Reviewer's report

Title: Nutritional Therapy and Infectious Diseases: A Two-Edged Sword

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Reviewer: Frank van Haren

Reviewer's report:

General
This paper addresses an important issue: the use and limitations of nutritional therapy in preventing or treating infectious diseases. It looks at this topic from an unusual and interesting perspective, not limiting itself to critically ill or peri-operative patients. It is well written and easy to read. However, there are some major concerns that need to be addressed.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. Background, page 3: It is unclear and not stated anywhere in the article exactly what inclusion and exclusion criteria have been used to identify suitable original articles for this review. Although the paper is not presented as a systematic review or meta-analysis, more information on search strategy and quality of presented studies is warranted to exclude significant author or publication bias. See also 2.
2. The presentation of the data/evidence to support the conclusions is not logical, unbalanced, and somewhat confusing. Two examples (but the raised issue is not restricted to these two examples): Early vs late nutrition (page 10-12) and gastric vs non-gastric enteral feeding (page 12-13). Here it seems that some smaller studies with limited "power of evidence" are presented almost randomly, before moving on to relevant meta-analysis. Why have these studies been chosen (see also 1.)? It would seem more logical to restrict the number of presented studies to the ones with the highest quality or highest level of evidence. One could also suggest to discuss the relevant meta-analyses in more depth and detail and specifically focus at important studies that contradict the conclusions drawn from these meta-analysis.
3. Page 6: ...The organization, Dietitians of Canada recommends......: Recommendations from organizations are probably based on the same evidence as presented, perhaps with additional "expert opinion". As such, this doesn't provide any additional evidence. It should be left out or moved to the end of that section following the conclusion (e.g. This conclusion is in keeping with current recommendations/guidelines).
4. Background: ...It will not review the pharmacological use of vitamins...: Many experts will debate whether nutrition in disease states is nutritional therapy or merely nutritional support. There is not a clear cut-off between those two entities and as a matter of fact, both definitions are probably defendable. However, the title of the manuscript mentions "nutritional therapy", so why exclude higher doses of vitamins while including so-called immunonutrition (page 15)?
5. Background: ...This review will not deal with nutritional interventions in populations which often suffer dietary deficiencies....: This exclusion criterium is a bit artificial and not used consistently. Page 9: ....cohort of 192 malnourished American veterans... etc. Malnutrition is very common in Western society (estimations in hospitalized patients often exceed 50%) and as such is not restricted to developing countries.
6. Pre-operative nutrition: There is good evidence that pre/peri operative enteral nutrition (as opposed to TPN) is beneficial and improves outcome in surgical patients. This should be added to this section including relevant references.
7. TPN versus enteral nutrition Page 13-15): Most experts agree that there are some major issues involved when one compares TPN to enteral: Most older TPN studies used hyperalimentation, this could be a confounding factor accounting for poor outcome rather than the use of TPN itself; current practice of thight glucose control in the ICU (vd Berghe et al) changes the landscape of nutrition completely, implementing this into clinical practice potentially ameliorates the negative effects of TPN, however, this remains to be proven; new developments in TPN such as the lipid composition (e.g. structured lipids) have shown to possess different immunomodulatory properties. These issues need to mentioned in order to provide a more balanced and updtodate view on TPN vs enteral.
7. Page 15: Immunonutrition in critically ill patients has been reviewed in more than 1 meta-analysis.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1. Page 15: ...boosting immunity...: this term is not entirely adequate, suggest to replace with immunomodulation.
2. Title page 3 Prevention of infection in non-hospitalized people: suggest changing it to ..in the general population - or something similar. Reason is that pre-operative enteral nutrition often is achieved in the pre-hospital setting = non-hospitalized.

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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