Medical Xpress

Pneumococcal DNA predicts course of infection

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In addition to revealing information about a patient's condition, pneumococcal DNA also appears to provide information about the course of an infection. In the next issue of *Clinical Infectious Diseases*, Radboudumc researchers describe several pneumococcal genes predicting whether a patient runs the risk of developing meningitis or dying from the disease. Use of such genetic tests can improve infection diagnostics.

Pneumococcus (Streptococcus pneumoniae) is an important cause of pneumonia, sepsis and meningitis. This bacterium commonly resides in the nasal cavity. Normally, this is not a problem but it can make weak patients very ill, quite often with a fatal outcome. Patient characteristics such as age, compromised immune system and comorbidity partly explain why some patients develop pneumonia and others meningitis. It was not known whether properties of the pneumococcus itself also determine how invasive pneumococcal disease manifests itself.

Pneumococci show huge genetic variability. This variation is often denoted using antibodies (sera) which recognize specific sugar capsules on the pneumococcal surface. More than ninety of such sugar capsules (serotypes) are known. Although there is a relationship between these serotypes and the course of the disease, the variation in pneumococci is not restricted to these differences in sugar capsules. Therefore, researchers at the Radboudumc in collaboration with the RIVM, CWZ, Maasziekenhuis Pantein, Imperial College London and the Sanger Institute in Cambridge have determined the entire DNA sequence of

pneumococci isolated from the blood of 350 patients. They could subsequently relate the genetic variation they found to more than twenty disease manifestations.

Blood-brain barrier

The researchers found several bacterial genes which appeared to be linked to the course of the infection. The presence of the slaA gene, for example, appeared to predict meningitis. This gene codes for the phospholipase A2 protein. Earlier research suggests that this protein is involved in inflammation and may also affect the blood-brain barrier. Bacteria carrying this gene could therefore be able to penetrate the brain. Another set of four genes predicted whether a patient would die within 30 days, particularly among those who were not expected to die at first sight. Marien de Jonge, head of the section Pediatric Infectious Diseases at the Radboudumc: "Earlier we found that one of these genes codes for a protein that activates blood platelets, which could lead to excessive blood clotting and an increased risk of death." The genes identified were also found in a second group of 500 patients.

The pneumococcal genes found can also be measured in the blood of patients. This provides diagnostic opportunities, says Amelieke Cremers, clinical microbiologist in training and first author of the article: "This study shows that modern DNA sequencing techniques can be used to improve the diagnostics of infectious diseases. Knowledge of the genetic variation within bacterial species can improve our risk assessment for individual patients with acute infections."

More information: Amelieke J H Cremers et al, The Contribution of Genetic Variation of Streptococcus Pneumoniae to the Clinical Manifestation of Invasive Pneumococcal Disease, *Clinical Infectious Diseases* (2018). DOI: 10.1093/cid/ciy417

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