified as a low-risk region with no registered cases thus far, the country has implemented all measures and strategies in line with the International and European standards to control the spread of MPXV.

Collaboration with other countries during the smallpox eradication program is another good example of how Albania can adopt international measures to control MPOX outbreaks and import vaccines.

SMALLPOX VACCINES IN ALBANIA

In 1959, the 12th World Health Assembly decided to implement a program to eradicate smallpox worldwide. In 1967, the Smallpox Eradication Program initiated more intensive actions, including training healthcare workers, isolating smallpox patients, and mass vaccinations. Smallpox was eradicated globally within a decade, with the last case identified in Somalia in 1977. WHO officially declared the eradication of smallpox in May 1980 (1). The timeline of smallpox vaccines used in Albania is depicted in Fig. 2.

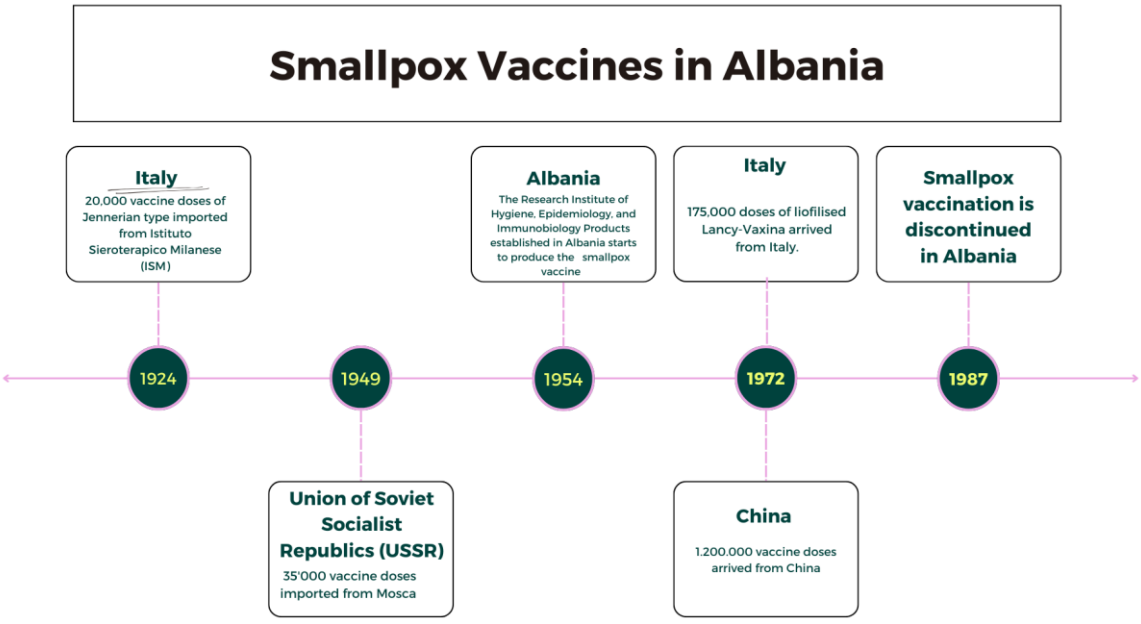

Figure 2. Timeline of smallpox vaccines used in Albania

The smallpox vaccine produced in Albania

The production of the smallpox vaccine in Albania by the IHE started in 1954. The vaccine was produced by infecting calves with the vaccinia virus. It was a glycerinated suspension of the vaccine pulp, which was stored at temperatures under 5 °C for 1 month after the date of production. The introduction of glycerol as a preservative was a major step forward in lymph production as it helped stabilize the virus and prevent bacterial multiplication. Cows were first used to produce vaccines in Italy in the early 19th century.

The usage of bifurcated needles started from 1968 onwards. The efficacy of the vaccine against smallpox in the Albanian population was reported 1.5 years after vaccination, showing an immunization level of 80%-92% across different cities, as sourced from a document provided by the Albanian IPH. This study demonstrated that vaccination with a bifurcated needle was better than vaccination with a pen. The quality control of the smallpox vaccine produced in Albania was tested in 1963 at the Statens Serum Institute of Copenhagen (Denmark). The bacteriological control was performed on the vaccine based on the presence of saprophytic bacteria, hemolytic streptococcus, and pathogenic anaerobic microbes (Table 1).

In 1962, WHO and UNICEF provided support for the development of the laboratories in developing countries, enabling them to produce their own vaccine. The Lister strain was used to prepare seed lots, which were given to local vaccine producers.

Vaccines against Smallpox imported from other countries

Smallpox vaccines arrived in Albania from other countries during the pre-smallpox Eradication Era (up to 1958)

During the years of monarchy (1920-1939), Albania was economically and politically dependent on Italy. In 1924, about 20,000 doses of the Jennerian vaccine arrived in Albania from the Italian Istituto Sieroterapico Milanese (ISM). In 1939, 50,000 vaccine doses arrived from the same Institute in Albania. The Lister strain was used in the United Kingdom since 1892 and in France since 1916.

Under the communist regime, Albania was allied with the USSR from 1944 to 1961. Data from the State Archive reveal that in 1949, approximately 35,000 vaccine doses arrived from Moscow to Albania. Up to 1966, the Tashkent strain was used for the production of smallpox vaccine, both for local use in the USSR and for donation to other countries. After 1966, the production of this highly pathogenic strain was interrupted in the USSR. The EM-63 strain, with a low pathogenicity, was the main strain used in the USSR between 1967 and 1970 for the production of vaccines, that were donated for the WHO Intensified Smallpox Eradication Program and for many bilateral aid programs.

Table 1. Schedule of Albanian vaccine production against smallpox

Composition_	Live viral suspension in 60% glycerin.
Appearance	Turbid, with a color ranging from yellow to white or darker, depending on the calf's skin.
Preparation	The vaccine was prepared using calves. The pus (pulp) of scarified calves infected with live poxvirus was diluted at a ratio of 1:3 to 1:8 in 60% glycerin, depending on the viral titer. The vaccine was preserved in 80% glycerin.
Therapeutical indication	Smallpox prophylaxis.
Technical requirements (according to the method presented for the approved technological process)	**Bacteriological Control** No more than 1000 saprophytic microbes/ml should be present; no development of hemolytic streptococcus; no development of pathogenic anaerobic microbes. **Virulence tests** **Scarification of the cornea of guinea pigs** Gins' method (1:5000-1:10000 dilution): a full lesion should be present. **Intradermal inoculation of rabbits** Grott method: the sum of the diameters of the infiltrates should be 20-30 mm. **Scarification of rabbits** No data regarding the site of scarification. **Inocuity** The vaccine should be harmless **Vaccination of the control group children** After passing all the tests, the vaccine should be inoculated into a group of unvaccinated children to observe the positivity rate and the post-vaccination reactions caused by the vaccine. Pustules should develop in at least 80% of vaccines.
Ampoules, labeling, packaging	0.5 ml suspension in an ampoule. Pack size of 10 ampoules. Each pack had a label that included the institution's name, the biopreparation's name, batch number, expiration date, and storage conditions. It also included a leaflet indicating that the material was fragile.
Distribution and transport	The production department distributed the smallpox vaccine according to the vaccination plan. The vaccine was transported in thermic boxes with ice.

Smallpox vaccines arrived in Albania from other countries during the Smallpox Eradication Program

From 1958 to 1966, the main smallpox vaccine used in Albania was the one produced by the Albanian IHE. During this period, almost all countries shifted from the first-generation vaccines to the second-generation vaccines produced using cell cultures, which led to fewer adverse events. The first cell-culture-derived smallpox vaccine originated by infecting primary rabbit kidney cells with the Lister strain in the late 1960s (16). Meanwhile, data from the State Archive of Albania show that the vaccine strain

was grown in fibroblast cell cultures. However, there is no data on whether the vaccine production was carried out using this method or not. The seed virus for the production was the same as the one used for the production of the calf lymph vaccine (17).

From 1967 onwards, the implementation of more standardized vaccine production methods, such as lyophilization and freeze-drying, ensured that vaccine batches had a higher potency, stability, and safety (18). Standardization and control of vaccine production were essential for the success of the smallpox eradication program (1). In Albania, the lyophilization technique was performed for vaccine preparation in 1978. However, there is no data on whether such vaccines were prepared using the lyophilization technique.

Smallpox vaccines arrived in Albania from other countries during the Intensified Smallpox Eradication Program (1967-1980)

During the Intensified Smallpox Vaccination Program, most vaccines were provided under bilateral agreements with the USSR, which donated more than 1400 million doses from 1958 to 1979 (1). All vaccine contributions were made through the WHO Voluntary Fund for Health Promotion.

During the intensified eradication program, coordinated by the WHO, more than 35 different strains of vaccinia virus were being used by 71 manufacturers worldwide for smallpox vaccine production.

Out of 35 strains, 7 strains were said to have been derived from variola virus: Dairen (Japan), Ikeda (Japan), Lister (United Kingdom), LMC (United Kingdom), Tashkent (USSR), Temple of Heaven (China), and Williamsport (USA) (19). The most widely used strains for vaccine production were Lister, New York City Board of Health (NYCBH), TianTan (also known as Temple of Heaven), and EM63, which have been inoculated into maybe one-third of the population worldwide since 1950. The Lister strain was employed by one-third of the producers, and its use increased by two-thirds of the producers by 1972.

During these years, many countries passed from more virulent, live first-generation vaccines to second-generation vaccines, which were produced using appropriate methods to render the vaccine heat-stable. Two new techniques were introduced: intradermal inoculation by a jet injector in 1967 and multiple puncture inoculations with the bifurcated needle in 1968. To facilitate the changing of strains, WHO collaborating centers produced quantities of the Lister strain seed virus and made it available to all producers.

In response to the 1972 smallpox epidemic in Yugoslavia, Albania conducted a mass vaccination campaign among individuals aged 6 months to 60 years. 1.2 million vaccine doses arrived from China. TianTan was the main strain used for vaccine production in China from 1926 to 1954 and from 1960 to 1980. Recent genomic analyses demonstrate that TianTan shares a common phylogenetic origin with the

Copenhagen strain. Another 175,000 vaccine doses arrived from Italy in the same year. The smallpox vaccine imported from Italy was a first-generation lyophilized smallpox vaccine known as Lancy Vaccinia, and derived from the Elstree strain. According to WHO requirements, this vaccine was manufactured on sheep's skin, using the Lister strain derived from the Lister Institute. The potential smallpox vaccine strains imported in Albania are summarized in Table 2.

Table 2. Possible smallpox vaccine strains imported into Albania

Year of importation	Country of origin	Strain
1949	USSR	Tashkent, EM63
1924	Italy	Lister
1939	Italy	Lister
1972	China	TianTan
1972	Italy	Lancy

Smallpox vaccination strategies implemented in Albania offer essential lessons for modern public health responses.

The coordination between the Institute of Public Health (IPH) and the district levels (epidemiological service), and between these levels and the peripheral capillary ones (child consultancies in towns and cities, health centers in communes, health posts, or ambulances in villages), provided access to vaccines, even in remote areas (7). This operational strategy underscores the significance of inter-institutional collaboration in addressing current public health challenges.

Albania also utilized multidisciplinary teams including doctors, vaccinators, and nurses, demonstrating the value of community healthcare in achieving mass immunization goals.

Moreover, concerns about vaccine efficacy and insufficient quantity of smallpox vaccine doses arrived from Moscow were reported by Dr. Benussi and his colleagues (11). This highlights that pharmacovigilance has also been considered since then. Meanwhile, community education was carried out through the distribution of informational bulletins across all districts of Albania. Public announcements regarding mass vaccination campaigns were also issued through propaganda initiatives. This approach was also evident in the strategies adopted for the control and prevention of smallpox cases in Albania during the outbreak in Yugoslavia in 1972 (11).

Thus, these historical insights remain important today, particularly in preparedness against emerging threats, such as MPXV.

CONCLUSIONS

Considering the recommendations of the Albanian Committee of Vaccination Experts, which suggest that people who have had close contact with monkeypox cases should be vaccinated with smallpox vaccines, it is crucial to understand the history, background, and epidemiology of smallpox vaccines in Albania. Although a smallpox vaccine was also produced in Albania by IHE since 1954, information related to control measures performed on calves before vaccine production is missing. Moreover,

no data is available regarding the vaccine strains imported from different countries and used in mass vaccination campaigns in Albania.

The global smallpox vaccination program, launched by the WHO in collaboration with major allies such as the USA and the USSR, played a pivotal public health role by enhancing their support for the low-income countries. Vaccination of nearly 100% of the global population was performed, which subsequently led to the eradication of smallpox (5). Vaccine access, international collaboration, and operational strategies tailored to local contexts achieved the program's success. Applying the same principles, such as global collaboration, access to vaccines for all, and rapid response systems, can support a response to future infectious disease threats. Albania has a strong immunization program with routine immunization coverage estimated at over 98% for all antigens (27). All vaccines included in the Albanian National Immunization program are procured through UNICEF, which supplies vaccines from only prequalified manufacturers (27). Country-specific immunization indicators are reported annually through the WHO/UNICEF Joint Reporting Form on Immunization reports.

Albania adopted multiple production methods, including cell-culture-based in vitro techniques and lyophilization.

Data retrieved from the State Archive is limited. Future studies should focus on evaluating the immune responses of individuals vaccinated with smallpox vaccines in Albania until 1987.

The scar survey conducted by Fenner and his colleagues (1, 12), later adopted by WHO, was a crucial key to measure smallpox vaccination coverage. However, even individuals who are not vaccinated against smallpox may have a scar on their arm left from the tuberculosis (vaccine, which can lead to misunderstandings and confusion about the smallpox vaccination status (23). This suggests to conduct immunological studies instead of scar surveys to understand the risk of exposure to MPXV infection or other orthopoxvirus zoonosis in individuals vaccinated or not against smallpox.

Dee et al. (24) investigated the prevalence of antibodies in individuals born before or after smallpox eradication in the UK in 1971. The serum from patients who may have been vaccinated against smallpox retained either anti-VACV antibodies or high levels of neutralizing and cross-neutralizing activity. They are protected from exposure to zoonotic infections such as MPOX, compared to people born after 1971. In addition, Xia et al. (25) evaluated the cross-reactivity of the antibody response to MPXV surface proteins in a small proportion of Chinese individuals with and without a history of smallpox vaccination after its eradication in 1980. Surprisingly, some unvaccinated young adults showed high titers of antibodies against MPXV, but no serum neutralizing activity against vaccinia virus. This is likely due to their exposure to other orthopoxviruses that circulate in animals, such as cowpox or ectromelia virus.

Therefore, it is important to administer smallpox vaccination to high-risk populations. Studying antibody responses in individuals with different vaccination histories could facilitate a deeper understanding and the development of more effective therapeutic antibodies.

Future studies could also include oral history interviews with healthcare workers and vaccinated individuals, as well as comparative policy analyses with neighboring Balkan countries.

Acknowledgement: None declared

Conflict of Interest Statement: The authors declare that they have no conflict of interest.

REFERENCES

1. Fenner F, Henderson DA, Arita I, Jezek Z, Ladnyi ID. Smallpox and Its Eradication; Geneva: World Health Organization; 1988.

2. Duggan AT, Perdomo MF, Piombino-Mascali D, Marciniak S, Poinar D, Emery MV, et al. 17th Century Variola Virus Reveals the Recent History of Smallpox. Curr Biol 2016;26(24):3407-3412. doi: 10.1016/j.cub.2016.10.061.

3. Republika e Shqipërisë, Instituti i Statistikave i Shqipërisë. Available from: https://www.instat.gov.al/ [Accessed 20 January 2025].

4. Biberaj E, Prifti PR. Albania. In: Encyclopaedia Britannica [Internet]. Encyclopaedia Britannica, Inc.; [cited 2025 January 10]. Available from: https://www.britannica.com/place/Albania.

5. Zickel RE, Iwaskiw WR, Keefe EK. Albania: a country study. U.S. Washington, D.C.: Federal Research Division, Library of Congress; 1994. Available from: https://www.loc.gov/item/93042885/[Accessed 20 January 2025].

6. Instituti i Shëndetit Publik. Historiku i ISHP. Available from: https://www.ishp.gov.al/ [Accessed 20 January 2025].

7. Kakarriqi E. Epidemiological background of infectious diseases in Albania (1960-2001) and their prevention and control in the context of natural disasters and infectious diseases. Tirana: Institute of Public Health; 2002. Available from: https://www.ishp.gov.al/wp-content/uploads/2023/10/Eduard-Kakarriqi-ALBANIA-INFECTIOUS-DISEASES-EPIDEMIOLOGY-1960-2001-and-NATURAL-DISASTERS-Monograph.pdf [Accessed 20 January 2025].

8. Moss B. Smallpox vaccines: targets of protective immunity. Immunol Rev 2011;239(1):8-26. doi: 10.1111/j.1600-065X.2010.00975.x.

9. Tiecco G, Degli Antoni M, Storti S, Tomasoni LR, Castelli F, Quiros-Roldan E. Monkeypox, a Literature Review: What Is New and Where Does This concerning Virus Come From? Viruses 2022;14(9):1894. doi: 10.3390/v14091894.

10. Monitor Magazine. Monkey pox, the National Immunization Committee convenes: Vaccination

for close contacts. Available from: https://monitor.al/en/monkey-pox,-the-national-committee-of-immunization,-vaccination-for-close-contacts-meets/[Accessed 20 January 2025].

11. Republika e Shqipërisë, Drejtoria e Përgjithshme e Arkivave. Available from: https://arkiva.gov.al [Accessed from 19 September 2024 to 20 November 2024].

12. World Health Organization. The global eradication of smallpox: Final report of the Global
Commission for the Certification of Smallpox Eradication Geneva, December 1979. Geneva: World Health Organization; 1980. Available from: https://iris.who.int/handle/10665/39253 [Accessed 25 May 2025].

13. World Health Organization. Epidemiologic aspects of smallpox in Yugoslavia in 1972. Geneva: World Health Organization; 1973. Available from: https://iris.who.int/handle/10665/67617 [Accessed 25 January 2025].

14. Ristanovic E, Gligic A, Atanasievska S, Protic-Djokic V, Jovanovic D, Radunovic M. Smallpox as an actual biothreat: lessons learned from its outbreak in ex-Yugoslavia in 1972. Ann Ist Super Sanita. 2016;52(4):587-597. doi: 10.4415/ANN_16_04_21.

15. Sánchez-Sampedro L, Perdiguero B, Mejías-Pérez E, García-Arriaza J, Di Pilato M, Esteban M. The evolution of poxvirus vaccines. Viruses 2015;7(4):1726-803. doi: 10.3390/v7041726.

16. Hekker AC, Bos JM, Rai NK, Keja J, Cuboni G, Emmet B, et al. Large-scale use of freeze-dried smallpox vaccine prepared in primary cultures of rabbit kidney cells. Bull World Health Organ 1976;54(3):279-84.

17. World Health Organization. 21st report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations. Geneva: World Health Organization; 1965. (WHO Technical Report Series, No. 307). Available from: https://www.who.int/publications/i/item/WHO_TRS_307 [Accessed 30 January 2025].

18. Wokatsch R. Vaccinia virus. In: Majer M, Plotkin SA, editors. Strains of human viruses. Basel: S. Karger; 1972: 241–257. Available from: https://karger.com/books/book/791/chapter-abstract/5602585/Vaccinia-Virus?redirectedFrom=fulltext [Accessed 1 February 2025].

19. Qin L, Liang M, Evans DH. Genomic analysis of vaccinia virus strain TianTan provides new insights into the evolution and evolutionary relationships between Orthopoxviruses. Virology 2013;442(1):59-66.
doi: 10.1016/j.virol.2013.03.025.

20. Gubser C, Hué S, Kellam P, Smith GL. Poxvirus genomes: a phylogenetic analysis. J Gen Virol 2004;85(Pt 1):105–117.
doi:10.1099/vir.0.19565-0.

21. Fine PE, Jezek Z, Grab B, Dixon H. The transmission potential of monkeypox virus in human populations. Int J Epidemiol 1988;17(3):643–650. doi: 10.1093/ije/17.3.643.

22. Poland GA, Kennedy RB, Tosh PK. Prevention of monkeypox with vaccines: a rapid review. Lancet Infect Dis 2022;22(12):e349–e358. doi: 10.1016/S1473-3099(22)00574-6.

23. Taube JC, Rest EC, Lloyd-Smith JO, Bansal S. The global landscape of smallpox vaccination history and implications for current and future orthopoxvirus susceptibility: a modelling study. Lancet Infect Dis 2023;23(4):454–462. doi:10.1016/S1473-3099(22)00664-8.

24. Dee K, Manali M, Bissett LA, Bone J, Magill C, Davis C, et al. Smallpox vaccination campaigns resulted in age-associated population cross-immunity against monkeypox virus. J Gen Virol 2024;105(6):001999. doi:10.1099/jgv.0.001999.

25. Xia A, Wang X, He J, Wu W, Jiang W, Xue S, et al. Cross-reactive antibody response to Monkeypox virus surface proteins in a small proportion of individuals with and without Chinese smallpox vaccination history. BMC Biol 2023;21(1):205. doi: 10.1186/s12915-023-01699-8.

26. See KC. Vaccination for Mpox (Monkeypox) Infection in Humans: From Basic Science to Real-World Effectiveness. Vaccines (Basel) 2024;12(10):1147. doi: 10.3390/vaccines12101147.

27. Mehmeti I, Bino S. Establishing immunization safety surveillance System in Albania. In: CBU International Conference Proceedings; Prague, Czech Republic. 2016; 4:634-41. doi: http://dx.doi.org/10.12955/cbup.v4.824.