Format for ANSWERING REVIEWERS

August 25, 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2429-review.doc).

Title: *Urological Manifestations and treatment of the Primary Systemic Vasculitides*

Author: Javeria Peracha, Matthew David Morgan

Name of Journal: *World Journal of Clinical Urology*

ESPS Manuscript NO: 02521413

Reviewer: ***00505788***

This is an extensive review on the urological manifestations of the vasculitides. It is very well written and provides an adequate background of these diseases, necessary for the readers of the journal who mainly, I suppose, belong to the Urologic community. Indeed I have no major comments for improvement of the manuscript. In the Introduction (apparently in page 4), the authors write that medium vessel vasculitides affect arteries and veins. This may be true to some extend only for Kawasaki disease and not for polyarteritis nodosa, which is the major entity of the group. To avoid this likely source of confusion, I would suggest that the authors delete the statements regarding the type of vessels involved by each one of the vasculitis classes at this particular part of the manuscript, something they can do separately at the discussion of each one of these entities later in the text. I would also strongly recommend a substantial.increase in the length of the Introduction section, which is too short compared to the size of the paper. In page 11 (top), the authors mention the FFS score. This score comes from data on both PAN and Churg-Strauss, and it is not very appropriate to be used here for PAN. At the same time I am not sure that this severity score has gained general acceptance. In page 16 (bottom), under Diagnostic Tests, for the appropriate information of their readers, the authors should clarify that c-ANCA correspond to anti-PR3 and p-ANCA to anti-MPO in the clinical setting of vasculitis. Finally, occasional typographical, grammatical and expression errors should be corrected.

Authors' response:

As suggested by the reviewer we have removed the statement in the introduction regarding the sizes of vessels involved in the different vasculitides (page 4).

The reviewer has suggested increasing the length of the introduction but as it is not clear what additional content is proposed to be included and as other reviewers have suggested the introduction is too long we have left it unchanged.

As the reviewer notes the five factor score was derived from clinical data including PAN patients we are not clear why it is considered unsuitable for inclusion here. The authors routinely use the FFS in the assessment of patients with PAN as this was the main determinant of inclusion into the French RCTs in PAN.

As suggested we have included a sentence to make clear to readers that cANCA is usually anti-proteinase 3 and pANCA usually anti-myeloperoxidase (page 17).

Reviewer: ***00739152***

Abstract: 1. please delete the abbreviation of "PSV", it is not popular and dose not mean excellent. 2. It is better to omit all other usual abbreviations from the abstract and if it is needed mention, those in the body of the abstract to minimize the abstract word count. 3. Side effect does not need "hyfen".4. Word count is 311, it is a little long, it is

better to reduce it. Key Words: Key words are acceptable Introduction: 1. In order to refer to type of vasculitis it is not needed to put a table, the reference you cited is enough. Table 1 is better to be deleted. 2. Please delete all the criteria tables and only refer them in the references. 3. Introduction part is too long with details, it is better to summarize it especially in discussion of each disease, and to highlight urological manifestations. 4. Anti-GBM disease (Goodpasture's Syndrome) is not a vasculitis, therefore should not be explained here. 5. Reference numbers are more than needed, please remove excess references. 150 numbers at most are enough. 6. Some references are too old and should be omitted absolutely, such as references: 180,185,160,… 6. There are several typographic errors. It should be edited again. 7. There are some biologic therapies like Rituximab, tocilizumab which have FDA approval for vasculitis treatment, with some concerns about pregnancy under treatment with them, if you can find related articles or refer to it according to text books it makes your article more valuable.

Authors' response:
In the abstract the abbreviation PSV is defined as meaning primary systemic vasculitis/vasculitides (page 2) and not "excellent".
As suggested we have removed the abbreviations from the abstract that are not reused in the abstract and defined them in the main text.
According to the Oxford English Dictionary side-effect should be hyphenated and so we have left this unchanged.
The editorial guidance for the format of a review article is that the abstract should be no fewer than 200 words. As it is currently 214 and words we do not consider that it needs any further shortening.
Table 1 has been replaced.
We have removed the majority of the criteria tables.
As there is disagreement amongst the reviewers as to whether the introduction is too long or too short we have elected to leave it unchanged.
Anti-GBM disease is an antibody mediated vasculitis of renal and alveolar capillaries and is a cause of haematuria and is therefore included in this review.
We are not clear what the basis is for stating that there should be no more than 150 references as the example review provided by the editorial team contains 168 references. Having reviewed our manuscript we have not identified superfluous references that need removing. We are also not clear what the reviewer's criteria are for stating that references are too old. As the purpose of this review is to inform readers of the reported urological manifestations of the systemic vasculitides the case reports cannot become "out of date".
As the management of systemic vasculitis during pregnancy is beyond the scope of this review on the urological manifestations of vasculitis we have not included a discussion of the use of biologic therapies in pregnancy. Toculizumab is not licensed for use in systemic vasculitis. Rituximab is only licensed for use in ANCA associated vasculitides.
We are not aware of the text books on the urological manifestations of vasculitis that the reviewer refers to.

Reviewer: ***00503179***
The purpose of the paper is to review urological manifestations and their treatment in primary systemic vasculitis. This is an interesting aspect among these diseases, although rare. The paper comprises a systematic review of urological complications in vasculitis. The revised Chapel Hill classification from 2012 was used as reference. The urological complications are mentioned, the clinical manifestations clarified and recommendations for treatment given regarding almost all types of vasculitis. The paper is well written, easy to read and gives useful information about the special urological problems in vasculitis. An extensive reference list is included. I think no 1 and 2 in the list refers to the same publication.

Authors' response: We thank the reviewer for pointing out the mistake in referencing and we have corrected this.

Reviewer: ***00143238***
Authors present an overview of the urological manifestations and treatment of the primary systemic vasculitides. Comments: authors should place more emphasis on the urological manifestations and include a table describing them. Same comment regarding treatment, manuscript should benefit if the authors add a table with specific

treatment modalities. In addition, nothing is discussed regarding IgG4-associated vasculitis (Perez Alamino R et al. Curr Rheumatol Rep 2013), which is also associated with urological manifestations.

Authors' response: We agree that a table outlining the urological manifestations of vasculitis is helpful and have included a new table 1.
Unfortunately the detailed management of the individual vasculitides is complex and beyond the scope of this review and so we have not included such a table.
We have not included IgG4-related vasculitis as there is no consensus as to whether this disease entity really exists and if it does whether it is a primary disease or a secondary manifestation of a variety of other diseases as detailed in the review article referred to by the reviewer.

Matthew Morgan