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REVIEW ARTICLE

Asthma and the Home Environment

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Key words: Allergens; Housing; Indoor environment; Nitrogen dioxide; Pollution; Sulfur dioxide; Volatile organic compounds

ABSTRACT

Recent years have seen a global increase in asthma prevalence. This has coincided with modifications to the home environment resulting in changes to the indoor air quality. This article considers the links between indoor pollution and asthma. Exposure to a range of substances is examined. Airborne allergens such as those from house dust mites may be important. Pollution from particulate materials associated with combustion and smoking is discussed, as is the role of chemical vapors and gases including nitrogen dioxide, sulfur dioxide, and volatile organic compounds. The efficacy of various environmental controls to limit the impact of these pollutants is explored.

INTRODUCTION

It is generally agreed that, in recent decades, we have experienced a global increase in asthma prevalence (1,2). Particularly in more economically developed and rapidly de-

veloping countries, rising prevalence has been accompanied by unprecedented changes in both lifestyles and environmental quality. One impact of development has been an upsurge in the proportion of inhabitants living in cities. A repercussion is that an escalating number of

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the population are exposed to the contaminants of urban air (3). Although this has led to concern that outdoor air pollution may be to blame in causing asthma, the findings of many studies are weak or contradictory (4). Consequently, there has been a shift of attention from outdoors to the situation indoors (5). It seems that changes in indoor air quality may be more important in explaining the increase in the number of asthma cases.

Until recently, the health impacts of indoor air pollution have been of little concern to much of the scientific community. Up until the mid 1970s, indoor air quality problems in residences were occasionally investigated, but the level of interest was generally low (6). Even today, most public and media attention is focussed on the effects of outdoor air pollution (7). To some extent this preoccupation with outdoor air is understandable; the frequently invisible nature of indoor air quality problems must be contrasted with the often only too obvious photochemical and particulate substances that characterize outdoor contamination. However, the fact remains that the average individual born today will spend more than 90% of their life inside (8). In the past, this figure was much lower. This trend has coincided with major changes to the home environment, in part driven by alterations to building design which were hastened by high fuel costs during the 1970s energy crisis.

Modern homes are much better insulated than was previously the case. Houses with ventilation rates as low as 0.2–0.3 air exchanges hr^{-1} are now widespread (9). In older properties, particularly those with open fireplaces, ventilation rates above 1 air exchange hr^{-1} are more common. Improved insulation has been accompanied by numerous other modifications. Many more houses have central heating and sealed-unit double-glazing for windows. For example, although only 29% of British homes were centrally heated in 1970, this figure had risen to more than 85% by 1995 (10). Fitted carpets have generally replaced loose rugs, and advances in construction technology have meant a greater use of synthetic building materials (11).

All of these transformations have undoubtedly led to more comfortable living condi-

tions. However, they have also resulted in warmer, more humid houses with a poorer availability of fresh air. These conditions provide an environment in which airborne contaminants are readily produced and may build up to much higher concentrations than are typically encountered outside (12). Of course, many other aspects of the internal and external environment have changed in recent years, and it is quite possible that these could partially explain the increasing prevalence of asthma. However, given the amount of time that most individuals spend indoors, it seems that the indoor environment may have an important role to play in allergic disorders.

As with all respiratory allergies, asthma is caused by an interaction between genetic and environmental factors (11). A great number of substances found in the environment can induce allergic respiratory sensitization and reaction (13), whereas many more precipitate or aggravate respiratory symptoms by nonallergic mechanisms (14,15). Various indoor exposures have been related to asthma, including house dust mites, molds and fungal spores, sulfur dioxide (SO_2), and nitrogen dioxide (NO_2) from cooking with gas (16). High concentrations of volatile organic compounds (VOCs) and formaldehyde have also been associated with the condition (17), as has particulate matter from smoking and biofuel combustion.

Concern over indoor air has now increased to such an extent that the United States Centers for Disease Control has classified indoor pollution as a factor of high environmental risk (18). Domestic air pollution is now seen as a major public health issue, and if the asthma problem is to be successfully tackled, a good understanding of the risks it poses may be vital (19). This article reviews the current state of knowledge on the relationship between indoor air quality and asthma, and outlines some of the interventions that may be required to reduce levels of exposure.

INDOOR ALLERGENS

Indoor allergens arise from a wide variety of sources (Table 1). However, the best under-

Table 1. Common Indoor Allergic Agents

SOURCE	GENUS	SPECIES	ALLERGEN
Dust mite	<i>Dermatophagoides</i>	<i>pteronyssinus</i>	<i>Der p</i>
	<i>Dermatophagoides</i>	<i>farinae</i>	<i>Der f</i>
	<i>Euroglyphus</i>	<i>maynei</i>	<i>Eur m</i>
	<i>Hirstia</i>	<i>domicola</i>	<i>Hir d</i>
	<i>Lepidoglyphus</i>	<i>destructor</i>	<i>Lep d</i>
	<i>Malayoglyphus</i>	<i>intermedius</i>	<i>Mal l</i>
	<i>Malayoglyphus</i>	<i>carmelitus</i>	<i>Mal C</i>
	<i>Sturnophagoides</i>	<i>brasiliensis</i>	<i>Stu b</i>
Cat	<i>Felis</i>	<i>domesticus</i>	<i>Fel d</i>
Dog	<i>Canis</i>	<i>familiaris</i>	<i>Can f</i>
Rodent	<i>Mus</i>	<i>musculus</i>	<i>Mus m</i>
	<i>Rattus</i>	<i>norvegicus</i>	<i>Rat n</i>
Cockroach	<i>Blattella</i>	<i>germanica</i>	<i>Bla g</i>
	<i>Periplanetta</i>	<i>americana</i>	<i>Per a</i>
Fungi	<i>Alternaria</i>	<i>alternato</i>	<i>Alt a</i>
	<i>Aspergillus</i>	<i>fumigatus</i>	<i>Asp f</i>
	<i>Cladosporium</i>	<i>herbarium</i>	<i>Cla h</i>

stood is the house dust mite. Ten species of mites can be found in temperate climates. They come from the genera *Dermatophagoides*, *Euroglyphus*, *Malayoglyphus*, *Hirstia*, and *Sturnophagoides* (11). In the United States and Europe it is thought that individuals of *D. pteronyssinus* and *E. maynei* comprise around 95% of all mites present in a typical house (20). In tropical climates the mite *Blomia tropicalis* is also commonly found, although house dust mites survive in the majority of homes. Undoubtedly the most researched mite is the common house dust mite, *D. pteronyssinus*. The mites prefer warm, humid conditions (Table 2). They inhabit a range of soft furnishings, including sofas, fabrics, carpets, sheets, duvets, pillows, and mattresses.

The droppings from the mite are a primary source of indoor antigens (21). The mites encase their feces in a coating of intestinal enzymes containing a protein which is a strong allergen. The function of the coating is not fully understood. It may protect the hind gut from physical damage, or act as an antioxidant (22). Although more than 10 different antigens have been characterized for *D. pteronyssinus* so far, the first to be identified, *Der p* 1, is the most commonly reported.

There can be up to 100,000 mite fecal particles, ranging from between 10 and 40 μm in

diameter, in a single gram of house dust (23). Their small size means that they do not remain airborne for long, although levels in disturbed rooms can be more than 1000 times higher than those observed in undisturbed environments (24). It is generally recognized that concentrations of *Der p* 1 above $2 \mu\text{g g}^{-1}$ (equivalent to 100 mites) of dust appear to represent a significant factor for mite sensitization (25), and $10 \mu\text{g Der p 1 g}^{-1}$ increases the risk of triggering an acute or severe asthma attack in mite-allergic individuals (26).

Table 2. Characteristics of the Common House Dust Mite

Size	250–350 μm
Growth cycle	Egg to adult in 25 days at 25°C
Optimal temperature	20–30°C
Minimum temperature	16°C
Maximum temperature	55°C
Optimal relative humidity	70%–80%
Minimum relative humidity	50%
Habitat	Sofas, fabrics, carpets, sheets, duvets, pillows, mattresses, and other soft furnishings

Typical *Der p 1* concentrations are below 5 $\mu\text{g g}^{-1}$ of dust (27). However, work of Friedman et al. illustrated that the actual concentration of mite antigen in a home will strongly depend upon a range of factors, particularly climatic variables (28). They reported mean concentrations of *Der p 1* and *Der f 1* of 3.98 and 8.17 $\mu\text{g g}^{-1}$, respectively, of dust in a sample of 15 New England homes during the month of June. In September the corresponding mean concentrations had risen to 21.43 and 14.53 $\mu\text{g g}^{-1}$, respectively.

The first documented observation that mites may be a cause of respiratory symptoms was made more than 70 years ago (29). Today, it is estimated that exposure to mite allergen may trigger attacks in up to 85% of asthmatics (30). The asthmatic response to exposure is generally in two stages (31). The early or immediate response is an episode of airway obstruction, which peaks between 10–20 min after inhalation and normally resolves within 1–2 hr. This is mostly due to bronchospasm in the lungs. A secondary response may develop some hours after exposure. This is usually associated with airway inflammation and may manifest itself as an acute asthma exacerbation, increased airway hyperresponsiveness, or recurrent nocturnal asthma.

Studies of the effects of dust mite allergen exposure are numerous. A recent Swedish study by Björnsson et al. found that nocturnal breathlessness and other asthma-related symptoms were most common in adults inhabiting homes with high compared to low mite populations (OR = 6.2 and 7.9, respectively) (32). In Australian children, Peat et al. found a positive association between wheezing in the previous year and exposure to dust mite *Der p 1* (OR = 7.0) (33).

As well as being a major trigger of attacks in asthmatics, there is also evidence that exposure to mite allergen, particularly among infants, may be an important factor in inducing the onset of asthma itself (34). In the United States, Call et al. found that the residents of homes with high concentrations of mites were more likely to be sensitized to mite allergen, and this in turn was associated with a higher prevalence of asthma (35). Sporik et al. reported that early exposure to mite allergen

was a significant factor for sensitization and the early onset of wheezing among 68 children living in an area of southern England (36). In an important study, Arshad et al. examined the role of early exposure to dust mite allergens in the development of allergic disorders among infants on the Isle of Wight (37). One hundred and twenty infants were randomly allocated to prophylactic and control groups. In the prophylactic group, the infants' bedrooms and living rooms were treated with chemicals to control mites, and concentrations of *Der p 1* were monitored. In the control group, no interventions were made. At 12 months the odds ratio for asthma was 4.13 (95% confidence interval (CI) 1.1–15.5) among the control group. After 24 months, the excess number of cases among the control group had narrowed, but still remained (38).

Like dust mites, cockroaches have been associated with the manifestation of symptoms in individuals with allergic asthma, and up to 60% of asthmatics test positive to cockroach allergen (39). Although cockroaches are generally indigenous to warm tropical climates, some species are able to thrive elsewhere due to the presence of central heating. The most commonly found cockroach in homes in Europe is the German cockroach, *Blattella germanica*, from which at least five antigens have been isolated (*Bla g 1–5*). In the United States, the American cockroach, *Periplaneta americana* is ubiquitous. Sources of cockroach allergens have been identified in body parts, as well as fecal extracts (40).

Cockroach antigen has a rather different distribution from that of dust mites. In particular, it is found in kitchen cabinets, kitchen floor dust, bathrooms, and basements (41). Van Wijnen et al. detected measurable concentrations of *Bla g 1* in 44% of a sample of 46 homes in Amsterdam (42). Mean concentrations ranged between 1.3 and 11 ng g^{-1} of dust. The highest level recorded in a single sample was 3899 ng g^{-1} . In general, concentrations were elevated in rooms with textile floor coverings. Similar findings were made in the United States by Rosenstreich et al. (43). They measured concentrations of the allergen in dust taken from 476 homes situated in various inner-city locations. They discovered that,

whereas concentrations of less than 9 U g^{-1} of dust were common, some houses had concentrations of more than 1000 U g^{-1} . The same authors found that asthmatic children allergic to cockroaches were three times more likely to be hospitalized for their asthma if they lived in a house with a large cockroach population. These children also exhibited significantly more days of wheezing and nights with lost sleep. The authors concluded that the problems of cockroach sensitization might be particularly severe among the residents of poor quality inner-city housing because these homes provide an ideal environment in which cockroaches can thrive.

Domestic cats and dogs are a further important source of allergens in the home, particularly in Northern Europe where the climate is less favorable to dust mites. Cat allergen (*Fel d*) is produced by cat sebaceous and salivary glands (22). It is generally carried on small particles ($<2.5 \mu\text{m}$), and hence can be airborne for many hours (44). Concentrations of the primary cat allergen, *Fel d* 1, in domestic dust can be very high, ranging from less than $1 \mu\text{g g}^{-1}$ to more than $10 \mu\text{g g}^{-1}$ (45). Airborne levels of the allergen vary between 2 and 20 ng m^{-3} , and Colloff found them to be highest in homes with more soft furnishings and fitted wool carpets (46). Recently, it has been proposed that a concentration of *Fel d* 1 of more than $8 \mu\text{g g}^{-1}$ in house dust should be considered as a threshold for both atopic sensitization and the development of asthma (11).

As with cat allergens, dog allergens are mostly found in saliva and danders. The major dog allergen has been termed *Can f* 1 (47). Concentrations of *Can f* 1 in dust are often similar to those of *Fel d* 1, although *Fel d* 1 can remain airborne longer due to its smaller particle size (48).

Interestingly, significant concentrations of both *Fel d* 1 and *Can f* 1 can be detected in homes without a cat (49). Because *Fel d* and *Can f* are readily transported by becoming attached to clothing, exposure to these allergens can even be a problem in public places such as schools, trains, and hospitals, where pets are not allowed. Custovic et al. recently sampled levels of mite, cockroach, dog, and cat allergens in the public areas in 14 British

hospitals (50). Although concentrations of *Der p* 1 and *Bla g* 1 were low, high concentrations of *Fel d* 1 (mean $22.9 \mu\text{g g}^{-1}$, range 4.5–58) and *Can f* 1 (mean $21.6 \mu\text{g g}^{-1}$, range 4–63) were measured. During the 10 days for which sampling was undertaken, airborne *Can f* 1 was detected on every occasion (range $0.12\text{--}0.56 \text{ ng m}^{-3}$), whereas airborne *Fel d* 1 was recorded on 7 days (range $0.09\text{--}0.22 \text{ ng m}^{-3}$).

Because of the small particle size, cat and dog allergen readily enters the lung and can produce a rapid and severe asthmatic response. This is illustrated by the work of Pollart et al. who found that 30 out of 188 asthma patients who were admitted to a hospital emergency department with severe acute attacks were allergic to cats, compared to 1 out of 202 controls ($p < 0.05$) (51).

Microorganisms are an often overlooked, yet extremely important form of biological pollution in homes. Numerous species of fungi are well adapted to the indoor environment, where their presence is often associated with the occurrence of organic matter (e.g., wall coatings, wood, foodstuffs) (26). High levels of humidity also provide favorable conditions for fungal growth (52), and colonies are frequently found in damp homes, especially those with structural faults, or basements and under-floor crawl spaces (47). An additional important source of indoor fungi and bacteria is the outdoor air, particularly during the summer and autumn months (53).

It can be difficult to produce representative estimates of airborne fungal spore levels, because concentrations often undergo large temporal variations (54). In the United Kingdom, Hunter et al. used air filtration to monitor 163 homes for the presence of fungi and bacteria over the period November 1990 to December 1992 (55). They reported a geometric mean count of 234 colony forming units (CFU) m^{-3} . A more detailed study of 35 of the houses showed evidence of variability in fungal concentrations that was associated with the function of rooms; mean counts were 912 CFU m^{-3} in living rooms, but only 818 CFU m^{-3} in bedrooms. *Penicillium* was the most frequently isolated fungus, found in 53% of samples. It was followed by *Cladosporium* and *Aspergillus*. In Norway, Dotterud et al. also found that

Penicillium was the most common microfungus in homes and schools, with *Aspergillus*, *Cladosporium*, and *Mucor* being regularly present (56). In a study in Japan, Takahashi reported that indoor concentrations of fungal CFUs ranged from between 13 to 3750 CFU m⁻³ (57), although Macher et al. measured rather less extreme spore concentrations of 198 CFU m⁻³ in an apartment in the United States (58).

Because exposure to fungal spores is associated with a range of conditions that produce asthma-like symptoms, it can be difficult to make a connection between concentrations of spores and asthma. Furthermore, many studies use indoor dampness (which is confounded with other factors such as house dust mite population size) as a surrogate measure of CFU concentrations, although some direct associations have been made. In a sample of almost 600 U.K. homes, Platt et al. found that elevated numbers of fungal CFU m⁻³ were associated with higher levels of self-reported wheeze in children, and breathlessness in adults ($p < 0.05$) (59). Also in the United Kingdom, Potter et al. detected allergic responses to nine different fungal allergens in a survey of 2000 patients with allergic respiratory disease (60).

It seems that fungal spores may be a particular risk factor for asthma symptoms in infants. In Sweden, Wickman et al. found that the presence of *Penicillium*, *Alternaria*, or *Cladosporium* molds in a home was associated with an increased likelihood of atopy in resident children (61), and Neas et al. reported that morning lung function was inversely associated with *Epicoccum* and *Cladosporium* spore concentrations among a panel of 108 children (e.g., a 60-spore m⁻³ increment in *Epicoccum* concentrations gave an OR of 1.8 for morning cough [$p = 0.05$]) (62).

Interestingly, very recent research on molds and fungi suggests that allergic reactions may not be the most important factor in the development of respiratory symptoms (63). Mycotoxins are toxic compounds produced naturally by numerous fungi (64). They give rise to a wide range of acute and chronic systemic effects that cannot be attributed to fungal growth within the host. Samson et al. provide evidence that mycotoxins are readily absorbed

through the membranes of the respiratory tract, and it could be that their presence in the lung affects the immune system, precipitating the onset of symptoms (65).

INDOOR PARTICULATE MATTER

Smoke from the combustion of cigarettes, wood, and fossil fuels produces an extremely complex mixture of pollutants, one of the primary constituents of which is respirable particles; aerosols that are of a small enough diameter to enter and remain in the lung (66). Many are around 6–7 μm in diameter although, in practice, a variety of particle size distributions may be related to a single respirable fraction (67). The particles comprise a mixture of organic and inorganic substances including aromatic hydrocarbon compounds, trace metals, nitrates, and sulfates (68). In the absence of significant indoor sources, indoor-to-outdoor ratios of respirable particles are generally slightly below unity (69,70). However, a significant consideration is that measurement techniques routinely used in reported studies are often not able to differentiate combustion-related particles from those from other sources (68). Hence, it can be difficult to formulate a direct relationship between specific exposure sources and asthma.

Cigarette smoke is an extremely important source of indoor particulate pollution. The term environmental tobacco smoke (ETS) has been used to describe the complex aerosol that is associated with the combustion of cigarettes in enclosed environments. Because a substantial proportion of the population are exposed to high concentrations of ETS on a regular basis, it is one of the most significant indoor air pollutants (71).

As information has become known about the generation and chemical composition of ETS, many irritants and toxins have been identified (Table 3). By inhaling ETS, nonsmokers are exposed to most of the toxins inhaled by active smokers, as well as some additional substances. For example, a "passive" smoker at a distance of 50 cm from a cigarette may inhale more than 10 times the amount of car-

Table 3. Emission Factors for Mainstream (MS) and Sidestream Smoke (SS)

SUBSTANCE	MAINSTREAM (μg PER CIGARETTE)	SS/MS RATIO	CALCULATED SIDESTREAM (μg PER CIGARETTE) ^a
Carbon dioxide	10,000–80,000	8.1	81,000–640,000
Carbon monoxide	500–26,000	2.5	1200–65,000
Oxides of nitrogen	16–600	4.7–5.8	80–3500
Ammonia	10–130	44–73	400–9500
Hydrogen cyanide	280–550	0.17–0.37	48–203
Formaldehyde	20–90	51	1000–4600
Acrolein	10–140	12	100–1700
N-Nitrosodimethylamine	0.004–0.18	10–830	0.04–149
Nicotine	60–2300	2.6–3.3	160–7600
Total particulate	100–40,000	1.3–1.9	130–76,000
Phenol	20–150	2.6	52–390
Catechol	40–280	0.7	28–196
Naphthalene	2.8	16	45
Benzo(a)pyrene	0.008–0.04	2.7–3.4	0.02–0.14
Aniline	0.10–1.20	30	3–36
2-Naphthylamine	0.004–0.027	39	0.02–1.1
4-Aminobiphenyl	0.002–0.005	31	0.06–0.16
N-Nitrosonornicotine	0.2–3.7	1–5	0.02–18

^aCalculated from ratio of SS to MS. Source: reference 71.

bonyl compounds actively taken up by the smoker (72).

Because of the complex nature of ETS, measurements of respirable particles are often used as indicators of indoor concentrations, with ETS-associated particle sizes ranging from 0.1 to 1.5 μm (73). Over several weeks, Spengler et al. observed particle concentrations in 80 homes (74). They found that a smoker of one pack a day contributed about 20 $\mu\text{g m}^{-3}$ to 24-hr indoor concentrations. Because cigarettes are not smoked uniformly throughout the day, the authors concluded that short-term particulate concentrations of 500–1000 $\mu\text{g m}^{-3}$ were likely when cigarettes were actually ignited.

Chest irritation is one of the most common health effects associated with exposure to ETS. Although ETS contains substances that can activate the immune system, and approximately half of allergy-prone individuals react to various extracts of tobacco leaf or smoke in skin tests, there is little evidence to link smoking in adulthood with the onset of asthma (68). However, exposure to indoor cigarette smoke has been connected to an increased incidence of

atopy and respiratory symptoms in infants. Indeed, among very young children, cigarette smoke may be an even more important cause of asthma than are house dust mites (9).

In Italy, Forastiere et al. examined the self-reported prevalence of asthma in 3239 children in the town of Civitavecchia and the city of Rome (75). They discovered that the prevalence of asthma was elevated in children whose mothers smoked (OR = 1.4, $p < 0.05$). Similarly, Gortmaker et al. found that the prevalence of parent-reported asthma in children aged 0–17 years increased from 5% to 7.7% for children with a mother or father who smoked, and the prevalence of severe asthma increased from 1.1% to 2.2% ($p < 0.05$) (76). Among British infants, Arshad et al. reported an odds ratio for asthma of 3.33 (95% CI 0.8–14.6) if one parent smoked and 11.0 (95% CI 2.5–48.2) if both parents smoked (37).

The mechanism by which exposure to ETS represents a risk for the development of asthma in infants is not fully understood, but may be associated with immune response or retarded bronchial growth, both known risk factors. Strong evidence is available that links

domestic ETS exposure and acute childhood lower respiratory tract illnesses (77), and a significant effect on the level and growth of lung function among juveniles has been observed (78).

Although domestic wood and coal combustion is less common than was once the case, the use of open fires and woodstoves for cooking and heating can still make a significant contribution to indoor particulate matter concentrations. Smoke from the burning of wood and fossil fuels produces an extremely complex mixture of pollutants in terms of its physical, chemical, and toxicological characteristics (79).

As part of the Harvard Six-City Study, Neas et al. recorded mean annual concentrations of particles less than $2.5\ \mu\text{m}$ in diameter ($\text{PM}_{2.5}$) in the order of $17\ \mu\text{g m}^{-3}$ in a sample of 470 nonsmoking homes (80). The presence of a smoker can greatly add to indoor levels, as discussed earlier. Traynor et al. found that indoor concentrations of respirable particles were slightly above background ($0\text{--}30\ \mu\text{g m}^{-3}$) during the use of airtight stoves, and substantially higher with nonairtight stoves ($200\text{--}1900\ \mu\text{g m}^{-3}$) (81). In general, it appears that homes with airtight woodburning stoves have about $4\ \mu\text{g m}^{-3}$ higher indoor concentrations than homes without stoves (81). Wood and coal burning in fireplaces also produces particulate pollutants, and Moschandreas et al. found that these concentrations can be much higher than those produced by stoves (82).

It is important to note that personal exposures to particles are often higher than ambient indoor concentrations, a phenomenon that has become known as the "personal cloud" effect. This is particularly the case during the daytime when individuals may be involved in activities that place them in close proximity to exposure sources (83). For example, Clayton et al. observed that daytime mean personal exposure to particles less than $10\ \mu\text{m}$ in diameter (PM_{10}) in a sample of individuals was more than 50% higher than either indoor or outdoor levels (84). Similar findings have recently been reported by Janssen et al. (70).

Despite the potential for high levels of contamination from domestic biofuel combustion,

there are still relatively little data available on indoor smoke and asthma in developed countries. Honicky et al. conducted a prevalence survey of respiratory symptoms in 62 children in Michigan (85). They discovered that the proportion of children reporting moderate or severe symptoms was much greater for those from homes with woodstoves (84% of children in this group reported at least one severe symptom, compared to 3% of the control group). In their investigation of six U.S. cities, Dockery et al. found an OR of 1.32 (95% CI 0.99–1.76) for respiratory illness in households with woodburning stoves compared with those using other sources of heating (86). Likewise, Koenig et al. reported that infants who were exposed to wood smoke were more likely to exhibit the symptoms of asthma (87).

NITROGEN DIOXIDE FROM GAS APPLIANCES

Nitrogen dioxide (NO_2) is a water-soluble red to brown gas with a pungent acrid odor. It is formed from the combination of nitrogen and oxygen during combustion at high temperatures (68). Hence, the presence of elevated concentrations of NO_2 is particularly associated with the operation of gas appliances, kerosene heaters, and woodburning stoves, as well as the smoking of cigarettes. The use of gas for domestic cooking is common practice in much of Europe and the United States. In the United States alone, it is estimated that up to 50% of hot meals are cooked on gas stoves, providing a significant source of NO_2 (88). Although outdoor air can act as an important origin for indoor NO_2 pollution, in many areas of the United States and Europe ambient outdoor NO_2 levels are relatively low (89).

There have been numerous studies of indoor concentrations of NO_2 . Where emission sources are not present, levels generally correlate well with those observed outdoors (90). In homes with gas cooking stoves in Albuquerque, New Mexico, Lambert et al. found that 2-week average NO_2 levels were 21 ppb (39 μg

m^{-3}) in bedrooms and 34 ppb ($63 \mu\text{g m}^{-3}$) in kitchens (91). In comparison, bedroom concentrations in homes using electric stoves averaged just 7 ppb ($13 \mu\text{g m}^{-3}$). On average, normal use of a vented gas cooking range adds 25 ppb ($47 \mu\text{g m}^{-3}$) of NO_2 to the background concentration in a home (92). One-week average levels of greater than 50 ppb ($94 \mu\text{g m}^{-3}$) have been reported in homes with unvented gas space heaters (93).

One factor that appears important in terms of the effect of NO_2 on asthma is that transient peak concentrations of the gas can greatly exceed average measurements during the operation of appliances. For example, Spengler et al. found that the use of a gas range in a sample of kitchens generated peak levels as high as 1000 ppb ($752\text{--}1880 \mu\text{g m}^{-3}$) (74). Because individuals operating the ranges will often work in close proximity to the appliance, personal exposures may be even greater.

Nitrogen dioxide is an oxidizing agent, and hence is an irritant to the mucous membranes of the lung (94). Because it is highly soluble in water, a large proportion of inhaled NO_2 is removed in the respiratory tract (79). It is thought to combine with water in the lungs to form nitric acid (HNO_3) and may react with lipids and proteins to form nitrite anions and hydrogen ions (95). Nitrogen dioxide within the airways is also converted into vapor phase nitrous acid (HONO) via heterogeneous reactions involving water vapor (96). Although it has been suggested that oxidant injury is the principal mechanism by which NO_2 damages the lung, substantial uncertainty remains (79).

In Pisa, Italy, Viegi et al. examined the effects of the home environment on respiratory symptoms of a general population sample (97). After controlling for potential confounding factors, they found that the use of bottled gas for cooking was associated with increased reporting of cough and phlegm in males. They also discovered that the presence of wheeze and shortness of breath in females was correlated with the use of a stove or forced air circulation for heating ($p < 0.05$). Similar results were found in England by Jarvis et al. (98). They surveyed the association between the use of domestic gas appliances, and respira-

tory symptoms and lung function in adults aged between 20 and 44 years. Women who reported they mainly used gas for cooking were more likely to mention an attack of asthma or asthma-like symptoms in the 12 months prior to the survey (OR = 2.07 for wheeze; OR = 2.32 for breathlessness; OR = 2.60 for asthma). Women who used a gas stove or had an open gas fire were also found to have reduced lung function, and increased airway obstruction ($p < 0.05$). These findings were not made for the men studied. The fact that these studies generally show the greatest effect for women might be because women are more susceptible to the products of gas combustion, or they may have greater exposure to high concentrations of these products.

Among a sample of asthmatic women and children, Goldstein et al. examined the relationship between mean 48 hr NO_2 concentrations in the subjects' kitchens, and their spirometric lung function (99). Exposure to NO_2 levels on the order of 300–800 ppb ($564\text{--}1504 \mu\text{g m}^{-3}$) was correlated with a reduction in lung capacity of around 10% ($p < 0.05$). Salome et al. reported a similar effect whereby the experimental exposure of 600 ppb ($1128 \mu\text{g m}^{-3}$) of NO_2 over a period of 1 hr led to a small but statistically significant increase in airway hyperresponsiveness among a sample of 20 asthmatics ($p < 0.05$) (100).

Exposure to NO_2 may act as a trigger for asthma in one of two ways (101). One possibility is that the pollutant itself causes a direct effect on the lungs by toxic damage. Another is that exposure may sensitize the lungs, making individuals more susceptible to allergic response upon contact with other indoor allergens. The second explanation is particularly pertinent to the home environment, where concentrations of common aeroallergens are high, and water produced by gas combustion may favor the growth of mold and dust mite populations. Evidence that the sensitization mechanism may be important comes from a study by Tunnicliffe et al. (102). In individuals exposed to 400 ppb of NO_2 for 1 hr previously, lung function (measured by forced expiratory volume) decreased by 19% within 2 hr after the inhalation of house dust mite *Der p 1* aller-

gen. There was a comparative reduction of just 14% in those exposed only to air.

SULFUR DIOXIDE

Sulfur dioxide (SO_2) is produced by the oxidation of sulfur impurities during the burning of coal and other fuels that contain sulfur (103). It is a colorless gas with a strong pungent odor that can be detected at about 0.5 ppm (0.9 mg m^{-3}). It is readily soluble in water and can be oxidized within airborne water droplets (68). Levels of SO_2 are most often lower indoors than outdoors, and indoor/outdoor concentration ratios between 0.1 and 0.6 are common in buildings without significant indoor sources. Sulfur dioxide levels can be elevated in homes with kerosene heaters and poorly vented gas and coal appliances. For example, average concentrations of 30 ppb ($78 \text{ } \mu\text{g m}^{-3}$) were recorded by Leaderer et al. in their study of 33 homes with kerosene space heaters in Connecticut (104), and mean values as high as 57 ppb ($149 \text{ } \mu\text{g m}^{-3}$) were measured in homes equipped with both kerosene heaters and gas stoves (105).

In terms of the impact of SO_2 on asthma, two substances may be important; the sulfur dioxide itself, and the acid aerosols that can be produced from the oxidation of SO_2 in the atmosphere. Because it is soluble in water, SO_2 is easily absorbed in the upper respiratory tract. The deposition pattern of acid aerosols within the lungs is dependent upon the size distribution of the droplets and the level of humidity indoors (68).

Although evidence from controlled chamber studies and occupational exposures suggests that exposure to extreme concentrations of SO_2 and acid aerosols can precipitate severe asthma symptoms (106), there are relatively few indications of significant acute impacts associated with typical indoor concentrations. However, there is research to suggest that long-term exposures to indoor SO_2 may lead to an elevated reporting of asthma and other chronic respiratory complaints. In the United Kingdom, Burr et al. found that residents of South Wales who had open coal fires were more likely than others to suffer asthma-like

symptoms of breathlessness and wheezing, and speculated that a high death rate from respiratory conditions among miners' wives may have been associated with exposure to SO_2 from the burning of concessionary coal (107). Recent studies in China, where the domestic burning of coal is still widespread, have also associated exposure to SO_2 with asthma symptoms (108).

VOCs AND FORMALDEHYDE

Organic compounds are chemical compounds that contain at least one carbon and a hydrogen atom in their molecular structure. Volatile organic compounds are organic compounds that have a low boiling point, typically between 50 and 260°C (68). Their low boiling point means that they will readily off-gas vapors into indoor air (109). However, because they exhibit the desirable characteristics of good insulation properties, economy, fire-resistance, and ease of installation, their use in construction projects is widespread (see Table 4).

Formaldehyde is the most widespread aldehyde found in the environment. Although it is a volatile compound, it is not detected by the gas chromatographic methods commonly applied to VOC analysis, and hence is often considered separately in epidemiological investigations (68). At normal room temperatures, it is a colorless gas with a strong odor. Domestic sources of formaldehyde include particleboard, medium-density fibreboard, plywood, resins, adhesives, and carpeting (110).

The indoor concentration of individual volatile compounds is very dependent upon the presence of important emission sources. Hence, the load of total volatile organic compounds (TVOCs) is often considered, rather than concentrations of individual compounds (111). A major study of TVOCs in 179 U.K. homes reported mean domestic levels of between 200 and $500 \text{ } \mu\text{g m}^{-3}$ (112). The maximum recorded value was $11,401 \text{ } \mu\text{g m}^{-3}$ in a living room. Mean concentrations were highest in main bedrooms, and lowest in second bedrooms. Similar findings have been reported by

Table 4. Sources of Common VOCs in Indoor Air

SOURCES	EXAMPLES OF TYPICAL CONTAMINANTS
Consumer and commercial products	Aliphatic hydrocarbons (<i>n</i> -decane, branched alkanes), aromatic hydrocarbons (toluene, xylenes), halogenated hydrocarbons (methylene chloride), alcohols, ketones (acetone, methyl ethyl ketone), aldehydes (formaldehyde), esters (alkyl ethoxylate), ethers (glycol ethers), terpenes (limonene, alpha-pinene)
Paints and associated supplies	Aliphatic hydrocarbons (<i>n</i> -hexane, <i>n</i> -heptane), aromatic hydrocarbons (toluene), halogenated hydrocarbons (methylene chloride, propylene dichloride), alcohols, ketones (methyl ethyl ketone), esters (ethyl acetate), ethers (methyl ether, ethyl ether, butyl ether)
Adhesives	Aliphatic hydrocarbons (hexane, heptane), aromatic hydrocarbons, halogenated hydrocarbons, alcohols, amines, ketones (acetone, methyl ethyl ketone), esters (vinyl acetate), ethers
Furnishings and clothing	Aromatic hydrocarbons (styrene, brominated aromatics), halogenated hydrocarbons (vinyl chloride), aldehydes (formaldehyde), ethers, esters
Building materials	Aliphatic hydrocarbons (<i>n</i> -decane, <i>n</i> -dodecane), aromatic hydrocarbons (toluene, styrene, ethylbenzene), halogenated hydrocarbons (vinyl-chloride), aldehydes (formaldehyde), ketones (acetone, butanone), ethers, esters (urethane, ethylacetate)
Combustion appliances	Aliphatic hydrocarbons (propane, butane, isobutane), aldehydes (acetaldehyde, acrolein).
Potable water	Halogenated hydrocarbons (1,1,1-trichloroethane, chloroform, trichloroethane)

Source: reference 68.

research in Denmark (113), Germany (114), and Sweden (115), and United States (116).

Because individuals are often situated close to emission sources, average VOC concentrations may give an inaccurate indication of personal exposures (117). This was illustrated by Wallace, who reported the results of measurements of personal exposure to 25 VOCs among 51 Los Angeles residents (118). Ambient indoor maxima ranged from 10 to 100 $\mu\text{g m}^{-3}$, whereas personal maxima were generally much higher, between 100 and 1000 $\mu\text{g m}^{-3}$.

In terms of the impact of VOCs on asthma, there is considerable uncertainty concerning the concentrations that might be required to induce a measurable response. However, Samet estimates that concentrations in indoor air of more than 0.1 ppm can lead to acute upper airway irritation, and levels above 5 ppm

can result in lower airway and pulmonary effects (119).

Norbäck et al. examined the association between asthmatic symptoms and VOCs and formaldehyde in the dwellings of 88 Swedish subjects aged between 20 and 45 years (120). They reported positive associations between the prevalence of reported nocturnal breathlessness and concentrations of both substances. In another Swedish study, Wieslander et al. examined the association between asthma symptoms and exposure to VOCs and formaldehyde from newly painted indoor surfaces (17). They found that recently painted surfaces were a risk factor for symptoms (OR = 1.5, 95% CI 1.0–2.4). Particularly strong effects were associated with newly painted wood details (OR = 2.3, 95% CI 1.2–4.5) and kitchens (OR = 2.2, 95% CI 1.1–4.5).

One recent theory proposes that the products of chemical reactions involving VOCs may be more important in causing asthma symptoms than direct exposure to the compounds themselves (121). This rationale is based on the fact that many epidemiological studies on outbreaks of symptoms recorded concentrations of VOCs at considerably lower levels than those found to induce asthma in experimental trials. This apparent anomaly could be explained by the increasing evidence that many chemical reactions take place on surfaces and in air in the indoor environment (122). Results from some epidemiological research suggests that reactions between indoor ozone and VOCs may produce irritant substances that could cause asthma exacerbations (123). Via the same mechanism, it seems that reactions involving nitrogen dioxide (124) and particles (125) may also be important.

INDOOR ENVIRONMENTAL CONTROLS FOR ASTHMA PREVENTION

The prevention of asthma involves both the prevention of the initial development of the condition (primary prevention), and the prevention of exacerbations in asthmatics (secondary prevention) (25). Although little is currently known about their impact on the prevalence of asthma, primary prevention strategies are obviously attractive. Secondary prevention encompasses interventions designed to avoid and treat the triggers of asthma symptoms.

Indoor Allergen Avoidance

Given the evidence that exposure to allergens in early infancy may precipitate the onset of asthma (38), indoor allergen avoidance is probably the most effective strategy for the primary prevention of asthma. It also carries obvious benefits for secondary prevention.

At its core, asthma is now considered to be a condition of disrupted immune regulation which manifests itself in the form of an ab-

normal immunological response to inhaled aeroallergens. Hence, it seems likely that avoidance measures will be most effective in preventing the development of asthma if employed in very early life when the immune system is still undergoing critical stages of development. Indeed, even prenatal avoidance of indoor allergens may pay dividends in reducing the likelihood of the newborn infant developing asthma (126).

Specifically, asthmatics fail to follow the normal pattern of immune maturation in response to aeroallergens that occurs in non-atopic individuals (127). It is now recognized that, during normal immune maturation, the early response to antigen challenges is governed by Th2 or uncommitted T-helper cells. These are associated with the production of immunoglobulin E (IgE), a characteristic of atopy and asthma. During the natural process of immunological development, the response shifts to Th1 T-helper cells which are specific and do not stimulate IgE production (127). This process is known as Th2/Th1 immune switching and it appears to be delayed or defective in many asthmatic subjects (128). Although many components of Th2/Th1 switching seem to be genetic, there is evidence that switching may also be disrupted by the presence of environmental influences at a critical time in early life (129). For example, responses to mite allergens *in vitro* have been observed in the cord blood of Swedish infants whose mothers were exposed to less than $0.4 \mu\text{g g}^{-1}$ *Der p 1* (130). Hence, it could be that repeated indoor aeroallergen exposure during early life may perpetuate a Th2 / IgE response, causing the immune system to indefinitely retain the primitive Th2 phenotype (129). Maternal and infant allergen avoidance may prevent this immune deviation from occurring.

Reducing domestic mite populations is an important but difficult task. The idea is to remove the habitat of mites and make what remains inhospitable for them. Thus, the main methods are physical measures designed to control the sites where mites grow. A range of short- and long-term objectives for reducing exposures to house dust mites are outlined in Table 5.

Table 5. Methods for Reducing Exposure to House Dust Mites

Priority objectives

- Cover mattresses and pillows. Damp wipe the mattress cover every 2 weeks
- Wash all bedding in hot cycle (~55°C) weekly. Replace duvets with dacron or orlon washable material
- Place small objects that accumulate dust in drawers or closed cabinets. Clothing should be stored in closed cupboards or closets
- Vacuum carpets weekly using a vacuum cleaner with an effective filter

Medium-term objectives

- If possible, remove carpets from bedrooms
- Replace curtains/drapes with washable cotton curtains or venetian/slat blinds
- Control humidity in the house by increasing ventilation or using central air conditioning. Use dehumidifiers in basements
- Treat carpets with acaricides or tannic acid

Choice of houses/apartments and fittings

- Avoid basement flats. Bedrooms should be upstairs
- If possible, avoid houses with carpets fitted to a concrete slab. All floors should have a primary polished floor (vinyl or wood) and carpets should be movable
- Upholstered sofas and chairs should be avoided
- Ensure air filters are kept clean on central heating and air conditioning equipment

Bedding is a prime breeding area for mites. The single most effective measure is to cover mattresses and pillows with plastic or vapor-permeable fabric covers. This entombs the existing allergen and cuts the mites off from their food source (131). Owen et al. reported that the use of vapor-permeable covers on mattresses reduced the mean concentration of mite allergen on the outside of the mattress from 20.3 to 0.3 $\mu\text{g Der p I g}^{-1}$ of dust (132). However, it is important to note that allergens may still continue to accumulate on top of and inside the casings, and hence it is important that all of the bedding be periodically washed to remove accumulations (133).

Cotton and wool blankets should be substituted with synthetic materials, which are less conducive to mite growth. Feather duvets and pillows can be replaced with synthetic fiber and foam rubber equivalents, because these are less likely to harbor dust mite populations. Duvets should also be encased with hypoallergenic covers, or regularly washed in hot water (>55°C) to kill mites (134). Although the use of cooler water will be effective in removing antigens, it does not kill all mites (22). How-

ever, a soluble form of benzyl benzoate (final concentration 0.03%) can be used to eliminate mites in a cool wash if high temperatures cannot be used (135).

The second priority for mite removal is the flooring and remainder of the bedroom. Whenever possible, the carpet should be replaced by wood or vinyl flooring that can be polished. Cool shampooing carpets has no effect on mites, and steam cleaning only reduces the mite allergen for about 1 month (131). The carpet is not only a source of airborne allergen, but can also harbor populations of mites which will reinfest bedding. If carpet removal is impractical, a number of different chemical treatments (acaricides and denaturing agents) are available for controlling mite populations. Generally, these are applied as a liquid spray, foam, or powder. However, although some controlled studies with acaricides have shown reductions in allergen levels (136), questions have been raised about the effectiveness of these agents, particularly about doses required to achieve a lasting noticeable effect (137).

In the rest of the house, high levels of mite

allergen can be found in sofas, chairs, carpets, curtains, and other materials. Indoor vacuuming is recommended once a week (25). This will help remove dead mite bodies and fecal pellets that are light enough to become airborne when disturbed. In the short term, however, vacuuming will also increase the concentration of airborne allergens (30). Consequently, if asthmatics must do the vacuuming, it is preferable that they wear a mask and stay out of the room for at least 30 min afterward. Vacuum cleaners with good suction and extra-thick bags may also help, as will the use of units fitted with high-efficiency particulate air (HEPA) filters or those with electrostatic filtration systems on the exhaust air (138).

For many areas of the house, the most effective treatment for mite populations is a decrease in overall levels of air humidity. Numerous studies confirm the association between indoor humidity and mite allergen levels (139). Relative humidity indoors should be kept below 50%, but not less than 30% (140). Reductions in humidity can be achieved in several ways. In temperate climates, increasing ventilation (for example, from 0.2 air changes per hour to 1 air change per hour) will be effective (141). The boiling of kettles and pans should be avoided in poorly ventilated areas, and structural faults that allow dampness to enter the home should be corrected. The indoor temperature should ideally be maintained at less than 25°C, because mites do not reproduce well below this.

The eradication of cockroaches from a home can be difficult because they reproduce quickly under ideal conditions. Professional extermination is probably the only method that will control a serious infestation (39). In an apartment block, even this can be difficult because cockroaches can quickly reinfest from neighboring apartments. Hence, management practices should aim to keep concentrations of allergen as low as practicable. Kitchen floors and cabinets should be kept clean and free from dust (142). During the night, the maintenance of a kitchen environment that is clear from food and food residues is particularly important, because cockroaches are usually more active during the hours of darkness. In

addition, paper bags and cardboard boxes should not be stored in the home; cockroaches often live and breed within them (39).

The elimination of allergens from pets is also important. Obviously, the best avoidance measure is not to keep pets in the house. However, finding a new home for a family pet is not always easy. Restricting animals to certain rooms is ineffective because the allowable rooms act as reservoirs, from which the allergen can be spread throughout the rest of the house (143). If the animal cannot be removed, a number of procedures can be adopted for reducing exposure. These include the lifting of carpeted flooring in rooms where dogs and cats will be housed, the adoption of a regime of regular vacuuming, the filtration of air, and regular washing of the pet (144). Glinert et al. found that washing cats, combined with purchasing washable furniture, may reduce levels of cat allergen by around 90% (145). Despite this, even with regular carpet vacuuming and steam cleaning, it can take many months to achieve a substantial decline in allergen levels.

Fungal growth can occur on any surface, and is primarily dependent on humidity, plus a source of organic matter. Removing or cleaning mold-laden objects can best reduce the number of fungal spores in indoor air. Surfaces that are especially prone to molds, particularly in kitchens or bathrooms, should be cleaned with chemicals such as chlorine bleach (144). Molds grow well in refuse containers, and these must be regularly emptied (131). Maintaining a low relative humidity is also important (9). Bathroom rugs and carpets are also a common source of fungal contamination, and should be washed frequently or disposed of as required (144).

Other Measures to Improve Indoor Air Quality

It is clear that asthmatics and their families ought to avoid smoking, and try to maintain a smoke-free indoor environment as far as possible. Where this cannot be achieved, commercial air purification devices can reduce the particulate load from cigarette smoke. In particular, the use of heating, ventilation, and air conditioning (HVAC) systems fitted with

HEPA filters has been shown to lower concentrations of particulate pollutants in indoor air (146). However, they will not eliminate the constituents of tobacco smoke that are in the gaseous phase, some of which are known respiratory irritants (119). Hence, the avoidance strategy, while not always easy, is by far preferable.

The management of indoor air quality problems not caused by cigarette smoke is often difficult and, depending on the interventions required, can be costly. Room dehumidifiers can be useful in helping prevent mold growth in particularly damp rooms, although there is little research on the efficacy of these devices in reducing asthma symptoms. The principal steps known to reduce exposure to indoor respirable particles from sources other than smoking are venting all furnaces to the outdoors and maintaining heating systems adequately (25). The use of an airtight wood stove is preferable to an open stove or an open fire, and the maintenance of good ventilation is important during operation. The use of ionizers to remove particulate materials from the air is not recommended because the particles are simply deposited around the ionizer from where they can easily be resuspended. Ionizers can also produce ozone, which is a known respiratory irritant.

To reduce exposure to NO_2 and SO_2 , all appliances should be regularly serviced, and have sufficient flues or ducts. When gas is used for cooking, an extractor should be used to improve ventilation in the kitchen. Although it is widely accepted that improving the supply of fresh, clean outdoor air in a home will reduce concentrations of airborne contaminants, it is also recognized that some ventilation systems may themselves contribute to the concentrations of indoor pollutants (147). Sources might include bacterial contamination, fungal mycotoxins, or VOCs from air filtration systems or maintenance ducts. Because of this, the provision of an appropriate supply of fresh air can be problematic in polluted urban environments, especially in countries with particularly hot or cold climates.

A better indoor environment can be achieved by the selection of building products and indoor fittings on the principle that the

emission of pollutants such as VOCs and formaldehyde must be as low as reasonably achievable. The use of insulation materials that emit formaldehyde should be avoided (115). This is often difficult when a new house is being purchased, because few people have any input into the materials used to build their home. The choice of an older property is not necessarily a solution, because it may suffer from structural defects such as rising dampness. Despite this, these considerations should be important for asthmatics who are moving their home, or planning home alterations.

The Role of Patient Education

Underpinning any efforts to improve the quality of domestic air must be a recognition of the significance of patient education; a central factor in the management of asthma is the patient's own understanding of the disease and its control.

It is, of course, of primary importance that information be conveyed concerning the day-to-day management of the disease itself. However, the patient with asthma and his or her family must also be provided with suitable material and training so that they can successfully manage their indoor environment so as to maintain acceptable conditions. A common finding of confidential enquiries into asthma deaths is a poor understanding of the condition among sufferers leading to, among other shortcomings, inadequate control (148).

A broad picture of studies into the effects of patient education suggests that the provision of information on its own may not be the most effective method of improving or stabilizing symptoms (25). Behavioral techniques which help patients acquire skills to manage their environment, detect changes in their condition, and take appropriate action have provided very encouraging results (149). Programs for patient education should involve a partnership, with frequent revision and reinforcement, between the asthmatic and health-care professionals. They could involve simple interventions such as the avoidance of smoky atmospheres. Alternatively, more holistic approaches could be adopted whereby the entire spectrum of indoor air quality issues is

examined and addressed within the patient's home. Whatever programs are implemented, they should aim to achieve guided self-management, giving patients the ability to control their domestic surroundings with guidance from knowledgeable professionals (25).

DISCUSSION

Over the last century, the design and management of houses has changed considerably. Modern homes are well-insulated, warm, and filled with soft furnishings and fitted carpets. These conditions encourage the production and concentration of indoor allergens and air pollutants. These have been associated with asthma, and a range of other allergic diseases. It may be that our immune systems are simply not made for 21st century domestic life.

In the past, the conditions prevailing in homes may not have been as comfortable as those we now enjoy, and some characteristics of the indoor environment were less than acceptable. Certainly an increased reliance on wood and coal burning to provide domestic heat meant that particulate pollution from these sources was generally much higher than is observed today. However, housekeeping practices dictated that our ancestors were not exposed to the same cocktail of allergens and pollutants that we are. In *The House of Mirth*, written by Edith Wharton in 1905, it is interesting to note how one of the characters, Mrs. Perniston, considers lifting carpets in the summer to be one of the cardinal rules of good housekeeping. Nowadays, fitted carpets mean that such practices are impossible.

Complacency over the risks posed by indoor air quality should be avoided; the asthma epidemic is a serious global issue. Yet as Roberts and Dickey point out, we continue to allow, in many homes, exposures to substances that would not be tolerated on the job or in the outdoor environment (150). This is simply because most people are not aware of the problem. There is undoubtedly a need for more high-quality research to further investigate the links between domestic air quality and asthma. At present, indoor-air-related research projects are funded at only around one-tenth of the level of those concerning the

health impacts of polluted outdoor air (151). This imbalance clearly needs to be addressed. Future research must fully acknowledge the complex nature of the indoor environment. Indoor air quality is the result of an intricate series of interactions involving numerous indoor and outdoor ventilation, microbiological, toxicological, and physical systems. Their interdependence may lead to the instigation of a multitude of synergistic processes that can result in many unexpected health impacts.

As the health effects of indoor air pollution become better understood, the legal and regulatory aspects of the issue will require careful consideration. Currently, indoor air quality and pollution is also a concern of the legal community. In this respect, their aim is to control the quality of indoor air through the passage of legislation and the development of regulations (152). When the U.S. Clean Air Act was passed in 1970, the Environmental Protection Agency was obliged to set national ambient air quality standards for common outdoor air pollutants. Unfortunately, no consideration was made of the health risks of indoor contamination. Despite revisions to the act in 1990, it still does not give the EPA clear authority to address indoor pollution. This lack of legislative power is complicated in the public policy arena by the scarcity of solid data. Although the 1996 United Kingdom National Environmental Protection Plan identifies indoor air quality as a key area (153), it provides no mandatory regulations. Indeed, across Europe, outside the Scandinavian countries, Holland, and Germany, policy on indoor air quality issues is generally poorly developed (154).

The introduction of new legislation may go some way toward reducing levels of contamination. However, it is important to remember that simple interventions by homeowners and building operators can also have major impacts. Allergen avoidance strategies need to be adopted by asthmatics or susceptible individuals. Sensitization to indoor allergens is strongly associated with the development of asthma. Recent clinical trials have shown that simple avoidance measures are effective in reducing asthma morbidity. Such interventions are also financially attractive; in the United States it has been estimated that an expendi-

ture of just \$10 for mite-proof mattress and pillow covers can significantly lower the risk of an asthmatic infant requiring a hospital visit (155). Patient education is also critical, and the medical practitioner has an important role to play. Good education provides a nonpharmaceutical option to managing asthma, and patients can be easily taught in the home, or in a primary care, hospital inpatient, or emergency department setting.

Avoidance measures provide a simple and effective solution to the problems caused by indoor air, and should be the prime focus in any asthma or allergy management program. In addition, a wider, more long-term view also needs to be adopted. Managing indoor air is not simply a challenge for the homeowner or the asthma sufferer. Governments need to set and enforce home building standards. Although problems with existing homes are difficult to overcome, house designers and builders must be educated so as to create better new structures. Improved data on the links between house design and health would have to precede the development and enforcement of new standards for building design. At present, we have only limited knowledge in this area. In part, this is due to the lack of gold standards that can be used to assess the quality of indoor air; although highly refined techniques are available for outdoors, the measurement and reporting of indoor air pollution is less advanced. These technologies must be developed.

A change of attitude may also be required with respect to the energy efficiency of buildings. Increased fuel costs could be one consequence of improved building design. However, these costs must be offset against potential reductions in the considerable financial burden from asthma and, for asthma prevention programs to adequately address the problems of indoor air quality, a policy shift from reactive to proactive mode may well be required.

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REFERENCES

1. Burney PGJ: Current questions in the epidemiology of asthma. In *Asthma* (Holgate ST, Austen KF, Lichtenstein LM, Kay AB, editors). Academic Press, London, 1993.
2. Haahtela T, Lindholm H, Björkstén F, Koskenvuo K, Laitinen LA: Prevalence of asthma in Finnish young men. *Br Med J* 301:266 (1990).
3. Lipfert FW: Air pollution and human health: perspectives for the '90s and beyond. *Risk Anal* 17:137 (1997).
4. Brunekreef B, Dockery DW, Krzyzanowski M: Epidemiologic studies on short-term effects of low levels of major ambient air pollution components. *Environ Health Perspect* 103(Suppl 2):3 (1995).
5. Hines AL: *Indoor Air: Quality and Control*. Prentice Hall, New York, 1993.
6. Stolwijk JA: Risk assessment of acute health and comfort effects of indoor air pollution. *Ann NY Acad Sci* 641:56 (1992).
7. LHEA (London Health Education Authority): What people think about air pollution, their health in general, and asthma in particular. Health Education Authority, London, 1997.
8. Robinson J, Nelson WC: *National Human Activity Pattern Survey Data Base*. United States Environmental Protection Agency, Research Triangle Park, NC, 1995.
9. Platts-Mills TAE, Woodfolk JA, Chapman MD, Heymann PW: Changing concepts of allergic disease: the attempt to keep up with real changes in lifestyles. *Allergy Clin Immunol* 98(Suppl):S297 (1996).
10. Office of National Statistics: 1996 Family spending: A report on the 1995–1996 Family Expenditure Survey. Office for National Statistics, London, 1996.
11. D'Amato G, Liccardi G, D'Amato M: Environment and development of respiratory allergy. II: indoors. *Monaldi Arch Chest Dis* 49:412 (1994).
12. Hyndman SJ, Brown DL, Ewan PW, Higenbottam TW, Maunder JW, Williams DRR: Humidity regulation in the management of asthma patients sensitized to house dust mites. *Q J Med* 87:367 (1994).
13. Lau S, Wahn U: Indoor environments and the development of allergy. *ACI News* 2:179 (1990).
14. Salvaggio JE: The impact of allergy and immunology on our expanding industrial environment. *J Allergy Clin Immunol* 85:689 (1991).
15. Molina CL: Respiratory manifestations induced by indoor air. *Proc XVth Congr EAACI Paris* 377 (1992).
16. Hasselblad V, Eddy DM, Kotchmar DJ: Synthesis of environmental evidence: nitrogen dioxide epidemiology studies. *J Air Waste Man Assoc* 42:662 (1992).
17. Wieslander G, Norbäck D, Björnsson E, Janson C, Boman G: Asthma and the indoor environment: the significance of emission of formaldehyde and vola-

- tile organic compounds from newly painted indoor surfaces. *Int Arch Occup Environ Health* 69:115 (1997).
18. Centers for Disease Control: National Health and Nutrition Examination Survey (NHANES III). U.S. Department of Health and Human Services, Atlanta, 1994.
 19. Cohen L: Indoor air quality a major public health issue, workshop told. *Can Med Assoc J* 153:92 (1995).
 20. Hart BL, Whitehead L: Ecology of house dust mites in Oxfordshire. *Clin Exp Allergy* 20:203 (1990).
 21. Kaliner MA, White MV: Asthma: causes and treatment. *Comp Ther* 20:645 (1994).
 22. Platts-Mills TAE, Vervloet D, Thomas WR, Aalberse RC, Chapman MD: Indoor allergens and asthma: Report of the third international workshop. *Allergy Clin Immunol* 100:S3 (1997).
 23. Platts-Mills TAE, Ward GW, Sporik R, Gelber LE, Chapman MD, Heymann PW: Epidemiology of the relationship between exposure to indoor allergens and asthma. *Int Arch Allergy Immunol* 94:339 (1991).
 24. Kalra S, Own SJ, Hepworth J, Woodcock A: Airborne house dust mite antigen after vacuum cleaning (letter). *Lancet* 336:449 (1990).
 25. World Health Organisation: Global strategy for asthma management and prevention. World Health Organisation, Geneva, 1995.
 26. Institute for Environment and Health: IEH assessment on indoor air quality in the home. Institute for Environment and Health, Leicester, UK, 1996.
 27. Verhoeff AP: *Home Dampness, Fungi and House Dust Mites, and Respiratory Symptoms in Children*. Posen & Looijen b.v., Wageningen, Germany, 1994.
 28. Friedman FM, Friedman HM, O'Connor GT: Prevalence of dust mite allergens in homes and workplaces of the Upper Connecticut river valley of New England. *Allergy Proc* 13:259 (1992).
 29. Ancona G: Asma epidemica da pediculoides ventricosus. *Policlinico Sez Med* 30:45 (1923).
 30. Platts-Mills TAE: Asthma and indoor exposure to allergens. *New Engl J Med* 336:1382 (1997).
 31. Cockcroft DW: Allergens. In *Asthma: Basic Mechanisms and Clinical Management*, 2nd ed. (Barnes PJ, Rodger IW, Thompson NC, editors). Academic Press, London, 1992, pp. 413–426.
 32. Björnsson E, Nörback D, Janson C: Asthmatic symptoms and indoor levels of micro-organisms and house dust-mites. *Clin Exp Allergy* 25:423 (1995).
 33. Peat JK, Tovey E, Gray EJ, Mellis CM, Woolcock AJ: Asthma severity and morbidity in a population sample of Sydney schoolchildren. *Aust N Z J Med* 24:270 (1994).
 34. Tariq SM, Matthews SM, Hakim EA, Stevens M, Arshad SH, Hide DW: The prevalence of and risk factors for atopy in early childhood: a whole population birth cohort study. *J Allergy Clin Immunol* 101: 587 (1998).
 35. Call RS, Smith TF, Morris E, Chapman MD, Platts-Mills TAE: Risk factors for asthma in inner city children. *J Pediatr* 121:862 (1992).
 36. Sporik R, Holgate T, Platts-Mills TAE, Cogswell JJ: Exposure to house-dust-mite allergen (*Der p 1*) and the development of asthma in childhood. *New Engl J Med* 323:502 (1990).
 37. Arshad SH, Matthews S, Gant C, Hide DW: Effect of allergen avoidance on development of allergic disorders in infancy. *Lancet* 339:1493 (1992).
 38. Hide DW, Matthews S, Matthews L, Stevens M, Ridout S, Twiselton R, Gant C, Arshad SH: Effect of allergen avoidance in infancy on allergic manifestations at age two years. *J Allergy Clin Immunol* 93: 842 (1994).
 39. Kuster PA: Reducing the risk of house dust mite and cockroach allergen exposure in inner-city children with asthma. *Pediatr Nurs* 22:297 (1996).
 40. Musmand JJ, Horner WE, Lopez MM, Lehrer SB: Identification of important allergens in German cockroach extracts by sodium dodecylsulfate-polyacrylamide gel electrophoresis and Western blot analysis. *J Allergy Clin Immunol* 95:877 (1995).
 41. Hannaway PJ: Exposure to high concentration of house dust mites as a possible precipitating factor in near fatal asthma. *J Allergy Clin Immunol* 17:105 (1993).
 42. van Wijnen JH, Verhoeff AP, Mulder-Folkerts DKF, Brachel HJH, Schou C: Cockroach allergen in house dust. *Allergy* 52:460 (1997).
 43. Rosenstreich DL, Eggleston P, Kattan M, Baker D, Slavin RG, Gergen P: The role of cockroach allergy and exposure to cockroach allergen in causing morbidity amongst inner-city children with asthma. *New Engl J Med* 336:1356 (1997).
 44. Luczynska CM, Li Y, Chapman MD, Platts-Mills TAE: Airborne concentrations and particle size distribution of allergen derived from domestic cats: measurements using a cascade impactor, liquid impinger and two-site monoclonal antibody assay for *Fel d 1*. *Am Rev Respir Dis* 141:361 (1990).
 45. Luczynska CM: Risk factors for indoor allergen exposure. *Respir Med* 88:723 (1994).
 46. Colloff MJ: Dust-mite control and mechanical ventilation: when the climate is right. *Clin Exp Allergy* 24: 94 (1994).
 47. Montanaro A: Indoor allergens: description and assessment of health risks. In *Indoor Air Pollution and Health* (Bardana EJ, Montanaro A, editors). Marcel Dekker, New York, 1997, pp. 201–214.
 48. Puerta L, Fernandez-Caldas E, Lockey RF: Indoor allergens: detection and environmental control measures. In *Indoor Air Pollution and Health* (Bardana EJ, Montanaro A, editors). Marcel Dekker, New York, 1997, pp. 215–229.
 49. Woodfolk JA, Luczynska CM, De Blay F, Chapman MD, Platts-Mills TAE: Cat allergy. *Ann Allergy* 69: 273 (1992).
 50. Custovic A, Fletcher A, Pickering CA: Domestic allergens in public places III: house dust mite, cat, dog and cockroach allergens in British hospitals. *Clin Exp Allergy* 28:53 (1998).
 51. Pollart SM, Chapman MD, Fiocco GP, Rose G,

- Platts-Mills TAE: Epidemiology of acute asthma: IgE antibodies to common inhalant allergens as a risk factor for emergency room visits. *J Allergy Clin Immunol* 83:875 (1989).
52. Sterling DA, Lewis RD: Pollen and fungal spores indoor and outdoor of mobile homes. *Ann Allergy Asthma Immunol* 80:279 (1998).
 53. Wanner HU: Sources of pollutants in indoor air. *IARC Sci Pub* 109:19 (1993).
 54. Flannigan B, Miller JD: Health implications of fungi in indoor environments—an overview. In *Health Implications of Fungi in Indoor Environments* (Sampson RA, Verhoeff AP, Flannigan B, Flannigan ME, Adan O, Hoekstra E, editors). Elsevier, Amsterdam, 1994.
 55. Hunter CA, Hull AV, Higham DF, Grimes CP, Lea RG: Fungi and bacteria. In: *Indoor Air Quality in Homes, the Building Research Establishment Indoor Environment Study, Part 1* (Berry RW, Brown VM, Coward SKD, editors). Construction Research Communications, London, 1996.
 56. Dotterud LK, Vorland LH, Falk ES: Viable fungi in indoor air in homes and schools in the Sor-Varanger community during winter. *Paediatr Allergy Immunol* 6:181 (1995).
 57. Takahashi T: Airborne fungal colony-forming units in outdoor and indoor environments in Yokohama, Japan. *Mycopathologia* 139:23 (1997).
 58. Macher JM, Huang FY, Flores M: A two-year study of microbiological indoor air quality in a new apartment. *Arch Environ Health* 46:25 (1991).
 59. Platt SD, Martin CJ, Hunt SM, Lewis CW: Damp housing, mould growth, and symptomatic health state. *Br Med J* 298:1673 (1989).
 60. Potter PC, Juritz J, Little F, McCaldin M, Dowdle EB: Clustering of fungal-allergen specific IgE antibody responses in allergic subjects. *Ann Allergy* 66: 149 (1991).
 61. Wickman M, Gravesen S, Nordvall SL, Pershagen G, Sundell J: Indoor viable dust-bound microfungi in relation to residential characteristics, living habitats, and symptoms in atopic and control children. *J Allergy Clin Immunol* 89:752 (1992).
 62. Neas LM, Dockery DW, Burge H, Koutrakis P, Speizer FE: Fungus spores, air pollutants, and other determinants of peak expiratory flow rate in children. *Am J Epidemiol* 143:797 (1996).
 63. Howden-Chapman P, Isaacs N, Crane J, Chapman R: Housing and health: the relationship between research and policy. *Int J Environ Health Res* 6:173 (1996).
 64. Hendry KM, Cole EC: A review of mycotoxins in indoor air. *J Toxicol Environ Health* 38:183 (1993).
 65. Samson RA, Flannigan B, Flannigan ME, Verhoeff AP, Adan OCG, Hoekstra ES: Health indicators of fungi in indoor environment. In *Air Quality Monographs*, Vol. 2. Elsevier, Amsterdam, 1994.
 66. Cooper JA: Environmental impact of residential wood combustion emissions and its implications. *J Air Poll Control Assoc* 30:855 (1980).
 67. Martonen TB, Katz I, Fults K, Hickey AJ: Use of analytically defined estimates of aerosol respirable fraction to predict lung deposition. *Pharm Res* 9:1634 (1992).
 68. Maroni M, Seifert B, Lindvall T: *Indoor Air Quality—A Comprehensive Reference Book*. Elsevier, Amsterdam, 1995.
 69. Wallace LA: Indoor particles: a review. *J Air Waste Man Assoc* 46:98 (1996).
 70. Janssen NA, Hoek G, Brunekreef B, Harssema H, Mensink I, Zuidhof A: Personal sampling of particles in adults: relation among personal, indoor, and outdoor air concentrations. *Am J Epidemiol* 147:537 (1998).
 71. Rando RJ, Simlote P, Salvaggio JE, Lehrer SB: Environmental tobacco smoke: measurement and health effects of involuntary smoking. In *Indoor Air Pollution and Health* (Bardana EJ, Montanaro A, editors). Marcel Dekker, New York, 1997, pp. 61–82.
 72. Schlitt H, Knöppel H: Carbonyl compounds in mainstream and sidestream tobacco smoke. In *Present and Future of Indoor Air Quality* (Bieva CJ, Courtois Y, Govaerts M, editors). Excerpta Medica, Amsterdam, 1989, pp. 197–206.
 73. Chen BT, Naneniyi J, Yeh HC, Mauderly JL, Cuddihy RG: Physical characterisation of cigarette-smoke aerosol generated from a walton smoke machine. *Aerosol Sci Technol* 12:364 (1990).
 74. Spengler JD, Dockery DW, Turner WA, Wolfson JM, Ferris BG: Long-term measurements of respirable particles, sulphates and particulates inside and outside homes. *Atmos Environ* 15:23 (1981).
 75. Forastiere F, Corbo GM, Michelozzi P, Pistelli R, Agabiti N, Brancato G, Ciappi G, Perucci CA: Effects of environment and passive smoking on the respiratory health of children. *Int J Epidemiol* 21:66 (1992).
 76. Gortmaker SL, Walker DK, Jacobs FH, Ruch-Ross H: Parental smoking and the risk of childhood asthma. *Am J Public Health* 72:574 (1982).
 77. Somerville SM, Rona RJ, Chinn S: Passive smoking and respiratory conditions in primary school children. *J Epidemiol Commun Health* 42:105 (1988).
 78. National Research Council: Environmental tobacco smoke: measuring exposures and assessing health effects. National Academy Press, Washington, 1986.
 79. Lambert WE: Combustion pollution in indoor environments. In *Indoor Air Pollution and Health* (Bardana EJ, Montanaro A, editors). Marcel Dekker, New York, 1997, pp. 83–103.
 80. Neas LM, Dockery DW, Ware JH, Spengler JD, Ferris BG, Speizer FE: Concentration of indoor particulate matter as a determinant of respiratory health in children. *Am J Epidemiol* 139:1088 (1994).
 81. Traynor GW, Apte MG, Carruthers AR: Indoor air pollution due to emission from woodburning stoves. Lawrence Berkeley Laboratories, Berkeley, CA, 1986.
 82. Moschandreas DJ, Zabransky J, Rector HE: The effects of woodburning on the indoor residential air quality. *Environ Int* 4:463 (1980).
 83. Furtaw EJ, Pandian MD, Nelson DR, Behar JV:

- Modelling indoor air concentrations near emission sources in imperfectly mixed rooms. *J Air Waste Man Assoc* 46:861 (1996).
84. Clayton CA, Perritt RL, Pellizzari ED, Thomas KW, Whitmore RW, Özkaynak H, Spengler JD, Wallace LA: Particle total exposure assessment methodology (PTEAM) study: distributions of aerosol and elemental concentrations in personal, indoor, and outdoor air samples in a Southern California community. *J Expo Anal Environ Epidemiol* 3:227 (1993).
 85. Honicky RE, Osborne JS, Akpom CA: Symptoms of respiratory illness in young children and the use of wood-burning stoves for indoor heating. *Pediatrics* 75:587 (1985).
 86. Dockery DW, Pope CA, Xu X, Spengler JD, Ware JH, Martha EF, Ferris BG, Speizer FE: An association between air pollution and mortality in six U.S. cities. *New Engl J Med* 329:1753 (1993).
 87. Koenig JQ, Larson TV, Hamley QS, Rebolledo V, Dumler K, Checkoway H, Wang SZ, Lin D, Pierson WE: Pulmonary lung function in children associated with fine particulate matter. *Environ Res* 63:26 (1993).
 88. Gold DR: Indoor air pollution. *Clin Chest Med* 13: 215 (1992).
 89. Chan CC, Yanagisawa Y, Spengler JD: Personal and indoor/outdoor nitrogen dioxide exposure assessments of 23 homes in Taiwan. *Toxicol Ind Health* 6: 173 (1990).
 90. Monn C, Brändli O, Schindler C, Ackermann-Liebrich U, Leuenberger P: Personal exposure to nitrogen dioxide in Switzerland: SAPALDIA team Swiss study on air pollution and lung diseases in adults. *Sci Tot Environ* 215:243 (1998).
 91. Lambert WE, Samet JM, Hunt WC, Skipper BJ, Schwab M, Spengler JD: Nitrogen dioxide and respiratory illness in infants—part II: assessment of exposure to nitrogen dioxide (research report 58). Health Effects Institute, Cambridge, MA, 1993.
 92. Samet J, Marbury MC, Spengler JD: Health effects and sources of indoor air pollution. Part 1. *Am Rev Respir Dis* 136:1486 (1987).
 93. Ryan PB, Hemphill CP, Billick IH, Nagda NL, Koontz MD, Fortmann RC: Estimation of nitrogen dioxide concentrations in homes equipped with unvented gas space heaters. *Environ Int* 15:551 (1989).
 94. Spengler JD: Nitrogen dioxide and respiratory illnesses in infants. *Am Rev Respir Dis* 148:1258 (1993).
 95. Postlethwait EM, Bidani A: Reactive uptake governs the pulmonary air space removal of inhaled nitrogen dioxide. *J Appl Physiol* 68:594 (1990).
 96. Spicer CW, Kenny DV, Ward GF, Billick IH: Transformations, lifetimes, and sources of NO₂, HONO, and NHO₃ in indoor environments. *J Air Waste Man Assoc* 43:1479 (1993).
 97. Viegi G, Carrozzi L, Paoletti P, Vellutini M, DiViggiano E, Baldacci S, Modena P, Pedreschi M, Mammì U, di Pede C: Effects of the home environment on respiratory symptoms of a general population sample in middle Italy. *Arch Environ Health* 47:64 (1992).
 98. Jarvis D, Chinn S, Luczynska C, Burney P: Association of respiratory symptoms and lung function in young adults with the use of domestic gas appliances. *Lancet* 347:426 (1996).
 99. Goldstein IF, Andrews LR, Hartel D: Assessment of human exposure to nitrogen dioxide, carbon monoxide, and respirable particles in New York inner-city residences. *Atmos Environ* 22:2127 (1988).
 100. Salome CM, Brown NJ, Marks GB, Woolcock AJ, Johnson GM, Nancarrow PC, Quigley S, Tio J: Effect of nitrogen dioxide and other combustion products on asthmatic subjects in a home-like environment. *Eur Respir J* 9:910 (1996).
 101. Jones AP: The main causative factors of asthma, available information on population exposure to those factors, and current measures of control. In *Asthma in Europe*. European Federation of Asthma and Allergy Associations (EFAAA), Holland, 1997, pp. 207–301.
 102. Tunnicliffe WS, Burge PS, Ayres JG: Effect of domestic concentrations of nitrogen dioxide on airway responses to inhaled allergen in asthmatic patients. *Lancet* 344:1733 (1994).
 103. Burr ML: Health effects of indoor combustion products. *J R Soc Health* 117:348 (1997).
 104. Leaderer BP, Koutrakis P, Briggs SLK, Rizzuto J: Measurement of toxic and related air pollutants. Proceedings of the EPA/Air and Waste Management Association International Symposium (VIP-17), United States Environmental Protection Agency, Washington, DC, 1990, p. 567.
 105. Leaderer BP, Stolwijk JAJ, Zagraniski RT, Qing-Shan M: A field study of indoor air contaminant levels associated with unvented combustion sources. Proceedings of the 77th Annual Meeting of the Air Pollution Control Association, San Francisco, CA, 1984.
 106. Islam MS, Ulmer WT: Threshold concentrations of SO₂ for patients with oversensitivity of the bronchial system. *Wissenschaft Umwelt* 1:41 (1979).
 107. Burr ML, St-Leger AS, Yarnell JW: Wheezing, dampness, and coal fires. *Commun Med* 3:205 (1981).
 108. Qin YH, Zhang XM, Jin HZ, Liu YQ, Fan DL, Cao ZJ: Effects of indoor air pollution on respiratory illness of school children. Proceedings of the 6th International Conference on Indoor Air Quality and Climate (Jantunen M, Kallickoski P, Kukkonen E, Saarela K, Seppänen A, Vuorelma H, editors). Helsinki, Finland, 1993, pp. 477–482.
 109. Burton BT: Volatile organic compounds. In *Indoor Air Pollution and Health* (Bardana EJ, Montanaro A, editors). Marcel Dekker, New York, 1997, pp. 127–153.
 110. Hines AL, Ghosh TK, Loyalka SK, Warder RC: *Indoor Air—Quality and Control*. Prentice Hall, Englewood Cliffs, NJ, 1993.
 111. European Commission Joint Research Centre: Total volatile organic compounds (TVOC) in indoor air quality investigations. European Commission, Luxembourg, 1997.

112. Brown VM, Crump DR: Volatile organic compounds. In *Indoor Air Quality in Homes, the Building Research Establishment Indoor Environment Study, part 1* (Berry RW, Brown VM, Coward SKD, editors). Construction Research Communications, London, 1996.
113. Wolkoff P, Clausen PA, Neilsen PA, Mølhave L: The Danish twin apartment study; part 1: formaldehyde and long-term VOC measurements. *Indoor Air* 4:478 (1991).
114. Adlkofer F, Angerer J, Ruppert T, Scherer G, Tricker AR: Determination of benzene exposure from occupational and environmental sources. In *Volatile Organic Compounds in the Environment*. Indoor Air International, Rotherfleet, U.K., 1993, pp. 511–518.
115. Norbäck D, Björnsson E, Janson C, Widstrom J, Boman G: Asthma and the indoor environment: the significance of emission of formaldehyde and volatile organic compounds from newly painted indoor surfaces. *Occup Environ Med* 52:388 (1995).
116. Hartwell TD, Pellizzari ED, Perritt RL: Results from the Total Exposure Assessment Methodology (TEAM) study in selected communities in Northern and Southern California. *Atmos Environ* 21:1995 (1987).
117. Rodes CE, Kamens RM, Wiener RM: The significance and characteristics of the personal activity cloud on exposure assessments for indoor contaminants. *Indoor Air* 2:123 (1991).
118. Wallace LA: Personal exposure to 25 volatile organic compounds. EPA's 1987 team study in Los Angeles, California. *Toxicol Ind Health* 7:203 (1991).
119. Samet J: Environmental controls and lung disease. *Am Rev Respir Dis* 142:915 (1990).
120. Norbäck D, Björnsson E, Janson C, Widstrom J, Boman G: Asthma. *Occup Environ Med* 52:388 (1995).
121. Wolkoff P, Clausen PA, Jensen B, Nielsen GD, Wilkins CK: Are we measuring the relevant indoor pollutants? *Indoor Air* 7:92 (1997).
122. Reiss R, Ryan PB, Koutrakis P, Tibbetts SJ: Ozone reactive chemistry on interior latex paint. *Environ Sci Technol* 29:1906 (1995).
123. Groes L, Pejtersen J, Valbjørn O: Perceptions and symptoms as a function of indoor environmental factors and building characteristics in office buildings. Proceedings of the 6th International Conference on Indoor Air Quality and Climate, Vol. 4, Nagoya, Japan, 1996, pp. 237–242.
124. Grosjean D, Williams EL, Seinfeld JH: Atmospheric oxidation of selected terpenes and related carbonyls: gas-phase carbonyl products. *Environ Sci Technol* 26:1526 (1992).
125. Schneider T, Bohgard M, Gudmundsson A: A semi-empirical model for particle deposition onto facial skin and eyes. Role of air currents and electric fields. *J Aerosol Sci* 25:583 (1994).
126. Wegmann TG, Lin H, Guilbert L, Mosmann TR: Bidirectional cytokine interactions in the maternal-fetal relationship: is successful pregnancy a TH2 phenomenon? *Immunol Today* 17:353 (1993).
127. Hanrahan JP, Halonen M: Antenatal interventions in childhood asthma. *Eur Respir J* 12:46S (1998).
128. Holt PG: Postnatal maturation of immune competence during infancy and childhood. *Pediatr Allergy Immunol* 6:59 (1995).
129. Holt PG, Sly PD: Allergic respiratory disease: strategic targets for primary prevention during childhood. *Thorax* 52:1 (1997).
130. Björkstén B, Holt BJ, Baron-Hay MJ, Munir AKM, Holt PG: Low level exposure to house dust mites stimulates T cell responses in early childhood independent of atopy. *Clin Exp Allergy* 26:775 (1996).
131. Mudd KE: Indoor environmental allergy: A guide to environmental controls. *Pediatr Nurs* 21:534 (1995).
132. Owen S, Morganstern M, Hepworth J, Woolcock A: Control of house dust-mite antigen in bedding. *Lancet* 335:396 (1990).
133. Kemp TJ, Siebers RWL, Fishwick D: House dust mite allergen in pillows. *Br Med J* 318:916 (1996).
134. Salerno MSR, Huss K, Huss EW: Allergen avoidance in the treatment of dust-mite allergy and asthma. *Nurs Pract* 17:53 (1992).
135. Bischoff ERC, Fischer A, Liebenberg B, Knies FM: Mite control with low temperature washing, I: Elimination of living mites on carpet pieces. *Clin Exp Allergy* 26:945 (1996).
136. Dietemann A, Bessot JC, Hoyet C, Ott M, Verot A, Pauli G: A double-blind, placebo controlled trial of solidified benzyl benzoate applied in dwellings of asthmatic patients sensitive to mites: clinical efficacy and effect on mite allergens. *J Allergy Clin Immunol* 87:738 (1993).
137. Woodfolk JA, Hayden M, Miller J, Rose G, Chapman M, Platts-Mills T: Chemical treatment of carpets to reduce mite allergen: a detailed study of the effects of tannic acid on indoor allergens. *J Allergy Clin Immunol* 94:19 (1994).
138. Reisman RE, Mauriello PM, Davis GB, Georgitis JW, DeMasi JM: A double-blind study of the effectiveness of a high-efficiency particulate air (HEPA) filter in the treatment of patients with perennial allergic rhinitis and asthma. *J Allergy Clin Immunol* 85:1050 (1990).
139. Sundell J, Wickman M, Pershagen G, Nordvall S: Ventilation in homes infested by house dust mites. *Allergy* 50:106 (1995).
140. ACP: *Mould Spore Allergy*, Allergy Control Products Inc., Ridgefield, 1990.
141. Platts-Mills TAE, de Blay F, Ward GW, Hayden ML: Allergen avoidance. In *Asthma: Basic Mechanisms and Clinical Management*, 2nd ed. (Barnes PJ, Rodger IW, Thompson NC, editors). Academic Press, London, 1992, pp. 515–526.
142. Pollart SM, Smith TF, Morris EC, Gelber LE, Platts-Mills TAE, Chapman MD: Environmental exposure to cockroach allergen: Analysis with monoclonal antibody based enzyme immunoassays. *J Allergy Clin Immunol* 87:505–510 (1991).
143. Wood R, Egleston P: Management of allergy to animal danders. *Immunol Allergy Clin Am* 12:69 (1992).

144. Wood R: *Taming Asthma and Allergy by Controlling Your Environment*. Asthma and Allergy Foundation of America, Baltimore, MD, 1995.
145. Glinert R, Wilson P, Wedner HJ: *Fel d I* is markedly reduced following sequential washing of cats. *J Allergy Clin Immunol* 85:327 (1990).
146. Antonicelli L, Bilo MB, Pucci S, Schou C, Bonifazi F: Efficacy of an air-cleaning device equipped with a high efficiency particulate air filter in house dust mite respiratory allergy. *Allergy* 46:594 (1991).
147. Simmons RB, Crow SA: Fungal colonisation of air filters for use in heating, ventilating, and air conditioning (HVAC) systems. *J Indust Microbiol* 14:41 (1995).
148. Wareham NJ, Harrison BDW, Jenkins PF, Nicholls J, Stableforth DE: A district confidential enquiry into deaths due to asthma in Norwich. *Thorax* 48:1117 (1993).
149. Wareham NJ, Hyndman S, Williams R: Asthma: the scope for prevention. East Anglian Regional Health Authority, Cambridge, U.K., 1994.
150. Roberts JW, Dickey P: Exposure of children to pollutants in house dust and indoor air. *Rev Environ Contam Toxicol* 143:59 (1995).
151. Seltzer JM: Effects of the indoor environment on health. *Occup Med* 10:26 (1995).
152. Tokarz AP, Potterfield PM: Regulatory and legal aspects of indoor air quality and pollution. *Indoor Air Poll* 14:679 (1994).
153. Department of the Environment: The United Kingdom national environmental health action plan. H.M. Stationery Office, London, 1996.
154. Harrison PTC: Health impacts of indoor air pollution. *Chem Ind* 17:677 (1997).
155. Washington State Department of Health: Comprehensive hospital abstract reporting system (CHARS). Washington State Department of Health, Olympia, WA, 1994.