Clinically Relevant Vaccine-Vaccine Interactions
A Guide for Practitioners

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Summary

The need for combination vaccines has been recognised for many years. Many children must have 9 or 12 injections in their first year, which places a considerable burden on the child and the health service. Combination vaccines or simultaneously administered vaccines need to generate a protective immune response to all vaccine components that is equivalent to the response when administered separately. This is not always the situation. Many vaccines should not be administered together because of adverse reactions known as vaccine-vaccine interactions, a phenomenon where one vaccine affects another vaccine, thus potentially causing loss of immunogenicity, loss of protective efficacy or induction of adverse reactions. It is important to remember that most vaccine-vaccine interactions are asymptomatic and may only be discovered when the immune status of the vaccine recipient is analysed or when the individual is challenged by the microbe. The interactions may occur because of physical or chemical interactions within the vaccine formulation, interactions between live vaccines or immunological interference. This review summarises known vaccine-vaccine interactions that have been critically analysed and categorised based on their clinical importance.
Children and travellers commonly receive 2 or more vaccines concurrently; indeed, a child may receive up to 6 vaccines simultaneously [diphtheria toxoid, tetanus toxoid and acellular pertussis (DTaP) + *Haemophilus influenzae* type b (Hib) + inactivated poliomyelitis virus (IPV) + hepatitis B (HBV)]. The reasons for combination vaccines are many; one reason is that it decreases the number of injections and visits to the doctor, which results in less discomfort for the child and the parent. Another reason is that it lowers the overall cost of immunisation programmes. However, simultaneous use of vaccines may give rise to adverse reactions called vaccine-vaccine interactions, a phenomenon in which one vaccine may affect the response of another vaccine. Vaccines may also interact with immune globulins and drugs,[1-3] but this paper will solely discuss the present knowledge about vaccine-vaccine interactions.

There is a common misunderstanding among many clinicians that most vaccines may easily be administered together or even mixed together, if possible. Very little attention is paid to vaccine-vaccine interactions, probably because the interactions are usually asymptomatic and may only be discovered if the immune status of the vaccine recipient is analysed. We must distinguish between simultaneous immunisation, when the vaccines are administered separately but simultaneously at different sites, and combined immunisation, when the vaccines are physically combined together in 1 formulation. Good examples of successfully combined vaccines are the 23-valent pneumococcal polysaccharide vaccines, the trivalent poliovirus vaccines and the annual mixture of 3 influenza vaccines (which was first approved in 1945). Combined vaccines may also contain antigens from different pathogens, such as the combined diphtheria, tetanus and pertussis vaccine (DTP), which is the oldest combination vaccine having demonstrated efficacy for over 40 years, and the measles, mumps, and rubella vaccine (MMR). An example of vaccines administered simultaneously, but at different sites, is the combined DTP vaccine and the *Haemophilus influenzae* type b vaccine (Hib).

Throughout history, the various benefits of combined vaccines have been recognised. They are more economical in terms of product cost, healthcare personnel time and simplifying medical record maintenance. For the vaccine recipient it is more convenient, because there are fewer injections and fewer visits to the physician or clinic. The ultimate goal would be the development of a single vaccine that would, with 1 dose, immunise a child for life against all vaccine-preventable diseases.[4] We still have a long way to go to reach that goal. For example, Gambian children must have 9 injections in their first year of life, which places a considerable burden on the health service. With the introduction of the Hib vaccine as a separate injection, it brought the number of injections in the first year up to 12,[5] which is traumatic for the child. These frequent injections are not conducive to compliance. Especially when new vaccines are introduced, it will be desirable to avoid the need for extra visits to the doctor and more injections will mean slower adoption of newly developed and recommended vaccines. At present it may be possible to administer 7 vaccines during 1 clinic visit, with 2 injections (DTP and MMR) and 1 dose of oral poliomyelitis vaccine (OPV).[6]

Although some vaccine-vaccine interactions affect the immune response, the interaction is not associated with any clinical risk for the vaccine recipient. For clinicians and other professionals, it would be an advantage if interactions could be classified based on their clinical importance and frequency. An example of a major and well documented interaction is the concurrent use of OPV and oral RIT 4237 rotavirus vaccine, where the OPV may reduce the seroconversion rate for rotavirus.[7] The time between 2 vaccinations is also an important factor which should not be forgotten, such as the optimum time between administration of 2 interacting vaccines or the time until an interaction may be observed.

Easily accessible information on vaccine-vaccine interactions is extremely important from a public health perspective. It is never the intention to cause ‘false security’, by administering 2 or