

Bio-aerosols as exposure agents in indoor environments in relation to asthma and allergy

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INTRODUCTION

Asthma, asthmatic symptoms and allergic sensitization are linked with a number of indoor exposures, such as VOCs, phthalates, tobacco smoke and biological agents. This paper focuses solely on the biological exposures. Exposures to allergens, microbial agents and other biological particles are risk factors to these health effects, but the exact causal connections or the mechanisms underlying the symptoms are still not well understood. Among the open questions are e.g. the importance of genetic-environmental interactions in the development of allergy, pathophysiological mechanisms of the development of asthma and the role of various exposing agents as causal or adjuvant factors of these diseases.

In general, any foreign protein may be a potentially sensitizing agent but not all agents are equally important as indoor exposures. Agents that have major importance as indoor allergens are listed below. In addition, many other biological molecules, such as lipopolysaccharide (endotoxin) have immunological potential, although they do not sensitize humans via IgE-mediated allergic pathway. The different types of key exposure agents of the indoor environment that may have a role in development of allergy and asthma are listed in the following.

Microbial agents of indoor environments:

- Endotoxin of Gram negative bacteria
- 1,3-beta-glucan of fungi
- Fungal spores and fragments
- Bacterial cells, spores and fragments
- Microbial metabolites, e.g. fungal and bacterial toxins and MVOC

Allergens of the indoor environments:

- House dust mites
- Storage mites
- Cockroaches, rodents, other pests
- Pets: dog, cat, rabbit, mouse, rat
- Fungal allergens

MICROBES IN THE INDOOR ENVIRONMENT

This paper deals with non-infectious microbes, the major groups of which are fungi and bacteria. Fungi contain allergens, and individuals may become sensitized to them. Among the fungal allergens that have been isolated are water-soluble glycoproteins, some of which are enzymes; some of them may also be high-molecular weight carbohydrates (1). Fungi and bacteria also contain other immunologically potential material that may have a role in the development of asthma or its symptoms. The sources from which fungi and bacteria derive may have importance in their health effects. Therefore, a short overview of their major sources is presented in the following.

The main source of fungi in the indoor environment is outdoor air. Outdoor fungi have remarkable diurnal and seasonal variations (2), the concentrations being highest in summer and fall, and lowest during the cold seasons. In climates with snow cover, the wintertime outdoor concentrations of fungi may be very low (3). Indoor concentrations follow in the seasonal fluctuations of outdoor air (4). As for the species profiles, outdoor air mycobiota is well represented in the indoor air but there are also indoor sources of fungi with somewhat different species profiles.

Among the common fungal genera present in indoor air are *Penicillium*, *Aspergillus*, *Cladosporium* and yeasts. The aerodynamic size of fungal spores is usually 2-10 μ m, although much larger spores also exist. Thus, fungal spores are retained relatively well in the filtering systems of the building ventilation, but in buildings with no filtering system, the spores enter indoors freely through open windows and doors. Those spores that enter the indoor environment, settle relatively easily on surfaces. Fungal spores are removed from the indoor environments by cleaning and by exhaust ventilation.

There also are indoor sources for fungi. Several everyday activities actually act as sources of indoor fungi. For example, handling firewood has been shown to elevate the fungal levels remarkably for several hours. Other such normal sources are handling of vegetables, fruit, houseplants and other organic material (5). Fungi are also carried indoors on people's clothing and on dog and cat fur.

All these sources of fungi are regarded as "normal" everyday phenomena. Fungal spores and particles from such normal sources may accumulate into the indoor environment and lead to elevated exposures. For example, settled house dust may contain large amounts of fungi and once the settled dust is resuspended, also fungal material may become airborne. The control of the fungal material from "normal" sources is limited to the filtering of intake air and proper cleaning practices.

For bacteria, humans are important sources in indoor environments. This has been shown using both cultural methods and by measurements of muramic acid, a chemical marker of bacterial biomass, the concentration of which has been shown to follow the number of pupils in a classroom (6). The majority of indoor bacteria are gram positive cocci originating from the human skin, but also Gram negative species are involved. Apart from the infectious agents that are not the topic of this paper, the majority of the skin bacteria belong to the normal human bacterial flora. Apparently, they do not have importance as allergens or agents involved in the development of allergy or asthma.

On the contrary, the present understanding is that exposure to bacteria, especially endotoxin and fungi in early childhood may be protective from allergy and asthma (7).

MICROBIAL EXPOSURES RELATED WITH DAMPNES AND MOISTURE

A quite different source of fungi and bacteria is any moist or wet site where fungal or bacterial spores may germinate and start to grow, or where non-sporing bacteria and yeasts are able to proliferate.

In general, building structures and indoor environments should be dry, without any mechanism that would cause constant or regular wetting of surfaces and structures. However, this is often not the case, and various problems with dampness, moisture and water damage are prevalent in all climates and building types. Such problems are strongly linked with respiratory and other adverse health effects (8, 9, 10). However, the causal agents of the health effects are not yet well understood.

As soon as any material gets wet, microbial growth starts. Microbial spores and cells are present everywhere, and therefore the only factor regulating the microbial growth is availability of water. In general, the microbial types that start their growth on building or finishing materials, originate from outdoor air and other natural sources. However, the substrate on which microbial growth takes place, has a crucial role on the microbial profile that will develop on it. Both the moisture content, availability of nutrients, pH and other characteristics of the material have importance. For example, the species profile that grows on moist wood is different from the species that derive on gypsum board (11).

Among the fungal species that grow typically on moist building materials but are not part of the “normal” microbial content of indoor environments, are *Aspergillus versicolor*, *Aspergillus fumigatus*, *Stachybotrys chartarum*, *Acremonium*, *Aureobasidium*, *Chaetomium*, *Phialophora* and *Trichoderma*. Among the bacteria that contaminate moist building materials are *Streptomyces* and *Mycobacterium*. In fact, it is a whole ecosystem that develops on moist building materials, including not only many species of fungi and bacteria but also protozoa such as amoebae (12). Amoebae may allow the growth of *Chlamydia* and other bacteria that do not proliferate alone in environmental habitats.

The factor that makes the difference between growing microbes and those transported in and out by “normal “ phenomena, is that growing microbes produce additional pollutants into the indoor air. They produce spores and small fragments of microbial material (13), and secondary metabolites that may be either volatile compounds, often with characteristic smell, or non-volatile compounds many of which are characterized as microbial toxins. Fungi and bacteria isolated from houses with moisture problems have shown both cytotoxic and immunotoxic characteristics (14, 15). Thus, having a source of growing microbes in the building structures or indoor environment means quite different exposure situation.

The evidence between dampness and “mold” and risk of allergy and asthma is strong, but the causal links are yet to be documented. A limiting factor in the health studies has been the lack of sensitive enough methods to characterize the microbial exposures. Currently, development of DNA based and other non-cultural methods will provide better tools to profoundly understand the exposures.

Even if the control of microbial exposures may be difficult due to their complex nature, the solution may be the control of their most important determinant, i.e., dampness and moisture. That can be done without numerical guideline values, based on down-to-earth advice and guidance.

INDOOR ALLERGENS

House dust mites are the best known indoor allergens that have a direct link to allergy and asthma. Mites belong to acarids, and the most common species are *Dermatophagoides pteronyssinus*, *D. farinae* and *Euroglyphus maynei*. Also storage mites are important allergens.

Mites live on skin scales and other organic debris and they are strictly dependent on the relative humidity of air. Mites are very common in humid climates and more rare in dry and cold conditions. For example, mite antigens were found in 38% of nearly 800 homes studied in Ohio, USA (16). Mites typically live in mattresses and padded furniture where they can survive long periods of time even if the ambient humidity has decreased. Mites are present in indoor environments wherever the conditions are favourable, i.e., relative humidity >55%.

Dust mite sensitivity is strongly associated with asthma as already reported in the late 1960ies. In some countries the mite sensitization among the asthmatics is so common that other indoor risk factors may not be very important. Control measures have been developed, e.g., mattress covers that would decrease the allergen exposure, but they have not necessarily been successful. In large cities, cockroach debris or rodent urine may be common allergens in house dust (1). The occurrence of these pests is closely related to housing conditions.

Allergen avoidance has long been part of the practice of asthma and allergy medication and health care and associated patient advice and training. Apart from pet allergens that can be avoided by not having pets, it may be beyond the possibilities of indoor air quality regulation to solve the many problems with allergen exposures.

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