

Executive Summary for April 2015 SAGE Session on Administration of Multiple Injectable Vaccines at a Single Visit

Due to the global introductions of pneumococcal conjugate vaccines (PCV) and inactivated polio vaccine (IPV), a majority of countries could soon have national vaccination schedules recommending administration of three or more injectable vaccines to infants during the same immunization visit. The evidence on the safety of administering multiple injectable vaccines, techniques for administering multiple injectable vaccines, and past experiences with healthcare provider and caregiver acceptance of additional injectable vaccinations were reviewed to help provide the basis for guidance in this area.

Summary of field study report: Post-IPV introduction assessment of the acceptability of three vaccine injections given to infants during clinic visits in South Africa, November 2014.

Since 2009, two of the five recommended vaccination visits in the first year of life in South Africa have included 3 injections in one visit, including IPV-containing vaccine at 6, 10 and 14 weeks of age. A cross-sectional survey of healthcare providers and infant caregivers at 21 public and 5 private clinics in two provinces was conducted. Most caregivers preferred that all recommended vaccinations be given in one visit rather than deferring one or more; however, the majority also reported that 3 injections or more were too many to give in one visit. Concerns were influenced by perceived infant pain and discomfort. Nevertheless, nearly all caregivers were willing to bring the child for visits with 3 injections again, and 96% of children were up to date for age for their immunizations. About half of the healthcare providers expressed concern about administering 3 injections in one visit. Caregivers' lack of knowledge and understanding of the reasons for 3 injectable vaccines was exacerbated by the limited communication with and information for caregivers from vaccinators. Strategies to improve immunization pain management and communication with caregivers may further improve acceptability of three injections.

Summary of field study report: Pre-IPV introduction assessment of healthcare providers and caregivers' perceptions of multiple injections for immunization in Tanzania, March 2015.

In preparation for IPV introduction in Tanzania (which would increase the number of injections at the 14 week visit to 3), focus group discussions and interviews with healthcare providers and infant caregivers were conducted across 6 regions of Tanzania in early 2015. The majority of healthcare providers believed the additional injection would not affect their work and were comfortable with administering 3 injections in one visit. The providers reported that potential challenges of increased injections included additional infant pain and a possible drop in vaccination coverage; potential benefits of not spreading out vaccinations included maximum protection against disease and increased efficiency for both parent and provider. The majority of caregivers accepted multiple injections as they perceived that young infants cannot rationalize fear of injections, that it is most efficient to get all recommended injections in one visit, and that infants are protected against disease at the youngest possible age. Both parents and providers identified current scenarios where children already receive 3 injections in one visit (such as children catching up on missed vaccinations), so there was already experience with multiple injections.

Summary of systematic review of experiences with provider and parental attitudes and practices regarding the administration of multiple injections during infant vaccination visits, 1970-2014

A systematic review was conducted to examine healthcare provider and infant caregiver concerns and practices related to the introduction of additional injectable vaccinations into routine childhood

vaccination visits. Forty-four articles were identified; 42 were from high income countries, including 21 from the U.S.A. Providers and parents reported concerns regarding multiple injections in one vaccination visit; these concerns increased linearly with the number of injections suggested in one visit. Common parental and provider concerns included apprehension about the pain experienced by the child, worry about potential side effects, and uncertainty about vaccine effectiveness. Multiple studies reported that a positive provider recommendation to the parent and a high level of concern about the severity of the target disease were significantly associated with parental acceptance of all injections. Providers often significantly overestimated parental concerns about multiple injections. Their overestimation of parental concerns may lead them to postpone recommended vaccinations, which may result in extra visits and delayed vaccination. More research is needed on interventions to overcome provider and parental concern about multiple injections, particularly in developing countries.

Summary of systematic review of safety and methods of administering multiple vaccines to infants

A systematic review was conducted in order to provide evidence on the safety and methods of administering multiple vaccines to infants in one visit. The review focused on IPV, DTP-HepB-Hib, and PCV vaccines, but other types of vaccines were included if study results were pertinent. In addition, literature reviews focused on specific subtopics and a grey literature review were conducted if little evidence was available in the initial search of peer-reviewed literature.

No studies were identified that evaluated the non-inferiority of giving two or more injections in the same limb compared to administration in different limbs for infants. In general, simultaneous administration of the relevant vaccines with other routine vaccines was well tolerated among infants; however, there were a few combinations of vaccines that resulted in reported increases in adverse events. Although multiple guidance documents recommend a 2.5 cm separation between injection sites on the same limb to allow for local reactions to be differentiated by vaccine type, no evidence from research was found to support this recommendation. Multiple published reviews have stated that the use of the deltoid muscle for intramuscular injections among infants is not preferable as the muscle is not well enough developed; the vastus lateralis muscle and ventrogluteal site are recommended alternative sites for vaccination. Additionally, studies have repeatedly shown that intramuscular administration of inactivated vaccines provides equal or greater immunogenicity and fewer local reactions than subcutaneous administration. No clear guidelines were identified on a preferred vaccine preparation process for a multiple injection visit.

Relevance of Findings to Country Immunization Schedules

There are 68 countries that have 3 or more vaccine injections scheduled for at least one visit in the country routine childhood immunization schedule. Twenty-six countries are including IPV as the 3rd injection in one visit by April 2016 (as of March 2015).

Key Conclusions and Recommendations (abbreviated)

- IPV (non-adjuvanted) can be safely and effectively given intramuscularly (IM) or subcutaneously (SC). However, the IM route is generally less reactogenic for inactivated vaccines.
- The vastus lateralis (thigh) muscle is a viable site with the ventrogluteal (hip) muscle as an acceptable alternative for intramuscular injections among infants. The deltoid (upper arm) muscle is another viable site for children 12 through 18 months, however the use of the deltoid may need to be delayed if the muscle is atrophied.

- Systematic comparisons of the risks and benefits of the various possible sites for administering infants DTP-Hepatitis B-Hib vaccine, IPV, and a PCV at the same visit are lacking, but injecting DTP-Hepatitis B-Hib vaccine in one thigh and IPV and PCV in another thigh can be done safely and effectively.
- Systematic studies of the best distance for separating vaccine injections are lacking, although a 2.5 cm distance between injections to the vastus lateralis (thigh) or deltoid is a viable option to allow any localized adverse events caused by the individual vaccines be distinguished.
- If multiple injectable vaccines are to be administered in one visit, vaccines needed for an infant should be prepared in a clean designated area, covering each clean needle with its cap using a one-hand scoop technique, and then administering of the indicated vaccines to the infant in quick succession is a viable approach.
- Countries introducing new vaccines should be strongly encouraged to:
 - Ensure healthcare providers receive information that the safety and biologic effects of providing all recommended vaccines in single visits are generally similar to those of providing them in separate visits, as well as training on communication techniques with parents with concerns about the child receiving multiple vaccine injections in a single visit.
 - Develop national vaccination schedules that include multiple vaccine injections in one visit unless specific evidence exists that there are negative repercussions which outweigh the benefits of administering multiple vaccines in one visit.
 - Monitor the acceptance and effects of simultaneous administration of injectable vaccines per their national vaccination schedule recommendations.
- Vaccination schedules should adapt to new data on the adverse events and immunogenicity of specific vaccine combinations as they become available