

# Viruses as the causative agent related to ‘dampness’ and the missing link between allergen exposure and onset of allergic disease

**Abstract** Asthma and asthma-like symptoms occur more often among people living in humid indoor climates. It has been postulated that the higher concentration of allergens in these environments is the cause for the increase in the number of affected people. However, poor correlations between allergen concentration and symptoms indicate a missing link between allergen exposure and onset of asthma. Respiratory viruses have been identified in up to 85% cases of asthma or exacerbations of asthma. The missing link between respiratory diseases and humid indoor climates could therefore be attributed to viruses. The infectious effectiveness of respiratory viruses depends strongly on the environment where the viruses are spread. For respiratory viruses, survival and infectivity are dependent on temperature and relative humidity. A direct link between virus-induced inflammation and the asthmatic process has been proposed. Therefore, a more effective spreading of viral infections in damp indoor climates is likely to represent the main cause for the increased prevalence of asthma in these environments. Moreover, the incidence of viral infections is higher in patients with asthma compared with that in control subjects. Therefore, a humid indoor climate could also represent a higher risk for persons already sensitized to one or more allergens.

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## Practical Implications

In epidemiological studies where the relationship between moisture in the indoor climate, respiratory symptoms and exposure to allergens is investigated it will be necessary to analyze the role of respiratory viruses in relation to respiratory symptoms. Today, the necessary techniques to address the presence of viruses [e.g. polymerase chain reaction (PCR), antibodies] are highly sensitive. In order to further our understanding of why the frequency of asthma and atopic diseases is still increasing, it is mandatory to implement these methods.

## Introduction

It has been known for many years that a humid indoor climate has a negative impact on health. A wet and clammy building offers optimal conditions for house dust-mites [relative humidity (RH) >40%], while molds grow on cold outer walls, bridges, window frames, etc. Moreover, asthma and asthma-like symptoms occur more often among people resident in humid indoor climates. Unfortunately, the causative agents related to ‘dampness’ and responsible for the onset of disease are still not known.

Recently, two multidisciplinary reviews NORD-DAMP (Bornehag et al., 2001a) (mite-exposure not included) and EUROEXPO (Bornehag et al., 2001b) (mite-exposure included) have been published. In these reviews, the connection between health and ‘dampness’ in buildings has been studied. It was concluded, that dampness in buildings is a risk factor for health effects,

such as cough, wheeze, asthma, general symptoms, and airway infections among atopic and non-atopic people, both in domestic and in public environments.

Concerning exposure to allergens, it has been shown that increased exposure to mite allergens will increase the risk of sensitization and allergic disease. Furthermore, the possible role of microbes/molds as (major) causative agents for dampness-related health effects remains unclear. The prevalence of sensitization to mold allergens is low. This is an indication that the causative agents have not been identified (Bornehag and Sundell, 2002). It is assumed that allergy is developed because of exposure to an allergen. The increase in the risk of allergy depends, to some extent, on the increase in exposure to the allergen. This has been shown in the case of the house dust-mite exposure (Bornehag and Sundell, 2002). But exposure to an allergen is by itself not sufficient to initiate the cascade of events leading to the differentiation of the

T lymphocytes to T-helper 2 lymphocytes (Th2). T cells need a co-stimulatory signal, which is provided through the interaction with cells specialized in antigen capture and successive sensitization (Chung and Adcock, 2000).

Different types of virus [rhinovirus, coronavirus, respiratory syncytial (RS) virus, influenzavirus, para-influenza 1, 2 and 3] have been identified in up to 85% cases of asthma or exacerbations of asthma (Johnston et al., 1995). Two major factors may account for this high rate of viral detection. First, the high sensitivity of polymerase chain reaction (PCR) permits the effective detection of viral DNA. Secondly, viruses are widespread in indoor environments and might be the causal agents of these diseases. How these viruses are involved in the onset of these diseases is probably achieved through mechanisms involved in inflammation (L.-G. Hersoug, unpubl. obs.).

### **Spread of respiratory viruses**

The necessary precondition for virus-induced increase in sickness in environments with high RH is that the spread of the relevant virus also correlates with the actual RH. Different viral particles display great variations in stability and 'survival' outside of the host. These differences are often correlated with the means by which viruses infect new hosts. Viruses that persist in the extracellular environment for considerable periods must be more stable than those that pass quickly from one host to the next (Strauss and Strauss, 2002a). Respiratory viruses are spread when a virus present in the respiratory tract is expelled as aerosols or in mucus. Transmission and infection begins when contaminated air is inhaled or when virus present in mucosal secretions is transferred to mucosal surfaces in the nose, mouth, or eyes. These viruses are often unstable outside of the body and spreading requires close person-to-person contact (Strauss and Strauss, 2002b). Studies on the survival time of RS virus from infected children transmitted to different surfaces, showed that samples from rubber gloves remained infective up to 1.5 h, from cloth and paper tissues up to 30–45 min, and from skin up to 20 min (Hall et al., 1980). The infectivity depends on the environment where the viruses are spread, and the respiratory viruses are especially dependent on temperature and RH. The risk of RS virus infection has indeed been positively correlated to temperature and RH (Chan et al., 1999).

The infectivity of aerosols with rhinovirus-14, which is a common cold-causing virus, has been studied in relation to RH (Karim et al., 1985). Aerosols containing viruses were maintained at 30, 50 and 80% RH at 20°C. Aerosols from 30 and 50% RH regimes lost the infectivity rapidly and after 2 h only 0.25% of the virus survived. At 80% RH, the half-life was 13.7 h and after

24 h nearly 30% survival was observed. Likewise, rhinovirus-14 showed a much better survival at 80% RH than on 30 and 50% on surfaces (Sattar et al., 1987).

On the contrary, a study on the infectivity of coronavirus 229E, another cold-causing virus, showed remarkable difference in survival. For this virus, the half-life was 26.8 h at 30% RH, 67.3 h at 50% RH and only 3 h at 80% RH (Ijaz et al., 1985).

Based on these findings, it may be concluded that the risk of being infected with a rhinovirus or a RS virus will increase on environments with a higher RH. The same applies for coronavirus, at least in the RH range 30–50%.

Overall, these findings suggest that common respiratory infections by viruses are strongly dependent on RH. As proposed previously (Arundel et al., 1986) the importance of RH on the incidence of infection may largely depend on the settling rate of aerosols and the survival of airborne pathogens.

The frequency of the most common viruses in 0–2-year-old children with rhinitis and viral infections in the upper respiratory tract is (approximately 40%) rhinovirus, (approximately 20%) RS virus and (approximately 10%) coronavirus (van Benten et al., 2003).

It has been shown that the incidence of rhinovirus infections is higher in patients with asthma compared with those in control subjects (Minor et al., 1974; Pattemore et al., 1992). In a study, where adult sensitized patients were exposed to both allergens and viral infections, it was shown that asthma patients were more susceptible to respiratory viruses (Green et al., 2002). Therefore, a humid indoor climate could represent a higher risk for persons already sensitized to one or more allergens.

### **Relationship between dampness and indoor RH**

Dampness in buildings is a risk factor for health-related problems, but it is not a concept as well defined as RH. The level of indoor RH mainly depends on the outdoor climate and the impact of ventilation. 'Dampness' includes both humidity in indoor air and moisture in the construction. Therefore, dampness and RH are intimately connected but not always in a simple manner. Different parts of the world have, at least partly, different types of dampness problems. In Scandinavia, visible mold and condensation on walls seem to be rather rare while humidity in the construction with indications such as bad odor is more frequent (Bornehag et al., 2001a). In more humid climates as in, e.g. Taiwan, the frequency of visible mold and condensation on walls is much higher. However, the estimated risk for health effects is in the same range regardless of the prevalence of such dampness indicators (Bornehag et al., 2001a). We spend more than

80% of our lifetime in indoor environments with frequent and close contact with other people. Therefore, a greater risk of acquiring a respiratory virus in the indoor environment exists. Both indoor RH and transmission of respiratory viruses are strongly dependent on outdoor RH. As an example, RS virus has a clear seasonal distribution, which is shown in a study of patients hospitalized with this infection in Hong Kong. Most cases occurred from April to September showing a significant positive correlation with temperature, relative humidity and rainfall (Chan et al., 1999). RS virus is typically seasonal in its incidence and has been responsible for epidemics throughout the world. In the temperate zones of the world, the infections peak during late autumn, winter or spring but not in summer (Kim et al., 1973; Mufson et al., 1973; Winter and Inglis, 1987). In tropical and semitropical countries, infection mainly peaks during the rainy season (Cherian et al., 1990; Spence and Barratt, 1968). Likewise, in tropical and semitropical countries, there is a higher risk of dampness conditions in indoor environments during the rainy season. The spread of RS virus is not only dependent on RH and temperature alone, but also on the timing of the first infections in the season, the number of infected individuals, the number of susceptible individuals and seasonal changes in behaviour. In the temperate zones, the scenario could be as follows: autumn is often the time of the year when the outdoor RH peaks and people begin to spend more time indoors. In early autumn, decreasing outdoor temperature will decrease the indoor RH and likewise the infectivity of the virus, but because of a higher number of infected individuals, the viruses will continue to propagate and could peak in late fall or during the winter or spring depending on the weight of the different parameters. In the temperate zone, autumn, winter and early spring is the period where the risk of 'dampness' peaks because of heavy rainfall and cold outer walls. As a consequence of this, if a RS virus epidemic is initiated in the humid early autumn it could have enough infective 'inertia' to peak even after the humidity in indoor air has decreased. In epidemiological studies where humidity, dampness and respiratory symptoms are recorded, the symptoms appear better correlated with dampness even if humidity is more directly correlated to the initiation of the RS virus epidemic. The mechanisms discussed here for RS virus are contemplated solely for the purpose of illustrating the mechanisms behind the impact of RH

and respiratory virus survival. Similar mechanisms will be applicable for other respiratory viruses with a similar seasonally distribution (rhinovirus, influenza virus, parainfluenza virus) (Monto, 2002).

### Conclusion

Asthma and asthma-like symptoms occur more often among people resident in humid indoor climates. It has been generally accepted that the higher concentration of allergens in these environments was the major cause to the increased frequency. But poor correlation between allergen concentration and symptoms indicate a missing link between allergen exposure and onset of the disease. Respiratory viruses have been identified in up to 85% cases of asthma or exacerbations of asthma. The link between respiratory diseases and humid indoor climates is therefore likely to be viruses. The infectivity of respiratory viruses depends on the environment where the viruses are spread, and the respiratory viruses are especially dependent on temperature and RH. Furthermore, a direct link between virus-induced inflammation and the asthmatic process has been proposed (L.-G. Hersoug unpubl. obs.). Therefore, a more effective spreading of viral infections in damp indoor climates is probably the main cause for the increased sickness in these environments.

Dampness in buildings has been identified as a risk factor for health-related problems. The infectivity of respiratory viruses is better correlated with RH and temperature than with dampness at least in temperate regions. A virological spreading mechanism 'infective inertia' is put forward to explain this apparent discrepancy.

Moreover, the incidence of rhinovirus infection is higher in patients with asthma compared with that in control subjects. Adult, sensitized patients exposed to both allergens and virus infections, showed that asthma patients were more susceptible to respiratory viruses. Therefore, a humid indoor climate could represent a higher risk for persons already sensitized to one or more allergens.

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