Global Polio Eradication: The Need for Inactivated Polio Vaccines (IPV)

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Outline:

• Polio: Background
• Global Polio Eradication Initiative
• Role of Inactivated Polio Vaccines (IPV)
• Features/ Use of IPV
Anyone can be a victim ...

– US President Franklin D. Roosevelt
– Francis Ford Coppola
– Donald Sutherland, Mia Farrow, Mel Ferrer
– Arthur Guyton (physiologist), Jack Niclaus
– Frieda Kahlo (artist), Katherine Jackson
– Neil Young, David Sanborn (saxophone player)
– Apolinaro Mabini
– Ma. Gracia Cielo "Grace" Magno Padaca
Background

POLIO:

• Highly contagious disease that causes permanent disability and even death.
• Caused by: **Poliovirus (types 1, 2, 3)**
  – Wild poliovirus (WPV)
  – Vaccine-derived polio virus (OPV)
• Person-to-person spread
• 1 in 200 infections → irreversible paralysis
  • Among those paralyzed, 5% to 10% die
• Children <5 years old most at risk.
• No cure
• Polio vaccine, given multiple times, can protect a child for life.

[WHO Polio Information](http://www.who.int/mediacentre/factsheets/fs114/en/)
Polio: Clinical Description

- **Asymptomatic infection**
  - Minor viremia
  - No symptoms
  
  **Most common outcome**

- **Abortive polio**
  - Minor illness
  - No neurologic symptoms

- **Paralytic polio**
  - Minor illness followed by Flaccid paralysis
  
  **Most severe form**

- **Aseptic meningitis**
  - Meningeal irritation (stiffness back/neck)
  - Mild & transient muscle weakness/paralysis

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Polio: What you see is only the tip of the iceberg

The poliovirus is sneaky, silent and highly contagious.

It doesn’t respect boundaries or social class – it is an equal opportunity paralyzer.

Even 1 case is an outbreak...

for every one case of polio
200 more kids are infected

http://www.cdc.gov/globalhealth/immunization/infographic/world-polio-day-2014.htm
The fight against Polio has lasted for over 70 years...

1908 - Landsteiner (Vienna) Viral etiology established
1938 - Viral etiology established
1955 - The Thomas Francis Field Trial of Salk’s Inactivated Polio Vaccine: the largest efficacy clinical trial ever done
1988 - Born from a coalition between WHO, Rotary, Unicef and US CDC, GPEI initiative is launched at 41st WHA with the objective to eradicate Polio by 2000.
2012 - Polio Eradication and End Game Strategic Plan 2013-2018 launched by the GPEI

WHO declares Ebola outbreak an international public health emergency

Director general Margaret Chan says west African countries' health systems need international help to manage infection

Maev Kennedy
The Guardian, Friday 8 August 2014 11.15 BST
May 26, 2012: World Health Assembly declared ending polio a “programmatic emergency for global public health.”

The Polio Eradication and Endgame Strategic Plan 2013-2018
- developed to capitalize on this new opportunity to end all polio disease.

www.polioeradication.org
Are we really very close to eradicating Polio?

- **Eradication**, not only Elimination:
  - Elimination:
    Reduction to zero of the incidence of a specified disease in a defined geographical area as a result of deliberate efforts; continued intervention measures are required.
    Example: neonatal tetanus.
  - 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.
    Example: smallpox.
Are we really very close to eradicating Polio?

**Polio in the world:**

- Since the GPEI was launched in 1988:
  - Reduced global incidence of polio by $> 99\%$ (1988 to 2012)
  - Reduced number of countries with endemic polio (from 125 to 3) Pakistan, Afghanistan, and Nigeria
  - Prevented paralysis in $>13$ million people

**Polio in the Philippines:**

- Year 1993: last polio case was recorded in the Philippines.
- Year 2000: the Philippines was certified polio-free.

**Answer:** Yes
GPEI Accomplishment: Significant Decline in Polio-paralyzed Children, 1988-2013*

*as of 31 December 2013

IPV Comprehensive Technical Module GPEI version date: Feb 10, 2014
Polio in 2014...

- **Wild Poliovirus (WPV) Cases**
  - Total: 359 cases, **all WPV Type 1**
  - Endemic countries: 340 cases (Pakistan, Nigeria, Afghanistan)
  - Non-endemic countries: 19 cases (Somalia, Cameroon, Equatorial Guinea, Syria, Iraq)

- 10 countries with active transmission, 4 have exported WPV to other countries.

- Not under control in Pakistan, (but shows significant progress in Nigeria and Afghanistan).

- Most recent: Jan 17, 2015

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http://www.polioeradication.org/Dataandmonitoring/Poliothisweek/Wildpolioviruslist.aspx
Polio in 2014...

- Circulating Vaccine-Derived Poliovirus (cVDPV) Cases
  - Total: 54 cases
    - Endemic: 51 cases  Non-endemic: 3 cases
    - all cVDPV type 2 except ...
    - cVDPV type 1:
      - 1 case Madagascar Sep 2014
      - 2011 previous case
    - cVDPV type 3:
      - Last case 2013

✓ General improvement in control
✓ Most recent: Dec 13, 2014

As wild polioviruses are eradicated, number of vaccine-derived cases exceeds wild poliovirus cases.

A hypothetical scenario of estimated VDPV cases compared to reported cases of wild poliovirus (as of 31 December, 2013)

IPV Comprehensive Technical Module GPEI version date: Feb 10, 2014
“As long as polioviruses circulate anywhere, all countries are at risk of reintroduction and epidemics of paralysis.”

Data in WHO HQ as of 03 February 2015
GPEI goal of interrupting transmission both WPV and cVDPV by end 2014 at extreme risk → Security/political situation remains fragile in some countries

In May 2014, the international spread of poliovirus was declared a public health emergency of international concern.
“complete the eradication and containment of all wild, vaccine-related, and Sabin polioviruses such that no child ever again suffers paralytic poliomyelitis.”
Polio Eradication and Endgame Strategic Plan 2013–2018

Objectives:

1. Detect and Interrupt Poliovirus
   – The plan provides a strategy to interrupt all wild poliovirus transmission by the end of 2014.

2. Strengthen Immunization Systems and Withdraw OPV

3. Contain and Certify
   – All regions must pass three years without a case to attain polio-free status, to be followed by global certification.

4. Plan Polio’s Legacy

GPEI Fact File. www.polioeradication.org
All children worldwide should be fully vaccinated against polio, and every country should achieve and maintain high levels of coverage.

WHO no longer recommends an OPV-only vaccination schedule.

For all countries currently using OPV only, at least 1 dose of IPV should be added to the schedule.
# Review of Polio Vaccines: Difference between OPV and IPV

<table>
<thead>
<tr>
<th></th>
<th>OPV (Oral Polio Vaccine)</th>
<th>IPV (Inactivated Polio Vaccine)</th>
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</thead>
<tbody>
<tr>
<td><strong>Vaccine type:</strong></td>
<td>Live attenuated</td>
<td>Inactivated “killed”</td>
</tr>
<tr>
<td><strong>Contains:</strong></td>
<td>tOPV: Polio Type 1, 2, 3</td>
<td>Polio type 1, 2, 3</td>
</tr>
<tr>
<td></td>
<td>bOPV: Polio type 1, 3</td>
<td></td>
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<tr>
<td><strong>Pros:</strong></td>
<td>Cheap, Easy to administer</td>
<td>• No risk of VAPP</td>
</tr>
<tr>
<td></td>
<td>• Good oral and intestinal immunity</td>
<td>• Highly effective</td>
</tr>
<tr>
<td></td>
<td>• Confers transmission to contacts and secondary vaccination</td>
<td></td>
</tr>
<tr>
<td><strong>Cons:</strong></td>
<td>Causes paralysis in very rare cases (VAPP &amp; cVDPVs)</td>
<td>More costly than OPV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Does not confer transmission to contacts and thus provide secondary vaccination</td>
</tr>
<tr>
<td><strong>Protection:</strong></td>
<td>≈ 50% immune after 1 dose</td>
<td>≥90% immune after 2 doses</td>
</tr>
<tr>
<td></td>
<td>&gt;95% immune after 3 doses</td>
<td>≥99% immune after 3 doses</td>
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Why stop using OPV?
OPV protects vs transmission but challenges the eradication of polio...

Rarely, OPV can cause:

- VAPP (Vaccine-associated Paralytic Polio)
- Vaccine-Derived Polioviruses (VDPV)
Polio type 2:

- Wild Polio Virus 2 eradicated globally in 1999
- OPV-related type 2 polio cases cause majority of cVDPV and VAPP cases
  - 40% of VAPP cases globally per year
  - 98% of cVDPV outbreaks in recent years
- OPV-2 now carries more risk than benefit
- Continuing OPV-2 unacceptable
- Plan: Shift: tOPV → b1&3 OPV → full IPV (Phased withdrawal of OPV)
Primary purpose of the IPV dose:

- To maintain immunity against type 2 polio during and after the global withdrawal of OPV2 and switch from tOPV to b₁&₃ OPV
- To reduce VAPP risks (depending on the timing of the IPV administration)
- To boost immunity against polio types 1 and 3 → hasten the eradication of these WPVs
Schematic description of technical rationale for use of at least one dose of IPV as part of the Endgame Strategy:

- **tOPV**: 3 rings of protection against types 1, 2, and 3
- **bOPV**: 2 rings of protection against types 1 and 3
- **bOPV + IPV**: IPV adds protection against type 2 & boosts immunity to 1 & 3 (enhancing bOPV effect)
Timeline for implementation of Objective 2: Strengthen Immunization Systems and Withdraw OPV

**Strengthen Immunization Systems and Withdraw OPV**

**Anticipated timeline**

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<tbody>
<tr>
<td>Last wild polio case</td>
<td></td>
<td></td>
<td>tOPV-bOPV switch</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPV in routine immunization</td>
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</table>

**Phase in IPV**

- **Before end of 2015**: introduce **one dose of IPV** in immunization programs of all countries

**IPV in routine immunization**

- **2016**: tOPV to bOPV switch globally

**Ongoing STRENGTHENING of routine immunization services**

**3 Stages:**

- **Introduction**
  - Before end of 2015: introduce **one dose of IPV** in immunization programs of all countries

- **Switch**
  - **2016**: tOPV to bOPV switch globally

- **Withdrawal**
  - **2019-2020**: withdrawal of bOPV after the world is certified polio-free in 2018 (use all IPV)

IPV Comprehensive Technical Module GPEI version date: Feb 10, 2014
- IPV is an additional dose to OPV (not a replacement)
- Minimum interval: 4 weeks
- Single IPV dose at 14 weeks of age with DTP3/OPV3
  - better immunogenicity of IPV vs earlier administration
- Late schedules (age > 3mos) may give IPV on 1st visit
- Countries may consider alternative schedules
  - (e.g. VAPP risks)
Inactivated Polio Vaccines (IPV)

**Salk IPV** (Enhanced-potency IPV/Conventional IPV)
- Available as stand-alone or in combination
  - (tetra-, penta-, hexavalent with diphtheria, tetanus, pertussis, Hepatitis B, or Hib antigens)
  - No interferences reported when used in combination
- Most are WHO pre-qualified
- Considered very safe
- Main drivers of immunogenicity:
  - Number of primary series injections
  - Age at first dose
  - Interval between doses
  - Ethno-ecological factors (transient maternal antibodies, etc.)
- Less effective than OPV in inducing mucosal immunity, but reduces quantity and duration of viral shedding in stools due to a certain degree of intestinal protection.

**Sabin IPV**
- JPRI (Japan), Kunming (China), Intravacc (NL)

Impact of one dose of IPV

- **Primary role of 1- dose IPV:** RISK MITIGATION strategy
- **Seroconversion against type 2** after one dose of IPV: **32-63%**.
- **Seroconversion rates higher** when vaccine is administered later in infancy presumably because of waning maternal antibody

<table>
<thead>
<tr>
<th>Author year</th>
<th>Country</th>
<th>Schedule</th>
<th>Type 2 Seroconversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>McBean 1988</td>
<td>US</td>
<td>2 mo</td>
<td>35%</td>
</tr>
<tr>
<td>Simasathien 1994</td>
<td>Thailand</td>
<td>2 mo</td>
<td>39%</td>
</tr>
<tr>
<td>Resik 2010</td>
<td>Cuba</td>
<td>6 wk</td>
<td>36%</td>
</tr>
<tr>
<td>Mohammed 2010</td>
<td>Oman</td>
<td>2 mo</td>
<td>32%</td>
</tr>
<tr>
<td>Resik 2013</td>
<td>Cuba</td>
<td>4 mo</td>
<td>63%</td>
</tr>
</tbody>
</table>

At least 2 doses of IPV (initiated $\geq 8$ weeks of age) will give high protection against type 2 poliovirus when we shift from tOPV to bOPV.

**IPV: Seroconversion against poliovirus Type 2**

- **1 dose IPV:** 32-63% (higher when given later)
- **2 dose IPV:** $>90\%$ when initiated after 8 weeks of age

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![Table showing seroconversion rates following 1–3 doses of inactivated poliovirus vaccine (IPV) in different routine immunization schedules](image)

Salk IPV

• **Efficacy**
  
  – Proven in several studies (Houston 96%, Canada >90%, India 92%, etc.)
  – (Senegal study during outbreak of Polio type 1)
    • 1 dose: 36%
    • 2 dose: 89%

• **Herd Immunity demonstrated**
  
  – US experience upon IPV introduction → case reduction more than expected

• **IPV-containing vaccines**
  
  – Licensed in > 100 countries
  – Yearly: 25-30 million newborns, 15 mil children, adolescents, and adults vaccinated

• **Used in different schedules**
  
  – IPV-only
  – IPV/OPV sequential schedules
  – IPV/OPV combined schedules

As of Jan. 2015, 75 countries have introduced IPV in their routine public infant/toddler National Immunization Program (and much more countries in their private markets)

WHO/IVB Database, as of 04 December 2014; Map production Immunization Vaccines and Biologicals (IVB), WHO
Different routine POLIO immunization regimens combining IPV & OPV can be implemented

<table>
<thead>
<tr>
<th>IPV-only supplemented by OPV SIAs</th>
<th>Mixed / combined IPV and OPV with OPV optional at birth</th>
<th>IPV-followed-by-OPV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mexico</strong>: IPV at 2, 4, 6 and 15-18 months of age completed by OPV NIDs twice a year in all &lt;5yrs</td>
<td><strong>Turkey</strong>: IPV at 2 and 4 months, and IPV &amp; OPV at 6 and 18 months</td>
<td><strong>US (from 1997 to end of 1999)</strong>: IPV at 2 and 4 months and OPV at 6 to 18 months and at 4 – 6 years</td>
</tr>
<tr>
<td><strong>Israel</strong>: IPV at 2, 4, 6 and 15-18 months of age completed by OPV NIDs twice a year in all &lt;5yrs</td>
<td><strong>South Africa</strong>: OPV at birth, IPV &amp; OPV at 6 weeks, IPV at 10, 14 weeks</td>
<td><strong>Russia</strong>: IPV at 3 and 4.5 months and OPV at 6, 18 and 20 months</td>
</tr>
<tr>
<td><strong>Brazil (since 2012)</strong>: IPV at 2 and 4 months and OPV at 6 and 15 months + OPV SIAs</td>
<td></td>
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</tr>
</tbody>
</table>

As of today 24 countries have implemented IPV-OPV combined regimen.

Several countries use all IPV-only, relying on IPV-containing combination vaccines

**Infant series:** 3 (sometimes 2) doses during 1\(^{st}\) year of life

**Booster doses:** toddler age and/or pre-school/early-adolescence (to ensure long term immunity)

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 + 1 + 0</td>
<td>Spain, Slovenia, Japan, Uruguay</td>
</tr>
<tr>
<td>3 + 0 + 1</td>
<td>New Zaeland, United States*, Greece*, Australia, Ireland, Portugal, South Korea, UK</td>
</tr>
<tr>
<td>2 + 1 + 1</td>
<td>Austria, United States*, Greece*, France, Sweden, Slovakia, Italy, Norway, Denmark, Finland, Iceland</td>
</tr>
<tr>
<td>3 + 1 + 1</td>
<td>Switzerland, Canada, Croatia, Israel, Romania, Hungary, Belgium, Luxemburg, Germany, Czech Republic, Netherland, Estonia, Latvia, Lithuania, Bulgaria, Cyprus, Liechtenstein, Malta</td>
</tr>
</tbody>
</table>

* Official recommendations are for 3\(^{rd}\) dose to be given any time between 6 and 18 months of age, therefore falling in the “2 + 1 + 1” or the “3 + 0 + 1” schedule. Consider also the “3 + 1 + 1” schedule as acceptable

Polio not included in combination vaccines used in Philippine NIP: can we improve coverage rates?

Philippine National Immunization Program Coverage: OPV 3

WHO and UNICEF estimates of national immunization coverage - June 27, 2014
IPV-containing combination vaccines are now integrated in many routine public infant / toddler National Immunization Programs
(and much more countries in their private markets)

- **Most of European Union countries**
  - DTaP-IPV-Hib (1997) and DTaP-IPV-HepB-Hib (2000)
- **Canada**
  - DTaP-IPV-Hib (1997) and DTaP-HepB-IPV-Hib (2007)
- **Australia & NZ**
  - DTaP-IPV-HepB-Hib (2004)
- **USA**
  - DTaP-IPV-HepB (2005) and DTaP-IPV-Hib (2008)
- **Taiwan**
  - DTaP-IPV-Hib (2007)
- **Mexico, South Africa, Turkey, Costa Rica**
  - DTaP-IPV-Hib (2007)
- **Malaysia**
  - DTaP-IPV-Hib (2008)
- **South Korea**
  - DTaP-IPV (2010)
- **Japan**
  - DTaP-sIPV (2012)
Conclusions

• **WHO:**
  - All countries currently using OPV only should add at least 1 dose of IPV to their NIP by 2015.
  - OPV cessation must occur for the world to be polio free.
• **Need for IPV in Polio Eradication:**
  - Maintain immunity vs type 2 PV during/after the switch from tOPV to bOPV
  - Reduce VAPP risks
  - Boost humoral and mucosal immunity against PV types 1 and 3 → hasten the eradication of these WPVs
• **Salk IPV:**
  - No risk of VAPP or cVDPVs
  - Predictable, consistent high immunogenicity with at least 2 doses
  - Wealth of data have proven safety, efficacy, and effectiveness
  - Different schedules alone or in combination with OPV
  - Can be included in combination vaccines → improve coverage
PHILIPPINES: INTRODUCED IPV IN THE NIP LAST OCT 6, 2014

Wendell Corregidor

- Polio victim: walks with crutches
- 36-year-old ex-paralympian
- Winner of gold medals from swimming competitions for the disabled.
- Saved 10 people, including six children, from drowning in gigantic storm surges during Supertyphoon “Yolanda” in Palo, Leyte.

**used his skills to save lives**

http://newsinfo.inquirer.net/575774/unlikely-hero-polio-victim-saved-10-lives#ixzz3RUcykzjY
What can PEDIATRICIANS do?
1. Educate parents about importance of eradicating polio.
2. Ensure patients are vaccinated against polio (incorporate at least 1 dose IPV).
3. Ensure that all patients travelling internationally receive recommended vaccines (IPV when appropriate).
4. Consider polio in the ddx of child presenting with AFP.