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December 20, 2012

Dear Editor:

I am pleased to submit the revised manuscript "*Clostridium difficile* enteritis: A report of two cases and systematic literature review" for consideration of publication in *The World Journal of Gastrointestinal Surgery*. The edited manuscript is included as a Word document (1098- EDITOR revisions SD 12.6.12).

Title: *Clostridium difficile* enteritis: A report of two cases and systematic literature review

Author: Sean Patrick Dineen, Steven Bailey, Thai Pham, Sergio Huerta

Name of Journal: *World Journal of Gastrointestinal Surgery*

ESPS Manuscript NO: 1098

We appreciate the thought critique given by the reviewer. The manuscript has been improved according to their suggestions:

1. Format has been updated
2. Revisions have been made according to the reviewer

Abstract:

- a. *C. difficile* is not the most common cause of healthcare associated diarrhea (antibiotics are), but the most common cause of healthcare associated infectious diarrhea. The reference number 3 (Loo et al) correctly states this in the first sentence of their article.
- b. This has been corrected in the abstract. The abstract has also been revised to 152 words per the editors request.**

Case 1:

- c. I would report how the enterococcal bacteremia was treated as this could have an impact on the efficacy of the treatment for the *C. difficile* infection.
- d. The patient was treated with i.v. vancomycin and this has been added to the case report.**

Discussion:

- e. See comment for the abstract about the most common cause of healthcare associated infectious diarrhea. This was corrected.**

- f. I think that it is too much of a stretch to say that the NAP1/BI/027 strain may be more capable of causing small bowel infections. This is pure conjecture. **We agree that there is no data to support causality of NAP1/BI/027 and enteritis. However, I think it is reasonable to suggest that more toxinogenic strains are more likely to cause enteritis. I have added a comment to make it explicit that we did not test our patients for the NAP1/BI/027 strain. Additionally, a sentence in a subsequent paragraph (page 6, last paragraph) was potentially misleading regarding NAP1/BI/027 treatment. This sentence was deleted.**
 - g. Toxin assays alone are actually poor diagnostic tools with low sensitivity. Combined testing with GDH/Toxin assay is provides much better sensitivity. **I agree this sentence was misleading and it was removed.**
 - h. I would use Zar et al's article "A comparison of vancomycin and metronidazole for the treatment of Clostridium difficile-associated diarrhea, stratified by disease severity" from Clinical Infectious Diseases instead of reference #46 to support your point. **This reference is, indeed, very useful and was included.**
 - i. There is a discrepancy in your discussion. Here you state that the patient was treated with Flagyl enemas, while in the case description (Case 1) you stated he received vancomycin enemas. **This issue has been clarified.**
 - j. In your cover letter you correctly pointed out one of the weaknesses of your review; namely that the apparent increased incidence of this condition may actually just reflect increased awareness, testing and reporting. This important caveat must be included also in the actual article. **A new paragraph has been included to address this important criticism.**
3. Revisions made in accordance with editor.
- a. The title has been changed to 12 words.
 - b. I lengthened the abstract
 - c. The reference format was corrected within the manuscript. The references were reformatted.
 - d. Table was deleted
 - e. The figures will be sent as editable ppt slides.

Thank you for your consideration.

Respectfully,



Sean Dineen, MD