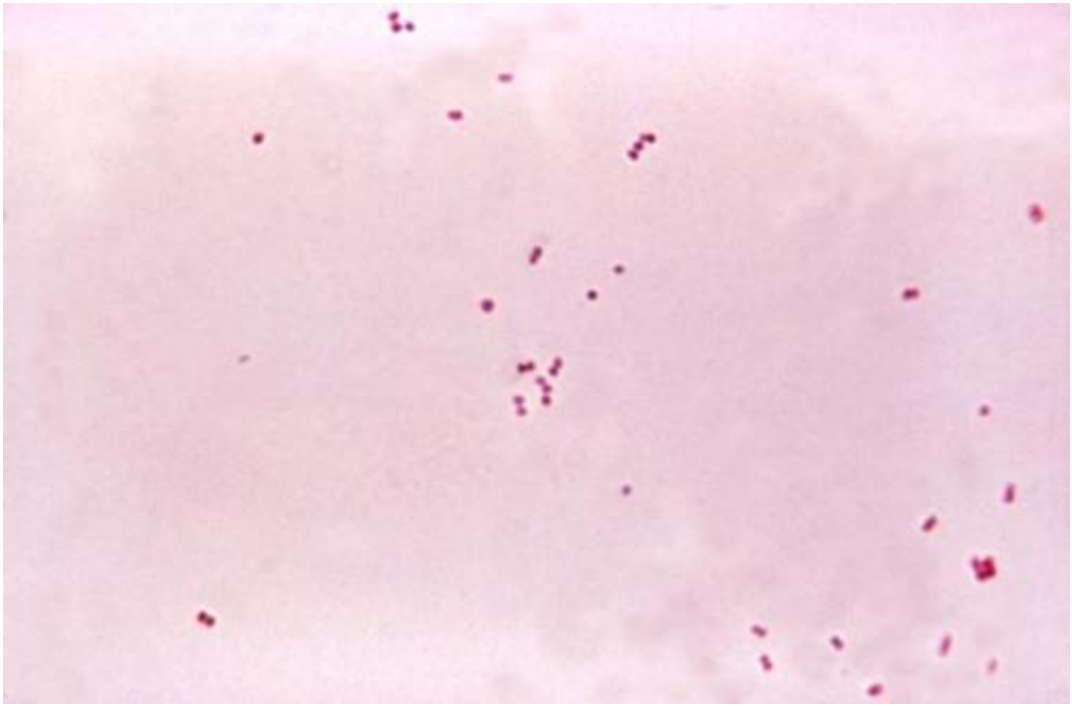
Research finds new way to determine protection of Men B vaccine against different strains

June 18 2018



Gram stain of meningococci from a culture showing Gram negative (pink) bacteria, often in pairs. Credit: public domain

Researchers at the University of Leicester and Meningococcal Reference Unit have developed a new approach to assess the effectiveness of the Men B vaccine, Bexsero, against different strains that cause meningococcal meningitis and septicaemia.

The new approach allows direct testing of blood samples from patients with meningococcal disease to find out if the strain they are infected with might have been prevented by the vaccine. Currently, it is estimated that the vaccine offers protection against 73-88% of strains responsible for meningococcal disease in England and Wales.

The approach is being assessed by Public Health England for its potential to routinely test all meningococcal disease cases.

The research was based on looking at one of the four antigens that make up the vaccine. More work is needed to look at the remaining three antigens.

Dr. Chris Bayliss, from the University of Leicester's Department of Genetics and Genome Biology, said: "This new research fills a gap in current testing capabilities that determine whether a disease-causing meningococcal strain is expected to be covered by the vaccine.

"We are currently unable to obtain and grow live bacteria from up to half of patients to determine whether the vaccine might have prevented the type of meningococcal disease they have, often because treatment with antibiotics has already killed them. There is a need for new tests to identify and measure the amount of antigen by obtaining meningococcal DNA directly from patient samples."

Bexsero is a vaccine that helps protect against group B meningococcal disease (MenB), developed by GSK. It was introduced into the UK infant immunisation schedule in September 2015 and has been shown to be highly effective in preventing MenB disease in vaccinated infants.

One of the protective components of Bexsero is an antigen called factor H binding protein (fHbp). Infants vaccinated with MenB vaccines produce antibodies against this protein, so that if they are exposed to

meningococcal bacteria that possess this protein, these antibodies will kill the bacteria.

In a study published in the academic journal *PLOS ONE*, funded by Meningitis Research Foundation (MRF), the researchers show how a combination of DNA sequences and statistical testing can be used to measure the amounts of fHbp present in disease-causing meningococcal bacteria.

Researchers and Mathematicians at the University of Leicester studied more than 2,000 disease-causing meningococcal isolates to measure how much antigen each strain produces.

They used their results to categorise each strain into three classes: 'covered'; 'not covered'; and 'at risk'. The 'not covered' groups included the ~12% of strains that will not be covered by the vaccine while the 'at risk' groups contains strains that are more likely to cause illness in vaccinated individuals.

Dr. Bayliss said: "Detailed molecular analyses of clinical samples are essential for understanding how efficient the new vaccines against meningococcal disease are at protecting people against different meningococcal strains.

"This novel approach has the potential to help measure the effectiveness of Bexsero more accurately.

"The detailed information collected on the fHbp protein could be important in helping to improve the next generation of MenB vaccines."

Linda Glennie, Director of Research at MRF, said: "Introducing the MenB vaccine into the UK immunisation schedule in 2015 was a major step forward. Vaccines are the only way to prevent bacterial meningitis

and septicaemia. The MenB vaccine has already been proven to be safe and effective and rates of MenB have been reducing since the introduction of the vaccine. Now that we have a vaccine in the schedule that gives good protection against MenB, these new testing techniques that the scientists have developed will give us crucial insights. Over the years, the strains that circulate in the UK have changed, and it is important to be certain about how much coverage the current MenB vaccines can provide, both now and in the future."

"We are very encouraged by the results of the study , though measuring the attribution of only one antigen, fHbp, alone, without taking the effect of the other three components of Bexsero into consideration, may underestimate its protective effect," said Rafik Bekkat- Berkani,MD. Global Medical Affairs Lead from GSK. "Bexsero's 4 distinct components target different mechanisms in MenB survival and disease development and offer the potential to protect against invasive MenB strains even when the expression of one component is low or antigenically different. We agree with the study's authors that more research is needed on Bexsero's additional three antigens potentially providing multiple targets for vaccine-induced antibodies. "

Shamez Ladhani, Paediatric Infectious Disease Consultant, Public Health England, said: "Since the introduction of the MenB vaccine programme in 2015, cases of Meningococcal B disease have nearly halved in infants under 1 year and in one and two year olds, who became eligible for the 12-month booster in May 2016. However, any case of meningococcal disease is tragic and, unfortunately, not all cases of meningitis and septicaemia are preventable through vaccines. This research is important in helping us understand how we can best protect those who are most at risk from a very serious disease."

More information: Caroline Cayrou et al, Clustered intergenic region sequences as predictors of factor H Binding Protein expression patterns

and for assessing Neisseria meningitidis strain coverage by meningococcal vaccines, *PLOS ONE* (2018). DOI: 10.1371/journal.pone.0197186