The Role of Vaccines in Eradicating and Eliminating Diseases

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CIRE Webinar
August 18, 2025

Disclosure:

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Walter A. Orenstein (Speaker): Consultant for CureVac SE, Seqirus, Merck, Krog, Sanofi, and ModernaTx

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Financial Support:

This project was supported by the Centers for Disease Control and Prevention of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award totaling $143,195 with 100 percent funded by CDC/HHS. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by CDC/HHS, or the U.S. Government. Additionally, the contents do not necessarily represent the official views of, nor an endorsement, by the North Dakota Department of Health and Human Services.

Disclosure

Dr. Orenstein reports they are a consultant for CureVac SE, Seqirus, Merck, Krog, Sanofi, and Moderna. All relevant financial relationships have been mitigated.

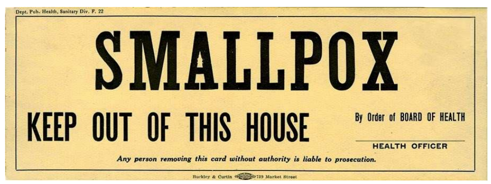
CEimpact PHARMACY EDUCATION

Objectives

- Define eradication and elimination and the criteria required for making a disease eligible for eradication
- Describe why disease surveillance, including whether cases are the result of vaccine failure or failure to vaccinate, plays a critical role in disease eradication and elimination
- Explain how investments by high income countries to support efforts to eradicate or eliminate vaccine-preventable diseases in low-income countries benefit both low- and high- income countries

Global Eradication

"The worldwide absence of a specific disease agent in nature as a result of deliberate control efforts that may be discontinued where the agent is judged no longer to present a significant risk from extrinsic sources (e.g., smallpox)"



Cochi SL, Dowdle WR eds., Disease Eradication in the 21st Century, Strungman Forum Reports, MIT Press, 2012, p5

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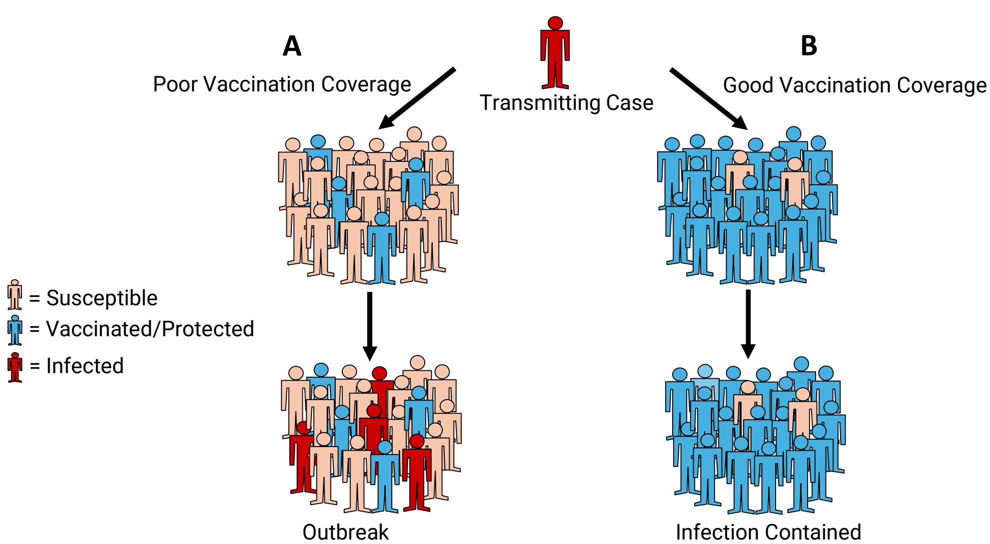
Community Protection



Biologic and Technical Feasibility Criteria For Disease Eradication

- An effective practical intervention must be available to interrupt transmission of the agent
- Practical diagnostic tools must exist with sufficient sensitivity to detect levels of infection that can lead to transmission
- There must be an absence of a nonhuman reservoir (when humans are essential for the life cycle of the agent), and the organism does not amplify in the environment
- Success of the eradication strategy must be demonstrated in a large geographic area or region

Cochi SL, Dowdle WR eds., Disease Eradication in the 21st Century, Strungman Forum Reports, MIT Press, 2012, p6

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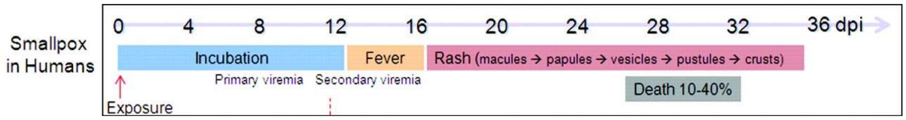
Smallpox



John Huggins et al. Antimicrob. Agents Chemother. 2009;53:2620-2625

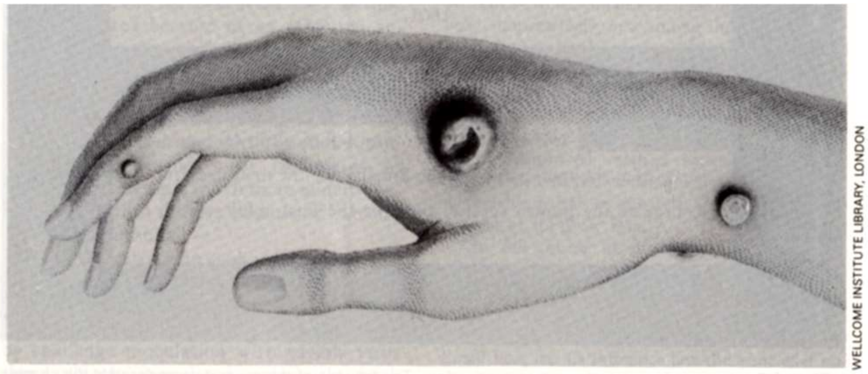


Plate 6.9. Accidental cowpox lesions on the hand of Sarah Nelmes (case XVI in Jenner's *Inquiry*) from which material was taken for the vaccination of James Phipps in 1796.

In Fenner F, et al. Smallpox and its Eradication, World Health Organization, 1988

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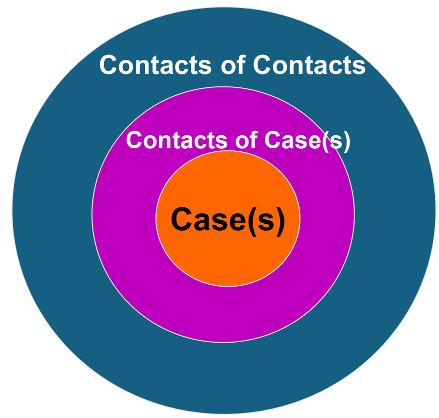
Search and Containment (Ring Vaccination)

- Search for cases
- Identify and vaccinate contacts
- Provide a ring of immunity around each case
- Used to eradicate smallpox
  - required to control disease in face of ‘routine immunization’
  - found the people who needed to be vaccinated
  - minimized adverse events



Provided by DA Henderson

Reasons for Success of Ring Vaccination

- Smallpox -easy to diagnose & no carriers
- Almost all transmission is by droplets
- No transmission until after patient becomes sick
- Vaccination protects up to 3 to 4 days after infection

Provided by DA Henderson

Summary

- Clinical diagnosis is comparatively straightforward. Few atypical cases
- Laboratory tests are definitive.
- Spread is slower than illnesses such as measles. Similar to rubella, diphtheria and mumps.
- Transmission almost always readily traceable to face-to-face contact.

Provided by DA Henderson

Knowledge Check

All of the following are criteria for a disease to be eligible for eradication EXCEPT:

A. An effective practical intervention to interrupt transmission
B. Practical diagnostic tools
C. Absence of a non-human reservoir for the pathogen
D. Global funding and political support

Smallpox eradication

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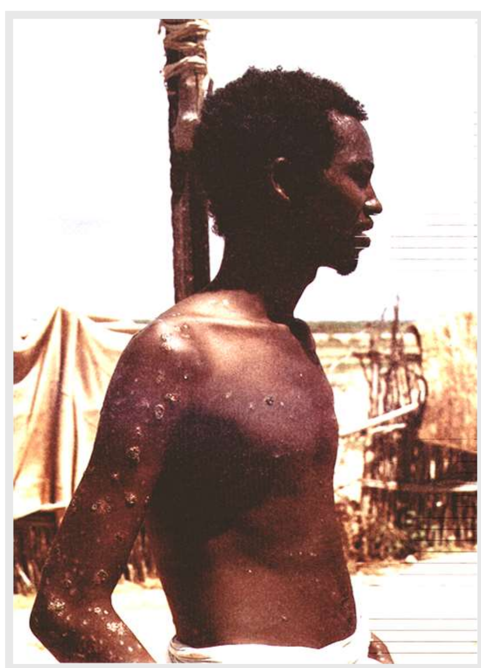

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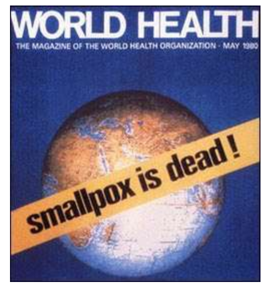
Smallpox Eradication Benefits*

- 1967 – intensified global eradication program begun
  - 44 countries with smallpox; 31 endemic
  - 217,218 cases reported; estimated 10-15 million cases; 1.5-2 million deaths**
- 1977 – last naturally acquired case
- Total investment of $300 million;
- Estimated benefits ~ $1 billion per year



*Henderson DA et al. Smallpox and Vaccinia in Plotkin SA, Orenstein WA, Offit PA. Vaccines 5th edition; 2008; pp 774-803
**Fenner F et al. Smallpox and its eradication WHO 1988 pp 1363

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Benefits of Smallpox Eradication to the US

Sencer and Axnick documented in the United States during 1968:

- 14.2 million persons were vaccinated of whom 5.6 million were primary vaccinations and 8.6 million were revaccinations.
- Because of vaccine complications, 238 required hospitalization
- 9 died, and 4 were permanently disabled.
- The total costs to the country, including the costs of quarantine services, were estimated to be US$150 million.

Source: Henderson DA et al. Smallpox and Vaccinia in Vaccines 5th edition, 2008

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Continuum of approaches to improve health

- Comprehensive health services
- Selective approaches
  - Basic package
- Targeted programs
  - Tuberculosis control
- Elimination
  - Measles
- Eradication
  - Polio

Provided by Alan Hinman

Control

Reduction of disease incidence, prevalence, morbidity or mortality to a locally acceptable level as a result of deliberate efforts; continued intervention measures are required to maintain the reduction.

Source: Dahlem Conference 1997

Provided by Alan Hinman

Elimination of disease

Reduction to zero of the incidence of a specified disease in a defined geographic area as a result of deliberate efforts; continued intervention measures are required

Source: Dahlem Conference 1997

Provided by Alan Hinman

Elimination of disease

- Absence of endemic measles transmission in a defined geographical area for $\geq$12 months in presence of a well performing surveillance system
- Interruption of local mosquito-borne malaria transmission
- Elimination of lymphatic filariasis (LF) as a *public health problem*
- Less than 1 case of neonatal tetanus per 1,000 live births
- Less than 1 leprosy case per 10,000 population
- Less than 10 cases of tuberculosis per 100,000 population by 2035
- By 2030, 90% reduction (compared to 2015) in new chronic hepatitis B and C infections and 65% reduction in deaths

Provided by Alan Hinman

Eradication

Permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts; *intervention measures are no longer needed*

Source: Dahlem Conference 1997

Provided by Alan Hinman

Knowledge Check

What was the first vaccine ever developed?

A. Diphtheria Toxoid
B. Tetanus Toxoid
C. Smallpox Vaccine
D. Polio Vaccine

Polio – a paralysing disease for life

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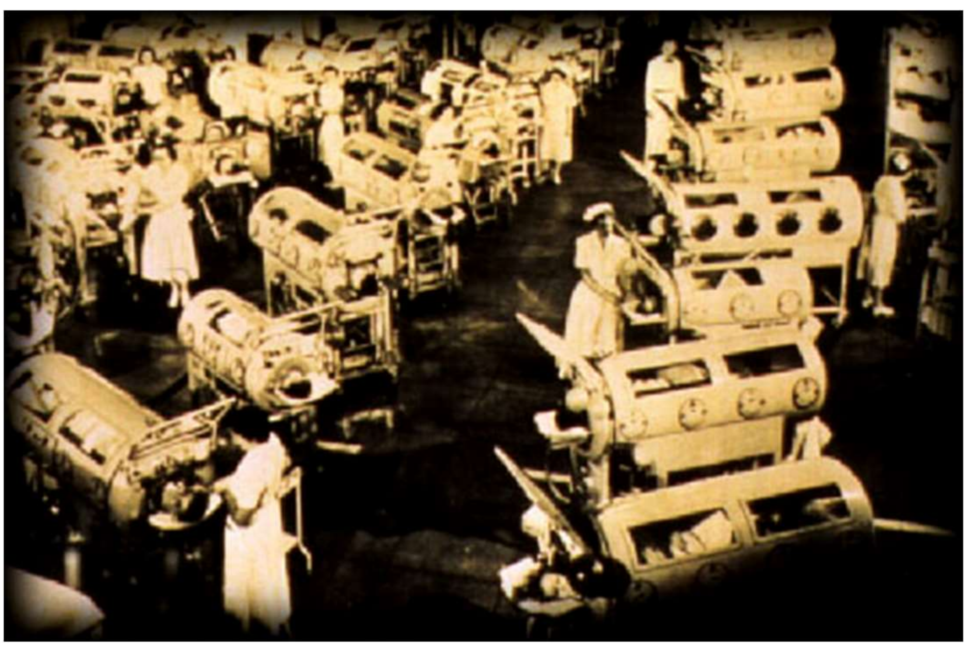

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Why is polio a candidate for eradication?

Eradication Principle	Polio characteristic
Humans required for pathogen lifecycle	• Poliovirus requires specific cell receptor (poliovirus receptor or PVR) expressed on human cells • High level primates can be infected orally but colony sizes are too small to maintain sustained transmission
Sensitive and specific diagnostic tools	• Acute flaccid paralysis (AFP) surveillance • Virologic testing of stool • Culture and now more commonly PCR • Genetic sequencing *asymptomatic infection is a challenge
Effective intervention	• OPV • IPV
Proof of principle	• Wild polioviruses have been certified as eliminated in 4 of the 6 WHO regions

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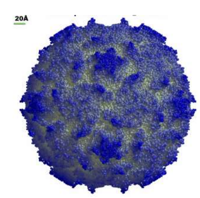
Exposure to Poliovirus



- Transmission: person-to-person
  - Oral-to-oral (developed countries)
  - Fecal-to-oral (developing countries)
- Exposure in susceptible person results in:

Consequence	Symptoms	% of infections
Inapparent infection without symptoms	None	72%
Minor illness	Transient illness; 1-3 days fever, malaise, drowsiness, headache, nausea, vomiting, constipation, or sore throat, in various combinations	24%
Nonparalytic poliomyelitis (aseptic meningitis)	Minor illness characterized as fever, sore throat, vomiting, malaise; 1-2 days later stiffness of neck or back; vomiting, severe headache, pain in limbs, back neck (lasts 2-10 days, recovery is usually rapid and complete)	4%
Paralytic poliomyelitis	**Minor illness for several days, symptom free period of 1-3 days, followed by rapid onset of flaccid paralysis with fever and progression to maximum extent of paralysis within a few days**	**<1%**

Sutter RW, Kew OM, Cochi SL, Aylward RB. 49- Poliovirus vaccine—live. In: Plotkin SA, Orenstein WA, Offit PA, Edwards KM, editors. Plotkin's Vaccines (7th Edition) Elsevier; 2018. p. 866–917. Available from: http://www.sciencedirect.com/science/article/pii/B9780323357616000481

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Paralytic Poliomyelitis

- Asymmetric
- Descending
- Diminished or complete loss of deep tendon reflexes
- Intact sensory system
- Paralysis may include
  - Spinal
  - Mixed spinal-bulbar
  - Bulbar involving primarily respiratory muscles
  - Paralysis is permanent. Yet, partial recovery can be achieved due to compensation of other, still functioning muscles (usually in first 6 months)

Sutter RW, Kew OM, Cochi SL, Aylward RB. 49- Poliovirus vaccine—live. In: Plotkin SA, Orenstein WA, Offit PA, Edwards KM, editors. Plotkin's Vaccines (7th Edition) Elsevier; 2018. p. 866–917.
Available from: http://www.sciencedirect.com/science/article/pii/B9780323357616000481

Basic Epidemiology

- Age group: mostly children aged 6-24 months
- Case fatality: ~ 5% (Cape Verde, 2000, 17/44 39%)
- Most infectious immediately before and 1-2 weeks after onset of paralysis
  - Excreted for 3-6 weeks in feces and 2 weeks in saliva
- Incubation period
  - Infection to first symptoms: 3-6 days
  - Infection to onset of paralysis: 7-21 days (range 3-35 days)
- Lab diagnosis: viral detection
  - >90% sensitive, nearly 100% specific
  - Gold standard test is detection of virus from stool specimens

Modified from "Introduction to Poliomyelitis". Training of STOP Team 34, Atlanta, May 2010

Types of Polioviruses

Wild
- 99% reduction in cases of wild poliovirus since 1988
- Type 1 (highest **case-infection** ratio)
- Type 2 (**eradicated - 2015**)
- Type 3 (**eradicated - 2019**)

OPV-related

VAPP**
- Vaccine-associated paralytic poliomyelitis (VAPP)**
- Overall risk in developing countries: 1 case 4-5 million OPV doses

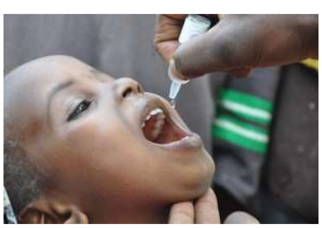
VDPVs*
- Most are circulating vaccine-derived poloviruses (cVDPVs)
- **Type 2 cVDPVs account for ~90% of cVDPVs**

** Platt LR, Estívariz CF, Sutter RW. Vaccine-Associated Paralytic Poliomyelitis: A Review of the Epidemiology and Estimation of the Global Burden. J Infect Dis. 2014 Nov 1;210(suppl 1):S380–9.

Vaccines against Polio

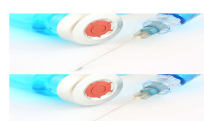
Oral Polio Vaccine (Sabin)

-live weakened virus



Inactivated Polio Vaccine (Salk)

-killed virus administered by injection



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Polio Eradication Strategy

- **Routine immunization**
- **National Immunization Days (NIDs)** vaccinating all children < 5 years of age regardless of vaccination status
  - Also known as Mass Campaigns or Supplemental Immunization Activities (SIAs)
- **Careful surveillance**
  - Acute flaccid paralysis (AFP)
  - Environmental sampling
- **Mop-up campaigns**

Modified from "Introduction to Poliomyelitis". Training of STOP Team 34, Atlanta, May 2010

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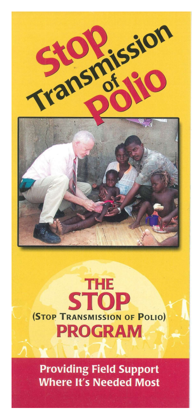
Critical Tools in Polio Eradication

- Disease Surveillance
  - Acute flaccid paralysis (AFP) surveillance
    - Indicators of quality
      - >2/100,000 cases of non-polio AFP among children <15 years of age, annually
      - >80% of AFP cases investigated have at least two stools collected within 14 days of paralysis onset and processed in an accredited laboratory
      - Global accredited laboratory network
  - Environmental Surveillance (sewage monitoring)
  - Coverage Monitoring
    - Routine Coverage
      - Immunization status of non-polio AFP cases
    - Supplemental Immunization Coverage Monitoring
      - Finger Marking
      - Independent monitors



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Modified from "Introduction to Poliomyelitis". Training of STOP Team 34, Atlanta, May 2010

Milestones towards Polio Eradication

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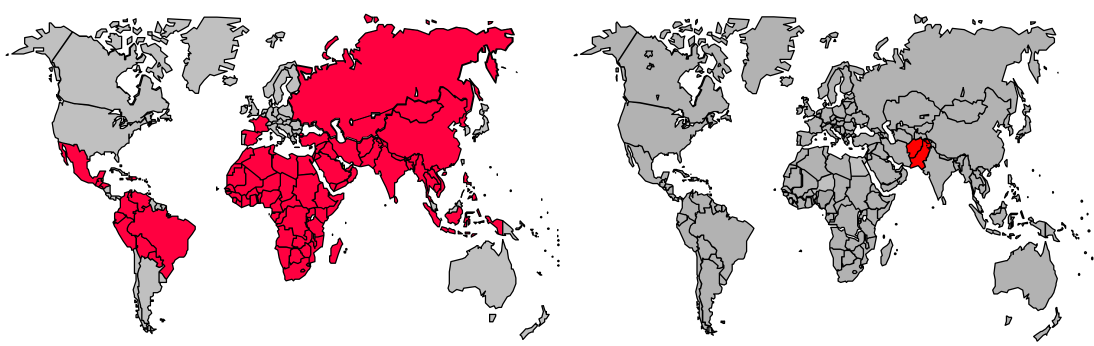
Year	Timeline
1985	Pan American Health Organization launches initiative to eradicate polio in the Americas by 1990
1988	World Health Assembly passes a resolution to eradicate polio by the year 2000
1994	Americas certified as polio-free, last case indigenous case 1991
1999	Last outbreak of wild poliovirus type 2: Aligarh, India
2000	Western Pacific region certified polio free
2002	Europe certified polio free
2012	Last detected case of wild poliovirus type 3 (WPV3) had onset Nov 10, 2012 in Nigeria
2014	India (entire WHO SouthEast Asian Region) declared polio free May 5, 2014: the Emergency Committee under the International Health Regulations declared polio a Public Health Emergency of International Concern
2015	Global eradication of wild poliovirus type 2 declared; Only 2 countries now considered endemic (i.e., potential reservoirs): Pakistan & Afghanistan
2016	Type 2 component of trivalent oral polio vaccine (tOPV) withdrawn in a globally synchronized switch
2019	Global eradication of wild poliovirus type 3 declared
2020	Africa certified as wild poliovirus free
2025	99 **WPV1** cases in 2 endemic countries. 100 **cVDPVs**, 0 **type 1**; 97 **type 2;** 3 **type 3**

Data in WHO HQ as of 5 Aug 2025

Wild poliovirus (WPV) cases



1988

- **350,000 cases**
- **125 endemic countries**
- **World Health Assembly voted to eradicate polio**

2025

- **99 WPV1 cases**
  - **25 in Afghanistan and 74 in Pakistan**
- **2 endemic countries (Afghanistan and Pakistan)**

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Data in WHO HQ as of 5 Aug 2025

Global Wild Poliovirus 2018 - 2025

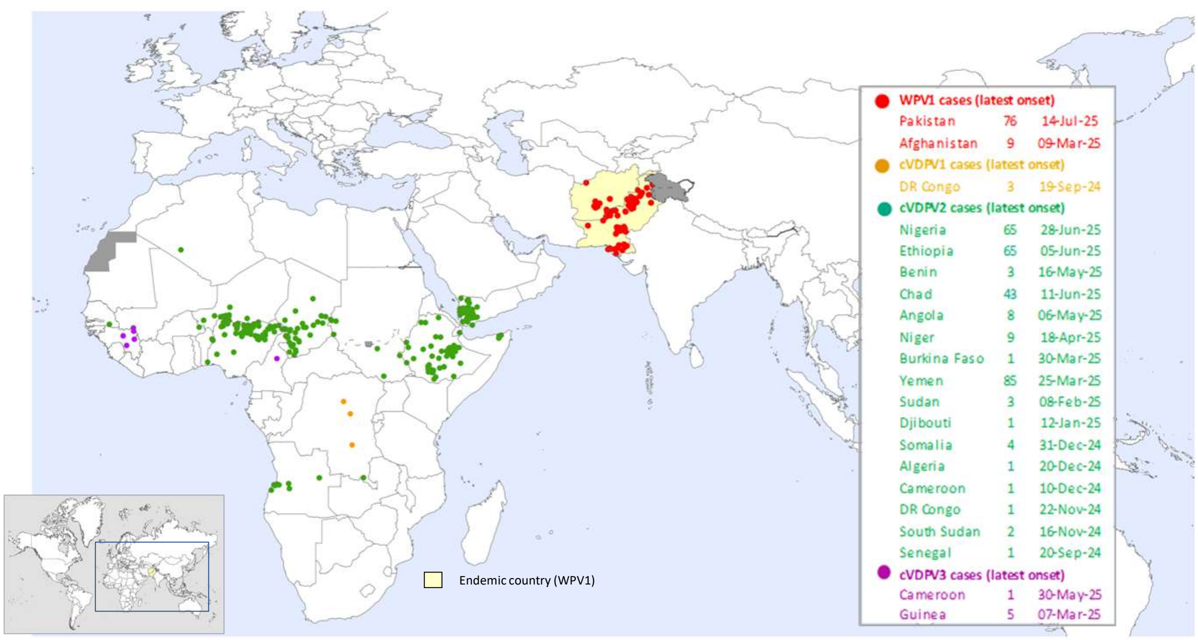
Country or territory	Wild virus type 1 confirmed cases										Wild virus type 1 reported from other sources[2]								
	Full year total							01 Jan-05 Aug[1]		Date of most recent case	Full year total							01 Jan-05 Aug	Date of most recent virus
	2018	2019	2020	2021	2022	2023	2024	2024	2025		2018	2019	2020	2021	2022	2023	2024	2025	
Pakistan	12	147	84	1	20	6	74	12	18	14-Jul-25	141	405	455	65	43	128	649	349	15-Jul-25
Afghanistan	21	29	56	4	2	6	25	11	2	09-Mar-25	83	60	49	1	22	62	119	41	23-Jun-25
Mozambique	0	0	0	0	8	0	0	0	0	10-Aug-22									
Malawi	0	0	0	1	0	0	0	0	0	19-Nov-21									
Iran	0	0	0	0	0	0	0	0	0	NA		3							20-May-19
Total (Type 1)	**33**	**176**	**140**	**6**	**30**	**12**	**99**	**23**	**20**		**224**	**468**	**504**	**66**	**65**	**190**	**768**	**390**	
Tot. in endemic countries	33	176	140	5	22	12	99	23	20										
Tot. in non-end countries	0	0	0	1	8	0	0	0	0										
No. of countries (infected)	2	2	2	3	3	2	2	2	2										
No. of countries (endemic)	3	3	3	2	2	2	2	2	2										
Total Female	18	72	59	2	10	4	43	4	8										
Total Male	15	104	81	4	20	8	56	19	12										

Countries in yellow are endemic. [1]Data reported to WHO HQ on week 32 in 2024 and 2025.

[2]Wild viruses from environmental samples, selected contacts, healthy children and other sources.

Data in WHO HQ as of 05 Aug 2025

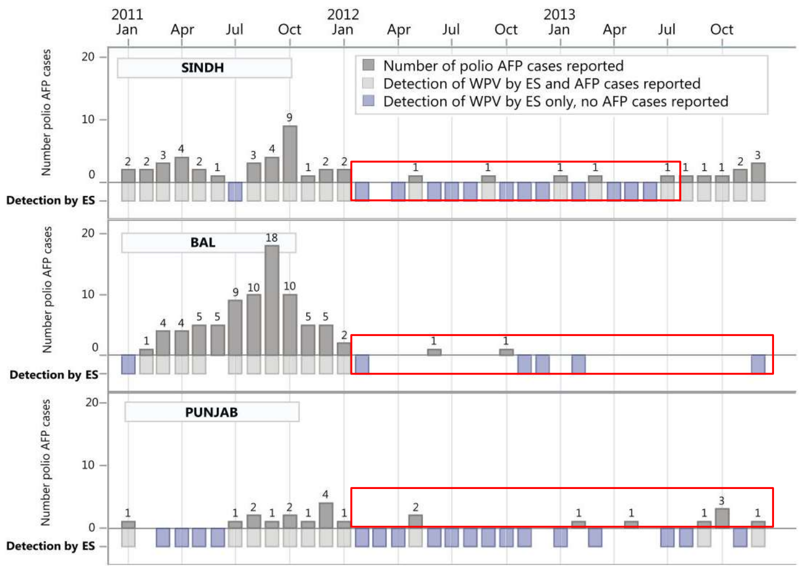
Global WPV1 & cVDPV Cases[1], Previous 12 Months[2]



[1]Excludes viruses detected from environmental surveillance; [2]Onset of paralysis: 06 Aug. 2024 to 05 Aug. 2025

Data in WHO HQ as or 5 Aug 2025

Environmental surveillance detected WPV before paralytic cases reported in Pakistan, suggesting silent transmission



Cowger et al. PLoS ONE 2017; 12(7)

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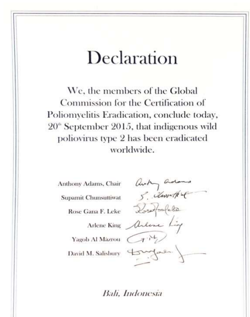
Type 2 Eradication

September 20th, 2015

- Global Commission for the Certification of Poliomyelitis Eradication (GCC) concluded that wild poliovirus type 2 (WPV2) has been eradicated worldwide
  - Review of formal documentation from global poliovirus laboratory network and surveillance systems
  - The last detected WPV2 dates to 1999, from Aligarh, northern India



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Type 3 Eradication

October 17, 2019

- Independent Global Commission for the Certification of Poliomyelitis Eradication (GCC) concluded that wild poliovirus type 3 (WPV3) has been eradicated worldwide
  - Review of formal documentation from global poliovirus laboratory network and surveillance systems
  - The last detected WPV3 dates to 2012, in northern Nigeria

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Knowledge Check

Which wild poliovirus serotypes have NOT been eradicated?

A. Type 1
B. Type 2
C. Type 3
D. Types 1 and 2
E. Types 2 and 3

Key Characteristics of Measles

Making it an indicator disease for immunization programs

- Highly contagious – most infectious of the vaccine-preventable diseases
- Distinct clinical syndrome
- Virtually all cases clinically apparent
- Good diagnostic tests
- Episodic in nature
  - Epidemics followed by low incidence as susceptibles accumulate fueling next epidemic
- Substantial complications including hospitalizations and deaths

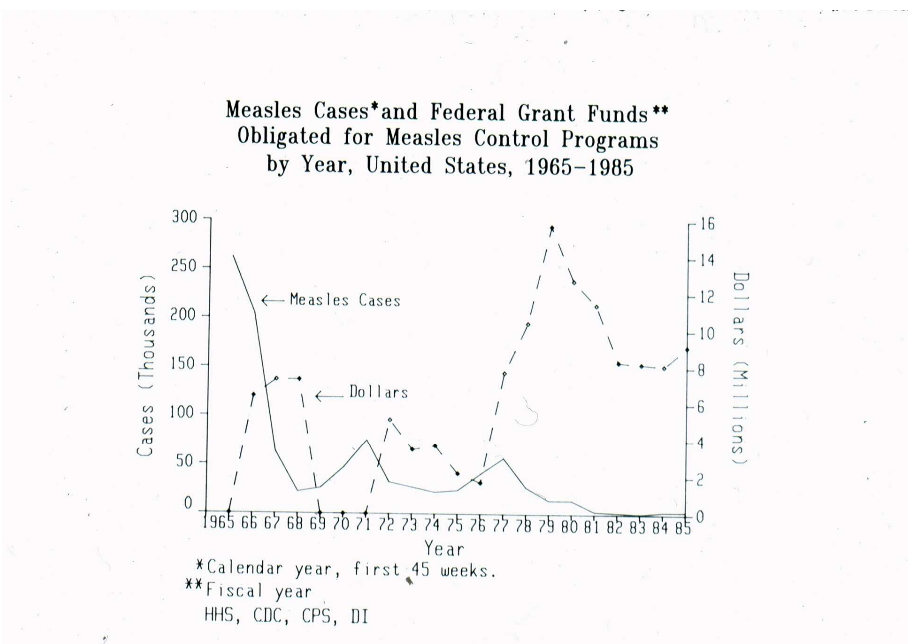
Initial Strategy for Eradication of Measles in 1967 †

- Routine immunization of infants
- Immunization on school entry
- Surveillance
- Epidemic control

† Sencer DJ, Dull HB, Langmuir AD. Epidemiologic Basis for the Eradication of Measles in 1967. Public Health Reports 1967; 82:253-256

Impact of Initial Measles Eradication Program 1966-1968

- >90% reduction in measles cases
  - >500,000 reported cases annually in pre-vaccine era to 22,000 in 1968
  - Actual cases in pre-vaccine era in the millions, many unreported
  - With improved reporting in the vaccine era, actual reduction likely much greater than 90%
- Funding for measles eradication program switched to rubella



Accumulating Knowledge 1969-1977

- Smallpox was being eradicated with "an outbreak control strategy"
  - Could measles be eradicated with a similar strategy?
- Demonstrating measles could be eliminated from the US could set the stage for potential worldwide eradication
- School laws make a major difference in controlling measles
- Need for continuous source of funding
- Surveillance documented a change in age pattern with a greater proportion of cases in middle and high schools
- Political leadership critical for success

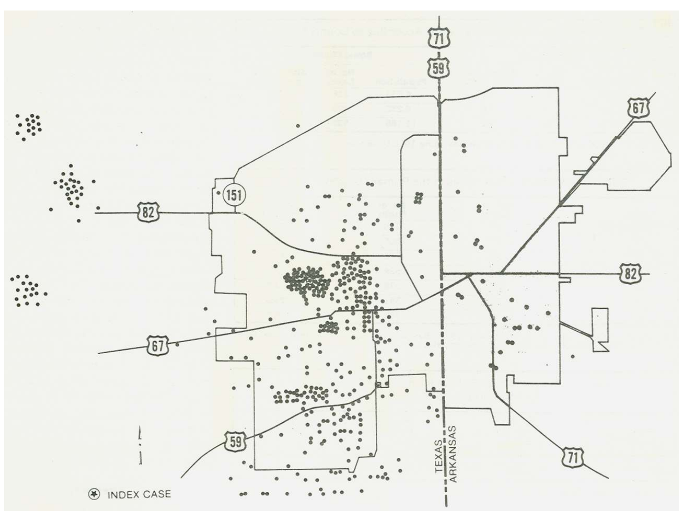


Figure 2. Cases of Measles, Texarkana, Tex-Ark, June 1970 to January 1971

From: Landrigan PJ, Epidemic Measles in a Divided City. JAMA 1972; 221:567-570

Measles, Los Angeles - 1977†

Mid January –	outbreak detected
Mid March –	2 deaths, 3 encephalitis cases, multiple pneumonia cases
March 31 –	school exclusion order issued for May 2nd, if no measles immunity
April –	clinics in most schools, night and weekend clinics
May –	~50,000 / 1.4 million students excluded within days, most back in school

† Orenstein WA, Hinman AR. Vaccine 1999; 17:S19-S24

Measles in 6 States Strictly Enforcing School Laws vs. Other States*

	Measles incidence †		
	1975-76	1977	1978 ‡
6 states ‡ ‡	47.0	40.6	2.7
Other states	50.4	90.3	35.2

* *MMWR* 1978; 27:303-4
† per 100,000 < 18 years
‡ 1st 31 weeks

‡ ‡ Alaska, Colorado, Hawaii, Maryland, New Mexico, South Dakota

US Experience with Focus on Measles & Building the Overall System

- Led to the enactment and enforcement of school and licensed day care immunization mandates covering all vaccines, not just measles
- Led to financing system to remove cost as a barrier for all childhood vaccines
- Led to a National Immunization Survey measuring immunization coverage of all vaccines for preschool children
- Led to two Presidential Initiatives

Measles Elimination – Lessons Learned

- Strong Scientific Base – vaccine science, epidemiology, health services research
- Limited number of measurable goals
- Compare and contrast good and poor performers – accountability
- Develop key partnerships to help build political base
- Focus not only on vertical measles elimination but also building the system

Knowledge Check

There are global goals to eradicate which of the following diseases?

A. Measles
B. Rubella
C. Polio
D. Tetanus

Critical Issues for Immunization Program Success I

- Understanding the Epidemiology of the Disease to Be Prevented
  - Who are the transmitters, who is most seriously affected, should a universal immunization program be implemented or a targeted one
- Knowing the effectiveness and safety in populations for whom vaccine is recommended
- Having a surveillance system in place to determine if cases are a result of vaccine failure or failure to vaccinate
- If vaccine failure, what is the reason (e.g., problems with cold chain, waning immunity, subpopulations with poor response, etc.) and take action based on what is found (e.g., booster doses if waning immunity)
- If failure to vaccinate, what is the reason (e.g., vaccine hesitancy, problems with access, not recommended for vaccination by NITAG)

Critical Issues for Immunization Program Success II

- Have an ongoing monitoring program in place to help in answering questions not answered when a vaccine is first approved
  - Vaccine Effectiveness assessment in observational studies when randomized placebo-controlled studies are not ethical or feasible
  - Vaccine Safety Evaluation to look for rare events and determine if such events are causally related or coincidentally related
    - If causally related, what are the characteristics of the persons with the adverse event. Can a contraindication be made for such persons. Do the benefits of vaccines continue to outweigh the risks.
- Having a strong communications system to deliver the right messages, by the right messengers, through the right communications channels – key groups – public health, healthcare providers, media, general public and more

Key Takeaways

- **Eradication vs. Elimination:** Eradication refers to global extinction of a disease, while elimination refers to stopping the spread of a disease within a defined geographic area.
- **Surveillance is Critical:** Effective disease surveillance helps track progress, identify outbreaks, and distinguish between vaccine failure and failure to vaccinate, guiding intervention strategies.
- **Global Collaboration Benefits Everyone:** Investments from high-income countries in eradication efforts in low-income regions strengthen global health security, reduce cross-border transmission, and protect everyone from re-emerging threats.

Thank you