Reviewer's report

Title: Fungal exposure in homes of patients with sarcoidosis

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Reviewer: Päivi Salo

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The authors’ goal was to examine whether fungal exposure in homes was associated with clinically established sarcoidosis in a case-control study in Slovenia. Although the article fits to the scope of the Journal, the manuscript suffers from methodological flaws and part of the sections are not adequately delineated. Furthermore, the manuscript would benefit from improved sentence structures and use of proper grammar. The manuscript presents information that would be of interest, but several issues limit the impact of the paper and reduce enthusiasm.

Major comments

1) The introduction is short and does not review the background adequately. Sarcoidosis is a disease of unknown etiology, but there is increasing evidence that microbial antigens may play a role in the pathogenesis. Although fungal exposure may contribute to the development of sarcoidosis, other agents (e.g., Propionibacterium, Mycobacterium) have also been considered important in etiology (Oswald_Richter and Drake, Semin Respir Crit Care Med 2010:31:375-9). While several epidemiological studies have reported adverse health effects with fungal exposures in indoor environments, the exact inflammatory and immunological processes behind the observed associations between the exposures and health outcomes are still largely unknown.

2) The authors give very little details on the sampling procedures. Readers may not be familiar with N-acetylhexosaminidase assessment method, which was developed to provide more practical method to quantify fungal biomass (ergosterol). For example, methods allowing quantification of mold on building materials are important when evaluating mold damage in buildings and the quality of the remediation efficacy. While concern about indoor mold exposures has increased over the past decades, the complexity of the fungal exposure assessment may not be clear to all readers.

3) It is well known that molds are commonly found in both outdoor and indoor air. Interpretation of possible indoor fungal exposure can be addressed using (1) indoor/outdoor total concentration ratios, (2) comparisons of the species compositions detected indoors and outdoors, and/or (3) the presence of indicator species that are associated with excess moisture problems (e.g. Aspergillus and Penicillium spp.). Did the authors assess fungal biomass concentrations outdoors? It is likely that the results from a sampling conducted at a single point...
in time may not represent exposure throughout the entire year because fungal exposure is prone to temporal, particularly seasonal, and spatial variations (LeBouf et al., J Air Waste Manag Assoc 2008;58:684-92).

4) Indoor exposures are of great importance in relation to many health outcomes because most people spend a large amount of their time indoors, especially at home. The authors do not consider potential confounding by other indoor air pollutants (e.g., emissions from gas/wood stoves, environmental tobacco smoke, pets, dust mites, or other indoor allergens) in their manuscript. Indeed, there is emerging evidence that cigarette smoking is a strong risk factor in the otherwise unknown etiology of chronic diseases. Can the authors think any other factors that could enhance inflammation in the cases? Do the total levels of total IgE suggest presence or absence of allergic inflammation? Furthermore, recent findings suggest that nutritional status may also influence sarcoidosis status (Boots et al., Respir Med 2009; 103:364-72).

5) Controls should be selected from the same population that gives the rise to the cases (Rothman and Greenland, Modern Epidemiology, 1998). Were all cases non-smokers like the controls (p.6)? In the abstract, the number of controls is 290 (p. 2) – however, in the tables the number of controls range from 28 to 30 (Table 1, 2, 3). How many controls were chosen for the study?

6) The presented results are unadjusted – no potential confounders were considered in the analysis. Any comments?

7) Socioeconomic status (SES) is often closely associated with health-related outcomes, and type of housing can influence indoor exposures. Did the authors collect any information on these factors?

8) An expanded discussion is warranted; the discussion in its current form is too short and it is not very well structured. The authors should carefully discuss differences and/or similarities of their findings with respect to previous findings. Furthermore, the authors should emphasize the novelty of their study design.

9) The manuscript would benefit from improved sentence structures and use of proper grammar.

Minor comments

1) The paragraph describing the study subjects should disclose information about consent procedures.

2) Population characteristics are generally presented in the Results section.

3) If the results were highly skewed, why the authors present mean concentrations? For skewed distributions, geometric mean is usually better measure of central tendency.

4) Proofread the manuscript carefully, correct typographical errors (e.g., add “comparable” to the first sentence on page 7 – “The groups were relatively
comparable, although…”

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

**Quality of written English:** Needs some language corrections before being published

**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