THE JOSEPH L. MAILMAN
SCHOOL OF PUBLIC HEALTH
COLUMBIA UNIVERSITY

Frank A. Calderone Lecture
April 5, 1999

Bioterrorism:
Myths and Realities

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The Frank A. Calderone Lecture and Prize Ceremony
The New York Helmsley Hotel
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It is, for me, a special pleasure to be here today to celebrate with you the 75th Anniversary of the Columbia School of Public Health. Hopkins and Columbia, two of the first Schools of Public Health in this country, have been at the heart of a 75 year era unprecedented in history during which infant mortality rates have plummeted, fertility rates have declined sharply, longevity has increased, the scourge of many infectious diseases has ebbed — and, lest any one forget, the lion's share of the credit for these extraordinary advances unequivocally goes to public health.

I appreciate especially being honored with the Frank A. Calderone Prize. The Calderones are, of course, public health legends to all of us — a remarkable team whose bold vision transformed public health. I feel a special kinship to Frank Calderone, a public health administrator whose career, like mine, included memorable service in the World Health Organization. He was married to the legendary Mary Calderone but probably wondered at times if he was not, in fact, wedded to Planned Parenthood, and to SIECUS, the organization that Mary founded. As one married to a former President of Planned Parenthood of Maryland and who is a continuing member of at least 4 or 5 different committees of that organization, I can more keenly appreciate the many and inevitable conflicts.

The subject of my presentation today is bioterrorism and, in particular, the threat of smallpox and bioterrorism. I should first like to tell you briefly about it. I should then like to relate this to public health in the 21st Century, for the threat,

surprisingly, has important implications. In December, 1979, just 20 years ago, the WHO Global Commission for the Eradication of Smallpox concluded its work of certifying that eradication had indeed been accomplished. The last case occurred on 9 October 1977. Two years of intensive search had been conducted in all previously endemic countries under the direction of the Commission. No cases had been discovered. Men and women from around the world celebrated. In all, 687 WHO staff from 73 different countries had worked in the field at some time during the program; upwards of 150,000 national staff had participated. It was tough, frustrating work and the program itself hung in the balance on many occasions. Finally, however, we prevailed. For the first time in history, a disease had been eradicated. The fact that throughout history it had been the most devastating of all the pestilential diseases, made the victory especially notable. Vaccination everywhere ceased in 1980. There have been no subsequent cases.

An exceptional feature of the program had been the amicable and close cooperation throughout the campaign between the two principal contributors, the USA and the Soviet Union, during some of the darkest days of the Cold War. The proposal in 1958 that smallpox be eradicated was a Soviet one; U.S. support, provided some eight years later, gave it needed momentum. Field epidemiologists came from both countries. Collaborating laboratories in Atlanta and Moscow conducted important research programs in support of the campaign; they provided diagnostic services as well as consultant services to other laboratories. The bulk of the contributed vaccines came from the Soviet Union and the U.S.

A Russian author inadvertently played an important role, through his writings, in driving the program through to its completion during the long months of search after the last known cases in order to confirm that eradication had indeed been achieved. It was a quotation from Solzenitzyn's "First Circle," termed "The Rule of the Final Inch." An abbreviated quote provides something of the flavor. "The rule of the Final Inch!... The work has been almost complete, the goal almost attained, everything seems completely right and the difficulties overcome...Finishing touches are needed...In that moment of fatigue and self-satisfaction, it is especially tempting to leave the work without having attained the apex of quality...the rule of the Final Inch consists in this; not to shirk this crucial work...And not to mind the time spent on it, knowing that one's purpose lies not in completing things faster but in the attainment of perfection." Staff everywhere regularly referred to the "final inch" as the final, tedious months passed, searching and searching, but finding no cases.

The Soviets at the highest level, both publicly and privately, took immense pride in the accomplishment of eradication. As they viewed it, the program was primarily their creation — and, indeed, it was. But there was a dark side, a betrayal of a commitment and a trust. This did not become apparent until many years later.

As the post-smallpox eradication era began, a special WHO committee oversaw publication of a book documenting the program; field studies of monkeypox infections to assure there was no threatening animal reservoir; and preserving vaccine and seed virus in case the vaccine should ever again be required.

As confidence grew that smallpox had really been eradicated, countries around the world grew increasingly more insistent that steps be taken to destroy the remaining stocks of smallpox virus in order to be that much more certain that they would not have to deal with this feared disease once again. The WHO committee proposed that destruction be delayed until a number of studies could be completed to more completely characterize the smallpox virus genome and to preserve it in the form of cloned virus fragments. Later, sequence maps of the virus were prepared for a number of stains. Finally, in 1993, five major national and international scientific bodies were formally approached by WHO and asked to consider whether they would support destruction of the virus. All provided written agreement assenting to this action. Few saw any reason to retain the virus. Essentially no research had been performed with the virus for more than ten years and none was planned, at least in Western countries. At the World Health Assembly in May, 1996, member nations voted to destroy the virus at the end of June, 1999. That decision will be debated finally at the World Health Assembly this May. Although some continue to question the desirability of virus destruction, I strongly support its destruction, as does the WHO Expert Committee.

It was with a touch of nostalgia that I realized that a subject which had dominated my life for more than 20 years was about to be consigned once and forever to history. In fact, I had no regrets. There are so many other challenges — from the new, such as AIDS, to the old, such as tuberculosis — which demand far more commitment and resources than are now being assigned.

The subject of smallpox was not to die so easily, however. In 1993, Dr. Ken Alibek, the deputy director of the Soviet Union bioweapons program defected to the United States. Meanwhile, in 1972, the Biological Weapons Convention was finalized and subsequently signed by most countries of the world, including the United States, the Soviet Union, and Iraq. All signatories pledged to abandon research on offensive bioweapons and to destroy such stocks as they had. However, reports obtained during the late 1980s suggested that, contrary to the Convention, the Soviet Union may have been conducting research on such weapons and perhaps producing them. Dr. Alibek brought the ultimate in grim news.

As he explained, Soviet authorities in the 1970s had viewed the acceptance of the Convention by virtually all countries as presenting an unusual opportunity for the Soviet Union to gain an important advantage in the Cold War. Accordingly, an extensive expansion of its bioweapons research and production capacity began. In 1980, at the time that many Russians were celebrating the demise of smallpox and Russia's important contributions to that effort, Soviet leadership saw yet another opportunity and embarked on an

aggressive program to weaponize smallpox and to produce it on a very large scale. As Dr. Alibek described in convincing detail, the task proved more difficult than had been anticipated, but finally, in the late 1980s, production of high titer smallpox virus in multi-ton quantities was achieved. It had been weaponized so as to be able to be transported in intercontinental ballistic missiles and to be dispersed effectively as an aerosol after reaching its target.

The massive bioweapons facility that undertook the research and development program, is called VECTOR. It is located in Koltsovo in Central Siberia. It continues to function today as a research enterprise, conducting studies of many exotic viruses, including Ebola, Marburg, and Venezuelan Equine Encephalitis — and, yes, smallpox. The WHO laboratory in Moscow that had collaborated with the smallpox eradication effort was closed, and its virus stocks transferred to Koltsovo. The major production facility for the smallpox virus is said to be at another location near Moscow, operated by the Ministry of Defense. It has never been opened to inspection.

Smallpox virus thus exists in Russia, probably at two sites, at least. How secure the stocks may be is uncertain, especially given the economic conditions in Russia today, and the fact that salaries for scientists are paid very late or not at all. Many have left their former institutions for other countries. Reasonable evidence exists that at least ten nations are now engaged in the development of bioweapons and some are actively recruiting scientists in Russia.

Two groups have reviewed the characteristics of organisms that might be used as bioweapons against civilian targets in order to ascertain which merit the greatest concern and would require special preventive or therapeutic measures. One group, a committee of Russian bioweapons experts, concluded in 1994 that smallpox was alone at the top of the list, followed by plague and anthrax. A Working Group of U.S. military and civilian experts convened at Johns Hopkins, reached similar conclusions.

Why smallpox? The factors which until 1980 made smallpox the most feared of all infections are, in fact, heightened today. Recall that until the 1970s, all countries conducted routine vaccination programs, even those that had not experienced the disease for decades. They feared the possible importation of the disease and its subsequent spread. Smallpox kills 30% of the unvaccinated; there is no treatment. Moreover, as many will remember, all travelers had to carry a yellow vaccination card attesting to the fact that one had been successfully vaccinated within the preceding three years.

Smallpox is a virus disease that normally spreads from person to person by airborne droplets. Twelve to 14 days after exposure, the patient develops very high fever, severe aching pains, and usually takes to bed. After two or three days, a pimple-like rash erupts over the body; the pimples gradually fill with pus. Some have described the disease as being similar to having thousands of boils all over the body.

By the second week, if the patient survives, scabs form. They fall off, leaving deeply pitted scars. Some people are left blind. There are reasons to fear this disease above others.

Today, in contrast to the past, very few persons have immunity, either acquired because of past infection or because of vaccination. Vaccination ceased in this country in 1972. Thus, effectively no one under the age of 25 has been vaccinated, and among those older, few now have sufficient immunity to protect against infection.

Smallpox in an aerosol form is very stable, and in a cool, dry environment would be expected to survive for at least 24 hours. Borne by wind currents, it would be wholly undetectable. If one were to suppose that as few as 50 to 100 persons were exposed, they would begin experiencing acute, severe illness some two weeks later. Brought primarily to physicians who have never before seen a smallpox case, the diagnosis would not be made for several days to perhaps a week. Meanwhile, each patient would have been in contact with many others. A second wave of cases would occur two weeks later with 10 or more new infections for every case in the first wave or, in other words, 500 to 1000 cases in all. Complicating the problem would be the fact that perhaps as many patients again would be experiencing unknown illnesses with rash and fever, such as chickenpox or a drug reaction, and would have to be treated as if they had smallpox until the diagnosis was certain.

Because of the risk of virus transmission in hospital, patients would need to be housed in rooms under negative pressure and the exhaust air filtered. How many such beds there are in New York, I don't know; in Maryland, we have only 80.

Meanwhile, vaccination would be needed for health care workers, patients exposed in hospitals and all the contacts of those with smallpox or suspect smallpox. The numbers possibly exposed and those clamoring for vaccine would quickly number in the tens of thousands, and at least with the second wave of cases, mass vaccination would become a necessity. Thus far, few cities have given serious thought as to how such a program could be carried out, although I would note parenthetically, that you in New York are probably further ahead than any city. Moreover, we now have only six to seven million doses of vaccine in reserve in the United States. There are presently no vaccine producers anywhere in the world and substantial new production would require 36 months or more. In brief, the vaccine supply would rapidly be exhausted; there are few reserves in other countries.

You can now appreciate why the release of even a small amount of smallpox causing a limited number of infections has such dire implications. Fortunately, under the aegis of Dr. Hamburg, comprehensive national planning has begun for this and other potential bioweapons. A component of the

plan is the provision of a national stockpile of smallpox vaccine. This effort, however, is at its earliest stages.

Meanwhile, on the national scene, billions of dollars are being expended on counter-terrorist activities, virtually all of this money being directed to dealing with a chemical or nuclear event despite the fact that experts rate the bioterrorist threat as potentially the more serious. A plan to train and equip so-called "first responders" (police, fire, and emergency rescue personnel) in 120 major cities is being implemented by personnel from the Department of Defense; emergency teams of National Guardsmen are being trained for the same purpose; the Federal Bureau of Investigation has been greatly strengthened.

However, for a bioterrorist attack, the key personnel are not the "first responders" who are now being trained, but infectious disease physicians, family physicians, emergency room doctors and nurses, health department epidemiologists, laboratory directors, and administrators. To date, none has received training. Moreover, the public health infrastructure that is essential to countering an attack has been allowed to deteriorate over recent years. Many state and local laboratories are but shadows of what once they were; epidemiologists are few and far between; significantly lacking is a network for reporting and information which connects the infectious disease specialist, family practitioners, emergency rooms, and hospital infections staff with state and federal resources. We are today ill-prepared to deal with a bioterrorist threat,

but then we are no better prepared to deal with the threat of new and emerging infections, the increasing tide of antibiotic resistant organisms, and the special challenge of food-borne disease as we internationalize and industrialize our food supply. We, as a nation, have quite forgotten that our present salubrious state of health did not happen by indirection. It had a great deal to do with public health measures.

Some have suggested that under threat of hostile action, many of our most important advances have materialized — to wit, our national network of interstate highways, supersonic transport, the internet and many others. Last year, the federal budget for counter-terrorism was somewhat over $11 billion; of that, less than 0.1% was provided to the Department of Health and Human Services, which at the federal level, bears the major responsibility for coping with bioterrorist attack. Increased funds have been provided for this fiscal year but the sums appropriated scarcely begin to meet the need. It seems to me that there is a good reason now to invest in a strong public health infrastructure not only as a defense against bioterrorism but to cope with the challenges and potential for good health in the 21st century.

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Dr. Henderson is an expert in worldwide immunization programs. Throughout his career, he has directed his interests and energies toward a population-based approach to the control of infectious and communicable diseases. He became a nationally-known public health figure as the director of the World Health Organization's (WHO) successful campaign to eradicate smallpox. To achieve the goal of disease eradication, hundreds of millions of people were vaccinated.

Dr. Henderson helped launch WHO's global program of immunization, which is now vaccinating 80% of the world's children against six major communicable diseases. The year 2000 is the target date for the eradication of poliomyelitis.

Dr. Henderson spent 1991-1995 in government service, first in the White House as associate director for life sciences, Office of Science and Technology Policy, Executive Office of the President, and then as deputy assistant secretary and senior science advisor in the Department of Health and Human Services. One of his prime undertakings was advancement of the "Child's Vaccine Initiative," to spur development of a single vaccine to protect children from infancy onward against the most dreaded communicable diseases.

For 13 years, Dr. Henderson was dean of the faculty of the Johns Hopkins School of Hygiene and Public Health and professor of epidemiology and international health. Today, he is the director of the Johns Hopkins Center for Civilian Biodefense Studies, doing pioneering research in the field of bioterrorism.

The Calderone Award is one of many honors Dr. Henderson has received from institutions and governments for his work. Thirteen universities have conferred honorary degrees on him, and 14 countries have honored him with awards and decorations. In 1986, he became the first public health professional to receive the National Medal of Science. He has been awarded the National Academy of Sciences' Public Welfare Medal and the Dana Foundation's Award for Pioneering Achievement in Health. Dr. Henderson and three colleagues received the 1988 Japan Prize. He is a member of the Institute of Medicine and a fellow of the American Academy of Arts and Sciences.

Frank A. Calderone, MD

Dr. Frank A. Calderone was born in New York's Lower East Side in 1901. He received his undergraduate degree from Columbia University and his M.D. from New York University. He was an instructor in pharmacology at NYU until 1936, when he enrolled at Johns Hopkins University to pursue a master's degree in public health.

Two years later, he returned to New York and accepted the position of district health officer of the Lower East Side for the Department of Health, and began his career in public health. He then spent four years as secretary of the Department, during which time his careful planning, operations management, and negotiating skills saved the City more than a million dollars.

In 1946, as director of the headquarters office of the United Nations Interim Commission of the World Health Organization (WHO), Dr. Calderone was instrumental in helping to shape WHO's organization, policies, and structure, and in raising funds to support its continuing operations. When WHO became a permanent organization, he was appointed chief technical liaison officer and New York office director. Subsequently, he was appointed medical director of the United Nations Secretariat Health Service.

Dr. Calderone was a fellow of the American Public Health Association. In addition to his public health responsibilities, he managed a family business of eight theatres and extensive real estate holdings, and enjoyed music, sailing, and family life.

The Frank A. Calderone Medal and Prize

Early this century, Salvatore Calderone, immigrant father of Dr. Frank A. Calderone, commissioned the renowned firm of Dieges and Clust to design and strike a "medal of merit" in solid gold. Only a few were made, and only one is still in existence. It was the model used by Tiffany & Co. for the creation of the Calderone Medal. Dr. Calderone arranged for the endowment of the $10,000 Prize and Medal in his will. The recipient is invited to give a lecture on the public health topic of his or her choice. The Calderone Prize is awarded by the Joseph L. Mailman School of Public Health of Columbia University to recognize and honor individuals who have made significant contributions in public health and public health research. It is one of the most important honors in the field of public health.

Recipients

1992	C. Everett Koop, MD
1994	Jonathan Mann, MD, MPH
1996	William Foege, MD, MPH
1999	D. A. Henderson, MD, MPH