Therapeutic Colonization With *Trichuris suis*

To the Editor.—In the May 2006 issue, Kradin et al[1] described the histology of live helminths and mucosa from a boy with highly refractory Crohn disease treated with *Trichuris suis* ova. Previous treatment with corticosteroids, cyclosporine, infliximab, methotrexate, thalidomide, azathioprine, and adalimumab had failed. A posttherapy computerized tomographic scan showed thickened terminal ileum and distal colon, and colonoscopy revealed diffuse colonic disease of variable severity, a rectal ulcer, a tight stricture at 25 cm, and a worm in the cecal region.

We would like to address several issues the authors raised.

1. It is highly unlikely that *T suis* causes prolonged colonization of humans. In our studies of *T suis* ova therapy in ulcerative colitis and Crohn disease, we performed colonoscopy in some patients and occasionally saw helminths of variable size and maturity.[2–4] Ova in the stool were never detected despite regular examinations, suggesting that the worms never reached maturity. In patients who had been off ova therapy for several months, including some patients who were taking various immunosuppressants, we never saw eggs in the stool or parasitic forms on colonoscopy. Also, farmers who are frequently exposed to *T suis* by close contact with colonized pigs never develop clinically associated disease or chronic *T suis* colonization. Thus, the authors' suggestion that prolonged parasitic colonization may be a concern is speculation.

2. The authors observed chronic inflammation in the mucosa that did not appear directed toward the helminths. It more likely was caused by active Crohn disease. In our cases, there was no increase in mucosal inflammatory cells, eosinophils, or histiocytes in the vicinity of worms. This is the typical host response to this helminth.

3. Helminths likely induce various immune modulatory effects. The authors noted a marked predominance of $CD4^+$, $CD20^+$, and small numbers of $CD8^+$ lymphocytes. It is known that helminths induce eosinophilia and T_H2 cytokines, and the authors have provided evidence supporting this concept. However, it is unlikely that helminths simply alter the T_H1-T_H2 balance. Recent studies indicate that helminths stimulate the development of regulatory T cells that reduce both T_H1 and T_H2 responsiveness.[5–8]

4. The authors cited an article that reported a case of severe colitis caused by *Campylobacter jejuni* in a patient with trichuriasis.[9] *Campylobacter jejuni* alone causes a severe life-threatening colitis[10] and it is highly speculative whether coinfection with *Trichuris* accentuates such infections. Although the abstract of the article reported *T suis* ova in the stool, the actual text stated that ''microscopy showed *Trichuris trichiura* larvae.'' *Trichuris* larvae are not normally seen in stool specimens, no adult forms were seen on colonoscopy, and improvement occurred prior to treatment with mebendazole. If this Somolian immigrant was colonized, it was almost certainly the result of a helminth other than *T suis.* We suspect this was an error that the authors failed to address.

5. As is often the case with far-advanced disease, none of the recognized therapies was effective, apparently including 5 oral doses of *T suis* ova. We suspect this patient had irreversibly altered intestinal function.

ROBERT W. SUMMERS, MD
DAVID E. ELLIOTT, MD, PhD
Department of Internal Medicine
University of Iowa Carver College of Medicine
Iowa City, IA 52242

JOEL V. WEINSTOCK, MD
Department of Gastroenterology/Hepatology
Tufts-New England Medical Center
Boston, MA 02111

1. Kradin RL, Badizadegan K, Aulich P, Korzenik J, Lauwers GY. Iatrogenic *Trichuris suis* infection in a patient with Crohn disease. *Arch Pathol Lab Med.* 2006;130:718–720.

2. Summers RW, Elliott DE, Qadir K, Urban JF Jr, Thompson R, Weinstock JV. *Trichuris suis* appears to be safe and possibly effective in the treatment of inflammatory bowel disease. *Am J Gastroenterol.* 2003;98:2034–2041.

3. Summers RW, Elliott DE, Urban JF Jr, Thompson RA, Weinstock JV. *Trichuris suis* therapy in Crohn's disease. *Gut.* 2005;54:87–90.

4. Summers RW, Elliott DE, Urban JF Jr, Thompson RA, Weinstock JV. *Trichuris suis* therapy for active ulcerative colitis: a randomized controlled trial. *Gastroenterology.* 2006;128:825–832.

5. Elliott DE, Setiawan T, Metwali A, Blum A, Urban JF Jr, Weinstock JV. *Heligmosomoides polygyrus* inhibits established colitis in IL-10-deficient mice. *Eur J Immunol.* 2004;34:2690–2698.

6. Wilson MS, Taylor MD, Balic A, Finney CA, Lamb JR, Maizels RM. Suppression of allergic airway inflammation by helminth-induced regulatory T cells. *J Exp Med.* 2005;202:1199–1212.

7. Ince MN, Elliott DE, Setiawan T, Blum A, et al. Cutting edge: *Heligmosomoides polygyrus* induces TLR4 on murine mucosal T cells that produce TGFβ after lipopolysaccharide stimulation. *J Immunol.* 2006;176:726–329.

8. Metwali A, Setiawan T, Blum AM, et al. Induction of CD8+ regulatory T cells in the intestine by *Heligmosomoides polygyrus* infection. *Am Physiol Gastrointest Liver Physiol.* 2006;291:G253–G259.

9. Shin JL, Gardiner GW, Deitel W, Kandel G. Does whipworm increase the pathogenicity of *Campylobacter jejuni*? A clinical correlate of an experimental observation. *Can J Gastroenterol.* 2004;118:175–7.

10. Centers for Disease Control and Prevention. Outbreak of *Campylobacter jejuni* infections associated with drinking unpasteurized milk procured through a cow-leasing program—Wisconsin, 2001. *MMWR.* 2002;51:548–549.