CONCLUSION

Serological assays and epidemiological studies have provided strong evidence that nearly all individuals living in regions of endemicity for LF have been exposed to filarial parasites. Characterizing the nature of antifilarial immunity in EN persons has been complicated by our inability to ascertain the true infection status of MF negative individuals who do not show any clinical symptoms of lymphatic filariasis. These individuals, in fact, represent a heterogeneous group that includes persons truly free of adult worms, individuals with single sex infections and individuals with pre or post patent infections. Many of the earlier studies have used criteria for selection of the study groups, especially EN and ASM, which is not unambiguous. For example, CH individuals, which comprise a heterogeneous group, many a times have been included without grouping them on basis of their MF status. Similarly EN individuals have been selected loosely only on the basis of MF status in finger prick blood.

To characterize immune response associated with the putatively immune state in bancroftian filariasis (that is both MF and CFA free) humoral and cellular response were compared among CFA and MF-negative, CFA-positive and MF-negative and MF-positive individuals, in a study by Dimock et al. (1996). These studies revealed that Th1-like antifilarial immune response predominate in antigen negative persons. The elevated Th1-like response in these individuals is consistent with the hypothesis that these responses contribute to protection in putatively immune individuals.

In the present study, we have used antigens (SDS-PAGE fractionated and NCP-bound) which have been fractionated on the basis of their reactivity with IgG4 antibodies present in the sera of EN and ASM individuals, on 1D and 2D immunoblot.
It is well established that early events in immune response stimulate the production of cytokines that direct the subsequent development of T-helper subsets producing discrete pattern of cytokines. These events are dictated by the nature of antigen that the immune system is exposed to as well as its dose and route of entry. Therefore, we have studied the response of PBMC of EN as well as ASM individuals not only to the total soluble antigens of BmA but also to its different molecular weight fractions which are differentially recognized by IgG4 antibodies present in their sera.

The profile of secretory cytokines against the different antigen fractions showed that the Fr. 4 and Fr.5 of BmA induced a polarized Th1/Th2 cytokine response; EN individuals showed a strong Th1 cytokine response whereas ASM individuals showed strong Th2 response. The Th2 cytokine response by ASM individuals is filarial-antigen specific as these individuals produce comparable quantity of Th1 cytokines like their EN counterparts against H37Rv whole cell lysate (a potent Th1 inducer).

To support our results, we focussed our studies on Fr.5 and analyzed the internal cytokines and their receptor expression profile and also expression of selected cell surface molecules, by flow cytometry. We selected the Fr. 5 antigens, as it is unique in its immunoreactivity (This fraction contains low molecular weight antigens (< 24 kd) which are exclusively recognized by the IgG4 isotype in the ASM individuals' sera.) These results correlate well with our earlier results on secretory cytokines.

The elevated Th1 like responses in our well characterized EN group (selected on the basis of the stringent criteria; MF -ve, CFA-ve, low antigen-specific IgG4 titer and longitudinal follow-up for at least three years) are consistent with the hypothesis that these responses contribute to protection in EN individuals. The Fr.5 antigens are able to induce such a response and therefore, these antigens are of diagnostic importance and merit further
investigation as a immunodiagnostic tool for diagnosing the carrier state among endemic population. Detailed antigenic analysis and characterization of the purified antigens in Fr. 5 may lead to development of immunodiagnostic test that may be cost effective and useful for rapid epidemiological survey for successful mass chemotherapy programmes in endemic countries like India. Study of antigens present in Fr.5 of *Brugia malayi* adult soluble antigens (BmA) may also throw some light about the mechanism of induction of IgG4 response in ASM individuals and its role, if any, in development of carrier state.