Pneumococcal Vaccination: Should We Kill the Enemy or Just Disarm It?

Manel Luján1,2 and Miguel Gallego1,2

1Respiratory Medicine Department, Hospital de Sabadell, Corporació Parc Taulí, Universitat Autònoma de Barcelona, and 2Ciber Enfermedades Respiratorias, Banyoles, Spain

(See the Major Article by Shigayeva et al on pages 139–47.)

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The burden of pneumococcal disease remains a major health problem, especially in the most vulnerable groups. Over the last 3 decades, a range of active immunization measures have been introduced to reduce the incidence in these at-risk populations. Despite these measures, however, a recent study in Europe found the average yearly incidence of invasive pneumococcal disease (IPD) to be 5.2 cases/100,000 inhabitants, with huge variations depending on patients’ age and baseline status [1].

In this of Clinical Infectious Diseases, Shigayeva et al [2] report data from an 18-year population-based surveillance study of IPD, which placed emphasis on the evolution of the disease incidence and serotype variability in immunocompromised hosts. They observed a slightly higher decrease in the incidence rates of IPD in immunocompromised patients over the duration of the study. In the initial phase of the study, the incidence of IPD in this group was >15 times higher than in immunocompetent patients but only 11.5 times higher at a later stage of the study in 2010–2011. During this period, antipneumococcal vaccination programs with polysaccharide 23-valent vaccine and 7-valent conjugated vaccine (PCV7) had been implemented in the area where the study was conducted. In addition, in agreement with other studies [3], an increase in the proportion of nonvaccine serotypes in immunocompromised patients was also documented.

These population immunization programs have had a major effect on the control of IPD because the largest declines have occurred mainly in the serotypes contained in the vaccine, especially in the ones with more immunogenic (conjugate) formulations. Besides the direct effect on the vaccinated population recently demonstrated in the CAPITA study [4], conjugate vaccines have shown an indirect (herd) effect in nonvaccinated populations, leading to a decrease in the incidence of serotype carriage and IPD in adults after pediatric vaccination [5,6]. This decrease in the incidence of IPD has also been accompanied by a proportional increase in serotypes not contained in the vaccine (known as the replacement effect). And last but not least, the introduction of major improvements in the management of certain chronic medical conditions should be considered as a contributing factor in the decrease in the incidence of IPD.

The most illustrative example is human immunodeficiency virus infection after the improvements in antiretroviral therapy, but there have also been important changes in the management of patients with highly prevalent chronic medical conditions, which may have contributed to preserving their immunologic capabili-
Practices (ACIP) for the administration of the 13-valent pneumococcal conjugate vaccine (PCV13). Another population-based study already showed that the presence of certain nonimmunocompromising comorbidities considered outside the group of ACIP indications for vaccine could present an increased risk for IPD, especially if >2 comorbidities converge in the same patient (risk stacking) [8]. In this setting, it would have been interesting to know the risk of IPD in patients with chronic medical conditions that are traditionally considered as nonimmunocompromising (eg, diabetes mellitus, heart disease, lung disease). In all of these entities not only an increase in IPD but also immunologic abnormalities that can explain this susceptibility have been shown: for example, in patients with diabetes mellitus, certain mechanisms of cellular and humoral immune dysregulation attributable to poor metabolic control are known [9].

The final purpose of this risk assessment is the recommendation of proportional preventive measures according to the risk of infection. The current recommendations for PCV13 administration may leave some patients who present a similar or even greater risk for IPD than those included in the ACIP documents (eg, those with multiple nonimmunocompromising disorders) unprotected. In the era of personalized treatments, it might seem paradoxical to recommend the same preventive measures in very high- and relatively low-risk situations. In this setting, Cordonnier et al have recently demonstrated the safety and enhanced immunogenicity of repeated doses of PCV13 in hematologic patients undergoing hematopoietic stem cell transplantation, thus opening up new preventive perspectives for immunocompromised higher-risk patients [10].

The other finding that deserves special attention is the partial emergence of nonvaccine serotypes in this high-risk population. Some results for serotype replacement in certain geographic areas suggest that the maximum benefit of PCV13 might have been achieved 4 years after its introduction [11]. In the coming years, we must ensure that this serotype replacement effect is not accompanied by other collateral effects on nasopharyngeal colonization and, possibly, on the incidence of infection by other microorganisms because increased rates of Haemophilus influenzae and Staphylococcus aureus colonization in PCV7-vaccinated children and their parents have been reported [12]. Hence, epidemiological follow-up of people at risk seems compulsory to monitor the potential side effects associated with changes in the nasopharyngeal flora. An alternative approach for the next generation of vaccines would be the use of formulations directed toward common pneumococcal virulence factors [13]. These formulations have the potential to offer serotype-independent coverage against pneumococcal diseases and may have a lower impact on nasopharyngeal colonization. In other words, in the future, it may be better to disarm the enemy than to kill it.

Note

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