

Commentary

Meningococcal Vaccines

To Eradicate the Disease, not the Bacterium

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ABSTRACT

Neisseria meningitidis is exclusively a human-adapted bacterium, most frequently found in asymptomatic carriage that promotes natural immunity. However, it is also the causative agent of severe invasive infections, such as septicaemia and/or meningitis that may lead to life-threatening septic shock. Vaccination with capsular polysaccharidic antigens (either plain or conjugated) induces serogroup specific protective antibodies. Meningococcal capsular polysaccharide vaccines are only available against serogroups A, C, Y and W135. There is no available capsular vaccine against serogroup B. Future strategies to develop meningococcal vaccine should be global strategies aimed to design a "universal vaccine" effective against meningococcal disease due to any strain, regardless its phenotype and genotype. However, these global strategies may be hindered by the high diversity of meningococcal isolates and their changing epidemiology. Alternatively, targeted or local vaccine strategies may be developed against specific isolates and can help particularly in controlling outbreaks while preserving benefits from carriage.

Infectious diseases are a major health threat and are still responsible for high mortality and morbidity worldwide, despite important advances in therapeutics and vaccines. The burden of several communicable diseases is also worsened by their epidemic potential. Vaccination is the optimal policy in controlling epidemic infections. They have achieved heroic success in controlling infectious diseases since the early 20th century; this has led to the quick assumption that eradication of the microbial agent of an epidemic infection through vaccination should permit a complete and definitive elimination of the disease. However, this "anti-microbial" strategy has several limitations, including the genetic diversity and variability of the agent, the coinfection with other microorganisms, the differences in clinical manifestations, and the existence of asymptomatic carriers and/or an animal reservoir. The "host/pathogen interaction" concept should replace the "anti-microbial" approach for developing optimal strategies to control infectious diseases. Meningococcal disease is one example for this viewpoint.

HOW/WHY MENINGOCOCCAL BIOLOGY SHAPES VACCINE DESIGN?

N. meningitidis is a bacterium exclusively found in humans, most frequently as a host of the commensal bacterial flora of the nasopharynx. Therefore, asymptomatic carriage may be detected in about 10% of people.¹ However, *N. meningitidis* is also responsible for severe invasive infections, including septicemia and/or meningitis, septic arthritis and pericarditis. These invasive infections occur as endemic or epidemic infections. Extensive phenotyping and genotyping of meningococcal isolates clearly showed that carriage isolates are highly diverse and differ from invasive isolates.² Indeed, epidemic isolates usually belong to a limited number of genetic lineages.³ Carriage isolates of *N. meningitidis* are more prevalent than invasive isolates, and invasive isolates are not drawn randomly from the carriage bacterial population.⁴ Virulence and transmissibility do not seem to be linked during the meningococcal life cycle, since bacteria that cross the upper respiratory tract epithelial barrier to invade the host are no longer transmitted to other hosts.⁵ *N. meningitidis* may hence be considered as an occasional pathogen.⁵ Isolates from cases of meningococcal disease seem to possess a higher invasive power upon acquisition by an immunologically naive host (touch-and-invade behavior). At the opposite, carriage isolates may have a low attack rate upon acquisition (touch-and-hide behavior). The carriage states of *N. meningitidis* and commensal *Neisseria* are therefore important in building herd immunity by inducing both IgG and IgM antibodies.^{6,7}

