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 British pounds 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 time period 1900–present.

Arthropod allergens are involved in three different atopic diseases: allergic asthma, allergic rhinitis and atopic 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 80% (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 the householder 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 multidisciplinary 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 (Patton and Evans, 1929; Burgess, 1990). In addition, arthropods secrete or excrete allergens provoking two different types of allergic diseases: atopy and insect venom allergy (Mygind *et al.*, 1996; Müller & Mosbech; 1993). This contribution will be restricted to inhalant allergens causing atopic disease.

Allergy means 'unusual reacting'. The term is used to describe the reaction on a substance that is generally not harmful, but causes an immune reaction giving rise to symptoms and diseases in some individuals (Mygind *et al.*, 1996). Such a substance is called an allergen. Allergens originate from different substances: pollen of plants and trees, moulds, food, and animal parts and products.

Atopy is a so-called Type-I allergy: IgE-mediated and with immediate phenomena (Mygind *et al.*, 1996). At first contact with an allergen, special 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 (Mygind *et al.*, 1996; Platts-Mills, 1992). Figures for mortality due to allergic diseases amount to 3 to 4 per 100.000 individuals per year for asthma in UK and 1 per 100.000 in the Netherlands respectively (Platts-Mills, 1992; Centraal Bureau voor Statistiek, 1993). Costs of allergic disorders accumulate to several hundreds or even billions of British pounds per year per European country, due to extensive use of health services and a high incidence of allergy related sick leave (Colloff *et al.*, 1992; van Mölken *et al.*, 1989).

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In this article we will describe the most relevant sources of arthropod allergens causing atopic disease and 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 by multidisciplinary 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. 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, atopic dermatitis, and allergic rhinitis. The prevalence of atopic disease in relation to arthropods is considerable (Table 1). About 40% of the human population have a hereditary predisposition to atopy, a so-called atopic constitution (Bronswijk, 1991). The inherited atopic constitution is polygenic and complex (Mygind *et al.*, 1996). 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 (Mygind *et al.*, 1996; Bousquet and Kjellman, 1986). 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 (Colloff *et al.*, 1992). 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 (Platts-Mills, 1992). 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 (Sporik *et al.*, 1990). 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 (Warner and Price, 1978,Mygind *et al.*, 1996). More than half of sensitized persons will develop an atopic disease (Mygind *et al.*, 1996).

Allergic asthma

Allergic asthma is a chronic inflammatory disease of the airways, in which bronchus obstruction occurs as a reaction on a variety of exogenous factors such as allergens, irritants, exercise and viral infections (Sheffer, 1992). Of these factors, allergens are considered to play the major role (Colloff *et al.*, 1992). The prevalence rate of atopic asthma is rising in Western Europe and North America

Table 1. Prevalence of atopic diseases in Western Europe and North America (Mygind *et al.*, 1996)

Disease	Prevalence
Allergic asthma	5–10%
Atopic dermatitis*	10–15%
Allergic rhinitis	10–20%

*Cumulative prevalence

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(Blumenthal *et al.*, 1993; Mygind *et al.*, 1996). Asthma is nowadays considered to be the most common chronic disease in children in the western world (Mygind *et al.*, 1996).

Asthma usually becomes evident at the age of 3–5 years. Its prevalence has two peaks: in childhood and during adult life. In women, the second peak occurs before the age of 30, while for men it is seen at the age of 50 (Mygind *et al.*, 1996; Nelson, 1991). During adolescence, asthma improves in 50% of cases, predominantly the mild ones. In 30% of the patients it returns during adult life (Mygind *et al.*, 1996).

The severity of asthma increased in the last decades as demonstrated by hospital admission rates in England, Wales, and the USA (Blumenthal *et al.*, 1993). Although asthma death rates remain low (4/100,000/year in the UK and 1/100,000/year in the Netherlands (Platts-Mills, 1992, Centraal Bureau voor Statistiek, 1993)), the mortality associated with asthma has risen lately, especially among asthmatic children (Jackson *et al.*, 1988).

In the Netherlands, about 20% of all work absenteeism and more than 20% of school absenteeism is related to asthma (Kersten and Ewalts-Willers, 1987). Total economic costs (National Health Services, sickness benefit, research, lost productivity and earnings) of asthma in the Netherlands amounted to 1.027 million Dutch guilders (approximately 350 million British pounds) in 1990 (van Mölken *et al.*, 1989). In the United Kingdom the total economic costs were estimated to be 946 million British pounds in 1987 (Colloff *et al.*, 1992).

Allergic rhinitis

Allergic rhinitis is also an atopic disease. It consists of inflammation of the nasal mucosa and is characterized by a mucous membrane hyper-reactive to allergens and irritants. Rhinitis has been defined as a combination of sneezing, discharge and blockage, lasting ≥1 hour in most occasions (Mygind *et al.*, 1996).

Allergic rhinitis is 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 (Lund, 1994).

The prevalence of allergic rhinitis is increasing (Mygind *et al.*, 1996, Lund, 1994). 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 (Pedersen and Weeke, 1981). In the USA, 75% of allergic rhinitis cases resided inside the city, compared to 25% who lived in the surrounding rural region (Broder *et al.*, 1974).

Most rhinitis patients have mild to moderate symptoms (Mygind *et al.*, 1996). 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 hospitalisation 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 (Lund, 1994).

Atopic eczema

Atopic eczema is also called atopic dermatitis. This inflammatory skin disorder has a chronic, relapsing course. It is characterized by itching, leading to scratching and excoriations (Mygind *et al.*, 1996).

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, 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, the head and neck are often involved. In 90% of patients the infliction develops within the first 3 years of age. Symptoms usually diminish and disappear in 80% of the cases during adolescence (Mygind *et al.*, 1996).

The cumulative prevalence rate of atopic dermatitis has increased worldwide over the last three decades from 2–3% before 1960 to 10–15% nowadays (Schultz Larsen and Hanifin, 1992).

The total economic cost of atopic dermatitis (including contact dermatitis) in the Netherlands can be estimated at 32 million Dutch guilders a year (12 million British pounds) (Ruwaard and Kramers, 1993). Similar to atopic rhinitis, the direct societal costs of eczema may not be high, however, in individual cases 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 80% of disease cases arthropods are (partly) responsible (Table 2).

A summary of the most common inhalant arthropod species involved in inhalant 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 as compared to the occupational environment. There are two reasons: (a) the humidity is generally higher in the domestic environment due to a higher water vapour production (cooking, bathing and washing), giving more insects and mites developmental possibilities, and (b) the exposure period is longer in the domestic environment as compared to 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 (Wickman *et al.*, 1993).

In essence the office and hospital environment are comparable to the domestic environment, with the exception of a lesser role for house dust mites (Janko *et al.*, 1995). Other occupations may call for intensified contact with special arthropods or arthropod products (Table 3).

Domestic environment

In cases of diseases originating in the domestic environment, the tenant (household) has the primary responsibility for prevention and care. In addition, the owner of the dwelling takes responsibility for the physical state of the building, by keeping it unattractive to arthropods. Health-care professionals, such as the family nurse in the Netherlands and in the UK (Bronswijk *et al.*, 1994; Hobbs and Lenney, 1994), provide information and guidance on the health aspects of pests and on keeping allergen exposure low in cases of atopy.

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: Pyroglyphids, Acarids, Glycyphagids, predatory mites and Oribatids (Bronswijk, 1981).

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

	European Union				North America
Arthropod allergens	United Kingdom	Netherlands	Scandinavia	Mediterranean	
House dust mites	80[1]	80[2]	2–27[3]	15–49[4]	24–78[5]
Storage mites	> 30[6]	65–70[7]	6–45[8]	10[9]	12[10]
Cockroaches	10[11]				7–69[12]

Sources: [1]: Sarsfield, 1974; [2]: Bronswijk *et al.*, 1994; [3]: Korsgaard *et al.*, 1985, Wickman *et al.*, 1993; [4]: Dal Monte *et al.*, 1992, Cabrera *et al.*, 1995; [5]: Kang *et al.*, 1993, Kang and Sulit, 1978; [6]: Cuthbert *et al.*, 1979; [7]: Bronswijk *et al.*, 1994; [8]: van Hage-Hamsten *et al.*, 1985, Korsgaard *et al.*, 1985; [9]: Dal Monte *et al.*, 1992; [10]: Warren *et al.*, 1983; [11]: Bessot *et al.*, 1994, Bronswijk *et al.*, 1994; [12]: Gelber *et al.*, 1993, Kang and Sulit, 1978

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	2
Apis mellifera Linnaeus	Honey bee	D/O	3
Blatta orientalis Linnaeus	Oriental cockroach	D/O	2
Blattella asahinai Mizukubo	Asian cockroach	D/O	2
B. germanica (Linnaeus)	German cockroach	D/O	2
Bombyx mori Linnaeus	Silk worm	O	2,4
Chironomus plumosus (Linnaeus)	Chironomid midge	D/O	5
C. thummi (Meigen)	European midge	D/O	2,6
Callosobruchus maculatus Fabricius	Bruchid beetle	O	2
Cladotanytarsus lewisi (Freeman)	'Green nimitti' midge	D	34
Cochliomyia hominivorax (=americana) (Coquerel)	Screwworm/American fly	O	3
Daphnia pulex (De Geer)	Water flea	D/O	3
Drosophila melanogaster Meigen	Fruit fly	O	2,3
Ephemera danica Muller	May fly	D	2,3
Ephestia kuehniella (Zeller)	Mediterranean flour moth	O	2
Galleria mellonella (Linnaeus)	Large bee moth	O	2
Lepisma saccharina Linnaeus	Silverfish	D	7
Liposcelis bostrichophilus Badonnel	Dust (book) louse	D	7
Locusta migratoria Linnaeus	Migratory locust	O	2,8
Macronema radiatum Pictet	Caddis fly	D/O	2,3
Musca domestica Linnaeus	Common house fly	D	2,3
Periplaneta americana (Linnaeus)	American cockroach	D/O	2
Psychoda alternata Latreille	Sewer fly	D/O	2,9
Schistocerca gregaria Forskal	Desert locust	O	2
Sitophilus granarius (Linnaeus)	Grain weevil	O	2,8
Tenebrio molitor Linnaeus	Common meal beetle	O	2,3
Trogoderma angustum Solier	Berlin carpet beetle	O	10
Vespula germanica (Fabricius)	German wasp	D	3
V. vulgaris (Linnaeus)	Common wasp	D	3
Zabrotes subfasciatus (Boheman)	Mexican bean weevil	O	2,8
MITES			
Acarus siro (Linnaeus)	Storage mite	D/O	11
Blomia tropicalis van Bronswijk, de Cock, Oshima	Storage mite	D/O	11
Dermatophagoides farinae Hughes	American house dust mite	D	11
D. microceras Griffiths & Cunnington	House dust mite	D	11
D. pteronyssinus (Trouessart)	European house dust mite	D	11
Euroglyphus maynei (Cooreman)	House dust mite	D	11
Glycyphagus domesticus (De Geer)	Storage mite	D/O	11
Lepidoglyphus destructor (Schrank)	Storage mite	D/O	11
Ornithonyssus sylviarum (Canestrini & Fanzago)	Northern fowl mite	O	3
Tyrophagus putrescentiae (Schrank)	Storage mite	D/O	8,11

[1]: Bagenstose *et al.*, 1980; [2]: Moscato and Dellabianca, 1994; [3]: Kagen, 1990; [4]: Harindranath *et al.*, 1985; [5]: van Kampen *et al.*, 1994; [6]: Witteman, 1995; [7]: Rijckaert *et al.*, 1981; [8]: Burge *et al.*, 1980; [9]: Gold *et al.*, 1985; [10]: Klaschka and Rudolph, 1980; [11]: Bronswijk, 1981

House dust mites are members of the mite family Pyroglyphidae. They account for more than 90% of the mite population in textiles in dwellings in the European Union and the USA (Platts-Mills, 1992; Bronswijk, 1981). Cosmopolitan species include *Dermatophagoides farinae*, *D. microceras*, *D. pteronyssinus* and *Euroglyphus maynei*. Pyroglyphids are comparatively small (0.1–0.5 mm in length).

Population growth of pyroglyphids requires protein-rich food, a relative humidity (RH) 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 (Bronswijk, 1981). Since human individuals shed 0.5–1.0 gram of mite edible skin scales a person every day (Voorhorst and Spieksma, 1972), mite food is not a restrictive factor. The niches of these mites are formed by textile materials such as beds, carpets, upholstered furniture, soft toys, and clothing (Platts-Mills, 1992). 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 (Nes *et al.*, 1993).

There exists a seasonal variation in mite numbers and amount of mite allergens. 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 may be measured between February and May (Vervloet *et al.*, 1982; Platts-Mills *et al.*, 1987). The decrease is due to lower indoor air humidities in the cold winter months (Nes *et al.*, 1993).

In countries with a moderate climate such as the United Kingdom and the Netherlands up to 80% of atopic patients have strongly positive skin tests to mite extracts (Sarsfield, 1974; Bronswijk *et al.*, 1994). 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% were sensitized (Wickman *et al.*, 1993).

At least 12 different allergens of house dust mites have been characterized (Table 4). Of these, the so-called Group I and Group II allergens are the most important: more than 80% of mite-allergic patients have IgE antibodies against these groups (Platts-Mills, 1992). A house dust mite produces 2–4 ng Group I allergen and about 1–2 ng Group II allergen per day (Colloff *et al.*, 1992).

Allergens of *Dermatophagoides* species are formed in the posterior midgut and the hindgut as digestive enzymes (Bronswijk, 1981), excreted in faecal pellets (10–40 μm in diameter) and in shed skins of mites. These allergenic parts are relatively large and will rapidly fall in undisturbed air (Platts-Mills, 1992, Platts-Mills *et al.*, 1991). However, in time the excrement pellets will crumble and become more easily airborne (Bronswijk, 1981).

In dwellings storage mites usually belong to the families Acaridae and Glycyphagidae. Typical species include *Acarus siro*, *Glycyphagus domesticus*, *Lepidoglyphus destructor* and *Tyrophagus putrescentiae* (Kort, 1994). 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 (Kort, 1994). 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% (Bronswijk, 1981).

On a global scale exposure rates to both pyroglyphid and storage mites vary according to altitude (Vervloet *et al.*, 1982; Charpin *et al.*, 1991), latitude (Bronswijk, 1981, Munir *et al.*, 1995) and continentality (Bronswijk, 1981; Munir *et al.*, 1995), 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 (Wickman *et al.*, 1993). In addition dust reservoirs became more extensive, due to the widespread practice of wall-to-wall carpeting that are not cleaned in depth in domestic, school and office environments (Custovic *et al.*, 1994).

The story of storage mites in Western European dwellings is more complicated. Before World

Table 4. Identified arthropod allergens (after Piao King *et al.*, 1995)

Allergen	Source
	INSECTS
Bla g I, g II	*Blattella germanica*
Chi t I	*Chironomus thummi thummi*
Per a I	*Periplaneta americana*
	MITES
Der f I,II,III	*Dermatophagoides farinae*
Der m I	*D. microceras*
Der p I-VII	*D. pteronyssinus*
Lep d I	*Lepidoglyphus destructor*

War II, allergy due to storage mite exposure was not uncommon in the urban environment (Kort, 1994). 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 products), seen in rural surroundings only (Kort, 1994). After the energy crisis (1973), and the resulting increased humidity indoors, mould and storage mite growth on walls and ceilings became common. Combined with less-intensive house-cleaning procedures (as mentioned above) exposure to storage mites increased. From the eighties onward storage mite allergy was reintroduced into the urban population (Kort, 1994).

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 (Garcia *et al.*, 1994). Cockroaches are omnivorous, but prefer sweet, humid and carbohydrate rich food (Stichting Vakopleiding Ongediertebestrijding, 1993).

Although exposure to cockroach allergens is more common in the USA, exposure to these allergens is becoming a medical problem in European countries too (Bessot *et al.*, 1994). 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 (Stichting Vakopleiding Ongediertebestrijding, 1993).

Cockroach allergies are especially common in crowded multifamily dwellings in deprived urban areas (Kang and Sulit, 1978; Gelber *et al.*, 1993; Garcia *et al.*, 1994). The increased number of flats equipped with air heating and block heating gives 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 (Stichting Vakopleiding Ongediertebestrijding, 1993). The prevalence of sensitization to cockroach in atopic patients is about 10% in Europe and 7–69% in the USA (Kang and Sulit, 1978; Bessot *et al.*, 1994).

The allergens of cockroaches include specific ones for a single cockroach species as well as shared allergenic components of different taxa (Helm *et al.*, 1990, Stankus and O'Neil, 1988). Cockroach allergens are found in their faeces 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 (Zwick *et al.*, 1991).

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 (Stichting Vakopleiding Ongediertebestrijding, 1993).

54–69% of atopic patients are sensitive to silverfish (Rijckaert, 1981, Bronswijk *et al.*, 1994). No specific allergens of silverfish have yet been purified and named. Research on the silverfish allergens is in progress at the Central Laboratory of the Red Cross Blood Transfusion Service in Amsterdam, The Netherlands (Witteman, 1995).

Dust lice

Dust (or book) lice belong to the order Psocoptera. They measure up to 4 mm, and have a white, grey or brown colour. Although some species have wings, they are not able to fly. Their jerky way of walking is characteristic (Stichting Vakopleiding Ongediertebestrijding, 1993). Dust lice avoid light and thrive at relative humidities of 80% or more, and a temperature between 20°C and 25°C (Stichting Vakopleiding Ongediertebestrijding, 1993). They devour moulds (Stichting Vakopleiding Ongediertebestrijding, 1993), making them common in modern humid housing (Kort *et al.*, 1989).

34–63% of atopic patients are sensitive to dust lice (Bronswijk *et al.*, 1994; Rijckaert, 1981). The effect of cross-reactivity with allergens of other arthropods such as the fungi-devouring storage mites 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, Kagen, 1990).

Pest extermination services

For the pest exterminator working in and around dwellings, cockroaches and carpet beetles (*Trogoderma angustum*) are the main target for extermination (Stichting Vakopleiding Ongediertebestrijding, 1993). The prevalence of allergies against these arthropods in pest exterminators is not mentioned in the literature. In atopics in the general population sensitization to carpet beetles amounts to 35% (Klaschka and Rudolph, 1980).

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 (Frankland and Lunn, 1965), the larvae of the bee moth (Stevenson and Mathews, 1967), locusts (Burge *et al.*, 1980; Frankland, 1953), chironomid midges (van Kampen *et al.*, 1994) and cockroaches (Steinberg *et al.*, 1987). See also Table 3.

Farming and food processing industry

In farm houses storage mites are found more often and in larger numbers than in urban dwellings, due to infested straw, hay and animal feed (van Hage-Hamsten, 1992). However, in the barn-area changes in agricultural practice will lead to a diminishing of occupational storage mite exposure (Kort, 1994). This will eventually affect dairy farmers who are nowadays abundantly allergic to storage mites (van Hage-Hamsten *et al.*, 1985). Occupation-specific allergic disease among poultry farmers concerns the northern fowl mite, a blood sucking parasite of fowl, producing allergen-containing excreta abundantly (Kagen, 1990).

Not only farmers are exposed to the arthropods living in foodstuffs and fodder, but also shipping workers (asthma due to grain mites and insects (Sheffer, 1992)), granary workers (itch or asthma due to storage mites (Sheffer, 1992)), bean sorters (atopic disease caused by the Mexican bean weevil (Wittich, 1940)), or employees in the fish food manufacturing industry (atopic disease due to midges (Sheffer, 1992)).

Silk industry

In the textile industry, silk production and processing result in an extensive exposure to allergens of the silk worm and moth. A high incidence of atopic disease is the result. Sensitization to silkworm-derived allergens is common among silkworkers (prevalence 12–52% (Harindranath *et al.*, 1985)).

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) and Gold *et al.* (1985) report asthma caused by sewer flies *Psychoda alternata* in sewage plant workers.

MANAGEMENT OF ARTHROPOD ALLERGENS

Effective management of arthropod allergies is required. Epidemiological studies in western countries have shown increasing prevalence rates of allergic asthma, allergic rhinitis and atopic dermatitis since the twenties (Dekker, 1930, Dekker, 1928; Mygind *et al.*, 1996), particularly in childhood and adolescence (Blumenthal *et al.*, 1993). In the Netherlands this trend is expected to continue into the next decade (Ruwaard and Kramers, 1993).

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 (Mygind *et al.*, 1996). The simultaneous increase in exposure to arthropod allergens, in consumption of exotic fruits, and the decrease in infant exposure to infections, indicate a multifactorial cause, with arthropod allergens playing an important role (Charpin and Vervloet, 1992).

Stopping the increase in allergies, as well as preventing new individual sensitizations and the development of allergic complaints, form the justifications of allergen management programs. A significant reduction of arthropod allergens has become a major goal in the management of allergic disease (Bronswijk, 1995). As has been mentioned before both the domestic and the occupational environment are relevant (Janko *et al.*, 1995).

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 and cockroaches only. Allergen management programs are effective if allergen concentrations remain below these thresholds. For the allergens produced by other arthropods no hygienic thresholds have been established. 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 (Platts-Mills, 1992). Guanine is the nitrogen excretion product of arachnids and correlates well with mite allergen concentrations in the indoor environment (Colloff *et al.*, 1992, Platts-Mills, 1992). For house dust mites the threshold level for sensitization has been set at 2 μg of group I mite allergens or 0.6 mg guanine per gram settled dust, 100 mites per gram bed dust, or 10 mites per gram floor dust (Platts-Mills and de Weck, 1989; Bronswijk, 1988). The threshold level for the development of an acute asthma attack in mite-allergic persons is 10 μg of Der p I or 3.0 mg of guanine per gram settled dust, or 500 mites per gram bed dust (Platts-Mills and de Weck, 1989). The threshold level for sensitization to cockroaches was proposed at 2–8 ng Bla g II allergen per gram dust (Gelber *et al.*, 1993; Call *et al.*, 1992).

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 (Stichting Vakopleiding Ongediertebestrijding, 1993; Schober *et al.*, 1992). Unwashable objects, such as furniture, may 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 are removed by the application of peroxide containing products (Kort *et al.*, 1993). Pesticides with a high sensitization potency, such as natural pyrethrins, are not acceptable in dwellings of atopic patients (Bismuth *et al.*, 1987).

Against house dust mites, washing at 60°C is most effective (Colloff *et al.*, 1992; Bronswijk *et al.*, 1994). The mites will be killed, and with the rinsing water dead mites as well as mite allergens are removed from textiles. Vacuum cleaning will not remove live mites out of home textiles. House dust mites cling strongly to the fibres of the home textile (Colloff *et al.*, 1992).

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 (Bronswijk, 1981).

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 (Colloff *et al.*, 1992).

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 (Colloff *et al.*, 1992; Bronswijk *et al.*, 1994).

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 (Koren, 1995).

A management concept for the domestic environment

Various disciplines are involved in avoidance of exposure to arthropod allergens (Figure 1. Unfortunately, hindered by feelings of shame, not all infested dwellings are presented for treatment. This decreases the effectiveness of extermination actions, especially in cases of cockroach infestation where whole blocks of dwellings should be treated together (Stichting Vakopleiding Ongediertebestrijding, 1993). Pest extermination personnel are best equipped to inform the public about arthropod pests in an open way, reaching all target groups.

Effective allergen avoidance is a step-by-step procedure with several Partners-in-Care (Bronswijk *et al.*, 1994) (Figure 1). First of all the patient and other members of the household should be motivated by the treating physician through assessing 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 (Custovic *et al.*, 1994).

The physician takes responsibility for diagnosing sensitizations and hyper-reactivities. 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 measures (Bronswijk *et al.*, 1994; Bronswijk, 1995).

The second step in arthropod allergen avoidance includes assessment of actual exposure, using a structured interview by a community nurse, over-the-counter tests, or laboratory techniques. In the Netherlands the household is supported by a community nurse, not only for exposure assessment, but also for choosing from the different effective measures and for a structured and feasible allergen

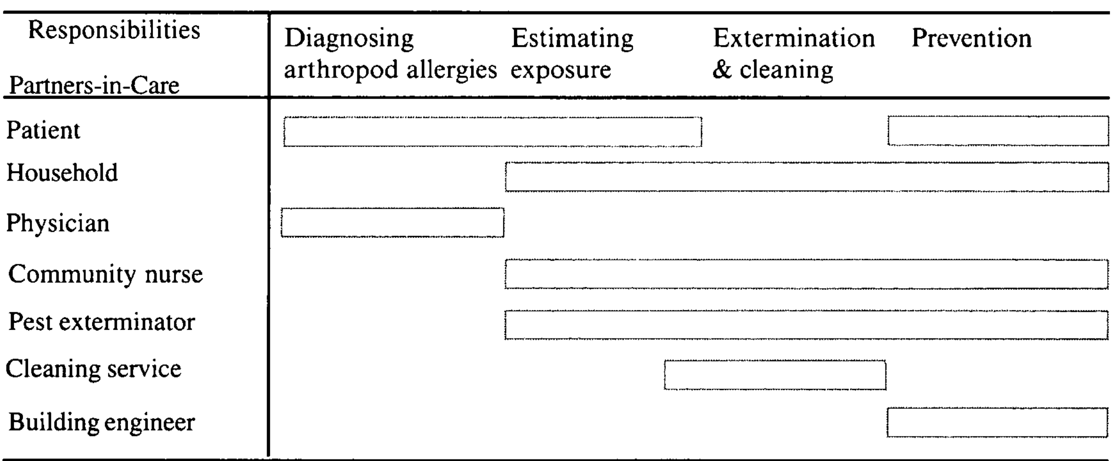

Figure 1. Partners-in-care in arthropod allergen avoidance in the domestic environment and their responsibilities.

avoidance program (Bronswijk, 1995).

The frequency of large scale surface treatment with pesticides or cleaning against allergens can be reduced by taking preventive measures, pursuing one or more of four tools that influence living conditions of the arthropods concerned: no entrance, no food, no shelter, no appropriate climatic conditions (Stichting Vakopleiding Ongediertebestrijding, 1993).

Relative humidity is the most important restricting factor for mite population growth. 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 (Brandt and Arlian, 1976, Maessen, 1995). By combining adequate ventilation and heating with a reduction of water vapour production through household activities, relative indoor air humidity will decrease, making living conditions for mites less favourable. In this way, in temperate regions, the diminished water vapour content indoors will result in a relative humidity below 50% during the cold winter months (Nes *et al.*, 1993).

Successful extermination of allergen producing cockroaches needs the expertise of the pest exterminator. When necessary the help of cleaning services can be called in. 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 engineer, will result in structural improvements (Seifert, 1991).

At half-yearly intervals household members or the community nurse should check to confirm that exposure levels remain below hygienic thresholds. If not the avoidance program should be repeated (Bronswijk, 1995).

Public buildings should be suitable to most possible users (Harber *et al.*, 1995). 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. No law prevents individual household members from behaving in an unhealthy manner, e.g. by keeping arthropod-prone conditions in the dwelling. Usually allergen avoidance management takes place after sensitization, disease or symptoms have developed (Colloff *et al.*, 1992).

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 organisation, the medical services of the organisation, and the employee themself (van der Poest Clement and Boere, 1994).

The individual worker is responsible for his or her own private health (Harber *et al.*, 1995). We may expect worker reports to the medical services of the organisation and managers, any allergies or health complaints experienced. The manager of the organisation takes responsibility for all working procedures and the assessment of health damage that could be evoked through these procedures (Harber *et al.*, 1995). The medical service of the organisation 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 (van der Poest Clement and Boere, 1994).

Facility managers coordinate all efforts relating to planning, design and management of buildings, including systems, equipment and furniture (Wagenberg, 1996). Their duties encompass setting health standards and contracting pest exterminators and cleaning services to attain these standards.

Architects and building engineers 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, the 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 favourable living conditions for allergenic arthropods or 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 multidisciplinary teamwork between patient, household members and professionals of various disciplines.

In the domestic domain a structured cooperation of pest exterminator, patient, other household members, cleaning services, building engineers, medical doctors and the family 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 organisation should work together to prevent sensitization and disease due to 'occupational' arthropods.

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REFERENCES

Bagenstose, A.H., Mathews, K.P., Homburger, H.A., and Saaveard-Delgado, A.P. (1980). Inhalant allergy due to crickets. *J Allergy Clin Immunol*, 65:71–74.

Bessot, J.C., de Blay, F., and Pauli, G. (1994). From allergen sources to reduction of allergen exposure. Review. *Eur Respir J*, 7:392–397.

Bismuth, C., Baud, F.J., Conso, F., Frejaville, J.P., and Garnier, R. (1987). *Toxicologie Clinique*. Flammarion, Paris.4th ed..

Blumenthal, M., Bousquet, J., and Burney, P. (1993). Evidence for an increase in atopic disease and possible causes. *Clin Exp Allergy*, 23:484–492.

Bousquet, J. and Kjellman, N.-I.M. (1986). Predictive value of tests in childhood allergy. *J Allergy Clin Immunol*, 78:1019–1022.

Brandt, R.L. and Arlian, L.G. (1976). Mortality of house dust mites, Dermatophagoides farinae and D. pteronyssinus, exposed to dehydrating conditions or selected pesticides. *J Med Ent*, 13(3):327–331.

Broder, I., Higgins, M.W., Matthews, K.P., and Keller, J.B. (1974). Epidemiology of asthma and allergic rhinitis in a total community. *J Allergy Clin Immunol*, 53:127–138.

Bronswijk, J.E.M.H.van (1981). *House dust biology for allergists, acarologists and mycologists*. NIB, Zeist, The Netherlands.

Bronswijk, J.E.M.H.van (1988). Niveaux d'allergènes domestiques tolérables par l'homme. *Rev fr Allergol*, 28(2):143–146.

Bronswijk, J.E.M.H.van (1991). Ziek van je huis, inaugural speech, Utrecht University.

Bronswijk, J.E.M.H.van (1995). Allergologische woningsanatie en de rol van de wijkverpleegkundige. In: *Astma, chronische bronchitis en emfyseem. Een professioneel kader*, ed. by M. Telkamp, et al, pp. 123–140. De Tijdstroom, Utrecht/Leusden.

Bronswijk, J.E.M.H.van, Kort, H.S.M., Koren, L.G.H., Nes, A.M.T.van, and Snijders, M.C.L. (1994). Allergen avoidance in the dwelling environment. In: *Eczema and the environment. On the 75th anniversary of dermatology at Utrecht university, The Netherlands (1919–1994)*, ed. by J.E.M.H.van Bronswijk, et al, pp. 83–98. Drukkerij Elinkwijk BV, Utrecht, The Netherlands.

Burge, P.S., Edge, G., O'Brien, I.M., Harries, M.G., Hawkins, R., and Pepys, J. (1980). Occupational asthma in a research centre breeding locusts. *Clin Allergy*, 10:355–363.

Burgess, N.R.H. (1990). *Public Health Pests. A guide to identification, biology and control*. Chapman and Hall, London-New York-Tokyo-Melbourne-Madras.

Cabrera, P., Julià-Serdà, G., Rodríguez de Castro, F., Caminero, J., Barber, D., and Carillo, T. (1995). Reduction of house dust mite allergens after dehumidifier use. *J Allergy Clin Immunol*, 95:635–636.

Call, R.S., Smith, T.F., Morris, E., Chapman, M.D., and Platts-Mills, T.A.E. (1992). Risk factors for asthma in inner city children. *J Pediatr*, 121:862–866.

Centraal Bureau voor Statistiek, (1993). CBS-publikatie. Overledenen naar doodsoorzaak 1993. Serie A1. CBS, Heerlen.

Charpin, D., Birnbaum, J., Haddi, E., Genard, G., Lanteaume, A., Toumi, M., Faraj, F., Brempt, X.van der, and Vervloet, D. (1991). Altitude and allergy to house-dust mites. A paradigm of the influence of environmental exposure on allergic sensitization. *Am Rev Respir Dis*, 143:983–986.

Charpin, J. and Vervloet, D. (1992). *Allergologie*. Médecine-Sciences Flammarion, Paris.3rd ed..

Colloff, M.J., Ayres, J., Carswell, F., Howarth, P.H., Merrett, T.G., Mitchell, E.B., Walshaw, M.J., Warner, J.O., Warner, J.A., and Woodcock, A.A. (1992). The control of allergens of dust mites and domestic pets: a position paper. *Clin Exp Allergy*, 22(2):1–28.

Custovic, A., Taggart, S.C.O., and Woodcock, A. (1994). House dust mite and cat allergen in different indoor environments. *Clin Exp Allergy*, 24:1164–1168.

Cuthbert, O.D., Brostoff, J., Wraith, D.G., and Brighton, W.D. (1979). 'Barn allergy': asthma and rhinitis due to storage mites. *Clin Allergy*, 9:229–236.

Dal Monte, A., Tomasini, C., Calipa, V., and Pederzoli, P. (1992). The role of the sensitization to storage mites in the diagnosis of allergic respiratory diseases. *Aerobiologia*, 8:419–422.

Dekker, H. (1928). Asthma und Milben. *Münch Med Wschr*, 75:515–516.

Dekker, H. (1930). Allergisches Asthma. In: *Praktikum der Allergischen Krankheiten*, ed. by K. Hansen, et al, pp. 69–137. Montana, Horw-Luzern.

Frankland, A.W. (1953). Locust sensitivity. *Ann Allergy*, 11:445.

Frankland, A.W. and Lunn, J.A. (1965). Asthma caused by the grain weevil. *Br J Ind Med*, 22:157.

Garcia, D.P., Corbett, M.L., Sublett, J.L., Pollard, S.J., Meiners, J.F., Karibo, J.M., Pence, H.L., and Petrosko, J.M. (1994). Cockroach allergy in Kentucky: a comparison of inner city, suburban and rural small town populations. *Ann Allergy*, 72:203–208.

Gelber, L.E., Seltzer, L., Bouzoukis, J., Pollart, S.M., Chapman, M.D., and Platts-Mills, T.A.E. (1993). Sensitization and exposure to indoor allergens as risk factors for asthma among patients presenting to hospital. *Am Rev Respir Dis*, 147:573–578.

Gold, B.L., Mathews, K.P., and Burge, H.A. (1985). Occupational asthma caused by sewer flies. *Am Rev Respir Dis*, 131:949–952.

Harber, P., Schenker, M.B., and Balmes, J.R. (1995). *Occupational and environmental respiratory disease.* Mosby-Year Book, Inc.,

Harindranath, N., Prakash, O., and Subb Rao, P.V. (1985). Prevalence of occupational asthma in silk filatures. *Ann Allergy*, 55:511–515.

Helm, R.N., Squillace, D.L., Jones, R.T., and Bremmer, R.J. (1990). Shared allergenic activity in Asian (*Blattella asahinai*), German (*Blattella germanica*), American (*Periplaneta americana*), and Oriental (*Blatta orientalis*) cockroach species. *Int Arch Allergy Appl Immunol*, 92:154.

Hobbs, J. and Lenney, W. (1994). How confident do practice nurses feel about managing paediatric asthma? *Eur Resp J*, 7 (Suppl 18):1s-521s.(Abstract)

Jackson, R., Sears, M.R., Beaglehole, R., and Rea, H.H. (1988). International trends in asthma mortality: 1970 to 1985. *Chest*, 94:914–918.

Janko, M., Gould, D.C., Vance, L., Stengel, C.C., and Flack, J. (1995). Dust mite allergens in the office environment. *American Industrial Hygiene Association Journal*, 11:1133–1146.

Kagen, S.L. (1990). Inhalant allergy to arthropods. Insects, arachnids, and crustaceans. *Clin Rev Allergy*, 8:99–125.

Kang, B. and Sulit, N. (1978). A comparative study of prevalence of skin hypersensitivity to cockroach and house dust antigens. *Ann Allergy*, 41:333.

Kang, B.C., Johnson, J., and Veres-Thorner, C. (1993). Atopic profile of inner-city asthma with a comparative analysis on the cockroach-sensitive and ragweed-sensitive subgroups. *J Allergy Clin Immunol*, 92:802–811.

Kersten, M.W. and Ewalts-Willers, R.A.M.A. (1987). *CARA verpleegkundig benaderd.* Spruyt, van Mantgem & De Does,

Klaschka, F. and Rudolph, R. (1980). Trogoderma-Allergie: Eine neue klinische Erfahrung. *Z Hautkr*, 55:1411–1416.

Koren, L.G.H. (1995). *Allergen avoidance in the home environment. A laboratory evaluation of measures against mite, fungal and cat alllergens.* (PhD Thesis) University of Technology, Eindhoven.

Korsgaard, J., Dahl, R., Iversen, M., and Hallas, T. (1985). Storage mites as a cause of bronchial asthma in Denmark. *Allergol. et Immunopathol.*, 13(2):143–149.

Kort, H.S.M. (1994). *A structured approach to allergen avoidance in dwellings with special emphasis on the ecosystem of humid indoor walls and room partitions.* (PhD Thesis). Einhoven University of Technology, Einhoven.

Kort, H.S.M., Bronswijk, J.E.M.H.van, and Schober, G. (1989). Moulds, mites and moisture, a preliminary report on six cases of fungal damage in dwellings. In: *Proceedings 'Present and future of indoor air quality.'*, ed. by C.J. Bieva, et al, pp. 389–393. Excerpta Medica, Amsterdam.

Kort, H.S.M., Koers, W.J., Nes, A.M.T.van, Young, E., Vorenkamp, J., Wolfs, B.G., and Bronswijk, J.E.M.H.van (1993). Clinical improvement after unusual avoidance measures in the home of an atopic dermatitis patient. *Allergy*, 48:468–471.

Lund, V.J. (1994). International Consensus Report on the Diagnosis and Management of Rhinitis. *Allergy*, Suppl 19:5–34.

Maessen, W.H. (1995). Overlevingskansen van huisstofmijtenpopulaties. Een onderzoek naar de invloed van ventilatie op de vermindering van een huisstofmijtenpopulatie op een begane grondvloer. M.Sc. Thesis, Eindhoven University of Technology, Eindhoven.

Moscato, G. and Dellabianca, A. (1994). Only Hymenoptera in the future of insect allergy? In: *Progress in insect allergy*, ed. by F. Bonifazi, et al, pp. 49–53. Kurtis, Milano.

Müller U, Mosbech H (eds). (1993). Subcommittee on Insect Venom Allergy of the European Academy of Allergology and Clinical Immunology: Position paper: Immunotherapy with hymenoptera venoms. *Allergy*, 48 (14 Suppl):37–46.

Munir, A.K.M., Björkstén, B., Einarsson, R., Ekstrand-Tobin, A., Möller, C., Warner, A., and Kjellmann, N.-I.M. (1995). Mite allergens in relation to home conditions and sensitization of asthmatic children from three climatic regions. *Allergy*, 50:55–64.

Mygind, N., Dahl, R., Pedersen, S., and Thestrup-Pedersen, K. (1996). *Essential allergy.* Blackwell, Oxford. 2nd ed..

Nelson, H.S . (1991). The natural history of asthma. *Ann Allergy*, 66:196–203.

Nes, A.M.T.van, Kort, H.S.M., Koren, L.G.H., Pernot, C.E.E., Schellen, H.L., Boven, F.E.van, and Bronswijk, J.E.M.H.van (1993). The abundance of house dust mites (Pyroglyphidae) in different home textiles in Europe, in relation to outdoor climates, heating and ventilation. In: *Proceedings of the 1st International Conference on Insect Pests in the Urban Environment*, ed. by K.B. Wildey, et al, pp. 229–239. BPCC Wheatons Ltd, Exeter, Great Britain.

Ordman, D. (1946). Sewage filter flies (Psychoda) as a cause of bronchial asthma. *S Afr Med J*, 20:32–35.

Patton, W.S. and Evans, A.M. (1929). *Insects, ticks, mites and venomous animals of medical and veterinary importance.* H.R. Grubb, Croydon, Great Britain.

Pedersen, P.A. and Weeke, E.R. (1981). Allergic rhinitis in danish general practice. Prevalence and consultation rates. *Allergy*, 36:375–379.

Piao King, T., Hoffman, D., Lowenstein, H., Marsh, D.G., Platts-Mills, T.A.E., and Thomas, W. (1995). Ed, Allergen nomenclature. *J Allergy Clin Immunol*, 96(1):5–14.

Platts-Mills, T.A.E. (1992). Eds, Dust mite allergens and asthma: Report of a second international workshop. *J Allergy Clin Immunol*, 89:1046–1060.

Platts-Mills, T.A.E. and de Weck, A.L. (1989). Dust mite allergens and asthma – a worldwide problem. *J Allergy Clin Immunol*, 83:416–427.

Platts-Mills, T.A.E., Hayden, M.L., Chapman, M.D., and Wilkins, S.R. (1987). Seasonal variation in dust mite and grass-pollen allergens in dust from the houses of patients with asthma. *J Allergy Clin Immunol*, 79:781–791.

Platts-Mills, T.A.E., Ward, G.W., Sporik, R., Gelber, L.E., Chapman, M.D., and Heymann, P.W. (1991). Epidemiology of the relationship between exposure to indoor allergens and asthma. *Int Arch Allergy Appl Immunol*, 94:339–345.

Rijckaert, G. (1981). *Fast releasing allergens from some organisms living in house dust.* Thesis.Catholic University of Nijmegen, Nijmegen.

Rijckaert, G., Thiel, C., and Fuchs, E. (1981). Silberfischchen und Staubläuse als Allergene. *Allergologie*, Jahrgang 4, Nr. 2:80–86.

Ruwaard, D. and Kramers, P.G.N. (1993). *Volksgezondheid Toekomst Verkenning. De gezondheidstoestand van de Nederlandse bevolking in de periode 1950–2010.* SDU, Den Haag.

Sarsfield, J.K. (1974). Role of house-dust mites in childhood asthma. *Arch Dis Childhood*, 49:711–715.

Schober, G., Kniest, F.M., Kort, H.S.M., de Saint Georges Gridelet, D.M.O.G., and van Bronswijk, J.E.M.H. (1992). Comparative efficacy of house dust mite extermination products. *Clin Exp Allergy*, 22:618–626.

Schultz Larsen, F. and Hanifin, J.M. (1992). Secular change in the occurrence of atopic dermatitis. *Acta Derm Venereol (Stockh)*, suppl 176:7–12.

Seifert, B. (1991). Das "sick building"-Syndrom. *Öff Gesundh-Wes*, 53:376–382.

Sheffer, A.L.(chairman). (1992). International consensus report on the diagnosis and management of asthma. International asthma management project. *Clin Exp Allergy*, 22(Suppl. 1):

Sporik, R., Holgate, S.T., Platts-Mills, T.A.E., and Cogswell, J.J. (1990). Exposure to house-dust mite allergen (Der p I) and the development of asthma in childhood. *N Engl J Med*, 323:502–507.

Stankus, R.P. and O'Neil, C.E. (1988). Antigenic/allergenic characterization of American and German cockroach extracts. *J Allergy Clin Immunol*, 81:563.

Steinberg, D.R., Bernstein, D.I., Gallagher, J.S., and et al., (1987). Cockroach sensitization in laboratory workers. *J Allergy Clin Immunol*, 80:586–590.

Stevenson, D.D. and Mathews, K.P. (1967). Occupational asthma following inhalation of moth particles. *J Allergy*, 39:274.

Stichting Vakopleiding Ongediertebestrijding, (1993). Syllabus A. Stichting Vakopleidng Ongediertebestrijding, Wageningen.

van der Poest Clement, P.E. and Boere, A.H.M. (1994). *Handboek ARBO-wet.* SDU, Den Haag.

van Hage-Hamsten, M., Johansson, S.G.O., Höglund, S., Tüll, P., Wirén, A., and Zetterstrom, O. (1985). Storage mite allergy is common in a farming population. *Clin Allergy*, 15:555–564.

van Hage-Hamsten, M. (1992). Allergens of storage mites. *Clin Exp Allergy*, 22:429–431.

van Kampen, V., Liebers, V., Czuppon, A., and Baur, X. (1994). Chironomidae hemoglobin allergy in Japanese, Swedish, and German populations. *Allergy*, 49:9–12.

van Mölken, M.P.M.H., Doorslaer, E.K.A., and Rutten, F.F.H. (1989). *Cara in cijfers, verslag van een pilot-studie.* Instituut voors Medische Technology Assessment, Maastricht, The Netherlands.

Vervloet, D., Penaud, A., Razzouk, H., Senft, M., Arnaud, A., Boutin, C., and Charpin, J. (1982). Altitude and house dust mites. *J Allergy Clin Immunol*, 69:290–296.

Voorhorst, R. and Spieksma, F.T.M. (1972). Prevention of asthma and vasomotor rhinitis due to house-dust-mite atopy. *Prevent*, 1:17–23.

Wagenberg, A.F.G.M. (1996). Facility management. Zoeken naar theoretische grondslagen. Inaugural speech, February 2, 1996. Eindhoven University of Technology, Eindhoven, The Netherlands.

Warner, J.O. and Price, J.F. (1978). House dust mite sensitivity in childhood asthma. *Arch Dis Child*, 53:710–713.

Warren, C.P.W., Holford-Strevens, V., and Sinha, R.N. (1983). Sensitization in a grain handler to the storage mite *Lepidoglyphus destructor* (Schrank). *Ann Allergy*, 50:30–33.

Wickman, M., Nordvall, S.L., Pershagen, G., Korsgaard, J., and Johansen, N. (1993). Sensitization to domestic mites in a cold temperate region. *Am Rev Respir Dis*, 148:58–62.

Witteman, A.M. (1995). *Quantitative aspects of the IgE-mediated reaction in patients with asthma and rhinitis.* (PhD Thesis) University of Amsterdam, Amsterdam.

Wittich, F.W. (1940). Allergic rhinitis and asthma due to the Mexican bean weevil (*Zabrotes subfasciatus boh*). *J Allergy*, 12:42.

Zwick, H., Popp, W., Sertl, K., Rauscher, H., and Wanke, T. (1991). Allergenic structures in cockroach hypersensitivity. *J Allergy Clin Immunol*, 87:626–630.