



Revised recommendations for the administration of more than one live vaccine

Introduction

For many years, Immunisation against Infectious Disease (the Green Book) has contained a recommendation that when two live vaccines are required in the same individual, then the vaccines should either be given on the same day, or separated by an interval of at least four weeks. This was based on early studies with measles and smallpox vaccines,¹ and supported by the theory that interferon production stimulated by the replication of first vaccine prevented replication of the second agent, thus leading to a poor response to the second vaccine.

Following the recent introduction into the routine schedule of two live vaccines not given by a parenteral route (live attenuated nasal influenza vaccine and oral rotavirus vaccine) the evidence to support this general recommendation was reviewed. Based upon the available evidence and on the different immune mechanisms used by the various vaccines, in February 2014 the JCVI² agreed that the guidance to either administer the vaccines on the same day or at four week interval period was not generalizable to all live vaccines. They concluded therefore, that intervals between vaccines should be based only upon specific evidence for any interference of those vaccines. Therefore, to ensure protection from live vaccines is offered to individuals in a timely manner, the JCVI agreed that the current immunisation guidance should be updated to reflect this change.

¹ Petralli JK, Merigan TC, Wilbur JR. Action of endogenous interferon against vaccinia infection in children. *Lancet* 1965;286(7409):401-405.

² Joint Committee on Vaccination and Immunisation (JCVI) 2014. Minutes of the February 2014 meeting. [internet] <https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation>

What are the new recommendations?

The recommendations for giving more than one of the live attenuated vaccines currently used in the UK are as follows:

Vaccine combinations	Recommendations
Yellow Fever and MMR	A four week minimum interval period should be observed between the administration of these two vaccines. Yellow Fever and MMR should not be administered on the same day.
Varicella (and zoster) vaccine and MMR	If these vaccines are not administered on the same day, then a four week minimum interval period should be observed.
All currently used live vaccines (BCG, rotavirus, live attenuated influenza vaccine (LAIV), oral typhoid vaccine, yellow fever, varicella, zoster and MMR)	Apart from those combinations listed above, these live vaccines can be administered at any time before or after each other.

What is the evidence for these recommendations?

MMR and yellow fever. Co-administration of these two vaccines can lead to sub-optimal antibody responses to yellow fever, mumps and rubella antigens.³ The recommendation is that a four week interval should ideally be left between the administration of Yellow Fever and MMR vaccines. Where protection is required rapidly then the vaccines should be given at any interval; an additional dose of MMR may be considered.

MMR and varicella. A study in the US⁴ showed a significant increase in breakthrough infections when varicella vaccine was administered within 30 days of MMR vaccine; suggesting that MMR vaccine caused an attenuation of the response to varicella vaccine. When the vaccines are given successfully on the same day, however, as in the combined MMR-V vaccine used widely in North America responses are adequate⁵. The recommendation is therefore that MMR and varicella

³ Nascimento, Silva JR et al (2011). Mutual interference on the immune response to Yellow Fever vaccine and combined vaccines against measles, mumps and rubella. *Vaccine*, 2011 29 (3). 6327-6334.

⁴ Mullooly, J. Black, S. (2001). Simultaneous administration of varicella vaccine and other recommended childhood vaccines. *United States*. Nov 30; 2001. 50 (47). Pp. 1058-1061. [internet] <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5047a4.htm>

⁵ Plotkin, S. Orenstein, W.A. Offit, P.A (2013). *Vaccines*. Measles vaccines. Elsevier Saunders, China.

vaccines should be given either on the same day, or at a four week interval. As the zoster (shingles) vaccine contains the same virus as varicella (chicken pox) vaccine, this recommendation is extrapolated to MMR and zoster, although these vaccines are rarely given to the same age group. Where protection is required rapidly then the vaccines should be given at any interval and an additional dose of the vaccine given second may be considered.

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