HOW IT WAS: THE GLOBAL SMALLPOX ERADICATION PROGRAM IN REMINISCENCES OF ITS PARTICIPANTS

To the 30th anniversary of smallpox eradication

"…This unprecedented achievement in the history of public health of all nations, which by their collective action have freed mankind of this ancient scourge and, in doing so, have demonstrated how nations working together in a common cause may further human progress."

Declaration of Global Eradication of Smallpox,
33rd World Health Assembly, May 1980

"…The eradication of smallpox will undoubtedly be ranked with the mastery of flight, the harnessing of nuclear energy, and the first steps in the exploration of space."

Halfdan Mahler,
the WHO Director-General during the Intensified Phase
of the Smallpox Eradication Program

"There has been no greater medical—or humanitarian—miracle in modern times than the eradication of smallpox…"

David Oshinsky, 2006 Pulitzer Prize winner

Cover photo:
A poster by a local artist from Bihar (India) allegorically depicting the victory over smallpox as the black monster covered with pockmarks; a young man in the pose of a winner stands in front of the defeated disease; he is armed with a bifurcated needle, which he just used to deliver a fatal blow to the monster (by the courtesy of Yu.G. Krivda)

Ministry of Health and Social Development
of the Russian Federation

Federal Service for Supervision of Consumer Rights Protection
and Human Well-Being

State Research Center of Virology and Biotechnology Vector

HOW IT WAS: THE GLOBAL SMALLPOX ERADICATION PROGRAM IN REMINISCENCES OF ITS PARTICIPANTS

Prof. S.S. Marennikova, Ed.

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How It Was: The Global Smallpox Eradication Program in Reminiscences of Its Participants
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This book is dedicated to the 30th anniversary of the global eradication of an extremely dangerous disease—smallpox. Its body is personal reminiscences of Russian participants of the Global Smallpox Eradication Program, launched by the World Health Assembly in 1958 by the initiative of the Soviet Union. The book comprises 20 separate chapters written by 17 authors. The first chapters acquaint the readers with the course of this program, the encountered difficulties, and victories as well as with the festive occasions connected with the 30th anniversary of the smallpox eradication. Subsequent chapters narrate the arduous and frequently heroic daily routine of the struggle with smallpox told by participants of these events who worked in India, Bangladesh, Pakistan, Afghanistan, Ethiopia, and other countries. A special focus in this description is put on the final intensified stage of this program, including eradication of residual smallpox foci in these countries.

A separate chapter deals with the activities of the WHO Collaborating Center for Smallpox and Related Infections in Moscow, which supported the program during its entire course (21 years). The book contains the materials on the control of imported smallpox outbreaks in the USSR during implementation of the program as well as the activities associated with the upgrading of the smallpox vaccine production at the Institute for Viral Preparations, Ministry of Public Health. The memorial chapter concludes the book. It is dedicated to the memory of the passed colleagues and friends who participated in the eradication program. The book is intended for epidemiologists, virologists, infectiologists, and other medical and veterinary specialists. It will be also interesting for historians of medicine and a wide range of readers. Students and young physicians will find there the worthy examples to follow.

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A Word to the Reader

Dear reader:

This book is dedicated to the 30th anniversary of the great event that freed out planet from smallpox, one of the most ancient and dangerous infectious human diseases.

Even in the middle of the 20th century, smallpox as an endemic disease affected the population of many countries in Asia, Africa, and South America. The countries that had eliminated this disease long ago, including the USSR, suffered from smallpox importation.

The book was published on the initiative and thanks to the tremendous efforts of Prof. Svetlana S. Marennikova and a team of her colleagues, who succeeded in finding and uniting almost all living participants of this ambitious project. All of them laying aside other concerns put down their reminiscences of what they had seen and experienced while working for the Global Smallpox Eradication Program.

Celebrating the victory over smallpox in 1980, the 33rd World Health Assembly called smallpox eradication an extraordinary achievement of the global public health. The word "extraordinary" is very succinct, on the on hand, denoting an event or phenomenon that has not been previously observed, and, on the other hand, used to reflect the immensity of natural or social phenomena. Both meanings are applicable to smallpox eradication. However, independent of the comparisons used to estimate this achievement, it is obviously among the greatest events of the 20th century.

We can be proud that our scientists put forward the global smallpox eradication project as the most important goal of the World Health Organization. This proposal was accepted and endorsed by the World Health Assembly in 1958.

The initiative of our country relied not only on the vast and successful experience of smallpox eradication in the USSR, but also on its real potential in implementation of this project. This includes the supply of a high quality smallpox vaccine, deployment of well-trained young epidemiologists to combat smallpox, as well as the scientific and practical support of the project provided by the National Smallpox Center, headed by Prof. Marennikova, later transformed into the WHO Collaborating Center for Smallpox and Related Infections.

The book provides the insight into how all the three factors acting in different directions altogether made a very significant contribution to the Program and greatly assisted in smallpox eradication.

It is obvious that the book *How It Was: The Global Smallpox Eradication Program in Reminiscences of Its Participants* is not only a document of our history, but also a magnificent example of commitment and a behavior model for young people starting their way in medicine.

***Prof. G.G. Onishchenko**, academician of the Russian Academy of Medical Sciences, head of the Federal Service for Supervision of Consumer Rights Protection and Human Well-Being, and Chief State Sanitary Doctor of the Russian Federation*

Foreword

Few of the past centuries were so full of great events that shook the world as the 20th century. Just recall the two world wars, which killed tens of millions of people as well as the revolutions and disasters that have changed the social and political landscape of the world. However, this century was marked by unprecedented advance and achievements in almost all spheres of human activities. The latter rightly includes the global eradication of smallpox, one of the most dangerous infectious diseases that have plagued humanity for millennia. Halfdan Mahler, the WHO Director-General during the period of smallpox eradication project, highly esteemed this victory: "...while presenting the history of the 20th century from the positions of the coming 21st century, the smallpox eradication will be equated with the great achievements of mankind, such as the exploration of space and development of nuclear energy." One can have different attitudes to this estimate but has to agree that the smallpox eradication worldwide was one of the greatest achievements in the public health and medical science. Here we omit the details of how many human lives were rescued and how much money was annually saved by the world community since the reader can find this information in the brief history of the Smallpox Eradication Program. The initiative on the global smallpox eradication belongs to Prof. V.M. Zhdanov and was proposed on behalf of our country in 1958 at the 11th session of the World Health Assembly (WHA).

Recall that the late 1950s were a rather difficult period for the WHO. It became clear at this particular time that the currently acting Global Malaria Program was on the verge of complete failure. Putting forward a new global initiative in these circumstances required some courage and the confidence that there was every reason to expect its successful completion. Prof. Zhdanov had both. The proposal was endorsed by the WHA in 1958. The combat against smallpox continued to the end of 1977 plus 2 years of certification activities that confirmed the complete smallpox eradication. The results of this ambitious project were summarized in the report of the Global Commission for the Certification of Smallpox Eradication. In the May of 1980, the 33rd WHA meeting officially declared that the world was free from smallpox.

However, it is not correct to regard the overall course of this program as a triumphal procession. There were mistakes, failures, and disappointments on the way, especially, during the first period, not to mention objective difficulties, including the absence of budget funding for the program. The turning point was in 1966, when the program was recognized as "one of the major goals of the WHO" thanks to the efforts of the participants of the 18th and 19th WHA meetings as well as got the budget funding and a specialized department at the WHO Headquarters. A great success was that D.A. Henderson (United States), a highly qualified epidemiologist and a talented organizer, was appointed the Program Manager. The results came soon: the last case of smallpox on the globe, according to the WHO, was reported 10 years later.

The results of the program were summarized in several monographs, including the fundamental WHO publication *Smallpox and Its Eradication* (1988). This book differs from others in that it is based on the reminiscences of our compatriots who directly participated in the struggle against smallpox and were working shoulder to shoulder with

experts and practitioners from over 70 countries. These reminiscences allow the readers to observe live pictures of real events with living personalities doing their work under severe and sometimes life-threatening conditions. The reader will see the flexibility and understanding of the local population's psychology that were necessary to achieve the goal. The Russian scientists of the WHO Collaborating Center for Smallpox in Moscow were the major contributors to the success of this program. Along with the diagnostic support for the program, the WHO Collaborating Center implemented a number of important research projects and gained international recognition. We would like to specially mention the memorial section of the book dedicated to the deceased colleagues and friends whose work and labor contributed to this great victory.

We hope that the book will be of interest to everybody who cherishes the history of the Russian medicine, and the younger generation will find examples of commitment to medical duty and the ideals of humanity worth to follow.

***V.V. Zverev**, Director of the Mechnikov Institute of Vaccines and Sera and academician-secretary of the Department of Preventive Medicine of the Russian Academy of Medical Sciences*

Introduction

The eradication of smallpox in the world is one of the largest and brightest medical achievements of the 20th century. This event is a milestone in the history of mankind: it is the first and so far only case when the world community eventually got rid of a severe infection under the approved Global Smallpox Eradication Program.

Several books have been written and a large number of articles have been published in periodicals on smallpox eradication. However, although the materials presented in these publications are of importance and scientific interest, they typically do not describe the heroic everyday work of eradicators with its diversity of specific situations. In our view, this aspect of the program implementation could be best demonstrated in the reminiscences of those who had been at the forefront of the fight against smallpox.

To prepare this book, we called for the living veterans of the program asking them to recall this heroic time and to share the vivid and colorful details of their noble mission in combating smallpox with the readers.

It was not an easy task to find and gather the participants of this epic mission. Life has scattered the people and the communication between teammates and colleagues was interrupted over decades. Unfortunately, too many people passed away before the 30th anniversary of smallpox eradication. It cannot be ruled out that the early death of at least some of them was associated with the great strain and difficulties of working under extreme conditions. Nevertheless, we managed to find and gather a group of living veterans who worked under the program in various countries.

According to our experience while preparing this publication, almost nobody of the participants of smallpox saga put down their impressions and observations during the work. Now that many of them are no longer with us, we have lost the opportunity to reconstruct many interesting facts that could complement this narration. In part, this "omission" is compensated for by a large number of photos provided by the authors of reminiscences. Not all the images are high quality but we hope that readers will understand this—after all, some photos are the only documentary evidence of those distant events or their participants.

While preparing materials for the book, we came across the publication dedicated to the staff of the Pasteur Research Institute of Epidemiology and Microbiology in Leningrad, which is poorly known to the general public[1]. One of the essays in this book described the work of two deceased participants of the program, A.Yu. Samostrel'skii and Yu.P. Rykushin, who managed to read this publication while still alive. It was important for us that their own stories about their work were there. Therefore, we considered it possible to include this material in our book. E.M. Slepchuk a candidate of medical sciences and a journalist, edited and somewhat abridged their narration.

The book starts with a portrait of V.M. Zhdanov, a famous Russian scientist, the man who launched the Smallpox Eradication Program. He not only proposed, but also substantiated the feasibility of this ambitious project. Unfortunately, we have to admit the recent trend, including the relevant publications, to conceal this fact and regard that the

[1] We are grateful to G.P. Oblapenko, G.F. Trifonov, and N.A. Chaika, candidates of medical sciences working with the Pasteur Institute, who not only showed us this publication, but also presented us the book.

program started in 1967, when the first governmental funding was allotted as well as the corresponding staff. We believe it incorrect to distort the history of the program giving people a wrong idea about it.

The reminiscences of veterans in the book are preceded by the chapters reviewing the analysis of the Smallpox Eradication Program and its importance for the global public health, the activities of the WHO Collaborating Center for Smallpox and Related Infections in Moscow, as well as commemorative events held at the WHO Headquarters in Geneva and some other countries. These materials are complemented by the description of the efforts made by the public health authorities of our country in support of the program.

Along with the infection control in smallpox-endemic countries, it was necessary to control it from time to time in the countries where the disease was eradicated long ago. Our country was no exception, and we thought that the book should include the reminiscences of those who participated in elimination of such imported outbreaks (including the imported outbreaks in Moscow). We also briefed the history of a large-scale production of smallpox vaccine at the Moscow Institute for Viral Preparations intended for both the domestic purposes and the Smallpox Eradication Program. The supply of our vaccine played a most important role in the overall effort to eradicate smallpox in many countries.

The last section of the book is memorial. We gathered the photos and brief description of smallpox eradication activities of our perished colleagues and friends. Unfortunately, although we did our best, some living and deceased eradicators have not been found; thus, only 45 names were included in the general list of compatriots who participated in the Global Smallpox Eradication Program. We hope that the readers will not remain indifferent and respond to our request to provide any information about our colleagues who are not mentioned in the memoirs.

To help our reader imagine the enemy that the authors of this book together with the other eradicators had to combat, we added unique color images reflecting different stages of skin lesions in various forms of smallpox.

We would like to emphasize the help and support of the following people, without whom the book could not be completed and see the light of day: V.V. Zverev, director of the Mechnikov Institute of Vaccines and Sera; A.N. Sergeev, director general of the State Research Center of Virology and Biotechnology Vector, and R.A. Martynyuk, a deputy director of Vector; and G.G. Onishchenko, head of the Federal Service for Supervision of Consumer Rights Protection and Human Well-Being, and to this institution as a whole. We are very grateful to all the listed institutions and their leaders. We also regard as our duty to thank our selfless helpers N.N. Yanov and E.V. Faizulloev, working with the Mechnikov Institute, for their assistance in searching for the necessary (often hardly accessible) documents and photographs.

We thank one of the authors, L.N. Khodakevich, for his significant contribution to preparation of the book for publication and the collaboration of a group of the program participants with the WHO Country Office in the Russian Federation, which he initiated. We would like to acknowledge the assistance of our colleagues G.D. Suleimanov, V.V. Fedorov, E.M. Slepchuk, and N.A. Khabakhpasheva, who earlier worked with the Moscow Center.

We are grateful to Dr. Luigi Migliorini, Special Adviser of the WHO Regional Office and N.P. Kolpakova, his deputy, for their interest and attention to this work and the willingness to provide any kind of support.

Prof. S.S. Marennikova, doctor of medical sciences

Victor M. Zhdanov

Geneva, the Palace of Nations, WHO Headquarters, May 1958, 11th World Health Assembly.

Prof. V.M. Zhdanov, the head of the Soviet delegation, Deputy Minister of Public Health of the Soviet Union, and well-known virologist and epidemiologist, is at the podium. In his speech, Zhdanov proposed the program for global smallpox eradication and substantiated its feasibility. This proposal was approved by the World Health Assembly, thereby actually launching this tremendous WHO program, which was completed in 1980 by declaring the world free from smallpox at the 33rd World Health Assembly

The World Triumphantly Celebrated the 30th Anniversary of Smallpox Eradication

S. S. Marennikova and L. N. Khodakevich

In 2010, medical science and public health celebrated the memorable date—the 30th anniversary of the global eradication of smallpox, one of the most severe and highly contagious diseases. Smallpox had been affecting the mankind throughout its history. According to recent estimates, 300 million people became its victims only in the 20th century. During the 30 years of freedom from smallpox, the world community saved at least 60 million human lives and $30 billion.

The preparations for the 30th anniversary of smallpox eradication began almost 2 years before the celebration. The initiative group from the Emory Global Health Institute (United States) established the Secretariat, Committee of Advisors, Committee for the development of the Program of the International Symposium, and so on. Three Russian experts—S.N. Shchelkunov, S.S. Marennikova, and G.D. Suleimanov—participated in these activities. The Secretariat succeeded in mobilizing considerable financial resources for organization of the International Symposium, commissioning of the monument in honor of this event, the publication of an illustrated history of smallpox and its eradication, etc. The brochure was published in paper form in English and French and in Russian it is available at http://www.globalhealth.emory.edu/programs/sec2010%20documents/graphicnovel_russian.pdf.

Numerous cosponsors of these events included Russian veterans of the Program: Lev Khodakevich, Valery Fedenev, and the Gromykos, the husband and the wife. A special meeting dedicated to smallpox eradication was held among festive events in May 2010 at the 63rd World Health Assembly (WHA) meeting. This was followed by the opening ceremony of the monument in honor of smallpox eradication (sculptor Martin Williams from Wales) in front of the WHO Headquarters. A bronze sculptural group portrays a married couple with a child and the figure of a

The monument in honor of the victory over smallpox (sculptor M. Williams, 2010, bronze) in front of the WHO Headquarters in Geneva, Switzerland

Edward Jenner vaccinating a child against smallpox (sculptor G. Monteverde, 1878, marble). The monument is in Boulogne, France

vaccinator performing a smallpox vaccination with a bifurcated needle. The bronze plaques on the pedestal have the following text in the six official languages of the WHO, including Russian:

"The conquest of smallpox was an unprecedented achievement made possible by all nations working together. On May 8, 1980, the thirty-third WHA declared the world free from smallpox."

In this regard, we would like to remind that the first steps of the era of smallpox vaccination were also commemorated in sculpture. One of the most impressive works of this kind is a marble sculpture by Giulio Monteverde, a famous Italian sculptor, who portrayed Jenner vaccinating a child, i.e., the episode from which the era of vaccination actually started. Both monuments represent the nearly a 200-year path that humanity had to go through before celebrating the eradication of this dangerous infection on a global scale.

The opening ceremony of the monument was attended by Dr. Margaret Chan, current WHO Director-General; Dr. Halfdan Mahler, the former WHO Director-General who worked during the main stages of the Smallpox Eradication Program; Dr. Donald Henderson, the program manager; the staff of the WHO Headquarters; the veterans of program from different countries (including Russia); guests; and press.

We believe that it will be interesting for the reader to get acquainted with the speeches of the main figures of this ceremony.

The opening ceremony of the monument in honor of smallpox eradication

The speech of Dr. Margaret Chan, the WHO Director-General:

"Dr. Mahler, Dr. Henderson, Mr. Roy, and of course, my old friend David, colleagues in public health, ladies and gentlemen, it is a great honor to welcome this statue to such a prominent place on the WHO grounds. It will remind staff and visitors alike of a truly remarkable success story with permanent gains for health in every corner of the world. I am likewise honored by the presence of people who played such a key role in this success story, Dr. Mahler, and of course, my teacher Dr. Henderson, and many others. Do you remember your coming to me when I was working in Hong Kong? You asked lots of questions, it was you who was mainly asking, and I was answering. And of course, many others mentioned by Mr. Roy."

"Leadership at WHO was important, but an achievement of this scale ultimately depended on tens of thousands of dedicated workers who literally crisscrossed this entire earth, by jeep, donkey, and fishing boats, on foot in jungle and desert journeys, from nomadic tribes in remote mountain areas to pavement dwellers in the scorching heat of Asia's slums. Do you remember it? Who remembers? Who of those present? Look, I am just telling what happened. It is you who worked and made history. When the intensified eradication program was launched, no one knew exactly what needed to be done, how progress would evolve, or even if the initiative would succeed. And there were indeed many near misses

and setbacks. The history of smallpox and its eradication has been written, and public health continues to benefit from the many lessons learned. Thank you for this."

Success has been attributed to a strong research component, an emphasis on epidemiology and surveillance, and the flexibility to adapt to new findings and change course when needed. The strategy of ring vaccination emerged and was validated, vastly simplifying operational and logistic demands. The bifurcated needle was invented, and some like to argue that the war against smallpox was eventually won by a modified sewing needle. I am not sure that this comparison is appropriate here. Smallpox fighters had to contend with war zones, vast population displacements, religious and cultural beliefs, fetishes, and traditional healers with their tin boxes of smallpox scabs. And yet despite the incredible odds, one of history's longest chains of virus transmission, dating back at least 3000 years, was broken in a small harbor on the Indian Ocean more than 30 years ago."

"Actually, the eradication of a disease requires the collaboration of all countries of the world. The history of smallpox eradication is also a story about the peaceful collaboration of the two superpowers throughout the hottest years of the Cold War. The monument standing in front of the building will remind of the significance of this achievement and of how resources available to WHO can be vastly magnified when the whole world unites for the sake of a common humanitarian goal. It will commemorate the time of great idealism that attracted talents and inspired commitment and personal sacrifice. Above all, it is a

The opening ceremony of the monument in honor of smallpox eradication, May 17, 2010, Geneva, Switzerland. *Standing in the center* is Margaret Chan, the WHO Director-General; *on her right*, D.A. Henderson, manager of the Smallpox Eradication Program; *on her left*, H. Mahler, the WHO Director-General during the Program implementation; *and next to them*, Program participants (photo from the archive of the Emory Global Health Institute)

reminder of the power of international health cooperation to do great and lasting good. And I want to thank each of you for having honored us by enabling the erection of the monument in front of the headquarters. Thank you very much. Now don't leave yet. I managed to convince Dr. Mahler to say just a few words. Dr. Mahler!"

The speech of Dr. H. Mahler, a former WHO Director-General:

"Dr. Chen, Dr. Henderson, friends! If I decided to analyze everything that relates to the eradication of smallpox, the first thing to note is that I have never met people so motivated as the group of enthusiasts who achieved the eradication of smallpox. I wish it was possible to write on a prescription, 'This is what should be done.' They achieved success inspiring each other for the incredible and almost unreal things. Despite the suffering and the fact that it was incredibly, incredibly difficult. Why are we all not able to act and to achieve the same success in the challenge no less daunting than the eradication of smallpox? It reminds me of what my friend, a poet, said in his mini-poem. After he stole my girl, he wrote me the following: 'The ability to fail gracefully may save the mankind one day and become a timeless virtue that we, average people, would consider a humiliation.' Because everybody had such feelings when Henderson and his colleagues travelled all over the world, and you heard about the incredible things they were doing, about the unheard victims, about the ingenuity they demonstrated to make this possible. So that one day the organization (WHO) could say: 'We had the great honor to lead the program that you successfully implemented.' Thank you."

The speech of Dr. D. Henderson, the manager of the Smallpox Eradication Program:

"Thank you very much. Dr. Mafubelu, current Director-General Dr. Chan, and former WHO Director-General Halfdan Mahler, my close friend! I am glad to be here. I am so happy to see so many people whom I haven't seen for a long time. Now when I hear about these achievements I understand that smallpox eradication was inevitable considering the effort and talent invested in it. By the way, I have to admit that many of you haven't changed over these 30 years, including myself. That's it! I would like to remind you that 30 years ago health workers gathered at a special plenary session of the 33rd Assembly of the WHO where Dr. Frank Fenner from Australia, the then Chairman of the Global Commission for smallpox eradication, declared: 'The Commission concluded that the global eradication of smallpox was achieved' and the Assembly endorsed this statement. It was a significant moment for many, especially for hundreds of thousands of global health workers whose commitment for 14 years made the eradication of smallpox possible. Many of them sacrificed much together with their loved ones. They sacrificed their careers, they sacrificed their time, and some of them even died. As now it is well known, a lot of people participated in this program. Much more people participated in this fight than could have been expected. I salute all of you with great respect and proudness. I was lucky to be a member of the team that was doing and accomplished this job. We were certainly in no small measure inspired by the award from the Lasker Foundation the WHO received in 1976. I quote what they said: 'We salute this historic milestone as one of the most brilliant accomplishments in medical and world history'."

"But smallpox eradication was not an end in itself, and in 1974 the Assembly agreed to launch a large-scale immunization program to ensure that the world's children would also be protected against measles, polio, diphtheria, pertussis (whooping cough), and tetanus. The goal was to achieve 80% coverage of children. UNICEF, international agencies, as well as a number of governments made this a priority. We were joined by many other organizations. The 80% mark was reached in 1990. A new era in the history of public health started due to vaccination."

"I have often been asked whether I thought the eradication of smallpox could have been accomplished in today's world with so much armed conflict in so many areas and with large populations inflicted by

natural disasters, such as in Chile, Indonesia, and Haiti. But how soon we forget! In the 1960s and 1970s, the Program was beset by major floods, famines, civil war, hundreds of thousands of refugees in various parts of Africa and Asia and we did not have then cell phones, we did not have e-mail, we did not have fax machines, we didn't have Facebook, we didn't have Twitter. In some areas where we worked, even the telephone was not always available. Telex was possible on some occasions but too expensive. I think it is a testimony to the skill and creativity of the international advisers from some 70 different countries as well as the ministers and health program staff who managed to overcome all of these and achieve what had been deemed impossible."

"I would particularly like to mention the work of several people who deserve special thanks. One of them is the WHO Director-General Halfdan Mahler who managed to ensure the implementation of the Program in a very difficult time, in spite of many difficulties. We highly appreciate it. And special thanks to Dr. Isao Arita who had been the Deputy Director of the Program since 1966 and in 1977 became the Manager of the Program until the certification of smallpox eradication. Today he is not here because he is present at the celebration in Kumamoto, which is taking place at the same time. The ability of Dr. Arita to be in two or three places at once is well known, but this time he failed to do it. I must say that today I wouldn't be so sure that we would be able to accomplish such global task in a 10-year period. There is too much bureaucracy and too many additional obstacles at the national and international levels. We start to suffocate under the weight of data and numerous reports, which replaced brief but, in my opinion, very informative, summaries on two–three pages. I even feel some anxiety. Now there are leaders that are challenging the traditional foundations and are able to reach a goal. But I believe that today as never before we need courageous health care workers who see the goal and know that it's necessary to find new ways and new forms of cooperation in order to achieve this goal. As time has shown, it is necessary to regularly review the established work practices.

S.S. Marennikova (*left*) and G.D. Suleimanov (*fourth from the left*) together with Brazilian and American veterans of the Smallpox Eradication Program

At the anniversary conference of the WHO Regional Office for Southeast Asia dedicated to the 30th anniversary of smallpox eradication. Awarding S.S. Marennikova with the medal "For Service to Humanity in Public Health in Southeast Asia"

And this is the key to the future of science, to a new revolutionary era for the sake of health improvement. Personally, I regret that now I do not work directly in the area of health care in this, possibly, the most interesting period in its history. And taking into account all the above, there is no doubt that the WHO existence in the future will be vitally important. So, congratulations to all those present and thank you all for coming. It is so great to see everyone again and to remember happy days. Thank you."

The celebrations in Geneva were the climax of the overall celebration of the 30th anniversary of smallpox eradication. However, different meetings covering the most important events and stages of the program were organized in many countries of the world before and after it. For instance, the United States celebrated 30 years of the victory over smallpox in West Africa where the last smallpox case on the globe was reported. In May 2009, the WHO Regional Office for Southeast Asia held a scientific and practical session in India, with participation of the countries of this region and speakers from the United States and Russia. Active members of the Program, including a representative of Russia, were awarded medals "For Service to Humanity in Public Health in Southeast Asia".

In Japan, the anniversary conference was held under the motto "Smallpox eliminated forever". The meetings were held in the national theatre. The conference brought together 1300 participants. Distinguished experts from both Japan and abroad were invited as speakers. They discussed the lessons of the Smallpox Eradication Program as well as the implementation of eradication programs for some other infectious diseases. Dr. I. Arita, the organizer of the conference and one of the former leaders of the Smallpox Eradication Program, stressed special importance for such programs to be based on research contributing to both the proper selection of main directions and resolution of specific issues. The anniversary was also celebrated in the Czech Republic and some other countries.

However, the main and most significant event of the anniversary became the 4-day International Symposium in Rio de Janeiro "Smallpox Eradication after 30 Years: Lessons, Legacies, and Innovations" with about 300 participants from 34 countries. The Minister of Health of Brazil and the Director General of the Pan American Health Organization were among the participants. The symposium analyzed the Smallpox Eradication Program as a whole (report by Dr. Henderson) and highlighted the progress in smallpox eradication in the most important endemic countries. Dr. Quadros described the situation in Ethiopia; Dr. Baptista Risi, the situation in Brazil; Dr. William Foege, in the countries of West and Central Africa; and Dr. Stanley Foster, in Bangladesh.

Some related problems were also discussed in addition to the issues associated with the program itself. The latter include an increased incidence of other orthopoxvirus infections in recent years, in particular, human monkeypox, and the harassing vaccinia-like infections in humans and animals in Brazil and some other countries. These questions were discussed at the special session with Prof. Marennikova as a chairman. Opening the session, she noted that in addition to the 30th anniversary of smallpox eradication,

the session coincided with the 40th anniversary of the discovery of a new human orthopoxvirus disease, caused by monkeypox virus.

The significance of this discovery consisted in eliminating the anxiety caused by the emergence of pox-like infections in the areas where smallpox had been already eradicated. The second important consequence was the start of a serious research into this previously unknown form of human pathology and the pathogen ecology.

The reports on human monkeypox were made at the session by Dr. Inger Damon, director of the WHO Collaborating Center for Smallpox and Related Infections at the Centers for Disease Control and Prevention, and Dr. Anne Rimoin, an epidemiologist from California, with close ties and a base in the Democratic Republic of the Congo. Rimoin's report analyzed the first outbreak of human monkeypox outside the African continent, in the United States, where the infection was imported with rodents from West Africa. The comparison of monkeypox virus strains isolated from patients in the United States

Participants of the International Symposium "Smallpox Eradication after 30 Years: Lessons, Legacies, and Innovations" held on August 27, 2010, in Brazil. D.A. Henderson, the Program Manager (*in the center of the first row*); Ciro de Quadros, an active participant in the fight against smallpox (*on his right*); and J. Bremen and S.S. Marennikova (*on his left*)

with the isolates from patients in the Congo River basin confirmed the data on the differences in the pathogen characteristics and the disease severity. Dr. Rimoin reported alarming on a sharp increase in monkeypox incidence approaching a 20-fold level according to her estimate. The rate of disease cases resulting from human-to-human transmission has also largely increased. We can agree with the author's conclusion that the reasons are associated with the cessation of vaccination, resulting loss of immunity to smallpox, and, as a consequence, increased susceptibility to infection when contacting animals (carriers of this virus) and human monkeypox cases. Prof. Shchelkunov presented his report titled "Genomic studies of orthopoxviruses pathogenic for humans". In particular, the author outlined his hypothesis on the origin of variola virus. The other sessions focused on the issues of the elimination and eradication of other infections (polio, measles, rubella, malaria, etc.), new approaches to vaccine development (in particular, malaria vaccine), state-of-the-art surveillance methods, research related to the eradication of diseases, and improvement of global public health.

The poster presentation mainly dwelling on the vaccinia-like infections of humans and animals in Brazil was also organized. The proceedings of the symposium were published in reputable scientific journals. The other activities of the Secretariat (SEC2010) included creation of the blog citing the names of the Smallpox Eradication Program participants and their reminiscences.

The following final statement was made at the closing ceremony of the symposium:

"Thirty years after smallpox eradication, we, 260 scientists, health professionals, historians, and other specialists from 34 countries who participated in the symposium, declare:

First, smallpox eradication freed humanity from the virus, which killed about 300 million people in the 20th century;

Second, after 1980, smallpox vaccination was stopped, which saved huge funds required for the implementation of vaccination programs, and eliminated severe complications frequently associated with vaccination;

Third, the Smallpox Eradication Program inspired a whole generation of health workers to develop several important programs such as:

• Expanded Program on Immunization, which provided high levels of protection against diseases worldwide and prevented a large number of deaths among children and adults;

• Widespread use of surveillance as a key tool in combating diseases; and

• Successful development of Polio and Guinea Worm Global Eradication Programs as well as Measles and Rubella Elimination Programs in the Americas;

Fourth, smallpox eradication proved that international cooperation and solidarity could make a significant contribution to the global public health improvement; and

Fifth, after the cessation of smallpox vaccination, the portion of susceptible population is constantly increasing. Given that the vaccine supply is limited, uncontrolled virus can cause a catastrophic global epidemic. Moreover, it is known that the virus is maintained in two WHO-designated laboratories. Despite the fact that these laboratories have emergency measures to prevent the release of the virus, no security system is free from the risk of a breakthrough. It cannot be also guaranteed that there are no unauthorized repositories of variola virus. More than 15 years have passed since the WHA agreed to postpone the destruction of the virus. Therefore, for the sake of the global security, the destruction of laboratory stocks of variola virus should be considered as soon as possible, when the current research to improve the vaccine quality and to develop effective antivirals and reliable models for studies involving animals endorsed by the WHO are completed. Finally, the possession and use of the virus outside organizations authorized by the WHO should be considered as a crime against the mankind."

In general, this statement correctly reflects the current problems. However, it does not in our view adequately reflect the important task of human monkeypox monitoring.

In Russia, the country that initiated the Smallpox Eradication Program and made an outstanding contribution to it, real steps to celebrate the anniversary were made too late and the original plan was not fully implemented. However, some work was done. The first event, an independent section "Thirty Years of the Victory over Smallpox and the Prospects for Eradication of Other Infections (Polio, Measles, and Rubella)" was held in May 2010 in St. Petersburg (Russia) at the 19th International Conference "AIDS, Cancer, and Public Health", organized by the conference chairman Prof. A.P. Kozlov and Prof. Marennikova. In addition to the introductory lecture analyzing the Smallpox Eradication Program and its significance for global health (presented by Marennikova), the information about the state and prospects of polio, measles, and rubella eradication programs in this country and Belarus was presented by M.A. Ermolovich, V.B. Seibel, and N.V. Yuminova. The corresponding data demonstrate a definite and most significant success in combating these infections, although there still are some unresolved issues, highlighted by Dr. Seibel, in combating polio that hinder its final eradication. Academician of the Russian Academy of Medical Sciences O.I. Kiselev described the prospects of combating influenza. Prof. Shchelkunov outlined his concept of the origin of variola virus based on the results of his own studies into the structure of orthopoxvirus genomes and the relevant data of ancient history.

In the summer of 2010, the Ministry of Health and Social Development instructed the Mechnikov Institute of Vaccines and Sera to arrange further events in the frame of the celebration of the anniversary. The Organizing Committee headed by Academician V.V. Zverev, director of this institute, was formed for this purpose.

In October 2010, an extended meeting of the Presidium of the Russian Society of Epidemiologists, Microbiologists, and Parasitologists together with the Scientific Council of the Mechnikov Institute of Vaccines and Sera was held. Presentations were made by Prof. Marennikova (who headed the WHO Collaborating Center for Smallpox and Related Infections for 25 years), Suleimanov (who worked under the eradication program in Pakistan and Ethiopia), V.D. Bychenko (a member of the smallpox eradication team in India), and M.O. Konovalova (who told of the Soviet mass vaccination mission for Iraqi population). We omit the details of these presentations here because they are included into this book.

In November 2010, another conference was organized by the Department of Preventive Medicine of the Russian Academy of Medical Sciences. The speakers were Prof. Marennikova, Prof. G.G. Onishchenko, L.N. Khodakevich, and N.V. Yuminova. The presentation by Marennikova was focused on the lessons of the Smallpox Eradication Program and that by Onishchenko, on the poorly known facts related to the fate of the two variola virus collections still remaining in the world (in the WHO Collaborating Centers in Russia and the United States). The difficult question of whether to destroy the virus or to preserve it as a biological species and use for research purposes for many years has been the subject of heated debate in both the scientific community and the WHO. During this time, the virus was maintained and used in most important studies approved by the WHO. The final decision about the fate of these collections has not been made yet. Khodakevich gave an interesting perspective in his report by making a comparative analysis of different approaches to smallpox and HIV eradication programs.

In addition to the anniversary for the eradication program, the year of 2010 is notable for another memorable event, namely, the 50th anniversary of the eradication of a severe smallpox outbreak in Moscow. The conference organized by the Federal Center of Rospotrebnadzor for Moscow focused on these two events and considered the issues related to these two dates. Prof. Marennikova described the course of the Global Smallpox Eradication and G.M. Manenkova, an epidemiologist of the highest qualification, made a detailed analysis of the Moscow outbreak and the measures to handle it (see more details about the 1960 outbreak in Moscow in the last essays of this book).

The round table discussion dedicated to the anniversary of smallpox eradication and the history of combating this infection in this country since the pre-revolutionary period and the stand with the relevant

materials were organized by joint efforts of the WHO Country Office in Moscow (T.P. Kolpakova, a deputy WHO representative in the Russian Federation) and the Russian State Library (thank to S.V. Martynyuk, a deputy head of department, and G.V. Shandurenko, chief librarian). The participants had the possibility to study rare documents and publications on this subject from the repositories of the State Library. A number of the eradication program participants made presentations during the round table discussion. The overall situation with the Smallpox Eradication Program was outlined by Corresponding Member of the Russian Academy of Medical Sciences D.D. Venediktov, the former Deputy Minister of Health of the USSR, who supervised these activities. Prof. Marennikova described the activities of the WHO Collaborating Center for Smallpox and Related Infections. Khodakevich shared his reminiscences about the research into monkeypox virus ecology and compared the approaches to smallpox eradication and the combat against HIV infection. The round table ended with a brief discussion with participation of both veterans of the program and guests.

Another round table discussion was organized and conducted by Kolpakova at the WHO Country Office in Moscow as the meeting of the eradication program veterans and the office staff. The audience was offered a series of presentations, which caused a lively discussion. After the round table, Dr. Luigi Migliorini, representative of the WHO Director-General, spoke with the eradication program participants. During this informal discussion, the veterans said that a book of reminiscences of the participants in the fight against smallpox was in preparation on the initiative of Prof. Marennikova. Dr. Migliorini welcomed this initiative and said that the WHO Office was willing to support our project.

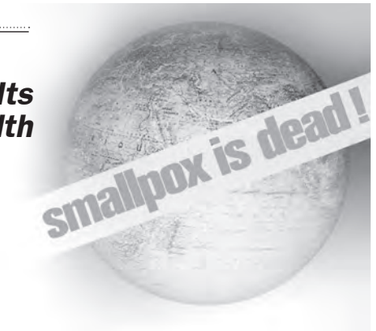
In addition, the State Research Center of Virology and Biotechnology Vector (Novosibirsk, Russia) in the frame of the smallpox eradication celebration published the book titled *30 Years after Smallpox Eradication: The Research Continues* (G.G. Onishchenko and I.G. Drozdov, Eds.).

The Presidium of the Russian Society of Epidemiologists, Microbiologists, and Parasitologists awarded medals and diplomas of honorary members of the Society to the Smallpox Eradication Program participants (Marennikova, Venediktov, Khodakevich, Suleimanov, Fedenev, Yu.G. Krivda, Bychenko, Oblapenko, Konovalova, and E.B. Gurvich) in recognition of their contribution to preventive medicine.

Regretfully, the most important mass media of Russia, such as TV and radio, completely ignored this significant international event despite that they had a good reason to tell our citizens that our country was the initiator of the Smallpox Eradication Program and made an outstanding contribution to its triumphant completion. This is doubly unfortunate since the smallpox eradication is one of the greatest medical achievements of the 20th century.

The Smallpox Eradication Program and Its Significance for the Global Health

S. S. Marennikova



The history of smallpox emergence in the human population and the place of its primary origin are still rather vague. According to a hypothesis, smallpox originated from one of causative agents of animal pox. It transformed into a purely anthroponotic infection when the population size was sufficient for the pathogen transmission within the human population.

Ancient findings and written evidence indicate that smallpox already existed in Egypt and India in the early 12th century BC. With an increase in the population size and density on the globe and development of connections between separate regions, smallpox colonized new areas and gradually became endemic in vast territories of Asia, Africa, and almost entire Europe. At the beginning of the 16th century, smallpox entered the American continent and destroyed a significant part of the population. A smallpox epidemic can only be compared with plague in strength and magnitude. Variolation (inoculation of the material from smallpox patients) as the attempt to prevent the disease was used for centuries from China to Europe. This practice gave certain protective effect but the risk of smallpox infection and its further spread. Nevertheless, variolation was used in Europe until E. Jenner in 1796 discovered the method of vaccination. Later, the vaccination became obligatory in several countries, decreasing the damage caused by this infection. However, world war in many European countries interfered with the final eradication of smallpox. This infection was at last eradicated in Europe in the next two decades, and its whole territory became free from this terrible disease.

The unprecedented experience of smallpox eradication in our country should be specially mentioned. The combat with smallpox in the USSR was especially difficult because the disease was abundant, the country was vast, and the living conditions, national customs, traditions, climates, etc., were most diverse not to mention the devastation and disruption of the national economy as a result of the

Prof. Svetlana S. Marennikova, virologist, doctor of medical sciences, honored scientist of the Russian Federation, and academician of the Russian Academy of Natural Sciences. She participated in the Smallpox Eradication Program starting from 1958 and headed the WHO Collaborating Center for Smallpox and Related Infections for 25 years; was a member of all program-specific research groups and expert committees of the WHO and a member of two International and Global Commissions for the Certification of Smallpox Eradication; was a Vice-Chairman of the ad hoc Committee on Orthopoxvirus Infections, established by the WHO in 1981 to oversee the implementation of recommendations for the post-eradication period

Civil War. Yet, despite all these difficulties, it took less than 20 years after the introduction of obligatory smallpox vaccination in 1919 for the complete eradication of smallpox throughout the country.

The experience gained by the USSR public health during smallpox eradication and control of its import from neighboring countries affected by smallpox formed the background for the International Global Smallpox Eradication Program proposed by the delegation of the Soviet Union at the 11th WHA in 1958 and approved by its members.

According to the WHO estimates, nearly 100 000 smallpox cases were annually recorded by the beginning of eradication program, which experts assessed as approximately only 1% of the actual number of cases. At least 2 million of them died. Unfortunately, the early years of the eradication program displayed a frustratingly slow progress towards the set goal. This resulted not only and not so much from the situation typical of the preparatory stage, especially, under such ambitious project. The reason was quite different. Three years before the endorsement of the Smallpox Eradication Program, the WHO initiated the unsuccessful Global Malaria Eradication Program, which took over 2 billion dollars for its implementation, to say nothing of the staff, technical resources, and so on. In addition, the Smallpox Eradication Program was rejected by Dr. M. Candau, the WHO Director-General at that time; he did not believe in its feasibility. This created a strange situation: instead of organizing a structure that would be able to plan, direct, and coordinate such a huge and complex program, its implementation was entrusted to one officer with the WHO Department of Viral Infections, whose function was to assist the countries in forming national smallpox eradication programs. In fact, the WHO activity at this time was a mere recording of the relevant events. Moreover, the eradication program for 9 years had no funding from the WHO budget. Representatives of the USSR (D.D. Venediktov, Sh.D. Moshkovsky, S.S. Marennikova, and others) as well as delegates from other countries regularly suggested improving the situation at the WHO meetings. However, it was only in 1965 when the WHO Assembly categorically demanded that the Director-General should radically change his attitude to this project. Thus, the next Assembly (1966) voted for allotment of special budget (2.4 million) for smallpox eradication (with a margin of just two votes). From that moment, a new phase of the eradication program, referred to as the Intensified Smallpox Eradication Program, began.

Nonetheless, the first stage of the eradication program (1958–1966) despite all these difficulties allowed 24 countries to eradicate smallpox. Mass vaccination campaigns were conducted in other countries (for example, in Iraq with approximately 75% coverage of the population) and/or draft national programs were developed. An important event of this period was the development of the international requirements for smallpox vaccines as well as an international reference preparation.

In 1964, the WHO Expert Committee summarized the results of mass vaccination and concluded that an 80% vaccination coverage was insufficient to eradicate the infection. Unfortunately, this analysis, similar to the initial proposal of the USSR on smallpox eradication, did not properly take into account the factors of epidemiological surveillance, control, and anti-epidemic measures in the infection foci; this is rather strange because surveillance always received the due attention in the practice of smallpox eradication in the USSR. Perhaps the prevailing idea was to simplify the tasks and to reduce the costs since the absence of funding made these tasks unfeasible. Our prominent epidemiologist Moshkovsky, who emphasized that vaccination campaigns must be supplemented with anti-epidemic activities, highlighted the importance of this factor in 1960 at the 13th World Health Assembly (WHA). However, some practical experience was needed before everybody could understand this. This major component in combating smallpox was fully implemented during the intensified stage of the eradication program. Characteristic of the intensified stage (besides the allotted funding) was organization of the structural unit with the WHO Headquarters headed by Donald Henderson (United States), a talented epidemiologist and brilliant manager.

Young, energetic, and knowledgeable professionals from different countries were enrolled for the work with the WHO Headquarters and regional offices as well as for field activities. Two WHO Collaborating Centers for Smallpox were organized using the promising and reliable facilities, namely, the Institute for Viral Preparations in Moscow and Centers for Disease Control and Prevention in Atlanta. Later, the Center for Quality Control of Smallpox Vaccine was organized in the Netherlands (Bilthoven, National Institute of Public Health and the Environment). The meetings of regional advisers were organized on an annual basis. The first meeting was held in Alexandria (Egypt) and discussed the draft guidelines for smallpox eradication programs in endemic areas along with the review of the local situations. In the future, these meetings became much more representative.

D.A. Henderson, M.D., Chief of Smallpox Eradication Unit at the WHO Headquarters during the intensified stage of the program

Special attention was paid to clarify the reasons of low efficiency of mass vaccination campaigns in the most problematic regions. In particular, high levels of immunization coverage in some areas of India resulted from vaccination of the same nearby objects (villages, schools, etc.). The analysis of the data made it possible to considerably improve the eradication program. Its structure was radically changed. The vaccinators were supplemented with supervisors, who

A meeting of regional advisers for the eradication program, 1967 (Alexandria, Egypt)

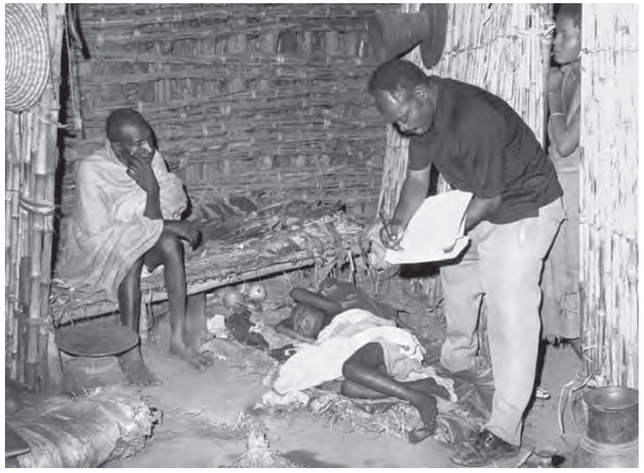
Inter-Regional Seminar on Smallpox Eradication, 1969 (Lagos, Nigeria)

assessed the inoculation procedure and recorded its results; an efficient system of reporting and inspecting was introduced; mobile teams were organized; vaccination schedules for different areas were developed. Efficient feedback between remote units of the program and the centers in WHO regional offices and headquarters was established. A characteristic feature of the eradication program was an immediate response to the changing situation.

The eradicators are proud of the fact that characteristic of the program were international solidarity and cooperation. In particular, this was the assistance from the USSR, Sweden, and other countries. Surprisingly, neither cold war nor other foreign policy complications affected the friendly and dedicated work at all levels of the complex mechanism of the eradication program. For example, representatives of 26 countries were working together with the local staff in India. Another impressive example: the team of two professionals—E.M. Shelukhina from the USSR and L. Matlovsky, a documentary photographer from the United States—was sent by the WHO to prepare a set of slides and other health education material. They made over 3000 images of smallpox patients in the midst of the epidemic in Karachi, discovering new foci and daily capturing the patients with different forms of smallpox from the onset of disease to its completion. These images proved to be invaluable, especially at the final stages of the eradication program, being a unique document in the history of medicine. There were lots of such examples throughout the Program.

The first large project of the intensified program stage was smallpox and measles eradication in 20 countries of West Africa. This special project, launched in January 1967, was organized and funded by the United States. Along with mass vaccination, the project included surveillance and anti-epidemic activities as its integral parts. During the attack phase, over 100 teams were simultaneously working throughout the region. On the average, up to 1 million people were immunized during 6 working days. At the end of the attack phase, 115 million people were vaccinated and 28 million additional vaccinations were

Registration of a smallpox patient



made during the maintenance phase. As a result, smallpox transmission was stopped in 20 countries by December 1969. Note that the anti-epidemic measures allowed for the smallpox eradication even on the background of incomplete (50%) vaccination coverage.

This project clearly demonstrated the importance of surveillance in the complex of infection control measures. On its basis, the strategy for combating smallpox was further adjusted and the experience of West Africa was extended to other smallpox-affected regions.

The proposal of our colleagues A.N. Slepushkin and V.A. Mukhopad proved to be very efficient, in particular, for India: intensive monthly searches (over a week) for smallpox patients who were not officially recorded. The first search in the state of Bihar detected over 1500 outbreaks and approximately 6000 human cases. This innovation was adopted in neighboring countries (Pakistan and Bangladesh). It was a significant addition to the surveillance system. In some cases, teenager groups were engaged in the search for new smallpox cases, which already had been practiced in Zambia and proved very efficient.

In general, the surveillance system, as well as all the components of the eradication program structure, became very flexible and rapidly adaptable to the changing circumstances and local conditions. Just two examples. The situation in Ethiopia was rather hard for implementing the eradication program: only donkeys and sometimes mules were available to search for smallpox patients or to perform vaccination in remote areas, making the anti-epidemic activities extremely difficult and slow. The problem was solved by using rented helicopters to deliver the staff.

Another example concerns a severe smallpox epidemic with a daily rate of 1000 new cases in Bihar; all the efforts to stop this wave of infection failed. It was decided to hire several

A team of teenager enthusiasts is providing invaluable assistance in the search for smallpox patients for a modest fee, 1967, Zambia, Northern Province (by the courtesy of I.D. Ladnyi)

tens of thousands of guards ordered to prevent the contacts of patients with others in smallpox foci. This measure radically changed the situation and the outbreak subsided.

Chronologically, the intensified phase of the program comprises three stages:

- 1967–1972, when smallpox was eradicated in South America, Indonesia, and most of African countries;
- 1973–1975, when all countries of the Indian subcontinent became free of smallpox;
- 1976–1977, when smallpox was eradicated in the remaining endemic countries of the Horn of Africa.

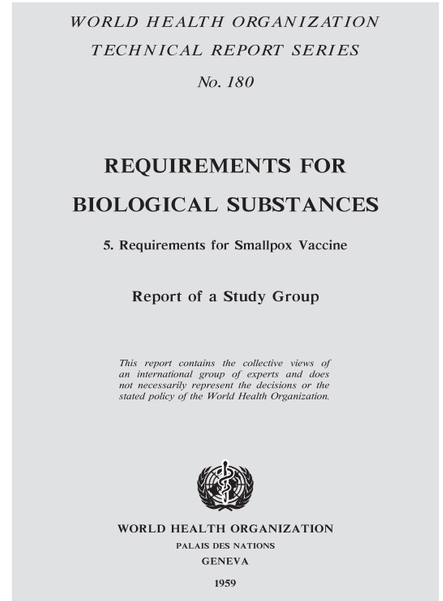
In particular, the last case of smallpox on the globe as a result of natural transmission was reported on October 22, 1977, in Somalia. Smallpox eradication in this region was very difficult and dramatic because the disease persisted among nomads migrating in a vast semidesert area with complete absence of roads as well as because of several other aggravating factors. It should be emphasized that the eradication program at this time was supported by many public agencies and countries.

The success of the intensified program is evident. However, we cannot agree with the recent trend to believe that the Smallpox Eradication Program was launched in 1967 (the beginning of the intensified stage) rather than in 1958, as it actually was. This trend is especially clear in various statements and publications of US experts. This could result from the fact that the United States were actively involved in the program implementation in its intensified phase. The United States undoubtedly made an outstanding contribution to the victory. However, no rationale can justify the distortion of historical facts related to the eradication program. This approach alters the real course of events completely rejecting what was done before 1967. The role of our country, which initiated the program and provided support and assistance throughout its implementation, thus disappears.

Completing the overview of the eradication program, we must mention two important questions, which are actually a crosscutting issue over the whole period of its implementation, namely, the smallpox vaccine and the WHO Collaborating Centers. As is already mentioned, the initial eradication strategy was based on mass vaccination of the population. Naturally, the major tool was the smallpox vaccine. Its quality influenced the level of collective immunity, the frequency of adverse reactions, and other important issues. Meanwhile, the used liquid glycerin vaccine rapidly lost its activity. Its administration required special storage conditions, unavailable in smallpox endemic countries. Another problem was the increased reactogenicity of some smallpox vaccines (including our vaccines). Their use provoked complaints and refusals to get vaccinated. In addition, the vaccines produced in different countries differed by one order of magnitude in their activities and other characteristics.

The WHO twice arranged the meeting of experts to address these issues. As early as 1958, the WHO Research Group developed the first international requirements for this preparation in the history; these requirements were stricter than those for most of the produced smallpox vaccines in several characteristics. This fully applied to the domestic vaccine. The enhancement of requirements was a hard work and demanded restructuring of the corresponding production facilities. Cannot but tell that when I returned from the trip and made the report, I was met with harsh criticism and accusations; in particular, I was accused of causing damage to the state. Despite all this, we soon managed to achieve the level of our vaccine that complied with the WHO requirements. It was very important because the Soviet Union was the largest donator of the vaccine. However, this was not the case at all the vaccine production facilities. In 1965, the WHO Expert Committee revised the 1958 requirements to the vaccine based on lessons learned and introduced a number of changes.

Unfortunately, the powerful lever as the international requirements was not sufficiently used for various reasons. It was found out later when the Center for the Vaccine Control commenced working based on the approved international requirements for the vaccine. Depressing facts were obtained during the first year of the Center's activity (1967): 70% of the supplied vaccine batches were substandard. The very fact of such control radically influenced the manufacturers and the number of substandard batches began to steadily



WORLD HEALTH ORGANIZATION
TECHNICAL REPORT SERIES
No. 180

REQUIREMENTS FOR
BIOLOGICAL SUBSTANCES

5. Requirements for Smallpox Vaccine

Report of a Study Group

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization.

WORLD HEALTH ORGANIZATION
PALAIS DES NATIONS
GENEVA
1959

Above, the title page of the first *International Requirements for Smallpox Vaccine* and *below*, the WHO Research Group that developed the first *International Requirements for Smallpox Vaccine*, Geneva, November 3–8, 1958

A meeting of the Expert Committee to revise the *International Requirements for Smallpox Vaccine*, Geneva, 1965; Chairman, F.P. Nagler (*in the center at the head of the table*), Vice Chairman, M.P. Chumakov; Secretariat: W.C. Cockburn, Director of the WHO Division of Viral Diseases, and A.S. Aushorn, Director of the Division of Biological Standardization (Secretary). A. Downey, an outstanding expert in poxviruses (*fourth to the left of the window*) and A. Benenson (*third to the left at the same side*) were also members of the Committee

decline, reaching 18% by the year of 1970. The prevalent trend at that time was switching to production of a dry thermostable vaccine. On sites, this process was slow and complicated. It was in this critical period that our country provided invaluable assistance to the eradication program by free delivery of hundreds of millions of the vaccine doses. As is mentioned, the USSR donated a total of about 1.5 billion doses to the program for the WHO and different countries under the bilateral assistance. Relevant research at the Moscow WHO Collaborating Center made it possible to eliminate an increased reactogenicity of the smallpox vaccines.

The inoculation procedure was significantly modified during the intensified eradication program stage. The bifurcated needle designed by Dr. Rubin (United States) was used for vaccination. This tool allowed vaccination to be simplified, standardized, and accelerated, saving up to 50% of used vaccine.

The activities of the WHO Collaborating Centers were most tightly connected with the needs of the eradication program in both the solving of practical problems (diagnostics) and research. It is enough to

mention that the number of diagnostic tests done at the Centers reached many thousands and in some cases their results were decisive for the on-site activities. The Centers implemented manifold research projects for the program. One of the most important results was the discovery of a previously unknown smallpox-like disease referred to as the human monkeypox at the Moscow WHO Collaborating Center. This discovery initiated a series of research projects aimed at the comprehensive study of the corresponding infection. The problem of monkeypox in humans is still a relevant issue.

The work of the Centers was highly esteemed by the WHO. One of the chapters of this book dwells on the activities of the Moscow WHO Collaborating Center.

A separate issue is the final stage of the program, namely, certification of smallpox eradication. Its goal was to provide the satisfactory evidence that smallpox did not exist on the globe anymore. As far as we know, there were no precedents of this kind with global coverage.

According to the recommendations of the WHO Expert Committee on Smallpox Eradication (1972), the duration of this period should be no less than 2 years from the last recorded smallpox case without taking into account clearly defined and controlled cases of imported infection. Only then we can speak about the actual cessation of smallpox transmission or its eradication. A 2-year period was chosen based on the field observations in different countries (Nigeria, Botswana, Indonesia, and Brazil); these data suggest that hidden infection foci can remain unknown for 10–34 weeks. Thus, the control period chosen by experts obviously overlapped these periods. Furthermore, the WHO Smallpox Eradication Unit assessed that a possibly missed smallpox outbreak that affected 100 people would in 2 years give a total of 5000 smallpox cases (assuming that each patient gives one disease case in the next generation). An event of this scale could hardly remain unnoticed by national and international health authorities for 2 years under ongoing almost universal active surveillance. The absence of smallpox cases for 2 years was a prerequisite for its eradication in any country or territory that had been endemic for smallpox.

The work on verification of smallpox absence was difficult and most important. It was performed according to the WHO methodology by the staff involved in implementation of the national program in each country. Color photographs (identification cards) of smallpox patients were widely used to attract the local population to the search for smallpox cases. The posters informed that a bonus of US $1000 (a huge sum according to the local standards) would be paid for finding any laboratory-confirmed case of smallpox. In addition, the samples from all individuals with suspicious skin lesions were taken for emergency laboratory testing at the WHO Centers.

Taking into account the exclusive responsibility of the act of declaring a country free of smallpox and possible severe consequences in the case of an error, the WHO developed and successfully used an additional control procedure—confirmation (certification) of smallpox eradication. Depending on particular conditions in individual countries (the scale, incidence, and duration of smallpox outbreaks in the past, the area of its territory, size and distribution of its population, the state of health services, the possibility of smallpox importation from neighboring countries, and some others), this system was implemented in four different versions:

- Examination of the country by International Commission;
- Report by the country on smallpox eradication submitted to the WHO followed by a control visit of a WHO representative;
- Report by the country on smallpox eradication submitted to the WHO; and
- The official statement of the government submitted to the WHO on the absence of smallpox on its territory.

The International Commissions were formed by the WHO and consisted of the experts and public health authorities from different countries (others than the certified country). During the certification period, the WHO arranged 21 International Commissions for the Certification of Smallpox Eradication in 61 countries.

Identification cards for detection of smallpox patients

A WHO poster that informs about the bonus of $1000 for finding a smallpox patient

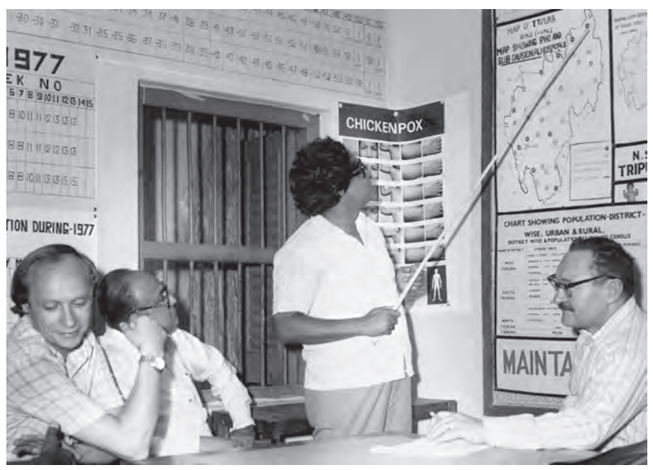
The materials collected by the participants of national programs and later by the members of International Commissions (who were assessing individual countries) were submitted for consideration to the Global Commission for the Certification of Smallpox Eradication, which prepared the report after analysis and summing up. The author of these lines (the only woman in the Commission) and one more member from the Soviet Union were among the 21 members of the Global Commission. Along with the report, the Commission developed 19 recommendations for the post-eradication era, the first of which prescribed universal cessation of smallpox vaccination. The members of the Commission also signed the declaration, which informed the world that smallpox no longer existed on the globe.

All materials of the Global Commission were considered and approved by the 33rd WHA in the May of 1980. On this occasion, the WHA made a special statement signed by the heads of delegations of the WHO Member States. Thus, the implementation of the recommendations became the roadmap for the WHO activities in the post-eradication era. Their practical implementation was entrusted to the remaining (in a reduced form) Smallpox Eradication Unit at the WHO Headquarters. In that period, the department was headed by I. Arita (1977–1985), one of the oldest participants of the Program, and later by Z. Jezek, who had been working in smallpox endemic countries for several years. For scientific advice to the department, on the recommendation of the Global Commission, the WHO Director-General in 1981 organized the Expert Committee on Orthopoxviruses, which included F. Fenner (Chairman), Marennikova (Vice-Chairman), C. Dambell (reporter), and Henderson. In 1981–1986, the Committee met in Geneva almost annually for critical evaluation of the progress in the post-eradication program and development of the activities for its further implementation.

A surveillance team interviewing local residents about the known smallpox cases, Ethiopia, 1978, Sidamo province (WHO archive)

The members of the International Commission for the Certification of Smallpox Eradication in India, April 1977; *from left to right in the first row*: Dr. G. Flamm, Dr. J. Cervenka, Dr. V.A.B. de Silva, Lieutenant General R.S. Hoop, Dr. F. Fenner, Dr. Jan Kostrzewski, Dr. V.T.G. Gunaratne, Dr. D.M. Mackay, Dr. A.M. Mustakil Haq, Dr. R. Roashan, Prof. V.M. Zhdanov, and Dr. Zein Nyunt; *in the second row*: Dr. W. Koinange-Karuga, Dr. N.B. Lundbeck, Dr. Kitamura, Dr. D. Senser, and Dr. M.F. Polak

V.M. Zhdanov (*sixth from the left*), a member of the International Commission, and V.G. Fedenev (*second row in the center*), a program staff member and the coordinator of smallpox eradication activities in the Northeastern States of India, with a group of national epidemiologists in the State of Assam, India (spring 1977)

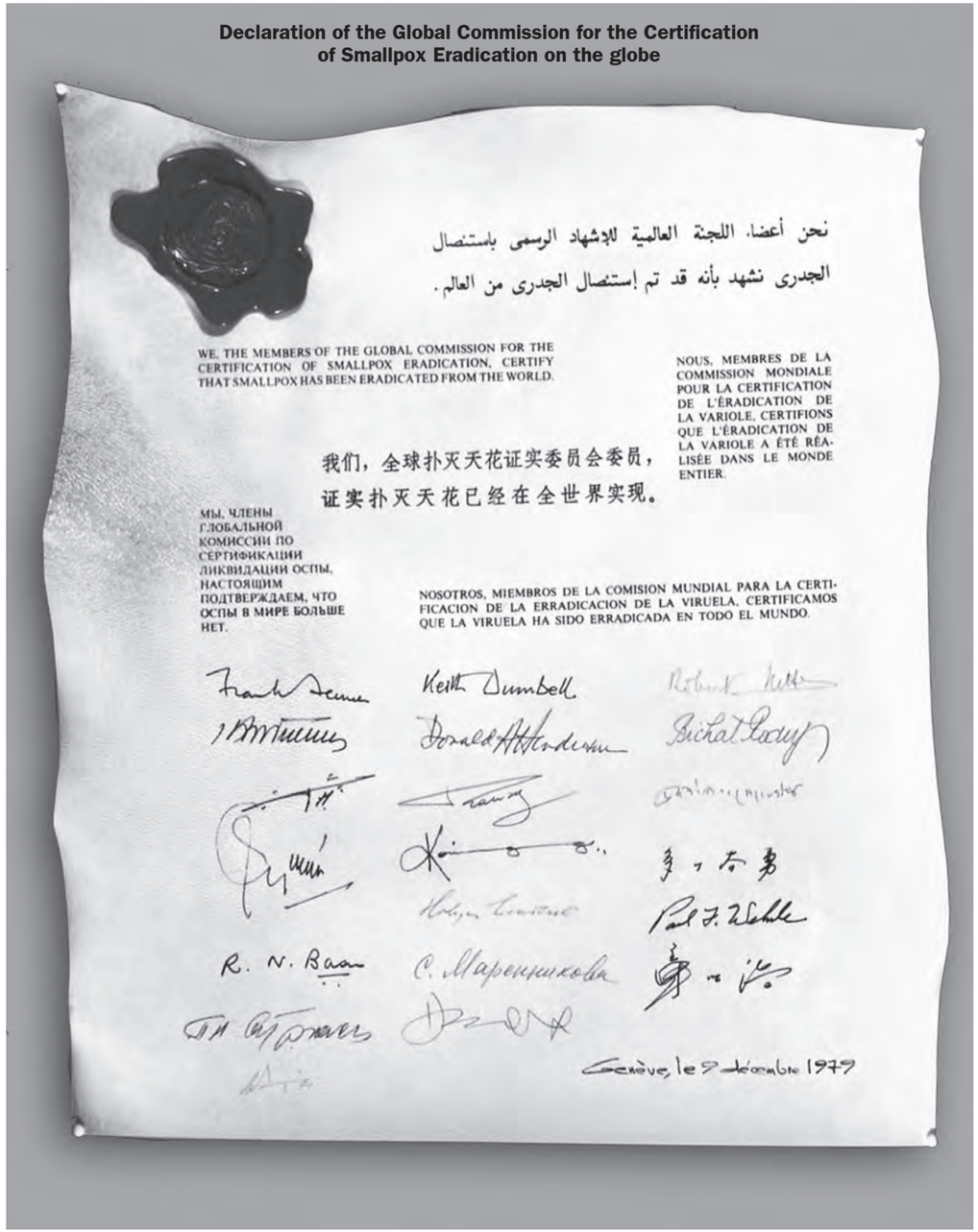


V.M. Zhdanov and V.G. Fedenev in the Primary Health Care Center in a rural area of the State of Tripura after reading the documentation

Now, after 30 years, we can say with satisfaction that almost all recommendations of the Global Commission have been implemented and some of them, intended for a long period, are still implemented. With regard to the certification principles developed by the WHO, they fully have justified themselves and are used in several other major programs.

Without any exaggeration, we can say that the significance of the Smallpox Eradication Program is really enormous. It was an epoch-making milestone in the history of humanity that with joint efforts succeeded in the total eradication of an infectious disease on a global scale. The victory over smallpox served as a powerful stimulus for activation of the control of other infections by overcoming passivity and self-doubt that arose after the failure of the first Global Malaria Eradication Program. The contribution of the Smallpox Eradication Program to the global health can hardly be assessed only by savings as was done in the early years after its completion. However, the figures are impressive: according to Dr. Arita's estimate, with the cost of the Program of 300 million dollars from 1967 to 1980, the annual savings in 1981 made up 1 billion dollars. Undoubtedly, the saving of human lives is more important, as is mentioned above. There are no longer post-vaccination complications, importation of smallpox, and so on.

Members of the Global Commission for the Certification of Smallpox Eradication (December 1979).
From left to right in the first row: S.S. Marennikova (Soviet Union), J. Azurin (Philippines), P.N. Burgasov (Soviet Union), F. Fenner (Australia, Chairman), J. Kostrzewski (Poland, Vice-Chairman), D.A. Henderson (United States), W. Koinange (Kenya), and Zhang Uvayhao (China); *in the second row*: P.F. Werle (United States, reporter), R.N. Basu (India), J.M. Aashi (Saudi Arabia), N.B. Lundbeck (Sweden), B.A. Rodrigues (Brazil), C.R. Dambell (United Kingdom), R. Netter (France), I. Tagaya (Japan), J.S. Moeti (Botswana), Kalisa Ruti (Zaire), P.N. Shrestha (Nepal), and A. Deria (Somalia)



Declaration of the Global Commission for the Certification of Smallpox Eradication on the globe

نحن أعضاء اللجنة العالمية للإشهاد الرسمى باستئصال
الجدرى نشهد بأنه قد تم إستئصال الجدرى من العالم.

WE, THE MEMBERS OF THE GLOBAL COMMISSION FOR THE CERTIFICATION OF SMALLPOX ERADICATION, CERTIFY THAT SMALLPOX HAS BEEN ERADICATED FROM THE WORLD.

NOUS, MEMBRES DE LA COMMISSION MONDIALE POUR LA CERTIFICATION DE L'ÉRADICATION DE LA VARIOLE, CERTIFIONS QUE L'ÉRADICATION DE LA VARIOLE A ÉTÉ RÉALISÉE DANS LE MONDE ENTIER.

我们，全球扑灭天花证实委员会委员，
证实扑灭天花已经在全世界实现。

МЫ, ЧЛЕНЫ ГЛОБАЛЬНОЙ КОМИССИИ ПО СЕРТИФИКАЦИИ ЛИКВИДАЦИИ ОСПЫ, НАСТОЯЩИМ ПОДТВЕРЖДАЕМ, ЧТО ОСПЫ В МИРЕ БОЛЬШЕ НЕТ.

NOSOTROS, MIEMBROS DE LA COMISION MUNDIAL PARA LA CERTIFICACION DE LA ERRADICACION DE LA VIRUELA, CERTIFICAMOS QUE LA VIRUELA HA SIDO ERRADICADA EN TODO EL MUNDO.

Genève, le 9 décembre 1979

B.V. Petrovsky, the head of the Soviet delegation and USSR Minister of Health, is signing the statement of the 33rd World Health Assembly on the complete eradication of smallpox from the world

According to many experts, the most important lessons of the Smallpox Eradication Program are that (1) the countries of our planet can work together and achieve a common goal despite any national, religious, and political differences and economic conditions and (2) this activity must be based on scientific research, which ensures efficient implementation of any project. The other lessons include the correct definition of goals and objectives, a clear structuring of the program, and professional management. Of course, all this works in full with the political support.

Implementation of the Smallpox Eradication Program drew an increased interest to vaccine prevention of infectious diseases and activated immunization practices. The interest in the development of new vaccines has significantly increased. One of the most efficient projects, later named the Expanded Program on Immunization (EPI), actually originated in the depths of the Smallpox Eradication Program in the early 1970s and is its direct legacy. For instance, simultaneous vaccination against smallpox and measles was started in West Africa. In Nepal and Uganda, co-immunization with smallpox vaccine and BCG became a common practice. By 1977, the EPI was endorsed by the WHO. At that time, the WHO took into account the negative experience of the initial period in the Smallpox Eradication Program: a coordinating center was immediately formed at the WHO Headquarters; and the staff and funds were allocated. The Program was and is most successfully implemented in the countries of the Western Hemisphere. It was based on a set of measures and structures borrowed from the Smallpox Eradication Program. The campaign that lasted several years led to that the last endemic polio case was reported in 1991. The attack on measles was resumed in 1996, when 240 000 cases were annually recorded. The endemic measles transmission stopped by the year of 2002. Now the Americas are free of endemic polio and measles. The new object is rubella.

We refer to these data to illustrate how it is possible to eradicate at least some socially important infectious diseases in a vast albeit a limited area with correct and good organization at a relatively low cost. The progress in combating these infections is achieved not only in the countries of the Western Hemisphere.

Celebrating the victory over smallpox, we must bear in mind the fact that the virus under certain conditions can come back to the human population. This could be, first and foremost, in the case of bioterrorism. It is supposed that in addition to the two official repositories of the smallpox (variola) virus at the WHO Collaborating Centers in Atlanta and Novosibirsk (where the former Moscow Center was transferred), the virus can be in the hands of certain terrorist organizations and/or be kept illegally in some countries. Despite the absence of direct evidence, it cannot be also ruled out that bodies of people who died of smallpox buried in the permafrost could become the source of the virus during natural disasters (for example, global warming). It is also possible that the variola virus-containing material can be occasionally stored in freezers of some lab. Obviously, bioterrorist attacks are most dangerous and real variants of the variola virus return. According to the Dark Winter senior-level bioterrorist attack simulation, one smallpox outbreak caused by a terrorist attack can lead to the death of about million people until the end of the fourth transmission generation.

Taking this into account, we should be prepared for such scenario. Further work is necessary to create new generation smallpox vaccines that combine high immunogenicity with complete safety. The development of highly efficient drugs for smallpox chemoprevention and chemotherapy is equally important. In particular, the need for such vaccines and chemotherapeutics is determined by the fact that the population immunity has actually been lost after 30 years since the total cessation of anti-smallpox vaccination, so that most people have never been vaccinated against this infection. As is known, this latter category is subject to significant risk of post-vaccination complications. Such situation took place in 2003 in the United States when it was decided to vaccinate employees of health services who in the corresponding cases would have to contact the sources of infection. The launched campaign covering about 350 000–500 000 people was stopped in about 3–4 months because of a large number of post-vaccination complications.

In contrast to the situation abroad where dozens of centers and research teams are working on this issue, very little is currently done in this country. Obviously, the above mentioned developments should be the most important part of a whole package of measures aimed at countering bacteriological attacks.

In addition to the above discussed, we cannot ignore the newly emerging hypotheses based on a comparative genetic analysis of the orthopoxviruses pathogenic for humans. According to these hypotheses, the causative agent of smallpox, which is strictly anthroponotic and highly pathogenic for humans, is the result of a long evolutionary transformation of an ancestral orthopoxvirus that had a wide host range, humans included (Prof. Shchelkunov).

Whatever our attitude to these assumptions is, we cannot afford to neglect the currently existing orthopoxviruses pathogenic for a wide range of animals as well as humans. Therefore, this hypothesis must be another incentive to arrange regular monitoring and investigation of the outbreaks of zoonotic orthopoxvirus infections, such as vaccinia-like diseases in humans and animals (recurring in Brazil and India) and the infections caused by cowpox virus in Russia and European countries. Particular attention should be paid to monitoring of the diseases associated with human monkeypox infections. It is this disease that has dramatically changed in Central Africa over the past decade and a half: the number of reported cases increased 20-fold and the rate of human-to-human transmission sharply elevated as compared with the infection from the natural carrier of the virus.

This disturbing dynamics is mainly related to a decrease in population immunity that results from the cessation of vaccination. Presumably, this factor is not the only cause of these changes. Indeed, no significant growth in the incidence of monkeypox is reported for another region, West Africa, which

is endemic for smallpox and where smallpox vaccination was also stopped. Perhaps, the WHO in this situation should revisit the purposefulness of vaccination in the foci of human monkeypox outbreaks. It would also be important to periodically study the genetic structure and biological properties of fresh isolates of this virus for timely grasping possible dangerous trends in its evolution.

In conclusion, it seems appropriate to quote the words of the former Manager of the Smallpox Eradication Program, Dr. Henderson that “Smallpox cannot be forgotten nor ignored”.

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Some International and Political Aspects of Smallpox Eradication Program

D. D. Venediktov

Dmitry D. Venediktov,
a corresponding member of the Russian Academy of Medical Sciences and doctor of medical sciences; Deputy Minister of Health of the USSR during implementation of the Smallpox Eradication Program; and member of the WHO Executive Committee. He supervised the assistance of the Soviet Union to the eradication program and actively contributed to the radical strengthening and support of the program by the WHO Headquarters

In 2010, the 30th anniversary of the worldwide elimination of one of the most severe and dangerous epidemic diseases, smallpox, was celebrated. This became the most important event in the long history of medicine from Aesculapius and Hippocrates to the sociomedical problems of the 20th century and new challenges of the third millennium.

The Smallpox Eradication Program has many dimensions. First, this is one of the greatest achievements in science, practical medicine, and systemic social activity. On the other hand, this is an experience of the international political cooperation between most different countries and, in particular, two rival superpowers of the 20th century—the United States and Soviet Union, in the frame of the international organization, United Nations. It is interesting to dwell on some aspects of this competition–cooperation. To a certain degree, I was lucky to participate in the discussion of preparation and progress of this program and to be acquainted with its direct participants, experts from all over the world.

The history of the Smallpox Eradication Program was far from simple. The initial WHO interests were focused on another disease, malaria, with over 700 million people suffering from it in the 1930s–1940s and over 3 million of lethal cases annually. Only a regular use of DDT (by the end of the World War II) and other residual insecticides to control mosquitoes, the vectors of the disease, malaria morbidity and mortality started to sharply decline in many countries. In June 1948, the first World Health Assembly (WHA) has already drawn attention to this fact; this gave the hope to malaria experts, above all in the United States and several Latin American countries, to eliminate malaria in Americas. In 1950, the Pan American Sanitary Conference supported this challenge, which was later approved by the 8th WHA (1955) after an enthusiastic presentation of Dr. M.G. Candau (Brazil), the WHO Director-General, which provided funding and wide terms of reference to Dr. Candau for the international antimalaria campaign.

However, the reaction of the European countries, still retaining at that time their colonies in Africa and Asia, was more reserved, while the Soviet Union (one of the WHO founders) did not participate in the WHO activities in 1948–1957 and could not significantly influence the formed concept and methodology of the Global Malaria Eradication Campaign. When the Soviet Union resumed its active membership in the WHO, the WHO authorities and delegates of the United States asked the Soviet Union to support the antimalaria program.

This issue was considered by S.V. Kurashov, the Minister of Public Health of the USSR and V.M. Zhdanov, the Chief Sanitary Inspector, with participation of prominent Soviet specialists in malariology (P.G. Sergiev, Sh.D. Moshkovsky, G.M. Maruashvili, and others) taking into account the arduous long-term experience of this country in integrated control of malaria, with the climate and other environmental conditions influencing the mosquito propagation and specific features of malaria spreading considerably differing from the tropical countries of Latin America, Asia, or Africa. The experts criticized methodological and organizational inconsistence of the American experts on the Global Malaria Eradication Program, underestimation of all links of the epidemiological process, excessive hopes for DDT in the absence of integration of the malaria eradication service with general medical network, and so on. The decision was to abstain from an active support of the Malaria Eradication Program. (Note that nobody knew at that time that mosquitoes can develop resistance to DDT and other insecticides as well as that DDT is so stable in environment that it is even detectable in the in penguins in Antarctic.) However, Zhdanov suggested submitting to the WHO the program for global smallpox eradication as the infection best "fitting" to its worldwide eradication. This was justified by several factors:

- Smallpox spreads by transmission of the virus from sick to healthy nonimmune individuals;
- Its natural reservoir is putatively absent among animals;
- The disease is relatively simply detectable at its early stages thanks to characteristic skin lesions;
- The vaccine that provides full immunity for 4–5 years after a single inoculation is available; moreover, the revaccination induces even higher and more prolonged immunity; and
- Finally, the available positive experience of smallpox eradication in the Soviet Union and some other countries (in this country, smallpox was eradicated by 1936 because of the obligatory vaccination campaign according to the decree of the Russian Federation *On the Obligatory Smallpox Vaccination* of April 10, 1919.)

In 1958, Zhdanov presented this proposal on behalf of the Soviet delegation at the 11th WHA. The approved resolution on this asserted that the worldwide smallpox eradication was timely; the WHO Director-General proposed to examine the financial, administrative, and technical consequences of the program aimed at smallpox eradication and to report the results of this analysis to the Executive Committee. This had to include the measures for promotion of production of the required number of full-fledged smallpox vaccine tolerant to temperature, suitable for long-term storage and use in tropical and subtropical areas, in national laboratories and institutes; training of vaccinators of the local population in the countries to be subject to mass immunization against smallpox; development of safety measures to address the possible complications of smallpox vaccination; and several other issues.

The USSR proposal was supported by the statement on free allocation of 25 million doses of smallpox vaccine to the WHO. In June 1958, the WHO Executive Committee expressed gratitude for this gift to the Governments of the USSR and Cuba (which also provided 2 million doses) and decided to further (in 1960) open a special account for financial and material donations to fund the smallpox eradication.

Despite the official announcement of the Global Smallpox Eradication Program, the attitude to it within the WHO was for several years rather ambivalent. This was associated with the ongoing priority support for the antimalaria program by the United States as well as with that the WHO Director-General, Dr. Candau, personally did not believe that smallpox eradication could be feasible. An additional important factor was the competition between the United States and other western countries versus the socialist countries with

the Soviet Union as the leader, on many issues, in particular in the organization of healthcare systems. As a result, the issues of malaria and smallpox were considered almost at every WHA and the WHO Executive Committee meetings; if one of the countries "forgot" the corresponding topic or insufficiently clearly formulated the relevant resolution, this error was "corrected" by either American or Soviet parties. In this process, the United States pumped mainly money into the malaria program, whereas the Soviet Union, with its deficiency in currency and high-level production of vaccines and sera, helped many developing countries (first and foremost, India) on a bilateral basis by supplying the smallpox vaccine and sending advisers to combat smallpox and other infectious diseases.

American delegates and officers of the Secretariat attentively supervised the malaria program: the Malaria Eradication Unit at the WHO Headquarters was one of the strongest, and the funding for this Program from the WHO and UNICEF was significant. As for the Soviet representatives, they did their best so that smallpox would not be forgotten (note that only one officer was involved in the smallpox program in Geneva and four additional specialists did the field work).

It became ever clearer that the ambitious program, such as global smallpox eradication, could not effectively run with funding from random sources and donations. The program needed stable regular funding from the WHO budget. The organization of special coordinating and guiding unit with the WHO Headquarters was equally necessary. These issues were raised in the speech of S.S. Marennikova, a member of the Soviet delegation, as early as 1962 at the 15th WHA.

As time went on, a successful completion of the malaria eradication program became ever more doubtful despite huge funding by the WHO and UNICEF, to say nothing of the high costs of technical assistance and expenditures of the countries themselves. By the year of 1959, the number of malaria cases in the world decreased to 140 million and of the lethal outcomes, to 980 000. However, most countries in Asia and the Americas, which conducted the malaria eradication campaign according the WHO principles, did not reach the expected results, while the spending of the WHO and other international antimalaria institutions increased almost eightfold (from 2 to 16 million dollars) and much more money was further necessary. The situation did not improve when all funding for malaria eradication was included in the WHO regular budget. This made the WHO to refer to the Soviet experience, think over the integration of malaria eradication services with general medical network, and to use mass medical chemotherapy and other mass practices under difficult epidemic conditions. In 1962, special training in malariology was organized in Moscow for WHO specialists and developing countries. Research was activated in the WHO as well as training of specialists for different countries as advisers on malaria (in 1966, their number reached 435). In the mid-1960s, the initial successes of malaria program in India, Pakistan, Sri Lanka, Laos, Thailand, Brazil, and other countries were erased by repeated outbreaks of malaria; moreover, any antimalaria activities were

The reception organized by the Soviet delegation, 15th World Health Assembly, 1962. S.V. Kurashov, head of the delegation, meets guests. *Left to right,* Mr. P. Coul, assistant to the WHO Director-General; S.V. Kurashov, Minister of Health of the USSR and Chairman at the 15th WHA; and delegates S.S. Marennikova and D.D. Venediktov

actually not started at all in the particularly endemic areas of Africa. In 1966, Prof. Sergiev in his speech at the 19th WHA on awarding him the International Prize and Darling Medal emphasized that "…we from the very beginning did not agree that malaria could be defeated using … DDT alone. The experience of our country has clearly demonstrated how insidious is this disease and how complex are sometimes epidemiological conditions; thus, … we cannot merely rely on DDT. Treatment of patients as the source of infection for mosquitoes is a task no less important."

As a result, malaria eradication campaign finally lost its prospect and no one even could predict the date for its completion; finally, the United States fully realized the failure of the malaria program and decided to change the vector and support smallpox program. This was stated by President L.B. Johnson at the UN anniversary meeting in San Francisco. Winds have changed in the WHO, while UNICEF considerably reduced its contribution to the antimalaria efforts. In May 1967, the 20th WHA adopted the resolution on revision of the global strategy for malaria eradication, although it actually consisted in replacing the word "liquidation" with the word "fight" against malaria. The program was continued by inertia. In 1968, the number of malaria-free areas did not increase but rather markedly decreased; moreover, the most dramatic return of malaria was observed in the countries that seemed to have achieved the greatest success in its elimination.

It was only in May 1974, when H. Mahler, the new WHO Director-General (who succeeded Dr. Candau, the Director-General for almost two decades), in his speech at the 27th WHA said that a high prevalence of malaria in many countries "gives rise to concern"; that "the program has lost prestige"; that international and bilateral agencies and a number of governments "have drastically reduced or interrupted funding of antimalaria activities"; and, finally, that "… we cannot even expect more progress". Then the WHO Executive Committee established the ad hoc Working Group on malaria, comprehensively considered the antimalaria programs in all regions, and recognized their prospects as highly uncertain. The 29th WHA had to accept this in 1976.

On the other hand, the international effort against smallpox despite all difficulties was gradually gaining support in many countries. Finally, when the United States changed its position and declared their readiness to support smallpox eradication, the program was revisited. In May 1965, the WHA adopted a resolution that stated the worldwide smallpox eradication as one of the most important goals of the WHO; according to the assessment of the Director-General, the smallpox could be eradicated in 10 years, which would require international funding of 23.5–31 million dollars in addition to the amounts that the smallpox endemic countries could allocate. The resolution highlighted the need to ensure extensive use of freeze-dried smallpox vaccine (up to 50 million doses annually) and the involvement of basic health services in implementation of the program in order to use them in the control of other infectious diseases. The smallpox eradication unit was organized with the WHO Headquarters in Geneva and D.A. Henderson, an American specialist, was invited to its leader position; Henderson was not an expert in smallpox and encountered with smallpox cases only during an outbreak in Argentina but was known as a very efficient manager. The USSR Ministry of Health even got worried that Americans just want to seize the initiative in this program. For its part, the American delegates and Dr. Candau himself insisted that Henderson was a good specialist obsessed with the idea to "kill the smallpox". After the personal acquaintance with Henderson, the USSR Ministry of Health decided to accept his appointment (and did not regret). Only many years later, Henderson revealed the background of his appointment. According to his memoirs Dr. Candau was an ardent enthusiast of the Malaria Eradication Program and believed the smallpox eradication unfeasible. When the United States representatives joined the Soviet Union demands to strengthen the smallpox eradication program, they asked the WHO general director to prepare appropriate suggestions in 1965, Dr. Candau "accomplished" this mission by proposing to increase the WHO budget for 1967 to 2.4 million dollars (by more than 16%), perhaps, hoping that the draft budget would not be accepted. The vote was tough: the budget was approved by only two votes (60 with 58 necessary). Dr. Candau demanded that the

United States put forward its own candidate for the head of the smallpox program so that the United States would be blamed in the case of failure (Dr. Candau did not doubt) rather than the WHO authorities. Two failing programs (malaria and smallpox) would be too much for the WHO (!).

A year later, the 19th WHA (May 1966) approved the funding of the Smallpox Eradication Program from the WHO budget. The WHO funding intended for assistance to developing countries in implementation of national smallpox eradication programs was correspondingly increased. The delegation of the Soviet Union congratulated the WHO on this decision and asserted the participation of the Soviet Union in the control of the Smallpox Eradication Program.

The working mutual understanding was achieved with Henderson, who headed the smallpox eradication unit at the WHO Headquarters and the program implementation intensified. Joint efforts of many professionals, including Soviet scientists (S.S. Marennikova, I.D. Ladnyi, G.P. Nikolaevskii, O.G. Andzhaparidze, A.N. Slepushkin, and others) resulted in the plan for particular antismallpox activities and research. New efficient methods for smallpox vaccination, namely, using bifurcation needles and needle-free injectors, were proposed and vaccine supply for the program was ensured. At that time, no other country except for the Soviet Union could produce more than 1–2 million doses of smallpox vaccine per year, whereas this country annually manufactured over 25 million doses; this annual contribution eventually accounted for over 80% of vaccine donated through the WHO.

Nearly 98 million dollars (in currency and material transfers) was spent for the international assistance to the Smallpox Eradication Program in 1967–1980; one-third was delivered through the WHO and other UN agencies and two-thirds were donated by individual countries, with the Soviet Union, United States, and Sweden as the major contributors. The first regional Reference Center for Smallpox (later, the WHO Collaborating Center) was organized in the Soviet Union. Soviet specialists were ever more actively involved in the work at the WHO Headquarters, as well as in the field projects in Africa, Southeast Asia, and other parts of the world.

The intensification of the Program actually started in 1967. By that time, smallpox foci remained in 30 countries and the number of smallpox cases reached 2.5 million worldwide. During the 5 years of intensive work (to 1972), the number of endemic countries was reduced to seven and the smallpox incidence, to 150 000 cases. The WHO recommended using only thermostable freeze-dried vaccine in endemic countries, organizing epidemiological surveillance services, and intensifying the research program. However, 12 imported smallpox outbreaks were recorded in 1964–1973 in Europe and 283 individuals were infected. The largest smallpox outbreaks were in the United Kingdom in 1966 (71 cases) and Yugoslavia in 1972 (175 cases).

The changes in the WHO leadership influenced the development of the program. The USSR representatives, paying tribute to Dr. Candau personally and his work as the WHO Director-General, nevertheless, were openly against his reelection for another 5-year term. As for the delegates from the United States, United Kingdom, and several other countries, they gradually agreed. In 1973, H. Mahler (Denmark) was elected the Director-General. The Smallpox Eradication Program gained a new motivation. An efficient system for detection of smallpox cases was introduced and the virus identification was organized at the WHO Collaborating Centers. The immunization coverage of population and vaccine quality were monitored on a regular basis. Rapid communication between the WHO Headquarters and field workers was undoubtedly provided by Henderson and his staff, including many Soviet specialists (Ladnyi, Khodakevich, Slepushkin, G.D. Suleimanov, and others). As a result, smallpox was eradicated from Latin America (1971) and significantly declined in other regions. In 1974–1975, the smallpox eradication campaign entered its final phase in the remaining endemic smallpox countries (India, Ethiopia, Pakistan, and Bangladesh).

It was high time to think about the future when it would be possible to stop the obligatory smallpox vaccination of population and about the consequences of assumed situation if some smallpox foci would

appear in nature. In addition, it should be born in mind that smallpox was regarded as one of the likely candidates for biological weapons in the discussion of the prohibition of biological (bacteriological) and chemical weapons in 1967–1970 (WHA Resolutions 20.54, 22.58, 23.53).

When discussing these issues at the 27th WHA in 1975, the importance of systematic vaccinations of population during the final stages of smallpox eradication was emphasized. It was also decided to summarize the results of the overall smallpox campaign in a fundamental treatise prepared by scientists and practitioners from different countries in order to analyze and thereby save for the humanity the unique historical experience of eradication of one of the most dangerous infections as a result of efficient international cooperation, which will surely be used in the programs against other infections. (The monograph *Smallpox and Its Eradication*, most comprehensive and profound in its content, was issued by the WHO in 1988.)

By the end of 1975, the Asian continent was declared free from smallpox and 2 years later, the disease was eradicated from Africa. The intensive search for new smallpox cases in different countries (with a cash reward for identifying new cases) demonstrated that this infection was no longer there. In 1979, the Global Commission for the Certification of Smallpox Eradication in the world confirmed the full elimination of smallpox. The certificate was signed by P.N. Burgasov and S.S. Marennikova from the USSR. The 33rd WHA in 1980 officially announced that smallpox was eradicated from the world.

The humanity entered a new smallpox-free era. However, bearing in mind that the first smallpox vaccine was made of vaccinia virus and that according to E.N. Pavlovskii concept on the natural foci of disease, no ecological niche remains free, the researchers continued their search for other potential natural niches housing variola virus. Their attention was attracted by the so-called “monkeypox” recorded in some countries in Africa (Zaire, Liberia, Nigeria, Sierra Leone, etc.). Monkeypox virus was shown to be similar to variola virus in its biological and antigenic properties; thus, the activation of monkeypox virus and its penetration to the human population after the cessation of vaccination against smallpox cannot be excluded. The more so since a human-to-human transmission of monkeypox virus is recorded. Thus, it was inferred that a long-term monitoring was necessary in combination with the WHO epidemiological surveillance of the cases complicated with fever and rash, especially, in tropical countries.

Later, the problem of the storage or destruction of variola virus laboratory stocks became relevant. The number of laboratories keeping live variola virus gradually decreased to two facilities, one in the United States and the other in Russia. Variola virus is still retained in these two specially protected laboratories, namely, the State Research Center of Virology and Biotechnology Vector (Koltsovo, Novosibirsk oblast, Russian Federation) and Centers for Disease Control and Prevention (Atlanta, Georgia, United States). Any studies with variola virus are under stringent control of the WHO ad hoc Advisory Committee, established according to the WHA resolution 52.10 (Proceeding of the 117th session of the WHO Executive Committee, January 2006). The relevant results are on a regular basis reported to the WHO Executive committee and WHA.

Another problem is the risk of possible illegal retention of variola virus as a biological weapons agent, especially with the current international threats of biological terrorism. The danger consists in that the world population now has not been vaccinated for at least 30 years and those born after the year of 1980 have no immunity to smallpox. In this situation, in the case the virus (or other biological or toxic agents) is used as a biological weapon, the number of infected persons in any big city may reach several hundred thousand with a 25–30% mortality rate.

In conclusion, a few words about the results and lessons of the smallpox eradication campaign. What it taught us and what we (the world) as if “have forgotten”.

Recently, some scientists proposed to resume the vaccination against smallpox; this is the issue that requires careful study and discussion. The smallpox vaccines used in the global eradication of smallpox and currently available in the world cause a high rate of adverse reactions, so that administration of such

vaccines could be justified only to the individuals facing a real risk of infection. However, the resumption of mass vaccination is reasonable in the case new generation vaccines, efficient but not reactogenic, are developed.

Henderson named one of his papers on the results and lessons of smallpox eradication from the world “Smallpox eradication—a cold war victory” (*World Health Forum*, 1998, no. 19, pp. 113–119). Eloquently, but this is the victory that all won and this is the main point. This is a lesson that says that we can solve all global problems relying on scientifically justified and joint systemic efforts.

The sphere of life and health care of the current and future generations encounters many such problems. Other WHO programs, such as polio eradication as a mass disease, experience in the tuberculosis control, and even anti-malaria, to which we returned on a basically new methodological, social, and political level, have clearly shown this. This also refers to the issue of violence in any of its forms, recently ascribed by the WHO to the universal (global) problems.

A monument was erected on the grounds of the WHO Headquarters in Geneva (Switzerland) to commemorate the 30th anniversary of the victory over smallpox and acknowledge the efforts of the program initiators and participants; this is a look into the future at the same time. All those who participated in the eradication program should be proud, while those who did not participate in it, should not be pity since there is still a lot of problems and challenges.

Moscow WHO Collaborating Center for Smallpox and Related Infections: Its History and Activities

S. S. Marennikova

The heads of the Smallpox Eradication Program during the overall period of its implementation constantly emphasized the significance of scientific research and regarded it as an integral part of the program. In particular, Dr. Isao Arita, who headed the program for several years, highly esteemed the role of scientific developments in the large projects, such as the Smallpox Eradication Program. The WHO Collaborating Centers—two major centers in Moscow and Atlanta, GA; the Center for Vaccine Control in Bilthoven; and several additional centers in the United Kingdom, Japan, and some other countries—formed the solid scientific backbone for the program.

The first of them, the Moscow Collaborating Center, was organized at the end of 1966 at the facilities of the Laboratory of Smallpox Prevention with the Institute for Viral Preparations of the USSR Ministry of Public Health. I had the opportunity to head this center for over 25 years during the implementation of the Smallpox Eradication Program and in the post-eradication period. It is fair to point that this team, residing in one of the oldest USSR institutes involved in microbiological research—Mechnikov Institute of Vaccines and Sera, actually started to work as early as 1953 with the newly organized Laboratory of Smallpox Vaccine. There, the laboratory resided in a cozy one-storied building, constructed over a century ago for the Moscow Pasteur Station. A portrait of Pasteur signed by him remained there since that time.

A group of recent graduates of medical institutes came to work there and started to energetically gain the knowledge in medical virology, the area new for them. At that time, I was a young candidate of science, and a laboratory to head was my first experience in guiding a research team and be responsible for its activities.

The initial team comprised Z.I. Ogorodnikova, E.M. Shelukhina, and E.B. Gurvich; M.A. Yumasheva

The very first team of the newly organized Laboratory of Smallpox Vaccine with the Mechnikov Institute of Vaccines and Sera (Moscow), 1956. *In the center*, S.S. Marennikova, head of the laboratory; *to the left*, Z.I. Ogorodnikova and *to the right*, E.M. Akatova-Shelukhina, researchers

and N.N. Mal'tseva came later. Eventually, Shelukhina, Mal'tseva, and Gurvich became doctors of medical sciences, while Ogorodnikova and Yumasheva became candidates of medical sciences. My colleagues and I always warmly remembered the staff of the Mechnikov Institute starting from its director, A.P. Muzychenko, who welcomed our young team and did his best to provide comfortable conditions for our research and work. There we were in the most favorable atmosphere.

Over a relatively short period, we succeeded in developing the technology for manufacturing the product quite new in this country—freeze-dried chick-embryo smallpox vaccine—and produced its pilot batches. The accumulated experience was summarized in my monograph titled *The Smallpox Ovovaccine* (1958). This vaccine differed from the traditional variant by that the chorioallantoic membrane of developing chick embryos was used as the substrate for virus cultivation. The advantage of this new vaccine was the absence of any bacterial flora, which was always present in the traditional preparation. My earlier work at the Tarasevich State Institute for Standardization and Control of Biomedical Preparation with Academician of the USSR Academy of Medical Sciences V.D. Solov'ev, whom I regard as my first teacher, gave me the experience that enhanced solution of several problems associated with the chick-embryo vaccine production and control. Soon the range of activities of our lab started to gradually change. In 1955, the USSR Ministry of Health sent me to the Surkhan-Dar'ya oblast (Uzbek Soviet Socialist Republic), where a putative imported smallpox outbreak was reported. The goal of my work there was to clarify the etiology of this outbreak and assist in its liquidation. This infection actually appeared to be smallpox according to a distinct clinical picture of the infected people.

Omitting the activities on liquidation of this outbreak, I cannot but tell that the outward appearance of these smallpox patients impressed me strongly. I encountered the suffering of these people and different forms of this disease, including the most severe variants (variola vera plana, late hemorrhagic, and confluent forms). The shock was so strong that I decided to get the insight into this problem. During my work there, I collected numerous and manifold specimens for variola virus isolation and brought them to my lab.

When I started to consult the literature, I was really amazed to find that the domestic scientific publications lacked any paper on the properties of variola virus and its isolation in a pure culture, while the available methods of smallpox laboratory diagnosis were hopelessly outdated. Thus, we had to become a kind of pathfinders in this country in this area. To process and analyze the specimens from Uzbekistan, we arranged an isolated facility by reconstructing the former shower room with an air-lock and by isolating it from the general ventilation system. All technical manipulations (preparation of glassware, materials, and tools as well as all procedures associated with deactivation of the infected object) were done by Anna G. Gladkikh, now deceased. She was fanatically committed and alone performed a colossal volume of work with amazing accuracy and responsibility. Working with such perfect assistant in our small and primitive facility, I succeeded in isolating no less than a dozen variola virus strains and comprehensively examined them together with my colleagues.

Working at the Laboratory of Smallpox Vaccine (*to the right*, S.S. Marennikova) with technical assistant

A year later, I had to work with another imported smallpox outbreak, this time in the Samarkand oblast, Uzbekistan. The specimens sampled there were also carefully examined; the variola virus strains isolated from the patients completely coincided in their characteristics with the earlier recovered isolates. These results were obtained using for the first time in this country the variola virus isolation and cultivation on chick embryos and in cell culture. Our data (published in 1956 and 1959) on the isolation and cultivation of variola virus in developing chick embryos and cell culture formed the background for introduction of newer and more accurate methods for smallpox diagnosis and control of the vaccine specific activity. The advantages of these methods and their significance were soon fairly estimated when eliminating the imported smallpox outbreak in Moscow in 1960. As for the cell culture, these studies were further continued and expanded (after our first publication in 1958).

A.G. Gladkikh, my top-class laboratory assistant and preparator in one

It was a lucky coincidence that we (in collaboration with the Laboratory for Immunoglobulin Production) by the same time produced antismallpox immunoglobulin from the sera of the animals hyperimmunized with vaccinia virus, which was also used during the 1960 outbreak in Moscow for treating ill individuals and preventing the infection in contacts. The results of this work were published in the *Bulletin of the World Health Organization* in 1962. Later, the antismallpox immunoglobulin was produced from the sera of the human cases recently vaccinated against smallpox; this immunoglobulin was actively used in the treatment of post-vaccination complications, including post-vaccination encephalitides. The observations demonstrated that its administration in many cases had a considerable therapeutic effect and radically treated individual patients.

Since 1957, new researchers came to work with our lab (V.A. Zuev, a postgraduate student T.I. Kaptsova, and later, in 1960, N.N. Mal'tseva), which was included into the Department of Viruses. I was proposed to head it. Prof. V.M. Zdanov was invited as a scientific advisor by the director of our institute. The erudition and recommendations of Prof. Zhdanov were of serious help and support to our work.

By the beginning of the Global Smallpox Eradication Program, the team of the lab had already a certain reputation in the area of poxvirus research. Thus, it was not unexpected when the WHO started to actively involve our lab in solving various questions. In particular, we took part in the tests of smallpox vaccines organized by the WHO and conducted in different countries. The goal of these tests was to select the international standard of this vaccine. The preparation produced by the Lister Institute (United Kingdom) was finally selected as the reference. During this period, I was invited to the WHO scientific group that developed the international requirements to smallpox vaccine (in 1965, these requirements were revisited according to the accumulated experience by the ad hoc Committee of WHO experts).

I always feel regret when recalling my first scientific group and recognizing the significance of the international recommendations that it elaborated. The point is that I failed to convince the members of this group that it was necessary to replace the fluid glycerin vaccine with the thermostable freeze-dried variant. As it was known, the vaccination campaigns in the countries with hot climate (where the necessary

equipment for vaccine storage was as a rule absent) frequently used the preparations with a poor specific activity, making these campaigns defective in terms of creating the immunity to smallpox.

This is a small addition to my reminiscences of this period. When I first came to Geneva to the WHO Headquarters, I felt rather uncertain not knowing the working conditions at this huge institution. But I was very lucky. My coach there was Prof. K.A. Vinokurov, one of the WHO authorities, our compatriot, and a wonderful personality. His constant patronage and valuable advice helped me to overcome my initial worry and fit the working climate of the scientific group. This truly intelligent personality with a high level of culture always remains in my mind. Later, I participated in the work of many scientific groups and expert committees on orthopoxviruses until the completion of the smallpox program and over two decades of the post-eradication period. However, let us return to the history of the Collaborating Center.

At the end of 1961, the overall lab was assigned to the newly organized Institute for Viral Preparations according to the order of the Ministry of Health, where we became the Laboratory of Smallpox Prevention. After this relocation, our team was supplemented with new researchers (I.A. Svet-Moldavskaya, G.R. Matsevich, K.L. Chimishkyan, and L.S. Shenkman). Here we continued our earlier studies. One of the most serious difficulties associated with the study of smallpox was the absence of its adequate experimental model. The first step in this direction was the work of our postgraduate student, T.I. Kaptsova, who developed the experimental smallpox model in white mice. Studying the age-dependent susceptibility of these animals to variola virus, Kaptsova discovered that they retained the susceptibility to this pathogen to a certain age. As it emerged, an intracerebral infection of 10-day-old mice induced a systemic infection appropriate for assessing the efficiency of chemotherapeutics as well as for solving some other problems. Later, R.A. Shafikova, our postgraduate student, created another model using more adult white mice (28–37 days old) exposed to γ-radiation and intracerebral infection.

Taking into account the recommendation of the mentioned WHO scientific group, we started a new project, namely, a comparative study of different strains used for production of smallpox vaccine in both this country and abroad. The very beginning of this work, performed by Gurvich and Ogorodnikova, demonstrated that several domestic and foreign production strains of vaccinia virus were genetically inhomogeneous and consisted of different virus clones. Considerable efforts of Mal'tseva allowed these clones to be isolated and assessed according to their biological characteristics. Some strains, which became genetically uniform after this "purification", were further used in production. This part of the work was performed in collaboration with several peripheral production facilities (in Minsk, Tashkent, and Tomsk).

In addition to research, the lab constantly assisted to practical healthcare visiting the sites with local outbreaks of smallpox-like infections among people and animals and helping in the case of severe post-vaccination complications to say nothing of imported smallpox outbreaks.

According to the order of the USSR Ministry of Health, the lab was turned into the National Center for Smallpox in 1965 and the WHO appointed it the WHO Collaborating Center on Smallpox and Related Infections in 1966 according to the agreement with the Ministry of Health. Naturally, the new terms of reference expanded the range of tasks and the volume of work.

The most important research direction, the results of which were really of a paramount importance for the eradication program, was to clarify why some smallpox vaccines displayed unacceptably high reactogenicity. As is mentioned above, the use of such preparations resulted in rejection of vaccination and caused rightful criticism of the healthcare agencies. Ten and a half smallpox vaccines manufactured in different countries were selected for these studies. Taking into account that the production conditions were different, pure chorioallantoic cultures of these production strains were obtained. Their biological characteristics were assessed under the same conditions using a wide range of parameters and different animal species, chick embryos, and cell cultures. As was shown, the tested strains considerably differed in their pathogenicity for animals. The subsequent analysis allowed these strains to be divided into three groups, namely, weakly pathogenic, moderately pathogenic, and highly pathogenic. A comparison of the

Researchers working with the Moscow WHO Collaborating Center, 1967. *Left to right*, G.R. Matsevich, T.I. Kaptsova, V.S. Brykina, E.M. Shelukhina, E.B. Gurvich, and M.A. Yumasheva; *in the center*, I.A. Svet-Moldavskaya

pathogenicity characteristics and the results of vaccination with the corresponding vaccines demonstrated the correlation between the pathogenicity of these strains for animals and the degree of severity of the vaccinal process. Thus, it was demonstrated that a high reactogenicity of vaccines resulted from specific biological features of the production strain, which, most likely, were determined by the pervious history of its cultivation. It also became evident that the reactogenicity of vaccines did not depend on the particular method of their production; thus, the quality of vaccine can be changed only by changing the production strain. This work took much time; in different periods, Mal'tseva, Chimishkyan, V.V. Fedorov, Shelukhina, and Shenkman participated in this study. In particular, Shenkman performed a large and complex study to compare the patterns of the vaccinal process developed in rabbits after epicutaneous infection with different vaccinia virus strains. Moreover, the dynamics of virus accumulation in the skin, lymph nodes, blood, and internal organs were monitored in each animal group. The results of this work were presented at international conferences in Berlin, Zagreb, and Utrecht and reported to the WHO. They formed the basis for rejection of highly reactogenic strains and their replacement with the single recommended strain used for manufacture of the reference smallpox vaccine preparation. Our studies of the strains were awarded a Kitasato medal. Mal'tseva was the major contributor to this work.

As is known, post-vaccination complications inevitably accompany the smallpox prevention by vaccination. One of the methods to prevent these complications is a two-stage immunization, comprising inoculation of inactivated vaccine followed after a certain interval by standard live vaccine. Matsevich, who worked at the WHO Collaborating Center, in collaboration with the Karpov Physicochemical Institute designed an original variant of inactivated vaccine: the virus in this case was inactivated by the exposure to Co^{60} γ-radiation rather than the earlier used chemical inactivation. Testing demonstrated that the new type of inactivated vaccine had certain advantages, in particular, more active humoral response to vaccination. The experience in administration of the two-stage vaccination using this new inactivated preparation to the individuals with an increased risk for post-vaccination complications showed a certain effect in prevention of complications; the method was adopted by practical medicine.

When referring to the imported smallpox outbreaks of 1955–1960, I mentioned a high efficiency of our methods, new for this country, for laboratory identification of smallpox and their role in containing of the infection. In this issue, both the WHO authorities and we ourselves were well aware that the accuracy and quickness of a diagnostic test was directly associated with the efficiency of anti-epidemic efforts, the more so for the Global Smallpox Eradication Program. Correspondingly, the development of the new methods for laboratory diagnosis of smallpox and related infections and the improvement of the exiting techniques

N.N. Mal'tseva,
a leading researcher of the Moscow WHO Collaborating Center

Prof. Nelya N. Mal'tseva, doctor of medical sciences, came to work with our team when we were still a unit of the Mechnikov Institute of Vaccines and Sera. She quickly mastered the methods used in virology and started the research activities. Nelya was a wonderful experimenter. Her works made a significant contribution to the issues associated with the correlation between the reactogenicity of smallpox vaccines and the production strains of the virus, development of new diagnostic manipulations for detection of poxvirus and herpesvirus diseases, and the research into these pathogens. She contributed to the discovery of the natural focus for cowpox virus and a new disease, human monkeypox. With her solid background, she successfully coped with rather distant activities, such as a field epidemiologist in India under the Smallpox Eradication Program, lecturer to WHO students, and advisor in organization of smallpox vaccine production in developing countries. The last period of her bright life was connected with the Laboratory for Herpesviruses as its head. A severe disease untimely cut Nelya's life in 2001.

were a crosscutting project throughout the overall eradication program. Omitting the technical and some other details hardly interesting to the reader, I outline our main results in this area.

Thus, we continued our study into the behavior of variola virus and other orthopoxviruses in cell cultures of different origins. These data, obtained mainly by Gurvich and Yumasheva, allowed for characterization of the specific features in the cytopathic effect (CPE) of different orthopoxviruses and the changes in the virus cells; moreover, the same studies were performed with the pathogens that induced the diseases frequently mistaken for smallpox, such as chickenpox and herpes. Based on these data, the differential diagnostic criteria were formulated. In addition, the test (hemadsorption phenomenon) was found that made it possible to detect the presence of an orthopoxvirus in cell culture before the CPE was observable in the cell monolayer, which significantly accelerated the assay response. The first enzyme immunoassay (ELISA) test system designed at our Collaborating Center in two variants—for detecting antismallpox antibodies and orthopoxvirus antigens—allowed for a qualitative leap in diagnosis. This method is highly sensitive, being comparable with the virus isolation in chick embryos, but gives the result in 3–3.5 h, so it may be regarded as a rapid test. Generation of the monoclonal antibodies to monkeypox virus allowed for designing of one more variant of highly specific ELISA test system for detection of this pathogen. This test kit was verified using field specimens of the cases suspected for human monkeypox and demonstrated its high information content in combination with rapid result. In particular, when we received specimens from Gabon, the presence of monkeypox virus in these specimens was reported to the WHO in 4 h. These developments were performed by a team of our researchers (Mal'tseva, N.A. Khabakhpasheva, and Matsevich). The monoclonal antibodies were produced with participation of F.G. Nagieva and G.M. Platonova.

Using this opportunity, I would like to express my heartfelt gratitude to my great friend, wonderful scientist, and personality Prof. Y. Ichihashi (University of Niigata, Japan), whose most valuable advice considerably reduced the way to generating the necessary hybrids and producing species-specific monoclonal antibodies to orthopoxviruses.

In addition to development and improvement of the methods for diagnosis of orthopoxvirus infections, we believed it important to focus part of our efforts on solving the same problems for other infections that

clinicians frequently take for smallpox, namely, the infections caused by herpesviruses. The studies performed by Mal'tseva, Gurvich, and V.G. Nikulina resulted in several techniques for identification of these viruses, namely, indirect hemagglutination test for detection of chikenpox agent, varicella zoster virus; hemagglutination retardation reaction for detection of the corresponding antibodies; detection of herpesviruses in cell cultures according to morphological criteria, and so on.

Our wonderful biochemist N.A. Khabakhpasheva

The differentiation between individual orthopoxviruses was one of the most important and difficult problems to be solved in the diagnostic research. Several developments at the Moscow Collaborating Center focused on this problem. In particular, we (Gurvich and Mal'tseva) found and tested the continuous pig embryo kidney (PEK) cell culture for distinguishing between variola and monkeypox viruses. PEK cell culture emerged to be nonpermissive for monkeypox virus unlike variola virus, which displayed full cytopathic effect pattern in this cell line. On request of the WHO, this cell culture was tested in several laboratories and the results confirmed our data. The use of PEK cell culture became a simple and available standard test in the diagnostic toolkit.

On the request of the head of the eradication program, we also developed a number of techniques for differentiation of variola and camelpox viruses, which is important for the regions widely using these animals. The point is that both pathogens induce almost indistinguishable lesions when cultivated on the chorioallantoic membranes (CAMs) of chick embryos under standard conditions. This considerably complicated diagnosing. By varying different cultivation parameters, we succeeded in finding the temperature regime that revealed distinct differences between these viruses.

In our diagnostic research, we every now and then encountered the situation when the specimens of patients contained a low amount of the virus. This created difficulties for electron microscopy examination, the major rapid diagnostic test. As the way out, we actively used immune electron microscopy. Developing this direction, we further turned to monoclonal antibodies, which considerably increased the test efficiency. N.N. Yanova, working with the interlaboratory group of electron microscopy and preparing her theses in our lab, as well as Mal'tseva and Matsevich performed the main part of electron microscopy examination. V.D. Lotte, the head of this group, consulted us for unclear cases.

Another important projects implemented at our center was the serological examination of the population in the Republic of Congo aimed at assessing the incidence of human monkeypox (this work was performed in 1984 by Shelukhina, Mal'tseva, and E.V. Efremova). The serum sampling among the Congo population was organized by A.I. Gromyko. One more serious project, implemented by Shelukhina, Shenkman, and A.E. Frol'tsova, was a comparative study of the variola virus strains isolated of patients in different regions of the world. In total, they examined 60 variola virus strains that circulated in 1960–1975 in Asia, Africa, South America, and Middle East. Only four of the numerous phenotypic characteristics of variola virus strains appeared to be informative. This suggested a certain correlation of the set of these four markers, such as pathogenicity for chick embryos, virus accumulation in the liver, neuropathogenicity for 10-day-old white mice, and differences in the virus infectious titers when cultivated under normal and elevated

(38.3°C) temperatures, with the smallpox lethality characteristics in the corresponding region. It was also found that one of the African strains, which were in general less pathogenic as compared with the Asian ones, contained one strain that could be ascribed to the *alastrim* viruses. Of the five South American strains, four belonged to *alastrim* viruses and one appeared to be a variola virus of an intermediate type.

When studying the ecology of monkeypox virus, we never missed the opportunity to get a deeper insight into cowpox virus as well. In particular, we were interested how this pathogen was transmitted to humans from environment (naturally, in the cases other than a mere infection by contacting an infected cow). A comprehensive analysis of the first solitary diagnosed human cowpox cases allowed us to reliably speak of infection transmission from certain rodents inhabiting the corresponding area. In our team, O.A. Zhukova focused on this problem. She collected, studied, performed all necessary tests, and recorded at least seven cases of human cowpox caused by the contact with rodents. Moreover, the four cases were confirmed virologically by isolating the cowpox virus from both the infection source (white rats) and patients. As for the remaining cases, a tight contact with rodents (mole and field mice) was recorded.

Evidently, the WHO and leaders of the eradication program always bore in mind the need in studying other orthopoxviruses pathogenic for humans and their ecology. Moreover, the recommendations of the Global Commission for the Certification of Smallpox Eradication set this goal for the post-eradication period as well. The Moscow WHO Collaborating Center was involved in the research into cowpox and monkeypox viruses along with smallpox and vaccinia viruses.

Our coworker, N.N. Yanova, from the group of electron microscopy, analyzing the specimens of smallpox cases received from the WHO

Before the beginning of our studies, it was believed since the time of Jenner that cattle were the natural reservoir of cowpox virus. However, the very pattern of how cowpox outbreaks emerged frequently bewildered everybody who dealt with them. Dr. Dixon (1963), a well-known expert in orthopoxviruses, not without reason called these outbreaks puzzling. Our research into the ecology of this virus started from clarifying the nature of the pathogen isolated by V.A. Krikun (1974) of ill white rats in one of the Moscow animal breeding facilities and referred to as pneumotropic rat virus. At our lab, the virus was identified as a cowpox virus.

Later, we investigated an outbreak of a severe infection with a vague etiology in the Moscow Zoo, which led to the death of almost all felines and giant anteaters, kept in the same area. The specimens of ill animals were examined by Mal'tseva, me, and N.N. Korneeva, who worked with the Moscow Zoo; it was demonstrated that cowpox virus was the agent of this disease. The disease followed two main courses. The clinical picture in part of lions, cheetahs, and a black panther was untypical of a poxvirus disease: it was a fulminant lethal pulmonary infection and was initially classified as influenza. Animals died as early as days 3–4. The autopsy showed serofibrinous pneumonia and massive (up to 3 L) pleural exudate containing high concentrations of virus. The other variant of the clinical course developed slower and

It is appropriate here to briefly tell about one of the first members in our team, Emma M. Shelukhina, doctor of medical sciences. Above and below, we repeatedly referred to the studies of Emma Shelukhina, including the research into the ecology of the orthopoxviruses pathogenic for humans (such as cowpox and monkeypox viruses). Here, I would like to say some words about her activities as a scientist and a personality. Emma came to work with our team almost immediately after graduation from the institute. She started to work with poxviruses and retained the interest to this issue during all her scientific career. As a scientist, she was diligent and interested in everything new; she had a talent to contact her colleagues and able to inflame her young colleagues. She had no fear to efficiently and dedicatedly work in dangerous regions, in the midst of severe smallpox outbreaks. Her open character and sincerity always attracted her colleagues. Now, when I am putting down these lines, Emma receives medical treatment for a severe illness. We all greatly regret that her illness prevented Emma, one of the most active participants of the eradication program, to attend the celebrations of the 30th anniversary of our victory.

E.M. Shelukhina,
a leading researcher of the Moscow WHO Collaborating Center

was accompanied by skin lesions. This disease pattern was observed in part of felines and both giant anteaters. An analogous outbreak developed in the zoo a year later but was smaller-scale and affected young pumas and Far East wild cats.

The key question for understanding the mechanism of outbreak development in the zoo was identification of the primary source of animal infection. Our analysis of the potential sources eventually allowed us to find out that the diet of some carnivores included living white rats. These rats were delivered from an animal breeding facility, where, as we later demonstrated, a cowpox outbreak occurred. We recovered several cowpox virus isolates from the white rats kept in this facility and they emerged to be identical to those recovered from the ill animals of the zoo. Thus, the role of white rats as a source of infection in the zoo was confirmed.

In connection with these events at the zoo, I dare add a small excursus. I recall that many foreign zoos when they came to know our results started to demand obligatory smallpox vaccination of all large predators that they bought from or exchanged with the Moscow Zoo. By the way, I every now and then did these vaccinations since the zoo staff had no such experience. The vaccination of a large Amur tiger, weighing about 200 kg, in a special immobilizing cage, was especially picturesque.

The logical consequence of our results was the need to clarify a set of issues associated with the outbreaks among white rats in the animal breeding facilities and vivaria. For this purpose, we (Marennikova and Shelukhina) investigated eight such outbreaks in Moscow and the Moscow oblast. The characteristics and durations of these outbreaks were in general rather similar. The observed minor differences were associated with the number of animals and the conditions of their keeping. The epizootics in some facilities continued for 4–5 months with a peak in morbidity after 1.5–2 months. The mortality rate in these outbreaks and epizootics was on the average 30% and higher.

In terms of clinical manifestations, the disease had different forms. The form that first attracted our attention was a pulmonary variant. The ill animal ceased feeding; became sluggish; developed panting, dyspnea, and progressive abdominal distention; and died in 3–4 days. Autopsy demonstrated a total or focal pneumonia with pleural serous or fibrinous exudate and almost empty swollen stomach and intestine with considerably thinned walls. This form of the disease had a 100% lethality rate; moreover, rats never ate

their corpses (unlike the death cases according to other reasons). The other form, cutaneous, had a milder course with typical development of red papular rash mostly localized to the hairless or poorly haired areas (tail, paws, and snout). The rash rapidly (in 1–2 days) got dry and was covered with scabs. Characteristic features of this form were pronounced conjunctivitis with sanguineous exudate (a thin red glasses-shaped band around the eyes and rhinitis). This form of disease progressed without any dramatic disturbances of the general state of animals and almost without any lethal outcomes. In some cases, necrosis of the affected parts of the tail and paws was recorded. A mixed variant of the disease was also observed, when the skin lesions were combined with pulmonary involvement. In part of the cases, a subclinical variant passing in 2–3 days was observed. During the disease, animals had decreased appetite, were sluggish, and had ruffled fur. The disease course and its severity were age-dependent. For example, suckling rats were infected and died without any apparent clinical signs. The disease had a mild course, cutaneous form, and no lethal outcomes in adult females. The virus was detectable in the lung tissue of over half rats with evident clinical signs; in addition, the virus was also recorded in the kidneys of 45.2% of these rats and at a lower rate, in the liver and spleen. Interestingly, the orthopoxvirus antibodies were detectable by different serological tests in 81.8–89.6% of the rats as early as the acute stage of disease. Up to 10% of the virus carriers were recorded among the apparently healthy animals examined at the end of the outbreak. This carriage was confined to a certain post-infection period. For example, the virus was detected in the urine of 50% of the examined individuals and in the feces of two individuals of the examined 12 ones 6 weeks after the beginning of the outbreak and was undetectable at all in the 41 examined rats 10 weeks after the outbreak.

Of special interest was the opportunity to create an experimental model for the asymptomatic infection course. We succeeded in obtaining such model in the experiments with the intranasal infection of 5-day-old rats with small doses of the virus. In this form of infection, some individuals displayed rather long-term, up to 4 weeks (the period of observation), persistence of the virus in the kidneys and the presence of antibodies to orthopoxviruses (Shelukhina) on the background of the absence of apparent clinical signs of the disease. An analogous study using even lower virus doses was conducted by A.D. Maiboroda and Z.I. Lobanova, our collaborators, with 1.5–2-month-old white rats; the animals developed an asymptomatic infection, which was confirmed by pathohistological alterations in the organs and serological deviations. These facts gave the grounds to regard that post-infection virus carriage by apparently healthy rats and their ability to discharge the virus to environment were in our view not only the main cause of long duration of epizootics, but also a putative model for the spread of infection in rodent populations in wildlife. As for the origin of the infection in white rat colonies, several indirect signs suggested that it was associated with the penetration of feral rodents, in particular, gray rats (*Rattus norvegicus*), living near the animal breeding facilities. This assumption is favored by the individuals with a combined coloration in the offspring of white rats. However, our initial attempts to isolate the virus from the wild rats trapped in the nearby area failed. On the other hand, serological screening of these animals for the presence of the antibodies to orthopoxviruses detected these antibodies although at a low rate (0.2%). Completing this part of our studies, we considered it necessary to test the effect of cowpox virus on the feral relatives of the laboratory white rats. It appeared that the infection caused by cowpox virus was easily reproducible in both the wild gray rats (Maiboroda) and the individuals of the same species grown in captivity (Marennikova and Efremova, unpublished data). The sensitivity of these animals, clinical manifestations of the disease, and mortality rate were almost the same as for the white rats. The disease followed the most severe course in the case of intranasal infection. The transmission without direct contact (when healthy rats were placed into the cages that previously housed ill animals) was observed. The virus was discharged with urine and feces for 11 to 35 days after infection.

Summing up this large research, the following conclusions were made:

- The pathogenicity range of cowpox virus appeared much wider than is was earlier believed and
- The totality of accumulated data suggests that the search for natural reservoir of cowpox virus should be focused on rodents.

In order to implement the new project, it was decided to start the search for this virus in a remote region. According to our plan, Dr. Ladnyi organized trapping of rodents in Turkmenistan (in desert and semidesert areas). Ogorodnikova, our former researcher, performed the primary examination of the trapped animas and recovered virus isolates at the local antiplague station, where the work with orthopoxviruses had never been done before. The isolated viruses were finally identified at the Moscow Collaborating Center. The animals were in parallel assessed by serological methods. In total, approximately 1000 rodents belonging to 10 species were examined and three isolates were recovered: two from the kidneys and spleen of the great gerbil and one from the kidneys of the yellow ground squirrel. The corresponding antibodies were most frequently detectable in the species from which the virus was isolated. Identification of the isolates confirmed that this was cowpox virus. The isolates of cowpox virus were for the first time recovered from wildlife. Simultaneously, this was the evidence that rodents represented the true natural reservoir of this virus. The presence of antibodies demonstrated that these isolates were not an accidental finding. In addition, special experiments showed that the carriers of this virus were highly susceptible to it and responded to infection by development of the disease differing in the degree of severity (from a rapid disease course with a high lethality to a subclinical variant). The disease could progress both with skin lesions (at a small infective dose) and without them.

Thus, direct and doubtless evidence was obtained that the wild rodents were the true natural reservoir of this orthopoxvirus species. These results were published in one of the leading virological journals, *Archives of Virology*, in 1978. This new look on the ecology of cowpox virus is now commonly recognized. Although no new isolates of rodents have been reported over the decades that elapsed since this publication (except for the isolates recovered under the Transcaucasia project), dozens of papers describe the results that in various aspects confirm our concept. This large innovative work, which sometimes resembled a real investigation and which allowed the traditional view on the cowpox virus ecology to be revisited, was performed by Marennikova, Shelukhina, Mal'tseva, and Ogorodnikova and, of course, Ladnyi, who was the main organizer of the Turkmenian search. This project was continued by Efremova and Zhukova. Unfortunately, which is rather a common situation, the references to our first publications are almost absent.

Later, another project was planned to further develop this direction, which we supported; this project covered Transcaucasia (Georgia) and was implemented by L. Sakvarelidze, Sh. Tsanava, and our researchers (Shelukhina and Yanova, 1989). The virus was also isolated from rodents in this region; the carrier was the Libyan jird. Among the individuals of this species, 11.3% displayed the virus-neutralizing antibodies to orthopoxviruses.

Another orthopoxvirus that attracted our attention was monkeypox virus. Chronologically, it was the last human-pathogenic virus added to the genus *Orthopoxvirus*. It was for the first time described by von Magnus et al. (1958) when studying an outbreak of a smallpox-like disease among the long-tailed macaques kept in the vivarium of the State Serum Institute in Copenhagen. Later, similar outbreaks were recorded in several monkey breeding facilities in the United States. However, the infection source was not found in all cases. The virus was regarded as nonpathogenic for humans since any cases of human infection from monkeys were absent. Yet many questions remained unanswered, for example, why these outbreaks emerged after rather long time (months and even years) after the animals were obtained, what geographic regions housed the natural reservoirs of the agent of this infection, who was the true natural carrier of monkeypox virus, what were the mechanisms underlying persistence of this virus in wildlife, and many others.

The similarity of the monkeypox clinical picture to that of smallpox and insufficient data on the pathogen forced the WHO to focus its efforts on assessment of the monkeypox prevalence among wild monkeys. The initial stage involved sampling of the sera of wild monkeys in Southeast Asia and later, in Africa. Serological screening for the antibodies to orthopoxviruses was conducted at the Moscow WHO

Collaborating Center in collaboration with four other WHO centers. It was assumed that this screening would help in defining the region of monkeypox virus circulation. Unfortunately, this huge and laborious work failed to make unambiguous conclusions.

During the same period, we studied the properties of several monkeypox virus strains isolated during the outbreaks in the United States and Danish monkey breeding facilities and vivaria (Marennikova and Gurvich). In order to discuss these data and other materials, the WHO organized the scientific group on monkeypox at the Moscow Collaborating Center (Institute for Viral Preparations, Ministry of Health of the USSR). The group analyzed the available data and recommended to continue the research into this virus and to assay the serum samples and organs of wild monkeys with a special focus on African countries.

The watershed in monkeypox research was the discovery of the earlier unknown human disease caused by monkeypox virus by Marennikova, Shelukhina, Mal'tseva, and Ladnyi. The brief history of this discovery is as follows. A specimen of an ill child from Zaire (Central Africa) with a clinical diagnosis of smallpox was received by the Moscow Center. It was an ordinary event for the diagnostic lab except for the most important fact that Zaire was regarded as a smallpox-free area. Taking into account that the situation was rather unusual, we examined part of the infected chick embryos earlier than it was typically done, after 48 h. The observed lesions looked typically of smallpox. However, they considerably changed 72 h after infection and acquired the appearance characteristic of monkeypox virus. We knew monkeypox

The first WHO scientific group on monkeypox, organized with the Moscow WHO Collaborating Center. Participants of the group with interpreter walking in Moscow after a session

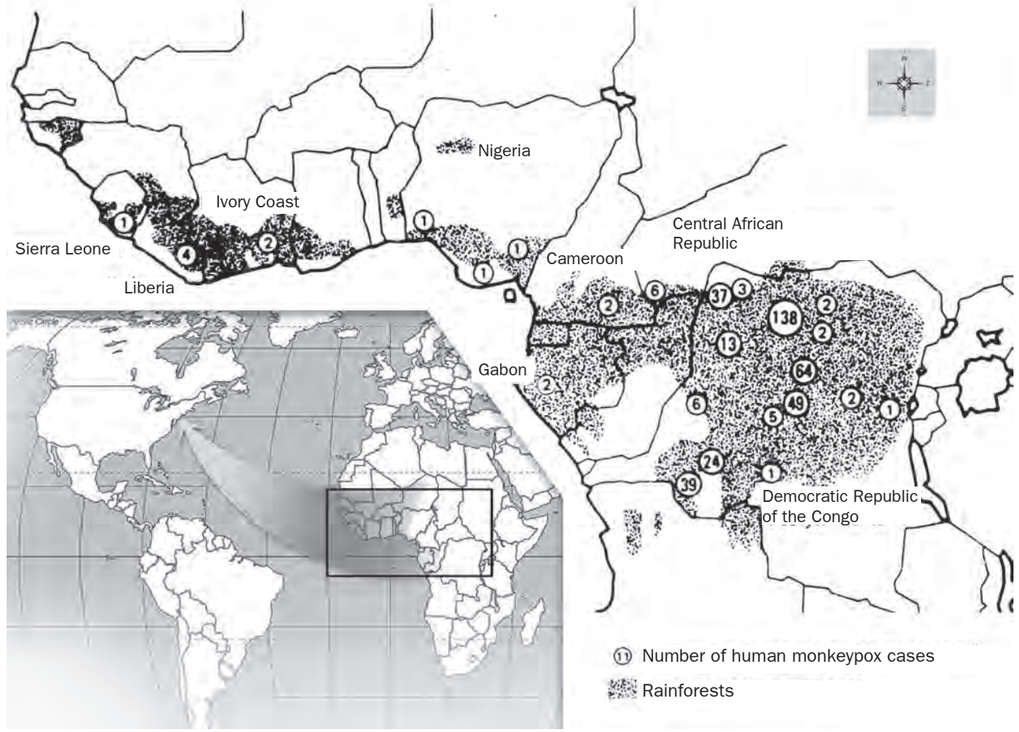
virus quite well because of our earlier studies of the isolates from monkeypox outbreaks in the United States and Danish monkey breeding facilities.

We reported to the WHO about this new case of human disease caused by monkeypox virus, discovered for the first time, on October 5, 1970. Note that shortly prior to this event, several cases of the disease with a clinical diagnosis of smallpox were recorded in West Africa (Liberia), also regarded as a smallpox-free region. The situation was aggravated by that the WHO Collaborating Center in Atlanta confirmed this diagnosis. These cases created anxiety among the staff of the program and could even cause doubts concerning the adequacy of smallpox eradication strategy. Based on our report, Dr. Henderson, manager of the eradication program, asked the Collaborating Center in Atlanta to repeat the assays of Liberian specimens using our protocols. The repeated assays confirmed that all West African specimens of as if smallpox cases contained monkeypox virus rather than variola virus. All this allowed the tension to be reduced. (These events are considered in such detail not only because they are really significant. The point is that, unfortunately, almost all international issues "forgot" about our priority despite that the history of this discovery is detailed in the final WHO monograph *Smallpox and Its Eradication* and the book *Human Monkeypox*.) Note that the peculiarity and guile of this infection consist in that it is almost indistinguishable from smallpox in its clinical manifestations (see the last photo in the Supplement).

The discovery of human monkeypox qualitatively changed the significance of this virus and the pathology it causes. Before this discovery, this virus was of interest merely as a new orthopoxvirus but now it acquired the value for medical science and public health as the agent of new human disease. In turn, this situation required a considerable increase in the scope of work in order to get the answers to the most important practical questions. Among them were the questions on the natural reservoir of monkeypox virus, the ways of its transmission to humans, the possibility of person-to-person transmission, main variants of clinical course, and the significance of this disease for public health care. The study of these and several other questions started under the aegis of the WHO and with its support. Find below the briefed results of our studies under his project.

Taking into account the ambiguity of the earlier serum screening of the wild monkeys trapped over a vast territory, we decided to tackle this problem in another manner. According to our request, Ladnyi organized serum sampling of the monkeys trapped immediately near the areas of human monkeypox foci close in time to recording of the disease. In total, four sets of examinations were performed according to this principle in the Equatorial Province of Zaire in January 1971–October 1973. In addition to me, Shelukhina, Shenkman, Mal'tseva, and Matsevich were involved in this work. We were very glad that this approach was a complete success. Of the 79 sera samples of wild monkeys, 20 specimens contained significant titers of hemagglutinins and/or virus-neutralizing antibodies to orthopoxviruses. Moreover, precipitins, demonstrating a recent contact with the virus, were detected in two cases (*Vopr. Virusol.*, 1975). Thus we were the first to detect the antibodies to orthopoxviruses in monkeys living in the region with recorded human monkeypox cases. Later, this principle was used by the researchers that examined monkeys and other animals in West African countries (Bremen et al., 1977) and in Zaire (Khodakevich et al., 1986).

The results obtained by our center suggested the possibility of monkey-to-human infection; moreover, local population used to eat monkeys in several areas of the Equatorial Province. However, it could not be excluded that both the monkeys and humans were infected from a certain other source. Thus, we continued our work on assessing the susceptibility of other animal species to monkeypox virus, the more so, since several studies reported the presence of orthopoxvirus antibodies in other animal taxa, including rodents. Special experiments were conducted by Shelukhina and Marennikova with five rodent species (rabbits, hamsters, guinea pigs, white rats, and white mice) to assess the species-level susceptibility of various rodents to monkeypox virus. Actually, this work continued the early studies by Dr. von Magnus (Magnus et al., 1959). We paid special attention to assessing the infection routes that were most probable under wildlife conditions, namely, intranasal and oral, as well as to modeling a contact infection route. These



West and Central Africa: localization of human monkeypox cases recorded in 1970–1991. Later, this disease was discovered in several countries of this region, in particular, in the Republic of Congo and Sudan. In 2003, human monkeypox was for the first time recorded outside Africa. An outbreak of this infection emerged in the United States and affected 79 persons in six states. The rodents imported from Ghana were the source of infection

methods were for the first time used in the studies with monkeypox virus. It was shown that monkeypox virus induced different types of response from a complete resistance to generalized infection with a lethal outcome depending on the animal species, animal age, and infection route. Of the five tested species, two—white mice and young (10-day-old) rabbits—appeared susceptible. In particular, oral infection of 10-day rabbits, unlike the adult animals, induced a generalized infection with skin lesions and a high mortality rate. From the ecological standpoint, the possibility of a contact transmission of this infection from ill young rabbits with generalized rash to the healthy individuals kept together was of special importance. In our view, this fact suggested the possibility of a horizontal transmission of monkeypox among the animals of the species other than primates, for example, among rodents (*Vopr. Virusol.*, 1975).

After our studies with rodents, the WHO together with the Centers for Disease Control and Prevention organized the serological examination of 43 animal species trapped in Northern Zaire (1979). In total, the antibodies to orthopoxviruses were detected in 17% of them. Representatives of rodents, namely, the red-legged sun squirrel (*Helioscinrus rufobrachium*), were also among the seropositive species (Jezek and Fenner, 1988).

Despite the interesting results, described above, many details of how monkeypox virus infected humans were vague. I believed that the on-site observation and study would be helpful in clarifying at least some of the yet unsolved questions. Thus, I agreed with the WHO my trip to Zaire, and my visit to the area with the highest incidence of human monkeypox was approved. I went there in 1982.

In Kinshasa, I was welcomed by Mark Szczeniowski, whose assistance was invaluable in the difficult situation in Zaire at that time. From Kinshasa, I flew on a small single-engine plane being the only passenger, to the northwestern part of Zaire to the upper reaches of the great Congo River. We travelled over endless dense rainforest with very few signs of human presence, marked by wooden decks above the land, the purpose of which was vague for me. On arrival, I was warmly welcomed by the team of program participants who worked in the equatorial area of Bumba Province. This team worked under most hard conditions. For example, they confessed that they had to save gasoline for a long time so that I could visit the hospital and the sites where human monkeypox cases were recorded. This small team did its best for the success of my trip.

I would like to use this occasion to cordially thank Szczeniowski, Monica Vernet, and the entire team for their kindness, hospitality, and priceless and manifold assistance during my mission.

I repeatedly observed how the local people prepared the carcasses of killed animals for cooking and the overall setting of this process and many things connected with possible infection routes became clear to me. My visit to the hospital in Yambuku and analysis of the case record of the hospitalized children made it possible to find out at least three generations of infection within the hospital. However, the most important result of my visit there was the detection and analysis of one case when the wildlife infectious source and the human monkeypox disease were evidently linked. It was a girl who found an apparently ill squirrel and carried it to her village for about half an hour. The child developed monkeypox approximately 9 days later. The girl did not contact any human monkeypox cases or other wild animals and was not vaccinated against smallpox. This case convinced me that there were serious grounds to regard tropical squirrels in addition to monkeys as one of the potential natural carriers of this virus.

Having reported to the WHO in Geneva about my mission, I proposed (taking into account my experience during the Smallpox Eradication Program) to announce rewards for finding ill squirrels with skin lesions and bringing them to the working team. This was soon done, and Dr. Khodakevich, who studied the monkeypox virus ecology in Zaire, got such squirrel. The specimens of this animal were shipped to the WHO Collaborating Centers in Moscow and Atlanta. Our examination (Marennikova, Shelukhina, and Yanova) detected the presence of monkeypox virus at a high concentration in the skin lesion specimens as well as in internal organs (lungs, kidneys, and spleen). Examination of the isolate recovered from the squirrel according to biological markers and DNA restriction assay demonstrated that it was identical to the strains earlier isolated from human monkeypox cases. The squirrel blood serum contained the antibodies to monkeypox virus. The results were reported to the WHO. The results at the Atlanta Center were analogous. I think that all participants of this work were most satisfied that this collaborative effort gave a significant result. However, one of the researchers of our center told me at the beginning of 1986 about the paper published in the *Lancet* in January by L. Khodakevich, Z. Jezek, and K. Kinzanzka titled “Isolation of monkeypox virus from wild squirrel infected in nature”. Unfortunately, nobody of the researchers who recovered, studied, and identified the isolate of squirrel was among the authors of this paper. This was quite unexpected for us and completely beyond our understanding of publication of collaborative works, especially, of a priority character.

The discovery of monkeypox in a squirrel induced us to continue the study into the susceptibility of rodents to this virus, now in the *Sciurus vulgaris* squirrels. A small group of these animals (each with a weight of about 300 g) were obtained after a 1-month quarantine at the Moscow Zoo. They were infected orally, intranasally, and epicutaneously with the monkeypox virus isolate recovered from the African squirrel. The disease symptoms appeared from the very first day. The disease progression was especially fast in

S.S. Marennikova (*second from the left*) with the field team that participated in the human monkeypox project (Lisala, Zaire, 1982); Dr. Paluku is in the center and Monica Vernet, a volunteer, to the right

the animas infected intranasally and orally. All animals died on days 7–8 after infection. Interestingly, no skin lesions were observable. This could be associated with a rapid development of the disease, resulting from a high infectious dose. We already noticed that the development of skin lesion were dependent on the infectious dose in our earlier experiments with cowpox virus. The internal organs of the squirrels contained high concentrations of the virus. These studies demonstrated that squirrels were highly susceptible to the virus infection via the routes most closely simulating the natural conditions (this part of the research was performed by Shelukhina and Zhukova). This was the first study that demonstrated a high susceptibility of squirrels to monkeypox virus.

Later, our data were confirmed and extended in the studies with African squirrels by Shelukhina, Khodakevich, D. Messinger, S.B. Pole, Szczeniowski, and others. These experiments were initiated by Khodakevich at the interim lab organized with the National Institute of Biomedicine in Kinshasa. The virological and serological studies in Kinshasa were performed by Shelukhina. The results also confirmed

our earlier observations, mentioned above, on the contact transmission of monkeypox virus among rodents form their ill congeners.

O.A. Zhukova, a researcher of the Moscow WHO Collaborating Center

Part of the specimens from the Kinshasa project was shipped to our center for a more comprehensive examination, performed by Shelukhina and Zhukova. Omitting several interesting directions in their work, I want to dwell on only one of them. When examining the specimens of African squirrels, they confirmed the observation made as early as by the discoverers of monkeypox virus—Dr. von Magnus et al. (1959)—who demonstrated that apparently healthy monkeys could be carriers of the virus. Shelukhina and Zhukova isolated monkeypox virus from the kidney and liver specimens of two apparently healthy squirrels that emerged to be seropositive. Presumably, this was either a post-infection carriage (as had been shown for cowpox virus) or asymptomatic disease course. In our view, both states could play a certain role in maintenance of virus circulation and infection spreading.

It is evident that the issue of post-infection carriage is of a paramount importance, including in our understanding the mechanisms underlying the virus persistence in nature. The further studies in this direction would perhaps reveal why the monkeypox outbreaks in the monkey facilities emerged with such delay, which has not been yet satisfactory explained.

An important part of the activities of our center, as is mentioned above, was diagnostic testing of the samples from patients, which was of an utmost importance for the eradication program. In this work, we used the methods designed and improved at our center (see above) along with the other assays. Typically, the specimens of patients were shipped to the center in difficult or unclear situations. The peak of this work was during the period of the certification of smallpox eradication, when all samples of the cases suspected for smallpox were sent to Moscow and Atlanta. At that time, we got 318 to 420 specimens every week. In total, 3047 specimens were examined from November 1977 to and through 1979; the agents of herpes virus group, monkeypox virus, and tanapox virus were detected in these samples. However, none of the specimens contained variola virus. In total, the WHO Collaborating Centers in Moscow and Atlanta in 1967–1979 analyzed over 16 000 samples.

During this work, we also encountered rather unusual things. In particular, the simultaneous presence of two pathogens—poxviruses and herpesviruses—was observable by electron microscopy in some specimens of patients. This directly confirmed the co-infection by poxviruses and herpesviruses. Such state could be hardly detected according to clinical observations. The use of electron microscopy also allowed us to clarify the situation at the Moscow Zoo that caused a considerable concern: a gorilla kept there developed numerous smallpox-like lesions. This concern was supported by the information about a smallpox infection of another higher primate, an orangutan, in the Jakarta (Indonesia) Zoo. The susceptibility of these animals to variola virus was known as early as the very beginning of the 20th century from the classical experiments by Brinckerhoff and Tyzzer (1906). As we managed to find out by electron microscopy, it was a mere chickenpox.

Another unusual situation arose when the WHO asked us to examine the specimens of an Italian mummy from a burial in one of the Naples cathedrals dated back to the 16th century. The specimen was taken from skin lesions of a child. The electron microscopy demonstrated characteristic poxvirus virions, which confirmed the diagnosis of smallpox. However, a concurrent serial passaging of this material in both chick embryos and cell culture demonstrated that the virus over the past four centuries had completely lost its viability.

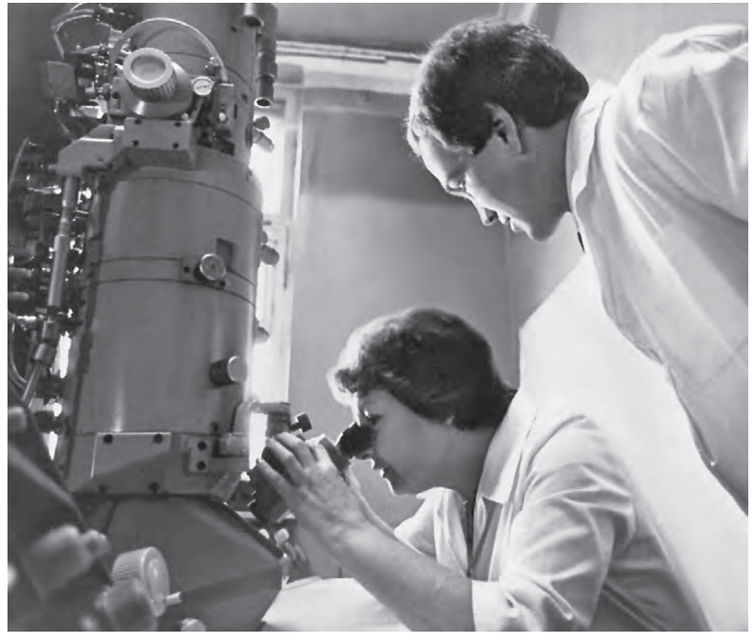
In general, the diagnostic activities were a real support for the eradication program and allowed for an adequate assessment of the situation. One of the results of this work was the first national collection of variola virus strains and other orthopoxviruses. First, this formed the real background for comparative studies and characterization of variola virus strains from different regions of the world (Shelukhina); later (in 1995), this collection as well as the WHO Collaborating Center was relocated to the State Research Center of Virology and Biotechnology Vector (Novosibirsk), where the strains were studied in terms of molecular genetics. When describing this collection, I cannot but tell that, unfortunately, its considerable part (including the unique isolates that had to be further examined) was destroyed according to irrational decision of the administration of the Institute for Viral Preparations. In our life, we also encountered other strange things unexplainable in the context of common sense. In particular, the administration of the institute in some period prohibited to report the results of diagnostic studies to the WHO by telegraph (we were told to send such reports only by regular mail). It was possible to return to the only practice acceptable in this situation only after Dr. Henderson, the manager of the eradication program, strongly protested against this strange decision. I mention these minor details to illustrate the working atmosphere at the Institute for Viral Preparations, which significantly differed from that at the Mechnikov Institute of Vaccines and Sera.

When describing the activities of the Moscow WHO Collaborating Center, I cannot but recall how we performed various tasks set by the WHO Headquarters by directly assisting on-site eradication program implementation. For this purpose, our researchers went to different countries as WHO advisors in different issues. For example, the WHO sent me to India at the beginning of the 1960s to estimate the state of program implementation and help the local manufacturers of smallpox vaccine. I visited a number of large production faculties and shared with them our experience in production of freeze-dried smallpox vaccine.

E.M. Shelukhina (*in the center*) with her Indian colleagues during her visit to India, 1965–1966

Shelukhina and Mal'tseva each spent a year in India training the local specialists in the modern methods for control of smallpox vaccines and laboratory diagnosis of smallpox as well as directly helping in these activities. Our colleagues sent under the eradication program to different countries also participated in field anti-epidemic work. In 1972, Dr. Mal'tseva was setting up the production of freeze-died smallpox vaccine in several Middle Eastern countries (Iraq, Syria, and Egypt) according to the task by the WHO as well as was delivering lectures and organizing seminars with the WHO courses in Thailand. Shelukhina had to implement a very difficult WHO mission. We have earlier mentioned the important WHO project aimed at preparation of the set of reference materials that would enhance recognition of smallpox patients and educational materials for diagnosing different smallpox forms and its distinguishing from other vesicular diseases. For this purpose, Shelukhina and L. Matlovsky, a documentary photographer from the United States, were sent to Pakistan to the area near Karachi to an ongoing smallpox epidemic. Working in the center of the epidemic, Shelukhina detected potential patients among the contacts and Matlovsky on a daily basis captured their states. In this work, they documented the dynamics of different smallpox forms from varioloid to its most malignant variants. This work was brilliantly performed. In total, they captured over 3000 images, which the WHO Headquarters used to create the mentioned guidelines (a set of color slides, posters, diagnostic charts, and so on), which were of essential help to the eradication program.

Another researcher of our center, Fedorov, spent 4 years in Afghanistan, one of the most difficult countries with respect to smallpox, and considerably contributed to the successful smallpox eradication there. On returning from his mission, Fedorov summarized the accumulated materials and successfully defended his candidate of science dissertation. Moreover, even before Afghanistan, Fedorov actively participated in several projects of the laboratory, including a comparative study of the vaccine strains.



S.S. Marennikova and V.V. Fedorov discuss the results of electron microscopy examination of a sample from a human case suspected for smallpox

The researchers of our center spent a great deal of time and effort on preparation of documentation for various scientific groups and expert committees organized by the WHO on the most important issues under the eradication program. I was their constant member (in some of them, a vice chairman). In total, our center had prepared 60 working documents. I also participated in the annual meetings of the regional advisors organized by Dr. Henderson, manager of the eradication program, to analyze the progress in program implementation and discuss the further plans and in different seminars. One of them was the travelling seminar on the smallpox vaccine quality. The participants of this seminar visited the leading vaccine production facilities in the Soviet Union (Moscow), Netherlands (Bilthoven), and United States (Philadelphia). The managers of these production facilities also participated in the seminar. The result of its work was development of the guidelines for modern production technology for the vaccine that met the international requirements to this preparation.

During the final stage of eradication program, I within the group of scientists and healthcare authorities (21 persons) was included into the Global Commission on the Certification of Smallpox Eradication. In addition, I was elected a member of two international commissions (in Kenya and Sudan) that verified the materials submitted by the national authorities. This verification consisted in on-site inspections. Each member of the commission visited the most remote places of these countries within the allotted territory to confirm the absence of any fresh smallpox scars and the presence of vaccination marks in population. The members of these commissions during their mission covered many hundreds of kilometers. In particular, I had to inspect the notorious Darfur Province, including the regions adjacent to Chad, in 1978. The report summarizing the results of the program was endorsed at the final meeting of the Global Commission and 19 recommendations for the post-eradication period were formulated. Completing their work, the members of the commission signed the Declaration announcing that the planet was free from smallpox.

A meeting of the WHO Expert Committee on smallpox eradication (Geneva, November 1971)

Participants of the travelling seminar on production of improved smallpox vaccine, 1968. *Left to right in the first row*, P. Fenier (Canada), S.S. Marennikova (Soviet Union), A. Hekker (Netherlands), J. Brown (United States), R. Wilson (Canada), and I. Arita (WHO); *in the second row*, F. McCartney (United States), M. Bierly (United States), G. Tint (United States), V. Milushin (Soviet Union), A. Bernstein (United States), K. Caplan (United Kingdom), D. Henderson (WHO), B. Rubin (WHO), and A. Fontes (United States); including the managers of vaccine production in Moscow (Milushin), Philadelphia (Bernstein), and Bilthoven (Hekker)

Participants of the travelling seminar acquainting with the process of vaccine manufacture at the National Institute of Public Health and the Environment in Bilthoven

S.S. Marennikova, a member of the International Commission for the Certification of Smallpox Eradication, examines residents of a village in Kenya to control their vaccination (October 1979)

S.S. Marennikova, a member of the International Commission for the Certification of Smallpox Eradication, signs the Declaration on the Global Smallpox Eradication

Prof. Frank Fenner (Australia) with researches of the Moscow WHO Collaborating Center during one of his visits (1983).
Left to right in the first row, N.N. Mal'tseva, F. Fenner, and S.S. Marennikova; *in the second row*, E.V. Efremova, E.M. Shelukhina, E.V. Chekunova, G.R. Matsevich, and N.A. Khabakhpasheva

E.N. Ivanov, the biosafety supervisor with the Moscow WHO Collaborating Center near the control terminal of the system for decontamination and discharge of fluid waste

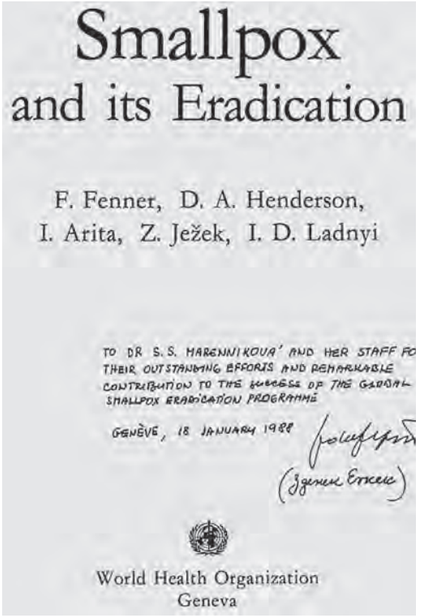
We constantly received participants of the eradication program and experts on poxviruses for training and exchange of experience. The list of our guests included many outstanding scientists, such as Fenner, A. Downey, C. Dambell, K. Caplan, J. Esposito, W. Ehrengut, and G. Stickl, to say nothing of Dr. Henderson and Dr. Arita.

The beginning of the 1980s brought us unexpected difficulties. The WHO decided to elevate the biosafety level at the Collaborating Centers for Orthopoxviruses and Related Infections, which according to the recommendations of the Global Commission for the Certification of Smallpox Eradication were retained for the post-eradication period. We had to fulfill the demands of the WHO to continue our work. This implied a large work on creating the conditions meeting the highest biosafety level. I cannot but notice that in this issue we met the understanding and assistance of the USSR Ministry of Health, administration of the institute, and WHO. Evgenii Ivanov, young, educated, and ambitious engineer was of invaluable help. On completion of the reconstruction, he provided for several years the failure-free operation of all technical biosafety systems.

The reconstruction was completed in record time and comprised installation of the air filtration system with highly efficient HEPA filters; the system for creation of negative pressure in the rooms used for diagnostic assays and manipulations with variola and monkeypox viruses; the equipment for decontamination of used specimens and fluid waste; and many others. The WHO inspection comprehensively examined and tested all systems and endorsed the modernized biosafety system during their very first visit.

I cannot but note that my description covers far from all work performed by the Moscow WHO Collaborating Center. In particular, I said nothing about the work of our lab as the National Center for Smallpox Prevention (control of post-vaccination complications and so on). I would like to separately emphasize the efficient work of the center and its success always relied on the committed team of like-minded people with high professional skills.

The WHO authorities and leaders of the eradication program highly esteemed the efforts and activities of the Moscow Collaborating Center. In the letter addressed to me and B.V. Petrovskii, the Minister of Public Health of the USSR, Dr. Mahler, the WHO Director-General, separately emphasized that the Moscow WHO Collaborating Center made an exceptional contribution to the Global Smallpox Eradication Program. Dr. Henderson in his monograph *Smallpox—The Death of a Disease* (2009) named the research and diagnostic activities of the world-level laboratory (Moscow Collaborating Center) among the critically important factors that contributed to the program by this country (along with the hundreds of millions of vaccine doses and highly qualified field epidemiologists). Finally, let me quote the acknowledgement by Zdenek Jezek, the head of the smallpox eradication unit, on the monograph *Smallpox and Its Eradication*, presented to our center by the WHO: "To Dr. Marennikova and her staff for their outstanding efforts and remarkable contribution to the success of the Global Smallpox Eradication Programme. Geneva, 18 January 1988, Zdenek Jezek".


Smallpox
and its Eradication

F. Fenner, D. A. Henderson,
I. Arita, Z. Ježek, I. D. Ladnyi

TO DR S.S. MARENNIKOVA AND HER STAFF FO
THEIR OUTSTANDING EFFORTS AND REMARKABLE
CONTRIBUTION TO THE SUCCESS OF THE GLOBAL
SMALLPOX ERADICATION PROGRAMME

GENÈVE, 18 JANUARY 1988

World Health Organization
Geneva

The cover page of the summarizing monograph *Smallpox and Its Eradication* with the inscription made by Dr. Z. Jezek, who headed the program during its post-eradication period

I have to admit that I could not for a long time find the appropriate place in my reminiscences to tell about the relations with the WHO members. Perhaps, this is high time to do it. During the initial stage of the program, it was Dr. W. Cockburn, head of the WHO Department for Viral Diseases, the contacts with whom were most frequent. We first met in Moscow (in the late 1950s as far as I remember) in the office of Prof. V.M. Zhdanov, Director of the Institute of Virology, USSR Academy of Medical Sciences, who at that time was the scientific advisor to our Department of Viruses with the Mechnikov Institute of Vaccines and Sera. Cockburn showed keen interest in our work related to poxviruses (creation of smallpox vaccine, study of the properties of variola virus strains, and so on). Later I repeatedly met him in Geneva, where I came to the meetings of the WHO expert committees and as a member of the Soviet delegation to the 15th WHA. Cockburn was a good-natured and optimistic personality with good English humor, enriching the interaction with him. He always asked where and how he could be helpful. As a partisan of active exchange of experience between scientists from different countries, Cockburn via the WHO organized for us several business trips (for example, to the Lister Institute in the United Kingdom and State Serum Institute in Copenhagen), which were most helpful. However, the working contacts with Cockburn ceased by evident reasons after the separate smallpox eradication unit was organized with the WHO and all the activities were transferred there.

For the first time, I met Dr. Henderson, the head of the smallpox eradication unit, in Moscow at the end of 1966 (before his formal appointment), when he told me that our laboratory was appointed the WHO Reference Center and, later Collaborating Center of Smallpox (note by the way that this was the first WHO center associated with the smallpox eradication program). It was interesting to work with Dr. Henderson but not easy. When speaking with him, I was always aware that he was the person who distinctly saw not only the final goal of the program, but also the ways and methods necessary for its implementation. This in no way meant that he never hesitated when considering some questions. He just was never satisfied with some generalities on a certain topic. He would accept only distinct and grounded opinions relying on actual facts. His high esteem of the role of research and diagnostic support by the collaborating centers was appealing to me as a researcher and to my colleagues. Most frequently, the research areas were associated with the need of the program; however, in some cases, Dr. Henderson asked to do certain studies in the areas that attracted his interest. Everybody all the time knew well that the essential conditions for normal working relations with him were commitment, professionalism, and high efficiency. In this case, it was possible to count on his assistance and support. During one of his visits to our laboratory, I showed him a baby rabbit which was orally infected with monkeypox virus and developed the disease with the characteristic skin lesions on the hair-free body areas. He was truly impressed and I heard in response that "for each my visit, you lab finds something unusual and interesting to amaze me." We still retain good friendly relations and were happy to meet during the 30th anniversary celebrations in Geneva and at the International Symposium in Rio de Janeiro.

I would like to recall one more member of the WHO smallpox eradication unit, Dr. Isao Arita, who worked there since the very moment of its organization. In 1977–1985, Arita headed this unit. The range of his activities and interest was rather wide: in addition to the current work on the national eradication programs, he initiated the search for the natural reservoir of monkeypox virus. Dr. Arita paid much attention to prevent using the vaccines that did not meet the international requirements in the program. I frequently contacted Dr. Arita in connection with different questions and he always was interested in what we were doing, was friendly, and eager to maximally help in solving any difficulties that we encountered in our work. I have repeatedly mentioned that he highly estimated the role of scientific research in the program implementation and, in particular, emphasized the significance of the discovery of monkeypox virus, made by our center. Dr. Arita organized and conducted the 30th anniversary celebrations in Japan; however, this prevented him from attending the ceremony of opening the monument in Geneva and the International Symposium in Rio de Janeiro. The participants of these events were sincerely pity because of his absence.

The last 2 years of activities of the WHO smallpox eradication unit, it was headed by Dr. Jezek, in collaboration with whom we performed several studies on monkeypox virus.

Out team established the tightest creative and research contacts with the late Dr. Ladnyi. He belonged to the type of people who are referred to as a self-made man. Originating from a family of peasants, he thanks to his inquisitive mind, insistence, determination, and amazing commitment graduated from medical institute and started successful research and teaching career in the area of his choice, epidemiology. His diverse gifts especially brightly manifested during his work with the WHO under the Smallpox Eradication Program. Our working contacts started when he was the WHO advisor in a large region covering 22 countries of East, Central, and West Africa. During our collaboration, a new smallpox-like human disease—human monkeypox—was discovered. So we commenced to search for the source of the human infection in wildlife and Ladnyi immediately responded to our proposal to change the approach to the search for the monkeypox virus among primates by focusing on the areas adjacent to the disease foci. Omitting some other directions of our collaboration, I would like to dwell on the project on the search for natural reservoir of cowpox virus, which ended in successful isolation of this pathogen from wild rodents. Dr. Ladnyi, who at that time worked with the USSR Ministry of Health, was not only the coauthor of this idea, but also made huge efforts for its practical implementation. I cannot but add that Ladnyi was sociable and keenly sensed everything new and promising in any proposed project or idea. I believe that my team and I were lucky to have Ladnyi among our colleagues.

Over several decades of the Smallpox Eradication Program and post-eradication period, I repeatedly visited the WHO Headquarters in Geneva for different purposes as well as the leading poxvirus centers and laboratories and met there many outstanding scientists involved in both the poxvirus research and adjacent areas. I was lucky to be well acquainted and, dare to say, be in friendly relations with two fathers in this area—Alan Downey and Frank Fenner. They both were representatives of the generation that came into science before World War II. In their company, one always felt the friendly atmosphere and never, the dominance of their tremendous scientific authority and numerous titles. They both followed the unwritten code of scientists (including the rule to always refer to their predecessors) and applied this to any person they contacted. Here, I recall the following episode. In one of our papers on the variola virus behavior in the human body, we reported the isolation of this agent from the urine of smallpox convalescents. Soon I received a polite letter from Downey, who paid attention to the point that he had described this phenomenon in his paper before our publication. Although we used to carefully check the references, this "failure" was an important lesson for us. Note here that ignoring of the earlier works of colleagues has become by now a rather widespread situation. As for Fenner, I recall the time when he visited our center to discuss my criticism as a referee on his chapters to the monograph *Smallpox and Its Eradication*. In our discussion, he did not approve any change without the comprehensive confirmations. When I informed Fenner that I was nominated as a member of the Russian Academy of Natural Sciences, he immediately sent the supporting

Prof. F. Fenner discusses the text of his chapters for the monograph *Smallpox and Its Eradication* with S.S. Marennikova, head of the Moscow WHO Collaborating Center (Moscow, 1986)

letter from Australia. It was a pleasure for me to know from his letter that I was one of the pillars of the Smallpox Eradication Program. This estimate was unexpected for me yet rather flattering. It is regrettable that these giants of science are no more with us.

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In the late 1980s, we were ordered by the Ministry of Public Health of the USSR to develop a diagnostic kit for HIV infection. The deadline was strict and I as the head of the center was appointed the manager of this project. We got some additional staff—L.G. Stepanova, doctor of medical sciences and an expert in cell cultivation, and M.N. Nosik, young scientist at that time and candidate of biological sciences and the head of the Laboratory of Lentivirus Biology now. This work, new and difficult for us, had to be performed without interruption of our main activities on poxviruses and required significant efforts of all participants, namely, Shelukhina, Matsevich, Khabakhpasheva, and Chekunova. T. Ulimova, a senior technician, was our constant assistant. Having overcome considerable difficulties, we succeeded in designing the first domestic test kit for serological diagnosing of HIV infection; the system was approved by the corresponding trials.

The years passed, and the administration of the institute continued to reduce the possibilities of our lab to work in its main area, the orthopoxvirus infections and their agents. Partial destruction of the unique collection of variola virus strains and other orthopoxviruses was commenced. Actually, the WHO Collaborating Center ceased its activities. In the mid-1993, I was forced to leave the institute, having worked there for over three decades. Almost immediately, I came to work to the State Research Center of Virology and Biotechnology Vector by the invitation of its director general, Academician Lev S. Sandakhchiev. The details on this new stage in my activities are beyond the scope of this essay, but I still want to say some words about my impressions of the Vector. There, I encountered the atmosphere of friendliness and mutual understanding as well as the academic freedom and democracy that stimulated the creative activity and high efficiency of scientific work. It did not take much time for me to understand that this rather infrequently met atmosphere was emanated and formed thanks to the personality of Vector's director, Lev Sandakhchiev. Unfortunately, this outstanding person passed away in 2006, without having done a considerable part of what he could. I am sure that many who had the opportunity to meet him and work with him preserve the memories of this personality.

The year of 1995 brought about an important event: the Government of the Russian Federation decided to relocate our collection of the variola virus strains to Vector. Ironically, I was a member of the special commission responsible for checking and withdrawing the collection from the Institute for Viral Preparations. Quite soon, the WHO Collaborating Center for Smallpox and Related Infections was organized at the Vector's facilities, where it resumed its activities, got new name, and is efficiently working until now.

As for the long way that my dear colleagues and I have travelled over the decades of joint work, which I tried to outline in this book, we all believe that it was a wonderful time filled with creativity, enthusiasm, and pride in the opportunity to participate in one of the greatest and noblest medical projects of the 20th century, which brought a complete victory over one of the most dangerous human diseases. On the other hand, I cannot help but express certain bitterness that the heroes of global smallpox eradication have not received the due attention in our country. Perhaps, it is still not too late…

(The author uses this opportunity to thank Petr Pesov for his efficient technical assistance in preparing this book.)

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At the Start of the Road: Indian Smallpox Eradication Program, 1962–1965

V. K. Tatochenko

The WHO Global Smallpox Eradication Program of 1966–1980, the triumph of humanity over one of the most dreadful infections, became feasible thanks to the experience amassed in different parts of the world. The largest national program in this field was carried out in India, and its experience, both positive and negative, was instrumental in the success of the global program. The Indian national program was actively supported by the USSR; the Soviet specialists took part in it later and actively worked in the eradication program in other countries.

There is ample evidence that smallpox was rampaging in India, China, and some other Asian countries in the 3rd millennium BC. Although this scourge hardly missed any country, the Indian subcontinent in the 20th century remained its main reservoir. In particular, India in 1953–1958 accounted for 74.15% of all smallpox cases in Asia and for 55% cases worldwide (Baroyan, 1962). The latter rate increased to 62.7% in the next 5 years, which indicated insufficient antismallpox activities in the country.

A sharp decrease in smallpox morbidity in Europe in the 19th century due to vaccination did not take place in India, since obligatory vaccination was introduced in colonial India only in 81% of the urban and 62% of the rural areas. In addition, the vaccination activities in many states were of very low quality. For example, obligatory vaccination in Bombay State was introduced only in 4.2% of the districts (*Report of the Health Survey Committee*, 1961). Correspondingly, smallpox morbidity was very high: the smallpox average mortality rate over 1900–1910 amounted to 40–50 cases per 100 000 population (with 50 000–170 000 annual mortality) and decreased by the late 1950s almost twofold. The mortality also decreased on the average to 58 000 annual cases in 1951–1959. Smallpox had clear epidemic pattern with the peak mortality during epidemic years reaching 50–80 cases per 100 000 at the beginning of the 20th century and 40 cases in the 1950s. The periodicity of epidemics changed from 2.7 to 4.5 years in this half

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a pediatrician, doctor of medical sciences, and honored scientist of the Russian Federation; in 1962–1965, the medical advisor to the UNISEF Bureau in Southeast Asia and active participant of the Smallpox Eradication Program in India

century. Highest morbidity in most states was recorded in the dry season at the beginning of the year. The endemicity level could be judged by the percentage of the weeks in a year with recorded smallpox cases: in big cities—Delhi, Bombay, and Madras—and many other areas, this rate reached 70% (Patnaik and Kapoor, 1965).

The distinguishing feature of smallpox in India was a high toll in children population. Although statistics is not very reliable, this can be assessed by the percentage of children among the smallpox victims. Thus, the share of infants in 1961 was 22.8% (11–33% in different states) and of the children of 1–10 years old, 48.1% (22–65.3%). Case mortality rate (the data of 1963 for infectious hospitals) among the vaccinated persons was 7.6% (children of 0–4 years, 16.2% and adults over 30 years, 10.9%) and among nonvaccinated, 39.6% (46.6 and 42.8%, respectively) (Tatochenko, 1968).

The Government of independent India recognized the gravity of smallpox problem. The country had 13 institutes producing the vaccine. In the 1950s, approximately 50–60 million people were annually vaccinated. However, these efforts could not alter the smallpox epidemiology since this failed to create a sufficient immune layer among the population. Besides, India produced only the liquid vaccine with a short viability period, and the hot climate further lowered the efficiency of vaccination.

In 1958, the Government of India proposed the Smallpox Expert Committee to recommend a program for smallpox eradication (*Indian Council of Medical Research*, 1959). The term "eradication" was meant the situation when the area would be smallpox-free and imported cases would not cause a significant spread of the disease. By the WHO definition, such situation is referred to as "elimination". The Expert Committee recommendations were supported by the Health Survey Committee and the activities commenced in 1962. The program was to last for 2 years with the goal to vaccinate 80% of the total population. According to the WHO Expert Committee, such immune layer could interrupt the transmission. Vaccination was to be done by the teams composed of one physician, 12 public health inspectors, three health educators, 12 recorders, and 60 vaccinators. One team was supposed to vaccinate 3 million people in 2 years; the country with 450 million population at that time required 150 teams, and they were formed in 1962–1963. Similar to the other health programs, this program should be funded in equal shares by the governmental budget and the budgets of individual states.

The program was facilitated thanks to supply of 600 million doses of the freeze-dried vaccine by the USSR. The WHO supplied 7 million doses. Substantial assistance came from the UNICEF in the form of equipment for manufacture of the freeze-dried vaccine installed in four vaccine institutes: this allowed for production of the required 200 million doses of vaccine per year. Another important UNICEF contribution was the assistance in developing Primary Health Centers (PHCs) in rural Indian areas that had almost no health service at all. Each PHC was planned for 100 000 people; in total, 5000 PHCs were planned. The UNICEF provided a set of medical supplies and equipment for each PHC and a motor vehicle that facilitated (and more often provided the only possibility of) the transportation for both PHC workers and vaccination teams. Of importance were also refrigerators (including kerosene-operated ones for the areas having no electricity) supplied to the PHCs, which ensured the safety of vaccine storage.

By 1965, 4500 PHCs were organized in the country. However, only 40% of them met the criteria agreed to by the Government of India, WHO, and UNICEF with respect to availability of a physician, other staff, building, and assistance from the UNICEF. Slow development of the PHC network was mainly explainable by insufficient funding from the states and failed to maintain the high state of population immunity achieved by the mass vaccination (Tatochenko, 1968).

The start of the mass vaccination program was not free of shortcomings. Thus, the smallpox transmission was not interrupted in Delhi despite a high (84%) reported vaccination coverage. When double checked, the actual coverage with vaccination and revaccination was only 63% with 86% of positive vaccination reactions. Thus, 45% of the population remained susceptible to smallpox. This was associated with incomplete registration of the newborns and a considerable inflow of migrants. The delay with reporting of

new cases and insufficient work with contacts also contributed to the spread of smallpox: for each imported case, there were 3.6 secondary cases. The correction of these flaws in the city reduced the case number from 470 in 1963 to 69 in 1964 with only two secondary cases per one imported case. In other regions of the country, the vaccination coverage was 76–84% and in some districts, less than 50%. This was the reason to continue the program for another 2 years.

By mid-1965, 45 million people were vaccinated and 326 million, revaccinated, thus bringing total coverage to 78.4%. In 1964, only 10 000 smallpox cases were recorded (2 per 100 000 population). By 1966, the total coverage of population increased to 83%; by March 01, 1967 over half billion people were vaccinated.

Despite these impressive figures, the smallpox program did not achieve the state of eradication, first and foremost, because of a poor "maintenance phase". The number of vaccinators in many regions did not exceed one vaccinator per 25 000–75 000 people, whereas the minimum appropriate ratio was 1 : 10 000–20 000. In fact, one vaccination team can vaccinate only 90–95% of a district with a population of 1.5 million. This means that 10% of those with unsuccessful vaccination were supplemented with 5–10% of nonvaccinated. The susceptible layer will increase in the next year by 4% at the expense of newborns, giving in total 18–23% of susceptible individuals, thereby creating the possibility for the infection to spread. Thus, the attack phase should be followed by accurate comprehensive vaccination of both the earlier nonvaccinated people and newborns.

The latter is particularly important because of the specific features in mother-to-newborn transmission of smallpox antibodies. Our (in collaboration with Dr. V. Vishnyakov) data on observation of over 3500 smallpox cases in the foci demonstrate that the transplacental immunity does not prevent newborn morbidity but rather can interfere with the development of vaccinal process. The infants of 0–3 months contracted smallpox and died of it (case fatality rate, 52.7%) irrespective of the maternal vaccination status (Vishnyakov and Tatochenko, 1968). However, the transplacental immunity influenced the vaccination efficiency: the infants with an age to 3 months whose mother had had smallpox were successfully immunized at a rate of 70% versus the children of the same age whose mothers were not vaccinated during the last 2 years—their vaccine take was 82.6%. These data suggested the demand in a total check of the newborn vaccination results and additional vaccination of those with negative results. Another important task was the revaccination of children at school entry and at the age of 10–15 years.

The efforts to train vaccinators allowed for minimization of the rate of vaccination complications: only 21 serious cases (seven of them fatal) were recorded for 250 million vaccinations. The main cause of complications was poor vaccination techniques (involving three to four incisions for children), but these cases were used to discredit the Soviet vaccine by the anti-vaccination group headed by one of right-wing Swatantra party leaders.

In general, the Program has to be considered as a success since it brought about a drastic decrease in smallpox morbidity and mortality in India. In a short period of time, a mass organization was established that included not only field teams, but also an efficient epidemiologic service. The major part of over half a billion Indian population was covered, albeit with some delay, with smallpox vaccination, laying the foundation for implementation of the WHO Smallpox Eradication Program approved in 1966.

The main lessons of the Indian Smallpox Program are the need to strengthen the primary health services in order to maintain the results of the mass campaign; to organize the epidemiological surveillance; and to quickly react to every smallpox case and to conduct vaccination around it. The experience with preservation of the smallpox vaccine (and many instances of its spoilage) was used in formulating of the WHO "cold chain" concept.

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The author of this chapter was serving as a medical advisor to the UNICEF Bureau for Southeast Asia from early 1962 to mid-1965. His terms of reference included the health programs implemented jointly with the WHO. Naturally, the UNICEF could not stay away of the smallpox program in India; its main efforts concentrated on the production of smallpox vaccine and strengthening of the PHCs, which for the first time in the history promoted the healthcare for millions of rural population. Substantial assistance was given to training of the health personnel of different levels from rural midwifes training to the improvement of pediatric and public health education in medical colleges.

The participation in the Indian National Smallpox Program required planning of the PHC development and staff training taking into account the local conditions in different parts of the country. This was conducted jointly with the WHO, Indian Ministry of Public Health, and administrations of the states with particular attention to the level of PHCs' preparedness for the activities they were supposed to perform. As a pediatrician, the author of the chapter could not refrain from looking into problems of child health and child health care in India, as well as from smallpox epidemiology. Some studies were conducted in collaboration with Dr. Vishnyakov, a WHO smallpox adviser from Leningrad and one of the world most competent smallpox epidemiologists. Dr. Vishnyakov for several years was fighting smallpox in Afghanistan, where the situation was hardly better than in India. Since 1963, he was a WHO regional smallpox adviser coordinating the programs in India, Afghanistan, Nepal, and other countries of the region. On his return home, we continued our friendship; he worked until his untimely demise, at the Institute of Influenza.

The supply of the Soviet smallpox vaccine to India was not without problems; some batches remained for a long time at customs, losing their potency. We rose this and other problems and addressed the corresponding Soviet authorities; as a result, two top specialists—Academician V. Zhdanov and Prof. S. Marennikova—visited India and did their best to improve the coordination of activities. Dr. E. Shelukhina, a smallpox specialist, was appointed to the newly created post of the WHO regional bureau. Participation of the Soviet specialists helped in solving of many problems of the Global Smallpox Eradication Program, which started soon after.

On his return home in 1965, the author continued his research work at the Institute of Pediatrics, the USSR Academy of Medical Sciences, in Moscow combining it with the activities in international health as an extraordinary chief of the International Health Department with the Semashko Institute and advisor to the Soviet delegations at the World Health Assemblies and WHO Executive Office. He participated in the monitoring of WHO Smallpox Eradication Program, of its successes and pitfalls, and in discussions and preparation of the WHA resolutions on the subject. The experience from India was of great help in this work.

It should be emphasized that the USSR delegations in supporting of the Global Smallpox Eradication Program collaborated with both the US delegation and Dr. D. Henderson irrespective of the current international situation and the relationship between these two countries. A significant WHO budget for smallpox eradication did not always meet with the approval of some developing countries, which regarded some other programs as having higher priority. However, the consensus of the Soviet Union and United States and their joint resolutions in support of the Smallpox Eradication Program allowed the WHO to bring it to the complete victory in 1980.

A "professional score" of the author to smallpox is also associated with his work as the Chief of the Infectious Disease Department. This department with the Institute of Pediatrics was collecting the children with complications of vaccination; over 95% of them resulted from smallpox vaccination. We always had 10–15 kids with vaccinal eczema, keratitis, and even fatal encephalitis. The eradication of smallpox implied cessation of the vaccination against this disease once the post-vaccination complications were so frequent. Once smallpox vaccination was stopped, the wards for complications stayed empty and were soon closed since other vaccines give very few complications.

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Afghanistan in the Intensified Phase of Smallpox Eradication Program

(The Country and People Kept in My Memory)

V. V. Fedorov

By force of circumstances, I had rather little time to write an essay for transforming it into a real book. Besides I had no opportunity to use any records since I kept no diary being overloaded with routine work in Afghanistan. Therefore, my recollections show the brightest and most important episodes of my 4-year Afghan period of life as well as the meetings with people that my memory has saved for long years.

The decision to send me on the business trip particularly to Afghanistan, probably, was determined by my "case history" with long-term business trips to the Soviet Republics of Central Asia to fight different diseases and, first of all, to eliminate the residual foci of malaria. The global program of malaria eradication in the world was started before the Smallpox Eradication Program. The former with varying success goes on up to now. Upon graduation from the special residency for training to work in hot countries, I changed my work place for the Smallpox Prevention Laboratory with the Moscow Institute for Virus Preparations, which was the WHO Collaborating Center on this range of problems, headed by S.S. Marennikova. Being guided by Svetlana Marennikova, I participated in the trials of the new vaccines against smallpox and methods of their administration.

The clear formulation of the final goal of the eradication program, availability of the means and methods for the fight, readiness of the world community on the proposal made by the USSR to unite the efforts and resources have made the Smallpox Eradication Program feasible. For the Soviet Union, the work was headed by Prof. Marennikova and the team she formed. This impression was confirmed by the character of negotiations on the matters of scientific and organizational components of the Smallpox Eradication Program with its leader Dr. Henderson (United States) during his visit to Moscow. The cooperation and confidential relations of Prof. Marennikova and Dr. Henderson, representatives of two superpowers, people with brightly expressed features of strong leaders, young, full of energy,

Vladimir V. Fedorov,
an epidemiologist, doctor of medical sciences, and health service authority. He worked at the WHO Collaborating Center for Smallpox and Related Infections and as a WHO expert under the Smallpox Eradication Program in Afghanistan (January 5, 1970–February 24, 1974). Later, he was a member of the Soviet delegation at WHA and other events arranged by the WHO. He was a counselor with the Permanent Mission of the USSR at the United Nations and other international agencies in Geneva (1983–1989) and worked in different structures of the state service of the Russian Federation

and beautiful personalities in the best way possible symbolized both the importance of the set up mission and the reality of its achievement.

During my briefing at the WHO Headquarters and the Regional Office for Eastern Mediterranean Countries, the opinion was repeatedly expressed that Afghanistan taking into account the level of its economic development still remained "the last bastion" of smallpox on the globe. According to the classification stated by the UN, it was included in the group of six "less developed countries among the developing countries of the world".

My information about the country (before my coming in the beginning of 1970) was confined to some reference data. At that time, Afghanistan was a constitutional monarchy in Southeast Asia. Its area was 647 500 km^2. As of 1968 UN estimate, the population was about 16 million people. More than half of them were Afghans in the South; Tajiks, Uzbeks, and Turkmen in the North; and Hazara in the center. The official languages were Afghan and Dari (Farsi). The prevalent religion was Islam. The agrarian population exceeded 80%. The level of health care could be characterized by such a criterion: one doctor had to take care of 21 thousand of inhabitants. Afghanistan is a mountain country divided diagonally into its north and south parts by the Hindu Kush Range of mountains, covered with permanent snow. The climate is continental and dry. Soviet Russia was the first country that established diplomatic relations with Afghanistan in 1921 after the victory of Afghanistan over England in the third invasive war against it. Afghans mentioned the fact very often. That helped us to establish good and sometimes trustful relations.

I came to Afghanistan in the status of a WHO's advisor in the January of 1970. I was waited for. An old desk was given to me at the Ministry of Health. And that was all.

By the time of my arrival, a number of measures for preparation to the transfer to the intensified smallpox eradication program were made. The General Director for the program was appointed. The country was divided into four operative zones named according to the largest city in their territory: Kunduz, bordering the USSR; Herat, adjoining Iran; and southern Kandahar and Kabul at the border with Pakistan. The management centers were organized in the zones and the national directors as well as the middle-level WHO staff (paramedics) were appointed. In Kandahar and Kunduz, the directors were L.I. Chicheryukina (Soviet Union) and Kin Mou Ai (Burma). Only in Herat zone, the special unit to control smallpox was not organized since it included four provinces with a low population density bordered with Iran, free of smallpox at that time. We visited the area to inspect the work of medical service units from time to time. The WHO satisfied the needs of the program in transport vehicles, deliveries of materials and equipment, and payment to the local staff for field work. The Soviet Union supplied the smallpox vaccine for the program.

I was entrusted to participate in forming of the Kabul operative zone, which comprised 11 provinces housing about 60% of the overall population of the country. Nothing happened during several days after my arrival, and Dr. Clement (France), the WHO representative in Afghanistan, advised me to familiarize myself with the situation in the operative zones. I would like to emphasize his large administrative and moral support, especially valuable during the first days of work in the unknown country. At our first meeting, he asked me whether he resembled anyone in my opinion. I supposed that he looked like Russian writer Turgenev and it was the point; this served as an occasion but not the cause for establishment of good working relations. Many times he protected the program from the attempts to use its human and technical potential for some other purpose.

Time passed but the problem of opening of the Kabul zone was still unsolved. Once National Director of the program Dr. Darmangar proposed that all his family and I should spend a weekend in the country. I said that I have not so far deserved the right to have any rest. Dr. Darmangar was astonished why I should be responsible for their bureaucratic red-tape with opening of the zone: "the red-tape is yours and Dr. Henderson would make his claims addressed to me but not to you". Two days later, Dr. Salekhy was appointed the Director of the eradication program in Kabul and as the process advanced. The self-

Movement of mobile teams for mass vaccination in the Kabul zone

sacrificing and honest work of the young Afghan doctors induced and allowed for the same work of their subordinates. Together with my colleagues, especially with the Director of the Kabul zone, I managed to visit the farthest and hard-to-reach districts, moving in jeeps, on horseback, or on foot.

After the decision to open the Kabul operative zone, we organized the director's office, mobile teams of vaccinators, and mobile groups of controllers; adjusted the vaccine storage system; and so on. The intensive training and improvement of professional skills of different categories of workers engaged in the Program were organized. By the time of Dr. Henderson's arrival (3 months after my arrival), the program was completely deployed in the Kabul zone and, correspondingly, in the country as a whole. In addition to a great stimulating effect, the visit of Dr. Henderson to Afghanistan strengthened the role of the active epidemiological surveillance. Dr. Henderson made essential changes in the report system relevant to the program activities. The system was simplified. In addition, it contributed to an increase in the reliability of the obtained results, eliminating any chances of accidental errors or any falsifications.

The completion of the intensified phase of the Smallpox Eradication Program revealed a number of its drawbacks and specific features poorly noticeable in the latent period. I faced the consequences of one of such errors just in the first weeks of mass vaccination of population in the Kabul zone. When planning the schedule of activities, the developers of the campaign had not considered the great differences in environment even in the neighboring provinces. One medieval Arabic traveler said about it better than others: "At the distance of two hours from Kabul one can find himself in a kingdom of permanent snow and a kingdom in which it never snows". The performance of our campaign in the mountains in winter despite the incredible difficulties and deprivations could not provide an adequate coverage of population with vaccinations, since many villages were inaccessible because of plenty of snow there. Besides, a part of inhabitants at that time of the year were engaged in distant-pasture cattle rearing in the terrains with warm climate, that is, in plains. My fair voluntary decision to immediately and completely change the order of priority of the immunization campaign in provinces did not meet any objections and even comments from both the Afghan governmental authorities and the WHO.

In my view, it was not the best decision made by the developers of the eradication program to send two women to the regional management bodies of the program activities. It was supposed that they would

promote a more complete coverage of women with vaccinations. However, the specificity of the country was not taken into account in this case. Travelers often called Afghanistan "the country of men" when sharing their impressions about this region. In fact, one could always see a lot of children and men with a proud bearing, often armed, in the streets of villages and towns (except for Kabul) and only most infrequently, a few timid figures of women in dull usually black hijabs during our trips through the country. Field parties of vaccinators were completely staffed with men and any attempts to include women in them turned to be a failure. Besides, two female paramedics were obviously not enough to implement the vaccination. The reality showed that the principal task of the WHO women workers (by the way, of men workers as well) was to give the advice to the national directors (doctors). That is why the successful work of two foreign female paramedics in "the country of men", say the least of it, may be called really heroic. In reality, the Afghan women did not play any considerable role in the transmission of smallpox in this country taking into account their secluded way of life, although they naturally also wanted to be protected from smallpox.

In particular, I want to emphasize that Chicheryukina enjoyed merited respect of her Afghan colleagues as well as WHO staff and other international organizations. Dr. Henderson in his letter of May 15, 1970 on the results of our trip to the Kunduz area expressed "his special gratitude for the good training of the Afghan participants of the program and the enthusiasm with which she performs her work". Using the high style (very valuable for workers in the field), the assurance was expressed that "the Northern Queen in her isolated kingdom would manage in short terms to achieve the reduction in smallpox morbidity rate down to a 000 level" (to reach the Kunduz zone from Central Afghanistan, it was necessary to surmount the Salang Pass, about 4000 m above the sea level).

Later, on completion of the contract with Chicheryukina, her functions were transferred to me. The program in the Kunduz zone, where the smallpox transmission had already been terminated by that time, was controlled by means of periodical trips. In the south where the threat of infection from Pakistan still existed, Mr. Agly (United States) was appointed to the post of Kin Mu Ai. He had the experience of work in different WHO programs in other countries.

Undoubtedly, the eradication program turned to be successful because the use of a simple inexpensive and efficient method of vaccination with the help of a bifurcated needle. I would like to emphasize the fact that this vaccination method was introduced everywhere in Afghanistan over 3–4 months. Several semi-automatic jet injectors of the American production (comparable in its cost to a Volkswagen Beetle) were earlier shipped from the WHO Headquarters for the program. Wide trials of these devices produced abroad and in the Soviet Union were held in our country under the aegis of the Moscow WHO Collaborating Center on Smallpox and Related Infections with the WHO support. A high efficiency of this vaccine application method was demonstrated, especially for immunization of large organized groups of population: schoolchildren, students, military men, and workers of industrial facilities. According to the published data, the use of these injectors in African countries for mass vaccination against smallpox and a number of other infections has shown to be highly efficient.

The only case of a successful application of the injector in Afghanistan known to me was the immunization of all members of the two chambers of the Parliament and officers of its Secretariat, which I personally did, since the Afghan doctors did not want to either deal once again with their deputies or with this "tricky" machinery.

The mass vaccination required mainly an individual approach and was implemented in a family-to-family manner. Many of the households directly proved the English proverb that "my house is my fortress". As a rule, it was necessary to give a delicate and patient explanation of the harmlessness and importance of vaccination against smallpox to obtain consent for vaccination. It was required to obtain a permission of a headman of a village and a mullah to make the action.

In the course of program implementation when its practical significance became ever more evident, the visits of our vaccination teams more and more often caused gratitude of the local population and

A talk with a mullah about the purposes of mass smallpox vaccination
(Helmand Province of the Kandahar zone, spring of 1970). V.V. Fedorov is on the left

full support of the local authorities. It is worth mentioning that it considerably expanded the information resources of the program since the local authorities and the population became involved in the process. The number of cases when the population informed about the diseases suspicious for smallpox considerably increased. Every such case was obligatory examined in any site of the country with participation of WHO workers regardless of the results of examination by local healthcare workers.

Despite the great improvement of smallpox diagnosis in the country, only part of the suspected cases was noticed by the local health authorities. For example, I would like to mention an episode that happened during my planned inspection trips over the country to the city of Khost, at the border with Pakistan. I found that batteries in my radio ran down. There were no batteries that I need in the first small shop and its owner after having invited me to sit down to drink tea went to search for wanted goods in the neighboring small shops. While waiting for him, I began to scrutinize his dwelling. Among many photos of the relatives on the walls, all of whom were very serious bearded men, my attention was attracted by a photo of an Afghan whose face seemed to be familiar to me. I recalled that I saw the same photo before in one of houses in Kabul during my examination of a patient with smallpox. The owner of the small shop said that it was his brother and a few weeks before he visited one of nearest villages. We examined this village and immediately found several dozens of unregistered old and new cases of smallpox, unknown to the local authorities. Naturally, the prompt anti-epidemic actions began in the district.

We think it expedient to mention two most vivid characteristics among different ones that we used in our work and reports. The first one is an increase in the number of smallpox cases from 250 in 1969 to 1044 in 1970. This fourfold increase in the annual smallpox cases at the beginning of the intensified phase, when a cyclic reduction in morbidity rate was expected, was the direct consequence that the search for the new cases became more efficient. The second one demonstrated a change in the epidemic situation and marked

Vaccination of a traveler met in the Paktia Province

the beginning of the end of infection transmission in the country during the first 6 months of 1973. Only 25 cases were registered in the year. The age composition of smallpox patients changed: traditionally, most cases were recorded among children, which were the focus group for mass vaccination; however, an increase in the specific weight of adult smallpox cases was noticed on the background of reduction in the total morbidity rate; moreover, only a comparatively small part of this cohort remained unprotected being either recovered after smallpox, vaccinated, or variolated.

The combat with smallpox in the disease foci comprised vaccination of the overall local population regardless of whether it was covered by mass campaign or not. Repeated visits to the foci became obligatory until the fact of eradication there was verified. In fact, our activities at the foci were limited to that. Hospitalization of smallpox cases in the local foci was often a greater threat of infection transmission than the refusal of hospitalization. An example is my first meeting with natural smallpox (variola) in Pakistan on my way to Afghanistan, where I was sent by the regional WHO office on my own request since although being a WHO expert I had seen human smallpox cases only in pictures. Accompanied by the local physicians, who covered their faces with handkerchiefs, I was escorted to a hangar in Karachi and entered it alone. It was hot inside and about 40 patients were lying on the floor on mattresses. They were at different stages of the disease with different degrees of severity. I found several persons among them with evident signs of chickenpox. I told the physicians waiting for me outside about it. I did not see these persons when I visited the hangar once again. The physicians told me that these patients were transferred to the wards of the main hospital building where the chickenpox patients were kept! I reported the episode to Dr. Adib-zade, a WHO advisor in Pakistan, who arrived to Karachi. At the same time, the WHO Headquarters ordered him to engage me in the search for the source of smallpox infection of a German hippie who brought the smallpox to Germany. The only thing we knew was his name and the fact that before his return to Germany he stayed in Karachi for a few weeks. Our intensive search allowed us to find the source of his infection in the poorest quarters of this multimillion city; moreover, we found there a large focus of smallpox unknown to health authorities. Afterwards, it emerged that 19 hospitalized people contracted the disease from him. After such lessons, it seemed to me that I was quite ready to work in Afghanistan.

The specific feature of the epidemic situation in Afghanistan was the method traditionally practiced by mullahs for smallpox prevention by variolation. Scabs of smallpox lesions, ground and suspended in water, were used for inoculation. The suspension was applied intracutaneously with needles connected with each other, i.e., similar to the modern method of inoculation with a bifurcated needle. Sometimes the fluid content of pustules was used. However, the procedure in some cases was accompanied by development of a generalized infection. The man-made smallpox focus thus resulted. The mullahs making variolation

moved along the country from one village to another and for a very low payment "vaccinated" all people who wanted. They often appeared in smallpox foci earlier than we did and contributed to either liquidation of a focus or transformation it into a fire. Any attempts to forbid this practice were inefficient because of a high authority of the variolators. The way out was withdrawal of the inoculation material and their replacement with the modern prevention means. The activities of variolators gradually ceased.

During the early stages of the program, we faced the problem of nomads which was either absolutely unknown to the program developers or they just did not take it into account considering of no importance. As for the Afghans, this cohort was not at all exotic. We paid attention to nomads and little by little began to understand their role in formation of the epidemic situation in the country, mainly by bringing the infection from Pakistan. The published data about this population cohort were scanty. According to the information obtained from Kabul University, the Ministry of Internal Affairs of Afghanistan, Ethnographic Museum, and several other sources, the number of nomads exceeded 2.5 million. Their main occupation was cattle breeding. On the average, a family owned 200 heads of cattle and small animals, several dozens of camels, and other pack animals. Nomads spent winter in the plains of Pakistan to move to high mountain pastures of Central Afghanistan in the early spring. They covered about 20 kilometers daily except for aged people and small children. The women (without hijabs) went together with men, who were armed with barreled rifles manufactured in all times and by all peoples. The checkpoints that we arranged for examination and

Dr. Dardmal (left) checks the results of mass vaccination in a remote high mountain region of Nuristan

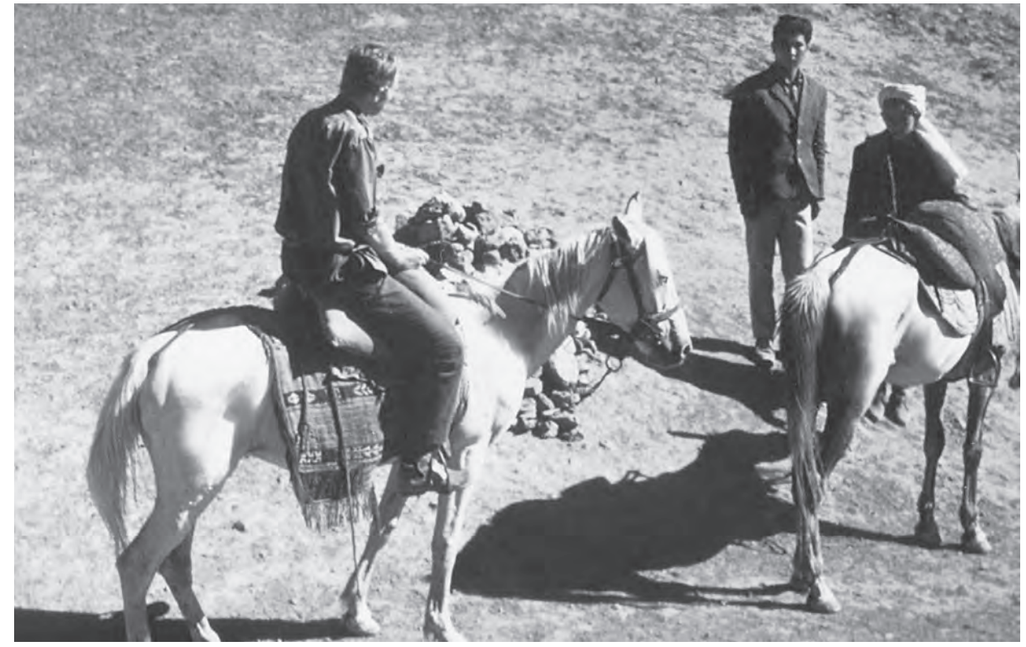
A smallpox case of a girl revealed in a Hazara family; repeated visit demonstrated that it was fatal (Central Afghanistan)

An inspection trip: crossing of the Panjshir River

vaccination of the people on way of their movement turned to be of low use, since nomads used many paths in the open terrain rather than the main roads. I well remember the time when Mr. Agly and I standing on a low hill saw a cloud of dust moving towards us. It covered the entire horizon. The nomads moved their herds. Perhaps, this picture was similar to that seen by the soldiers of Iskander (Alexander) in their battles with huge armies of Persians, we decided. According to the proposal by Mr. Agly, we organized several mobile teams for active epidemic surveillance and vaccination of nomads during their stop or at their camps.

One more part of my stay in Afghanistan is of interest. It seems to have nothing to do with the program mission. In the evening of my very first working day in the country, the WHO management in honor of my arrival arranged a large reception and invited the heads of all 28 diplomatic missions in Kabul. The invitation was accpeted by all ambassadors except one. My first meeting with the Ambassador of the Soviet Union took place approximately 18 months later, after the Prime Minister in his talk with the Ambassador highly appreciated the work of Dr. Fedorov.

The inattention to my work on the part of the USSR Embassy might be explained by the fact that the Soviet Union at that time was the major trade partner of Afghanistan. The large number of large-scale projects was implemented with the assistance of our country both in the field of the local industry, agriculture, urban construction, road construction, and development of irrigation systems and educational programs on site and in various institutions of the USSR. Our physicians worked in many hospitals. A team of Soviet specialists in malaria actively worked in the north along the border with the USSR. Our specialists usually worked within large groups and took part in various joint activities. Except for me, only



There is no traffic road ahead. I had to learn basic principles of riding astride (Central Afghanistan)

a few individualists sent for some international missions under the UNDP (United Nations Development Program), UNESCO, and FAO. The office of economic advisor with USSR Embassy to which we belonged often held meetings of advisors, naturally, in its working hours. This made difficulties for me because I had to participate in urgent anti-epidemic actions when “any delay is similar to death”. Thus, I asked to invite me for these sessions only after the end of a working day. After several requests of this type, I never again had to take part in these sessions. A propos, the subject of the last session that I attended was “The problems of the large block construction in the USSR”.

In other words, a very limited set of people was aware of my work. My direct curator was an officer of our Embassy, comrade Ezhov[1] (one of the best experts on the problems of Iran and Afghanistan). He helped me in my work in every possible way. Once some officers of the Ministry of Health of Afghanistan asked me to assist them in renewal of vaccine deliveries from our country. The reserves of the vaccine were exhausted. As for the Government of Afghanistan, it was ready to address the UN with the request for an urgent delivery of the vaccine from another source. I was not informed about this critical situation since the vaccine was delivered free of charge under a bilateral agreement between our countries. I managed to find out that a person from the office of the USSR economic advisor had thus decided to accelerate the repayment of debts made by the Afghan party for a batch of sugar imported earlier. An active actions of my curator, who in series of phone calls and negotiations as if joking used “the notorious potential” of his family name, has led to a quick restoration of the Soviet vaccine supply program.

[1] Nikolai Ezhov was the People’s Commissar for Internal Affairs of the USSR (NKVD) from 1936 to 1938; however, they were not relatives.

An event when a smallpox patient came himself to be registered by an epidemic surveillance team (a village in the vicinity of Jalalabad)

I suppose that many our specialists (and not only ours) who worked in international organizations had certain difficulties in keeping a balance under conditions of frequently conflicting interests and claims made by different parties of the international cooperation. Coming back to the program, I would like to emphasize that it was always supported by the leaders of Afghanistan regardless of its state system or political situation. The example of it is my own experience. I was the first of the foreign specialists who was officially authorized to go out of Kabul and to visit any regions of the country despite of imposing the martial after the coup d'etat in 1973.

A few years later on my return to Moscow and the confirmation of the smallpox eradication in the world, I was awarded the gold medal for participation in smallpox eradication by the Government of Afghanistan. The award was handed by the Minister of Health of Afghanistan during an official visit to our country. (When I was in Afghanistan, Dr. Omar was a deputy minister.) The minister said that the decision to award me was approved by the King and it was then confirmed by other representatives of the leaders of the country. Such award was conferred to several foreign participants of the program, namely, Dr. Henderson, the head of the Global Smallpox Eradication Program; the head of the Regional Office at the WHO for the Countries of Eastern Mediterranean (Dr. Taba, Iran); and the heads of the Regional Smallpox Eradication Program (Dr. Shafa and Dr. Hajan, Iran) as well Dr. Rangaraj, an Indian expert (he was the last person who took part in the preliminary phase up to the official statement on eradication of smallpox all over the world).

Only now I began to realize that many erroneous tactical approaches of the initial plan of actions, which we had to correct already in the progress of implementation of the program, were not accidental but rather systematic. The initial version of the program was intended for a mass vaccination on the plain terrain with a high density of the non-Moslem population (say, the jet injectors and the women participants sent to work under the field conditions), while the principal type of economic activities in Afghanistan was cattle breeding rather than crop farming. Even the system of reporting was intended for another level of health care development.

As is mentioned above, at the very beginning of our work, we had to face the fact that developers of the program had not considered the specific features of Afghanistan in many respects: its natural conditions,

customs, and morals of its population. Nevertheless, we have managed to cope with these problems. The proof of more serious consequences of similar errors, I deeply regret to say, at present are unsuccessful efforts made by individual foreign countries or their coalitions to impose their will to peoples of Afghanistan based on their best intentions, perhaps.

Now I became convinced that the program originally had pronounced "Indian features". It may be explained by the fact that Afghanistan just before the beginning of the intensified phase of the Program was included into the region of Eastern Mediterranean because of the sudden change in the political situation in the Southeast Asia with its regional office in Dehli, where it had been before and where the draft program had been developed. The success of the Smallpox Eradication Program in Afghanistan and all over the world was mainly determined not only by its correct strategy and tactics, availability of required resources, and means, but also by considerable operating flexibility and ability to solve scientific and practical problems arising at all levels of its implementation. In my case, if all specific features of Afghanistan had been taken into account in the draft program, the character of my recollections would undoubtedly be quite different.

In conclusion, I would like to describe my first impression of Afghanistan. It was growing dusky. It was cold especially after Pakistan, since Kabul is located at a height of 2000 m above the sea level. I was met by a small group of Afghans in the airport. We shook hands. Why do I consider this event so important? This is because one of the persons who came to meet me was my future driver Assadoulla. I always added "khan" to his name with profound respect regardless of his youth. During the time when I was in Egypt and Pakistan on my way to the place of my assignment, all drivers appointed to serve me clad in new jackets of a military pattern and caps always stood still like upon the command "ready" near the back doors of their cars but Assadoulla-khan just shook my hand. We have worked together all the 4 years and without particular proofs of his devoted friendship I would not participate in work over the book now.

The medal awarded to a group of national and international participants of the Smallpox Eradication Program by the Government of Afghanistan

Smallpox Eradication Campaign in Pakistan and Ethiopia

G. D. Suleimanov

Through the 4-year span of my staying with the Global Program of Smallpox Eradication, I was witness to a superficial understanding of its meaning and essence. I recollect one episode that occurred during one of my annual leaves, spent in Moscow. Here, in the corridor of the Ministry of Health, I incidentally came across one of my mates from Martsinovsky Institute. On his query about my work in Pakistan, I started to talk but soon was abruptly interrupted by his peremptory remark: "Oh, I know, I know—you were there just roaming over hills and vaccinating people".

But significantly more surprising, and shocking, for me and other young WHO staff members was to meet with strikingly skeptical attitudes towards the program from some key persons in the WHO Headquarters in Geneva. One of them, briefing me and Vyacheslav Mukhopad on his way to India, stated frankly that he, personally, had no trust in the success of our venture and believed that we, as epidemiologists, were unable to imagine the problems waiting us in our respective duty-stations. We decided to disregard them.

The WHO in 1967 decided to change principally the strategy of the global campaign against smallpox since it had become evident that mass vaccination in endemic countries did not yield the expected results—interruption of transmission. Instead, the WHO Assembly approved an Intensified Program that was targeted on disease eradication in a predictable future. To strengthen the expertise and the Organization's role in particularly problem zones, foreign specialists would be enrolled for the task. To select the first group of Soviet epidemiologists, the Head of the WHO/Smallpox Eradication Unit, Dr. D.A. Henderson himself arrived from Geneva to meet Ministry of Health personnel. Altogether four specialists, graduates of the WHO Courses on Epidemiology, were selected for the task, namely A. Gromyko, G. Marchenko, V. Mukhopad, and G. Suleimanov.

Gassan D. Suleimanov,
a medical epidemiologist, participant of the Smallpox Eradication Program. In January 1971–May 1973, he headed the eradication campaign in Pakistan; in June 1973–October 1974, was responsible for anti-epidemic activities in Gojjam, Ethiopia, and then in seven provinces in the south and west parts of this country. Thanks to the new developed method, the disease in this region was eradicated by the fall of 1974. Later, he participated in the WHO malaria projects in Africa and Asia

The WHO Courses on Epidemiology, Moscow, 1969. *Right to left*: the first is A. Gromyko; second, G. Suleimanov; fourth, D. Henderson; and fifth, S. Marennikova; *from the left*: third, V. Mukhopad and fourth, G. Marchenko

Smallpox Eradication Program staff policy. Dr. Henderson from Centers for Disease Control and Prevention (CDC), Atlanta, United States was appointed as the first Chief of Smallpox Eradication Unit/WHO HQs.

Some curious circumstances accompanying his official appointment for the post and the choice of an American as a priority of political importance, was disclosed in the interview he gave to the CDC "Oral History" project. According to him, he agreed to accept the appointment against his will, under pressure from senior American Administrators. It should be recognized that this choice demonstrated their wisdom. It was supported by my 4-year personal experiences of direct contacts with him. Excellent specialist, epidemiologist with a vast field practice, extremely hard-working, target oriented, always open to new possibilities and demanding of himself, and, of course, from his subordinates. Staff selection for the program he saw decisive for its success; field fitness of proposed candidates was the most important. Besides the abilities for nonstandard thinking ("imagination potential" and "imagination in solving of current problems") plus physical shape and "thermo-resistance" were required from any program member. I recollect well my astonishment by his persistent attempts to understand my ability to stand heat during our first meeting in Moscow in 1970. As to my lengthy summer expeditions in southern Azerbaijan and Turkmenistan, he only shook his head rather dubiously. His worries I appreciated later on, upon arrival in Pakistan.

The overwhelming majority of personnel were young people in their thirties from national health services and research institutions. An exception should be mentioned—Dr. Kurt Weithaler. Austrian by nationality, Senior Epidemiologist for the Ethiopia Project, he was far beyond his fifties. Beginning in 1972, young people 20–25 years of age were recruited in numbers to support field activities. Most of them were Peace Corps Volunteers from the United States, but also from Japan and Austria. Among them

were some rather exotic personalities. One of the Japanese volunteers assigned to help me in Ethiopia, previously served as a fire-fighter in Tokyo City.

However, the operational and methodological core was formed by trained epidemiologists, whose number reached the figure of 687, from 73 countries with contracts ranging from 3 months up to 10 or more years. The Soviet Union provided 12 epidemiologists (I. Ladnyi, G. Nikolaevskii, A. Slepushkin, A. Gromyko, V. Mukhopad, G. Marchenko, G. Suleimanov, V. Fedorov, L. Khodakevich, V. Fedenev, brothers Bychenko, A. Samostrel'skii, and R. Aslanyan). They served for periods of 2 or more years each. There were also a number of short-term consultants. Particularly of notice was the only Russian woman in the Project, L.I. Chicheryukina, a nurse, who was assigned to work in extremely hard conditions in Afghanistan.

At this point, it would be appropriate to ask was it necessary to deploy foreigners in national programs? In fact, the WHO members approved the resolution that all smallpox-endemic countries agree to establish smallpox programs with adequate structures and material support from the WHO. The international staff in the field was in technical support and advice in implementing the overall strategy.

Author's participation in the eradication campaign. As a staff-member, a WHO inter-country epidemiologist, I served in the two out of five remaining endemic countries on the eve of the 1970s, namely, in Pakistan and Ethiopia. Before assignment, I was given training as a postgraduate in Martsinovsky Institute of Tropical Medicine (Moscow) and then the WHO Courses on Epidemiology in Geneva and in Alexandria University, Egypt.

At the end of 1970, I received the official assignment to Pakistan and the next January left Moscow for duty-station. My assignment was defined as an "inter-country" implying high mobility, prompt transfer, with minor bureaucratic involvement, from one region to another in accordance with decision of the Unit Chief in Geneva. This could, potentially, lead to certain frictions with Dr. Hajian, the senior advisor for the Eastern Mediterranean Office in Alexandria. Actually, I cannot recollect even a single example of misunderstanding. Direct guidance and permanent supervision by Unit Chief in Geneva over field operations proved its efficacy, at least in my case. Recently, when I started to look through my smallpox archives, I found 19 letters, mainly hand-written to me from Dr. Henderson. They were preserved among other documents. It can be assumed that total correspondence was more voluminous. And these messages were not at all short notices but usually rather spacious texts with scrupulous situational analysis and best operational variants. I think this shows perfectly the Chief's rare efficiency and devotion to our common task. It needs to be noted that he maintained the similar correspondence with numerous addressees. Regrettably, in those times postal services were the only mean of communication left for us. It should be kept in mind that 45 years back, cell and satellite phones, printers, faxes, PC and similar devices were still not existent. Luckily, the diplomatic pouches from Geneva were regularly delivered to my office in Pakistan with only 3–4 day delay. It should be emphasized, therefore, that the simple, effective organizational structure and operational leadership directly from Headquarters was the second, after personnel policy, which was a novelty of this program.

Protracted briefing in United States and WHO Regional Office. Prior to my departure to Geneva, I knew there would be delays with my arrival at my duty-station—an air ticket was issued with stops in Geneva–Atlanta–Boston–Cairo–Karachi with open dates. In our first meeting, Dr. Henderson said that the Government of Pakistan decided, for the time being, to prohibit any cross-border movements for foreigners, including international staff. The reason I knew perfectly well. Pakistan armed forces were using all means in an attempt to suppress a national uprising in East Pakistan (my destination was West Pakistan). A new independent state, Bangladesh, was born as a result of fierce fighting.

Anyhow, the WHO could not permit me the luxury of hanging around idly. Thus, after a short briefing by Headquarters staff I was sent on a learning trip to the United States. Some 2 months were spent at CDC

and at the School of Public Health of Harvard University. Particularly, I benefited most from Dr. Thomas Mack who had just returned from Pakistan and from W. Foege, Chief of CDC's Smallpox Unit.

Intensified Program implementation in Pakistan

My first duty-station was in Baluchistan. I arrived at the end of April, 1971. Here, the true reasons for delays became more evident. Factually, the program was not yet existent. Personnel decisions, allotment of office premises, furniture, transport, etc., were taken only upon my arrival in Quetta, provincial capital. Management included my counterpart, Dr. Kamal Khan Mandohel, specialized in surgery, and Mr. Mohammad Balooch.

Baluchistan and Punjab in the early 1970s: some factors essential for the program. Desert–semidesert territories in the country west and northwest were proclaimed as a province only in 1970. Therefore, I was involved, simply due to our activities, in the province establishment as such. Each of Pakistan's provinces enjoyed an independent existence in the matters related to public health.

The public health system was absolutely inadequate. Besides a Central Provincial Hospital there were no more than five district hospitals, each staffed by a single Medical Doctor.

Privately run hospitals in Guadar Town were well equipped and adequately staffed but there were few public health centers scattered over the province. Qualified health services were accessible only in Quetta City.

For Punjab in 1970, there were altogether 14 430 beds available in the state and privately owned clinics, out of which rural health institutions had 174 beds (less than 2%), although 80% of the population here lived in countryside.

For better understanding of the specific problems, the program's most important problem in this province was geography in its broadest sense. Out of Pakistan, 804 000 km^2 belonged to Baluchistan. Most of it represented the lands less suitable for man's survival than in any other place in the world. The rocky dry desert stretches from Mecran coast in the west to the wall of Hindukush Mountains, which protected Indus valley from the desert in the east. Rare water streams dry up in early spring and only rare oases are scattered within distances of 100–150 km from each other. Daytime air temperatures from March till November rarely drop below +40°C. Thus, WHO advisor was compelled to use night hours for driving, brushing aside the security risks.

Communications: there were only two asphalt roads crisscrossing the province from west Iranian border to Quetta in the east and from Afghani border in the north to Karachi in the south. Dry river beds were widely used practically throughout the year, although the risks of sudden floods had to be kept in mind. Regular postal services were nonexistent, as well as telegraph, for the most districts. To alleviate the situation, the Government provided radio transmitters to District Administrators and police stations and distributed a number of transmitters with electric generators among loyal tribal chiefs.

Regrettably, the political background worsened at the very outset of the Program operations. The course of events indicated inevitable collision with neighboring India; all signs showed that both sides were waiting for the end of hot season to start attacks. As it is now known, Pakistani armed forces were defeated by Indian Army supported by armaments supplied by its ally, Soviet Union. Predictably, this defeat caused profound shock and unrestrained civil disturbances all over the country. Frankly, I was prepared for the worst but, surprisingly, neither here, in Baluchistan, nor in other provinces were there the slightest signs of animosity.

Surveillance mechanism foundation in Baluchistan. The new strategy adopted by the Program demanded establishment of appropriate surveillance and, in first turn, case detection, as its key component. Therefore, leaving the Project Director in Quetta coping with personnel recruitment and managerial

At the headquarters of provincial smallpox eradication program in the city of Quetta, Baluchistan (Pakistan), 1971. *From left to right*: Dr. Kamal Khan Mandohel, director of the provincial program; G.D. Suleimanov; and Mr. Mohammad Balooch, administrator

problems, I undertook several routes to farthest corners of Baluchi part of the province—Mecran coast, Punjgur, and Khuzdar Districts. Investigation of several real outbreaks and some false reports were also checked. But the principal task in this stage was to establish a notification network through visits to officials, elders, and tribal chiefs, particularly those with transmitters. In due course, Provincial Governor's Office was asked to issue an order distributed to District Administrators, Levy, and police stations obliging them to notify all cases of suspected smallpox. But this, passive, case notification system was unable to reveal a complete picture. For the purpose, some 20 assistant sanitary inspectors, all young males that graduated the nursing school affiliated to provincial hospitals were recruited to be established in rural Primary Healthcare Centers (PHCs). However, unexpectedly, within days, all people sent to PHCs in the Baluchi part of the province returned back to Quetta. All of them were Pashtuns and simply could not stand the hardships of rural life. Thus, other candidates were hastily hired. Anyhow, before midsummer, a force of 15 assistant sanitary inspectors and superintendents of vaccination together with several dozen vaccinators were available. The WHO provided bicycles to all, although this kind of transport was not very suitable. In each of the 10 districts, mobile groups of four–five vaccinators started the active search for the cases followed by containment operations. In the Project headquarters, five mobile teams, composed of one–two superintendents, two vaccinators and one recorder were formed, using cars or motorcycles. Correspondingly, it could be stated that in a short time, a more or less functioning surveillance was established in the province.

The problem of nomads, common to northern Pakistan, needs to be mentioned. For centuries, caravans of nomads, locally called Kuchis, are crossing the Afghan border on their way to Indus valley in early spring and back in late autumn. Due to their mode of life, nomads were practically deprived of even the scarce health services available to the settled population. Fortunately, nomad routes are restricted by numbered passes and valleys, timing is known. Thus, the duties of one of the mobile teams were interception, interviewing, and vaccination of these groups.

Epidemiological situation in 1971–1972. As expected, the project establishment led to a rise of smallpox incidence in the province. The incidence in 1971 increased 2.5-fold and in 1972, the rise was even more impressive, sevenfold. By the end of 1971, the infection transmission in oases of western desert was stopped with relatively minor efforts.

Meantime, by the spring of 1972, the national program showed more and more anxiety over the state of affairs in Punjab, the largest province with 60% of the country population at that time. The year before, a mass vaccination campaign was carried out. Nevertheless, transmission did not cease. The vaccination coverage was substantially higher than 80% in all administrative units, some of them reported the coverage close to 100%. Therefore, the Chief of Smallpox Eradication Program Unit in Geneva, with agreement from the

Participants of the Smallpox Eradication Program in Punjab Province (Pakistan), 1972. *Left to right*, G.D. Suleimanov, Majid (administrator), and Dr. Mansur (epidemiologist)

national Ministry of Health decided to transfer me from Quetta to Lahore City to take necessary measures. During this period, the civil unrest became extreme in Pushtun populated parts of the country. The WHO adviser field trips now were escorted by police truck, inevitably hampering contacts with local population. Remarkably, my Soviet colleague, Dr. Marchenko, who was in charge of the operations in neighboring Northwest Frontier Province, could not return to Peshawar City and was, instead, sent to Ethiopia.

Smallpox Eradication Program status in Punjab in mid-1972. Officially, I took responsibilities for the Punjab Project activities in May 1972. The situation in this province was essentially different from the one in Baluchistan. The population represented two-thirds of the country, some 50 million people with a considerable proportion of urban dwellers, residing in 23 672 villages. They were about 800 in average population. Communications were satisfactory: each of the tehsils (districts) had telephone and telegraph links with the provincial capital. All-weather roads provided access to any spot by car.

The smallpox eradication activities here had been under the aegis of the WHO for almost 3 years. The total force of 46 different personnel was assigned to the Project by the Directorate of Health, including two medical doctors, administrator, eight assistant sanitary inspectors, statistician, book-keeper, 16 vaccinators, drivers, and 10 servants. My counterpart, Dr. Mohammed Rafique, was a qualified specialist with a solid background of public health service at a district and a provincial level. In districts and municipalities, some 1500 vaccinators were still on the list of the project. Two years back, the WHO provided 1300 bicycles for the province and three–four motorcycles for each district. There was a sufficient stock of the Soviet-made vaccine available both in provincial headquarters and in districts.

Thus, the material and human resources were definitely enough for the project implementation. However, there were understandably bitter feelings prevailing after the recent war combined with meager positive results of mass vaccinations conducted. Then, initially, some time was spent in attempts to raise the people spirits through friendly discussions and training sessions primarily with the project management. New tactics and approaches were talked over and explained.

Establishment of epidemiological surveillance and case reporting system. The WHO advisor realized that surveillance, in the proper sense, did not yet exist in the province. Simply, at the end of each month, the project director was supposed to compile a report based on the reports sent to him, by mail, by the district health officers. At the project director's request, the provincial health secretary issued circular letters addressed to district officers obliging them to report, weekly on a fixed day, to the Smallpox Eradication Project. Telephone messages followed by mail. The reports to the statistician started to arrive, irrespective of the presence or absence of cases during the period. In this manner, 52 weekly reports should be sent by the end of each calendar year to the provincial headquarters. A different reporting form, some of them rather elaborate, included 15 questions to be answered, was the duty of adviser. Any delay with

regular reporting from districts led to inquires, followed by the visit of headquarters team headed usually by adviser or director, or both. This system worked smoothly for a general situation. For the second half of 1972, the project office received in due time 81.4% of expected reports. Weekly summaries were submitted on weekends directly to the Smallpox Eradication Program in Geneva. For monthly reports, diplomatic pouches were used with subsequent copies to the Pakistani Ministry of Health and the Secretary of Health of Punjab. For this report, the foci surveys pro forma for each focus were also added. In fact, these data were used to compile the weekly WHO Smallpox Eradication bulletins.

However, in the early autumn of 1972, I discovered that the national Ministry of Health (MOH) sent to the WHO its monthly report for July, province-wise. To my surprise, the Punjab data differed from those reported by the advisor. I could only assume that the MOH Statistic Department decided to classify as smallpox cases the acutely sick patients with fever and vesicular or pustular rash. Ultimately, MOH was forced to recognize my stand, since practically all cases were detected with my personal participation. The WHO headquarters with SEARO (South-East Asia Regional Office) was on my side, and by their letter of September 27 the order was adopted, which required that only the data provided by provincial projects were recognized as official. This episode proves the utility of the WHO staff presence at a field level since some national governments were tempted to beautify the real picture.

Population immune status. Before the start of the active operations, 3 to 5% of the province population had a history of naturally acquired infection. In 1969–1971, 25 521 904 persons were vaccinated, of which 1157 566 got primary inoculation. Thus, the overall population coverage was roughly 74%. A survey throughout the province demonstrated that only 3.7% had neither pock marks nor post-vaccinial scars. But the figures reflecting the situation in age groups, as well as different social and religious groups were inaccessible. Besides, it was difficult to rely on the results of previous mass campaign vaccinations since the liquid vaccine of unknown potency was used. Nevertheless, the study showed good residual immunity among those vaccinated in the past. Of the 762 vaccinated contacts, only 30 (3.9%) contracted infection, including 10 vaccinated who had been vaccinated 15 or more years before. Of the 255 unvaccinated contacts, 159 (60.8%) became sick. Several "pockets" missed by the vaccination campaign were discovered in large urban areas.

In Model Town, the slum quarters of Lahore, out of the 514 examined, only 40.9% had pock marks or post-vaccinial scars. Among young children, the unprotected accounted for 84%. The district population coverage by mass vaccination was variable, from 63 to 93%, and only 8 of 19 administrative divisions showed 80% or more. Thus, these data demonstrated uneven, patchy population immunity level before the start of the new phase of the program.

Variolation problem. The practice of variolation never posed any real threat. During the entire period of our activities, only a single episode of this kind was registered. Rahim-Yar Khan district reported several importations from the nearby Sind Province. The surveillance team found that five local peasants undertook variolation in nine villages and, in due course, 49 persons developed rashes. Apparently, the neglect of duties by local health authorities, as well as by program staff, was responsible for this outbreak. Adequate measures were taken immediately and subsequent WHO advisor's visits indicated that variolation here had been abandoned.

Operational targets determination. The preliminary population immunity assessments singled out the most vulnerable territories, those with the lowest immunity, as primary operational targets. In Punjab, however, the infection's geographic distribution did not coincide with the territories of lowest immunity. The majority of case reports were coming from districts with the rates of 80% and higher. The data analyses indicated that the capital, Lahore City, constituted the real problem for the program. In 1972, more than 69.0% of provincial incidence was recorded in this municipality.

More thorough surveys of the reported foci revealed the existence of population strata missed in the course of mass vaccination campaigns. Almost all cases came from the slum areas inhabited by poor newcomers from the countryside, "red light" quarters, and populations isolated by occupation or religion such as sewer-system cleaners and Catholics.

Keeping in mind the magnitude of the problem, we together with the provincial program director decided to organize a special Program for Lahore and submitted our plan to the Secretary of Health, as additional provincial resources would be required. The idea was supported both by the province and by the Smallpox Eradication Program Unit Chief in Geneva. At the beginning of 1972, a special program was launched.

Organizational structure of the Punjab Program. In each of the 19 major administrative units there was one divisional supervisor of vaccination and 72 assistant superintendents of vaccination, each of which had a permanent team of up to 30 vaccinators, based on the area's population. In total, the manpower involved in the Punjab Eradication Campaign execution was 1100–1300 personnel.

To illustrate, let us take Sheikhupura Division, where approximately 1.6 million people lived. Under the Divisional Chief Surgeon's operational guidance, a Sanitary Inspector (SI), an assistant SI, and 28 vaccinators were deployed specifically against smallpox. Each vaccinator was attached to four rural Union Councils with a population, on average, of 40 000. The vaccinator's main duty was the registration of newborns and their vaccination within the first 3 months of life. (This system dated to 1885, when the country was under British rule, and was considered to be effective in vaccinating 95% of newborns.)

There were four channels of information in a division. The first, and main one, consisted of 28 vaccinators, who were obliged to report to the District Health Officer (DHO) through the SI, or directly. The others were the 92 Malaria Control Program personnel, stationed all over Punjab; schools; and medical institutions. The schools and malaria personnel were asked to report only suspected cases to the DHO or Chief Surgeon. Special reporting forms were distributed among vaccinators to be sent weekly by mail to the DHO office. The scheme worked rather efficiently, lacking only sustained attention from health authorities. Essentially, the system relied on the sense of responsibility among state employees. This was periodically jeopardized by delayed payment of wages to vaccinators.

A mass vaccination campaign was performed here in 1971. It was well-conducted, and did not leave any sizable missing "pockets". Health services were generally considered reliable. However, in the first quarter of the 1973 intensive campaign, only half of all cases reported were by divisional health services; the remaining were detected through active case search done by the provincial program personnel.

The special program for Lahore City. The difficulties in dealing with smallpox transmission in this city were compounded by the multiplicity of specialized health services independent of the Provincial Health Department, including armed and police forces, railroads, religious groups, and so on. The program director organized several meetings with these services and, as a result, additional personnel with transport became available for a coordinated effort. All personnel received one week training at the Program headquarters.

The problematic slum territories were divided into four operational sectors. One mobile group of two–three vaccinators headed by an SI or an assistant SI was attached to each sector. Daily systematic house-to-house searches with wide use of the WHO colored posters were started. The surveillance groups were instructed to work in places where people gathered—bus stops, cinemas, and markets—with special attention given to private clinics and pharmacies. If a case was detected, the family members and the immediate neighbors were promptly vaccinated. A group of 10 vaccinators was reserved to conduct more extensive circle vaccination when foci were found.

A short digression from the theme. *In Pakistan, the bifurcated needles and Soviet-made freeze-dried vaccine were used. One day, my national counterpart told me that his office was not happy with the vaccine. Its qualities were not questioned; its potency was highest and it satisfied the WHO standards. The problem was opening the vials—the glass was too sturdy. The next day I sacrificed several vials in the presence of the superintendents of vaccination to demonstrate the groundlessness of claims. Oddly, the same situation recurred later in Ethiopia.*

The bifurcated needle proved to be the ideal tool for the work in Pakistan in comparison with the jet-injector. The house-to-house case searches with simultaneous vaccination of family members were the only practical method to guarantee high level coverage. Some specific obstacles were presented by many of the Muslim populations. One was that the newborns were given several names to camouflage them from the devil; the real name was not used until the child was 6 years old. Thus, a lot of time was spent in persuading parents to disclose the children's real names for registration. The second obstacle was the requirement that an adult male of the household be present during team visits. The team revisited missed households 5-6 days later.

For case search/containment operations, an additional force of 75 vaccinators was formed by the Lahore municipality under the guidance of a medical doctor. In August, a short training was given by program staff to this group, part of which was deployed in 14 vaccination stations opened in problem areas.

A talk after the seminar in Karachi (Pakistan), 1972. *Left to right*, Dr. Young (United States), G.D. Suleimanov, and Dr. W. Foege, Chief of CDC's Smallpox Unit (Atlanta, United States)

From the beginning of active operations, the WHO advisor realized that reporting of only two statistical parameters—the number of foci and number of cases—was insufficient for operational analyses. Therefore, a new reporting form included an additional parameter—the promptitude of detection of the first case of an outbreak. The ideal situation was that foci would be discovered within 2 weeks of rash appearance on the first case. Longer delays resulted in spread of infection and the need for more control activities. This innovation was immediately supported by Dr. Henderson (see the letter at the end), who introduced it for a routine use by all Global Eradication Program staff for assessment of operations efficacy.

The Special Program for Lahore City was under the WHO adviser's permanent control; most of his time was spent with mobile teams. One day, two foci were discovered in which the index case developed rash after hospitalization in a noninfectious ward of the Municipal Hospital. A visit to the hospital revealed that the two infectious wards were not effectively isolated. All wards shared the same premises and doors were left open to alleviate the heat. The Central Municipal Hospital was acting as a stable focus of infection, essentially contributing to the maintenance of transmission. The Directorate of Health stopped admittance of smallpox cases to all health institutions of the province.

Here, I would like to mention a more successful method of isolation I found in Baluchistan. In early June 1971, information arrived about an outbreak at the Punjgur oasis, some 400 km from Quetta, the provincial capital. We left Quetta the next morning and upon arrival visited the house

indicated by the local assistant health inspector, but found it vacant. Neighbors explained that the whole family, including the healthy members, had moved into the desert. We went on foot to the place, about 2 km distant, and discovered, in sandy dunes, a make-shift tent, where the family of seven was residing. There were three patients, one convalescent, and two with crusts. Food and water for the family was regularly provided, without coming into contact with the patients, by relatives and neighbors. All belonged to the Gulam ethnic group, occupying a separate sector in Punjgur, with minimal interrelations with the other oasis populations. They have Negroid features and are said to be descendants of slaves brought centuries back to the Mecran coast by Arabic merchants. A thorough survey of the Gulam sector proved the absence of clinically ill or convalescent cases. Nevertheless, the total population of the sector and of the selected adjoining streets was vaccinated. There were no more reports from this oasis.

An intensified phase in Punjab was initiated at the end of June 1972. Very soon, there were positive results. For the first 2 months and at the low transmission season, some 396 cases in 52 foci were detected (94.1% reported by the program mobile teams). The foci detection rate for the first 4 months of active operations increased substantially—156 (65.5%) of 238 foci were detected within 1 month of symptom development in the index case.

In the middle of October, like a bolt from the blue, a sizable outbreak was discovered in Kumharpura, a city slum area. The most disturbing was the fact that this particular outbreak was known from the beginning of the intensified phase and all necessary measures were seemingly taken. Nonetheless, transmission recurred two months later and spread to nearby slums in the cantonment. The investigation confirmed that infection had continued to smolder here unabatedly. Only in March of the next year, the outbreak was finally extinguished after a house-to-house search and vaccination done under the daily supervision of the WHO adviser.

Smallpox diagnosis at field and mortality. Smallpox symptoms were well known to the native population of Pakistan. Only in three cases I was compelled to send materials for laboratory confirmation.

The mortality in Punjab Province according to the available data ranged from 13 to 22%. But mortality rates could be higher; local healthcare personnel may be unable to confirm a cause of death because of the necessity for a funeral before sunset. Death occurred only twice in my presence. One case was the small girl described previously. However, a more profound impression is still deeply preserved in my memory—the death of a young man from Baluchistan.

One day, during a case search in a Tribal Belt village of Baluchistan, one of the villagers, an old man, asked me through an interpreter to examine his sick son. He believed that only a foreign doctor could help him. We agreed to visit his house and when I stepped into the room, some time was needed for sight adaptation. The windows were shut because of the local belief that darkness was good for a patient's recovery. When I adapted and asked to open a window, I saw a terrible picture. There was a young man lying on a bed. He was totally black with skin covered by numerous knobs. They resembled crocodile skin to the touch. They were incompletely developed pustules. His eyes and teeth were particularly distinct in the dim light of the room. The young man had fallen ill 4 days before. He was fully conscious and able to communicate. This was a case of hemorrhagic smallpox, the so-called "black smallpox". With heavy hearts we left this house, feeling complete powerlessness. The next morning the young man died.

By the spring of 1973, active measures aimed at detection and containment of the foci brought the expected results—the absence of smallpox infection in Punjab Province. In March, the traditional peak of smallpox, only eight cases were registered—in the previous year, this figure was 202. Half of these eight cases were importations from Sind Province, where an epidemic was raging. The four remaining cases were infected in the capital city of Lahore. The first case was reported from Gujranwala town,

The active search for smallpox foci with the help of WHO posters, Punjab Province (Pakistan), 1973

80 km north of the capital, detected in due time and contained properly. The second case was traced to the Central Municipal Hospital where smallpox admissions still continued in violation of the order. From this patient, two more residents of the cantonment contracted disease, the latest one being detected on March 21.

To confirm the interruption of transmission, a mass screening of potentially vulnerable localities was launched on March 14. During the next 6 weeks, 96 villages in the vicinity of Lahore and 46 quarters in the city itself were surveyed; 19 mosques, 18 schools, 75 cafeterias, 19 private clinics, and 4 PHCs were visited. The participants visited 958 households and interviewed more than 20 000 persons, including 3120 schoolchildren. During this search, only a single case was found. During the next month, only three cases were reported. All cases proved to be imported.

By the spring of 1973, the Program Headquarters in Geneva became more confident of the improvement in Punjab and Dr. Ehsan Shafa in his letter of April 6 asked the WHO advisor to support the activities in Sind Province. This had unexpected negative consequences for the Program in Punjab. In the advisor's absence, the Directorate of Health effected a complete administrative reorganization, under the assumption that smallpox in the Punjab was under control. The national program director no longer reported directly to the Secretary of Health, and was required to seek pre-authorization for all field trips. I tried in vain to convince the authorities that the magnitude of control measures should be increased not reduced, at the lowest level of transmission. Smallpox transmission continued in neighboring provinces and the risk of reintroduction was high. Active searches by the program staff were responsible for identifying no less than the half of Punjab's outbreaks. Simultaneously, both Dr. Henderson in Geneva and Dr. Hajian in the Regional Office were informed but their attempts to revive the program were equally in vain.

My forebodings were realized at the end of the year, when in November several outbreaks were reported from Lahore and districts. The Secretariat of Health was forced to restore the Program and the renewed activities succeeded in the final smallpox elimination throughout the country in August, 1974.

As the recognition of my personal assistance in this achievement, the WHO and the Government of Pakistan sent me official praise and congratulations.

The fight with Smallpox in Ethiopia

In June of 1973, after a short briefing with Dr. Henderson in Moscow, I arrived at my new duty station in Addis Ababa. The new appointment was absolutely different from the previous program, starting with the countries general characteristics.

Terrain, population, communications, health services. The major part of the country occupies the massive mountainous central plateau; some heights reach 3000 m and more above the sea level. In the

southeast, along the border with Somalia, is the Ogaden desert. There are two distinctive climatic seasons in the country: dry season, from September till April, and wet season, from May till August, with regular torrential rains.

The population consists of numerous ethnic and religious groups, the most numerous of which are Amhara, Galinja, Wollega, and Tigrinja, mountain residents. The Ogaden desert is sparsely populated by nomadic Affars and Issas and the savannas, by Nilotic groups. Christian Orthodox Church followers are most numerous but Muslims and pagan tribes prevail in many provinces. The Amhars, source of the hereditary ruling dynasty, claimed to be dominant and could be proud to obstinacy and less cooperative with outsiders.

The population is dispersed all over the country. The typical landscape is represented by tukuls (huts) separately standing in fields. After sunset, the family members and their stock (cattle, chickens, etc.) gather under the roof, shutting down the door for security reasons. Villages are rare and most of them are spread along main roads.

All-weather roads link the country center in Addis Ababa with all provincial capitals, but usually only the first 100 km are asphalt; the remainder is gravel. In the rainy season, long trips off the main roads are possible only on horseback or, preferably, muleback. For the program staff, this was the most important factor hampering the work. In addition, the WHO staff, due to the lack of personnel, frequently traveled alone and, of course, unarmed. Minor incidents were inevitable. I myself was robbed twice in the middle of the road. To survive in the field, all of us were forced to develop the physical qualities of cross-country racers.

> *One episode is engraved in my memory. One day, our group of four (two local assistant sanitarians; John, our tall bright Peace Corps volunteer; and me) went to investigate a report from a village 40–50 km west of the Lake Tana. It was in the dry season, so we could use a Land Cruiser. Local people on the main road gave us directions and we started across the savanna. Eventually, we sighted our destination, a small village located on the opposite side of the river, over which a wooden bridge was thrown. But there was a problem—the bridge was made of thin eucalyptus logs, 7–8 cm in diameter. We had serious doubts that the bridge could withstand the car's weight, but decided to take the risk and moved on cautiously. The front wheels had reached the far end of the bridge when I felt something wrong and exclaimed. John promptly pressed the accelerator and we found ourselves in safety. When we looked back, the right side of the bridge was gone.*

The practical absence of telecommunications was a factor that seriously impaired adequate coordination of activities in the field. In the autumn of 1973, the Government of Japan provided a number of powerful radio-transmitters and installed them in all program cars. Now, the WHO advisors could contact the radio center at headquarters and exchange operational news with each other from the remotest corners of the country.

Ethiopia was a classic pastoral country with negligible industry. Cattle breeding and cultivation of tef (a local variety of millet) were the principal occupation of the majority of the population. Droughts and starvation occurred with appalling regularity.

The general health profile of the population was typical of many African countries with regard to communicable and noncommunicable diseases. Typhus was a major problem and, in the central plateau, from one-quarter to half of all hospital admissions were typhus patients, with accompanying mortality. In the lowlands, tropical malaria with high death rates was endemic.

Smallpox, although found countrywide, was the variola minor variety, which had a relatively low mortality rate. The perception of smallpox as relatively harmless was a major stumbling block in implementation of the Program. (Dr. Weithaler's personal intervention with the Emperor was instrumental in getting government support.) Variolation was widely practiced as a control measure, while vaccination was sometimes associated with ill effects, such as stopping the milk of nursing mothers.

The Program's organizational set-up. The lack of the national counterparts to the WHO staff required special organizational features. Due to the scarcity of personnel of even elementary qualification, the Government could assign only assistant sanitarians in the provinces to cooperate with the foreign staff. In June 1973, when I arrived in Addis Ababa, the WHO program chief/senior epidemiologist was Dr. Kurt Weithaler, a remarkable personality who in his youth fought in the Wermacht against us, Russians, on the Eastern front. Before his selection for the smallpox program, he had been Chief Surgeon to the Emperor's bodyguards and the Emperor's family doctor. The WHO group included Drs. Petrus Koswara and Ciro de Quadros from Indonesia and Brazil, respectively. Dr. Genadii Marchenko of the USSR spent almost a year with the program but departed just before my coming.

Ethiopia was the only endemic country where mass vaccination was not even attempted. The program personnel were involved exclusively in the case search/containment activities. The surveillance teams included US Peace Corps volunteers and some volunteers from Japan and Austria. All of them were young people below 25 years of age with different backgrounds—a Vietnam war veteran and a Tokyo fire-fighter, for example. Before going into the field, all attended a 1-month orientation and training course in Addis Ababa. The national Ministry of Health delegated 38 assistant sanitarians and some 54 vaccinators.

Program performance in 1973. By the middle of the year, the majority of provinces were considered as approaching smallpox-free status. Three provinces remained seriously affected, namely Gojam, Begemdir, and Hararge. The Gojam Province remained the most problematic. I was given the task to solve this problem. For some time, a team of four to six Peace Corps volunteers, three assistant sanitarians, and ten vaccinators were engaged in the activities. Three vehicles, including the WHO advisor's vehicle, were allotted. The team was based in Debre Marcos, the capital, a minor town with a population of 10 000–15 000 residents. The active operations were initiated in the second half of 1971, almost 2 years before my arrival. The surveillance team's activity was reflected promptly in reported statistics. For the second half of 1971, over 600 cases were reported and in 1972, additional 2427 cases. The most essential part of the work consisted in collection of information. There were many official sources of information—administration in Awrajas (districts) and Woredas (communities), a few functioning health centers and leprosy clinics, and the malaria program personnel. However, only 24% of all reports came from these sources. A more fruitful method was interviewing people in traditional gatherings, namely, markets, prayers, or celebrations. Remarkably, the clerics themselves were usually not eager to cooperate with the program staff; much time and patience were required to gain their support. Thus, it was not surprising that a substantial share of the Amharic population in Gojam was not cooperative (later, in 1975, villagers killed two Ethiopian surveillance team members).

When a suspect case report was received, a route was drawn up based on the data provided by local people since no maps were available. The type of transport was selected—car, mules, or by foot. In many instances, the final destination could be reached only by foot. If the information proved to be correct, the next, no less easy, task was to convince contacts to be vaccinated. Nowhere else did I have to revaccinate myself to prove the vaccine was harmless. It was a time-consuming operation, often requiring long walks from house to house or village to village. Location and vaccination of contacts were, in some outbreaks, unachievable. It is to be noted that surveillance teams carried out vaccination even in the absence of cases (or contacts) in the visited localities. That is why in 1973, vaccination immunity in Ethiopia reached 30% and, in some provinces, 70 to 80%.

The success of the Program in the Gojam Province was complicated by the 1973 drought in the neighboring provinces. Fleeing from hunger, numerous crowds started to fill the major settlements, particularly along the main road to Addis Ababa. In June, it was concluded that available resources were insufficient for simultaneous actions in all Awrajas. It was decided to concentrate on the western lowland part of the province, gradually ascending to the mountains, where the approaching dry season would make movement easier. Four of the province's seven Awrajas were selected for an active case search: Debre

Marcos, Bichena, Damot, and Bahr-Dar. The plans were, indeed, implemented. The incidence for the year of 1973 showed a significant decrease as compared with the previous year. What was more important, the transmission continued to decline in the dry season, when an increase usually occurred. It was felt that the disease was well suppressed in all but Bahr Dar Awraja, and the surveillance teams shifted their attention to the three Awrajas in the east. But it was soon apparent that there were no grounds for optimism. Cases began to be reported from the areas thought to be smallpox-free. There were two major reasons. First was the work of variolators, who refused to abstain from this practice, their only source of income. Second, there was the need for quality control of the containment component of operations. For this purpose, the vaccinators needed to revisit the foci and vaccinate the missed vaccinees. For Gojam, there were insufficient personnel to do this.

The situation in Gojam Province was discussed in April 1974 with Drs. Henderson and Hajian, from the Regional Office. The responsibility for Gojam was transferred to Dr. Ciro de Quadros, and I was assigned to six provinces in the predominantly Muslim west and southwest, namely, Kaffa, Arussi, Bale, Sidamo, Wolega, and Illubabor.

Kaffa Province, 1974. Over a span of 7 months, from October 1973, no cases were reported from this province and it was referred to as a smallpox-free. However, in April 1974, the signal was received in Addis Ababa headquarters about a renewed transmission in one of its districts.

The eradication activities in Kaffa started in January 1971 and were untypical of Ethiopia. A mass vaccination campaign was carried out. During 1971–1972, the program personnel supported by provincial health services vaccinated 1.1 million out of a population of 1.2 million, i.e., some 90%! But a more attentive look at the figures revealed that old census data had been used and the actual rates were somewhere in the range of 50–60%, with uneven districtwide coverage. In 1971, Kaffa was recognized as the most severely affected region of the country. Its five districts reported 5024 cases, although the actual number of cases was definitely much higher.

In 1972, when case notification improved, the incidence dropped sharply, to 3034 and in 1973, only 308 cases were detected. Analyses showed that 78.6% of them belonged to Jimma Awraja and all of them were from a single Woreda, Dedo. Here, 48 foci were detected. The sources of infection were traced for only half of them, all but three by program personnel. According to reporting forms, 10% of the family contacts reported having had smallpox previously; 78% had no vaccinial scars.

G.D. Suleimanov on his way to a smallpox-affected area in the Kaffa Province (Ethiopia), 1974

The foci reported in April 1974 were detected by the program staff in the course of a routine visit to a primary school in the village of Ebu, the administrative center of Mana Woreda. The index case was identified as an adult student of a religious school in Dedo Woreda, who lived there from May till October of 1973, at which time he returned to his home in Ebu. At the beginning of November, he presented a typical clinical picture. He was the source of a chain of infection comprising 73 cases in 33 households. Transmission lasted for 5 months, unnoticed either by the program staff or by general health services. The outbreak team of four surveillance workers (out of the five assigned to the province) headed by the WHO adviser, carried out house-to-house surveys; some 1500 persons were vaccinated. An interesting note—seven successful vaccinations of the patients in the incubation period on days 8, 6, 5, 4, 3 and 1 before the rash appeared. The foci in Ebu persisted till the beginning of May, when 3 weeks of subsequent searches confirmed the absence of infection in the province. Meanwhile, a survey performed in the index case's village in Dedo Woreda confirmed the absence of recent foci there. All persons with pockmarks reported having had smallpox at least a year earlier.

I found it disturbing that the source of infection was not traced for half of the foci. To prevent further spread of infection, it was decided that in the households infected in March and April, a vaccinator would be stationed from morning till sunset, with the task of vaccinating any visitor without a fresh vaccinial scar. There was no need for vaccinators to stay with these families at night as there were no movements in the country due to security reasons.

The situation in Sidamo Province. In June–July, events in the neighboring Sidamo Province required special attention. These events were similar to Kaffa. In 1972, there were 2520 cases, and in 1973, only 262 cases. The source of infection resembled Kaffa—70% came from Wollamo Awraja and one-third of cases (91), from Bolosso Woreda. In 1973, the transmission in this Woreda went uninterrupted from January to the end of the year. The last case was reported on December 14; in five villages, the infection lingered for 8 to 11 months. The source of infection here was not identified in 37% of cases, compared to the rest of the province, where it was 9%. The WHO advisor accompanied by two surveillance teams with Land Cruisers and then on muleback arrived in the early June in Bolosso Woreda. During two weeks of intensive case search, 62 clinically ill patients in 12 foci were found. The suspected chain of importation from Kaffa was not proved; the origin of the epidemic was clearly indigenous. The appropriate containment measures were aided by a campaign of flour distribution in this famine-stricken province. All visitors to food distribution centers were vaccinated. In total, 14 000 out of 16 000 Bolosso residents were protected and, consequently, transmission in the province was stopped. As a result, the number of smallpox-free provinces increased from six to eight.

The summer of 1974 was spent in analogous activities in other provinces under my responsibility (Arussi, Bale, and Illubabor).

Critical phase in the SEP in Ethiopia. By the spring, the program plans were seriously hampered by dramatic worsening of the internal sociopolitical situation, shortages of manpower and material, plus deterioration of security. Attacks on WHO personnel took place; public demonstrations and rioting military personnel became a routine phenomenon of daily life. Twice, in the WHO adviser's presence, bayonet-charging solders dispersed demonstrating civil crowds. Administration, both in the capital and in the provinces, gradually started to collapse; the Emperor was dethroned and later executed.

The Global Program's senior management in Geneva, seemingly, was slow to grasp the essence of the happenings, though recently, as I understood from Dr. Henderson's interview for CDC's Global Chronicles, mid-1974 represented critical points for the program in both India and Ethiopia. I myself left Addis Ababa in the fall of 1974, but it seems that the lessons of the preceding period were useful and resulted in a radical change of tactics. The victorious revolutionary government proclaimed the Smallpox Eradication Program to be a national priority. The national force was increased from 30 national health staff to 1200. Simultaneously, international support was drastically increased. The WHO staff was enlarged to 24 advisors; donations, transport, and helicopters were provided. Two years of persistent fighting ultimately brought the long-awaited results. The last case of smallpox in Ethiopia occurred on October 26, 1976.

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In conclusion, I would like to make some general observations:

- The Smallpox Eradication Program demonstrated the importance of epidemiology as a science. Its employment in an adaptive, flexible system of epidemiologic surveillance was decisive in achieving eradication. Inexpensive, low-maintenance, easy to use tools, such as bifurcated needle used with freeze-dried vaccine, are indispensable, obligatory prerequisites for similar ventures;
- The purposefulness of the Smallpox Eradication Program leadership, the dedication of both national and WHO staff, team work, and high international spirits served as unique examples worthy of imitation. Moreover, the appointment of someone like Dr. D.A. Henderson as Chief of the Intensified Program was crucial for success; and
- Paradoxically, from my point of view, the Cold War rivalry between two superpowers, who tried their best to demonstrate their will for cooperation, also contributed to implementation of the program. Surprisingly, the modern Russian government seems to be hardly aware of their predecessors' achievements, so the general public remains ignorant of relatively recent history.

Finally, I wish to state that for me personally, the main treasure acquired during my years in the Global Program is the feeling of honor in my participation. The good memories of my colleagues from both continents—Drs. D.A. Henderson, William Foege, Ahmad Hajian, Ehsan Shafa, Petrus Koswara, Ciro de Quadros, Kurt Weithaler, Kamal Khan Mandohel, Mohammed Rafique, to mention but a few, will always be with me.

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Find below the letters by Dr. Henderson, which I mentioned above. Both were indeed on the official printed form of the WHO.

Dr. G.D. Suleimanov
Smallpox Eradication Programme
P.O. Box 1358
Lahore
Pakistan

12 August 1972

Dear Dr. G.D. Suleimanov,

I read your second quarter report with very great interest. It would seem that, no less than elsewhere on the subcontinent, there is inevitably the continuing problem in sustaining a high level of interest on the part of administrators as well as surveillance teams in tracking down the last residual foci. In the summer months, this constitutes indeed an even more difficult problem. Much can be done in this regard by the WHO SE staff and national staff and this, I sense, you are doing. You emphasis on Lahore as being of special priority is sound. As you know only too well, the major cities are a problem all to themselves and as Mack and his colleagues demonstrated, they serve as a reservoir of infection, periodically infecting villages over a vast geographical area. If one can stop transmission in the city and keep it free of smallpox, one's task elsewhere is vastly simplified. Such as your sweepers' colony requires special attention, of course, if this is to be done.

Table III was of special interest to me as I don't recall that anyone has ever complied data in this manner. It is not only interesting but provides a very useful index of the efficiency of the surveillance mechanism. I am especially struck by the fact that 80% of cases are investigated within one month after onset. Although I have no other data to compare this with, it would seem to me that this is a comparatively high figure which reflects most favorably on the surveillance activities. With detection such as this and with a reasonably effective containment effort, it would seem that transmission ought to be able to be interrupted reasonably rapidly.

I would hope that with the aggressive measures you have in operation that you could rapidly interrupt transmission in northern and central Punjab, say in the next 6 to 8 weeks and that you would then be in a position to launch a truly all-out attack on the foci in the south, working in close cooperation with those from Sind and Quetta. Adibzadeh feels reasonably that the problem in NWFP should be finished by the end of the year and Chamsa feels similarly from Quetta. If we could soon narrow our area of concern to the 4 million or so persons in Sind and attack this with all our resources, it would seem to me that the problems in Pakistan could very rapidly dissolve. It means a very great deal of field work, of course, but from this distance, it would seem to me that you are rapidly approaching this point.

With all best regards in your efforts

Sincerely yours

D.A. Henderson, M.D.
Chief, Smallpox Eradication Unit

Dr. G.D. Suleimanov
Smallpox Eradication Programme
P.O. Box 1358
Lahore
Punjab
Pakistan

18 October 1972

Dear Dr. G.D. Suleimanov,

It is seldom that one receives a paper so gratifying as your paper on Lahore. You have done a perfectly magnificent job! I wonder how many more years it will take before we finally learn the lessons which you so beautifully document. Personally, I think we'd best start learning dam soon if we expect to interrupt smallpox transmission in the next 18 months. I'm counting on this paper especially to dive home a few lessons for the participants in the Karachi seminar as there are many urban problems still remaining.

I've edited the paper for clarity and to de-emphasize a bit the WHO role as I feel this may be the more effective way to present the information. I've done my best, however, to retain all points which you have made. We will have it reproduced for distribution at the Seminar but, in the meantime, will send you a copy as soon as it is prepared.

Again, one beautiful piece of work. Now how about rapidly finishing off the rest of Punjab.

With all best personal regards,
Sincerely yours

D.A. Henderson, M.D.
Chief, Smallpox Eradication Unit

Smallpox Eradication in the World and Some Remarkable People I Met and Worked with in the Program[1]

(It also includes some adventures during the period of my participation in the Program[2])

L. N. Khodakevich

Initiatives on celebrating the anniversary of the smallpox eradication in the world

In 2010, 30 years after a brilliant achievement of mankind—freedom from smallpox, one of the most dangerous diseases known to man. Dr. Mahler, the WHO Director-General stated in 1987 that "... When the history of the 20th century is written from the standpoint of the 21st, the eradication of smallpox will undoubtedly be ranked with the mastery of flight, the harnessing of nuclear energy, and the first steps in the exploration of space."

In August 2008, the Smallpox Eradication Commemoration 2010 Secretariat was launched at Emory University's Global Health Institute in Atlanta. Its mission was to plan for events in 2010, commemorating the 30th anniversary of the worldwide eradication of smallpox. The Secretariat was led by Jean A. Roy, the Director of the SEC2010. SEC2010 had three ambitious projects:

• Commissioning and erecting a bronze monument at the World Health Organization's Headquarters in Geneva, Switzerland;

• Commissioning and publishing an easy to read illustrated history of smallpox and its eradication: "Smallpox Zero"; and

• Organizing a major international symposium in Rio de Janeiro in August 2010 on the lessons, legacies, and innovations resulting from smallpox eradication.

Lev N. Khodakevich,
an epidemiologist, doctor of medical sciences, and participant of the Smallpox Eradication Program in India and other countries of Southeast Asia; a WHO advisor on organization of the post-eradication epidemiologic surveillance and coordinator for the Global Commission on the Certification of Smallpox Eradication (1973–1979); member of the WHO Headquarters Smallpox Eradication Unit responsible for planning, organization, and coordination of the research into monkeypox ecology in the countries of Central Africa (1983–1987). Later and until now, he was involved in the control of HIV/AIDS epidemics in the programs of the WHO and other international agencies

[1] This story does not pretend to be an exhaustive description of the events occurring during the program implementation. It is based on photos and slides made by the author during the time he participated in the program. Unfortunately, the practice of documenting the events was occasional. Consequently, I regret that many episodes and participants of the program are not included in this brief memoir. (Some photos are borrowed from colleagues or copied from official documents.)

[2] The adventures and events that do not have a direct relation to the Program are described in italics in order not to overstrain the reader.

By December 2010, SEC2010 had successfully accomplished its commitments and initiated several legacies:

- *The newly created David J. Sencer Smallpox Eradication Fellowship*. At its last meeting on December 15, 2010, the SEC2010 Board approved this Fellowship at the Emory Global Health Institute. It will enable graduate students from all disciplines to participate in short term international disease control projects;
- *Two publications: Smallpox Zero and the forthcoming supplement to the journal Vaccine summarizing the proceedings of the Rio Symposium, "Smallpox Eradication after 30 Years: Lessons, Legacies, and Innovations*", which will appear during the first half of 2011;
- The superb *bronze vaccination monumen*t at the entrance to the World Health Organization; and
- *Future support to the Jenner Museum* in the United Kingdom can perpetuate the eradication legacy and inspire younger generations.

The 30th anniversary was widely celebrated in many countries around the world. The program participants now living in Moscow and other Russian cities have also contributed to the anniversary celebrations. Prof. Svetlana Marennikova initiated this movement. One year prior to the anniversary, Prof. Marennikova developed the plan of activities to celebrate this anniversary. She motivated other veterans of the program living in Russia to participate. The calls for support were sent to various public health authorities and branches of the mass media.

Prof. S.S. Marennikova at work

Prof. Svetlana S. Marennikova: Honorable scientist of the Russian Federation, academician of the Russian Academy of Natural Sciences, WHO expert on smallpox and related orthopoxvirus infections, Chief of the WHO Moscow Collaborating Centre on Smallpox and Related Orthopoxviruses. It is true to say that Prof. Marennikova was a key figure in this country in the interaction of the Soviet Union with the WHO Global Smallpox Eradication Program not only in relation to developing vaccines and diagnostics, but also in the formulation of the program strategy. The laboratory she headed started cooperating with the WHO right after the program was launched. Under the program, the laboratory was involved in comparative studies of the smallpox vaccines produced in different countries. As a result of this work, the reference vaccine was chosen. That same year, the WHO Expert Committee, with the participation of Prof. Marennikova, developed the first International Requirements for Smallpox Vaccine. The importance of this event was that the vaccine had never before had any standard indicators of quality. She participated in almost all WHO expert committees and scientific groups related to the eradication program. In 1978–1980 during the certification of smallpox eradication, Prof. Marennikova was actively involved in this process. She was a member of the international commissions in Kenya and Sudan and a member of the Global Commission. The Declaration of the Global Commission on Smallpox Eradication, dated May 1980, was signed by 19 members, one of whom is Marennikova, the only woman among the members of the Commission.

Mass media had responded by producing several publications in Russian periodicals. Eventually, the Secretary of the Chairman of the RF Council, through the Ministry of Health and Social Development, had charged the Mechnikov Institute of Vaccines and Sera with the implementation of the plan. The institute established the Organizing Committee that arranged a number of events and organized a series of activities. In particular, on September 12, 2010, a session of the Presidium of the Board of the All-Russia Scientific and Practical Society of Epidemiologists, Microbiologists, and Parasitologists together with the Academic Council of the Institute of Vaccines and Sera was held, where some veterans of the program made presentations on the program implementation. During this session, they were awarded memorial decorations "For Practical Contribution to Strengthening of Health of the Nation" and diplomas of Honorable members of the All-Russia Scientific and Practical Society of Epidemiologists and Microbiologists.

On December 14, 2010, several veterans of the Program made presentations at a session of the Bureau of the Branch of Preventive Medicine of the Russian Academy of Medical Sciences. Simultaneously, in cooperation with the WHO Country Office in Moscow, the Russian State Library prepared an exhibit devoted to the anniversary and organized a meeting of the WHO staff in the country with participants from the Global Smallpox Eradication Program. On February 8, the WHO Country Office in Moscow arranged a special meeting of the Office staff with some Russian participants of the program. At this meeting, Prof. D.D. Venediktov, former Deputy Minister of Health of the USSR, presented his views on the systemic issues of public health and international cooperation. Prof. Marennikova reported on the role of the Moscow WHO Collaborating Centre in development of the standard for smallpox vaccine, control of vaccine quality, research, and testing of the samples from patients in the endemic areas and animals subject to the monkeypox ecological studies. Dr. L. Khodakevich presented a comparative analysis of two infections, smallpox virus and HIV, as well as different approaches to their control and the outcomes.

Among other activities, the Organizing Committee decided to publish the reminiscences of program veterans, in particular, the WHO staff and consultants who worked in the program. That is how this essay was initiated.

My participation in the WHO Global Smallpox Eradication Program

In the summer of 1973, Dr. Donald Henderson, the Chief of the Global Program, asked the Ministry of Health of the USSR to provide several specialists for work in the countries where the final phase of eradication of smallpox was commenced. The Ministry of Health offered some experts, one of which was the author of this essay.

By that time, I had already gone through several assignments as a young epidemiologist: tuberculosis control, organization of medical aid to newborns and children in the USSR Republic of Bashkiria, and a special postgraduate course at the Martsinovsky Institute of Medical Parasitology and Tropical Medicine. The events at that time developed quickly, and in October of the same year, I was in New Delhi and reported to the Smallpox Eradication Program Unit for the Southeast Asian countries (SEARO).

I was assigned to work as an epidemiologist in the state of Madhya Pradesh, the central lands of India, with a population of about 80 million people. This state was one of the four endemic for smallpox and the least affected among them, in spite of the fact that more than one case of smallpox was registered in 1973 in 23 of the 44 districts of the state. The first steps in this work were carried out with the support of Dr. Nicole Grasset, the Head of the Smallpox Unit at SEARO (WHO Regional Office for the countries of Southeast Asia).

At first, I learned the WHO strategy on surveillance and containment used during the intensive phase of the program (from Nicole); the system of registration and monitoring of smallpox outbreaks (from Larry Brilliant, a WHO epidemiologist from the United States, and Zdenek Jezek, a WHO epidemiologist from Czechoslovakia); and clinical diagnosis of the disease.

My terms of reference included provision of technical, operational, and financial support to the state Government and the staff involved in the eradication activities. It was a multitudinous and not a simple task, considering the need for early detection of EACH new case of smallpox on the territory of the largest state in the country. The work in the endemic states was carried out following the two components of the WHO strategy approved by the World Health Assembly in May 1966, which included:

• Vaccination of 80% of the population using heat-stable, freeze-dried vaccine and

• Filing weekly reports of all smallpox cases using the hospitals and clinics reporting system, investigation of each reported case, and vaccination of individuals in a large circle of houses around each case to prevent the disease spread (containment).

Subsequently, when it was found that the routine reporting was insufficiently effective in revealing new cases of smallpox (the program estimates of the number of reported cases in some countries showed only 1 to 10% of the cases that actually occurred), the program added reporting through active periodic household surveys in all settlements.

Dr. Donald Ainslie Henderson (called simply D.A. by his colleagues), Prof. of Medicine, worked in the intervals between the academic institutes in 1955–1957 and 1960–1966 at the Center of Communicable Diseases (now the Centers for Disease Control and Prevention, CDC) where he created a unit for epidemiological surveillance on smallpox, which dealt with smallpox importations to the United States. In 1966, Dr. Henderson, then aged 38, was appointed as the Chief of the Smallpox Eradication Unit at the WHO Headquarters in Geneva, heading the Global Eradication Program until the last case of smallpox in the world was registered in Somalia. In the program, Henderson showed many outstanding abilities: "well-educated, strong-willed, perspicacious, and perfectly well seeing through people, he had been recognized as the reliable leader"; his qualities as they were summarized by A. Turbin, a Russian writer, in his documentary novel *The Long Pursuit*. D.A. was able to listen and hear signals from the "field". During the intensive program stage in Africa, Dr. William Foege, a WHO epidemiologist from the United States, due to lack of smallpox vaccine, suggested to use the so-called ring vaccination around the households affected by smallpox. The experience showed that this strategy was successful, and Henderson promoted its expansion to other endemic areas. Later on, he supported and expanded the practice of carrying out periodic weekly drives for case finding proposed by the Soviet epidemiologists A.N. Gromyko and A.N. Slepushkin. During the period of the "cold war", Henderson, considering the initiative and contribution of the Soviet Union to the program development, showed the qualities of an erudite diplomat and highly skilled manager. Thanks to his initiative, one of the first WHO Collaborating Centers on Smallpox was organized with the Moscow Institute of Virology of the USSR Academy of Medical Sciences, which, under the direction of Prof. Marennikova, carried out methodological, diagnostic, and research work on smallpox until the end of the program. Henderson had promoted a wide use of specialists from the USSR as consultants and program staff. He repeatedly visited Moscow, interviewed the candidates proposed by the Ministry of Health, and selected experts for the program. As a result, dozens of specialists from the Soviet Union took part in the program. For having achieved the eradication of smallpox as well as other merits, Donald Henderson was decorated with five medals, three of them national, and numerous other awards.

Dr. Donald Henderson, New Delhi, 1975

Fortunately, unlike many developing countries, India had a reasonably good infrastructure of public health services, namely, a broad network of Primary Health Centers (PHCs) pretty well staffed with medical professionals. While the physicians in charge of these centers preferred to provide mainly medical aid to the population that offered them additional benefits and popularity, the PHCs had several health inspectors involved in anti-epidemic activities among the population. The PHC's work was supervised by the Regional Health Departments, which had two branches. One, responsible for epidemiological activities, was headed by an epidemiologist or public health manager (Public Health Officer, PHO) and the second, for coordinating and providing medical aid to the population, headed by a Civil Surgeon (CS). Apart from the national health network, four to seven (in various periods of time) specialized teams supervised and carried out the surveillance for smallpox cases and containment of outbreaks. The teams were composed of epidemiologists and sanitary inspectors assigned from the state of Madhya Pradesh and from the other states of the country. The work of these teams and maintenance of their mobility were subsidized by the WHO. Periodic weekly drives for revealing smallpox cases in all households of each settlement were an essential component of the epidemiologic surveillance.

Nicole Grasset, the daughter of a well-known Swiss microbiologist, worked at the Pasteur Institute in Paris after graduating from medical school and as an advisor to the Red Cross in Nigeria. In 1971, she was appointed as the senior WHO adviser to head the WHO Program Eradication Unit at the Regional Office for the countries of Southeast Asia (SEARO). Her work included technical support and coordination of the Program activities in the countries of the region most affected by smallpox; supervision of the teams of international and national epidemiologists; organization of an active search for smallpox cases and containment activities: receiving and analyzing the information from the countries; and monitoring epidemiological situation. Nicole proved to be a strong leader and strong-willed person. D.A. spoke of her as a vigorous, unshakable, and charismatic leader and mentioned that except for the nursing staff, she was the only woman in the program in the whole region. In 1979, Nicole served as a member of the Commission for the Certification of Smallpox Eradication in Djibouti. Considering her devotion to improving health of people and perfection in clothes choice, she was named a great angel, mother Teresa in Dior attires. After working on smallpox eradication, Dr. Grasset went on to help as an advisor in the creation of Larry Brilliant's nonprofit organization, the Seva Foundation, and devoted several years to support the National Program of fighting blindness in Nepal.

Nicole Grasset is marking active smallpox outbreaks on the map of an Indian state

The health workers visited families, showed the so-called identification cards (photos of smallpox patients), and enquired about the people with lesions similar to those on the card. Special attention was paid to the search in schools, which represented populations of surrounding villages. The reported cases were initially investigated by local paramedical staff and physicians. The patients suspected of smallpox were eventually seen by WHO epidemiologists. Samples were collected from all patients with skin eruptions without a definite clinical diagnosis and sent to the WHO Collaborative Centers in Moscow and Atlanta. After clinical confirmation of the case as smallpox, or a suspicion of it, local physicians and paramedical staff initiated the containment activities.

Halfdan Mahler (*left*) discusses the issues of eradication of smallpox with his colleagues

Dr. Mahler, a Danish pediatrician and tuberculosis specialist, was elected as the WHO Director-General in 1973. He vigorously supported the Smallpox Eradication Program and considerably strengthened the support to Henderson in its implementation. Ivan D. Ladnyi (*in the center*), an epidemiologist from Kharkov, doctor of medical sciences, worked as a WHO advisor supervising the program of smallpox eradication in the countries of East, Central, and South Africa in 1965–1971. From 1976, he worked as the Assistant to the WHO Director-General, with the control of communicable diseases as the major area of his responsibilities. Dr. Ladnyi served as a member of the International Commission on the Certification of Smallpox Eradication in West Africa and was one of the authors of the authoritative WHO monograph *Smallpox and Its Eradication*. In 1985, he published the monograph titled *Eradication of Smallpox and Averting Its Return*.

All contacts of smallpox patients, prior to and after the onset of the disease, were traced to reveal the source of infection and potential future cases. The patients were isolated from visits by relatives and friends, and the so-called "ring" vaccination was initiated starting from the affected household and expanding to the periphery of the village. The villages with suspected sources of infection were also included. Any outbreak remained under observation and considered as "pending" until 4 weeks elapsed after the last patient in the settlement recovered; then the outbreak was considered "closed".

The results of the surveillance and containment operations were reviewed at the state level on a monthly basis. The heavily affected areas were also reviewed at the district capitals and summaries were reported to SEARO.

Ranchi city, Bihar state, India. Review of the situation and progress in the activities. Larry Brilliant (*left*) and D.A. Henderson (*right*). Search results are noted on the board: names of the districts, results of search assessment, and numbers of active smallpox outbreaks

Generally people learned how to prevent the spread of smallpox long before Edward Jenner discovered the vaccine. The methods varied depending on the cultures and habits. In densely populated areas of the Indian peninsula, for example, relatives and close friends were invited with their children to the house where smallpox occurred. The people knew that the earlier a child would get smallpox, the less severe would be the disease and lower the chance that the child would die from it. Brides with pockmarks on their face were preferred to girls with clean skin, who may eventually be victims of the disease. In the mountainous areas in the north of the peninsula where the concentration of the population was much lower, the villagers built temporary houses in higher hills. They brought to the doorsteps of these houses water and food until all members of a family got well and recovered from smallpox. In some countries of Africa, the settlements affected by smallpox were fenced off by branches of acacia with long sharp thorns, which were burned out. In central India, the population long ago knew about the ways of transmission of some diseases. People recount that during devastating epidemics, when most of the people died and the survivors did not have enough strength for burials in traditional ways, the corpses of people who died of cholera were burned, while those who died from smallpox were simply dumped into rivers.

According to plan, each household during weekly searches was to be visited to enquire about smallpox. However, as in many public services, involvement of government staff in the program activities quite often depended on personal responsibility and, more important, on the professional interest and enthusiasm of the staff member.

For example, in one of the PHCs, the physician in charge was spending hours sitting in an armchair and chewing paan, and in response to my query regarding the smallpox situation in the PHC area, he answered that this was not within his responsibility. At another PHC, a young graduate from a medical institute was ready to walk tens of kilometers in order to personally check a report (the so-called rumor) on a suspected case of smallpox. One more example: in the regional center of the Sagar district, the head of the Medical Department, after finishing the outpatient session and operating on his patients, found time and energy to visit a couple of PHCs to assist in their medical work and, at the same time, to see the reports of paramedical staff responsible for vaccinations.

Prof. A.N. Slepushkin, doctor of medical sciences, professor, and honored scientist of the Russian Federation, worked in the program in 1971–1976 at the Smallpox Eradication Unit of the WHO Headquarters. From there, he traveled to various countries and participated in the national programs in India and Pakistan in 1972–1976. He proposed a highly efficient way of active detection of smallpox cases through monthly household surveys. On his recommendations in 1973, this technique was included in the programs in these two countries; in addition, it was successfully used in Bangladesh. Slepushkin was awarded a commemorative medal and a certificate of honor from the Government of India, and received from WHO the "Bifurcated Needle" and a medal "The Smallpox Is Eradicated". Prof. Slepushkin was the supervisor of my studies for my candidate of sciences dissertation and acted as an official opponent for the doctor of sciences dissertation.

Anatoly N. Slepushkin
(by the courtesy of
Dr. Marennikova)

In contrast, the Regional Epidemiologist was sitting in his office and receiving reports from his subordinates from the Primary Health Centers.

In general, an enthusiast was in almost each medical institution who because of the personal interest and with small material support from the WHO was ready to spend days traveling by car, bicycle, or by foot for checking up the rumors on smallpox cases and then to stop and stay overnight in the settlement where cases were found in order to begin the immediate vaccination of population.

So, day by day, with a couple of paramedical staff, we moved from district to district, from PHC to PHC, checking the activities, giving special attention to the areas where outbreaks were recently registered, where suspected cases required verification, or where poor program implementation was expected. Apart from purely epidemiological work, the program required field epidemiologists to oversee the work of the national employees who received subsidies from the WHO; to support their field work; to distribute money; to supply fuel for vehicles and repairs of cars; as well as to collect reports on expenses, collating and sending summary reports to New Delhi. My colleagues joked: when I was coming to the bank in Bhopal (the Madhya Pradesh state capital) to receive the monthly remittance from Delhi, the employees of the bank respectfully rose in recognition of the amounts, which were transferred to my account. I had to clarify that this was not my personal money, but the WHO's support to the eradication program in the state.

The author is taking samples from the skin lesions of a smallpox patient for laboratory tests

As for the monetary support from the WHO, it consisted of payments of small, by WHO standards, amounts to national employees as daily allowances for the work they did away from their homes. Although it could significantly enhance the mobility of the staff badly needed by the program, paying additional allowances to the national staff was an issue for the National Ministry of Health. Negotiations by the WHO with the authorities in Delhi, supported by Dr. M.I.D. Sharma, Director of the National Institute of Communicable Diseases, and Dr. R.N. Basu, the assistant to the Director General of the Health Service of the Government of India, were successful. We saw the positive consequence of such an agreement in the field: the staff in the periphery became highly mobile and could start work immediately wherever the situation required.

Dr. M.I.D. Sharma,
a great supporter to the WHO during the intensive phase of smallpox eradication in India

Whatever the efficiency in detection of cases could be, it did not come to the level of perfection in reaching hundreds of thousands of settlements and millions of households. A mechanism was required

that would allow communicating with the large population to have additional sources of information on smallpox and reconfirm the data already available through the periodic search operations. For this purpose, we promoted the use of weekly markets, the events widely spread in the central state of India, as places of contacts with population. The idea was not new, since the searches for smallpox cases at markets were sporadically used in some states of India before 1974. In 1972–1973, in Rajasthan (Western India), an attempt was made to assess the share of the rural population that participated in the weekly markets. On the basis of these initiatives and their experience, we designed a methodology for work at the markets and the documentation for planning, recording, and reporting such activity. The details of these elaborations and the results are described in several publications.[3]

Girija Brilliant, Lidia Khodakevich, and Larry Brilliant in Bhopal, 1974

During the coming years, this system of surveillance was used in other states of India and appeared to be especially useful for remote areas. In the post-eradication surveillance, 20 to 30% of all reports on the patients with skin eruptions in four states of India were received through enquiries at the weekly markets.

But this was later on. Now let us come back to Madhya Pradesh. Towards the end of 1975, the program was persistently clearing the state from the last outbreaks, and in the following year the vigorous actions of the state public health system with relatively limited support from the WHO had freed the state from smallpox. During the 14 months beginning from October 1973, 604 outbreaks with 2464 patients had been registered and contained.

During this period, I received many useful lessons in relation to working abroad, cooperation with international and national colleagues, and improving my English (which prior to my arrival in India could not yet be considered at a "working" level). Out of numerous useful lessons I learned from my colleagues, two received from Larry Brilliant are worth mentioning.

We worked with a national team in an unusually large outbreak with a dozen cases. It offered a good opportunity to receive the data on the rates of secondary cases in unvaccinated cohort and those who were vaccinated in various periods of time prior the onset of the disease.

After the investigation of the outbreak was completed, I broke the team into two groups. One carried out the ring vaccination in the village and the other started a population census with registration of the vaccination status and the time of the last vaccination. After a day of work, Larry came to the village to have a look on the progress. He had quickly realized that the work was performed in two directions and rearranged it by mobilizing all available workers exclusively for vaccination. Within a day this work was finished. "And now," he said, "you can continue the census". A word on this episode was sent to Delhi.

[3] Rao, H.N. and Khodakevich, L. Weekly market search in mountainous areas—a study, Swast Hind, July 1976, vol. 20, no. 7, pp. 215–218; 224–225; Basu, R.N. and Khodakevich, L. Surveillance at weekly markets in the Smallpox Eradication Program in India, *Ind. J. Pub. Health*, 1978, vol. 22, no. 1, pp. 44–49; Khodakevich, L. and Rao, H.N. Search at weekly markets for detection of smallpox outbreaks which occurred during the previous year, *Ind. J. Pub. Health*, 1978, vol. 22, no. 1, pp. 51–55.

Apparently, it did not have any serious repercussion for me, but I learned a lesson. The second example was when Larry strongly insisted on including me as a co-author in the publication for the WHO Bulletin.[4] I neither investigated the patient nor did I make a large contribution to the preparation of the paper. This was a second lesson, or a message: I should get involved in research and publish results (prior to this I had a single publication prepared jointly with the scientists of the Martsinovsky Institute, based on the results of the blood tests on filariasis among students from African countries). However, neither Larry nor any one else taught me to keep diaries on the activities, which I deeply regret now.[5]

West Bengal

At the beginning of 1975, the WHO initiated my transfer to the state of West Bengal. By that time, the local transmission of smallpox in this state was interrupted but crowds of refugees had poured into India from Bangladesh, where smallpox transmission continued and these immigrants could import infection to India.

It was not possible to stop immigration, and no effort was made to do so, as the immigrants were the Hindus who had settled in Bangladesh after the division of Pakistan into two parts. The task was to set up a barrier on these borders of India in order to reveal EVERY SINGLE smallpox patient and to extinguish outbreaks before the infection crossed the western borders of West Bengal.

At that time Dr. Isao Arita, sent here on a mission from WHO Headquarters, strengthened the program in the state from the WHO side. A Japanese, with a nice soft character, was not happy (nor was the Delhi WHO Office) with the unfolding events there. Several jeeps provided to the state by the WHO were distributed among senior officers together with the subsidies for fuel and maintenance but were hardly involved in the program activities. Supervision of the field work on smallpox case detection from the Government side was poor. Paramedical staff had little motivation to work and limited capacity for travel through the countryside.

India. The city of Bhopal, the capital of Madhya Pradesh, is in the center of the country. To the east is Calcutta (now Kolkata), the capital of West Bengal. To the northwest of Bangladesh, between Bangladesh, Bhutan, and Burma are the seven states of northeastern India. These are the areas where I worked in 1973–1978

Apparently Isao was happy to see me there. While staying in Calcutta for a couple of weeks after my arrival, he, being the WHO Headquarters representative, told me to do anything I considered necessary to change this situation.

[4] Brilliant, L.B., Nakano, J.H., Kitamura, T., Khodakevich, L., and Bharucha, P.B. Occupationally-acquired smallpox in an Ig M-deficient health worker, *Bull. WHO*, 1981, vol. 59, no. 1, pp. 99–106.

[5] By the way, Gregory David Roberts had written his book Shantaram unfortunately only 30 years later. This guy who had the life full of dangerous adventures and, as he writes in the book, he had a good habit to note down to minor details on any piece of paper coming to his hands of what was happening with him every day: meeting, fights, chats, cloths, impressions of the faces, emotions, etc. In the evenings, he scrupulously rewrote his scribbling into notebooks that eventually built up an odyssey of over 800 pages, which became a bestseller of the beginning of this century. But this lesson came too late for me.

In West Bengal (in comparison to Madhya Pradesh), everything had been organized in a big way. The program had a large office. The administrative and financial issues were handled by a specially assigned WHO officer. A WHO epidemiologist with a team supported the state program. Some teams were headed by national employees from the state of West Bengal and from other states of the country. All this allowed me to concentrate my efforts on coordinating the surveillance and containment activities. The most important was intensifying the search for cases. Dr. R.N. Mukerjee, the Head of the State Program, was mainly involved in bureaucracy. Claudio Amaral, the WHO epidemiologist from Brazil, was in the Darjeeling area, in the north, and I had to take care of the central and southern areas of the state.

Fortunately, working in this state, I found full support from Dr. K.S. Basu Mallick, the then Director of Health Services and Secretary of the State Department of Health. He had upgraded ten epidemiological teams, which, supported by the WHO subsidies for fuel and DSA, covered all 15 districts. (The only thing Dr. Basu Mallick could not implement was the use of motorcycles, which the WHO could provide to paramedical staff, as the state legislation did not provide insurance in case of accidents, which may have incurred during their work.)

Surveillance posts were established on the major passages of the immigrants from Bangladesh, who were arriving to the central and southern areas of the state mainly by railway. The appearance of the refugees was depressing. Exhausted, emaciated women picked up between ties the kernels falling down from passing trains and carefully carried them in their palms to the equally emaciated children. The program did not have humanitarian purposes and had no funds for them, but the families and relatives of smallpox patients were very glad with our presence, as during isolation in the outbreaks, we had a possibility to support them at least with food. The news about our activities quickly spread among the refugees and local population, which helped us finding more patients with rash. The program consequently helped some families to survive, although not many, and not for a long time, but still…

The isolation methods were basically standard, but some cases required inventions. For example, in Calcutta, a city of three million people, a smallpox affected teenage beggar was found. He was asked to list all beggars whom he knew. Through his friends, all of them were invited in a small tent camp set up in a park in the center of the city. The beggars were fed free of charge, given water, and provided with all daily necessities, including monetary compensation in the amounts close to their "earnings" from begging on the condition that they would not leave the camp for 4 weeks. It worked well since no secondary case had occurred. Certainly, such kind of isolation was possible only with technical and financial support from the WHO.

Dr. K.S. Basu Mallick (*from the Journal of Communicable Diseases*, the Indian Society for Malaria and Other Communicable Diseases, vol. 7, August 15, 1975, no. 3)

Temporary surveillance teams were also posted at the camps of refugees. The local teams carried out periodic surveys among local populations, with special attention to the settlements where refugees temporarily stayed. As a result of these actions, 19 importations of smallpox from the neighboring country had been detected within 5 months and all outbreaks were contained. NOT A SINGLE of the smallpox patients had crossed the western border of the state until they fully recovered. As the monsoon season approached, the flow of immigrants gradually subsided.

The successes achieved in West Bengal had, nevertheless, negative repercussion for me. Some heads of the Public Health Services were unhappy that they had lost their individual transport and other privileges received earlier from the WHO. In Delhi, the national authorities were displeased that I released a couple of national epidemiologists sent to the State by the Central Government and subsidized by the

WHO, who had plainly neglected their duties. The reports went to the WHO in Delhi. In June 1975, the Regional Office, using a convenient and well-founded pretext, proposed to move me to the state of Assam, located to the north from Bangladesh. It was necessary to strengthen surveillance in the seven northeastern states: Meghalaya, Assam, Arunachal Pradesh, Nagaland, Manipur, Tripura, and Mizoram. As smallpox transmission still continued in the north of Bangladesh, importations could be expected to these states.

Trip to Bangladesh

By the fall of 1975, smallpox transmission was thought to be completely interrupted in Bangladesh. Following a lapse of 6 weeks after recovery of the last known patient, Daniel Tarantola, the Head of the WHO advisors in the country, signed a telex report concerning the termination of the last outbreak in the country. Only moments after this message was sent, a message arrived: on the island Bhola, the largest island in the Delta of the Meghna River, in the lower reaches of Ganges and Brahmaputra, a fresh case of smallpox was found. The news caused a shock! Investigation and containment were urgently carried out and the outbreak was terminated. On this island, the last case in Asia caused by variola major occurred on October 16, 1975.

The remaining undetected transmission on the island occurred as a result of peculiar circumstances. To understand them, we will make a small excursus. The southern areas of Bangladesh are basically islands in the Meghna River estuary. These islands grow gradually, gaining the territory from the Bay of Bengal. During monsoonal rains, the rivers bring huge volumes of sand and silt to the estuary, raising the level of the ocean floor and forming some hills. Some of them reach the water level of the ocean and, after the floods subside, they become new islands. During the following years, grass and bushes grow wildly on them thanks to the high fertility of the soil and the abundance of warmth and humidity. They strengthen the soil and keep the islands from being washed away during the next floods. A few years later, trees grow and eventually people start settling on these islands.

In spite of the risks, these islands with highly fertile soil are gorgeous presents to the densely populated valley occupied now by Bangladesh. (People say that this process has been going on for millenniums and

Daniel Tarantola (*left*) in Delhi during the time of work of the International Commission on the Certification of Smallpox Eradication in India; Prof. Jan Kostrzewski (*right*), the Chairman of the Commission, and Dennis Olsen, the administrator of the Smallpox Unit at SEARO

it pushed away the ocean from the foothills of the Himalayas southward to the borders we know today, having built up millions of acres of fertile earth, cultivated by humans.) Possibly, the history of how the Bhola Island appeared was similar. In 1970, a cruel typhoon lifted the water level over the island and massive water streams washed away a majority of its settlements and took half a million lives. The medical rescue teams, which arrived from various countries of the world, had to deal with one of the most frequent traumas: the injuries on the internal surfaces of their arms. Trying to escape from being washed away, people clasped trunks of trees, spending many hours in such a position, until the water level came down.

Once the water receded, new groups of people started moving to the island. The Government authorized the measures for prevention of epidemics by vaccinating all new settlers, including the vaccination against smallpox. Orders are orders, but the implementation appeared to be defective. These so-called "taken measures" weakened the attention of the Smallpox Eradication Program to proper surveillance on the island. (By the way, another flood disaster occurred on the island in 1995, although with smaller human victims, but having left nearly 500 000 persons without houses.)

Having learned this lesson, Daniel decided not to risk any more with reports concerning interruption of transmission, unless he was absolutely sure that there was no other gaps in the surveillance. He invited some experienced WHO epidemiologists from the region to check the quality of surveillance in the whole lower delta area. He also called me and allocated to me three districts adjoining the state of West Bengal of India. By random sampling together with the local epidemiologists, we chose some 3% of all settlements in the area for visits. The lists were made easily, but reaching villages required developing a special plan for each of them. The estuary consists of numerous islands and peninsulas divided by small rivers and channels of various widths, with the roads and paths hardly reflected on the maps. But fortunately, the local workers knew how to access almost each village (a very good sign, since it meant that they had already been there). According to the plans developed, in the mornings, we loaded motorcycles and bicycles into jeeps and the teams went to the targeted villages. The jeeps would go to the first small river.

Bangladesh, the Bhola Island

There, the motorcycles or bicycles were shifted to local ferries or boats. Once on the other bank, the motorcycles or bicycles took us as far as they could, then we would continue on foot until we reached the settlements. The return trips required the same effort. Our evenings were occupied by reports: when and who was seen in the settlement? What he or she had spoken about? Was the local school visited? What did the children know about smallpox? As well as numerous other matters.

As a result, we could not find any major shortcomings in the surveillance.

A friendly and highly encouraging attitude by the administrative and health leaders of the districts, both to the WHO supported program and to this final exercise for the assessment of the surveillance, left a very good impression about this trip. One episode shows the care and attention I received from the Chief of one district. On New Year's Eve, I stayed in the capital of the district where a rabble group was expected. Small remaining forces of the opposition, which had killed the President

Mujibur Rahman and the majority of members of his family, being pursued by the Government troops, were expected to reach the district capital. The District Chief was informed of the expected invasion. He came to the guest house I was staying at, told me about possible troubles, and proposed that I should be hidden somewhere in case this group reached the city. Official establishments and families of the heads of the city should be excluded as they could be targeted for attacks. I made a helpless request, "Please, propose what you consider the safest action". The offer was interesting: to move me in a mosque, which would probably not be attacked. I agreed. On my arrival to the mosque, its watchman made a good dinner and flavored it with a large bottle of coconut vodka, a rough violation of the Muslim traditions, but an exception was made considering that it was on the eve of the coming new year. That was how I met the New Year of 1976. The next day, a message came from Dhaka that the group of insurgents was intercepted some tens of kilometers from the regional center.

We continued to work according to the plan. In a month's time, the work in the area was finished and the administrators of the three districts solemnly, and with gratitude, sent me to Dhaka.

(It is probably worthwhile to mention that from 1987 onward I worked for several years under Daniel's supervision in the WHO Special Program on AIDS (SPA). It was in the summer of 1987 when Jonathan Mann, the Program Director, and two Program staff members, Daniel Tarantola and Manuel Carballo, locked themselves in the Office of the Director for three days and developed a draft of the document on AIDS prevention, which eventually became the basis for the corresponding WHO strategy. Since then, the basic components of the prevention have not changed essentially, except for the prevention of HIV in drug users, which was separated from the "transmission through blood" and became a major component of the Program.)

In January 1976, I returned to India.

The geography in the Northeast India is very different from the rest of India. Mountainous areas are more sparsely populated than the mainland of the peninsula by the people with Mongoloid types of faces. They are more open, straightforward, and hardworking. Ethnic and cultural features of the people in these states differed notably from the Bengalese. These were the states that later on, in the 1990s, provided the routes for smuggling illicit drugs from the Golden Triangle to India and further on to Europe. Smallpox transmission was interrupted here earlier and the states were running the post-eradication surveillance.

Driving from Assam to Meghalaya one evening, we came to one of the PHCs. The physician in charge of it, a woman in her early twenties (I unfortunately do not remember her name, and no diary was kept), had recently graduated from medical school. We checked the documents, the results of household visits, and periodic reports. All were in order. We were about to leave the PHC to continue the trip to the other centers when a man came, the teacher of the local school, to tell that he had heard about smallpox in one of the villages served by this center.

(In India, as in other endemic countries during the later stages of eradication, compensations were announced and widely publicized for reports on suspected smallpox patients. The initial amounts were meager: a hundred Indian rupees, equivalent to US$ 2.50–3.00. By 1975, the sum was raised to US$1000.) The doctor translated his report and turned to me with an inquiring glance and asked: "What should we do?" I replied: "What would you have done, if I were not here?" She responded that she would go to the village and see the patient. Then I said that I would go with her. Further enquiries about the location of the village revealed a difficult task in front of us: about 15 km by jeep and a further 3 to 5 km on foot, while the sun was approaching the horizon. The doctor called three health assistants and asked them to bring torches for the five of us. The torches were made from the reserves of the dried sticks of the pine tree wood kept in each house of the area. After everything was ready, we started our expedition. Lidia stayed at the PHC. At the beginning of the trip, with darkness approaching, the doctor asked whether I was afraid of running

into a bear. I considered it a joke and told her that I had a knife in my bag, thinking to myself that with torches, bears are not dangerous.

We were walking on a cow track. From time to time, the doctor let us go ahead and stopped behind. I ask the health assistants what was happening with her, whether she was sick. No, she was not. She was simply removing leeches from her body. And then I realized why the skin on my shins was itching terribly. I lifted the bottom of my trousers, and discovered several leeches hanging on each leg. My companions explained that leeches creep up on bushes and when a herd of cows or other animals pass on and shake the branches, the leeches fall down and stick to their skin. This time they attacked "cows" without wool! I removed the bloodsucking leeches, stuffed the trouser-legs into my socks and continued the journey. It started drizzling. The path went through the hills, 300–400 m up on a relatively gentle slope, and then passed a stream before climbing again 300–400 m. We ascended and descended an incalculable number of times. When darkness finally fell, we lit the torches. We reached the village by 11 in the evening. Here the village constructions were unusual: all houses stood on wooden piles about 3 m high, for protection from predators, snakes, and leeches. We entered the house. It had one big room with everything included: kitchen, dining room, and bedroom. The doctor went to look at the patient. The man suffered from malaria and had no rash. She gave him medicine and was ready to go back. I was sitting at the door, breathing hard and totally exhausted. The health assistant looked at me and said that we should go or otherwise we would lose the respect of the people.

Then the same ups and downs. The drizzle turned into rain and the small streams became rivulets, which we had to cross stepping onto bamboo logs, keeping one hand on the bamboo handrail, and the other on the torch. A kilometer and a half from the car the torches almost burned out, and without them one could not make a step. The doctor collected all the remaining sticks and two health assistants went with them to the nearest village to collect more torches. They returned some 40 min later and we were able to continue walking. I remembered about the leeches only after we reached the car—my back was itching and I rubbed it against the car seat. We returned to the PHC at 3 o'clock in the morning and lit candles. In the room, I turned to the exit, and Lidia exclaimed: "What happened to your back, the whole shirt is soaked with blood?" I had enough strength for humor and replied with a joke: "When we began the journey, the doctor cautioned that we could meet a bear!" We removed all the leeches and I rinsed myself before collapsing into bed as if dead.

Before I was transferred to Delhi, Lydia almost always traveled with me during the field trips in the states of India. Once in Delhi, I started traveling by air. Lydia mainly remained at home where she found good friends among compatriots working in USSR missions and with their families.

Another rather amusing story: Once I was to go from the state of Manipur to the next state, Mizoram. I asked the Chief of one health center the permission to leave Lydia behind for a couple of days to avoid going through the rough mountain roads. She settled in with the family of the center's Chief. At that time, the weekly household visits were on, and the Chief of the center personally supervised this work. She suggested that Lydia go with her, and Lydia agreed. That day they walked some 20 km, selectively checking the houses scattered on slopes of the hills. Lydia returned, her feet worn out. For the second day, to make it easier, the host chose a more remote village in a more plain area, near the border with Bangladesh. After they finished their household visits, already after sunset, they returned to the car. The engine did not start, the battery was dead. There was no electricity in the village, no other cars, and no other means of recharging the battery. The India–Bangladesh frontier post was the nearest point of "civilization" and the driver went there to look for help. The frontier guards drove back to the village with him and decided that returning to the Center with the uncharged battery was too risky. They took the women with them to the frontier post, entertained them with their soldier's food, and arranged a bed under their greatcoats. The next morning, they got the engine running and sent them home. On my return to Manipur, they told me this story and we all cheerfully laughed at it.

At the dinner, the Center Chief admitted that she thought that I had left Lydia with her in order to see how she was doing her job and then to report to me. Therefore, she chose the most difficult terrain and most remote settlements for the visits. This was followed by more laughter. Laughing is fine, but later on Lydia told me that the next time she would go with me and ready to face any kind of difficult roads rather than stay behind.

Lydia asking the woman holding her child with smallpox to step out of the shade for me to examine the patient and take samples for laboratory tests

After several months of work in the northeastern states, I was transferred to New Delhi to work with the Smallpox Unit at SEARO. My previous position was taken over by Dr. Valerii Fedenev, an epidemiologist from the USSR. The unit was chaired by Dr. Nick Ward from the United Kingdom. Several endemic countries of the region at that time were coming to the end of the two years of the post-eradication period before the certification of the smallpox eradication. I was assigned to assist in facilitating the work of the national and international certification commissions. Larry Brilliant was also specially invited to facilitate this mission.

The certification in the countries was organized under the following scenario. At the beginning, each country built up a national commission. These commissions included national experts in public health and epidemiologists who took part in the eradication program. The commissions also included national specialists from the medical services and individuals who were skeptical of the possibility of eradicating smallpox and criticized the program itself. The commissions checked the reports on the periodic household surveys; the results of the studies on the presence of scars left by smallpox on the faces of people affected in various years; and reviewed the results of the laboratory tests of the

Rafi Aslanyan, Valerii Fedenev, and Connie Davis (United States), WHO consultants and staff involved in the Program

samples taken from the patients with all skin eruptive diseases identified during the last two years. The details of the work of the commissions are described in several publications.[6]

All reports were randomly checked on site during the visits to public health and medical institutions that participated in the program. Based on these observations, national commissions prepared reports for the international commissions. The international commissions were created from world famous experts in the fields of public health, medicine, and virology. These commissions carried out basically the same activities, but they were empowered to have the last word on the extinction of smallpox transmission in each country. With support from the experts in the countries, the commissions made assessments in India, Nepal, Bangladesh, Burma, and Butane. In 1978, the region with a population of more than a billion people was declared free from smallpox.

Prof. Frank Fenner, an Australian virologist and microbiologist, played an important role during the intensive phase of the eradication program. Virologist and microbiologist, he became a national hero in Australia in the early 1950s, when he helped direct a program to control the spread of feral rabbits, which were nibbling their way through the country's pastureland, with the help of myxoma virus.

A pilot study on the myxoma virus showed a rabbit mortality rate of more than 99%. In order to reassure Australians that the myxoma virus would not infect humans, Fenner and two fellow researchers injected themselves with a dose potent enough to kill 1000 rabbits. They survived and the Government initiated a pest-control campaign using the myxoma virus. In 1969, after doing research on poxviruses including the variola virus, Fenner began advising the WHO on its campaign to eradicate smallpox. In 1977, he was named the Chairman of the Global Commission for the Certification of Smallpox Eradication. As the campaign neared its goal, he was able to demonstrate that there were no animal carriers of the disease, an important step in declaring the victory over the disease. In May 1980, as the Chairman of the Global Commission, Fenner officially declared during a session of the World Health Assembly that smallpox was eradicated from the world. A few years later, in 1987, the work was completed on the book Smallpox and Its Eradication, an important and fundamental edition of the WHO on all aspects of the illness and its eradication. Prof. Fenner played a key role in this work.

Donald Henderson and Frank Fenner discussing the process of certification of smallpox eradication in the countries of Southeast Asia

During the last stage of the work in this region, Nick Ward left the program and I acted as the Chief of the Unit. It was the time for finalizing the documents of the commissions, winding up the administrative and financial matters, and transferring the program equipment and transport to the countries. Dennis Olsen and Tony Scardaci, the administrative and financial officers, were running these activities. The work was completed by the end of 1978. Isao asked me to continue the work and move to Ethiopia. In March 1978, following a brief respite in Moscow, we were in Addis Ababa.

[6] Basu, R.N. and Khodakevich, L.N. The National Commission for Assessment of the Smallpox Eradication Program in India. *Ind. J. Pub. Health*, vol. 22, no. 1, January–March, 1978, pp. 16–30; Eradication of Smallpox in India. Report of the International Smallpox Assessment Commission. *Ind. J. Pub. Health*, vol. 22, no. 1, January–March 1978, pp. 8–15; Fenner, F., Henderson, D.A., Arita, I., Jezek, Z., and Ladnyi, I.D. Smallpox and Its Eradication, World Health Organization, 1988, ISBN 92 4 156110 6.

Viktor Zhdanov and Donald Henderson celebrate the eradication of smallpox in India

Prof. Viktor M. Zhdanov

In 1951, when Zhdanov was appointed the Head of the Sanitary and Epidemiological Services of the USSR, he showed active interest in the concept of eradication of diseases. His enthusiasm was boosted by the successful termination of smallpox transmission on the whole territory of this country by 1936 and by successful elimination of dracunculiasis (guinea worm disease) in the republics of Central Asia in 1932. Eradication of diseases attracted Prof. Zhdanov from the economic point of view as the concentration of resources during a short period of time would lead to considerable savings in the economy in the long term. In 1958, Zhdanov, the Deputy Minister of Health of the USSR, as the head of the Soviet delegation to the 11th World Health Assembly (WHA) proposed to set up a program for global eradication of smallpox. Keeping in mind that the WHA took place in the United States, Zhdanov began his report with the citation from Thomas Jefferson, the President of the USA, in a letter addressed to Edward Jenner in 1806, in which he wrote, "Thanks to your opening... future nations will know by history only that the loathsome smallpox has existed and by you has been extirpated". The WHA supported the proposal and the WHO initiated the world war against smallpox. During the final stages of the program, Prof. Zhdanov served as a member of the International Commission on the Certification of Smallpox Eradication in India and Bhutan.

According to A. Turbin, a Russian poet, "He is a highly volatile person, not only in outward appearance, but also volatile internally, optimistic, and changing. He should be irritating and tiring for the people inclined to follow once established order in the system; and such people were extremely boring to him." With numerous publications, three inventions and 30 monographs to his credit, Zhdanov also found time for other "nonprofessional" engagements. An inveterate philatelist, he possessed a unique memory and could cite contemporary popular poems and songs.

Ethiopia

I was assigned as a senior advisor to the WHO team that included two WHO epidemiologists: P. Arbani from Indonesia and C. Amaral from Brazil, and the WHO administrative and finance manager, O. Ismail from Egypt. Dr. Ato Yemane Tekeste, a very tactful and progressive epidemiologist and public health manager, led the national program and facilitated the cooperation between the WHO and the Government. The eradication program in Ethiopia, a country with 30 million people, had practically no health infrastructure, which greatly differed from the situation in India. The work was carried out by a thousand field workers paid from the WHO funds, who worked under the supervision of 15 national health inspectors also subsidized by the program for their travels to the field. In addition, the WHO supplied the program with transport, blankets, and stationary for recording and reporting on the field activities.

Smallpox transmission was already interrupted in the country and the eradication program concentrated on the surveillance of skin eruptive diseases and collection of samples for laboratory testing.

Once per quarter, these field workers visited many thousands of tukuls (households) scattered through the hills of the Ethiopian highlands as well as all houses in the towns and cities. During the 2 years of surveillance, no cases of smallpox were found. In thousands of samples collected from patients with rash, the WHO Collaborating Centers found no variola virus. In the second half of 1979, the team facilitated the work of the national and international commissions, which certified Ethiopia among the last African countries to be free from smallpox. The goal of the program in this country and in the whole world had been completed.

As a result of the campaign, the last case of smallpox in the world was registered on October 26, 1977, just 19 years after the world community declared its intention to wipe out the disease that had been killing human beings for over 10 thousand years. During the intensive phase of eradication program, from 1967 through 1979, the WHO was spending US$ 5 to 13 million annually. Its total expenditure for the campaign amounted to US$ 98 million.

The eradication of smallpox was an extraordinary achievement by mankind during a rather short period of time. In 1966 (at the beginning of the intensified campaign), smallpox was registered in 43 countries, 31 of them (with a population of a billion people) reported more than 2.5 million cases annually.

Isao Arita and Jan Kostrzewski are discussing the organization of work of the commissions on the certification of smallpox eradication in the countries of East Africa. Isao was working for several years as a member of Henderson's team at the WHO Headquarters, and from 1977, he chaired the Smallpox Eradication Unit until it was closed in 1987. Prof. Jan Kostrzewski, the Secretary of the Medical Division of the Polish Academy of Sciences, was a member of the international commissions for India, Bhutan, Nepal, and Ethiopia

The pessimists and opponents of the eradication program were prostrated. As Jack Hopkins recalled,[7] one of the high-ranking WHO officials said to D.A. that if the WHO campaign in India would ever succeed, he "will eat a tire from a jeep". After the last case was registered, D.A. sent him a jeep tire.

Back at home

All reports were randomly checked on site during the visits to public health and medical institutions that participated in the program. Based on these observations, national commissions prepared reports for the international commissions. The international commissions were created from world famous experts in the fields of public health, medicine, and virology. These commissions carried out basically the same activities, but they were empowered to have the last word on the extinction of smallpox transmission in each country. With support from the experts in the countries, the commissions made assessments in India, Nepal, Bangladesh, Burma, and Butane. In 1978, the region with a population of more than a billion people was declared free from smallpox.

Svetlana Marennikova and Aleksandr Gromyko after a session of the Certification Commission for Kenya. In the middle, Dr. R.N. Basu, one of the leaders of the National Program in India and a member of the Commission for Kenya

A considerable amount of funds had been accumulated, and the Government and UNEP agreed to use this money for training in the USSR the epidemiologists and veterinarians from Asian, African, and South American countries on the control of zoonoses. The agreement was signed 6 months before, but the institution put in charge of the project did not have sufficient capacity to implement it. A meager part of the budget was used and the Ministry of Health was eager to boost the development in order to fulfill its obligation to the international organization. I started working the next day. The project was implemented successfully during a period of 3 years as planned, but details of this work are in no way related to smallpox.

Study on the seasonal variation of smallpox incidence

In Moscow, I started processing the materials on smallpox that I accumulated in India and the other countries of the region with an attempt to find out the reasons for seasonal fluctuations of the disease incidence. This work is reported here in a very concise version.

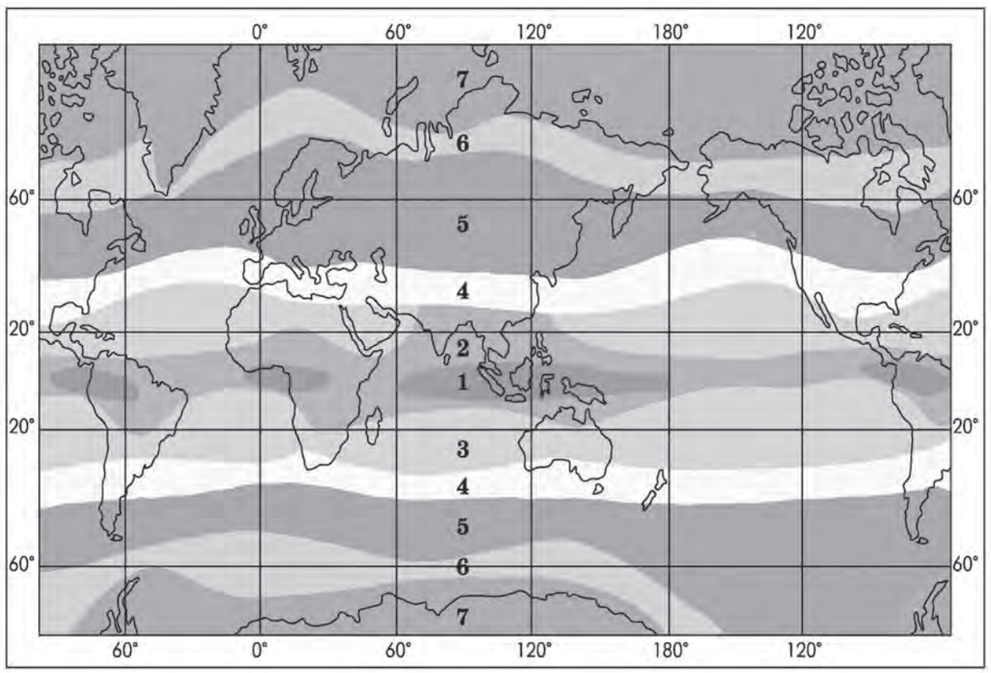
The seasonal fluctuations of smallpox in the endemic areas are considered to have various reasons. Fenner at al.[8] having analyzed numerous sources showed that the seasonal fluctuations of incidence

[7] Hopkins, J.W. *The Eradication of Smallpox: Organizational Learning and Innovation in International Health,* Boulder, CO: Westview Press, 1989.

[8] Fenner, F., Henderson, D.A., Arita, I., Jezek, Z., and Ladnyi, I.D. *Smallpox and Its Eradication*, World Health Organization, 1988. ISBN 92 4 156110 6, pp. 179–182.

(or death rates from smallpox) varied in different countries and depended on the geographical situation and climate. In Bangladesh, the maximum number of cases was observed from January through the end of April, and in Brazil, located in the southern hemisphere, from August until the end of October. In Indonesia, the peak was observed in January, and the cases were rather evenly distributed among the other months. In Madras, India and in Zaire, the incidence was more or less uniform during the year. On the basis of this analysis, Fenner concludes that the smaller the variations of humidity and seasonal rains, the lower are the fluctuation of the incidence. All three areas of the low variations (Brazil, Zaire, and Madras, in the extreme south of India) are located in the Equatorial belt with constantly high temperatures and hot and humid equatorial climate throughout the year.

Further, Fenner analyzes three possible reasons for seasonal variations. The first is the changes in viability of the virus. The second, by analogy to flu, a change in susceptibility of the host, in connection with seasonal changes of permeability of the mucous membranes of the respiratory tract. And the third is the social factor: dispersion of the population occupied with planting work during the rainy season, while numerous festivals and social contacts occur during the dry seasons and promote broader virus dissemination. The role of this factor (among the other observations, that are seasonal variations in the size of the smallpox affected settlements, age and sex of the patients, and the persons transmitting infection within and between the villages, and some others) was a subject of my interest in the study of the seasonal incidence variations. For the analysis, I used personal observations in Madhya Pradesh and the documents of the program in Bangladesh and Burma.



The climatic zones of the world; 1 and 2 show the Equatorial and Subequatorial belts

The long-term observations showed that for the countries studied, a significant increase in the incidence was observed in January–April and the lowest figures were recorded during the rainy seasons. Our analysis showed that these variations can hardly be linked purely to the seasonal changes in temperature or humidity, levels of rainfall, or a change in bactericidal action of sun rays or the other physical factors mentioned above. The change in high humidity and the level of rainfalls, for example, can not affect the incidence as the significant decrease in the number of cases starts at the beginning of summer, that is, about 2 months before the rains start and humidity sharply rises.

More likely, as suggested by Fenner, the incidence depended on the social phenomena related to the economic and social activity of the population. To prove this assumption, a tool was required that would show the intensity of infection transmission, or the rate of reproduction of infection: an average number of new cases originating from one case in the previous generation during one turnover of infection. Such an instrument would have allowed the period of the turnover to be linked with the change in incidence in different periods of the year.

The period of turnover of infection (the average number of days between two generations of cases) is quite a stable indicator. For the state of Madhya Pradesh, it was, by our calculations, 18.31 days with the range of 16.29 to 20.33 days. The publications showed that this period in the United Kingdom, Poland, and Sweden ranged from 16.31 to 17.57 days. However, I did not know how to connect this indicator with the change in the monthly incidence.

The help came from my friend, a mathematician. After I described the issue, he proposed a formula and explained how it was deduced. The equation appeared simple enough and easy to use:

$$R_1 = (n_2/n_1),\ t/T \quad or R_1 = \exp(t/T_1 \times \ln n_2/n_1), \text{ where}$$

R_1 is the indicator (rate) of the intensity of transmission of infection within month 1;

n_1 is the number of cases registered in the month for which R_1 is defined;

n_2 is the number of cases registered within the following month;

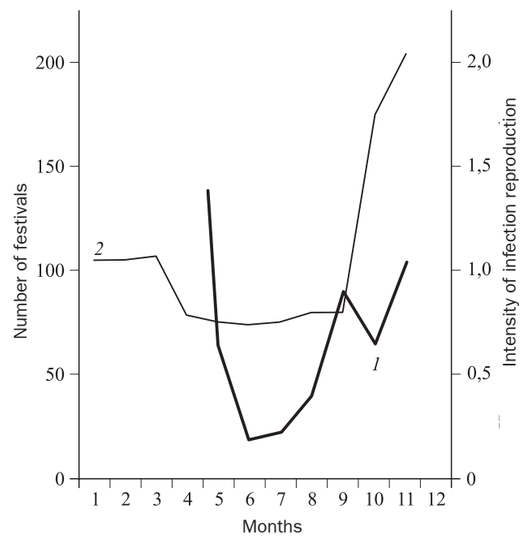
t is duration of the period of the turnover of infection (days); and

T_1 is duration of the period of the reporting (number of days in the month under calculation).

The use of this equation, taking into account the delay in case reporting, equal approximately to one month, allowed for calculation of the intensity of infection transmission for each month of the year. The calculations showed that during the period from April through September, in one infection turnover, one case produced 0.74 to 0.81 secondary cases, i.e., the intensity of transmission was decreasing. In October, when the humidity of air still remains high, the intensity of transmission was sharply increased, reaching a maximum of 2.04 in November. Within the 3 following winter months, when the highest incidence is observed, the rate of intensity slightly exceeded unity.

The next step was to find out the cause–effect relation between the social events and the rates of transmission in different periods of the year. In the first 1.5–2 months of the rainy season, the overwhelming majority of the rural adult population (some 75–80% of the country population) was occupied with sowing and care of agricultural fields. This kept people in or near their villages. In the second half of this season, the volume of agricultural works was decreasing, but did not end. Besides, the population movement to long distances is limited by rains. The seasonal migration sharply increased after the end of monsoons, in September–October. For a quantitative assessment of the migration, we used the data from the population census, which registered the numbers of the traditional festivals by month in the state of Madhya Pradesh. Superimposing the indicators of the transmission rates on the numbers of festivals per months showed that the increase in transmission in October and November comes straight after the sharp increase in the number of festivals during religious holidays, registered in September and October.

Interrelation between the frequency of traditional festivals and the rates of transmission, by months. On the left is the number of festivals (50–100–150–200) and on the right, the rate of transmission (0.5–1.0–1.5–2.0). The number of holidays is shown by the heavy line. The months of the year are shown below[9]



Thus the cause–effect relation between the social and cultural activities and the seasonal variations in smallpox incidence, as advocated by Fenner, looks obvious. I did not pretend that I made a discovery, but I think I added a mite in advancement of our understanding of these relations.

This study was a section of my dissertation titled "Some epidemiological aspects of smallpox and the program of its eradication", which was successfully defended in Moscow at the Ivanovsky Institute of Virology and was awarded a degree of candidate of medical sciences, an equivalent to PhD.

Back to the eradication program

In 1970, when the WHO was unfolding the Intensive Phase of the Program in Eastern Africa and Southeast Asia, a new smallpox-like disease was found in some countries of Central Africa. This so-called monkeypox much resembled smallpox, although it was a less severe disease, and it was thought to be contracted by man from monkeys. This discovery was considered by the Committee on Smallpox and Related Orthopoxvirus Infections a potential threat to smallpox eradication. At the end of 1983, Dr. Isao Arita, at that time the Head of the Smallpox Eradication Unit in Geneva, planned, in pursuance of the Committee's recommendations, to sort out the ways this virus circulated in nature. With this objective, Isao invited me to Geneva and assigned me to the planning and coordination of the research on the monkeypox ecology. The research strategy was formulated in Geneva on the basis of the data received from the epidemiological surveillance on monkeypox in Central Africa and on the previous ecological studies. The field work was to focus on Zaire, from where most of the cases were reported.

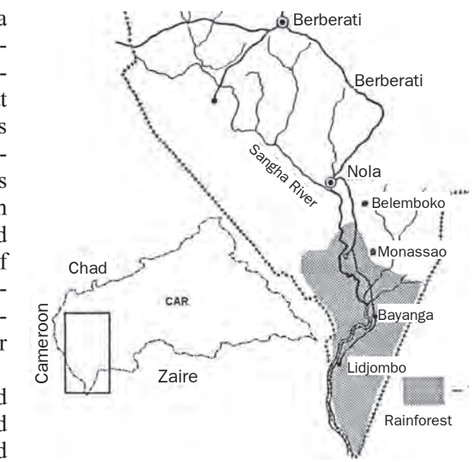
One event at the beginning of 1984 had slightly delayed the expeditions to Zaire. In February, a message was received from the Central African Republic (CAR) on suspected cases of smallpox. We immediately flew to the CAR to investigate this report with Ross Widy-Wirski, a WHO epidemiologist, who worked in this country earlier and knew well the local conditions.

The message came from the southwestern part of the country, covered with tropical rainforest, situated some 800 km from Bangui, the country capital. Our investigation of the report revealed six patients with a disease resembling light forms of smallpox in a pygmy settlement consisting of 50 persons, several kilometers away from the village Lijombo. The village was located some 50 km north from the joint borders of the CAR, Cameroon, and Congo.

[9] This and the other figures are scanned from the pages of my dissertations, on which I pasted some texts in English, when necessary, for better understanding. Not because I was lazy to redraw them, but in order to show the original sketches.

The head of one of the two affected families was a hunter. Several weeks prior, he had brought back a monkey with the body covered with lesions, similar to pustules, and a gazelle with almost identical lesions. Meat of the killed animals was divided between the members of the hunter's family and shared with some other families of this settlement. A few days later, first the hunter's wife, then within 3 days, their five children aged from 10 months to 10 years, got sick. All the patients lived in three huts adjacent to each other out of a total of 12 huts in the settlement. The inhabitants of the settlement informed us that they had been living there for several months without having had any contact with other tribes.

This episode was worth mentioning since it showed that pygmies were susceptible to monkeypox virus, and all six patients in the settlement probably got infected from one sick animal.[10]



The southern part of the Upper Sangha (Central African Republic) where the suspected cases occurred

Once monkeypox was found in humans, we decided to conduct a survey of wild animals in the surrounding area. Ross arranged with a Yugoslavian timber company working in the same area to set up a base for studies approximately 10 km from the affected settlement. American Peace Corps volunteers were invited from Bangui to participate in the study. Transport was provided by the Ministry of Health. The team had collected a number of wild animals and samples were sent for laboratory testing. None gave positive results.

Here, in the CAR, there was one episode which caused excitement. One morning after refueling the tank of the car, I stepped down from the cab to pay for the fuel. On return to my seat in the car, I found that the field bag left on the right seat was missing. Adrenaline hit my blood. Besides the camera with flash, the tape recorder borrowed from the WHO, and money, there was something of far greater value in the bag—the three photo films that I shot during the visits to the pygmy settlement. Ross spoke to the local health assistant working with us and told me not to get too upset. We returned to the same fuel point in the evening. The assistant was sitting and drinking beer, and in front of him was my bag which he had found in the bush behind the fuel post. Money and the tape recorder were gone but the camera and films had no apparent value for the thief. So, thanks to Ross and the local assistant, I was able to show the pictures of pygmies and monkeypox in the CAR to my colleagues at the WHO, to include them in my publication, and in this essay. Almost a week and a half after my return from a trip to the CAR, I felt skin burning on the top of the heel above the edge of the shoes, where I noticed a chain of whitish pustules. I phoned Ross, and he told me that he had the same kind of lesions, but they did not surprise him, as it was not for the first time. The pustules were caused by the tropical sand flea called jiggers. The female of the flea jumps up from the ground, reaches the skin of animals or men, penetrates it and lays its eggs.

[10] Further details on this outbreak are described by: Khodakevich, L., Widy-Wirski, R.I., Marennikova, S., and Nakano, J. Orthopoxvirus Simienne de l'Homme en Republique Centrafricaine, *Bull. Soc. Path. Ex.*, 1985, pp. 311–320.

Three of the six monkeypox patients among pygmies in the CAR: a 10-month-old baby (*left*) and a 2-year-old child with his 22-year-old mother also affected by monkeypox (*right*)

When the process is over, the pustule breaks, the eggs are freed, and disseminate to the soil to continue the further stages of development. In the WHO medical unit, the contents of the pustules were put under a microscope. Numerous whitish round-shaped formations were seen: the eggs of Tunga penetrans or Pulex penetrans. In a couple of weeks, all pustules opened and the skin cleared up with no complications. During the following visit with Ross to the pygmy settlements, we deliberately looked for people with similar lesions and saw several affected children. The local women used sharply shaped wooden sticks to open the pustules and remove their contents on the palms and legs of their children.

Pygmies in their settlement. During the day, only women and children stay in the village, while the men are occupied hunting. In the background, the huts in which the pygmies live

Ross with a local assistant in the CAR with the recovered bag on the table. For some years, Ross, a professional venereologist, worked as a WHO expert in Central African countries, including the CAR. Here, he studied the prevalence of STDs and yaws and treated patients as well. In the CAR, he built an OPD clinic for STD patients for testing, treatment, and follow-up

The ecology of monkeypox virus: theoretical presumptions for the study

The monkeypox virus was first isolated in 1958 at the State Serum Institute in Copenhagen. In the summer of that year, two outbreaks of a pox-like disease occurred among the captive monkeys shipped by plane from Singapore on April 29, i.e., 2 months prior to the appearance of the disease. The second episode happened in October of the same year among the monkeys shipped from Singapore on September 18, approximately 2 months after the animals were imported. On the basis of these and other early reports on occurrence of monkeypox among the captive animals in Europe and the United States, it was assumed that monkeypox in animals could have either a long incubation period or infection could develop without visible clinical manifestations. Our analysis of several related communications caused a doubt that such forms of infection could play any essential role in the maintenance of the virus circulation in nature. One reason was a high similarity of the natural course of the two diseases, smallpox and monkeypox, in humans. The results of the laboratory tests of wild animals were quite different: the cultivation of liver tissues of about 300 monkeys from various African countries, including those seropositive for orthopoxviruses, failed to isolate the virus. The efforts to isolate the virus from the samples of kidneys and spleen of 930 animals, including 227 seropositives, also gave negative results. Additionally, several outbreaks of monkeypox in captive monkeys occurred among the animals imported from the countries where monkeypox was never registered in man.

On the basis of this analysis, we built up a working hypothesis that the virus transmission from an infected animal is possible only during the active periods of the disease. Appearance of infection in captive

animals imported several months prior to the onset of outbreaks could only be explained by settling newly imported mammals in the same captive spaces. Such newcomers would have arrived from an African country more recently (a week or so), during their incubation period or with active stages of the disease, because they did not have proper veterinary inspection or quarantine on their arrival into captivity.

The interest in the ecology of the virus had risen sharply after the appearance of monkeypox in man. However, several specially organized studies among wild animals in the West African countries in 1970–1972—in Ivory Coast in 1971; in Ivory Coast, Mali, and Upper Volta in 1973–1974; and in Zaire in 1979—had not brought the researchers any closer to the understanding of how the virus circulated in nature.

Based on the results of these studies and theoretical presumptions, we expected that the natural reservoir host of monkeypox virus could be a group of mammals with a permanently maintained high population density and frequent contacts among susceptible members of the group that could allow for an uninterrupted transmission of the virus among their congeners. This group would most likely be rodents, which form dense populations.

Such a hypothesis was generated with support from Prof. Vitalii D. Belyakov who at that time was holding the Chair of Epidemiology of the Sechenov Moscow Medical Academy. Prof. Belyakov was delivering a series of lectures on the role of heterogeneity of populations in self-regulating parasitic systems. After one of his lectures, we met with Belyakov and he, after learning that I was working on smallpox eradication, justified the possibility of eradication using the theory he was actively promoting. He listed the features of the virus that made the infection eradicable, including the following: (1) during its evolution, the virus had lost the possibility of frequent mutations and, therefore, adaptation to other kinds of animals; (2) the virus had selected human species as the only animal in which it could effectively replicate; (3) thereby, it had lost the possibility of transmission and circulation among the populations of other animals, having left for itself only one way to sustain itself in the population by circulating within the human community; (4) since the virus does not survive in the environment for more than several days, it has no possibility of being transmitted except through direct contacts between patients and other

Prof. Vitalii D. Belyakov, an outstanding Soviet scientist, epidemiologist, and lecturer; academician of the Russian Academy of Medical Science and Russian Academy of Natural Sciences; doctor of medical sciences and Major-General of Health Services, belonged to the galaxy of graduates of the Kirov Army Medical College, in Leningrad. He made a huge contribution to the development of national public health. When he was a student of the Kirov Medical College in Leningrad (now St. Petersburg), he won a highly valued Stalin stipend. In the fall of 1941, together with friends, he was among the fighters looking for and suppressing the incendiary bombs dumped by German aircrafts on the city. From 1982, Belyakov headed the Chair of Epidemiology of the Moscow Medical Academy. His colleagues say that he inherently was a reformer both in the field of teaching and in science. Prof. Belyakov believed that the heterogeneity of populations of the host and parasite, as well as their changeability in the process of interactions, was the only mechanism for self-regulation of parasitic systems.

Vitalii D. Belyakov
(by the courtesy of Dr. I.N. Briko, Chair of Epidemiology, Moscow Medical Academy)

susceptible persons; and (5) the persons who survived smallpox develop a lifelong immunity, while the others died along with the virus particles they carried. The summary was short but capacious: the lack of heterogeneity within the viral population was one of the leading factors that gave man a chance to eradicate the disease.

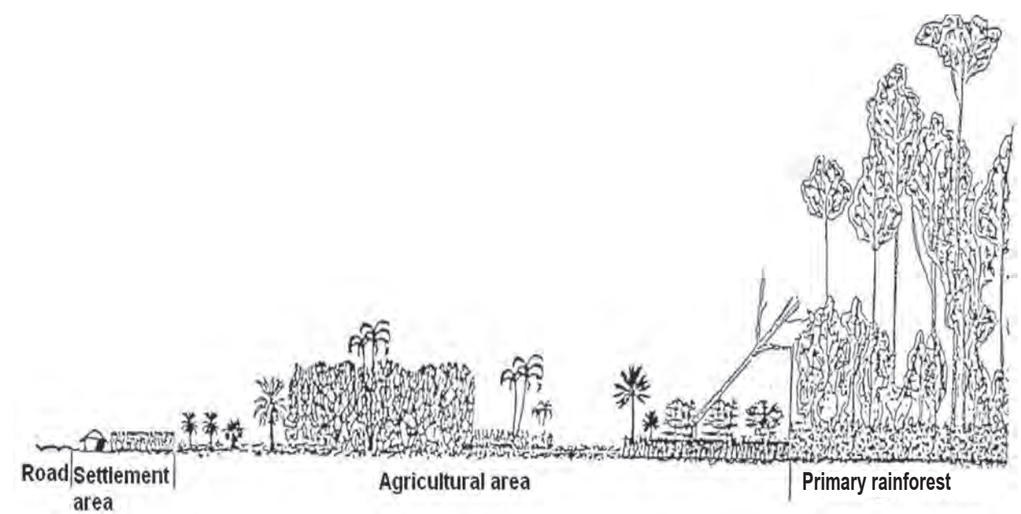
In the following years, when I was involved in the studies on the ecology of monkeypox virus, I met Prof. Belyakov on numerous occasions while coming to Moscow during the annual leaves. I shared with him the plans and results of the studies that got him very interested and somewhat involved in the research. After the studies were completed and summarized in the dissertation “Ecological and epidemiological aspects of smallpox of monkeys”, Prof. Belyakov kindly agreed to play the role of an official opponent in its presentation.

Our studies on the ecology of monkeypox virus

The research was organized in several stages. In the beginning, we reviewed the analysis of the results of monkeypox over nearly 10 years of surveillance among the unvaccinated populations in the countries in Equatorial Africa. The results appeared interesting and mysterious: children between 3 to 9 years contributed the majority, 64.8%, of the primary cases and the highest incidence was recorded in the children of 3–7 years of age, while 6.6% were teenagers from 9 to 14 years, and 3.5% were the persons older than 15 years. Paradoxically, it looked like the adults who reportedly hunted wild animals, skinned them, and handled the raw organs while preparing food, had the lowest risk of getting infected.

This observation led to the next stage of the research, specifically, to the study of the places of habitation and the day-to-day behavior of people of different ages. The Bumba zone, situated in the northwest of Zaire, with one of the highest number of human cases, was chosen for the field studies.

The settlements are usually located along roads. The population practices shifting agriculture. The villagers first burn out some areas of the tropical forest, clear away the wood, and then plow up the earth. For several years, these sites are planted with a variety of cultures.



Zaire, ecological features of the territories surrounding human settlements

Richard Olio (*right*). By an occasional and favorable coincidence, Richard and his wife were near the area of our studies. A biologist from the United States, he studied the structure of tropical rainforests. Having heard the subject of our research, he willingly agreed to participate in the ecological description of the areas surrounding human settlements and thereby contributed his professional skills

After the soils lose their fertility, these fields are abandoned and new areas of the forest are explored. Blessed by the high humidity and abundance of year-round sunlight, wild vegetation starts growing vigorously like "mushrooms after a rain". At the beginning, it is grass, then bushes, and between them the palm trees and the trees of the future closed dense forest. These growths form the secondary tropical rainforest, which quickly becomes populated by numerous kinds of small mammals living at the ground and arboreal levels, mainly squirrels and other rodents, and birds. This real densely populated paradise is totally different from the closed rainforest. In a closed forest, there is a vacuum of fauna at the earth level, while all animals occupy the medium and upper arboreal layers. On the bottom of the closed forest, one can see the trunks of large trees and lianas hanging down from them. Only ants, whose bodies form black or brown vertical and horizontal threads on the trunks of trees, move between the earth and the upper layers of the forest. It is possible to walk freely for kilometers until rivulet streams or fallen old trees create an obstacle. The empty spaces left in the umbrella of the forest earlier occupied by the crown of fallen trees let sunbeams reach the ground below. On such spots, the tropical paradise develops similar to that on the sites of the abundant agricultural areas surrounding human settlements.

Behavior of the population

The children below the age of 3–4 years usually stay in the houses in the village or in temporary huts when the family moves closer to their remote agricultural fields. At this age, either the mother or some elder sibling keeps an eye on them. Beginning from the age of 4–5 years, they join their senior mates who go hunting in the areas left idle after cultivation. Here, they catch and shoot various small animals, skin

Some of the volunteers from the American Peace Corps who were working in the Bumba zone, in Zaire:
Shannon Hager, Brad Otto, and Jennifer Clegern, resting after a day of hard work

them on site, and eat their organs often without any thermal processing. The parenchymatous organs are the greatest delicacies as they are probably easier to chew.

This looked like a clue to where we should look for the animals that could be the source of infection for humans. In parallel with the ecological and human behavioral studies in the areas surrounding villages, the team of volunteers from the American Peace Corps and workers from the local public health services started taking blood samples for monkeypox virus antibodies from wild animals and pets living in the villages and surrounding area. A monetary award was announced for the local people who would bring an animal with pox lesions on the skin.

The squirrel coded eventually under number 249
(*by the courtesy of Brad Otto*)

The announcement of the award eventually worked. It happened in the village of Yambuku, at the Belgian Catholic mission providing medical aid to the local population, where the WHO research team was based. On July 21, on the eve of my birthday, when we returned from the field, the nurse heading the Mission dispensary showed us a package made of bamboo leaves, which was brought by a woman from

a nearby village. We unfolded the leaves and found a dead squirrel (later coded under number 249). Brad Otto made a photo of the squirrel, which is shown above.

On the belly of the animal, we noticed some crusts somewhat similar to pox lesions. I could not keep myself from exclaiming: "This is a real gift for tomorrow's celebration". Eventually, the WHO Collaborating Centers isolated monkeypox virus from the lesions sampled from this squirrel.

It was the first case of isolation of the virus from a wild animal infected in nature.[11]

Rodents were the prime targets for the laboratory testing for monkeypox antibodies. At the same time, we also took blood samples from domestic cats, assuming that they could become infected from rodents eaten by them; from small cattle, expecting that these animals could be infected from contaminated grass; and from household and wild rodents, including squirrels as potential victims of the virus. The samples of blood were frozen in liquid nitrogen and periodically sent through Kinshasa to Geneva, and from there to the WHO Collaborating Centers in Atlanta, United States and Moscow, Soviet Union. This system of storage and transportation of samples worked perfectly and within a couple of months we were receiving the laboratory results of the tests from both collaborating centers.

Delfi Messinger, an American Peace Corps volunteer

Delfi Messinger is an extremely brave and hardworking woman, with a great love for animals. She trained the other Peace Corps volunteers and local workers on the methods for dissecting animals, sampling the body tissues and blood for laboratory tests, their preservation in the field, and transportation. Together with the field laboratory, she made a long trip of 1000 km by jeep from Bumba to Kinshasa, where she set up a vivarium and continued experimental studies on virus transmission in wild animals. Later on, she wrote in her book called *Grains of Golden Sand*: "I was an animal conservationist in Africa for 14 years. During a major uprising in Zaire, when bullets were flying, I did not flee. Instead, I spray-painted the word "AIDS", in blood, on the entrance of the compound where I had struggled for years to rescue orphaned bonobos—a rare ape found only in that country. I stayed on and 5 years later, I managed to get 6 bonobos to safety in a Dutch zoo, where several and their offspring reside to this day."

[11] More details about this case are in the paper by Khodakevich, L., Jezek, Z., and Kinzanzka, K. Isolation of monkeypox virus from wild squirrel infected in nature. *The Lancet*, 1986, vol. 327, no. 8472, pp. 98–99.

In total, more than two and a half thousand samples were tested for antibodies, including 1398 samples from wild terrestrial rodents, 74 household rodents, 816 squirrels, 157 monkeys, 67 house cats, and 120 house goats and sheep. Among all samples, antibodies were found in 8% of monkeys and in 21% of squirrels.[12]

Estimation of the disease incidence among various groups of animals and man

The data on the prevalence of monkeypox virus antibodies found by this study allowed us to estimate the disease incidence. For this, we used the formula proposed by Freeman and Hutchison in 1980 (Freeman, J. and Hutchison, G.B. Prevalence, incidence, and duration, *Am. J. Epidemiol*., 1980, vol. 112, pp. 285–294):

$$I = p/(t/2) \times 1000,$$

which connected the average life expectancy of groups of animals (and man), t, with the antibody prevalence, p, and gave the expected incidence, I.

For the striped squirrels (*Funisciurus* spp.), it was 240 cases per 1000 animals in the population; for the sun squirrels (*Heliosciurus* spp.), 75; for monkeys, 23; and for man, 0.04. The results of the analysis indicated that various species of striped squirrels could sustain transmission of monkeypox virus in nature.

Ecology and behavior of squirrels of the tropical rainforests

I was lucky that by the time of the studies Dr. L. Emmons, an American biologist, had summarized in her thesis for a doctorate degree[13] a huge amount of data she collected on the ecology and behavior of squirrels in the African rainforests. Her work helped to make a number of key conclusions confirming the potential of squirrels in maintaining a stable and permanent circulation of monkeypox virus in nature, in particular:

- Squirrels are one of a few groups of mammals of the tropical rainforest that have a very high population density;
- Various forms of contacts among individuals of the same species of squirrels and with different other species provide a good opportunity for transmission of infections that may ensure a stable virus circulation in nature; and
- The populations of the striped squirrels get renewed in a rather short period of time for mammals (on the average, in 2 years).

The *Funisciurus* species occupy the African tropical rainforests, which widely inhabit the palm trees (*Elaeis guineensis*). (By the way, Zaire, thanks to huge growths of this plant, was one of the large producers of palm oil in Africa.) As Emmons described, the squirrels feed on small fat fruits of the palm trees, using ants as a dessert, whose acid helps to decompose the nut fat. This plant maintains squirrel population of very high density (up to a thousand and more individuals on a square kilometer), which, accompanied by frequent contacts among squirrels, can provide a constant circulation of the virus in nature.

[12] Results of these studies were published in several scientific journals, namely, Khodakevich, L., Szczeniowski, M., Mambu-ma-Disu, Jezek, Z., Marennikova, S., Nakano, J., and Meier, F. Monkeypox virus in relation to the ecological surrounding of human settlements in Bumba zone, Zaire, *Trop. Geogr. Med.,* 1987, vol. 39, pp. 56–63 and Khodakevich, L., Szczeniowski, M., Mambu-ma-Disu, Jezek, Z., Marennikova, S., Nakano, J., and Messinger. D. The role of squirrels in sustaining monkeypox virus transmission, *Trop. Geogr. Med*., 1987, vol. 39, pp. 115–122.

[13] Emmons L.H., *Ecology and Behaviour of African Rainforest Squirrels*, Cornell University, 1975.

Mark Szczeniowski (*right*) with a team working in the Bumba zone; Delfi is *to the left*

Mark Szczeniowski, a citizen of the United States of Polish origin, worked from 1967 to 1970 in Africa as an American Peace Corps volunteer. In 1971, Mark was employed by the WHO to lead one of the epidemiological teams responsible for smallpox surveillance in Zaire. Since 1980, Mark coordinated the surveillance on monkeypox and viral hemorrhagic fevers in Zaire, and since 1984, he played a key role in the organization of the expeditions and laboratory research on the ecology of monkeypox virus in Zaire. Before that, he had traveled all over the country, getting to know people, the habits and traditions of the population, and gained great experience in resolving problems, which later on arose during our joint work. In Bumba zone, Mark set up a camp based at a clinic of a Belgian Catholic mission where the team of five–seven persons worked during several months. He organized the local people to capture and shoot wild animals, created conditions for sampling animals, and storage and transportation of animal organ specimens and blood samples to Geneva. At the end of the field work in Bumba and in the other areas of Zaire, Mark successfully negotiated with the administration of the National Institute of Biomedical Research in Kinshasa on creating an experimental laboratory for studying virus transmission among wild animals with the vivarium of the Institute and ensured provision of everything needed for successful work in the laboratory. He morally supported people working with him under difficult circumstances and encouraged them not to lose their spirit if that happened. I do not know of any obstacles that were beyond Mark's ability to overcome. It was not by chance that later on, some time after Mark was transferred to the WHO Headquarters, he was assigned to the high position of the Coordinator of General Support Services, supervising a team of over 150 people in the General Management branch of the WHO, where he was working until his retirement.

A journey across the equator on the way to Bumba, Zaire

Here, it is probably worthwhile to recall our trip with Mark Szczeniowski to Bumba. We flew from Kinshasa to Kikwit, a distance of approximately 300 km. From Kikwit, we had to drive about 1000 km by jeep. People say that during the colonial times this could be made by a Plymouth sedan just in 10 hours. By the 1980s, this once magnificent road had turned to something unimaginable. The former embankments evolved into shapeless hills, and the cuts in the hills turned into ravines and rivers whenever it rained. Only some concrete roadside drains here and there reminded that this was a "road". Actually a road going through the rainforest is similar to a tunnel covered by crowns of the trees growing on the road sides. The sides of the crowns striving to catch more sun from the opening over the road are thicker and heavier then those facing the other trees. Naturally when the tree gets old and perishes, it falls down only to one direction—across the road, and not simply across, but perpendicular to the road.

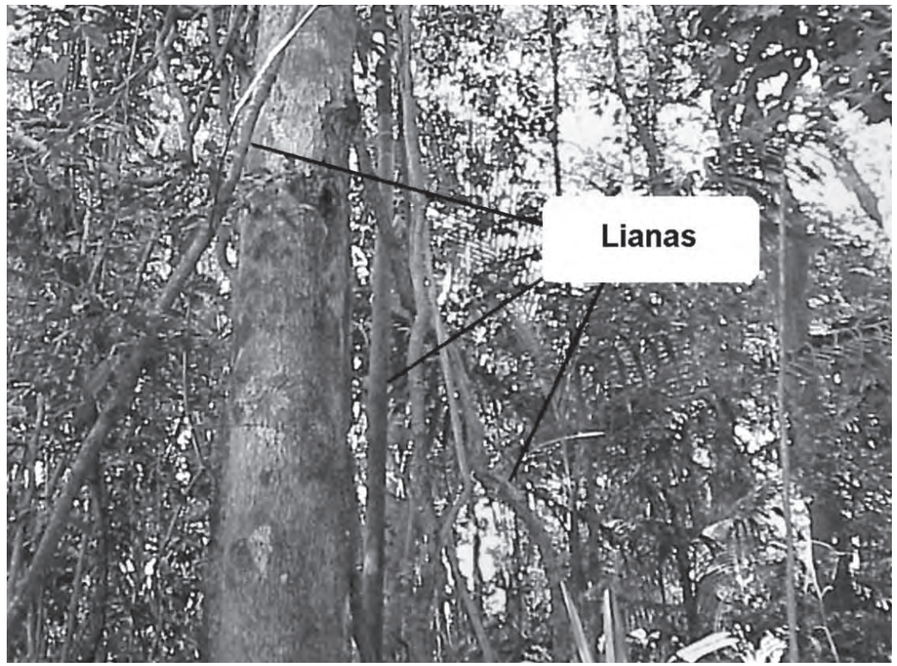
In the afternoon, we started our trip to Bumba by a British Landrover. It is an excellent jeep, and the local drivers deserve writing poems on them, both performed exceedingly well on these wretched roods during this trip. In about 150 km, the road was blocked by a tree of 70–80 cm in diameter. The driver left the car, took a machete and cut the tree trunk in two places allowing a cut slightly wider than the width of the jeep. The log of about two meters cut away from the trunk was pushed by the Landrover bumper forward, then aside and the road was cleared. The whole exercise took about an hour and a half. We continued further in pouring rain. In one of the water-filled ravines, the car started slipping to a stop. Water rose in the cabin covering the floor. We lifted our bags and put them on the seats and the driver went out to manipulate with the jack. We were sitting in the car, which was leaning to the left and then to the right. In half an hour, the driver lifted one by one all four wheels and put branches of trees under each of them. Eventually he got the jeep out of its captive situation. Time was running towards midnight. Mark said that the nearest mission was half an hour drive away. At those times, dozens of missions from several countries of Europe were working in Zaire on various projects from agriculture to improvement of children health. These missions established quite a good communication system using powerful Motorola portable radio stations and maintained a good tradition of mutual aid in extreme situations.

The prospect of being able to rest in a short time was invigorating. Then suddenly there once again appeared a large tree across the road. The driver again used a machete in his attempts to cut it. But his attempts produced nothing more than fountains of sparks. Mark said that this tree had petrified at the root before falling down and no machete, axe, or saw would cut it. What to do? Mark reassured me that the driver would manage somehow. The road stretched on the bottom of a ditch approximately a meter and a half below the ground level. The driver took a lantern and went out in the dark of the forest to find a shorter way to bypass the tree. On his return, he started digging an alternate pass for the jeep. Thank God, the ground around was sandy and easy to dig. After some 5 meters were cleared, he turned the car and drove it into this new passage. Then he drove it back and forward. The front of the car rose and hung on the lianas. He chopped them, releasing the front of the car down on the ground again. He repeated these maneuvers a dozen of times, going around the root of the fallen tree back to the road.

Very soon we reached the mission, where people were waiting for us; Mark was keeping them informed about our movement over the radio. The mission was a small island of civilization in the midst of the dense forest. It had solar batteries on the roof that provided sufficient energy to charge batteries during the day. There was enough power to keep a small refrig-

erator running and feed a couple of fluorescent lamps in the nights. People here knew Mark, and welcomed me while congratulating me for spending my first night on the Equator. It was literally on the geographic equator of the earth! The rain stopped. The sky was clear and absolutely dark with numerous stars sparkling brightly. The forest was full of loud whistles and songs produced by various insects.

The next morning we continued the drive to the north through the same type of roads and similar obstacles encountered the previous day. In the middle of one of the following days, the driver stopped the car when we heard something knocking the rear of the jeep. He went down under the car and brought back a broken bearing of the cardan. Even the Landrover could not stand such tests. Mark switched on the Motorola, spoke to someone, and in a couple of hours a car from the nearest mission came to bring a replacement for the broken bearing. There were many more similar adventures for the rest of the journey and by the end of the fifth day we reached Bumba at last. One thousand kilometers in five days!



Rope-like vines, called lianas, hang in the canopy of almost every jungle in the world. They grow up from the jungle floor, through the understory and loop through the canopy tree tops. (I did not make any photos during the trip to Bumba, so I took this photo from Internet. Lianas are very well seen here, though they appear not in a closed forest, since on this photo one can see the sky among the crowns of the trees. In a really closed tropical rainforest it is semi-dark at the ground level because the crowns form a thick umbrella impenetrable to sunrays)

Experimental studies

The conclusions made on the basis of the variations in the prevalence of antibodies and the estimated incidence were one side of the story. The susceptibility of squirrels to monkeypox virus needed to be proved and the possible ways of viral transmission among them needed to be identified. For these purposes, we proposed to set up an experimental laboratory in a vivarium of the National Institute of Biomedical Research in Kinshasa. The Smallpox Unit in Geneva supported the idea but the Department of Communicable Diseases of the WHO Headquarters was reluctant, reasonably fearing that the infection could leak out of the laboratory located in the center of a big city in Central Africa, especially as a result of the experimental work financed by the WHO. A positive decision was made by Dr. Sergei K. Litvinov, at that time in the position of the Assistant to the WHO Director-General. He was convinced that our proposed precautions were sufficient enough to prevent release of infection, and eventually the plan was approved.

At the laboratory in Kinshasa, the administrative and financial matters were handled by Mark Szczeniowski, the operational aspects by Delfi Messinger, and the research was guided by Dr. Emma Shelukhina and Dr. Sergei Pole.

The conditions of the experiments allowed a separate study of the air-born transmission and the combined ways (air-born and contacts). During the experiments, we observed a high degree of "communicability" and physical contacts between the individuals of the same species and between different species of squirrels as well as a case of cannibalism. The experiments showed a high efficiency of all studied ways of transmission. Besides the clinical appearance and the course of the disease, its duration and lethality were recorded. Out of 54 animals involved in the experiment, 34 were infected artificially (intranasally and orally) and by a natural way, through the air. All except the two, which on arrival to the vivarium had high titers of antibodies to monkeypox virus (obviously as a result of earlier infection in nature), developed clinical symptoms of monkeypox.

Emma Shelukhina and Sergei Pole working in the experimental laboratory in Kinshasa

From each of the 13 animals that survived and fully recovered, the samples were taken from four to six internal organs. The WHO Collaborating Centers failed to isolate the virus from them, while it was isolated

from almost all animals in the active stages of the disease. Although the sample was not large, these results offered an additional argument that the virus does not survive after recovery of squirrels from monkeypox.

Emma Shelukhina, a virologist from the laboratory of Prof. Marennikova (who earlier worked in the eradication program as a physician and epidemiologist in the countries of Southeast Asia), in Kinshasa was collecting the samples from animals and carried out some simple immunological tests, which could be performed in the field, away from the principal laboratory. Sergei, a research worker from the Central Asian Plague Research Institute, Ministry of Health of the USSR, in Alma-Ata, with good work experience with mammals, carried out the taxonomic identification of animals used in the experiments, organized the studies on the behavior of squirrels in captivity, the type of contacts among them, and set up the experiments to study different ways of the virus transmission.

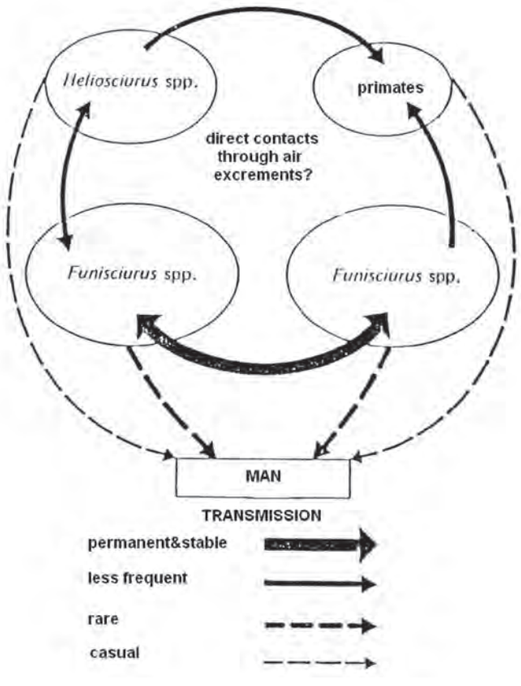
On the basis of the data we obtained on the antibody prevalence and the estimated incidence of monkeypox in various groups of animals (and man) and considering the high susceptibility of squirrels to the virus shown in the experiments, we constructed a scheme of the virus circulation in nature. A permanent stable circulation of the virus in nature continues throughout the year among various species of the genus *Funisciurus*, living in the secondary forests of the tropical belt of Africa. Through the contacts with other animals inhabiting the borders of the closed rainforest and secondary forests, the larger squirrels of *Heliosciurus* spp. and primates accidentally get infected. Occasionally and very seldom, man gets infected through contacts with one or other sick animal.

Besides these conclusions, I feel that this work can shed the light on two other issues (the subject not reported anywhere earlier): the first is the **area of circulation** of monkeypox virus in nature; and the second, the **place of origin** of smallpox. The identification of the reservoir host of monkeypox virus and the results of Emmons' research on the area of the natural habitat of the *Funisciurus* species make it possible to outline the geographical area of the virus circulation in nature and the possibility of man contracting the infection.

This area stretches in the geographical space from 15° N to 9° S and occupies the territory of 15 African countries with an area of two million square kilometers. As to the areas of the tropical belt outside the African continent, it is hard to deny the absence of monkeypox virus and there may be several reasons why it was not revealed there, including:

- The absence of virus circulation in nature of the tropical belt in South America and Southeast Asia;
- The absence of the types of contacts of man with wild animals that can facilitate virus transmission; and
- The lack of research in wild animals.

The second most important issue is the place of origin of smallpox. The earlier



The scheme of circulation of monkeypox virus in nature

Tropical rainforests in the world

assumptions on the origin of smallpox in India, China, or Egypt were based mainly on archaeological findings. Genetic research indicates that smallpox and monkeypox viruses are not the closest relatives. However, the similarity of the natural course of the two diseases in man, in spite of the genetic remoteness, suggests that monkeypox virus was a direct or indirect predecessor of variola virus. This may hopefully be sorted out by future research. Whatever was the direct parent of the variola virus, our studies suggest that this transformation took place in the area of the tropical rainforests of Central Africa. This geographical area was also, in our opinion, the native land of smallpox.

It looks like the end of the story. But I was tempted to summarize the studies in one piece since a dozen different publications on the research have gone to different journals and did not create a comprehensive picture on the entire work.

In 1989, when working with the WHO Special Program on AIDS in Ethiopia, I started preparing my doctorate dissertation with the support of Prof. Marennikova and Prof. Belyakov. The work, which was registered in the Institute for Viral Preparations, was completed in about 2 years. In 1990, I brought the work to Moscow and presented it to Prof. S.G. Drozdov, the Director of the Institute of Poliomyelitis and Viral Encephalitides. I had never met Prof. Drozdov in person earlier and was pleasantly surprised by his attention to the subject and to the dissertation.

Prof. S.G. Drozdov, a doctor of medical sciences, academician of the Russian Academy of Medical Sciences, and winner of the State Award of the Russian Federation and the Award of the Council of Ministers of the USSR, and Director (at that time) of the Chumakov Institute of Poliomyelitis and Viral Encephalitides of the Russian Academy of Medical Sciences. Prof. Drozdov made essential contributions to the development of medical virology and epidemiology of viral infections in the USSR and Russia (tick-born encephalitis, rotaviral gastroenteritis, and poliomyelitis). Under the guidance of Prof. M.P. Chumakov, he proved the epidemiological efficiency of the live attenuated poliomyelitis vaccine received from Dr. Sabin, which was successfully used in the USSR and many other countries. He was the first to show that it was possible to eradicate poliomyelitis on the territory of a region by using the live vaccine. As a WHO advisor, he laid down the foundations for the epidemiological surveillance of poliomyelitis in different regions of the world. He was an active participant of the WHO Program on Eradication of Poliomyelitis by 2000 and a member of the Global Commission and the WHO Regional Commission on the certification of eradication of poliomyelitis.

Prof. Sergei G. Drozdov

Sergei Drozdov asked me to describe the work and, after an hour of discussion, asked the Secretary of the Institute Scientific Council to organize a concise presentation of it at a meeting of the Scientific Council. The presentation was well received, although there was an unpleasant episode after my report. One of the council members made a remark during the discussion that he had been working in Africa (apparently in Sierra Leone). He saw these chipmunks and, he said, they transmitted no disease. He knows how these WHO officers make dissertations: they screen the reports and cut and paste their publications from them. Although he presented it as an exclusively personal view and the Council did not pay much attention to it, adrenalin struck my head. However, the lesson was useful: the final presentation I ended with a photo (which appears here), showing me training local workers in Zaire. In December of the following year, the dissertation was successfully defended and endorsed unanimously by the members of the Council.

And before the end of my story, I would like to place a picture and say a couple of words about one more person, my friend Andrei E. Belyaev.

Andrei E. Belyaev

Andrei Belyaev did not work in the Global Smallpox Eradication Program but he played an important role in the preparation of my dissertations. At present he, an associate professor, works as a senior lecturer of the Chair of Tropical and Parasitic Diseases of the Russian Academy for Advanced Medical Studies. After the postgraduate course at the Martsinovsky Institute of Medical Parasitology and Tropical Medicine, Andrei participated in the research of zoonotic cutaneous leishmaniasis in Turkmenistan (1967–1971). In this complex work, guided by Prof. A. Lysenko, he was responsible for the epidemiological studies. As a result of the research, an epidemetric mathematical model was developed as a tool for measuring the intensity of infection transmission. The results of this achievement have received international recognition and they are still quoted today. In the late 1960s, a large malaria epidemic occurred in the USSR, in the Republic of Azerbaijan, where the transmission was thought to be already interrupted. In 1971, a group of scientists, including Andrei, was sent there under the guidance of Prof. Lysenko. During the containment of this epidemic, it became obvious that the earlier understanding of the *Plasmodium vivax* life cycle did not explain the observed epidemiological features. This issue became a subject for intensive brainstorming, which resulted in the development of a hypothesis on heterogeneity of malaria sporozoits (please, refer to heterogeneity mentioned earlier), which already existed in a mosquito body. This theory was published in the *WHO Bulletin* in 1977. As at that time there were neither laboratory models for *P. vivax* nor any methods for its cultivation, an experiment in man was the only choice. Andrei made a plan for the experiment. He and 11 other young scientists infected themselves through bites of infected mosquitoes. The disease developed in eight volunteers, including Andrei, in much longer time periods than the theory predicted. Subsequently, Andrei, as the recognized expert, worked in many countries of the world as a WHO advisor on malaria. It is necessary to note that his interests go far beyond these two research achievements and include the history, geography, sociology, and many other aspects of science. He works freely in English and French and reads in many other languages. The aspiration to learn all and everything was possibly the reason why Andrei, with enthusiasm, agreed to read both my dissertations, and thanks to his encyclopedic brain, made essential comments. Last year, he acted as the leading editor of the Russian version of the illustrated history *Smallpox Zero*, written by Jonathan Roy, which the Secretariat of the SEC2010 asked me to translate into Russian.

The author training local members of the research team in Zaire

30 years later

On May 17, 2010, numerous participants of the Smallpox Eradication Program from various countries came to Geneva to participate in the unveiling ceremony of the sculpture devoted to the program, which took place at the front entrance to the main WHO building. Several people came from Russia.

At the ceremony, D.A. said that he was often asked if smallpox eradication could have been accomplished in today's world, which is so swamped by armed conflicts in so many areas, and with so many large populations afflicted by natural disasters such as Chili, Indonesia, and Haiti. But we have forgotten that in the 1960s and 1970s, the eradication program was affected by conflicts, wars, and hundreds of thousands of refugees in various parts of Africa and Asia and that we did not have cell phones, we did not have e-mail, we did not have fax machines, we did not have facebooks, and we did not have twitter. In fact, telephone service was scarce in many parts of the world that we worked in. Telex machines were possible

Geneva, May 17, 2010. *From left to right*: Aleksandr Gromyko, Gassan Suleimanov, Donald Henderson, Svetlana Marennikova, Lev Khodakevich, and Joel Breman, a Program participant from the United States. The statue is on the background

on some occasions but it was too expensive. And it is a real testimony to the skills and creativity of the advisors from some 70 different countries as well as the ministries and health program staff who managed to overcome all that and achieved what was deemed as impossible.

The 30th celebration year has gone. The participants of the Rio Symposium, held on August 24–27, 2010, listed numerous legacies that arose from smallpox eradication, such as the great achievements in the elimination of several communicable diseases with the consequent prevention of large numbers of deaths of children and adults and the widespread use of epidemiological surveillance as a key tool in public health improvements around the world. Concurrently, they summarized several issues that remained despite the achievement. Several of them represent some or certain threats to humanity and would probably continue over the coming decades' jubilees. Just to mention some: with an increasing share of the world population becoming susceptible to smallpox, given the current limited supplies of smallpox vaccine, a release of smallpox virus into environment, either intentionally or through leaks from the high safety laboratories, could cause a catastrophic global epidemic. Another concern was expressed about the rapidly growing number of monkeypox cases in Africa in the populations that lose herd immunity after the cessation of smallpox vaccination. And all these will have to be witnessed by other remarkable people who will work in the decades to come…

Acknowledgement

I am grateful to a number of people who have gone through the drafts of this paper, first of all to Prof. Svetlana Marennikova, who insisted that I should describe the events related to the participation in the Smallpox Eradication Program. In addition, she read a draft and commented on several issues.

Then the draft was edited by Mark Szczeniowski, mentioned in the paper, Veena Lakhumalani, a staff member and consultant of the British Council, who was involved as a consultant of the WHO and UNAIDS while I was working with HIV/AIDS, and by Jean Roy from the Emory Global Health Institute, who coordinated the SEC2010 events and recommended this write up to make accessible to public. I would also like to note with high appreciation that D.A. Henderson had found time to read a draft of my recollections, noted with interest the details of the research on the monkeypox virus ecology, and supported the idea for its circulation.

The Bihar Mixing Vessel

V. D. Bychenko

The first impression when the plane landed in Delhi was a smell of the rotten earth and feeling of hot air as in a sauna. It was a middle of October 1973, when I arrived to India. Before departure, the chief of epidemiological department at the Ministry of Health of the USSR encouraged me that the Government telegram about my arrival to the WHO office in Delhi was sent and that they would surely meet me. The plane arrived early in the morning on Saturday but nobody met me at the airport. I attentively listened to announcements and examined people around. Although I learned English all my life both at school and institute and then took special course at the Academy of Medical Sciences, which completed with honors, the English speech of announcer at the airport was rather unclear for me. Just suddenly, I heard that the WHO representative won't meet me but the hotel in the downtown was reserved. I quickly estimated the situation: I had only $5 in my pocket, knew nobody in the city, and was not guided. At this time, I saw the crew of our plane going to an exit from the air terminal. Having grabbed a suitcase, I rushed behind crew, explained the situation, and asked for a lift to the consulate. There I was fed and brought to my hotel. So, my live and work in India began.

In the first few days of my stay in India, it was very difficult to adapt: the heat was over 40°C. In addition, I had to learn how to understand the peculiar accents of the people around—American, French, Czech, Polish, and Indian—but very rarely English. The intense epidemiological situation forced to quickly get into gear; therefore, the WHO employees tried to quicker end the formalities and push me out into the "field". At the end of the first week of my stay, I took off for Patna (capital of Bihar) together with Dr. Z. Jezek to participate in the meeting on the organizational issues related to the Smallpox Eradication Program in Bihar. I had then no idea of who are the people I was to meet and carefully prepared for the presentation; however,

Vladimir D. Bychenko,
a clinical epidemiologist, candidate of medical sciences, and participant of the Smallpox Eradication Program in India. Since 1973 to July 1974, was the coordinator of the program in the Bihar State and since August 1974 through 1975, was responsible for several districts of this state

Bihar people: representatives of a Hindu community

the participants of the meeting could not understand me. Yet my debut passed well. At the meeting, I got acquainted with the management of the Ministry of Health of Bihar and the leading experts and drew up the plans of collaboration for the future.

The epidemiological situation on smallpox in India by the end of 1973 was as follows: 86.9% of the cases were registered in four states—Bihar, Madhya Pradesh, Uttar Pradesh, and West Bengal. Bihar accounted for 20.7% of all cases; Uttar Pradesh, for 39.1%; West Bengal, for 21.0%; and Madhya Pradesh, for 6.1%. From these states, smallpox spread across India and beyond its borders. The Indian government and the WHO took all measures to improve the situation. Additional staff resources, materials, and equipment were attracted and funding was allotted. Correspondingly, three epidemiologists from the Soviet Union were sent by the WHO for a long-term mission, namely, Dr. V.A. Mukhopad, to Uttar Pradesh; Dr. L.N. Khodakevich, to Madhya Pradesh; and me, to Bihar.

I worked with the WHO as a medical officer under the Smallpox Eradication Program in India since November 16, 1973. During my mission, my duties included advising the State Government of Bihar on all aspects of smallpox eradication; conducting full epidemiological investigation of all smallpox outbreaks (source tracing, case detection, forward tracing, and specimen collection); managing the containment of all smallpox outbreaks, including wide vaccination, appointment, and supervision of watch guards and vaccinators, initiation of local searchers, and follow-up visits for assessment; developing surveillance techniques, such as monthly house-to-house searches, surveillance teams, supervision of junior medical officers, and so on; training of local staff at all levels through training courses and participation in field work to develop and supervise a satisfactory reporting system in my zone; participating in the meetings at all levels; and consulting, training, and reporting to the relevant Bihar authorities and the WHO.

Bihar became a real stumbling block for the eradication program. This is a densely populated state of India. In 1973, its population was 65 million people. In the north, Bihar bordered Nepal; in the south, Orissa state; in the west, Uttar Pradesh; and in the east, West Bengal. Bihar was regarded as the poorest and one of the most dangerous states of India.

A northern flat half of Bihar is divided into two parts by the Ganges River, running from the mountains of Nepal and crossing the state from west to east; the rainforests account for 25% of the area in this state. The official language is Urdu along with Hindu and English; however, over 20 local languages are also in use. The Hindu regard that Bihar is the cradle of Buddhism and the state has many sites associated with Buddha life. Even the name of the state comes from a Sanskrit word *vihara* for a Buddhist monastery. Mahavira, the founder of Jainism, was born in Bihar. Patna, the capital of Bihar, was once the center of a large empire, Magadha, the first of the great empires of India and part of the Mogul Empire. This state also houses many religious shrines of Hinduism and Islam. Many thousands of pilgrims not only from India, but also from many countries of the world visit these sites every year. Thus, it is no wonder that many

smallpox cases "exported" from Bihar were recorded in different parts of India, Nepal, and other countries of Southeast Asia. It was there where many ethnic, religious and social problems met as in a mixing vessel and constantly fanned the flame of infection. It is now quite clear why this state played an important role in the Smallpox Eradication Program not only in India, but also in the overall Southeast Asia.

After the meeting, I returned to Delhi to finish the formalities with registration for the work and to get acquainted with the specific features of the activities under the eradication program. At the end of the third week of my stay, I was suggested to leave for a smallpox focus to practically examine on-site the surveillance, epidemiologic investigation, and containment activities. Certainly, the first visit to a smallpox focus in an Indian village impressed me indelibly. After a 300-km jeep trip at a temperature of 43°C, we arrived to the village where some cases of smallpox were recorded. At that time, the sun set and it at once became dark. The village had no electricity. I could see 500 brick one-storey houses with earthen floors covered with tiles. Their cattle were kept in the yards near the house. When we entered a house, I saw a patient lying on a trestle bed with no bed linen. The room was lit with an oil lamp. The state of the patient was awful; all his body was covered with rash. Around the bed, the heap of the smallpox crusts rolled and the cloud of flies curled. The patient was in a most severe condition. The members of the family including children surrounded the patient; part of them was not vaccinated against smallpox. After examination of the patients and diagnosing—and I had to touch his lesions with my hands—I went outside to wash the hands. They had neither tap water nor towel, and I had to use my handkerchief instead. Besides, we were dressed in shorts and shirts with short sleeves. All this was most unusual for me although I pretended to be calm knowing that I was attentively watched. Certainly, I knew well that, being vaccinated, I could not get smallpox. Thus, I passed this exam!

By the fall of 1973, the program leaders changed the strategy for the smallpox control. The focus of the eradication activities changed from the practice of mere mass vaccination to an active search for the smallpox foci and their liquidation. The new strategy also included

• Strict isolation of the patients at home and vaccination of all family members and visitors to the epidemic focus;

• Detection of the infection source and vaccination of all people living in 40 nearest houses; and

• House-to-house examination for an active search for potential smallpox cases in the area with a radius of 10 km from the epidemic focus.

As for Bihar, the new, intensified, eradication program in 1973 implied organization of epidemiological surveillance in the overall state as well as the adequate anti-epidemic measures on-site in all smallpox foci; in 1974, to decrease the smallpox morbidity to a minimum; and in 1975, to interrupt the epidemic process.

The surveillance implied periodic active search for smallpox cases (1 week in a month); all personnel of all services was involved in these activities; every person had to visit a

A control visit of the WHO staff to verify the efficacy of house-to-house examination

specified number of villages or city quarters. Identification tables were used when questioning people and all fever and rash cases were attentively examined. Any found smallpox case was immediately reported to the healthcare services and authorities. Every village, city quarter, and crowded area, including schools, markets, cookshops, bus and train stations, and nomad camps, were searched for smallpox. Each person involved in house-to-house examination knew well that the work is controlled and once it was poorly done, it should be done again.

A high-quality freeze-dried vaccine was used for vaccination. It was timely delivered using the necessary "cold chain". The rules for reporting the smallpox cases were strict and included the information even about suspicious cases. With a decrease in smallpox morbidity, the informers reporting smallpox or suspicious cases were awarded if their information was confirmed by laboratory tests.

During the first 3 months, my terms of reference comprised coordination of the local healthcare services in the activities under the eradication program and organization of special activities under the WHO funding. The intensified campaign and search activities revealed that the smallpox problem in many areas was considerably more severe than the routine reports and the earlier field surveys had suggested. The second search in Bihar covered 70% of the villages and towns and resulted in 2459 detected cases in 484 villages and 21 municipalities. By the end of 1973, the endemic areas had been reduced in size and better outlined. The surveillance and containment activities were introduced in these areas. Thus, the reported smallpox incidence much more accurately reflected the epidemiological situation. During this period, I was sent for 2 months to the Nepal border to the north of Bihar to prevent the smallpox export from India to Nepal, where smallpox was eradicated. In that period, I got a good field practice. The third search, conducted throughout the area, which I was responsible for, revealed 218 cases in 35 villages and two municipalities. Thus, the rational anti-epidemic activities allowed over 20 smallpox foci to be eliminated

Active smallpox detection in a civilian crowded area, a market place

during 2 months. The epidemiological situation in the region was stabilized. My task was carried out!

My activities in 1974

More than 67% of all smallpox cases reported during 1974 occurred in Bihar. From January to December 1974, the goal was to reduce the smallpox transmission in the state to a minimum or to arrest it at all. However, the program in Bihar was slow in starting, largely due to extensive floods and the diversion of resources to deal with that emergency. It was not until the spring of 1974 that a really effective search for cases started. From mid-February onwards, smallpox explosively spread, exceeding the capacity of the existing health structure to deal with the situation. The search operation greatly improved during the first half of 1974. Just before and during the monsoon, the most seriously affected districts started their most intensive efforts. In Bihar, 45 international short-term (3 months) epidemiologists and more than 100 physicians and PMAs (paramedical assistants) from other states of India assisted thousands of the state, district, and local medical staff for surveillance and containment. Over 150 special containment teams operated throughout the state and more than 150 vehicles were provided by WHO as well as the TATA Industries Ltd. and OXFAM.

Vaccination in a smallpox focus

At the beginning of the year, I was transferred to work to the right bank of the Ganges River. During the year I took part in organization of ten search operations and was an advisor in eight districts of Bihar. In this period, 41 877 smallpox cases, 14 900 foci, and 771 outbreaks were recorded in the areas under my responsibility. I personally conducted full epidemiological investigation and managed containment of 115 smallpox outbreaks and 226 foci with 4118 smallpox cases. Unfortunately, the progress in Bihar was less rapid than had been hoped. The number of foci in the state steadily decreased from 3320 in July to 205 by the end of the year, but there was was still a high number of them to potentially return the disease transmission. This suggested that the bottleneck was inefficient containment. The smallpox vaccination was slow; unvaccinated visitors came to affected houses and infected persons every now and then

A detected smallpox case in a child

were found moving about from place to place. At the end of December 1974, endemic smallpox was believed to be confined to Bihar. The average number of cases in each focus was less than five and about one-third of all foci were single-case outbreaks.

My activities in 1975

January–November

In 1975, a total of 839 smallpox cases and 98 deaths were reported in Bihar. It was less than 1% of the incidence reported in 1974. In January 1975, all affected areas showed a downward trend. A 40% decrease in the number of smallpox outbreaks was monthly observed. Expectations of reaching a "zero-status" by the onset of monsoon seemed ambitious but realistic.

In 1975, I was responsible for six districts in the Chota Nagpur Plateau. This area was covered by seven searches with full containment procedures. And so it happened. The last case of smallpox was found in May, 1975 in the Ranchi district.

The last case of smallpox, found in the city of Ranchi, 1975

Some episodes

A smallpox focus was found during the search in the district of Munger. However, a control check demonstrated that the necessary procedures were not conducted there in due time. At the meeting, I asked the district medical and health officer (DMHO) for the reasons and he explained that he was just tired to do the same things several times without any success and stopped it. He convincingly asked me to help him in managing the containment. The next day, I with the state containment team moved forward to this epidemic focus. Having arrived to the village, we found a woman of 35 years old suffering hemorrhagic smallpox. The man of the house was absent, he was on a trip, and there were only women and children in the house. As it appeared, part of them had no smallpox inoculations. For a long time, we explained and persuaded the members of the patient's family to get a vaccination but they refused. Finally, the paramedic lost patience and tried to vaccinate the contact children. I saw through the window that neighbors from the nearby houses began to pool out stakes from fencing and understood they would beat us. To save the team and myself from beating I gave the command to run to the vehicle. Immediately we were in tour jeep and left the village. The crowd of the furious inhabitants armed with stakes pursued us. As a result, we had to devise a special technique how to persuade the families that refused to be vaccinated. For this purpose, the head of the village and religious leaders were attracted and the local residents were hired and trained as vaccinators. They were supplied with the vaccine and necessary materials and got the corresponding payment for the job. Later, we widely used this practice for the anti-epidemic activities in the districts where the population refused to be vaccinated.

The DMHO of Munger, who was also responsible for the healthcare in local jail, asked me to help in containment activities among the prisoners, because there were some smallpox cases there. Next day,

I went to the jail without any hesitations. However, my enthusiasm somewhat faded when we approached this sort of medieval fortress with the walls about 20 m high and 4 meters thick. Turrets located on the top of the walls every 25 meters housed Bengalese shooters with large gauge guns. I shuddered when the jail gates closed behind me—nobody knew where I was and nobody would help me out if something happened. The jail was overcrowded. I won't describe the horrors of prisoners' existence there. Part of them was in an open space with the temperature of 52°C in the shadow. After carrying out all necessary procedures for containment, I left the jail with relief and sense of fulfilled duty.

The climate of India may be quite an ordeal for a foreigner. I recollect the following situation. It happened in Buddha-Gaya in summer. During the whole day, I carried out the containment activities in the rural area. I went to spend the night in a local hotel for administration, a two-room house. I had some documents with me and some money for payment to the staff. The electricity was absent. After 20 minutes indoors, I understood that I would die of overheating because the outside temperature reached 52°C. Then I put on wetted sheets, undressed to pants, put the money and documents in a money-belt, and went to the flat rooftop of the hotel, where easy whiff of breeze was felt. Wet sheets and easy whiff of "zephyr" allowed me to survive through that night, although as I was told that heat strokes here were quite often observed at night.

In general, the epidemiological situation in areas of actions was extremely adverse. Districts were endemic for cholera, manifold intestinal infections, tropical malaria, tropical parasitosis, leprosy, typhoid fever, hepatitis, and so on. My driver, a local resident, who worked with me for nearly 2 years and constantly accompanied me in my trips, ate and slept with me in one room, had typhoid, hepatitis, malaria,

A team of epidemiologists in the district of Munger. *In the first row (right),* V.D. Bychenko

and dysentery during this period of his job. Some epidemiologists from the United States and Europe, participating in the program, suffered from intestinal infectious diseases since they preferred to eat at the restaurants with European cuisine, namely, liked beefsteaks with greens and garnish, and greens were known to be poorly washed. As for me, I during my trips used to eat in roadside cookshops where the food was cooked in my presence and with a heat treatment and to drink only bottled water or freshly brewed tea. Thus, in half a year, I became an "old-timer" there. Because of these difficult conditions of work and life in this state, no WHO epidemiologists except for me stayed more than half year.

The organization of sanitary and epidemiological surveillance, active detection of smallpox cases, and rapid high-quality anti-epidemic measures in the foci has led to a drastic reduction in the species morbidity. Just compare that 20 800 outbreaks were recorded in 1974 versus only 11 300 in 1975; finally the last smallpox case was recorded in the May of 1975.

Find below an example of the set of measures in Ranchi in July 11–31, 1974.

In 1974, Ranchi Municipal area (with the population of about 1000 000 people) remained free from smallpox incidence until week N 16 (April). During week N 16, only six smallpox cases were detected. The active campaign included three searches—Search 6th (weeks NN 18–22), Search 7th (weeks NN 23–27), and Search 8th (weeks NN 28–29). The special center was formed for searches and containment measures in order to plan and supervise these activities. All reports from search and containment teams were sent to the center. The center staff comprised an epidemiologist, chief sanitary inspector, municipal medical officer, PMA, and clerk. The center planned all surveillance and containment activities. Nonmedical staff was used for search operation. Two search teams were formed, each team of 36 workers. The municipal staff worked as a "guide". Search workers were mainly through volunteers (students of the Mansera House and persons employed by OXFAM and WHO). The teams had a minivan at their disposal. Additional ten search teams were formed by other companies. The search was conducted according to a house-to-house scheme. Each searcher received every morning a special search form, prepared and reported to me every day on completing their activities. When any case of rash and fever was found, the label "urgent" was put at the top of the form. In the team, the participants worked in pairs and each pair examined approximately 100 houses daily. One member of each team was assigned responsible for the area allotted to the team. The search activities were supervised on a random basis by a medical officer and the sanitary inspector of the municipality, even the preliminary results revealed a large number of smallpox cases that remained unreported. During the searches in Ranchi Municipality, 32 city wards were examined, which was more than 18 441 houses. The result was five detected smallpox outbreaks and 126 foci with 264 cases. The containment measures met the WHO guidelines and were performed in parallel with the search. The containment vaccination covered the infected house and 30 surrounding ones. On receiving the information about a suspected smallpox case from the search teams, all such cases were examined and confirmed by a special confirming team. Four containment teams were formed, each including one PMA and six vaccinators. The teams had two jeeps. The follow-up visits were performed by eight municipal vaccinators by bicycles. Their task was to vaccinate those residents of the affected regions who were absent during the previous visit. This follow-up visits continued for 6 weeks. Selective vaccination also covered the slum areas of Ranchi and were performed by a special mobile team of 27 internees of the Rajendra Medical College. The routine vaccination was also continued. In total, approximately 10 000 people were vaccinated during the containment activities. In parallel, the surveys were continued at the railway station, airport, and bus stations. A checkpoint was organized near the gate to the railway station; it detected suspected smallpox cases, confirmed them, and took immediate containment. The booking clerk issued tickets together with smallpox leaflets. One vaccinator station was intended for vaccination of all contacts of the smallpox cases as well as everybody who wanted to be vaccinated. All conductors were supplied with the WHO recognition cards. If they met in the train any person with the visual symptoms resembling smallpox, they had to ask

him/her information about the illness and contacts and inform police and medical authority. The searching and containment activities were organized simultaneously during weeks NN 18–29 at Ranchi municipality. In addition to the municipal and WHO staff, local resources were used. The smallpox drive was done with limited resources. Containment vaccination, selective vaccination at slum areas, and routine vaccination were performed simultaneously with the survey at Ranchi municipality, railway station, airport, and bus stations.

OXFAM staff participating in the eradication program

One more episode of my work there. The duties on the search in the Ranchi district were distributed between Dr. D.P. Dhar, an Indian WHO epidemiologist, and me in the following way: I as a younger one was responsible for rural areas and he, for the city quarters. Before leaving, I asked him to pay special attention to the sanitary and epidemiologic situation in the infectious disease hospital of Ranchi, in particular, to exclude any smallpox speeding from it. As was mentioned, the WHO guidelines required that the smallpox cases were not hospitalized but isolated on site. However, it emerged from the reports that smallpox patients in three localities contracted the disease when being at the municipal hospital. The following fact was revealed when investigating these cases. The hospital was a one-story building, actually a barrack, housing several divisions for different diseases, which were not isolated from one another. And one section had smallpox patients. On my question why patients with smallpox were hospitalized in the hospital—after all, it contradicted the program requirements—the superintendant of the hospital answered that they were hospitalized according to life-threatening conditions; otherwise, the administration of the hospital would be subjected to "obstruction". On the question why patients of other sections were not protected against smallpox according to epidemic indications, the superintendent and Dr. Dhar declared that they had contraindications for vaccination because of their diseases. This was the lesson for rest of my life: If you want a thing well done, do it yourself.

Summing up, during my work under the Smallpox Eradication Program in Bihar, I prepared 16 proposals, trained 11 local and 14 international WHO epidemiologists, as well as directly supervised and participated in eradication of 321 smallpox outbreaks and 227 infection foci.

During my mission in Bihar in 1973–1975, I worked with heroic colleagues from our country, including Drs. B. Bychenko, A. Gromyko, V. Fedenev, Yu. Krivda, V. Mukhopad, G. Oblapenko, Yu. Rykushin, A. Samostrel'skii, and A. Slepushkin, experienced and top-class specialists, who fulfilled their professional duties under most severe climatic and epidemiological conditions. I believe that my work performance during the WHO Smallpox Eradication Program was satisfactory.

Operation "No Return to Smallpox": Smallpox Goddess Leaves Bihar

Yu. G. Krivda

This was the final year of the Global Smallpox Eradication Program in Southeast Asia. While European countries, the United States, and Soviet Union had already forgotten about this dreadful disease, here in India, the mythical Goddess of Smallpox, Sheetala Mata, still continued to collect her deadly toll on the population.

The national program to combat smallpox began in the country in 1962. Introduction of the mass vaccination policy made it possible to significantly reduce the incidence in southern states; however, the relevant outcomes had been less successful in other regions. Two subsequent innovations in vaccination practices, such as introduction of the bifurcated needle in 1967 and replacement of a liquid vaccine with a heat-resistant freeze-dried vaccine in 1971, raised the vaccination capacity to almost 100%. However, more than 10 000 outbreaks were registered in 1974. About 30 000 people died of smallpox and 75–85% of them resided in the state of Bihar, located in the northeastern part of India, bordering Nepal.

In view of a rather complex situation prevailing in the country at that time, Indira Gandhi appealed to the people pleading them to provide all-round support to local doctors and international experts and actively participate in updating them on any possible new cases. She also sought assistance from local producers and entrepreneurs. Some of them responded to this appeal. For example, a well-known industrial group TATA donated 40 jeeps to the program in addition to financial assistance of US$ 600 million. Certain funds were also received from other sources. As a result, the activities within the national program increased significantly thanks to the funds allocated by the Government of India, the WHO, and the Swedish International Development Agency.

Yurii G. Krivda,
a medical epidemiologist, candidate of medical sciences, and participant of the Smallpox Eradication Program in India in 1975. Later, he worked under other WHO projects, in particular, the Expanded Program on Immunization in Africa and Asia

Sheetala Mata, the goddess of smallpox, was considered to be one of the most revered goddesses in Northern India, Nepal, Bangladesh, and Pakistan. According to folk belief, Sheetala, moving through the land, scattered grains of rice along her path, and every grain turned into a pock. Consequently, the life of a patient depended on whether or not Sheetala washed off such seeds with water from her jar

Inhabitants of the villages and urban areas affected by smallpox were thoroughly registered and vaccinated. The outcomes of such measures were not long in coming, and the number of outbreaks dropped significantly by the end of 1974.

In order to conclusively reverse the situation, the WHO decided to detach additional group of international experts to India on a short-term basis, and I was included in this group. Nominees to be included in the group were personally selected by the program manager, Dr. Donald Henderson, and during the interviews with him they had to demonstrate a good command of spoken English in addition to professional skills. Unfortunately, this requirement represented an insurmountable obstacle for many of my colleagues.

Yu.G. Krivda with a group of young Indian doctors.
Office jeep with the inscription "SMALLPOX ERADICATION PROGRAM" is a donation from TATA group

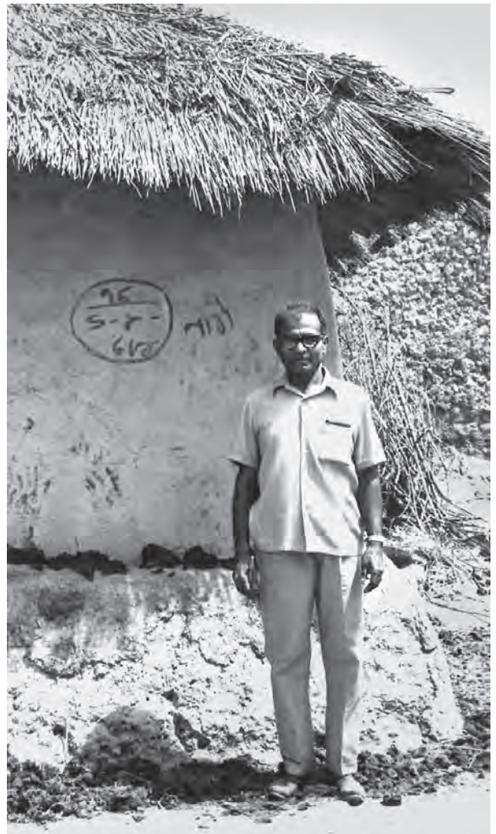
In 1975, India launched the final operation referred to as "No Return to Smallpox" and on April 7 of the same year, the WHO Health Day was held under this motto.

Our group of three experts was detached to the state of Bihar, where the most dramatic situation had evolved. I was accompanied by Georgii Oblapenko from Leningrad and Leonid Korobov from Odessa. Each of us was assigned to several provinces.

Vaccination was carried out with the Soviet-made freeze-dried vaccine, and it is worth noting that during the whole period of our work not a single complicated case was identified. Initially, when the number of people to be vaccinated was quite significant, we used injectors, while later on we switched to bifurcated needles. We were applying an active search system proposed by Anatolii Slepushkin, virologist of the Smallpox Eradication Unit in the WHO Headquarters. This method proved to be very effective and deserves to be elaborated in more detail.

The overall catchment area was divided into sectors. At a certain preset time, we were moving out to planned sites together with local physicians and vaccinators trained from local inhabitants. Essentially, it was a continuous door-to-door visiting of households. In case of any suspected case of smallpox, biological material was sampled from every patient and sent to the virological laboratory. Such rounds of visits were implemented on a monthly basis during one week. In this period we managed to cover all assigned settlements and visit each household. I supervised three provinces—Darabanga, Samastipur, and Begusaray.

After careful examination of all inhabitants of a given household, relevant inspector drew a circle with a special felt-tip pen on the outside beat-cob wall, indicating inside such circle a number of examined/vaccinated persons in a fraction form, i.e., 15/10, as well as his personal identification number. During the next round of visits a different geometric shape was used, as agreed in advance. In order to eliminate any possibility of "formal" attitude, inspectors were followed by supervisors. They interviewed residents, asking them how and when they were examined and when drawings appeared on their house walls. If any flawed work was uncovered, the corresponding inspector was either fired or strictly instructed to repeat the examination. The system functioned quite effectively, and once, during a personal 'get-together' I asked Anatolii Slepushkin, how he came up with such a bright idea. It turned out that this idea had been invented much earlier; Russia struggled with typhus in the 1920s in a similar fashion.



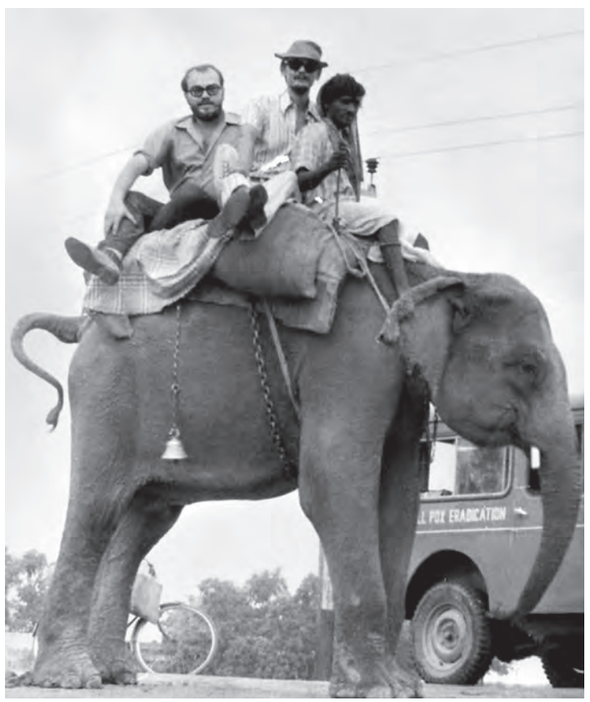
The inspecting Indian physician assured himself that all epidemic control measures had been carried out in a given household, which is indicated by the sign on the outside wall of the house

While traveling around the country, we encountered a number of unexpected problems. The appalling poverty of the local population was combined with terrible unsanitary conditions. When a waiter in one local roadside cafe waved his napkin, black clouds of flies rose in the air to go down again on your table and your food. Consequently, I did not refuse when a couple of times vaccinators invited me to share the meal with them. Indians would rather miss some important meeting then their lunch and they take their meals quite seriously. So once staying outdoors, we used open fire to cook rice with a delicious sauce consisting of a variety of vegetables and fruits. Wide banana-tree leaves were used as napkins to put plates with food and bottles with water on them. I still remember this exotic lunch with great pleasure.

Most of all we were afraid of the amoebic dysentery since almost all water was contaminated with these parasites. We drank mostly bottled water and Coca-Cola. A bottle was wrapped with a damp cloth and hanged outside the car window to cool it with the wind.

I noticed that my Indian colleagues did not suffer from thirst. They maintained their bodily water balance in quite an original way. I had to put up with the fact that they were constantly chewing something and spitting brightly red-colored saliva. My assistants explained that they were chewing so-called "pan" (in Africa, betel nut) and it helped them to keep agile during the long hot working day. Indeed, the pan was always served on a special tray before dinner. National dishes in India are tasty but too spicy and Indians wash them down with plenty of water, at least one-and-a-half or two liters for lunch. Once we arrived to a village where the water was in extreme deficit. Our drinking supplies ran out and I decided to try some pan offered to me. It looked like a part of a young coca leaf, wrapped in a shape of an envelope with black tobacco and a tiny piece of chalk or lime inside and pinned with a toothpick. After chewing this treat, I also spat red saliva like the locals. However, the most surprising result was that quite soon I had a feeling of cheerfulness, the thirst was gone, and during 3–4 hours I did not even think about water. I did not repeat this experiment but in that critical situation it saved me.

We were also impressed by the fact that there was no such thing as traffic rules on Indian roads. Everyone is driving where he wants and can turn without warning at any time and in any direction. Drivers give way only to heavy vehicles and only because no one wants to be caught under their wheels. Fortunately, my driver, an Indian guy named Uma, was quite deftly finding his way in this chaotic Brownian motion and we somehow managed to avoid serious accidents.



An elephant, a jeep, and a bike—one could see such picture quite often on Indian roads

My driver Uma is changing a flat tire

In the evening time, each of us did some accounting work, balancing the sheets and meticulously counting expenses. For this purpose, we completed a special training course on accounting and book-keeping in the WHO Regional Office in New Delhi. We were accountable for every dollar spent and regularly send financial reports. In this regard, I recall one funny incident.

Once I included in my report a purchase receipt for 370 rupees for a soccer ball in a sports shop. Naturally, we did not practice any sports. However, by accident out car crushed a ball used by school students to play soccer near my office. Children's reaction was so aggressive that I began to fear for the safety of our jeep, which became an unwitting culprit of this accident. In order to restore good-neighborly relations, we presented students a new ball and meticulous auditors recognized my somewhat strange purchase as appropriate in this situation.

Local people were actively helping us to look for the patients infected with smallpox.

Crowded places, especially farmers' markets, were convenient sites to distribute identity cards

Near a local church together with residents of an Indian village after interviews. Yu.G. Krivda is *in the center*

We were using a system which received the name "Call". Program participants in regional centers were given two-sided cards with a child's face covered with smallpox vesicles on one side and dorsum of a hand with the same elements of the smallpox rash, on the other. These demonstrative cards (ID cards) were reprinted from a photograph made by Dr. Emma M. Shelukhina, a virologist working in India under the program. We left dozens of envelopes with such ID cards in villages and anyone who saw something like that image could send us a letter with the return address. Such call was immediately followed by the visit of medical professionals and if the diagnosis was confirmed by laboratory tests, the "caller" received some sum of money. This ceremony was always performed in a public place in a very festive atmosphere. More recently reported cases usually involved chickenpox; however, all messages were checked. The amount of remuneration had been going up with the decrease in the numbers of identified patients. At first, it was 25–50 rupees, then 100 rupees; and later US$ 100. The latest figure reached US$ 1000. However, as I recall, nobody managed to receive this amount of money.

Any village with identified smallpox patient was declared a ten mile quarantine zone. Such quarantine area was defined rather simply. One leg of compasses was put on patient's house on the map and the circle was drawn. Everything inside this circle was included in the quarantine zone. The "guard" (watchman) was assigned in the house to try to limit the number of visitors and record all incoming people in a special log. Usually, the functions of such guard were performed by one of the older family members. This situation was complicated by the fact that it was usually unrealistic to completely stop visiting such house. By custom, many relatives are required to express their sympathy for a sick person. In those years, the surrounding population was usually vaccinated, thus reducing the risk of infection.

In view of the fact that the program was at its final phase, each new case became an important event and was subjected to careful analysis. Once I personally provoked quite a bit of anxiety in one regional center. In mid-April, we received some written information about an infected 3-year-old girl with the rashes on

the body resembling smallpox in a village in the province of Samastipur. After arriving to this area and examining the nature of this baby's rashes as well as the epidemiological history, I realized that this is a new case of smallpox. According to the instruction, the contents of the vesicles were taken for laboratory testing and all the epidemiological control measures were carried out in full. Later on, I regularly visited the village observing the development of the elements of a classic rash and monitoring implementation of quarantine measures. Soon a commission of several Indian physicians appeared who were engaged in the program as experts. After listening to my report and consulting with each other, they delivered a verdict: "This is a case of chickenpox, and the consulting physician from WHO makes misleading statements and spends money unjustifiably for unnecessary activities." I continued to insist on my initial diagnosis. Then, as a means of differential diagnostics, they proposed a test that they referred to as "the quenching phenomenon". This meant that a smallpox vaccine should be inoculated to the infected child and the nature of the vaccinal process signs (general and local reaction) would allow for the right conclusion. If this is an actual smallpox case, there will be no reaction because the vaccine antigen will be bound by the antibodies developed in the human body. By contrast, in case of chickenpox, all reactions will be pronounced and the disease may even go through the complicated version. For the first time I heard of such a risky test, which I frankly told colleagues. Fortunately, soon the laboratory confirmation of my diagnosis arrived. It was one of the last five cases of smallpox in India.

The last victim of smallpox in India was a 30-year-old woman from the state of Assam, who contracted the disease during her trip to Bangladesh. She fell ill on May 24, 1975, and the epidemiological control measures were immediately launched that prevented the occurrence of any secondary cases.

Time passed quickly and my assignment was coming to an end; after sending out all the reports, the three of us met again at the WHO Office in Patna. We exchanged our impressions and experiences and could not go to sleep for a long time. Finally, I asked my colleagues what was their best experience in

We stand in front of the poster, on which a local artist represented the final phase of the smallpox eradication program in India, Soviet physicians, epidemiologists Yu.G. Krivda, G.P. Oblapenko, and L.I. Korobov (*from right to left*)

India? The answer from Zhora Oblapenko, a Leningrad dweller, was diplomatic. He liked the fact that one can buy a real Indian tea in any remote and run-down village. Lenya Korobov's answer was short and gave him out as an Odessa native, "Here your underwear dries-up very quickly", he said.

Saying goodbye to the Center staff, I also mentally wished "farewell" to the brave fighter against smallpox depicted on the colorful poster by a local artist: on a broad background, a man in the pose of a winner stands in front of the defeated black monster covered with pockmarks; the man is armed with a bifurcated needle, which he just used to deliver a fatal blow to the monster. We took pictures in front of this poster upon our arrival to Bihar and had a deep emotional feeling of our own involvement in this undoubtedly significant victory, which embodied the potential of joint efforts of physicians around the world.

Nevertheless, we still had 2 years ahead of us of hard work involving enhanced epidemiological surveillance (the certification phase). Subsequently, an international commission of experts from different countries asserted that smallpox was eradicated in India.

Now 35 years after these events, I am absolutely convinced that the participation in the Global Smallpox Eradication Program in 1975 was a unique opportunity, or a gift of fate, to become a witness and participant of the international health project, the likes of which has never appeared in the history of mankind, and unlikely will appear in the near future.

Concluding Stage of Smallpox Eradication and Post-Eradication Activities

A. I. Gromyko

In 1974, Dr. D. Henderson, Head of the Smallpox Eradication Program, came to the USSR Ministry of Health in search for the candidates to participate in the eradication program. He met some candidates and I was one of them. During the interview, I frankly confessed that I had never seen a smallpox patient but knew the clinical symptoms and epidemiology of infectious diseases including smallpox, as I had graduated from the First Medical Institute in Moscow. Dr. Henderson appreciated my honesty and chose me to work in the program. In 1975, he suggested me to work as international consultant in the state of Bihar in India and so I did.

Initially for the first two weeks, I worked with Dr. V. Bychenko and then continued on alone. At that time, the smallpox in Bihar was in full outbreak, which left me wondering what me almost alone just with an assistant provided under the program and a driver could achieve. My first action was the attempts to convince district administrators and public health workers to increase vaccinations of all not yet infected. I even went out and vaccinated people myself but all that seemed futile in a state of such widespread epidemic.

I was fortunate to connect with some private companies in the district of Dhanbad whose employees happened to include Soviet workers. Through talks and lectures, I was able to raise a small amount of funding for vaccinators, gas, and a few cars. I had the vaccine, since the Soviet Union supplied it free of charge; so I found younger people who would be willing to work as vaccinators for just a small fee. In a short period of time, I created 10 mobile vaccination teams each consisting of ten men and sent them out to vaccinate around the rural areas affected by smallpox.

To vaccinate around the affected part of a village or all villages was the key part in WHO strategy in combating the smallpox outbreak. Each evening, we would discuss everything we did during the day and

Aleksandr I. Gromyko,
a medical epidemiologist, doctor of medical sciences, and participant of the Smallpox Eradication Program. In 1975–1976, he headed the WHO eradication activities in the Indian state of Bihar; in 1977–1983, worked with the WHO Headquarters and participated in the coordination of activities of national and international commissions on the certification of smallpox eradication and was involved in examination of the suspected human monkeypox cases in Central and West Asia

plan our activities for the next day. The searches for smallpox cases were sometimes quite unusual. For instance, when I was relocated to the district of Dhanbad, the capital of the district was regarded as smallpox free despite that many smallpox causes were still recorded in the surrounding villages. When I arrived to the city early in the morning, yet having not met with district medical team, I saw some local teenagers near the market. I showed them the photo of a smallpox patient and asked whether they had seen anyone with similar symptoms. They said "yes" and were eager to show me where the affected persons lived. Having obtained evidence first hand, I met with the district medical team and asked them if they had any cases of smallpox. To their "no", I offered them a visit to the houses where I encountered the cases earlier. My demonstration was convincing to start the active search for smallpox cases in the city. Within the next few days, over 500 smallpox cases were identified and an active vaccination campaign began.

Coming from the Soviet Union here for the first time, I had to learn the capitalist way of management: immediate dismissal of careless workers and praise of those who worked with enthusiasm. My work was viewed very positively by the leadership of the program and Dr. Henderson suggested inviting me to work at the WHO Headquarters in Geneva, where I worked for 6 years, in 1977–1983, at the Smallpox Eradication Unit.

My primary work there was travelling to search for, examine, and diagnose the suspected cases that were regularly reported to WHO from Asia (Bangladesh and Burma) and Africa (Ethiopia, Congo, Kenya, Nigeria, Benin, Uganda, and Ivory Coast).

I would be sent to various countries to assist international experts and local programs working there and would even encounter some dangerous situations. One particular example that comes to mind is when I and three other international experts were in the Ethiopian desert of Ogaden, which borders Somalia. From there, we could quickly travel to investigate suspected smallpox cases in the area. However, Somalia at the time was on the brink of war and Somali guerrilla activity was high in the surrounding areas. Many roads were blocked with landmines. Unfortunately, one of our experts, Dr. Amaral from Brazil, was taken hostage and released after three weeks in captivity only with the assistance of the UN Secretary General. All this time, he was under constant threat of execution and we all were under the risk of such dangerous fate. We were able to get out of the desert 2 days before military action started and the desert was captured by the Somali army. Although none of the investigated cases in the area were confirmed, Somalia continued to have many smallpox cases, with the last one recorded in October 1977.

A.I. Gromyko at the Smallpox Eradication Unit at the WHO Headquarters during one of the short breaks between field travel to Asia and Africa

As a result of these epidemiological investigations, I was travelling to the countries with very different levels of development. I even ended up living with the pygmies in the northern part of the Democratic Republic of Congo. It was well know that cannibalism was still practiced among them and I remember feeling very uneasy as they kept staring at me. At one point, I wondered if they were imagining me as a pot roast. Luckily, I was not eaten.

Under the program's directive, I would often travel to Asia and Africa where later the international committee members would follow to confirm whether full eradication had taken place. I assisted the WHO staff and national representatives in the committee work, as well as in the discussion of the epidemiological situation in these countries and background of the work done locally. I would plan the travel itinerary to visit the areas, towns, and villages of the countries that were selected by the committee members, participated in the visits, and examined the population. I participated in the executive committee sessions where decisions would be made whether the country was deemed smallpox free or if there was a risk they kept smallpox virus samples.

Safekeeping of the international stockpile of smallpox vaccine was done by the WHO headquarters in Geneva. I personally oversaw the storage conditions and replenished the vaccine reserves. I regularly checked the vaccine storage temperature levels and sent samples of vaccines provided by different countries for testing of the activity levels.

During the 6 years that I worked for the WHO, I participated in the preparation of smallpox eradication documents for the WHO General Assembly. I repeatedly spoke in front of the General Assembly on the workings of the program.

It was my duty to maintain and publish the reports on possible vaccine complications in the post-eradication period. I maintained a comprehensive vaccine-complication register of the countries that were still vaccinating their population. Publication of these reports led to reduction in the number of countries that continued vaccinations.

It is not a secret that certain countries would officially declare that the smallpox virus samples collected from patients for diagnostic purposes were destroyed but then WHO would receive the reports that the samples were still being found in lab refrigerators. To investigate these reports, I would travel with the international committee to Uganda, Congo, and the Ivory Coast since storing smallpox virus in non-sanctioned laboratories posed an enormous threat to the success of the program.

After the global eradication of smallpox, the WHO turned to monitoring the emergence of monkeypox cases in the human population. I would often travel to different countries in Africa to investigate the cases that were suspected to be monkeypox. Most of the confirmed cases were in Zaire but epidemiological investigations were carried out in the Democratic Republic of Congo, Serra Leone, Nigeria, Benin, and the Ivory Coast.

I remember one particularly long investigation in Nigeria, when we first had to search for the suspected patient in different places of this country and then in the neighboring Benin. It turned out that the patient was a local untrained "medicine man" and was travelling from place to place "treating" others. Full details of that investigation carried out together with Dr. M. Doromola, a local medical worker from Nigeria, were published in WHO documents.

Another memorable travel episode was the mission to Serra Leone. I was accompanied by a French expert, Jean Paul Rist, who discovered the last natural outbreak of smallpox in Somalia in the October of 1977. We had to examine a patient who was suspected of having monkeypox. The situation with the patient was quickly resolved; however, the events that followed developed into a detective story which I will not forget. Jean Paul and I were on the coast by the ocean and decided to go for a swim as it was unbearably hot. As soon as we got in the water, a local man ran out of the bushes, snatched my clothing, and disappeared into the jungle. We immediately ran out after him but could not catch him. To this day, I get shivers when I imagine what would have happened if I had the USSR diplomatic and UN passports on me and they

were stolen. It would have been an immediate end to all my work with the UN. It was pure luck that I had left them at the hotel that day even though it was strictly forbidden by the USSR embassy not to have the passport on you at all time.

I walked in my underwear all the way through the town back to my hotel stopping by the police station, which of course did nothing to catch the thief. One could only image the reaction of the local population, but nothing would have been worse than if the passports were gone.

My work in the Smallpox Eradication Program is in part reflected in the WHO book *Smallpox and Its Eradication*, wherefrom is my photograph at the program office.

Eradication of Smallpox in India: Reminiscences of a Field Epidemiologist (District Level)

G. P. Oblapenko

Variola vera. Smallpox. These words stirred a complicated mix of emotions: anxiety and benign envy towards the epidemiologists of the old days… Our epidemiology professor, Viktor A. Bashenin, gave lectures in an interesting, absorbing way. While telling us about the epidemiology of diseases, not only did he give historical and epidemiological data, but also quoted fiction. I do not know why but at that time I had the impression that the history of smallpox was virtually over: so much was known, so much had been done. True, smallpox still existed and was still registered but that was somewhere far, far away…

I could hardly foresee that I would chance to encounter smallpox face to face—what is more, to become an active participant of a unique event, the Global Program on Smallpox Eradication.

As it is often the case, everything started in an unexpectedly ordinary way. It was in 1974. I was working as a researcher at the Leningrad Pasteur Institute of Epidemiology and Microbiology. My epidemiology teacher, Yurii P. Rykushin, had been urgently assigned to India, where a large-scale smallpox epidemic was raging. He had spent four months there, in Bihar, the most affected state. On his way back, Rykushin visited the WHO Headquarters, where he reported on the results of his work; there he suggested several epidemiologists as potential candidates for subsequent missions. I was on his list…

And so, on March 1, 1975, a new group of Soviet epidemiologists flew from Moscow to Delhi. There were three of us: Leonid I. Korobov, the chief of Odessa Harbor plague control station; Yurii G. Krivda from the epidemiology department of the First Moscow Medical Institute; and me.

Georgii P. Oblapenko,
an epidemiologist, candidate of medical sciences, and participant of the Smallpox Eradication Program in India: field epidemiologist in Bihar, 1975; coordinator for the northern region of Uttar Pradesh, 1976–1977; member of the National Commission for the assessment of India's readiness for the certification of smallpox eradication

The state of Bihar

India struck us with heat. It was morning. We were met by a representative of the WHO Regional Office for the Southeast Asia, who took us to our hotel and explained where we were to report for duty on Monday, March 3.

The day started somewhat oddly. The truth of the matter is that our Health Ministry had not given us a penny of any currency. So, Leonid, being a man of experience, who had already worked abroad, suggested going to our embassy in order to try and get some rupees there. And so we did. When we got to the embassy, I was left with the taxi driver as collateral, while Leonid and Yuri left. The taxi was standing in the full blaze of the sun, and it was getting hotter and hotter. The time seemed to be flowing rather slowly… The cabbie kept glancing at me with more and more mistrust. And then there they were, my partners, content, joyful, and with money! They were accompanied by a charming couple, the Orlovs, Irina and Valery. Valery (I had met him earlier in Moscow) was working at the WHO Regional Office as an advisor on the malaria control program. Irina and Valery took us under their patronage—they organized a car tour of Delhi and invited us for dinner. We talked about life in India and about field work under the Smallpox Eradication Program (which was of special interest for us). Valery had already spent several years working at the WHO Regional Office; what is more, he had greeted and seen off a number of epidemiologists who had come to fight with smallpox, so he could give us some valuable advice. Among other things, he suggested that we use the next day (Sunday, March 2) to visit the Taj Mahal. We protested, saying that it would be better to see that beauty on our way back. Valery finished our discussion with a weighty argument, "Of course, it's your decision. But bear in mind—now that you are fresh and full of energy, the impression will be deep and mighty. After 3 months of hard field work, given the Indian sun… it would be much harder to dare to go on this wonderful trip to the Taj Mahal."

We made up our minds to go and never regretted it! It really was a fantastic trip! One of our most vivid and cherished memories! The Taj Mahal is rightly called one of the wonders of the world!

The morning of March 3 marked the start of busy days full of intensive work. Altogether, the international group of epidemiologists who had come under the auspices of the WHO consisted of about 30 people. Three days flew by in special briefings. They dealt with a wide range of subjects and included practical aspects of an epidemiologist's field work from purely technical ones (the best ways to look for and identify smallpox cases, how to carry out work in a smallpox focus, and reporting forms) to practical and administrative ones (budgeting and cost accounting, monitoring petrol consumption by field teams). The truth of the matter is that a WHO epidemiologist in the Smallpox Eradication Program was a "multifunctional figure", being not just an epidemiologist, but also an administrator as well (he directly financed and supervised the work of several field teams headed by national epidemiologists). At the same time, a WHO epidemiologist coordinated all smallpox eradication work in the region and was responsible for weekly reports provided by primary health centers. Therefore, the briefings consisted not only of lectures and discussions, but also of practical work with epidemiological and financial documents. We needed to understand and master our responsibilities and different reporting forms in a short period of time.

I have organized and participated in a lot of seminars both before and after that trip and I am convinced that the instructive seminars and workshops arranged by the Smallpox Eradication Program at the WHO Regional Office were highly efficient. These briefings were well-organized and clear-cut. Despite the abundance of various documents (most of which were absolutely new for many participants), we were explicitly briefed on our tasks and possible actions. Our queries were answered in detail. Of great help for our subsequent work was the fact that we analyzed specific real situations and discussed field work experience. How were we to keep large amounts of money? What were we to drink in the field? (Obviously, raw water was out of the question. But what was not?) How to reduce "excessive petrol consumption" by some drivers? What to do in case of a road accident? How to keep in contact (if any) with the press? How to organize house-to-house searches for smallpox cases in the event of a newly registered case (not known before)? How much and how to pay a village vaccinator, a mobile vaccinator, an assistant of a national epidemiologist (a paramedical assistant)? These and many other questions were raised and discussed, and we were given advice or clear-cut instructions on how to act and keep records and reporting documents.

I especially remember the lecture by Dr. Bill Foege, one of the Program's coordinators. He spoke about the epidemiological specifics of smallpox in India, the tactics of epidemiological activities in a fresh

focus of smallpox, and the Program's achievements. For example, 100–200 new outbreaks of smallpox were registered a day in May 1974 in Bihar alone! In India, the total number of registered outbreaks had been 8300, whereas at present there were only 115! In conclusion, Dr. Foege said, "Get ready for hard everyday work. You will have to work from dawn to dusk, sometimes until midnight, because you will be vaccinating late in the evening when villagers get home from the fields. You will have no days off. Your Jeep will be both your office and your bedroom. And I believe that you will make it! Good luck!" Early in the morning on March 6, a plane took a new group of epidemiologists (including us) to Patna, the capital of Bihar. We were met by international epidemiologists, who loaded us into Jeeps, and we set off along the dusty roads of Bihar. By nightfall, we reached our overnight accommodation and got an invaluable present for one night from a Swedish epidemiologist—a mosquito net! In India one needs to take serious precautions against malaria. Early next morning, we quickly got ready, once again took our seats in the Jeeps, and went to a village where there was a fresh outbreak of smallpox. For the first time in our lives, we saw a person suffering from SMALLPOX! On February 19, a member of that family died of measles (?). And now his brother and sister are ill… The face cannot be seen—it is nothing but a mask consisting of pustules and blood crusts stuck together. A heavy cough… BLACK SMALLPOX. A terrible, depressing picture… Several days passed in such "field training": we come to villages, examine patients, and analyze the measures taken and mistakes made. It is quite telling and extremely useful!

On Monday, March 9, we returned to Patna. Just as we were told before, on March 10 we are given our assignments: Yuri goes to the northeast of the state, while Leonid and I proceed south, to Gaya Division. There we got final instructions as to who goes where; each of us is given a Jeep, a bag (containing a blanket, mosquito net, torch, medicine kit, and airbed)… We hugged each other goodbye… By lunch time, I reached the town of Nawada standing on the bank of a dried-up river. It is the center of a newly-established district, so problems (interruptions in power and water supplies) are not infrequent. I was

An epidemiological team entering a village: training of newly arrived epidemiologists; Nalanda District, Bihar, March 7, 1975

An epidemiological team collecting data on suspicious cases (with rash and fever), Dr. Datta making notes; Varsaliganj Block, Nawada District, Bihar, March 14, 1975

allotted accommodation in a state-owned "guest house"—such houses exist in all administrative territories and are to provide overnight accommodation to travelling state officials. A small room with a table, a couple of chairs, an armchair, built-in shelves for personal possessions, a bed with a mosquito net in the middle of the room, a shower, and a toilet, but… as I am told, water is supplied only early in the morning and around 6 pm in the evening. Nearby there is a building where a workroom (an "office", so as to say) is rented. So I took over and checked incidence reports from medical centers. The last smallpox case in the district was registered 2 weeks before. Therefore, my task would be to keep the district free from smallpox! Just as I was beginning to draw up a plan of immediate activities, the lights went off…

At that time, the main activities of the Smallpox Eradication Program in India were the detection of smallpox cases and organizing control actions. This work included the identification of exposed people, vaccination in their immediate circle, and observation of the exposed, as well as house-to-house searches in territories of risk aimed at detection of suspected smallpox cases. That is why I decided to start with visiting all primary health centers and getting to know the primary care physicians as they were the key figures in detecting suspicious new cases with fever and rash. They carried out primary diagnostics of smallpox and were responsible for timely reporting as well as arranging house-to-house searches, which were periodically organized in the state. As far as I could understand, one of the most common errors was late and incorrect diagnostics together with the passiveness of local doctors.

No sooner said than done? Well… good and quickly seldom meet. The tempo of life in India is "somewhat different" from the one we got used to at home. As soon as you arrive at a health center (something like our rural district hospital), you… have tea with the doctor. This is accompanied by small talk (although talking business is also possible), but, first of all, it is a Ritual. A process to show Courtesy and Respect for the guest! Sometimes plans had to be changed abruptly owing to an emergency. For example, I make an appointment with Dr. D.N. Singh, the district doctor of Nawada medical center, to plan the organization of house-to-house searches on the territory of his district bordering another district where smallpox was registered. No sooner have we started talking than a letter is delivered. An urgent one! He opens it to find out that there is smallpox in one of the villages!!! We drop everything, get into our Jeeps,

and set off. Here is the village. Following traditions, we go to the house of the village headman (community leader), introduce ourselves, and explain the purpose of our visit. Then we have tea. At last, we go to the house in question and examine the patient. Thank goodness, it is not smallpox, just chickenpox. We heave a sigh of relief. Then we find out that there are more patients "with fever and rash". It turns out that there is an outbreak of chickenpox in this village.

The roads of Bihar… They deserve a story in their own right! As a rule, a road goes between paddy fields, which are flooded with water. So, at the same time, it serves as a dam. The road surface is, needless to say, topsoil. So dust is in abundance! When you get home by nightfall, you are either pinkish or grey, depending on the color of soil in the places you have been to. Of course, asphalt roads do exist. But they connect cities, while Bihar is, mainly, an agricultural state. Going over bridges… It is a separate ceremony! Generally, bridges are narrow but they have a couple of widened sections enabling cars to pass by. During the rush hour, some bridges are manned by policemen, who control the traffic: they stop the traffic flow either from one, or from the other direction. In a couple of instances, we had to wait rather long, giving way to a herd of cows. The cows were taking their time, walking with dignity. Sacred animals indeed!

The end of March was spent in the appraisal of the quality of house-to-house searches and in the preparation of a function dedicated to the International Health Day, April 7. The appraisal was made using the method of random follow-up visits to the "territories of risk", i.e., the remotest villages, difficult to access. It was important to have evidence that house-to-house searches had taken place everywhere and that the data received by us were trustworthy. Besides, house-to-house searches provided the information on suspicious cases (with fever and rash) that necessitated visiting such patients by a doctor in order either to verify the diagnosis of smallpox or to dismiss it. Such visits were carried out by me, a local doctor, or a specialist from a field epidemiological team. From early morning till late evening I rolled along dusty roads…

The second important task was organizing the celebration of the International Health Day on April 7. It is the day of the founding of the World Health Organization and it is celebrated every year. Each year, a theme is selected that highlights a priority area of public health. In 1975, the motto suggested by WHO was "Smallpox—Point of No Return". Announcing that event, Dr. Halfdan Mahler, the WHO Director-General, wrote in his letter that that day marked the beginning of the final stage of a great campaign aimed at the eradication of smallpox on the Earth and also heralded the beginning of a new era for the WHO, which was able to demonstrate what could be done to eliminate a disease when all nations join in one coordinated effort. I decided to organize a function for a wide audience, including both the medical community and politicians of the district. I explained my vision of the event and discussed my idea with Mr. C.S. Prasad, the governor of Nawada District, and Dr. D.N. Lal, the district health officer. My suggestion

Vaccination in the village of Gonarbigha, Hisua Block, Nawada District, April 13, 1975. Vaccination is carried out by assistant epidemiologist Ram Singh (*right*) under the supervision of block doctor, Dr. V.K. Singh

Stuck! The epidemiological team's Jeep got stuck on the road to Rajauli Block near the village of Biglen, Nawada District, April 17, 1975.

A tricky situation! Racindar, my Jeep's driver, is convincing the cow's owner to clear our way; the man answers that he has already tried to persuade the cow to get up, but… "she wouldn't move"… One has to be extremely polite with cows! Akbarpur Block, Nawada District, April 12, 1975

was accepted with enthusiasm. The governor suggested holding the function in the town hall. I ordered colorful invitation cards at the print house. My idea was to organize a big "tea cocktail party" with sweets for all invited and after that a small VIP reception. The function was scheduled for April 5. I sent out invitations to Mr. John Dresher, WHO coordinator in Gaya Division, a big number of WHO epidemiologists working in the state, and to the WHO Regional Office. I decided to hand in some cards personally—to VIP guests (for example, to the Chief of Police); as for the rest, the governor undertook to distribute them using his own channels. The function was a big success even before its start. For instance, the Chief of Police invited me to make a speech at a district police meeting and I suggested that police officers be involved in epidemiological surveillance: they could promptly inform us about suspicious cases and migrants from Bangladesh (where a large-scale smallpox epidemic had started).

Saturday, April 5, was a hot day. In the morning, a scorching, as if from a desert, wind started to blow, and everything was sinking in that scalding misty dust… They said it was almost +40°C! Early in the morning, I went to the district police headquarters where I made a brief report on the state of affairs and our achievements in smallpox eradication in Bihar. I explained how the police could help us in reaching "zero point" in smallpox incidence. I was anxious that the heat might ruin the planned function. However, all my worries were for nothing. Streams of cars and Jeeps started flowing to the town hall building—physicians in private practice and doctors from district hospitals were coming. The WHO coordinator from Gaya came together with Dr. Lal. After the heat of the streets, it was so pleasant to sit in the air-conditioned town hall auditorium. Thank goodness, there were no power cuts at that time! A short introductory speech was made by Mr. Prasad. Then it was my turn to speak about the achievements (we were keeping Nawada free from smallpox!), the situation, and our tasks. After that the head of the health service specified the goals of house-to-house searches, emphasizing once again the importance of timely information. The function went very well. Everyone was delighted (I was told that much by the participants, who thanked me). In accordance with local customs, after the function there was an amateur performance with Indian songs and dances, and even I had to take the floor and sing a song about my native Leningrad.

At the end of March, an important extraordinary event took place, which is engraved in my memory. It was Holi, an Indian festival. It is a big national celebration meant to welcome spring. It continues for several days during which bands play everywhere and people dance in the streets, pouring colored water over each other, showering coloured powders, flowers and all kinds of paints. Long before the festival, we received a memo from the chief of WHO epidemiologists in the state strictly ordering us not to work and to park all Jeeps in a safe guarded place. I and Leonid Korobov arranged that I would visit him in Aurangabad. It was quite a big district center and living conditions (in the "guest house" where he lived) were, according to him, "much better and more comfortable". But of course, the main reason was that for several weeks we had been rather isolated, communicating only in English, letters from home being a very rare occasion. That is why we preferred to spend those festive days in friendly conversations rather than in solitude. When the working day was over, I steered my Jeep for Aurangabad, where I got only by midnight. The morning turned out to be not so hot; however, I took a shower several times, getting the best out of the advantages of that "guest house". (As I mentioned before, water in Nawada was supplied in the morning but after the time I had to leave for field work and in the evening, well before my return from work!) There were actually just the two of us left in that building. Only the security guards eyed us with curiosity while we were sitting on the terrace, enjoying our conversations, the sun, and marvelous Indian tea. Leonid told me that the previous day had been a great holiday for them—the last smallpox outbreak was done away with! It happened on March 25, 1975. We argued about when and where there would be the last focus in India. Eventually, we agreed that it would be in the state of West Bengal. Later it became clear that we were seriously mistaken! From behind the walls of the garden surrounding the "guest house" we could hear distant drumbeat and sounds of music… However, we stayed calm thinking that all those "Holi horrors" told us by veteran epidemiologists were heavily exaggerated.

But in that we were gravely mistaken, too! Next morning, the thunder of music got closer. It seemed that the drummers were pounding right under our walls even though the streets were deserted. Not a single car! We were visited by a military jeep, though. The tommy gunners came up to us and asked who we were. We explained that we were WHO staff from Russia helping to eradicate smallpox. So, we talked about smallpox in India. The patrolmen asked us to revaccinate them, and Leonid promised to do it right after the festival. The patrol left. No sooner had we sat down to work (we wanted to prepare reports on the assessment of house-to-house searches) than a crowd of Indians painted in all colors of the rainbow approached the house. The drums were thundering and it seemed to me that there was also a trumpet insistently calling somewhere. Upon the sight of us—clean, half-naked, and relaxed—the crowd roared, pushed the security guard aside, and surrounded us. After a short pause, we were sprinkled with something orange. To play along, we smiled pretending it was cool. At that moment a couple of activists with cans in their hands jumped from behind and started painting us accompanied by the laughter and cheering of the audience. The crowd was exuberant! The trumpet was howling. The drum was on the verge of explosion. Someone was painting on our backs with their palms! The security guard was dying of laughter, literally rolling on the grass. The electrified crowd urged us to go to the street but we politely refused. It took us about two hours to wash ourselves in the shower… We locked the doors of the room and drew the blinds. The festival was still raging behind our windows! By nightfall, shooting began—it was a fireworks display. Holi was continuing gaining momentum. Several times there was a prolonged pounding on our door. But we did not open it…

April brought intense heat. Every day it was getting hotter and hotter. The lack of fresh air made it impossible to sleep at night. A temporary, for a couple of hours, remedy was a wet sheet. But as soon as it dried out, you woke up. Under the sun, the Jeep quickly got sweltering, making you feel like in a sauna.

Holi festival. Georgii Oblapenko (*left*) and Leonid Korobov (*right*) have just got rid of “unwelcome guests”, who left absolutely delighted having got a chance to decorate foreigners. Aurangabad, March 25, 1975

Every evening, I filled my thermos flask with tea and in the morning squeezed a lemon into it. Such a drink was a salvation, especially when it was necessary to get to remote villages across the fields under the scorching sun. In order to adapt to the heat, we had to rearrange our working hours. We started work early in the morning, at 6 o’clock we were already on our way so that we could hide into the shade by midday. Later on, we went “to the field” again: visited villages to assess the quality of house-to-house searches or to examine suspicious patients. Once I had to drive along the bed of a dried-up river. That was because I, together with the district doctor, had decided to visit some remote villages inaccessible after the beginning of the rain season. So, in spite of the hot day, we drove to that faraway place. It was a really extraordinary experience! The sand crunching under our wheels… The low steep banks of the dried-up river… The scorching sun! The scalding wind! Once you close the window, it is impossible to breathe! Opening it makes things even worse owing to the hot wind, which fills the cabin with sand! At long last we got there!!!

Having left our Jeeps in the shadow of a tree, we… marched some more kilometers across the fields. Completely exhausted and sweating, we entered the village. Observing the proprieties, we made our way to the house of the headman (the leader of the village community). We were greeted with hospitality and curiosity. They invited us to try some cold sorbet drink. I am looking forward to enjoying the cool liquid! But… they pull a bucket of water out of a well and ask us if we have a handkerchief. Alas, we don’t. At this moment the assistant epidemiologist, whose head is covered with a piece of light-coloured cloth, offers it instead… “Will do!” says the headman happily. They put sugar onto the cloth, tie it up and, put the bundle into the bucket with water waiting until the sugar dissolves. Then, they pick some lemons from a tree and squeeze them into the same bucket… The sorbet drink is ready! Well, I think to myself, since there is lemon juice, there certainly can’t be cholera in there! I drink two glasses. Lovely! After that we examined several patients with measles and chickenpox. We found out that there were no visitors from Bangladesh there. Relieved, we set off on our journey back…

The heat was growing! Tea in a “roadside café”. Nawada District, April 1975

As I have already mentioned, the work on the detection of suspected smallpox cases and their subsequent examination and, if necessary, follow-up was our main task. The information about such cases was collected using different methods. We arranged special visits to schools and talked to children showing them photographs of patients with a typical clinical picture of smallpox and inquiring if anyone had seen such cases. An active search for and collection of such information were organized at markets frequented by residents of many villages. There we put up colorfully decorated tents with special posters and large photographs (a smallpox patient: stage of eruption, stage of pustules, etc.). We displayed notices in prominent places promising a reward of 100 rupees for information about a confirmed smallpox case. Trained medical staff talked to people, answering their questions and finding out whether anyone had seen victims of such a disease in the neighborhood. The data on suspicious cases were logged into special registers, Fever and Rash Cases Registers. Subsequently, such cases were visited on a compulsory basis by a doctor or an epidemiologist. It should be mentioned that the Jeeps used by epidemiological teams and doctors were also decorated with posters and photographs. Several times, we were stopped on our way by passersby who said that just in the vicinity there was a village with cases we were looking for. We carefully wrote down the address, made a U-turn, and went to look for suspicious cases in order to examine them and decide what their illness was. Until then, all detected cases that we (i.e. doctors and epidemiologists) had seen were chickenpox or measles.

At the beginning of May, there was an episode worth describing in detail. In March and April, as a result of active searching for new smallpox cases and anti-epidemic measures in foci, their number had fallen dramatically. By mid-April, as few as 30 outbreaks of smallpox had been registered in India and

An epidemiological team's post at a market. The post personnel are explaining the clinical picture of smallpox and collecting data on suspicious cases; the second on the right is Ram Singh, an assistant epidemiologist. Gobindpur Block, Nawada District, April 1975

In order to get to a hard-to-reach remote village, we drove along the blistering bed of a dried-up river. Hisua Block, Nawada District, May 1975

15 of them, in Bihar. On April 14, it was announced at the meeting of epidemiologists working in Gaya Division that a new outbreak of smallpox was registered: eight sick and one dead. The focus had been detected too late owing to the local doctor's mistake. Of course, we used this information to motivate doctors and medical staff emphasizing the importance of TIMELY detection of suspicious cases and their examination. And there you are—at the end of the afternoon of April 30, I am told that I urgently need to go and examine a suspected smallpox case! I arrive at the village with a population of about 5000. I find out that the family in question has come from Bangladesh… The father reported on the sick child having learnt about a 100-rupee award. We go to the house, talk to the father, and ask him to show us the sick child. It's an 11-months-old girl, who hasn't been vaccinated against smallpox. Her face is covered with pustules. We carefully examine the character of pustules—they are late lumps, which have already started to dry. There is rash on palms and soles. We drive to the local hospital and discuss the situation with the local doctor. We decide on the first measures to be taken—carrying out vaccination in the village (in an orderly way, without panic!) and detecting all exposed. Next morning I drove to the office of Dr. Lal to inform him about the focus and told him that I was going back there because I wanted to examine the patient once again and check how the vaccination of the villagers was going on. He decided to go with me. But first of all we got through to the office of division coordinator John Dresher and reported on a very suspicious case of possible smallpox.

Vaccination in the village was in full swing! The place was noisy and crowded. The day was quite hot. We carefully examine the sick girl and… see a youth of about 12 or 14 about to leave the house who is covered with fresh rash. A typical clinical picture of chickenpox! We sighed with relief and even smiled. We returned to Nawada with good news. No sooner had we set out to phone John Dresher than he entered the room! He was delighted with our news! However, that was not the end of the story. A day later, a representative of the WHO office in Patna arrived and asked us to escort him to the village for final monitoring, so as to say. Our visit came in really handy: the father was demanding the promised reward and only the authority of the representative from the state's capital, who in the course of a heated discussion in Hindi explained him the reasons for the refusal, calmed him down. And that's how this troublesome story ended.

Two weeks later, at a weekly meeting of the division's epidemiologists in Gaya, we were given a touching farewell party. A lot of warm words were said. We sang songs, joked a lot, but when the time came to hug each other goodbye, we felt sad…

Here in Bihar, we had met a lot of nice and interesting people. We had been all doing one big thing. Everybody understood that we would probably never meet again… And the last words were, "Have a safe journey! Don't forget us!"

Here in Bihar, we were leaving a part of our souls. I couldn't even imagine that almost in a year's time, I would be back in India again taking part in the preparation of the documents necessary for the certification of the country as a territory free from smallpox.

The state of Uttar Pradesh

Not so much time elapsed before I received, in October 1975, a letter from D. Henderson, the head of the WHO Global Smallpox Eradication Campaign, inviting me to come to India again and take part in the last stage of the Program—the preparation of the country for the certification of the freedom from smallpox. Having agreed, I arrived to New Delhi early in the morning on October 2, 1976. Two days of briefings at the WHO Regional Office passed very quickly. Having finished with paperwork, I flew to Lucknow, the capital of Uttar Pradesh, on October 8. The morning was spent in a detailed instructive conversation with Dr. Agarwal, national Smallpox Eradication Program coordinator. He told me that the WHO coordinator in the state, Dr. Paul Rotmil, was checking the quality of house-to-house searching campaign but would be back in a couple of days and finalize my duties. Paul Rotmil, an epidemiologist from Sweden, turned out to be a nice young man with a magnificent bush of black hair and a big black beard. He said that he wanted to appoint me as the work coordinator for the northern part of the state but meanwhile was asking me to work in Lucknow, where a series of house-to-house searches were just finished and assess their quality. He

Farewell to Bihar. The last photo as a memento, Aurangabad, May 24, 1975. *First row, from left to right*, epidemiologists Yurii Krivda, Singh, and Khan; *second row*, I.C. Jensen, S. Chakravarti, Georgii Oblapenko, and Leonid Korobov

added that in October he was going on holiday to Nepal to take photos of Mt. Everest (Chomolungma) and was planning to leave me in his stead, i.e., as an acting WHO coordinator in Uttar Pradesh. My main task would be the organization and quality control of the last national campaign of house-to-house searches in November, helping doctors of all levels with the preparation of documents necessary for the certification of India as a smallpox-free country, as well as field epidemiological work. Field work involved examining suspected smallpox cases and maintaining a high level of the follow-up of the "patients with fever and rash".

As I found out later, the character of work, in general, was not different from what I did in Bihar in 1975. I do not want to repeat myself, describing administrative and organizational matters or road trips. However, two events I was involved in were quite special and they are worth talking about in detail.

Kumbha Mela (the festival of jars) at Prayaga, which takes place in the city of Allahabad every 12 years, stands out among the Hindu religious festivals. The city lies at the confluence of three holy rivers—the Ganges, Yamuna, and Saraswati. The legend has it that the festival of jars is associated with a battle between gods and demons for a jar containing a potion of strength. It is believed that drops of that potion fell to earth in four places—Prayaga (the old name of the city of Allahabad), Hardwar, Ujjain, and Nasik. The date of the festival is determined in accordance with the position of stars but generally it happens in January. Thousands and thousands of pilgrims go to these holy places to bathe in the holy rivers and thus purify their bodies and souls. Astrologers said that in 1977 it would be a special festival. It was expected that between 30 and 50 million pilgrims, not only from India but also from neighboring countries as well, would visit Allahabad for ceremonial bathing.

Needless to say, it was decided to use this event to carry out a large-scale epidemiological survey to make sure that smallpox was not present. As early as on November 1, Dr. Agarwal, Paul Rotmil, and I drew up a work plan including organizational matters, such as the preparation of leaflets and posters, arranging of a tent camp for medical staff, calculation of required funds, and so on. On November 10, we visited Allahabad, where we had a meeting with the health officer who was responsible for medical support during Kumbha Mela. We decided that 33 medical aid posts (checkpoints) would be deployed to vaccinate people against smallpox and cholera, while suspicious cases would be hospitalized; came to an agreement on the work of epidemiological teams, which would actively look for cases with fever and rash in the city and in the main pilgrims' camp; and discussed the question where to place medical staff and the cost of such a camp. When we went to look at the campsite, we found out that it had already been fenced and several tents had been pitched.

At the end of November, Dr. Agarwal and I had to go to Delhi to plead our cause in the Health Ministry and WHO

Georgii Oblapenko is examining a patient with chickenpox and taking a specimen for virological testing. Moradabad District, October 1976

Regional Office. The discussion was professional and to the point. We were offered to concentrate our efforts on health education, collecting data on cases with rash and taking specimens (from chickenpox cases), and forwarding them for laboratory tests. They suggested excluding any active search (house-to-house searches and visiting tents).

It was with some apprehension that I was approaching Allahabad on January 9, 1977. The first checkpoint that stopped us was 12 km away from the city. People were passing in groups; medical staff were talking to them and checking them for vaccination scars and cholera vaccination certificates. I drove to our tent camp. There they told me that the peak of pilgrim inflow was expected on January 13 and 14 but the most important days for bathing would be from 17 to 21. Pilgrims usually come 2 or 4 days in advance and after bathing go home. The main tent camp for the pilgrims was brightly illuminated with lamps of various colors and decorated with balloons. The spirit of the festival was felt everywhere! And the pilgrims kept coming! In the middle of the night, I was woken by thundering drums. The tempo was accelerating accompanied by singing "Ram! Ram! Ram!" Suddenly everything went quiet but in a couple of minutes the drumbeat and singing were gaining momentum again.

In the morning, I drove on my rounds of checkpoints. The work everywhere was going on without trouble. I visited seven posts on the roads leading to the city and two ones at railway stations. The medical staff said that the number of pilgrims passing their checkpoints varied between 1000 and 10 000. On return to our camp, we saw a colorful procession: a column of people was entering the main gate headed by three men, their bodies painted. They were carrying big orange flags with "Praise God!" written on them in Sanskrit. They were followed by a column of honorary citizens wearing wreaths. After them, there were flag-bearers with multi-colored flags and several bands trying to outdo each other; they were tootling,

Quality assessment of house-to-house searches and people's awareness: interviewing schoolchildren. Local doctor Fatan Singh and epidemiologist Georgii Oblapenko. Paliya Block, Kheri District, November 1976

chanting, and drumming. I got the impression that the main instrument was the drum! In their wake, a cavalcade of elephants was moving in a stately and dignified manner! The elephants and their drivers were also decorated with wreaths made of flowers. Bringing up the rear was a column of women, who, following an unseen command, suddenly produced shrieked cries and threw up their arms…

We went on with organizational work: arranged with the local radio the broadcasting of appeals and announcements (about what to do if a rash case is detected); negotiated televised addresses and the display of specially prepared posters; got special passes for the Jeeps of epidemiological teams (the entry of vehicles into the pilgrims' camp was strictly limited); and checked the location and equipment of field hospitals in tents and their accessibility in terms of the transportation of patients.

In the evenings, it wasn't just cool but really chilly! We lent a special heater, so we sat around it, drank tea, and discussed the day's results. Once a duty doctor called on us; he said that the most important days for bathing were January 14, 19, and 21 (that had been established according to the position of stars). It was expected that from 4 to 9 million people would be coming on these days! "So far," he said, "it has been rather quiet: from 500 000 to 600 000 pilgrims a day have been coming."

And the pilgrims kept coming, more and more of them! The processions were, generally, like each other (flags, musicians, musicians on camels, a column of honorary pilgrims and, by all means, elephants). But once the police stopped us, asked to switch off the engine and wait on the side of the road. We saw a magnificent and extraordinary procession! Those were pilgrims from Bihar, from Ranchi region (it is quite a rich region, where iron and steel works are located). At the head, flag-bearers were proudly marching. Trumpets were blowing loudly, drums were thundering. Then there were warriors with pikes. They were followed by a silver and gilt litter carrying the holy book "Gita"; a handsome Hindu man was walking by its side with a little brush, removing dust from the book! And, of course, there were elephants!

Deliberations at a bridge, "Will we be able to cross or not?" on a road to remote villages of Kheri District

Quality control of house-to-house searches in a village: talking to villagers

Epidemiological inspector Georgii Oblapenko puts the date of his visit to a village and his signature in a place indicated by a special sign. Lucknow District, November 1976

Kumbha Mela is one of the biggest festivals in Hinduism. It is celebrated every year but once in 12 years it is a special holiday: pilgrims from all neighboring countries come to Allahabad for a ceremonial bath in the waters of the Ganges. Allahabad, tent camp, January 11, 1977

A lot of them! They were splendidly decorated both with flowers and with cloth. On their backs, next to the drivers, “the elders” were solemnly sitting. At the sight of the elephants with the elders, the public lining the road prostrated themselves, putting a coin into an elephant’s trunk. The elephant gracefully passed the coin to the driver. However, one of the elephants playfully and skillfully threw the coin up… hitting the elder in his forehead. As punishment, the driver hit the animal on its forehead with an iron rod, and the elephant howled loudly…

One day on my rounds of checkpoints in one of the main directions (southern), I drove onto a bank of the Yamuna River. The view from there was spectacular. The place where the two rivers flew together was clearly seen but for quite a long distance below this spot the greenish waters of the Yamuna did not mix with the yellow waters of the Ganges. The setting sun was illuminating the famous island of Sangam, the main bathing site! Numerous boats full of pilgrims were heading for the island from three campsites. The red disc of the sun (“Tomorrow it will be windy”, I thought to myself) seemed to hang still for a moment and then… plunged into the waters of the Ganges. That’s what it was like—Kumbha Mela at Prayaga…

However hard we tried, no smallpox cases were detected during the festival. We checked several suspicious cases but they all turned out to be chickenpox. We were very pleased! It was just another proof of the fact that smallpox had disappeared from the Indian subcontinent.

The Government of India and WHO Regional Office took the country's certification very seriously. That is why it was decided to set up a national commission for the assessment of smallpox eradication efforts. It consisted of national specialists, staff of the WHO Regional Office, and temporary staff (WHO epidemiologists). The National Commission had the following tasks: to appraise all aspects of the process of smallpox surveillance; to look for any evidence of the existence of smallpox foci after the last registered smallpox case; to motivate medical staff of all levels to maintain high-quality smallpox surveillance until the arrival of the International Certification Commission; and to recommend a field work plan for the first quarter of 1977. Each state was visited by a group of commission members, who spent 4 or 5 days there inspecting primary health centers as well as regional health offices and state health authorities. We talked to medical staff, examined and appraised documentation, paying special attention to the organization of surveillance and special work in high-risk territories. We randomly visited towns and villages to check the people's awareness of what to do if there was a case with rash. As a member of the National Commission, I visited the states of Odisha (Orissa) and Bihar. It was pleasant to see how much serious work had been done in the vast majority of primary health centers and the way epidemiological surveillance was carried out. Of course, we did find some loose ends. But there was enough time before the visit of the International Commission to tie them up. On January 20 and 21, 1977, the National Commission met up in Delhi for the last discussions and approval of the final report. The main conclusion of the National Commission was that there was no evidence of the existence of smallpox cases in the country. The commission noted with

Kumbha Mela. Crowds of pilgrims coming in! Allahabad, January 14, 1977

satisfaction that the quality of surveillance had improved in most states. The commission's recommendations on the correction of shortcomings found in the organization of epidemiological surveillance were discussed at the local level and reported to the health authorities of each state.

At last, the time came for the final stage of the many years of huge and hard work on smallpox eradication in India. The International Certification Commission, including 16 specialists from different countries of the world, arrived to Delhi. On April 4 and 5, its members met with national coordinators, WHO field epidemiologists, and the staff of the WHO Regional Office who supervised the Smallpox Eradication Program. After studying the documents and discussions, the commission decided on the forms of future work and on the territories for "field visits". H. Lundbeck, a professor from Sweden, was to fly to us in Uttar Pradesh. Thus, on April 7, I was already leading a convoy of Jeeps (with the member of the International Commission, Paul Rotmil, and representatives of the health ministry of the state) along the road to the town of Kheri, the district center. This territory, bordering Nepal, had several risk zones (hard-to-reach villages located in forests and regularly flooded after heavy rains). The inspection was meticulous but I kept calm seeing how much Dr. Kapur had improved the organization of epidemiological surveillance. Prof. Lundbeck was especially interested in the situation and surveillance in the zones of risk. Dr. Kapur replied that they had recently conducted two extra series of house-to-house searches there (as Dr. George Oblapenko had recommended!) and examined all suspicious cases found. These had turned out to be just chickenpox cases! The inspectors were content. Before the departure, Dr. Kapur came up to me,

Checking the work of a field infectious diseases hospital. During Kumbha Mela celebrations, special active epidemiological surveillance was organized in order to detect the cases suspected of smallpox, with subsequent urgent hospitalization and examination. Nag-Baski hospital, Allahabad, January 15, 1977

At the meeting of the National Commission on India's certification, WHO Regional Office, Delhi, January 21, 1977. Dr. F. Lowen, Deputy Regional Director (*right*); Ivan Masar, WHO epidemiologist and chief epidemiologist of Slovakia (*middle*); and Georgii Oblapenko (*left*)

gave me a hug, and said, "It's thanks to you, Doctor George, that everything has gone so well today. I'm very grateful!" I was really touched by his words and remembered how I had explained the basics of epidemiology to him and persuaded him to carry out the active search for cases with rash (i.e., do house-to-house searches in the zones of risk). Prof. Lundbeck decided to visit several primary health centers, where he also scrutinized the documents and talked to the staff. He was satisfied. By April 9, our convoy of Jeeps, which had considerably thinned, reached a wonderful town in the foothills of the Himalayas. This beautiful place was called Nainital. We arrived there quite late, because the mountain road had been clogged with lorries. Dr. Gupta, the chief physician, suggested visiting the observatory. I had already been to Nainital several times and knew that there was a well-known observatory at this place, famous for its crystal-clear mountain air. In winter, when I was there with members of the National Commission and we were literally freezing, the director of the observatory showed us the rings of Saturn. It was a fantastic sight! "What are they going to treat us with today?" I was wondering on our way to the observatory. What we saw was unforgettable! The picture is still before my eyes… We saw Jupiter's five moons!

And in the morning there was intensive work again: studying documents, discussing the results of the last series of house-to-house searches, and the general questions of surveillance of smallpox and the cases with rash. D. Gupta repeatedly praised my recommendations on the improvement of epidemiological surveillance. It was unexpected and pleasant.

There, in Nainital, I said goodbye to Prof. Lundbeck and those accompanying him—they went to inspect other territories of the state, which had other coordinators. While we were driving down to the valley, Paul Rotmil got into my car for a parting conversation. He was sorry that I was leaving, thanked me for good work, and said that he had enjoyed working with me. Bidding farewell, he said, "Maybe one day we'll meet again". "That would be lovely!" I answered. We hugged each other. We have never seen each other again…

Meanwhile, I had to finish with administrative matters, which included collecting financial reports from field teams, final payments, and preparation of my own report for the WHO Regional Office. On April 17, I was to fly to Geneva, and from there, finally, home!

Little did I know then that in a couple of days I would have to go to the village of Patonagar, where, according to a local newspaper, "smallpox was raging"! It was right on the eve of my flight from Lucknow to Delhi. I drove to the village, convinced that it was just the journalist's sensationalist scheme. I was right. There was an outburst of chickenpox in the village. I examined the patients: it was a "beautiful" classical clinical picture of chickenpox…

I flew home being absolutely sure that the International Commission would certify the eradication of smallpox in India. I had seen the pains specialists from different countries were taking to achieve this noble

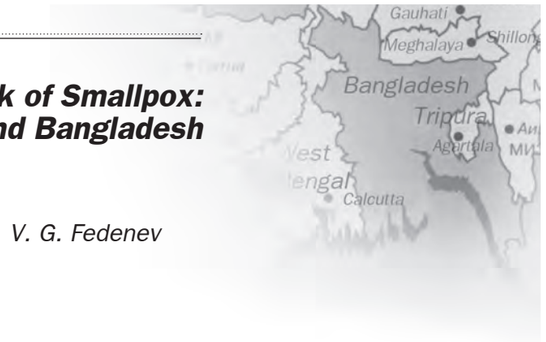
goal and could appreciate the success reached. I was convinced that all these efforts were bound to lead to the eradication of smallpox. And, indeed, it happened. But I was to learn about it later, being already in Geneva. I was told the news by Ivan D. Ladnyi, then a Deputy Director-General of the WHO. He said that on April 23, 1977, the International Commission declared that smallpox had been eradicated from India!

It was not until much later that many people and experts believed that such a tremendous thing had really happened—a terrible disease taking numerous lives had been eliminated on the Earth. I remember a scientist from our institute (Leningrad Pasteur Institute of Epidemiology and Microbiology), Yu.P. Rykushin, returning in 1978 to Moscow from Africa, where, as a member of the International Commission, he visited Uganda to certify the eradication of smallpox. As it was the rule, sanitary control people told him to produce his smallpox vaccination certificate. It took him quite long to find it. Finally he showed it and announced, "This paper will no longer be necessary!"—"??? Why are you saying this?!"—There is no more smallpox in the world! Do you understand? Nowhere in the world!" "No way!" they retorted sharply. "If there is a place for smallpox, it is definitely India. It has always been there and it will never go away!"

When he told them that he had personally taken part in the eradication of smallpox in India and that the country had been certified in 1977, they objected again, "It is just impossible! There are a lot of jungles, and smallpox is still hiding somewhere. You'll see!"

I am writing these reminiscences in March 2011. Almost 34 years have passed since the International Commission declared the eradication of smallpox in India. Time has definitely proved the effectiveness of the Global Smallpox Eradication Program. And we have never seen smallpox since then!

The foothills of the Himalayas on the way to Nainital, October 1976



On the Track of Smallpox: India and Bangladesh

V. G. Fedenev

The offer to go to India to participate in the WHO Global Smallpox Eradication Program was not only unexpected and tempting, but also exciting. Although there was no reason to feel the excitement since I already worked with smallpox before. However, it was the WHO, it was the known as ambitious program, and it was initiated by the Soviet Union and announced in due time by Academician V.M. Zhdanov at the 11th World Health Assembly (WHA).

Dr. I.D. Ladnyi, the head of the Main Board for Quarantine Diseases with the Ministry of Health of the USSR, who earlier worked on the eradication of smallpox in Africa, successfully promoted our specialists to work in the WHO Smallpox Eradication Program as short-term consultants in different countries of Africa and Southeast Asia. At that time, I was his colleague and, besides, I already had had an experience working in the foci of smallpox.

It was in the city of Aral'sk (Kazakhstan) in the fall of 1971, where people suddenly began getting sick with smallpox. Some 10 people fell ill, three or four died. In fact, my colleague, a professor and specialist in communicable disease, and me at that time were in Turkmenistan to conduct an epidemiological survey and anti-epidemic measures on cholera. Dr. Ladnyi organized at the Health Minister of Turkmenistan an urgent transfer for us to Aral'sk by air ambulance aircraft. Ivan Ladnyi was already there and leaded the anti-epidemic activities. We did not know why we were moved so urgently to Aral'sk and were very much surprised to see soldiers with machine guns at the airfield. Still onboard the plane, we tried to guess what could have happened given that we were summoned by Dr. Ladnyi. Our conclusion was that it was a serious infection, even more serious than cholera. Well, as soon as we were offered to be vaccinated against smallpox at the airport, all became clear.

Professor immediately started working with smallpox patients in the hospital and I was involved in the work of the team of epidemiologists, which conducted a door-to-door search for identifying the febrile patients and people with skin rashes.

Valerii G. Fedenev,
a medical epidemiologist and participant of the Smallpox Eradication Program in India (August 1975–May 1977) and Bangladesh (May 1977–January 1979). He was involved in organization of surveillance and was the coordinator of anti-epidemic activities in five northeastern states of India and southeastern regions of Bangladesh and contributed to the preparation and work of the national and international commissions on the certification of smallpox eradication in these countries. On completion of the Smallpox Eradication Program, he continued his activities in Bangladesh under the WHO Expanded Program of Immunization; later, he worked with the WHO Headquarters (1985–1989 and 2006–2008) and with the WHO Regional Offices in India and Egypt (1992–2003)

We also visited all the plants of Aral'sk. Schools and other institutions were already closed. During the searches, we vaccinated or revaccinated all people without any exception regardless of the availability of vaccine scars. People suspected for smallpox were isolated and the contacts were also kept in isolation ward.

Strict quarantine was organized in Aral'sk, which excluded any contacts with the outside world. The city was cordoned by a ring of special military forces; trains were passing through in transit without stopover. An exception was made for us because we came to work in the center of the epidemic. The hospital where the patients with smallpox were treated was in a decrepit single-story wooden house with wooden floors with slots. Scabs of patients, which were numerous, could freely get under the floor boards. To communicate with patients in a hospital and to record their personal medical histories, we had to wear a full "anti-plague suit" and the hospital staff worked wearing the same gowns. After discharge of the last patient, the hospital was just burned out: disinfection in such a construction would be completely ineffective.

Epidemiologists were anxious to know whence smallpox could emerge since it was liquidated in the USSR as long ago as 1936. There were some imported cases but without any epidemic consequences. The main version of the source of infection which was strongly imposed on us was the following: the smallpox virus could have been imported with the smuggled belongings from Afghanistan via Turkmenistan. It was a pretty dubious assumption. The more so since the local residents and employees of the Aral'sk anti-plague station said that there was a military bacteriological laboratory with a field test site on an island in the Aral Sea and the virus could have come from there. However, it was a restricted topic, which we did not discuss. Later, it was confirmed. Dr. P.N. Burgasov, at that time Deputy Minister of Health and Chief Sanitary Physician of the USSR, disclosed in the open press the secret of the Aral smallpox outbreak after 20 years (Evgeniya Kvitko, *Smallpox is Also a Good Weapon*, Moskovskie Novosti, November 14, 2002; Dmitrii Mel'man, *The Historian of Death*, Moskovskii Komsomolets, April 7, 2006).

Thus, I was to go to India for smallpox. Long clearance, quick packing, and finally Aeroflot brought me to New Delhi. It was in mid-August 1975. The door of the plane opened and immediately a blow of unforgettable and unusual hot and humid air rushed in, despite early morning. Everything was unusual: the air with some spicy touch of odors, low-rise city immersed in the green, numerous cyclists and scooter riders hurrying to work, clothes of men and women, and a hotel with open-air corridors and small rooms but with air-conditioner. By the way, some words about the hotel. It was Lodhi hotel, accommodating most of those who came for the WHO Smallpox Eradication Program in India.

The very same morning, I went to the WHO Regional Office. I met the staff of the program and visited the Indian Ministry of Health to appear before health authorities; then, the 5-day briefing at the WHO office, which included technical, administrative, and financial matters, as well as some advice of the specific features of behavior and communication with the local population, taking into account the local culture, customs, religions, etc. There were people from about eight different countries. Almost all of them were allocated to the states of Uttar Pradesh and Bihar, located in northern India. These states were the most densely populated and poor and, which was the most important, they were the most affected by smallpox. I was assigned to Bihar.

An hour and a half flight to Patna, the capital of Bihar, and immediately after I went to a large gathering of all epidemiologists working on smallpox in the state. There were discussion on the strategy of the program, reports by epidemiologists, tasks and plans for the near future, meeting with the local program leadership and other epidemiologists already working there. I must confess that it was quite difficult with my English: lack of practice and different pronunciation and accents of interlocutors, all from different countries and with different levels of English command. It was much easier to understand our compatriots.

I was lucky. I was assigned to the State of Bihar, where the last local smallpox case was registered in India. It happened on the May 17, 1975, two and a half months before my arrival, in a very remote Pachera village in Katihar district. By the way, 2 years later (already working in Bangladesh), I have had the

opportunity to accompany to this village a group of Japanese reporters, who were shooting a documentary about the eradication of smallpox.

The Smallpox Eradication Program in India by that time entered its last phase, referred to as Target Zero (Operation Smallpox Target Zero), implying the goal of decrease in the number of smallpox cases to zero. The program strategy somewhat changed to intensify the search activities for suspect smallpox cases and similar diseases. Although the frequency of regular searches reduced, house-to-house surveys were introduced instead of a village-to-village scheme. The searches were also conducted at weekly markets, during religious festivals, melas, where up to a million people could gather, as well as at other local festivals, and this was a very important task. Special attention was given to the surveillance in the high-risk areas, such as difficult to access villages and the sites where a smallpox case were recently detected, as well as in areas previously not covered by surveys for some reasons.

Great attention was paid to the system of registration and notification of information about any cases with fever and rashes. Such information was subject to verification. All these I had to deal with during the next 2 months in the district of Katihar.

It was a long journey from Patna to Katihar on a locally made jeep. Prior to this, the Administrative Officer in Bihar, Mr. Page, explained in detail what to do and how to monitor the drivers to prevent them from stealing gasoline, how to hire assistants, to pay for their work, and to cope with other administrative matters.

A typical rustic family, Katihar district, Bihar

A search team with a jeep at a river ferry, Bihar State

Dr. V.G. Fedenev on a river crossing

We traveled together with Dr. W.R. Forrester, whom I replaced, and he talked about the life in Katihar. He managed to negotiate with the head of the district to occupy a guest house at his residence, where later I stayed. The living conditions were rather modest; it was a small room with windows without glass and minimum of furniture: beds with mosquito nets, a table and a fan on the ceiling. This fan did not help much at night even if there was electricity; it blew hot air, which could not get through a mosquito net. As a result, one would wake up in the morning in a puddle of his own sweat. But there was a shower and a lot of water, unfortunately undrinkable. There was a large jug with drinking water, strongly smelling of iodine, rather undrinkable too. One way out was to boil water. Each of us had received a large kit with sleeping bag, bed sheets, mosquito nets, and a small set of medicines and prevention remedies, including the tablets for water disinfection, which I never used.

Dr. Forrester left after 3 or 4 days, and I began an independent work. Almost every day, I had to travel to different villages to verify the rumors about smallpox cases and to visit the rural primary healthcare centers, in which, as a rule, young doctors, graduates from local medical institutions, were working. Many of these places were not reachable by jeep, so I had to ride a motorcycle or a bicycle provided by the eradication program. I abandoned a motorcycle after falling into water from a narrow bridge over a thin stream. All turned out well because the height of the bridge was less than a meter. But more often I had to walk under the scorching sun between rice paddies. Neither water nor food was available on the way. One would be lucky to meet along the way the so-called tea stall. This is typically a small hut covered with palm leaves with one shop and a small oven where tea is prepared. Small glasses for serving tea were washed in one bucket, so you can make the idea of local sanitation and hygiene. For Hindus, the water is sacred: it is always considered pure and clean even if it is from a dubious source. In the absence of another source

Another type of our transport

A tea stall

of water, I had a serious risk but once drank water from a well at the edge of which women washed clothes… and nothing happened to me.

Our jeep was plastered with posters with a photo of a boy suffering from smallpox and the announcement of a reward for information about any person with smallpox. During the searches in markets and sites of melas and other festivals, we used an amplifier with loudspeaker calling to report any cases resembling smallpox and announced the reward for such information if it would be confirmed as a smallpox case. This gave us an opportunity to receive quite a lot of information that was checked by our team onsite of the incident. Twice we have had a chance to visit the place of the last smallpox case to verify such rumors. This was a very remote village and we had to go first by train and then riding skinny Indian horses bareback about 15 km, feeling each and every bone of the horse spine. There were no other transport means and roads because of a flood.

The 2 months ended pretty quickly and I did my way back to Delhi, where I was suddenly offered an extension for another 2 months and a job as an epidemiologist to coordinate the smallpox activities in the Karnataka state, with the capital in Bangalore, in South India.

Karnataka state is considerably different from Bihar. Economically, it was one of the richest Indian states with developed industry and agriculture and a good scientific potential. The cities were more modern and better maintained; the population was more literate than in the north. Correspondingly, the health infrastructure was better developed and better equipped, both technically and with competent staff. The south of the country, in general, was less affected by smallpox. The last case in the state of Karnataka was registered in May 1974, a year earlier than in Bihar. In general, the smallpox incidence in this state for several years was sporadic and amounted to six–ten recorded cases annually. However, the health authorities of the state and in some its districts lost the interest in work on the smallpox program and we had to conduct the forthcoming fall search and continue to support the surveillance on smallpox during the next 2 years until the certification of the smallpox eradication. It was necessary to motivate the national

The head of the search team staff gives job to its members, Katihar district, Bihar state

eradication program authorities. For this purpose, I often invited the program manager to take part in field visits to towns and rural areas of the state to organize searches and hold meetings with the health care leaders of different levels as well as with the medical staff at the grass-root level at primary health care centers. We also attended departmental and private medical centers with a view to involve them in the work during the search and further surveillance. The work was done and the search conducted. More than 70% of villages and other administrative entities were visited by search teams and smallpox was not found in any of them.

Upon returning to the WHO Regional Office in New Delhi, I was pleasantly surprised that I was selected to the position of a long-term staff to continue the work in this program for another 2 years.

I returned to India in February 1976 and was sent to work as a coordinator of the smallpox program in five northeastern states, namely, Assam, Meghalaya, Tripura, Manipur, and Nagaland. I replaced Dr. Lev Khodakevich, who worked there before. For about a week, we worked together traveling to the Assam and Meghalaya, visiting the national smallpox eradication program managers and primary health care centers, which allowed me to acquaint with the situation in detail. This region of India was practically restricted to foreigners; entry permit was mostly given only to the people from socialist countries, whereas Arunachal Pradesh and Mizoram were completely closed. These restrictions were introduced by the Government of India because these states were close to the border with China, with which they had recently a military conflict, and also because of on-going separatist activities in these states.

It was the last phase of the smallpox eradication going on in India, a 2-year period after the last smallpox case and preparation for the certification of smallpox eradication by the International Commission. I was fortunate again: in Assam, the last case of smallpox imported to India from Bangladesh was registered on May 24, 1975. The city of Guwahati, the capital of Assam, was my headquarters with a small office and a few staff. This office coordinated all activities on smallpox surveillance in the post-liquidation period in these states and the work of national epidemiologists as well as organized the regular and ad-hoc searches in the areas where smallpox was recently registered and in remote and inaccessible areas and in mountainous re-

Dr. L.N. Khodakevich (*right*) and Dr. V.G. Fedenev (*second left*) with the staff working on Smallpox Eradication Program, state of Assam

Dr. V.G. Fedenev (*second left*) with the staff of the Smallpox Zero office in Assam

gions of the states. Great attention was paid to the system of notification and registration of the suspect cases. We also worked on the preparation of the documents for the National Commission for the certification of smallpox eradication and for the corresponding International Commission. We developed standard sets of illustrative materials for medical facilities and offices at various levels of health service structure (including regional statistics on demography and economics, availability of medical facilities and staff, equipment, incidence of smallpox and other similar diseases, terrain maps, information about anti-epidemic activities carried out in the area, surveillance on smallpox-like diseases, etc.). It should be noted that all the work was carried out in close collaboration with our colleagues and health authorities, especially with the National Smallpox Eradication Program managers in the states.

I was happy enough to work and to accompany one of the members of the International Commission for the certification of smallpox eradication, Dr. V.M. Zhdanov, Director of the Institute for Virology

Dr. V.G. Fedenev (*second left*) with members of the National Commission for smallpox eradication, Nagaland

Drs. V.G. Fedenev (left), V.M. Zhdanov (center), and Z. Jezek (right) discuss the work plan of the International Commission for the Certification of Smallpox Eradication, Assam

of USSR Academy of Medical Sciences, a nice, intelligent man and a great storyteller. We visited three states—Assam, Meghalaya, and Tripura. Viktor Zhdanov studied the materials and talked to the local healthcare professionals and health authorities. We visited two or three districts in each state and two or three health centers of different levels, including a number of remote and inaccessible areas. This important event was widely covered by the local press. Despite a tight work schedule, we visited the famous Kaziranga National Park in Assam to glance at the untouched nature and some of the wild animals, such as Bengal tiger and rhinoceros.

Thus, the Indian epopee ended but not the work on smallpox in other places. I was transferred to Bangladesh. There was a period of 2 years after the last smallpox case and surveillance activities were in full swing. At the end of May 1977, we flew by Thai Airlines to Dacca, the capital of Bangladesh, and got into severe turbulence. The aircraft was hurtled so badly that all the passengers probably would have flown around the cabin. All of us were terribly frightened but everything turned out well. Beneath us lay the land of Bangladesh, or rather, some islands of the ground were lying beneath, everything else was under the water. It was the rainy season and the monsoon was in full progress.

The last case of smallpox was recorded in Bangladesh on October 16, 1975. It was the very last case in the overall Southeast Asia. Surveillance on smallpox in Bangladesh was slightly different from the Indian one. The searches during the post-liquidation period were normally combined with other health programs. The search teams, which included other program staff, had not only to collect the information about any cases with fever, rash, and death, but also to distribute antimalaria drugs and vitamin A capsules. A significant increase in the number of employees of search teams permitted to change strategy and shift from a village-to-village to a home-to-home or a door-to-door scheme.

The surveillance in remote areas with a low population density was a particular problem. In the Chittagong Hill Tracts, which was my area of responsibility, it was necessary to organize two special searches in June–July and October–November. It was necessary to collect information not only on the cases similar to smallpox, but also register all persons with the vaccination scars and smallpox scars on the face. The last search was prepared especially carefully in view of the fact that due to geographical features and difficulties in accessing, the total number of searches conducted in those areas was less than in the country as a whole. Attention was paid to the recruitment, preparation, and motivation of the staff. We developed the work schedules and reporting forms, etc. As a result of the thorough work during the last search, we were able to cover about 60% of all households in these areas. The main result of this search was that not a single person with fresh smallpox marks and not any child with smallpox scars born after the last case were found.

The International Commission for the Certification of Smallpox Eradication in Bangladesh was fully satisfied with the results of the work carried out in the past 26 months and confirmed the eradication of smallpox in the country. The work was completed… but not for me. I and another WHO medical

officer had to develop a strategy and tactics for the Expanded Program on Immunization fitting the specific conditions in Bangladesh and taking into account the experience of the Smallpox Eradication Program. The immunization schedule layout was developed. The suppliers of vaccines were identified, the storage and cold chain system was designed, and the demand in vaccine and other materials was estimated. For these purposes, we used the epidemiological statistical information collected during the biennial smallpox post-liquidation surveillance. In other words, we have prepared a bridgehead for launching the Expanded Program on Immunization in Bangladesh.

Pasteur Scientists Have Always Been in the Center of an Epidemic Doing the Hardest Work

E. M. Slepchuk

Just three decades have passed but modern young people can learn about the agony and sufferings brought by smallpox only from books or from the words of their relatives. It was justifiably called the "black death" not as long ago as the last century, devastating smallpox epidemics wiped out millions of people and disfigured the survivors. The whole world was fighting with it. It was a long, hard, and persistent struggle. Doctors were exhausted by strenuous and dangerous work, which took away both their power and health. Many of them have passed away by now. We as well as the next generations ought to remember these people. The purpose of this book is to pass the knowledge about these great people to the next generations because they must not be forgotten.

Yurii P. Rykushin and Aleksei Yu. Samostrel'skii were honored members of the oldest scientific and educational Russian institute, St. Petersburg Pasteur National Institute of Epidemiology and Microbiology. The Pasteur scientists were always sent to the "eye of the storm" of an epidemic and did the hardest work. They were fighting with black smallpox during the first years of Soviet state and were saving Leningrad from epidemics during the Siege. After the war, many of them had to face diseases forgotten in Russia outside their motherland.

Yurii Rykushin confessed to his friends that the least of all he, a war veteran, expected was that he would not only have to fight against smallpox, but do it in the faraway India. This was not his first business trip abroad; Africa became his "baptism of fire". In 1965, Rykushin as a head of the WHO project against tuberculosis in Uganda travelled throughout the country, moving from one small village to another, from one tribe to another over hill and dale. Tuberculosis became a national disaster in the country, which recently gained independence. Smallpox cases often occurred in high mountain areas but there were no major outbreaks due to scarce population.

Elena M. Slepchuk,
a medical virologist, candidate of medical sciences, journalist, and member of the Moscow Union of Journalists

Yurii P. Rykushin

Mr. Rykushin and Mr. Ladnyi, head of the smallpox campaign in Africa, propounded to combine the smallpox and tuberculosis vaccinations into a single procedure. This plan was accepted by both the Government of Uganda and the WHO. Congo and Kenya joined in. While working at the WHO Headquarters, this Leningrad scientist showed himself as a top class professional, brave, responsible person. Accordingly, when some time later skilled experts were required to fight smallpox in India, Mr. Rykushin again received an invitation from Geneva.

The WHO representatives understood that the fate of Smallpox Eradication Program may well be decided in this country. Vast and densely populated India with its ethnic, religious, and social conflicts was a fertile ground for spreading of the infection. Hundreds of thousands of smallpox cases were registered in this country in 1974, with tens of thousands of deaths. Four states in northeast India formed the so-called "epidemic incubator", and even among them, the state of Bihar consistently held the first place in the number of smallpox cases. Thus, it was not surprising that the WHO assigned a large number of experts to Bihar; Rykushin was among them. Mr. Rykushin was an experienced practitioner; in addition, he was one of the few epidemiologists who advocated for a new program implementation tactic. Instead of mass vaccination, which covered 80% of the local population within several years, experts proposed to actively identify and "seal" infection outbreak sites in order to block the virus transmission. This course of action demanded a wide and active cooperation with local populations, as well as training of large numbers of vaccinators, not always from the medical community, but also engaging local residents and volunteers.

The situation was improving gradually; however, money, means of transportation, and medical staff were in deficiency. Mr. Rykushin in cooperation with Dr. L. Brilliant (United States), a New Delhi-based WHO epidemiologist, sought help from the local business community. The Government of India also called for active support to the international program team. Sponsors were found; for instance, the major industrial company TATA in addition to money transfers also granted some 40 jeeps and even an airplane.

This airplane once helped Rykushin to convince a chieftain of a tribe where smallpox cases occurred in the need of vaccination. Initially, the chieftain was utterly opposed to smallpox vaccination arguing that it was the will of the wrathful Smallpox Goddess Sheetala Mata. On the occasion, Mr. Rykushin asked pilots to spread leaflets and photos of children disfigured by smallpox over the territory occupied by the tribe. Astonished chieftain dropped on his knees in front of the "messengers of heaven" and was the first to thrust out his hand to receive the inoculation. The others followed his example. They parted as good friends.

The cases like that were exceptional; local people usually demonstrated friendly attitude towards medical personnel and thought of them as their saviors. Rykushin was often invited to weddings, and many children in Bihar were given an uncommon name Yurii in honor of the Russian physician.

After completion of the assignment, Rykushin returned to his alma mater institute and was appointed the head of the Chair of Epidemiology. His colleague, Mr. A.Yu. Samostrel'skii, also from Leningrad, replaced him on assignment in India.

Aleksei Samostrel'skii also received extensive field training. In the late 1960s, he as a WHO expert headed the smallpox eradication program in Somalia. Once, by lucky occasion the two compatriots met at an airport of a small town in Uganda. Both Rykushin and Samostrel'skii were going to Kinshasa to an interregional WHO meeting. As it turned out, the purposefulness of mass smallpox vaccination was

questioned and debated already at that time. Samostrel'skii was interested in the vaccination practices directly in the infection foci. It was a relevant issue in Somalia. The population density in deserted areas was low, with many isolated nomadic tribes; thus, the disease was spreading mostly within families.

Aleksei Yu. Samostrel'skii

Consequently, when in a few years he arrived to India being assigned to the same state of Bihar, Samostrel'skii saw his mission quite clearly. He was working in Purnia, the border crop-producing area of this state adjacent to Nepal. Monsoon rains start there in November; the Great Ganges River overflows its banks and floods the surrounding villages. Large numbers of refugees accumulate in different settlements separated by flooding waters, which promoted infection spreading. Moving knee high or waist high in the water, the vaccinator teams led by Samostrel'skii made their way from village to village on foot, in Land Rovers, or even riding elephants. Later Samostrel'skii recalled that they had to spend nights in deserted dwellings and even in abandoned palaces of rajahs. Numerous snakes also were escaping flood, so everyone had a stick at hand in case of an unexpected meeting with a king cobra.

The identified infection foci sites were encircled by a 10-mile quarantine zone where everyone who had not been vaccinated received vaccination. Subsequently, such villages remained under surveillance for 6 weeks; later, this period was reduced to 4 weeks. Apart from their primary work task, the vaccinator teams often administered different medical aid: set bones, put compresses, supplied medicines, and treated malaria. Sometimes, they deliberately made themselves the second smallpox vaccination to show that it was harmless. Indian people often invited doctors for dinner, and not to offend hospitable hosts, they had to follow the family traditions. "If the family ate with fingers, we did the same," recalled Samostrel'skii, "Other vaccinator teams followed us; therefore, our behavior determined how they would be met and received." All information immediately spread around through the village. Samostrel'skii introduced weekly reports and often monitored the performance of his subordinates despite huge workload.

When Samostrel'skii appeared in his institute on return from India, his colleagues hardly recognized him. They were joking that only one half of him was left but of course the better half. Subsequently, Samostrel'skii became the head of the Laboratory of Microbiology and Intestinal Infections in his Institute.

Before the completion of the program, Samostrel'skii was urgently summoned by Mr. D. Henderson and sent to Africa, where an unexpected smallpox outbreak took place once again. The devious virus attempted the last attack but soon was completely defeated. Two years later, the International Commission confirmed this fact. Mr. Rykushin was also a member of one the commissions for the certification of smallpox eradication, that in Uganda. It was in this country that he started fighting smallpox and there he witnessed its complete eradication in 1978. He examined 36 000 preschool children and did not found a single child under 6 years pitted with smallpox scars. However, several suspicious samples were sent to the WHO Collaborating Center in Moscow. Neither of the samples from Uganda or other African countries demonstrated the presence of variola (smallpox) virus. It was the victory indeed!

The Soviet Mission in Iraq

O. M. Konovalova

After the WHO adopted the Global Smallpox Eradication Program, the Soviet Government implemented a number of measures to meet this challenge. One of the steps was to send a team for mass vaccination to Iraq, where about 2000 smallpox cases were recorded in the previous year. The Soviet Union committed to provide the necessary materials for the campaign, including the freeze-dried smallpox vaccine. The Iraqi Government welcomed the proposal and the corresponding intergovernmental agreement was signed on March 16, 1959. By the beginning of 1959, over 6.4 million people lived in the 14 provinces. The natural conditions of the country are rather diverse—from high mountain ranges in the north to the mouth of the Shatt al-Arab River, residing southward in the foothill area, most part of which is considerably swamped. Deserts occupy approximately 47% of the territory and house nomadic cattle herders. During dry and hot summer, which takes about 7 months, the temperature rises to 40 and even 50°C in the shadow. Arabs were the major population and the north was mainly inhabited by the Kurds. The larger part of the population was illiterate. The living conditions in the rural areas were most severe: clay houses with a low ceiling, narrow windows, and earthen floors. As a rule, the farmers who had cattle kept them in the house, in the rooms with the same exit. The average lifespan in Iraq at that time was 28–30 years and 300–350 newborns of every thousand died.

Before 1958, the state allotted scant funding for the public healthcare. The general sanitary and anti-epidemic activities were sporadic and any scheduled preventive measures were absent at all. It was several times attempted to organize vaccination of the Iraqi population with the help of French, English, and American specialists.

Olga M. Konovalova,
a virologist, candidate of medical sciences, and a member of the anti-epidemic team sent by the Government of the Soviet Union to Iraq to perform mass vaccination of the population against smallpox (1959)

However, these campaigns did not include total and obligatory smallpox vaccination. Correspondingly, only a minor part of the population had been vaccinated against smallpox.

All these factors enhanced the spread of numerous communicable diseases, in particular, smallpox. Since the ancient times, the peoples inhabiting the territory of Iraq suffered from this disease. Some epidemic outbreaks wiped out cities and villages.

The Mechnikov Institute of Vaccines and Sera, headed by A.P. Muzychenko, was the organization base for establishing the anti-epidemic team for performing the mass anti-smallpox vaccination in Iraq. The team included Anna A. Demina, Olga M. Konovalova, and Leonid V. Salmin from the Mechnikov Institute as well as physicians from Zaporizhia, Leningrad, and other cities of the USSR. Most laboratory assistants working with the team were from the Mechnikov Institute. Paramedics and laboratory assistants were also recruited from the Sklifosovsky Institute, First Medical Institute, and other institutions. In total, the team comprised six physicians and 15 laboratory assistants and was headed by Aleksandr V. Zakaryan from Yerevan.

Short-term seminar courses and training in particularly dangerous and parasitic infections were organized in Moscow for the team. At these seminars, well-known specialists—virologists, microbiologists, and parasitologists—delivered lectures on the relevant topics in their sciences. The practical training for the members of the team on the anti-epidemic measures in smallpox foci and vaccination technique was performed by the staff of the Department of Viruses of the institute. The guidelines on smallpox vaccination were issued in Moscow in Arabic to enhance training of the local vaccinators. The large-scale vaccination

The team of physicians and paramedics before leaving for Iraq, June 1959. A.P. Muzychenko, director of the Mechnikov Institute of Vaccines and Sera is in the center and A.V. Zakaryan, head of the team, to the right

campaign was supplied with all needed, including 25 million doses of freeze-dried smallpox vaccine, inoculation tools, materials, and drugs.

The first group of six left for Iraq on June 22, 1959. Our goal was to completely cover the Iraqi population with vaccination against smallpox during 5–6 months. The Soviet party initiated organization of the Committee for Smallpox Liquidation with emergency powers. Along with our physicians from the anti-epidemic team, this committee included representatives of several Iraqi ministries (Ministries of Health, Internal Affairs, and Education) as well as members of different religious creeds (mostly Muslim) and nongovernmental organizations.

On August 19, 1959, the Iraqi Ministry of Health held the press-conference on the mass smallpox vaccination campaign. Later, wide sanitary and educational activities were deployed in all institutions and agencies involving all mass media. Information displays were also used, such as posters and so on. Literate representatives from all provinces were trained as vaccinators and after passing the corresponding exam were approved for this work. In addition to medical staff, students and military men were allowed to do vaccination.

In order to completely cover the population with vaccination, we used house-to-house surveys and organized special vaccination posts. The latter were also set along large roads, at railway stations, and so on. All Iraqi inhabitants were vaccinated starting from the age of 3 months. The vaccination campaign was started in the northern provinces and ran through the central part of the country to the southern region. The inoculation in Iraq was earlier made using only one incision, whereas we did the vaccination with two

Soviet physicians A.V. Zakaryan and O.M. Konovalova on the way to a Muslim center in Iraq to perform vaccination (the author is in Islamic dress to enhance the contact with population)

incisions. Our data that the intensity of immunity in the vaccinees depended not only on the quality of the inoculated material, but also on the inoculation technique agreed with the WHO data. The work experience in Iraq confirmed that the Soviet freeze-dried smallpox vaccine was sufficiently stable in the hot climate of this country.

Note that our team was welcomed most enthusiastically and friendly. Only 1 year passed since the revolution in Iraq and the Soviet Union was among the first to recognize the Iraqi Republic. With few exceptions, not only high governmental, public, and religious leaders, but also students and common people tried to express their gratitude and provide the assistance they can. Just one example—Dr. Shaker, a high-qualified physician from the city of Basra first met us with a kind of distrust, asking directly, "What for do we need you?" However, he later developed respect and confidence and not only actively participated in the campaign, but also gave most valuable advice and recommendations.

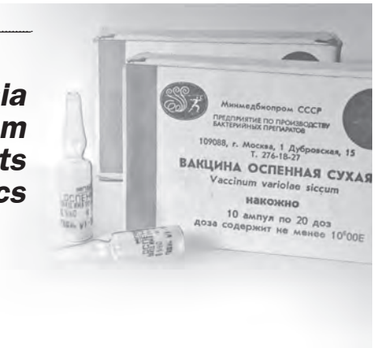
The smallpox vaccination campaign was performed under most severe conditions. In addition to hot climate, poverty of the population, and total unsanitary, the language barrier significantly complicated our communication with local residents. The number of interpreters was next to none. Traditions of the country interfered with the vaccination of women and girls by foreigners; correspondingly, the women of our team dressed as or similar to Muslim women in some provinces, for example, in Karbala, where the Islamic laws were very strict. In some provinces, our specialists together with local physicians crossed the mountain areas using the Soviet UAZs, perfect off-road vehicles. As for the southern regions, we were shipped via shallow channels by boats.

The mass smallpox vaccination campaign in Iraq took 6 months. Over this period, the vaccination coverage reached 75% of the total population and not a case of vaccination complications was recorded. The vaccination results were randomly checked in two regions of the country and vaccination success was observed in 90–95% of the cases.

In the November of 1959, the attempt to assassinate Abd al-Karim Qasim, the Prime Minister, luckily ended in wounding. This fact destabilized the situation in the country although for a short period. Nonetheless, our specialists in collaboration with the Iraqi healthcare services worked efficiently, which allowed the mass vaccination campaign in this country to be successfully completed in due time. Abd al-Karim Qasim in his letter to N.S. Khrushchev, Chairman of the Council of Ministers of the USSR, of December 17, 1959 highly esteemed the activities of the Soviet specialists in the control of smallpox and thanked for the selfless help. Later, the vaccination of the population in this country, including newborns, was continued.

The huge work carried out by Soviet specialists freed Iraq from endemic smallpox. Since the end of our work until the complete smallpox eradication in the world, only one imported smallpox outbreak took place in Iraq.

Smallpox Vaccine Production in Russia for the Global Smallpox Eradication Program and Some Aspects of Post-Eradication Politics



Yu. Z. Gendon

The USSR was one of the countries where the officially approved smallpox vaccine prevention scheme was most accurate and faithfully met. In addition to the initial vaccination, revaccination was carried out at different ages. This country had several production facilities for manufacturing the smallpox vaccine. By the end of the 1950s, all these facilities produced the freeze-dried vaccine differing from each other however by the vaccine strain and the passage scheme in animals. Given the population size and the frequency of smallpox vaccination, a considerable amount of the vaccine was demanded. The available capacity has provided the domestic needs for the vaccine; however, the produced volume was insufficient to assist the WHO Smallpox Eradication Program. In 1958, two additional factors appeared. The WHO approved the Global Smallpox Eradication Program, proposed by our country, and the WHO special scientific group developed the first *International Requirement to Vaccine Preparation* and certified the reference vaccine. These requirements in a number of characteristics were stricter compared to the standards of this country. All these facts together highlighted the establishment of large-scale production of the smallpox vaccine that completely met the international requirement. This need was emphasized by the fact that the first donation of the Soviet Government—25 million of vaccine doses—was rejected by the WHO because they did not meet the requirements on bacterial contamination and thermostability. In addition, the strain used for vaccine production emerged to be genetically heterogeneous (although the latter was not formally conditioned by the requirements).

This situation induced the decision that the Institute for Viral Preparations would be responsible for organizing the production of smallpox vaccine to meet the WHO requirements in quite a short

Yurii Z. Gendon,
a virologist, doctor of medical sciences, professor, and Honored Scientist of the Russian Federation. He considerably contributed to the introduction of the production technology for manufacture of freeze-dried smallpox vaccine used in the USSR; in 1985–1995, chief virologist with the WHO Headquarters

period of time. The Director of the Institute of Viral Preparations, O.G. Andzhaparidze, ordered to equip the facilities for vaccine production, while the Laboratory of Live Vaccines, under my supervision at that time, was assigned responsible for elaboration of the production technology. Assuming that the smallpox vaccine production technology in our plants was outdated, we decided to address Academician of the USSR Academy of Medical Sciences M.A. Morozov for assistance. Mikhail Morozov was already rather old but still headed a laboratory of the Gamaleya Institute of Epidemiology and Microbiology and was recognized as most prominent expert on smallpox in this country. Morozov accepted me and my colleague F.B. Genkina and, above all, showed us a microscope, where, as he said, he had made great discoveries. Then he took us into the stall where a calf was kept. At that time, he wanted to prove that the vaccinia virus, used for vaccine production, had evolved from variola (smallpox) virus. The vaccinia virus was cultivated on the one side of this calf and variola virus, on the other. He explained that it was possible to isolate vaccinia virus from the side infected with variola virus and this was a clear proof that vaccinia virus had originated from variola virus. However, we noticed that the calf first rubbed its one side on the wall and than its other side on the same wall, which could cause some questions on the conclusions he made.

Unfortunately, M.A. Morozov failed to give us any useful tips and it was decided to improve technology for production of the vaccine that was used in the USSR but to make it more stable during storage and eliminate the bacterial contamination. In addition, it was necessary to choose the most optimal vaccine production strain.

Since the smallpox vaccine rejected by the WHO was produced using the vaccine strain from the Gamaleya Institute of Epidemiology and Microbiology, we decided to use the vaccine strain Tashkent, used in some USSR production facilities. However, the virus yield in experiments was not standard, displaying high titers in some batches and low, in others. Then the Laboratory of Viral Genetics examined the Tashkent strain and demonstrated its genetic inhomogeneity by plaque assay in cell culture. This structure formed both large and small plaques. The clones forming only large or only small plaques were derived; the clones from large plaques gave high yield and from small plaques, low yield. Therefore, a large-plaque clone of the Tashkent strain, with its stable high virus yield, was further used for vaccine production.

However, even with the cloned Tashkent strain, the challenge to improve the smallpox vaccine production technology remained and, first and foremost, to develop the technique allowing to eliminate the bacterial contamination and increase the vaccine stability. It was known that one of the best smallpox vaccines in the world was the vaccine produced in the United Kingdom; they used Freon treatment of the sheep skin detritus to avoid bacterial contamination and peptone as a stabilizer during drying. However, these technical steps were patented, and we had no idea about the used Freon concentration, time of processing, method of its removal, kind of peptone, and its concentration.

Nevertheless, thanks to the qualified chemists and biochemists (A.V. Mikheeva) from our lab, we rather quickly succeeded in elaborating the technique that allowed for eliminating bacteria from the detritus. However, we encountered serious difficulties when using peptone as a stabilizer during drying. I must say that the vaccine drying technique proposed by highly qualified specialists (B. Parizh and L. Metreveli) was well elaborated but we had no experience with peptone as a stabilizer. At that time, peptone was produced in Baku. A researcher from our institute was sent to Baku and brought several cans with peptone. The first experiment with drying when the peptone of one of the cans was most successful; however, the second attempt with the peptone from another can just failed. The peptones from different batches appeared to be quite different. Out colleague again went to Baku to bring back several cans from each produced batches; we selected the best batch and bought it all. Unfortunately, we had to repeat this procedure every time when a "good" batch came to an end.

Validation of the improved vaccine showed that it met all international requirements. However, with all its advantages, this vaccine still had a most important disadvantage in terms of its practical

The staff of the Department of Smallpox Vaccine, Institute for Viral Preparations, 1962.
First row, head of Department of Vaccine Drying B. Parizh (*leftmost*), next to him, chief engineer L. Metreveli, and head of Department F. Genkina (*fifth from left*); second row, research consultant of department Yu. Gendon (*leftmost*) and deputy head of Department, V. Milushin (*second from the right*)

use—it was highly reactogenic. The studies conducted at the WHO Collaborating Center in Moscow showed that the quality of the vaccine depended not on the production technology but rather on the biological characteristics of the production strain. Thus, further efforts were focused on switching of the vaccine production to other production strains with milder reactogenicity. Two strains were tested: one strain was EM-63 (Ecuador-Moscow, 1963), it was used in Ecuador and proved to be less reactogenic in animal experiments and human vaccination and the other, Elstree, used in the United Kingdom (Lister Institute) for the production of smallpox vaccine in sheep. This strain was significantly less reactogenic for animals than the Tashkent strain. At the Institute for Viral Preparations, this strain was adapted for cultivation on the calf skin and got the name L-IVP. This strain made it possible to obtain a higher yield as compared with the EM-63 strain. Thus, the strain L-IVP was selected for large-scale vaccine production. The subsequent vaccine controls at the Institute for Viral Preparations confirmed the high quality of this vaccine at the specialized WHO Center for the Vaccine Control for the Smallpox Eradication Program (Utrecht) and its full compliance with the international requirements.

The Production Smallpox Vaccine Department was initially leaded by F.B. Genkina, then by V.N. Milushin and G.M. Stepanov. About 150 million doses of the vaccine were annually produced; part of this amount was shipped to the WHO. The smallpox vaccine production was continued at our Institute until 1980, when the WHO General Assembly (WHA) declared the complete eradication of smallpox in the world and recommended to stop the vaccination against smallpox.

Note that along with the production of large quantities of smallpox vaccine, our institute was developing new technologies for this vaccine production. In particular, our laboratory in collaboration with laboratories leaded by E.M. Dosser and L.G. Stepanova developed a technology for producing the dry smallpox vaccine using a human diploid cell line; our data describing the technology were published in the journal *Voprosy Virusologii* (Problems in Virology) in 1965. Unfortunately, our institute at that time had no possibilities to organize the vaccine production according to this technology, although the smallpox vaccine produced using cell culture could be less reactogenic as compared with dermal vaccine.

After the complete eradication of smallpox and termination of vaccination against it, several problems to be solved still remained. Therefore, the WHO launched the post-eradication program. The special (Ad-Hoc) Committee of Experts was formed for this purpose. Of the Russian specialists, it included Prof. S.S. Marennikova, elected as its Vice Chairman. As an expert at the WHO Headquarters working in Geneva, I was assigned to participate in this program since 1987. The task of the post-eradication program included organization of the laboratory for analyzing the specimens of human cases suspected for smallpox and organization of annual meetings of the WHO Expert Group on Smallpox at the WHO Headquarters to discuss the important emerging problems.

The first part of the program goals consisted in monitoring the reported cases of any infection similar to smallpox, collecting specimens from these patients, and shipping these specimens to one of the WHO Collaborating Centers, in the USSR (Moscow, headed by Prof. Marennikova) or in the United States (headed by Dr. Esposito), for laboratory examination. Note that none of the specimens suspected for smallpox contained the variola virus. If there were multiple suspicious cases of such diseases, it was necessary to identify on site the nature of these diseases. Variola virus was not identified in any of them. There were, however, some anecdotal situations. One of the major newspapers published a sensational message that a smallpox outbreak was discovered in one of the Southeastern countries and over 100 people fell ill. This message seriously disturbed the WHO staff but the analysis of this publication on site demonstrated that these cases were mere chickenpox. The “sensation” was the result of an error of one of translators who informed the newspaper.

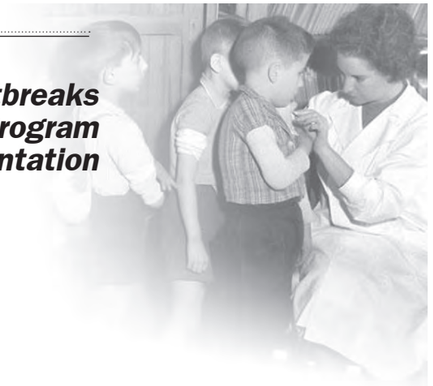
At the meetings of the Expert Group, the most excited debates concerned two issues: the preservation of vaccination of the army and the fate of the smallpox virus strains kept in two WHO Collaborating Centers, in the United States and Soviet Union. The opinions on the issue of army vaccination divided: during the first meeting for retention of vaccination, the US experts voted for vaccination and the experts from the Soviet Union, against; however, the situation at the second meeting was opposite. Finally, it was decided that the recommendation would not be universal so that the countries themselves would decide whether to vaccinate the army or not.

A more emotional debate was about the fate of the variola virus strains. After the smallpox eradication, the WHO decided to contain the work with variola virus strains to only two WHO Centers for Smallpox, namely, the Centers for Disease Control and Prevention (CDC; Atlanta, GA) in the United States and the Institute for Viral Preparations (Moscow) in the Soviet Union. The WHO invited all countries to either destroy all variola virus strains in laboratories of the country or to transfer them to one of the WHO Collaborating Centers for the Smallpox and confirm in writing that the WHO recommendation was implemented. Thus, the variola virus strains officially were only in these two centers. In 1990, the WHA recommended to analyze the whole DNA nucleotide sequences of at least of two variola virus strains at the WHO Smallpox Center in CDC and the State Research Center of Virology and Biotechnology Vector (Novosibirsk, whereto the USSR collection of variola virus strains was relocated from the Moscow WHO Smallpox Collaborating Center). The researchers from Vector were first to cope with this task. In addition to the analysis of the whole genome of two variola virus strains, the plasmids carrying almost all genes and genome regions of these viruses were constructed.

At this stage, the discussion about the fate of the variola virus strains started again. The experts who insisted on keeping the virus believed that the liquidation would make it impossible to restore the virus when it would be needed, taking into account that individual variola virus proteins could be very useful in treatment of certain human diseases. In addition, it was noted that the destruction of the variola virus strains in the collections of the two WHO centers still did not guarantee its unofficial preservation. Those who believed it necessary to destroy all variola virus strains noted that millions of people after the cessation of smallpox vaccination did not and would not have the immunity to this virus and any case of accidental laboratory infection or a terrorist accident could cause a huge epidemic. As for the study of viral proteins, this could be done using the constructed plasmids, being absolutely safe.

As the expert opinion did not agree, I organized an open discussion at the next National Congress of Virologists in Glasgow (1993), which was attended by approximately 1000 virologists from around the world; several hundreds of virologists attended this discussion and about 40 expressed their views. The attempt to reach a consensus failed again.

Nonetheless, the WHO by 1994 to a certain degree agreed with a number of countries on the advisability of liquidation of the variola virus strains, and I was requested to prepare the relevant decision for the WHA in 1994. However, the day before the WHA session, it was asserted that this decision would not be discussed but delayed to the next Assembly. After this event, over 15 years passed but the decision about the future of the variola virus strains is still delayed from one Assembly to another…



The Control of Imported Smallpox Outbreaks in the Soviet Union during Program Implementation

It Was This Way

V. A. Zuev

On a clear January morning in the 1960s, the author of these lines came in high spirits to work at the Mechnikov Moscow Institute of Vaccines and Sera. Carrying a suitcase in my hand and humming a simple song, "Adventure time, come on tell your friends—we are *going* to very *distant lands*!" (I was going to the first in my life business trip to Leningrad), a young candidate of sciences, junior researcher, was about to say a warm goodbye to his fellow workers. It is so hard to imagine the depth of my disappointment when Head of the Department of Viruses, Prof. S.S. Marennikova, announced without a shadow of a smile on her face that my trip had been canceled due to …extraordinary (?) circumstances. Moreover, Dr. Marennikova asked me to get ready for the arrival to our lab of Academician of the USSR Academy of Medical Sciences M.A. Morozov, who was well known as the main expert in the country on the problems of smallpox and vaccination against smallpox.

...A few days before, artist K. Kokorekin, who had just returned from India, was admitted to Botkin Hospital in Moscow. The painter had witnessed the burial service of a Brahmin who had died of smallpox. He had even held out his hand over the bonfire, which, as usual, is made on the place where the deceased lived, and touched the amazingly beautiful fabric, which he had admired very much. On his way back to Moscow, already on the plane, the artist fell unwell: his temperature rose, he began to cough, and on arrival home he asked for help at Botkin Hospital.

Having learnt where the patient had arrived from, a young intern at the hospital admissions set, as is said, without a moment's hesitation the diagnosis of variola (smallpox). A venerable professor made fun of the young professional and diagnosed the patient with flu. Of course, the flu! What else could it be? It is already winter outside—a regular seasonal outbreak of influenza has begun and is developing in Moscow. A special division for patients with influenza was long ago

Viktor A. Zuev,
a virologist, doctor of medical sciences, professor, Honored Scientist of the Russian Federation, honorary vice president of the Russian Academy of Natural Sciences, member of the New York Academy of Sciences, and active participant of the liquidation of the Moscow smallpox outbreak in 1959–1960

formed at Botkin Hospital, and a new patient, the artist, was admitted to the hospital ward designated... for influenza patients.

The artist is getting worse and worse. In the meantime, the hospital workers are becoming ill too: the receptionist who completed the artist's registration and admission, the throat specialist who examined him, the doctors and nurses from the same hospital division, and even a plumber who was just passing through the corridors of that unit. And, of course, new symptoms started to appear in the patients who were in the same ward with the artist. In the end, the artist dies. The autopsy shows a picture that is not characteristic of either flu or complications attributed to it. So, what is it?

Pathologists expressed an array of very different assumptions. For some days, those symptoms were even attributed to "the plague in question" (and this is in Moscow!!!). And then Botkin Hospital sent a microscope slide with a swab of the purulent material from the cutaneous lesions (pustules) taken from the physician, otolaryngologist T., who had become ill after being infected from the artist, to the Department headed by Prof. S.S. Marennikova.

The arrival of the venerable Academician to the Department headed by Prof. Marennikova was not accidental. Just a few years before, Marennikova was sent to Uzbekistan to study the outbreak of naturally occurring smallpox and brought a number of isolates of that virus, which is referred, as it is well-known today, to the first group of biohazardous infectious agents of pathogenic diseases (this group in those years included, besides the smallpox virus, the plague pathogen). The fruitful results of this and other similar trips of Prof. Marennikova to the places where the natural cases of smallpox occurred (including foreign countries) were noticed by the leadership of the USSR Ministry of Health and the scientific community also due to her practically pioneering studies devoted to the findings in the field of developing of new original methods for successful laboratory diagnostics of smallpox using chicken embryos.

In the mean time, I was frantically getting ready for the arrival of the famous Academician: took a microscope out, set light, prepared paper and a pen, and even (just in case) boiled a kettle.

On his arrival, Academician Mikhail A. Morozov picked up a microscope slide with the specimen, treated it using "Morozov's method" (a well-known throughout the world silver staining method of

Moscow Botkin Municipal Hospital, the 1960s

Morozov), and drawing together his gray eyebrows, clung to the eyepiece of the microscope. He was moving the sample stage for a long time, thoroughly examining every detail of the specimen, and only after a while he muttered, "Young man! Sit down, please, and write the report to the Minister of Health of the USSR!" I wrote with a trembling hand under the dictation of the Academician: "Paschen bodies are found in the material collected from patient T." Yes, exactly so! Paschen bodies are particles of variola virus. Many years before, Paschen suggested staining them and examining under a conventional light microscope because of their large size. Does it mean that the VARIOLA (SMALLPOX) VIRUS has come to Moscow?!

The headquarters for the fight against smallpox was established with an unprecedented urgency. Literally the total vaccination of all Moscow's residents began. Special Commission identified and immediately hospitalized anyone who had been in contact with the artist or the members of his family, and even those who had contacted the latter ones. As a result, there occurred about 5000 of them.

Botkin Hospital was confined to barracks (visiting the patients is prohibited; all the hospital workers live in the hospital; and the hospital territory is cordoned off by the militia). By the way, the staff at Botkin Hospital even that time consisted of several thousand people. There were enough beds, enough mattresses, but too little linen. The Council of Ministers of the USSR promptly issued a special Decree according to which the access to the emergency linen supply for the Air Defense became available!

For obvious reasons, it is the laboratory headed by Marennikova that was in charge of the laboratory diagnostics of all the incidents of existing and newly emerging suspicious diseases. And it also meant the daily collection of the material from the patients at Botkin Hospital and the analysis of the material from the city (the author of these lines even had to go to the embassies) because many people tended to think that they had already had the onset of smallpox (fear has big eyes!).

On the next day, when we were asked the question "Who will go to Botkin Hospital to collect samples from the infected patients?" I, having understood that it would be my only chance to see a patient with smallpox, did not hesitate (full of "virological romanticism") to express a strong desire and, accompanied by spiteful sneers of my fellow workers, solemnly headed to Botkin Hospital in a luxury ZIM limousine belonging to the Chief Physician, carrying a large metal box full of a wide variety of material for obtaining samples from the patients. It turned out that the procedure was not as romantic as I innocently had imagined: stripping naked, shower. I put on hospital linen, on top—two patient gowns (one above the other), a medical cap, two pairs of rubber gloves, and a gauze mask with a huge lump of cotton wool. There is a problem with rubber boots: my shoe size is 45, but they offered a choice of either 42 or 43 but both right. I chose the latter option and went to the patients staying in isolation wards... for 5 hours.

Each time before entering the ward, I put on one more patient gown and another pair of gloves in the vestibule. This entire seemingly superabundant "burden", as it eventually turned out, saved me. The matter is that the process of collecting material from the patients includes, among others, scrapings of the skin lesions, which need to be done, bending low to the skin surface of the patient; taking swabs from the throat and nose, which, of course, is accompanied by patient's coughing and sneezing into your face. And I, as it turned out later, was very poorly vaccinated against smallpox. So eventually, the "burden" turned out to be the "muse" of health for me.

The outbreak was not allowed to grow and spread and at the early winter of 1960, it was completely eliminated. Unfortunately, three out of the infected 46 people died. The development of the so-called "varioloid", that is, smallpox occurring in the people who have previously been vaccinated, was observed in a number of cases.

The pattern of the so-called "black smallpox" developed in one of the deceased patients (it is the mentioned above unlucky plumber, who only passed through the corridors), when blood instead of pus accumulates in skin vesicles (pustules) and after they dry the skin occurs covered as if with a black crust. The last days of that patient's life were painful. Prof. Marennikova tried to save him with the help of a newly

developed anti-smallpox gamma-globulin. However, the extent and severity of the disease in that patient, who unfortunately appeared unvaccinated, was too great for successful treatment.

The colleagues of Prof. Marennikova did their best working all the time as hard as they could, as the saying goes "without cease". It will be easy to understand if we remember that in addition to the everyday study of the material received from Botkin Hospital, an endless stream of samples from other hospitals and polyclinics in Moscow was continuously arriving at the laboratory, among which, for obvious reasons, there was a large amount of material from smallpox patients.

And all this work was carried out by a small but very friendly team, which consisted of only five researchers, including E.M. Akatova-Shelukhina, E.B. Gurvich, M.A. Yumasheva, Z.I. Ogorodnikova, and the author of these lines. In all fairness, it should be also noted that the entire technical part (preparation of laboratory glassware, sterilization of materials, preparation of solutions, elimination of infectious material, and many others) was provided by one technician A.G. Gladkikh.

So, at the beginning of 1960, the outbreak of the disease was eliminated. However, a few months later smallpox once again reminded of itself.

In the summer of the same year, one of the staff members from the laboratory, Akatova-Shelukhina, was assigned by the USSR Ministry of Health to go to the Afghanistan border where there was a natural outbreak of smallpox. Some time after her return to Moscow (and to work!), she felt unwell: there were characteristic symptoms of the cold with a slight rise in body temperature. Of course, they could be ignored, but for one "but"... The "but" consisted in the fact that the signs of ill health appeared on the 13th day after her arrival from the trip, and the incubation period of smallpox does not exceed 14 days.

An experienced eye of Marennikova saw in this unhealthiness only a common cold but she shared her considerations with Dr. A.V. Eremyan, who during the outbreak had examined almost all individuals having a contact with the smallpox patients and those who had contacted the exposed ones. Dr. Eremyan, in turn, shared this information with Moscow's Chief Epidemiologist Dr. Samvelova and...

... In the middle of the work day, when every staff member in the laboratory was doing the work, the neighborhood of the Mechnikov Institute of Vaccines and Sera was suddenly filled with a deafening sound of sirens. Several ambulances literally dashed into the territory of the institute. Pouring out of them was a special team of epidemiologists equipped with protective clothing...

Yes, the law is the law!

So, all the staff members from the laboratory headed by Prof. Marennikova and several other people who had communicated at work with Akatova-Shelukhina after she came back from this trip were immediately taken to the Clinical Hospital for Infectious Diseases, "Sokolinaya Gora", to observe a two-week quarantine, wherein each was placed in an isolation ward. The following day, each quarantined person was examined by Prof. Bilibin, the most prominent infectious disease specialist of the country, who, though, seemed to have forgotten that he was examining the individuals who had repeatedly and thoroughly (and Akatova-Shelukhina especially!) been vaccinated, since most of them had been working in the areas with smallpox outbreaks for several years. Fortunately, this story ended after 2 weeks and we all safely returned home and to work.

However, it would be unfair to finish the story of "our" fight against smallpox (even on "our" limited scale) like this. The outbreak in Moscow, despite all its dramatic nature, was just one of the numerous so-called imported outbreaks, which occurred in the countries free of smallpox. They served as a sort of reminder of the huge areas in Asia, Africa, and South America where variola remained an endemic disease that in various ways continued to spread, arriving to smallpox-free parts of the world.

The Global Smallpox Eradication Program, initiated by the Soviet Union and approved by the WHO, was the only radical way to solve this problem. Our Russian scientists made the decisive contribution to implementation of the program by producing the vaccine (more than 1.5 billion of doses of thermostable vaccine were given free), by personal participation in organizing and conducting mass vaccination

campaigns in different Asian and African countries, and, finally, by a number of important scientific developments. All in all, the hard work and efforts were not in vain—smallpox was totally eradicated all over the world. The last case of naturally occurring smallpox in humans was recorded in Somalia in 1977.

In 1978, the Executive Board of the World Health Organization, comprising 21 representatives from 19 countries, approved the establishment of the Global Commission for the Certification of Smallpox Eradication in the world. The Commission included two representatives from the Soviet Union—Deputy Minister of Health of the USSR P.N. Burgasov and Permanent Member of the WHO Committee on Variola Virus Research Prof. Marennikova.

On December 9, 1979, P.N. Burgasov and S.S. Marennikova together with other members of the Commission put their signatures on the WHO Declaration certifying the global eradication of smallpox. Then, in May 1980, the World Health Organization officially declared that smallpox had been eradicated from the world.

Emma B. Gurvich,
a virologist, doctor of medical sciences, and participant of the Smallpox Eradication Program in 1959–1969 at the Moscow WHO Collaborating Center for Smallpox and Related Infections; she conduced laboratory diagnostic research for the program and worked under the projects related to the program, participated in eradication of imported smallpox outbreaks in the Soviet Union, and studied the post-vaccination complications and the mechanisms of their development

Galina M. Manenkova,
a high level certified medical epidemiologist; in 1970–1980, leading specialist with the Department of Especially Dangerous Infections of the Center of State Sanitary and Epidemiological Surveillance Agency in Moscow; she was responsible for sanitary border protection and organization of vaccination against the smallpox and participated in assessment of different smallpox vaccines and testing of attenuated smallpox vaccination techniques

The Smallpox in Moscow, 1960: Facts and Figures

E. B. Gurvich and G. M. Manenkova

The year of 2010 was marked by two significant dates for the public health: one of them has an international significance—this is the 30th anniversary of the completion of the Global Smallpox Eradication Program, and the other one is the 50 years since the smallpox outbreak occurred in Moscow.

Recalling the 1950s–1970s, lethal disease, such as the smallpox, was almost forgotten in this country, and no smallpox cases took place in Moscow for 25 years. Nowadays, one can hardly ever encounter the people whose faces are disfigured by pockmarks—the traces of smallpox "lesions". Due to the cessation of the immunization against smallpox in the end of 1979, modern young people have no scars from smallpox vaccinations, which used to be mandatory for children who had reached the age of 1–2 years with revaccination at 8 and 16 years. However, smallpox just a short while ago existed in more than 80 countries around the world and affected over 100 thousand people annually. Moreover, 20–40% of smallpox patients died, while many others got blindness and deafness "as a souvenir".

Less than 100 years ago, in 1919, 186 805 people got smallpox in this country only according to the official data (certainly underestimated because people do not always seek medical help and, in such cases, the patients were not registered). Then, 18 months later (April 10, 1919), a decree signed by V.I. Lenin was published demanding mandatory vaccination of all newborns; all people enrolled at educational institutions, orphanages, and boarding schools; all those mobilized in the army and navy; workers and employees of all plants and agencies; as well as convicts in prisons and other places. All expenses of the vaccination campaign had been paid by the state. According to the resolution of the Council of People's Commissars of the RSFSR of October 18, 1924, free primary vaccinations of infants and revaccination at the age of 10–11 years and 20–21 years were legally mandated. Those who escaped the vaccinations could be prosecuted under art. Criminal Rule 118 of the Russian Federation with punishment of up to 6 months of forced labor or a charge of up to 500 rubles. Thus, the mandatory vaccination was not only declared, but also financially and legally provided. In the middle of the 1920s, the tactics of active patient identification started to be applied together with vaccination in the smallpox outbreak foci, total or selective vaccination according to epidemic indications, and so on. Such tactics against the smallpox used by the Soviet epidemiologists in the mid-1920s was later used in India, Bangladesh, Ethiopia, and other countries.

The incidence of smallpox in the Soviet Union declined steadily, although even in 1932, 59 857 cases were still registered. In 1936, 414 people contracted smallpox; these were the last endemic cases

of the smallpox in the Soviet Union. At the end of the 1930s, many parts of the country had been freed from smallpox. In the subsequent years, only individual events of smallpox carried over from the countries where it remained endemic had been observed in this country. The Central Asian and the Transcaucasian republics of the Soviet Union, bordering Afghanistan, Iran, etc., were particularly vulnerable.

We tend to quickly forget the past. This often leads to unforgivable repetition of the past mistakes and costs dearly. No one can guarantee that in the future the infection will not return. This may occur due to the natural process of evolution of an orthopoxvirus or due to bioterrorism. Taking this into account, we consider useful and even necessary to remind about the causes of smallpox disease in Moscow, the dynamics of the outbreak, and the enormous efforts and activities that were required for its suppression.

When describing this outbreak, I used some data published in the papers by K.V. Golubchikova and S.A. Samvelova (at that time, working with the Moscow Department of Public Health and Moscow Sanitary and Epidemiological Station) and E.A. Gal'perin (in: *Smallpox*, S.S. Marennikova, Ed., Moscow, 1961, pp. 13–26 and 29–52, respectively [in Russian]).

As already mentioned, smallpox was imported to Moscow by a 53-year-old artist, K. Kokorekin, returning from a trip to India where he had stayed for 2 weeks. On the day of his arrival to Moscow by plane (December 23, 1959), he felt unwell. On December 24, he appealed to the Polyclinic no. 1 of the Ministry of Health of RSFSR with complaints of fever, head pain, and general weakness.

There he was diagnosed with "flu". On December 26, rash appeared on the skin and the next day he was hospitalized to Botkin hospital with a diagnosis of "flu, drug rash, typhus?" The patient died on the night of 29 to 30 December. Neither during the life of the patient nor after his death was diagnosis of "smallpox" suspected. On December 30 during the autopsy, numerous and abundant hemorrhages had been found and it was suggested that the cause of death was a hemorrhagic form of plague, so the autopsy and burial were carried out with the necessary anti-epidemic measures. The basis for the isolation of his contacts was prepared. However, the isolation was delayed until receiving the results of the laboratory tests. On December 31, the diagnosis of plague was canceled and the final diagnosis was formulated as acute vascular purpura. Restrictive measures for the contacts were canceled.

The subsequent events developed as follows: on January 12, artist N. was hospitalized to Botkin Hospital from the Polyclinic no. 2 of Krasnopresnensky district with the diagnosis "toxic flu". Her report of the close contact with artist K., who had arrived from India and was dead, was the first lead in the discovery of the smallpox outbreak. During the investigation, it was found that on January 11, a doctor and a nurse who had contacts with the patient K. in Botkin Hospital were hospitalized with a diagnosis of "influenza and chickenpox". Smallpox was suspected and the specimens were sampled for laboratory tests. Clinical and epidemiological diagnosis of smallpox was confirmed at the laboratory. Later, another 13 people who had contacted K. were identified applying to various clinics in Moscow with complaints of weakness, headache, fever, and skin rashes. They were diagnosed with various clinical forms of the smallpox.

Intensive anti-epidemical work started on January 16. All-day-round shifts of the specialists on communicable diseases and doctors from disinfection stations were set up; a mandatory system organized to alert of the detected smallpox cases and strict regime activities were conducted in hospitals; and an active search for the contacts of the patients was initiated.

By January 18, 75 individuals having had contacts with K. had been identified in 15 Moscow districts; 19 of them were ill. In turn, another 410 people were in contact with them, while two sick individuals traveled to Leningrad and Riga, where they contacted local residents. The number of people who contacted with each sick person ranged from 1 to 120. For example, patient T., an otolaryngologist, a few days before hospitalization had received 117 patients from Moscow, Moscow oblast, and other cities.

Patient B., a lecturer at the Institute of Railway Engineers, while in the incubation period of the disease, had taught student classes. She had contacted 120 persons, all of whom were hospitalized. Among the identified persons who contacted the sick, 324 people lived in the Moscow oblast and 35, in different

cities of the Soviet Union. In Moscow and the Moscow oblast, 9342 people were under surveillance of physicians, including 1200 "primary" exposed, who were hospitalized to the 2nd Hospital for Infectious Diseases and 286, to hospitals in the Moscow oblast. "Secondary" exposures were also monitored: 3586 people at their homes and 1220 in hospitals. They were followed up for 14 days. Special ambulance cars were assigned to transporting the patients with suspected smallpox.

In the city of Moscow, there were two foci of infection. In one of them (family-based focus, comprising the relatives and friends of patient K.), it was relatively easy to limit the spread of infection. From January 16 to 20, all family members of patient K. and the majority of those who contacted them were hospitalized. The second focus on the territory of Botkin Hospital was harder to isolate, as nine employees of the hospital contracted smallpox and there were cases of nosocomial infection in other buildings. In total, 2092 patients and 2600 people among the stuff were under observation at the hospital. There were also 600 people discharged from the hospital during the period when patient K. was there. The hospital held a complete vaccination of staff and patients against smallpox. The discharge and admission of new patients were ceased; visits, delivery of letters, objects, etc., were prohibited. The hospital was overcrowded; quarantine was declared in seven buildings. The kitchen staff and economical and technical staff were in quarantine. There was a strict access control and police was guarding the territory. During the outbreak, 46 people living in 15 districts of the city contracted smallpox; three of them died.

During the first wave of the smallpox outbreak, 19 people were infected by K., including seven members of his family and friends. Among the staff of Botkin Hospital, nine people were infected, including two doctors and two nurses. There were three cases of nosocomial infection: a child, 13 years old, hospitalized with Botkin disease, who was on the second floor above the box where the patient K. was placed; a patient from the nearby box; and the patient who contracted the disease in the first therapeutic department, whereto the infection brought by a therapist who examining patient K. (the doctor himself did not contracted smallpox).

During the second wave, 23 people were infected, including five members of the hospital staff, three members of their families, and two more as a result of nosocomial infection in the therapeutic department (visitors). Nine people contracted smallpox directly from the family members of patient K., two in their families and two more via random contacts. The latest were an insurance agent who visited the apartment of K. and woman B., who contacted the sick wife of K. on January 6 in the Sanduny baths, where they stayed for 2.5 h.

During the third generation, three people were infected: the husband and son of the mentioned, already sick, B. (a friend of the wife of K.) and sister of a receptionist in the outpatient department of Botkin Hospital. Among these cases, three persons died. Two of them had suffered from severe concomitant diseases at the time they became infected (subacute bacterial endocarditis, rheumatic heart disease in the stage of decompensation, and Hodgkin's disease).

The incubation period for the majority of cases was 9–13 days; 65.2 % of them were adults over 29 years old. They all had been vaccinated against smallpox in the childhood and 10 persons were revaccinated in 1957. In 1960, 23 persons were revaccinated prior to disease and 14, during the disease. The clinical picture was as follows according to the severity of the disease and skin lesions: severe smallpox in two cases, moderate smallpox in two cases; varioloid (a mild clinical form), in 39 cases; and smallpox without rash was observed in three cases.

During this outbreak, enormous work was conducted on the immunization of the population starting with children of 2 months of age. In total, 8522 vaccination teams and 3391 vaccination points were organized. The mass vaccination began on January 21. During 5 days, 6464 865 people were vaccinated. Up to 1.3–1.5 million people were vaccinated daily regardless of contraindications. In less than a week, more than 8 million people were vaccinated in Moscow and the surrounding areas. In fact, the risk of

further spread of the infection was eliminated in Moscow already by January 25 (10 days after the initial diagnosis of smallpox).

The fast localization of smallpox infection in Moscow became possible only due to the enormous efforts, strict organization, and concerted activities of the sanitary and epidemiological service. The prevalence of light clinical course of the disease and a favorable outcome in the majority of cases resulted from the regular mandatory vaccination of the population against the smallpox.

The Moscow smallpox outbreak became "the test site" for the practical verification under conditions of epidemic distress of the sensitivity and reliability of laboratory diagnostic methods developed at the Virus Department of the Mechnikov Institute of Vaccines and Sera in the 1950s–1960s. What is the most important, the use of these methods allowed not only for detection, but also for differential diagnostics of hard-to-distinguish related viruses, such as the variola and vaccinia viruses. Nonetheless, certain difficulties were often encountered when diagnosing diseases and distinguishing between a mild form of smallpox and the complications caused by mass vaccination during the outbreak. The laboratory methods of diagnostics included the virus isolation on chorioallantoic membrane of developing chick and in the cell culture in view of the nature of cytopathic (damaging) effect of the virus; the identification of cytoplasmic inclusions (Guarnieri bodies) in the cell culture infected with variola virus, and assessment of the content and dynamics of anti-hemagglutinin accumulation in the blood serum. These methods had replaced the old fashioned tedious microscopic study of smears for identification of elementary Paschen bodies, silver staining according to Morozov, and Paul test (scarification of rabbit eye cornea). During the outbreak, specimens of 108 individuals with suspected smallpox were examined in the lab. The samples of skin lesions (vesicles, pustules, and dry crusts), nasopharyngeal swabs, blood, and sectional materials were studied. Thanks to the improved methods of diagnostics, it was possible to attribute a significant part of the disease cases to the post-vaccination complications caused by vaccinia virus. Among 39 observed patients with clinical diagnosis of smallpox, the virus was detected in 23 patients (at different times and with different clinical courses of the disease; (for details, see the description of comparative assessment of the laboratory diagnostics used during this outbreak in Marennikova, S.S. et al., in: *Smallpox*, Moscow, 1961, pp. 63–79 [in Russian]). The benefits of the cell culture method of diagnostics allowed us to recommend it for the *Guidelines for Laboratory Diagnostics of Smallpox*.

The live smallpox vaccine that provided immunity driving the resistance to smallpox infection and essential for smallpox eradication was highly efficient but the most harmful among all prevention medicines. Thus, its application was accompanied by the intense research to improve the vaccine with the aim of reducing its side effects. In 1960, during the mass vaccination of the population without regard to medical contraindications, in total 67 112 sick leave certificates had to be issued due to the development of adverse responses to the smallpox vaccine. Complications have been reported in 163 cases of vaccination. They mostly consisted in allergic and local reactions (115), inoculation of the virus (19); generalization of vaccine process (7, generalized vaccinia); and neurological complications (22), mostly in adults over 20 years of age (19), including meningoencephalitis, meningomyelitis, and encephalitis. All patients had recovered, except for one patient who developed severe hemorrhagic syndrome with hemorrhagic glomerulonephritis.

Because of the global smallpox eradication—a unique medical victory—the immunization against the smallpox was canceled in 1980. At present, the older generation in Russia has lost the immunity against the smallpox and the young people born after the end of 1979 have not been vaccinated, so the population is not protected from this lethal infection. The current situation stresses the need for conducting the wide-ranging research to improve the prevention and treatment, develop safe vaccines, and design new test systems for indication and identification of variola virus and other orthopoxviruses. The smallpox, if it ever comes back, must not catch the humanity unawares.

The Beginning of the Path: Some Episodes from the Recent History of the Smallpox Control

E. B. Gurvich

…The beginning of 1960. It has already been a year and a half since I started working at the Virology Department of the Mechnikov Research Institute of Vaccines and Sera in Moscow, having stumbled upon the job by accident after reading a newspaper advertisement for the vacant post of researcher. Despite all the obvious benefits of my previous experience in independent work after graduation, I am still enjoying having left behind my everyday life as a young epidemiologist: boring house calls during various disease-related campaigns, examining dog bites, overseeing kitchens in schools and daycare centers, giving oversimplified lectures on hygiene, as well as being busy with other everyday concerns. However, even then I did not miss an opportunity to go deep into the problem and, therefore, succeeded in publishing three papers on typhoid fever having identified the cause of the outbreak… Now I work enthusiastically, getting interested in everything: I am working in a totally novel field of science that has just opened a path for entering the microcosm of subcellular structures and viruses…

I have learned (not in a day!) to maintain cell cultures, to detect cellular response to viral infection, and to maneuver in the search for optimal solutions. The Head of the Virology Department, S.S. Marennikova, seemed to foresee that all these skills would be required in the near future. In 1959, the first results were obtained in our laboratory that allowed us to identify the smallpox virus in specimens from patients, and as early as January 1960, we applied the newly developed method during the smallpox outbreak in Moscow. Our lab was prepared to conduct laboratory diagnostics not only of the smallpox virus itself, but also of the diseases causing similar clinical symptoms. This was crucial for designing the appropriate strategy for clinicians and epidemiologists! By the 1960s, the smallpox had become rare. It was thus not surprising that diagnosing the smallpox in the first patient who got the disease, artist K., who just returned from India, caused great difficulties. Experienced clinical doctors were proposing various diagnoses based on his symptoms: toxic flu, acute vascular purpura, typhus, plague, or drug dermatitis but the true cause of patient K.'s illness was recognized neither before nor after his death.

The year of 1960 was the peak of interesting work, exciting in its novelty, its practical necessity, and requiring the dedication and a certain degree of courage. After all, it involved direct contact with extremely contagious, exceedingly dangerous infection during the collection of research specimens from patients (throat swabs, blood samples, contents of smallpox pustules, and crusting dried pustules), as well as the laboratory work with the smallpox virus itself. Our bravery can be explained in part by the young age of most scientists (we were 28–30 years old). But at the time, I and my namesake Emma M. Akatova had just had babies: my daughter Olya was born on May 15 and Emma's son Misha, on May 21, 1959. Due to the specifics of my work, Olya had been vaccinated against the smallpox at the age of 3 months and I guess Misha was vaccinated as well.

In Moscow, the extraordinary precautions were taken because of the epidemic situation that had arisen at the time. As in the movies, when we with Akatova drove along the Garden Ring Road from the laboratory of the institute to Botkin Hospital, where suspected smallpox patients and their contacts were hospitalized, our car sounded a loud siren, while the driver and epidemiologist inside wore full-body anti-plague suits. The huge responsibility of avoiding the transmission of smallpox to our relatives, including little children, forced us to strictly follow the hygiene requirements of the anti-epidemic regime and carry out sanitization when leaving the hospital's infectious boxes after collecting materials for diagnostic purposes.

I still remember a patient with the smallpox—otolaryngologist T., 61 years old. He was very ill, all his body was abundantly covered with pustules. Realizing that I was going to enter his isolated box, he raised his hand and gestured to me asking not to do it. Only in few days, when his condition improved, I could

see through the glass wall of the box that he gestured inviting me to come. I entered and collected a "rich harvest" of smallpox scabs (a full tube). The isolated virus (strain T) remained active for many years and was used for research.

In 1961, however, Moscow epidemiologists, having learned the hard lesson of missing the smallpox in the first patient, which had led to the 1960 outbreak, were cautious and vigilant. We directly felt this when all of a sudden the ambulances entered the courtyard of the Mechnikov Institute of Vaccines and Sera, scaring everybody by sirens, forced the whole staff of the lab into the cars, and proceeded to the 2nd Hospital for Infectious Diseases. Here, we had been placed in boxes, while our luggage had been sent to disinfection. The background story of this quasi-detective epic is as follows. A few days before these events, one of our colleagues, E.M. Akatova-Shelukhina, returned from a trip to Tajikistan, where she participated in the elimination of an imported smallpox outbreak in the Pyandj district, bordering Afghanistan. In addition to the elimination activities, she monitored the progress of treatment and collected specimens from the skin lesions of patients for further study. Back in Moscow, 2 days later, she reported having a low-grade fever. Taking into account the fact that Akatova-Shelukhina, like all of us, was vaccinated against smallpox and had experience with the causative agent of this infection, we were convinced that smallpox was out of the question. Nevertheless, we took her pharyngeal swab and blood for the case-control study, while she was left in the lab overnight. The next day, the situation changed dramatically: learning about the situation from a telephone conversation with Marennikova, the Head Physician of the 2nd Hospital for Infectious Diseases, Dr. A.V. Eremyan, reported this fact to the Health Inspection Service, which led to the dramatic situation that I have described above.

Our stay in quarantine was not quite ordinary since we had left the laboratory before the results of testing the Akatova-Shelukhina specimens were ready. The doctors of Hospital for Infectious Diseases, seeing no signs of developing smallpox coupled with the disappearance of the previously observed sub-febrile temperature, were at a loss. The situation was helped by the Chief Infectious Disease Specialist of the country, Prof. Bilibin, who decided to continue the already initiated laboratory diagnostic study of her specimens. The tests confirmed the absence of smallpox but the quarantine period was not reduced. Despite the fact that all ended safely, our whole team spent 2 weeks in individual boxes under the supervision of physicians surrounded by caring medical staff, leaded by the chief doctor of the hospital, Aykas Eremyan.

I remember that in the morning, we (in the box, we were two—me and Marina Yumasheva) saw through the upper half of the glass partitions between the suite boxes (the lower one was opaque) the hands of Victor Zuev, doing morning exercises, and gladly joined him. This added a bit of fun to our monotonous and isolated life. While placed in the neighboring box, Zlata Ogorodnikova found ways to send us poems of K.M. Simonov, as well as her own. Of course, she did not remain without a reply. I have kept these letters until today as evidence of the extraordinary events in our lives and of our friendship.

However, our stay in quarantine had also a tragic side. During those days, the beloved mother of our laboratory head, Marennikova, was dying from cancer. No prayers and requests to permit Marennikova visit her and say goodbye had any effect. When the quarantine was over, the mother had died, and Svetlana saw her only in a coffin.

I should say that our young laboratory team was tightly knit and friendly both in the early years of laboratory work and also later, when we were joined by N.N. Mal'tseva, K.L. Chimishkyan, G.R. Matsevich, V.S. Brykina, T.I. Kaptsova, V.V. Fedorov, and L.S. Shankman. We were all about the same age, had recently graduated, and understood each other well. Many issues were resolved in cooperation and it was common to help one another.

We were almost at the same level in learning the new tasks, especially in the beginning, were able to consult each other, to discuss, and to enjoy the others' success. What a pleasure it was to see in the eyepiece of a microscope a focus of viral infection of cells that confirmed the clinical diagnosis of a disease! Or to detect for the first time a novel pattern of changes… is it caused by a virus? How not to share the news with

The team of researchers of the Moscow WHO Collaborating Center, 1971. *From left to right*, K.L. Chimishkyan, G.R. Matsevich, T.I. Kaptsova, V.S. Brykina, E.M. Shelukhina, and E.B. Gurvich; *in the center*, M.A. Yumasheva and I.A. Svet-Moldavskaya

a colleague and, at the same time, to get your finding confirmed! A little bit later, Inna Svet-Moldavskaya joined the laboratory staff. We shared with her a common project aimed at the effects of variola virus on the human blood cells. The data we obtained on the transformation of human lymphocytes by variola virus were published in the *Doklady Akademii Nauk SSSR* (Proceedings of the USSR Academy of Sciences) and in the *Nature* (London).

In January 1969, Svetlana Marennikova took me to Tajikistan. There in the village of Novabad, Shaartuz district (foothills of the Pamir Mountains), an outbreak of smallpox was reported. Along the way, our car was stopped by avalanche in the Varzob Gorge; the avalanche blocked the road. Our guide Said Ali Saidov reassured us that this was a common event in the area. This imported smallpox outbreak in Tajikistan proved to be the last one (for details, see the next chapter).

Directly in the epicenter of the outbreak of the smallpox in the Novabad village, Marennikova and I worked together with the investigation team from Dushanbe, which consisted of the Deputy Minister of Health of the Republic, K.M. Chernovskii; Chief epidemiologist V.G. Arskii; Head physician of the Republican Health Inspection Services, Kh.B. Berdyev; Head of the Department of the Hospital for Infectious Diseases in Dushanbe, N.I. Krupnik; and Chief of the Main Sanitary and Epidemiological Agency V.S. Maiboroda.

During the inspection, we saw the hospital for the smallpox patients that was organized in the infectious disease department of the local clinic and was equipped with an observation ward for the contacts, isolation ward for patients with fever, and repository for medical records. We examined patients and checked the results of the revaccination of population against smallpox performed because of outbreak.

During the investigation, it was found that the first patient who got sick with the smallpox (Kh.N.) had not in fact been immunized against smallpox; the vaccination he had received earlier did not take (apparently, the vaccination protocol was not properly followed), and he did not have a skin scar that signifies successful inoculation of the smallpox vaccine. The patient developed a severe case of smallpox complicated by pneumonia. The delayed hospitalization of the first patient led to the spread of infection. Prior to his isolation, this first patient infected a child, S.D., who lived close to him and was found during the inspection of households. He was not vaccinated against the smallpox because of contraindications (eczema); he suffered a discrete smallpox of moderate severity. The child, S.D., isolated only on day 5 of the disease, had in turn become a source of infection for three people, as revealed by the household

inspections. One of them (a schoolgirl N.G.) suffered the smallpox of moderate severity; another (K.Sh.), a modified form of smallpox (varioloid); and the third girl, 5 months old, (I.-Kh.S.) had not been vaccinated and, therefore, suffered a severe smallpox form.

It is clear that isolation of the patient as early as possible is crucial for preventing the spread of infection. But it was not always possible, even despite our daily household inspections that we performed in the Novabad village. Local doctors told us that the inhabitants of this remote village in the foothills of the Pamir Mountains, with their traditional lifestyle and customs, were initially hiding their children from the visiting health workers fearing that the children would be taken away from them and put into the hospital. The mothers stopped resisting only after they saw that their kids actually do come back to them nice, clean, and unharmed. There were no complications with conducting the vaccination: the only requirement was that women had to be examined and vaccinated by women only. Interestingly, the men in thick cotton robes, belted with wide color sashes, stayed away from us with marked dignity not taking any part in the events, while the women curiously followed our every action looking over the mud fences of their homes. They had thin black braids with black threads artfully woven into their hair. The braids ended with ornate tassels, garlands of colored beads. I remember a curious detail that, as we were told, the unusual and flowery baby names often originated from the things that the mother experienced right after the birth. These could be natural phenomena, such as “it is raining”, “ray of sunshine”, or any other event, for example, a loud knock. I was surprised that people throughout their lives had to bear the names witnessing the first impression of their mothers upon giving birth.

The work in this smallpox epicenter had firmly convinced me that vaccination was a unique and valuable approach to saving lives in the case of a lethal smallpox infection. We could clearly see that the severe disease developed strictly selectively, only in those who, in an exception to the general rule, had not been vaccinated for some random reasons.

It happened that I was not at the forefront of the work under the international Smallpox Eradication Program: my participation was limited by the borders of this country. I have repeatedly had to travel and examine the cases of suspected smallpox infection. Sometimes, these trips involved using medical aviation; they were always urgent and often fell on the weekends, disrupting family plans. On site, we had to examine the clinical documentation, see the patient, collect specimens, and bring them back to our lab or perform a preliminary (tentative) diagnosis right away. It was a hard work and a lot of responsibility. The conditions for carrying out the necessary studies were not always optimal, and, on top of that, the dangerous nature of the infection, with its potential to cause epidemics, worried the local authorities, who constantly bothered us with the barrage of phone calls, asking for the results of our research, since the positive response might have required from them the appropriate quarantine measures.

I remember how I was called on to travel to Novgorod. We went with G.R. Matsevich on a small Czech plane Morava L-200 to examine a Czech girl suspected of having contracted smallpox from a resident of India. The work was hard, the diagnosis had to be clear. Fortunately, the disease had turned out to be chickenpox. The tension was relieved only by the night; we decided to take a breath of fresh winter air before going to our hotel, Volkhov, and went towards the Volkhov River. Tired, we were totally rewarded by a fairy-tale view of the elegant St. Sophia Cathedral silhouetted against the backdrop of the night sky that was dimly lit by the falling snow. I must say that Novgorod fascinated me at the first sight. Even while approaching the city, when our four-seater plane (pilot, navigator, and two passengers) was circling central Novgorod, we could see the 12th century Yuriev Monastery and many cathedrals and churches in the city and its surroundings.

There were also some peculiar cases. One of the trips (1963) was to examine an Indian citizen (Tampikuta, 28 years old) who had stayed for 5 months in the USSR and was going to marry a Russian girl. To me, this trip was exciting from the very beginning: it was early spring and the flooded Volga could only be crossed by a military helicopter, and this was just what I did (to my great joy). During the flight,

I was surrounded by locals who mostly carried flour, since the connection with the city was temporarily lost. I found the Indian to be a handsome strong man with expressive clever eyes, without any signs of suffering on his face. He had prominent rash all over his body with skin elements in various phases of development, some of which were filled with liquid. I have kept his picture with clearly visible skin lesions. Of course, in this case there were no obvious reasons to suspect smallpox, but the fact that the patient was from India where the smallpox still existed worried the health workers. This was a typical case of chickenpox, which in adults may be more severe than in children, especially if they encounter the infection for the first time. The disease ended in complete recovery. I hope that the guest from India successfully married and is raising children and grandchildren in Russia or in India.

Marennikova, perhaps, also remember the business trip to Omsk (1969) since we were there together; we flew by a recently developed TU104 plane to examine a suspected smallpox case. We carried boxes of smallpox vaccine; due to their loading the flight was somewhat delayed; while approaching Omsk, we heard a loud announcement on the intercom that the passengers should pass into the sanitary control point for vaccination as "there is smallpox around the city" (!). I should add that the trains at that time were passing the Omsk station without stopping by the request of the Epidemical Service. The disease of a soldier proved to be chickenpox and the reason everyone got worried was that he had received a package from Tula (where there was no smallpox at the time…). Well, in some cases, better to be too cautious.

Meanwhile, the laborious multifaceted scientific work in the lab was going on as usual. Performing experiments, defending dissertations… The results obtained during the study of the properties of variola virus, the improvement of diagnostics and differential diagnosis of variola virus and the viruses that cause the diseases similar to smallpox were summarized in a series of papers in the *Acta Virologica* (S.S. Marennikova, E.B. Gurvich, and M.A. Yumasheva) and other national and international publications. There were also small "discoveries" that made us happy as we added something new to the knowledge about the variola viruses, such as a differential diagnostic test making it possible to distinguish monkeypox from vaccinia virus and variola viruses by their ability to replicate in a continuous PEK cell line—this was my little scientific success!

When working late at night in the laboratory or being on vacation, we often sang guitar songs that we composed by ourselves—the songs about our colleagues, our fascinating work, and our lab, which became a second home for us. And now, remembering, I see them all—young, inspired, serious, and cocky, generously sharing their knowledge in the highly specialized field of infectious medicine with doctors who came to the laboratory from different parts of the country and during numerous congresses in Moscow, Yekaterinburg (Sverdlovsk at that time), Angarsk, Pyatigorsk, and so on…

I want to finish with a confession—my life has been incredibly lucky: I worked with engagement, with joy, and, moreover, in a great team. Remembering the years of my youth, I have something to tell. The deep knowledge obtained in the laboratory allowed me to continue doing exciting research during the next stages of my career (the study of smallpox post-vaccination complications and the mechanisms of their development). Svetlana Marennikova, who had opened the path to the science for countless future candidates and doctors of sciences, was for me the example of a person deeply devoted to science for the rest of my life. Even when I did not work under her supervision, I often consulted with her in my mind in difficult situations.

Unfortunately, Nelly Mal'tseva, Tat'yana Kaptsova, Inna Svet-Moldavskaya, and Kornelii Chimishkyan are no longer with us, we remember them and every one of them has made a contribution to Science.

The Last Imported Smallpox Outbreak in the USSR, Tajikistan, 1968

E. B. Gurvich

In November 1968, there was a smallpox outbreak in the Tajik SSR. In accordance with the Order of the Ministry of Health of the USSR no. 3-k of January 3, 1969 and the telegram signed by Deputy Minister of Health of the USSR A. Burnazyan, a team was created consisting of E.I. Varshavskii, S.S. Marennikova, Z.I. Ogorodnikova, E.B. Gurvich, and V.E. Vishnyakov. We were instructed to investigate the smallpox outbreak and to assess the organization of anti-epidemic and preventive activities related to the smallpox outbreak in the village of Novabad (population, 863 people), Shaartuz district, in Tajik SSR, where five people got smallpox during November 9–December 17, 1968. Here, it looks appropriate to present the records "Results of examination of the preventive and anti-epidemic measures in the outbreak of smallpox in Shaartuz district, Tajik SSR, in November 1968–January 1969", compiled by the team of specialists, especially since these materials have never been published.

The first patient, Kh.N., 35 years old, on the day of return (November 9) from the city of Dushanbe and the Leninskii district, where he stayed for 5 days, felt ill and noticed a rash on the body on November 13. He requested medical care from the local medical worker in Novabad only on November 15. On day 12 of the disease, he was hospitalized with a temperature of 39.9° and tentatively diagnosed with "smallpox". The patient suffered from a severe form of smallpox complicated with pneumonia in the lower lobes of both lungs. He was dismissed from the hospital 35 days later. On the day of admission, the patient was sampled for laboratory tests, including throat and nasal swabs, contents of the pustules, and blood. Clinical diagnosis of smallpox was virologically confirmed by isolation of variola virus in chick embryos (72 h after infection of embryos); Paul positive test; and serologic assays (antibody titers in hemagglutination inhibition with 4 AU 1 : 160 on the day of hospitalization). During the investigation, it was found that the patient was not immunized against smallpox. Vaccinations carried before (last time, in 1966) failed; this was indicated by the lack of vaccine scars, a sign of a successful vaccination. The patient did not have a permanent job, was periodically engaged in mail and water delivery, and in black market trade. According to the inhabitants of the village, he had the opportunity to visit the border area of Afghanistan, where smallpox cases had been documented.

All 11 people who had contacts with the first smallpox patient were isolated. They were revaccinated according to the epidemiological indications, given Methysazon preventively (four-day course) and intramuscular injections of donor gamma-globulin (6.0 mL twice with an interval of 2 days). All family members of the patient had vaccine scars from previous vaccinations, and his mother had had smallpox earlier. The contacts of the patient who developed high fever were placed in boxes. Among 11 isolated people, high fever was noted in six cases. One was diagnosed with the right-sided pneumonia; had respiratory events (cough) on the background of subfebrile temperature; in two cases, the cause could have been a response to vaccination; and two people had an increase in temperature to 39–39.6° within 3–6 days, accompanied by throat hyperemia. It is possible that these people suffered a modified smallpox (pharyngeal form or smallpox without rash) due to the fact that they had been repeatedly vaccinated against this infection.

On the first notice, rapid anti-epidemic measures were taken in the area: emergency immunization among the population, daily household inspections in order to identify new case, and disinfection. Monitoring was carried out by the Tajik Republican sanitary staff directed to the district. However, the delayed hospitalization of the first patient had led to the spread of infection.

Prior to the isolation of the first patient, he had infected a child (S.D., 3.5 years old) who lived at a distance of 20–30 meters. The child was hospitalized only on December 4, although he got ill on Novem-

ber 30. He was not vaccinated against smallpox because of contraindications to vaccination (eczema). During examination, he had a dense papular rash; eczema traces on the body, feet, and hands; petechia on the palate; seropurulent nasal discharge; and fever of 38.4°. Later, vesicles and pustules appeared on his face. During 7 days, the fever remained high (39.7–40°). The final diagnosis was a discrete smallpox form of moderate severity. The child was dismissed from the hospital on January 6, 1969, 34 days after hospitalization.

In the second case of the disease, eight family members who had contacts with S.D. were isolated (on the next day after hospitalization). Two of them—the father, who was constantly with his child, and the mother—had had smallpox in the past. Two sisters, 5 months old and 15 years old, had fever of 37.7° and 37.2°, respectively, during one day. One of the brothers, 11 years old, had the pharynx hyperemia coupled with a temperature rise to 38° for 3 days (December 7–9). He was isolated in a box. Other family members did not have any pathological symptoms.

Three people became infected after contacting the sick child, S.D.; they were all found during the household examinations. One patient, N.G., 8 years old, lived at about 50 meters from the house of S.D. She got ill on December 10; on December 12, rash on the face was observed; on December 14, fever rose to 38.2° and large dense papules on the skin and a rash on the mucous membranes were observed. The girl was hospitalized. She had a moderate smallpox form with the characteristic clinical manifestations, including development of skin elements (vesicles and pustules) on the palms and feet. However, the disease was accompanied only by subfebrile temperature (temperature of 38.3° was recorded once). The smallpox diagnosis was confirmed in laboratory by virus isolation in chick embryos (72 h after infection), the Paul positive test, and the presence of antibodies in hemagglutinin inhibition test (1 : 320). The patient had a poorly visible vaccine scar and was revaccinated on December 20 because of the first smallpox case in the village. On the day of hospitalization of N.G., only one man was isolated, the father who contacted the girl. He had a temperature of 39.2° and throat hyperemia. Schoolchildren who contacted N.G. were not isolated but were revaccinated on the first day of her disease according to the epidemiological indications and received placental gamma-globulin to smallpox.

Next case: K.Sh., 36 years old. She became ill on December 16, was detected during the household surveys, and hospitalized on December 21 with vesicles on the face, body, and hands and a temperature of 37.2°. From medical records, she had a temperature of 39° on December 17 and 37.7° and 37.2°, December 18 and 19, respectively. She had a papule rash on December 19 and enlarging papules on December 20. As it turned out later, on December 19–20 during the backyard surveys, she was hiding. In the hospital, a low fever continued for 3 days (December 21–23), and the temperature returned to normal in the following next days. The patient suffered a mild form of modified smallpox, varioloid, mainly with subfebrile fever. The mild clinical course of smallpox, apparently, was possible because of the pre-existing immunity: she had been successfully vaccinated against smallpox in the past (she had a significant vaccine scar); she was revaccinated three times with a negative result (the last time on December 17). Eight contacts of the patient were isolated: one child, 7 years old, had a single temperature rise to 37.4°; another one, 4 years old, had temperature rising to 39°; he received Methysazon and gamma-globulin (6 mL); other family members did not have any pathological symptoms during the observation period.

The last case: I.-Kh.S., 5 months old, was revealed during a house-to-house survey and hospitalized on December 21. Her skin was covered with abundant dense papular rash and her forehead and cheeks, with vesicles and mucosa, with spots. According to her mother, the girl got a fever from December 17 and rash appeared on December 19. In the hospital, the fever from subfebrile values to 39° lasted for 11 days. The girl had a severe form of smallpox. She was not vaccinated against the smallpox. Her 12 contacts were isolated: two of them had a slight rise in temperature (37.2–37.4°) within 1–2 days, while her 9-year-old sister was isolated because of increased body temperature to 37.8–38.2° in 3 days.

After December 21, no new cases of smallpox in the village of Novabad were recorded. It was possible to quickly stop the spread of infection thanks to the timely anti-epidemic measures and, above all, the isolation of the contacts. The rapid outbreak elimination was enhanced by the fact that most of the residents were immunized in accordance with the existing requirements for the population of Central Asia, especially in the border areas. It should be emphasized that many residents of the village had earlier had smallpox, when the infection showed up from time to time, and were thus protected from repeated illnesses. Note also that the preventive treatment with Methysazon and immunoglobulin to smallpox led to a more benign disease course or the absence of clinical manifestations of the infection. However, as it can be seen from the above materials, despite the surveillance of the smallpox outbreak loci and house-to-house surveys, the smallpox cases were not identified on the first day of illness but only on days 4 or 5. The explanation is that this village was remote and isolated and the residents were unwilling to cooperate with the medical staff, whom they considered “city people”.

Because of the emergence of the smallpox outbreak in Novabad epidemiological surveillance and control measures were also carried out in the other potential smallpox outbreak sites, namely, in Dushanbe (in the house where the first patient stayed for 2 days) and in the Lenin collective farm in the Leninskii district. The work was conducted by the staff of the Division of especially dangerous infections of the Tajik Republican Sanitary Service. The commission performed random tests of 12 medical stations and 55 regional and four local hospitals in seven districts of Tajikistan (Shaartuz, Kumsangir, Pyandj, Parharsk, Moscovskii, Kolkhozabad, and Leninskii) including five border districts; the work of the sanitary control of Nizhny Pyandj; and the documents on smallpox vaccination campaign in the Republic. The conclusions were drawn about the state of collective immunity, and epidemiological study of the border village Aivadj was conducted.

The commission concluded that the source of the smallpox infection was outside the territory of the Soviet Union (in Afghanistan) and that the contact between Soviet and Afghan citizens was possible in the border village of Aivadj. The location of the first patient, who had a vagrant mode of life without permanent work, during the most likely exposure (5 days), could not be identified. It was the last outbreak of the smallpox imported to the Soviet Union.

The Soviet Citizens Who Participated in the Global Smallpox Eradication Program

Strange it may seem, but we have encountered serious difficulties when listing the Soviet participants of Smallpox Eradication Program. First, the time has elapsed and now separates us from these distant events and, second, the collapse of the Soviet Union, resulted in that some participants live in different countries or have changed their place of residence. It should also be borne in mind that the radical changes in the societies of newly formed states made inaccessible the necessary documents or they have been merely lost.

Another difficulty is that there are no strict criteria who should be considered the participant of the Smallpox Eradication Program and who not. In part, this is because the activities underlying the program implementation, from field epidemiologists engaged in the on-site struggle with smallpox and researchers involved in important projects providing the diagnostic support to the manufacturers of high-quality vaccines meeting the international requirements, and so on. Moreover, this is far from a complete set of activities that provided the success of the program (just recall the development of basic documents, guidelines, consulting, certification activities…).

Thus, that the list of the participants may differ in different editions; yet we believe it purposeful to present here this list based on the set of available documents, reminiscences of the program's veterans, and other materials.

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Presenting this list of participants, we are completely aware that it is incomplete. The fate of some participants of the program is unknown to us, in particular, O.M. Karban, T.S. Kereselidze, and O.I. Sirenko. We will continue the search of the available data and the search for new documents about the veterans of the program.

We would also appreciate any information about the fate and current locations of our colleagues at the Mechnikov Institute of Vaccines and Sera, Department of Science Organization, N.N. Yanova:

Malyi Kazennyi per. 5a, Moscow, 105064 Russia
e-mail: natyanova@mail.ru

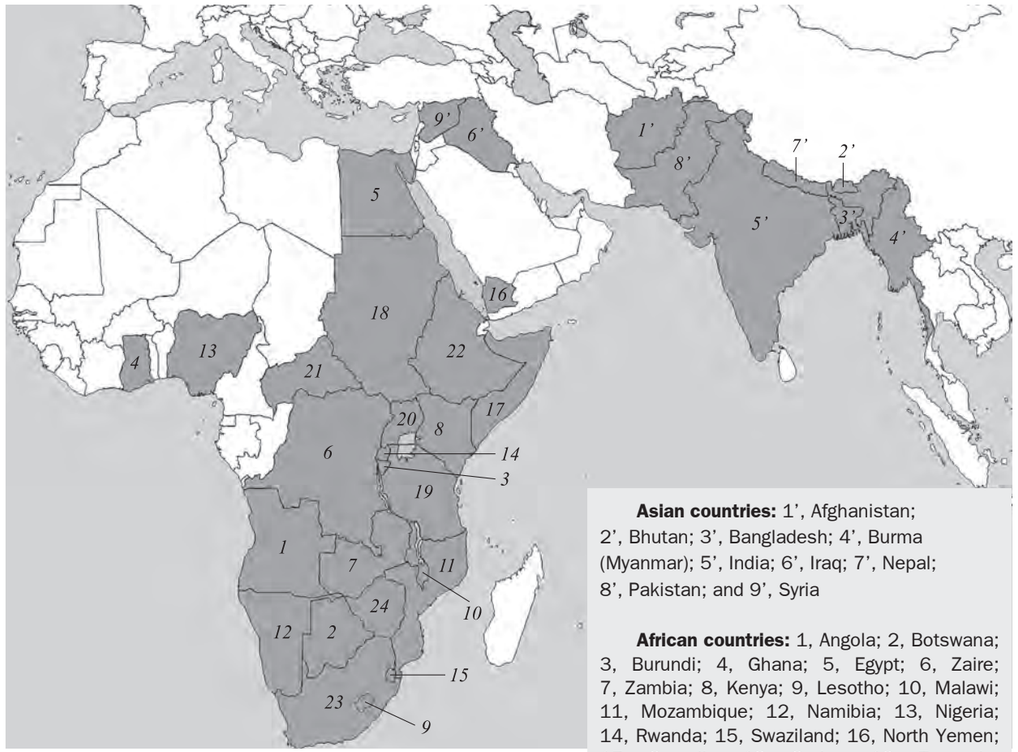
Participants of the Global Smallpox Eradication Program

Otar G. Andzhaparidze
Levon A. Arevshatyan[1, 2]
Rafi G. Aslanyan
Viktor F. Bulk
Petr N. Burgasov
Boris D. Bychenko
Vladimir D. Bychenko
Lyudmila I. Chicheryukina
Anna A. Demina
Valerii G. Fedenev
Vladimir V. Fedorov
Aleksandr I. Gromyko
Emma B. Gurvich
O.M. Karban[2]
Tamaz S. Kereselidze[2]
Lev N. Khodakevich
Olga M. Konovalova
Leonid I. Korobov
Igor M. Kozlov[1, 2]
Yurii G. Krivda
Ivan D. Ladnyi
Sergei K. Litvinov[1]
Nelya N. Mal'tseva
Gennadii P. Marchenko
Svetlana S. Marennikova
Gennadii R. Matsevich
Vladimir N. Milushin
Vyacheslav A. Mukhopad
Nikolai I. Neuimin
Georgii P. Nikolaevskii
Georgii P. Oblapenko
Yurii P. Rykushin
Leonid V. Salmin
Aleksei Yu. Samostrel'skii
Yaroslav M. Selivanov
Emma M. Shelukhina
O.I. Sirenko[2]
Analolii N. Slepushkin
Andrei A. Stroganov
Gassan D. Suleimanov
Vladimir K. Tatochenko[1]
Dmitrii D. Venediktov
Valentin E. Vishnyakov
Aleksandr V. Zakaryan
Viktor M. Zhdanov

[1] The specialists who worked under other WHO programs and considerably contributed to the Smallpox Eradication Program.

[2] The participants about whom we failed to collect sufficient information by the moment the book was issued.

The Soviet specialists who participated in the eradication program worked in different regions of Asia and Africa, covering a total of over 30 countries. In the below map, these countries are shaded and listed in the caption.



Asian countries: 1', Afghanistan; 2', Bhutan; 3', Bangladesh; 4', Burma (Myanmar); 5', India; 6', Iraq; 7', Nepal; 8', Pakistan; and 9', Syria

African countries: 1, Angola; 2, Botswana; 3, Burundi; 4, Ghana; 5, Egypt; 6, Zaire; 7, Zambia; 8, Kenya; 9, Lesotho; 10, Malawi; 11, Mozambique; 12, Namibia; 13, Nigeria; 14, Rwanda; 15, Swaziland; 16, North Yemen; 17, Somalia; 18, Sudan; 19, Tanzania, 20, Uganda; 21, Central African Republic; 22, Ethiopia; 23, South Africa; and 24, Southern Rhodesia (Zimbabwe)

Getting acquainted with the materials of this book, the reader could see how selflessly and tirelessly our colleagues fulfilled their humanitarian mission. Their noble activities were appreciated by the public authorities of the countries where they worked. This included honorary diplomas, letters, other forms of gratitude, and even, as was the case in Afghanistan, the highest award of the country. The WHO also highly esteemed the activities of almost all in the list above. The participants were awarded the badge of honor "Bifurcated needle". To illustrate this, we show the images of this award and one of the registered certificates accompanying this sign. In addition, many participants were awarded WHO commemorative medals.

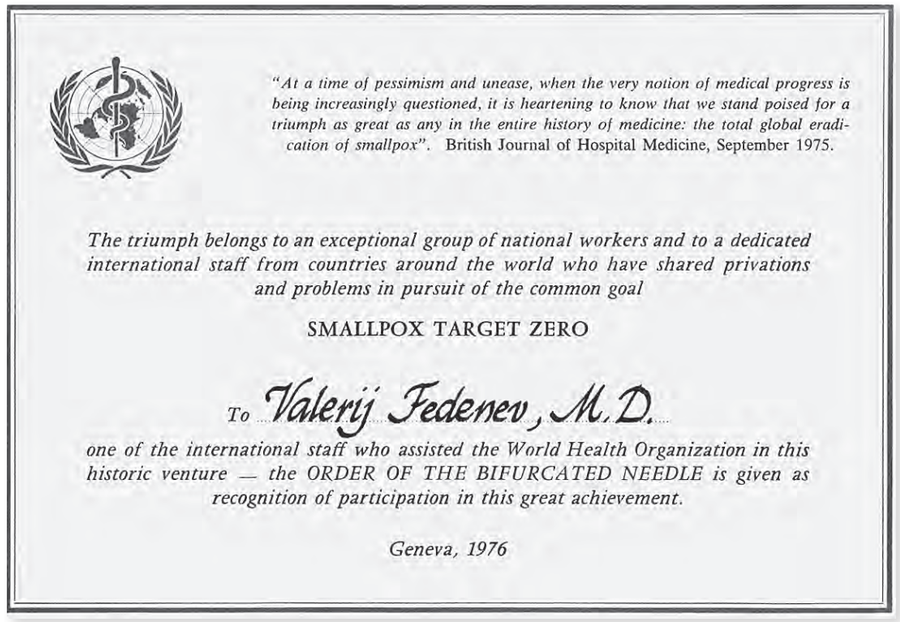
Badge of honor "Bifurcated needle"

Bifurcated needle is the tool for smallpox vaccination which was adopted during the intensified phase of the Smallpox Eradication Program. Its use drastically increased the vaccination efficiency and considerably reduced the vaccine spending. The use of bifurcated needle played an important role in the success of the program

WHO commemorative medal "Smallpox is eradicated"

Released by the WHO in 1980 by declaration of the victory over smallpox at the 33rd World Health Assembly

A certificate accompanying the badge of honor "Bifurcated needle"



"At a time of pessimism and unease, when the very notion of medical progress is being increasingly questioned, it is heartening to know that we stand poised for a triumph as great as any in the entire history of medicine: the total global eradication of smallpox". British Journal of Hospital Medicine, September 1975.

The triumph belongs to an exceptional group of national workers and to a dedicated international staff from countries around the world who have shared privations and problems in pursuit of the common goal

SMALLPOX TARGET ZERO

To Valerij Fedenev, M.D.

one of the international staff who assisted the World Health Organization in this historic venture — the ORDER OF THE BIFURCATED NEEDLE is given as recognition of participation in this great achievement.

Geneva, 1976

In Memory of Our Deceased Colleagues Who Participated in Smallpox Eradication Program

Time and tide wait for no man. We should sadly emphasize that many of our colleagues and coworkers, brothers-in-arms, did not live to see the great events of the 30th anniversary of the Global Smallpox Eradication, which was celebrated in Geneva, Brazil, and many other countries. All our dearly departed colleagues involved in the fight against this terrible infection exemplified a devotion to their official duty, Hippocratic Oath, and selfless modesty. Unfortunately, while alive they have not received any appreciation of their state.

This final part of this publication was written with the aim to preserve the memory of their names and work for our contemporaries and the future generations. We can only express once again our deep regret that this book is the only opportunity to honor their blessed memory and to express the words of gratitude for their heroic deed. We hope that their names will be kept in records of national medicine.

Working on the captions for the photos, we did not aim to show a detailed biography of our colleagues. The period of their lives directly related to the Smallpox Eradication Program was specially emphasized. We apologize to the readers for the fact that we have not yet managed to collect the materials of all deceased veterans for objective reasons but the work will continue.

The photos of our deceased colleagues are arranged in alphabetical order. The only exception was made for V.M. Zhdanov, the person who proposed the global eradication of smallpox.

Viktor M. Zhdanov
1914–1987

A professor, academician of the USSR Academy of Medical Science, outstanding Russian virologist, epidemiologist, organizer of public health. For 26 years, he headed the Ivanovsky Institute of Virology—the leading research center of our country in this field of science. Possessing the gift of scientific prediction, in his speech at the 11th World Health Assembly, he proposed and justified (together with V.I. Vashkov and M.A. Morozov) the program of global smallpox eradication. As a Deputy Minister of Health, he actively supported this program. At the final stage of the program, he was a member of the International Commission for the Certification of Smallpox Eradication in India and Bhutan. The history has confirmed his excellent foresight: in 1980, the 33rd session of the World Health Assembly informed that smallpox no longer existed in the world. Zhdanov was awarded the WHO badge of honor “Bifurcated needle” as the recognition of the participation in this great achievement.

Otar G. Andzhaparidze
1920–1996

A professor, academician of the Russian Academy of Medical Sciences, for many years Director of the Institute for Viral Preparations with the Ministry of Health of the USSR, later, Academy of Medical Sciences of the USSR. A large-scale production of freeze-dried smallpox vaccine, in particular, for the needs of the Smallpox Eradication Program was organized at the facilities of the institute. In total, about 1.5 billion doses of the vaccine were supplied (for the WHO and bilateral assistance), which played an important role in the fight with this infection in different regions of the world.

Rafi G. Aslanyan
1936–2003

A candidate of medical sciences and senior researcher with the Gamaleya Institute for Epidemiology and Microbiology. For the first time, he was invited to work in the Smallpox Eradication Program as a short-term consultant (3 months) in West Bengal in March 1976. On expiration of the contract, he was offered the next contract and then, a long-term contract under which he worked until the end of the program in India. In 1980–1987, he worked as an advisor in the Expanded Program on Immunization at the WHO Regional Office for Southeast Asia; in 1989–1999, at the same position in Alexandria at the Regional Office for the Mediterranean region. He was awarded the WHO badge of honor “Bifurcated needle” as the recognition of his contribution to this great achievement.

Viktor F. Bulk
1932–1995

A candidate of medical sciences; he worked with the Mechnikov Moscow Institute of Vaccines and Sera first as a technician and then as clinical microbiologist. In 1959, he was a member of the Soviet mission in Iraq, which carried out mass vaccination of the population against smallpox. During the intensification phase of the Smallpox Eradication Program, he worked to in North Yemen (1970). He was awarded the WHO badge of honor “Bifurcated needle” as the recognition of his contribution to this great achievement.

Petr N. Burgasov
1915–2006

An epidemiologist, specialist in highly dangerous infections, professor, academician of the Russian Academy of Medical Sciences and the Academy of Medical and Technical Sciences; in 1965–1986, Deputy Minister of Health and Chief State Sanitary Inspector. He participated in the Smallpox Eradication Program as a member of the Global Commission for the Certification of Smallpox Eradication, which confirmed the victory over this infection in the world. He was one of the authors of the final document on the results of the program. Among other members of the commission, he signed the Declaration on the smallpox elimination on earth. He was the author of research papers and monographs on the highly dangerous infections. In 1972, together with G.P. Nikolaevskii, he published the monograph *Smallpox*. He has awards of the governments of the Soviet Union and several foreign countries.

Boris D. Bychenko
1931–1998

A candidate of medical sciences, epidemiologist, microbiologist, and professor. In 1974–1975, he worked in the Smallpox Eradication Program in India and participated in the elimination of over 150 smallpox foci and outbreaks. Together with his brother, V.D. Bychenko, he proposed and introduced the practice of training local residents as vaccinators and other technical personnel. His work was highly esteemed by the WHO Regional Director, Dr. Gunaratna, who wrote: "The secret of Bychenko's success, like many other Soviet specialists, is a combination of excellent training that Soviet doctors receive with rich experience, commitment to the program, deep understanding of its aims and, most important, the honest attitude." Bychenko also possessed the gift of scientific prediction coupled with great capacity for work and ability to work in team. He was awarded the WHO badge of honor "Bifurcated needle" as the recognition of his contribution to this great achievement.

Anna A. Demina
1924–2007

A doctor of medical sciences, professor, researcher with the Mechnikov Moscow Institute of Vaccines and Sera, microbiologist, member of the Soviet anti-epidemic team that performed the mass vaccination of Iraqi population against the smallpox (1959).

Leonid I. Korobov
1928–2006

A candidate of medical sciences, epidemiologist, and Honored Doctor of Ukraine; participated in the Smallpox Eradication Program in India, in the state of Bihar, severely affected by this infection (1975). As many other Soviet specialists in Bihar, he managed to organize the complex measures accelerating smallpox eradication. He was awarded the WHO badge of honor "Bifurcated needle" as the recognition of his contribution to this great achievement.

Ivan D. Ladnyi
1927–1987

An epidemiologist, doctor of medical sciences, and one of the most active participants of the Smallpox Eradication Program. His work was always initiative and highly productive. In 1965–1971, he headed the program in the 22 countries of the African continent. Dr. Henderson, the head of the program since 1967, in his monograph *Smallpox: The Death of a Disease* (2009) called him a key figure catalyzing the Smallpox Eradication Program in the East, Central, and South Africa. Since 1976, Ladnyi was Deputy Director-General of the WHO; his terms of reference were the control of infectious diseases. He was a member of the International Commission for the Certification of Smallpox Eradication in West Africa. He was among the discoverers of a previously unknown human monkeypox and the natural reservoir of cowpox virus. He is the author of the monograph *Smallpox Eradication and Prevention of Its Return* (1985) and a coauthor of the final WHO monograph *Smallpox and Its Eradicatio*n (1988).

Nelya N. Mal'tseva
1934–2001

A virologist, doctor of medical sciences, professor, and an active participant of the Smallpox Eradication Program over entire period of its implementation. As a leading expert of the Moscow WHO Collaborating Center for Smallpox, she participated in the research projects and diagnostic studies for the program. Frequently, she traveled as a WHO consultant to the Middle East and India to provide practical assistance in establishing the production of smallpox vaccines and their control. Together with the other staff of the Moscow WHO Collaborating Center, she compared the vaccine production strains. The resulting conclusions formed the basis for rejection of the highly reactogenic strains and their replacement by moderately reactogenic. In 1977, she participated in the post-liquidation surveillance in India. She is a coauthor of the discovery of human monkeypox and the natural reservoir of vaccinia virus. She was awarded the WHO badge of honor "Bifurcated needle" as the recognition of her contribution to this great achievement.

Gennadii P. Marchenko
1938–1992

A Ukrainian epidemiologist and candidate of medical sciences. As a WHO advisor, he participated in the Smallpox Eradication Program since 1971. The first stage of his activities was Pakistan, the Northwest Frontier Province, where he organized (as his colleague G.D. Suleimanov in other provinces of Pakistan) the control measures leading to a significant reduction in the incidence of smallpox. After the start of the Indo-Pakistan war, he was transferred to Afghanistan and continued his mission in fight with smallpox. At the end of 1972, he was sent to Ethiopia, where he joined a group of WHO staff operating in the remaining endemic areas of the country. In mid-1973, he was sent to India to participate in the final stage of the eradication program. Later, he worked on other WHO projects. He was awarded the WHO badge of honor "Bifurcated needle" as the recognition of his contribution to this great achievement.

Vladimir N. Milushin
1930–1995

A candidate of medical sciences and the head of the smallpox vaccine production at the Institute for Viral Preparations. He was one of the main developers of the large-scale production technology for dry heat-resistant smallpox vaccine. The ready vaccine fully met the international requirements; it was delivered free of charge (either through the WHO or under bilateral agreements) to the countries of Asia and Africa fighting against smallpox under the Smallpox Eradication Program. As a member of a WHO special seminar, he participated in development of the WHO guidelines for production of advanced dry smallpox vaccine. After completion of the program, he worked at the WHO Headquarters.

Vyacheslav A. Mukhopad
1937–1981

An epidemiologist from Kiev and candidate of medical sciences. Since 1971, he worked as a WHO advisor in the most populated Indian state, Uttar Pradesh, where he organized the smallpox eradication campaign. Being highly skilled expert overcoming incomprehension and direct resistance of local officials, he trained epidemiological teams as well as reorganized and streamlined the identification and registration of smallpox cases. He introduced the system of weekly repeated searches of smallpox cases involving local health services, teachers, students, and others, which was fully justified. As Dr. I.D. Ladnyi wrote, "this system has become the prototype of incidence monitoring across the country". His mission in India was completed in 1976, when the whole country was free of the smallpox. He was awarded the WHO badge of honor "Bifurcated needle" as the recognition of his contribution to this great achievement.

Georgii P. Nikolaevskii
1928-1994

An epidemiologist, candidate of medical sciences; in 1967–1971, worked at the smallpox eradication unit with the WHO Headquarters. He was engaged in planning of national programs for smallpox eradication; participated in organizing and conducting eradication campaigns in Zaire and Uganda; and worked on evaluation of the smallpox eradication in several states of India. When working in Zaire, he prepared photo material to create a series of slides illustrating various forms of smallpox in the region. He participated in the preparation of the WHO guidelines for the laboratory diagnosis of smallpox (1969). Together with P.N. Burgasov, he published the monograph titled *Smallpox* (1972). He was awarded the WHO badge of honor "Bifurcated needle" as the recognition of his contribution to this great achievement.

Yurii P. Rykushin
1923–1995

An epidemiologist, candidate of medical sciences, and researcher at the Pasteur Institute of Epidemiology and Microbiology (St. Petersburg). Since 1965, he worked in Uganda under the tuberculosis control program and proposed combined vaccination against tuberculosis and smallpox, which proved to be effective. In 1973, he was sent by the WHO to work for the Smallpox Eradication Program in India. Having devised a system for active detection of hidden foci and individual smallpox cases involving social forces and organizations, he made a significant progress in the fight against smallpox. He was a member of the International Commission for the Certification of Smallpox Eradication in Uganda. He was awarded the WHO badge of honor "Bifurcated needle" and WHO commemorative medal "The smallpox is eradicated" as the recognition of his contribution to this great achievement.

Leonid L. Salmin
1930–2001

An epidemiologist, candidate of medical sciences, and researcher with the Mechnikov Institute of Vaccines and Sera. In 1959, as a member of the anti-epidemic team, he participated in the mass vaccination campaign against smallpox in Iraq. Later, he worked in the Department of Science of the Central Committee of the Communist Party of the Soviet Union, supervising the sanitary and epidemiological service and as a Deputy Director of the Tarasevich Institute of Standardization and Control of Biomedical Preparations.

Aleksei Yu. Samostrel'skii
1929–2000

An epidemiologist, microbiologist, candidate of medical sciences, and researcher with the Pasteur Institute of Epidemiology and Microbiology (St. Petersburg). Since the late 1960s, he was the head of Smallpox Eradication program in Somalia. In the early 1970s, the WHO assigned him to the smallpox eradication in India. In both Somalia and India, he has proved as highly skilled manager and epidemiologist. He was awarded the WHO badge of honor "Bifurcated needle" and WHO commemorative medal "The smallpox is eradicated" as the recognition of his contribution to this great achievement.

Yaroslav M. Selivanov
1929–1998

A virologist and candidate of medical sciences; he worked under the Smallpox Eradication Program in India and Bangladesh, where he in collaboration with national services arranged broad measures against the smallpox in remote parts of West Bengal and the north of Bangladesh, often suffering from flooding. Along with solving the epidemiological and organizational issues, he conducted the relevant research. He was awarded the WHO badge of honor "Bifurcated needle" and WHO commemorative medal "The smallpox is eradicated" as the recognition of his contribution to this great achievement.

Anatolii N. Slepushkin
1929–2009

A virologist, doctor of medical sciences, professor, and Honored Scientist of the Russian Federation. In 1971–1976, he worked under the Smallpox Eradication Program with the smallpox eradication unit at the WHO Headquarters. In 1972–1976, he was directly involved in the smallpox control in India and Pakistan. He proposed a highly efficient method of active search for unregistered smallpox cases through monthly surveys. According to his recommendation in 1973, this technique was used in the intensified phase of the program in these countries and later, in Bangladesh. He was awarded a medal and honorary certificate by the Indian Government as well as the WHO badge of honor "Bifurcated needle" and commemorative medal "The smallpox is eradicated". On completion of the Program, he headed the Laboratory of Influenza at the Institute of Virology of the Russian Academy of Medical Sciences.

Valentin E. Vishnyakov
1929–1992

An epidemiologist and candidate of medical sciences; in February 1962–April 1967, worked as an advisor at the WHO Regional Office for Southeast Asia. He was involved in the organization of anti-epidemic measures and smallpox vaccination companies in Afghanistan, Nepal, and India and advice and methodological assistance to the local experts as well as also conducted the research important for the program, which contributed to further development of strategic approach to smallpox eradication. He is the author of numerous research papers and the monograph *Smallpox Eradication in Asia*. He was awarded the WHO badge of honor "Bifurcated needle" as the recognition of his contribution to this great achievement.

Aleksandr V. Zakaryan
1920–2008

A doctor of medical sciences, epidemiologist, professor, Honored Doctor of the Armenian SSR; he headed the anti-epidemic team that performed the mass vaccination of Iraqi population against the smallpox (1959).

Skin Lesions in Smallpox

Few Introductory Remarks

Since the entire book deals with smallpox control, we would like to allow our readers to get visual acquaintance with this infection. Our wish was also stimulated by the fact that we succeeded in finding the color captures of smallpox cases only in two books issued in this country (P.N. Burgasov and G.P. Nikolaevskii, 1972; I.D. Ladnyi, 1985). We selected for illustration the high-quality photos displaying the smallpox lesions in all detail.

Several forms are distinguished in the clinical course of smallpox. In most cases, these forms are classified according to the differences in skin elements (pocks) and their number. We present the most frequent common form of smallpox and its variants—discrete and semiconfluent. The latter is distinguished by that the pocks merge in some skin areas. In addition, we show the photos of a patient with one of the most malignant smallpox forms—the so-called flat smallpox, which, as a rule, has a lethal outcome. The specific feature of this form is flat pocks, as if submerged in the skin, rather than typical convex pocks. A patient suffering with the confluent variant of flat smallpox is shown. The photos reflect the dynamics of the disease course in all three patients.

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All these photos are the courtesy of Dr. E.M. Shelukhina, whose activities have been repeatedly described in this book. As a leading specialist of the Moscow WHO Collaborating Center, she in collaboration with L. Matlovsky, a photographer from the United States, succeeded in capturing the dynamics of development of specific skin lesions of smallpox patients. This is the good occasion to thank her and Mr. Matlovsky for their job.

Discrete form of smallpox: patient M. (different body parts)

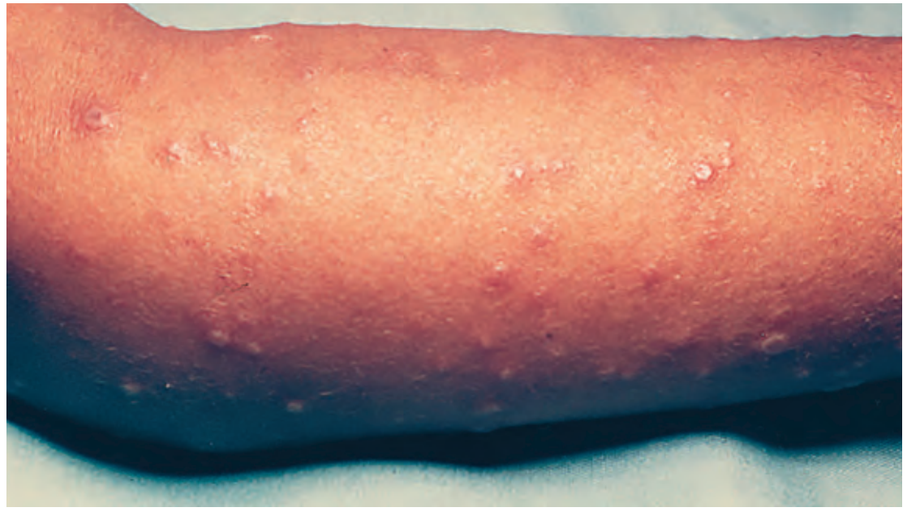
Stage of papules (nodules) with progression to vesicles (fluid-filled elevation of the skin)

Stage of vesicles

The same patient

Stage of pustules (pus-containing skin elevations)

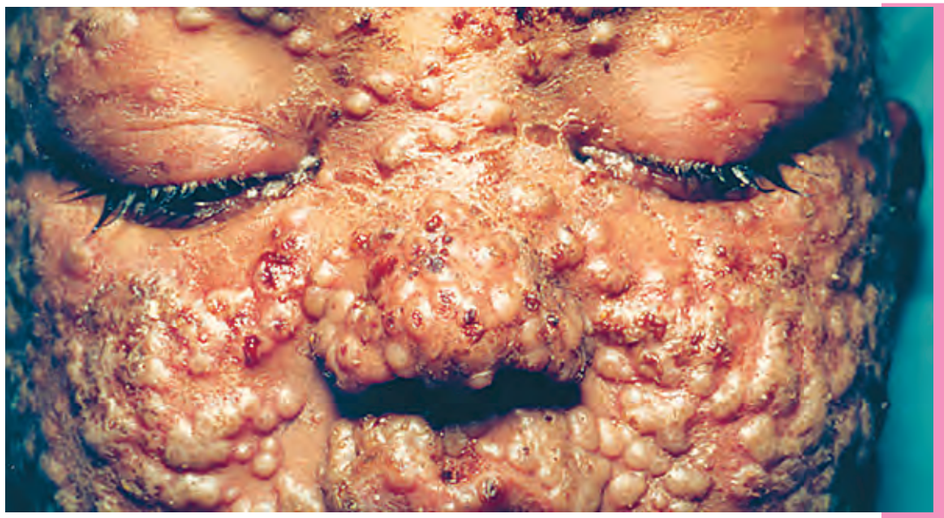
Stage of pock drying and scab formation



Stage of vesicle formation

Stage of vesicles

The same patient



Stage of vesicle maturation and their transformation into pustules; confluence of pocks is observed

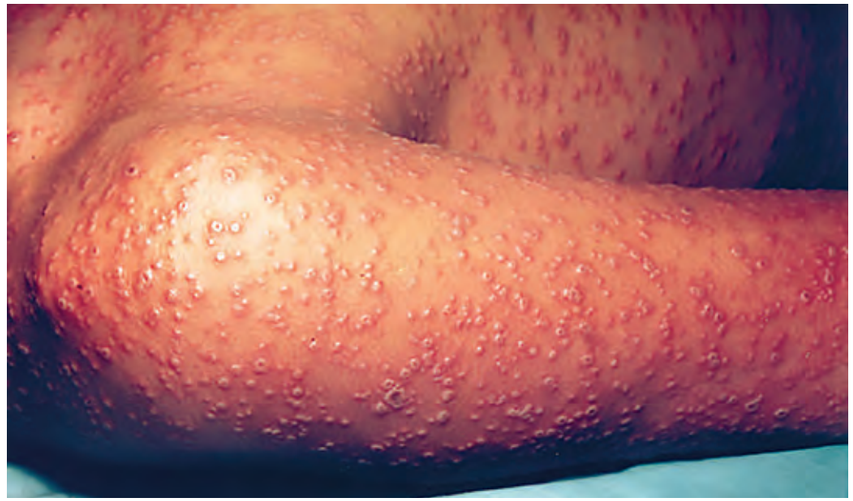
Pustules on the face begin to dry

The same patient

Part of scabs on the face shed; pustules on the limbs are drying

Stage of scab shedding

Emergence of papular rash



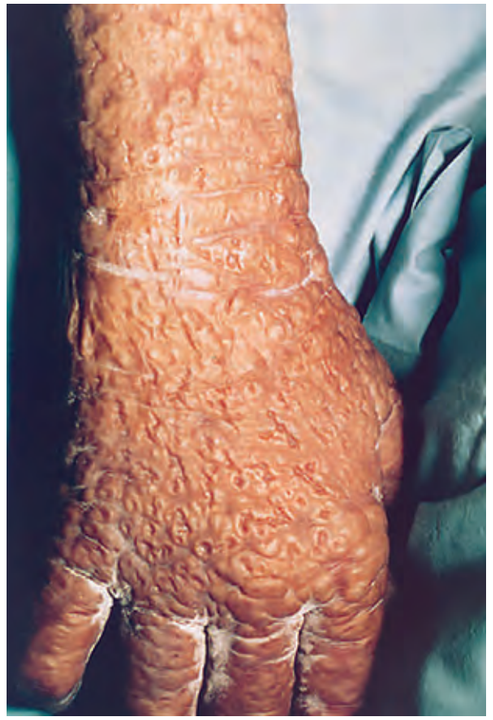
Transformation of papules into vesicles; note that pocks in this smallpox variant are flattened and as if submerged in the skin

The same patient

Stage of vesicle maturation and their transformation into pustules; beginning of pock confluence

Further confluence of pustules

The same patient



Almost entire body surface is covered with pus-containing lesions, which from a kind of armor; this case had a lethal outcome

Clinical manifestations of smallpox and human monkeypox

Rashes on the neck, back, and limbs of a smallpox patient on day 7 of infection

Rashes on the neck, back, and limbs of a monkeypox patient on day 7 of infection

These photos (by the courtesy of I.D. Ladnyi) demonstrate an amazing similarity between the skin manifestations of smallpox and the recently discovered disease, human monkeypox. This explains why the latter disease remained unknown to science for such a long period. It was discovered thanks to professional virological research.

This photo is given to illustrate the chapter "Moscow WHO Collaborating Center for Smallpox and Related Infections: Its History and Activities" (see p. 49).

Scientific publication

How It Was:
The Global Smallpox Eradication Program
in Reminiscences of Its Participants
(to the 30th anniversary of the victory over smallpox)

The quality of photos corresponds to the materials
supplied by the authors

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