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Review article

Endotoxin levels and contribution factors of endotoxins in resident, school, and office environments — A review

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HIGHLIGHTS

- Mean endotoxin loads in settled floor dust were 660–107,000 EU/m^2.
- Mean airborne endotoxin concentrations in indoor air were 0.04–1610 EU/m^3.
- There were several strong determinants for the endotoxin loads.
- The presence of pets was extremely strong determinant for the endotoxin concentration.
- Literature findings concerning several determinants were inconsistent.

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ABSTRACT

As endotoxin exposure has known effects on human health, it is important to know the generally existing levels of endotoxins as well as their contributing factors. This work reviews current knowledge on the endotoxin loads in settled floor dust, concentrations of endotoxins in indoor air, and different environmental factors potentially affecting endotoxin levels. The literature review consists of peer-reviewed manuscripts located using Google and PubMed, with search terms based on individual words and combinations. References from relevant articles have also been searched. Analysis of the data showed that in residential, school, and office environments, the mean endotoxin loads in settled floor dust varied between 660 and 107,000 EU/m^2, 2180 and 48,000 EU/m^2, and 2700 and 12,890 EU/m^2, respectively. Correspondingly, the mean endotoxin concentrations in indoor air varied between 0.04 and 1610 EU/m^3 in residences, and 0.07 and 9.30 EU/m^3 in schools and offices. There is strong scientific evidence indicating that age of houses (or housing unit year category), cleaning, farm or rural living, flooring materials (the presence of carpets), number of occupants, the presence of dogs or cats indoors, and relative humidity affect endotoxin loads in settled floor dust. The presence of pets (especially dogs) was extremely strongly associated with endotoxin concentrations in indoor air. However, as reviewed articles show inconsistency, additional studies on these and other possible predicting factors are needed.

1. Introduction

There is great concern about the potential health hazard of biological components in airborne particulate matter (bioaerosols),

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including endotoxins, in indoor environments. Endotoxin is a biologically active lipopolysaccharide that is a component of the outer membrane of gram-negative bacteria (Duchaine et al., 2001; Rennie et al., 2012; Todar, 2015) and has been shown to cause health responses among occupants. Epidemiologic and toxicologic studies provide evidence associating elevated endotoxin levels with increased asthma severity and bronchial hyperresponsiveness (Rabinovitch et al., 2005; Thorne et al., 2005), and it has been reported recently in a review study (Kanchongkittiphon et al., 2015) that there is sufficient evidence of an association between indoor endotoxin exposure and exacerbation of asthma. Although some studies have suggested a protective role of endotoxin exposure in infancy (Liu, 2002) or at school age (Norbäck et al., 2014), exposure to endotoxins later in life appears to have a detrimental effect in both individuals with asthma and other respiratory conditions and in healthy volunteers (Michel et al., 1996; Gehring et al., 2001; Thorne et al., 2009). Thus, to reduce endotoxin exposure may be important for the control of detrimental effects, and examine the association between indoor characteristics and endotoxin levels is prerequisite in reducing.

Although several studies were carried out worldwide to assess indoor exposure to endotoxins mainly through quantification of endotoxin loads in settled dust samples collected by vacuum cleaners (Noss et al., 2008; Samadi et al., 2010; Frankel et al., 2012b), and a few studies were conducted to measure endotoxin levels in ambient air (Park et al., 2000; Heinrich et al., 2003; Morgenstern et al., 2005; Dales et al., 2006; Wheeler et al., 2011), an overall overview of the data about the loads and concentration of endotoxin in different indoor environments is not available. Duquenne et al. (2013) reviewed examples of the airborne inhalable endotoxin concentration levels measured at the workplace but not in other indoor environments, such as residences. In addition, despite the reported sources and predictors of endotoxin – such as dairy farming, pets, cigarette smoke and dampness (Park et al., 2001a; Bischof et al., 2002; Tavernier et al., 2005; Mazique et al., 2011; Bari et al., 2014) – a systematic summary of the different predictors of endotoxin loads in indoor settled dust and endotoxin concentrations in indoor air is needed. Moreover, there is a need to rank the different predictors in indoor settings in terms of their importance.

With this motivation in mind, the aim of the present review study was (1) to summarize the reported endotoxin loads in settled floor dust (expressed as EU/m^2) and airborne endotoxin concentrations (expressed as EU/m^3) in school, office and residential indoor environments; (2) to summarize the different predictors of endotoxin in settled dust and indoor air; and (3) to rank the predictors of endotoxin in terms of their importance.

2. Material and methods

2.1. Literature search and selection

A PubMed search of the literature published between 1958 and 2016 was performed at http://www.ncbi.nlm.nih.gov/pubmed/ (National Library of Medicine (NLM), a division of the National Library of Medicine (NLM) at the National Institutes of Health (NIH)). Altogether, 52 search terms (See Table S1 in supplementary material (SM)) as well as different combinations of those terms were used. Searches included combinations of at least three terms simultaneously, and the terms endotoxin and indoor air/floor dust were used each time. Original peer-reviewed scientific articles and literature reviews were included in the search. Then, a search was done in the lists of references of relevant articles (based on their title and abstract) that included measurements of endotoxins in settled floor dust (expressed as EU/m^2) and/or in the air (expressed as the EU/m^3) as well as environmental factors affecting the levels of endotoxins. From the lists of references, relevant articles (based on their titles) were chosen for a detailed search. A few often-cited authors (Park, Chen, Gehring, and Thorne) were also added as search terms. Personal contacts with experts in the field were also established in order to collect relevant data. The basic search was performed from April 2013 to February 2014 and updated from September 2015 to July 2016.

A total of 290 abstracts were selected based on the eligibility of their titles, 200 of which were read based on the eligibility of their abstracts. Review of the whole articles was subject to their availability in the electronic databases of Aalto University, QUT (Queensland University of Technology), FIOH (Finnish Institute of Occupational Health) library subscriptions, or as free downloads from the Internet.

In the next step, 122 publications were selected for inclusion in the analysis. Indoor environments in this work include residential, school, and office buildings.

2.2. Relationship between environmental factors and the endotoxin loads in settled dust and the concentrations of airborne endotoxins

The relationship between environmental factors and the endotoxin loads in settled dust and the concentrations of airborne endotoxins were classified into three categories: 1) Extremely strong scientific evidence (several ($\geq$6) empirical studies from peer-reviewed journals and/or several systematic reviews, as reviewed herein); 2) Strong scientific evidence (at least three empirical studies from peer-reviewed journals and/or at least three systematic reviews, as reviewed herein); and 3) Scientific evidence was found (one or two empirical studies from peer-reviewed journals).

3. Results and discussion

3.1. Endotoxin loads in settled surface floor dust in different indoor environments

We found 11 residential studies from 3160 residents (n = 9049), three school studies (n = 95) from 42 school buildings and two office studies (n = 630) from two offices that reported the loads of endotoxins in settled floor dust expressed as EU/m^2. A summary of these studies is presented in Table 1 and detailed information of studies is available in Table S2 in the SM. In all of the selected studies settled floor dust samples were collected by using vacuum cleaners. In all the studies, endotoxins were evaluated with a LAL based bioassay (e.g. kinetic turbidimetric LAL, endpoint chromogenic LAL or kinetic chromogenic LAL) (Chun et al., 2002; Thorne et al., 2009). Other detailed information about the selected studies is presented in Table S2 in the SM.

In a residential settings, the reported average loads of endotoxin in the floor dust collected by vacuum cleaners varied between 660 EU/m^2 (in the Netherlands) and 107,000 EU/m^2 (in Cincinnati and Northern Kentucky, USA) (Douwes et al., 1998; Wouters et al., 2000; Gehring et al., 2002; Wickens et al., 2003b; Thorne et al., 2005; Perzanowski et al., 2006; Gehring et al., 2008; Noss et al., 2008; Thorne et al., 2009; Johansson et al., 2013; Adhikari et al., 2014; Holst et al., 2015a). In a study comparing farming and non-farming households, the endotoxin loads in settled floor dust were higher in farming households (geometric mean [GM]: 28,400–29,900 EU/m^2) than in non-farming households (GM: 11,500–14,460 EU/m^2) (Noss et al., 2008).

In a school environment, mean (GM) endotoxin loads in the settled floor dust collected by vacuum cleaners varied between 2200 and 48,000 EU/m^2 (Foarde and Berry, 2004; Ebbehøj et al., 2005; Salonen et al., 2013; Holst et al., 2015a). The lowest and