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Long-term effectiveness of MenAfriVac

Published Online February 8, 2019 http://dx.doi.org/10.1016/S1473-3099(18)30725-4

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A conjugate vaccine for *Neisseria meningitidis* serogroup A (MenAfriVac) was introduced through mass campaigns in people aged 1–29 years in the African meningitis belt and is now being added to national infant immunisation programmes.[1] Following the mass campaigns in 2010–17, incidence of *N meningitidis* serogroup A meningitis has declined from a hyperendemic pattern with regular epidemics to a few sporadic cases.[2] The hope is that control of the disease will be long lasting. The mechanism for such control would be the initial interruption of circulation of *N meningitidis* serogroup A in the population through the effect of the vaccine against asymptomatic nasopharyngeal infection, followed by sustained direct protection against disease, including in new birth cohorts. The duration of persistence of antibodies is a major variable in this scheme.

In *The Lancet Infectious Diseases*, Michael White and colleagues report results from a mathematical model,[3] originally developed for natural malaria infection but used here to estimate the kinetics of *N meningitidis* serogroup A-specific serum bactericidal antibodies (SBAs) in the African meningitis belt. The model uses serological data obtained in clinical trials[4,5] before and up to 2 years after vaccination with MenAfriVac. These trials tested a single dose of MenAfriVac in children and adults aged 12 months to 29 years.[4,5] The model predicts that vaccine efficacy after 20 years will be 52% (95 credible interval 29–73) among 12–23 month-old children and 70% (60–79) among older children and adults. These results suggest that no booster vaccination would be needed for people vaccinated with MenAfriVac at age 2 years or older.

This research is an important complement to two other approaches: first, the two clinical trials[4,5] followed SBA persistence up to 5 years after vaccination and found that after a substantial decline of 40–80% during the first year after vaccination, antibody titres were stable in all age groups between 1 and 29 years. One limitation of these estimates is that, unlike the current situation of quasi-elimination, *N meningitidis* serogroup A continued to circulate in trial populations and natural boosting might have maintained higher antibody levels. White and colleagues overcome this limitation in their model by simply not assuming any such boosting effect and also provide a long-term estimate up to 20 years after vaccination. Second, from a series of population-level cross-sectional studies in Burkina Faso and exponential extrapolation of the decline, we estimated that SBA antibody titres would return to pre-vaccination levels after 12 years at the earliest.[6] Although our work's strength was that it reflects the real-life situation of immigrating unvaccinated individuals, its ecological design and lack of document-based vaccination status for most participants in subsequent surveys was a limitation.

The results we obtained, however, shed light on an important limitation of all current work: there is no confirmed correlate of protection against *N meningitidis* serogroup A in the meningitis belt, neither for meningitis nor for asymptomatic infection. We have previously shown that the seroprevalence of putatively protective SBA titres against the *N meningitidis* serogroup A reference strain (≥1/8 or ≥1/128) does not correlate with meningitis incidence.[7] This finding was not surprising, given that the seroprevalence of these titres was more than 70% among children and adults already in the pre-vaccination era. As an alternative serological measure, we proposed the SBA against strain 3125, which should be specific for vaccine-induced protection.[8] Among children vaccinated before 5 years of age, the return to pre-vaccination levels

of these 3125-SBA titres would be expected after 8 years.[6] These results suggest that a MenAfriVac booster vaccination would currently be required for this group to maintain immune protection.

This uncertainty around the correlate of protection raises some concern. It is worrying that the pathophysiology of serogroup A meningitis found in the African belt is not well understood. One hypothesis is that under the extreme climatic conditions during the dry season (high aerosol load and low air humidity), meningococci can invade the meninges directly from the nasopharynx through the lymphatic tissue along the olfactory nerve.[9] In this scenario, conjugate vaccines are effective primarily, or perhaps only, through their capacity to protect against nasopharyngeal infection. In any case, it is widely accepted that the interrupted pathogen circulation is the main determinant of strong and persistent impact of high-coverage conjugate vaccine programmes.[1] The key factor to evaluate, then, is the mucosal immunity induced by conjugate vaccines. Unfortunately, there is even less understanding of how this mucosal immunity works. No validated measures are available, although salivary antibodies might be candidates.[10,11] For now, the sole way to evaluate the vaccine-induced protection against asymptomatic infection is through large and costly carriage studies.

The pragmatic approach is to acknowledge that conjugate vaccines work well, particularly because of indirect protection, and that further evaluation is necessary only if *N meningitidis* serogroup A epidemics re-emerge. Furthermore, a vaccine against five meningococcal serogroups (A, C, W, X, and Y) is being developed[1] and its introduction through mass campaigns will provide a booster against *N meningitidis* serogroup A.

To move forwards, my wish would be to see the development of a simple, specific test of mucosal immunity against meningococci, which would allow for the follow-up assessment of protection against asymptomatic nasopharyngeal infection among trial participants and vaccinated populations. Mathematical modelling based on such data will allow estimation of the duration of both direct and indirect protection after vaccination and thus offer a powerful tool to develop strategies for long-term control of meningococcal meningitis.

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I declare no competing interests.

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Twitter to engage, educate, and advocate for global antibiotic stewardship and antimicrobial resistance

The WHO Global Action Plan on Antimicrobial Resistance recommends countries work together to improve awareness and understanding of antimicrobial resistance, including through social media.[1,2] Twitter disseminates news in seconds around the world in real-time to anyone with an internet-connected