Medical History

International Contributions toward the Conquest of Polio


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INTRODUCTION

In October 1986 Paul Mellon flew his own jet to Aldergrove, thence to Ulster-American Folk Park near Omagh. To Mellon’s surprise, he was met by a delegation headed by Park Director Denis MacNeice. Paul Mellon was then escorted to Camp Hill Cottage, where his grandfather, Thomas Mellon had been born in 1813. His grandfather left in 1817 for Baltimore, Maryland (memoir published privately 1885). The visages of Grandfather Thomas and Paul, both in their 70s are remarkably similar1 (Fig. 1).

THE GOLDEN YEARS

The recruitment of noted virologist George Williamson Auchinvole Dick by Eric Ashby2,3,4, Paul Mellon’s friend and beneficiary, led to vital improvements in the production and safety of polio vaccine (Fig. 2). Dick was to be awarded by Johns Hopkins University the title “Hero of Public Health”5. Eric Ashby became Lord Ashby of Brandon4.

Fig 1. Paul Mellon, oil on canvas, by William Franklin Draper (1912-2003), 1974, 48.25 x 40.12 inches, image no. 183.75.1, from the collections of the U.S. National Gallery of Art, Washington, DC, and reproduced with permission. Paul Mellon wrote, “While flying [in his jet] on the return journey from Belfast to Heathrow my thoughts continually reverted to my grandfather. Would he have seen me as an effete wastrel or as the son of a sensible son”1. The Mellon family having moved from Ulster to Pittsburgh, in 1948 they funded the founding of the University of Pittsburgh School of Public Health to support Jonas Salk. They also supported Eric Ashby in the founding of Clare Hall and the maintenance of Clare.

Fig 2. Lord Ashby of Brandon (1904-92), oil on canvas by Ruskin Spear, CBE, RA (1911-1990) 1960. From the Queen’s University Belfast Art Collection, and reproduced with their permission. Eric Ashby, Kt, Ph.D., F.R.S., Vice Chancellor, President and Chancellor of the Queen’s University, Belfast, entered the City of London College in 1916 and proceeded to Imperial College and the University of Chicago. In 1931, Ashby returned to Imperial College to marry Helen Farries. At Imperial College “They came together in an entirely appropriate manner for two plant scientists—collaborating in the use of an incinerating system”4.

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In 1929 Eric Ashby and Robert Maynard Hutchins came to the University of Chicago. Ashby was 24 and Hutchins 29 years of age\textsuperscript{4,6}. Ashby was a Harkness Commonwealth Scholar from Imperial College, London\textsuperscript{4}. Hutchins came from a youthful deanal professorship at Yale Law School\textsuperscript{6}.

Twenty-nine-year-old Hutchins was determined as the new Head of the University of Chicago, to redefine and by example to improve Research Universities. Ashby was determined to improve the practice and teaching of Ecology and Plant Pathology. Hutchins lectured frequently on University Governance and himself chose and vetted the Professoriate, University of Chicago staff, and architects. Ashby listened and learned. In 1932 Ashby returned to the Faculty of Imperial College. Polio was rampant in both the United States and Northern Ireland and would so remain\textsuperscript{3,9,10} (Table 1, Table 2). The effect of polio on agricultural ecology and urban life was profound. Ashby was successively Professor of Botany at the Universities of Bristol and Sydney. From Sydney in World War II, the Australian Government sent Ashby as Scientific Liaison Officer to Moscow. Ashby thought Lysenko an opportunist but not a charlatan\textsuperscript{4}. Introduced to Stalin and many of the Soviet Scientific Establishment, Ashby later returned to Sydney where he was offered the leadership of the University of Sydney and sequentially the National University in Canberra. The Ashbys decided to return to the United Kingdom\textsuperscript{4}.

Ashby decided to follow Hutchins’ teaching and precepts. According to the Royal Society, of all Ashby’s Queen’s Scientific Professorial appointments made, all when they were in their 30s, all were elected to Fellowships of the Royal Society\textsuperscript{4}. Ashby served as the Vice-Chancellor of Queen’s University, Belfast, where he succeeded David Lindsay Keir who had such a leading role in the development and organization of Orthopaedics for the World War II Allies\textsuperscript{11}.

DEVELOPMENT OF ANTI-POLIO VACCINES: KOPROWSKI, SABIN, ENDERS, SALK, DICK AND THEIR TEAMS

In 1953, my\textsuperscript{*} tutor at Clare, Michael P. Stoker, told me that polio was “Antigenicity versus Infectivity”. That in order to have hope of an academic career, I should study the history of the vaccines and their funding\textsuperscript{15}, starting with Paul Mellon and FDR\textsuperscript{16}. In 1955 I moved to Barts and Michael Stoker to Glasgow as the first British Professor of Virology.

KOPROWSKI ATTENUATED POLIO VIRUS

Warsaw native Hilary Koprowski received a medical degree from the University of Warsaw in 1939, concurrently studying music at the Warsaw Conservatory. After the German invasion, Koprowski left Warsaw with his family for Rome, where he continued his musical studies. He then relocated to Rio de Janeiro and a position with the Rockefeller Foundation’s Yellow Fever Research Service. The Koprowskis emigrated to the United States in 1944 where Dr. Koprowski obtained a position at Lederle Laboratories in Pearl River, New York\textsuperscript{17}.

\begin{table}
\begin{center}
\begin{tabular}{lcccc}
\hline
\textbf{YEAR} & \textbf{CASES NOTIFIED} & \textbf{NORTHERN IRELAND DEATHS} & \textbf{N.I. DEATH RATE/10\textsuperscript{5} POP} & \textbf{U.S. DEATH RATE/10\textsuperscript{5} POP} \\
\hline
1938 & 11 & 2 & 0.2 & 0.4 \\
39 & 12 & 3 & 0.2 & 0.6 \\
40 & 4 & 4 & 0.3 & 0.8 \\
41 & 20 & 12 & 0.9 & 0.6 \\
42 & 21 & 9 & 0.7 & 0.4 \\
43 & 13 & 6 & 0.5 & 0.9 \\
44 & 13 & 2 & 0.2 & 1.0 \\
45 & 36 & 14 & 1.1 & 0.9 \\
46 & 22 & 7 & 0.5 & 1.3 \\
47 & 208 & 30 & 2.2 & 0.4 \\
48 & 17 & 2 & 0.1 & 1.3 \\
49 & 40 & 4 & 0.3 & 1.8 \\
50 & 272 & 25 & 1.8 & 1.3 \\
51 & 80 & 10 & 0.7 & 1.0 \\
52 & 142 & 7 & 0.5 & 2.0 \\
53 & 290 & 15 & 1.1 & 0.9 \\
54 & 54 & 4 & 0.3 & 0.8 \\
55 & 52 & 0 & 0 & 0.6 \\
1956 & 49 & 5 & 0.4 & 0.3 \\
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\caption{POLIOMYELITIS CASES WITH MORTALITY IN NORTHERN IRELAND}
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\hline
1957 & 297 & 9 & 0.6 & 0.1 \\
58 & 55 & 5 & 0.4 & 0.1 \\
59 & 19 & 0 & 0 & 0.3 \\
60 & 12 & 1 & 0.1 & 0.1 \\
61 & 16 & 3 & 0.2 & 0 \\
62 & 35 & 1 & 0.1 & 0 \\
63 & 1 & 1 & 0.1 & 0 \\
64 & 0 & 0 & 0 & 0 \\
65 & 4 & 0 & 0 & 0 \\
66 & 1 & 0 & 0 & 0 \\
1967 & 1 & 0 & 0 & 0 \\
\hline
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\caption{POST-VACCINE DEPLOYMENT POLIOMYELITIS CASES WITH MORTALITY IN NORTHERN IRELAND}
\end{table}

During the late 1940s, Hilary Koprowski and his team at Lederle Laboratories in Pearl River, New York, set out to attenuate polio type 2 virus through monkeys and cotton rats (\textit{Sigmodon hispidus}). He achieved attenuation of neurovirulence after cotton rat and monkey to monkey transfer. In January 1948, Koprowski ingested the resultant vaccine himself\textsuperscript{17} and then in 1950, with the physician-in-
chief of twenty mentally disabled children at Letchworth Village, Rockland County, New York, they all drank the vaccine. Safety and immunogenicity were demonstrated and the Koprowski vaccine was approved and successfully used in the Soviet Union.

Later Koprowski, with the support of Nobel-Prize winner John F. Enders of Harvard, rejuvenated the Wistar Institute of Philadelphia as Director and became a Professor at the University of Pennsylvania. Progress in development and refinement of vaccines continues at the University of Pennsylvania.

**GEORGE DICK AND THE BELFAST LABORATORY**

George William Auchinvole Dick (1914–1997) was a son of the Manse in The Gorbals. Dick was educated in Glasgow before medical studies at the University of Edinburgh. After becoming a Colonel in the RAMC he served in the Colonial Medical Service until 1951. He then was awarded a Rockefeller Fellowship to their University in New York, which was followed by a year at Johns Hopkins from where he was recruited to the British Medical Research Council. In 1954 Dick accepted Ashby’s offer of a Professorship of Microbiology at Queen’s Belfast. His group with Clare-Dane and McKeown formed a virus research group and institute supported by Vice Chancellor Ashby and Dean John Henry Biggart. Sir Hugh Casson designed the Microbiology Building. In January 1957, the George Dick group published the three previously noted consecutive papers and the first showed that Koprowski’s TN type II attenuated poliovirus vaccine caused paralysis in monkeys, after passage through the intestinal tracts of vaccinated humans, so that “the laboratory characteristics of attenuation shown by TN type II virus which made it appear suitable for trial as a vaccine are not maintained after multiplication in human gut.” Similar results were obtained using Koprowski’s SM type I virus vaccine. Many lives were saved by the more stringent standards required as a result of this trio of Dick, Dane and McKeown papers.

**JOHN ENDERS AND THE NOBEL PRIZE: HARVARD UNIVERSITY**

John Franklin Enders (1897–1985) (Fig. 3) was educated in Hartford, Connecticut where his father was head of the Hartford National Bank. From Hartford, in 1912, John Enders was further educated at St. Paul’s Boarding School in Concord, New Hampshire. In 1915 Enders entered Yale. In 1917 he became a U.S. Navy pilot. Subsequently he served as a lieutenant flight instructor. He returned to Yale post World War I and graduated BA in 1920. In 1922 as an English teacher he received an MA from Harvard. For the next three years he taught philology. In 1927 he married and entered a doctoral program in Bacteriology under Harvard’s famous Hans Zinsser. Enders was a Harvard Instructor from 1930 to 1935 and then Assistant Professor until 1942. Late in 1939 with Harvard Medical student Thomas H. Weller and Dr. A.E. Feller, Enders cultivated vaccinia virus in roller cultures of chicken tissues. In 1940 Hans Zinsser died. Enders’ wife, Sarah Frances, died of acute myocarditis in 1943. Enders expanded his own research on mumps. In 1946, Dr. Charles H. Janeway, previously of Harvard’s 5th General Hospital during World War II, and Dr. Sidney Farber asked Enders to set up a laboratory at Boston Children’s Hospital and become Head of the Research Division of Infectious Diseases at that institution.

In 1947 Dr. Thomas Weller commenced biological studies on infections. Next year Dr. Frederick C. Robbins joined the Enders laboratory and started work on a strain of mumps virus that they propagated in vitro for the first time. In March 1948 Weller tried with varicella virus propagation using human embryonic skin and muscle. “A few unused cultures were spiked with polio virus, Lansing strain”. After three weeks of culture and three changes of medium, injection into mice produced paralytic polio. Enders suggested to Robbins that he use “cultures of intestinal tissue obtained at the autopsy of a premature human infant”.

In the Yale Archives there are just over twenty years of correspondence during the years 1946-1967 between John Enders (Fig. 3) and Hilary Koprowski during the latter’s stay at Lederle Laboratories, and later at the Wistar Institute, Philadelphia. Enders supplied advice and tissues for the Koprowski-Lederle anti-polio vaccine which was at first successful. Then George Dick and his laboratory at Queen’s

*Fig 3. John Franklin Enders, NAS, FRS. Oil on canvas, 60” x 44” by Janis Lejins (1899-1990), 1960. From the collection of Boston Children’s Hospital and the Harvard University Portrait Collection and reproduced with their permission.*
Belfast showed in their BMJ consecutive trilogy that human alimentary passage of the polio virus increased its virulence.\textsuperscript{12,13,14}

As a result of the ramification and later U.S. confirmation of the Dick team’s studies of polio vaccines, the UK avoided the fiascos of the Cutter incident\textsuperscript{28} which led to sixty separate civil lawsuits\textsuperscript{28}. The resolution of the first, Gottsdanker \textit{v. Cutter Laboratories}\textsuperscript{36}, set a precedent for a finding of breach of product warranty\textsuperscript{28}. The Salk killed polio vaccine was approved in the UK on April 25, 1955\textsuperscript{37,38}. In the same month of April, a quarter of a million U.S. children had been given a defective Salk polio vaccine. Forty thousand of these children developed polio; within days 200 children were paralysed and ten died\textsuperscript{28}. The first U.S. mass vaccination programme against polio was promptly abandoned. Salk’s protocol for formaldehyde inactivation of poliovirus in the vaccine produced by two companies had failed. Enders, Sabin, Dick and their research groups criticized Salk\textsuperscript{29}.

The United States courts found that Cutter Laboratories had not been negligent in failing to kill all the live allegedly non-toxic polio viruses of Jonas Salk’s Mellon funded University of Pittsburgh vaccine. Unfortunately the ruling that the vaccine manufacturer should be held responsible for post-vaccine disability and vaccine-associated death led to drug companies not producing vaccine supplies and halting of funding for vaccine production.

The Enders laboratory showed type 1 polio virus could be propagated using excised human foreskins\textsuperscript{39}.

I had the opportunity to meet John Enders when his second wife Carol (Carolyn) was admitted seriously ill to the Children’s Hospital, Boston, and occasionally consulted for ventilation but recovered completely. My wife Tessa was, at the time, Electron-Microscopist in the Enders Building at Children’s Hospital Medical Center, was appointed Assistant Director in 1949. The Enders laboratory showed type 1 polio virus could be propagated using excised human foreskins\textsuperscript{39}.

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Robbins had left Boston for Cleveland shortly after winning his share of the Nobel Prize. Tom Weller, who after wartime service in the U.S. Army Medical Corps, in 1947, joined Enders in his new, Research Division of Infectious Diseases at Harvard Medical School’s Children’s Hospital Medical Center, was appointed Assistant Director in 1949. The Harvard Medical School’s Department of Comparative Pathology and Tropical Medicine was transferred to the Harvard School of Public Health and renamed the Department of Tropical Public Health. In July 1954, Weller was appointed Richard Pearson Strong Professor of Tropical Public Health and Head of the Department\textsuperscript{41,42}. Weller was a superb consultant to the nearby Beth Israel Hospital’s Respiratory Surgical Intensive Care Unit; Max Finland\textsuperscript{43} by night and Weller by day were consultants. Professor Sir Michael Stoker, when he came to Boston, said to me he hoped I had learned more from Weller than I had from himself as my tutor at Clare. Apparently Eric Ashby smiled when told of this.

**MELLON SUPPORT OF SALK’S RESEARCH**

Jonas Salk was, or seemed to be, the only person John Enders disliked\textsuperscript{44}. Salk worked at the University of Pittsburgh. Paul Mellon was responsible for financing the extension and conversion and modification of the Salk group’s laboratories. Paul Mellon’s money came from his father, Andrew Mellon, Secretary of the U.S. Treasury for three presidents, before FDR, partly crippled by polio, was instrumental in founding the March of Dimes. Previously Andrew Mellon (1855-1937) had been the most financially successful U.S. businessman of the 19th Century and the leading citizen of Pittsburgh\textsuperscript{45}. The Mellons in the 20th Century were to give away well over 1,000 million Pounds Sterling of which several hundred million went to Paul’s college, Clare, and to the founding of Clare Hall and the very generous Mellon fellowships both ways between Clare and Yale University.

Paul Mellon was awarded three Bronze Medals as a Major in World War II for Bravery under Wild Bill Donovan, head of OSS, precursor of the CIA\textsuperscript{1}. After World War II Mellon money and influence was used to attract Francis F. Foldes as Head of Anaesthesia at Mercy Hospital in Pittsburgh from the Massachusetts General Hospital, and later supported the appointment of Foldes as Professor at Albert Einstein College of Medicine in New York City\textsuperscript{46}.

Born of an English mother, Paul Mellon (1907-1999) was baptised in St. George’s Chapel at Windsor Castle. He majored in Literature at Yale and then proceeded to Clare College, Cambridge for two years of further study. An excellent rower and horseman he left Clare in 1931 and returned home to Pittsburgh. When I was at Clare from 1952-1955 the Master of Clare used to regale us with descriptions of his luxurious flights in the Mellon Gulfstream II Jet which was decorated with work by George Braque, Paul Klee and Ben Nicholson. Paul Mellon presented the U.S. National Gallery and its holdings on behalf of his late father and himself to President FDR on March 17, 1941; FDR accepted this gift on behalf of the American people\textsuperscript{1,47}. Later Paul Mellon chose I.M. Pei as the architect of the East Building of the U.S. National Gallery, originally planned by his father Andrew to house the expanded collections of the future, with groundbreaking ceremony in 1971\textsuperscript{47}.

For the Museum of British Art in New Haven, Connecticut, Paul Mellon chose architect Louis Kahn\textsuperscript{48}. In turn Jonas Salk chose Louis Kahn on Paul Mellon’s recommendation to design the Salk Institute in La Jolla, California\textsuperscript{1,44,48}. For Clare and Clare Hall, Paul Mellon was an indispensable advisor to Eric Ashby, Master of Clare and to A. Brian Pippard as the founding Master of Clare Hall\textsuperscript{49,50}.

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LEGAL CONSEQUENCES OF POLIO SEQUESTRATION

The legal consequences of the Cutter trials are still such that generally the drug companies have to organize reimbursement for patient injury from vaccine injuries and consequent deaths. The result is few if any drug companies are interested in vaccine development without government guarantees. Very few legislators or insurance companies are willing or able to step into this role. To some extent the Gates Foundation is filling this void. In the second decade of the 21st century polio has, through vaccination almost been eliminated from our world, but late sequelae are still a world-wide burden.

ALBERT B. SABIN

Born in Bialystok, Poland, then part of the Russian Empire, in 1906, Albert B. Sabin arrived in New Jersey with his family in 1921 after an 18-month journey. Fluent in Yiddish, Hebrew, Russian and German, only after intensive tutoring in English by his Americanized cousins, was he ready at age fifteen to enroll in Paterson, New Jersey’s Public High School. He excelled and graduated after two years. With the support of a dentist uncle he enrolled at New York University School. He excelled and graduated after two years. With the support of a dentist uncle he enrolled at New York University School. He excelled and graduated after two years. With the support of a dentist uncle he enrolled at New York University School. With the support of a dentist uncle he enrolled at New York University School. With the support of a dentist uncle he enrolled at New York University School.

In 1935 he returned to New York with an appointment in the Department, Albert J. Saubermann, a Visiting Fellowship which enabled him to study virology during 1934-1935. Sabin determined to change course and, Dr. Park, also Director of the Public Health Laboratories of the City of New York, helped Sabin obtain scholarships for medical school as well as lodging at Harlem Hospital in exchange for “chores” in the Pneumonia Laboratory. There he developed a method for rapid typing of pneumococci before his 1931 graduation from New York University’s Medical School. Before settling into an internship at Bellevue Hospital, he returned to Dr. Park’s Bacteriology Laboratory just as a severe polio epidemic began in July 1931. Here, Park instructed Sabin to confirm Claus Jungeblaut’s earlier immunological studies of the polio virus at Columbia University. When Sabin was unable to do so, Park, Sabin and Jungeblut collaborated and published the revised finding that no one, without previous infection, was naturally immune to polio. Thus began Sabin’s campaign to control poliomyelitis.

After a two-year internship and residency at Bellevue Hospital, Sabin applied for a National Research Council Fellowship which enabled him to study virology during 1934 at the Lister Institute of Preventive Medicine in London. In 1935 he returned to New York with an appointment in the virus research laboratory of Dr. Peter Olitsky at the Rockefeller Institute for Medical Research; in 1936 Sabin and Olitsky established that poliovirus could be grown in human tissue cultures.

The National Foundation for Infantile Paralysis had been founded in 1938 by FDR, with Basil O’Connor serving as president. O’Connor recruited Dr. Thomas Rivers of the Rockefeller Institute, who enlisted the aid of his Rockefeller colleague, Albert Sabin, who, in turn, was offered a five-year appointment funded by the National Foundation, later renamed March of Dimes, to work exclusively on poliomyelitis at Rockefeller. In 1939, Sabin chose instead to develop a polio research program at the Children’s Hospital Research Foundation at the University of Cincinnati. In a 1941 paper, co-authored with Dr. Robert Ward, Sabin demonstrated the transmission of poliovirus through the digestive tract, and that this pathogen was seldom found in the nasal passage.

In 1939, while in Cincinnati, Sabin was appointed a civilian advisor to the Army Epidemiological Board, and eventually enlisted in the U.S. Army as a commissioned officer at the rank of Major in February 1943. During the war he researched diseases affecting the military and developed vaccines for a South Pacific variety of dengue fever and for Japanese encephalitis. After the war he returned to his Cincinnati laboratory.

In 1951, aware that Koprowski had attempted to develop an attenuated live polio vaccine, Sabin had contacted Dr. John F. Enders at Harvard and also sent an assistant to Salk’s Pittsburgh laboratories to study tissue culture techniques. Sabin continued this Cincinnati-based work on attenuated live vaccine. The 1955 Cutter Incident increased interest. At Children’s Hospital, University of Cincinnati, Sabin developed his live attenuated virus polio vaccine from polio virus that Hilary Koprowski had attenuated.

During the late 1950s the Sabin vaccine was tested in field trials in Mexico, Chile, Holland, Sweden, Japan, Singapore, Czechoslovakia and the UK. The most noteworthy field trial was Sabin’s work with the Soviet Union’s Dr. Mikhail P. Chumakov in which the vaccine was tested initially in over ten million persons. By 1960 more than 90 million persons had received Sabin anti-polio vaccine.

ASHBY

In his post-Clare Mastership Lectures and conversations, Ashby was wont to say that his recruitment of young Professors to Queen’s Belfast ranked first in importance in his own career. George Dick and Clare-educated David S. Dane had saved Britain and the United States from future polio catastrophes like the Cutter incident. Second in order was the admission of women to Clare and third was his role in the Mellon funding of Clare Hall with Arthur Brian Pippard as founding Master. Pippard had returned to Clare in 1947 as director of studies in Physics. In 1955 Pippard married Charlotte Dyer and immediately thereafter they left for their next year at the University of Chicago to join the Fermi Laboratories and work on Fermi surfaces of copper. Fermi himself had died of cancer of the stomach the previous November.

In the early 1970s, I was referred to Brian Pippard by Eric Ashby. I had tried to get a Harvard post-doc in my Department. Albert J. Saubermann, a Visiting Fellowship to accompany his training position in the Cavendish
Laboratory. Ashby said ‘No’ to Clare. Brian Pippard said ‘Yes’ and asked me to lunch. We decided that Mellon money should be involved, and that the long-term goal should be an eponymous chair at Einstein Medical College in New York City, preferably to be held by our trainee, Albert J. Saubermann.

After the Mastership of Clare, in 1976 Ashby was called to the Walgreen Visiting Professorship at the University of Michigan. Charles R. Walgreen, founder of the drugstore chain, had previously in 1935 sued President Robert Hutchins and the University of Chicago for indoctrinating his niece with communist ideology. Hutchins had supported the academic freedom of his faculty to teach as they wished. Hutchins by dint of “character, knowledge and charm” persuaded Walgreen to drop the suit, and later to endow a series of lectures on democracy. One of the duties of Ashby, as Walgreen visiting Professor in 1976, was to lecture at Harvard where “Individual members of the teaching faculties have full control over and responsibility for their methods of teaching.” As a result of Ashby’s Tanner Lecture at Harvard, the Charter originally written in Seventeenth Century Puritan English, approved in 1650 and subsequently revised over the years, remained in effect.

EPILOGUE

Some dozen years later, in April 1988, the plan to install our Mellon’s anti-polio research.

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