in the thymus and await experiments that specifically address this issue.

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Pertussis infection and vaccination induces Th1 cells

In the recent *Viewpoint* article, Rook and Stanford[1] suggest that increased incidence of allergies can be explained by decreased exposure to T helper 1 (Th1)-inducing pathogens and increased exposure to Th2-inducing vaccines. Evidence for the former is growing, however the latter, for the most part, hinges on the assertion that current vaccines, and pertussis vaccines in particular, are strong Th2 inducers. This is clearly not the case. Indeed, a considerable body of evidence has demonstrated that whole-cell pertussis vaccines, similar to natural infection with *Bordetella pertussis*, selectively induce Th1-type responses in infants[2,3] and mice[4,5]. Furthermore, the new acellular pertussis vaccines[3], as well as diphtheria and tetanus toxoids (K.H.G. Mills *et al.*, unpublished) induce T cells with a mixed Th1/Th2 cytokine profile in humans.

The article also suggests that the protective effect of most vaccines is largely mediated by neutralizing antibodies, however the contention that 'Th2 responses are adequate' does not follow. This notion has arisen from the simplistic dogma that Th1 cells only mediate cellular immunity and Th2 cells stimulate humoral immunity. However, it is clear that protection generated by killed or attenuated bacterial or viral vaccines is most often mediated by Th1 cells. Th1 cells mediate protective neutralizing antibody responses against poliovirus[6] and influenza virus[7]. Furthermore, we have shown that protective immunity induced with the pertussis whole-cell vaccine requires both humoral and cellular responses and is largely mediated by Th1 cells[5,8,9].

Rook and Stanford claim that *B. pertussis* is a 'powerful Th2-inducing adjuvant' and assert that pertussis vaccination may increase the incidence of Th2 disease. Experimental evidence does not support this view. The adjuvant properties of the whole-cell pertussis vaccine are mediated, in part, by lipopolysaccharide (LPS) and by residual active pertussis toxin (PT)[10,11]. LPS enhances Th1 responses[10], whereas PT enhances both Th1 and Th2 responses[11]. In this situation the Th1 response is dominant, which explains the polarized Th1 response observed with the whole-cell pertussis vaccine. It has been demonstrated that purified native PT can augment interleukin 4 (IL-4) production and IgE responses to co-injected antigens, but it also enhances interferon γ (IFN-γ) production[11]. However, the results obtained from systems where the response to model antigens has been examined should not be confused with the more complex events following pertussis vaccination. Booster immunization with certain acellular pertussis vaccines enhances Th2 responses and IgE specific for *B. pertussis*, but is not associated with enhanced atopic disease[12] or IgE responses to common allergens in children (L. Nilsson *et al.*, unpublished).

The authors claim that depriving the immune system of the early input historically provided by infection may lead to increased allergy. In fact the reverse is true for active infection with *B. pertussis*: allergic sensitization is slightly increased in children with a history of pertussis[12,13]. In this situation it is the infectious 'input' and not input deprivation that is associated with allergy. This cannot be explained by inadequate priming of Th1 activity as convalescent infants develop a Th1 response[2], a result confirmed in murine models of infection[4,5,9]. Whether the immune system has evolved to 'anticipate' appropriate inputs in an appropriate sequence after birth has not yet been resolved. Our opinion is that this would be an inflexible approach to immunity and that it is more likely that each pathogen (and the very large and diverse numbers of commensals that comprise the normal flora) is dealt with according to different criteria, such as physiological niche, toxin production and perhaps even danger.

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