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4. **Hsu**, S.J.; Tseng, P.H.; Chen, P.J.: *Trichuris suis* therapy for ulcerative colitis: Non-responsive patients may need anti-helminth therapy (correspondence). – *In:* Gastroenterology, (**2005**), **vol.** **129**, no. (2), pp. 768-769

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Reply. As a busy clinician who sees almost exclusively patients with esophageal disease, I share Dr. Radwin's desire to offer our patients with GERD more and better treatment options. Several points in his letter deserve further consideration.

The comparison that Dr. Radwin makes of efficacy and complication rates between Enteryx and surgical fundoplication is inappropriate. Enteryx is indicated for and has been tested in PPI-responsive patients only. Its performance in those with hiatal hernias of greater than 3 cm is not known. Clearly, many of the patients we send to surgery do not fit these criteria. Comparing outcomes data from surgical anti-reflux trials to Enteryx data is comparing apples to oranges. A randomized study comparing the 2 modalities would be a welcome addition to the literature. Because Enteryx to date has only been compared with no therapy, it is difficult to know where to put it in our current algorithms of care.

I agree with Dr. Radwin that lumping all of the endoscopic anti-reflux devices into one category is not advisable. It is probable that these devices will have different efficacy and side-effect profiles. In including discussion of the Stretta device, the main point was that in both the Enteryx and the Stretta "sham" trials, it is likely that a good proportion of subjects were unblinded as to their group assignments, due to side effects of the therapy. Unblinding is a possible explanation for why subjective measurements of GERD improved in each study while objective measures did not.

Dr. Radwin notes "many tremendous successes" and "infrequent failures" using Enteryx. Given the paucity of literature available on the use of the device, his report of these many cases in a medical journal would be welcome by all of those treating GERD patients. Since almost all existing reports feature less than 100 patients with follow-up of a year or less, Dr. Radwin's claim of "sufficient peer-reviewed data" is not substantiated by the literature.

Dr. Radwin asks, "Has academia with its strict evidence-based process become too onerous to be useful to frontline, practicing gastroenterologists looking for guidance?" Evidence-based medicine is not the province of academics, but rather is the duty of everyone who takes care of patients. In fact, early adopters of a technique such as Enteryx should be the ones clamoring most loudly for rigorous studies of it. After all, these practitioners have staked their patients' health based on short-term follow-up data. If long-term data show unforeseen complications (a situation hardly novel in the medical literature), their patients will pay the price.

With respect to academicians' attempts to incarcerate clinicians by "ball and chain. . .in the dungeon of the ivory tower" of academia: due to rising property values in Chapel Hill, our ivory tower has gone condo, and our dungeon has been remodeled into garden apartments. Therefore, we are no longer able to keep practitioners captive there. I must admit, however, that I have been called worse than an "intractable custodian of the evidence-based ivory tower."

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Trichuris suis Therapy for Ulcerative Colitis: Nonresponsive Patients May Need Anti-Helminth Therapy

Dear Sir:

Summers et al[1] reported in the April 2005 issue their interesting results about a therapeutic effect of ova from one animal parasite, *Trichuris suis*, in ulcerative colitis patients. The authors also found this novel therapy safe by both physical and laboratory examinations. However, a few issues should be addressed before appreciation of this new therapy.

Current trial gave viable ova to ulcerative colitis patients for 12 weeks. The ova could develop into immature or mature helminths that stimulate a particular profile of mucosa immunity beneficial to UC patients. *T. suis*, the porcine whipworm, though is genetically related to *T. trichiura*, usually does not infest and propagate in the human intestinal tracts. It is therefore generally assumed to be not a human pathogen. The rationale of safety of this treatment is quite clear. About 40% of patients in this trial responded to ova therapy, indicated by a significant decrease of UCDAI scores. With this indirect evidence of *T. suis* treatment effects, it might justify the persistence of *T. suis* ova or helminths in the guts of clinically responsive patients. However, there were about 60% of patients did not respond after ingestion of *T. suis* ova. We are concerned about the fate of these *T. suis* ova, which were not therapeutic but could be detrimental, in these patients.

Beer had reported *T. suis* ova recovered from one human experiment still infectious.[2] A recent case report from Canada found a human case with life-threatening colitis associated with *Campylobacter jejuni* and concomitant *T. suis* ova in feces.[3] This indicated a colonization, or even an infection of *T. suis* in human. Admittedly, the possibility is very low but not negligible. Therefore, the authors may have the obligations to reduce the possibility and take active steps to help clear any residual ova or helminths in these patients. For example, the subjects in nonresponsive group should receive anti-helminth agents, such as albendazole or ivermectin, after the completion of trial.[4]

Besides, whether the processing of *T. suis* ova fulfilled Good Laboratory Practice (GLP) was not clearly described in the study. This is also an important point to consider. While making efforts to pursue a novel remedy, physicians always have to put the safety of patients first.

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Reply. We would like to thank Drs. Hsu, Tseng, and Chen for their letter in response to our recent article that described a double-blind trial of *Trichuris suis* ova therapy in ulcerative colitis.[1] We strongly support their recommendation that "physicians always have to put the safety of patients in first place . . . when pursuing a novel remedy." However, we cannot support their suggestion that helminths be eradicated in patients who failed to respond to helminth therapy. Such a suggestion is unfounded and unnecessary.

In support of their suggestion, they raised the issue of a single recently reported human case of colitis that was associated with concurrent *Campylobacter jejuni* and possibly *T. suis* ova in the feces.[2] A Somalian immigrant developed abdominal pain, diarrhea, and renal insufficiency after eating at a local restaurant and was found to have *C. jejuni* in the stool culture. Although the abstract mentions the presence of *T. suis* ova in the stool, the main article mentions only the presence of *T. trichiura* larvae by light microscopy. Thus, that report is unclear and it is unknown whether the patient had *T. suis*, *T. trichiura*, or another organism. It is not possible to distinguish either the larvae or ova of *T. suis* and *T. trichiura* on morphological appearance alone. Neither *T. trichiura* nor *T. suis* release larvae in their host. These helminths release immature eggs that require several weeks of incubation in the soil to mature into a form that contains larvae. Thus, it is impossible to interpret the parasitology findings contained in this case report. *C. jejuni* has the potential to cause serious colitis by itself and it is unnecessary to invoke concern regarding co-colonization with a helminth. A recent outbreak of colitis due to *C. jejuni* was reported in 75 persons who drank unpasteurized milk and 23% developed bloody diarrhea.[3] The suggestion that either *Trichuris* species increases susceptibility to *C. jejuni* remains unproven.

We have treated more than 120 patients with *T. suis* ova for both ulcerative colitis and Crohn's disease.[1,4] Subjects enrolled in a double-blind study were crossed over to the alternative therapy for an additional 12-week period, and in addition, patients who requested to continue the therapy as an open trial were allowed to do so. Our experience represents more than 2000 individual doses of eggs, and some subjects were on treatment for more than 4 years. According to our protocol, stools were routinely examined for the presence of ova and they were found in only 2 instances when the collection was inadvertently made one day after administering the ova therapy. Eradication was entirely unnecessary because *T. suis* is not a human parasite, and it is spontaneously eliminated over a few weeks without drug therapy even in the immunocompromised host. We would have treated our patients with an antihelminthic if there had been any adverse effects attributable to the agent, but there were none. Hundreds of additional patients have now been treated with *T. suis* in Europe without reported incident.

The ova used in our trial were treated with an antiseptic and were negative for bacterial and viral pathogens by culture prior to administering them to the subjects. They were standardized for viability and purity and the preparation of the ova satisfied the standards of our Institutional Review Board. We did not detect any instance of a bacterial infection. We appreciate the comments, but are not convinced that subjects who failed to respond should have been treated with an anti-helminthic agent.

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Liver Transplantation Is a Time-Dependent Prognostic Predictor in Cirrhotic Patients With Esophageal Varices

Dear Sir:

We have read with interest the paper published in a recent issue of GASTROENTEROLOGY.[1] This randomized study compared the treatment efficacy and long-term survival in cirrhotic patients with high-risk esophageal varices undergoing different treatment approaches. The authors concluded that patients undergoing endoscopic banding ligation had a significantly better outcome compared with the propranolol group. Notably, a distinct feature of this study is that 27.4% of 62 patients had undergone liver transplantation some time during the follow-up period. A major concern with such a high transplantation rate is that this could well be the main reason to explain why a statistical difference can be generated with relatively few case numbers in this study.

Since it is not foreseeable which patient will receive a liver transplant at the time of enrollment and the survival data will be censored at the time of transplantation, this important prognostic factor needs