Reviewer's report

Title: Spectrum of Gluten-Related Disorders: Consensus on New Nomenclature and Classification

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Reviewer: Geoffrey Holmes

Reviewer's report:

As the authors point out there has been a tremendous interest in coeliac disease (CD) world wide in the last few years. In addition it has become increasingly clear that CD is only one aspect of the wide spectrum of disorders related to gluten gluten. This paper is a useful review of the spectrum of gluten related disorders in the light of recently obtained experimental data. I have some comments.

Minor essential revisions.

1. Figure 2 requires attention. There is no dark green on this as mentioned in the legend. On page 9 there is mention of the 33-mer having 6 overlapping epitopes. Figure 2 is cited here but it is not clear how this relates to Figure 2. I would exclude this Figure or add more information to make it intelligible

2. Figure 3 requires attention. It looks as though this has been down loaded from Google. What do the boxes A, B and D signify? What is the bottom line of the Figure there for? I suspect these need to be deleted. Otherwise the Figure is informative.

3. Figure 4 is difficult to interpret (see legend and page 19). It might be better to leave this out.

4. What is the evidence that in the West wheat is regarded as an inferior food? I have never come across this notion (page 9)

5. Gluten sensitivity unrelated to CD is not a new diagnosis as the authors claim (see for example the second paragraph of the conclusions section). A paper by Cooper et al - Gluten-sensitive diarrhoea without evidence of celiac disease (Gastroenterology 79:801-806;1980)commented on this over 30 years ago. At this time few believed the concept and the paper got "lost".

6. The authors point out the huge increase in the sale of gluten free products globally and in the USA. This raises the question of how much of this is appropriate and how much unnecessary. Those with a disease for which little can be done are likely to try anything to see if it will confer benefit. Through the years GFDs have been tried in schizophrenia, multiple sclerosis, autism and dementia to name a few. There is no evidence that the diet is effective in any of these. "Allergy" is all the rage and I gather many are on a GFD particular in the USA especially children for no sound medical reasons but because it was recommended by an Allergist. The GFD is expensive and inconvenient and this is bad practice. Food manufacturers are anxious to get their gluten free products
on the market and the claims made for benefit may in some cases be spurious. I wonder whether the authors might add a short section pointing out some of these difficulties so that those with chronic, troublesome symptoms are spared going on an expensive, inconvenient diet which confers no advantage. Clinicians need to be aware of this.

7. The article is well constructed and well written but there are a few errors of expression.

Introduction - end of first paragraph - widely should be wide
Methods - first paragraph - than should be then
Sort out the apostrophes on page 6
On page 10 - beginning of second paragraph - as an initial test for CeD
On page 14 - The deposition is most pronounced
Top of page 15 - why include - once exposed to CNS
On page 16 - second paragraph - claimed should be claim and raised raises
On page 17 - better to say normal rather than negative histopathology
On page 18 - diabetogenic factor
On page 19 - was associated with an increased expression of Toll Like receptors-2 (TLR2) and a significant reduction etc
On page 20 - first paragraph - compared with the placebo
Algorithm incorrectly spelled

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests