POLIO GLOBAL ERADICATION INITIATIVE

Multiple Injections: Acceptability and Safety

This version has been adapted by the Pan American Health Organization/World Health Organization (PAHO/WHO) for the Region of the Americas, from the original document prepared by the communications sub-group of the Immunization Systems Management Group (IMG)/Global Polio Eradication Initiative (GPEI). IMG is responsible for the overall management of the activities under Objective 2 of the Polio Eradication & Endgame Strategic Plan 2013-2018.

For more information on the introduction of IPV, OPV withdrawal and strengthening routine immunization, see: www.paho.org/immunization/polio

Pan American Health Organization

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Introduction

Humankind is drawing increasingly closer to securing polio eradication. Over the past 30 years, ceaseless efforts have been made to achieve global vaccination and high uniform coverage making this goal possible. Since 1991, thanks to multiple interventions and the social mobilization of millions of people, the Region of the Americas has managed to curb the circulation of poliovirus. However, one final push is needed so that children throughout the world remain free of this disease that causes death and severe disability.

All indications now suggest that the wild type 2 poliovirus has been eradicated globally, but the oral vaccine-related type 2 virus still causes sporadic outbreaks of circulating vaccine-derived poliovirus (cVDPV) in some countries and cases of vaccine-associated paralytic poliomyelitis (VAPP). As a result, the type 2 component of the oral polio vaccine (OPV) poses more of a risk than a benefit and is hindering global eradication efforts.

In January 2013, the World Health Organization (WHO) Executive Board approved the goals, targets, and timelines of the Polio Eradication and Endgame Strategic Plan 2013-2018. This plan has four main objectives:

1. Detect and interrupt all poliovirus transmission
2. Strengthen immunization systems and **withdraw OPV**
3. Contain poliovirus and certify interruption of transmission
4. Plan the legacy of the fight against poliomyelitis.

To minimize risks following OPV withdrawal, the Strategic Advisory Group of Experts on Immunization (SAGE), which advises WHO on matters relating to immunization, recommended that all countries gradually phase out OPV, starting with the type 2 component and introduce at least one dose of the inactivated polio vaccine (IPV) into their routine vaccination programs by the end of 2015.

The rationale to introduce IPV in routine vaccination programs is based on the following:

- To contribute to the final phase of polio eradication
- To reduce risks associated with OPV withdrawal
- To maintain immunity against the type 2 poliovirus while countries use bOPV (which will protect against type 1 and type 3).

PAHO/WHO's Technical Advisory Group on Vaccine-preventable on Diseases (TAG) recommends that, ideally, countries administer IPV during the first and second vaccination visits, followed by two or three doses of OPV. If a country decides to introduce only one IPV dose, this should be administered during the first vaccination visit, followed by three or four OPV doses, as indicated in the following table:

TABLE 1. Vaccination Schedule recommended for the introduction of inactivated poliovirus vaccine (IPV) in combination with the oral poliovirus vaccine (OPV).

Schedule	Basic			Booster	
	1st	2nd	3rd	1st	2nd
First option	IPV	IPV	OPV	OPV	OPV
Alternate option	**IPV**	**OPV**	**OPV**	**OPV**	**OPV**

How to communicate that a new injectable vaccine is to be introduced into routine vaccination programs?

While preparing and implementing the introduction of IPV, a social mobilization and communication strategy addressing internal and external publics should be designed and carried out.

Adequate and timely information on IPV should be made available to the public (especially parents or caregivers of newborn babies) so that they may seek out the health services and facilitate child vaccination.

Of equal importance, the communication strategy should also consider internal audiences (i.e., professionals, healthcare workers, and health promoters) as essential recipients of the communication messages and resources.

Health professionals are the primary promoters of vaccination and play a vital role in ensuring that parents or caregivers are informed about and agree to the vaccination of their children.

If not informed in a timely and adequate manner, parents or caregivers may not understand why their child needs another polio vaccine and may worry about the child having so many injections during the same visit.

It is undeniable that fear of needles and injections is frequent and widespread in the community and that this affects children and parents alike.

Although there are no contraindications to administering the vaccines at the same time or in the same limb (as long as the injections are about 2.5 cm [1 inch] apart), mothers and healthcare workers are increasingly concerned about the child's discomfort and possible local reactions.

Thus, there is an increasing need for an appropriate social communication and dissemination process to reduce pain during vaccination, as there are a growing number of available vaccines that should be administered simultaneously.

Giving multiple injections

When infants need three injections during the same visit, the first two vaccine injections are given in one thigh, with injection sites separated by at least 2.5 cm. The third injection is given in the other thigh.

Vaccination schedules that involve multiple injections during the same visit are based on many years of pre-licensure and post-licensure safety and effectiveness data, including concomitant use studies.

Advantages of multiple vaccinations

Giving a child several vaccinations during the same visit offers three major advantages:

1. **Protecting children**: Immunizing children as soon as possible provides protection during the vulnerable early months of their lives. Often, diseases are more severe in babies.
2. **Fewer vaccination visits:** Giving several vaccinations at the same time means parents and caregivers do not need to make as many vaccination visits.
3. **Increasing efficiency:** It means that health care providers are able to more efficiently provide and deliver other health services by reducing the time they need to spend providing vaccinations.

Children in many countries receive multiple vaccine injections

Globally, most middle and high-income countries have been using multiple injections for more than a decade without any untoward effects to infants or to the country immunization program. Data from middle and high-income countries have reinforced the well-established record of safety and acceptance of multiple injections. For example, in the United States, infants often receive 3 or more injections during each of the primary series vaccination visits.

Recently, more low and middle income countries have begun using multiple vaccine injections with the addition of pneumococcal vaccine and recently, inactivated poliovirus vaccine (IPV). For example, South Africa and Brazil have been using 3 simultaneous injections in their Expanded Program on Immunization (EPI) routine childhood immunization schedule.

Case study – Brazil

In Brazil, communication strategies targeting healthcare workers, professional societies, opinion leaders, and parents included materials and messages that focused on the safety of multiple injections. The result was successful acceptance of multiple injections, including high IPV coverage (>90%) among infants after the first year after vaccine introduction, similar to DTP. National surveillance for events supposedly attributable to vaccination or immunization (ESAVIs) demonstrated that multiple injections were well-tolerated and not associated with adverse events (and this included not being associated with fever, convulsions or hypotonic-hypo-responsive episodes).

Common health care provider and parent/ caregiver questions about multiple injections

It is common for the administration of multiple vaccines or injections to cause health care providers and parents to have questions or concerns. Typical questions and concerns about multiple injections include:

- Concerns about child's pain during vaccinations, such as "Will the child experience more pain or discomfort?
- Confidence in vaccine effectiveness, such as "Will the vaccines be as effective as if given alone?"
- Concern about adverse events, such as "Is there a greater likelihood of a child experiencing an adverse event?"

As a result, immunization programs should be prepared to provide information related to those concerns and questions, and health care providers should be prepared and able to answer parent or caregiver questions about multiple vaccine injections. This document will help immunization programs and providers address the most common questions.

Health care providers play important roles in parent/caregiver acceptance

Research and experience have shown that a health care provider's recommendations to parents and caretakers are very important. Parents and caregivers are willing to have their children receive multiple injections during the same visit if recommended by the provider and the provider can effectively address parent/caregiver questions and concerns about the safety and effectiveness of multiple vaccinations.

Will a child experience more pain or discomfort during vaccination when there are multiple injections?

Health workers should acknowledge that children will likely experience slightly more pain or discomfort when there are multiple injections. However, they should remind parents the pain or discomfort from vaccination is very brief – and that even one injection can cause pain or discomfort, with children often not noticing the pain or discomfort caused by subsequent injections. If more immunization visits are used to provide children with needed vaccinations, that will mean there will be more times when children will experience pain or discomfort from vaccinations.

What helps parents become willing to have their children receive two or more injections during the same vaccination visit?

There are three things that health care workers can do to help make parents become more willing to have their children receive two or more vaccine injections during the same visit:

1. **Provide reassurance**: A strong health care provider or worker endorsement of administration of multiple injections is essential to increase parent or caregiver acceptance.
2. **Provide clear responses to caregiver questions**: Health care providers or workers need to be able to effectively answer or address parent/caregiver concerns and questions related to the safety of multiple injections, the effectiveness of the vaccines, and child pain or discomfort.
3. **Minimize pain during immunization**: Health care providers or workers should take appropriate steps to decrease pain during immunization.

It is important to remember that additional vaccination visits mean children will have more stressful and painful vaccination experiences – not fewer. Also, spreading out vaccinations means parents/caregiver will have to schedule additional visits and bring children back. It may be very difficult for parents/caregivers to bring children back, and if children are not brought back, they will be unprotected from serious diseases.

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Are there things that health care providers or workers can do to decrease or minimize the pain from multiple vaccine injections?

Yes. There are things that health care providers can do when providing multiple injections to minimize pain. Studies have found that pain during immunization can be decreased by:

1. Having the child sit up to receive injections or by having a caregiver or provider hold an infant during the vaccinations;
2. Stroking the skin or applying pressure close to the injection site before and during injection;
3. Injecting the least painful vaccine first when two vaccines are being administered sequentially during a single office visit;
4. Performing a rapid intramuscular injection without aspiration;
5. Breast-feed the baby during and after vaccination or provide some sweet-flavored drinks; and
6. Use distracting techniques.

How can health care providers reduce the risk of local reactions after vaccination?

If the following recommendations are followed, possible errors related to the vaccination program can be greatly reduced and, as a result, parents' confidence in the vaccination program is maintained:

1. Use sterile injections.
2. Use correct vaccine administration procedures: check expiration date on vial, store vaccines at correct temperature, and do not freeze.
3. Use correct injection techniques, ensuring that two injections are separated by at least 2.5 cm (1 inch).
4. Do not massage or rub the skin after administering the vaccine.

Is it safe for children to receive two or three injections of vaccines at one time?

Yes. Children are given vaccines at a young age because this is when they are most vulnerable to polio, diphtheria, whooping cough (pertussis), Hib and pneumococcal disease. Vaccination schedules that involve multiple vaccine injections during the same visit are based on many years of pre-licensure and post-licensure safety and effectiveness data, including concomitant use studies. An infant's immune system is more than ready to respond to the very small number of weakened and killed antigens (bacteria and viruses) in vaccines. However, if exposed to a disease without

having been vaccinated, an infant's immune system may not be strong enough to fight the disease.

Wouldn't it be safer to separate vaccine injections and spread them out?

No. Spreading out vaccinations leaves babies unprotected for a longer time. Further, the available scientific data show that simultaneous vaccination with multiple vaccines has no adverse effect on the normal childhood immune system. A number of studies have been conducted to examine the effects of giving various combinations of vaccines simultaneously. These studies have shown that the recommended vaccines are as effective in combination as they are individually.

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Is IPV effective and safe when given in combination with other vaccines?

Yes. IPV is equally effective when given alone or with the other vaccines. IPV does not interfere with mounting a good immune response to the other vaccines, and giving IPV simultaneously with other vaccines is as safe as giving the vaccines without IPV.

Can IPV be administered during the same visit as DTP/Penta, PCV or rotavirus vaccine?

Yes. IPV can be administered together with vaccines routinely given to infants and children during immunization visits. Rotavirus vaccine can be administered together with DTP/Penta vaccine, Hib vaccine, IPV, hepatitis B vaccine, and pneumococcal conjugate vaccine. Available evidence suggests that rotavirus vaccine does not interfere with the immune response to these vaccines.

Is there any evidence that some multiple injections of vaccines may increase the risk for adverse events?

In most cases, multiple injections carry no greater risk for adverse events. However, a recently published study found simultaneous administration of PCV13 and trivalent inactivated influenza vaccine resulted in greater incidence of fever in children under 12 months old and in children in the second year of life, increased febrile seizures. These risks must be balanced against the risk of disease if one of the vaccinations is deferred.

For example, in the U.S., where this study was performed, the National Immunization Technical Advisory Group still recommends simultaneous vaccination.

As noted above, numerous studies have shown adding IPV immunization does not result in higher incidence of significant adverse events.

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Can many vaccines, given so early in life, overwhelm a child's immune system, suppressing it so it does not function correctly?

There is no evidence that the recommended childhood vaccines can "overload" the immune system. In contrast, from the moment babies are born, they are exposed to numerous bacteria and viruses on a daily basis. Eating food introduces new bacteria into the body; numerous bacteria live in the mouth and nose; and an infant places his or her hands or other objects in his or her mouth hundreds of times every hour, exposing the immune system to still more antigens. When a child has a cold they are exposed to at least 4 to 10 antigens and bacterial infections of the throat and tonsils (e.g., "strep throat") bring exposure to about 25 to 50 antigens.

Adverse Events Associated with Childhood Vaccines, a 1994 report from the United States Institute of Medicine, states: "In the face of these normal events, it seems unlikely that the number of separate antigens contained in childhood vaccines ...would represent an appreciable added burden on the immune system that would be immunosuppressive."

Sources

U.S. Centers for Disease Control and Prevention, Frequently Asked Questions about Multiple Vaccinations and the Immune System, Vaccine Safety website http://www.cdc.gov/vaccinesafety/Vaccines/multiplevaccines.html

Children's Hospital of Philadelphia, Too Many Vaccines? What you should know. http://vec.chop.edu/vaccine-safety/vaccines-and-immune-system.html

Risk of Fever After Pediatric Trivalent Inactivated Influenza Vaccine and 13-Valent Pneumococcal Conjugate Vaccine, Stockwell et al., JAMA Pediatics. Published online January 06, 2014 http://archpedi.jamanetwork.com/article.aspx?articleid=1809378

Parental Attitudes Toward Multiple Poliovirus Injections Following a Provider Recommendation, Kolasa et al., Public Health Reports, July-August 2001; 116; 282-288. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1497352/

Addressing Parents' Concerns: Do Multiple Vaccines Overwhelm or Weaken the Infant's Immune System? Pediatrics 2002; 109; 124. http://pediatrics.aappublications.org/content/109/1/124.full

Reducing the pain of childhood vaccination: an evidence-based clinical practice guideline, Taddio et al., Canadian Medical Association Journal, December 14, 2010 vol. 182 no. 18 http://www.cmaj.ca/content/182/18/E843.full

Physical interventions and injection techniques for reducing injection pain during routine childhood immunizations: systematic review of randomized controlled trials

and quasi-randomized controlled trials, Clinical Therapeutics, 2009:31 Suppl 2:S48-76; S104-51. http://www.ncbi.nlm.nih.gov/pubmed/19781436

Neonatal and early life vaccinology, C.A. Siegrist, Vaccine 2001; 10; 3331-3346 http://www.ncbi.nlm.nih.gov/pubmed/11348697

Developmental Change in Infant Cortisol and Behavioral Response to Inoculation, Ramsay and Lewis, Child Development, 1994, 65, 1491-1502. http://www.jstor.org/stable/1131513

Further Reading:

- GPEI Polio Eradication and Endgame Strategic Plan 2013-2018
- PAHO/WHO Final report of the XXI Technical Advisory Group (TAG) Meeting on Vaccine-preventable Diseases
- PAHO/WHO Practical Guide: Inactivated Poliovirus Vaccine (IPV) Introduction
- PAHO/WHO Polio Field Guide, Third Edition, (2006)
- PAHO/WHO Immunization Polio Webpage
  - FAQs on the Introduction of Inactivated Poliovirus Vaccine (IPV)
  - Background and Technical Rationale for Introduction of one dose of Inactivated Polio Vaccine (IPV) in Routine Immunization Schedule
  - Brief on IPV Introduction, OPV Withdrawal, and Routine Immunization Strengthening