

Polio Vaccine Policy & Evaluation

26 FEB 1997

^{in vac. develop.}

Course is intended to illuminate policy issues and provide to you some sense as to how ~~policy~~ ^{policy} issues ^{are} developed and resolved.

Profrax - work about policy formulation + policy offices -

During 3 yrs. as VP - perception of a mystique about the process.

Working com. → draft policy document / options / pros + cons → recs. ^{cost-benefit analysis, 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 prejudices, ^{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.

(~~DATA~~ 1955 IPV lic.; ^{Chif. Dir.} 60's c lic. of OPV; est ACIP;

launched EPI; 85 → VAD; 88-91 Clin. Glob. Cons. to Poli Erad.)

Polio - bx of disease curions

1st epidemic in 1890's - few 100 cases

1916 27,000 cases / 6,000 deaths in U.S. - Canadian border closed

Some outbreaks in 20's and 30's

Paralysis of FDP - ^{Proxy for} ~~low incidence~~ ^{tomorrow balls}

Arg. by FDP had partners.

Green into the NFIP (1938) R & rehab. of polio cases - A unique foundation.

^{Policy} Decision to support ~~basic~~ ^{basic} desires which might result in a vaccine.

REMARKABLE POLICY ! ~~Support~~ ^{Support} ~~of~~ ^{of} ~~the~~ ^{the} ~~policy~~ ^{policy}

(like now)

reactors

1944, Polio ^{incidence} sharply increased <10,000 cases to 25,000 to 30,000
Enormous concern - ~~not as large but many~~ victims in their teens and 20's
- ~~not restricted~~ to the poor - many cases, esp. older in SE.

govt. - no money to play.
Health comm. & stock market

Movie theaters, pools, schools.

NFIP Resources ↑ and research ↑ (note: NIH resources 1940s)
~~Small~~ centers funded - 60

OVERHEAD

- 1) Harvard - Enders, Ribbin, Weller 1949 - (Noted 1954)
- 2) Hopkins (SHPH) Others: Yale, Cincinnati, Pittsburgh, New Orleans, Toronto.
- 3) Pittsburgh. - Green stools. [Salk began work in 1952]

NFIP policy - need to raise funds - get a respectable young scientist - Jonas did a good job representing the foundation & doing phases I and II trials.
(NOTE: PATENTING THE VACCINE)

Mar 53
Dec 1953

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.

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

NFIP - wanted the vaccine ad fast. (57,000 cases in 50)

All agreed a trial was needed - Jonas argued vs. "control" trial - unethical
State epidemiologists provided 1 who made the vaccine one year
449,000 placebo controlled trial. 1,000,000 shared control.

Code broken in April 12th 1955 - licensed the same day / vac. began the fl. work.

Within 10 days - cases ^{July} began to occur in vaccinees. - GOVT. INVOLVED FOR FIRST TIME

OVERHEAD

Cotton incident. - the inactivation curve.

- + Dir DPHS / SGE / Society.
- + CDC Surveillance.

Echo 1936 - Parvovirus

"Panic" "? loss of faith in vaccine" "? eroded public trust (Lemon for PSE)

New policy - test every batch
& in potency of IPV.

M. Simon: Who owns the patent?
Chick: There is no patent.
Could you patent the gene?

licensed in 1962 & considerable success

OVERSEAS - P&S

S.O.S. program - broke the private
within 1 year -

limited

23 cases -

~~Access~~ & Availability - special
Rural

cc

Problems to the vaccine:

①

- Nupth ⁸³ -

- Piter -

②

- 0

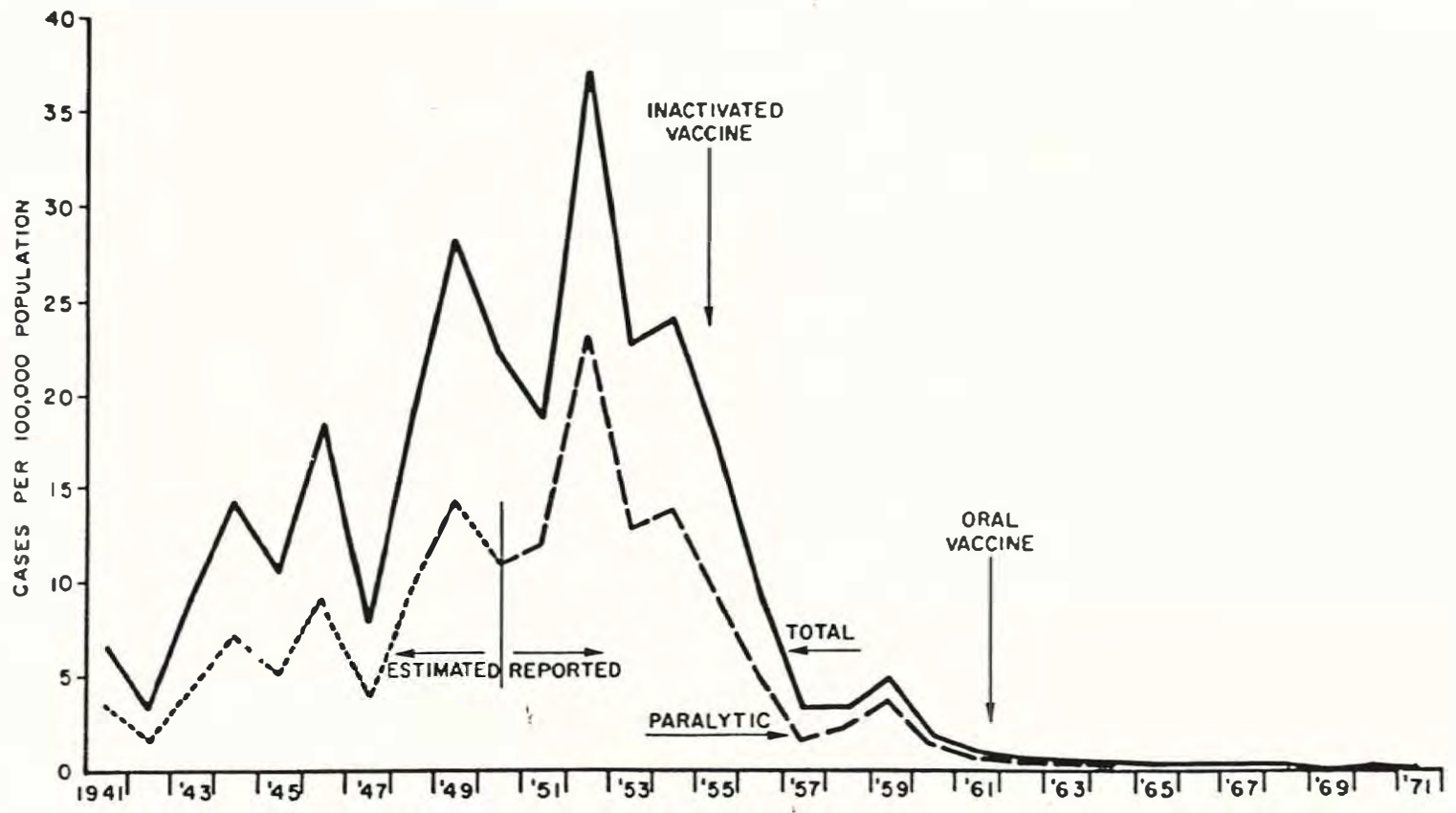
WAD - cold chain

(chick & milk a better regulator)

1974 EPI - 5 to 20%
1983 UNICEF - Rotary International -
~~in America~~

1988 Decision for polio eradication.
Strategy - ↑ vac. to 80%⁺ → WID (Cuba/Brazil)
- SURVEILLANCE + lab. confirmation.
↓ 500 hospitals. - weekly report → 20,000
Cases of Type III polio.
- CONTAINMENT - (different than epid).
→ - "Mapping up" ^{"high risk areas"} derived from epid. experience.
~~1988~~ - Difficult time for the CDC S.P. Director -

IVP Problem runs its head yet again -
eIFV developed Mammals Caught.



CUTTER INCIDENT 1955

Cause --The inactivation curve

Morbidity

260 cases : 192 paralytic

Vaccinees . 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

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

Immune contacts

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

Source: Gelfand, et al. 1959

Problems with the Oral Vaccine

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

Strategies for polio eradication

- o 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

- o National Immunization Days**

- + twice each year**

- + children under 5 years**

- + during low point in season (cool period)_**

- o House to House Vaccination in High Risk Areas**

- + slum areas and areas reporting 1+ cases in
prior 3 years**

- o Routine Vaccination in Health Centers**

- o Vaccination in Outbreak Areas**

ISSUE: Will there be fewer VAPP?

VAPP CASES BY IPV STATES (1961-64)

NUMBER OF DOSES OF IPV

	<u>0</u>	<u>1-2</u>	<u>3</u>	<u>4+</u>	<u>?</u>	<u>Total</u>
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

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

1955 (May) Cutter episode--262 cases

1960 Simian virus (40) discovered in vaccine

1952 NIH = \$14 x 10⁶
Roadside
rec'd > \$500,000

- ① ^{44's} Research on polio and, broadly, ^{rel.} basic research funded thro 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 - SOM - Bodian, Howe, Morgan, Maxcy.

o Salk came on the scene rather late -
Basically: - figured out formalin inactivation curves
- did phase I/II vaccine trial.

o 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
Inactivation curves a problem → less immunogenic vaccine but 90% by 1962. The Francis trial results announced.
 - ③ Simian virus - 40 - oncogenic
- ④ ~~Effect on pharyngeal and fecal excretion~~
~~Epidemiology~~ - droplet trans. primarily used at upper classes vs fecal-oral in poorer.
By 1960s - 50% reduction in polio cases 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 ser. vacines.

① Intestinal immunity

② Speculatively - longer duration of protection.

③ Practical utility in epidemic control.

② PHS ^(FDA) however, was not in a hurry to license. Why?

Cultor incident - Benjamin of Tech/SG/Dir. Div. of Biol. St. (a liaison-fairly quiet) was transferred overnight into a regulatory agency)

Reversion to virulence - demonstrable but ~~these~~ would this mean less access.

YES! - with strains produced by Cox at bedside.

③ because of massive outbreaks in Russia and Eastern Europe.

② Possibility of reversion - DOTS (advantages to both) vs. Red Book. implications of not making one were different. OPV had one

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 middle/higher class
and indus. countries.*
 - **Fecal oral**
- 3) **Enhanced levels of community protection** -
ex. where fecal-oral spread important.

RECOMMENDATIONS OF 1988 IOM COMMITTEE

- The mixed eIPV/OPV program is not 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
arguing the desirability of using their eIPV at a cost per dose which was ~~75~~⁷⁵ x
greater than OPV. Needless to say, the advantages of eIPV were
presented in an unimpaired, favorable light and various sweeteners
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
"sweeteners".

READ RECOMMENDATIONS

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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