Reviewer's report

Title: The influence of persistent pathogens on circulating levels of inflammatory markers: a cross-sectional analysis from the Multi-Ethnic Study of Atherosclerosis

Version: 1 Date: 4 August 2010

Reviewer: Chih-Hao Wang

Reviewer's report:

Comments from reviewer:

Major comments:

This article examined circulating levels of interleukin-6 (IL-6), C-reactive protein (CRP) and fibrinogen in relation to 5 common “persistent” pathogens: cytomegalovirus, herpes simplex virus-1, Hepatitis A virus, Helicobacter pylori and Chlamydia pneumoniae by using data from the Multi-Ethnic Study of Atherosclerosis. The authors conclude that high antibody response to pathogens was a more consistent predictor of inflammatory outcomes compared to seropositivity alone. High antibody response to multiple pathogens was the “strongest” predictor. The major concern of this reviewer relates to the lack of novelty of the study.

The reviewer is also concerned about:

1) In table 3b, the fully-adjusted model 4 (adjusted for age, gender, race/ethnicity, education level plus BMI, alcohol intake, smoking, diabetes, medications and self-rated health) failed to show high antibody response to multiple pathogens had a positive association with all 3 inflammatory makers of IL6, CRP and fibrinogen by multiple linear regressions. Only in model 1 adjusted by age and gender, we observed an association of high antibody response with 3 inflammatory makers. Therefore, the results might have limited significance and applicability.

2) Still in figure 1 and 2; the trend tests did not adjust for any of the variables (age, gender, race/ethnicity, education level plus BMI, alcohol intake, smoking, diabetes, medications and self-rated health). Both figure simply showed crude trend test without any adjustment. Still the results might restrict its interpretation, significance and applicability.

3) Conclusion “high antibody response to pathogens was a more consistent predictor of inflammatory outcomes compared to seropositivity alone. High antibody response to multiple pathogens was the strongest predictor.” The conclusion might need to be significantly modified.

4) Because of inadequate adjustment in the analysis, the conclusion and discussion need a major revision.

Minor comments:
1) It seems to me that “marker” is a better term than “predictor” due to the cross-sectional study in design.

2) Is it appropriate to define hepatitis A infection as persistent infection?

3) Page 7 line 6 HAV below a standardized calibrated rate should read HAV above

4) Page 11. “When seropositive pathogen burden and high antibody response to multiple pathogens were included in models simultaneously (data not shown), results were similar to those in Table 3b.” This statement is unneeded and could be deleted.

Level of interest: An article of limited interest

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.