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Anti-Capsular Polysaccharide Antibody-Mediated Agglutination

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Editorial

Herd immunity has been credited with the efficacy of the pneumococcal conjugate vaccine (PCV) to reduce transmission by preventing colonisation. We demonstrate how mucosal immunoglobulin G (IgG) to capsular Poly Saccharide (CPS) mediates carriage protection in humans, based on findings from a mouse model. We employed a flow kilometric test to measure antibody-mediated agglutination and found that hyper immune sera produced against an encapsulated mutant agglutinated weakly. When compared to agglutinating antisera generated against the encapsulated parent strain, passive vaccination with this antiserum proved unsuccessful in preventing colonisation. Samples were taken from PCV and control-vaccinated people in the human challenge model. IgG levels to CPS in serum and nasal wash were higher in PCV-vaccinated participants (NW). After inoculation, IgG to the injected strain CPS decreased in NW samples, indicating that it was sequestered by colonising pneumococci. Pneumococci were highly agglutinated in post-vaccination NW samples compared to pre-vaccination samples in carriage-protected participants. Our findings suggest that pneumococcal agglutination mediated by CPS-specific antibodies is an important strategy for preventing carriage. Capsules may be the sole vaccine target that can elicit substantial agglutinating antibody responses, resulting in carriage protection and herd immunity production [1].

In the fight against respiratory infections, the human nasal mucosa is the first line of defence. Some bacteria, such as Streptococcus pneumonia (The Pneumococcus), can inhabit the upper respiratory tract asymptomatically (The Carrier State). Although most cases of pneumococcal carriage do not result in disease, the organism may use its niche on the mucosal surfaces of the upper airways to obtain access to normally sterile locations in its human host. As a result, mucosal immune responses are crucial in the defence against pneumococcal infections because they determine the fate of host–pathogen interactions at the mucosa [2].

The production of mucosal antibodies is ineffectual at removing the organism once carriage is established, according to murine studies. Mucosal antibody, if present before stable colonisation, can inhibit acquisition through its agglutinating action, which is independent of Fc, complement, and opsonophagocytosis and is dependent on its multi-valence. The capacity of agglutinating antibody to prevent mucosal colonisation could be explained by more efficient mucociliary clearance of bigger particles and the need for a higher colonising dosage [3]. Because pneumococci enzymatically inactivate the agglutinating activity of human IgA1, the most prevalent type of immunoglobulin on the airway surface, enough mucosal levels of other subclasses, such as immunoglobulin G, are required to prevent colonisation (IgG). The capacity of the pneumococcus to target and escape human-specific components of humeral immunity highlights the need of studying mucosal protection mechanisms in natural hosts [4].

Anti-capsular antibodies inhibit transmission by blocking the acquisition of colonisation, as evidenced by the serotype-specific success of the pneumococcal conjugate vaccine (PCV) in reducing rates of carriage of vaccine-type strains in immunised populations. PCV immunisation causes significant quantities of serum IgG to reach the mucosal surface in vaccinated children, but the exact mechanism by which this vaccine provides mucosal protection is unknown. In an experimental human pneumococcal carriage (EHPC) investigation, we found that PCV reduced carriage acquisition by 78 percent compared to a control group after inoculation of adults with live type 6B pneumococci [5].

Our study provides insight into the mechanisms of mucosal defence against pathogens and how humeral immunity generated through vaccination contributes to protection. We demonstrate that the ability of antibody to block the establishment of colonization in the human host, the first step in pathogenesis of disease caused by S. pneumonia, correlates with its agglutinating activity [6]. Our focus was on IgG because it is generated in high concentrations in response to systemic immunization and has been shown to be sufficient to promote agglutination on the mucosal surface. We have measured both IgA1 and IgA2 in NW samples pre- and post-inoculation with pneumococcus and IgA1 was the dominant IgA subclass in the nasal mucosa (data not shown). Secretory antibodies are unlikely to be sufficient factor in agglutination owing to the activity of pneumococcal IgA1 protease and the moderated increase of S-IgM levels post vaccination [7].

This study required a sensitive method to quantify agglutination. Through use of technology that simultaneously provides images of individual events detected during flow kilometric analysis, we confirmed that flow characteristics were a sensitive and specific measure of the magnitude of antibody-induced agglutination [8]. By comparing hyper immune sera generated to isogenic strains differing only in expression of CPS amount and type, we showed that type-specific antibody to CPS was necessary for agglutination. Data from the EHPC study with parenteral administered PCV confirmed that anti-CPS IgG is protective from colonization and is sufficient to generate mucosal agglutinating activity [9]. This observation provided mechanistic understanding of the effectiveness of CPS-based immunity in reducing rates of mucosal infection and conferring herd immunity in the population. This same mechanism may be applicable to vaccines using the CPSs of other encapsulated pathogens that also impact mucosal colonization. In our study using whole pneumococci, only antibody to CPS was agglutinating. Yet, it remains possible that a sufficient amount of antibody to another pneumococcal target or combination of targets could elicit agglutinating antibody. It also remains possible; however, that CPS is the only pneumococcal target that may elicit agglutination by specific antibodies [10].

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Conflict of Interest

None

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