Author's response to reviews

Title: Fungal exposure in homes of patients with sarcoidosis

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Comments to points raised by reviewer Salo.

Major comments

1) This study may not justify any recommendations regarding fungal remediation; no remedial actions were performed in the study. To investigate whether remediation affects exposure levels and health outcomes (sarcoidosis/other outcomes), information on exposure(s) and outcome(s) is needed before and after performing remedial actions. Reword your conclusions (Abstract, p. 2).
   A. We agree in principle although it can always be debated at what level of certainty one should undertake actions directed against a disease. Text has been adjusted

2) N-Acetylhexosaminidases have been shown to be universally distributed among most types of living organisms, both prokaryotic and eukaryotic (Slámová et al., #-N-Acetylhexosaminidase: What's in a name…? Biotechnology Advances 28 (2010) 682–693). There is some evidence that the effects of fungal exposure on respiratory health may be modified by bacterial exposure (Park et al., Fungal and endotoxin measurements in dust associated with respiratory symptoms in a water-damaged office building. Indoor Air 2006;16:192-203). Did the authors assess airborne bacterial exposures? Damp indoor environments are known not only to promote fungal growth, but also to influence bacterial growth (IOM:Damp Indoor Spaces and Health, The National Academies Press, Washington, 2004 ). As mentioned before, fungal exposure may contribute to the development of sarcoidosis, but other agents (e.g., bacteria) have also been considered important in etiology.
   A. The comments on the presence of NAHA in other organisms are well taken.
However, in our previous work (ref 19) we found a very strong relation between 
NAHA and the presence of moulds. As bacteria, particularly Gram-negative 
bacteria, require water for growth, we think that one can conclude that the major 
part of NAHA as measured indoors is due to fungal cell biomass. Another reason 
why we focus on fungi is that fungal cell wall agents such as #-
glucan and chitin 
initiate inflammatory processes that related to the formation of granulomas. 
There is no good evidence of a relation between exposure to bacteria and the 
risk of sarcoidosis. The text has been adjusted.

3) Studies have demonstrated that tobacco smoke contains bacterial (e.g., 
endotoxin, muramic acid) and fungal components (Larsson et al., Identification of 
bacterial and fungal components in tobacco and tobacco smoke. Tobacco 
Induced Diseases 2008;4:4; Sebastian et al., Elevated concentrations of 
dendotoxin in indoor air due to cigarette smoking. J Environ Monit 2006;8:519-22; 
Hasdey et al., Bacterial Endotoxin Is an Active Component of Cigarette Smoke. 
Chest 1999; 115:829–835). Can the authors ascertain that the source(s) of 
airborne NAHAs was other than tobacco smoke? What proportion of the cases 
were smokers? Do NAHA concentrations correlate with smoking status or other 
smoking related variables? Studies have shown that a smoking habit affects the 
morphologic and functional correlations in pulmonary sarcoidosis (Terasaki et al., 
Pulmonary Sarcoidosis: Comparison of Findings of Inspiratory and Expiratory 
High-Resolution CT and Pulmonary Function Tests Between Smokers and 
Nonsmokers.AJR 2005;185:333-38). The authors need to provide additional 
information on smoking.

A. It is well known that smokers are at lower risk for sarcoidosis than 
non-smokers. In the patient material there were very few smokers. The amounts 
of tobacco derived endotoxin and other components in the air in connection with 
smoking are negligible in comparison to the amounts of NAHA found in the 
homes investigated here. In view of the small number of smokers, we feel that an 
extended discussion on the matters raised above is not warranted. Information 
on smokers in the material studied has been added.

4) Because all controls were non-smokers, the control group may not be a 
representative sample of the source population.

A. See comment above.

Minor comments
1) Check the manuscript for typographical errors. For example, replace “ocular 
inspection” with either “visual inspection” or “ocular inspection” (p. 8).

A. OK done