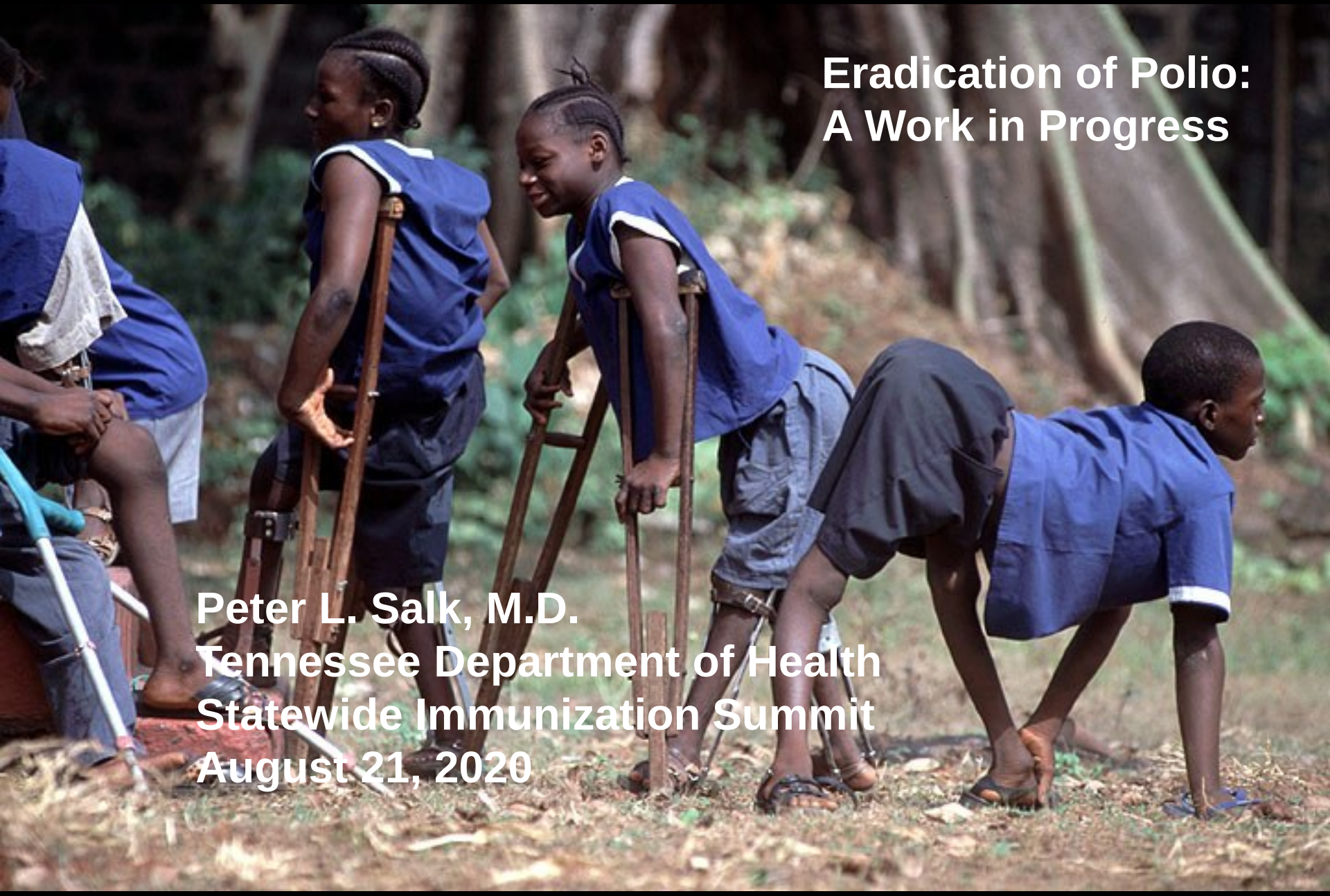
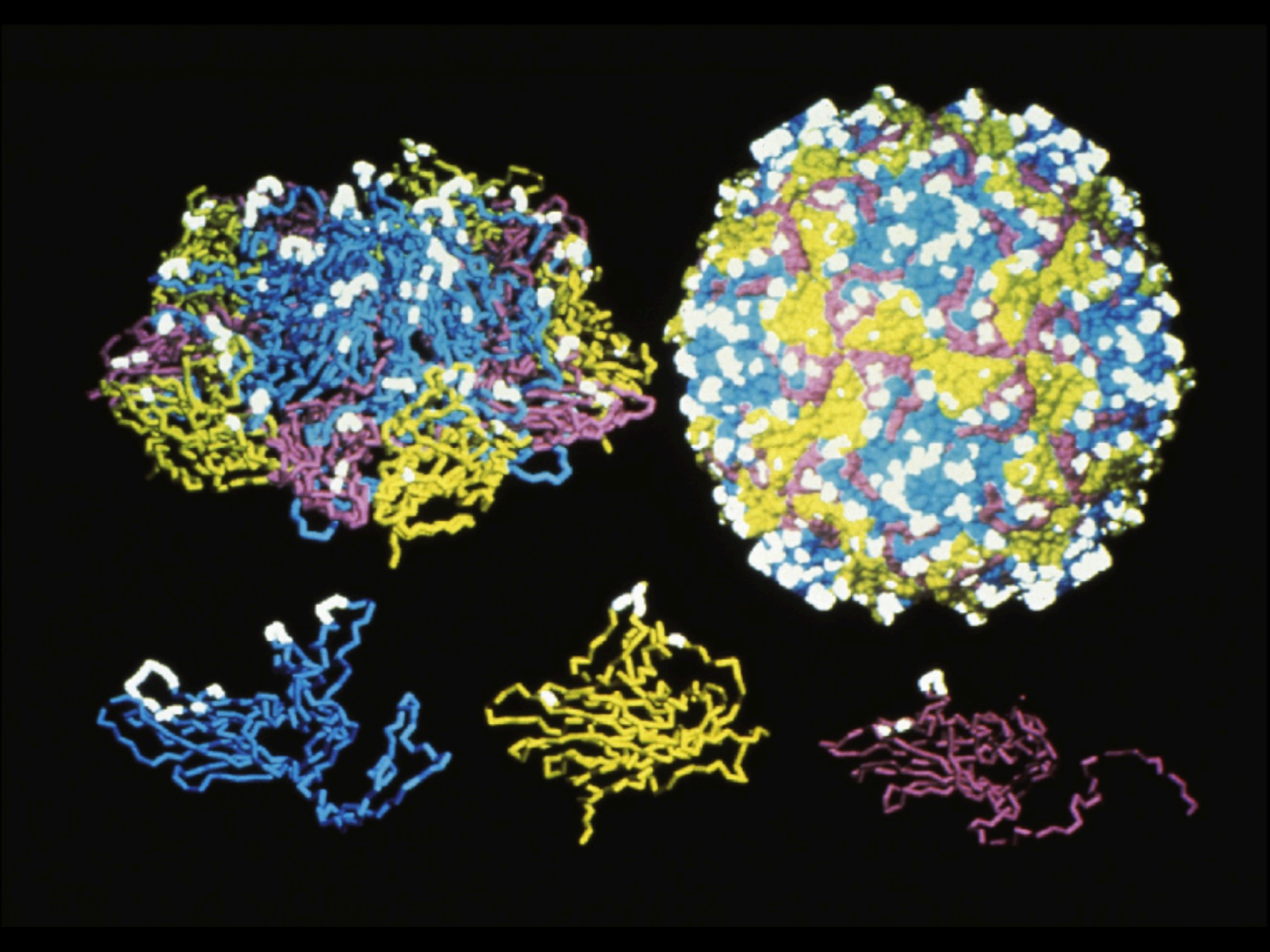


Eradication of Polio: A Work in Progress

Peter L. Salk, M.D.
Tennessee Department of Health
Statewide Immunization Summit
August 21, 2020



Poliovirus Characteristics (1)

- Enterovirus (genus) / Picornavirus (family)
- Nonenveloped; icosahedral symmetry; 30 nm
- Single-stranded, positive-sense RNA genome (c. 7,500 nucleotides)
- 3 antigenic types (serotypes 1, 2 and 3)
- 60 copies each of 4 capsid proteins: VP1, VP2, VP3, VP4
- Attaches to and enters cells via glycoprotein receptor (PVR, CD155)

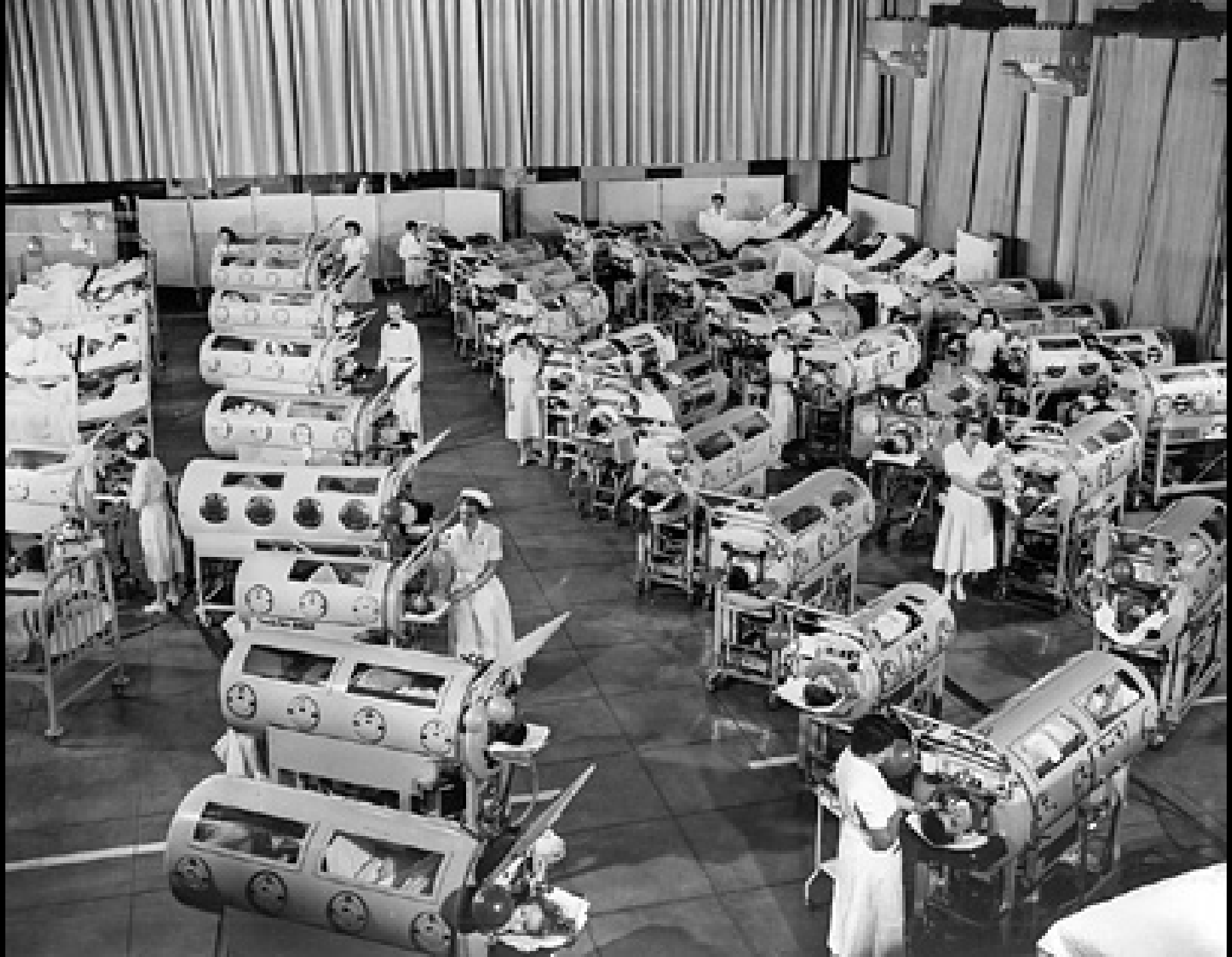
Poliovirus Characteristics (2)

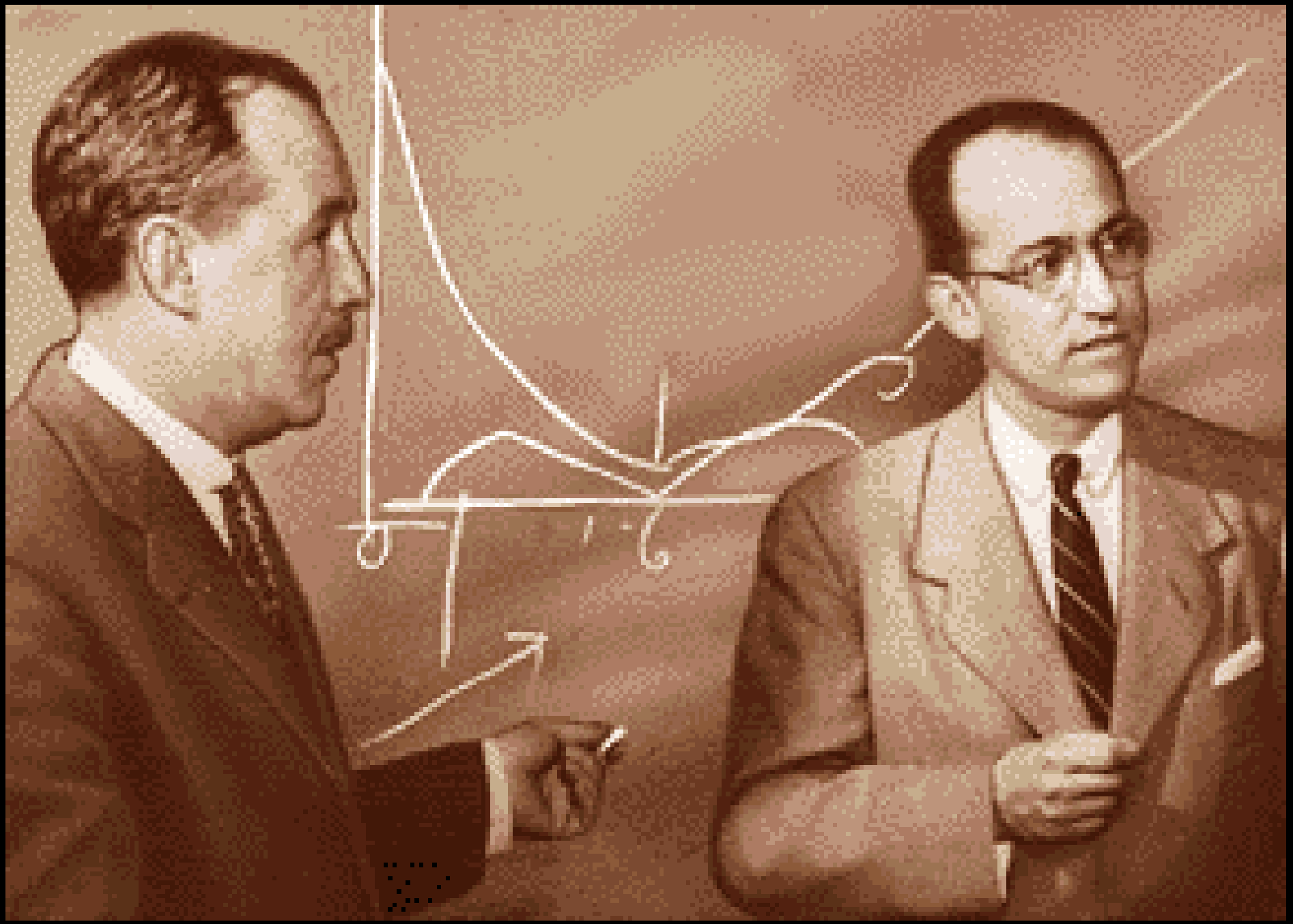
- Oral entry
- Replication in oropharynx, intestines and draining lymph nodes
- Enters bloodstream and can spread to CNS
- Excreted in feces
- Humans are the only reservoir

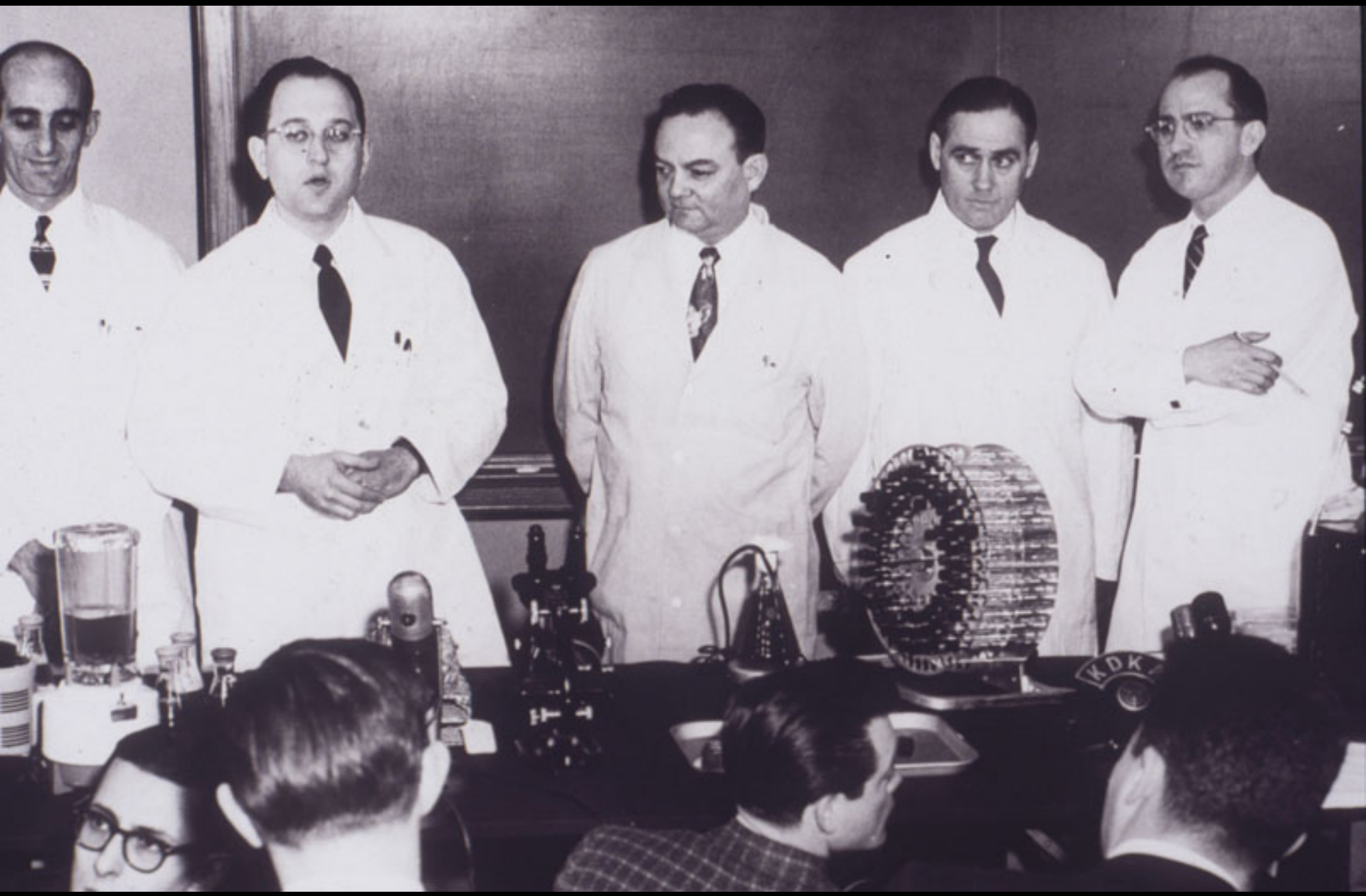
Clinical Course

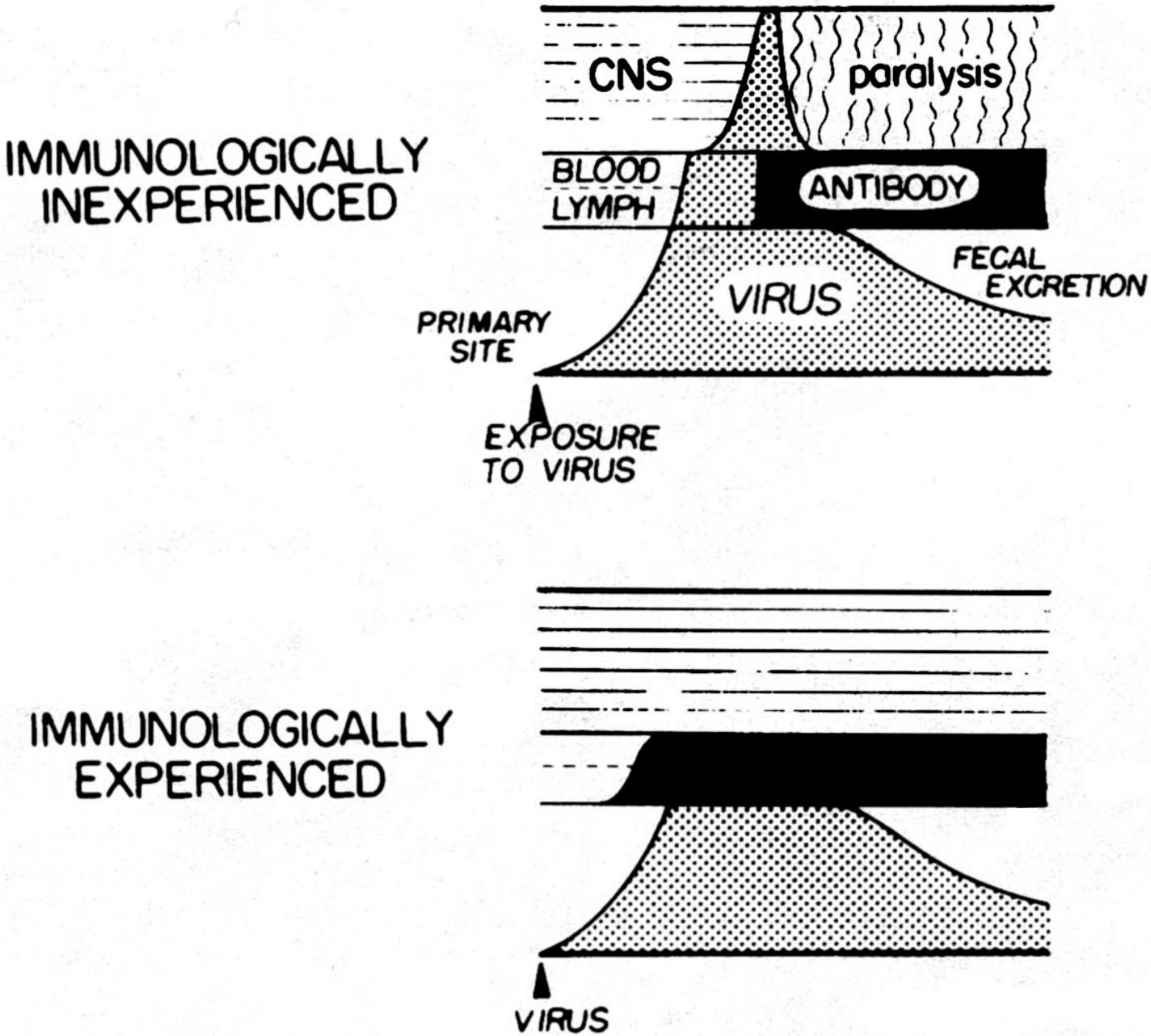
- Only 1 in 100-200 infected individuals become paralyzed
  - Inapparent infection (72%)
  - Minor illness (e.g., fever, malaise, headache, nausea, vomiting) (24%)
  - Nonparalytic polio (aseptic meningitis) (4%)
  - Paralytic polio (<1%) (minor illness, symptom-free 1-3 days, then rapid onset of fever and flaccid paralysis)

- Supportive treatment
- Physical therapy, bracing, orthopedic surgery
- Recovery of function in some
- Postpolio syndrome (25-40%)






KDK


IMMUNOLOGICALLY INEXPERIENCED
CNS
paralysis
BLOOD
LYMPH
ANTIBODY
FECAL EXCRETION
VIRUS
PRIMARY SITE
EXPOSURE TO VIRUS
IMMUNOLOGICALLY EXPERIENCED
VIRUS

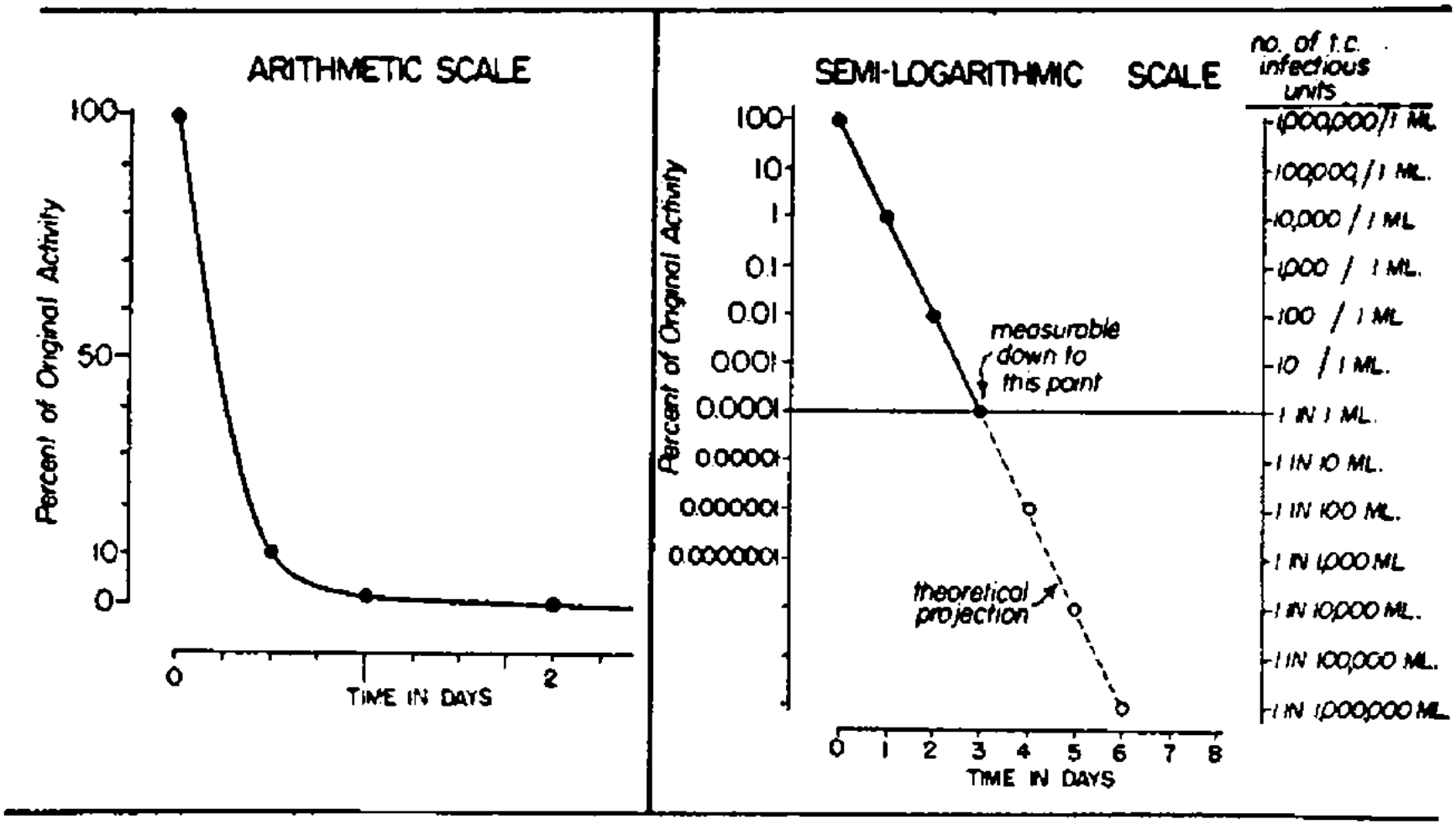
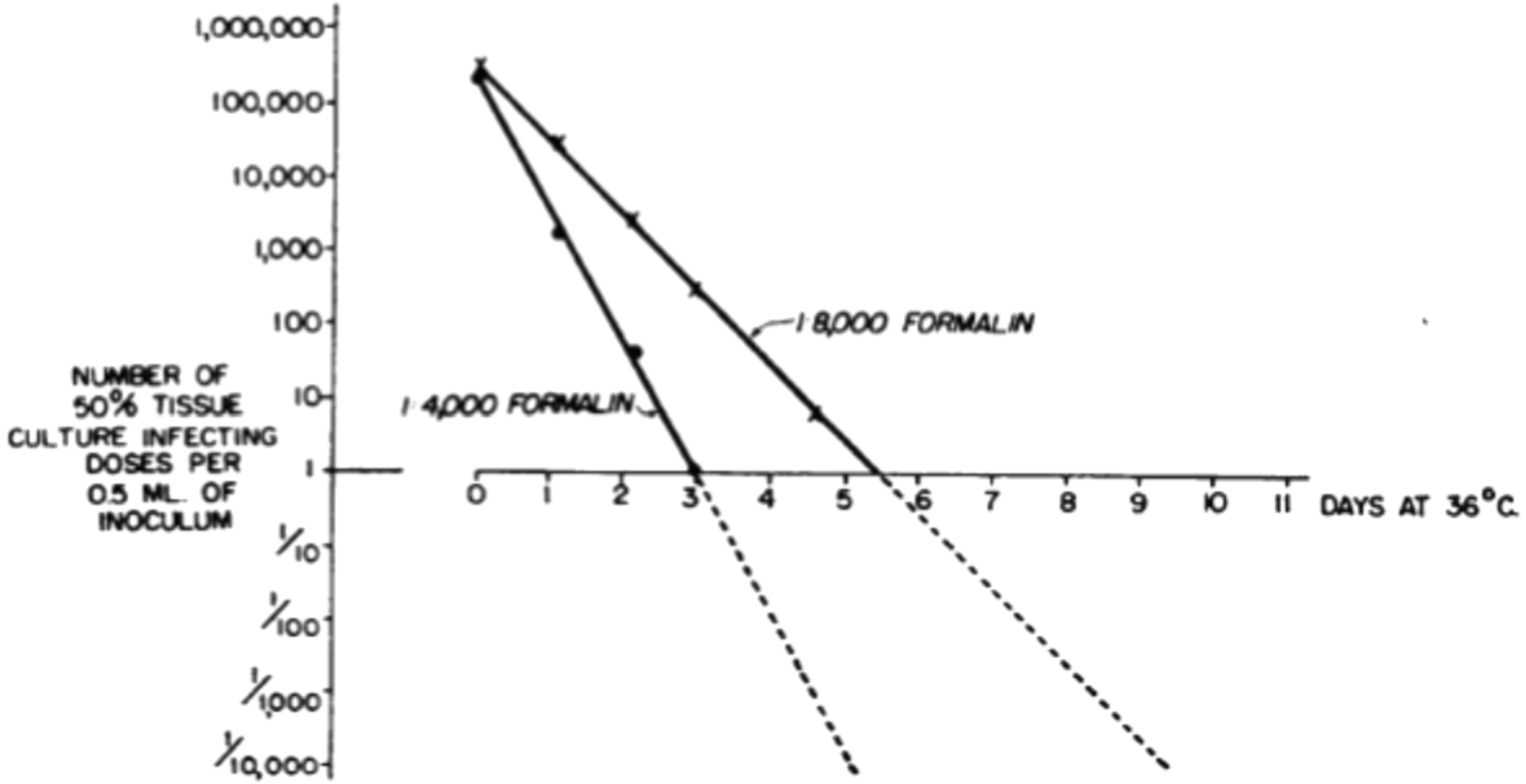
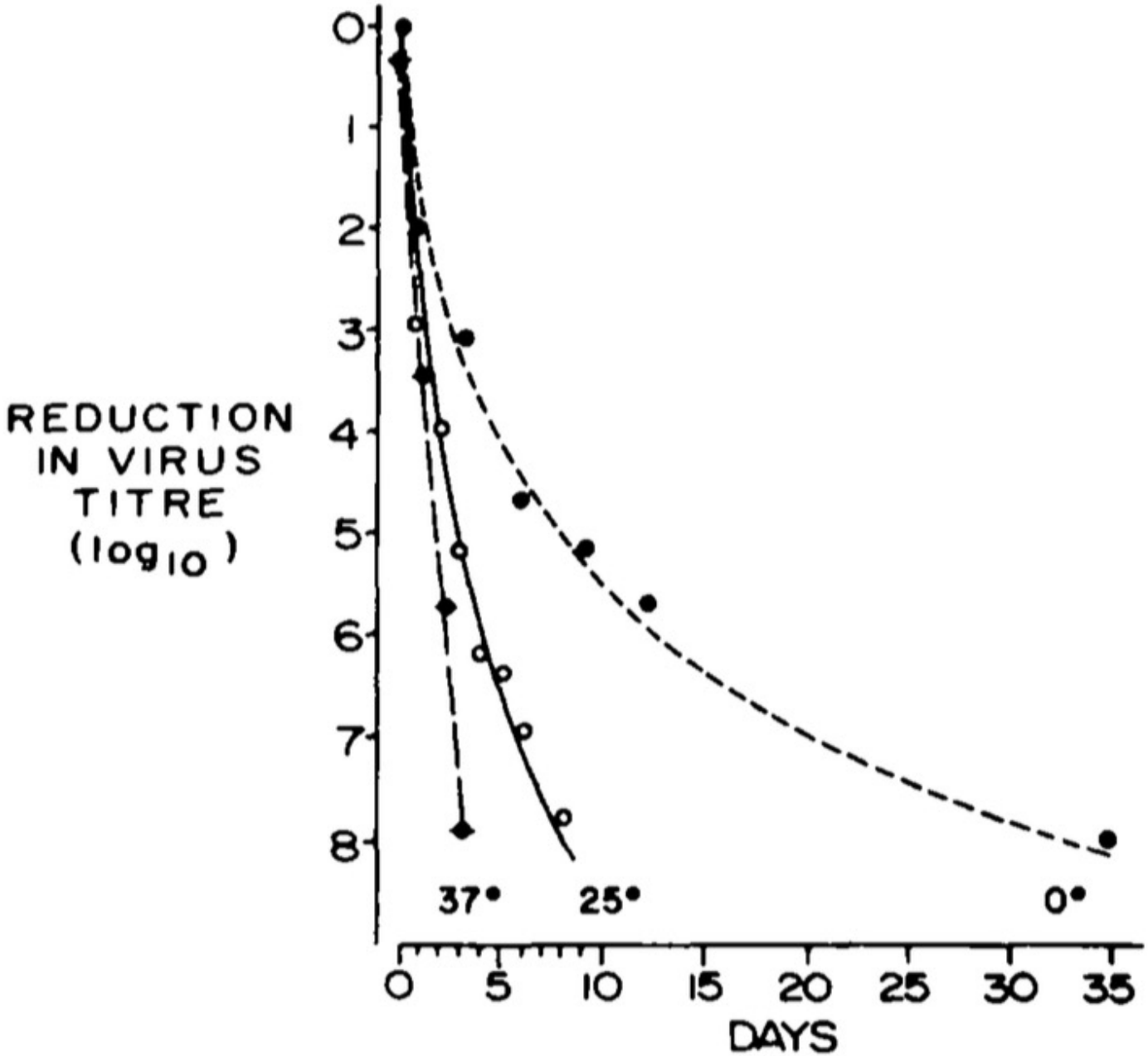


Fig. 1.—Rate of destruction of poliomyelitis virus infectivity at 37 C in presence of 1:4,000 formaldehyde solution (Formalin) at pH 7.


1,000,000
100,000
10,000
1,000
100
10
1
1/10
1/100
1/1,000
1/10,000
NUMBER OF 50% TISSUE CULTURE INFECTING DOSES PER 0.5 ML. OF INOCULUM
1:8,000 FORMALIN
1:4,000 FORMALIN
0
1
2
3
4
5
6
7
8
9
10
11
DAYS AT 36°C.


REDUCTION IN VIRUS TITRE (log_{10})
0
1
2
3
4
5
6
7
8
37°
25°
0°
0
5
10
15
20
25
30
35
DAYS

RX R-099 TYPE Mahoney DATE 4-15-
BULK FORMALIN RATE TEST
TIME: 14 HRS.
RX R-099 TYPE Mahoney DATE 4-15-
BULK FORMALIN RATE TEST
TIME: 25½ HRS.
RX R-099 TYPE Mahoney DATE 4-
BULK FORMALIN RATE TEST
TIME: 38 HRS.
RX R-099 TYPE Mahoney DATE
BULK FORMALIN RATE
TIME: 45½ HRS.

Vaccine A Pool
T89 T87 T90
1:4000 Form./Neut.
2xF.G.Fil
500cc
17 Dec 54
#2
Vaccine A Pool
T89 T87 T90
1:4000 Form/Neut.
2xF.G.Fil
500cc
17 Dec 54
#5
Vaccine A Pool
T89 T87 T90
1:4000 Form/Neut.
2xF.G.Fil
500cc
17 Dec 54
#7
Vaccine A Pool
T89 T87 T90
1:4000 Form/Neut.
2xF.G.Filtered
500cc
17Dec54
#3

THE NATIONAL FOUNDATION FOR INFANTILE PARALYSIS

CERTIFIES THAT

Helen Wright

HAS BEEN ENROLLED AS A

POLIO PIONEER

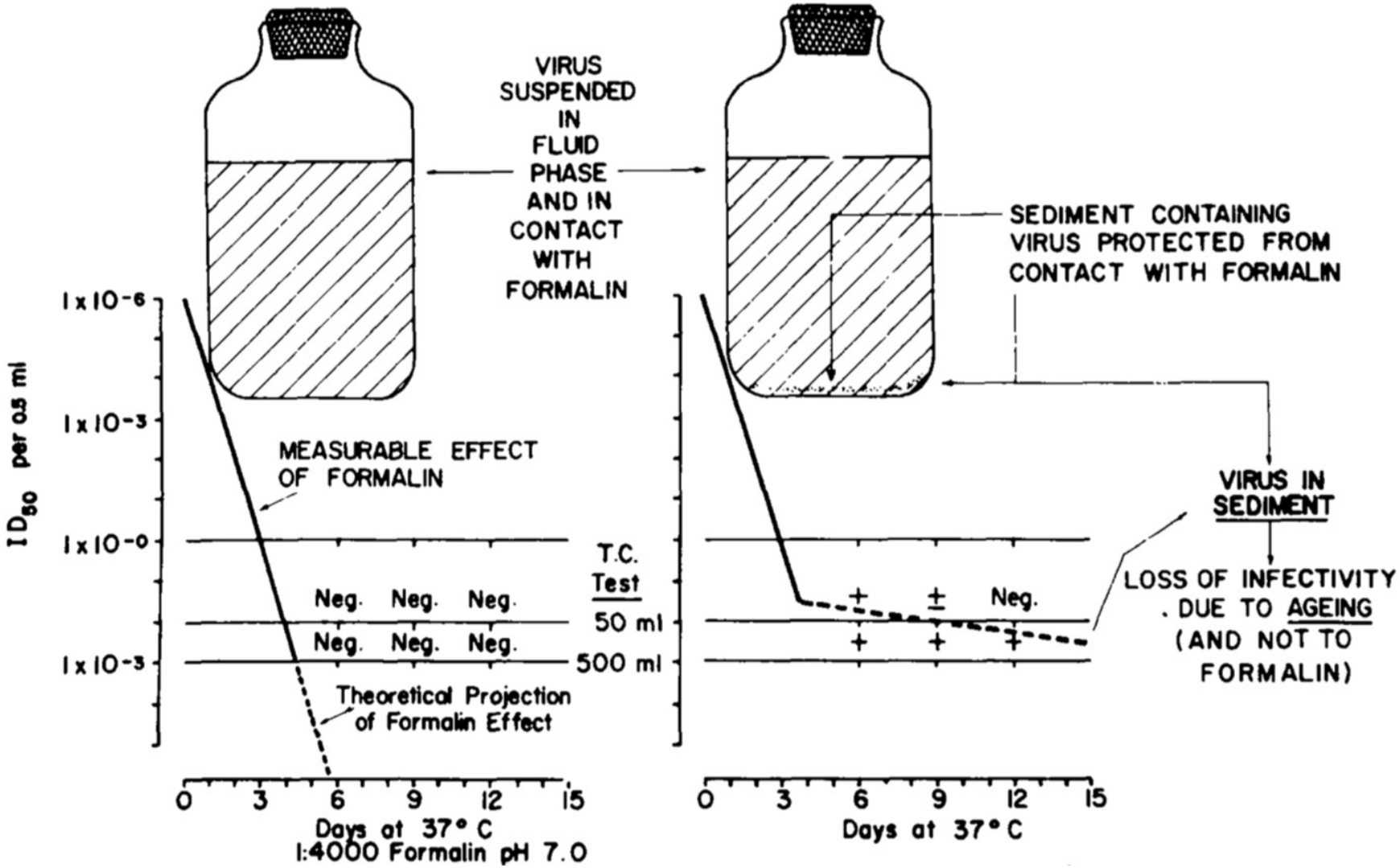
and this certificate of membership is
hereby presented for taking part in the first national tests
of a trial polio vaccine conducted during 1954.

Basil O'Connor PRESIDENT

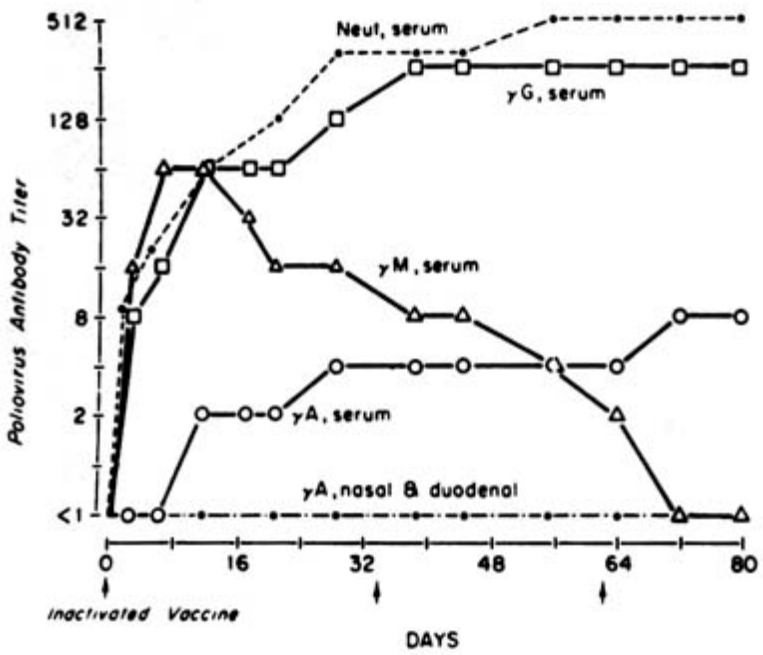
THE Cutter Incident

HOW AMERICA'S FIRST POLIO VACCINE LED TO THE GROWING VACCINE CRISIS

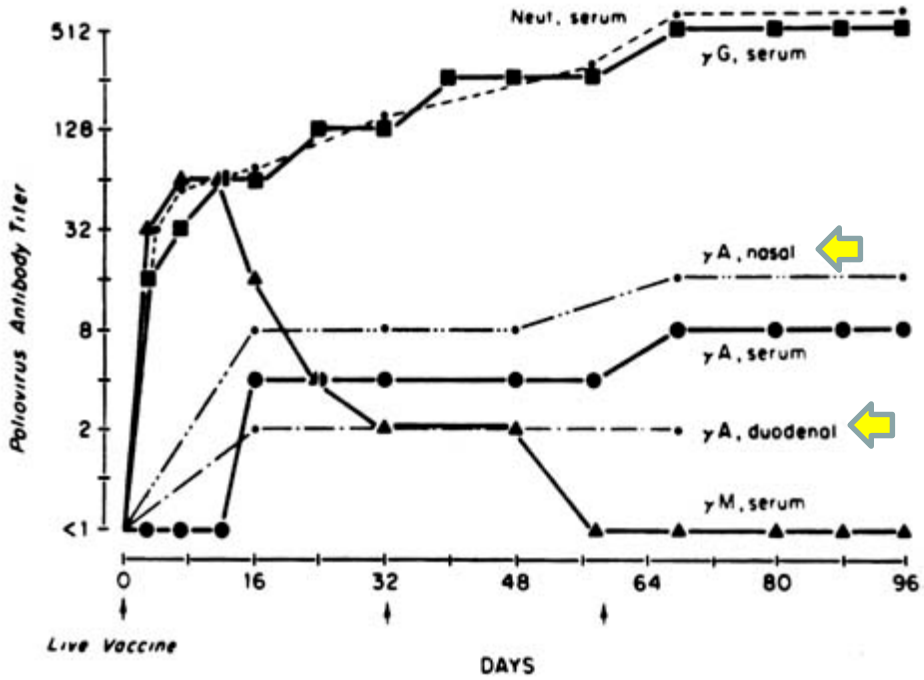
Paul Offit, M.D.


VIRUS SUSPENDED IN FLUID PHASE AND IN CONTACT WITH FORMALIN
SEDIMENT CONTAINING VIRUS PROTECTED FROM CONTACT WITH FORMALIN
ID_{50} per 0.5 ml
1 x 10-6
1 x 10-3
1 x 10-0
1 x 10-3
MEASURABLE EFFECT OF FORMALIN
Neg. Neg. Neg.
Neg. Neg. Neg.
Theoretical Projection of Formalin Effect
T.C. Test
50 ml
500 ml
+ ± Neg.
+ + +
VIRUS IN SEDIMENT
LOSS OF INFECTIVITY DUE TO AGEING (AND NOT TO FORMALIN)
0 3 6 9 12 15
Days at 37° C
1:4000 Formalin pH 7.0
0 3 6 9 12 15
Days at 37° C

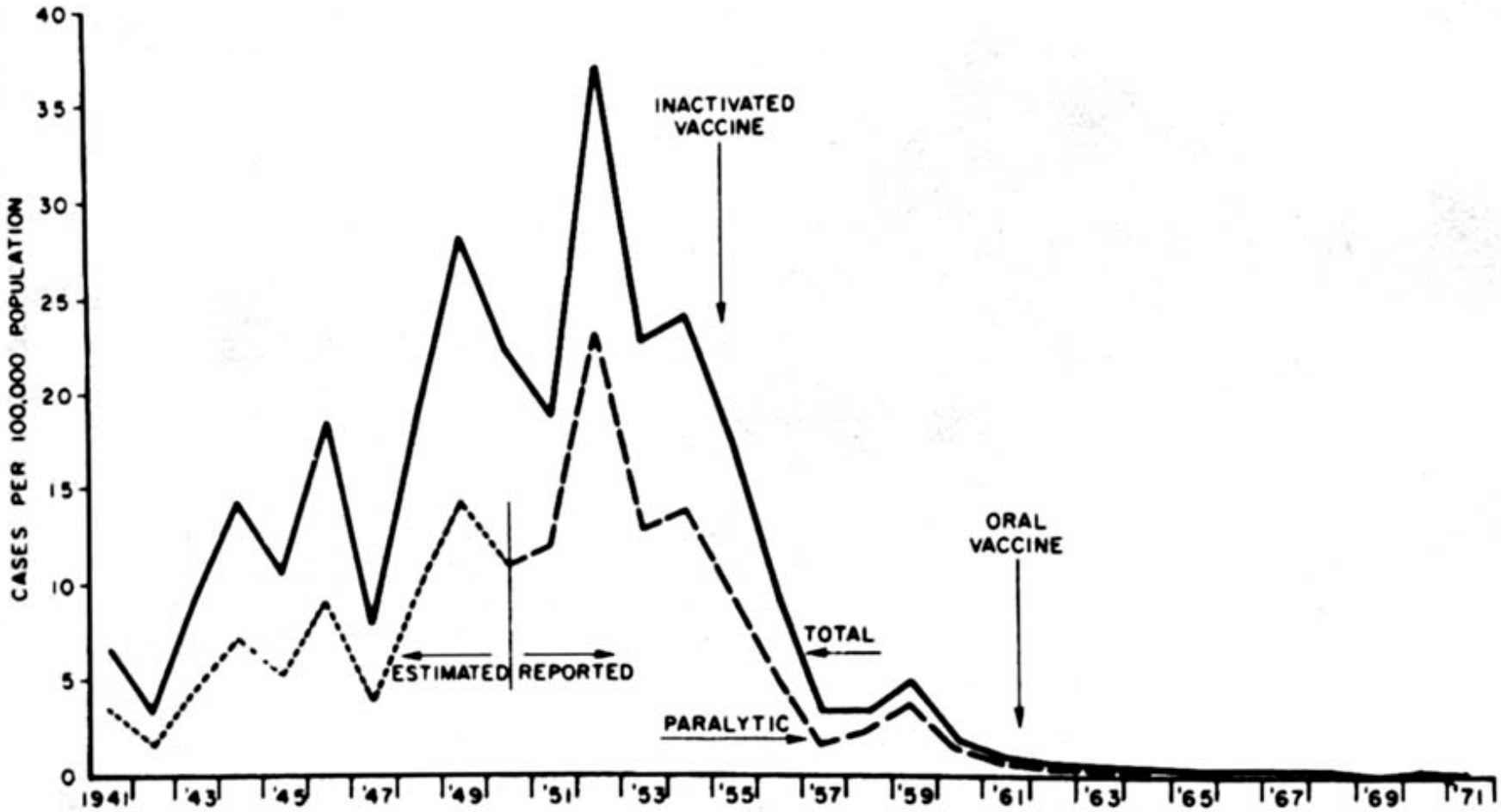
Inactivated Poliovirus Vaccine



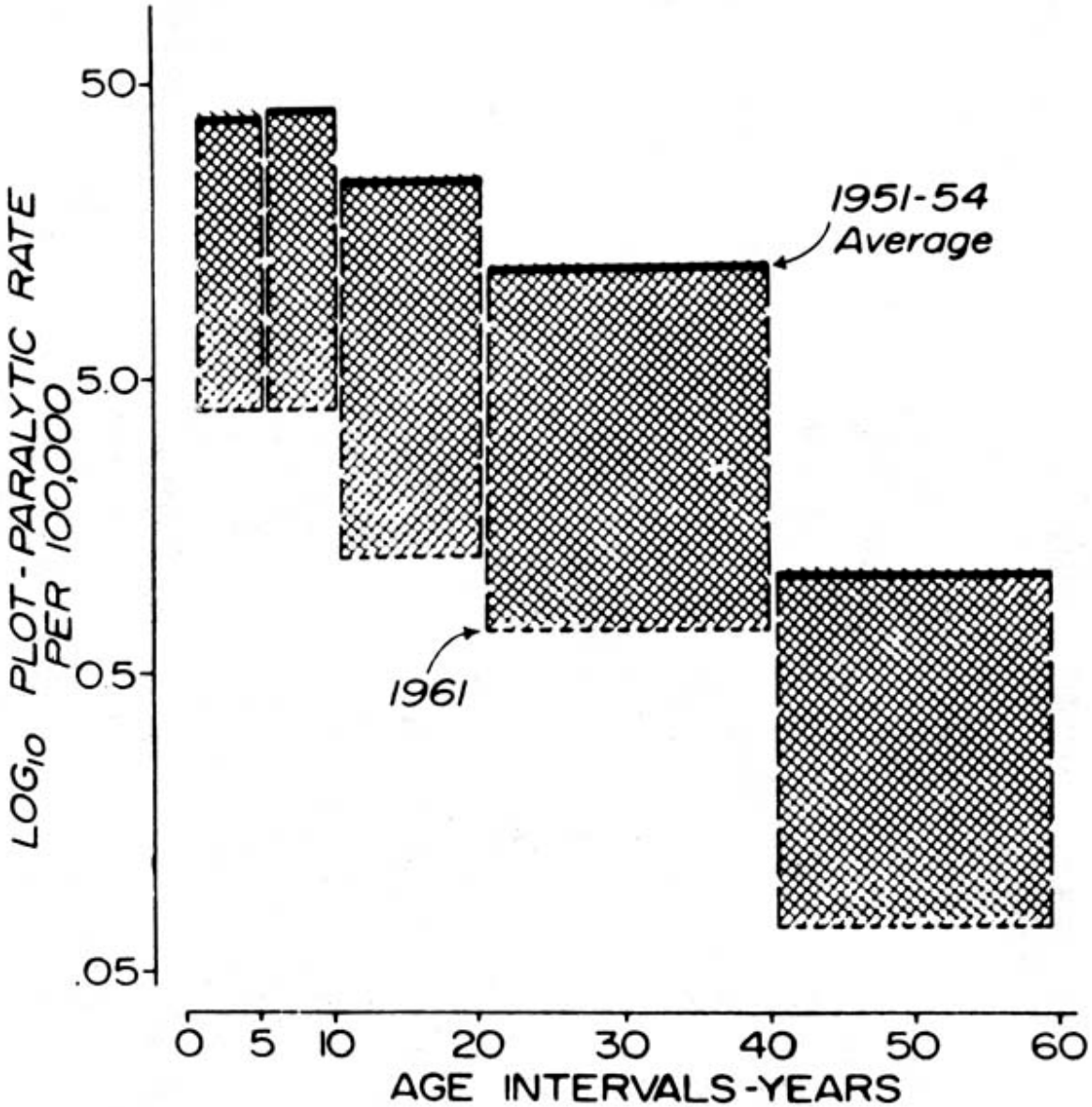
Live Poliovirus Vaccine

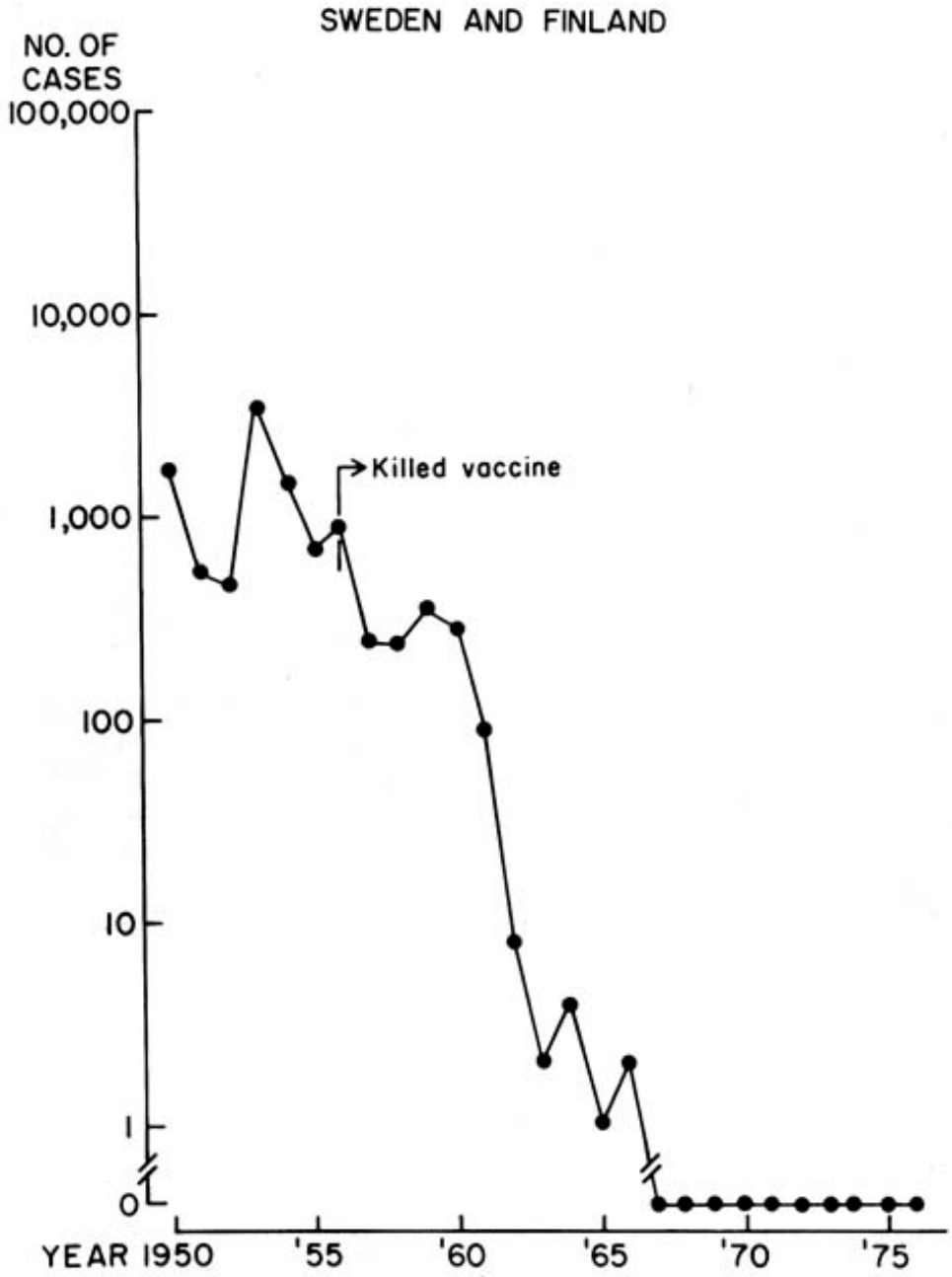


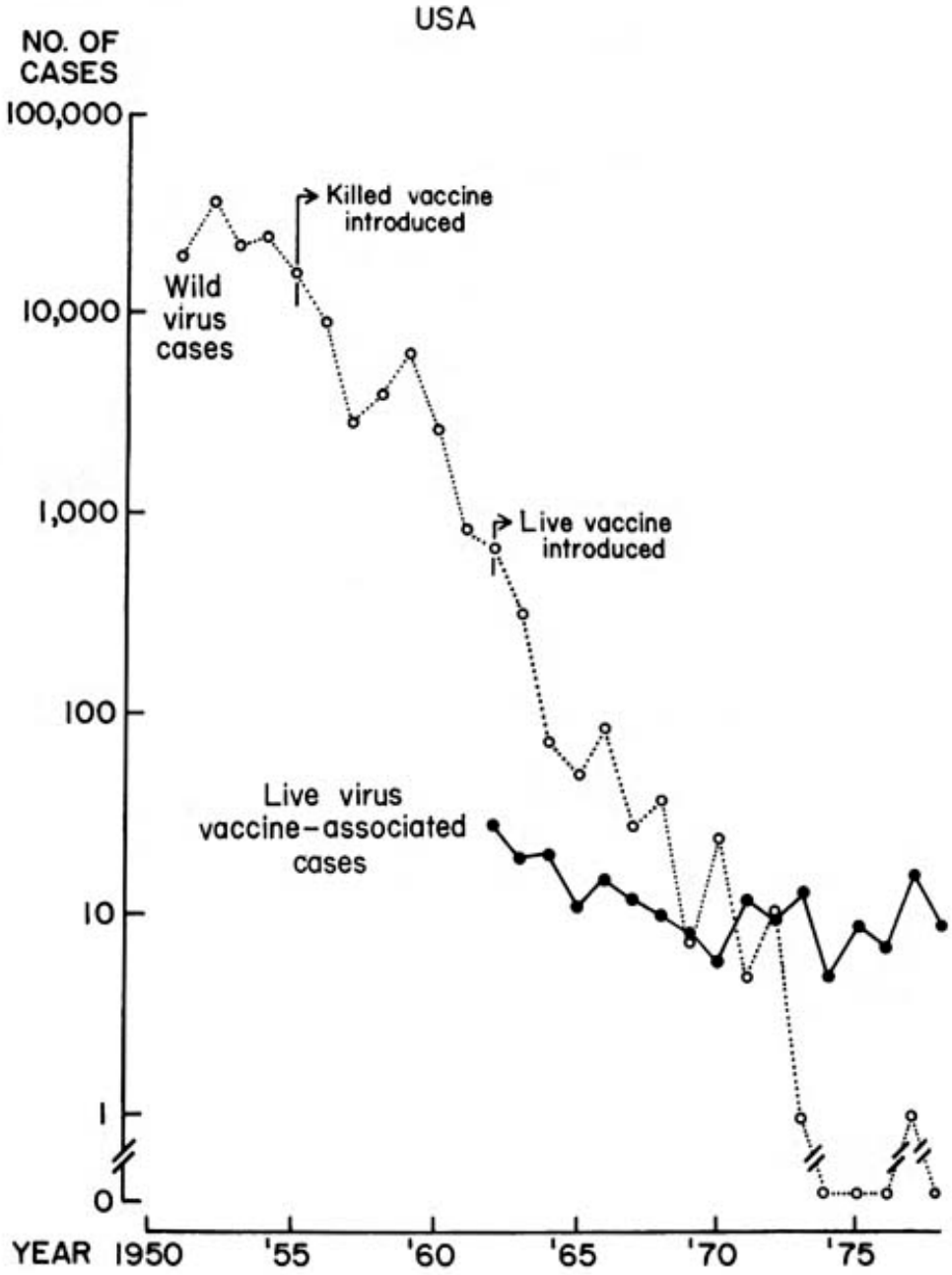
PL Ogra et al., NEJM 1968 (per D Salk & J Salk, Vaccine 1984)


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

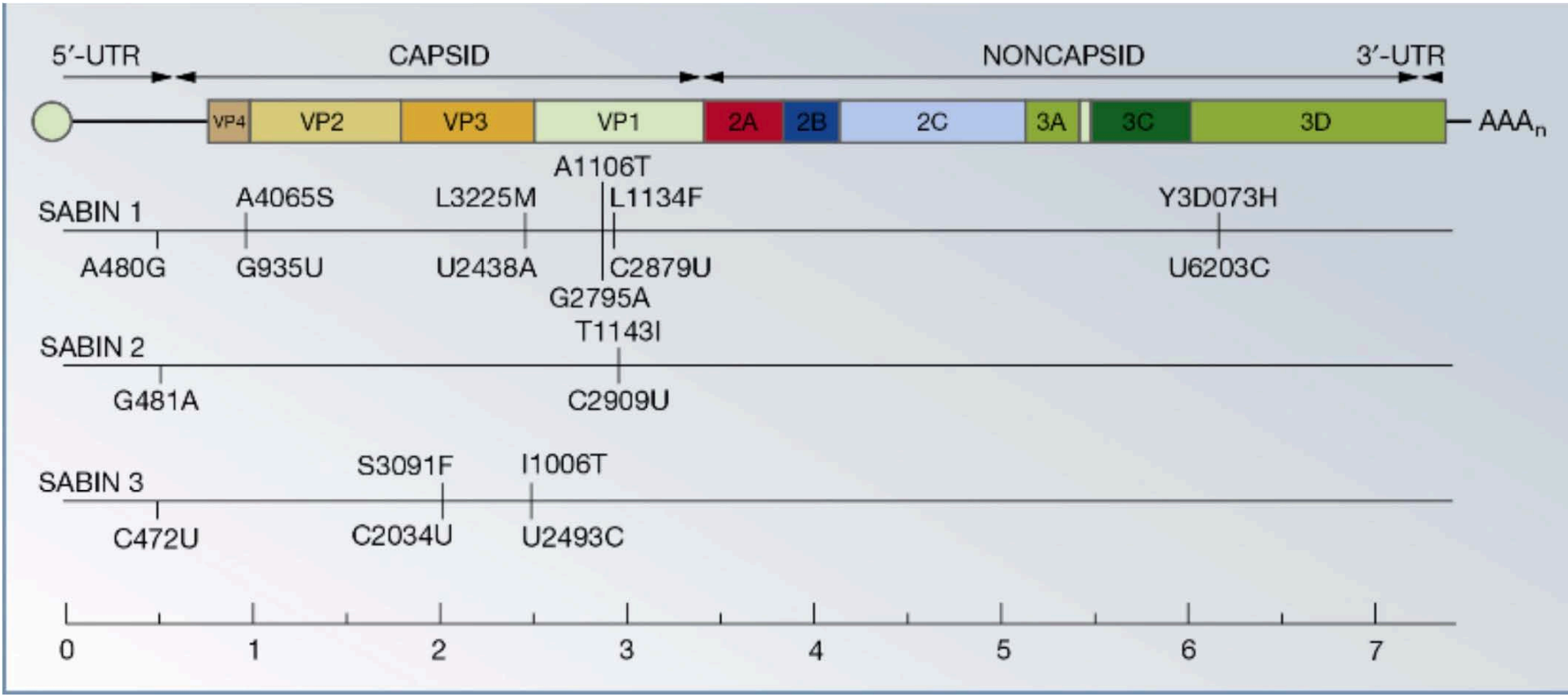
Herd Effect of Inactivated Poliomyelitis Vaccine: Attack rates in unvaccinated individuals




SWEDEN AND FINLAND
NO. OF CASES
100,000
10,000
1,000
100
10
1
0
Killed vaccine
YEAR 1950
'55
'60
'65
'70
'75


USA
NO. OF CASES
100,000
10,000
1,000
100
10
1
0
Killed vaccine introduced
Wild virus cases
Live vaccine introduced
Live virus vaccine-associated cases
YEAR 1950
'55
'60
'65
'70
'75

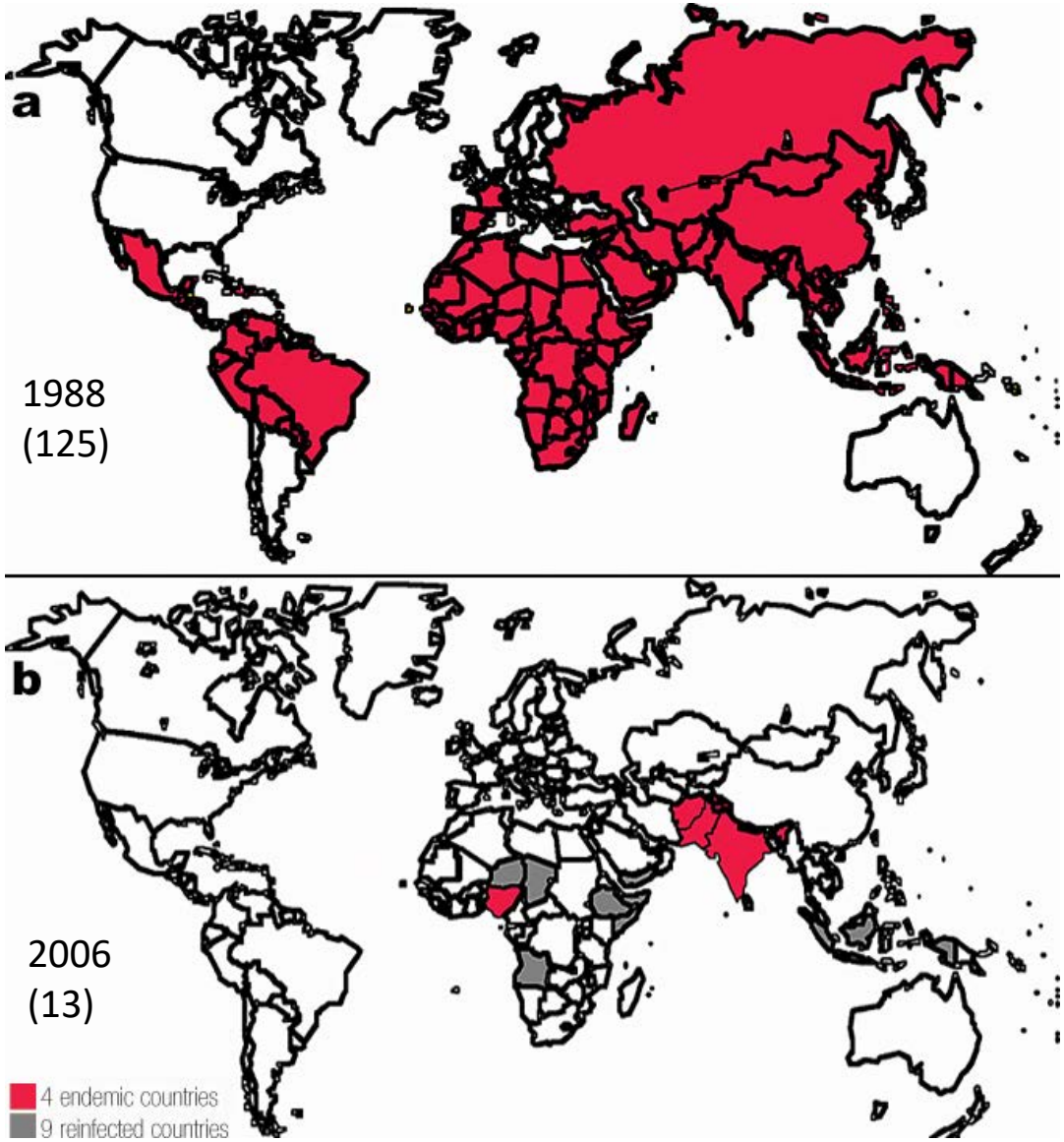
Attenuating Mutations in Sabin OPV Strains

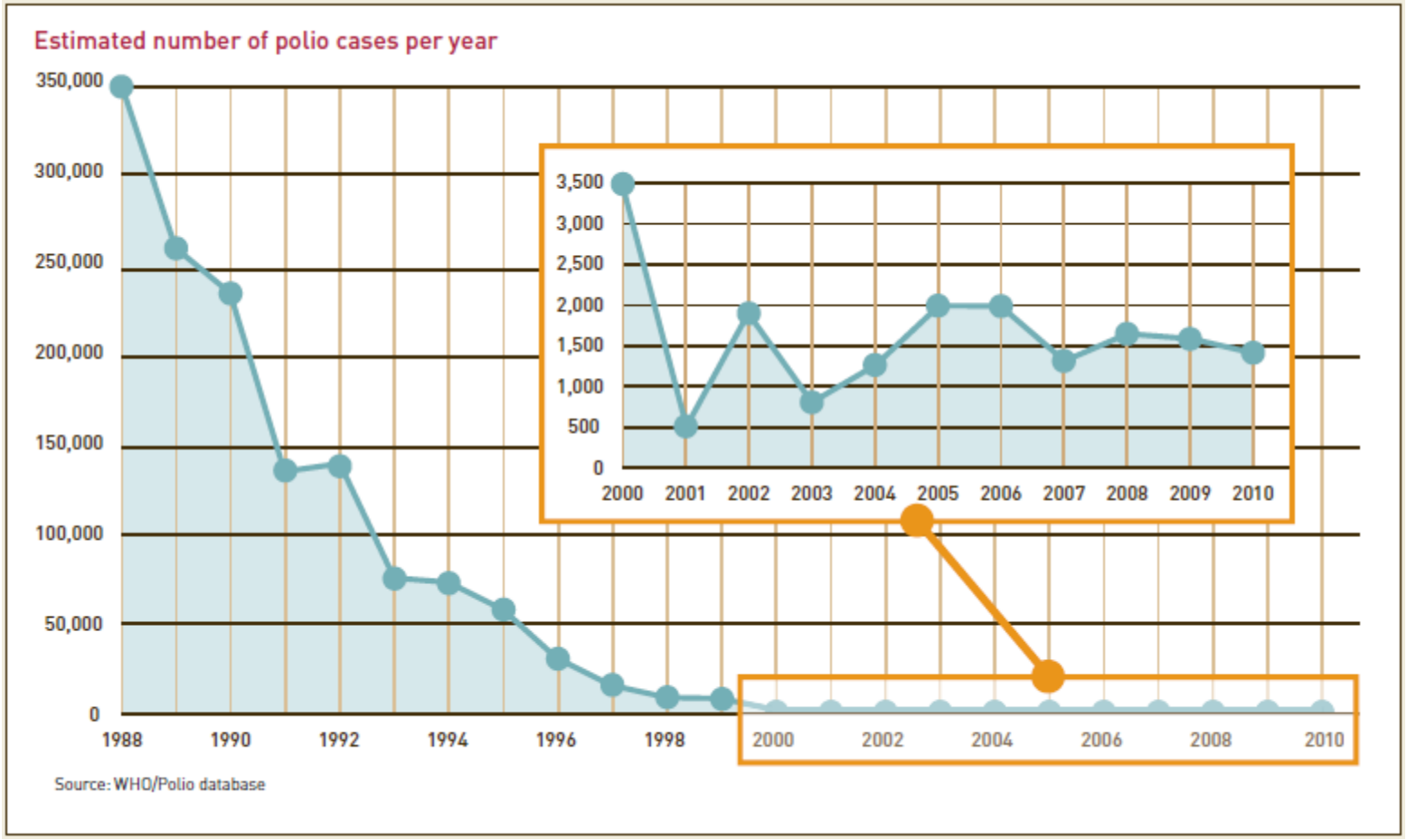


Upper entries = amino acid substitutions
Lower entries = nucleotide substitutions

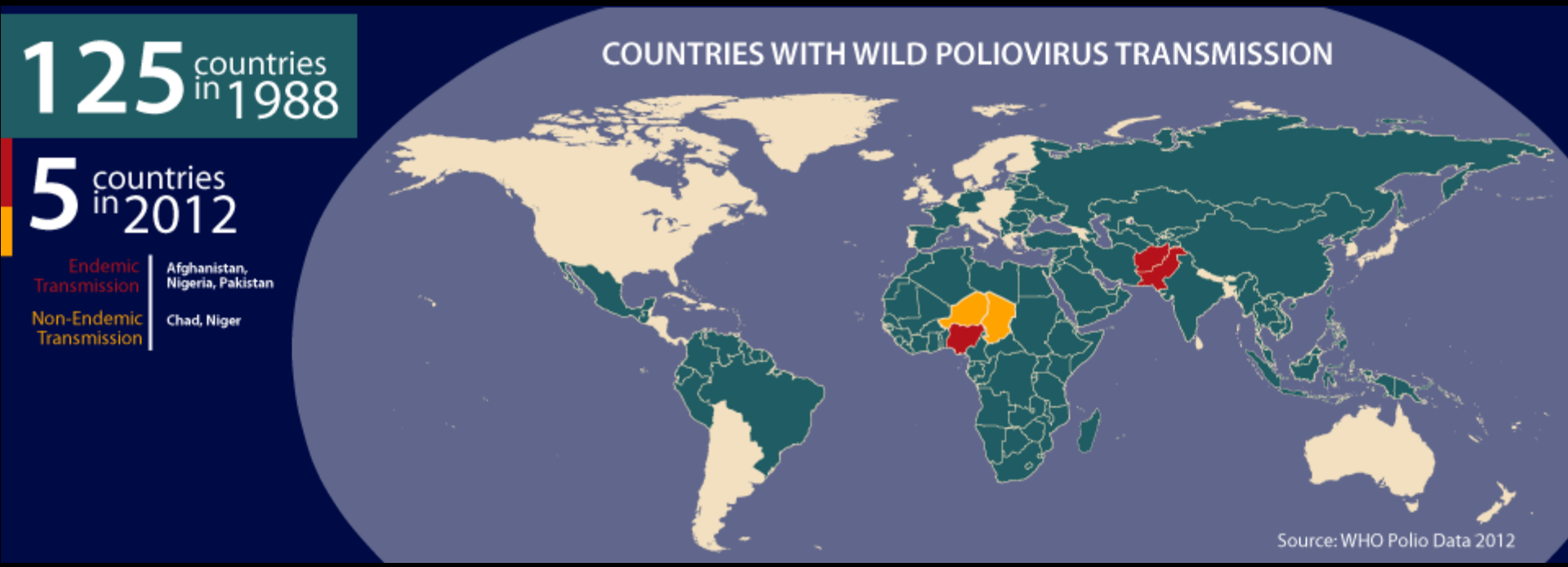
Sutter, Kew, Cochi, Aylward: Vaccines 6th Ed. 2013

Countries with Naturally-Occurring Polio: 1988-2006

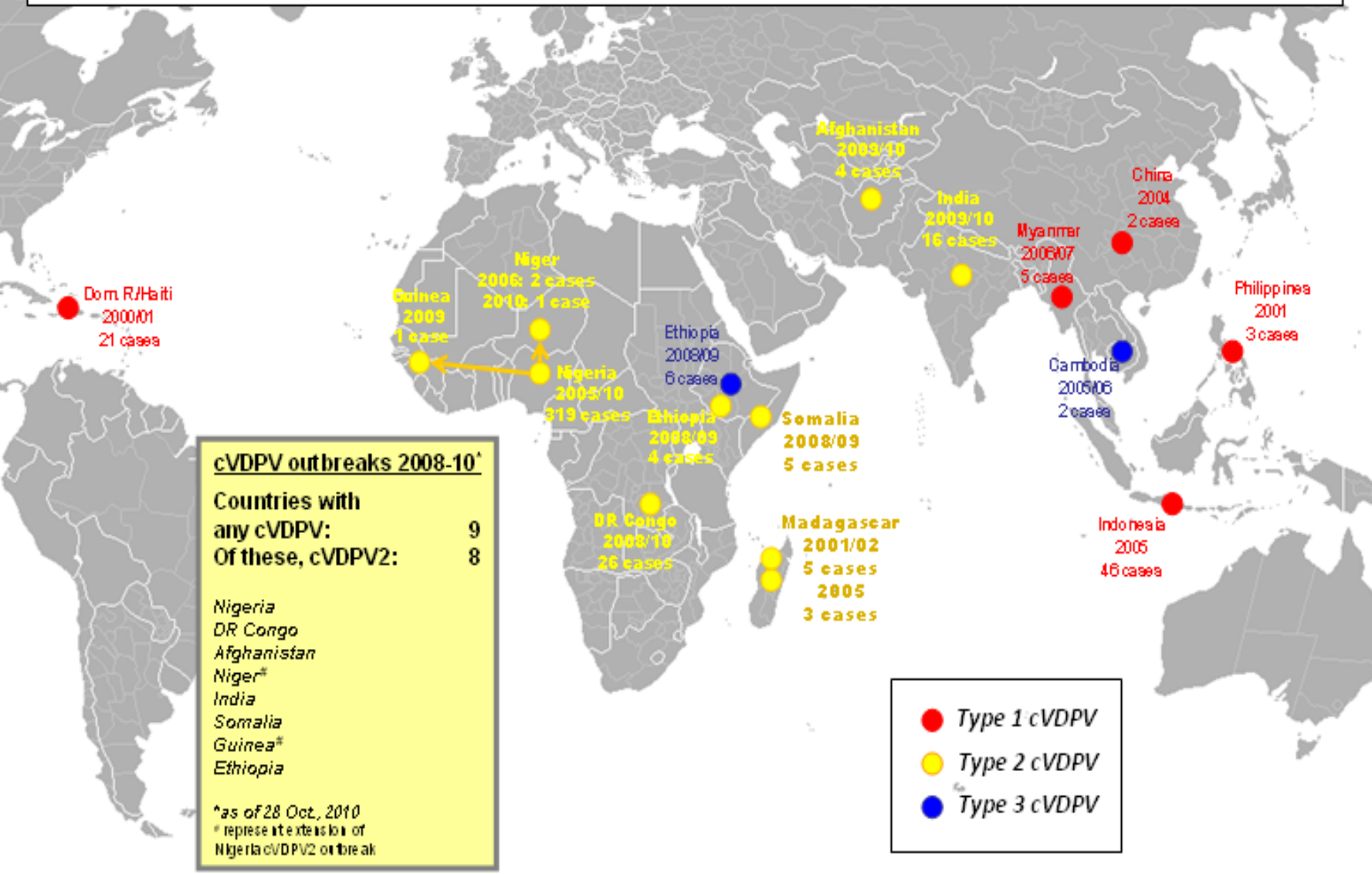




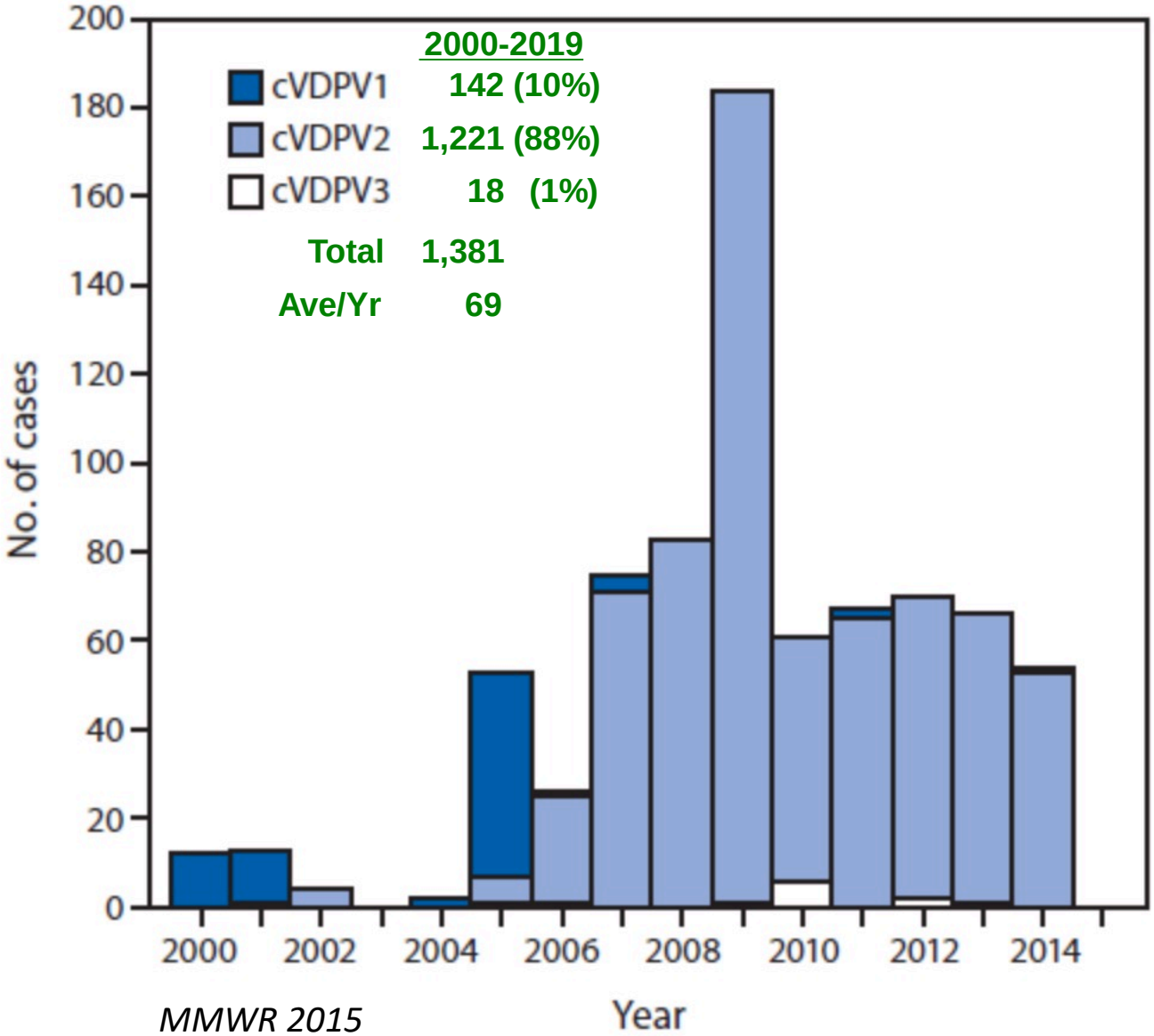
Bill Gates Annual Letter 2011


125 countries in 1988
5 countries in 2012
Endemic Transmission
Afghanistan, Nigeria, Pakistan
Non-Endemic Transmission
Chad, Niger
COUNTRIES WITH WILD POLIOVIRUS TRANSMISSION
Source: WHO Polio Data 2012

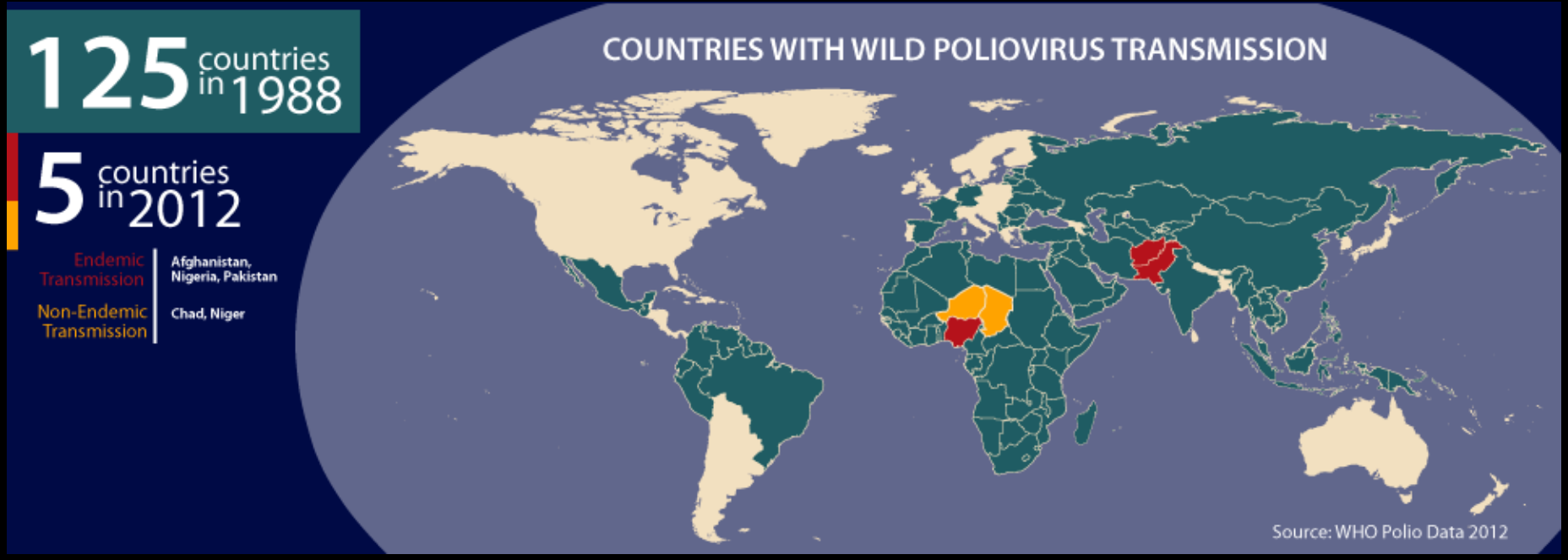
Outbreaks of circulating vaccine-derived poliovirus (cVDPV), by serotype, 2000 to end-October, 2010



Global Cases of Polio Caused by cVDPV 2000-2014 // 2000-2019

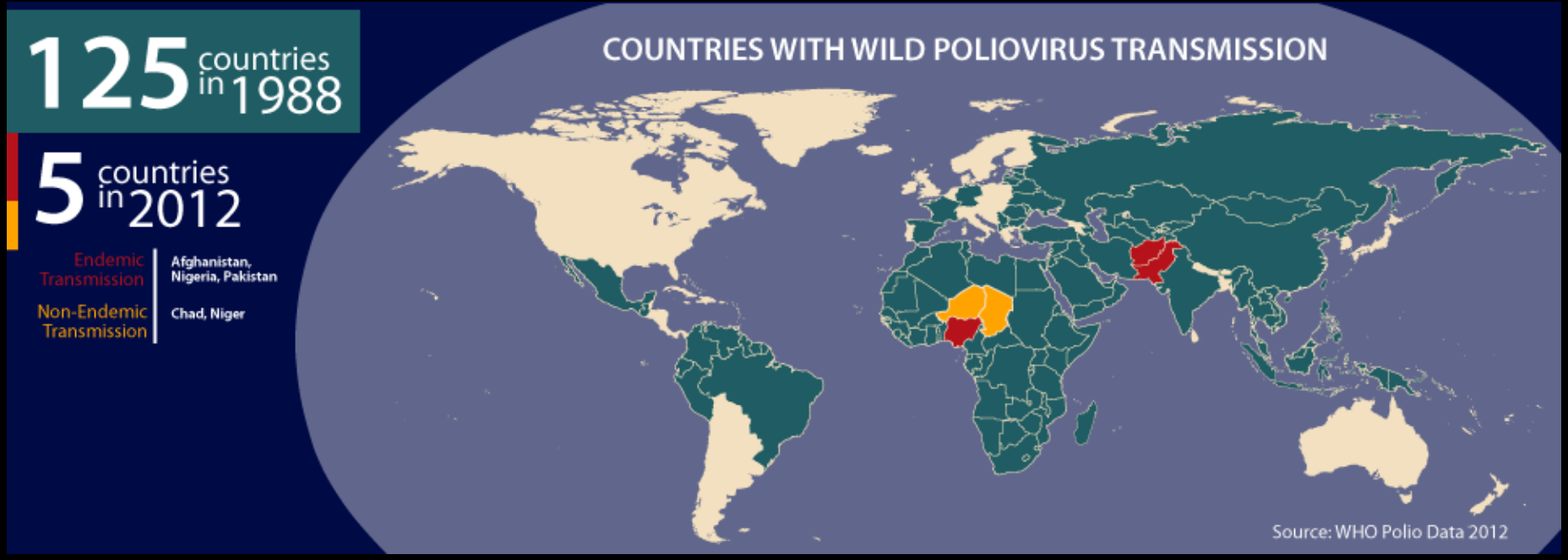


MMWR 2015



Annual Global Cases of Polio Caused by Polioviruses (No. of Countries)

	Wild	cVDPV	VAPP
1955:	c. 600,000 (All)		
1988:	c. 350,000 (125)		
2010:	1,352 (20)	60 (8)	c. 400
2011:	650 (16)	67 (7)	c. 400
2012:	223 (5)	71 (9)	c. 400
2013:	416 (8)	66 (8)	c. 400
2014:	359 (9)	56 (5)	c. 400
2015:	74 (2)	32 (7)	c. 400
2016:	37 (3)	5 (3)	c. 300?
2017:	22 (2)	96 (2)	c. 300?
2018:	33 (2)	104 (7)	c. 300?
2019:	176 (2)	369 (20)	c. 300? → → c. 100?



Annual Global Cases of Polio Caused by Polioviruses (No. of Countries)

	Wild	cVDPV	VAPP	c. % from OPV
1955:	c. 600,000 (All)			
1988:	c. 350,000 (125)			
2010:	1,352 (20)	60 (8)	c. 400	25
2011:	650 (16)	67 (7)	c. 400	42
2012:	223 (5)	71 (9)	c. 400	68
2013:	416 (8)	66 (8)	c. 400	53
2014:	359 (9)	56 (5)	c. 400	56
2015:	74 (2)	32 (7)	c. 400	85
2016:	37 (3)	5 (3)	c. 300?	89
2017:	22 (2)	96 (2)	c. 300?	95
2018:	33 (2)	104 (7)	c. 300?	92
2019:	176 (2)	369 (20)	c. 300? [→ c. 100?]	79

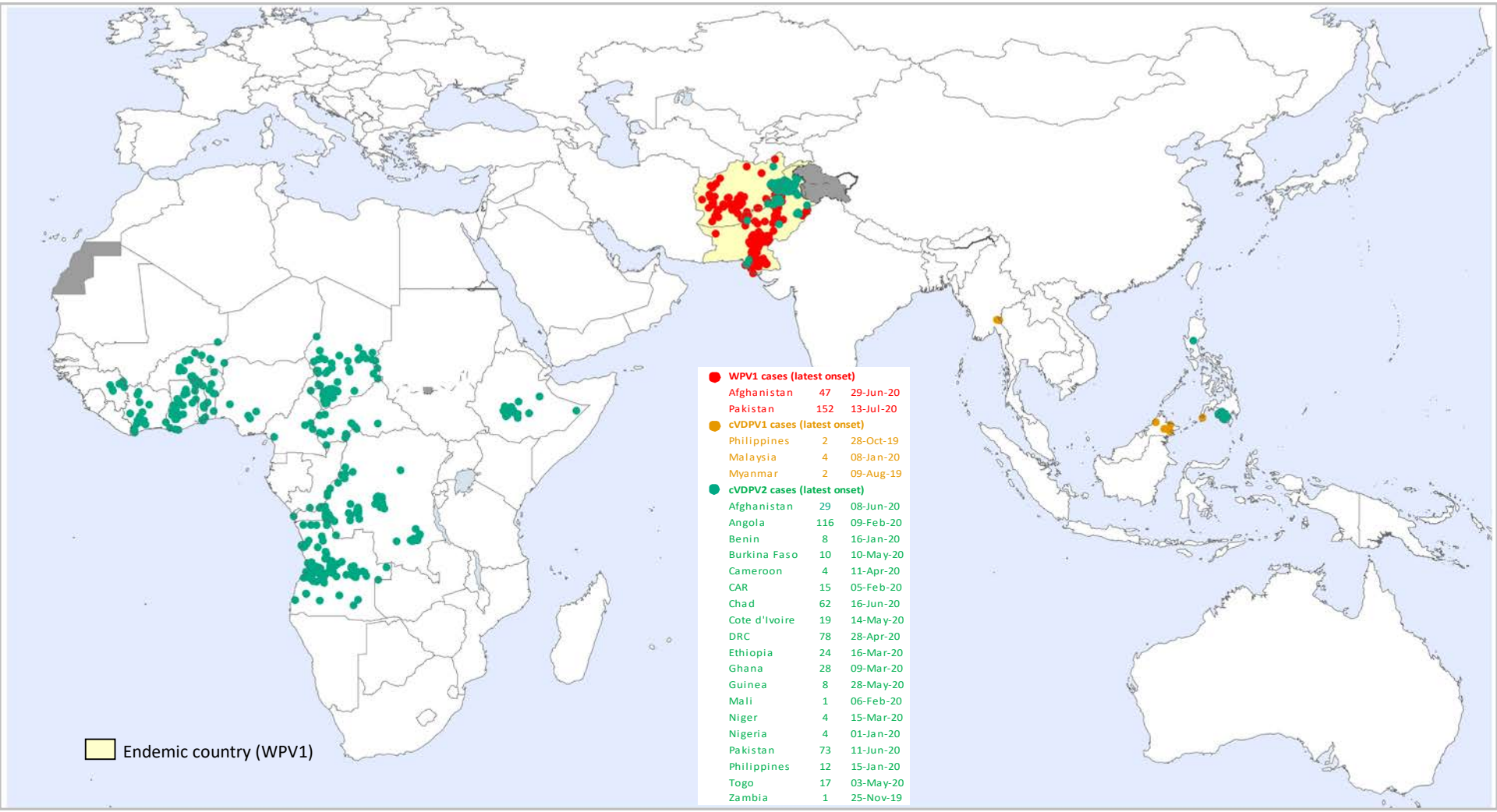
Polio 2019 vs. 2020: Year-to-Date (8/18/20)

Number of Cases (Number of Countries)

	WPV	cVDPV
2019 Total:	176 (2)	369 (20)
2019 YTD:	66 (2)	53 (11)
2020 YTD:	102 (2)	303 (22)

Global WPV1 & cVDPV Cases[1], Previous 12 Months[2]

World Health Organization



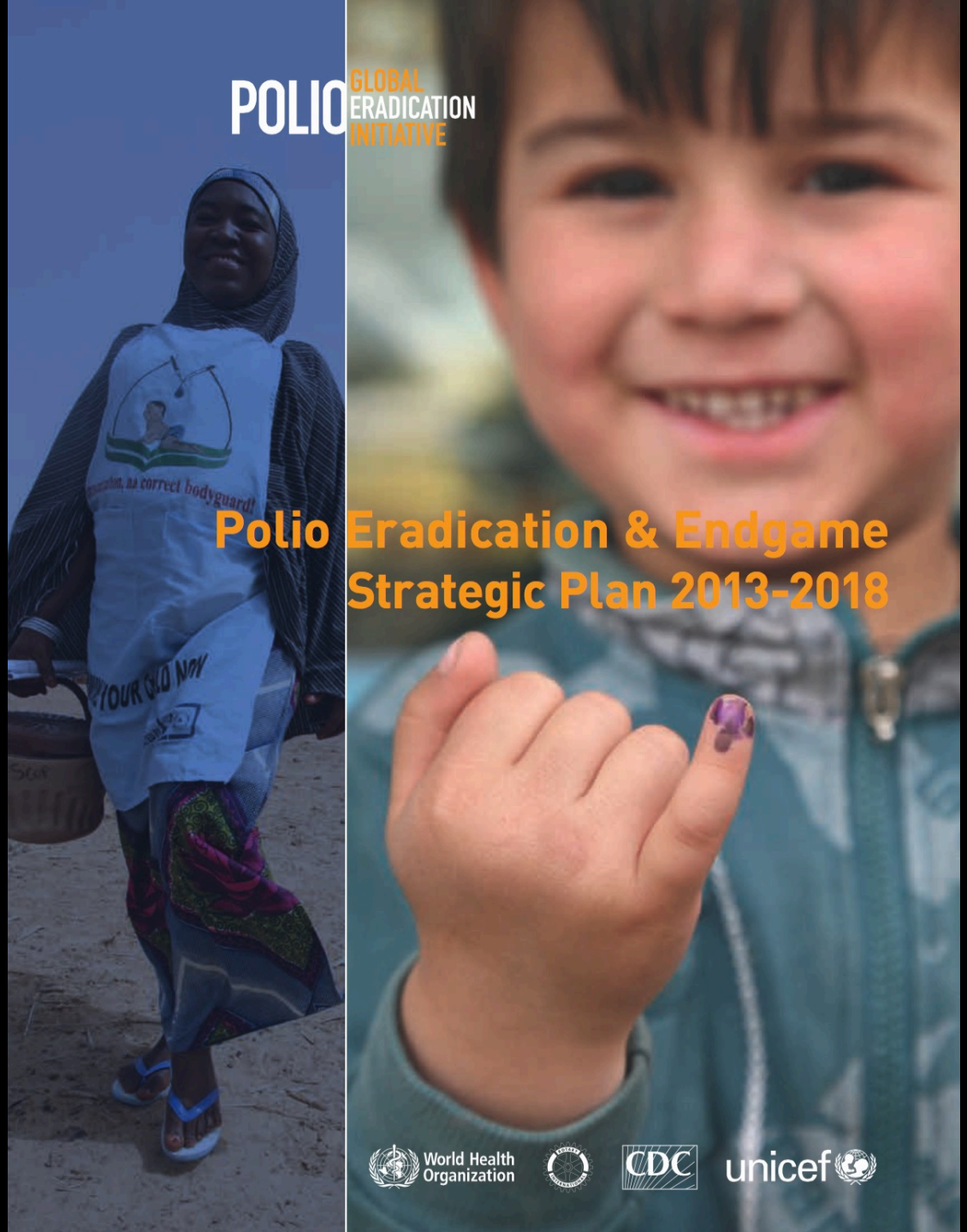
[1]Excludes viruses detected from environmental surveillance; [2]Onset of paralysis 05 Aug. 2019 – 04 Aug. 2020

Data in WHO HQ as of 04 Aug. 2020

BOUTER LA
POLIOMYELITE
HORS D'AFRIQUE

POLIO GLOBAL ERADICATION INITIATIVE

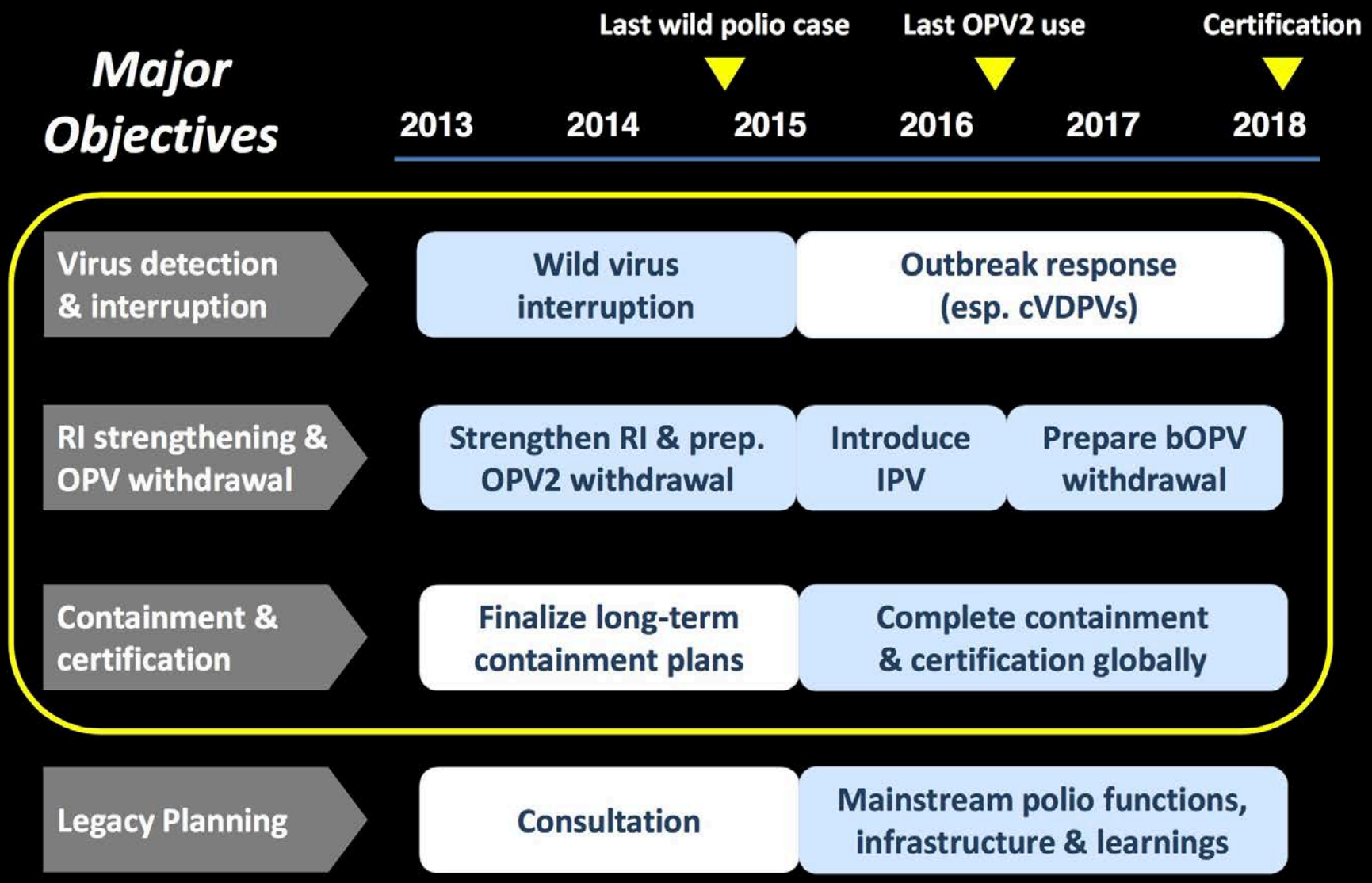
Polio Eradication & Endgame Strategic Plan 2013-2018



World Health Organization

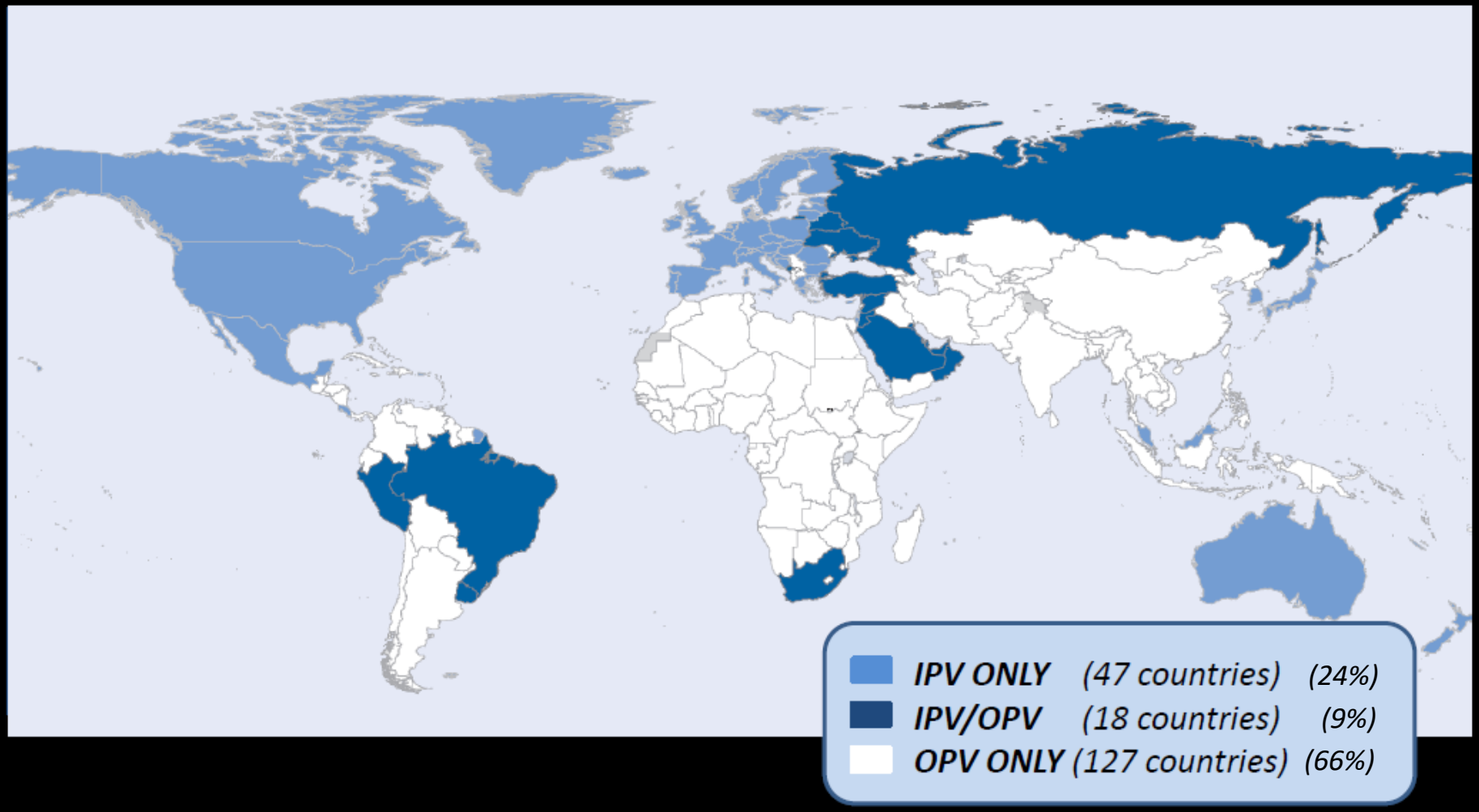
CDC

unicef



Bruce Aylward 2013

The Challenge: IPV into 125 'OPV-only' countries
2013



UNICEF Nigerian Polio Vaccine Contaminated with Sterilizing Agents Scientist Finds

KADUNA, Nigeria, March 11, 2004 (LifeSiteNews.com) - A UNICEF campaign to vaccinate Nigeria's youth against polio may have been a front for sterilizing the nation. Dr. Haruna Kaita, a pharmaceutical scientist and Dean of the Faculty of Pharmaceutical Sciences of Ahmadu Bello University in Zaria, took samples of the vaccine to labs in India for analysis.

2 Polio Workers Killed in Pakistan

By ISMAIL KHAN JUNE 16, 2013

Anti-Polio Worker Slain in Pakistan

By SALMAN MASOOD DEC. 9, 2014

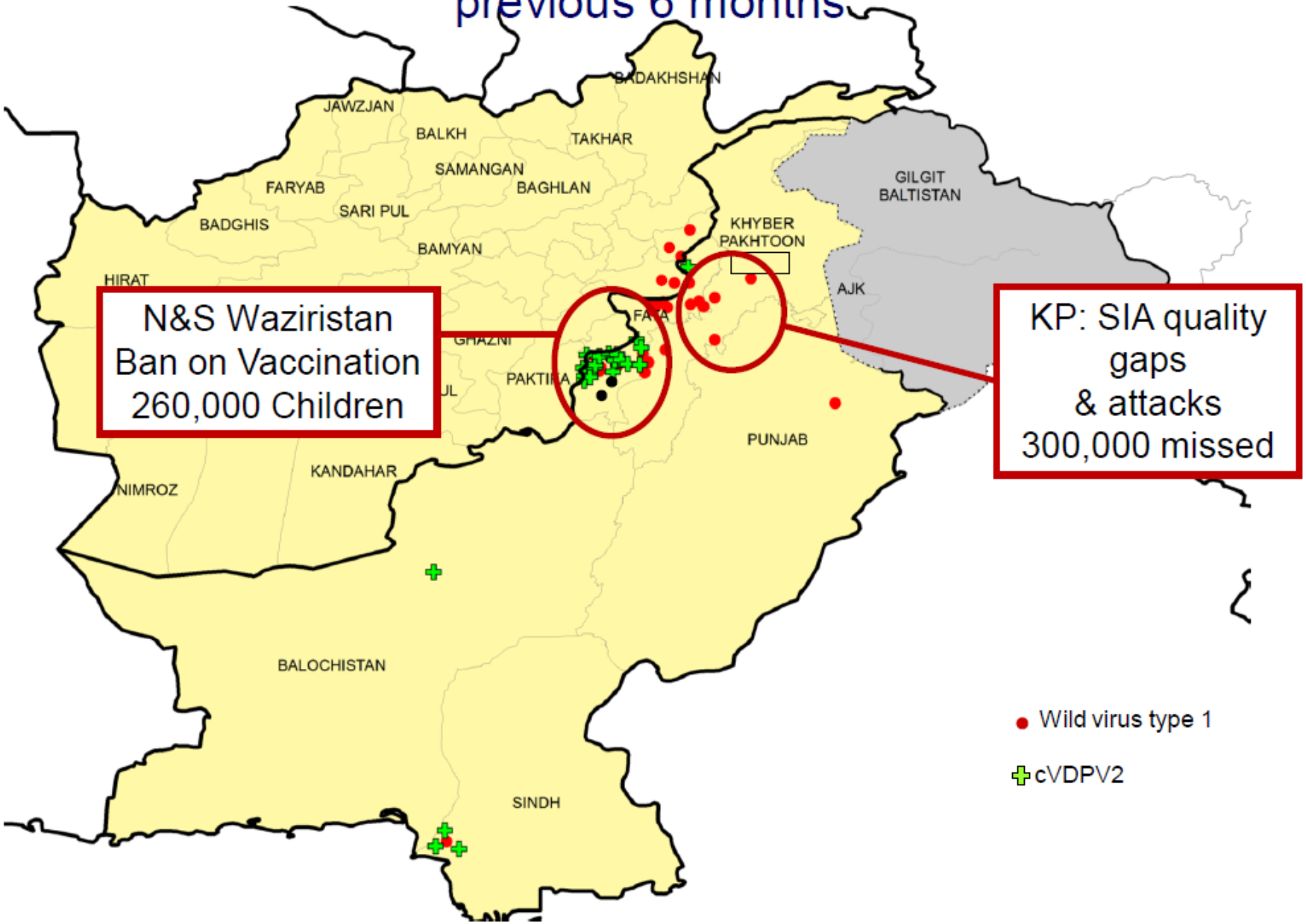
Polio Team Attacked in Pakistan

By SALMAN MASOOD FEB. 14, 2015

Gunmen Kill Health Workers From Pakistan Polio Drive

By THE NEW YORK TIMES MARCH 17, 2015

Wild and cVDPV2 Poliovirus, Pakistan and Afghanistan, previous 6 months*

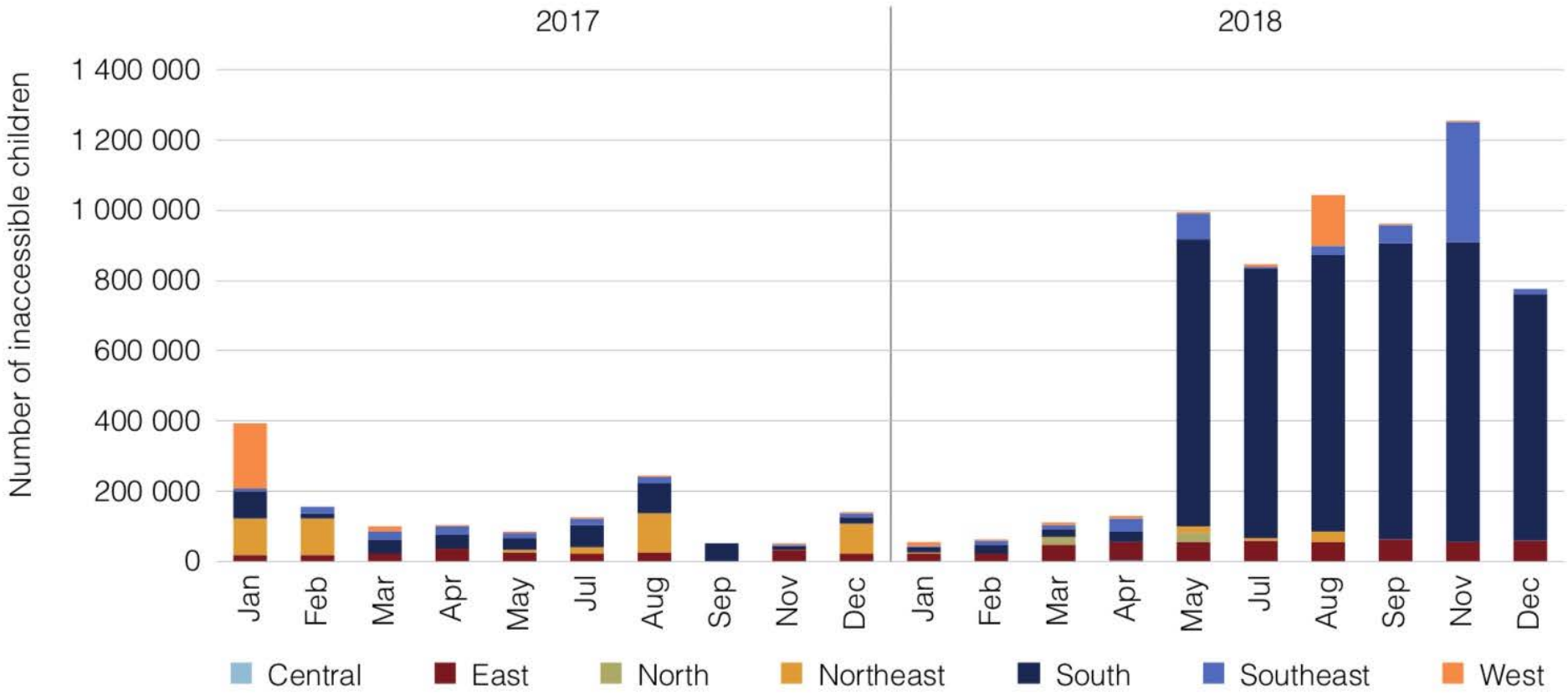


* 25 March – 24 Sep 2013 (Data in WHO/HQ as of 24 Sep 2013)

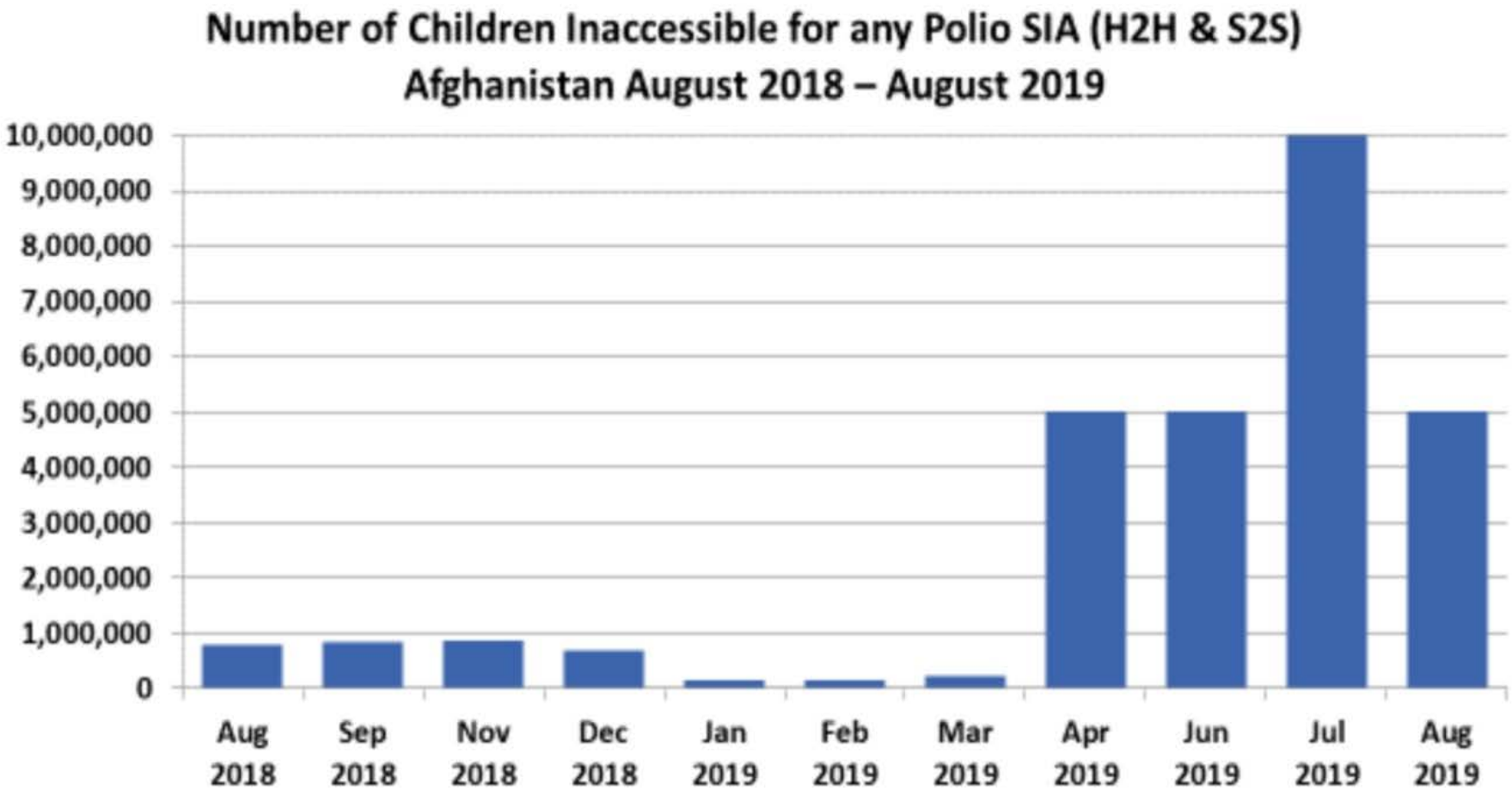
INACCESSIBLE CHILDREN CONCENTRATED IN EASTERN AFGHANISTAN

* “A fifth of the world’s polio cases in 2016 occurred in a part of the Shigal District where 1000 people live.” (IMB Report, August 2016)

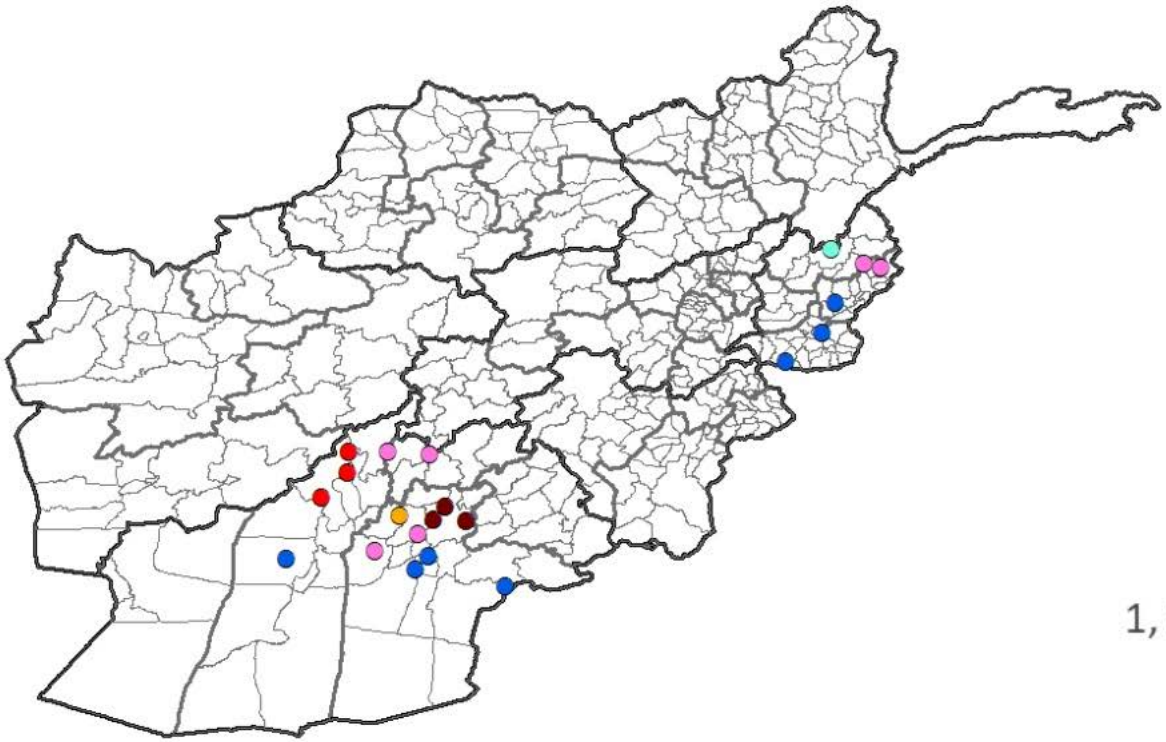
Inaccessible children in Afghanistan by region, 2017 and 2018

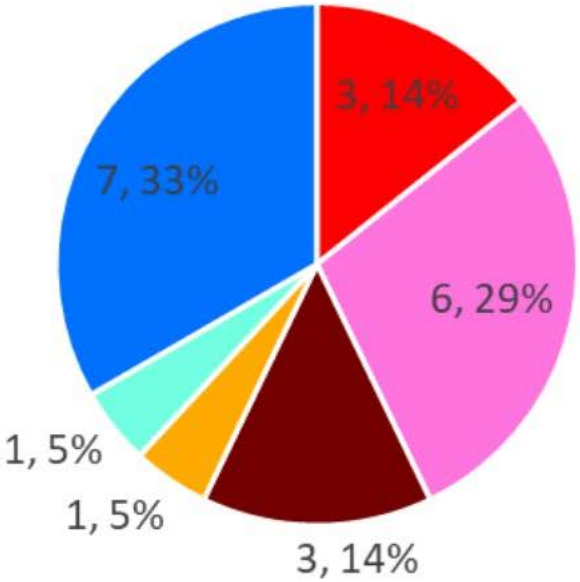


Source: National Emergency Operations Centre, Afghanistan. Presentation to Technical Advisory Group; January 2019.


Number of Children Inaccessible for any Polio SIA (H2H & S2S)
Afghanistan August 2018 – August 2019
10,000,000
9,000,000
8,000,000
7,000,000
6,000,000
5,000,000
4,000,000
3,000,000
2,000,000
1,000,000
0
Aug 2018
Sep 2018
Nov 2018
Dec 2018
Jan 2019
Feb 2019
Mar 2019
Apr 2019
Jun 2019
Jul 2019
Aug 2019

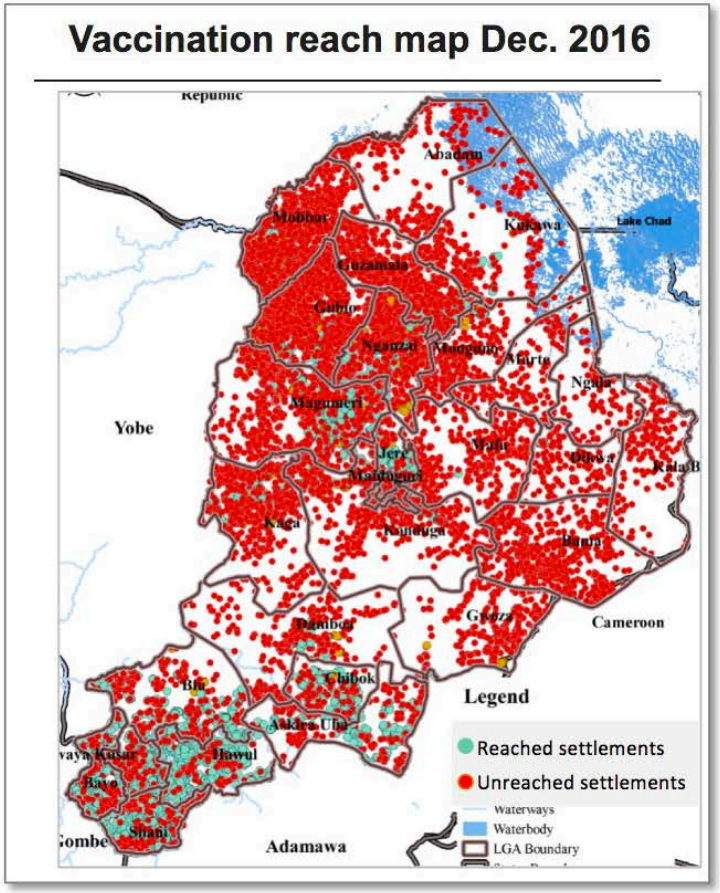
Investigation Results of WPV Cases
Afghanistan 2018

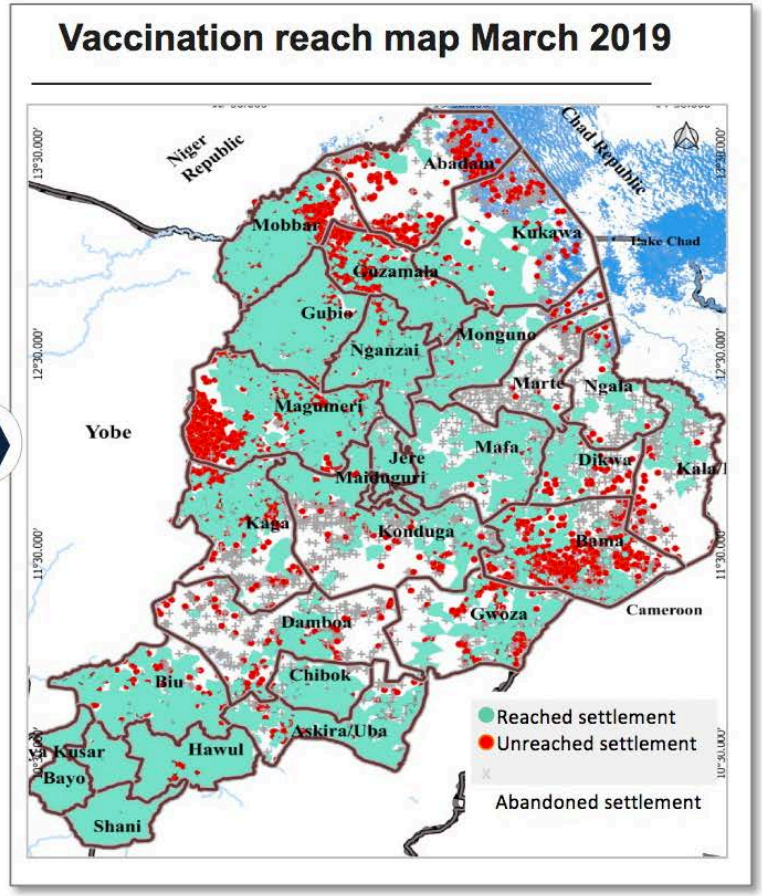




- Inaccessible
- Chronic Refusal
- Chronic Refusal / Inaccessible
- Program issue / Inaccessible
- Immunized as per age and # of SIAs conducted
- Adequately immunized (≥7 SIA doses)

Nigeria : No WPV detected in 2.5 years





Source: Borno EOC data team analysis

- Last virus 27 September 2016 in healthy child in Borno
- **August 2016, ~ 600,000 children** unreached across over 10,000 communities
- **February 2019, ~ 60,500 children** remain unreached in ~ 3,000 settlements

TABLE 28-12 Intestinal Immunity in Vaccinated (OPV or IPV) and Naturally Immune and Susceptible Children

Constructed from data in Fine and Carneiro,[206] Global Programme for Vaccines and Immunization,[614] and Ghendon and Sanakoyeva.[368]

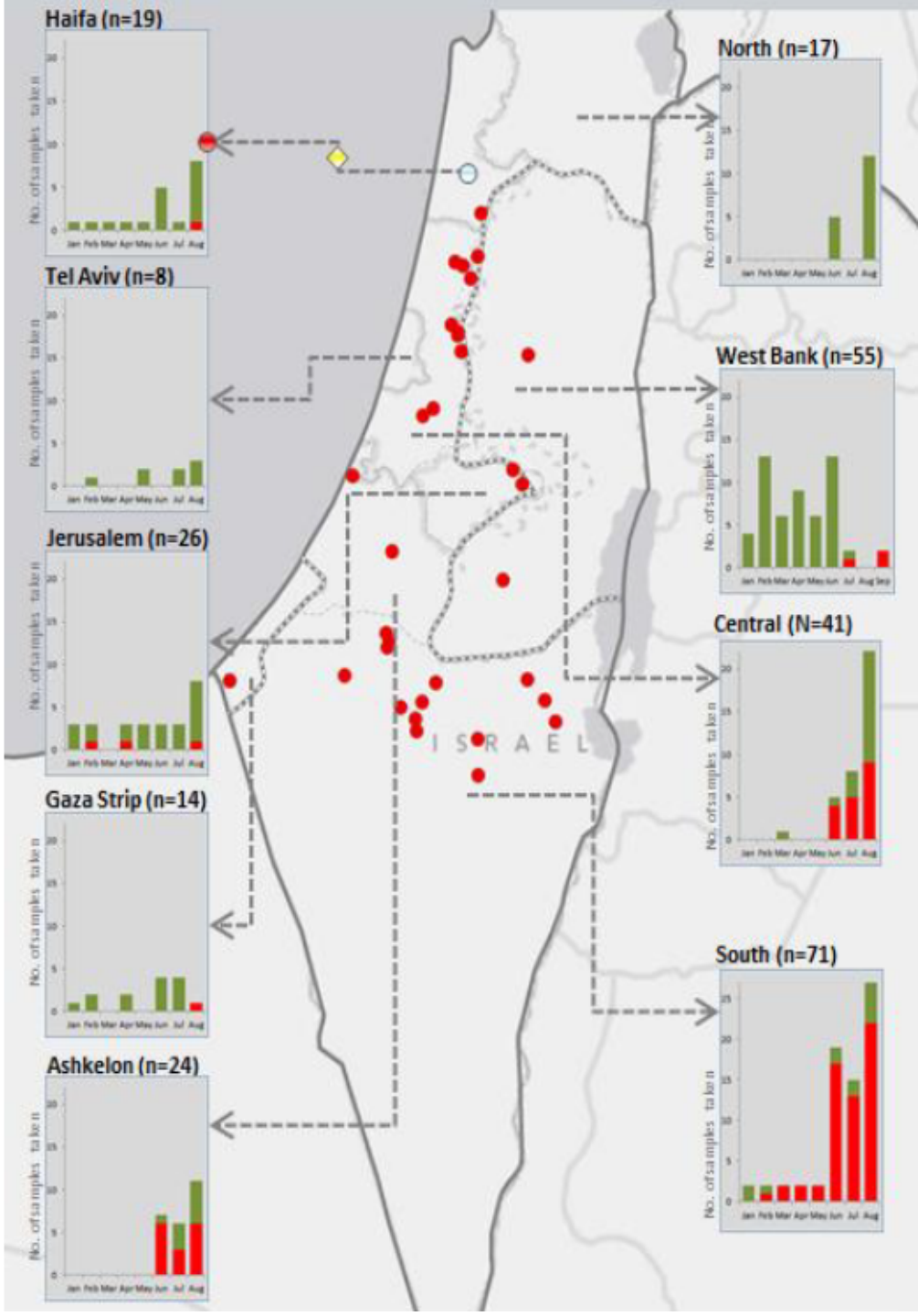
Study group	Proportion excreting	Mean duration of excretion (d)	Mean titer of virus excreted (log $TCID_{50}$)	Excretion index (million)*	Reduction in viral excretion (%)
Susceptible control subjects	0.80	20.4	5.15	2.305	Reference
IPV-vaccinated	0.74	12.3	4.11	0.1173	95
OPV-vaccinated	0.37	4.6	2.18	0.00022	99
Naturally immune	0.37	5.4	2.03	0.00022	99

IPV, inactivated poliovirus vaccine; OPV, oral poliovirus vaccine; $TCID_{50}$, median tissue culture infective dose.

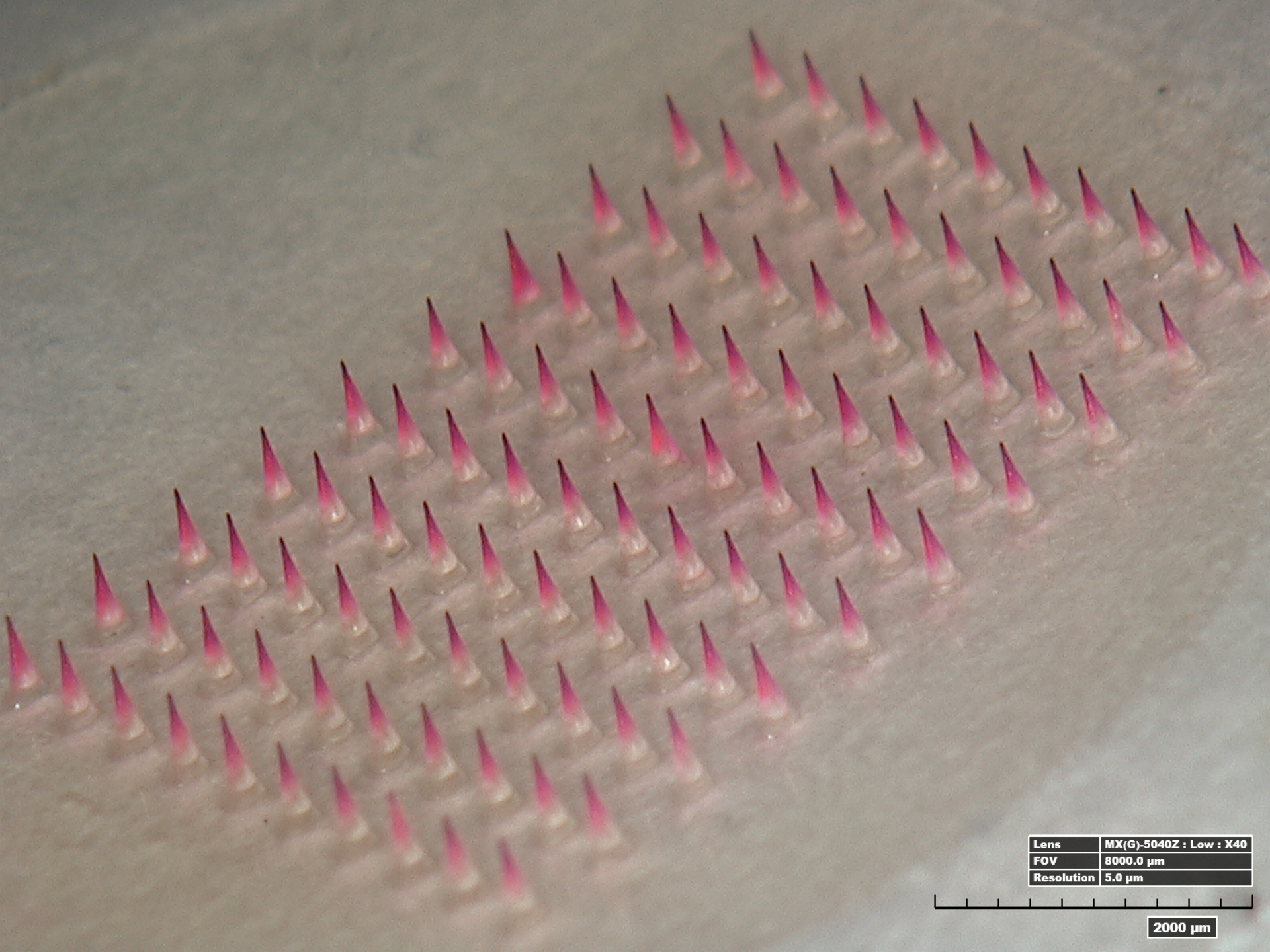
R.W. Sutter et al., Vaccines (6th Edition), 2013

Detection of WPV1 in Environmental Samples, Israel, West Bank & Gaza Strip Jan – 10 Sep 2013

- First detection in May
- Samples from February +ve
- South, Ashkelon, Central: increasingly +ve
- WPV1 detection in West Bank (July, Sept) and Gaza Strip (August)



Poliovirus Vaccine
Inactivated (IPV)


Lens
MX(G)-5040Z : Low : X40
FOV
8000.0 µm
Resolution
5.0 µm
2000 µm

THE LANCET

Published: June 04, 2019

The safety and immunogenicity of two novel live attenuated monovalent (serotype 2) oral poliovirus vaccines in healthy adults: a double-blind, single-centre phase 1 study

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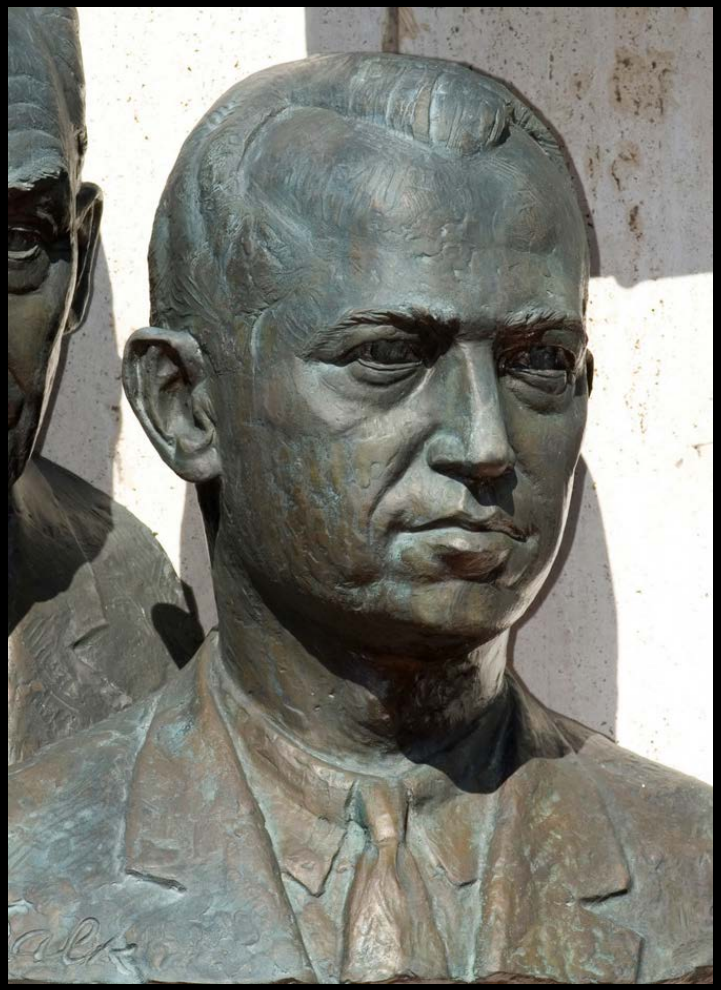
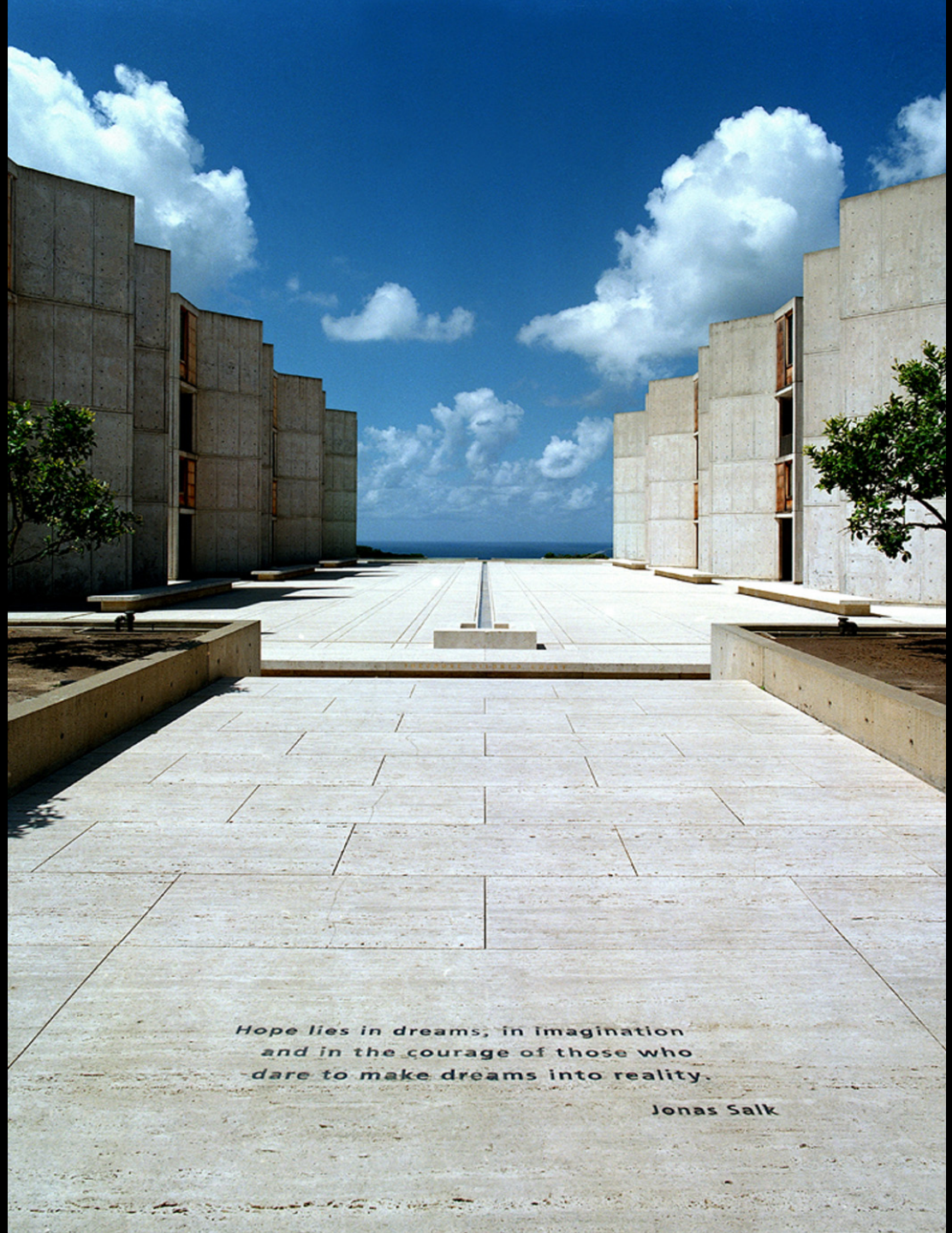


Sabin
Photography by Wanda


Hope lies in dreams, in imagination
and in the courage of those who
dare to make dreams into reality.
Jonas Salk