POLIO GLOBAL ERADICATION INITIATIVE

IPK INSTITUTO DE MEDICINA TROPICAL «PEDRO KOURÍ»

Lecciones aprendidas en la erradicación de la Poliomielitis: Contribuciones de Cuba al Programa Mundial de Erradicación

Dra. Sonia Resik, PhD, IPK, Cuba
sresik@ipk.sld.cu

III Congreso Internacional de Inmunizaciones
Vacunación Humanizada para una Ciudad Saludable
Medellín, Colombia

EVERY LAST CHILD

World Health Assembly Resolution: 1988

...polio eradication by the end of the year 2000…

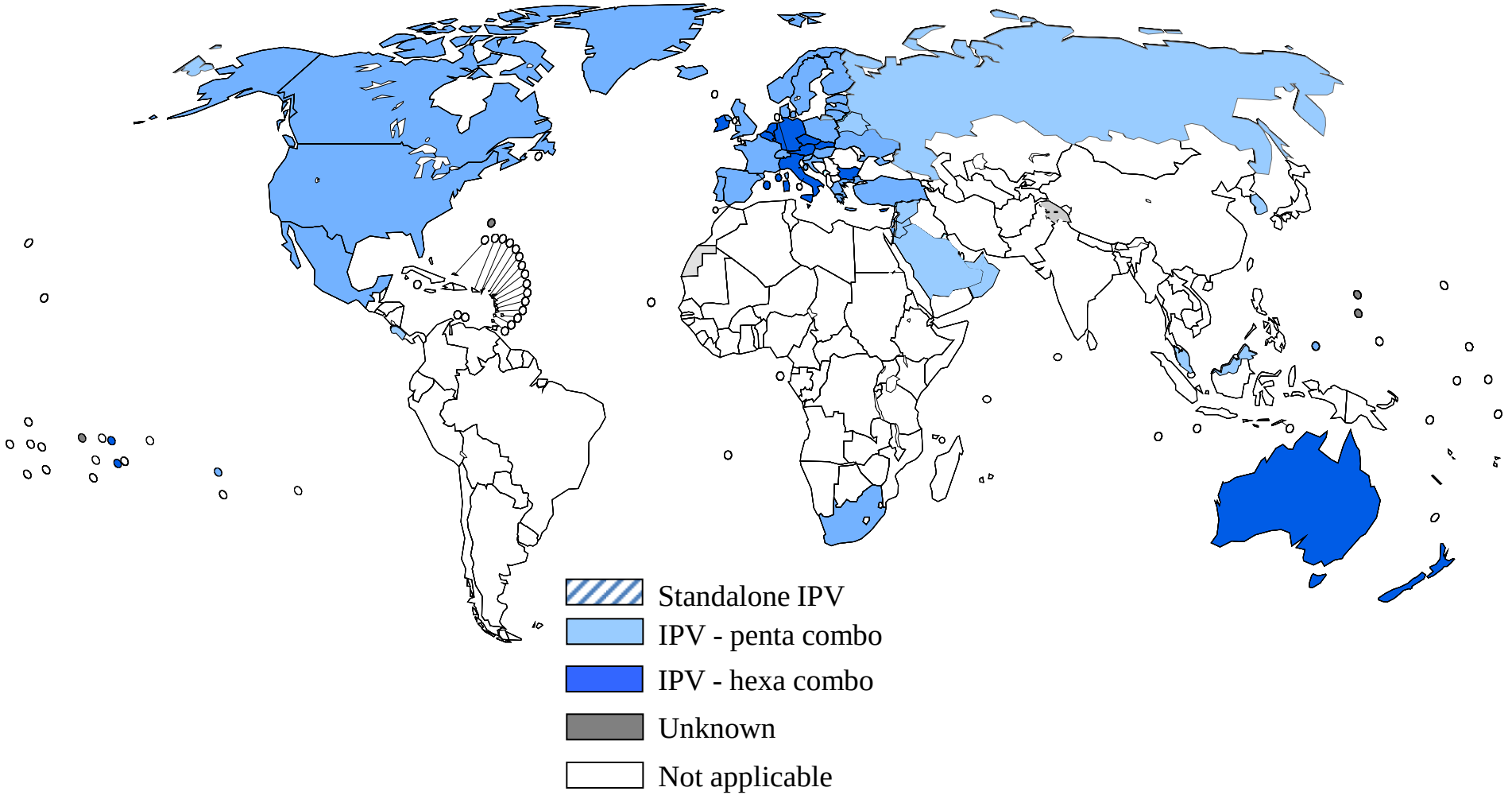
Expert Consultation on Vaccine-derived Polioviruses (VDPVs), Sept 2003, Geneva

After interruption of wild poliovirus, continued use of OPV would compromise the goal of a polio-free world.

Prerequisites for OPV Cessation

1. Wild virus certification & containment.
2. Global surveillance & notification.
3. mOPV stockpile & response.
4. **Affordable IPV** & use in PV-retaining areas.
5. Synchronization of OPV cessation.
6. Containment of Sabin virus.

Countries with IPV Use



Data in WHO HQ as of Sep 2010

WHO

61st World Health Assembly Resolution (2008)

Requests DG/WHO to:

…develop appropriate strategies and products for managing risks, including ***safer processes for IPV production & affordable strategies*** *for its use…*

Affordable IPV Strategy: Different Approaches

- Schedule
  - Routine schedule for IPV use in tropical areas
- Dose Reduction
  - Intradermal administration of 1/5 fractional IPV dose
- Schedule & Dose Reduction
  - 2-dose fractional schedule (DTP4 & measles)
- Adjuvants
  - Evaluate adjuvants for antigen reduction
- Seed strains for IPV production (Sabin & alternate strains)
  - Permit production of IPV in developing countries
- Needle-free Device to Administer IPV Intradermally
  - Easier administration of fractional doses & use of volunteers

Why Cuba?

- Epidemiology
- Infrastructure
- Interest & commitment

Epidemiology

- Poliomyelitis was eliminated from Cuba in the early 1960s.
  - earliest example how to eradicate polio using mass campaign.
- Unique campaign approach to maintaining polio-free status
  - Biannual NIDs since 1962 without Polio vaccine available at any other time.
  - Scientific evidences of limited circulation of VDPV during 3 months after NIDs.

Infrastructure

- Accredited polio laboratory at IPK
  - virus isolation & serology (neutralization)
- Vaccine field trial site in Camaguey
  - with necessary trial infrastructure
- National regulatory authority & ethical review committees
  - to review, approve and regulate trials
- Well-trained & interested staff at all levels

Interest & commitment

- Government
- Ministry of Health
- IPK
- Camagüey Provincial Health Office

Example 1: Immunogenicity of OPV

- *Study:*
  - seroprevalence survey in young children
- *Outcome:*
  - 3 doses of OPV insufficient to induce immunity against polioviruses
- *Implications:*
  - multiple dose of OPV are required

Más Lago P, et al. Bull WHO 1994;72:221-5

Example 2: Vaccine-associated polio

- *Surveillance:*
  - monitoring vaccine-associated paralytic poliomyelitis (VAPP) in Cuba from 1963-2006
- *Outcome:*
  - definition of VAPP risk
- *Implications:*
  - confidence building that risk is very low

Más Lago P, et al. Rev Cuba Hig Epidemiol 2008; 46(2)

Example 3: OPV virus persistence

- *Study:*
  - length of circulation of OPV polioviruses after campaign (stool surveys, environmental sampling, and seroprevalence surveys)
- *Outcome:*
  - circulation is limited to ~8-12 weeks
- *Implications:*
  - in well-immunized population in tropical developing countries, vaccine virus will die out after stopping OPV

Más Lago P et al. Int J Epidemiol 2001;30:1029-34

Más Lago P et al. Int J Epidemiol 2003;32:772-7

Example 4: Schedule evaluation

- *Study:*
  - assess schedule & mucosal immunity after IPV (6,10, 14 weeks vs 2, 4 mos)
- *Outcome:*
  - 2 doses at 2 + 4 mos provided similar immunity as 3 doses at 6, 10, 14 weeks
  - excretion following challenge of OPV was >90% in all three arms (including placebo arm)
- *Implications:*
  - re-confirmed data from IPV-using industrialized countries

Cuba IPV Study Collaborative Group. N Engl J Med 2007;356:1536-44

Example 5: "Affordable" IPV

- *Study:*
  - evaluation of a fractional dose IPV (1/5 of dose) administered intradermally at 6, 10, and 14 weeks
- *Outcome:*
  - demonstrated feasibility of intradermal fractional-dose approach
- *Implications:*
  - suboptimal immunity (need later start and longer intervals between doses)

Resik S, et al. J Infect Dis 2010;201:344-52

Example 6: Priming after IPV

- *Study:*
  - priming after a single IPV dose at 4 mos of age
- *Outcome:*
  - >95% of those not seroconverting after IPV dose responded with priming immune response after full-dose IPV and ~90% to a fractional dose
- *Implications:*
  - one-dose IPV could be used for inducing an immunity base against poliovirus
  - provided foundation for new polio endgame plan 2013-2018

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

Immunogenicity of a single dose of IPV administered at age 4 months

Study summary	Poliovirus type 2
1st dose seroconversion	63%
Priming	98%
1st dose seroconversion & priming	99%
Cumulative two-dose seroconversion	100%

rom the Pedro Kouri Institute, Havana S.R., M.D., L.S., G.G., M.F., L.H.H.), and he Provincial Health Office, Camagüey A.T., N.A.) — both in Cuba; the World Health Organization, Geneva (R.W.S., .-L.K., A.B., R.B.A.); and the Pan American Health Organization, Washington, DC J.M.L.). Address reprint requests to Dr. utter at 20 Ave. Appia, CH-1211 Geneva 7, Switzerland, or at sutterr@who.int.

l Engl J Med 2013;368:416-24.
)OI: 10.1056/NEJMoa1202541

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 (one fifth of a full dose) administered intradermally with a full dose administered intramuscularly in Cuban infants at the ages of 4 and 8 months. Blood was collected from infants at the ages of 4 months, 8 months, 8 months 7 days, and 8 months 30 days to assess single-dose seroconversion, single-dose priming of immune responses, and two-dose seroconversion. Specimens were tested with a neutralization assay.

Early versus later IPV administration

				seroconversion[1]
Author year (ref)	Country	Schedule	N	Type 2
Intramuscular administration of 1 dose				
McBean 88 [45]	US	2 mo	309	35%
Simasathien 94 [46]	Thailand	2 mo	103	39%
Resik 10 [40]	Cuba	6 wk	177	**36%**
Mohammed 10 [47]	Oman	2 mo	186[2]	32%
Resik 13 [39]	Cuba	4 mo	153	**63%**
Intramuscular administration of 2 doses				

Baseline (4-month IPV dose):

63% seroconversion, 98% priming; 99% seroconversion & priming

Later administration (potential gains):

?seroconversion (>63%), ?priming (>98%)

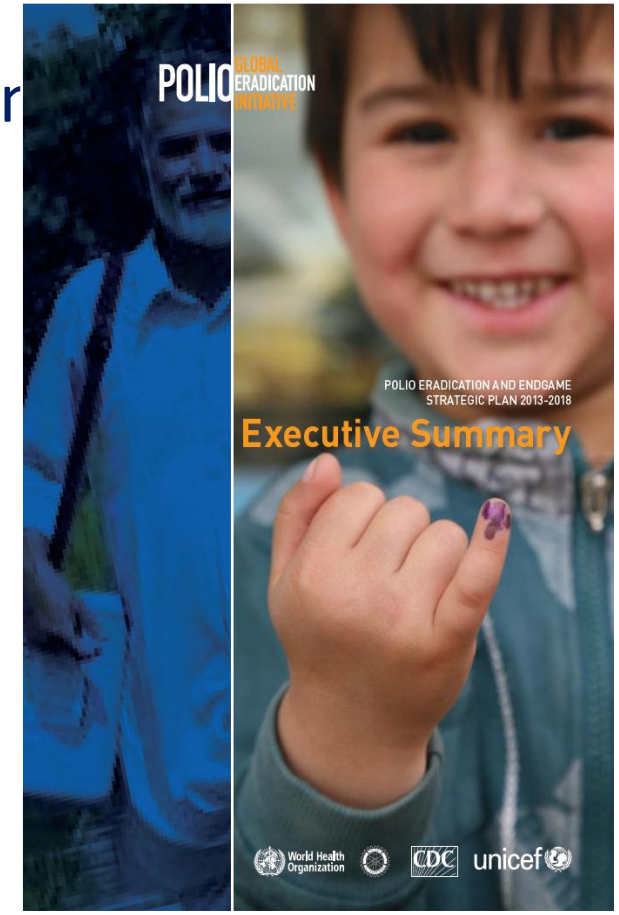
Earlier administration (potential losses):

seroconversion decreased (32-39% vs 63%)

2-dose IPV studies suggest priming also lower by early IPV(<90% seroconversion)

Endgame Plan, 2013-18

- Polio detection & interruption *(by 2014)*
- Immunization systems & OPV withdrawal *(by 2016)*
- Containment & Certification *(by 2018)*
- *Legacy Planning (by 2015)*



What is the new endgame?

- Strategic framework for the sequential cessation of Sabin strains, starting with Sabin type 2.
- For Sabin type 2, cessation means that tOPV must be replaced with bOPV in a synchronized manner globally.
- For risk mitigation, the framework includes at least one dose of IPV included in the routine EPI (starting ≥6 months before switch from tOPV to bOPV).

Example 7: Mucosal immunity

- *Study:*
  - mucosal immunity after 2 doses of IPV (challenge with 1 and 2 doses of OPV) (phase II of priming study)
- *Outcome:*
  - IPV has modest effect on excretion following challenge (prevalence, stool titer, length of excretion)
- *Implications:*
  - re-inforced the need for live-virus contact to mucosal surfaces

Laboratory work in progress

Example 8: New device evaluation

- *Study:*
  - evaluation of different needle-free devices to administer fractional-dose IPV intradermally
- *Outcome:*
  - one newly developed jet injector would facilitate the administration of fIPV intradermally.
- *Implications:*
  - help determine future direction of area-of-work

Resik S et al. Vacccine 33 (2015) 307-313
Resik S et al. Vaccine 07/2015; DOI:10.1016/j.vaccine.2015.06.071

Example 9: Sabin-IPV evaluation

- *Study:*
  - phase 1 study of Sabin-IPV in adults
- *Outcome:*
  - further demonstrated safety & immunogenicity of Sabin-IPV
- *Implications:*
  - assisted in decision to accelerate technology transfer to developing country manufacturers

Resik S et al. Vaccine 32 (2014) 5399–5404
Resik S et al. Trials in Vaccinology 4 (2015) 71-74

Example 10: Rapid evaluation

- *Study:*
  - assessment of intussusception after OPV (context of rotavirus vaccine)
- *Outcome:*
  - no increased risk demonstrated in Cuba
- *Implications:*
  - OPV confidence-building

Galindo MA, et al. Euro J Epidemiol 2001;17:783-7

Summary

- Collaboration between Cuba & WHO has provided important scientific data and has been hugely influential to shape polio vaccination policy
- Collaboration is a pillar for GPEI research and product development

Acknowledgement

CUBA IPV STUDY GROUP

Instituto Pedro Kourí

Dr. Manuel Díaz
Lic. Magilé Fonseca
Lic. Lay Hueng-Hung
Lic. Yenisleidis Martinez
Tec. Damarys Concepción
Tec. Niurka Pereda
Lic. Luis Morier
Lic. Dianeya Mendoza

Camagüey

Dr. Alina Tejeda
Dr. Nilda Alemany
Dr. Gloria García
Dr. Maria D Valdes
Dr. Marila Rivero
Dr. Liugmila Vasconcelos
More than 100 doctors and nurses from 15 Policlinics

IPK

Dr. Alina Llop
Dr. María G. Guzmán
In memory of Professors Gustavo Kourí and. Pedro Más

MINSAP

Prof. Miguel Galindo
Dr. Marlén Valcarcel

WHO – IVR

Dr. Roland Sutter
Anna-Leah Kahn
Leila Kadri
Dr. Anthony Burton
Dr. Hiromasa Okayasu
Dr. Ondrej Mach

PAHO/WASHINGTON

PAHO/HAVANA

Parents, infants and all volunteers

… until the time when polio will be eradicated from all countries, polio free countries will be under threat…

Thanks