

DESCRIPTION FOR THE GENERAL PUBLIC

Infections caused by *Streptococcus pneumoniae* (pneumococci), remain an important cause of morbidity and mortality worldwide, despite the availability of effective vaccines. Recent WHO data show that pneumococci are responsible for approximately half a million deaths in children under 5 years of age each year. Pneumococcal infections affect chiefly two most vulnerable groups: small children and the elderly. The most common invasive infections caused by pneumococci are bacteremic (or septic) pneumonia, sepsis and meningitis. Invasive pneumococcal disease (IPD) is associated with a high mortality and also with a high proportion of serious complications in patients who survive infections. This bacterium may also be responsible for more common, non-invasive infections of respiratory tract and plays role as a frequent asymptomatic colonizer, especially in small children.

At present, from the public health perspective, increasing bacterial resistance to antibiotics is one of the most important problems, affecting also the pneumococcal population. Until recently, it was typically penicillin resistance; however, infections are now caused more often by multidrug resistant isolates (MDR), non-susceptible to at least three different antibiotics. The rise of MDR pneumococci is of considerable public health concern as the therapeutic options that remain available are limited or very limited.

Polysaccharide capsule provides protection from the human immunological system and represents the main virulence factor of pneumococci. Differences in capsule composition and antigenic properties are the basis of discerning of over 90 serotypes. The vaccines that are currently in use are composed of capsular polysaccharides. The implementation of anti-pneumococcal conjugate vaccines (7-, 10- and 13-valent) have dramatically decreased the number of infections caused by vaccine serotypes. However, in consequence non-vaccine serotype strains have started to replace the vaccine serotype ones. Following the introduction of 7-valent vaccine, a significant increase in serotype 19A pneumococcal infections occurred. Importantly, an increase in 19A has also been observed in countries where vaccination was not routinely implemented. Nowadays, this serotype is one of the most common cause of invasive pneumococcal infections in Europe, moreover, it is the most resistant to antibiotics.

In Poland, vaccination against pneumococci is not part of the routine immunization schedule, with the exception of some risk groups, and is available only at the patient's own expense. Despite this, there has been an increase in the number and percentage of invasive 19A observed over the past few years. These isolates are also the most resistant among Polish pneumococci, with the majority being multi-drug resistant.

We suppose that a significant increase of invasive pneumococcal infections associated with pneumococci of serotype 19A, previously rare in our country, is associated with an introduction of epidemic, high-risk clone(s) from other countries. We consider our local conditions (lack of mass vaccination, high antibiotic consumption) as favorable for an additional diversification of 19A clone(s). We also suppose that the particular "success" of 19A clone(s) is due to their specific features, such as multidrug resistance and advantaged growth.

In the proposed project we would like to verify the above hypotheses by performing a detailed molecular analyses, involving whole genome sequencing, and growth ratio comparisons that will allow to explore of 19A pneumococci responsible for invasive infections in Poland, to investigate the relationships of these strains to other pneumococcal clones in Poland and other countries, and to explore antimicrobial resistance and virulence.

The 19A pneumococci epidemiology represents now a real "hot-topic", considering the increasing frequency of this serotype both worldwide and in Poland, its virulence, changeability, multi-drug resistance and the possibility of exchange of virulence and resistance genes with other strains, associated with a natural competence of pneumococci to release and uptake DNA. As discussed above, Polish situation concerning vaccination against pneumococci is complex and specific, so the results of the proposed project likely will bring new, original observations and broaden knowledge of pneumococcal infections, of interest for scientists in the country and abroad, as well as for clinical microbiologists, medical doctors and health policy makers.