Effective mite allergen avoidance in households with asthmatic children : clinical, technical and behavioral aspects

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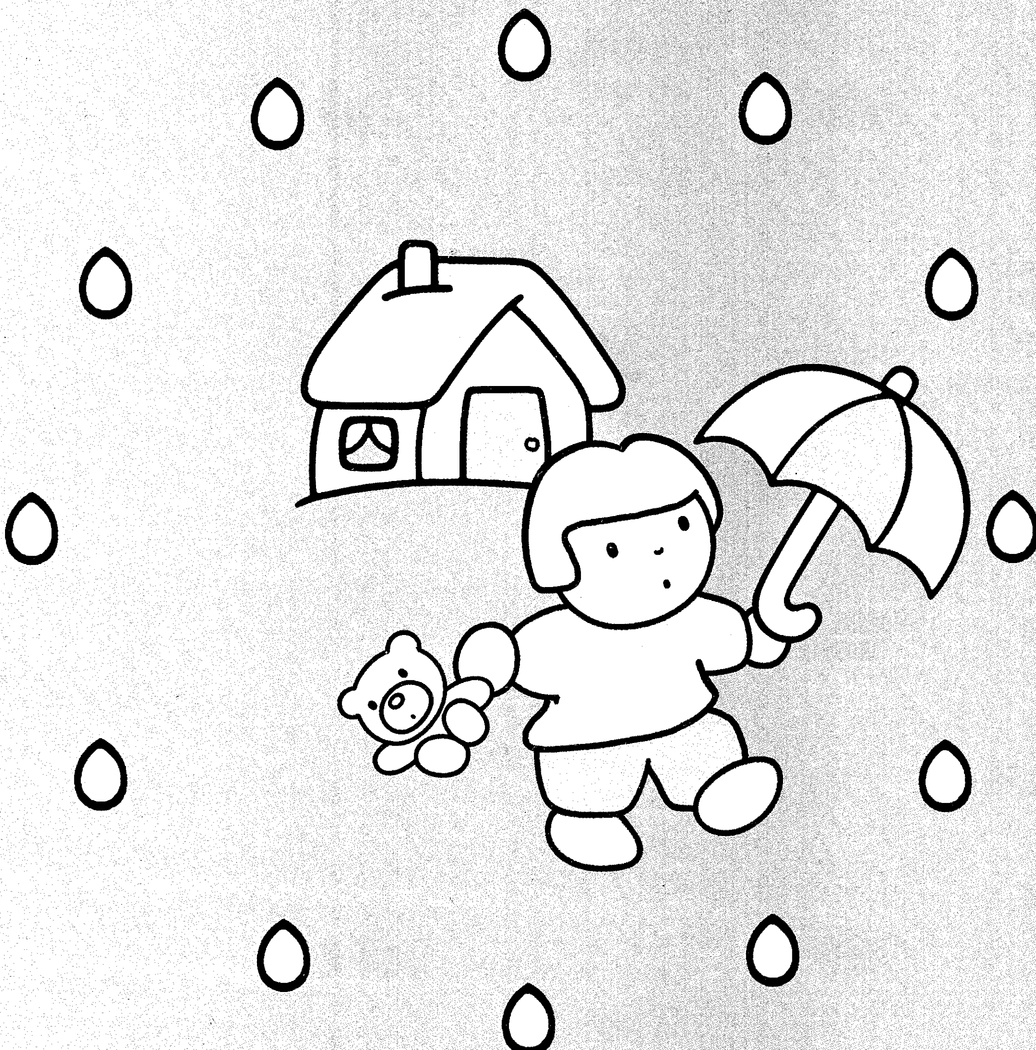

Anneke M.T. van Lynden-van Nes

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Effective mite allergen avoidance in households with asthmatic children

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door

Anneke M.T. van Lynden-van Nes

geboren op 5 juni 1965 te Utrecht

Dit proefschrift is goedgekeurd door de promotoren:

prof.dr. J.E.M.H. van Bronswijk
en
prof.dr. C.A.F.M. Bruijnzeel-Koomen

The work presented in this thesis was performed at the Laboratory for Biological Agents of Biomedical and Health Care Technology, Eindhoven University of Technology (until February 1994: Laboratory for Ectoparasitology and Domestic Hygiene, Faculty of Medicine, Utrecht University), within the frame work of the Interuniversity Task Group 'Home and Health' (1988-1998) of Eindhoven University of Technology and Utrecht University.

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'To laugh often and much;
to win the respect of intelligent people and the affection of children;
to earn the appreciation of honest critics
and to endure the betrayal of false friends;
to appreciate beauty;
to find the best in others;
to leave the world a bit better,
whether by a healthy child, a garden patch or redeemed social condition;
to know even one life has breathed easier because you lived.
This is to have succeeded.'

'Embracing the child', Ralph Waldo Emerson (1803-1882)

Ter nagedachtenis aan mijn vader
Aan mijn moeder
Aan Frans, Lotte en Anne-Fleur

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Niet alleen effectieve allergeen-vermijding duurt een leven lang, ook de ontwikkeling van een mens. Een promotie-onderzoek vormt daarbinnen 'een groeistuip': een intensieve periode waarin gestreden wordt voor inzicht en 'opeens' het licht wordt gezien. Door het multi-disciplinaire onderwerp 'allergeen-vermijding' heb ik met deskundigen uit vele disciplines mogen samenwerken. Door hun voorbeeld en kritiek op cruciale momenten is niet alleen dit 'boekje', maar ook 'de onderzoeker' tot ontwikkeling gekomen. Zonder compleet te kunnen zijn, wil ik daarvoor enkelen met name bedanken.

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Section 1

Introduction

In the last decades prevalence and severity of atopic diseases, such as allergic asthma, allergic rhinitis and atopic dermatitis, have risen in the western world, particularly in childhood and adolescence. In Chapter 1.1 a global overview is given of arthropodal allergens that may be met indoors as well as outdoors. In up to 90% of disease cases in the European Union and North America domestic mite allergens (house dust mites and storage mites) constitute the major sensitizations. Success of mite allergen avoidance programs appears to be limited. Chapter 1.2 discusses the factors that may influence the outcome of these programs and develops the aim of this thesis. Only when mite allergen avoidance procedures are both technically (=sufficient exposure reduction) and clinically effective and feasible in households, can these measures be incorporated into individual therapeutic concepts; otherwise, preventive or health protection schemes need to be incorporated into health education programs and building codes.

1.1 Medical impact of arthropod allergens
A.M.T. van Lynden-van Nes, L.G.H. Koren, M.C.L. Snijders, J.E.M.H. van Bronswijk.

1.2 Factors influencing effectiveness of mite allergen avoidance
A.M.T. van Lynden-van Nes

Chapter 1.1

Medical impact of arthropod allergens

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Abstract

In the European Union and the USA allergens of arthropods comprise a rising health problem. Atopic diseases resulting from insect or mite exposure cost several hundreds of millions euros per European country per year. This article is devoted to major sources of inhalant arthropod allergens, the cause of their rising abundance and resulting morbidity, and possibilities for effective management. For this review, literature was collected from the period 1900 to April 1996 plus two consensus reports published after 1996.

Arthropod allergens are involved in three different atopic diseases: allergic asthma, allergic rhinitis and atopic dermatitis (eczema). About 40% of the human population has a hereditary predisposition to develop atopic allergies. The atopic diseases show a rising trend in both prevalence and severity. Nowadays, 2-27% (Scandinavia) to 60-90% (the Netherlands, United Kingdom) of atopic patients are sensitized to one or more allergens derived from arthropods. In the United States up to 70% of asthmatics have a cockroach allergy.

Major arthropods producing relevant allergens include house dust mites, storage mites and cockroaches. Arthropod allergen exposure indoors has increased due to changes in building construction, household management and facility management.

Pesticides may be used to diminish pest populations producing inhalant allergens, but diminishing medical symptoms or preventing sensitization is only possible when the remaining allergens are removed by cleaning.

The prevention of atopic disease demands avoidance in both the domestic and the occupational domain. Responsibility for the prevention and management of arthropod derived disease in the domestic environment is shared between household and owner of the dwelling. Health professionals have an advising and therapeutic role. In the occupational domain, architect, facility manager, work manager and employee share responsibility for prevention and care.

In the domestic and occupational domains different multi-disciplinary task groups should be formed to solve the problem of arthropod allergens. Pest exterminators have a (public) health task in both domains.

Introduction

The presence of arthropod pests in the urban environment results in a variety of medical problems. These organisms are renowned vectors of bacterial and viral infections, and of food poisoning microbes. Adequate management and efficient use of pesticides have reduced the impact of these diseases[15,65]. In addition, arthropods secrete or excrete allergens provoking two different types of allergic diseases: atopy and insect venom allergy[59,60]. The work presented here will be restricted to inhalant allergens causing atopic disease.

Allergy means 'unusual reacting'. The term is used to describe the reaction to a substance that is generally not harmful, but causes an immune reaction giving rise to symptoms and diseases in some individuals[60]. Such a substance is called an allergen. Allergens originate from different substances: pollen of plants and trees, molds, food, and animal parts and products.

Atopy is a so-called type-I allergy: IgE-mediated and with immediate phenomena[60]. At first contact with an allergen, specific antibodies of the IgE-class against the allergen are produced in blood and tissues. In case of a subsequent exposure these IgE-antibodies have a medical impact within 20-30 minutes after contact. Several hours later, delayed-type reactions may occur in addition.

In the last decades, the prevalence and severity of atopic allergies have risen in both the European Union and the USA[60,68]. Costs of allergic disorders accumulate to several hundreds or even billions of euros per year per European country, due to extensive use of health services and a high incidence of allergy related sick leave[21,57].

In this article we will describe the most relevant sources of arthropod allergens causing atopic disease. We focus on the role of arthropods in the increasing prevalence and severity of allergic diseases. Finally, we will discuss how exposure to arthropod allergens in domestic and occupational environments may be reduced below hygienic thresholds in a multi-disciplinary teamwork of different partners-in-care.

Literature search

Literature was collected with the aid of Index Medicus (1966-April 1996) and the reprint collection (1900-1985) of the Interuniversity Task Group 'Home and Health', Utrecht/Eindhoven, the Netherlands. Two consensus reports published after 1996 were also included[27,69]. References were reviewed that contained the keywords 'allergen' or 'allergy', combined with one of the following: insect, arthropod, mite, house dust, storage, cockroach, locust, silverfish, dust lice, silk worm, midge, chironomid, carpet beetle, occupational, work, laboratory, and environmental.

Atopic diseases

Atopic diseases are allergic asthma, allergic rhinitis and atopic dermatitis. The prevalence of atopic disease in relation to arthropods is considerable (Table 1). About 40% of the human population has a hereditary predisposition to atopy, a so-called atopic constitution[10].

The inherited atopic constitution is polygenic and complex[60]. A child inherits a predisposition for:
1. atopic disease in general;
2. involvement of certain organs; and
3. severity of the symptoms.

A child of parents with severe asthma is therefore at greater risk of developing asthma than a child of parents with mild rhinitis[5,61]. The relevance of arthropod pests in allergy can be understood from the hereditary predisposition of allergic diseases and the allergic sensitization to arthropod products.

Sensitization to allergens and a subsequent development of disease only occurs after prolonged exposure to allergens that may take place by inhalation, by skin contact or by ingestion[21]. In essence, all species of arthropods are candidates for medically relevant allergens. In practice, the length and massiveness of actual individual exposure governs medical importance[68]. Sensitization to a specific allergen is demonstrated using blood tests, skin tests or allergen provocation tests.

The risk of sensitization is increased by exposure early in life[81]. In temperate climates, children born in autumn when dust mite allergens are at peak levels, have a higher risk of sensitization to dust mite allergens than those born in other seasons[60,89]. More than half of sensitized persons will develop an atopic disease[60].

Table 1. Prevalence of atopic diseases in Western Europe and North America[60]

Disease	Prevalence (%)
Allergic asthma	5-10
Allergic rhinitis	10-20
Atopic dermatitis	10-15*

* Cumulative prevalence

Allergic asthma

Allergic asthma is a chronic inflammatory disease of the airways, in which bronchus obstruction occurs as a reaction to a variety of exogenous factors such as allergens, irritants, exercise and viral infections[80]. Of these factors, allergens are considered to play a major role[21]. The prevalence rate of allergic asthma is rising in Western Europe and North America[4,60]. Asthma is nowadays considered to be the most common chronic disease in children in the western world[60].

The prevalence of asthma has two peaks: in childhood and during adult life. Asthma usually becomes evident at the age of 3-5 years, although it can appear at a younger age. During adolescence asthma improves in 50% of cases, particularly if the case is a mild one. In 30% of the patients asthmatic symptoms return during adult life[60]. In women, the second peak occurs before the age of 30, while for men it is seen at the age of 50[60,61].

The severity of asthma has increased in the last decades as demonstrated by hospital admission rates in England, Wales, and the USA[4]. Although asthma death rates remain low (4/100,000/year in the UK and 1/100,000/year in the Netherlands)[18,68], the mortality associated with asthma has risen lately, especially among asthmatic children[40].

In the Netherlands, about 20% of all work absenteeism and more than 20% of school absenteeism is related to asthma[46]. Total economic costs (National Health Services, sickness benefit, research, lost productivity and earnings) of asthma in the Netherlands with 14.5 million inhabitants amounted to 466 million euros in 1985[57]. In the United Kingdom, with 57 million inhabitants, the total economic costs were estimated to be 1345 million euros in 1987[21].

Allergic rhinitis

Allergic rhinitis is also an atopic disease. It consists of inflammation of the nasal mucosa and is characterized by a mucous membrane hyperreactive to allergens and irritants. Rhinitis has been defined as a combination of sneezing, discharge or blockage, lasting $\geq$ 1 hour on most occasions[60].

Allergic rhinitis is mostly diagnosed from the age of 4 or 5 years upward. Prevalence of the disease increases to reach 10-15% in adolescence. Allergic rhinitis is rare in individuals over 65 years of age[54].

The prevalence of allergic rhinitis is increasing[54,60]. Allergic rhinitis appears to be more common in urban than in rural areas. In Denmark the prevalence of allergic rhinitis among patients attending general practitioners was 19% in Copenhagen and 6-14% in surrounding rural areas[66]. In the USA, 75% of allergic rhinitis cases resided inside the city, compared to 25% who lived in the surrounding rural region[7].

Most rhinitis patients have mild to moderate symptoms[60]. In severe cases, the disease can interfere with the patient's daily activities, school or work performance. Although the direct societal costs of rhinitis may not be high, as few patients require hospitalization or extensive use of health services, the economic impact on patients may be considerable, due to loss of earnings attributable to sick leave and reduced productivity, and the financial burden of special avoidance measures. In addition, medication may not be available through national health or personal insurance schemes[54].

Atopic dermatitis

Atopic dermatitis is also called atopic eczema. This inflammatory skin disorder has a chronic, relapsing course. It is characterized by itching, leading to scratching and excoriations[60].

Based on the age of the patient and distribution of the eczema lesions over the skin surface, atopic dermatitis has three stages. In the infantile stage from 2 months to 2 years of age, cheeks and scalp are first affected. During exacerbations, lesions spread to neck, trunk, arms and legs. In the childhood stage, age 4 to 10 years, the eczema is more localized, typically involving the flexural sides of elbows and knees. From the age of 12, the adult stage sets in. In this stage, head and neck are often involved as well. In 90% of the patients the infliction develops within the first 3 years of age. Symptoms usually diminish and disappear in 80% of the cases during adolescence[60].

The cumulative prevalence rate of atopic dermatitis has increased worldwide over the last three decades from 2-3% before 1960 to 10-15% nowadays[60,78].

The total economic costs of atopic dermatitis (including contact dermatitis) in the Netherlands was estimated at 14.5 million euros in 1988[75]. Similar to allergic rhinitis, the direct societal costs of eczema may not be high. In individual cases, however, costs may be considerable.

Allergens and arthropods

Atopic diseases are provoked by allergens. The association between sensitivity to arthropod allergens and atopic diseases is strong. In up to 90% of disease cases arthropods are (partly) responsible (Table 2). A summary of the most common inhalant arthropod species involved in allergic diseases is listed in Table 3. Arthropod allergens that are already purified and named are listed in Table 4.

Exposure to arthropod allergens is more extensive in the domestic than in the occupational environment. There are two reasons: (a) the humidity is generally higher in the domestic environment due to a higher water vapor production (cooking, bathing and washing), giving more insects and mites developmental possibilities, and (b) the exposure period is longer in the domestic environment than in the occupational domain. The exact nature and intensity of additional occupational exposure to arthropod allergens depend on the type of working environment.

In general, indoor exposure to arthropod allergens has increased in the last 20 years due to energy saving campaigns, leading to less ventilation and resulting in improved (more humid) conditions for arthropods[91].

In essence, the office and hospital environment are comparable to the domestic environment, with the exception of a lesser role for house dust mites[41]. Other occupations may call for intensified contact with special arthropods or arthropod products (Table 3).

Domestic environment

We will discuss allergen producing arthropods that may be encountered in abundance in the domestic environment.

Mites

Mites are small arachnids, measuring 0.1-1 mm in length. In the domestic environment, more than a 100 mite species have been found. Most common and abundant are: Pyroglyphidae, Acaridae, Glycyphagidae, predatory mites and Oribatidae[8].

House dust mites are members of the family Pyroglyphidae. They account for more than 90% of the mite population in textiles in dwellings in the European Union and the USA[8,68]. Cosmopolitan species include *Dermatophagoides farinae*, *D. microceras*, *D. pteronyssinus* and *Euroglyphus maynei*. Pyroglyphidae are comparatively small (0.1-0.5 mm in length).

Population growth of pyroglyphids requires protein-rich food, a relative humidity of 50% or more, and indoor temperatures between 10 and 30°C. They survive a temperature range of -28°C for six hours to +60°C for 1 hour[8]. Since human individuals shed 0.5-1.0 gram of mite edible skin scales a person every day[87], mite food is generally not a restrictive factor. The niches of these mites are formed by textile materials such as beds, carpets, upholstered furniture, soft toys, and clothing[68]. However, the potential for mite breeding (and hence the amount of allergen produced) is related to the micro-climate found in a particular home textile[62].

Table 2. Prevalence (in %) of sensitization to arthropod allergens in atopic patients in different areas of Western Europe and North America

	Western Europe				North America
Arthropod allergens of	United Kingdom	Nether-lands	Scandi-navia	Mediterra-nean	
House dust mites	80[76]	60-90[12,13,27]	2-27[50,91]	15-49[16,24]	24-78[44,45]
Storage mites	> 30[23]	65-70[12]	40-45[35,50]	10[24]	12[90]
Cockroaches	<-------------- 10[2,12] ------------->				7-69[32,44]

Sources: Superscripts refer to reference numbers

A seasonal variation in mite numbers and amount of mite allergens exists. In Western Europe maximum levels of living mites are seen in June. Dead mite counts have their peak value in August-September, while highest allergen concentration is reported from August to December. The lowest level of both mite and allergen concentrations are measured between February and May[67,86]. The decrease is due to lower absolute indoor air humidities in the cold winter months[62].

In countries with a moderate climate, such as the United Kingdom and the Netherlands, up to 60-90% of atopic patients are sensitized to mite allergens[12,13,27,76]. In the colder and drier Scandinavian countries house dust mite allergy is less common. In northern Sweden 2% of atopic children appeared to be sensitized to house dust mite, whereas in southern Sweden 12% was sensitized[91].

At least 16 different allergens of house dust mites have been characterized (Table 4). Of these, the so-called Group 1 and Group 2 allergens are the most important: more than 80% of mite-allergic patients have IgE antibodies against these groups[68]. A house dust mite produces 2-4 ng Group 1 allergen and about 1-2 ng Group 2 allergen per day[21].

Allergens of *Dermatophagoides* species are excreted in faecal pellets (10-40 μm in diameter) and in shed skins of mites[8]. These allergenic parts are relatively large and will rapidly fall in undisturbed air[68,70]. However, in time the excrement pellets will crumble and become more easily airborne[8].

In dwellings, storage mites usually belong to the families Acaridae and Glycyphagidae. Typical species in temperate regions include *Acarus siro*, *Glycyphagus domesticus*, *Lepidoglyphus destructor* and *Tyrophagus putrescentiae*[51]. Storage mites feed on fungi. In urban areas they are found in low quantities in home textiles and in higher quantities on fungal ridden wall and ceiling surfaces[51]. They are more desiccation-sensitive than house dust mites and need a continuously humid environment for fast development, with a relative humidity of 70 to 98%[8].

On a global scale exposure rates to both pyroglyphid and storage mites vary according to altitude[19,86], latitude[8,58], and continentality[8,58], all influencing indoor air humidity. Exposure rates to house dust mite products in urban and rural areas are rising in Western Europe and the USA. Energy saving measures in these temperate climate zones have induced a more humid indoor climate, favourable to moulds and mites[91].

In addition, dust reservoirs in domestic, school and office environments became more extensive. This has three causes. First of all, small rugs that could be cleaned by beating have been replaced by wall-to-wall carpeting. These textiles are not cleaned in depth by vacuum cleaning only[22]. Secondly, housekeeping activities have decreased in both popularity and esteem. As a result spring-cleaning has been terminated.

The story of storage mites in Western European dwellings is complicated. Before World War II, allergy due to storage mite exposure was not uncommon in the urban environment[51]. In the sixties, urban dwellings were usually too dry to support extensive population growth. In that time period, exposure to storage mites was an occupational problem (in old and mouldy grain, straw and hay products), seen in rural surroundings only[51].

Table 3. Arthropod species causing atopic disease in domestic and occupational environments

Arthropods Scientific name	Common name	Domestic/ Occupational	Source
INSECTS			
Acheta domesticus (Linnaeus)	House cricket	D/O	1
Alphitobius diaperinus (Panzer)	Lesser mealworm	O	56
Apis mellifera Linnaeus	Honey bee	D/O	42
Blatta orientalis Linnaeus	Oriental cockroach	D/O	56
Blattella asahinai Mizukubo	Asian cockroach	D/O	56
B. germanica (Linnaeus)	German cockroach	D/O	56
Bombyx mori Linnaeus	Silk worm	O	37,56
Chironomus plumosus (Linnaeus)	Chironomid midge	D/O	43
C. thummi (Meigen)	European midge	D/O	56,92
Callosobruchus maculatus Fabricius	Bruchid beetle	O	56
Cladotanytarsus lewisi (Freeman)	'Green nimitti' midge	D	37,42
Cochliomyia hominivorax (=americana) (Coquerel)	Screw worm/American fly	O	42
Daphnia pulex (De Geer)	Water flea	D/O	42
Drosophila melanogaster Meigen	Fruit fly	O	42,56
Ephemera danica Muller	May fly	D	42,56
Ephestia kuehniella (Zeller)	Mediterranean flour moth	O	56
Galleria mellonella (Linnaeus)	Large bee moth	O	56
Lepisma saccharina Linnaeus	Silverfish	D	74
Liposcelis bostrichophilus Badonnel	Dust (book) louse	D	74
Locusta migratoria Linnaeus	Migratory locust	O	14,56

Macronema radiatum Pictet	Caddis fly	D/O	42,56
Musca domestica Linnaeus	Common house fly	D	42,56
Periplaneta americana (Linnaeus)	American cockroach	D/O	56
Psychoda alternata Latreille	Sewer fly	D/O	33,56
Schistocerca gregaria Forskal	Desert locust	O	56
Sitophilus granarius (Linnaeus)	Grain weevil	O	14,56
Tenebrio molitor Linnaeus	Common meal beetle	O	42,56
Trogoderma angustum Solier	Berlin carpet beetle	O	48
Vespula germanica (Fabricius)	German wasp	D	42
V. vulgaris (Linnaeus)	Common wasp	D	42
Zabrotes subfasciatus (Boheman)	Mexican bean weevil	O	14,56
MITES			
Acarus siro Linnaeus	Storage mite (Flour mite)	D/O	8
Blomia tropicalis van Bronswijk, de Cock, Oshima	Storage mite	D/O	8
Carpoglyphus lactis (Linnaeus)	Sugar mite	O	8
Dermatophagoides farinae Hughes	American house dust mite	D/O	8,28
D. microceras Griffiths & Cunnington	House dust mite	D	8
D. pteronyssinus (Trouessart)	European house dust mite	D/O	8,63
Euroglyphus maynei (Cooreman)	House dust mite	D	8
Glycyphagus domesticus (De Geer)	Storage mite (Furniture mite)	D/O	8
Lepidoglyphus destructor (Schrank)	Storage mite	D/O	8
Ornithonyssus sylviarum (Canestrini & Franzago)	Northern fowl mite	O	42
Tyrophagus putrescentiae (Schrank)	Storage mite (Cheese mite)	D/O	8

After the energy crisis (1973), and the resulting increased humidity indoors, mold and storage mite growth on walls and ceilings became more common. Combined with less-intensive house-cleaning procedures exposure to storage mites increased. From the eighties onward storage mite allergy was reintroduced into the urban population[51].

Cockroaches

Most common in Europe is the German cockroach *Blattella germanica*. In the United States the American cockroach *Periplaneta americana* and the oriental cockroach *Blatta orientalis* are abundant[31]. Cockroaches are omnivorous, but prefer sweet, humid and carbohydrate rich food[85].

Table 4. Identified arthropod allergens[47,69]

Allergen	Source
	INSECTS
Bla g 1, g 2, g 4, g 5	*Blattella germanica*
Chi t 1	*Chironomus thummi thummi*
Per a 1, a 3	*Periplaneta americana*
	MITES
Blo t 5	*Blomia tropicalis*
Group 1, 2, 3, 5, 7, 10,	*Dermatophagoides spp.*
Der p 4, 6, 8, 9	*Dermatophagoides pteronyssinus*
Eur m 1	*Euroglyphus maynei*
Lep d 2	*Lepidoglyphus destructor*

Although exposure to cockroach allergens is more common in the USA, exposure to these allergens is also becoming a medical problem in European countries[2]. Cockroaches are found in private dwellings, as well as in public environments with access to food such as restaurants, grocery stores, bakeries, hotels, hospitals, on board ships and on rubbish dumps[85].

Cockroach allergies are especially common in crowded multi-family dwellings in deprived urban areas[31,32,44]. The increasing number of flats equipped with air heating and block heating give cockroaches more shelter and migrating possibilities. These heating systems connect all living units in a flat, creating entrances between dwellings. This also complicates effective treatment with pesticides[85]. The prevalence of sensitization to cockroach in atopic patients is about 10% in Europe and 7-69% in the USA[2,44].

The allergens of cockroaches include specific ones for a single cockroach species as well as shared allergenic components of different taxa[38,82]. Cockroach allergens are found in feces as well as in shed skins and different body parts. The proteins derived from epithelial cells of the intestinal tract and the Malpighian vessels, equivalent in function to kidneys, are assumed to be the most important allergens of cockroach allergy[94].

Silverfish

Silverfish belong to the family Lepismatidae. They measure 3-12 mm, have 3 tail appendages and are covered with shiny scales. The common silverfish *Lepisma saccharina* prefers dark and humid (relative humidity above 75%) places in the home, and may be found in any room or indoor space. They feed primarily on carbohydrates: starched cloth, bookbindings, wallpaper paste, and stored grains[85].

Of atopic patients, 54-69% are sensitive to silverfish[12,73,74]. No specific allergens of silverfish have yet been purified and named. The high figures of sensitivity may be due to cross-reactivity with other allergens[92].

Dust lice

Dust (or book) lice belong to the order Psocoptera. They measure up to 4 mm, and have a white, grey or brown color. Although some species have wings, they are not able to fly. Their jerky way of walking is characteristic[85]. Dust lice avoid light and thrive at relative humidities of 80% or more, and a temperature between 20 °C and 25 °C[85]. They devour molds[85], making them common in modern humid housing[52].

Of atopic patients, 34-63% are sensitive to dust lice[12,73,74]. The effect of cross-reactivity with other allergens needs to be studied.

Occupational environment

Some occupations result in a massive exposure to certain allergens, inducing specific work-related allergies. As high risk occupations we selected the pest exterminator, employees of insect and mite laboratories, farmers and other workers in the food processing industry, workers in the silk industry, and sewage handlers (compiled from Moscato and Dellabianca, 1994[56] and Kagen, 1990[42]).

Pest extermination services

For the pest exterminator working in and around dwellings, cockroaches and carpet beetles are the main target for extermination[85]. The prevalence of allergies against these arthropods in pest exterminators is not mentioned in literature. In atopics in the general population sensitization to carpet beetles amounts to 35%[48].

Insect and mite laboratories

Laboratory workers occupied with breeding or testing arthropods were reported to have a high incidence of atopic disease due to allergens of the grain weevil[30], the larvae of the bee moth[84], locusts[14,29], chironomid midges[43] and cockroaches[83]. See also Table 3.

Farming and food processing industry

In farmhouses storage mites are found more often and in larger numbers than in urban dwellings, due to infested straw, hay and animal feed[34]. However, in the barn area changes in agricultural practice resulting in dryer storage conditions will lead to a diminishing of occupational storage mite exposure[51]. This will eventually affect dairy farmers who are nowadays abundantly allergic to storage mites[35]. Occupation-specific allergic disease among poultry farmers concern house dust mites[28,63] and the northern fowl mite[42], both producing allergen-containing excreta. The latter is a blood sucking parasite of fowl[42].

Not only farmers are exposed to the arthropods living in foodstuffs and fodder, but also shipping workers (asthma due to grain mites and insects[80]), granary workers (itch or asthma due to storage mites[80]), bean sorters (atopic disease caused by the Mexican bean weevil[93]), or employees in the fish food manufacturing industry (atopic disease due to midges[80]).

Silk industry

In the textile industry, silk production and processing result in an extensive exposure to allergens of the silk worm and moth resulting in a high incidence of atopic disease. Sensitization to silkworm-derived allergens is common among silkworkers (prevalence 12-52%)[37].

Sewage handling

Sewage handling plants are attractive to *Psychoda* species, locally known as sewage filter flies or sewer flies. Their numbers may be enormous during warm months (spring until fall). Ordman, 1946[64] and Gold et al, 1985[33] report asthma caused by sewer flies *Psychoda alternata* in sewage plant workers.

Management of arthropod allergens

Effective management of arthropod allergies is required. Since the 1920s, epidemiological studies in western countries have shown increasing prevalence rates of allergic asthma, allergic rhinitis and atopic dermatitis[25,26,60], particularly in childhood and adolescence[4]. In the Netherlands this trend is expected to continue into the next decade[75].

Since a change in genetic factors cannot occur over a few decades, the explanation of the increase in atopic diseases must be sought in environmental factors[60]. The simultaneous increase in exposure to arthropod allergens, in consumption of exotic fruits, and the decrease in infant exposure to infections, indicate a multi-factorial cause, with arthropod allergens playing an important role[20]. Stopping the increase in allergies, as well as preventing new individual sensitizations and the development of allergic complaints, form the justifications for allergen management programs. A significant reduction of arthropod allergens has become a major goal in the management of allergic disease[11]. As has been mentioned before, both the domestic and the occupational environment are relevant[41]. In Chapter 1.2 effective measures and programs will be discussed in more detail.

Hygienic limits

At the base of an effective allergen management program stands the establishment of hygienic exposure limits for sensitization and for the development of allergic symptoms. Until now these threshold levels have been established for mites only. For cockroaches threshold levels have been proposed. Allergen management programs are expected to be effective if allergen concentrations remain below these thresholds. For the allergens produced by other arthropods there are no hygienic thresholds yet. A management program for these species will aim at the maximum reduction technically possible.

Mite allergen exposure is measured in settled dust as mite allergen concentration, number of mite bodies, or guanine concentration[68]. Guanine is the nitrogen excretion product of arachnids and correlates well with mite allergen concentrations in the indoor environment[21,68]. For house dust mites the threshold level for sensitization has been set at 2 µg of Group 1 mite allergens or 0.6 mg guanine per gram settled dust, 100 mites per gram bed dust, or 10 mites per gram floor dust[9,71]. The threshold level for the development of an acute asthma attack in mite-allergic persons is 10 µg of Group 1 mite allergens or 3.0 mg of guanine per gram settled dust, or 500 mites per gram bed dust[71]. The threshold level for sensitization to cockroaches was proposed as 2-8 ng Bla g 2 allergen per gram dust (recalculated after Gelber[32] and Call[17]).

Pest extermination

Removal of pests with or without pesticides forms the heart of a management plan for arthropod allergens. Effective pesticides against mites and cockroaches include benzyl benzoate, chloropyrifos, and synthetic pyrethroids[77,85]. Unwashable objects, such as furniture, can also be treated with pesticides against house dust mites, in combination with moist cleaning, including vacuum cleaning to remove the loosened dirt. Storage mites living on mouldy spots on walls and ceilings can be removed by the application of peroxide-containing products[53]. Pesticides with a high sensitization potency, such as natural pyrethrins, are not acceptable in dwellings of atopic patients[3].

To eliminate house dust mites, washing at 60 °C or higher is most effective[12,21]. The mites will be killed, and with the rinsing water dead mites as well as mite allergens are removed from textiles. Vacuum cleaning does not remove the majority of live mites out of home textiles. House dust mites cling strongly to the fibers of the home textile[21].

Washable textiles that do not tolerate high temperatures can be treated effectively by freezing at -20 °C during one week followed by washing at a low temperature to remove killed mites and active mite allergens. Both treatments should be repeated at a six-weekly interval, in case the indoor climate is appropriate for the proliferation of mites[8].

Reduction of inhalant allergens

Pesticides diminishing arthropod populations are not effective in preventing sensitization, development of disease, or health complaints. The remaining allergens have to be removed, e.g. by thorough wet or moist cleaning, before a clinical effect becomes evident[21].

Washable or cleanable smooth surfaces of floors, walls, ceilings and furniture, avoidance of cracks and crevices, and barrier covers around bed parts prevent the build-up of allergens, at the same time facilitating the required cleaning program[12,21].

Inactivation of arthropod allergens is attempted by application of tannine or tannate formulations to textiles. The effectiveness of this procedure has been studied with RAST-inhibition tests. However, doubts on efficacy in vivo remains, since these preparations also denature enzymes used in the RAST-inhibition test[49].

A management concept for the domestic environment

Various disciplines are involved in avoidance of exposure to arthropod allergens (Figure 1). Unfortunately, feelings of shame are often a hindrance to reporting all infested dwellings for treatment. This decreases the effectiveness of extermination actions, especially in case of cockroach infestation where whole blocks of dwellings should be treated at the same time[85]. Pest extermination personnel are best equipped to inform the public about arthropod pests in an open way, reaching all target groups.

Selective allergen avoidance has a step-by-step procedure with several partners-in-care (Figure 1)[12]. This procedure is used by asthma nurses in the Netherlands as a management tool[11].

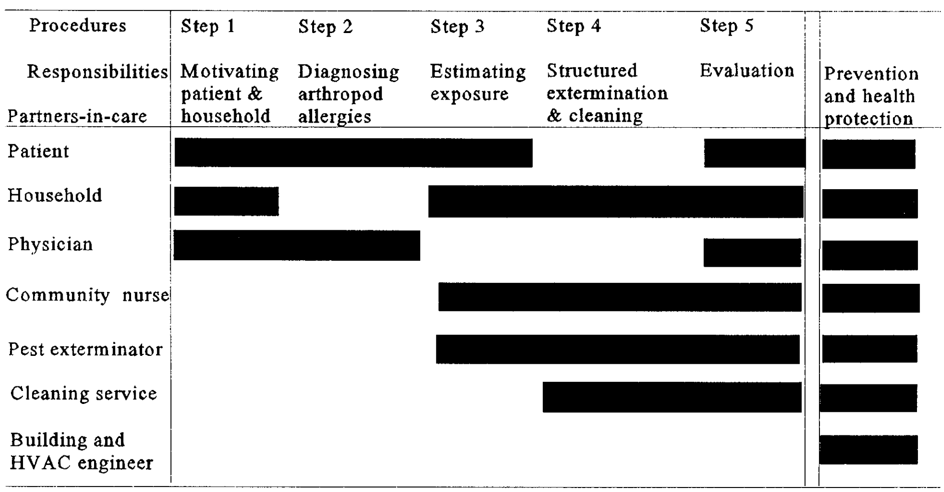

Figure 1. Partners-in-care in arthropod allergen avoidance in the domestic environment and their shared responsibilities. (Adapted from van Bronswijk[11] and van Bronswijk et al.[12])

First, the patient and other members of the household should be motivated by the treating physician through assessment of the degree of health improvement to be expected from an effective avoidance. Disadvantages of avoidance for household members include the effort in time and costs needed. Actual avoidance motivation is a balance between advantages and disadvantages for the household members.

In step 2, physician and patient take responsibility for diagnosing sensitizations and hyperreactivities. In addition to indoor allergens and irritants, food allergens and outdoor allergens (pollen and some insects) are taken into account in the diagnosing process. The physician further prescribes drug treatment, and periodically evaluates the clinical effect of both medication and allergen avoidance procedures (step 5)[11,12].

The third step in arthropod allergen avoidance includes assessment of actual exposure, using a structured interview by a community nurse combined with over-the-counter tests and/or laboratory techniques. In the Netherlands and the United Kingdom the household is supported by a community nurse, not only for exposure assessment, but also in choosing from the different effective measures and in supervising a structured and feasible allergen avoidance program (fourth step)[11,12,39]. Cleaning services can be called in. Successful extermination of allergen producing cockroaches needs the expertise of the pest exterminator.

The frequency of large-scale surface treatment with pesticides or cleaning against allergens can be reduced by taking preventive measures aimed at health protection, pursuing one or more of four goals that influence living conditions of the arthropods concerned: no entrance, no food, no shelter, no appropriate climatic conditions[85].

Relative humidity is the most important restricting factor for mite population growth. It forms a valuable tool in mite allergen avoidance. Human beings need a relative humidity between 30-70% to feel comfortable. When indoor air humidity remains below 50% for several weeks mites will die[6,55]. By combining adequate ventilation and heating with a reduction of water vapor production through household activities, relative indoor air humidity will decrease, making living conditions for mites less favorable. In this way, in temperate regions, the diminished water vapor content indoors will result in a relative humidity below 50% during the cold winter months[62].

For prevention of cockroach infestation it is important to reduce cockroach entry routes to a minimum. Block heating and hot air heating are important access routes. Cooperation of pest exterminator and HVAC (Heating, Ventilating and Air-Conditioning) engineer, will result in structural improvements[79].

At half-yearly intervals household members or the community nurse should check to confirm that exposure levels remain below hygienic thresholds (fifth step). If this is not the case, the avoidance program should be repeated[11].

Public buildings should be suitable for most possible users[36]. Here, management of arthropod allergens is mainly of a global preventive nature. This is in contrast with the situation in the private, domestic domain that is only meant for family and friends.

Management in the occupational environment

To prevent allergic manifestations due to work, different partners-in-care are called for. Fundamentally, five partners are responsible for the well-being of the employee at work: architect and building engineer, facility manager, manager of the organization, the medical services of the organization, and the employee himself[72].

The individual worker is responsible for his own, private health[36]. We may expect from him that he reports to the medical services of the organization and his superior, any allergies or health complaints experienced. The manager of the organization takes responsibility for all working procedures and the assessment of health damage that could be evoked through these procedures[36]. The medical service of the organization should - when possible - remove the worker from harmful exposure. When the worker has to stay in the same working environment, the industrial hygienist should supply information on the use of protective devices to minimize exposure, e.g. dust masks or respirators[72].

Facility managers coordinate all efforts relating to planning, design and management of buildings, including systems, equipment and furniture[88]. Their duties encompass setting health standards and contracting pest exterminators and cleaning services to attain these standards.

Architect and building engineer may, by design and materialization of the building, take precautions to prevent access by pests, and to make the building easily cleanable, while securing adequate ventilation capacity to keep the indoor air dry and clean.

Conclusions

In the past, medical impact of arthropods was mainly associated with vector status for infectious micro-organisms and microbes causing infectious diseases and food poisoning. But nowadays in Western Europe and North America, produced allergens have a greater impact on (public) health. Increased exposure to arthropods plays a role in the rising prevalence of atopic diseases in the European Union and the USA.

House dust mites, storage mites and cockroaches are the main arthropods relevant to allergic disease. Other pests in the domestic and occupational environment, and species reared in biological laboratories are of lesser public health importance. Energy saving programs, changed cleaning regimens, block and air heating systems have created more favorable living conditions for allergenic arthropods and increased allergen exposure of man.

In prevention and treatment of arthropod allergies, reduction of exposure to below hygienic thresholds plays a role of increasing importance. It can best be performed by multi-disciplinary teamwork between patient, household members and professionals of various disciplines. Assessment of threshold levels for arthropods other than mites and cockroaches will be helpful.

In the domestic domain a structured cooperation of pest exterminator, patient, other household members, cleaning services, building engineers, medical doctors and the community nurse is needed to tackle daily health problems. In the occupational environment the architect of the premises, the facility manager and the manager of the organization should work together to protect health by preventing sensitization and disease due to 'occupational' arthropods.

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Chapter 1.2

Factors influencing effectiveness of mite allergen avoidance

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Introduction

Mite allergen avoidance is a part of the prevention and treatment of atopic diseases such as allergic asthma, allergic rhinitis and atopic dermatitis. In Europe and North America up to 90% of atopic patients are allergic to mites (Chapter 1.1). Since people spend a considerable part of the day at home, mite allergen avoidance in the domestic environment seems a practical option.

There are numerous reports in scientific and clinical literature on effective avoidance measures (Table 1). On the other hand, when these measures are incorporated into programs, some controlled home studies show little clinical benefit[26,46,63], while others are strikingly effective[25,39,40,58,59,62,67,68,81,93,141,148,159]. Success of mite allergen avoidance seems 'erratic', resulting in conflicting views held by allergists as to the incorporation of mite allergen avoidance in the therapeutic plan of atopic patients.

To be able to discuss effectiveness of measures and programs we should first have a clear definition. An effective allergen avoidance program has been defined as a set of measures to reduce exposure to relevant allergens or irritants (technically effective), leading to a reduction of clinical symptoms (clinically effective)[20]. The feasibility to perform such a program is not included in this definition.

In practice, clinical effect is influenced by three factors: technical effectiveness, clinical effectiveness and feasibility. *Technically effective measures* are able to reduce relevant allergen exposure both to below sensitization threshold and more than 10-fold. The *technical effectiveness of a program* is determined by the total exposure reduction of allergens and irritants. *Clinical effectiveness* is demonstrated when clinical symptoms or another clinical parameter improves significantly compared to a control group as a result of an estimated exposure reduction. Since allergies are chronic diseases and the predisposition to develop an allergy is hereditary, allergen avoidance should be suitable to be performed life-long (*behaviorally effective*).

In this chapter the influence of different factors on a clinical effect are discussed and the aim of this thesis is developed.

Technical effectiveness of mite allergen avoidance measures

Avoidance measures are technically effective if they are able to diminish mite (allergen) concentrations both to below threshold levels for sensitization[16,123] and more than 10-fold[122]. Threshold levels are set at 2 μg group 1 allergen and 0.6 mg guanine per gram dust, and at 100 mites per gram mattress and upholstery dust and 10 mites per gram floor dust[17,123]. For mite densities a threshold level of 24 mites per m^2 has been used[157].

Technically effective measures are based on:
1. Deterioration of living conditions for mites (shelter deterioration or moisture reduction).
2. Extermination of mites (physical procedures and chemical treatment).

Both have to be combined with removal or denaturation of allergens[15]. An overview of these measures and their effectiveness in laboratory and home studies is given in Table 1.

Deterioration of living conditions

To flourish, mites need shelter, protein-rich food, and an appropriate microclimate. They find shelter in textile materials or rough surfaces where dust collects. Protein-rich food is abundantly shed in skin scales of human beings and pet animals. Between temperatures of 10 and 30°C mites multiply (Chapter 1.1). Relative humidity should be at least 45% for mite survival and 50% for mite population growth (Table 2), whereas for human beings 30% relative humidity is a minimum (Chapter 1.1). Since human comfort conditions have to be met, only shelter and relative humidity can be addressed in mite allergen avoidance.

Concerning shelter, textile floor coverings and upholstered furniture can be replaced by smooth or hard floors and smoothly covered furniture to decrease shelter possibilities (Table 1). Bed materials may be covered with special mite and allergen impermeable covers (Table 1). These covers are usually effective. In some studies mite exposure was not reduced according to the definition of technical effectiveness at the end of the trial. These studies were performed in Sydney, Australia[99,142,143], Cape Town, South Africa[72] and London, United Kingdom[124]. There, climatic conditions favor high house dust mite concentrations in all types of home textiles (see below). Under these circumstances, mites from non-treated home textiles rapidly recolonize the bedding covers[99,142]. The replacement of a home textile by a new textile material has only a temporary effect. Mite shelter remains[23,107]. Dust and allergens will build up again[162].

The other potentially restricting living condition is the relative humidity in home textiles and on rough surfaces[87,123]. The relative humidity in a home textile depends on available air humidity and temperature in the object. Absolute indoor air humidity consists of a build-up of absolute outdoor air humidity, leakages through the building envelope, and the net indoor moisture production by household activities that remains after ventilation. Indoor moisture is produced by activities such as cooking, washing and bathing as well as breathing and sweating[140].

Outdoor air humidity is the only factor that we are not able to control. It influences global mite exposure in a region. In warm climates absolute outdoor air humidity is high enough to allow mite population growth in all types of home textiles. This is seen in parts of Australia[21,99,142,143] and South Africa[72], and results in a short-lasting effect of bed covers as demonstrated before. In high mountainous areas the contribution of the absolute outdoor air humidity is too low to reach a suitable climate in most home textiles[133,136,146]. In other regions the contribution of net indoor moisture production, leakages, ventilation and temperature will determine whether mites will live in a home textile. However, the influence of outdoor humidity on mite abundance has not yet been studied systematically for the European Union. This is one of the aims of this study.

Leakages through the building envelope include rising damp, penetrating damp and defects in water conduits, rain water pipes and sewerage. These need a constructional solution.

In a heating climate both ventilation and heating facilities should be present. Even when ventilation and heating facilities are present, indoor humidity in a dwelling also depends on the use of them.

Indoor moisture production is diminished when water vapor produced during household activities is removed out of the dwelling before it can spread within the dwelling. Ventilation can be used to diminish relative humidity below 50% (the threshold for marginal mite population growth). Ventilation rates necessary to obtain a relative humidity below 50% at a room temperature of 20°C have been calculated for Denmark and the Netherlands[59,85,130]. Continuous heating with no temperature differences between rooms contributes to a decrease of relative indoor air humidity in winter. Underfloor heating is most suited to achieve an even room temperature and low relative humidity[43,90].

A health classification of Dutch dwellings (based on the national Building Code) has recently been devised which addresses humidity and temperature requirements of the mites, actual ventilation rates, and thermal insolation of Dutch homes.

Portable dehumidifiers, heating blankets and heating carpets are not effective in sufficiently reducing relative humidity in home textiles. The capacity of portable dehumidifiers is too low since most humidity is stored in finishing and furnishing materials and mites start to die below 45% relative humidity only (Table 2)[24,35]. Electric heating blankets decrease mattress humidity only locally. Using these blankets, mite densities were only reduced at the surface of the mattress[108]. Presumably mites migrated deeper inside the mattress, and from there can easily recolonize the superficial layers[14]. Electric heating carpets are common in Japan. While these carpets considerably increase room temperature, they are not continuously used; this suppresses their effect on house dust mites[135].

Extermination of mites

When the above-mentioned procedures to deteriorate living conditions for mites are not effective or available due to climatic, economic or behavioral factors, extermination of mites is needed. Methods for killing mites are numerous and comprise physical procedures and chemical treatment (Table 1).

Physical procedures

Freezing in a domestic freezer for 1 week is effective in small objects such as soft toys[19,114]. Liquid nitrogen acts as an instant killer by deep freezing[29,39,55,74,131]. In Sydney, Australia, solar exposure of carpets placed pile-side down on a concrete slab in the direct summer sun from 9.15 a.m. to 3.00 p.m. created relative humidities in carpets to below 24% which were fatal for mites and eggs[144]. After all these procedures, mite corpuses and allergens are still present in the treated objects and should be removed afterwards.

The thermal death point of mites lies at 58°C. Washing at temperatures of 60°C and higher kills mites. The dead mite bodies and allergenic excrements are removed with the rinsing water[2].

No convincing evidence as to the mite killing properties of steam cleaning has been reported. Steam cleaning was used in a laboratory experiment. Up to 114 days after treatment no live mites were found, but three days after the start of the experiment as much as 99.96% of the mites on the control carpet pieces without steam cleaning could also not be recovered[32]. In a home study mean *Der p 1* (mite

Table 1. Mite allergen avoidance measures in the domestic environment and their technical effectiveness (in laboratory and home case studies and controlled trials). All formulations tested in dwellings are included.

++ in the laboratory: significant reduction compared to control and more than 10-fold of baseline, in a dwelling: reduction to below threshold and more than 10-fold of baseline;
\+ in the laboratory: significant reduction compared to control and more than 10-fold of baseline, in a dwelling: reduction to below threshold, but less than 10-fold;
± effectivity seen in some types of home textiles;
– not effective; between ( ) uncontrolled study. Numbers denote reference number.

Measures	Technical effectiveness											
	in the laboratory				in dwellings							
					by professionals				by household members			
	++	+	±	–	++	+	±	–	++	+	±	–
Deterioration of living conditions												
based on shelter deterioration												
smooth or hard floor									65,137, (129)		161	84,148
smoothly covered or hard furniture												
mite/allergen impermeable bed cover					25,40,61, 67,68, 113,156, (103)	49,62,63		72,99, 124,143, (142)	26,46,65, 148			
based on moisture reduction in home textile												
reduction of water vapor production										83		84
ventilation						56-59,85	86	44	138		158	84,102
heating	13	12,77										

Extermination of mites												
Physical procedures												
mite extermination alone												
freezing in freezer	19,114											
liquid nitrogen application	29,55,130				29,39		74					
solar exposure					144							
mite extermination + allergen removal												
washing at ≥60°C	2,79,130						130					
Chemical treatment												
mite extermination alone												
alcohol + glycol ether (Allerite)		94						94				
benzoic acid, terpineol, salol, thymol (Paragerm AK)		55,117, 119	131			118,119						
benzyl benzoate + detergent (Acarosan)	7,10,55, 60,64,82, 131,132	73			42	6,80	8,9,37, 41,115, 116	4,25,40,60, 62,74,91,98, 134,156	76	26,159	48	70, 106, 128
benzyl benzoate + detergent (Acarosan) + extra detergent (Metsan)								72,98				
bioallethrin, esbiol, piperonyl butoxide (Acardust)		55,71	109, 131				27,139					5
natamycin (Tymasil)		22, 53-55, 92	93	82, 131, 132	93							31,126
pirimiphos methyl (Actelic 50)	55,64,105		131			105						
mite extermination + allergen removal												
cold water washing + benzyl benzoate	11,79											
cold water washing + essential oils		101										
mite extermination+allergen denaturation												
benzyl alcohol+tannic acid (Allersearch DMS)	52	82			141		150	52,99,124,143				
benzyl benzoate + tannic acid (Allerbiocid)						104						

allergen) concentration in bedroom carpet dust fell by 64% after steam cleaning. However, pretreatment levels were already below sensitization threshold. Steam cleaning causes an increase in indoor humidity, resulting in more conducive conditions for mite population growth[34]; this side-effect implies that it is also not effective for removal of allergens.

Drying home textiles at a temperature of more than 55°C for 20 minutes has been suggested to kill mites[122]. This drying procedure has not yet been studied. However, if it would kill the mites, allergens will still be present afterwards.

Chemical treatment

There is a large variety of chemicals (called acaricides) which kill mites under laboratory conditions. Studies in homes showed a more extensive variability in technical effectiveness (Table 1). Table 1 lists all products that have been tested in homes. Effectivity in homes has not been demonstrated for dry cleaning, which uses perchlorethylene as active substance. Although dry cleaning kills mites under laboratory circumstances[100,130,145], this has not been demonstrated at the dry cleaner; generally fatty dirt and dust are removed, but it does not remove or denature allergens.

Acaricides are available in various formulations on the market such as powder, foam and spray. As additive in washing detergent-formulations benzyl benzoate or essential oils are available, making washing at temperatures below 60°C effective in mite killing[11,79,101]. The suitability of the various formulations differs according to type of furnishing[121]. Powder used in powder cleaning can be difficult to remove from certain types of carpets, especially cord-type carpets[25,128,156]. Sprays should have a sufficiently high application rate to penetrate deep in the treated home textile[143].

Application is not uniform. Climatic conditions determine required concentration, duration and frequency. Under more favorable living conditions for mites than tested by the manufacturer, for complete extermination higher concentrations or longer application time[60,70,73,120] are needed than recommended[54,124,131,143]. Under mite-prone living conditions one application may not be sufficient to reduce high mite concentrations to below the no-sensitization threshold in a treated object[5,52,72,91,98,99,106,116,124,128,143], while the technical effect is temporary[52,70,91,99,107,122]. Frequency of application should match the speed of recolonization and is generally 2 to 4 times a year under Dutch climatic conditions[82].

Table 2. Thresholds of relative humidity for mite survival and population growth[18]

	Relative humidity (%)
Mite survival	45
Marginal mite population growth	50
Significant mite population growth	60

Allergen removal or denaturation

Mite killing measures have to be followed by allergen removal or denaturation to be clinically effective. Washing[100], vacuum cleaning[110,131,153-155] and beating[30,155] remove allergens. Tannic acid denaturates proteins, probably including allergens[51,82,160]. In washing procedures allergen removal is included. In Allersearch DMS and Allerbiocid an acaricidal and allergen possibly denaturating agent are combined (Table 1).

Ionizers and filtration devices are not recommended for removal of allergens from the air. Too little supportive data are available and none for temperate humid climates such as seen in Western Europe[3,112,127,151]. Such devices do not affect the large reservoirs of mite allergen which function as local sources of exposure[3,45,63,127,149].

Technical effectiveness of mite allergen avoidance programs

A mite allergen avoidance program in the domestic environment is technically effective when mite exposure in all possible niches is permanently reduced below the threshold for mite sensitization. To achieve this a program may consist of a combination of various effective measures to attack all relevant exposure sites. Which (combination) of ++ and + effective measures listed in Table 1 are applicable depends on the level of mite exposure before intervention and the preferences of those who perform the program. It might be expected that in mite-prone areas with mite exposure exceeding more than 10-fold the sensitization threshold only ++ measures will be effective. In climates with lower mite concentrations also + measures could be useful in a program. Design and building of dwellings determine also the effectiveness and needed application frequency of measures.

In the above-mentioned health classification of Dutch dwellings, homes are divided into 3 classes based on inhabitant behavior required to prevent the build-up of mite allergens. A ✚-dwelling meets the Building Code requirements for a 'healthy' building. However, in these dwellings asthmatic inhabitants are not allowed free choice of furnishing and finishing; an extensive use of ventilation and heating facilities and special housekeeping activities are required. In a ✚✚✚-dwelling, construction and facilities are appropriate to prevent sensitizations; there are no restrictions or special requirements for furnishing, finishing, use of the dwelling or special cleaning and maintenance measures. The condition of a ✚✚-dwelling is situated between these two[97].

To monitor mite allergen levels in the entire individual environment of patients is essential. When a program consists of avoidance measures performed "blindly" on a selection of the furnished objects at home, the program might not be effective. Not treated and monitored home textiles may also contain relevant exposure. This may not become "visible", while in intervention studies only those objects are monitored that have been treated. However, mite exposure varies between pieces of home textiles, different rooms, individual dwellings and local climates, since furnishing and indoor climate vary[21]. As demonstrated in Table 1, effective measures in the laboratory are not always effective in homes due to recolonization from non-treated home textiles. This brings us to the possible presence of more relevant exposure sites at home than those that have been included in the program.

Traditional mite allergen avoidance programs are advised without detailing the individual mite exposure pattern. In these programs measures are based on two principles:

1. Removing dust from the patient's home by changing the furnishing in combination with wet or dry cleaning.
2. A general advice concerning dehumidification of the dwelling by heating and ventilating[75].

Selective mite allergen avoidance was first formulated by van Bronswijk in 1988 and later further developed by Kniest, Schober and Kort[15,78,87,130]. It has a stepwise structure (Chapter 1.1, page 20). This concept has gradually been accepted worldwide[122], but is still to be included into consensus reports on the treatment of allergic asthma[38,47,66,152], allergic rhinitis[33,96] and atopic dermatitis[28,95]. In current consensus reports, no or only traditional mite allergen avoidance programs are mentioned, although their technical and clinical effectiveness were generally not thoroughly studied. When studied in comparison to selective mite allergen avoidance their technical effectiveness was less pronounced[81].

In a recently published meta-analysis of randomized, controlled mite allergen avoidance trials, no clinical effect in mite-allergic asthmatics has been demonstrated[50]. However, exposure was reduced in only 6 of the 23 included trials[25,39,40,69,148,151]. In 5 trials exposure was not assessed making it impossible to ascribe any clinical effect on mite allergen avoidance. In 12 of the 23 trials allergen exposure was not reduced; in this latter group avoidance measures were either not effective or not effectively applied. Not all effective avoidance measures were taken into account, since only randomized controlled trials were included in the meta-analysis. In fact, only 23 of 229 relevant studies met the inclusion criteria. Measures such as mini-risk dwellings (in Århus) and 'climate' therapy (in high mountainous areas) were excluded; such measures can not be blinded as in placebo-controlled medication studies. This is also the case for measures which have to be performed by household members, such as most moisture-reducing measures, smooth furnishing and finishing, and washing (Table 1).

Clinical effectiveness of mite allergen avoidance programs

Clinical effectiveness is demonstrated by improvement of at least one clinical parameter as compared to a control group. Clinical effect can only be demonstrated when follow-up is long enough[26,46]; one year is advised[122].

In a trial, clinical effectiveness may only be demonstrated when severity of symptoms and degree of sensitization or hyperreactivity are high enough to show a significant reduction[49,62,93,141,148]. When symptoms are mild, clinical improvement will only be noted statistically when large patient groups are studied. This is usually difficult to realize.

A number of factors may obscure the outcome of a trial. When no manifest mite allergy has been demonstrated, mite allergen avoidance will have no direct clinical results[30]. It is preventive only. In case sensitization to other allergens is also relevant, reduction of mite exposure alone may be ineffective or only partly effective[26,30,147]. The concomitant use of medication may reduce symptoms, while hyposensitization may diminish sensitization level[111]. When no or only a temporary mite allergen exposure reduction is achieved, no clinical effect may be expected[98,99]. Non-treated textiles with exposure above sensitization threshold at home or in other environments that are visited by the patient may also be relevant for the clinical condition of the patient[36,46,62,72,125]. In fact the program is technically ineffective, when non-treated but polluted textiles have been forgotten. If, before intervention, exposure levels are below the threshold level for sensitization even technically effective programs will show no clinical improvement[46,62]. Exposure to irritants such as cigarette smoking may interfere with the clinical outcome of the intervention[1].

If we take all these restrictions into account and use the longest observation period for data which are recorded at several points in time, 13 of the 16 controlled studies with sufficient exposure reduction were clinically effective[25,39,40,58,59,62,67,68,81,93,141,148,159] and 3 were not[26,46,63]. In 11 cases a more than 10-fold exposure reduction was achieved[25,26,39,40,46,62,67,68,93,141,148]. Of these, only two were not clinically effective[26,46]. In the trial of Frederick et al. only encasement of mattresses, duvets and pillows (median *Der p 1* at baseline above 10μg/g dust) took place. It might be expected that other home textiles contained high mite allergen exposure as well, which may have interfered with the clinical effect[46]. In the study by Chang et al. beds were covered and carpets of bedroom and most commonly used room were treated with Acarosan. However, baseline allergen exposure was just above sensitization threshold[26]. Both intervention studies were executed by household members for 3 months only, while exposure to other relevant aero-allergens remained.

In the above-mentioned meta-analysis, measures were performed by household members and exposure was reduced in only the study by Huss et al.[69].

Behavioral effectiveness of programs

An avoidance program that is technically and clinically effective in the hands of researchers is not always effective, when performed by household members[89].

For long-lasting clinical effect an allergen avoidance program should be not only technically and clinically effective but also feasible as a life-long endeavor. Up till now programs including all relevant exposure in the home environment[80,88] and the working or school environment[88] have been executed by professionals, not by household members (Table 1). The professionals included specialized laboratory personnel, community nurse or other health educators (Table 1)[80,88]. There is one exception; after exposure tests Kroidl et al. offered households an acaricidal cleaning program for all home textiles. No clinical improvement was found[89].

Feasibility of these programs for execution by the household members will depend on sociological factors. Experienced advantages and disadvantages of measures will be weighted. This includes costs, complexity, laboriousness, influence on other daily activities, and perceived clinical benefit. Timing of the introduction of a program might be influenced by an exacerbation of disease, presence of disturbing life-events or a new activity not yet incorporated in daily activities.

Costs may be considerable[80]. In the Netherlands, financial compensation is possible for mattress and pillow covers of the patient, leaving expense of other covers and other products for the household budget. However, time consumption is even higher. Kniest calculated one hygienic cleaning of the dwelling to consume almost 6 working hours[80]. No study has been performed to investigate the relative importance of behavioral effectiveness and contribution of specific knowledge to clinical effectiveness. This subject will be addressed in this thesis.

Aim of the study

The study aims at feasibility of an effective allergen avoidance program. How does an effective but minimal program vary between different regions of the European Union? Which tools are available to discriminate between dwellings and households where avoidance is effective and those where it is not? Which advantages and disadvantages of such programs are experienced by the patient and other household members? How can the experienced problems be resolved?

Technically effective mite allergen avoidance measures and actual mite exposure in a geographic region are determined by outdoor climate (**Section 2**). We first investigated which climatic variable(s) might predict mite numbers (**Chapter 2.1**). These variables are used to draw a map of Europe that shows the regions where mite problems might be expected and mite allergen avoidance could be part of an allergen avoidance program (**Chapter 2.2**). The geographic mite model on which this map was based has also been tested outside Europe (**Chapter 2.3**).

Non-mite allergens relevant for allergen avoidance are subject of **Section 3**. Indoor, outdoor and food allergens and irritants in the Netherlands have been investigated (**Chapter 3.1**). The possible allergenic role of the skin yeast *Pityrosporum* was examined (**Chapter 3.2**).

An individual, selective mite allergen avoidance program has been attempted in households with mite-allergic asthmatic children (**Section 4**). This program was executed by the household members during one year, and structured and supervised by the author. Household members could choose between various effective measures. Avoidance materials were supplied free of charge in the treatment group but not in the control group who also did not receive individual coaching. Exposure reduction and clinical effect were studied (**Chapter 4.1**), as well as avoidance behavior and feasibility of measures (**Chapter 4.2**).

In **Section 5** (General discussion) the results of Sections 2 to 4 are evaluated and reviewed in the context of relevant scientific literature.

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Section 2

A geographic mite model

Allergen-producing mites need certain living conditions for survival and population growth. Climate is the most important determinant of mite-prone living conditions. By quantifying the climatic factor we are able to predict the chance that a certain dwelling or home textile contains mite allergen concentrations above the sensitization threshold. Based on these predictors a technically effective allergen avoidance program can be made for a specific climatic region.

2.1 The abundance of house dust mites (Pyroglyphidae) in different home textiles in Europe, in relation to outdoor climates, heating and ventilation
A.M.T. van Nes, H.S.M. Kort, L.G.H. Koren, C.E.E. Pernot, H.L. Schellen, F.E. van Boven, J.E.M.H. van Bronswijk

2.2 Limiting factors for growth and development of domestic mites in Europe
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Chapter 2.1

The abundance of house dust mites (Pyroglyphidae) in different home textiles in Europe, in relation to outdoor climates, heating and ventilation

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Abstract

In Europe, house dust mites of the family Pyroglyphidae are abundant producers of allergens in dwellings. Their prevalence in dwellings as well as their distribution among different types of home textiles vary among different localities in Europe.

The main limiting factors for mite population growth are water activity of surfaces and relative humidity in the surrounding boundary layer of air. Water activity and relative humidity in the mite niche are influenced by outdoor temperature and absolute air humidity, heating and ventilation.

The mean January outdoor air temperature was determined to characterize outdoor climates. Based on outdoor temperatures and absolute air humidities, the length of heating season and length of mite population growth season in different home textiles were defined. These variables have been validated with published data on mite abundance in mattresses and on floors in climatically distinct areas in Finland, Denmark, United Kingdom, the Netherlands, France, Switzerland, Italy and Poland.

Length of mite population growth season - abbreviated to mite season - can be shortened by efficient ventilation and heating. Therefore, minimal required ventilation rates, to keep the relative humidity in the mite niche below the hygienic moisture limit for mite population growth, in European countries, have been collected.

No significant correlation was demonstrated between length of heating season and mite numbers in any of the home textiles. Between mean January outdoor air temperature and mite numbers in mattresses; and between length of mite season and mite numbers in mattresses, significant correlations were seen (Spearman rank correlation test, $p<0.05$). On floors, none of the climatic variables showed a significant correlation with mite numbers. Minimal required ventilation rates have been published for Denmark and the Netherlands only.

In contrast to length of heating season, mean January outdoor air temperature and length of mite season in mattresses can predict the overall abundance of house dust mites in mattresses in a climatic area. To predict the overall mite burden on floors, the influence of outdoor climate should be examined in larger studies in combination with soil drainage and constructional factors. To shorten the length of the mite population growth season minimal required ventilation rates should be assessed.

Introduction

Prevalence of house dust mites (Pyroglyphidae) in dwellings as well as their distribution among different types of home textiles vary in different European countries[2,3,9,10,12,14,15,21,25-27]. Exposure to house dust mite allergens may cause sensitization in persons with an atopic constitution, in Europe 20-40% of the total population[6]. The sensitization threshold for house dust mites has been set at 10 mites per gram floor dust or 100 mites per gram mattress/upholstery dust. For their major allergen (group 1: Der p I and Der f 1) the sensitization threshold is 2 μg per gram dust[20].

Mite population growth depends mostly on the availability of water. Water activity of the mite inhabited surface correlates closely to relative air humidity in the boundary layer of air, forming the mite niche. When relative humidity in the mite niche is 50% at room temperature (about 20°C), the sensitization threshold for house dust mites will be reached. Schober calls this humidity the hygienic moisture limit for mite sensitization[22].

Relative humidity in the mite niche is determined by temperature and absolute humidity in the mite niche. Under equilibrium conditions and without air-conditioning, absolute humidity in the mite niche is the sum of absolute outdoor air humidity, and water vapor production by household activities, remaining after ventilation[28]. During winter, the contribution of absolute outdoor air humidity will be low due to lower outdoor air temperatures in Europe. In the Netherlands and Germany, a relation has been seen between lowering mean January outdoor air temperature and decreasing guanine positive floor dust samples[8].

This suggests that outdoor air temperature and humidity, heating and ventilation determine the differences in mite numbers in climatically distinct areas in Europe. To test this hypothesis, we defined variables in which these factors are taken into account. Validation of the predictive value of these variables has been done with published information on mite numbers on floors and in mattresses in Europe.

Materials and methods

Outdoor air temperature and humidity

Hourly data of simultaneously recorded outdoor temperature and relative air humidity were obtained from European Test Reference Years (TRY). TRYs are given of climatically homogeneous areas in Denmark, United Kingdom, Ireland, the Netherlands, Belgium, France, and Italy[11]. Monthly climatic data of Finland, Poland, and the Mt Ventoux region (France) were obtained from Müller[19]. For Davos, these data were supplied by the Schweizerische Meteorologie Anstalt in Zürich, Switzerland. From these data, mean January outdoor air temperatures are taken.

Heating season

In previous studies length of heating season was considered a limiting factor[5,6]. Heating season is defined as the number of months in which the mean daily outdoor air temperature falls 2.5°C or more below the lower comfort level of indoor air temperature, T_{lc}[13].

The perceived lower comfort level of the indoor air temperature varies in different countries: in the Netherlands at 18°C, in Denmark and Sweden at 17°C, in the United Kingdom at 15.5°C, in Germany and Italy at 19°C, and in France at 17.5°C[4,17]. We set the lower comfort level for Poland at 19°C (as Germany), for Switzerland at 18°C (in between France and Germany), and for Finland at 17°C (as Denmark and Sweden).

Mite population growth season (mite season)

Length of mite population growth season - abbreviated to mite season - was defined as the number of months in which the mean monthly relative humidity in a home textile rises above 50% at room temperature, the hygienic moisture limit for mite sensitization[22]. An estimation of length of mite seasons is shown in Figure 1.

Bedroom conditions

Bedroom conditions were considered during the non-occupied period, between 8.00h and 24.00h. During occupation, human heat and sweat will contribute to the humidity of the mattress. However, the relative humidity in the mite niche during the non-occupied period can form a limiting factor for mite population growth[5]. Mite population growth will be determined by the combination of length of drying out period and lowness of relative humidity in home textiles during this period[7].

When not occupied, we assumed the bedroom would not be heated above the lower comfort level of a country. The bedroom air temperature was set at the lower comfort level of that country, if the outdoor air temperature was below this level. If the outdoor air temperature was above the lower comfort level, the outdoor air temperature was used (Figure 1).

In this non-occupied period we did not add water vapor by household activities to the absolute outdoor air humidity. The contribution of water vapor production by human sweat is negligible within 2-4 hours after the bed has been vacated[5].

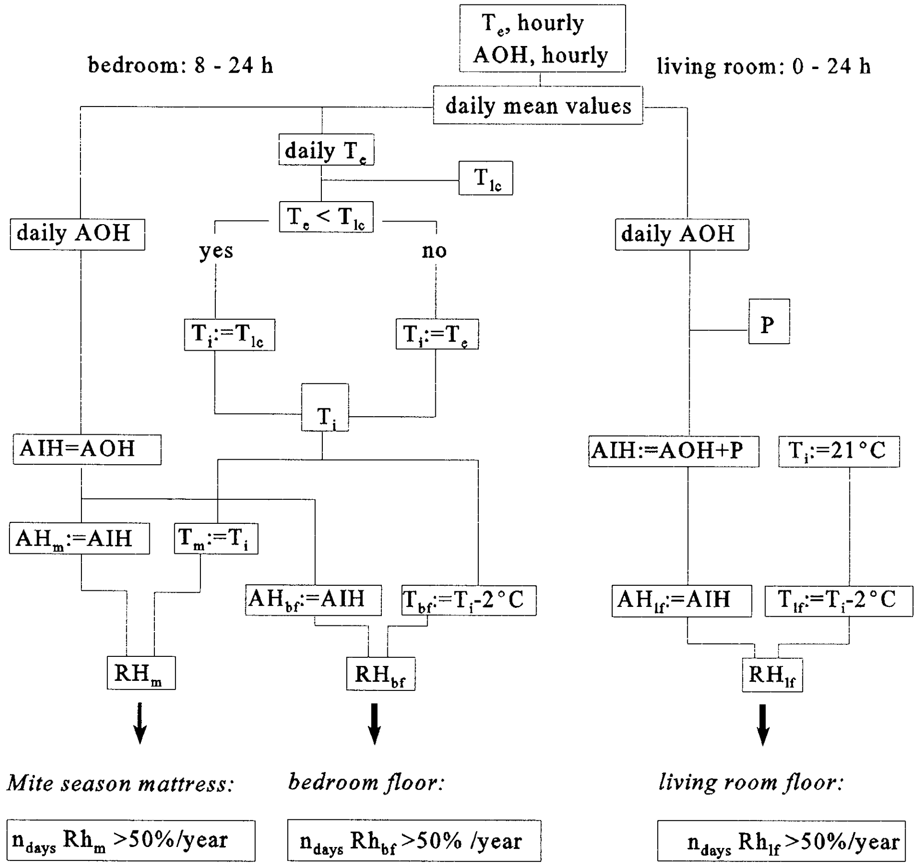

Figure 1. Flow diagram for the estimation of length of mite season in mattress, bedroom and living room floor (in days/year). All bedroom data are based on the non-occupied period only, 8-24 hours

AH = absolute humidity in g water vapor/m^3 air
AIH = absolute indoor air humidity in g water vapor/m^3 air
AOH= absolute outdoor air humidity in g water vapor/m^3 air
P = water vapor production by household activities in g/m^3 air
RH = relative humidity in %
T = temperature in °C
n_{days} = number of days

bf = bedroom floor
e = outdoor
i = indoor
lc = lower comfort level
lf = living room floor
m = mattress

Length of mite season in mattresses

For mattresses, mean temperature during non-occupation equals mean bedroom air temperature. Absolute humidity in mattresses was equated with absolute bedroom air humidity during non-occupation (Figure 1).

Length of mite season on bedroom floors
For bedroom floor temperature we subtracted 2 °C from bedroom air temperature[1]. As in mattresses, absolute bedroom floor humidities were equated with absolute bedroom air humidities (Figure 1).

Living room conditions
We assumed that in all European countries a comfortable living room air temperature of 21 °C is maintained[1]. In this preliminary model we did not take any night-reduction of heating into account. For absolute indoor air humidity in the living room, we added the maximal water vapor production by household activities remaining after ventilation, to the absolute outdoor air humidity belonging to a certain outdoor air temperature[28].

Length of mite season on living room floors
Temperature on living room floors was set at 19°C, 2 °C below the living room air temperature[1]. Absolute living room floor humidity was equated with absolute living room air humidity (Figure 1).

Ventilation

Ventilation can diminish the contribution of water vapor production by household activities[28]. Therefore, minimal required ventilation rates to keep the relative humidity in the mite niche below 50% in different European countries have been collected. Data were collected with the aid of Index Medicus (1966 up to March 1993) and the collection of the Interuniversity Task Group 'Home and Health', the Netherlands.

House dust mite data

The usage of mean January outdoor air temperature and our definitions of length of heating season and mite population growth season to predict mite abundance are to be validated by published information on numbers of house dust mites on floors and mattresses. These data were collected with the aid of Index Medicus (1966 up to March 1993) and the collection of the Interuniversity Task Group 'Home and Health', the Netherlands. Quantitative data of Pyroglyphid mites or the major allergen *Der p I* were recorded (Table 1).

When available, median values of mite or allergen densities were preferred to mean values (Table 1). For comparative purposes both median and mean values were divided by the sensitization threshold for house dust mites to obtain the so-called exposure rate. To compare quantitative data on allergen *Der p 1* with those on Pyroglyphid mites, the allergen load was divided by a factor of 20 for mattresses and a factor of 200 for floors, being the ratios between the sensitization thresholds for allergens and for mites.

Statistical analyses

For mattresses and floors Spearman rank correlation test is used to test relations between mean January outdoor air temperature and exposure rate; between length of heating season and exposure rate; between length of mite season and exposure rate; between mean January outdoor air temperature and length of mite season; and between length of heating season and length of mite season. The correlation between mean January outdoor air temperature and length of heating season was tested independent of type of home textile[24].

Analyses of differences in length of mite season between mattresses and bedroom floors, mattresses and living room floors, mattresses and floors, and bedroom and living room floors are performed using the Mann-Whitney U test[24]. Only house dust mite data with an exposure rate $\geq$ 1 are taken into account.Confidence levels have been set at 5%.

Results

House dust mite data

From all 13 areas mite or allergen data were available. Numbers of Pyroglyphid mites[2] were given, or could be calculated from the number of all mites[3,10,14,15,21,25]. In some cases only the combined counts were present of *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae* and *Euroglyphus maynei*[26,27]. For Denmark[12] numbers of *Dermatophagoides pteronyssinus* only are given. In France[9] allergen *Der p 1* was measured (Table 1 and Figure 2).

The period and method of sampling, and extraction technique were not uniform in different areas and no exact description of floor covering, textile or non-textile, was given.

In Denmark, the Netherlands and the United Kingdom, more house dust mites per gram dust were found in mattresses than on floors; and more on bedroom floors than on living room floors (Table 1). From Finland, France, Switzerland, Italy and Poland no comparative data on house dust mite numbers in different home textiles were mentioned.

In 8 of the 13 areas, mite or allergen densities in mattresses and on floors exceeded the sensitization threshold several times. This was not the case in mattresses from De Bilt[15], Briançon[9a], East-Finland[27] and Katowice[14], and on living room floors from Davos[26] (Figure 3).

Table 1. Description of mite (allergen) data extracted from literature

Weather station (Country)	**Sampling locality † (Country)**	**Textile sampled * (n of samples)**	**Mites/ Allergen #**	**Numbers/ Amount √**
Eskdalemuir (United Kingdom)	Glasgow [10] (UK)	mattress (n=65) br-carpet (n=27)	tot Pyr	729 (mean) 283 (mean)
Aberporth (United Kingdom)	Cardiff [21] (UK)	mattress (n=50) br-floor (n=32)	tot Pyr	1318 (mean) 810 (mean)
Kew (United Kingdom)	Birmingham [3] (UK)	mattress (n=19) br-carpet (n=5) lr-carpet (n=5)	tot Pyr	1800 (median) 882 (median) 252 (median)
Copenhagen (Denmark)	Aarhus [12] (DK)	mattress (n=24) br-floor (n=24)	*D. pter*	390 (median) 170 (median)
De Bilt (The Netherlands)	Utrecht [15] (NL)	mattress (n=20) br-carpet (n=14) lr-carpet (n=16)	tot Pyr	83 (median) 55 (median) 43 (median)
Vlissingen (The Netherlands)	Leiden [25] (NL)	lr-floor (n=150)	tot Pyr	12 (mean)
Mt Ventoux (France)	Briançon [9a] (F)	mattress (n=115)	*Der p I*	0.36 (mean)
Nice (France)	Marseille [9b] (F)	mattress (n=126)	*Der p I*	15.8 (mean)
Milan (Italy)	Milan [2a] (I)	mattress (n=15)	tot Pyr	185 (median)
Rome (Italy)	Naples [2b] (I)	mattress (n=6)	tot Pyr	419 (median)
Davos (Switzerland)	Davos [26] (CH)	lr-floor (n=4)	tot Pyr	1 (mean)
Punkaharju (Finland)	Uukuniemi/ Ilomantsi [27] (SF)	mattress (n=7)	tot Pyr	24 (median)
Krakow (Poland)	Katowice/Bytom [14] (PL)	mattress (n=21)	tot Pyr	5 (median)

* br-carpet = bedroom carpet ; br-floor = bedroom floor;
lr-carpet = living room carpet ; lr-floor = living room floor.
tot Pyr = all mites of the family Pyroglyphidae;
D. pter = Dermatophagoides pteronyssinus.
† Number after sampling locality relates to numbered paper in reference section.
√ Numbers are specified or calculated (mean or median) pyroglyphid mites per gram dust or amount of mite 1 allergens in μg/g dust.

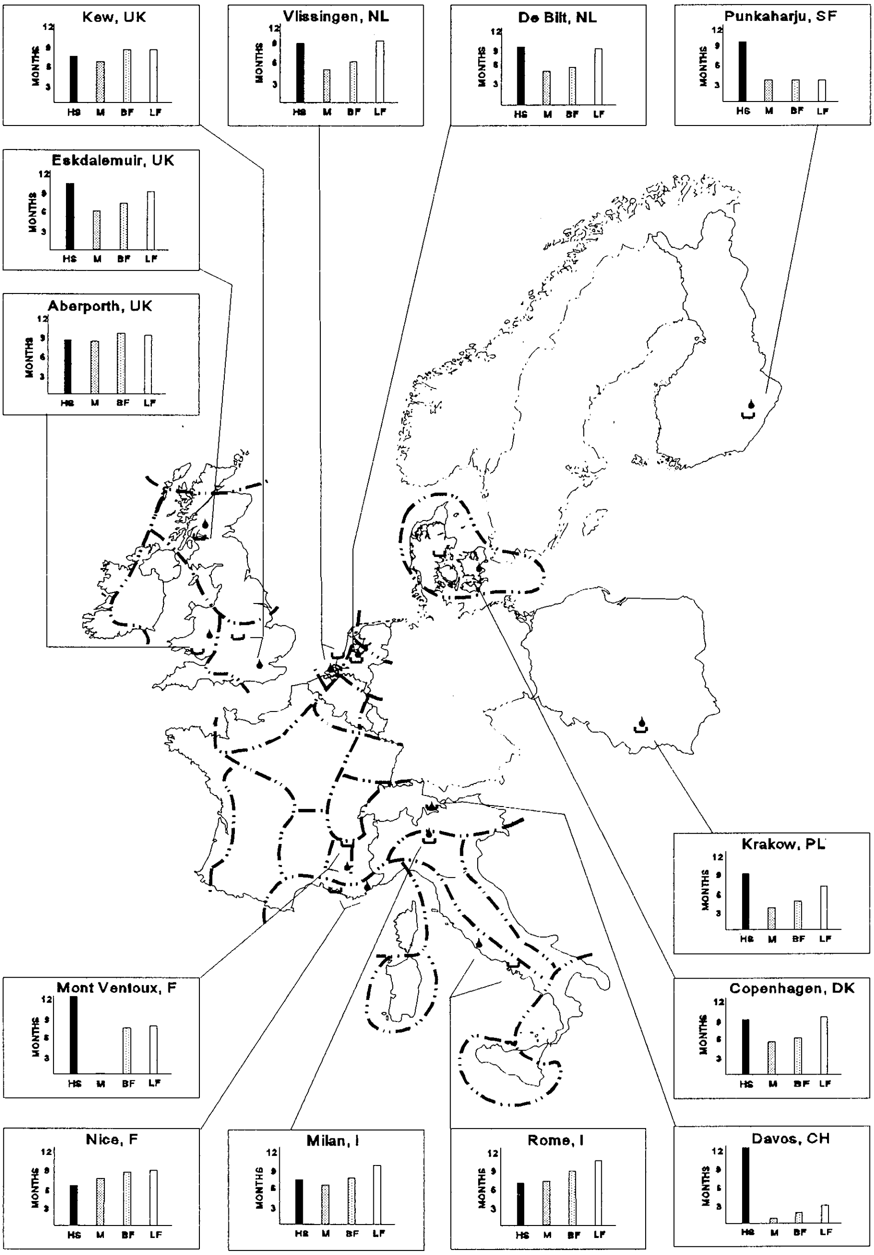

Figure 2. Map of weather stations and sampling localities. ▲ = weather station; ∪ = sampling locality; •• — = climatic regions; In squares: vertical axis: number of months; horizontal axis: HS = length of heating season; M, BF, LF = length of mite season in mattresses, on bedroom floors, and on living room floors, respectively

Mean January outdoor air temperature

A significant correlation was found between mean January outdoor air temperature and exposure rate in mattresses (Spearman rank correlation test, $p<0.05$); no significant correlation was seen for floors (Figure 3).

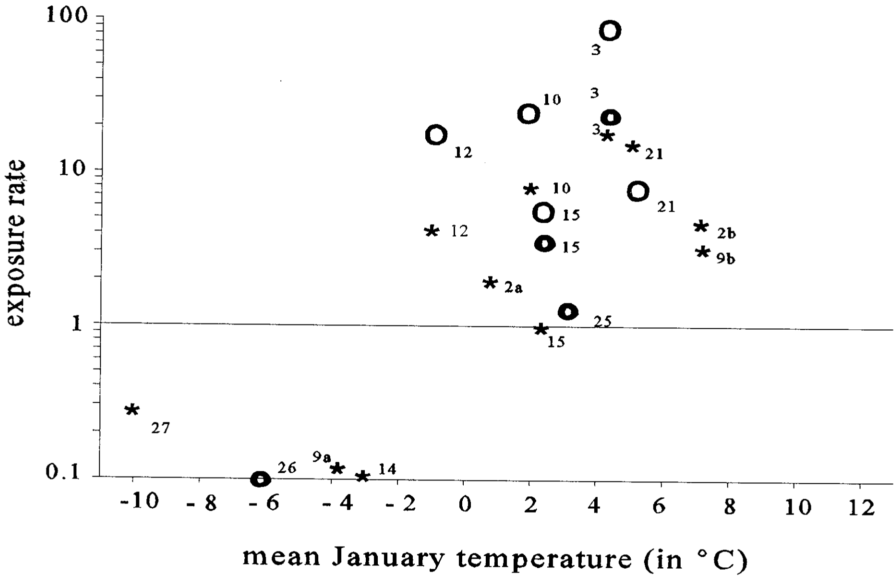

*Figure 3. Mean January outdoor air temperature, and exposure rate to mite /allergen (densities found divided by sensitization threshold) in different home textiles. Line indicates sensitization threshold for house dust mites. Mean January temperature = mean January outdoor air temperature. * = mattresses; O = bedroom floors;* **O** *= living room floors. Numbers refer to sampling localities in Table 1*

Heating season

In all areas, heating season was longer than 6 months (Figure 4). In those areas where mite numbers did not exceed the sensitization threshold for house dust mites, the heating season lasted 9 months or more[9a,14,15,26,27]. However, the reverse relation was not seen. Spearman rank correlation test revealed no significant correlations between length of heating season and exposure rate.

Mite season

The correlation between length of mite season and exposure rate in mattresses was significant ($p<0.05$). No significant correlations between length of mite season and floors, bedroom and living room floors separately or combined, were demonstrated by Spearman rank correlation test.

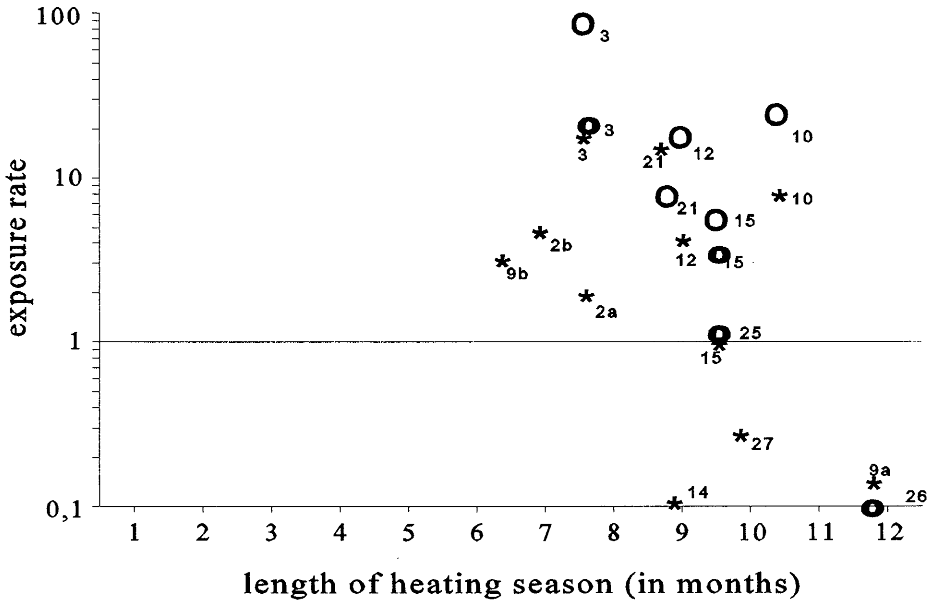

*Figure 4. Length of heating season (in months) and exposure rate to mite /allergen (found densities divided by sensitization threshold) in different home textiles. Line indicates sensitization threshold for house dust mites. * = mattresses; O = bedroom floors;* **O** *= living room floors. Numbers refer to sampling localities in Table 1*

Mite densities above the sensitization threshold for house dust mites were found in mattresses when the defined mite season was longer than 5 months; on bedroom floors longer than 6.5 months; and on living room floors longer than 8.5 months (Figure 5). Using Mann-Whitney U test the minimal required mite season in mattresses was significantly shorter than the one on living room floors ($p<0.05$).

Mean January outdoor air temperature was significantly correlated with length of mite season in all home textiles, apart from living room floors. An inverse relation between length of heating season and length of mite season was seen. This relation was significant in mattresses only. The inverse relation between mean January outdoor air temperature and length of heating season was significantly correlated (Spearman rank correlation test, $p<0.05$).

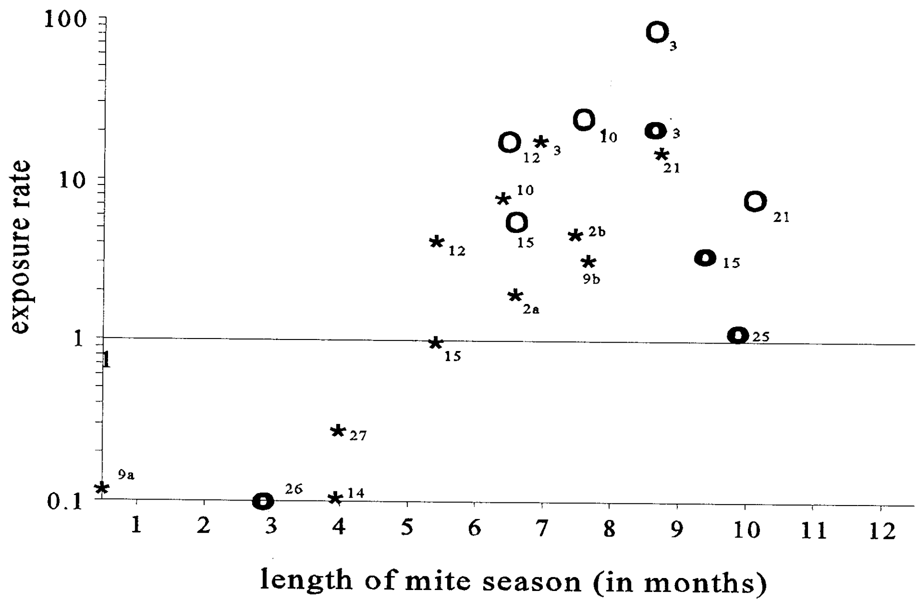

*Figure 5. Length of mite season (in months) and exposure rate to mite/allergen (found densities divided by sensitization threshold) in different home textiles. Line indicates sensitization threshold for house dust mites. *=mattresses;O= bedroom floors;* **O***=livingroom floors. Numbers refer to sampling localities in Table 1*

Ventilation

Data on ventilation rates in dwellings required to keep indoor air humidity below the hygienic moisture limit for mites for a considerable time in a certain outdoor climate have been published for Denmark and the Netherlands, only. In Denmark, mean daily relative indoor air humidity will theoretically be below 50% relative humidity for 7 months, November until May, if the minimum ventilation rate is 1,0 ACH (Air Changes per Hour) during those months[16,23]. Schober extrapolated from the Danish data the minimal required ventilation rate in the Netherlands[23]. In Dutch dwellings the minimal required ventilation rate is 1.0 ACH during the months November until April, 1.5 ACH in May and October, and even higher in the remaining months.

Discussion

In those climatic areas where mite numbers did not exceed the sensitization threshold for house dust mites, the heating season lasted 9 months or more[9a,14,15,26,27]. However, no correlation between length of heating season and exposure rate was demonstrated in any of the home textiles.

In 1981, Bronswijk found almost no house dust mites in Scandinavia, where the heating season was longer than 9 months[6]. In the cool marine climate of Northern Scandinavia the outdoor temperature will stay below 6.1 °C during 6 to 9 months[18]. During these months the contribution of absolute outdoor air humidity to indoor air humidity will not be sufficient to exceed the hygienic moisture limit for mite sensitization (50% relative humidity at room temperature) most of the time, if no water vapor is added by household activities.

The dryness indoors during the heating season, rather than the length of this period, is important[7]. Therefore the combined data of outdoor air temperature and absolute humidity should be used. These data are directly or indirectly incorporated in the values of the climatic variables mean January outdoor air temperature and length of mite season.

January is the coldest month in all tested climatic areas[2a,2b,3,9a,9b,10,12,14,15,21,25-27]. During this month the contribution of absolute outdoor air humidity to the relative humidity in the mite niche might be too low to exceed the hygienic moisture limit for mite sensitization.

In the definition of length of mite season, outdoor air temperatures and absolute humidities during a year are taken into account. Not only the dryness but also the length of the drying out period is described by this climatic variable.

Mean January outdoor air temperature and length of mite season showed significant correlations with the exposure rate in mattresses. These climatic variables seem useful tools to predict overall mite abundance in mattresses in a climatic area.

On floors, no significant correlations were seen between mean January outdoor air temperature and exposure rate; nor between length of mite season and exposure rate. This can be caused by several factors. In Kew and Davos the number of floors sampled were only 5 and 4, respectively (Table 1). No data on floor covering, textile or non-textile, and on which floor level rooms were situated, were recorded.

However, the most important factor in the length of mite season on floors is the floor temperature. In all countries floor temperature was set 2 °C below indoor air temperature. Differences in thermal insulation of floors, in soil drainage and construction were not taken into account.

In our model, bedroom conditions are defined during non-occupation only. This may have consequences especially for mattresses and the predicted length of mite season in mattresses may be too short, with no contribution of sweat during occupation taken into account. Defined length of mite season seems shorter in mattresses than on floors. This might explain why in climatic areas with borderline climatic conditions for the survival of house dust mites, the mattresses may be a hazard to atopic patients, while the floors are not[8].

The length of mite season could be reduced by effective ventilation. Minimal required ventilation rates to keep relative humidity in the mite niche below 50% were calculated previously for Denmark and the Netherlands[16,23]. To give suitable advice for allergen avoidance measures in other climatic areas minimal required ventilation rates should be assessed in every region.

In the present study, we found that the mean January outdoor air temperature and length of mite season can predict the overall mite abundance in mattresses in climatically distinct areas in Europe. For floors, the influence of outdoor air temperature and absolute humidity should be examined in studies:
1. with textile floor coverings only (mites need shelter for their development),
2. with rooms situated on floor levels with comparable floor temperature,
3. taking into account the influence of soil and constructional factors and,
4. with enough samples from a particular climatic area and enough sampling localities for statistical analyses.

To predict the mite burden in an individual dwelling, measurement of the absolute indoor air humidity and room temperature is needed. There is an extensive variability in mite numbers between dwellings in a climatic area[2,3,9,10,12,14,15,21,25-27].

Acknowledgments

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Chapter 2.2

Limiting factors for growth and development of domestic mites in Europe

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Abstract

A quarter to half of European households are at risk of health damage due to mites in their homes. House dust mites (family Pyroglyphidae) and storage mites (families Acaridae and Glycyphagidae) are present; both groups being specific for different ecosystems: ecosystem of textiles (mites) and the ecosystem of humid smooth surfaces (storage mites).
Due to the protection mites receive from the human inhabitants, only few limiting factors are active: humidity, niche, fungal growth, and protein content of the dust.
A diagram presentation has been developed to show the relationships between temperature (in °C), absolute air humidity (in g water vapor/m^3 air), and relative humidity (in %). Climatic requirements of house dust mites, local outdoor conditions, thermal insulation of floors and net indoor moisture production have been taken into account to explain seasonal variation in mite survival and development.
The building engineer may manage humidity by means of heating, ventilation, thermal insulation of the building envelope, and dehumidification of indoor air.
As an example of geographic diversity, and based on mean values of January outdoor temperature, Europe was divided into six zones with different risks for mite problems in carpeting. The resulting map is helpful in explaining mite distribution patterns, mite sensitization prevalence, and reported avoidance effectiveness.

Mite relevance and ecosystems

In Europe, allergic disease, such as bronchial asthma, allergic rhinitis and atopic eczema, is commonly associated with mites. In case of mites both the northern and the southern part of the continent show a lower incidence of mite sensitization than the western-central part. Sensitization to storage mites (families Acaridae and Glycyphagidae) is common in both northern and western-central Europe, but low in the Mediterranean (Table 1).

The prevalence of clinically active mite allergy ranges from 5-10% of the European population depending on the region concerned. Another 5-20% is not yet sensitized but born with the hereditary trait to atopic reaction. This means that 10-30% of the 375 million Europeans in the European Union, or 24-58% of the 145 million European households are at risk for dwelling-related mite allergies[9,15].

Let's introduce the tiny health threateners (Figure 1). Mites (Acari) have no distinct head: the body appears as an oval structure with legs and mouth parts protruding. Mites in houses usually belong to the Astigmata. These creatures have no special structure for gas exchange. Oxygen, carbon dioxide and water vapor pass through the chitinous skin, which also serves as mite skeleton. Within the mite, the free flowing blood carries out transport of gases, nutrients and waste products. Mites excrete nitrogenous waste in the form of guanine, partly in the feces, and partly under the (dorsal) skin to be removed during moulting together with the old skin. They partly regulate water vapor loss by secreting an appropriate amount of oily liquid and spreading it over the skin. Astigmatic mites have no eyes, nor ears as we know them. Some parts of the body are light-sensitive to distinguish between day and night. Sense organs for hearing, tasting and heat perception are located in special hairs (called solenidia) present on legs and mouth parts. Mite allergens are commonly digestive enzymes used by the mite to digest its food. The allergenicity of these enzymes for man is accidental[5,45].

In urban houses, the two main mite categories inhabit different niches. Textiles soiled with human skin scales and other organic particles are the home of the ecosystem with pyroglyphid mites and xerophilic fungi as most abundant inhabitants of the community. Abundance of pyroglyphid mites expressed as number/m^2 area (an ecological measurement) is high and about the same in Dutch bedding, upholstery and carpet products in bedroom and living room (Table 2). Abundance on walls and smooth floor coverings is low. Other niches found infested with house dust mites by us (and others) include air-conditioning installations, childrens' soft toys, clothing and footwear[40,55].

Presence of pyroglyphid mites on walls, room partitions, ceilings and smooth floors signifies exchange with another indoor ecosystem, the storage mite eco-system of humid smooth surfaces.

Table 1. Prevalence of sensitization to mite allergens in atopic patients in different areas of the European Union[33]

	Prevalence in %			
Allergen source	Scandinavia	United Kingdom	Netherlands	Mediterranean
House dust mites	2 - 30	80	60 - 90	15 - 50
Storage mites	40 - 45	> 30	65 - 70	10

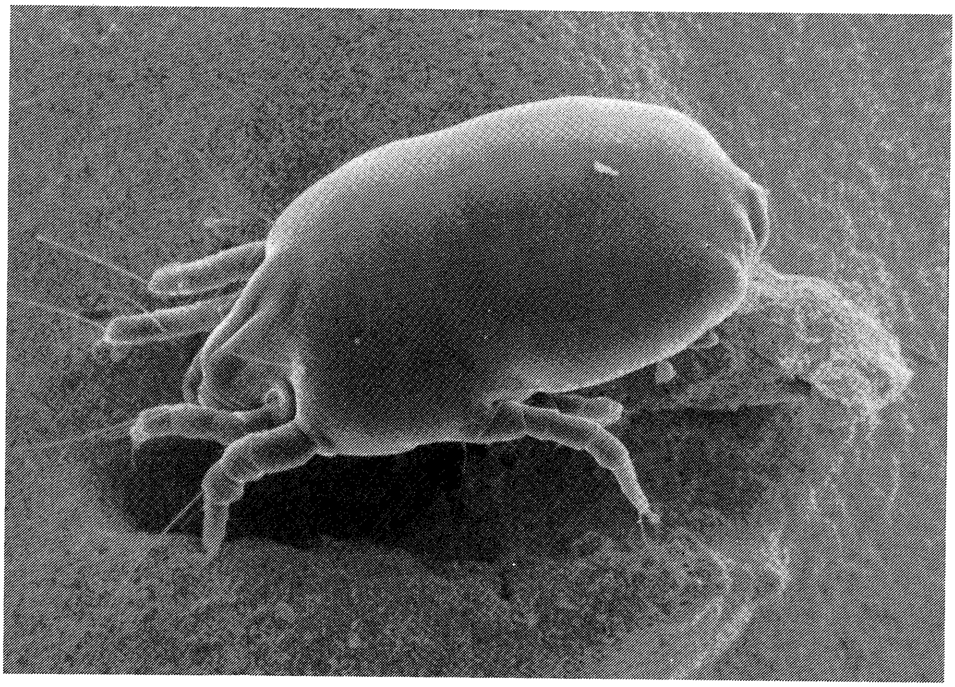

Figure 1. Astigmatic mite (Dermatophagoides pteronyssinus) as seen under the scanning electron microscope. Actual length of the nymphal mite is around 0.3 mm. Photo by J.E.M.H. van Bronswijk & A.W. Dicke

The latter system is characterized by storage mites, dust lice, xerophilic and meso-hygrophilic fungi[28]. Occasionally the storage mite ecosystem is visible to the naked eye due to the brilliant colors of some moldy surfaces. On other occasions the almost colorless and transparent mites have completely grazed off the fungal meadow leaving no visible material damage.

Limiting factors for mites

Ecology studies the distribution and abundance of organisms, such as mites. Flow of energy through the ecosystem, cycling of nutrients, conditions of existence for the organisms, and interactions between organisms are governing factors in most ecosystems[43].

Table 2. Distribution of mites in homes of mite-allergic patients in the Netherlands (June 1988). Dust collected by vacuuming whole surfaces at a speed of 1 m^2/min. Within columns, the same superscript letters A, B, C, D, E, P, Q, and R denote no significant difference at $p = 0.05$[6]

Habitat sampled		n	Mite numbers per m^2 surface area: median	per m^2 surface area: maximum	per g collected dust: median	per g collected dust: maximum
Mattress	bedroom	60	12^{A}	209	30^{P}	450
Upholstered furniture	bedroom	29	8^{A}	835	40^{P}	555
	living room	28	9^{A}	167	34^{P}	500
	other spaces	6	13^{A}	31	33^{P}	177
Carpet	bedroom	42	10^{A}	331	9^{Q}	64
	living room	25	7^{A}	228	8^{Q}	280
	other spaces	38	$2^{A/B}$	777	$5^{Q/R}$	92
Smooth floor covering	bedroom	15	0.1^{C}	2.1	$1^{Q/R}$	17
	living room	8	0.4^{C}	0.9	$1^{Q/R}$	3
	other spaces	26	0.0^{C}	4.9	0^{R}	3
Wall and room partition	bedroom	34	0.0^{C}	11	0^{R}	196
	living room	37	$0.0^{C/D}$	0.5	0^{R}	19
	other spaces	8	$0.0^{C/E}$	0.5	0^{R}	125

The house dust ecosystem of textiles and the ecosystem of humid smooth surfaces in housing depend for energy and nutrients on organic soiling. The protein content of carpet dust is sometimes limiting[25]. As to 'conditions of existence', such as light, temperature, water and a place to live, the availability of water (vapor) is most relevant. With respect to the other factors, man and mite share the range of acceptable conditions in the home. Mite ecosystems in the home are pioneer systems with a simple structure. Interactions between organisms with-in the ecosystem are limited, but the storage mite ecosystem is completely dependent on the presence of fungal growth, a staple food for storage mites and dust lice. Predatory mites have little influence on mite population growth in the home[5,28].

The question arises how we can use limiting factors for long-term decrease of population growth and allergen exposure. Removal of all suitable niches is a possibility. In case of the storage mite ecosystem this means the use of fungi-resistant finishing materials. For house dust mites, removal of all textiles is a theoretical possibility. However, bedding is considered essential for healthy life, while upholstered furnishings and carpet products increase comfort in indoor environments for a number of inhabitants. In fact, carpet products are found on 70-80% of domestic floors in the Netherlands[52]. Therefore we consider the total removal of textiles as unrealistic.

Removal of fungi and protein-containing dust as well as living mites, the next limiting factors, is dealt with by domestic cleaning. Several authors found vacuuming of home textiles inefficient against mites as well as mite products[10,48,61]. Steam cleaning was used in one experiment, where it removed a considerable proportion of the allergen present. Also up to 114 days after treatment no live mites were found, but three days after the start of the experiment as much as 99.96% of the mites on the control carpet pieces without steam cleaning could also not be recovered, making new tests of mite extermination necessary. A hot wash in a domestic washing machine suffices to exterminate a mite colony; the effect of dry cleaning being slightly less efficient. In addition, special cleaners for low-temperature machine washing, and for cleaning carpeting and upholstery were developed that showed a high mite extermination result[3,4,11,23-25,34,35,47].

The last remaining limiting factor, humidity, is the basis for a number of effective long-term mite avoidance procedures. The storage mite ecosystem exists only when humidity conditions allow for massive fungal growth: water activity of the finishing material of 0.70 or more (relative humidity of 70% or higher near the surface)[28]. Humidity in relation to mites will be addressed in the following section.

Mollier, outdoor climate, heating and cooling

Assuming equilibrium conditions, relative humidity (in %) may be calculated from temperature (in °C) and absolute air humidity (in g water vapor/m^3 air). Mollier was one of the first (in 1923) to describe these relationships in a simple diagram[36]. Absolute air humidity is limited at its maximum by temperature. The lower the temperature, the lower is the maximal absolute air humidity. The same relative humidity is correlated with different absolute air humidities, again depending on temperature. The relationship is non-linear (Figure 2). We added the global ranges for survival and for development of mites (*D. farinae* and *D. pteronyssinus* combined) and mean outdoor conditions. The total diagram is climatically specific and can be constructed for any community.

In Europe, outdoor air temperature and absolute humidity show seasonality. At the meteorological station of De Bilt, a village in the central region of the Netherlands, this results in mean outdoor relative humidities ranging from 95% in January (coldest month) to 75% in July (warmest month). In case no humidity is added to air or removed from it, heating will result in a lower relative humidity value and cooling in a higher one (Figure 2 and Table 3).

In the greater part of Europe, heating houses in winter is normal. Building engineers denote the corresponding outdoor climates as heating climates (heating of buildings with a proportional decrease of relative indoor humidity). In the Mediterranean, high summer temperatures call for cooling (cooling climate with a proportional increase of indoor relative humidity). When air-conditioning is practiced for cooling, the air may be dried in an extra treatment step resulting in a lower humidity[27,31,56].

Absolute indoor air humidity has absolute outdoor air humidity as its base value; the water vapor production indoors remaining after ventilation is added. At De Bilt this amounts to an indoor relative humidity of 40-45% in January and 65-75% in July for not-air-conditioned dwellings (Table 3). But mites are not directly exposed to air conditions; the little creatures do not live air-borne, but on surfaces.

In beds and upholstery absolute air humidity is increased due to transport of sweat from skin to textile. During use, gradients are established of both temperature and relative humidity: near the skin of the user 32 °C is measured and room temperature is measured at the furnishing's far end.

At De Bilt this results in 40-50% relative humidity near the skin of the user, which is not conducive to mite growth. At the edge of the furnishing 75-90% relative humidity occurs in January, while condensation may take place in summer (Table 3).

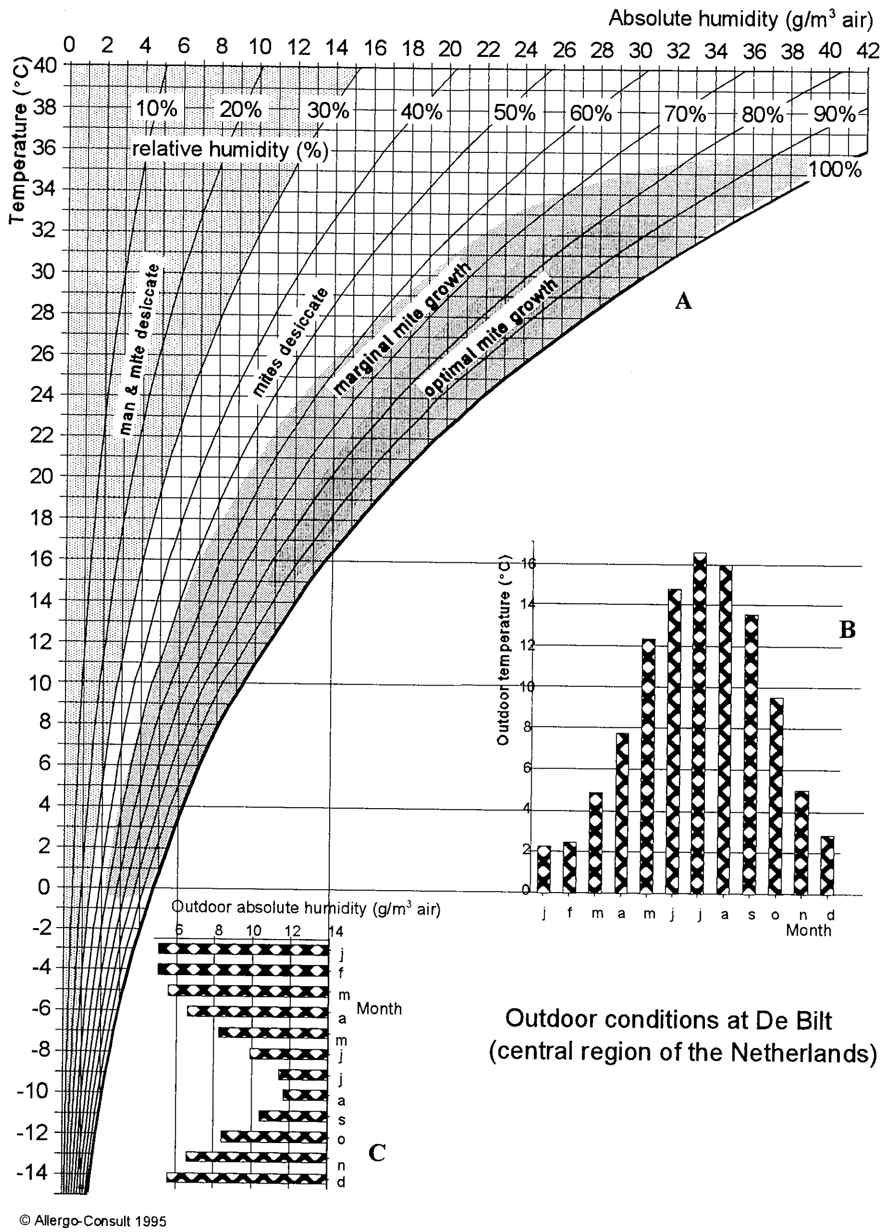

Figure 2. Relationships between moisture, temperature and house dust mites[7,54]
A. Mite development and survival; B. Monthly means of outdoor temperature;
C. Monthly means of outdoor humidity

In winter, mites may still desiccate in upholstered furnishings at De Bilt, providing the drying time in between periods of use is long enough and dry enough. Because of the hygroscopic nature of furnishing materials several consecutive dry indoor months are needed for mite extermination.

Carpeted floors do not usually receive sweat directly from skin. Floors with no heated rooms underneath and no floor heating, show a temperature drop (in relation to air temperature) depending on the temperature on the other side of the

Table 3. An example of relative humidity calculations (RH in %) for the Dutch village De Bilt, using prevailing monthly mean outdoor air temperatures (in °C) and absolute air humidities (AH in g water vapor/m³ air, RH in %)[7,30,54]*. It is assumed that no moisture penetrates the building envelope from the outside*

Compartment studied	Variate	Mean level in: January	July
Outdoor	Temperature	2	17
	AH	5	11
	RH	95	75
Indoor: room air	AH	7	11.5
	RH at 18 °C air temperature	45	75
	RH at 21 °C air temperature	40	65
Indoor: bed and upholstery (in use)	AH	14	16.5
	RH at edge, at 18 °C air temperature	90	condensation
	RH at edge, at 21 °C air temperature	75	90
	Temperature at skin of user	32	32
	RH near user	40	50
Indoor: floor (central section)	Temperature at 18 °C air temperature	16	16
	Temperature at 21 °C air temperature	19	19
	AH	7	11.5
	RH at 18 °C air temperature	50	85
	RH at 21 °C air temperature	45	70

floor and the level of thermal insulation of that floor. In the central part of the Netherlands this temperature drop is 2°C. At De Bilt this leads to 45-50% relative humidity in January, and 70-85% in July. 'Winter dryness' is supported by heating and thermal insulation, in addition to ventilation.

The smaller the temperature difference between indoor air and inner surface of the building envelope in winter, the higher the surface temperature and the lower the relative humidity will be in the boundary layer near surfaces of floor (in carpeting), wall or ceiling. To yearly exterminate mites and storage mites which may have been introduced in summer, one would expect thermal insulation levels to be dependent on outdoor winter temperature with higher values at lower temperatures. However, this is not the case. In the maritime Netherlands, for instance, mean January outdoor temperature is around 2°C and a thermal resistance of 2.5-3.5 $m^2 \cdot K/W$ is considered sufficient for a ground floor[2,21]. In continental (former) Czechoslovakia with a lower winter mean January outdoor temperature (-3°C in Prague) the national building code demands a thermal resistance for ground floors of only 1.0-1.5 $m^2 \cdot K/W$[1,16]. It has been reported earlier that floor temperatures differ within Europe[41]. Having building codes aim at limiting mite-exposure risk, should be a European wide future endeavor. Both thermal insulation limits and required ventilation levels are to be considered. In a recently introduced asthma classification of Dutch homes these data are incorporated[32].

An example:
dust mite distribution on carpeted floors

Harving et al. in Scandinavia used dry indoor winter climate to stop mite population growth[17,18]. However, Custovic et al. considered the strategy of reducing mite populations by lowering the domestic humidity not particularly useful in the U.K.[12], and Dornelas de Andrade et al. in Marseille (Mediterranean France) considered outdoor humidity conducive to indoor mite growth the whole year around[13].

The relevance of outdoor humidity to mite development is at variance within Europe[41]. We discussed earlier that mean outdoor January temperature values are a tool to predict the developmental possibilities of mites[8]. To extend this hypothesis further for carpeting, data were collected on mean January temperature[39], and on carpet dust analyses performed in late summer in different European sites[8,14,20,22,29,37,38,44,46,49,50,52,57,60,62]. Some unpublished results from

Charpin et al. (Hôpital Sainte-Marguerite, Marseille) could also be included. Noxious mite (allergen) levels were defined as ≥2 μg Group 1 allergens or 10 pyroglyphid mites or 0.6 mg guanine/g carpet dust, or Acarex® values from slightly positive onward[9,45].

All samples originated from houses of atopic patients. Some authors found that these were associated with a higher mite load, and some did not[26,38,53]. We expect therefore the collective body of data to be little influenced by the patient status of the households. Dwellings with air-conditioning were excluded from the calculations, because the air may be dried in an extra treatment step. Dust analyses from either the northern and the southern borders of Europe were scarce, and concern in some cases carpet dust mixed with dust from bedding or upholstery (probably leading to false higher probabilities), or with dust from smooth floors (only the Mediterranean, leading to false lower probabilities)[37,46].

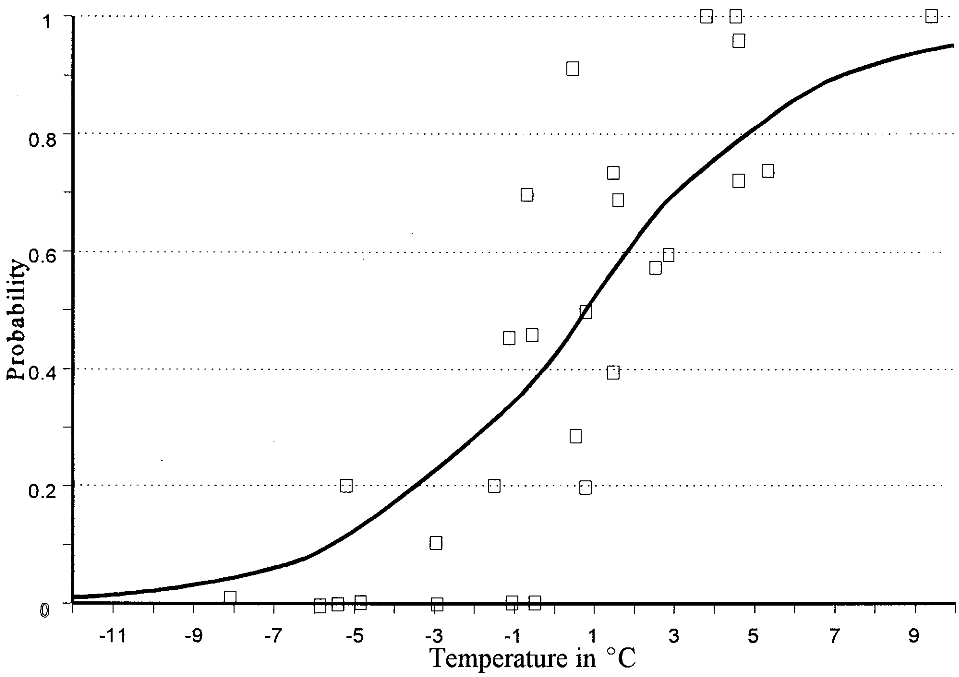

Figure 3. Probability of noxious mite (allergen) concentration in carpet dust in Europe based on monthly January outdoor temperature (T January) (1193 dust samples from 28 different locations □; logistic regression analysis: p = $1/(1+e^{+0.33-0.44 * T\ January}) * 100$; *Wald statistics: p<0.00005)*

With logistic regression analysis using one independent variable (mean January temperature in °C) the probability of noxious, mite-allergenic carpet dust occurring, has been estimated (Figure 3)[42]. Of all data, 73% were predicted by the model.

Noxious carpet concentrations were scarce when mean outdoor January temperature was -6 °C or lower. At higher temperatures the prevalence of significant mite pollution increases with temperature. Above 7 °C, the probability to have a carpet dust sample with a noxious mite (allergen) concentration surpasses 0.9 (Figure 3).

Now that the hypothesis has been accepted, the construction of a European mite-map for carpets and rugs is possible. For this first global map (Figure 4), we assume:

(a) 45% relative humidity at floor temperature of 15°C as the mite survival threshold (Figure 2);
(b) 60% relative humidity as limit for significant mite population growth (Fig. 2);
(c) a mean outdoor relative humidity in January of 100%;
(d) a mean temperature in all rooms of 20°C;
(e) a winter floor temperature of 15-16 °C for poorly-insulated floors of the lowest building level ('ground floors') and 17-19 °C for well-insulated ground floors or floors on higher storeys;
(f) rooms well ventilated with a net moisture production of Dutch indoor climate class II[19];
(g) heating in winter day and night, and in all rooms;
(h) a building envelope practically impermeable for moisture from the outside;
(i) no water leakages present
(j) no air-conditioning.

Taking into account outdoor temperature and prevailing floor temperatures (while outdoor air is considered saturated), six different risk areas may be distinguished: mean January temperature below -12 °C (*dark green*), -12 to -8 °C (*middle green*), -8 to -3 °C (*light green*), -3 to +4 °C (*yellow*), +4 to +7 °C (*orange*) and above 7 °C (*red*) (Table 4, Figure 4).

In the *dark green* area no living mites are expected in carpeting. In the *middle green* regions mites will survive on poorly-insulated ground floors only. It is generally too dry for mite population growth in winter. Improved thermal insulation of the building envelope, especially the lowest floor, will reduce mite populations.

Table 4. Calculated upper-limits of mean January temperature for 'no survival' and 'no development' of house dust mites on carpeted floors with different temperatures

Mite condition	Mean January temperature in °C / *Color denotes upper limit of the area in Figure 4*				
	Poorly insulated ground floor		Well insulated ground floor or floor of higher storey		
	floor 15°C	16°C	17°C	18°C	19°C
No survival (RH ≤45%)	≤ -12 *dark green*	≤ -10	≤ -8 *middle green*	≤ -6	≤ -3 *light green*
No population development (RH ≤60%)	≤ -3 *light green*	≤ +1	≤ +4 *yellow*	≤ +5	≤ +7 *orange*

RH = relative humidity

Light green Europe shows mite survival in winter on all textile-covered floors but no population growth. Only when winters are short, not all mites will be exterminated and some population development may occur in summer. Here too, an improved thermal insulation of the building envelope may decrease mite-allergen levels. An annual check in spring of mite-allergen pollution of carpeting will suffice to manage mite development.

In the *yellow* areas mites survive on all floors in textile floor coverings. Population growth may still be prevented by a high thermal insulation level of the floor. A spring and autumn check of mite pollution on floors is indicated from this region onward.

In the *orange* areas mites survive on all carpeted floors and mite population growth occurs on poorly-insulated and some well-insulated ground floors especially along the outer rims of the dwelling, as well as on some floors of higher storeys. Here, humidity is no longer a powerful limiting factor for mite survival or development. Improving thermal insulation of the ground floors will have a low impact.

Finally, in the *red* areas, mites survive and develop luxuriously on all carpeted floors in winter. When summers are hot and dry, cooler floors (with little thermal insulation) are mite-suitable in summer.

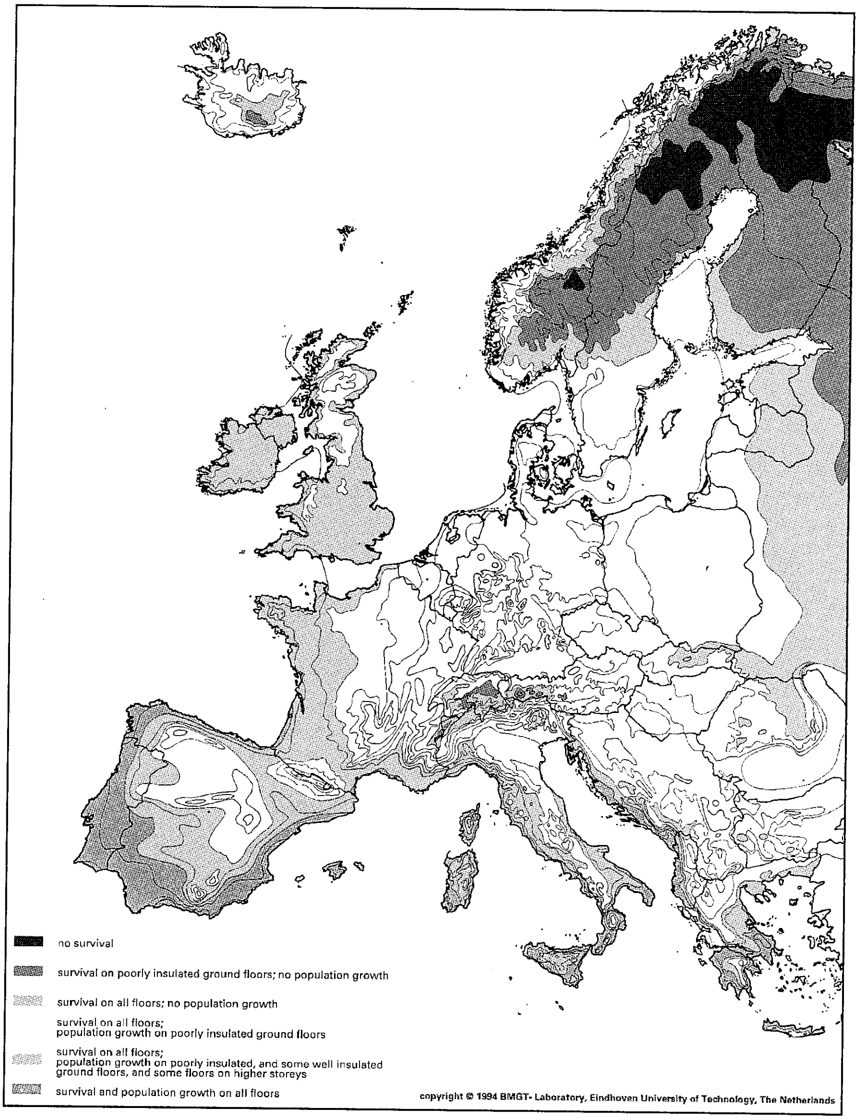

Figure 4. Six global risk-level areas for mite growth and survival in winter in carpeting of well-ventilated, heated rooms in Europe based on mean actual January outdoor air temperature. Outdoor temperatures are taken from Steinhauser[51] and Wallén[58,59]. In this thesis, this map is referred to as the European mite map

Conclusion

Manageable limiting factors for mite growth and development include humidity, availability of mite niches, fungi present, and protein content of the dust. Humidity management is a powerful tool in mite reduction in most, but not in all, European regions.

The distribution of mite abundance explains, in part, the differences in the prevalence of mite sensitization (Table 1). The lower value for mite sensitization in Scandinavia as compared to western-central Europe has been substantiated. The lower sensitization prevalence in the Mediterranean for the two mite categories, probably has a different basis. Here, more time is spent outdoors and ventilation levels in homes are high for comfort, both leading to less exposure to indoor mite allergens.

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Chapter 2.3

Mite exposure from carpeting in Ankara, Turkey, compared to similar climatic areas in Europe

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Submitted

Abstract

We investigated carpets in dwellings of Ankara (Turkey) to further test the outdoor climate hypothesis for mite allergy risk. Dust samples were collected from bedroom and living room carpets of 95 randomly selected homes in Ankara. Data on outdoor climate and housing characteristics were obtained. Of the tested bedroom and living room carpets 19% and 17%, respectively, had dust mite concentrations above the threshold level for sensitization. In the mite model, mean January outdoor air temperature predicts the percentage of carpeting with clinically relevant house dust mite concentrations.

According to data found and the mite model, outdoor climate in Turkish conditions (Ankara) is suitable for mite survival in carpeting on all floor levels in all seasons. Mite population growth in winter is possible on some poorly-insulated ground floors only. Thus, a minority of carpets present in dwellings in Ankara is relevant for mite-allergic patients. Individual variations in mite concentrations are explained by housing characteristics influencing floor temperature and relative humidity. The geographic mite model could be refined by also including outdoor humidity in January.

Introduction

House dust mite allergy is the most common allergy in Turkey[9,13,14], but the number of mites per infested textile has not yet been reported[1,2,4,12,21].

The global percentage of clinically relevant carpeting can be predicted[6]. In climates where houses are artificially heated, highest mite concentrations are found at the end of the non-heating period[6,18]. Length and dryness of the preceding heating period determine the level of mite pollution during this peak season[18]. A good indicator for length and dryness of this period is the mean January outdoor air temperature[18]. A model based on mean January outdoor air temperature has been validated with mite data from Europe. Based on this model a mite-risk map for Europe has been drawn[6].

In this report, house dust mite data in carpeting in Ankara are used to validate the geographic mite model for a heating climate outside Europe.

Materials and Methods

Data on Ankara

To validate the model for a heating climate outside Europe, we collected data in Ankara, Turkey: mean January outdoor air temperature and relative humidity were obtained[17], and dust samples were collected.

Dust samples were collected from bedroom and living room carpets of 95 homes located in different parts of the city of Ankara. Samples were taken during the peak season for house dust mites (July and August) in 1991. Homes were randomly selected irrespective of the presence of an atopic person in the dwelling. In 89 homes both bedroom and living room carpet were sampled. In one house carpeting was restricted to the bedroom, in another to the living room. Four dwellings consisted of one room only. Carpeting covered one-third to two-third of the floor surface in most cases.

House dust samples were taken by vacuuming one square meter in the center of the carpets for five minutes (Electrolux model D.728, 675 Watt, Västervik, Sweden). Mite numbers were assessed by the flotation method according to Bronswijk[5]. The percentage of carpets with more than 10 house dust mites per gram dust was determined[7].

To explain the influence of housing characteristics on individual differences between homes in Ankara, information was collected by a questionnaire on thermal insulation (construction materials of the dwelling), floor temperature (type of heating, floor level and type of smooth floor covering beneath the carpet), and relative water vapor production by the inhabitants (number of inhabitants divided by the number of rooms, with bathroom, toilet and kitchen excluded).

Model to predict percentage of clinically relevant carpeting

The model that calculates which floors have relative humidities above 45% during the coldest and driest winter month (January) was used (Chapter 2.2)[6]. It also predicts which floors will allow mites to multiply during winter (relative humidity above 60%). The relative humidity in a home textile depends on absolute humidity and temperature of the object. Absolute indoor air humidity consists of a build-up of absolute outdoor air humidity, leakages through the building envelope, and the net indoor moisture production by household activities that remains after ventilation[22]. For water vapor coming from outdoors with infiltration and ventilation air the absolute outdoor air humidity of saturated air is used. The model assumes that the building envelope is practically impermeable for moisture from the outside and that no water leakages are present. Remaining water vapor production during household activities was based on net moisture production in well-ventilated rooms of Dutch indoor climate class II (SBR publication[11]).

For the estimation of floor temperature we assume a continuous indoor air temperature of 20 °C in all rooms during winter. Well-insulated ground floors and floors of higher storeys have a floor temperature of 17-19 °C, whereas in poorly-insulated ground floors this is 15-16 °C[6].

The model has been validated earlier with mite data in late summer, when mite numbers are high[6]. The relation between mean January outdoor air temperature and percentage of clinically relevant carpeting could be described with the following formula:

$$p = 1/(1+e^{+0.33-0.44*T\ January})*100$$

p = percentage of carpets with clinically relevant mite (allergen) concentrations;
T January = mean January outdoor air temperature (in °C).
(Logistic regression analysis: 73% of data predicted, Wald statistics: $p < 0.00005$)

Statistical analysis

Influence of type of heating, floor level and smooth floor finishing on house dust mite numbers in carpeting was examined with Mann-Whitney U-test. Kruskal-Wallis was used to investigate the influence of construction materials. Both tests were used one-way. With Spearman rank correlation test corrected for ties the correlation was evaluated between relative water vapor production by inhabitants and mite numbers in carpeting. In all tests the confidence limit was set at 5%. Statistical analysis was performed by use of SPSS/PC version 4.0.1[19].

Results

The mite model predicted that 39% (95% confidence interval: 35 to 42%) of carpeting contains clinically relevant mite concentrations, since mean January outdoor air temperature in Ankara is -0.3 °C. When assigned to a mite risk area, Ankara belongs to mite risk area IV (Figure 1). Clinically relevant house dust mite concentrations were found in 17 (19%) of bedroom and in 15 (17%) of living room carpets (Table 1).

These results include 10 homes in which both living room and bedroom carpet exceeded the sensitization threshold. One out of four one-room homes contained a house dust mite concentration above sensitization threshold.

In bedroom carpets, significantly higher mite concentrations were found in homes heated by a stove than by central heating (Table 2). On both bedroom and living room carpets significantly higher mite concentrations were found on ground floor level and below than on higher floor levels. Bedroom floors finished with

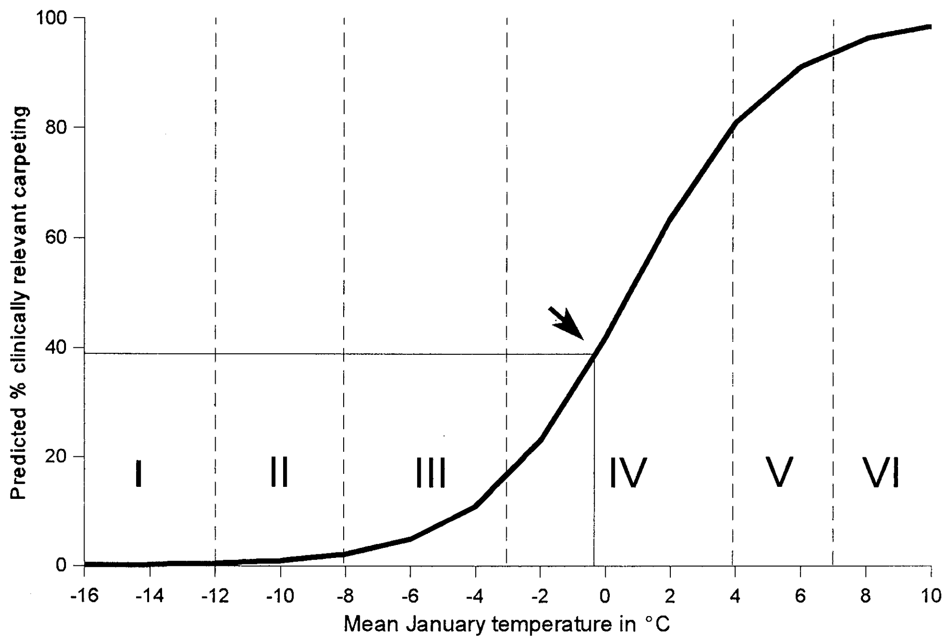

Figure 1. Mean January outdoor air temperature in relation to predicted percentage of carpeting with clinically relevant mite concentrations. Roman numerals refer to mite risk classes (after van Lynden-van Nes, et al.)[6]. ➛ denotes situation for Ankara

vinyl, mosaic or tiles showed significantly higher mite concentrations than wooden floors. Construction materials of the dwelling had no significant influence on mite numbers in carpeting.

The relative water vapor production by inhabitants has a significant influence on house dust mite concentrations in carpeting (Spearman rank correlation coefficient 0.45 for bedroom (p=0.00001) and 0.25 for living room carpeting (p=0.02).

Discussion

According to the mite model 39% of carpeting in Ankara should contain clinically relevant mite concentrations. The actually found percentage of clinically relevant carpets is considerably lower (17% for bedrooms and 19% for living rooms).

Table 1. Species list and occurrence of mites in carpet dust of bedrooms, living rooms and combined bedroom/living rooms in n (%) infested homes in Ankara. In bold Pyroglyphidae concentrations above 10 mites/g dust

	bedroom (n=90)	living room (n=90)	bed/living room (n=4)
	n (%)	n (%)	n (%)
ACARI	63 (70)	53 (59)	4 (100)
ASTIGMATA	58 (64)	51 (57)	4 (100)
Acaridae	30 (33)	26 (29)	1 (25)
Glycyphagidae	4 (4)	2 (2)	0 (0)
Pyroglyphidae present	52 (58)	43 (48)	4 (100)
Pyroglyphidae > 10 / g dust	**17 (19)**	**15 (17)**	**1 (25)**
Dermatophagoides farinae	2 (2)	2 (2)	0 (0)
D. pteronyssinus	51 (57)	42 (47)	4 (100)
Euroglyphus maynei	3 (3)	0 (0)	0 (0)
PROSTIGMATA	26 (29)	15 (17)	1 (25)
Tetranychidae	1 (1)	2 (2)	1 (25)
Cheyletidae	19 (21)	9 (10)	0 (0)
Tarsonemidae	7 (8)	3 (3)	0 (0)
Pyemotidae	2 (2)	1 (1)	0 (0)
Oribatidae	2 (2)	0 (0)	0 (0)
GAMASIDA	15 (17)	10 (11)	0 (0)
UNIDENTIFIED MITE	1 (1)	0 (0)	0 (0)

When allocated to a mite risk area both calculated and actual percentages refer to mite risk area IV (16-81% of carpeting contains clinically relevant mite exposure). In risk area IV mites will survive in textile floor covering on all floor levels in all seasons. Mite population growth is possible in winter on some poorly-insulated ground floors only[6].

The influence of collection and analysis of dust samples is difficult to estimate since the original data used to build the geographic mite model were not uniform.

Table 2. Housing characteristics and mite infestation of carpet dust. Significance levels between mite numbers (p) are shown per housing characteristic and room. Data in bold denote a significant difference (p<0.05)

		bedroom		living room	
	n	mite numbers median (range)	*p*	mite numbers median (range)	*p*
Construction materials					
concrete[1]	58	1.0 (0-117)	*0.22*	0.0 (0-145)	*0.17*
concrete+brick[2]	29	2.2 (0-150)		1.0 (0-230)	
concrete+brick+roof tiles[3]	3	5.0 (0-80)		2.0 (1.4-50)	
Type of heating					
central heating	41	**0.0 (0-117)**	***0.04***	0.0 (0-145)	*0.34*
stove	46	**2.0 (0-150)**		0.5 (0-230)	
Floor level					
above ground floor	53	**0.0 (0-80)**	***<0.001***	**0.0 (0-50)**	***0.03***
at or below ground floor	37	**3.0 (0-150)**		**1.0 (0-230)**	
Type of floor finishing					
wood	54	**1.0 (0-117)**	***0.02***	0.0 (0-145)	*0.12*
vinyl, mosaic or tiles	36	**2.6 (0-150)**		1.2 (0-230)	

1 concrete = floor, walls and roof made of concrete
2 concrete+brick = floor and roof made of concrete, brick walls
3 concrete+brick+roof tiles = concrete floor, brick walls, and roof tiles

In Ankara, dust samples were taken from one square meter in the center of the room. Next to cold outer walls relative humidity is higher than in the center of a room[6]. This would seem to diminish mite numbers when only central sections are vacuumed.

Presence of an atopic inhabitant was a selection criterion for the original mite data used to build the mite model. In homes of atopic patients, mite numbers might be higher since sensitization occurred[10,15], or lower when cleaned with mite-killing products or when relative indoor air humidity is reduced to avoid mite infestation[6]. We therefore assume no influence of presence of an atopic dweller.

A continuous indoor air temperature of 20 °C in all rooms during winter is another assumption in the mite model. In Ankara indoor temperatures are usually higher resulting in less humid living conditions for mites.

Another assumption of the mite model is that floor temperature on poorly-insulated ground floors is 15-16°C, and 17-19°C on well-insulated ground floors or floors of higher storeys during winter[6]. However, floor temperature depends not only on room temperature but also on insulation of the floor and the temperature beneath the floor. Almost 60% of the 90 homes were apartments situated above ground floor with heated spaces underneath (Table 2). This would increase floor temperature and lower relative humidity in carpeting while decreasing mite comfort[3].

Mean January relative outdoor air humidity in Ankara (78%) is somewhat lower than in the European areas for which the mite model has been built originally (on average 83%)[17]. This too could explain lower mite numbers than calculated by the model.

As has been demonstrated in other studies, we found the following housing characteristics associated with increased mite exposure: stove heating as compared to central heating[8]; basement or ground floor instead of higher floors[23]; and increased water vapor production by inhabitants[6,15,20]. All these factors increase relative humidity in carpeting. Vinyl, mosaic and tiles used as a floor finishing covered by carpet will increase relative humidity in the carpet, since they do not absorb household moisture leaving it all in the carpet. This is in contrast to wood on concrete as floor finishing. We could not demonstrate any influence of construction materials of the floor, since all floors were made of concrete.

In the future, mite exposure in a particular dwelling can be more specifically predicted when all characteristics influencing housing are included in a regional classification for homes. The recently developed health classification of Dutch dwellings is based on the national Building Code and may be used as example[16].

In conclusion, the geographic mite model can be applied to heating climates outside Europe as well. Since it is based on several assumptions, the current formula may only assign a climatic area to one of the six mite risk areas. In the future the geographic mite model could be refined by taking into account the actual outdoor air humidity in winter and asthma classification of a particular home.

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Section 3

Clinical relevance of common Dutch allergens

Although mite exposure is of primary importance for atopic diseases, other environmental factors may also influence the severity of the disease. Sensitization and exposure to other allergens may lessen the clinical outcome of mite allergen avoidance. This includes allergens that reach the patient by ingestion, inhalation or dermal contact. For some allergens, such as products of the skin yeast *Pityrosporum*, the question arises whether prophylactic therapy should be advised on a regular basis.

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Chapter 3.1

Towards an effective allergen avoidance

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Introduction

After an allergic infliction (expressed as rhino conjunctivitis, rhinitis, asthma or eczema) has been diagnosed, and treatment of the more serious symptoms initiated, avoidance of causal allergens may be discussed with the patient and other members of the household.

The therapeutic success of the different allergen avoidance measures depends on the individual clinical relevance of the allergens avoided, as well as on the efficacy of the measures actually taken[12].

Anamnestic results and laboratory data (such as Phadiatop results) collected to arrive at the diagnosis 'allergic disease' do not usually provide a complete basis for an effective avoidance plan. In this chapter we present a structured way to arrive at effective allergen avoidance procedures.

Sensitization and exposure

Biological and allergological investigations have shown that, under normal circumstances, people are exposed to a number of different allergens. At least 35 allergens of immunologically proven pathogenicity form a 'background exposure' shared in Western and Central Europe. They include members of the skin flora (only relevant in case of atopic eczema), food, and inhalant allergens of the indoor and outdoor environment. Intramurally, pets, house dust mites, pest rodents, pest insects, storage mites and fungi are common confectioners of indoor allergens (Table 1). In individual cases, additional exposures may be relevant, e.g. to guinea pigs when kept as a pet, to the mite *Carpoglyphus lactis* when working in the sugar industry, or to the fungus *Paecilomyces* when a saw mill is visited frequently.

Unfortunately, it is difficult to obtain extracts of all relevant allergens for routine diagnostic purposes. In all cases an attempt should be made to ascertain by history taking that no clinically relevant allergen remains unnoticed. As an example, the results are presented of specific serum IgE determinations in 50 adult atopic patients attending the outpatient clinic or admitted to hospital because of atopic eczema (Figure 1). Thirteen different allergens from the standard list of Table 1 were tested in at least 30 of these 50 patients. The percentage of positive results ranged from 23 to 88%, more than half of the number of patients being

Table 1. Common allergen exposure of proven pathogenicity in the built environment in Western and Central Europe (scientific names in italics)

SKIN FLORA (relevant in atopic eczema only)	
Pityrosporum orbiculare	
Staphylococcus aureus (only an irritant?)	
FOOD	
Potato (*Solanum tuberosum*)	
Egg white (*Gallus domesticus*)	
Hazelnut (*Corylus avellana*)	
Codfish (*Gadus morhua*)	
Cow's milk ((*Bos taurus*)	
Peanut (*Arachis hypogaea*)	
Wheat flour (*Triticum aestivum*)	
INDOOR INHALATION ALLERGENS	
Brown rat dander and urine (*Rattus norvegicus*)	
Cat dander (*Felis catus*)	
Dog dander (*Canis familiaris*)	
Dust lice - Psocoptera (*Lepinotus, Liposcelis*)	
Fungal mites - Tarsonemidae (*Tarsonemus*)	
German cockroach (*Blattela germanica*)	
House dust mites - Pyroglyphidae (*Dermatophagoides, Euroglyphus*)	
House mouse dander and urine (*Mus musculus*)	
Non-xerophilic fungi :	*Alternaria*
	Cladosporium
	Merulius lacrymans
	Penicillium brevicompactum series
	P. chrysogenum series
	P. frequentans series
	Scopulariopsis brevicaulis
Silverfish - Lepismatidae (*Lepisma, Thermobia*)	
Storage mites - Acaridae (*Acarus, Tyrophagus*)	
Storage mites - Glycyphagidae (*Glycyphagus, Lepidoglyphus*)	
Xerophilic fungi :	*Aspergillus glaucus* group
	A. restrictus group
	Phoma
	Wallemia sebi
OUTDOOR INHALATION ALLERGENS	
Birch pollen (*Betula*)	
Fungi :	*Alternaria*
	Cladisporium
	Helminthosporium
Mugworth pollen (*Artemisia vulgaris*)	
Grass pollen - Gramineae (*Lolium perenne, Secale cereale*)	

After van Bronswijk[3], Nilsson[10], Motala[16], Burgess[5], de Groot[9], Kieffer[11], Kort[14] and de Maat-Bleeker[15] sensitized to at least 7 of the 13 allergens (namely: house dust mite, dog dander, *Pityrosporum*, grass pollen, cat dander, wheat flour, peanut), and two showing relevant specific IgE values to only one of the 13 allergens. In 10 of the 50 patients, specific serum IgE against *all* 13 allergens was measured. Egg white and cod fish were positive in a minority of patients, the other 11 allergens were positive in the majority. One wonders what the results would have been had cockroaches and storage mites been included in the list to be tested.

More detailed analysis of the data on the 50 patients showed that when the number of different sensitizations is high, there is usually -clinically as well as immunologically (serum IgE-concentration) - a top group of 2 to 6 different allergens: the candidates for allergen avoidance.

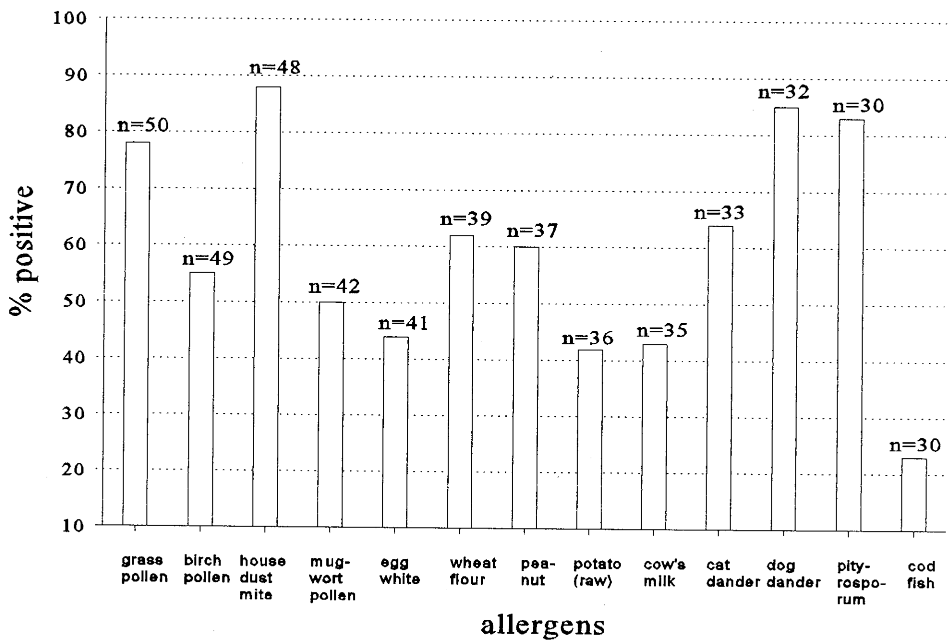

Figure 1. Sensitization to 13 different allergens in 50 atopic eczema patients measured with the Pharmacia CAP system. Serum values higher than 0.35 kU/l were considered to indicate sensitization[8]. Allergens are arranged in the order of frequency of testing. 'n' denotes the number actually tested

After the sensitization pattern of the patient has become clear, the actual exposure levels should be assessed. Here again anamnestic data play a key role, in addition to information on local allergen sources, composition of different food products, and ascertainment of indoor flora and fauna.

Routine assessment of exposure levels to indoor allergens can be performed with simple methods (Table 2); however, assistance of a trained biologist is usually needed.

Table 2. Assessment of exposure levels to indoor allergens (including skin flora) as performed routinely in the University Hospital of Utrecht, the Netherlands

Allergen source	*Assessment method*
SKIN FLORA	
Pityrosporum orbiculare	Culturing from skin
Staphylococcus aureus	Semi-quantitative culturing from skin
INDOOR INHALATION ALLERGENS	
Brown rat	Anamnestic
Cat	Anamnestic
Dog	Anamnestic
Dust lice	Sticky traps placed in cupboard or near outer wall *
Fungi - 1. in home textiles	Dilution plate method with vacuum cleaner dust**
2. on walls	Microscopic examination and culturing of scotch tape samples
German cockroach	Sticky traps placed in cupboard or near wall or room partitions *
House mouse	Anamnestic
Mites - 1. in home textiles	Semi-quantitative determination guanine content***
2. on walls	Mite flotation vacuum cleaner dust **
Silverfish	Sticky traps placed near wall or room partitions *

* = Sold as Trap-a-Roach Hoyhoy (manufacturd by Earth Chemical Co. Ltd., 3218 Sakoshi, Ako, Hyogo, Japan)

** = Bronswijk 1981[3]

*** = Sold as Acarex test (manufactured by Allergopharma J. Ganzer KG, Reinbek/Hamburg, Germany)

The actual clinical relevance of allergens for which sensitization and exposure are proven should be checked by history or, if possible, with trials of natural exposure (elimination diet, visits to places when certain inhalant allergens are in abundance). This will usually diminish the list of clinically relevant allergens for the individual patient. The resulting short-list forms the basis of the allergen avoidance plan.

Physician's role

At this point, the patient could be counseled by a specialist other than the treating physician. In some countries, specially trained nurses instruct the household members on the different avoidance options. Whatever the case, it is essential that some guidance is given and that the avoidance process is supervised. Murray[17] points out that in all reported successful mite allergen avoidance studies inspections were carried out.

The exception to the rule is, of course, treatment of the skin infecting species, such as *Pityrosporum* or *Staphylococcus*, which is purely a task for the physician[6,18].

For dietary measures to avoid food allergens, the patient should be referred to a qualified dietician and receive a list of the offending foods. The dietician must assure a complete nutrition when 'noxious' alimentary products are omitted[1,7].

Since the actual exposure to outdoor allergens depends on seasonal influences and local variability, the allergen avoidance advice given will include recognition of offending plants and avoidance of their neighborhood in the season of pollen flight or fungal dissemination. Plantings in the garden of the patient's home should also be discussed.

A common indoor pollutant is cigarette smoke. Although it acts as an irritant rather than an allergen it is an important contributing factor to the severity of respiratory symptoms[2]. If smoking cannot be prevented in the home or the work place, the success of anti-allergen measures will probably be limited.

Pets are not recommended in households with one or more allergic members. This includes pet species to which the patient is not yet sensitized. Sensitization might occur when the pet stays half a year to two years, or longer. Usually, it is harder to change the appreciation of household members towards pets than to pet allergens. The levels of most other indoor allergens are less dependent on behavior patterns of the inhabitants of the dwelling. Building construction and actual ventilation, together with interior decoration and cleaning performed, establish the success of allergen-producing rodents, house dust mites, storage mites and fungi in the home. Cockroaches are accidental intruders, but quickly adjuste to the home and increase in numbers; in this case a thorough chemical extermination program performed by a qualified exterminator is strongly advised.

Since mites are common in homes and sensitization is largely universal in the atopic population, we will address mite allergen avoidance in more detail[12,19]. It has been calculated that on the West coast of Europe allergy symptoms could be diminished by 50% after house dust mite extermination[4].

Avoidance of mite allergens

House dust mite avoidance starts with a simple plan of the home involved, drawn by the patient or another member of the household. Every room should be included, even attic and cellar spaces. On the plan the types of floor coverings are noted as well as the presence of furniture. From every area, two dust samples are taken by vacuum cleaner (1 min vacuuming for every m^2), one involving the complete surface of floor textiles, another consisting of the surface of furniture, bedding and mattresses. Vacuuming should not be performed by the patient, because of the resulting exposure to allergenic dust.

The different dust samples are tested for their mite product content by immunological, biological or chemical tests. A color reaction to guanine (a mite marker) that can also be used by household members is available (Table 2). The results of the mite product tests are noted on the home plan which reveals how the noxious mite concentrations are distributed over the home. This distribution pattern is the basis for the actual avoidance measures that may be taken.

When mites occur only at certain locations in the home, only localized measures are needed, e.g. removing a particular home textile from the dwelling, and washing it in a washing machine at 60°C.

When noxious concentrations are more widespread, a heating or ventilation problem may existc, causing a humid atmosphere[19]. In the long-term, ventilation should be increased and temperature inside the home be kept as constant as possible during the heating season, not allowing more than 2°C difference in the various rooms where textile is present, and between day and night[3]. It is also possible that the moisture problem is caused by rising or penetrating damp; a building engineer can be consulted about this. However, moisture reduction measures will reduce allergen exposure only after one or more seasons[19].

Therefore, in addition to these long-term measures, short-term chemical methods may be used. First choice is the household washing machine. Washing at 60°C or higher is effective in exterminating mites and removing allergen. For textiles that do not fit in a washing machine, special cleaning powders (for carpet) and foams (for furniture, mattresses) are on the market in most European countries[13]. Benzyl benzoate (an acaricide) is enveloped in particles fine enough to be devoured by the mites, and cleaning chemicals are added that remove allergen together with other dirt. Benzyl benzoate is a natural component of cinnamon, and is widely used in sweets to improve taste. This chemical mite-avoidance product has been extensively tested for efficacy, safety and practicality[12,19].

Cleaning of home textiles with powder or foam is a time-consuming process that must be performed at least 1-2 times a year. Household members may prefer to remove some of their textiles or buy new ones that are washable. All bedding, and even mattresses, are available nowadays that are washable in a household washing machine.

Washing and chemical treatment frequencies can be reduced when the improvements in heating, ventilation or insulation from rising or penetrating damp have resulted in a decrease of the water activity of textile surfaces to 0.55-0.60 or lower[19]. The necessity to treat may be assessed by the Acarex test.

A life-long project

It is wise to inform the patient that allergen avoidance is a life-long project. Choice of this type of therapy may change the outlook of the patient and other household members towards eating, house furnishing and cleaning, sports and outdoor activities.

It is important to instruct household members on how to handle the new situation, as well as showing them the advantages of choosing freely among different options, and remaining in control of their own situation.

After the patient has been informed about the real risks involved, some experimentation with allergen avoidance measures to establish under which circumstances allergic symptoms increase or decrease, may be encouraged in the household. These exercises, when properly supervised, will enable the household members to absorb allergen avoidance in their daily life. Then, allergen avoidance is no longer viewed as a form of medical therapy, but has become a chosen way of life. Formulating allergen avoidance measures as "do and don't" will not stimulate cooperation of the household members, resulting in less favorable results.

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Chapter 3.2

The skin yeast *Pityrosporum* is of minor clinical importance in atopic children aged 4 to 7 years

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Abstract

The antigenicity of the skin yeast *Pityrosporum* is subject to debate. To investigate whether colonization should be treated in atopic children, we studied exposure, sensitization, presence and severity of atopic manifestations in 27 asthmatic children with (n=11) and without atopic dermatitis (n=16) and 14 healthy controls aged 4 to 7 years. *Pityrosporum* could be cultured from the skin of all individuals. On normal skin, colonization was similar in both atopics and non-atopics, except on the forehead more *Pityrosporum* colony forming units were found in children with current atopic dermatitis. On eczematous skin significantly more *Pityrosporum* colony forming units were found than on comparable non-eczematous skin. The number of *Pityrosporum* colony forming units was significantly correlated with the severity score of flexural atopic dermatitis, but not of allergic asthma and rhinitis. Specific IgE antibodies were slightly elevated in less than a quarter of the atopic children. In all these cases specific IgE antibody levels comprised less than 3% of total IgE value, whereas levels to other allergens were much higher.

In conclusion, *Pityrosporum* belongs to the normal skin flora in children aged 4 to 7 years. Although skin colonization with this yeast can result in sensitization in atopic children, in this age group it is not a potent allergen source and does not need treatment on a regular basis.

Introduction

The skin yeast *Pityrosporum* has been cultured in 0-87% of the skin of young children aged 4 to 7 years[1-3,7,14,17]. No remarkable differences between atopics and non-atopics have been found[2,3,14]. However, skin colonization might lead to sensitization, especially in patients with atopic dermatitis. Sensitization against *Pityrosporum* has been demonstrated in 0-40% of atopic children of this age group[2,3,10,11,15].

The allergenic role of *Pityrosporum* in young children is not clear. In *Pityrosporum* sensitized children Nordvall and Johansson found more eczema, asthma and IgE-mediated food allergy. Sensitization against this yeast was correlated with severity of asthma. However, antibody levels were generally low or moderate and may not be clinically relevant[11]. In a later study, Nordvall et al. reported that in patients, aged 7 to 71 years with total IgE$\geq$3000 IU/ml, high IgE antibody levels to *P. orbiculare* were of the same magnitude as those to animal danders and pollens. However, of the 16 patients younger than 20 years, only three had elevated levels of *P. orbiculare* IgE antibodies[12].

In the treatment of adults with a positive prick test reaction to *Pityrosporum* and atopic dermatitis restricted to 'head and neck', antimycotics have been effective. In contrast, antimycotics were not effective in those who also had atopic eczema at other body sites[4]. For children aged 4 to 7 years such data are not yet available.

To investigate whether skin colonization with *Pityrosporum* should be treated with antimycotics in atopic children aged 4 to 7 years, we studied exposure and sensitization in relation to presence and severity of atopic manifestations.

Patients and methods

Patient selection

Twenty-seven atopic children, aged 4 to 7 years, were selected from the outpatient clinic of the University Hospital for Children and Youth `Wilhelmina Children's Hospital'. Healthy controls were selected from the outpatient clinic (n=2) and St. Dominicus primary school, Utrecht (n=12). All atopic children had moderate to severe asthma. In addition, 10 had concomitant atopic dermatitis and allergic rhinitis, 9 allergic rhinitis, and one atopic dermatitis. In the past, all had allergic rhinitis and 20 atopic dermatitis. Medication use was recorded. Approval of the Hospital Medical Ethics Committee, and parental informed consent were obtained.

Severity of allergic asthma was based on the international consensus report on asthma diagnosis and management and assessed by a paediatric pulmonologist (moderate asthma treated with sodium cromoglycate or nedocromil rated 2; treated with inhaled corticosteroids rated 3; severe asthma rated 4)[16].

Atopic dermatitis was diagnosed according to Diepgen et al.[6]. Local severity was estimated according to Costa by two independent dermatologists[5]. 'Extensiveness' of the simple scoring and 'severity' of the more elaborate scoring system were used. Extensiveness was rated 0 to 4 for feet, knees, legs, hands, arms, face, scalp, buttock, anterior and posterior aspects of the trunk (Cohen's kappa for inter-observer and both intra-observer validities based on 16 slides were 0.77, 0.23 and 0.36, respectively)[13]. Severity was rated 0 to 3 for erythema and oedema (0.27, 0.49, 0.41); vesicles, pustules and crusts (0.47, 0.47, 0.40); excoriations and cracking (0.08, 0.54, 0.06); scaling and dryness (0.09, 0.44, 0.19); and lichenification (0.50, 0.64, 0.40). For each topographic site we multiplied the extensiveness by the severity score (maximum score 4x3x5=60). Because of low inter- and intra-observer validities and the subjectivity of pruritus and loss of sleep, we did not use a total atopic dermatitis score[5].

The rhinitis symptom score of Kniest et al. was used after modification for primary school children[9]. Presence and duration of symptoms in the previous two weeks were rated:
1. itching of nose or sneezing;
2. nose secretion, nasal blockage, or nose bleeding;
3. itching or irritation of the eye.

Duration of symptoms was recorded for both day and night:
0. no symptoms;
1. symptoms present for 0-1 hours;
2. symptoms present for 1-3 hours; or
3. symptoms present for more than 3 hours.

All scores were summed (maximum score 3x2x3=18).

Determination of skin colonisation with Pityrosporum

All children were sampled using the 'tape-method' of Wikler et al.[18]. Samples were taken by "stripping" the skin with 1 cm^2 tape. Tapes were placed over a drop of sterile olive oil on a Sabouraud medium. Plates were incubated at 37°C. After 6-7 days *Pityrosporum* colonies were counted. No advice was given about stopping topical or oral treatment, or washing before sampling. None of the children used antimycotics. No antimycotics or antibiotics were added to the growth medium.

Samples were taken from two seborrheic (forehead between eyebrows, and behind ear) and two non-seborrheic areas (antecubital fossa and lumbal vertebral column) in children without atopic dermatitis. In children with atopic dermatitis samples were taken in each area from eczematous (preferably face and antecubital or popliteal fossa) and non-eczematous skin (forehead and antecubital fossa).

Immunological investigations

Of atopic children, concentrations of total serum IgE and specific IgE antibodies against *Pityrosporum orbiculare* and common allergens in the Netherlands were determined by Alastat-EIA (Diagnostic Products Corporation Nederland bv, Apeldoorn, the Netherlands). Tested were: birch, *Blattella germanica* (German cockroach), brown rat, cat, cow's milk, dog, egg white, grass, house dust mite

Dermatophagoides pteronyssinus, house mouse, mugwort, peanut, rabbit, storage mites *Tyrophagus putrescentiae* and *Lepidoglyphus destructor*, and a mould mixture (*Penicillium notatum*, *Cladosporium herbarum*, *Aspergillus fumigatus*, *Candida albicans*, *Alternaria tenuis*). Specific IgE antibody concentrations ≥ 0.35 IU/ml are considered positive.

Statistical analysis

Statistical analysis was performed by use of SPSS/PC version 4.0.1[13]. Mann-Whitney U-test was used to compare groups and the Spearman rank correlation test to determine correlations between variables. All results were one-way tested, confidence limit at 0.05.

Results

The number of *Pityrosporum* colonies could not be assessed in one child with atopic dermatitis and one control because of mould growth on the growth medium (an *Aspergillus* and a *Penicillium* species, respectively). Not enough serum was collected to estimate specific IgE in one atopic child without atopic dermatitis.

Pityrosporum could be cultured in all children in whom culture procedures were performed correctly. On non-eczematous skin, colonization was similar in atopics without atopic dermatitis and healthy controls. In atopic children with current atopic dermatitis, significantly more *Pityrosporum* colony forming units on the forehead were found than in healthy controls (Figure 1). At eczematous skin sites higher numbers were found than on comparable non-eczematous skin (Figure 2).

Atopic dermatitis score of the flexures was correlated with the number of *Pityrosporum* colony forming units ($r_s = 0.80$, $p = 0.02$, $n = 8$) (Figure 3). Severity scores for allergic asthma and rhinitis were not related to the number of *Pityrosporum* colony forming units. The use of medication was not associated with the number of *Pityrosporum* colony forming units.

Specific IgE against *Pityrosporum orbiculare* was slightly elevated in three of the 11 atopic children with atopic dermatitis and three of the 15 without, and comprised maximal 3% of total IgE value (Table 1). In all cases sensitization to other allergens was more prevalent, being above 100, up to 700 IU/ml. In children with atopic dermatitis *Pityrosporum* sensitization was inversely related to colonization on the non-eczematous forehead ($r_s = -0.67$, $p = 0.03$, $n=10$).

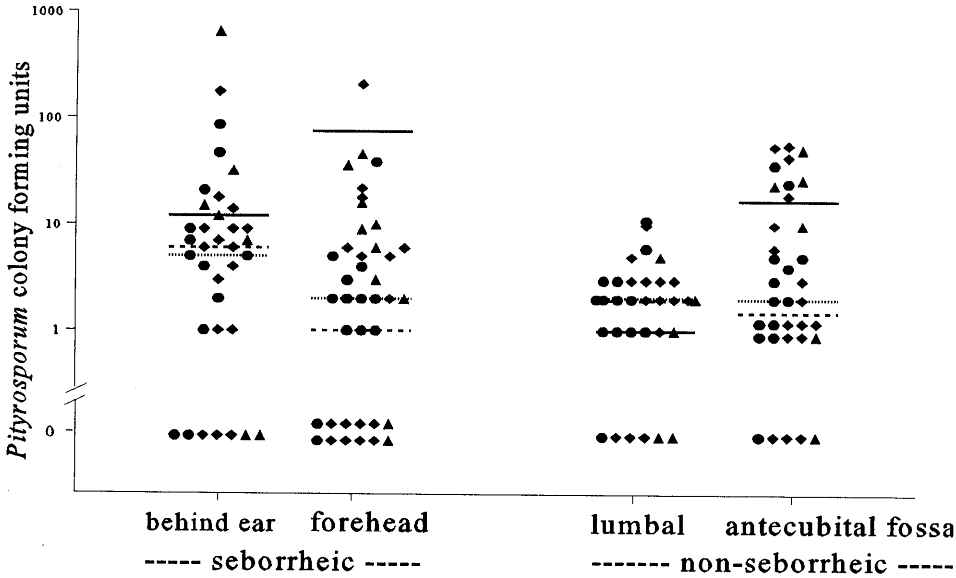

Figure 1. Number of Pityrosporum colony forming units cultured from different non-eczematous skin areas in healthy controls (●, median ·····), asthmatic children without (◆, median - - -) and with atopic dermatitis (▲, median ——).

No correlation between presence of current or previous atopic manifestation and specific IgE antibodies alone or as percentage of total IgE was found.

Discussion

Pityrosporum was detected in all children studied and successfully cultured. In similar studies on children of comparable age, the prevalence of *Pityrosporum* colonization was lower, ranging from 0-87%[1-3,7,10,14,17]. This difference might be caused by variation in sampling procedures. We used tapes[18] which have better access to all skin areas than contact plates[1,3] or the detergent scrub technique[7], and sampled four skin areas, including eczematous lesions and predilection sites for atopic dermatitis[8].

In contrast to others[1,3,7], we did not add antibiotics to the growth medium. Antibiotic supplements have no direct antimycotic effect. An indirect negative effect

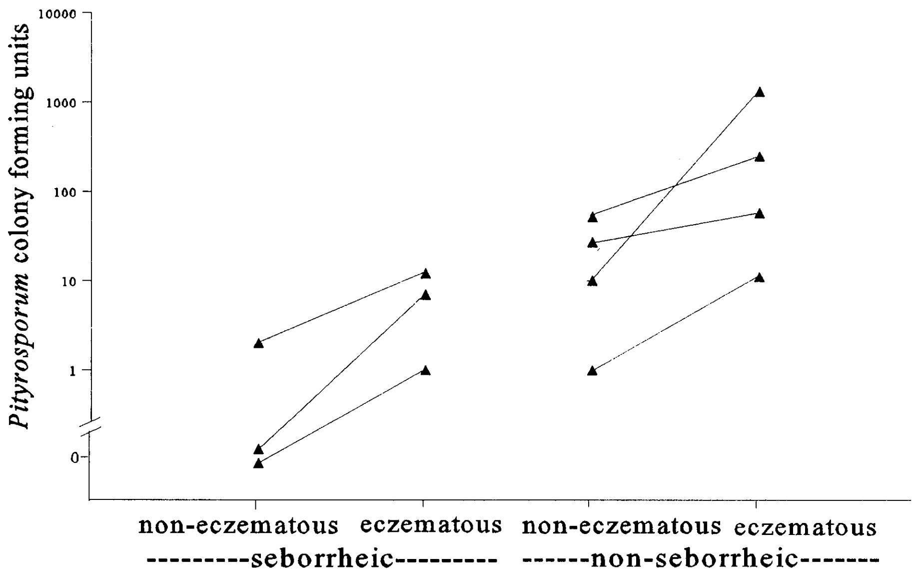

Figure 2. Number of Pityrosporum colony forming units cultured from different skin areas in children with atopic dermatitis. Lines relate number of Pityrosporum colony forming units cultured from non-eczematous and eczematous skin in the same patient.

on the metabolism of *Pityrosporum* is not yet established. We found no relation between topical or oral medication use and *Pityrosporum* numbers, suggesting no influence of medication on colonization.

In atopic children without atopic dermatitis no differences in colonization were demonstrated compared with healthy controls. Of these atopic children without atopic dermatitis, more than 80% was not sensitized to *Pityrosporum,* the remainder having only slightly elevated specific IgE antibodies to *Pityrosporum orbiculare*. In atopic children aged up to 10 years without atopic dermatitis (n=20), Broberg et al. reported no elevated specific IgE antibodies against *Pityrosporum*[3]. Nordvall and Johansson, investigating an older age group (7-18 years), reported elevated specific IgE antibodies to *Pityrosporum orbiculare* in 24% of the children with asthma (n=96), and in 21% of the children with rhinitis(n=108). In our study, skin colonization with *Pityrosporum* was not related to presence or severity of allergic asthma and rhinitis (current or in the past). These data suggest that although skin colonization with *Pityrosporum* may

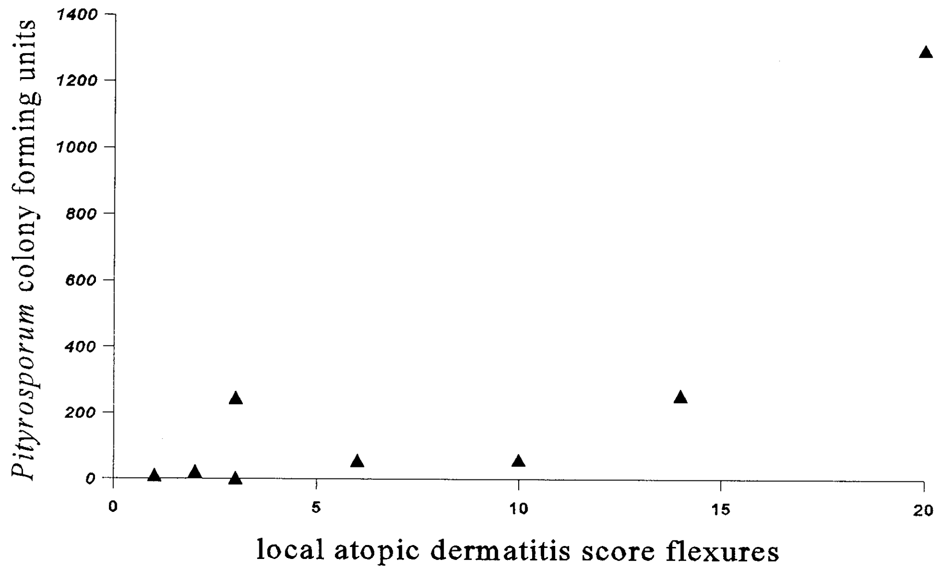

Figure 3. Local atopic dermatitis score of the flexures in relation to the number of Pityrosporum colony forming units

result in sensitization, it plays no important role in the etiology of allergic asthma and rhinitis in this age group.

In atopic children with current atopic dermatitis, significantly more *Pityrosporum* colony forming units were found on the forehead than in healthy controls. From eczematous skin significantly more *Pityrosporum* colony forming units were cultured than from comparable non-eczematous skin. Atopic dermatitis score at the flexures correlated with the number of *Pityrosporum* colony forming units (Figure 3). (While inter- and intra-observer validities were low, we must be cautious with the latter finding. However, we expect these validities would have been higher when measured in vivo instead of from slides.) These data suggest that *Pityrosporum* colonization might play a causal role in eczematous skin lesions. We found slightly elevated specific IgE antibodies against *Pityrosporum orbiculare* in only 27% of the atopic children with atopic dermatitis. Others also reported a small percentage of children with atopic dermatitis having elevated specific IgE antibodies[3,10,11,15].

In all atopic children, specific IgE antibodies against *Pityrosporum* levels comprised less than 3% of total IgE value. Specific IgE antibody concentrations

Table 1. Total serum IgE and specific IgE antibodies against common allergens in the Netherlands in 6 atopic children with elevated specific IgE antibodies against Pityrosporum orbiculare

	with atopic dermatitis			without atopic dermatitis		
	A	B	C	D	E	F
Total IgE	403	3126	422	471	751	398
birch	2.3	16.8	70.4	0.10	0.83	2.6
Blattella germanica	0.05	0.03	0.16	0.01	0.01	0.07
brown rat	0.20	0.34	0.39	0.01	0.01	0.05
cat	115.4	380.8	0.83	0.11	167.3	60.6
cow's milk	0.22	15.3	11.6	0.02	0.02	0.11
Dermatophagoides pteronyssinus	501.8	4.0	12.1	107.2	403.1	1.0
dog	57.6	255.3	0.64	0.08	0.42	19.0
egg white	2.1	220.0	11.3	0.02	0.01	0.33
grass	2.7	77.9	0.97	0.21	0.09	418.9
horse	n.d.	17.4	700.5	n.d.	0.20	n.d.
house mouse	0.15	0.36	0.12	0.02	0.01	0.03
Lepidoglyphus destructor	0.65	0.23	0.21	0.05	0.19	0.07
moulds	0.03	3.1	7.5	0.05	0.04	8.2
mugwort	1.2	0.50	0.15	0.17	0.06	0.99
nuts	20.1	417.4	13.1	n.d	0.28	0.78
peanut	75.3	437.0	4.7	0.21	0.23	1.1
Pityrosporum	11.4	3.0	5.7	1.5	0.75	4.3
rabbit	0.12	4.4	0.20	0.01	0.01	2.2
Tyrophagus putrescentiae	0.05	0.16	0.11	0.02	0.03	0.03

n.d. = not done

against other allergens were much higher (Figure 4). Lindgren et al., who studied 119 atopic dermatitis children aged 4 to 16 years, also found sensitization to

Pityrosporum less prevalent than to inhalant allergens[10]. Since *Pityrosporum* colonization is generally found in children aged 4 to 7 years, sensitization may occur gradually. In this age group, prophylactic therapy with antimycotics may produce undesired side-effects that are not warranted by the relatively low clinical importance of *Pityrosporum.* Avoidance of other relevant allergens might have less side-effects and make a more important contribution to the clinical outcome of allergen avoidance.

In conclusion, *Pityrosporum* belongs to the normal skin flora in children aged 4 to 7 years. Although skin colonization with this yeast can result in sensitization in atopic children, it is not an important allergen source and does not need treatment on a regular basis in children of this age group. Therefore, we did not include *Pityrosporum* evaluation in our randomized controlled mite allergen avoidance trial (Chapter 4.1).

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Section 4

Effectiveness of selective mite allergen avoidance achieved by households

Selective mite allergen avoidance meets the requirements of both technical and clinical efficacy. The advice has been proven effective when performed by professionals. We studied its effectiveness in the normal household situation with mite-allergic, asthmatic children, aged 4-7 years, in the Netherlands. Technical (= sufficient exposure reduction) and clinical effectiveness are described in Chapter 4.1. Because behavioral effectiveness is not optimal a separate chapter will be devoted to this topic (Chapter 4.2).

4.1 Selective mite allergen avoidance performed by households with asthmatic children: a randomized controlled trial
A.M.T. van Lynden-van Nes

4.2 Behavioral effectiveness of selective mite allergen avoidance in households with asthmatic children
A.M.T. van Lynden-van Nes

Chapter 4.1

Selective mite allergen avoidance performed by households with asthmatic children: a randomized controlled trial

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Abstract

Selective mite allergen avoidance addresses individually relevant allergens and irritants in the patients' whole environment; this has been proven effective in adult rhinitis patients when performed by professionals. We studied its effectiveness in asthmatic children when executed by the parents.

Twenty-eight households with moderately to severely asthmatic, mite-allergic children, aged 4 to 7 years, were included in an assessor blind, randomized, controlled trial for one year. Half of the households received individualized advice, the others general advice concerning mite allergen avoidance. Mite allergen exposure (measured as guanine exposure), total and specific IgE values, eosinophils, FEV_1, bronchial hyperreactivity and asthma severity were assessed before and after the trial. Symptom scores, peak flow and medication scores were recorded twice daily by one of the parents.

In both groups, parents executed the program incompletely. After one year, not all relevant mite allergen exposure sites had been removed. Guanine exposure was significantly reduced in beds in the treatment group as compared to the control group. No exposure reduction was seen in upholstery or in textile floor covering in both groups. Although no advice had been given concerning the school environment, exposure in upholstery was relevant in some cases. Clinical parameters did not alter in time and no differences were seen between the two groups.

Individualized advice proved to have no better clinical outcome than general advice, due to incomplete execution of avoidance programs by the household members. An analysis of avoidance behavior by parents is needed.

Introduction

After conflicting outcomes of many home studies of mite allergen avoidance (Chapter 1.2), a recently published meta-analysis of 23 randomized, controlled trials demonstrated no clinical effect in mite-allergic asthmatic patients[9]. The lack of clinical effect remained when only trials with proven exposure reduction were included in the analysis. In these latter studies, measures were restricted to patients' bedroom (n=4), or patients' bedroom and living room (n=2). In no case were all spaces in the home included in the avoidance program. The authors suggested that the lack of effect might be due to incomplete exposure reduction or to remaining exposure to other relevant allergens and irritants.

Selective mite allergen avoidance has the potential to be clinically effective[15]. It addresses all individually relevant allergen and irritant exposure in the whole patients' environment, and can be adjusted to the needs and skills of the household members. Individualized programs consist of measures of proven technical efficacy that are able to reduce mite allergen exposure 10-fold and below sensitization threshold. In a double-blind randomized trial, selective mite allergen avoidance proved to be effective in adult rhinitis patients when performed by professionals during one-year follow-up[15].

We aimed to investigate whether selective mite allergen avoidance at home would also be effective in young mite-allergic asthmatics when performed by their parents. Children aged 4 to 7 years, however, spend a part of their day at school. In schools in the Netherlands, exposure to mite allergens has been studied on floors only, but not in upholstery[29,33,34]. Therefore, before and after the one-year period in which the parents performed avoidance measures in their homes, mite exposure was also monitored at school.

Materials and methods

Set-up of study

The study was approved by the Hospital Medical Ethics Committee, and informed written consent from the parents was obtained prior to inclusion into the study.

In September-November 1994, 28 asthmatic children, aged 4-7 years, were selected from the out-patient clinic of Wilhelmina Children's Hospital, University Hospital for Children and Youth, Utrecht, the Netherlands. Patients included in the study were allocated to the treatment or control group at random. One child in the control group was removed from analysis due to moving house during the trial. Thus, the treatment group consisted of 14 children, whereas the control group of 13 children.

All children visited the outpatient clinic before avoidance advice was given (September-November 1994) and one year later (September-November 1995). Asthma severity, FEV_1 and bronchial hyperreactivity were assessed at both visits. Venous blood was collected for measurement of total IgE, specific IgE to common allergens in the Netherlands and eosinophil count. A pediatric pulmonologist examined all patients at both visits. Use of maintenance medication was continued during the study period. During the whole study parents recorded peak flow, medication use, and symptom scores for asthma, rhinitis and atopic dermatitis on diary cards daily. In this study we focus on asthma; rhinitis and atopic dermatitis symptom scores are not reported.

Dwellings and schools were visited in September 1994 and September 1995. Dust samples from all home textiles were collected and exposure to other indoor allergens was assessed. Time spent by the children in different environments was collected by means of a questionnaire before, halfway and after the trial. Although indoor moisture influencing activities (ventilation, heating and water vapor producing activities) were recorded, these data are not discussed in this study. In the Netherlands, attempts to dehumidify indoor climate will reduce mite numbers only after a few winters[23].

In January-February 1995 avoidance advice was given to the parents. The clinical assessor was unaware of the advice allocation group. Those who visited the homes (the author and a constructional engineer) were unaware of the clinical results collected by the pediatric pulmonologist or recorded by the parents during the study.

Patients

All patients had moderate to severe asthma[24] and were treated with inhaled corticosteroids (beclomethasone dipropionate or budesonide 200-1000 microgram daily) and short-acting bronchodilators (salbutamol or terbutalin) on demand. All children showed increased total IgE levels (≥25 IU/ml) and specific IgE against the house dust mite *Dermatophagoides pteronyssinus* (≥0.70 IU/ml). Those with a manifest food allergy had an allergen-free diet for at least 6 months before the trial that was continued during the trial. Sensitization and exposure to other allergens were also monitored.

In the treatment group 8 patients also had rhinitis, and 5 had atopic dermatitis. In the control group 11 also had rhinitis and 6 had atopic dermatitis. At the start of the intervention there were no significant differences between the groups, except for complaints at night and total days of school absence (Table 1).

Dwellings

All dwellings were situated in and around the city of Utrecht, the Netherlands. Most were one-family houses with living rooms on ground floor level and all bedrooms on higher storeys (in the treatment group 13 of 14, in the control group 11 of 13 dwellings). One treatment dwelling was an upstairs flat with all rooms on the first and second floors. In the control group, 2 households lived in an apartment above ground floor level. All homes were centrally heated, except for 2 family houses that were heated by a stove (1 in treatment, and 1 in control group). All homes had at least one home textile with a guanine concentration above the sensitization threshold for house dust mites (measured with Acarex tests).

Table 1. Baseline characteristics of the patients (September-November 1994). Mann-Whitney U-test on differences between treatment and control group, 1-tailed tested, α=0.05

	Treatment group		Control group		
	n	median (min - max)	n	median (min - max)	p-value
Bronchodilator use[1]	13	0 (0 - 21)	12	4 (0 - 18)	0.12
Asthma symptom score[1]	11	2 (0 - 30)	12	3 (0 - 44)	0.15
- complaints at night	11	0 (0 - 7)	12	1 (0 - 11)	0.04
- shortness of breath	11	0 (0 - 7)	12	1 (0 - 12)	0.11
- coughing	11	0 (0 - 8)	12	2 (0 - 15)	0.17
- physical activity	11	0 (0 - 8)	12	0 (0 - 10)	0.36
Total days of school absence	11	0 (0 - 0)	12	0 (0 - 5)	0.01
PFER mean daily variability (%)	12	6 (4 - 14)	9	8 (2 - 23)	0.27
FEV_1 (% of predicted)	14	102.5 (37-124)	13	94 (49-120)	0.18
PD_{20} (methacholine provocation dose steps) [doses in mcg]	14	4.5 (0 - 9) [34 (0-784)]	13	4 (0 - 8) [24 (0-392)]	0.45
Total IgE (IU/ml)	14	464 (99-5384)	13	578 (241-6000)	0.30
Specific IgE against the house dust mite (IU/ml)	14	145 (1-5247)	13	233 (2-12030)	0.42
Eosinophils absolute (10^9/l)	14	0.7 (0.3 - 1.7)	13	0.6 (0.1 - 1.8)	0.44
Eosinophils relative (%)	14	8 (2 - 16)	13	8 (3 -14)	0.43

n; number of patients
[1] median week score over 6 weeks

Mite allergen avoidance advice

Treatment group
At the start of the study, parents were informed about all sensitizations, hyperreactivities, and exposure relevant for their child. Sensitizations to relevant allergens were assessed anamnestically by the pediatric pulmonologist and confirmed serologically.

Hyperreactivities to irritants, such as environmental tobacco smoke, were mentioned by the parents. The level of hyperreactivity was measured by methacholine provocation. Baseline allergen and irritant exposure in the domestic environment was assessed by laboratory personnel.

The household members, assisted by the author, made an individual avoidance program based on the above information. The performance of the programs was checked after 3 months and at the end of the trial by means of a questionnaire (see Chapter 4.2). Feed-back was given to the parents after 4 months by the author during a home visit. During all home visits actually performed avoidance behavior was also observed, without mentioning this to the household members.

Households were given a choice between different measures by which mites are killed and their allergens removed. Mite-infested home textiles could be washed at 60°C, or put for one week in the household freezer at -20°C and washed at a lower temperature afterwards (every 6 weeks). Non-washable mite-infested home textiles could be treated with an acaricide 4 times yearly (Acarosan powder for carpets, or foam for bed materials and upholstered furniture, Allergopharma J. Ganzer KG, Reinbek/Hamburg, Germany). Special mite and allergen impermeable covers were available for daily used mattresses, quilts and pillows with guanine concentrations above sensitization threshold (Allergocover, Allergopharma J. Ganzer KG, Reinbek/Hamburg, Germany). Acaricidal application to encased bed materials was recommended twice yearly instead of 4 times yearly, because of the barrier function of the covers.

Households were advised to assess guanine exposure semi-quantitatively in non-covered home textiles every 3 months and in covered bed materials every 6 months, and to adjust their program according to the results. Acarex tests (Allergopharma J. Ganzer KG, Reinbek/Hamburg, Germany) were made available. Acarex is an over-the-counter test that measures guanine concentrations in 4 classes; it can easily be performed by household members. Households could order Allergocovers, Acarex and Acarosan free of charge.

Visual mold growth could be removed by peroxide-containing cleaning materials. Polluting indoor air by (tobacco) smoking and keeping pets indoors was discouraged. When a pet was present and the child was sensitized to that pet, removal of the pet followed by wet cleaning of all surfaces was advised. Specific humidity-reducing advice was given for each room of the dwelling. It was stressed that the entire individual program should be completed.

Control group

The control group received routine avoidance information, based on the - at that time - current Dutch general practitioner standard for asthma in children[4]. Advice included not to smoke at home, to vacuum clean regularly (2-3 times a week), and to wet clean smooth surfaces. In the bedroom, smooth floor covering and synthetic covers for mattress and pillow could be considered. Allowing pets in the home was discouraged. Reducing indoor moisture was advised, without mentioning how to achieve this.

Health classification of dwellings

To prevent individualized programs being more elaborate than needed to prevent asthma, we classified the participating homes according to the health classification of Dutch dwellings (Table 2). This classification is based on the extent of compulsory guidelines for inhabitant behavior to prevent asthma[19].

In this study, health classes of the dwelling were based on the lowest class reached by any of the following criteria:

1. the presence of heating facilities to heat the whole dwelling continuously
2. the presence of permanent ventilation facilities of rooms most visited by the children (patients' bedroom, parents' bedroom and living room).

Although thermal insulation of the building envelope will influence local relative humidity, this criterion was not used to classify the dwellings in this study. Other criteria of the health classification for dwellings are not directly related to living conditions for mites and were also not used[19].

Our advice was based on dwellings fulfilling the minimum qualities of the Dutch Building Code (✚-dwellings). However, our advice concerning changes in furnishing was not obligatory, and special covers were only optional for mite-infested beds (washing at 60°C was given as alternative).

Assessment of exposure

Dust samples were taken from all home textiles. Dust was collected from the outside of a cover if mattress, quilt or pillow were encased in a special mite and allergen impermeable cover. Dust was collected with a Hoover S 2856 (700 W, van Setten Hoover Service Center, Haarlem, the Netherlands), by vacuuming the whole surface with an intensity of 1 min/m^2. Dust samples were stored at -20°C for at least one week to kill any living mite present.

In the treatment group, Acarex tests were performed on dust of all textile-covered objects at the start of the study. A selective mite allergen avoidance program was made based on these results. If any of the objects had an Acarex test result that was not negative, that type of home textile was considered as mite infested. Samples were also considered mite infested when not enough dust was available for Acarex test.

For more accurate exposure assessment, HPLC (High Performance Liquid Chromatography) analysis was performed on samples from the main sites. These were: in the patients' bedroom the patients' bed, other beds, upholstery and textile floor covering; in the living room upholstery and textile floor covering; and in all other.

Table 2. Health classification of Dutch non air-conditioned dwellings based on the presence of permanent heating and ventilation facilities and required activity of inhabitants to prevent mite-based allergic asthma

Class		Building characteristics		Compulsory guidelines to prevent asthma
+++	Aim:	relative humidity ≤ 45% on floors and room partitions in all rooms during at least 3 successive winter months	Furnishing:	- no restrictions - special bed covers not needed
	Heating:	all rooms continuously in heating season	Cleaning:	no special cleaning needed
	Ventilation:	$> 2.0 \cdot 10^{-3}$ $m^3/s.m^2$ with 100% outdoor air		
++	Aim:	relative humidity ≤ 55% on floors and room partitions in all rooms during at least 3 successive winter months	Furnishing:	- no restrictions - special covers for mite infested beds
	Heating:	all rooms continuously in heating season	Cleaning:	during spring special cleaning if needed
	Ventilation:	$> 1.4 \cdot 10^{-3}$ $m^3/s.m^2$ with 100% outdoor air		
+	Aim:	Dutch Building Code quality level	Furnishing:	- no carpeting on ground floor - no upholstered furniture - special bed covers for all beds
	Heating:	no guidelines		
	Ventilation:	$> 0.9 \cdot 10^{-3}$ $m^3/s.m^2$ with 50% outdoor air	Cleaning:	frequent mite-exterminating cleaning
□	Aim:	not meeting Dutch Building Code criteria	Furnishing:	- no textile surfaces
	Heating:	no guidelines	Cleaning:	special cleaning will not result in a healthy dwelling under normal domestic conditions
	Ventilation:	$< 0.9 \cdot 10^{-3}$ $m^3/s.m^2$ with 50% outdoor air or less		

rooms the beds used daily To monitor exposure at school, dust samples were obtained from floor and upholstery in the child's classroom. In the classroom, upholstery was only sampled at the end of the trial to prevent alterations in cleaning habits during the trial.

HPLC was performed as follows. Dust samples of 50 mg (minimum 30 mg) were extracted in 0.6 ml 0.16 M natriumhydroxide (NaOH) and 20% methanol (MeOH). Homogenization of extracts was followed by centrifugation at 3800 rev/min for 1 minute. After extraction, remaining pellets were washed with 1 ml 20% MeOH followed by centrifugation two times for 1 minute each. Afterwards, filters were washed two times with 1 ml 20% MeOH. The extracted fluid was supplemented to 10 ml with demineralized water. Extracts were kept frozen at -20°C until analysis.

Guanine was measured using reversed-phase HPLC. Aliquots (100 µl) of the sample were injected into a HPLC system, consisting of a 996 Photo Diode Array Detector, 600S Pump Controller, 626 Non-metallic Pump, Millennium 2010 Data system (Millipore-Waters™, Marlborough, MA, USA), and a reversed phase column 250 x 4.6 mm I.D. (particle size 5 µm; Supelcosil LC-18-S, Supelco, Bellefonte, PA, USA). Column effluents were monitored at wavelength 260 nm. The flow cells had volumes of 100 µl.

Elutions were performed with a programmed non-linear gradient, starting with 96% 0.025 M potassium dihydrogenphosphate in 1% methanol (buffer A) and 4% 0.0375 M in 15% methanol (buffer B). After 5 minutes, this changed to 40% buffer A and 60% buffer B within 2 minutes. All mobile phases were degassed by continuous helium purging. The solvent flow rate was kept constant at 1.25 ml/min, the pressure at approximately 15,000 kPa and temperature at room temperature. The run-time was 10 minutes, followed by a 5-minute equilibration period. The correlation coefficient for guanine was at least 0.996[1]. Guanine concentrations in the dust (mg/g) were calculated. The detection limit was 0.01 mg/g dust.

Visual mold growth was observed by the naked eye and by smell, by the first author and a constructional engineer. Insect exposure was estimated with the use of sticky traps (Trap-a-Roach, RIWA BV, Breda, the Netherlands).

Serological assessment of sensitization

Concentrations of total serum IgE and specific IgE antibodies against common allergens in the Netherlands have been determined by Alastat-EIA (Diagnostic Products Corporation Nederland bv, Apeldoorn, the Netherlands). Investigations were performed on paired sera taken at the beginning and end of the trial, temporarily stored at -76°C, and assessed in the same test run. A reference system was run in all assays. We tested: house dust mite *Dermatophagoides pteronyssinus*, storage mites *Tyrophagus putrescentiae* and *Lepidoglyphus destructor*, German cockroach *Blatella germanica*, cat, dog, rabbit, house mouse, brown rat, birch, grass, mugwort, egg white, cow's milk, peanut and a mold mixture (*Penicillium notatum*, *Cladosporium herbarum*, *Aspergillus fumigatus*, *Candida albicans*, *Alternaria tenuis*). In individual cases, allergens to which allergic reactions were mentioned by the parents were also added to the test series. Specific IgE antibody concentrations ≥ 0.35 IU/ml were considered positive.

Absolute and relative eosinophil numbers in peripheral blood were counted at the start and end of the trial. The precision of counts was $0.01 \cdot 10^9$/l and 1%, respectively (Cell teller H1, Bayer, Mijdrecht, the Netherlands).

Assessment of asthma severity

At the end of the study, both the assessing pediatric pulmonologist and the parents were asked to grade the severity of the child's asthma as compared to the start of the study. They could choose between better, same or worse. The physician's evaluation was based on the patients' medical dossiers. The parents' evaluation was based on their own observation.

Lung function

Lung function tests were performed using a pneumotachometer system (MasterScreen Pneumo, Erich Jaeger, Germany)[8]. When the patients had optimized their technique, the best of at least 5 flow-volume loops, according to the ATS criteria[2], was taken for the calculation of baseline FEV_1 as a percentage of predicted for height. Methacholine provocation was performed according to a standardised protocol by dosimeter[8]. Methacholine was administered in steps of doubling doses 3, 6, 12, 24, 50, 98, 196, 392 and 784 microgram methacholine. Provocation was continued until the dose at which FEV_1 had dropped 20% or more from baseline was reached (PD_{20}). Hyperreactivity was defined as a methacholine $PD_{20} < 784$ mcg (= 9 dose steps)[25]. To exclude the influence of variability over the day, all respiratory tests before and after the trial were performed in the same patient at the same time of the day. Tests were performed after withholding all bronchodilators for at least 8 hours. Reference values were taken from Zapletal[32].

Diary cards

Parents recorded:

1. peak expiratory flow rates (PEFR) (twice daily: before breakfast and bedtime medication; best of three blows with mini-Wright peak flow meter of Glaxo Wellcome B.V., Zeist, the Netherlands),
2. symptom scores (daily), and
3. medication use (daily) throughout the study period using a 2-week diary card.

Data were included in the analysis when more than 2 weeks were recorded completely.

The *PEFR* meters utilized were calibrated and no data were used if the rate, as measured by stimulated peak flows of 340 L/min, varied by more than 10% from the calibrated meter (Dept. of Pediatrics, subdivision Respiratory Medicine, Erasmus University Rotterdam, Sophia Children's Hospital, Rotterdam, the Nether-lands). PEFR recordings of 3 patients of the control group differed by more than 10% from the calibrated meter at the end of the study; these data were excluded from analysis.

Mean daily variability of PEFR was estimated by the formula[5]:

$$variability(\%) = \frac{max\,PEFR - min\,PEFR}{mean\,PEFR} * 100$$

The median variability per 6-week period was used in calculations.

Symptom scores were developed for

A. nocturnal symptoms
 0=no complaints;
 1=slept well, but slightly wheezing and/or coughing;
 2=awakened 1 to 3 times due to shortness of breath and/or coughing;
 3=slept inadequately due to shortness of breath and/or coughing,

B. daytime cough and C. daytime wheeze and shortness of breath
 0=no symptoms perceived;
 1=symptoms present for less than one hour;
 2=symptoms for 1 to 3 hours;
 3=symptoms for more than 3 hours,

D. daytime activity
 0=not restricted;
 1=slightly restricted (needs occasional rest during activities);
 2=moderately restricted (needs rest during activities);
 3=severely restricted (is not able to perform activities).

Twenty-four-hour asthma symptom scores were calculated by adding the 4 item scores for one day; 24-hour scores were summed per week. The median of six-week scores at the start of the trial and one year later were used for calculations. Numbers of days absent from school due to asthma were also counted in these 6-week periods.

Medication. Consumption of maintenance medication and bronchodilators was recorded daily. Scores of each medication type were summed per week and the median of six-week scores at the start of the study and one year later were used for calculations.

Statistical analysis

To compare data before and after one-year intervention, data on guanine exposure, total IgE, specific IgE, eosinophilia in blood, mean PEFR daily variability, FEV_1, symptom and medication scores after one year were indexed by dividing these by the values at the start. To prevent zero-values, 1 was added to symptom and medication scores and 0.1 was added to days of school absence before the calculation. In case of methacholine provocation dose steps, the start value was subtracted from the end value.

Mann Whitney U-test was used to compare changes in time within and between groups. To study differences between groups, end data indexed by values at the start were used. The correlation between physician's and parents' evaluation of the course of asthma was tested with Spearman rank correlation coefficient. The confidence limit was set at 0.05. Statistical analysis was performed by use of SPSS for Windows version 7.5.

Results

The physician's assessed score of the course of asthma severity was not recorded in one child of the treatment group. On diary cards, for one child of the treatment group parents scored symptoms only during one week at the end of the trial. No reliable recordings of peak flow rates and symptom scores were available in two other patients in the treatment group and one patient in the control group. No reliable recordings of bronchodilator use could be obtained from one patient in each group. Number of hours spent at home and at school were not recorded for one child in the control group. All these data were excluded from analysis.

The number of home textiles analyzed by HPLC differed per home and time point (Figure 1). This was due to the presence of home textiles and group allocation (dust had been used for Acarex tests to make a selective avoidance advice in the treatment group only). In the treatment group 1 to 5 (median 3.5) dust samples per home were analyzed before, and 1 to 8 (median 3) one year later. In the control group these figures were 3 to 7 (median 5) before, and 2 to 7 (median 6) one year later.

Health classification of dwellings

Our selective mite allergen avoidance advice was based on dwellings only just meeting Dutch Building Code criteria (✚-dwellings) (Table 2). However, one treatment and one control household lived in a ✚✚✚-dwelling (household number 10 in Figure 1a, and 6 in Figure 1b, respectively). In both latter dwellings no guanine concentrations above sensitization threshold were found in any of the dust samples analyzed by HPLC before advice. (During the selection stage Acarex tests were mildly positive in some home textiles.) Patients in both households were exposed to tobacco smoke during the trial, and both recently introduced a pet (to which no elevated specific IgE concentrations were - yet - detectable).

Achieved effectiveness of program

Behavioral effectiveness
Before advice, most households had smooth floor covering in patients' bedrooms (10 in both groups). Only 2 treatment and 3 control households had specially covered patients' bed in part (mattress and pillow), according to the Dutch asthma treatment guidelines[4]. In all those cases in which the patients' beds were covered the bedroom floor was smooth. In both groups, none of the households had previously been instructed how to assess guanine exposure and how to perform acaricidal cleaning.

In the treatment group, all households executed avoidance measures at least once after advice was given (based on results of baseline guanine exposure assessment by our laboratory). Covering of mite- infested beds was performed by all. Of 14 households, 7 continued guanine exposure assessment, followed by mite-exterminating cleaning measures if necessary. Of these, 3 households did this 3-monthly (i.e., 4 times a year) as advised. One household tested every 3 months all home textiles established as mite infested at baseline. In none of the households were all home textiles included in the follow-up treatments.

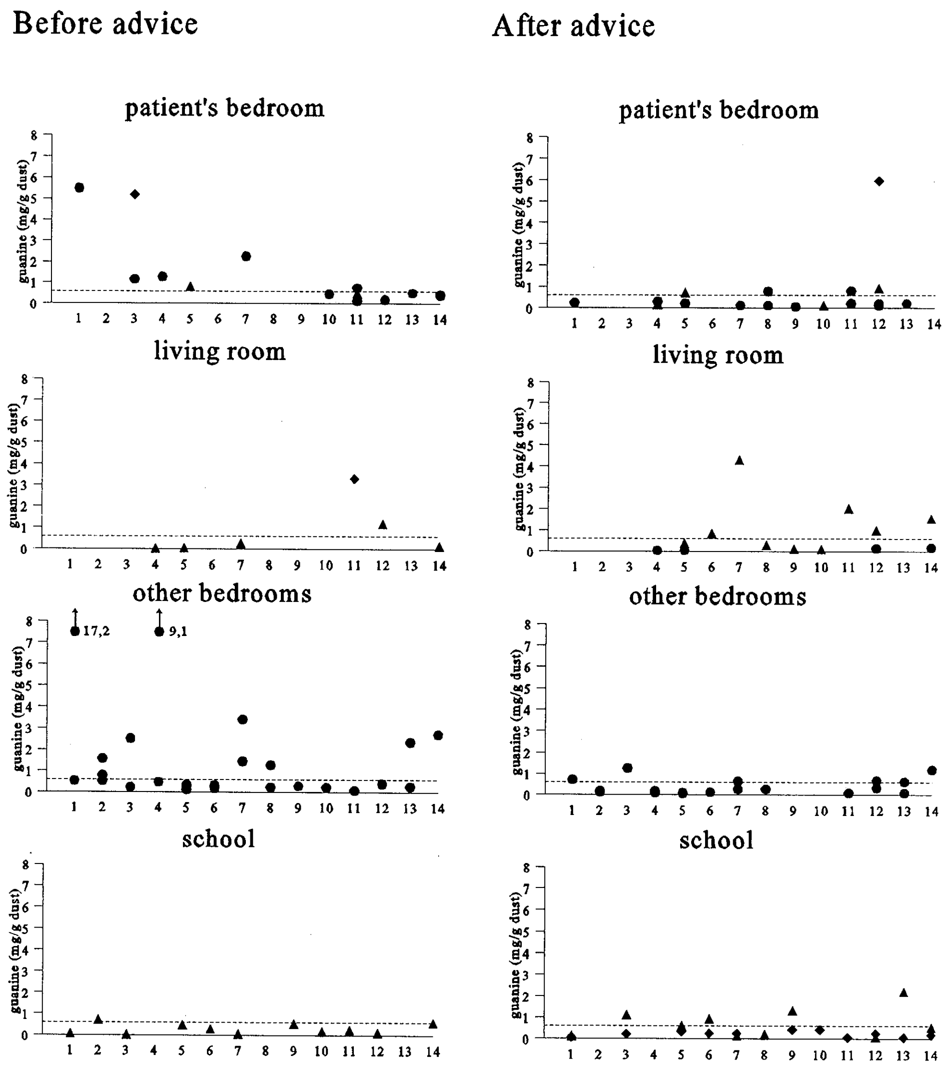
In the control group, no mite-exterminating cleaning measures, such as washing at 60°C or applying an acaricidal cleaning agent, were performed for the first time after advice was given. None ordered covers for mattress or pillow during the trial. Only one child moved from a room with textile floor covering to a room with smooth floor covering.

Technical (i.e. exposure reduction) effectiveness of measures
Beds Of all beds in all bedrooms of both groups, 53% were mite infested (contained guanine concentrations above sensitization threshold) before intervention.

In all treatment households mite-infested beds were treated (Table 3). However, in 5 beds the special quilt covers were removed during the study period because the cover caused sweating, or because the quilt with cover slipped off the bed. These quilts had been treated with an acaricide and contained no noxious guanine concentrations after the trial.

Patients' bedroom. Before intervention, of 5 of 27 patients' beds, mattress and pillow were already encased with mite allergen impermeable covers (2 in the treatment; 3 in the control group). Three of 4 beds analyzed by HPLC, had guanine concentrations above sensitization threshold on the outside of the cover.

a. Treatment group



b. Control group

Before advice / After advice

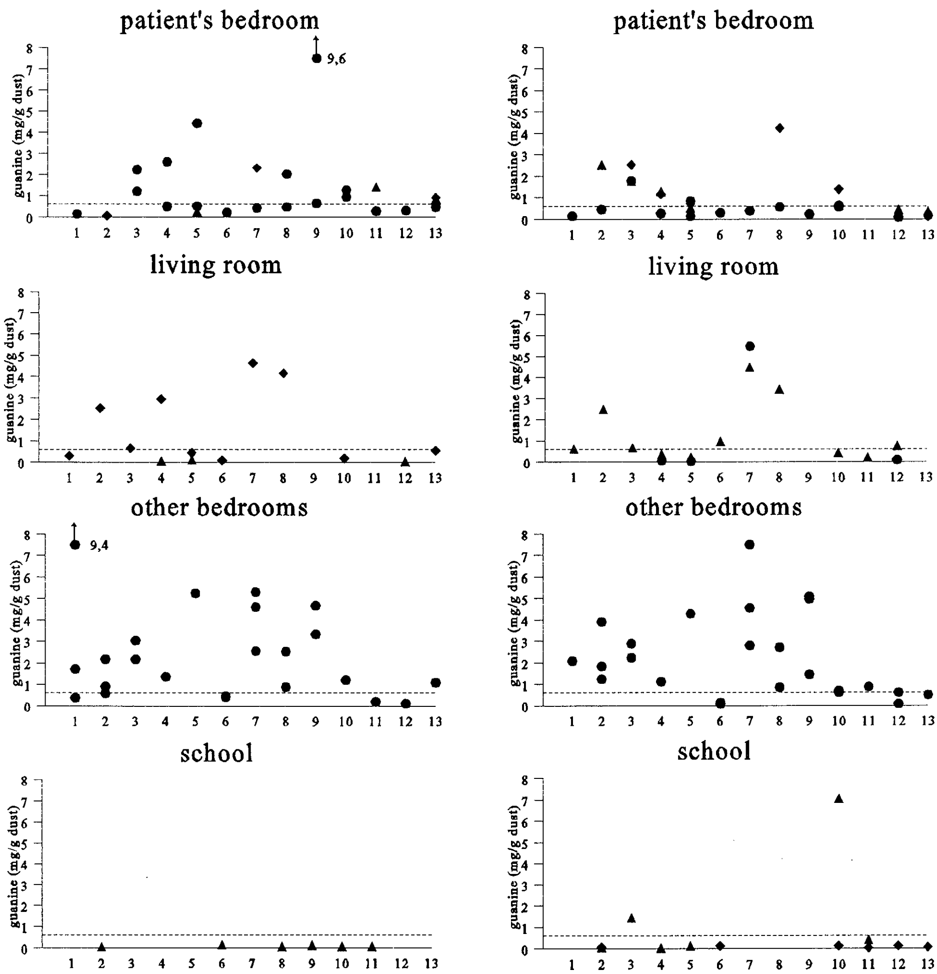


Figure 1. Guanine concentrations in beds (●), upholstery (◆) and textile floor covering (▲) in different rooms per household before and one year after advice was given a. in the treatment group; b. in the control group. At the x-axis: numbers refer to the individual households. Dashed line indicates threshold for sensitization to mites. Guanine concentrations above 8 mg/g dust are indicated with an arrow.

Table 3. Mite exposure before and after the trial (guanine in HPLC > 0.6 mg/g dust) and performed avoidance measures in the treatment group

Room	Home textile	Performed avoidance measure	guanine analysis (positive/total) Before	After
Patient's bedroom	patient's bed (n=14)	all covered[1] (n=9)	2/6	0/5
		covered[1] or washed (n=3)	2/2	0/2
		covered[1] in part (n=2)	0/2	0/2
	other beds (n=3)	all covered[1] (n=2)	1/2	0/1
		covered[1] or washed (n=1)	0/0	1/1
	upholstery (n=12)	washed (n=6)	1/1	2/3
		washed or acaricide (n=2)	0/0	0/1
		acaricide (n=4)	0/0	0/0
	floor textile (n=6)	acaricide (n=4)	1/3	1/3
		no treatment[2] (n=2)	0/0	1/2
Living room	upholstery (n=13)	washed (n=2)	0/0	0/0
		washed or acaricide (n=1)	0/0	0/1
		acaricide (n=7)	1/1	3/5
		no treatment[2] (n=3)	0/0	2/3
	floor textile (n=5)	acaricide (n=4)	0/3	0/2
		no treatment[2] (n=1)	1/1	0/1
Other bedrooms	parents' bed (n=14)	all covered[1] (n=13)	5/10	3/7
		covered[1] in part (n=1)	1/1	0/0
	siblings' bed (n=16)	all covered[1] (n=9)	3/9	0/8
		covered[1] or washed (n=4)	0/3	2/3
		covered[1] in part (n=1)	0/1	0/0
		no treatment[2] (n=2)	0/0	1/1

n; number of households
[1] bed materials were also treated with an acaricidal cleaner every 6-months
[2] no mite-exterminating treatment

In the treatment group, all patients' beds were covered. (Covers of the 2 beds that were covered before the trial remained in situ.) After covering, none of the covered beds contained noxious guanine concentrations (Table 3). Guanine exposure diminished significantly from 0.5 (median, range 0.1 - 5.5 mg/g dust; n=9) to 0.2 (0.1 - 0.3; n=9) (p=0.01) (Figure 1).

In the control group, only one patient's bed was covered with a mattress and pillow encasing, and the quilt was washed at 60°C every 6 weeks throughout the study period. This bed contained no relevant guanine exposure after the trial, whereas not enough dust was available to assess guanine exposure at the start of the trial. In the control group, 3 of the 10 patients' beds analyzed by HPLC contained noxious guanine concentrations. Guanine concentrations did not change significantly [before 0.5 (median, range 0.1-2.2; n=12); after 0.3 (0.1-1.8; n=12)] (Figure 1).

Parents' bedrooms. In the treatment group, mattresses, pillows and quilts were covered with mite and allergen impermeable covers in 13 cases. Of the 7 beds analyzed by HPLC, 3 still contained guanine concentrations above sensitization threshold after the trial (Table 3). In the control group, beds were not treated. When comparing both groups, there was no significant change in guanine exposure.

Siblings' bedrooms. In the treatment group, mattresses of 4 siblings' beds were covered but pillows and quilts were only covered in part and regularly washed in part. Of the 3 beds analyzed by HPLC, 2 beds still contained noxious guanine concentrations (Table 3). These beds had no noxious concentrations at the start of the study. One was washed at a lower frequency than recommended, the other was in a humid dwelling (Silver fish present). Also, a newly bought bed of a younger sibling was not treated and contained noxious mite concentrations at the end of the study (Table 3). In the control group, beds were not treated. At start, guanine exposure in the treatment group was significantly higher than in the control group (p<0.01). Guanine exposure in beds in siblings' bedrooms reduced only in the treatment group (p=0.03).

Upholstery. In the treatment group, guanine exposure could be assessed by HPLC in soft toys of only one patient's bedroom (5.2 mg/g dust) and upholstered furniture of one living room (3.3 mg/g dust) (Figure 1). Dust had been used for Acarex tests before. Of all upholstery of both groups, 56% contained guanine concentrations above sensitization threshold before intervention.

In patients' bedroom, guanine concentration was 0.4 mg/g dust (median, range 0.1-0.9; n=4) after advice in the treatment group (Figure 1a). Soft toys were washed at 60°C in 6 households (Table 3). Of the 3 households in which soft toys were washed and analyzed by HPLC, 2 still contained guanine concentrations above sensitization threshold after the trial. In both, treatment frequencies were lower than advised.

In the living rooms, guanine concentration in upholstery of living rooms was 0.8 (0.1-4.3; n=9) after advice in the treatment group (Figure 1a). Upholstered furniture was treated with an acaricidal cleaner in 7 households (Table 3). Of the 5 analyzed by HPLC, 3 still contained a guanine concentration above 0.6 mg/g dust after one year (Table 3); however, these objects had been treated only once (n=2) or 6-monthly (n=1) instead of 3-monthly. In 3 living rooms, upholstered furniture was not treated with a mite-exterminating method (Table 3). In 2 of them, guanine concentrations were above sensitization threshold after intervention.

In the control group, soft toys were washed at 60°C monthly in only one patient's bedroom. In this case, not enough dust was obtained to assess guanine exposure before and after intervention. In this group, guanine exposure did not change (Figure 1).

Textile floor covering. Guanine concentrations were rather low at the start of the trial in textile floor covering in patients' bedroom and living room (Figure 1). Of all textile floor covering, 27% contained guanine concentrations above sensitization threshold.

Neither treatment of carpeting with an acaricidal cleaner (treatment group) nor regular vacuum cleaning (control group) were able to significantly lower the already low guanine concentrations in patients' bedroom and living room.

Technical (i.e. exposure reduction) effectiveness of whole program

Only 2 treatment and 1 control households achieved a decrease of guanine content to below sensitization threshold in all home textiles estimated by HPLC (household numbers 2 and 4 in Figure 1a, and household number 13 in Figure 1b, respectively).

A high baseline guanine concentration (above 6.0 mg/g dust) was found in 2 dwellings of the treatment group and 2 dwellings of the control group (household numbers 1 and 4 in Figure 1a, and household numbers 1 and 9 in Figure 1b, respectively). A more than 10-fold reduction of these high baseline levels to below the sensitization threshold was achieved only in the 2 treatment households. In both households, these high guanine concentrations were found in parents' beds and assessment of guanine exposure followed by acaricidal cleaning had been executed 3-monthly. After one year, no other relevant exposure site was detected. In the control group exposure was reduced, but not all reduction was to below sensitization threshold (Figure 1).

Clinical effectiveness

Most clinical parameters did not improve significantly in both groups (Table 4). No significant differences were seen between treatment and control group at the end of the trial (Table 4). Consumption of maintenance medication did not change in the 2 groups.

According to the physician, in the treatment group asthma improved in 9 children, worsened in 2 children, and did not change in 2 children. In the control group these figures were 5, 0, and 8, respectively. No difference was found between the 2 groups.

According to the parents, in the treatment group asthma improved in 8 children worsened in 1 child, and did not change in 5 children. In the control group these figures were 7, 1, and 5, respectively. In both groups, the assessment by the physician correlated with that of the parents ($p<0.01$).

In the 2 patients of the treatment group living in houses in which a more than 10-fold guanine exposure reduction of the high baseline guanine concentration (above 6.0 mg/g dust) to below sensitization threshold was achieved, clinical parameters improved in one patient.

Exposure at school

Of the 168 hours constituting the time period of one week, children (n=26) spent a median of 130 (range 104-143) hours at home, of which they slept 81 (63-91) hours. Per week, 24 (range 22-30) hours were spent at school; and 11 (2-41) hours per week somewhere else.

No school used special mite-exterminating cleaning measures in the treatment of textiles. Textile floor covering was present in 19 of the 27 classrooms. No significant differences in guanine exposure were seen between start and end of the study period, or between the 2 groups. Only one school rug contained a slightly elevated guanine concentration before intervention (Figure.1).

Table 4. Clinical data of patients after one year avoidance advice (September-November 1995). Values given are indexed on values at the start (see Table 1 for absolute values at the start). Mann-Whitney U-test on differences between the groups after the trial, 1-tailed tested

	Treatment group		Control group		
	n	median (min -max)	n	median (min -max)	p-value
Bronchodilator use[1]	13	1 (0 - 15)	12	1 (0 - 3)	0.1
Asthma symptom score[1]	11	1 (0 - 3)	12	1 (0 -5)	0.3
- complaints at night	11	1 (0 - 2)	12	1 (0 - 8)	0.2
- shortness of breath	11	1 (0 - 4)	12	1 (0 - 8)	0.2
- coughing	11	1 (0 - 7)	12	1 (0 - 8)	0.3
- physical activity	11	1 (0 - 1)	12	1 (0 - 2)	0.5
Total days of school absence	8	1 (1 - 1)	12	1 (0 - 3)	0.3
PFER mean daily variability	12	0.9 (0.5-1.8)	9	0.9 (0.4-2.9)	0.5
FEV_1	14	1.0 (0.8-2.4)	13	1.1 (0.9-2.7)[2]	0.2
PD_{20} (methacholine provocation dose steps)	14	+2 (-6 to +7)	13	+1 (-2 to +6)	0.4
Total IgE	14	1.2 (0.2-3.1)	13	1.0 (0.2-3.1)	0.2
Specific IgE against the house dust mite	14	0.7 (0.3-6.2)	13	1.1 (0.1-6.5)	0.3
Eosinophils absolute	14	1.0 (0.2 - 2.4)	13	1.1 (0.4 - 5.1)	0.2
Eosinophils relative	14	0.9 (0.0 - 4.5)	13	1.3 (0.7 - 3.7)	0.1

n; number of patients

[1] median week score over 6 weeks; [2] significantly improved in this group

Guanine concentrations in textile floor coverings at school did not differ from those in living rooms, but were significantly lower than in bedrooms.

Upholstery was present in 23 classrooms. Of 16 analyzed by HPLC, 6 contained elevated guanine concentrations, with a maximum of 7.0 mg guanine/g dust (Figure 1). Guanine concentrations in school upholstery were not significantly lower than in living rooms or bedrooms before advice was given.

Other allergens and irritants

Parents of 7 of the 14 patients of the treatment group and of 5 patients of the control group were smoking at home before intervention (Table 5). After advice, in the treatment group one father stopped smoking completely and one mother smoked outdoors only; in the control group, one mother smoked outdoors only. In all 3 cases in which smoking indoors was terminated, one parent was smoking at home before advice. Bronchial hyperreactivity was present in all 3 patients before and after the trial, and this did not change.

In comparison to sensitization to house dust mites (Table 1), sensitization to storage mites and molds was rather low. Specific IgE concentrations against storage mites never exceeded 1.1 IU/ml, and against molds never exceeded 11.0 IU/ml. Six patients were sensitized to molds (Table 5). In these latter patients, specific IgE concentrations decreased: in the treatment group from median 7.5 (range 0.5-11.0) IU/ml to 4.4 (0.2-7.0) IU/ml, n=5; and in the control group from 3.1 to 2.6 IU/ml (n=1).

Of sensitizing pets, only cats were kept indoors. In the treatment group, a neighbor's cat was visited regularly; after advice the cat was no longer allowed to enter the dwelling. In the control group, one cat was re-housed after hospitalization of the child because of an asthma exacerbation; removal of the cat was not followed by wet cleaning of all surfaces. No clinical effect could be related to removal of the sensitizing pet.

Discussion

When performed by households, selective mite allergen avoidance advice did not result in clinical improvement in young mite-allergic children. None of the investigated clinical parameters improved significantly, and no differences were found between the 2 groups. In the control group only FEV_1 increased; this might be due to the improved technique of performing lung function tests. Because of their young age, some of the children had lung function measured for the first time at start of the study. In the treatment group FEV_1 was already higher at baseline than in the control group.

The use of maintenance medication might have obscured the clinical effect of avoidance measures. Asthma was well-controlled in both groups before and during intervention. Especially in the treatment group, baseline bronchodilator use

Table 5. Number of patients with hyperreactivity in relation to exposure to tobacco smoke at home, and number of patients sensitized to indoor allergens in relation to number of homes in which sensitized patients are exposed

	Treatment group (n=14)				Control group (n=13)			
	Sensitization[1]/ Hyperreactivity[2]		Exposure at home		Sensitization[1]/ Hyperreactivity[2]		Exposure at home	
	Before	After	Before	After	Before	After	Before	After
Irritants								
Smoke	13	14	7	5	13	11	5	4
Allergens								
House dust mite	14	13	12[3]	10[3]	13	13	11[3]	13[3]
Storage mites	3	3	3	2	5	5	5	4
Molds	5	4	4	1	1	1	1	1
Cockroach	0	0	0	0	0	0	0	0
Mouse	0	0	0	0	1	0	0	0
Rat	1	1	0	0	1	0	0	0
Cat	10	10	0[4]	0	8	10	2	1
Dog	12	12	0	0	12	12	0	0
Rabbit	4	4	0	0	6	7	0	0
Birds	1	0	0	0	0	0	0	0

[1] Serum values ≥ 0.35 IU/ml were considered to indicate sensitization
[2] Hyperreactivity to smoke is defined as a methacholine PD_{20} < 784 mcg
[3] Based on home textiles in which guanine exposure was assessed by HPLC
[4] In one home, a neighbor's cat visited regularly

and symptom scores were low, and lung function tests were already almost normal. However, clinical parameters that are not directly influenced by maintenance medication did not improve either. It is known that total IgE can decrease within one year[6,15,30], and a decrease of bronchial hyperreactivity -more methacholine provocation dose steps - is also possible[7,10,30]. In our study, however, neither of these parameters changed.

The number of households included was small; a large study population is needed to detect a small change in clinical parameters. However, the study population was large enough to detect a clinical improvement of 50% compared to a general advice, if selective mite allergen avoidance was completed as advised[15].

Exposure reduction could have been too limited for clinical effect. Only when all exposure sites to all relevant allergens and irritants are removed can programs be clinically effective; this has been demonstrated when professionals executed the whole program[15,17]. In the present study, not all exposure sites to relevant allergens and irritants were removed, although the advice consisted of effective procedures.

The advice given in this study was only partly followed by household members. In both groups, not all avoidance measures were included in housekeeping activities before intervention. In the control group, effective avoidance measures against mites consisted of covering beds and smooth surfaces only. These measures were almost never performed for the first time during the trial. This might be due to the fact that both measures were optional. In case of covers, assistance might have been needed on how to order them, and their clinical benefit must be emphasized to the household members.

Seven of the 14 treatment households repeated mite allergen exposure assessments followed by acaricidal cleaning if necessary. In only 3 households was this done 3-monthly as advised. Only one household treated all mite-infested home textiles. However, in no household was exposure in all the home textiles monitored and treated according to our advice. One might speculate whether individualized programs were too elaborate to be feasible to perform in their entity.

Samples containing insufficient dust for Acarex tests were considered as mite-infested; this might have enlarged the extent of advised programs more than necessary. However, household members were expected to take over the program and to assess mite exposure themselves. In a later stage, they would have been able to adjust the program accordingly.

In the Netherlands, programs are elaborate when dwellings only just meet Dutch Building Code criteria. In these dwellings special mite-exterminating cleaning must be repeated 3-monthly and all beds should be covered. In the present study 24 of the 27 included homes met - at the most - Dutch Building Code criteria (✚-dwellings according to asthma classification of homes). Therefore, the advice that was given in this study seems justified.

Found percentages of mite-infested home textiles seem to justify an extensive program. Guanine concentrations above sensitization threshold were found in 53% of all beds, 56% of all upholstery, and 27% of all textile floor covering. These percentages were lower than found by others in the Netherlands. Kniest et al. studying houses in the same region, found 77, 48, 50%, respectively[14]. Also, our geographic mite model predicts a higher percentage of mite-infested carpeting (60%)[20]. The concentrations found might have been lower due to avoidance measures that were already in use[26].

The complexity of our program is not exceptional. In other climatic regions included in the meta-analysis in which exposure reduction was demonstrated[3,6,7,13,30,31], comparable (Berlin, Germany[7]; and Washington, USA[13]) or even higher (the United Kingdom[3,6,30,31]) exposure levels than in the Netherlands are found[20,21,28]. Winters in these regions are similar or less cold, favoring mite population growth, as has been demonstrated in Section 2 of this thesis. In these regions similar or even more elaborate programs than in the Netherlands are needed[20]. However, in all of these studies, avoidance measures were restricted to patients' bedroom and/or living room, leaving other exposure sites unaddressed. By treating and monitoring only a few objects, relevant exposure sites originating from not-included home textiles might have been overlooked; this might explain why no clinical effect could be observed. In the present study, no relevant exposure was found in patients' bedroom or living room of some dwellings, whereas excessive high concentrations were found in other rooms, e.g. parents' bedrooms.

Koren et al. demonstrated that a change in global exposure correlates with a change in symptoms in rhinitis patients. Therefore, he calculated a global exposure for the whole dwelling based on a median of 8 dust samples per home in the Netherlands[16]. In our study a median of 3 to 6 dust samples, depending on time period and group allocation, could be analyzed; this number was restricted, because the amount of fine dust was sometimes insufficient for guanine assessment by HPLC. Unfortunately, these numbers are too low to calculate a global guanine exposure for the whole dwelling.

Partial exposure reduction does not result in clinical improvement. Covering of beds is often advised as a solitary measure, but seems ineffective in the Dutch situation. Of beds covered, 75% contained guanine concentrations above sensitization threshold before intervention. Also, significant guanine exposure reduction achieved in beds was not enough to result in clinical improvement. Covering of beds should be accompanied by measures that also reduce mite exposure in other home textiles to prevent rapid recolonization in the current Dutch situation[20,21,28].

To eliminate textile floor covering 'blindly' (read: before assessment of actual exposure) is advised in general guidelines. Although not treated with mite extermination procedures, in the present study baseline exposure of textile floor covering was low. Removal of mite-low home textiles will not reduce mite allergen exposure substantially. These data suggest that there seems no reason to eliminate textile floor covering 'blindly'.

In upholstery guanine concentrations were high. Since textile floor covering did not contain high guanine concentrations, and exposure in mite-infested beds could be significantly diminished by covers, remaining exposure in upholstery seems relevant for the clinical outcome.

A more than 10-fold reduction of a high baseline exposure to below sensitization threshold has the potential to be clinically effective[22]. In the present study, in most dwellings baseline exposure was rather low. In only 2 treatment houses was a high baseline exposure sufficiently reduced. Clinical improvement was seen in one patient. A more than 10-fold exposure reduction in a treated home textile correlated with clinical benefit in other studies [3,6,7,10-12,18,27,30].

Theoretically, places other than the home visited by the patient might be of relevance. Children of this age group spend 24 hours a week at school. At school, low mite exposure on floors has also been found by others[29,33,34]. In practice, smooth furnishing and finishing is advocated in schools; however, assessment of mite allergen exposure seems worthwhile before removal of carpeting.

Of upholstery at school, almost 40% contained guanine concentrations above sensitization threshold. Guanine concentrations found in upholstered furniture at school were similar to those in homes. As far as we know, mite allergen exposure in schools in the Netherlands has only been studied for floors, not for upholstery[29,33,34]. Mite allergen avoidance measures at school were not advised in our program, but would have been relevant in some schools.

Sensitization and exposure to allergens other than house dust mites may also determine clinical effectiveness of mite avoidance (Chapter 1.2 and Chapter 3.1). Sensitization to storage mites, molds and pests (mice, rats, cockroaches) played a minor role. Specific IgE concentrations against these allergens were below 10% of concentrations found against house dust mites. Pets, especially cats, were of importance in a few patients. Exposure to pet allergens remained, since pet removal was not followed by wet cleaning of all surfaces. The same was true for smoking indoors. A diet was prescribed to children with a manifest food allergy;

however, not all followed these diets strictly (data not shown). Allergy to pollen is common, but seasonal. Its influence might have been similar before and after the trial. Both clinical assessments were performed outside the pollen seasons (September - November). In the recently published meta-analysis of randomized, controlled mite allergen avoidance trials, continuous exposure to other allergens and irritants was also suggested to have caused no clinical effect[9].

To investigate why avoidance programs were only partly performed, analysis of household behavior is necessary. This is particularly important since, in daily practice, mite allergen avoidance programs should be performed by household members life-long and a change in behavior is usually needed. Therefore, behavioral patterns in adopting mite allergen avoidance in daily activities will be addressed in Chapter 4.2.

In conclusion, asthmatic children do not benefit from either an individualized avoidance advice or a general advice given to the parents. Avoidance programs are only partly executed. A clinical effect is only observed when high baseline exposure is reduced more than 10-fold to below sensitization threshold. High exposure sites are not restricted to patients' bedroom or living room. Since selective mite allergen avoidance programs have to be performed as a whole to be clinically effective, analysis of avoidance behavior is needed.

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Chapter 4.2

Behavioral effectiveness of selective mite allergen avoidance in households with asthmatic children

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Abstract

Effectiveness of selective mite allergen avoidance in households with asthmatic children depends on the completeness of performance of programs.
Behavioral effectiveness was studied in 14 households. They formed the treatment group of a randomized, controlled avoidance trial. This trial concerned mite-allergic asthmatic children, aged 4 to 7 years. Families received intensive assistance with individual advice based on actual exposure. During one year behavior, knowledge, attitude, and perceived behavioral control of adult household members towards mite allergen avoidance were followed.
To be able to construct an individual avoidance program the knowledge of the household members had to be improved. As long as the costs for special bed covers are reimbursed, application was acceptable to all households. Continuous ventilation and heating in winter was achieved in half of the households only. Presence of draught, risk of burglary, and energy-saving schemes discouraged some families from applying these measures. Three-monthly special cleaning of mite-infested home textiles was performed by 20% of households during the time they were supervised. Most households considered time and personal energy investment too high to balance with perceived clinical improvement. Three-monthly special cleaning activities were feasible for - at the most - 14 items, only in case the household members were motivated by the expected (clinical) benefit, strongly believed that they could perform the measures, had a structured organization of housekeeping activities (not disturbed by life-events or other not yet incorporated time-consuming activities), and were flexible enough to change housekeeping activities.
In the humid temperate climate of the Netherlands, it is barely feasible for a household with young children to complete an effective allergen avoidance program. Elaborateness of needed special cleaning may be diminished by shelter and moisture-reducing measures. Given that it is possible to design and build dwellings with no mite problem, upgrading or moving to a dwelling with a **+++**- health classification seems the most sanitary and sustainable solution.

Introduction

Selective mite allergen avoidance is based on diminishing relevant exposure to allergens and irritants in the complete individual environment[4,15,18,26]. It consists of measures directed towards tobacco smoking, keeping pets, indoor moisture reduction (water vapor producing activities, ventilation, and heating), furnishing and special cleaning. When performed by professionals, it proved effective in reducing mite allergen exposure, resulting in clinical improvement in rhinitis patients[17]. When performed by parents of asthmatic children, no relevant exposure reduction and clinical effect were observed (Chapter 4.1). This was not due to ineffective measures or incomplete avoidance advice, but to incomplete execution of the avoidance programs.

Individualization of the program will facilitate to address all relevant exposure sites[5,13]. A selective mite allergen avoidance program is tailored to the needs and skills of a household in the following manner:
1. households receive information about relevant exposure in their situation;
2. they can choose between several effective measures;
3. they are instructed how to perform these measures;
4. they are instructed how to monitor the effectiveness of their program;
5. and are assisted during this process by asthma nurses in the Netherlands[5,22].

Behavioral effectiveness of complete programs addressing the whole domestic environment have not yet been studied (Chapter 1.2). Since atopic diseases are chronic, allergen avoidance should be maintained lifelong by household members to result in lasting clinical benefit[28]. Knowledge of behavioral determinants influencing the performance of behavior can be useful in designing information to persuade households to change behavior. Models exist to explain the relationship between information and behavior through several determinants.

In their theory of reasoned action, Fishbein and Ajzen (Fishbein 1967, Fishbein and Ajzen 1975) introduced a model that mediates observed relations between attitudes and behavior. The *attitude* towards a behavior describes the evaluation one makes to engage in a behavior. Attitudes influence behavior by their effect on the *intention* to perform a behavior. Intentions are not only determined by attitudes toward behaviors, but also by their subjective norm. The *subjective norm*, consists of a person's belief about whether significant others think that he or she should engage in the behavior. Significant others are individuals whose preferences about a person's behavior in this domain are important to him or her[1].

The theory of reasoned action is restricted to the class of behaviors that is volitional, since it suggests that behavior is under the control of intentions. This theory excludes behaviors requiring skills, resources, or opportunities that are not necessarily available, and thus not fully volitional (e.g., applying acaricidal cleaning products, the use of ventilation and heating facilities). It also disallows the possibility that attitudes sometimes elicit behavior with little or no intervening thought (e.g., smoking). It also excludes behavior that may occur independently of attitudes, because it is habitual (e.g., water vapor producing household activities, such as cooking, bathing, washing and drying laundry). In this theory a strict distinction between behaviors and behavioral outcomes (or goals) is made.

The theory of planned behavior (Ajzen and Madden, 1986) substantially enlarges the model of reasoned action[1]. It includes behaviors that are not wholly under control and regards every behavior as a goal (Figure 1). *Perceived behavioral control* is included in this model, as well as attitude and subjective norm. Perceived behavioral control describes the conviction that one can successfully execute a behavior. Perceived behavioral control affects behavior in 2 ways: through intention and directly.

The model of planned behavior will be used to describe the behavioral effectiveness of selective mite allergen avoidance, when performed by parents with asthmatic children and assisted by a healthcare provider during one year. We will address which measures are acceptable; which factors explain performance quality; and how we can distinguish between good-performers and low-performers.

We expect that our information (the selective mite allergen avoidance advice) will increase *knowledge*. An increase in knowledge on consequences of behavior may influence the attitude towards selective mite allergen avoidance. An increase in knowledge on how to perform behavior may influence perceived behavioral control. Both attitude and perceived behavioral control are expected to influence avoidance behavior. The behavior, or trying to perform the behavior, will lead to feedback that may, in turn, influence the determinants attitude, subjective norm and perceived behavioral control. Due to the low number of included households (n=14), this survey must be seen as exploratory.

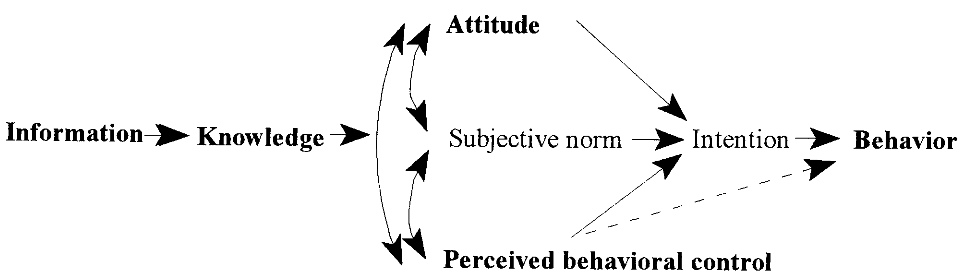

Figure 1. Model of planned behavior, adapted from Ajzen and Madden, 1986[1]. Items investigated more extensively in this study are printed bold

Materials and Methods

Selection of households

Fourteen households participated who had children, aged 4 to 7 years, with physician-assessed moderate to severe asthma[27]. All children had a manifest house dust mite allergy (specific IgE antibodies against *Dermatophagoides pteronyssinus* ≥ 0.70 IU/ml) and at least one home textile in their home with a mite allergen concentration above the sensitization threshold for house dust mites[24]. For further selection criteria of households see Chapter 4.1.

Set-up of study

The present study was restricted to the 14 households of the treatment group of the randomized, controlled trial described in Chapter 4.1. The study was approved by the Hospital Medical Ethics Committee, and informed written consent from the parents was obtained prior to inclusion in the study.

In September 1994 all 14 homes were visited and dust samples were taken of all home textiles. Dust was analyzed for mite allergen content (measured as guanine) by laboratory personnel (Chapter 4.1). Exposure to molds and other pests was assessed by the author and a constructional engineer (Chapter 4.1). In January - March 1995 indoor moisture influencing behavior was observed. Afterwards, households received an individual avoidance advice. Feedback on performed avoidance behavior was given during a home visit 4 months after advice was given. Before the advice, and 3 and 9 months after advice a behavioral questionnaire was filled in by the household coordinating parent (in 13 cases the mother, once the father).

Behavioral questionnaires and advice were pretested in various settings with parents of children who did not meet all inclusion criteria in the selection stage (mild asthma or mild house dust mite sensitization). Questionnaires were reviewed by 3 experts in mite allergen avoidance programs and a pediatric pulmonologist before administration to the parents in the present study.

Avoidance advice

Parents were informed of all relevant actual sensitizations (specific IgE antibodies ≥0.35 IU/ml) and hyperreactivities of their child (Chapter 4.1). They received background information on asthma, allergy, allergens and irritants in a booklet. Exposure sites were pointed out to them in their home environment. To assist the construction of an individual avoidance plan parents obtained a list of all potentially effective avoidance measures (Table 1). New or unfamiliar measures were demonstrated. To help the parents to monitor mite infestation in the different objects they were taught to use the Acarex test.

Table 1. Advised avoidance measures

Object	Advised avoidance measures
Removal of sources other than mites	
Smoking	not allowed indoors; smoking outdoors as alternative
Keeping pets	not allowed indoors; remove sensitizing pet and wet or dry clean all surfaces
Mold growth	reduce indoor moisture; remove visual mold growth with peroxide cleaning agent every 3 months
Other pests	call a pest exterminator
Moisture reduction	
Leakages	repair water leakages; close openings between dwelling and humid crawl space
Reduce water vapor production	dry laundry outdoors, in dryer or continuously ventilated room; ventilate maximal during and 10 minutes after bathing and cooking
Ventilation	24 hours/day; all year
Heating in winter	all rooms heated 24 hours/day; Temperature not below 15°C at night, not below 18°C during daytime
Shelter reduction	
Smooth floor	optional
Bed covers	all mite-infested beds in use
Special cleaning	
Exposure assessment	guanine assessment 3-monthly (= 4 times per year)
Bed materials	a. wash at 60°C (6-weekly), or b. freeze 1 week followed by low-temperature wash (6-weekly), or c. acaricidal cleaning 6-monthly when covered, or d. acaricidal cleaning 3-monthly when not covered
Upholstery	a. wash at 60°C (every 6 weeks), or b. freeze 1 week followed by low-temperature wash (every 6 weeks), or c. acaricidal cleaning (every 3 months)
Textile floor	acaricidal cleaning (every 3 months)
Smooth floor	dry or wet clean (twice a week)

Materials as Acarex test-sets, mite-exterminating cleaning products (acaricides), and special mite and allergen impermeable covers were supplied free of charge (Acarex, Acarosan, and Allergocover, Allergopharma J. Ganzer KG, Reinbek/Hamburg, Germany).

Households were assisted by the author in their choice between effective avoidance measures. Written information was supplemented with oral explanation. Parents were encouraged to ask for additional information during the study.

The content of written advice was checked by 3 experts in allergen avoidance. The readability was checked by 2 parents of asthmatic children who did not meet all inclusion criteria.

Behavioral questionnaire

Since behavior in selective mite allergen avoidance has not been studied previously we developed a new questionnaire. Performed behavior was asked in open questions. Knowledge, attitude and perceived behavioral control were assessed in closed questions (see for items asked Tables A, B and C of the Appendix). Allergen avoidance behavior was divided in 8 main behavior categories that are most relevant for indoor allergen avoidance:

1. smoking,
2. keeping pets,
3. water vapor production (e.g., laundry drying),
4. ventilation,
5. heating,
6. choice of a type of floor covering,
7. covering beds, and
8. special cleaning.

Not of all behavioral categories, all behavioral determinants were asked in the questionnaire. Concerning use of covers, no knowledge and attitude items were asked. Encasing beds with special mite and allergen impermeable covers was originally included in the behavioral category 'special cleaning', since this is one of the options to treat mite-infested bed materials. Only in the perceived behavioral control questionnaire items were asked concerning this measure. After giving the advice, open questions were used to ask parents if they had known of their existence. Side-effects of using these covers were recorded during the trial. Concerning choice of type of floor covering, only knowledge and attitude were asked, since this was an optional measure. We did not expect that type of floor covering would be significantly changed within one year.

Behavior

Performance and frequency of behavior were asked in detail for all 8 behavioral categories by means of open questions. For example: 'Which rooms and spaces are ventilated? Which type of ventilation facility is used in each of these rooms/spaces? To what extent is each facility open? How many hours a day and during which months is each facility used?'. (The use of ventilation and heating facilities was also observed by the author during home visits in the winter months. Households were not aware of these observations.)

Behaviors were scored as follows:
1. Smoking: no smoking indoors by parents (each 2 points); by visitors (1 point); maximal score=5 for 2 parents (n=13), 3 for a 1-parent household (n=1).
2. Keeping pets: kept indoors and child sensitized 0 points; kept indoors, but child not sensitized (4 points); no pets indoors (5 points); maximal score=5.
3. Laundry drying: part of laundry that is dried outdoors, in tumble dryer or in a continuously ventilated room; maximal score=1.0.
4. Ventilation: number of rooms that are continuously ventilated; rooms included are living room, patients' bedroom, parents' bedroom, siblings' bedroom and hobby room (each 1 point); maximal score=5.
5. Heating: number of rooms heated day and night ≥ 15°C; rooms included are living room, patients' bedroom, parents' bedroom, siblings' bedroom and hobby room (each 1 point); maximal score=5.
6. Choice of type of floor covering: rooms included are living room, patients' bedroom; textile 0 points, smooth 1 point; maximal score=2.
7. Covering of mite-infested beds: included are beds in patients' bedroom, parents' bedroom and siblings' bedroom; for each bedroom: not applied 0 points, in part 1 point, in total 2 points; maximal score=6.
8. Special cleaning: frequency of performing Acarex tests, followed by acaricidal cleaning if necessary, during the whole study period:
   0 = not done,
   1 = in part done after baseline exposure assessment only,
   2 = in total done after baseline exposure assessment only,
   3 = done after baseline assessment and once in part by household,
   4 = done after baseline assessment and once in total by household,
   5 = done after baseline assessment and twice in part by household,
   6 = done after baseline assessment and twice in total by household;
   maximal score=6. (Since at the most one cleaning could have been performed after 3 months, no score was made 3 months after advice).

In analysis all scores were divided by their maximal score.

Mite allergen avoidance in the domestic environment of asthmatic children aged 4 to 7 years is performed by parents. Four months after advice the coordinating parent was asked if his or her partner was 'supporting', 'indifferent to', or 'disapproving' the performance of their program. All partners were supporting the coordinating parent in performing the program, except one father who was described as being indifferent. This concept was not further investigated.

Attitude

The attitude of a person to a certain behavior can be estimated by asking for every consequence how likely it is that the consequence will occur ('belief') and how that person evaluates that consequence ('evaluation'). To estimate the attitude towards a specific behavior for each consequence, matching belief and evaluation are multiplied. The general attitude towards a specific behavior is estimated by summing all these multiplications[1].

For the attitude questionnaire addressing the 7 above-mentioned behavioral categories (covering beds was not asked) a list of salient consequences of behavior was made based on literature[22] and experiences of allergen avoidance experts (n=3) and parents (n=30). These consequences were completed in open interviews by telephone with parents of not selected children (n=4). All 7 behavioral categories and corresponding consequences were presented to another 10 not selected households. Of these, 9 returned the filled-in questionnaire. Of each behavioral category consequences were selected that:

1. had a high score on belief and/or evaluation, or
2. were expected to alter due to the advice, or
3. were not uniformly answered at the pretest, or
4. a combination of 1-3.

The submitted attitude questionnaire consisted of 70 items. Since the 8 items concerning smoking were not uniformly interpreted during the baseline assessment, this subject was excluded from further analysis. The remaining 62-item survey addressed the 6 other behavioral categories. Cronbach's alpha was .09. Cronbach's alpha may be low since the attitude items addressed different issues, such as 'Cleaning materials have irritating smells', 'Ventilation increases the risk of burglary in my home', and 'Because my child must avoid contact with pets, then he/she is seen as being different from other children'. The questionnaire was constructed with five-point rating scales for belief rated 1 (= it is not very likely that consequence will occur) to 5 (= it is very likely that consequence will occur), and for evaluation −2 (very negatively evaluated) to +2 (very positively evaluated).

The attitude of the coordinating parent towards each behavioral category was estimated by asking him/her for every consequence how likely it is that the consequence will occur ('belief') and how he/she evaluates that consequence ('evaluation'). The general attitude towards a behavioral category was estimated by multiplying for each consequence matching belief and evaluation and summing all these multiplications, followed by dividing by the number of consequences belonging to a behavioral category times 10 (maximal score of belief times evaluation)[1].

Perceived behavioral control

Perceived behavioral control was asked of each advised measure by questions such as 'Will you be able to ventilate the living room 24 hours a day?' and 'Will you be able to treat upholstered furniture with Acarosan foam 3-monthly, if needed?'. Two items were removed from analysis since no household performed these procedures (freezing of soft toys and of carpeting every 6 weeks). The 24 remaining items (α=.80) were measured using a six-point bipolar rating scale (1 = no certainly not, 5 = yes, certainly), including a 'not applicable' category. For statistical analysis per behavioral category, applicable answers were summed and then divided by the maximal score (= number of applicable items times 5).

Knowledge

For the knowledge questionnaire, needed knowledge and misconceptions for each behavioral category were obtained in face-to-face interviews, recorded on tape, with 4 parents of not-selected children. The questionnaire consisted of 26 items (α=0.68). Two items were excluded from analysis due to lack of uniform interpretation ('Dry air is good for asthma' and 'A heated bedroom is good for a child's asthma', leaving 24 items. Questionnaires were constructed in a 'true-false' format. For statistical analysis the number of correctly answered items was divided by the number of items per behavioral category.

Time investment

Time investment by households was calculated according to Kniest[16]. For assessment of guanine exposure: dust sample collection takes 1 minute per m^2 surface area; performance time of an Acarex test was estimated at 5 minutes. For acaricidal treatment of a home textile application time was set at 2 minutes per m^2 surface area followed by vacuum cleaning afterwards also 2 minutes per m^2 surface area (drying time of the cleaning agent not included).

The author made home visits for intake (60 minutes), first introduction of the advice (30 minutes), explanation of the advice (120 minutes) and feedback (90 minutes).

Statistical analysis

From the 8 investigated behavioral categories factor analysis was used to detect subsets of mite allergen avoidance behavior. Mann-Whitney U test was used to test changes over time. Spearman rank correlation coefficient was used to test the correlations between mentioned behavior, knowledge, attitude and perceived behavioral control of each behavioral category. The significance level was set at 0.05. Statistical analysis was performed by the use of SPSS for Windows version 7.5.

Results

None of the households completed the program as advised. In this small study group (n=14), factor analysis could not identify subsets of behaviors, so each of the 8 behavioral categories will be discussed separately. For each behavioral category, Table 2 shows the number of households that adhered completely to advice.

Since part performance of an advice may be seen as a gain in behavioral effectiveness, Table 3 shows to which extent each avoidance behavior improved during intervention. Data on knowledge, attitude and perceived behavioral control are shown in detail (Tables A to C) and in general (Tables D to F) of the Appendix. The relations of knowledge, attitude and perceived behavioral control; and of attitude, perceived behavioral control and avoidance behavior are shown in Tables G and H of the Appendix, respectively.

No behavioral data were missing. Of the attitude scores, only one evaluation item on floor covering was missed by 2 parents before advice; 1 parent missed one belief item on heating and one on keeping pets 3 months after advice; whereas another parent missed one belief item on ventilation 9 months after advice. Of perceived behavioral control, no items were missed. Concerning knowledge, only one parent missed one item on floor covering before and 3 months after advice; one respondent missed an item on ventilation 9 months after advice.

Table 2. Advised conduct in households (n=14) and number of households adhering completely to advice measured before, and 3 and 9 months after advice was given

Advised conduct	*Adherence*		
	Before	*After 3 months*	*After 9 months*
Removal of sources			
Smoking indoors not allowed (by parents and visitors)	2	2	2
Keeping sensitizing pets indoors not allowed	14	14	14
Moisture reduction			
Drying all laundry in dryer, outdoors or in well-ventilated room	6	10	10
Continuous ventilation of all rooms	0	6**	8***
Continuous heating of all rooms 15°C 24 hours a day	2	4	5
Shelter reduction			
Bed covers on all mite-infested beds in use	0	13***	10***
Smooth floor in bedroom of patient and living room (optional)	7	7	5
Mite extermination			
Exposure assessment, and special cleaning if needed, 3-monthly	0	n.m.	1

* $p<0.05$, ** $p<0.01$, *** $p<0.001$ compared to values before advice (Mann-Whitney U-test, 1-tailed tested); n.m. = not measured, since just started

Table 3. Median values (range) of performed conduct of households (n=14) before, and 3 and 9 months after advice was given

Performed conduct	*Adherence (0.0 -1.0)*		
	Before	*After 3 months*	*After 9 months*
Removal of sources			
Smoking indoors not allowed (by parents and visitors)	0.6 (0.2-1.0)	0.8 (0.2-1.0)	0.8 (0.2-1.0)
Keeping sensitizing pets indoors not allowed	1.0 (0.2-1.0)	1.0 (0.2-1.0)	1.0 (0.2-1.0)
Moisture reduction			
Drying all laundry in dryer, out-doors or in well-ventilated room	0.9 (0.1-1.0)	1.0 (0.2-1.0)*	1.0 (0.1-1.0)
Continuous ventilation of all rooms	0.2 (0.0-0.8)	0.8 (0.0-1.0)**	1.0 (0.0-1.0)***
Continuous heating of all rooms 15°C 24 hours a day	0.4 (0.0-1.0)	0.7 (0.3-1.0)*	0.7 (0.3-1.0)*
Shelter reduction			
Bed covers on all mite-infested beds in use	0.0 (0.0-0.2)	1.0 (0.0-1.0)***	1.0 (0.5-1.0)***
Smooth floor in bedroom of patient and living room (optional)	0.8 (0.0-1.0)	0.8 (0.0-1.0)	0.4 (0.2-1.0)***
Mite extermination			
Exposure assessment, and special cleaning if needed, 3-monthly	0.0 (0.0-0.0)	n.m.	0.4 (0.2-1.0)***

* $p<0.05$, ** $p<0.01$, *** $p<0.001$ compared to values before advice (Mann-Whitney U-test, 1-tailed tested)
n.m. = not measured, since just started

The results will be discussed per behavioral category:

Smoking

Smoking indoors was not done by parents and visitors in only 2 of the 14 households throughout the trial (Table 2). Smoking at home by parents was observed in 7 dwellings before intervention and in 5 homes after. After advice, in 2 different households one parent stopped smoking completely and one started to smoke outdoors only: both these parents mentioned that they stopped smoking because of its negative effect on their childs' asthma. In both households, the other parent was not a smoker.

Knowledge concerning smoking was already good before advice and could not be improved (Table D of Appendix). Perceived behavioral control towards smoking did not change (Table F of Appendix). Knowledge and perceived behavioral control were correlated at the end of the trial (Table G).

Keeping pets

A sensitizing pet indoors was not kept in any of the households (Table 2). Three households kept a pet to which the child was not - yet - sensitized. In one household a sensitizing neighbor's cat regularly visited. After our advice the cat was no longer allowed to enter the dwelling. The parents knew that presence of a pet could aggravate asthma. However, a relation between the cat and their child's asthma was not experienced earlier.

Knowledge on keeping pets indoors was good and did not improve (Table D). General attitude towards keeping pets indoors did not change (Table E). Knowledge on keeping pets was strongly correlated with perceived behavioral control at start (Table G). Perceived behavioral control did not change (Table F) and was correlated with mentioned behavior at all time points (Table H).

Mite allergen avoidance

Mite allergen avoidance measures investigated consisted of moisture-reducing activities, shelter reduction and special cleaning.

Moisture-reducing activities
Activities that were investigated in detail included drying laundry, ventilation and heating.

All households could dry their laundry outdoors or in rooms with permanent ventilation facilities. All except one also owned a tumble dryer. All laundry was dried outdoors, in a dryer or in a continuously ventilated room in 6 households before and in 10 households after advice was given (Table 2). Of these, only one household dried a part of their laundry outdoors. In 2 households, laundry was still partly (20%) dried in rooms with no permanent ventilation facilities after advice.

Parents knew that drying laundry indoors influences indoor air humidity (Table A). General attitude towards drying laundry in a tumble dryer improved only temporarily (Table E). Laundry drying outdoors or in a tumble dryer was not believed to diminish asthma complaints, although it was believed to reduce indoor moisture ('house becomes less humid') at all time points (Table B). Perceived behavioral control increased at both time points after advice (Table F).

Ventilation facilities that can be used continuously, were present in all investigated rooms in all 14 dwellings. These facilities were in 2 patients' bedrooms, 5 parents' bedrooms and 12 living rooms not sufficient to achieve an air exchange rate above $0.9 \cdot 10^{-3}$ $m^3/s.m^2$ as advised in our national Building Code[19]. Non-maximal use of these facilities resulted in insufficient ventilation in 12 patients' bedrooms, 12 parents' bedrooms and 12 living rooms before advice.

Ventilation increased after advice. In our advice, we did not mention a minimal rate, but only advised to ventilate all rooms continuously. Before advice, continuous ventilation of rooms was not done in any house. After advice, all households ventilated more (Table 3), of which 8 ventilated all rooms continuously (Table 2).

In general, knowledge concerning adequate ventilation could be improved significantly (Table D). Especially the following items improved: 'a dwelling becomes drier by ventilating', 'a window must be wide open to ventilate well' (= misconception), 'ventilation must be done 24 hours a day'. Knowledge items concerning ventilation were not correctly answered by two households at the end; they did not know that ventilation must be done 24 hours a day; and they did not ventilate any of the rooms continuously.

Attitude towards ventilation did not change (Table E). The consequence 'house becomes less humid' became more important (Table B). In those 6 households that insufficiently ventilated, risk of burglary (n=3), draught. (n=3), polluted air coming from outside (n=4), the room becomes cold (n=4) and increased fuel consumption (n=4) were mentioned as expected unpleasant side-effects.

Perceived behavioral control towards continuous ventilation of all rooms did not change (Table F). General knowledge about ventilation was significantly correlated with perceived behavioral control 9 months after advice (Table G). Perceived behavioral control was in its turn highly significantly correlated with performed behavior 3 months and 9 months after advice (Table H).

Heating facilities to heat all rooms continuously were present in all (central heating), except one that was heated by a stove. During the study, heating facilities were not altered. However, the household with stove heating seriously considered to move home.

Before advice only 2 households heated all rooms continuously. Nine months after advice 5 households did this (Table 2). The percentage of rooms that were continuously heated increased significantly (Table 3). The living room was heated at 15°C or higher during daytime by all before advice. After advice, night reduction below 15°C was no longer done in the living room, whereas this was done by 7 households before advice. Bedrooms were not continuously heated in 10 of 13 centrally heated houses before advice. Of these, 5 households started to heat bedrooms permanently after advice.

Parents knew that indoor air becomes drier by heating (Table A). Heating bedrooms was considered important to diminish asthma complaints 3 months after advice, but not 9 months after advice (Table B). That a bedroom becomes less humid seems most important (Table B). A warm bedroom was more positively evaluated after our advice (Table B). Energy-saving considerations mainly prevented sufficient heating in both bedroom and living room (Table B). Attitude towards heating patient's bedroom became more positive (Table E). Our advice did not change general perceived behavioral control towards heating patients' bedroom or living room (Table F).

All investigated moisture-reducing activities were performed completely according to our advice by no household before advice, and by 4 after one year intervention. Before advice all knew that in humid houses more house dust mites are present than in dry houses (Table A).

Shelter reduction

Special mite and allergen impermeable bed covers were in none of the households on all mite-infested beds (Table 2). Parents knew about their availability in 9 cases before advice. Of these 9 parents, 2 had covered the mattress and pillow of their child's bed. (Only mattress and pillow covers of patients' beds are insured in the Netherlands.) Four parents had not ordered covers since they thought these would not benefit their child. Three others became aware of the presence of these covers after the selection stage for this trial.

While available free of cost, all households ordered and applied covers for mite-infested beds. Covers for quilts were found too smooth (risk of sliding) in 6, and causing sweating in 4 cases. This deterred some households from keeping all mite-infested beds encased. Three months after advice 13 of the 14 households had all mite- infested beds encased. Nine months after advice this number was decreased to 10 households. In case covers were removed, quilts were not washed at 60°C 3-monthly instead. Perceived behavioral control decreased after advice (Table F) and was correlated with performed behavior 9 months after advice (Table H).

Costs seem to be a restricting factor. If paid by themselves, only 7 of the 14 parents would have ordered covers for their child's bed.

Smooth floor covering was optional in our advice. Half of the floor coverings in patient's bedroom and living room were already smooth before intervention (Table 2). After advice, two purchased a rug for the patient's bedroom. Although knowledge improved significantly (Table D), misconceptions such as 'carpeting is never allowed for a mite-allergic child', 'in woolen carpeting, there are more mites than in synthetic carpeting' and 'in high-piled carpeting, there are more mites than in low-piled' were persistent (Table A). Throughout the trial, textile floor covering was considered less easily cleanable and worse for child's asthma than smooth floor covering (Table B). Warmth insulating properties were significantly more ascribed to textile floor covering after advice (Table B). That textile floor covering is more sound-proof than smooth floor covering became significantly less important (Table B).

Special cleaning

Time investment for assessment of mite exposure in all home textiles present was 3 hours and 46 minutes (median, range 2 h 14 min - 5 h 56 min). Acaricidal treatment of all these home textiles by Acarosan will take 8 h 12 min (3 h 56 min - 14 h 4 min).

One special cleaning program - based on exposure assessments made by our laboratory - was performed by all. Seven households repeated exposure assessment, followed by mite-exterminating cleaning if necessary, during the trial. Only 2 households assessed exposure 3-monthly, as advised. Another executed a third mite-exterminating cleaning without assessment before, since the mother considered - after two assessments - cleaning frequency known.

None of the 7 households that repeated exposure assessment tested all home textiles. Only 1 household assessed exposure of all (at baseline) mite-infested home textiles 3-monthly (Table 2). The other 6 households tested a selection of their home textiles. Number of items tested at one time ranged from 6 to 14, whereas 20.5 (range 15-29) items were present per household.

Knowledge concerning special cleaning was good before advice was given, but could be improved (Table D). The use of Acarex and Acarosan was new for all households and also intensive - without acaricidal additive - cleaning of home textiles was unusual. Of the 14 coordinating parents, 5 knew that acaricidal cleaning products were on the market, but were considered not necessary in their case.

General attitude towards cleaning did not change (Table E). Parents believed that their new cleaning program removed house dust mites better than their original program; however, it was not better associated with diminishing asthma complaints (Table B).

Personal energy needed for their new special cleaning was significantly more than for their original cleaning program (Table B). Asked in open questions, all considered time and personal energy investment too high to complete every 3 months in a household with young children. This was also demonstrated in a highly significantly decreased perceived behavioral control concerning special cleaning during the trial (Table F).

After the trial, two parents mentioned that they would not have ordered acaricidal foam anymore: one because of irritation of the skin and the other preferred to cover beds and wash upholstery at 60°C. Four households would not order powder: two households since they had only a small, mite-infested carpet at the stairwells; one household considered replacement of all textile floor covering by smooth floor covering; and 1 household because of financial considerations. Acarex tests would not have been ordered by 3 of the 14 households. They considered these tests unnecessary, since treatment was known. All households considered dust collection for Acarex tests time consuming.

A clinical effect of mite allergen avoidance is only seen when all relevant exposure to allergens and irritants is eliminated (Chapter 4.1). Exposure to mite allergens is only directly reduced by shelter reducing and mite-exterminating cleaning. Since the application of special bed covers forms no problem as long as the costs are reimbursed, it will be interesting to know in which households special cleaning can be incorporated. (Moisture reduction will need at least 2 winters to result in a relevant exposure reduction in the Netherlands[26], and thus facilitating the required cleaning program.)

How to distinguish households in which special cleaning can be incorporated

Only 3 households performed special mite-exterminating cleaning 3-monthly as advised ('good-performers'), whereas 4 households did this twice ('moderate-performers') and 7 households only once during the 9 months following the advice ('low-performers'). Due to these low numbers no statistics have been performed. A suggestion is made how to distinguish households in which special cleaning can be incorporated.

First of all, household members must be motivated to change cleaning habits; they must expect - directly or indirectly - clinical benefit. Good-performers did not believe that their original cleaning program optimally reduced allergen exposure, whereas low-performers strongly believed that their original program reduced allergen exposure and diminished asthma complaints (Table 4).

Secondly, perceived behavioral control towards cleaning all types of home textiles must be high at start (> 0.90). This was seen in both the good- and low-performers group (Table 5). The reason why households in the low-performers group did not complete the program as advised was presumably due to the presence of disturbing life events or other new activities, that were not yet incorporated in household activities. In the low-performers group 3 coordinating household members had concomitant life events (a divorce; disease and death of a relative; and the birth of a baby, which had medical problems). Two others in this group, recently introduced a time consuming new activity in their daily activities (working and studying, respectively), that was not yet incorporated in daily activities.

All 7 low-performers did not repeat assessment of mite allergen exposure, followed by special cleaning if necessary. None of them made an avoidance plan within 100 days after advice was given.

The 3 good-performers were flexible to change housekeeping activities. They facilitated the program by removing home textiles and trying various measures. The program obtained a 'routine', that was incorporated in daily activities. These households continued estimating mite exposure, followed by special cleaning, after finishing the trial.

Table 4. Parental attitude of low-, moderate- and good-performers of special cleaning program (median values)

Consequences	Low-performers (Cleaned once) (n=7)			Moderate-performers (Cleaned twice) (n=4)			Good-performers (Cleaned 3-monthly) (n=3)		
	Before	After 3 months	After 9 months	Before	After 3 months	After 9 months	Before	After 3 months	After 9 months
House becomes dust-free	5	4	5	5	8	8	4	4	3
Diminishes asthma complaints	10	10	10	7	7	8	8	6	8
Reduces allergen exposure	10	10	10	6	10	7	3	10	5
Removes house dust mites	8	10	8	6	10	5	8	5	5
House looks clean	4	5	3	4	4	4	4	4	3
House smells clean	4	4	3	5	4	2	0	0	0
Cleaning materials have irritating smells	-3	-3	-2	-1	-1	-3	-1	-1	-1
Consumes much personal energy	0	0	0	-1	-5	-3	0	0	-4
Is time consuming	0	0	0	-3	-7	-2	-4	-4	-5
Spend little money on cleaning	-2	0	0	-6	-2	0	5	0	0
General attitude special cleaning	.29	.30	.34	.22	.22	.27	.29	.07	.15

Table 5. Parental perceived behavioral control of low-, moderate- and good-performers of special cleaning program before, and 3 and 9 months after advice was given (median values)

	Low-performers (cleaned once in 9 months) (n=7)			Moderate-performers (cleaned twice in 9 months) (n=4)			Good-performers (cleaned 3-monthly) (n=3)		
	Before	After 3 months	After 9 months	Before	After 3 months	After 9 months	Before	After 3 months	After 9 months
Cleaning mite infested bed materials	1.00	0.76	0.80	0.90	0.74	0.76	0.96	0.80	0.84
Cleaning mite infested upholstery	0.97	0.60	0.60	0.80	0.60	0.60	1.00	0.73	0.53
Cleaning mite infested textile floors	0.90	0.90	0.80	0.90	0.80	0.85	1.00	0.80	0.80
Cleaning mite infested smooth floors	1.00	0.80	1.00	1.00	0.90	0.80	1.00	0.80	0.80
General cleaning	0.97	0.72	0.76	0.86	0.73	0.75	0.94	0.76	0.72

Discussion

All participating households intended to complete the program at start. However, none completed the program as advised. Only 20% of the households performed special cleaning of - a part of - their home textiles every 3 months. To improve patient adherence to selective mite allergen avoidance program, implementation and assistance may be adjusted.

Program

There is a gradient from measures which are most commonly incorporated to measures which are almost not incorporated in housekeeping activities. Indoor moisture-reducing measures (e.g., continuous ventilation of all rooms) and shelter-reducing measures (the use of special covers for mite-infested beds) were most commonly incorporated. In contrast, special cleaning was only partly performed in all except one household. Measures against other well-known indoor sources such as smoking and keeping pets did not change.

Indoor moisture-reducing measures

Indoor moisture-reducing measures need appropriate facilities. Appropriate heating facilities were present in all but one household. Although all dwellings had permanent ventilation facilities, these facilities were insufficient to achieve an air exchange rate above Dutch Building code level in all rooms in 12 of the 14 households[19,25].

In addition to the needed technical requirements, heating and ventilation facilities should have no hindering side-effects for adequate use. Six households did not use ventilation facilities continuously because of expected side-effects as risk of burglary, draught, polluted air coming in from outside, the room becoming cold and increasing fuel consumption. This may be solved by the use of ventilation facilities, that provide air exchange rates sufficient to prevent mite population growth without these side-effects. In fact, such facilities are available[6,21].

All rooms should be continuously heated at 18°C or more to kill mites[19]. This became known after our trial[19]. Heating all rooms continuously at a lower temperature (15°C) was not yet feasible in two-third of the households. This was particularly seen in bedrooms, although the attitude towards heating patient's bedroom became more positive.

Shelter-reducing measures

Shelter-reducing measures consisted of special covers and smooth floor covering; the latter was optional. Using covers around mite-infested bed materials was done by all, as long as the costs were reimbursed. Knowledge of the benefit of covers and how to order those was not widespread at the time of intervention (1995) and needs attention. Covers were available free of cost in this study. However, their price (around 140 euro for a single mattress cover)[2], might deter half of the households to order covers for all mite-infested beds. In the Netherlands only covers for mattress and pillow of the patient are paid by the insurance company. The covers used in this trial were considered the best in a recently published study[2]. However, the covers for quilts should be adapted to more 'user-friendly', since risk of sliding and causing sweating deter some users to keep these on.

Type of floor covering was optional in our advice, since this can be monitored by the household members on mite exposure and treated if necessary. In 2 households a rug was ordered for the patients' bedroom, whereas textile floor covering in patients' bedroom or living room was removed in none after our advice. Freedom of choice for furnishing and finishing, with the consequences of needed special cleaning, responds to the wishes and needs of household members.

Special cleaning

Special cleaning - the only repetitive measure - was repeated every 3 months by 20%, as long as assisted by a healthcare provider. All items were tested and treated according to advised frequency in only one of the households.

The special cleaning programs were considered too complex and laborious for perceived clinical benefit. This resulted in cessation of the program in half of the households. Also, not more than 14 items were treated at a time. All considered time and personal energy investment too high to complete every 3 months in a household with young children. Also, the dramatically decreased perceived behavioral control concerning special cleaning suggests that advised programs were too elaborate. This information should be discussed before and during introduction of a program, so that patient and physician can consider whether allergen avoidance will be included in their treatment plan. This is particularly important since any clinical effect may be seen only several months after all mite-infested home textiles have been treated[17,24].

The elaborateness of programs may be adjusted by removal of mite-infested home textiles (a reduction of number of exposure sites) and/or indoor moisture reduction (a reduction in mite concentrations per home textile). By assessment of mite exposure before cleaning, time investment will decrease. Not all items need special cleaning, since not all will contain mite allergen concentrations (measured by the Acarex test as guanine) above the sensitization threshold. Frequency of needed special cleaning activities can be estimated by performing Acarex tests first every 3 months, and when negative (= no mite concentration above the threshold for sensitization to mites) with a longer time interval. This advantage of exposure assessment is not yet experienced as such by all households. Not all households would have ordered Acarex tests.

Sources other than mites
If smoking is continued or sensitizing pets are kept indoors no clinical effect can be expected from mite allergen avoidance[5].

Smoking at home continued in 12 households. In 2 of the 7 households in which parents were smoking, the smoking parent stopped smoking indoors because of its effect on their childs' asthma. Although the observed number of households is too low to draw firm conclusions, it seems worthwhile to stress the negative influence of indoor smoking on their childs' asthma. Even when it is in general known that smoke may aggravate asthma. In fact, knowledge and perceived behavioral control were only correlated at the end of the trial, suggesting that knowledge how to eliminate indoor air pollution by tobacco smoke can be more optimally used to prevent smoking indoors.

In this group none of the households kept sensitizing pets indoors; also no new pets were introduced. In Chapter 4.1 it has been demonstrated that sensitizing pets are removed when the child has a severe asthma exacerbation. Similar to smoking indoors, it seems worthwhile to stress the negative influence of keeping sensitizing pets indoors and inform the household how to remove the pet from indoors. At the moment the child has a severe asthma exacerbation, this information will be recalled.

Implementation

All households intended to include mite allergen avoidance in their daily activities before advice was given. In fact, all households performed special cleaning once. Presumably performance of special cleaning led to feedback that negatively influenced the behavioral determinants. In future studies it will be interesting to monitor intention also during intervention; thus investigating more directly which situational factors are important to perform avoidance behavior.

Investigated behavioral determinants of model

To be able to construct an individual avoidance program, the knowledge of the household members had to be improved. Knowledge could be improved concerning moisture reduction (in particular investigated for ventilation), shelter reduction (type of floor covering and the use of special covers) and special cleaning. Knowledge about removing other sources, such as smoking and keeping pets, was already good.

No hard conclusions can be drawn on which behavioral determinant(s) must be addressed to be able to implement avoidance behavior most successfully in households. This is due to the low number of participating households, the influence of habits in housekeeping activities, and differences in specificity of investigated determinants. Most housekeeping activities are habits; habits might have influenced the performance of avoidance behavior. The subjective norm has only roughly been assessed during the trial. Items in the perceived behavioral control and behavioral questionnaire were more specified than of the attitude and knowledge questionnaires; however, a behavioral category consisting of several specific conducts (as mite allergen avoidance), can better be predicted by a general attitude than by one specific attitude[3].

Information to change avoidance behavior through a change in perceived behavioral control seems most promising; this is demonstrated by the correlations between keeping pets, ventilation and covering beds and perceived behavioral control. In its turn, knowledge correlated with perceived behavioral control; this was demonstrated for smoking, keeping pets, and ventilation. Of drying laundry and heating, only one knowledge item (its effect on air humidity) was asked. Since this is a consequence of behavior, it is more likely to influence attitude, than perceived behavioral control. To investigate the influence of knowledge on perceived behavioral control, items addressing 'How to perform a measure' should be asked in future studies. Of type of floor covering no items on perceived behavioral control were asked, since this conduct was optional and was not likely to be performed during the course of one year. No knowledge items on the use of covers were asked, since this was originally included in 'special cleaning'.

By understanding avoidance principles, perceived behavioral control of household members will be improved. As a result, household members will be able to adjust their advice and adhere to it[12].

Our advice did not influence behavior by changing attitude towards advised avoidance conducts, except for heating the child's bedroom. After our advice, heating of bedroom was more positively evaluated; and more bedrooms were continuously heated. To change heating behavior, a more positive attitude is needed. Information should stress the consequences of not heating. Attitude towards drying laundry in a tumble dryer became only temporarily more positive; this did not result in a significant change in drying laundry behavior.

Tools for implementation
Implementation can be improved by setting mutual goals of household and healthcare provider more specifically before and during introduction of the program[12]. This will give household members the opportunity to form a more realistic perceived behavioral control. In this study outcome expectations were not explicitly used in setting goals. When outcome expectations change during the process of implementing allergen avoidance measures, treatment plans should be adjusted.

Implementing a program gradually will improve adherence to it. In this study the whole program was offered at one time. Since patients can tackle only one or two changes at a time, a gradual implementation of the program may increase performance[12].

By implementing avoidance measures in the following order, avoidance programs have the highest potency to be clinically effective.

1. All relevant irritants and allergens other than mites should be removed, before a clinical effect will be attributed to the avoidance of mite allergens[5].
2. The elaborateness of special cleaning may be adapted by reducing shelter possibilities for mites (smooth floor coverings; encasing beds with special covers) and by reducing the percentage of mite-infested home textiles (by indoor moisture reduction).
3. Special cleaning measures, that are unknown, have a low frequency performance and are considered time and personal energy consuming, might be more easily performed if the second requirement is fulfilled.

Follow-up of avoidance trials should be longer in order to study how elaborate a special cleaning program might be to be performed lifelong. Although a follow-up of one year is long for medical studies (effect of medication is judged within weeks) a year is short to implement new behavior with a low frequency, such as special cleaning. Adapting shelter possibilities and reducing indoor moisture will need even more time.

Assistance

Households may need assistance to obtain a realistic view on outcome expectations, needs and skills to complete a program; to structure housekeeping activities; and to supervise the performance. Asthma nurses are best equipped for these tasks[7,9,10,23]. Other professionals or interactive instruction systems that are well-informed about effective mite avoidance and the needs and skills of an individual household can be consulted on some occasions in the process of implementing mite allergen avoidance.

Since half of the households was no longer motivated to continue special cleaning after the first special cleaning, it seems worthwhile to assess motivation before and during implementation of the program.

By structuring housekeeping activities an asthma nurse can assist household members to incorporate new activities. Help may consist of demonstrating and supervising new techniques and how to overcome barriers, but also stepping down to a former step. Although selective mite allergen avoidance was set up with a step-arise structure (see Chapter 1.1, Figure 1 on page 19)[4,15,18,26], the possibility to step down to a former step or to cease allergen avoidance must be optional at all time points.

Assistance should not be restricted to one home visit, but continue until the program is completely incorporated in daily activities[12]. In this study, homes were visited 4 times within 6 months to structure and supervise households with the implementation of their program. A home visit costs approximately 70 euros in the Netherlands. To reduce costs, home visits can be replaced by visits to the outpatient clinic and, sometimes, phone calls. Households can be assisted in increasing their knowledge of mite allergen avoidance by interactive instruction systems[11,20]. However, home visits remain indispensable in assessing dwelling and household characteristics and monitoring exposure. Also, informing the household members by letting them 'see, feel, and smell' exposure sites might increase behavioral effectiveness.

How we can distinguish between good-performers and low-performers

Only 20% of households partly performed special cleaning every 3 months as long as supervised. These households were characterized by:

1. Motivation by the expected (clinical) benefit for their child.
2. A perceived behavioral control high enough to accept perceived avoidance load.
3. A flexible personality of the coordinating household member to change housekeeping activities.

These factors influencing motivation to continue the program should be discussed before and during the introduction of a special mite allergen avoidance program. Households meeting all these requirements, may wish to delay introduction of a program when life events or new time-consuming activities are introduced. Under these circumstances, housekeeping activities will be temporarily less structured.

Constructional solution

Since a total mite allergen avoidance program is hardly feasible in the Netherlands, prevention of mite infestation in homes will be the most sanitary and sustainable solution. This demands a constructional solution based on continuous moisture reduction. Requirements to design and build dwellings with no mite problem are already laid down in European building legislation[8]. Provision has been made in the Dutch Building Code to replace Dutch standards by harmonized European standards as soon as they are available[14]. Although this is done, this has not yet resulted in a reduction of mite exposure. Concerning ventilation, proposed air exchange rates are 2.5 fold higher in the European directive than in our national Building Code[14]. In a recent health classification for Dutch dwellings, these requirements were used to classify dwellings. In ✚✚✚-dwellings mite exposure will not be relevant for asthmatic patients[19]. These dwellings are already present, as was seen in Chapter 4.1.

Conclusion

An effective mite allergen avoidance program can hardly be completed by the majority of households with young asthmatic children. Particularly special cleaning is considered too elaborate. An individual program may be incorporated, only when household members are motivated by the expected clinical benefit for their child, they strongly believe that they can clean all types of home textiles, the organization of household tasks is sufficiently structured in current housekeeping activities and the coordinating parent is flexible to change housekeeping activities. Concomitant life events negatively influence structuring of housekeeping activities and increase perceived avoidance load. Before and during the introduction of an avoidance program, physician and household will need the assistance of another professional or automated coach to assess and monitor motivation and actual performance.

Since only a complete allergen avoidance protocol will reduce disease load, a technical solution is most promising to prevent mite infestation in dwellings. Shelter-reducing measures and indoor moisture-reducing measures will eventually diminish the elaborateness of cleaning programs. In fact, requirements for design and building of dwellings with no mite problem are already laid down in European building legislation, and was called ✚✚✚-class in a recent health classification for Dutch dwellings.

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Section 5

General discussion

In this section the results of Sections 2 to 4 are evaluated and used for the content of a minimal but effective mite allergen avoidance program in different regions in Europe. It will be discussed for whom and when it will be effective. A proposal is made how and by whom a program must be implemented.

A mite allergen avoidance program has a long-lasting clinical effect when it meets the following requirements: technically effective (= sufficient exposure reduction), clinically effective and feasible as a life-long endeavor (behaviorally effective) (Chapter 1.2).

Therefore, the following items have been addressed in this thesis:
- What is the content of a minimal but effective program in different regions of Europe?
- For whom (in which dwellings and for which patients) will a mite allergen avoidance program be effective? Which tools are available to distinguish dwellings and households in which avoidance will be effective? And what is the influence of their present dwelling?
- When can a program be introduced?
- How must a program be implemented to optimize adherence? Which advantages and disadvantages of such programs are experienced by the patient and other household members? How can the experienced problems be solved?
- By whom should implementation of a program be assisted? What are the responsibilities of the various professionals/healthcare providers?

What is the content of a minimal but effective program?

Nowadays, mite allergen avoidance programs with the same content are advised in different climatic regions. This results in conflicting outcomes of exposure reduction and clinical effect (Chapter 1.2). In Section 2 it has been demonstrated that effective mite allergen avoidance programs differ among climatic regions, since mite allergen exposure varies. Avoidance load depends on indoor moisture (climatic variable), and furnishing and finishing. Presence and type of furnishing and finishing are also strongly influenced by prevailing habits in a country and of a religion (cultural variable).

To be able to predict regions with and without a high mite risk, mite distribution in homes in relation to various outdoor climatic variables was investigated. This was studied in regions with dwellings heated in winter but not cooled in summer, so-called heating climates (Chapter 2.2). Discriminating variables appear to be: mean January outdoor air temperature, ventilation rate and heating intensity (Chapter 2.1). With the use of these variables a model has been made by which the risk of relevant mite exposure in carpeting of dwellings in heating climates can be predicted. This was tested successfully in and outside Europe (Chapters 2.2

and 2.3, respectively). Based on these data we can give a minimal but adequate advice about nature and frequency of effective avoidance measures in a particular climatic region in Europe (See the European mite map, page 84 of this thesis).

The Netherlands (and other regions with a comparable outdoor climate)

We first studied the content of a minimal but effective program in the Netherlands (mean January outdoor air temperature 1.7°C). In the Netherlands, mite exposure above sensitization threshold is found in most types of individual environment. This includes all rooms and spaces at home, at school, at work and in public places (Chapter 4.1). Koren et al. have demonstrated that in the Netherlands a change in mite allergen exposure (measured as guanine exposure) was only significantly correlated with a change in symptom score if all home textiles in a dwelling were taken into account[24].

There are only a few studies in which mite allergen avoidance in the whole dwelling has been compared with avoidance in a part of the dwelling (Chapter 4.1 and Kniest et al.[23]). It seems that for a guaranteed clinical effect all home textiles have to be included. Most clinically effective is a more than 10-fold exposure reduction of a high baseline exposure to below sensitization threshold[31].

The clinical benefit of mite allergen avoidance is approximately 50% if all relevant exposure sites (including exposure to other relevant allergens and irritants) are attacked. This was seen after acaricidal treatment by professionals of all home textiles at 3-monthly intervals in Utrecht and environs (the Netherlands) during one year[22,23]. A similar clinical effect was seen in asthmatic patients moving to a 'healthy' home with mechanical ventilation systems that reduced indoor moisture in Århus, Denmark[16]. The outdoor climate in Denmark is comparable to the Netherlands (both are yellow areas on the European mite map, page 84 of this thesis), though, winter temperatures are somewhat lower in Denmark.

If only a part of the home textiles is monitored and treated it will have a clinical effect less than 50%, since we do not know if the (most) relevant exposure site(s) are included. Covering of patients' bed resulted in a more than 10-fold reduction of high baseline exposure in beds in Berlin (Germany). Bronchial hyperreactivity diminished significantly compared to a control group after 8 months, but symptom scores are not recorded[13]. Covering of all mite-infested beds was well-performed by all households and resulted in a significant guanine exposure reduction in beds during the randomized, controlled trial in this thesis (Chapter

4.1). However, no clinical improvement was seen (Chapter 4.1). Exposure from other home textiles, especially upholstery, remained at a too high level. Also, continuing exposure to other relevant allergens or irritants, especially tobacco smoke, might have reduced its clinical effect.

To be technically effective a program should reduce **all** relevant mite allergen exposures, preferably below sensitization threshold. Measures should be able to reduce mite allergen exposure in a home textile more than 10-fold, and to a level below sensitization threshold (Chapter 1.2). In dwellings that conform to the Dutch Building Code level of quality (✚-dwelling), measures include:

- encasing of mattresses, quilts and pillows of all beds with special mite and allergen impermeable covers,
- washing of fully washable blankets and pillows every 6 weeks, if not encased
- special cleaners for mite-infested home textiles (3-monthly),
- increase of air exchange rates (at least $2.0 \cdot 10^{-3}$ $m^3/s.m^2$),
- and continuously heating of all rooms in winter (at 18°C)[26].

(For building characteristics and compulsory guidelines for inhabitant behavior of □-, ✚- ✚✚- and ✚✚✚-dwellings see Table 2 on page 134)

To be clinically effective, a program should also include **all other** relevant exposures to allergens and irritants. In the intervention study of this thesis sensitization to storage mites, molds and pests (mice, rats, cockroaches) played a minor role, whereas pets, especially cats, were of importance (Chapter 4.1). Relevant exposure is not restricted to the indoor environment of dwellings. It also includes outdoor allergens and irritants and nutritional elements (Chapter 3.1). Yeast flora of the skin, *Pityrosporum*, proved to be of minor importance in children aged 4 to 7 years, even in those with atopic dermatitis (Chapter 3.2).

In most home trials, as in daily practice, avoidance procedures are restricted to the patients' bed, bedroom, or bedroom and living room[9,17,18]. Avoidance measures extended to the school or work environment have rarely been reported[25]. Consensus reports of physicians on the treatment of allergic asthma do not recommend to treat the whole individual environment (at home and elsewhere)[11,14,19]. In the recently introduced guideline for Dutch asthma nurses, treatment of the whole individual environment is advised[30], but even then only 20% of households will benefit (Chapter 4.2).

Other regions in Europe

In most of Scandinavia, and at high Alps

In these regions mean January outdoor air temperature remains below -8°C (dark and middle green areas on the European mite map, Figure 4, page 84). Here it is generally too dry indoors for mite population growth in winter (Chapter 2.2.). Insulation of the building envelope, ventilation and heating are sufficient. Since relative indoor air humidity is below 45% in winter, mite populations will stay low the year round (Chapter 2.2). Dwellings in these regions are comparable to the Dutch ✚✚✚-dwellings[26]. In Dutch ✚✚✚-dwellings no special inhabitant behavior is needed to prevent sensitization to mite allergens.

Current advice in these mite-low areas (Sweden and Switzerland) is the same as in less cold regions of these countries (middle green, light green and yellow areas on the European mite map), making programs more elaborate than needed[1]. This includes removal of textile floor covering and special cleaning. In leaflets for patients general advice on ventilation and heating is given[1]. In contrast to the situation in the Netherlands, bedrooms are advised not to be heated above 18°C. This is needed to prevent dessication of humans in these cold regions: indoor air humidity must remain above 30% (Chapter 2.2).

Less cold regions of Scandinavia, the Alps and the Ural

In these regions (mean January outdoor air temperatures between -8 and -3°C), some mite population development in carpeting may occur in summer (light green regions on the European mite map). In most dwellings, a once-yearly check of mite-allergen pollution in home textiles, followed by special mite exterminating cleaning if needed, will suffice to manage mite development. This is comparable to Dutch ✚✚-dwellings. An improved thermal insulation of the building envelope (especially on mite-prone sites) and appropriate presence and use of ventilation and heating facilities will upgrade the asthma classification of dwellings to ✚✚✚-dwellings, making these once-yearly checks unnecessary.

As mentioned before, advice given includes special mite cleaning. In Austria, Acarex tests are used and Acarosan is applied to upholstery twice-yearly[1]. This requirement will be less, if rooms are continuously ventilated and heated.

Western and central Europe, Scotland and coastal Scandinavia

Here, as in the Netherlands (mean January outdoor air temperature between -3 and +4°C), a check 2 to 4 times per year of mite pollution on carpeted floors is indicated in most dwellings (yellow regions on mite map). In these areas normal quality dwellings can be compared to Dutch ✚-dwellings, if we look at prevailing living conditions of mites. Mite allergen avoidance programs will be less complex and time consuming when shelter places for mites and/or indoor moisture are reduced. Less shelter places will be available when the number of home textiles is restricted. Indoor moisture-reducing measures will reduce mite numbers in present home textiles, resulting in less home textiles to be treated (or at least with a lower treatment frequency). If the asthma class of dwellings is upgraded to ✚✚✚-dwellings by moisture reduction, home textiles such as carpeting, upholstered furniture and beds will need no special treatment. This was seen in both ✚✚✚-dwellings participating in the randomized controlled trial of Chapter 4.1.

In Germany, advice given is comparable to the Dutch selective mite allergen avoidance advice[1]. Also, controlled indoor air regulation and floor heating are included. In most countries, measures are mostly directed to the patients' bedroom. Covers are advised for bed materials. Other, non-washable textile objects should be removed (Belgium), or treated with an acaricidal cleaner yearly (Hungary)[1]. For clinical effectiveness extending the advice to other rooms, and more frequent special cleaning might be needed.

A part of France, coastal Greece, Ireland, coastal Italy, Portugal and Spain and the United Kingdom

In the orange areas on the European mite map (mean January outdoor air temperatures between +4 and +7°C) moisture reduction can not be used as a limiting factor for mite survival or for mite development, since relative humidity remains above 55% throughout the year (Chapter 2.2). All beds should be encased with special mite and allergen impermeable covers; and special mite cleaning remains necessary for other home textiles if present.

In the United Kingdom most attention is given to the patients' bedroom and living room[1]. Covering mattresses, quilts and pillows is advised. It is also advised to remove as many soft furnishings as possible, all carpeting in the bedroom and from concrete floors. These are effective solutions to reduce shelter possibilities for mites. It is also advised to seal concrete floors with a vapor barrier and to cover these floors with a non-textile floor covering, since concrete floors trap moisture. However, sealing a concrete floor with a vapor barrier will not be effective, since water vapor is produced indoors. Acaridal cleaning of carpets 2 to 3 times per year, as advised, may reduce mite allergen exposure insufficiently. Washing of pillows, blankets and quilts at 60°C once or twice a week seems justified to reduce mite allergen exposure, but may be too time consuming and costly in practice. It is also advised to set central heating a few degrees lower (especially in bedrooms). However, a lower room temperature will increase relative humidity and thus mite growth. Therefore, required treatment frequencies is augmented.

Southern Atlantic and Mediterranean coastal areas
In these areas mites survive and develop luxuriously in all home textiles in winter (red regions on the European mite map; mean January outdoor air temperature above +7°C). Dwellings will not meet the requirements of any of the Dutch asthma classes for dwellings. But still the problem is smaller than in the Netherlands, due to a very extensive air exchange with outdoors, scarcity of home textiles, and prolonged periods of persons being outdoors. During the warm summer months dwellings are usually completely closed during daytime. However, air is dry and the inhabitants spend most of the time outdoors. There is almost no need to incorporate mite allergen avoidance in the treatment plan. However, when dwellings are cooled in summer mite growth will be luxuriously, asking for extermination procedures. In their cooled homes people spend more time indoors. This will result in high exposure to mite allergens. The no-shelter procedures (e.g. covering beds, smooth furnishing and floors) are best advised.

In Spain and Italy, the no-shelter procedures are indeed advised[1]. Advice is mostly restricted to the patients' bedroom, leaving other relevant exposure sites unaddressed. In Italy, solar exposure of sheets, pillow, quilt and mattress is one of the advised measures to kill mites in home textiles[1].

The geographic mite model, that has been developed in Section 2, could be transformed into a geographic information system (GIS). With the use of such a GIS, required ventilation rates and heating intensity can be calculated from mean January outdoor air temperature for any European region. Also, other variables of the asthma classification for Dutch dwellings, such as thermal insulation of the building envelope, the use of home textiles and cleaning frequency can be adjusted for the particular situation in a region. Eindhoven University of Technology and the European Federation of Asthma and Allergy Associations (EFA) started such a GIS project for Europe in 1999. The information obtained will be used to develop an automated guide, adaptive to the needs of the individual user. It can help patients and their families in mite allergen avoidance at home. It can also be used to assess the risk of allergic reactions at holiday and recreational locations.

Mite exposure, and thus the content of an effective mite allergen avoidance program, differs among various climatic regions. Therefore, meta-analyses of avoidance trials should be performed for each of these regions and not for a mix of regions. Nevertheless, such a meta-analysis was performed, but could not demonstrate any clinical effect[15]. Meta-analyses must be restricted to non air-conditioned dwellings in a particular climate with similar mean January outdoor air temperature.

For whom will an avoidance program be effective?

In the Netherlands, a selective mite allergen avoidance program has proved to result in sufficient exposure reduction and clinical effect only when performed by professionals[22,25]. No effect was seen when performed by household members with mite-allergic, asthmatic children, aged 4 to 7 years (Chapter 4.1). This was due to behavioral ineffectiveness (Chapter 4.2). Only one of the 14 participating households was able to perform a complete selective mite allergen avoidance program as needed in ✚-dwellings. (For codes of □-, ✚-, ✚✚- and ✚✚✚-dwellings see Table 2, on page 134 of Chapter 4.1.)

A recently developed health classification for Dutch dwellings can be used to distinguish dwellings and households in which mite allergen avoidance will be effective (Table 2, on page 134 of Chapter 4.1).

In a ✚✚✚-dwelling compulsory inhabitant behavior is not needed to prevent mite concentrations above sensitization threshold. Municipal health services and dwelling inspection authorities should preferably refer atopic persons to vacant dwellings of the ✚✚✚-class.

In case mite-allergic patients live in a ✚✚-dwelling, a ✚-dwelling or a □-dwelling, special mite cleaning must be performed at least 1, 2-4, or ≥4 times per year, respectively (Chapter 4.1).

A once-yearly check of mite allergen exposure might be feasible only if
1. Household members are motivated by the expected (clinical) benefit for their child.
2. They strongly believe that they can clean all types of home textiles.
3. The organization of household tasks is structured in current housekeeping activities and not disturbed by concomitant life-events or other new activities that are time and personal energy consuming and are not yet incorporated in daily activities.

These households can live in ✚✚- and ✚✚✚-dwellings.

To incorporate special cleaning measures with a low performance frequency (2-4 times per year) in daily routine, household members must also be able to deviate from old habits: a flexible personality of the coordinating household member is needed. These households are also able to live symptom-free in a ✚-dwelling. However, only a minority of households (20%) is motivated, had a level of perceived behavioral control towards special mite-exterminating cleaning, was structured by design, and flexible enough to change their housekeeping activities (Chapter 4.2).

If households are not able to perform special mite cleaning measures until their dwelling is upgraded to a ✚✚✚-dwelling, it is better to move directly to a ✚✚✚-dwelling.

When can a program be introduced?

When exposure to tobacco smoke and sensitizing pets continues, a mite allergen avoidance program should not be incorporated. No effect may be expected of either mite allergen avoidance procedures or moving to a new dwelling (Chapters 4.1 and 4.2).

If the coordinating household member meets life-events or time consuming activities that are not yet incorporated in daily life, it is better to postpone the introduction of a mite allergen avoidance program (Chapter 4.2). The coordinating household member will not be as organized in its current housekeeping activities as needed, and the expected avoidance load of special mite cleaning will be too high. Information on mite allergen avoidance may still be given. In that case, household members can start mite allergen avoidance as soon as their situation changes.

A clinical effect of mite allergen avoidance will be seen not earlier than, mostly 3, months after avoidance procedures have been started[23]. Therefore it is necessary that:

1. high baseline exposure sites are reduced to below sensitization threshold, preferably more than 10-fold (Chapter 4.1), and
2. households are capable to continue their avoidance program completely (Chapter 4.2).

How must a program be implemented?

In the current Dutch situation, to complete a selective mite allergen avoidance program is not feasible in most households with young asthmatic children. How can this situation be improved?

The program

Selective mite allergen avoidance has the advantage that households can choose between different measures, which are all effective. To make a selective mite allergen avoidance plan feasible, avoidance products and procedures should not only be effective, but also easy to incorporate into existing household routines. In this respect, acaricides are produced as washing additives for washable objects which cannot be washed at 60°C[5,21,28].

Special mite exterminating cleaning is most difficult to incorporate since household members are not familiar with these activities. Although these activities should be performed with a low performance frequency, these activities are considered elaborate and time consuming (Chapter 4.2). Using shelter reducing measures, such as encasing bed materials and smooth floors and upholstery, an avoidance program is less elaborate. Shelter reducing measures are easily incorporated as long as financial considerations are not a limitation. Households that made their cleaning program less elaborate by shelter reduction were also the most flexible to complete avoidance (Chapter 4.2).

In the Netherlands, increasing the air exchange rate to $2.0 \cdot 10^{-3}$ $m^3/s.m^2$ in combination with continuous heating (without night reduction) is energy consuming[7]. A solution is a dynamic ventilation, regulated by actual - continuously measured in a room - indoor air quality. In combination with self-regulating ventilation gaps and sensors this can be used to reduce energy consumption[8]. Increasing thermal insulation of building construction of especially mite-prone sites will decrease needed ventilation rate[26].

European reports advise to solve the discrepance between indoor air quality and energy saving schemes by choosing appropriate ventilation facilities and rates. When these requirements are met, energy saving facilities can be included as long as they do not harm personal health[2]. This clause is incorporated in Dutch legislation, but not yet put in practice.

Implementation

It takes time to incorporate a program with new, repetitive measures. Selective mite allergen avoidance has a step-wise structure in itself. However, in the Netherlands assessment of actual allergen and irritant exposure, planning and performing a mite allergen avoidance program are considered too elaborate (Chapter 4.2). To implement a program gradually, the introduction of an education program might be useful[29,32]. New directives on how to order covers, apply acaricidal foam or powder can be demonstrated and household members can be guided. Effects of measures can be simulated by interactive instruction systems[27]. These can be supplied on CD-ROM for personal computers or are available on World Wide Web. Currently programs are often given in one time, without any guidance or feedback. Introducing no more than one or two new activities at a time will increase adherence to the program (Chapter 4.2).

Since motivation to continue a program is determined by perceived avoidance load and clinical benefit, both should be realistic. Therefore, knowledge should be increased. Household members should know that any clinical effect may be seen only after several months. Feedback, in short term, should be included. Due to the blind set-up of the trial, we were not able to give information about the clinical effect to the patient and their household, or to the physician about achieved exposure reduction. This might have negatively influenced adherence. Household members did not experience Acarex as a feasible feedback for exposure reduction. People are not used to perform these tests and consider them time consuming, especially collecting dust (Chapter 4.2).

Costs of avoidance measures were not taken into account in the intervention study (Section 4). Although costs are often mentioned as a deterrent to executing avoidance measures, time consumption forms the restricting factor in most households (Chapter 4.2). In only a small part of households special mite cleaning is temporarily feasible. It will be interesting to study the influence of financial considerations in this selected group.

Follow-up was one year in this trial. Although this is a long time for medication studies, it is short for implementing new behavior with a low performance rate (Chapter 4.2). In future selective mite allergen avoidance trials, follow-up should be longer if performed by household members.

By whom should implementation of a program be assisted?

Various disciplines are involved in mite allergen avoidance: physicians, household members, asthma nurses, building policymakers, architects, building engineers, dwelling inspection authorities, housing corporations, real estate developers, etc. All have their own task in this multi-disciplinary domain.

Physicians

Physicians play a coordinating role in allergen avoidance. They are coaches in the management of childhood asthma[6,11,19,34]. They assess to which allergens a patient is sensitized. If patients are sensitized to mite allergens, they can discuss with the patient or his parents whether mite allergen avoidance should be included in the treatment plan.

If disturbing life-events and/or time consuming not yet integrated activities are present in a household, the introduction of a mite allergen avoidance program may be postponed. Physicians can give patients general information, preferably written, that can be recalled when patients feel ready to perform avoidance measures. For further selection criteria physicians will need the help of an asthma nurse or other healthcare provider who regularly visits the home of a patient (Chapter 4.2).

Physicians should check the motivation of patient and household during the whole process of implementing mite allergen avoidance. If a whole mite allergen avoidance program is not - yet - feasible, they should advise the household members to - postpone performance or - not to start it. They can inform households that the most 'healthy' alternative will be to move to a ✚✚✚-dwelling.

Physicians must ascertain that the following conditions are fulfilled before mite allergen avoidance is introduced.

1. Mite allergy must be diagnosed.
2. In case of relevant food allergy a dietician is involved.
3. In case of sensitization and exposure to pests a pest exterminator must be called.
4. Sensitizing pets must be removed
5. Exposure to tobacco smoke indoors must be eliminated[6].

Exposure to pollen is not avoidable. Hyposensitization and symptomatic relief during the pollen season are the only solutions[6,11,19,34].

Physicians' prescription is needed to get mite allergen impermeable covers reimbursed by insurance companies. Since 1 April 1999 covers for mattresses, quilts and pillows of all beds in patients' bedroom are reimbursed in the Netherlands[4]. Although physicians are not actively involved in exposure assessment, planning and assisting the performance of a selective mite allergen avoidance program, they should know its content. Physicians must stress that a whole program has to be completed to have a long-lasting clinical effect. If during the process of exposure assessment, setting up and execution of an avoidance program, the household judges the avoidance load too heavy, physician and patients (or parents) must adapt the asthma management program. As an alternative, the physician can increase medication.

Household members

Household members should be motivated to implement mite allergen avoidance in their daily activities. In order to judge whether mite allergen avoidance is feasible in their situation, household members should assess mite allergen exposure in all home textiles. They must know the content of an effective program in their situation before actually starting any mite allergen avoidance measure[6]. If a complete program is not feasible, they should consider moving to a ✚✚✚-dwelling.

Asthma nurses

Usually, an asthma nurse or other health-related professional is needed to coach the household through the burdens of an effective mite allergen avoidance program in the Netherlands.

Asthma nurses can assess the motivation of the household to complete a mite allergen avoidance program. They can assist households in assessing relevant allergen and irritant exposure, in structuring and supervising the execution of a mite allergen avoidance program until totally integrated into daily household activities[10,11,14]. They inform the physician of the results of measures taken.

In at least 80% of home visits by asthma nurses, allergen avoidance is a subject of advice[6]. However, generally the nurse visits homes only once or twice in the total process of implementing mite allergen avoidance. Since allergen avoidance is complex in the Netherlands, only nurses working extramurally (i.e., outside the hospital) should be involved in household advising. Intramural nurses must know the content of programs, but leave guidance of households to their extramural colleagues, who have actually observed the patient's environment. These nurses need an adaptive automated coach including both architectural and behavioral aspects, though, to increase their coaching effectiveness[33].

Building legislation

Building legislation should be adapted. This should include not only the requirements to achieve sufficient ventilation rates and heating intensity, but also conditions to ascertain 'healthy' inhabitant behavior in using ventilation and heating facilities. Municipal, regional, national and international (European) policymakers can take up this challenge.

Architects and building engineers

By designing and building dwellings with a high health class, the need for elaborate special mite cleaning will be reduced. Moisture-reducing activities are feasible when permanent facilities are present and can be used continuously without hindering side-effects as draught, risk of burglary and energy saving schemes.

Designing +++-dwellings would be a natural task for architects and building engineers. However, the prevailing energy-saving schemes make it difficult to provide healthy indoor conditions[7]. Moreover, architects do not aim their work at patients.

The interpretative document 'Hygiene, health and the environment' of the European Council Directive, 89/106/EEC Construction products', explicitly recommends limitation of increased deposit of house dust mites by providing appropriate air exchange and humidity of incoming or indoor air[12]. In the Dutch Building Code, provisions have been made to replace Dutch standards by harmonized European standards[20]. Although the replacement of Dutch standards by harmonized European standards is mentioned in our national Building Code, this has not resulted in a reduction in mite allergen exposure. Ventilation rates to protect against dust mite growth are 2.5 fold higher than mentioned in our national Building Code[8,20]. Architects and building engineers should include these rates in their work.

Municipal health services

Since 1901 inspection of public health has been laid down by Dutch law[3]. This law is active since 1902. Municipal health services are local or regional services concerned with public health, including health protection schemes. Prevention of chronic diseases is one of their aims. Nowadays, in the Netherlands they are active in trying to increase ventilation, especially in households with asthma. But for an asthma classification of dwellings the health services are less equipped. They should refer the households to dwelling inspection authorities, housing corporations or real estate developers, that are familiar with the Dutch classification of healthy dwellings.

Dwelling inspection authorities

These municipal authorities are best informed about building characteristics. In the Netherlands, they check building and housing permits. These authorities are the most appropriate to include asthma classification for dwellings when assigning households with mite-allergic persons to a healthy dwelling.

Housing corporations and real estate developers

Housing corporations and real estate developers have a varied supply of dwellings. Dwelling inspection authorities can help them to classify their dwellings. Then, they can direct households with mite-allergic children to a dwelling with the appropriate asthma classification. Medical intervention is then no longer needed to buy a 'healthy' dwelling.

Other experts

Asthma nurses need the help of other partners in care in case they lack expertise. A pest exterminator for a pest problem other than dust mites, a plumber for leakages, cleaning services for a special mite-exterminating (spring) cleaning, etc. School and facility management can be involved if measures at school or work place should be taken. This is not yet common practice.

Conclusion

The content of a minimal but effective mite allergen avoidance program differs among different regions in Europe. In the Netherlands, households with one or more asthmatic children can move to a dwelling that demands no compulsory inhabitant behavior (in other words: they can live as others do). They can seek the help of municipal health services and dwelling inspection authorities to find such a dwelling. A minority of households is able to continue special mite-exterminating cleaning. They can stay in their own dwelling and upgrade the dwelling to ✚✚✚-level by moisture-reducing measures. Household members could need the assistance of a qualified asthma nurse, who can call in other experts if needed.

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Summary

Young children with asthma owe a great deal of their airway complaints to inhalation of mite products from beds, upholstered furniture and textile floor covering. One option to diminish airway complaints is to reduce the number of mites in home textiles in the dwelling. However, success of mite allergen avoidance seems 'erratic', resulting in conflicting views held by allergists as to the incorporation of mite allergen avoidance in the therapeutic plan of atopic patients.

Therefore, we investigated which effective allergen avoidance program fits within the current activities and habits of a household with young children living in dwellings meeting the current national Building Code criteria in the Netherlands. Selective mite allergen avoidance advice proved clinically and technically (=sufficient exposure reduction) effective when performed by professionals. In this individually tailored advice all relevant allergens and irritants are addressed. Included are measures that kill mites and remove their allergens by cleaning, or deteriorate their living conditions by reducing moisture and shelter.

The feasibility of generalization of these results to other regions within Europe and environs is investigated. The dissemination of various types of allergens in the home depends on indoor climate and furnishing. Both outdoor climate and cultural habits of furnishing homes differ in Europe and environs. Their influences on needed cleaning and maintenance programs, ventilation and heating schemes, and 'allowed' furnishing to prevent high mite allergen concentrations has been studied.

An experimental design has been chosen in which first the content of a minimal but effective program was determined. Therefore, certain factors are investigated separately, such as the dissemination of allergens of house dust mites, and exposure and sensitization to the skin yeast *Pityrosporum*.

The effectiveness of a potentially effective program was studied in average Dutch dwellings when performed by households. Twenty-eight households were included with children aged 4 to 7 years with moderate to severe asthma based on a house dust mite allergy in an assessor-blind, randomized, controlled trial. The households were allocated to two groups. One group received only general, written advice concerning allergen avoidance, whereas the other group received intensive assistance and an individual advice based on actually measured exposures. During the course of one year, the following items were observed and measured: knowledge, attitude and perceived behavioral control of the coordinating adult

household member towards allergen avoidance, the mite allergen reducing activities, the level of mite allergen exposure at home and at school, and the course of asthma in the children.

There seems no need to include antimycotics against *Pityrosporum* in the treatment plan of allergic children in this age group. Although *Pityrosporum* is commonly present on the skin of children, its allergen does not play an important role in allergic diseases.

In the Netherlands, no clinical effectivity was seen after either the general, written advice or the individual advice with personal assistance. Mite allergen exposure might have been relevant in some upholstery at school. It is most likely that no clinical improvement was seen, since programs were only partly performed resulting in insufficient mite allergen exposure reduction. Only 20% of the households with an individually tailored advice was able to perform a potentially effective program for the most part.

Actions which have to be performed continuously, gave the least problems. However, factors such as the presence of draught, risk of burglary, and energy saving schemes discouraged some from providing sufficient ventilation and heating. The most difficult measures for most households are those which are uncommon or have to be repeated infrequently, such as acaricidal cleaning. Type and amount of actually performed anti-mite measures depend on how motivated the adults are by the expected clinical benefit for their child, how strongly they believe that they can perform the measures, how structured they are in the organization of household activities and how flexible to change housekeeping activities.

In the damp climate of the Netherlands, it is barely feasible for a household with young children to complete an effective anti-mite program. It is possible to design and build dwellings with no mite problem, so-called +++-dwellings in a health classification of dwellings. Therefore, it seems reasonable to search for a constructional solution to diminish asthma, from which 15-20% of the children of the Dutch population currently suffers.

The content of a minimal but effective mite allergen avoidance program will differ in different climatic regions in Europe and environs. Different mite allergen exposure levels, as a result of different living conditions for mites, can be predicted by mean January outdoor air temperature, ventilation rate and heating intensity in the dwelling. In other parts of Europe and environs it may be easier or harder to build dwellings with a low risk for mite exposure. Clinicians are hardly aware of these geographical variations.

Samenvatting

Bij jonge kinderen met astma wordt een aanzienlijk deel van hun luchtwegklachten veroorzaakt door het inademen van mijtenproducten uit bedden, textiele vloerbedekking en gestoffeerd meubilair. Eén van de manieren om deze luchtwegklachten te verminderen, is het reduceren van de aantallen mijten in meubilering en stoffering van de woning. Echter, het succes van mijtenallergeen-vermijdingsprogramma's lijkt willekeurig. Dit resulteert in tegenstrijdige visies van allergologen over het opnemen van mijtenallergeen-vermijdingsprogramma's in het behandelplan van atopische patiënten.

Daarom is onderzocht welk effectief allergeen-vermijdingsprogramma past binnen de huidige activiteiten en gewoonten van een huishouden met jonge kinderen, wonend in een woning die voldoet aan de huidige Bouwbesluit criteria in Nederland. Een selectieve woningsanering bleek zowel klinisch als technisch (lees: voldoende blootstellingsvermindering) effectief wanneer uitgevoerd door deskundigen. Met dit op de individuele situatie afgestemde advies worden alle relevante allergenen en irritantia aangepakt. Het advies omvat maatregelen die mijten doden en hun allergenen verwijderen door schoonmaken, of die hun leefomstandigheden verslechteren door vocht en aantal beschuttingsplaatsen te reduceren.

De mogelijke generalisatie van deze resultaten naar andere landen in Europa en daarbuiten komt aan bod. De verspreiding van verschillende typen allergenen in huis hangt af van het binnenklimaat en de stoffering. Zowel het buitenklimaat als de culturele gewoonten om een huis te stofferen verschilt binnen Europa en in de omliggende landen. De invloed van deze factoren op de benodigde schoonmaak- en onderhoudsprogramma's, ventilatie- en verwarmingsschema's, en 'toegestane' stoffering om schadelijke concentraties aan mijtenallergeen te voorkomen, is bestudeerd.

Gekozen is voor een proefopzet, waarin eerst de inhoud van een minimaal maar effectief programma werd bepaald. Daarvoor zijn sommige factoren apart onderzocht, zoals de verbreiding van allergenen van huisstofmijten en de blootstelling en overgevoeligheid voor de huidgist *Pityrosporum*.

De effectiviteit van een potentieel effectief programma is bestudeerd in gewone Nederlandse woningen, uitgevoerd door de huishoudens zelf. Achtentwintig huishoudens met kinderen van 4 tot 7 jaar oud, die aan matig tot ernstig astma leden op basis van een huisstofmijt-allergie, deden mee in een gerandomiseerde, gecontroleerd opgezette studie. De huishoudens werden in twee groepen verdeeld. De ene groep kreeg louter algemene, schriftelijke adviezen tegen allergeenvervuiling, de andere werd intensief begeleid bij een individueel advies op basis van de daadwerkelijk vastgestelde vervuilingen. Van de volwassene, die het huishouden coördineerde, zijn kennis, attitude en ervaren gedragscontrole ten opzichte van woningsanering gemeten. Daarnaast zijn gegevens verzameld van de mijtenreducerende activiteiten, de mate van mijtenblootstelling in huis en op school, en van het beloop van het astma gedurende het jaar dat de studie duurde.

Het lijkt niet nodig om antimycotica tegen *Pityrosporum* op te nemen in het behandelplan van allergische kinderen in deze leeftijdsgroep. Aan het allergeen van *Pityrosporum*, hoewel algemeen aanwezig op de kinderhuid, kon namelijk geen belangrijke oorzakelijke betekenis worden gegeven.

In Nederland waren noch de algemene schriftelijke noch de individuele adviezen met persoonlijke begeleiding klinisch effectief. In sommige gevallen kan blootstelling aan allergenen van mijten in gestoffeerd meubilair op school relevant geweest zijn. Er werd geen klinische verbetering gezien doordat programma's slechts deels zijn uitgevoerd. Hierdoor is de blootstelling aan mijten-allergeen onvoldoende verminderd. Nog geen 20% van de huishoudens die persoonlijk werden begeleid bleek in staat een mogelijk effectief programma grotendeels uit te voeren.

Doorlopende acties geven de minste problemen, hoewel tocht, de kans op inbraak en energiebesparing enkele huishoudens van voldoende ventileren en verwarmen weerhouden. Voor de huishoudens zijn die maatregelen het moeilijkst, die niet gebruikelijk zijn en die met tussenpozen herhaald moeten worden, zoals het reinigen met mijten-dodende producten. De aard en hoeveelheid anti-mijtmaatregelen die daadwerkelijk worden genomen, hangen af van hoe gemotiveerd de volwassenen zijn door het voor hun kind verwachte klinisch effect, hoe sterk ze erin geloven dat ze de maatregelen kunnen uitvoeren en hoe flexibel ze zijn om hun huishoudelijke taken te veranderen.

Een effectief anti-mijtenprogramma vormt in het vochtige Nederland een dermate grote belasting voor een huishouden met jonge kinderen dat het zelden geheel kan worden uitgevoerd. Het is echter mogelijk woningen te bouwen waarin het mijtenprobleem niet optreedt, namelijk de ✚✚✚-woningen volgens een ziekterisico-classificatie (GCW). Daarom lijkt het voor de hand liggend een bouwkundige weg in te slaan voor het terugdringen van het astma, waaraan nu 15-20% van de kinderen binnen de Nederlandse bevolking lijdt.

De inhoud van een minimaal maar effectief mijten-allergeen-vermijdingsprogramma zal variëren in de diverse klimaatgebieden in Europa en daarbuiten. Verschillende blootstellingsconcentraties aan mijtenallergeen - als een resultaat van regionale leefcondities voor de mijten - kunnen aan de hand van de gemiddelde januari buitentemperatuur en de mate van ventilatie en verwarming van de woning voorspeld worden.

In andere delen van Europa is het vaak makkelijker of juist moeilijker om woningen met een laag mijtenrisico te bouwen. Artsen zijn zich vaak niet bewust van deze geografische variaties.

Curriculum vitae

De schrijfster van dit proefschrift werd op 5 juni 1965 geboren te Utrecht. In 1983 behaalde zij het eindexamen gymnasium-ß aan het Sint Bonifatius College te Utrecht. Hierna studeerde zij Geneeskunde aan de Rijksuniversiteit Utrecht, waar zij in juni 1991 het artsexamen behaalde. Aansluitend deed zij bij de Interuniversitaire Werkgroep 'Woning en Gezondheid' (Technische Universiteit Eindhoven en de Universiteit Utrecht) onderzoek naar allergeen-expositie en sensibilisatie bij constitutioneel eczeem. Tijdens dit onderzoek werd haar het onderhavige promotie-onderzoek aangeboden. Alvorens daaraan te beginnen was zij gedurende enkele maanden werkzaam als 'house officer' chirurgie bij Medway Health Authority te Gillingham, Engeland. In oktober 1992 kon het in dit proefschrift beschreven onderzoek van start gaan.

In 1996 trouwde zij met Frans van Lynden. In 1997 werd hun dochter Lotte geboren, in 1998 hun dochter Anne-Fleur.

Appendix

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Table A. Parental (n=14) knowledge about mite allergen avoidance per item

item	n Correctly answered		
	Before	After 3 months	After 9 months
Smoking			
Tobacco smoke can provoke or increase asthma	14	13	12
Smoking is allowed, when my child is not at home [1]	13	14	14
Keeping pets			
Pets, to which allergic, might provoke asthma	14	14	14
Only pets, to which allergy is proved, must be avoided [1]	10	10	9
By taking a pet at home, one can become allergic	13	11	11
Pet allergy is reduced by frequent contact with the pet [1]	13	14	14
Indoor moisture			
More mites are present in humid than in dry dwellings	14	14	13
Laundry drying			
Laundry drying does not influence indoor air humidity [1]	12	14	14
Ventilation			
A dwelling becomes drier by ventilation	10	14*	13[2]*
Only rooms in use have to be ventilated [1]	14	14	14
A window must be wide open to ventilate well [1]	6	12*	13**
Ventilation must be done 24 hours a day	7	12*	12*
Ventilation must be done all year	12	13	14
Heating			
Indoor air becomes drier by heating a room	12	12	13
Choice of a type of floor covering			
Carpeting is never allowed for a mite-allergic child [1]	4[2]	9[2]*	10*
More mites are present in woolen than in synthetic carpeting[1]	2	5	7*
More mites are present in high-piled than in low-piled carpeting[1]	1	4	4
Less mites are present on smooth floors than in carpeting	14	14	14
Special cleaning			
Mites are only present in not properly cleaned homes [1]	13	14	13
To wet clean removes mites from smooth floor covering	12[2]	13	14
Thoroughly vacuuming removes mites from carpeting [1]	9	12	10
Washing pillows at 40°C is effective against mites [1]	10	14*	13
Mites must only be removed from rooms where child stays[1]	13	14	14
To remove mites cleaning is never too often [1]	6	7	11*

[1] Misconceptions; [2] Answered by 13 respondents instead of 14; * $p<0.05$, ** $p<0.01$, $p<0.001$ compared to values before advice (Mann-Whitney U-test, 1-tailed tested)

Table B. Parental (n=14) attitude towards mite allergen avoidance per consequence (median values)

Consequences	Before			After 3 months			After 9 months		
	Belief	Evaluation	BE	Belief	Evaluation	BE	Belief	Evaluation	BE
No pets kept indoors									
Diminishes asthma complaints	5	2	10	5	2	10	5	2	10
Reduces allergen exposure	5	2	10	5	2	10	5	2	8
Prevent child from becoming allergic to pet	4	1	5	5	2	5	5	2	5
My child is seen as being different	3	-2	-5	3	-1*	-3*	3	-2	-3
Prevents my child from getting used to pets	4	-1	-1	3*	-1	-1	3	-1	-1
Other household members have no pet either	5	0	0	5	0	0	5	-1	-2
Textile compared to smooth floor covering									
Is more cosy	3	-1	-2	3	-1	-2	3	-1	-2
Feels warmer	5	1	5	5	1	5	5	1	5
Is more warmth insulating	4	1	4	5	1	5	5*	1	5
Is easier to keep clean	1	2	2	1	2	2	1	2	2
Is cheaper	2	-1	-1	2	0	0	1	0	0
Feels softer	5	1	5	5	1	5	5	1	5
Is better for asthma of my child	1	2	2	1*	2	2*	1	2	2
Is more soundproof	5	1	4	5	1	3	5	0*	0*
Holds dust better	5	-2	-10	5	-2	-10	5	-2	-10
Easier to slip	1	-1	-1	1*	-1	-1	1	-1	-1

Consequences	Before			After 3 months			After 9 months		
	Belief	Evaluation	BE	Belief	Evaluation	BE	Belief	Evaluation	BE
Drying laundry in tumble dryer									
Laundry quickly dry	5	1	5	5	1	5	5	1	3
Laundry becomes soft	5	0	0	5	1	2	5	0	0
House becomes less humid	5	2	5	5	2	7	5	2	10
Spend little money on laundry drying	1	-1	-1	1	0	0	1	0	0
Laundry smells fresh	2	1	2	3	1	3	3	1	2
Is time consuming	1	0	0	1	-1	-1	1	0	0
Consumes much personal energy	1	0	0	1	0	0	1	0	0
Diminishes asthma complaints	3	2	6	3	2	6	3	2	6
Occupies little room indoors	5	1	5	5	1*	5*	5	1	5
Drying laundry outdoors									
Laundry quickly dry	4	1	2	3*	1*	3	3	1	1
Laundry becomes soft	1	0	0	1	1	1	1	0	0
House becomes less humid	5	2	5	5	2	5	5	2	10
Spend little money on laundry drying	5	-1	0	5	0	0	5	0	0
Laundry smells fresh	5	1	5	5	1	5	5	1	5
Is time consuming	5	0	0	5	-1	-3	4	0	0
Consumes much personal energy	5	0	0	5	0	0	4	0	0
Diminishes asthma complaints	3	2	6	3	2	6	3	2	6
Occupies little room indoors	5	1	5	5	1	5*	5	1	5

Consequences	Before			After 3 months			After 9 months		
	Belief	Evaluation	BE	Belief	Evaluation	BE	Belief	Evaluation	BE
Ventilation									
Living room becomes cold	5	-1	-5	4	-1	-4	3*	-1	-3
Bedroom child becomes cold	5	0	0	4	-1	-1*	3*	-1	-1
Causes draught	4	-2	-5	4	-1	-4	3	-1	-2
Air becomes fresh	5	2	7	5	1	5	5	1	5
Polluted air can come in from outside	5	-2	-8	4*	-2	-4*	5	-1*	-5*
Polluted air can go out from inside	5	2	10	5	2	7	5	2	10
House becomes less humid	5	2	5	5*	2	9*	5*	2	10*
Increases risk of burglary in my home	3	-2	-4	4	-2	-6	3	-2	-4
Consumes energy (fuel)	3	-1	-2	4*	-1	-4*	4	-1	-4
Diminishes asthma complaints	3	2	6	4	2	8	3	2	6
Heating bedroom									
Bedroom becomes warm	5	0	0	5	1*	5	5*	1*	5
Bedroom becomes less humid	5	1	5	5	2*	10	5	2*	10*
Diminishes asthma complaints	3	2	6	4*	2	8*	3*	2	6
Consumes energy (fuel)	5	-1	-5	5	-1	-5	5	-1	-5
Heating living room									
Living room becomes warm	5	1	5	5	1	5	5	1	5
Living room becomes less humid	5	2	7	5	2	10	5	2	10
Diminishes asthma complaints	3	2	6	4*	2	8*	3	2	6
Consumes energy (fuel)	5	-1	-5	5	-1	-5	5	-1	-5

Consequences	Before			After 3 months			After 9 months		
	Belief	Evaluation	BE	Belief	Evaluation	BE	Belief	Evaluation	BE
Special cleaning									
House becomes dust-free	4	1	5	4	1	5	4	1	5
Diminishes asthma complaints	4	2	8	4	2	8	4	2	8
Reduces allergen exposure	5	2	9	5*	2	10	5	2	7
Removes house dust mites	4	2	8	5*	2	10	5*	1*	5
House looks clean	4	1	4	4	1	4	4	1	3
House smells clean	5	1	5	4*	1	4	3*	1	3
Cleaning materials have irritating smells	4	-1	-1	2	-1	-2	3	-1*	-2
Consumes much personal energy	4	0	0	5	0	0	5*	0	0
Is time consuming	4	-1	-3	5	-1	-4	5	-1	-2
Spend little money on cleaning	3	-1	-2	3*	-1	-1	3	0	0

* Mann-Whitney U-test, 1-tailed tested , $p < 0.05$

Table C. Parental (n=14) perceived behavioral control towards mite allergen avoidance per item. Median values (range) of a 5-point scale 1 to 5.

Item	Before	After 3 months	After 9 months
Smoking			
Respondent does not smoke at home	4 (1-5)	5 (1-5)	3 (1-5)
Partner does not smoke at home	4 (1-5)	5 (1-5)	4 (1-5)
Brothers+sisters do not smoke at home	4 (1-5)	5 (2-5)	4 (2-5)
Visitors do not smoke at home	4 (1-5)	4 (1-5)	3 (2-5)
Keeping pets			
Prevent pets to visit indoors	5 (1-5)	5 (1-5)	5 (1-5)
Moisture reduction			
Drying all laundry outside or in dryer with outlet	2 (1-5)	3 (1-5)	3 (1-5)
Drying laundry in continuously ventilated room	not asked	4 (1-5)	4 (3-5)
Ventilate all rooms 24 hours a day all year	4 (1-5)	4 (1-5)	4 (1-5)
Heating all rooms continuously, no T < 15°C	4 (1-5)	3 (1-4)	3 (1-5)
Cleaning mite-infested beds			
Mattresses: Acarosan foam 6-monthly	5 (4-5)	4 (3-5)*	4 (2-5)*
Mattresses: in mite allergen impermeable cover	5 (5-5)	4 (3-5)*	5 (4-5)*
Pillows/quilts: wash at 60°C 6-weekly	5 (4-5)	4 (1-5)*	3 (1-5)*
Pillows/quilts: Acarosan foam 6-weekly+cover	5 (3-5)	4 (2-5)*	4 (2-5)*
Bedding: wash at 60°C once a week	5 (3-5)	4 (1-5)*	4 (2-5)
Cleaning mite-infested upholstery			
Soft toys: wash at 60°C 6-weekly	5 (3-5)	4 (1-5)*	4 (1-5)*
Soft toys: freeze, followed by washing, 6-weekly	3 (1-5)	2 (1-4)*	1 (1-2)*
Soft toys: Acarosan foam 3-monthly	5 (1-5)	4 (1-4)*	3 (1-5)*
Furnished upholstery: Acarosan foam 3-monthly	5 (4-5)	4 (3-5)*	4 (1-4)*
Cleaning mite-infested textile floor covering			
Carpeting: Acarosan powder 2- to 4-yearly	5 (4-5)	4 (3-5)*	4 (2-5)*
Bath rug washing at 60°C 6-weekly	5 (1-5)	5 (2-5)	5 (4-5)
Cleaning smooth floor covering			
Smooth floor: dry or wet clean twice a week	5 (2-5)	4 (1-5)*	4 (1-5)*

* $p < 0.05$ compared to values before advice (Mann-Whitney U-test, 1-tailed tested)

Table D. Median values (range) of parental (n=14) general knowledge about mite allergen avoidance behavior before, and 3 and 9 months after advice was given

Conduct	n items	Part of items answered correctly (0.0 -1.0) Before	After 3 months	After 9 months
Removal of sources				
Smoking	2	1.0 (0.5-1.0)	1.0 (0.5-1.0)	1.0 (0.5-1.0)
Keeping pets	4	1.0 (0.5-1.0)	1.0 (0.5-1.0)	1.0 (0.5-1.0)
Moisture reduction				
In general	1	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (0.0-1.0)
Laundry drying	1	1.0 (0.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Ventilation	5	0.7 (0.2-1.0)	1.0 (0.4-1.0)***	1.0 (0.6-1.0)***
Heating	1	1.0 (0.0-1.0)	1.0 (0.0-1.0)	1.0 (0.0-1.0)
Shelter reduction				
Textile compared to smooth floor covering	4	0.3 (0.3-0.8)	0.5 (0.3-1.0) *	0.5 (0.3-1.0)**
Mite extermination				
Special cleaning	6	0.8 (0.3-1.0)	0.8 (0.7-1.0) *	1.0 (0.5-1.0) *
General knowledge	24	0.8 (0.4-0.9)	0.9 (0.6-1.0)**	0.9 (0.6-1.0)**

* $p<0.05$, ** $p<0.01$, *** $p<0.001$ compared to values before advice (Mann-Whitney U-test, 1-tailed tested)

Table E. Median values (range) of parental (n=14) general attitudes (belief x evaluation) towards mite allergen avoidance behavior before, and 3 and 9 months after advice was given

Conduct	*Attitude (-1.00 to +1.00)*		
	Before	*After 3 months*	*After 9 months*
Removal of sources			
No smoking indoors	not measured	not measured	not measured
No pets kept indoors	.15 (-.03 to .52)	.28 (.00 to .40)	.15 (-.03 to .55)
Moisture reduction			
Laundry drying in dryer	.21 (.01 to .43)	.30 (.08 to .50) *	.22 (.06 to .46)
Laundry drying outdoors	.18 (.04 to .44)	.28 (-.04 to .52)	.18 (.06 to .49)
Ventilation	.08 (-.11 to .23)	.03 (-.05 to .27)	.07 (-.04 to .28)
Heating patients' bedroom	.20 (-.10 to .40)	.38 (-.08 to .53) *	.35 (-.10 to .70)**
Heating living room	.33 (.15 to .53)	.43 (.18 to .63)	.35 (.18 to .70)
Shelter reduction			
Textile compared to smooth floor covering	.10 (-.07 to .27)	.10 (-.05 to .31)	.03 (-.14 to .26)
Mite extermination			
Special cleaning	.29 (.13 to -.49)	.24 (.06 to .57)	.26 (.01 to .48)
General attitude	.20 (.13 to .26)	.26 (.12 to .34) *	.20 (.06 to .38)

* $p<0.05$, ** $p<0.01$, compared to values before advice (Mann-Whitney U-test, 1-tailed tested)

Table F. Median values (range) of parental (n=14) general perceived behavioral control towards mite allergen avoidance behavior before, and 3 and 9 months after advice was given

Performed conduct	*Perceived behavioral control (0.0-1.0)*		
	Before	*3 months after*	*9 months after*
Removal of sources			
Smoking indoors not allowed (by parents and visitors)	0.8 (0.2-1.0)	0.9 (0.2-1.0)	0.7 (0.4-1.0)
Keeping sensitizing pets indoors not allowed	1.0 (0.4-1.0)	0.9 (0.2-1.0)	0.9 (0.5-1.0)
Moisture reduction			
Drying all laundry in dryer, out-doors or in well-ventilated room	0.4 (0.2-1.0)	0.7 (0.5-0.9)*	0.7 (0.4-1.0)*
Continuous ventilation of all rooms	0.7 (0.2-1.0)	0.7 (0.2-1.0)	0.8 (0.2-1.0)
Continuous heating of all rooms 15°C 24 hours a day	0.8 (0.2-1.0)	0.7 (0.2-0.8)	0.7 (0.2-0.9)
Shelter reduction			
Bed covers on all mite-infested beds in use	1.0 (1.0-1.0)	0.8 (0.6-1.0)***	1.0 (0.8-1.0)**
Mite extermination			
Special cleaning of all home textiles	0.9 (0.8-1.0)	0.7 (0.4-0.8)***	0.7 (0.4-0.9)***
of beds	1.0 (0.8-1.0)	0.8 (0.1-1.0)***	0.8 (0.6-1.0)**
of upholstery	0.9 (0.7-1.0)	0.6 (0.1-0.8)***	0.6 (0.1-0.9)***
of textile floor covering	0.9 (0.6-1.0)	0.8 (0.6-1.0)**	0.8 (0.6-1.0)**
of smooth floor covering	1.0 (0.4-1.0)	0.8 (0.2-1.0)**	0.8 (0.2-1.0)**
General perceived behavioral control score	0.8 (0.6-1.0)	0.7 (0.6-0.9)**	0.7 (0.5-0.9)**

* $p<0.05$, ** $p<0.01$, *** $p<0.001$ compared to values before advice (Mann-Whitney U-test, 1-tailed tested)

Table G. Spearman rank correlations of parental knowledge of avoidance behavior, and attitude and perceived behavioral control per behavioral category before advice was given, and 3 months and 9 months after advice (n=14)

Parental knowledge	Spearman rank correlation coefficient (r_s)					
	Attitude			Perceived behavioral control		
	Before	After 3 months	After 9 months	Before	After 3 months	After 9 months
Smoking	not measured			0.39	0.38	0.61*
Keeping pets	0.04	0.33	0.14	0.88***	-0.20	-0.08
Laundry drying in dryer	-0.03	n.d	n.d.	0.35	n.d.	n.d.
Ventilation	0.36	0.13	0.38	-0.14	0.50	0.62*
Heating living room	-0.48	0.41	0.35	-0.23	-0.21	-0.14
Heating child's bedroom	-0.41	0.14	0.38	-0.23	-0.21	-0.14
Choosing floor covering	0.40	-0.03	0.28	not measured		
Covering beds	not measured			not measured		
Special cleaning	-0.35	-0.53	-0.05	-0.24	-0.09	-0.05

n.d. = not done, since behavior is constant

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ compared to values before advice (Mann-Whitney U-test, 1-tailed tested)

Table H. Spearman rank correlations of avoidance behavior, and attitude and perceived behavioral control per behavioral category before advice was given, and 3 months and 9 months after advice (n=14)

Avoidance behavior	Spearman rank correlation coefficient (r_s)					
	Attitude			Perceived behavioral control		
	Before	After 3 months	After 9 months	Before	After 3 months	After 9 months
Smoking	not measured			0.38	0.43	0.49
Keeping pets	0.02	-0.29	0.02	0.83***	0.59*	0.77***
Laundry drying in dryer	-0.04	0.02	0.26	0.11	-0.25	0.18
Ventilation	0.58*	0.07	0.25	0.27	0.79***	0.80***
Heating living room	-0.67**	0.02	0.19	0.10	0.35	0.07
Heating bedroom	-0.03	0.21	-0.12	0.10	0.35	0.07
Choosing floor covering	not measured			not measured		
Covering beds	not measured			n.d.	0.22	0.56*
Special cleaning	n.d.	n.d.	-0.51	n.d.	n.d.	-0.02

n.d. = not done, since behavior is constant

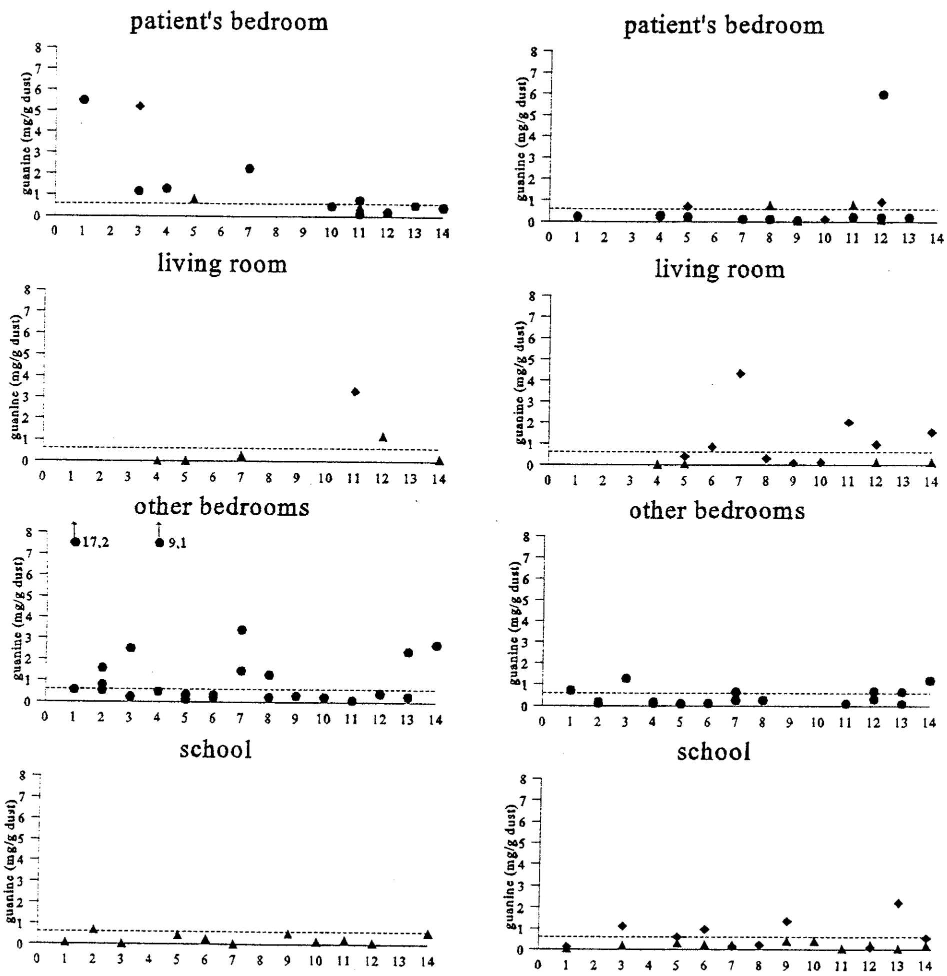
* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ compared to values before advice (Mann-Whitney U-test, 1-tailed tested)

ERRATUM

a. Treatment group

Before advice

After advice



ERRATUM

b. Control group

Before advice After advice

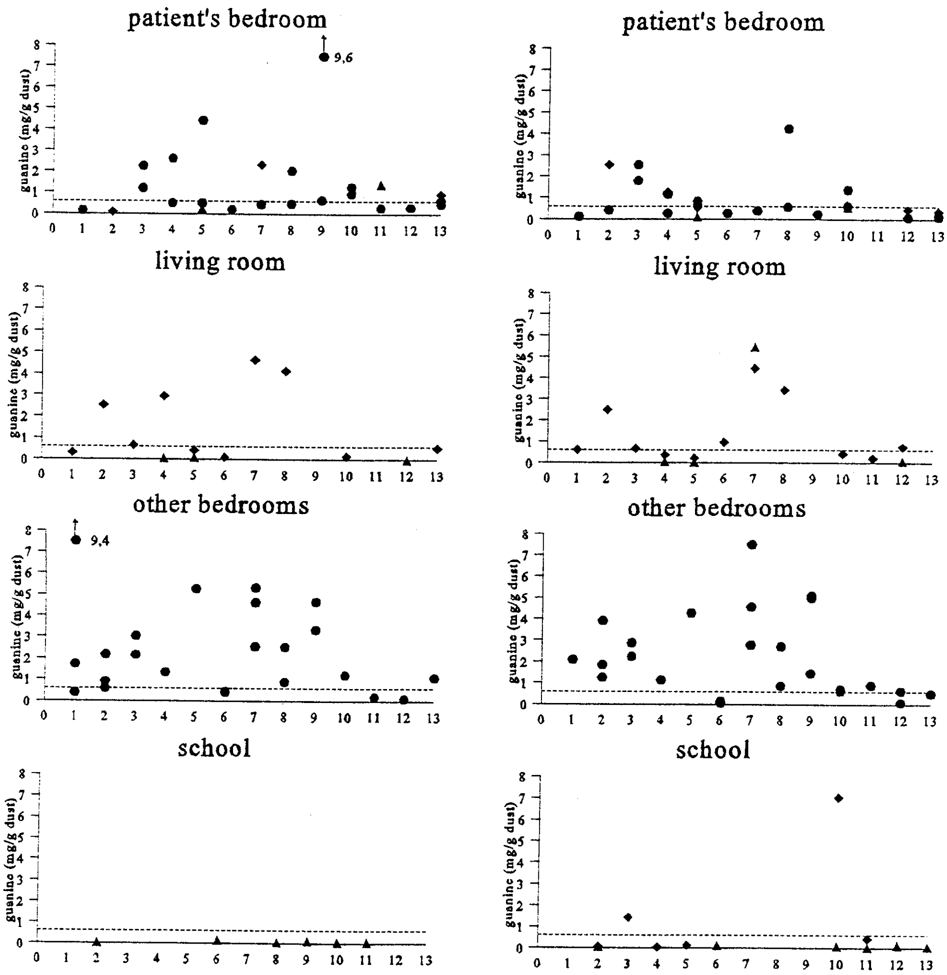


Figure 1. Guanine concentrations in beds (●), upholstery (◆) and textile floor covering (▲) in different rooms per household before and one year after advice was given a. in the treatment group; b. in the control group. At the x-axis: numbers refer to the individual households. Dashed line indicates threshold for sensitization to mites. Guanine concentrations above 8 mg/g dust are indicated with an arrow.