Reviewer's report

Title: Periodontitis and COPD - Epidemiological or Causal Association

Version: 2 Date: 14 February 2013

Reviewer: David Scott

Reviewer's report:

Thank you for the opportunity to referee the interesting review article by Usher and Stockley et al. The manuscript, entitled “Periodontitis and COPD – Epidemiological or Causal Association” is clearly within the scope of BMC Med.

The review serves a good introduction to the topic, although it is by no means exhaustive.

There are a number of issues that require attention, as follows:

- Major Compulsory Revisions

1. There is no search strategy noted. How did the authors select which literature to include – or exclude - in the review?

2. Please provide the epidemiological evidence of an association between COPD and periodontitis in a table. It seems rather premature to be writing a review of mechanisms that may underlie a phenomenon that has not been established. In other words, please “sell” the concept much more strongly and upfront. “respiratory conditions” do not correlate with COPD. Worse oral health does not correlate with periodontitis, etc (Ref 28, 29). Obviously, some referenced studies are more robust. Please discuss the strength of the epidemiological evidence using language similar to most evidence-based reviews. This reviewer finds it difficult to come to a conclusion on any epidemiological association, as written. What evidence is lacking to allow a more definitive conclusion to be made?

3. The negative studies receive less attention in the text. Please expand.

4. Figure 1. Oxidants and particulates, as well as systemic smoke-derived insults, are key inducers and / or exacerbators of inflammatory periodontal diseases. The Figure implies this is only true for COPD. Also, while there may be similarities in the mechanisms of disease progression in COPD and periodontitis, it is difficult to accept that the processes are “identical”, as claimed.

5. Please define what is meant by “periodontitis”. It is assumed the authors refer to chronic periodontitis rather than aggressive, etc?

6. Please check terminology throughout (periodontitis is a group of diseases/ C-reactive protein induces cytokines but is it a cytokine itself? / interchangeable
use of COPD and emphysema).

7. There are a number of extensive reviews on the role of neutrophils in periodontitis and COPD; and smoke-immune/disease interactions that are not referenced.

8. The authors support the hypothesis that abnormal neutrophil function is associated with COPD and perio. Please discuss the alternate, that normal neutrophils whose prolonged recruitment and activation to and by inflammatory stimuli (e.g. smoke / bacteria) lead to tissue destruction over long periods of time.

9. The authors tell us that “periodontitis” occurs in half of adults. What is the equivalent for (a) COPD and (b) both diseases simultaneously?

10. The Abstract should include a statement on whether the authors conclude that the association is epidemiological or causal.

- Minor Essential Revisions

11. Were the MMP studies discussed controlled for smoking status?

12. It is unclear why the authors argue that socio-economics are not related to periodontitis risk (e.g. Am J Public Health. 2006; 96: 332–339 / Contemp Clin Dent. 2010; 1: 23–26)?

13. The authors tell us that, presumably systemic, cytokine levels are raised in both perio and COPD. Can they provide some data? Are the increases similar in both diseases? Is there any evidence of disease synergy wrt cytokine levels.

14. The importance of bacteria in periodontitis is clearly established. The importance of bacteria in COPD has not and is contentious. The manuscript, however, is attempting to equate the two.


16. Considering that deep periodontal pockets are anoxic or microaerophilic, how important is ROS production likely to be? Are non-oxygen dependent killing mechanisms likely to be more prominent? Please delineate cell and soluble anti-oxidants. Also, discuss smoke and anti-protease inactivation.

17. It is unclear why NETs are discussed (a) in the context of periodontal destruction (rather than bacterial control) without specific evidence of their potentially destructive nature and (b) why they are discussed if there is no evidence of them as common mechanisms in perio and COPD.

Quality of written English: Acceptable
**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