

Format for ANSWERING REVIEWERS

June 11, 2014, 2012



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: DietaryHyperoxaluriaWJNR1.doc).

Title: Nephropathy in dietary hyperoxaluria: a potentially preventable acute or chronic kidney disease

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Name of Journal: *World Journal of Nephrology*

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The manuscript has been improved according to the suggestions of the editors and reviewers:

1 The format has been updated. All suggestions of the editors in the edited version of the original submission of this report were complied with. Specifically, the new title of the report has 12 words ([WL1]), postcodes of the addresses of the authors were added ([WL2]-[WL9]), a core tip section was added ([WL10]), the duplicate references were removed and the numbers of the references in the text were corrected ([WL11]). Finally a file of Figure 1 in Chemdraw that allows editing was attached ([WL12]).

2 Revision has been made according to the suggestions of the reviewers. Specific answers to each reviewer comment are presented below:

Reviewer 1:

- a) The sentence "which is a major interest of this journal" was omitted from the Introduction.
- b) The information on SLCs in the gastrointestinal absorption of oxalate subsection was moved and is now in sequence with the paragraph on SLCs in the section on renal excretion of oxalate.
- c) The words "(Sun et al, in preparation)" were removed from the legend of Figure 2. To answer the concern of the reviewer, different sets of figures are prepared for both the imaging and histology of the case report in preparation.
- d) Scale bars were added to Figure 4.

Reviewer 2.

- (a) Separate subsections or sections were created for oxalate homeostasis by the liver, intestine and kidneys (please see also point d)
- (b) A whole section is now devoted to the renal handling of oxalate. The section is moderately enlarged.
- (c) The revised subsection on hepatic synthesis of oxalate is devoted exclusively to this process. This should make understanding of the process clear. Figure 1 is a critical part of this section. The text has a sentence indicating the need to consult this Figure in order to understand oxalate synthesis.
- (d) We believe that the reviewer proposed moving the subsections on each category of diseases directly after the segment discussing the normal physiology of the relevant topic (e.g. discussing primary hyperoxaluria immediately after hepatic synthesis of oxalate). We suggest that such a

rearrangement would not be beneficial for the following two reasons: (I) Understanding of the whole metabolism of oxalate (synthesis, absorption, excretion) is necessary for any discussion on hyperoxaluria regardless of its pathogenesis. (II) Although two of the discussed categories of hyperoxaluria (primary and enteric) result from disturbances of a single physiologic mechanism (hepatic synthesis and gastrointestinal absorption respectively) and could be placed after the discussion of the relevant physiologic processes, the other two categories may result from disturbances in more than one function. As discussed in the text, there is evidence supporting underlying disturbances in synthesis, gastrointestinal absorption and renal tubular secretion of oxalate in idiopathic hyperoxaluria. Also, the source of hyperoxaluria is increased synthesis, not increased absorption of oxalate, in certain conditions that fit the definition of dietary hyperoxaluria (ascorbate intake, ethylene glycol intake, pyridoxilate intake)..

We want to express also our thanks to the editorial staff and both reviewers for their kind and thoughtful reviews. My coauthors and I will be proud to see this manuscript published in the *World Journal of Nephrology*.

Sincerely yours,

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