EDITORIAL

Cellular immunity in pertussis

Considerable advances have been made recently in our understanding of the pathogenesis and the immunological mechanisms involved in the prevention and control of infection by Bordetella pertussis. Traditionally, research on protection has focused on the role of humoral immunity and several reports have shown that passive transfer of antibodies against several putative protective antigens, including pertussis toxin (PT), filamentous haemagglutinin (FHA) and pertactin, can confer a level of protection in mice against intracerebral or respiratory challenge. However, the results of a clinical trial in Sweden, as well as a number of active immunisation experiments in mice and rabbits, have also failed to find a correlation between serum antibody levels to B. pertussis components and protection. While circulating antibodies do play a role, both in toxin neutralisation and in preventing bacterial attachment following transudation into the lungs, evidence is now emerging that cell-mediated immunity may also be required for protection against B. pertussis.

Recent reports have suggested that B. pertussis is not exclusively an extracellular pathogen. It has been shown that B. pertussis can be taken up and survive within mammalian cells including macrophages in vitro. Furthermore, organisms have been found within alveolar macrophages from the lungs of HIV-infected individuals. These findings suggest that cell-mediated immunity would be required to control an intracellular state of B. pertussis, which could escape immune defences mediated by antibody.

The earliest studies on the cellular immune response to B. pertussis described the induction and specificity of proliferative CD4+ T cells in human subjects and mice after immunisation or infection. De Magistris and colleagues demonstrated T-cell responses to PT, FHA and pertactin in adults who had suffered from pertussis in childhood. CD4+ T-cell clones specific for FHA and pertactin were established by re-stimulation following transudation into the lungs, evidence is now emerging that cell-mediated immunity may also be required for protection against B. pertussis.

In recent investigations, undertaken at NIBSC, we have also found that immunisation of mice with a whole-cell pertussis vaccine induces a good Th1 response and moderate antibody levels. In contrast, immunisation with an acellular vaccine comprising PTd FHA and pertactin generated a strong antibody
response and T cells that secreted IL-5, but not IL-2 or IFN-γ; a lymphokine profile characteristic of Th2 cells, which are considered to be the true helper T cells for stimulating antibody response to foreign antigen. The slower bacterial clearance after respiratory challenge of mice immunised with the acellular vaccine, when compared with mice immunised with the whole-cell vaccine or convalescent mice, is considered to reflect the failure of the acellular vaccine to induce B. pertussis-specific Th1 cells. However, the pattern of bacterial clearance in mice immunised with the acellular vaccine is compatible with the role of antibody, stimulated by Th2 cells, in reducing the numbers of organisms in the lungs early in the course of the infection.

In conclusion, the findings from murine models, as well as circumstantial evidence from studies in man, suggest that, while antibody plays a role in preventing colonisation and combating toxin-mediated disease, complete bacterial clearance requires cellular immune responses mediated by Th1 cells. Th1 cells could operate to stimulate the recruitment, phagocytic function and intracellular killing of B. pertussis by macrophages. Th1 cells could also function through their cytotoxic activity against the infected macrophages and thereby allow subsequent destruction of the intracellular reservoirs of the bacteria. Whatever the mechanism, it is now established that T cells are induced by immunisation and infection, and that these T cells play a vital role, not only in regulation of the antibody response, but in direct cell-mediated immunity against B. pertussis.

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References