Polio Vaccine Policies & Eradication

26 FEB 1997

Course is intended to illuminate policy issues and provide (in vac. directly) to give some sense as to how policy issues are developed and resolved.

Prof. – work about policy formulation & policy offices –
During 3 yrs. OSTP – perception of a mystique about the process.
Working com. → draft policy document ← options / pros + cons → recs.
(cost-benefit/risk etc.)
"Sometimes" this happened but seldom.

Most policies seemed to emerge & evolve in an often messy process of meetings, back-office discussion, precipitating crises. Seldom an orderly process —
For all made of cost-benefit analyses, I can't recall one which influenced policy one way or the other. After policy decided – cost benefit to justify.

Product of science, personalities, historical prejudice, prospects for commercial profit, political realities
Development & licensure of polio vaccine thru its evolution to eradication program bore all of these characteristics
Not well-described in most of the text books.
(DNA 1955 IPV lic.; Christmas 60's & lic. of OPV; est ACIP;
launched EPI; 85 → TAG; 88-91 Chm. Global Com. on Polio Eradn.)

Polio – Hx of disease cessions
1st epidemics in 1890's – few 100 cases
1916 27000 cases / 6000 deaths in U.S. – Canadian border closed
Some outbreaks in 20's and 30's
Paralysis of FDR. – Proxy torn Rotary balls
Org. by FDR has partners.
Grew into the NFIP (1938) Rx & rehabilitation of polio cases – A unique foundation.
Policy decision to support basic science which might result in a vaccine.
REMARKABLE POLICY !

(like WW2)

OVERHEAD 1944, Polio ~~rates~~ incidence sharply increased <10 000 cases/yr. to 25000 to 30 000

Enormous concern — ~~~~ no. not so large but many victims in their teens and 20's

- ~~included~~ not restricted to the poor — many cases, esp. older in the SE.

Movie theaters, pools, schools.

govt. — no role to play. health primarily state subject

NFIP Resources ↑ and research ↑ (note: NIH resources 1940s)

~~Small~~ No. of centers funded — so

OVERHEAD ① Harvard — Enders, Robbins, Weller 1949 — (Nobel 1954)

② Hopkins (SHPH) Others: Yale, Cincinnati, Pittsburgh, New Orleans. Toronto.

③ Pittsburgh. — ~~Broers studio~~ [Salk began work in 1952]

NFIP policy — need to raise funds — get a personable young scientist — Jonas

Jonas did a good job representing the Foundation & doing phase I and II trials (Mar 53 Dec. 53)

(NOTE: PATENT NO [illegible])

④ Cincinnati — Sabin
⑤ Western Inst. — Koprowski

POLICY debate: Inactivated vaccine or live vaccine?

Inact. vaccine would clearly be first and easiest — influenza vaccine model.

but what of duration of immunity. — No precedent

Live vaccine — smallpox, yellow fever. ~~[illegible]~~

Those working on live vaccine — saw inact vaccine as a stopgap. —

NFIP — wanted the vaccine and fast. (57000 cases in 52)

All agreed a trial was needed — Jonas argued vs. "control" trial — unethical

State epidemiologists prevailed / Who made the vaccine One year

749 000 placebo controlled trial 1 000 000 observed control.

Murrow: Who owns the patent? Salk: There is no patent. Could you patent the sun?

Code broken in April 12th 1955 — licensed the same day / vac. began the fol. week.

Within 10 days — cases of polio began to occur in vaccinees. — GOVT. INVOLVED FOR FIRST TIME

OVERHEAD Cutter incident. — the inactivation curve.

+ Dir DBS / SG / Secty.

+ CDC surveillance.

Echo 1936 — Brodie vs

"Panic" "? loss of faith in vaccine" "? swift publication (lesson for BSE)

New policy — test every batch

↓ in potency of IPV.

Acceptance of vaccine —

Return to polio curve — might we have stopped polio? Intro. of IPV problems

The IPV – OPV debate continued. Who knows.?

Salk / Sabin / Koprowski / Cox — often consulted in different rooms.

How to test OPV — monkeys.

Note reversion to virulence (monkey test)

How many — ? 1 x 1000 000. Not in U.S.

OVERHEAD OPV development —

1st large scale trial in Singapore 200 000

1959 Russians 15×10^6 1960 100×10^6

Berlin episode

Vonka strain — type III — implications

Neurovirulence marker called into question.

Licensed in 1962 & considerable reservations.

OVERHEAD – RRL's

S.O.S. program — broke the private practice barrier.

Within 1 year — VAPP 23 cases —

Anxiety — special committee

Russian experience.

OVERHEAD SPREAD OF OPV IN FAMILIES

? ~~Research to develop a new strain~~ —

Problems ⊖ the vaccine:

① VAPP — With SS —

② Antigenically — Better —

③ Heat stability — ⊖

WHO – cold chain

(akin to making a better vaccine)

1974 EPI — 5 & 20%

1985 ~~UNICEF — Latin America~~ — Rotary International —

1985 Decision for polio eradication.

Strategy — ↑ vac. & 80%+ → NID (Cuba/Brazil)

— SURVEILLANCE + lab. confirmation.

↓ 500 hospitals. — weekly report → 20 000

Cases of Type III polio.

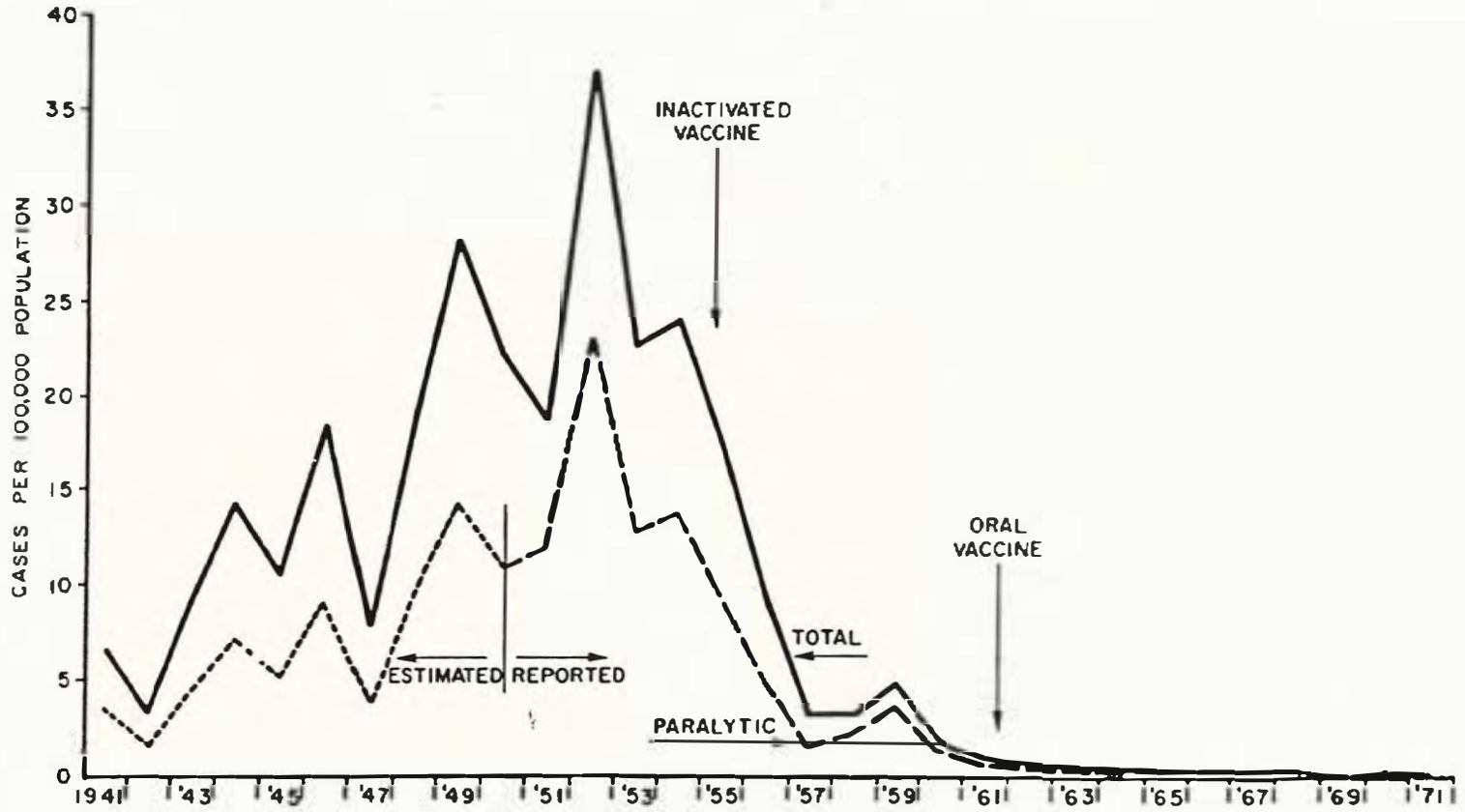
— CONTAINMENT — (different than eps).

→ — "Mopping up" (high risk areas) derived from eps epid. experience.

~~1988~~ — Difficult time for the CDC E.P. Director —

IVP Problem rears its head yet again —

cIPV developed Merieux Connaught.


CASES PER 100,000 POPULATION
40
35
30
25
20
15
10
5
0
INACTIVATED VACCINE
ORAL VACCINE
TOTAL
PARALYTIC
ESTIMATED
REPORTED
1941
'43
'45
'47
'49
'51
'53
'55
'57
'59
'61
'63
'65
'67
'69
'71

CUTTER INCIDENT 1955

Cause --The inactivation curve

Morbidity

260 cases : 192 paralytic

Vacinees	94
Family contacts	126
Community contacts	40

Outcome

CDC Poliomyelitis Program

Reorganization of the Division of Biologic Standards

DEVELOPMENT OF ORAL POLIOVACCINE

Principal Strains

Lederle-Cox
Wistar-Koprowski
Sabin

Neurovirulence measurements

Rhesus monkeys

Phase III Trials (Illustrative list of locations)

Belgian Congo
Costa Rica
Russia
Berlin -- 280 000 vaccinees
46 cases of polio

The Vonka strain

SPREAD OF OPV IN FAMILIES

Susceptible contacts

	Upper economic		Lower economic	
Virus	No.contacts	Infected	No.contacts	Infected
1	29	2	22	9
2	9	0	36	14
3	25	3	31	22
	63	5 (8%)	89	45 (51%)

Immune contacts

1	26	0	18	1
2	7	0	39	8
3	10	0	48	18
	43	0	105	27 (26%)

Source: Gelfand, et al. 1959

Problems with the Oral Vaccine

- Vaccine-associated paralytic poliomyelitis
- Diminished antigenicity in developing countries
- Poor heat stability

Strategies for polio eradication

- Surveillance for acute flaccid paralysis

  + Weekly reports from hospitals, rehab centers, later, all health units

  + All reported cases investigated within 48 hours by clinician and epidemiologist

  + Stool specimens collected within 14 days from all suspected cases

  + Vaccination of all children under 5 years in a defined area, usually 2000 persons

Vaccination strategies

- National Immunization Days
  - + twice each year
  - + children under 5 years
  - + during low point in season (cool period)_

- House to House Vaccination in High Risk Areas
  - + slum areas and areas reporting 1+ cases in prior 3 years

- Routine Vaccination in Health Centers

- Vaccination in Outbreak Areas

ISSUE: **Will there be fewer VAPP?**

VAPP CASES BY IPV STATES (1961-64)

NUMBER OF DOSES OF IPV

	0	1-2	3	4+	?	Total
Age 0-15	4	1	5	3	0	13
Adults	31	1	0	7	5	44
TOTAL	35	2	5	10	5	57

LANDMARKS IN POLIO VACCINE DEVELOPMENT

(1)
1949 Polio virus grown in tissue culture (Enders, Robbins, Weller)

1940s Pathogenesis of polio involves viremia (Bodian)

1948 Formalin inactivated polio induces antibody in monkeys (Morgan)

1949 Three immunological types identified (Bodian, Morgan, Howe)

1952 Humans develop antibody when given inactivated polio (Howe)

1953 Prophylactic gamma globulin protects against disease (Hammon)

1954-55 Francis field trial

1955 (April 12) Salk vaccine licensed

(2) **1955 (May) Cutter episode--262 cases**

(3) **1960 Simian virus (40) discovered in vaccine**

1952 NIH = $14 x 10^6
2 decades
rec'd > $350,000

(1) • Research on polio and, broadly, [1940's] [[?]] basic research funded thru NFIP
+ NFIP – funds in 40s larger than NIH
Run by Basil O'Connor (Roosevelt law partner)
Scientific Director – Tom Rivers –
Major unit at SHPH – joint c̄ SOM – Bodian, Howe, Morgan, Maxcy.
• Salk came on the scene rather late –
Basically: – figured out formalin inactivation curves
– did phase I/II vaccine trial.
• Salk identified by NFIP – highly effective PR office – as spokesman. & did this well.
But as a scientist not highly regarded by the broader comm.
(2) Note – ~~Short~~ time between '1945-1955 – licensed + into distribution on the same day the Francis trial results announced.
Inactivation curves a problem → less immunogenic vaccine but 90% ↓ by 1962.
(3) Simian virus – 40 – oncogenic

~~(4) Infectivity of polio ... effect on pharyngeal and fecal excretion.~~
~~Epidemiology – droplet trans. primarily oral & upper airways vs fecal oral in former~~
~~By 1965 – 90% reduction in polio incid and ... disease.~~

LANDMARKS IN POLIO VACCINE DEVELOPMENT

1962 Oral polio vaccine is licensed

+ PHS recommends neither OPV or IPV in preference to the other

+ Red Book Committee (1964)

"evaluation of the virtues and limitations of killed and live polio vaccines reveals a clearcut superiority of OPV from the point of view of ease of administration, immunogenic effect, protective capacity and potential for the eradication of polio."

① OPV Research also funded by NFIP but with increasing reluctance after 1955.
Much more difficult to attenuate the virus, to prove it was attenuated and to be certain it stayed attenuated.
SABIN – The principal figure in this effort.
Virologists, in general, favored the attenuated vaccine approach for several reasons.
(1) Intestinal immunity
(2) Specificity – longer duration of protection.
(3) Practical utility in epidemic control.
② PHS, (FDA) however, was not in a hurry to license. Why?
Cutter incident – Rejection of Salk / SG / Dir Bio. of Biol St. (a laissez-faire practice was transformed overnight into a regulatory agency)
Reversion to virulence – demonstrable but would this mean diseases.
YES! – with strains produced by Cox at Lederle.
③ Necessary for massive trials in Russia and Eastern Europe.
implications of mil making OPV took over.
② Recommendation – DPTS (advantages to both) vs. Red Book.

SPECIAL FACTORS TO BE WEIGHED

1) **Comparative duration of immunity** – theoretical vs. actual.
? any difference.

2) **Effect on patterns of transmission**

   - **Respiratory** – IPV - epidemiological effect in mild/hyperclean and indust. countries.
   - **Fecal oral**

3) **Enhanced levels of community protection** -
esp. where fecal-oral spread important.

RECOMMENDATIONS OF 1988 IOM COMMITTEE

- **The mixed eIPV/OPV program is <u>not</u> recommended if DTP and eIPV must be given separately because of cumbersome administration and greater cost.**

- **Simplicity in vaccination schedules is important because of continuing problems with inadequate immunization rates in pre-school children.**

1990-91 Pasteur Merieux detail men - all over Latin America, Europe and Asia
acquire the desirability of using their eIPV at a cost premium which was 7½ x
greater than OPV. Needless to say, the advantages of eIPV were
presented in an unwarranted favorable light and various assertions
were being offered to Ministers and others.
Difficult problem for WHO and UNICEF - Threatened the eradication effort.
Not easy to counter the many slick presentations and covered the distortions
let alone figure out what to do when you have no recourse to the
"investors"

ROAD TO ROTAVIRUS

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ISSUE: How many inoculations?

VACCINATION SCHEDULE

2 months	• Hep B	• DTP	• Hib	
4 months	• Hep B	• DTP	• Hib	
6 months	• Hep B	• DTP		
12-15 months		• DTP	• Hib	• MMR