Letter to the Editor

Response to Villanacci et. al.

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We would like to thank Dr Villanacci and colleagues for their letter, and are pleased that they agree with our conclusion that mucosal healing by both endoscopic and histological healing should be a target for therapy in ulcerative colitis.1 We are of course aware of their paper in this journal, concluding that the combination of basal plasma cells and eosinophils is a good diagnostic indicator for IBD.2 Both elements [basal plasmacytosis and mucosal eosinophilia, albeit not basal], were also found to be valid criteria for predicting relapse, in the paper by Bessissow.3

What are less clear are the criteria for defining basal plasmacytosis. This is invariably more abundant in the left colon than the right, to the point where plasma cells can be found normally in the vicinity of the ileo-caecal valve [ICV], which is a feature that probably applies more in adults than in the children, so may be age related. The corollary of this is that an absence of basal plasmacytosis as an indicator of long-term remission is probably far more meaningful in the left colon than the right, especially in adults. This raises a difficult issue, because if basal plasma cells are normal in the region of the ICV, their presence in this location should not be associated with an increased risk of relapse in ulcerative colitis [UC]. However, we see no contradiction in the presence of basal plasma cells in some patients when initially diagnosed, but not later in relapse.

As we also pointed out, even in the left colon there remains no threshold for the number of basal cells that may be significant in increasing the risk of relapse. Indeed, as we stated, the Geboes system scores the presence of plasma cells as part of chronic inflammation. A grading system for basal plasmacytosis is required to clarify these issues. Villanacci et al. use, as their criterion for basal plasmacytosis, ‘the presence of plasma cells between the base of the crypts and the muscularis mucosae’.2 They quote Tanaka et al as stating ‘the presence of at least three plasma cells around [deep 1/5th of the lamina propia] or below the crypts, alongside or penetrating the muscularis mucosae’, although the actual wording in the Tanaka paper was ‘at least three plasma cells per crypt diameter found below the crypt bases’. This does provide a definition, but it depends only on the uniformity of crypt diameter, and is also an arbitrary figure. The need for an evidence-based definition that is relevant to mucosal healing in IBD therefore remains.

Villanacci et al. state that ‘the presence or absence of neutrophils should be considered the hallmark for the differentiation between the active and the quiescent [resolving] phases of the disease’. This has long been the practice in pathology reporting, despite the fact that there is poor correlation between symptoms and histopathology. We need to be aware that the reading of pathology may be extreme to the point where some pathologists search for [or even dot on the slide] single neutrophils or single crypt abscesses, as if a single neutrophil [or even a crypt abscess] is of proven clinical significance when related to clinical symptoms. Thus the definition of ‘active’ disease also needs to be revisited.

The final point made is that ‘to reach higher interobserver agreement among different pathologists, it is necessary to avoid any form of morphological score in the evaluation of colonic mucosa, because, as widely demonstrated in the review these are extremely complicated and subjective’. Unfortunately we must disagree. Clearly some form of grading system is required, because there must be a difference in significance between a biopsy with an occasional neutrophil and one with myriad crypt abscesses and erosions. Whether it is necessary to use anything other than a semiquantitative system, or objective criteria [eg image analysis and counting] to set the guidelines, remains to be seen. On the other hand, this seems a reasonable way to begin.

Conflict of interest:
The authors have no conflicts of interest.

References