Global Polio Endgame and tOPV to bOPV Switch

Dr Thulani Mhlanga
Poliomyelitis
POLIOMYELITIS

Virology

- Three serotypes: Poliovirus types 1, 2, 3
- Family: Picornaviridae
  - Genus: Enterovirus
  - Species: Poliovirus

Melnick JL in Plotkin SA, Mortimer EA (eds) Vaccines 1994 (7) pp155-204c
Poliomyelitis Pathogenesis

*Infection may cause paralysis in a matter of hours*

1. **Exposure** (ingestion, inhalation)
2. **Adhesion/entry into gastrointestinal mucosa**
3. **Local multiplication of poliovirus** (tonsils, peyer’s patch of ileum, lymph nodes)
4. **Dissemination via lymph & blood**
5. **Invasion of central nervous system**
   - Destruction of motor neurons
   - Paralysis

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[32] WHO. Online
Clinical Aspects of Paralytic Disease

- Incubation period 6-20 days (range 3-35 days)

- **Prodrome [ biphasic ]**
  - Initial symptoms minor
  - Major symptoms evident 7 days later
    - Intense myalgia and hyper-reflexia of involved limbs

- **Paralytic symptoms begin 1-10 days after prodrome**
  - Asymmetric weakness, flaccid paralysis, diminished deep tendon reflexes
  - No sensory loss experienced
  - Proximal >> distal muscle involvement
  - Legs >> arms

- **Bulbar involvement in 5% to 35% of cases**
  - Dysphagia, difficulty with secretions
  - Anxiety
# Types of polioviruses

<table>
<thead>
<tr>
<th>Wild</th>
<th>OPV related</th>
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<tbody>
<tr>
<td>• 99% reduction in cases of wild poliovirus since 1988</td>
<td>VAPP**</td>
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<tr>
<td>• Type 1 (359 cases in 2014)</td>
<td>• Vaccine-associated paralytic poliomyelitis (VAPP)**</td>
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<tr>
<td>• Type 2 (eliminated worldwide in 1999)</td>
<td>• Estimated ~250-500 globally per year</td>
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<tr>
<td>• Type 3 (none detected since November 2012)</td>
<td>• Type 2 accounts for about 26-31% of VAPP</td>
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<table>
<thead>
<tr>
<th>VDPVs*</th>
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<tr>
<td>• Vaccine derived polioviruses (VDPV)</td>
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<tr>
<td>• Most are circulating VDPVs (cVDPVs)*</td>
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<tr>
<td>• ~54-185 per year from 2008 to 2014</td>
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</tr>
<tr>
<td>• Type 2 cVDPVs account for 97% of cVDPVs</td>
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† More up-to-date numbers can be found at [http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx](http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx)

*Other extremely rare VDPVs include primary immunodeficiency VDPVs (iVDPVs) and ambiguous VDPVs (aVDPVs)

**Refers to spontaneous reversion to neurovirulence of one of the attenuated viruses in OPV. VAPP occurs in OPV recipients or their close contacts in contrast to cVDPVs which are widely transmitted in a community and are not likely to be related to contact with a recent vaccine recipient.
POLIOMYELITIS

Epidemiology

1988
> 350,000 cases
> 125 endemic countries

2012
205 cases (4 Dec)
3 endemic countries –
Nigeria (114),
Afghanistan (39),
Pakistan (73)

Last polio case in South Africa in 1989
Polio is getting closer to being « history »
2015 was a landmark year; 2016 off to a good start

- 2016 YTD: only 2 cases of Wild Polio Virus - Pakistan
  - 2 cases of cVDV1 – Lao

- Positive environmental samples still found both in Pakistan (Feb) and Afghanistan (Dec) = circulation ongoing

Polio Status in 2015

- **WPV cases in endemic countries**
  - Afghanistan 20
  - Pakistan 54

- **cVDPV identified**
  - Type 2: Guinea, Nigeria, Pakistan
  - Type 1: Ukraine, Madagascar, Laos

2015 Key milestones

- Global Certification Commission certified wild poliovirus (WPV) type 2 as eradicated
- World Health Organization removing Nigeria from the list of polio-endemic countries
- 14 months after the last polio case was identified, Polio outbreak in Somalia officially declared over
- 3 years with no wild poliovirus (WPV) type 3
Type 2 wild poliovirus

*as of 31 Dec 2014; (current numbers: http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx

Last case of type 2 polio
As wild polioviruses are eradicated, number of circulating vaccine-derived cases exceeds wild poliovirus cases.
circulating Vaccine-Derived Poliovirus Outbreaks (cVDPVs), 2000-2011

>90% of cVDPV polio cases are due to type 2

Type 1 (79 cases)
Type 2 (478 cases)
Type 3 (9 cases)
Type 2 component of tOPV has to be withdrawn because it is responsible for >97% of all *circulating vaccine derived poliovirus (cVDPV)* in recent years.

*as of 31 December 2014; (current numbers: [http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx](http://www.polioeradication.org/Dataandmonitoring/Poliothisweek.aspx)*
Oral Polio Vaccines (OPV) in routine and supplementary immunization activities globally

- **Types of OPV**
  - Trivalent OPV (tOPV): types 1, 2, and 3
  - Bivalent OPV (bOPV): types 1 and 3
  - Monovalent OPV (mOPV): types 1 or 2 or 3

- Currently, **TRIVALENT** is the most commonly used OPV in routine immunization globally, while **BIVALENT** is more commonly used in supplementary immunization activities.
Live attenuated Poliovirus Vaccine (OPV)

- Developed by Sabin in 1961
- Attenuated and then produced in monkey kidney cell culture
- Minimum 3 doses for primary immunisation
- Immune response depends on replication of live attenuated viruses in the gut

Dr. Albert Sabin administers oral poliovirus vaccine. Photo courtesy of WHO.
Enhanced Inactivated Poliovirus Vaccine (eIPV)

- Inactivation of wild-type poliovirus strains
- New production techniques
- High potency
- Licensed in the US in 1987
Since January 2013, the following countries have introduced IPV: Kazakhstan & Peru (July 2013); Libya (March 2014); Albania (May 2014); Panama (July 2014); Nepal & Tunisia (September 2014); Philippines (October 2014); China (December 2014); Comoros, Senegal & Serbia (January 2015); Colombia & Nigeria (February 2015); Bangladesh & Maldives (March 2015); DPR Korea, DR Congo and Gambia (April 2015); Madagascar (May 2015)
Member states and recognized territories using tOPV to date

Countries currently using tOPV (156 countries or 80%) representing 149 Member States and 7 recognised territories)

Countries not using tOPV (45 countries)

Not applicable

Data Source: WHO/IVB Database, as at 19 March 2015  Date of slide: 19 March 2015  Map production: Immunization, Vaccines and Biologicals (IVB), World Health Organization
GPEI endgame is moving forward on April 2016 switch to bOPV

**Global Polio Eradication Initiative timelines**

- **“OPV switch confirmed”**
- **By July 2016**: Introduction of at least 1 dose of IPV
- **April 2016**: Universal switch from tOPV to bOPV
- **By 2020**: Total OPV cessation & maintain IPV vaccination

**IPV introduction* – Where do we stand?**

- Introduced to date* (158 countries or 81%)
- Introduction planned in February 2016 (3 countries or 1.5%)
- Introduction planned in March 2016 (3 countries or 1.5%)
- Introduction planned in April 2016 (9 countries or 5%)
- Introduction planned after April 2016 (21 countries or 11%)
- Not available

* Including partial introduction in Haiti, India & Venezuela

Data source: WHO/IVB Database, as of February 2016
## South African EPI schedule 2015

<table>
<thead>
<tr>
<th>VACCINES</th>
<th>Birth</th>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
<th>Booster 1</th>
<th>Booster 2</th>
</tr>
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<tbody>
<tr>
<td>BCG</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>tOPV</td>
<td>0</td>
<td>6w</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>DTaP-IPV-HB-Hib</td>
<td>6w</td>
<td>10w</td>
<td>14w</td>
<td>18m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV</td>
<td>6w</td>
<td>14w</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>PCV</td>
<td>6w</td>
<td>14w</td>
<td></td>
<td>9m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td>6m</td>
<td>12m</td>
<td></td>
<td></td>
<td>6y</td>
<td>12y</td>
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<tr>
<td>Td</td>
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The Plan differs from previous eradication plans because it addresses paralytic cases associated with both wild polioviruses and vaccine-derived poliovirus/VAPP.

**Eradication**
- refers to wild virus

**Endgame**
- refers to management of VDPVs and VAPP
The Plan addresses the Endgame through three distinct stages

**Introduce**
- at least one dose of IPV
- into routine immunization

**Switch**
- tOPV to bOPV

**Withdraw**
- of bOPV & routine OPV use

Before end 2015

2016

2019-2020

Ongoing STRENGTHENING of routine immunization services
The Endgame Plan calls for OPV cessation globally by 2018-2019

- The world must ultimately stop using OPV to be polio free…but first

Endgame

- Plan refers to management of VDPVs and VAPP
Rationale for THE SWITCH from tOPV to bOPV in 2016

Currently, risks of type 2 component of tOPV outweigh the benefits

- Type 2 wild poliovirus eradicated since 1999
- New diagnostics and experience suggest that type 2 component of tOPV causes >97% of VDPVs
- Type 2 component of tOPV causes approximately 40% of VAPP today
- Type 2 component of tOPV interferes with immune response to types 1 and types 3
- Immunity against type 2 will be provided through IPV introduction
Rationale for introducing at least one dose of IPV prior to the tOPV-bOPV switch

*IPV protects children against poliovirus types 1, 2 and 3. Introducing IPV prior to the tOPV-bOPV switch will maximize the proportion of the population protected against type 2 polio after OPV2 cessation. One dose of IPV will:*

- **Reduce risks** associated with type 2 cessation
  - Lower risk of re-emergence of type 2 polioviruses
- **Facilitate interruption of transmission** with the use of monovalent OPV2 if type 2 outbreaks occur
- **Boost immunity** against types 1 & 3 thus hastening polio eradication
Rationale for continuing use of OPV until Polio Eradication & Global Certification

<table>
<thead>
<tr>
<th>Wild poliovirus still circulating</th>
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<tbody>
<tr>
<td>• As long as there are susceptible persons in other countries, there is risk of export of the virus to these countries.</td>
</tr>
<tr>
<td>• <strong>Endemic in 3 countries</strong> – reservoirs for re-infecting others (Pakistan, Afghanistan, Nigeria)</td>
</tr>
<tr>
<td>• <strong>In 2013, polio cases in 5 other countries</strong> previously polio free countries (Somalia, Kenya, Ethiopia, Cameroon, Syria)</td>
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<table>
<thead>
<tr>
<th>Eradication requires OPV</th>
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<tr>
<td>• <strong>OPV is a critical component of the eradication strategy until polio transmission is interrupted</strong> globally &amp; the world is certified polio-free,</td>
</tr>
<tr>
<td>• <strong>Risk of polio spread into other regions of the world is real</strong> without the continued use of OPV</td>
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<tr>
<th>OPV is appropriate for eradication</th>
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<tr>
<td>• Inexpensive</td>
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<td>• Easy to administer</td>
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<tr>
<td>• Offers good oral and intestinal immunity—needed for interruption of person to person transmission</td>
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Rationale for retaining Types 1 & Types 3 components of OPV (bivalent OPV) until global certification of polio eradication

- Type 1 causes all polio cases related to wild virus today
  - Few VDPV cases are type 1
  - Few VAPP cases in immunocompetent individuals

- Type 3 last detected in November, 2012 (as of 20 November 2013)
  - Few VDPV cases are type 3
  - Most VAPP cases (60%) in immunocompetent persons are type 3
  - While lack of detection since November 2012 is promising, the period without detection to date is not long enough to assume eradication—due to potential silent transmission, certification of eradication requires at least 3 years without detection of virus
  - Supply & licensing considerations of mOPV1
Risks associated with OPV2 cessation

- **Short-term risks**
  - Time-limited risk of cVDPV2 emergence, highest 1-2 years after OPV2 cessation

- **Medium & long term risks**
  - Poliovirus re-introduction from a vaccine manufacturing site, research facility, immune deficient persons, diagnostic laboratory, or bioterrorism

- These **risks are mitigated** by strengthening routine immunization and introduction of IPV
Mitigating the risks of OPV2 cessation

● High population immunity before switch
  ● higher risk countries to conduct tOPV SIAs in Q4 2015 and Q1 2016

● Discontinuing tOPV production & distribution

● IPV introduction

  ▪ Switch in the month of April (2 weeks period) RSA-20 April 2016
    ▪ “low polio season” for countries with endemic polio or recent polio

● Synchronizing switch globally
  ● reduce risks of re-emergence and importation/exportation of type 2 cVDPVs from ongoing use of tOPV; the more simultaneous the switch across and within countries, the lower the risk of emergent cVDPV2s
Management and Operational Oversight

Plan

Prepare

Implement

National Switch Management Committee

Regional Switch Committees

Switch Support Teams

Validate

Independent National Certification Committee

Switch Monitors
Example of National Switch Process
April 2016

<table>
<thead>
<tr>
<th>Sun</th>
<th>Mon</th>
<th>Tue</th>
<th>Wed</th>
<th>Thu</th>
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</tbody>
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- **National Switch Day**
  - Stop use of tOPV and remove tOPV from the cold chain. Begin use of bOPV

- **National Validation Day**
  - Two-week window for disposal
  - All tOPV must be disposed of by this date.
OPV Production Capacity

- Val de Reuil site: Sanofi Pasteur the main suppliers of oral polio vaccines (OPV)
Marcy l’Étoile and Toronto: IPV will be critical to eradication efforts, we have been investing for years to increase our production capacity in order to reach today’s unmatched level.

In total, over 1 Billion doses of Sanofi Pasteur’s IPV containing vaccines have been distributed worldwide since 1982.
Sanofi Pasteur’s Commitment

- Ensure adequate vaccines supply for routine Immunisation
- Support the tOPV to bOPV switch process
- Supply and Support SIAs, Immunisation Awareness campaigns
- Projects
tOPV removal bags

- For disposal
- Do not use
- Not to be kept in the cold chain

Facility: ___________________________
Number of tOPV vials: __________________
Date: ___________________________
Without OPV, Polio Eradication is Impossible

Without IPV, Polio Eradication is Impossible
The world is moving ahead
The Polio Endgame is in reach
Sanofi Pasteur supports as partner

Thank you