

Journal club



CORRELATES OF PROTECTION AGAINST NEISSERIA MENINGITIDIS

Over the past two decades, the leading cause of meningitis in childhood and the leading infectious cause of death in the UK has been *Neisseria meningitidis*. There is now the potential for broad control of this serious disease by vaccination. Following on from programmes since 1999 to control disease caused by capsular group C *N. meningitidis*, and more recently by capsular groups A, C, Y and W, a multi-component capsular group B meningococcal (MenB) vaccine was introduced in 2015 in the UK for all infants. The first results suggest high vaccine effectiveness (83% against all MenB strains after two doses) (Parikh *et al.*, 2016). Because the disease is rare, these vaccines were all licensed without efficacy trials on the basis of data accumulated over the past century showing that bactericidal antibody is the correlate of protection. This insight can be traced back to a

“susceptibility to disease correlates with lack of specific antibody”

paper published in 1921 by George Heist and colleagues, involving observations from 172 individuals.

They showed that meningococci isolated from patients with associated disease were more resistant to killing in whole blood than were bacteria taken from the throats of healthy carriers. The blood of carriers was found to be better at killing meningococci than the blood of non-carriers, which the authors took to suggest that immunity was induced by pharyngeal exposure. They also showed that defibrinated blood supported the growth of all meningococcal strains and was used as a positive control, as was the blood of ‘Man H’, which was also an excellent growth medium for *N. meningitidis*.

We now know that the meningococci were killed in these experiments by complement-mediated lysis directed to the bacterial surface by specific antibody present in the serum of immune individuals. Susceptibility to disease correlates with lack of specific antibody and with complement deficiency. Defibrinated blood lacks complement and therefore supported the growth of bacteria

despite the presence of antibody.

Man H was the lead author of the paper, George Heist. He died, aged 36, of meningococcal meningitis in the year before the paper was published. Five male members of his family are said to have died in a similar way, including his father at the age of 24; it therefore seems quite possible that he had an X-linked complement deficiency. These carefully observed studies are a stark reminder that simple experiments in the laboratory and tragic experiments of nature can provide the key information to underpin vaccine development and point to correlates of protection.

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The author declares competing interests: see [Web version](#) for details.

ORIGINAL ARTICLE Heist, G. D., Solis-Cohen, S. & Solis-Cohen, M. A study of the virulence of meningococci for man and of human susceptibility to meningococcal infection. *J. Immunol.* **7**, 1–33 (1922)

FURTHER READING Parikh, S. R. *et al.* Effectiveness and impact of a reduced infant schedule of 4C MenB vaccine against group B meningococcal disease in England: a national observational cohort study. *Lancet* [http://dx.doi.org/10.1016/S0140-6736\(16\)31921-3](http://dx.doi.org/10.1016/S0140-6736(16)31921-3) (2016)