

Smallpox

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Smallpox eradication was a remarkable achievement for the World Health Organization, for its member countries and for the ~~dedicated~~ team of national and international staff who worked so tirelessly in achieving the ultimate victory. What is little known is that the eradication program was, from the first, an unwanted step-child of WHO -- a program thought to be destined for failure as was malaria eradication. In fact, the Intensified Program, begun in January 1967, was approved by the World Health Assembly over the objections of the Director General by a margin of only two votes in one of the most openly contentious budgetary debates of ~~WHO~~ ^{and the Organization.} Even as late as 1974, seven years into the program, eradication was considered by many to be as unlikely an event as it had been at the turn of the century.

The year 1900 found virtually every country in the world with endemic smallpox -- the only exceptions being ~~Norway and Sweden~~ ^{Scandinavia} where vaccination was diligently practiced and ~~Australia, New Zealand and New Zealand~~ ^{Australia} where isolation and rigid quarantine measures prevented all but the occasional importation. ① Vaccine technology had significantly improved during the latter half of the 19th century making vaccination less problematic than the arm to arm transfer of vaccinia. Vaccine began to be grown on the flank of a calf and bactericidal glycerol was added to stabilize the lymph, permitting it to be packaged in capillary tubes for easier distribution.

Until 1897, variola major, with a case-fatality rate of 30%, appears to have been the only form of smallpox but, that year, a mild form of smallpox, called alastrim, appeared in Florida and within a few years spread across the country, to Brazil, to Canada and to Britain. Less than 1% died. By the late 1920's, variola ^{minor dominated} ~~was replaced~~

~~from~~ North America. Why it did not spread to Mexico, let alone across the world, remains a mystery. Until the mid-1930s, the U.S. recorded between 30,000 and 100,000 smallpox cases each year but then cases plummeted. ^{The reversal of the P-H-S-} Sandy Guillian attributed this to the availability of refrigeration and better preservation of a thermolabile vaccine--shades of a later polio vaccine problem.

By the end of WWII, smallpox incidence in the industrialized world had reached very low levels but throughout the developing countries, epidemic disease prevailed everywhere. Some control was possible in the larger cities utilizing calf, sheep or water buffalo to grow the vaccine but distributing a potent product was a problem. The animal was often led from door to door as pustular material was scraped off the skin and transferred directly to the vaccinee. Protection of ^{a significant proportion} ~~most~~ of the population was simply not possible.

A heat stable vaccine was a critical need. Dutch, French and American scientists had experimented with some success with air dried and, later, freeze-dried vaccines but the methods were cumbersome; the product often contaminated; and the quantities were limited. In the early 1950s, Leslie Collier of the Lister Institute in Britain perfected a technique for large-scale production of freeze-dried smallpox vaccine. That product remained potent even when exposed to 37°C. for 4 months or more. Finally, an appropriate technology was available that ~~could~~ ^{could} make eradication a feasible proposition.

② In 1953, WHO's first Director General, Dr. Brock Chisholm, proposed that the Organization undertake a smallpox eradication campaign as a practical demonstration of the importance of WHO to all Member States. Developed and developing countries alike summarily rejected this proposal as impractical, uneconomical, complicated and, in failing, likely to damage the reputation of WHO.

Five years later, in 1958, the ^③USSR returned to active membership in the UN and WHO. At the World Health Assembly, Dr. Viktor Zhdanov, Deputy Minister of Health of

the Soviet Union proposed that WHO undertake the global eradication of smallpox. He noted that the USSR had succeeded in interrupting smallpox transmission during the 1930s in areas of Russia where the health services and transportation infrastructure were as primitive as in many developing countries. Why not undertake eradication as an international initiative? He quoted President Thomas Jefferson who had written to Edward Jenner: "It is owing to your discovery that in the future the peoples of the world will learn about this disgusting smallpox disease only from ancient traditions." Anxious to encourage Soviet activity in the Organization, the Assembly voted approval. But WHO was then immersed in a vast and costly malaria eradication effort and allocated neither resources nor personnel to the ^{smallpox} effort.

At each Assembly, the Russians expressed their anger that more was not being done. Finally, in 1965, the United States committed to support the program and joined with the Russians in proposing that \$2.4 million in Regular Budget funds be allocated ^{each year} for this effort. Some countries objected to any increase in the WHO budget; others objected that one more failed eradication effort was not what the Organization needed. UNICEF ^{flatly} stated ^{that} it had no interest in supporting another eradication program and ~~stated that~~ would provide no support -- a promise it kept. The Director General blamed the Americans for putting WHO in an unwelcome position and demanded that an American be appointed Director so that when the program failed, the United States would be seen to be ^{substantially} ~~partly~~ responsible. It was not an auspicious beginning for a young Public Health Service officer who was assigned responsibility for at least getting the program underway.

How many ^{smallpox} cases and deaths had occurred ^{since 1900} ~~up to the time~~ is, of course, pure speculation. Reporting was poor everywhere: few countries had death registration. After the program had begun, we undertook a number of surveys of the prevalence of facial scars and from this, an estimate of disease incidence was possible. For 1967, just

over 100,000 cases were reported; surveys, however, indicated that between 10 and 15 million cases and 2 million deaths had occurred ^{that year.} Since the turn of the century, it is probable that at least 300 million persons ~~were~~ died of smallpox.

- Smallpox - 1967 - (4)
- Face of smallpox - (5) (6) (7)
- Blindness (8)
- Factors favoring eradication (9)
- Strategy (10)
- Most important -

- A heat stable vaccine (11)
- Contr. batches of vaccine (12)
- The greatest invention (13)

Not an army - Not more than 100 ^{with} advisers
 WHO staff in GVA - 5 prof. / 3 sec'tys.
 1/3 of time in the field

- 1967 - (14)
- 1970 (15)
- 1973 (16)

The Subcontinent (17) (18) (19)

The Search (20)

1976 (21)

Ethiopia roads (22) (23)

Epidemic curve (24)

Ali, Maalin (25)

WHA declares (26) (27)

EA I (28) (29)

Right technology -
 Surveillance
 Production in down up the field -
 not from behind the desk and
 not in computer models.

→ Total cost 1967-88 Amer. just over \$740⁰⁰

? more 2 yr. later - what next do we calculate
 question was asked during program
 2 yr. later.

celebrated as an
 achievement, not

Then ^{ended} ~~started~~, so we thought, the saga of smallpox.

An Expert Committee, chaired by the world's foremost orthopox virologist, the Australian Frank Fenner, oversaw a carefully considered program, including sequencing of representative strains, that would permit destruction of known smallpox virus stocks. It was a program in which the U.S. was the principal advocate but a program supported by ~~all~~ the principal scientific societies and by virtually all coventors. In March last year, the U.S. abruptly and inexplicably reversed its position and requested ~~that~~ the Assembly vote to retain the virus to 2002 so that an antiviral drug could be developed. With anger and considerable bitterness, this was agreed, but the Assembly made clear no further extension would be given. And so a program begun in doubt ends with a whimper. ~~And was a program~~

Historical Landmarks in Eradication

VETERINARY INITIATIVES

1884 - Bovine contagious pleuropneumonia
5 year campaign

1890's - Eradication of vet.diseases - U.S./ Europe

HOOKWORM

1909 - Rockefeller F. campaign

YELLOW FEVER

1902 - Cuba

1915 - Rockefeller Foundation campaign

1928 - Jungle Yellow fever discovered

VECTOR ERADICATION

1934 - *Aedes. aegypti*

1939 - *Anopheles gambiae* eradication in Brazil

1944 - *Anopheles gambiae* eradication in Egypt

Historical Landmarks in Eradication - II

HUMAN DISEASE ERADICATION last 50 years

YAWS

- 1950 Region of the Americas
- 1966 Eradication efforts concluded

MALARIA

- 1950 Region of the Americas
- 1955 Global eradication
- 1973 Eradication efforts concluded

SMALLPOX

- 1953 Global program proposed by DG
- 1959 Global program agreed upon
- 1967 Global program actually launched
- 1980 Eradication certified

POLIOMYELITIS

- 1985 Region of the Americas
- 1988 Global program - goal 2000

DRACUNCULIASIS (Guinea Worm)

- 1986 Global program - goal 1996

CANDIDATE DISEASES FOR ERADICATION

	<u>Spx</u>	<u>Polio</u>	<u>Meas</u>	<u>HepB</u>	<u>TB</u>
Immunity after recovery	+	+	+	o	o
Man the only host	+	+	+	+	o
Importance to countries	+	±	+	±	+
Vaccine					
Affordable	+	+	+	±	+
Long-term protection	+	+	+	+	o
Easily applied	+	±	+	±	+
Transmission interrupted					
Developed country	+	+	±	o	o
Developing country	+	+	±	o	o

Why so Little Vaccine R & D

1. A demand issue -- physicians are trained to treat not prevent disease.

o 5% coverage

o Dentist / vet, car mechanic

2. A second demand issue -- developing country health centers are primarily curative -- often Western-style "Doc in the Box"

o Tents

o Vac. M hope / hth ctr.

3. Vaccine production is usually performed by a small unit of a large pharmaceutical house. Whether vaccine production flourishes or not is immaterial.

o liability

4. Incentives for developing new vaccines are limited

o vaccines vs. other Rx.

5. Public health professionals frequently express antipathy to research, especially bench science

o polio

6. Special circumstances of AIDS

+ The hubris of the basic scientist

+ The antipathy of the victims

Bottom line - haven't begun to reach potential in development and use of vaccines - see Gates - whether vaccination or not, however, it's beside the point

Problem elements in the malaria eradication strategy

- 1. An autonomous, wholly independent staff, reporting to the head of state is essential to success**
- 2. The technology and how to apply it is known; no further research is necessary**
- 3. A highly detailed plan applicable to all countries and meticulously executed is the key to success**
- 4. Measurements as to numbers of cases of malaria is not required until disease transmission is on the verge of interruption**