

Correspondence

Looking into the future of *Trichuris suis* therapy

To the Editor:

We were recently intrigued by the findings of a clinical trial using *Trichuris suis* ova as treatment for patients with allergic rhinitis.¹ *T suis* ova are prime candidates for the clinical therapy of allergic and inflammatory diseases in the growing field of helminth immunomodulation, having previously been successfully applied in patients with Crohn disease.² A plethora of epidemiologic and laboratory studies have brought the beneficial effects of helminth infections into focus in recent years. Loss of helminth infections (including *Trichuris trichiura*) through deworming of children living in endemic regions resulted in a consequent increase in skin reactivity to house dust mite allergens.^{3,4} Similarly, we were able to show that helminth infection abrogated clinical symptoms and key immunologic parameters in a murine disease model of airway hyperreactivity.⁵

During the trial performed by Bager et al.,¹ 100 patients presenting with grass pollen-induced allergic rhinitis symptoms received doses of 2,500 live *T suis* ova every 3 weeks. However, no clinical parameters, such as grass-specific IgE levels, were significantly altered. This led to the conclusion that *T suis* ova therapy might not be applicable in human subjects to treat allergic rhinitis or other allergic airway diseases.

However, the trial might have failed to yield positive therapeutic results because of problems with the study design. Although a dose of 2,500 ova every 21 days might be sufficient for therapeutic effects when directly delivered to diseased tissue, such as the colons of patients with Crohn disease, it might be insufficient to effectively alter systemic responses, considering the lack of colonization and rapid clearance of *T suis* ova.

Furthermore, the 96 patients who completed the trial received only 3 doses before the onset of the pollen season. It is currently unknown by which mechanisms *T suis* ova mediate their therapeutic effects or how many repeat exposures are necessary. Moreover, timing of helminth exposure is clearly important because early infections with *T trichiura* in human subjects directly correlated with reduced skin test reactivity to 7 common allergens.⁶ Thus a study in which all patients received a consistent and high number of doses before allergen exposure might prove more efficacious.

One attractive possibility to exploit the therapeutic effects of helminth treatment is to isolate the potent immunomodulatory

components produced by these worms, and we recently reported the striking effects of the filarial worm-derived protein Av17 in suppressing airway hyperresponsiveness in a murine model.⁷ Interestingly, our laboratory now has evidence suggesting excretory/secretory products of *T suis* larvae are also highly effective in preventing the onset of airway hyperreactivity in the mouse. In such a system administration of *T suis* excretory/secretory products before antigenic airway challenge resulted in a complete ablation of clinical symptoms, cell recruitment, and cytokine production (unpublished data).

Thus despite the findings of Bager et al.,¹ there is considerable hope for the future of *T suis* therapy, and the characterization and production of recombinant *T suis* products might be an effective way to bring this tool to the clinic.

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