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Exposure to hookworms in patients with Crohn's disease: authors' reply

Shale and Travis have raised several important points.[1] Immune responses to hookworm are influenced by a number of factors, the most important of which is continuing presence of the worms. Active hookworm infection is characterised by a mixed Th1/Th2 response with production of both Th1 (IFN-γ, IL-12) and Th2 (IL-4, IL-5) cytokines.[2] When infection is eradicated by chemotherapy, the same individuals exhibit a significant increase in Th1 (IFN-γ) response to hookworm antigens.[2] In our study, only two Crohn's disease patients and five controls had hookworm detected on serial stool examination.[3] Annual mass administration of albendazole to eradicate lymphatic filariasis in endemic areas could have contributed to the control of hookworm. Therefore, we believe that the demonstration of IFN-γ responses to hookworm antigens is entirely consistent with previous exposure to hookworms.

We had *a priori* excluded patients with disease duration longer than 2 years, as well as patients currently receiving steroid treatment; none of our patients ever received infliximab. The IFN-γ response to phytohaemagglutinin was preserved in Crohn's disease patients, making it unlikely that there was a nonspecific suppression of cellular immune response in these patients. A link between BCG vaccination status and helminth infection is not noted in all populations/communities.[4] We did not record vaccination status of participants in this study. The BCG vaccination coverage exceeds 80% of the population in India,[5] and in (unpublished) observations, we have noted BCG scars in equal numbers of healthy controls (66%) and Crohn's disease patients (69%).

Parasite antigens are notoriously cross-reactive across species; nevertheless in our area, hookworm was the most prevalent helminth infection (62%) followed by *Hymenolepis nana* (26%).[6]

Host genes, yet to be identified, play a variable role in predisposition to hookworm infection and burden.[7, 8] It would be interesting to investigate whether these genes are in linkage with genes conferring susceptibility to Crohn's disease.

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