1. JCVI and its meningococcal sub-committee have considered:
   - the epidemiology of meningococcal disease in the UK;
   - the impact of the current meningococcal serogroup C conjugate (MCC) vaccination programme;
   - if and when the current vaccination programme needs to be changed to include additional protection against meningococcal serogroup C and other serogroups; and
   - the likely effectiveness and cost-effectiveness of any changes to the current vaccination programme.

**Epidemiology of meningococcal disease in the UK**

2. JCVI noted that the number of cases of invasive meningococcal disease (IMD) in the UK has decreased since the introduction of the MCC vaccination programme in 1999. IMD caused by serogroup C meningococcal disease has fallen by over 95 per cent and cases are at an extremely low level (figure 1). Serogroup B meningococcus now causes 88% of all IMD in England and Wales. Serogroup Y meningococcus accounts for much of the remainder of IMD (4.2% of all IMD in England and Wales); the majority of serogroup Y cases are in people aged 45 years and over, often with co-morbidities; a small number of cases of serogroup Y disease are seen in teenagers. Similar epidemiological profiles are also reported in Scotland and Northern Ireland.

**Figure 1:** Number of laboratory confirmed serogroup C meningococcal cases in England and Wales, 1998-2010. Source: Health Protection Agency

---

Impact of, and protection offered by, the serogroup C meningococcal vaccination programme

3. The MCC vaccination programme was introduced into the routine childhood immunisation programme in 1999. At the time of introduction, the routine schedule was three doses of MCC vaccine given in the first year of life or two doses for infants over five months and less than 12 months of age. In addition to the introduction of MCC vaccine into the routine immunisation programme in 1999, a catchup programme for children and young people aged one year to less than 18 years, using one or two doses of MCC vaccine, was undertaken over a two-year period (1999-2001). In 2002, the catch-up campaign was extended to include all adults less than 25 years of age.  

4. In 2006, following studies that showed two doses of MCC vaccine provided good protection in the first year of life and that protection waned during the second year of life, the primary immunisation course was changed to two doses at three and four months of age and a booster dose at 12 months of age to extend the duration of protection. 

5. A number of studies show MCC vaccination in early childhood provides a short-term protective immune response but vaccination later in childhood provides higher levels of antibody that persist for longer. JCVI notes that studies have shown that levels of antibody considered to be protective, wane rapidly in infants and children aged under six years of age who were vaccinated with the MCC vaccine, such that only around twelve per cent are considered to have protective levels four years after vaccination. Other studies also suggest that antibody declines quickly to below protective levels even after a booster dose at 12 months of age for children who received the primary course as infants. However, if children are immunised when they are over six years of age then around fifty per cent still have protective levels of antibody in early adolescence. In contrast, antibody levels considered to be protective in individuals vaccinated from the age of ten years or older are markedly higher and protection therefore persists until at least early adulthood and possibly longer. Other studies have shown that the MCC vaccination campaign significantly reduced nasopharyngeal carriage of serogroup C meningococcus. This reduction in carriage provides indirect protection to unvaccinated and susceptible vaccinated members of the population through herd immunity. 

6. JCVI concludes that the low levels of serogroup C meningococcal disease achieved by the infant and catch-up MCC vaccination-programmes are due to both individual direct protection and indirect protection or herd immunity. Adolescents vaccinated as part of the catch-up programme are likely to continue to have high levels of protective antibodies and thus individual protection. In contrast, individual protection in vaccinated infants and toddlers does not last long. However, disease is very low and therefore, toddlers and young children are most likely being protected by herd immunity when individual protection wanes. It is extremely difficult to predict precisely and with confidence when indirect protection would be insufficient to maintain the current level of disease control. The only true indication that indirect protection has diminished would
be observations of increases in serogroup C meningococcal disease. JCVI strongly advises against using increasing disease as an indicator. Instead, a pre-emptive precautionary approach should be taken to maintain indirect protection and to provide individual protection in older children, who may become exposed (for example when travelling to a country where meningococcal serogroup C is still circulating).

**Need for an extra dose of MCC vaccine for older children**

7. JCVI concludes that herd immunity could be maintained by introducing a booster dose in older children to increase protective antibody levels. Studies have shown that boosting younger children after the age of six years produces high levels of antibody for at least one year; however, there are no longer term data following boosting in this age group. In contrast, primary vaccination in adolescence generates more persistent antibody responses. JCVI therefore advises that a booster dose of MCC vaccine should be provided during adolescence. Direct evidence on the immune response following boosting during adolescence is limited to one MCC vaccine. However, indirect evidence on immune responses following primary vaccination of children suggests that protective and persistent antibody responses should be expected following boosting during adolescence with any of three MCC vaccines. The sub-committee looking at adolescent vaccinations should consider the timing of an adolescent dose of MCC.

**Protection against other meningococcal serogroups**

8. There is a choice of licensed conjugate vaccines that protect against serogroup C meningococcal disease that could be offered to adolescents; serogroup C meningococcal vaccine or the quadrivalent ACWY vaccine. JCVI has considered whether protection of adolescents should be extended to other meningococcal serotypes such as A, W135 and Y. The Committee notes that whilst there may be appreciable carriage of serogroup Y meningococcus in adolescents there are relatively low levels of disease. A serogroup Y-containing meningococcal vaccine should only be used if the available vaccines do not compromise the response to meningococcal C, and would be supported by further evidence of how this may affect serogroup Y carriage. Some data to inform this consideration will come from a carriage study being conducted for serogroup B meningococcus that is also looking at the effects of an ACWY conjugate vaccine.

**Economic aspects of introducing an adolescent serogroup C meningococcal vaccination**

9. JCVI considered the health and economic implications of changing the immunisation programme to extend the protection offered by the MCC vaccination programme. Since the cost-effectiveness of an additional dose of MCC cannot be determined in the absence of disease, the Committee noted that a cost-neutral approach could be to move one of the current infant doses of MCC vaccine to an adolescent opportunity. A

---

*Menjugate kit® or Meningitec® (both CRM197-conjugated) or NeisVac C (tetanus toxoid-conjugated)*

*http://clinicaltrials.gov/ct2/show/NCT01214850*
clinical trial demonstrates that a single dose of one of two MCC vaccines at three months of age is sufficient to prime infants against meningococcal serogroup C disease and provide protection for the first year of life. This study shows that the priming effect of and protection offered by one dose of MCC vaccine is similar to that achieved from the currently administered two doses and that no differences are measured in the ability of the Hib/MenC vaccine to boost the immune response if children have been primed with one or two doses of MCC vaccine.

10. The committee noted data that suggests that it may be preferable to use a tetanus-toxoid conjugated MCC vaccine as a single priming dose in infants as this would likely provide a better immune response when boosted with a tetanus toxoid-conjugated Hib/MenC vaccine given at 12 to 13 months. However, the committee recognises that it is vital that continuity of supply for MCC vaccine is maintained. NeisVac C® or Menjugate® kit, the MCC vaccines currently used in the childhood immunisation programme, can be used to provide protection as a single dose in infants, however, this indication would be ‘off-label’ as none of the available MCC vaccines are licensed for a single dose in infancy.

Conclusion

11. Given that evidence suggests:
   (i) one dose of serogroup C meningococcal vaccine offers protection to infants; and
   (ii) one dose of serogroup C meningococcal vaccine would provide longer-term protection to adolescents and maintain herd protection to infants and younger children,

the committee advises that an adolescent dose of serogroup C meningococcal vaccine be introduced and a dose of serogroup C meningococcal vaccine in infants be removed.

12. The sub-committee looking at adolescent vaccinations should consider the timing and implementation of an adolescent dose of MCC vaccine to ensure that coverage is sufficiently high to maintain herd immunity.

References


* Menjugate kit® (CRM197-conjugated) or NeisVac C (tetanus toxoid-conjugated)
following primary series with an acellular pertussis-containing pentavalent vaccine given concomitantly with meningococcal group C conjugate vaccine, and response to a booster dose of an acellular pertussis-containing quadrivalent vaccine. Vaccine 27(37): 5096-102.


14. de Whalley PC, Snape, MD, Kelly, DF et al. (2011) Persistence of serum bactericidal antibody one year after a booster dose of either a glycoconjugate or a plain polysaccharide vaccine against serogroup C Neisseria meningitidis given to adolescents previously immunized with a glycoconjugate vaccine. Pediatr Infect Dis J. 30(11) e203-8.
