Public Health England

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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 JCVI [2] agreed that the guidance to either administer the vaccines on the same day or at four week interval period should not be generalised to all live vaccines. They concluded therefore, that intervals between vaccines should be based only upon specific evidence for any interference of those vaccines. To ensure timely protection from live vaccines, therefore, the JCVI agreed that the current guidance should be updated (table).

[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

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Table: Recommendations for giving more than one live attenuated vaccine in current use in the UK

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 should be observed between vaccines.
Tuberculin skin testing (Mantoux) and MMR	If a tuberculin skin test has already been initiated, then MMR should be delayed until the skin test has been read unless protection against measles is required urgently. If a child has had a recent MMR, and requires a tuberculin test, then a four week interval should be observed.
All currently used live vaccines (BCG, rotavirus, live attenuated influenza vaccine (LAIV), oral typhoid vaccine, yellow fever, varicella, zoster and MMR) and tuberculin (Mantoux) skin testing.	Apart from those combinations listed above, these live vaccines can be administered at any time before or after each other. This includes tuberculin (mantoux) skin testing.

Background evidence

Yellow fever and MMR: 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 should be considered.

Tuberculin skin testing (Mantoux) and MMR: Administering tuberculin (Mantoux) within 28 days of MMR vaccine may result in decreased reactivity of the tuberculin and the false

[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.

negative reporting of results.[4].For this reason, a four week interval period should be observed before tuberculin testing is initiated. If tuberculin testing has already been initiated, MMR should be delayed until the skin test has been read. If protection against measles is urgently required, then the benefit of protection from the vaccine outweighs the potential interference with the tuberculin test. In this circumstance, the individual interpreting the negative tuberculin test should be aware of the recent MMR vaccination when consider how to manage that individual.

Tuberculin can be administered at the same time or at any time before or after inactivated vaccines and all other live (including non-injectable) vaccines. Whilst there is no evidence of decreased reactivity or interference from other live vaccines, those interpreting the results of the tuberculin skin test should be aware of any recently administered live injectable vaccines.

Varicella and MMR: A study in the US[5] 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 on the same day, however, as in the combined MMR-V vaccine used widely in North America, the responses have been shown to be adequate.[6] The recommendation is therefore that MMR and varicella vaccines should be given either on the same day, or at a four week interval from each other. As the zoster (shingles) vaccine contains the same virus as varicella (chicken pox) vaccine, this recommendation has been extrapolated to MMR and zoster, although these vaccines are rarely given to the same age group. Where protection from either vaccine is required rapidly then the vaccines can be given at any interval and an additional dose of the vaccine given second should be considered.

[4] Statens Serum Institute (2011). Description of Tuberculin PPD RT 23. [internet] http://www.ssi.dk/English/Vaccines/Tuberculin%20PPD%20RT%2023%20SSI/Description%20of%20Tuberculin%20PPD%20RT%2023.aspx

[5] 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

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

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