Research for polio policy making: Lessons learned

GVIRF 2018, Bangkok, Thailand

Overview

- Thinking then and now
- Issues & responses
  - Low OPV immunogenicity
  - Chronic excretors of poliovirus & emergence of circulating vaccine-derived poliovirus
  - Understanding IPV immunogenicity (especially mucosal immunity)
- Lessons learned
- Opportunities & needs

Thinking in 1988 when eradication goal adopted and what has been learned - I

THINKING IN 1988

- Need to eradicate three wild polioviruses (WPV 1,2,3)
- Trivalent OPV would be adequate
- OPV could cause vaccine-associated polio in vaccine recipients or close contacts
- Acute flaccid paralysis (AFP) surveillance was adequate to find virus

THINKING IN 2018

- Need to eradicate six polioviruses (WPV 1,2,3 and Sabin vaccine viruses 1,2,3)
- Need monovalent and bivalent OPV
- OPV, through mutations, could reacquire phenotypic characteristics of WPVs leading to outbreaks (cVDPVs)
- AFP surveillance is not enough; environmental surveillance offers much in detecting virus

Thinking in 1988 when eradication goal adopted and what has been learned - II

THINKING IN 1988

- Primary immunodeficient chronic shedders (iVDPVs) of vaccine virus could develop polio but were not a danger to the community
- Inactivated Polio Vaccine (IPV) had no role in achieving eradication in developing countries with poor sanitation and hygiene

THINKING IN 2018

- iVDPVs could theoretically reseed a community and lead to cVDPVs and polio outbreaks
- IPV may have a role in achieving eradication but will be very important in sustaining eradication as Sabin Vaccine Viruses are withdrawn

Thinking in 1988 when eradication goal adopted and what has been learned - III

THINKING IN 1988

- Sustaining eradication, with a major focus on containment, was not a part of decision-making
- Vaccination could be stopped once polio eradication was certified, as was done with smallpox

THINKING IN 2018

- Sustaining eradication, with the need to contain and collect or destroy specimens (such as virus-containing stools), is an important part of current decision-making
- There is a need to continue vaccination for some period and potentially indefinitely after WPV is eradicated and Sabin viruses are withdrawn

Thinking in 1988 when eradication goal adopted and what has been learned - IV

THINKING IN 1988

- Everything needed for eradication was already known

THINKING IN 2018

- Continuing need for an extensive research program dealing with issues such as:
  - Development of safer vaccines
  - Development of vaccines that not only provide individual protection but community protection
  - The role of IPV and the optimal schedule, and how to make it cheaper
  - Detecting primary immunodeficient shedders and developing antivirals

Low immunogenicity of trivalent oral poliovirus vaccine (OPV)

New Strategies for the Elimination of Polio from India

Nicholas C. Grassly,[1]* Christophe Fraser,[1] Jay Wenger,[2] Jagadish M. Deshpande,[3] Roland W. Sutter,[4] David L. Heymann,[4] R. Bruce Aylward[4]

The feasibility of global polio eradication is being questioned as a result of continued transmission in a few localities that act as sources for outbreaks elsewhere. Perhaps the greatest challenge is in India, where transmission has persisted in Uttar Pradesh and Bihar despite high coverage with multiple doses of vaccine. We estimate key parameters governing the seasonal epidemics in these areas and show that high population density and poor sanitation cause persistence by not only facilitating transmission of poliovirus but also severely compromising the efficacy of the trivalent vaccine. We analyze strategies to counteract this and show that switching to monovalent vaccine may finally interrupt virus transmission.

The World Health Assembly committed to the global eradication of polio in 1988. Since then, the eradication initiative has achieved great successes, eliminating polio from the Americas, the Western Pacific, and Europe. However, in recent years the number of reported cases has increased after export of infection from the handful of remaining endemic countries. The difficulty in eliminating these last reservoirs of poliovirus transmission has led some to question the feasibility of eradication (*1*). Particularly worrying is the ongoing transmission in India, the source of half the world's reported paralytic cases over the past decade. Children in India have re-

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Table 1. Estimates of trivalent OPV efficacy in India, 1997 to 2005. The per-dose protective efficacy of the vaccine was estimated from the reported number of OPV doses received by polio AFP cases compared with matched nonpolio AFP controls, using conditional logistic regression (*6*). Regression model 1 provides an estimate for all India, whereas model 2 includes an interaction term between efficacy and location.

Poliovirus	Regression model	Location	Cases	Matches	Vaccine efficacy (%) (95% CI)
Type 1	Model 1	All India	4421	1627	13 (10–16)
	Model 2	Rest of India	1512	361	21 (15–27)
		Bihar	387	158	18 (9–26)
		Uttar Pradesh	2522	1108	9 (6–13)*
Type 3	Model 1	All India	1204	474	13 (7–18)
	Model 2	Rest of India	221	79	21 (8–33)
		Bihar	136	53	22 (4–36)
		Uttar Pradesh	847	342	9 (3–15)

*Significantly different from rest of India, $P < 0.01$

Articles

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 16, 2008 VOL. 359 NO. 16

Monovalent Type 1 Oral Poliovirus Vaccine in Newborns

Nasr El-Sayed, M.D., M.P.H., Yehia El-Gamal, M.D., Ph.D., Ahmed-Amr Abbassy, M.D., Ph.D., Iman Seoud, M.D., Ph.D., Maha Salama, M.D., Amr Kandeel, M.D., M.P.H., Elham Hossny, M.D., Ph.D., Ahmed Shawky, M.D., Heba Abou Hussein, M.D., Ph.D., Mark A. Pallansch, Ph.D., Harrie G.A.M. van der Avoort, Ph.D., Anthony H. Burton, B.S., Meghana Sreevatsava, M.P.H., Pradeep Malankar, M.D., Mohamed H. Wahdan, M.D., Ph.D., and Roland W. Sutter, M.D., M.P.H.T.M.

Immunogenicity of bivalent types 1 and 3 oral poliovirus vaccine: a randomised, double-blind, controlled trial

Roland W Sutter, T Jacob John, Hemant Jain, Sharad Agarkhedkar, Padmasani Venkat Ramanan, Harish Verma, Jagadish Deshpande, Ajit Pal Singh, Meghana Sreevatsava, Pradeep Malankar, Anthony Burton, Arani Chatterjee, Hamid Jafari, R Bruce Aylward

Lancet 2010; 376: 1682–88
Published Online October 26, 2010
DOI:10.1016/S0140-6736(10)61230-5
See Comment page 1624

World Health Organization, Geneva, Switzerland (R W Sutter MD, M Sreevatsava MPH, P Malankar MD, A Burton,

Summary

Background Poliovirus types 1 and 3 co-circulate in poliomyelitis-endemic countries. We aimed to assess the immunogenicity of a novel bivalent types 1 and 3 oral poliovirus vaccine (bOPV).

Methods We did a randomised, double-blind, controlled trial to assess the superiority of monovalent type 2 OPV (mOPV2), mOPV3, or bOPV over trivalent OPV (tOPV), and the non-inferiority of bivalent vaccine compared with mOPV1 and mOPV3. The study was done at three centres in India between Aug 6, 2008, and Dec 26, 2008. Random allocation was done by permuted blocks of ten. The primary outcome was seroconversion after one monovalent or bivalent vaccine dose compared with a dose of trivalent vaccine at birth. The secondary endpoints were seroconversion after two vaccine doses compared with after two trivalent vaccine doses and cumulative two-dose seroconversion. Parents or guardians and study investigators were masked to treatment allocation. Because of multiple comparisons, we defined

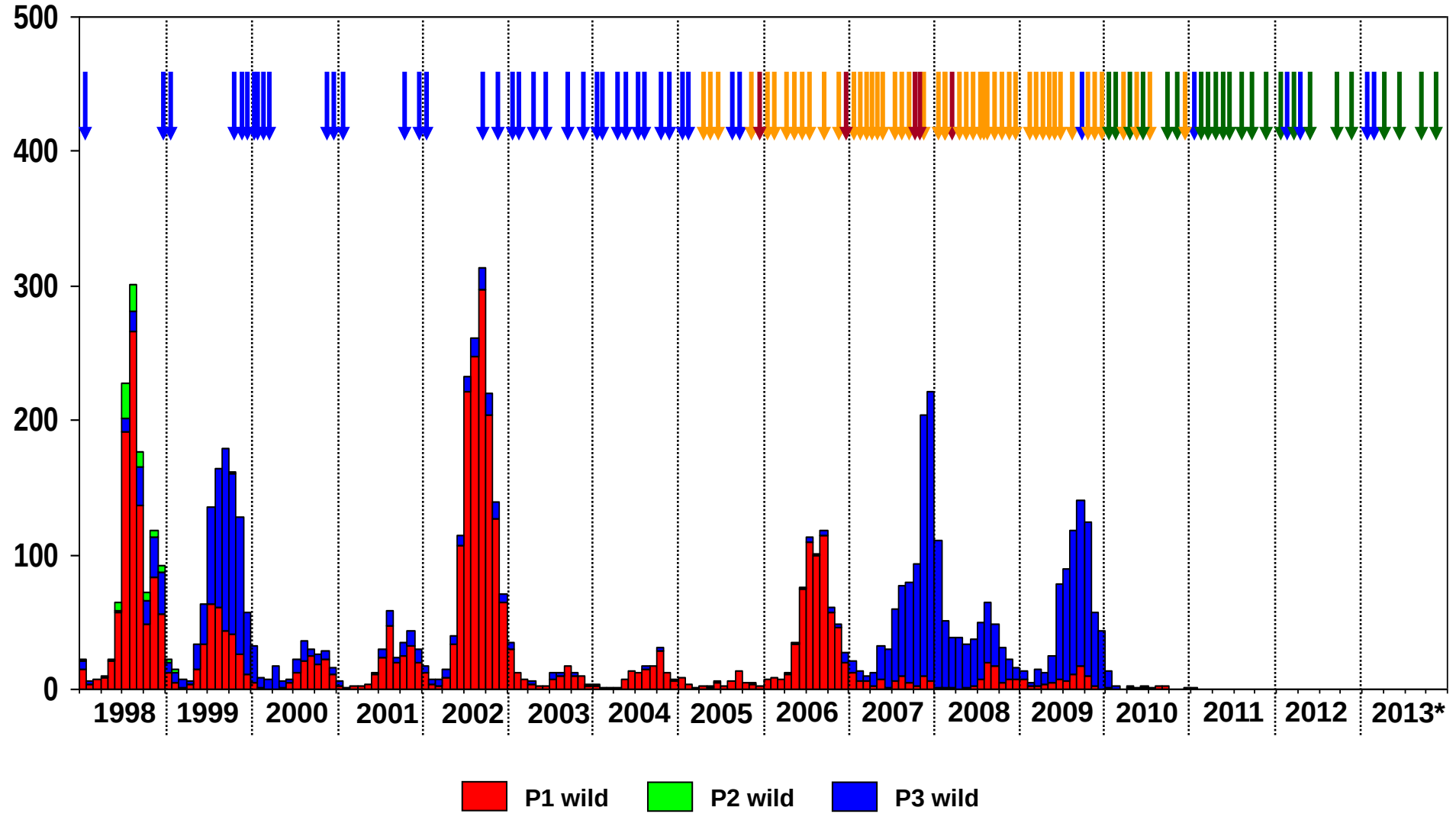
Quest for more immunogenic OPV

Product	Initial license year	Country	Initial study	Comment
tOPV	1963	USA	Control	
mOPV1	2004, 2005	India, France	55% mOPV1 vs 32% tOPV	Birth dose study in Egypt*
mOPV2	2007, 2008	India, Belgium	90% mOPV2 vs 91% tOPV	2-dose study in India (birth + 30 days)+
mOPV3	2005	India	84% mOPV3 vs 52% tOPV	+
bOPV (types 1+3)	2009	India, Belgium	bOPV 86% P1, 74% P3	type 2 interference removed+

*El-Sayed N, et al. N Engl J Med 2008;359:1655-65.
+Sutter RW, et al. Lancet 2010;376:1682-88

*Poliovirus cases, 1998 – November 2013**

(4 high-priority States: Bihar + Delhi + Uttar Pradesh + West Bengal)



** data as on 23 November 2013*

Policy decisions

- *Policy recommendations:*
  - Supplementary immunization activities (SIAs)
    - mOPV1 or mOPV3 (or bOPV)
  - Outbreak control
    - type-specific mOPV
  - Routine EPI schedule (after OPV2 withdrawal)
    - bOPV (replaced tOPV)

Longterm excreters of poliovirus & vaccine-derived poliovirus

AL OF CLINICAL MICROBIOLOGY, Oct. 1998, p. 2893–2899
137/98/$04.00+0

Prolonged Replication of a Type 1 Vaccine-Derived Poliovirus in an Immunodeficient Patient

OLEN M. KEW,[1]* ROLAND W. SUTTER,[2] BALDEV K. NOTTAY,[1] MICHAEL J. McDONOUGH,[1] D. REBECCA PREVOTS,[3] LINDA QUICK,[2] AND MARK A. PALLANSCH[1]

Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases,[1] and Divisions of Eradication of Vaccine-Preventable Diseases[2] and Epidemiology and Surveillance,[3] National Immunization Program, Centers for Disease Control and Prevention, Atlanta, Georgia 30333

Received 11 March 1998/Returned for modification 5 June 1998/Accepted 26 June 1998

VP1 sequences were determined for poliovirus type 1 isolates obtained over a 189-day period from a poliomyelitis patient with common variable immunodeficiency syndrome (a defect in antibody formation). The isolate from the first sample, taken 11 days after onset of paralysis, contained two poliovirus populations, differing from the Sabin 1 vaccine strain by ~10%, differing from diverse type 1 wild polioviruses by 19 to 24%, and differing from each other by 5.5% of nucleotides. Specimens taken after day 11 appeared to contain only one major poliovirus population. Evolution of VP1 sequences at synonymous third-codon positions occurred at an overall rate of ~3.4% per year over the 189-day period. Assuming this rate to be constant throughout the period of infection, the infection was calculated to have started ~9.3 years earlier. This estimate is about the time (6.9 years earlier) the patient received his last oral poliovirus vaccine dose, approximately 2 years before the diagnosis of immunodeficiency. These findings may have important implications for the strategy to eliminate poliovirus immunization after global polio eradication.

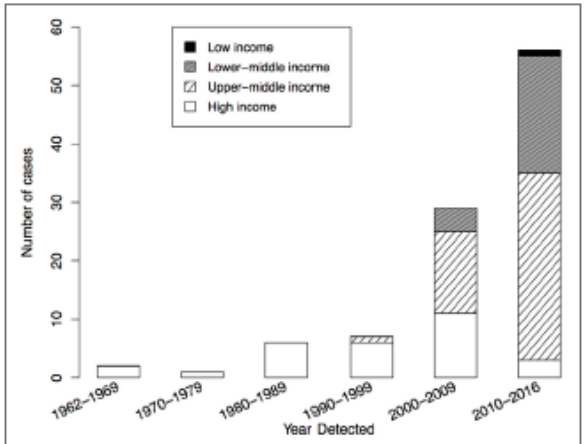


FIGURE 1 | Year of detection of 101 reported chronic and prolonged immunodeficiency-related vaccine-derived poliovirus cases from 1962 to 2016, by income classification of country of residence: low income ($n = 1$), lower-middle income ($n = 24$), upper-middle income ($n = 47$), and high-income ($n = 29$). Income classification based on 2016 World Bank Classification.

Failure to clear persistent vaccine-derived neurovirulent p infection in an immunodeficient man

Calman MacLennan, Glynis Dunn, Aarnoud P Huissoon, Dinakantha S Kumararatne, Javier Martin, Paula O Ronald A Thompson, Husam Osman, Philip Wood, Philip Minor, David J Wood, Deenan Pillay

Summary

Background Individuals who chronically excrete neurovirulent poliovirus of vaccine-origin are of considerable concern to the Global Polio Eradication programme. Chronic infection with such polioviruses is a recognised complication of hypogammaglobulinaemia.

Methods We did a series of in-vitro and in-vivo therapeutic studies, with a view to clearing persistent neurovirulent poliovirus infection in an individual with common variable immunodeficiency, using oral immunoglobulin, breast milk (as a source of secretory IgA), ribavirin, and the anti-picornaviral agent pleconaril. We undertook viral quantitation, antibody neutralisation and drug susceptibility assays, and viral gene sequencing.

represents a risk to the strategy to vaccination once global eradication has be

Lancet 2004; **363:** 1509–13

Introduction

Chronic poliovirus excretion (>6 mo recognised as a complication of primi ciency, specifically hypogammaglobulin Since then, 19 individuals have been ide of the virus for more than 6 months, a been antibody-deficient.[2] Most have poliomyelitis,[3–5] although a few have be carriers.[1,6] No carrier state has been immunocompetent individual.[7]

Outbreak of Poliomyelitis in Hispaniola Associated with Circulating Type 1 Vaccine-Derived Poliovirus

Olen Kew,[1]* Victoria Morris-Glasgow,[2] Mauricio Landaverde,[3] Cara Burns,[1] Jing Shaw,[1] Zacarías Garib,[4] Jean André,[5] Elizabeth Blackman,[2] C. Jason Freeman,[1] Jaume Jorba,[1] Roland Sutter,[6] Gina Tambini,[3] Linda Venczel,[3] Cristina Pedreira,[7] Fernando Laender,[8] Hiroyuki Shimizu,[9] Tetsuo Yoneyama,[9] Tatsuo Miyamura,[9] Harrie van der Avoort,[10] M. Steven Oberste,[1] David Kilpatrick,[1] Stephen Cochi,[6] Mark Pallansch,[1] Ciro de Quadros[3]

An outbreak of paralytic poliomyelitis occurred in the Dominican Republic (13 confirmed cases) and Haiti (8 confirmed cases, including 2 fatal cases) during 2000–2001. All but one of the patients were either unvaccinated or incom-

																	cVDPV type 2			
Country	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Onset of most recent case
DRCongo									13	5	18	11	17					22		22-Dec-17
Syria																		74		21-Sep-17
Pakistan													16	48	22	2	1			17-Dec-16
Nigeria						3	22	71	68	155	27	34	8	4	30	1	1			28-Oct-16
Guinea															1	7				14-Dec-15
Myanmar																2				05-Oct-15
South Sudan															2					12-Sep-14
Cameroon														4						12-Aug-13
Niger							2			2	1	1		1						11-Jul-13
Chad											1		12	4						12-May-13
Afghanistan											5	1	9	3						13-Mar-13
Somalia									1	6	1	9	1	1						09-Jan-13
Kenya													3							29-Aug-12
China													2							06-Feb-12
Yemen												9								05-Oct-11
India										15	2									18-Jan-10
Ethiopia									3	1										16-Feb-09
Madagascar		1	4			3														13-Jul-05
Total type 2	0	1	4	0	0	6	24	71	85	184	55	65	68	65	55	12	2	96	0	

Macklin G, et al. Front Immunol 2017 (online)

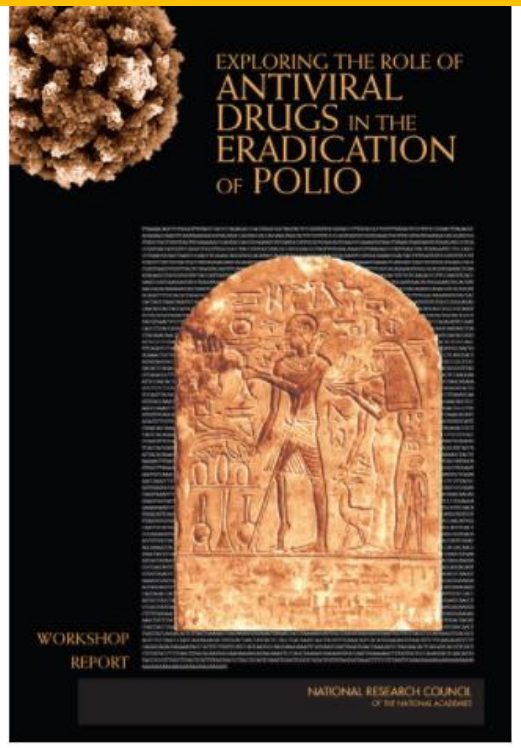
Vaccine-associated paralytic poliomyelitis (VAPP) & circulating vaccine-derived poliovirus (cVDPV)

Attributes		VAPP*	cVDPV+
Occurrence		Sporadic	Epidemic (transmission)
Presentations		Paralysis	Paralysis
Risk factors	Individual susceptibility	+++	+++
	Immunodeficiency	+++	-
	Species C NPEV prevalence	-	++
	Tropical enteropathy	-	++
Virus	Recombination	Rare	Typical
	Sequence diversity in VP1	-	>0.6% P2, >1% in P1 or P3
Control	Prevent OPV exposure	+++	-
	High population immunity	-	+++

*Terry L. Report of the Surgeon General. Washington, DC: US Department of Health, Education and Welfare,1962.
+Kew OM, et al, Science 2002;296:356-359.

Response & Policy decisions

- Research studies on VAPP
- WHO registry for iVDPV
- IOM 2006: Review
- Antiviral initiative in TFCH
  - Single drug Pocapavir under IND
- SAGE 2017: Decision to screen individuals with signs of immunodeficiency disorders for poliovirus excretion



The Journal of Infectious Diseases
MAJOR ARTICLE

Antiviral Activity of Pocapavir in a Randomized, Blinded, Placebo-Controlled Human Oral Poliovirus Vaccine Challenge Model

Marc S. Collett,[1] Jeffrey R. Hincks,[1] Kimberley Benschop,[4] Erwin Duizer,[4] Harrie van der Avoort,[4] Eric Rhoden,[2] Hongmei Liu,[2] M. Steven Oberste,[2] Mark A. McKinlay,[3] and Marianne Hartford[5]

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al List › Front Immunol › v.8; 2017 › PMC5622164

frontiers in Immunology

Front Immunol. 2017; 8: 1103. PMCID: PMC5622164
Published online 2017 Sep 25. doi: 10.3389/fimmu.2017.01103

Prolonged Excretion of Poliovirus among Individuals with Primary Immunodeficiency Disorder: An Analysis of the World Health Organization Registry

Grace Macklin,[1,*] Yi Liao,[1,2] Marina Takane,[1] Kathleen Dooling,[1] Stuart Gilmour,[2] Ondrej Mach,[1] Olen M. Kew,[3,4] Roland W. Sutter,[1] and The iVDPV Working Group

Author information ► Article notes ► Copyright and License information ►

Understanding IPV immunity contributions

		Tropical developing	Industrialized
Immunogenicity	Humoral	+++	+++
	Priming	++	++
	Mucosal	-	-
Risk factors	Maternal antibodies	+++	+++
	Acute malnutrition	+	+
Boosting	Humoral	+++	+++
	Mucosal (only OPV)*	+++	+++

* POLIO ERADICATION

Efficacy of inactivated poliovirus vaccine in India

Hamid Jafari,[1]* Jagadish M. Deshpande,[2] Roland W. Sutter,[3]† Sunil Bahl,[1] Harish Verma,[3] Mohammad Ahmad,[1] Abhishek Kunwar,[1] Rakesh Vishwakarma,[1] Ashutosh Agarwal,[1] Shilpi Jain,[4] Concepcion Estivariz,[5] Raman Sethi,[1] Natalie A. Molodecky,[3] Nicholas C. Grassly,[6] Mark A. Pallansch,[5] Arani Chatterjee,[4]‡ R. Bruce Aylward[3]

Inactivated poliovirus vaccine (IPV) is efficacious against paralytic disease, but its effect on mucosal immunity is debated. We assessed the efficacy of IPV in boosting mucosal immunity. Participants received IPV, bivalent 1 and 3 oral poliovirus vaccine

Jafari H, et al. Science 2014;384:1505-12.

*

Effect of a single inactivated poliovirus vaccine dose on intestinal immunity against poliovirus in children previously given oral vaccine: an open-label, randomised controlled trial

Jacob John, Sidhartha Giri*, Arun S Karthikeyan, Miren Iturriza-Gomara, Jayaprakash Muliyil, Asha Abraham, Nicholas C Grassly†, Gagandeep Kang†*

Summary

Background Intestinal immunity induced by oral poliovirus vaccine (OPV) is imperfect and wanes with time, permitting transmission of infection by immunised children. Inactivated poliovirus vaccine (IPV) does not induce an intestinal mucosal immune response, but could boost protection in children who are mucosally primed through previous exposure to OPV. We aimed to assess the effect of IPV on intestinal immunity in children previously vaccinated with OPV.

John J, et al. Lancet 2014;384:1505-12.

One dose IPV

Table 2. Rates of Seroconversion and Priming Immune Response after One or Two Doses of Inactivated Poliovirus Vaccine for Poliovirus Types 1, 2, and 3.*

Immune Response	Fractional IPV Dose (N=157)	Full IPV Dose (N=153)	P Value	Between-Group Difference (95% CI)
	no./total no. (%)			*percentage points*
Poliovirus type 1				
Seroconversion after first dose	26/157 (16.6)	71/153 (46.4)	<0.001	29.8 (19.2 to 39.6)
Priming response	119/131 (90.8)	80/82 (97.6)	0.1	6.8 (–1.3 to 13.7)
Seroconversion between visits 3 and 4	2/12 (16.7)	2/2 (100)	0.13	83.3 (–3.2 to 97.1)
Seroconversion after second dose	121/131 (92.4)	82/82 (100)	0.01	7.6 (0.9 to 14.0)
Cumulative seroconversion	147/157 (93.6)	153/153 (100)	0.002	6.4 (2.0 to 11.7)
Poliovirus type 2				
Seroconversion after first dose	74/157 (47.1)	96/153 (62.7)	0.008	15.7 (4.1 to 26.6)
Priming response	78/83 (94.0)	56/57 (98.2)	0.42	4.3 (–5.4 to 12.5)
Seroconversion between visits 3 and 4	2/5 (40.0)	1/1 (100)	>0.99	60.0 (NP)
Seroconversion after second dose	80/83 (96.4)	57/57 (100)	0.41	3.6 (–4.7 to 10.9)
Cumulative seroconversion	154/157 (98.1)	153/153 (100)	0.26	1.9 (–1.5 to 5.9)
Poliovirus type 3				
Seroconversion after first dose	23/157 (14.6)	49/153 (32.0)	<0.001	17.3 (7.5 to 26.9)
Priming response	120/134 (89.6)	102/104 (98.1)	0.01	8.5 (1.5 to 15.5)
Seroconversion between visits 3 and 4	3/14 (21.4)	1/2 (50.0)	0.90	28.6 (NP)
Seroconversion after second dose	123/134 (91.8)	103/104 (99.0)	0.018	7.2 (0.9 to 13.7)
Cumulative seroconversion	146/157 (93.0)	152/153 (99.3)	0.006	6.4 (1.6 to 11.9)

* Seroconversion was defined as an increase in the antibody titer that was four times as high as the expected decline in maternally derived antibodies. Cumulative seroconversion reflects the sum of the seroconversions occurring after the first and the second dose. P values were calculated with the use of chi-square tests (with the Yates-corrected test, or with Fisher's exact test if the number of participants in a cell was 5 or fewer). NP denotes not presented (i.e., the numbers of participants in the cells were too small to calculate meaningful 95% confidence intervals).

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Priming after a Fractional Dose of Inactivated Poliovirus Vaccine

Sonia Resik, M.D., Ph.D., Alina Tejeda, M.D., Roland W. Sutter, M.D., M.P.H.&T.M., Manuel Diaz, M.D., Luis Sarmiento, Ph.D., Nilda Alemañi, M.D., M.Sc., Gloria Garcia, M.Sc., Magilé Fonseca, M.Sc., Lai Heng Hung, M.Sc., Anna-Lea Kahn, M.Sc., Anthony Burton, B.S., J. Mauricio Landaverde, M.D., M.P.H., and R. Bruce Aylward, M.D., M.P.H.

ABSTRACT

BACKGROUND

To reduce the costs of maintaining a poliovirus immunization base in low-income areas, we assessed the extent of priming immune responses after the administration of inactivated poliovirus vaccine (IPV).

METHODS

We compared the immunogenicity and reactogenicity of a fractional dose of IPV

Resik S, et al. N Engl J Med 2013:368:416-24.

Policy decisions: The roadmap (WHA)

- Sequential removal of Sabin strains from OPV
- Starting with type 2 in 2016
- bOPV replacing tOPV
- IPV introduced in routine EPI schedules as risk mitigation

- 2 fractional IPV doses better than one full IPV dose (SAGE 2016)

WHO, Geneva, 2013

Lessons learned

- *Priority setting:* "if you don't know where go, any road will get you there"
- *Partnership:* Agenda, priority, labour division
- *Infrastructure:* Ethical Review Committee, standing DSMB, Polio Research Committee (PRC)
- *Public sector:* CDC/FDA/NIH, NIBSC, NIID, GPLN, Academia
- *Dedicated longterm funding support:* Allow rapid implementation of priority research
- *Collaboration:* Long term relationship with capacity building
- *Licensing studies:* Key studies sponsored / funded by GPEI

Opportunities / Needs

- *Priming*:
  - Duration, efficacy in preventing paralytic disease
- *One-dose IPV:*
  - Sufficient for long term immunity
- *iVDPV surveillance:*
  - How to screen population (10 warning signs – J Modell Foundation)
- *Containment:*
  - Replace neutralization assays
  - Eliminate infectious processes for vaccine production (VLPs)
- *Vaccine development:*
  - Mucosal immunity induced by inactivated vaccine ("holy grail")
  - New genetically stable OPV
  - Virus-like particles (VLPs)

Thank you for your attention!

EMORY UNIVERSITY

Computational and Structural Biotechnology Journal 15 (2017) 456–462

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COMPUTATIONAL AND STRUCTURAL BIOTECHNOLOGY JOURNAL

journal homepage: www.elsevier.com/locate/csbj

Are Circulating Type 2 Vaccine-derived Polioviruses (VDPVs) Genetically Distinguishable from Immunodeficiency-associated VDPVs?

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Comparative genomics

ABSTRACT

Public health response to vaccine-derived poliovirus (VDPV) that is transmitted from person to person (circulating VDPV [cVDPV]) differs significantly from response to virus that replicates in individuals with primary immunodeficiency (immunodeficiency-associated VDPV [iVDPV]). cVDPV outbreaks require a community immunization response, whereas iVDPV chronic infections require careful patient monitoring and appropriate individual treatment. To support poliovirus outbreak response, particularly for type 2 VDPV, we investigated the genetic distinctions between cVDPV2 and iVDPV2 sequences. We observed that simple genetic measurements of nucleotide and amino acid substitutions are sufficient for distinguishing highly divergent iVDPV2 from cVDPV2 sequences, but are insufficient to make a clear distinction between the two categories among less divergent sequences. We presented quantitative approaches using genetic information as a surveillance tool for early detection of VDPV outbreaks. This work suggests that genetic variations between cVDPV2 and iVDPV2 may reflect differences in viral microenvironments, host-virus interactions, and selective pressures during person-to-person transmission compared with chronic infections in immunodeficient patients.

Policy decisions

- *Technical oversight committees:*
  - Before 2005: Technical Consultative Group (TCG) on the Global Eradication of Poliomyelitis
  - 2005-2010: Advisory Committee for Polio Eradication (ACPE)
  - After 2010: SAGE (with WG on Polio support)