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: 18 August 2010

Reviewer: Jorge M Luna

Reviewer's report:

To the authors:

This manuscript details the findings of a cross-sectional analysis of the MESA cohort, specifically assessing the association of the independent predictor “persistent infectious burden” and the dependent variables consisting of continuous biomarker levels of IL6, CRP and fibrinogen. Persistent infection is operationalized as aggregate counts of pathogens with high antibody titer. Linear regression was used to assess the association after adjustment for age, sex, race/ethnicity, education, BMI, current alcohol intake, cigarette smoking, diabetes, medications and self-rated health. For each additional pathogen with high antibody titers, there was a significant 4.4% increase in IL6 levels (95% CI, 0.0 to 8.9). Conclusions point to the importance of distinguishing between heterogeneous antibody responses to pathogens and its relationship to inflammation.

Discretionary Revisions:

- The question of interest is clearly developed and the methods are appropriate to test the hypothesis.
- This is important work and definitely adds to the ongoing discussion of developing an effective and standard measurement for infectious burden. Not all immune responses to chronic pathogen are equal, and using antibody levels to assess pathogen impact is important to understanding the variability of pathogen effects on chronic system inflammation.
- Social economic position (SEP) is a predictor of both infectious disease status and inflammatory biomarker levels. Are there any other measured factors for your cohort that may help adjust for residual confounding by individual SEP? Or any family or community level SEP markers?
- In your analysis, you adjust for non-specific self-rated health status, but you do not make any distinctions recent viral infections (such a common cold or flu) that may impact inflammatory biomarker profiles. Do you think acute infection may influence observed associations?
- The Discussion Section provides a fair and thorough assessment of the manuscript’s limitations.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.