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Job for Mucosally Dynamic Antibodies against Pneumonia

Ruaidhrí Jackson*

Department of Immunobiology, Yale University School of Medicine, USA

Editorial

The Pneumococcal pneumonia is a life-threatening disease with high mortality and morbidity among children under 5 years of age, the elderly and immunocompromised individuals worldwide. Protection against pneumococcal pneumonia relies on successful regulation of colonization in the nasopharynx and a brisk alveolar macrophage-mediated immune response in the lung [1]. Therefore, enhancing pulmonary mucosal immunity (which includes a combination of innate, humoral and cell-mediated immunity) through mucosal vaccination might be the key to prevention of pneumococcal infection. Current challenges include a lack of information in humans on mucosal immunity against pneumococci and a lack of suitable adjuvants for new vaccines. Data from mouse models, however, suggest that mucosal active vaccines will enhance mucosal and systemic immunity for protection against pneumococcal infection [2].

Prevention of pneumococcal pneumonia: current strategies Streptococcus pneumonia (the pneumococcus) is a Gram positive aerobic commensal bacterium which forms part of the normal flora in the nasopharynx . The pneumococcus can evade the immune system through a combination of surface expressed and secreted virulence factors to cause mucosal diseases such as otitis media, sinusitis and pneumonia, as well as systemic diseases such as bacteraemia and meningitis. These diseases, collectively termed pneumococcal disease, can be classified as invasive or non-invasive disease [3]. Otitis media, sinusitis and non-bacteraemia pneumococcal pneumonia are examples of non-invasive disease which are confined to the mucosal surface, whereas bacteraemia pneumonia, bacteraemia and meningitis are examples of invasive disease.

Bacteraemia pneumococcal pneumonia, defined as having pneumonia and a positive blood culture, is more common in HIV-infected patients. Invasive pneumococcal disease is thought to progress from colonisation to bacteraemia, with or without pneumonia, only a minority of cases developing meningitis. Pneumonia accounts for 19% of all under 5 year old deaths worldwide, which makes it the most deadly infectious illness for this age group. The pneumococcus is the leading cause of pneumonia in children and it has been reported to cause over 50% of severe pneumonia cases in Africa. Pneumococcal disease is most prevalent in the young and the elderly, but is also very common among HIV-infected individuals, who are 20–40 times more likely than uninfected adults to suffer from this illness [4]. Pneumococcal pneumonia is treatable using antibiotic therapy. However, where treatment is delayed or unavailable mortality is high. Previously, the developing world had focused on treating pneumococcal disease rather than preventing it, but with the current increase in antibiotic resistance and the HIV pandemic, it is widely accepted that prevention is the key to minimizing the disease burden. Vaccination offers the most efficient and cost-effective method of preventing this disease. However, there are more than 90 pneumococcal serotypes which make development of a vaccine to provide universal protection a big challenge [5].

There are two formulations of pneumococcal vaccines that have been licensed thus far: polysaccharide vaccines (PPVs) and protein conjugate vaccines (PCVs). The 23-valent pneumococcal polysaccharide vaccine, which contains purified capsular polysaccharide antigens from 23 serotypes, offers some protection against invasive pneumococcal disease in adults but is not effective in either children less than 2 yea of age or immune compromised adults. PCVs, which contain purified capsular polysaccharides conjugated to a carrier protein, offer protection against both pneumonia and invasive disease in children and immune compromised adults.

The currently licensed 7- valent conjugate vaccine (containing 7 capsular polysaccharides conjugated to a diphtheria CRM197 protein) is being used as part of childhood immunization programmes in several countries but others are waiting for the licensing of 10-valent and 13-valent vaccines. The disadvantages of PCVs are that they are expensive, have limited serotype coverage, can be associated with an increase in disease caused by serotypes not included in the vaccine and are less effective against radiological pneumonia (20–37% efficacy) than against invasive disease (77–83% efficacy). In African children, PCVs appear to provide no protection to unvaccinated children (herd immunity) and is not very effective against colonization (39% against vaccine serotypes, 0% against all serotypes) [6]. There are several key developments that would result in a breakthrough in the global control of pneumococcal disease. Use of the PCV is an important landmark but the use of conserved proteins in a universal vaccine would allow a single vaccine to be deployed in all geographical regions without regard to the prevalent serotype patterns. In addition, the development of mucosal active vaccines might reduce mucosal disease including pneumonia and otitis media, but this will require the identification of safe and effective mucosal adjuvants for successful vaccine delivery [7]. This review will focus on recent advances in our understanding of mucosal immunity relevant to pneumococcal infection and, in particular, the critical immune responses that must be augmented by new vaccines.

Mucosal immunity against Streptococcus pneumonia Host response against pneumococcal colonization Pneumococcal colonization of the upper respiratory tract precedes infection of the lower respiratory tract, but is normally asymptomatic and not usually followed by disease [8]. The local host immune response plays an important role in regulating the containment of pathogens with in the nasopharyngeal cavity [9]. A brisk local host immune response to S. pneumonia involving phagocytes (neutrophils and macrophages), B cells (antibodies against pneumococcal polysaccharides and proteins) and T cells rapidly eliminates colonization, whereas a poor mucosal immune response results in protracted colonization. Both innate and adaptive immunity play a role in these host defence responses against

***Corresponding author:** Ruaidhrí Jackson, Department of Immunobiology, Yale University School of Medicine, USA, Tel: +1 (143) 476–72910; E-mail: ruaidhri_jackson@hms.harvard.edu

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S. pneumonia. Innate immune response during colonization Innate factors (including C-reactive protein, CRP) play a crucial role in the host defense against colonization with S [10].

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