New millennium: The conquest of allergy

(Supported by a grant from Novartis Pharmaceutical Corp., East Hanover, NJ)

Series editors: Donald Y. M. Leung, MD, PhD, Stanley J. Szefler, MD, and Harold S. Nelson, MD

The role of intervention in established allergy: Avoidance of indoor allergens in the treatment of chronic allergic disease

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Avoidance of exposure to indoor allergens is an important element in the treatment of allergic disease. The results of several studies provide strong evidence in support of a role for allergen avoidance; however, strategies that optimize allergen reduction in houses have not been determined. Complex issues regarding the efficacy of physical and chemical measures that target house dust mite, pet, and cockroach allergens in the home are discussed. The greatest challenge is to educate allergic patients so that they can play an important role in controlling their own disease. (J Allergy Clin Immunol 2000;106:787-804.)

Key words: *Allergy, indoor allergens, intervention*

Abbreviations used

A/C:	Air conditioner
AD:	Atopic dermatitis
BHR:	Bronchial hyperresponsiveness
HEPA:	High-efficiency particulate air
RH:	Relative humidity
TA:	Tannic acid

Identifying and controlling exposure to causal agents have always been an important part of the management of allergic disease. However, the realization that indoor allergens play a central role in chronic inflammatory disease has presented a challenge to develop practical and effective methods of reducing exposure to allergens derived from sources such as dust mites, domestic animals, and the German cockroach. For both asthma and atopic dermatitis the primary model for demonstrating inflammation in the lungs or skin is to apply allergen to specifically allergic individuals with use of either bronchial challenge or the atopy patch test.[1-5] In addition, prolonged avoidance of allergens in a hospital or sanatorium can control inflammation and the associated bronchial hyperreactivity.[6-9] Thus logically allergen avoidance should be the first line of anti-inflammatory treatment. The importance of this approach has also increased because patients want to know what is causing their disease and how to control it, many of them do not like having to take medicines regularly (especially antihistamines and steroids in any form), and the pharmaceutical agents are expensive.

For some allergens (ie, shellfish, stinging insects, or laboratory rats) demonstrating sensitivity may not be necessary to convince the patient about causality because the relationship between exposure and symptoms is obvious. By contrast, the relationship between chronic exposure, particularly indoors, and diseases such as perennial rhinitis, atopic dermatitis (AD), and asthma is not obvious to the patient. It is also increasingly clear that allergen avoidance protocols should be allergen specific. Thus any patient with chronic symptoms of one of these diseases should have skin tests or blood tests to evaluate the presence of IgE antibodies. Interestingly, this implies that allergen exposure is only relevant to those individuals who have specific IgE antibodies. The reasons for believing this come from three types of experiments: first, the epidemiologic evidence about the relevance of allergen exposure to allergic diseases relates to patients with skin tests or IgE antibodies[10,11]; second, the controlled and uncontrolled trials of avoidance only relate to allergic individuals; and third, in studies on cat allergen, rat urinary allergen, and bee venom individuals who make IgG antibodies without IgE antibodies do not have an increased risk of asthma or rhinitis.[12-14] Thus everything that we propose about avoidance should be taken to apply to individuals who have both allergic symptoms and evidence of specific immediate sensitivity.

The significance of house dust in asthma was first recognized by Kern[15] (1921) and he and others[16] talked about advising patients to control dust exposure. However, the first real experiments were those of Storm von

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Received for publication Aug 7, 2000; accepted for publication Aug 8, 2000.
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0091-6749/2000 $12.00 + 0 **1/1/110548**
doi:10.1067/mai.2000.110548

Leuwen et al[17] in 1929. They developed a "climate chamber" that was meant to be dust free and that collected clean air by constructing a "chimney" that went 100 feet above the building. At that time there was no available technique to filter the air. The authors reported that many patients with asthma improved in the climate chamber. Shortly after that, Rost[18] reported using a similar chamber to show that most patients with AD also improved when they were moved out of their houses. The inspiration for those experiments was the realization that patients with asthma who went to Davos and other sanatoria often improved dramatically. Interestingly, when Rackeman[19] defined intrinsic asthma in 1947, one of the features that he described as characteristic of these patients was that they "didn't get better in hospital." Thus he considered that the improvement of patients with asthma in hospital was in large part due to decreasing extrinsic allergen exposure. The next finding was that mite-allergic patients not only improve clinically when they move to sanatoria, but that they will have progressive decreases in nonspecific bronchial hyperreactivity.[6-8] When we demonstrated that decreased bronchial hyperresponsiveness (BHR) to histamine could also be achieved by moving mite-allergic patients into an allergen-free hospital room in London,[9] it was clear that decreased BHR should be the objective of avoidance treatment. In that study the air in the rooms was passed through a high-efficiency particulate air (HEPA) filter, the rooms had polished floors, and we showed that mite allergen decreased from 13.7 µg/g at home to <0.2 µg/g in the hospital room. Thus the real question posed is not whether allergen avoidance is good for allergic patients with asthma but whether the changes that have been consistently demonstrated in a sanatorium or hospital room can be achieved in real homes.

CONTROLLED TRIALS OF ALLERGEN AVOIDANCE FOR ASTHMA

In all controlled trials it is essential to establish that the patient complied with the treatment, that the treatment achieved its proposed objective, and also to ask whether the patient received benefit. The majority of published controlled trials of avoidance have not achieved the proposed objective (ie, significant decrease in allergen in the home). Clearly, the implications of a failure to reduce allergen are different from an experiment where decreasing allergen exposure does not help the disease. Our analysis of the published studies suggests that those studies that decreased exposure for a prolonged period were effective clinically.[20] In keeping with that, three committees/workshops that reviewed the data concluded that avoidance of dust mite allergens should be a routine part of the management of allergic asthma.[11,21,22] By contrast, a meta-analysis published in 1998 reached a different conclusion.[23] However, there was a major flaw in the design of that study. The authors evaluated 27 published controlled trials, including several by one of the authors who had used methods that were most unlikely to reduce mite allergen concentrations.[24] Including all these studies, they chose to study three outcome variables. With use of the outcome variables chosen on the basis of the whole group, they evaluated the subgroup of studies that reported for those variable results and that had documented decreased exposure, and they found no significant effect on asthma.[23] However, the outcome variables chosen excluded two of the most effective studies,[25,26] and they did not include nonspecific BHR, which is the variable most consistently studied and decreased in both controlled and uncontrolled trials of avoidance.[9,25-28] In five of six studies that have documented that exposure was decreased for 6 months or more, there was a significant improvement in the active group.[20]

The results of the avoidance studies not only provide a rationale for the use of this treatment and evidence that current exposure is relevant to the disease but also form a basis for deciding which measures are most effective. The evidence is strongest in relation to physical measures (ie, covering bedding, removing carpets, and hot washing of blankets). None of the successful studies had a major component of chemical treatment. However, it is important to remember that in each of the published studies several different measures were used and it is not possible to prove that one measure taken alone would help patients.

PHYSICAL BARRIERS

When it was first realized that mattresses contained large numbers of mites, weekly vacuum cleaning of mattresses was recommended as an avoidance measure. Not surprisingly, compliance with this proposal was extremely uncommon. When plastic covers were recommended, there was initial concern that mattresses would deteriorate or become moldy. This concern proved unfounded and there is a strong case for using plastic covers that have a zipper to enclose the mattress. Such covers may be uncomfortable but by using a washable mattress pad on top of the cover they are acceptable to most patients. Nonetheless, many individuals do not tolerate plastic mattress covers and very few find plastic pillow cases acceptable. This has created a demand for vapor- or air-permeable covers, which will prevent the passage of allergens but are comfortable. There are many different varieties of permeable and semipermeable allergen-proof fabrics ranging from plastic sheets containing small pores to very finely woven fabrics, including those that are vapor permeable (eg, Acb Elite [John]) and those that allow airflow (eg, Pristine [John]) and also nonwoven synthetics (eg, Softek, National Allergy Supply, Allergy Control Products)[29] (Table I).

The fine-woven fabrics are interesting because they can be produced with different pore sizes and allow different degrees of airflow. Several techniques for testing fabrics have been developed, including one that can test airflow and leakage of dust as assessed by measurement of the allergens Der p 1 and Fel d 1[29,30] (Fig 1). These fabrics were originally designed as typewriter ribbon and are currently used as surgeons' gowns. Pore sizes can be varied from ~2 µm up to 20 µm, and as shown in Fig 2,

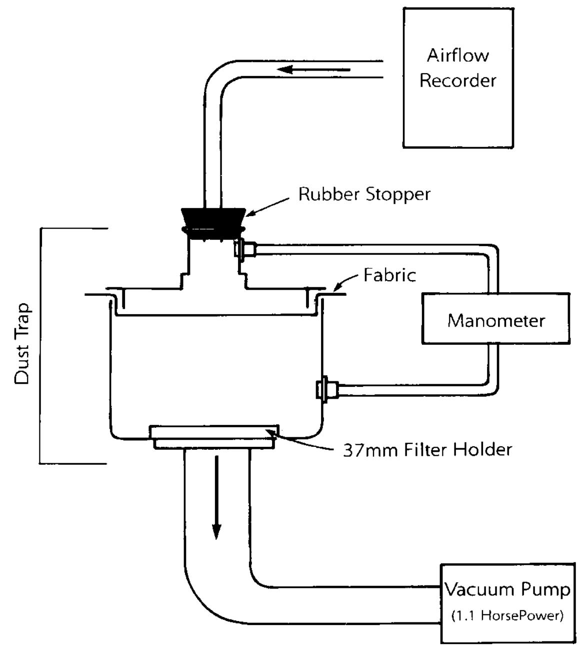

FIG 1. Diagrammatic representation of a modified Fussnecker dust trap showing placement of fabric during testing, location of flow meter, pressure gauges, and the direction of airflow.

TABLE I. Testing of materials recommended for encasing pillows and mattresses

Fabric tested	airflow through fabric tested (L/min)	Fel d 1 recovered (ng)	Der p 1 recovered (ng)
Controls			
Laboratory control	21.9	3087	280
Retail control	21.6	837	113
Poly cotton placebo	21.4	599	133
Commercially available fabrics			
Woven			
Pristine	18.4	7.4	<2.0
Pristine (washed 22 times)	17.7	3.5	<1.2
Microfiber (Priorities)	14.8	2.0	<3.1
Nonwoven synthetic			
Softek (National Allergy Supply, Allergy Control Products)	22.3	4.7	<1.2
Medibed (Comtrad Industries)	21.9	2.7	<1.2
Wondertex (GSI)	17.8	1.1	<2.0
Propore (3M)	1.3	2.3	<2.4
Acb Elite*	<0.1	<1.8	<3.6
Satin Soft (National Allergy Supply, Allergy Control Products)*	<0.1	<1.8	<3.6
Clean Living Vinyl (Sears)	<0.1	NT	<3.6

NT, Not tested. (Data taken from Vaughan JW, McLaughlin TE, Perzanowski MS, Platts-Mills TAE. Evaluation of materials used for bedding encasement: effect of pore size in blocking cat and dust mite allergen. J Allergy Clin Immunol 1999;103:227-31.)
*Vapor permeable.

the ease of airflow is directly related to pore size.[29] However, pore sizes of 6 to 10 μm will allow little or no leakage of mite allergen, and a pore size of 6 μm prevents leakage of cat allergen (Fig 2). Currently marketed fabrics were chosen on the basis of experiments of this kind.

By including the new fabrics, it is now possible to recommend mattress, box spring, duvet, and pillowcase covers to all allergic patients. However, it is essential to make sure that patients or parents understand the relative prices. A reasonable compromise is to use inexpensive plastic covers on the mattress and good-quality fine-woven fabric for the pillowcases. The picture showing a mite illustrates the fact that mites cannot penetrate some fabrics that will nonetheless allow airflow (Fig 5).

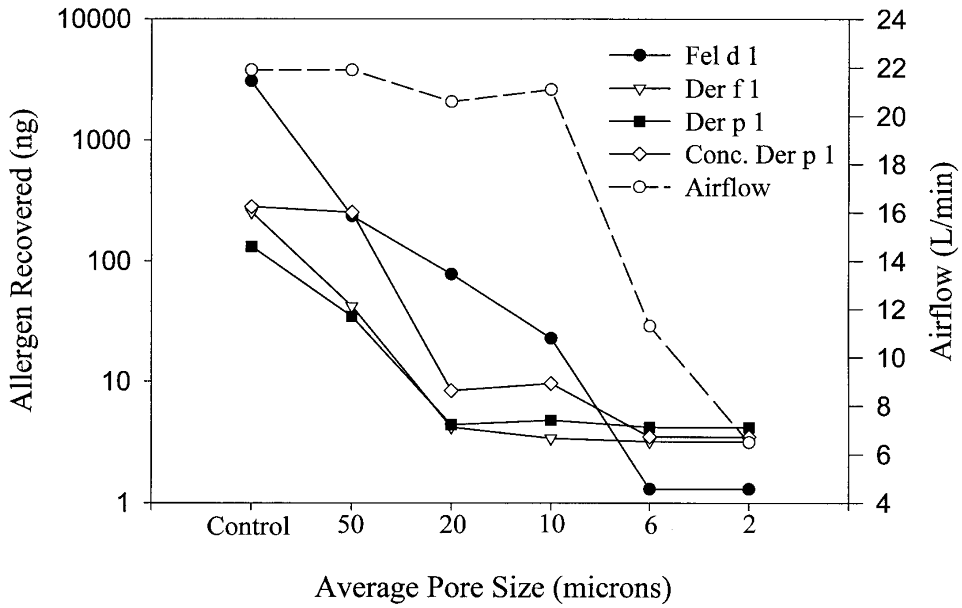

FIG 2. Allergen recovered from filter after testing fine-woven fabrics with 1.0 g of dust containing 510 μg/g Fel d 1, 5.5 μg/g Der f 1, 3.7 μg/g Der p 1, or 26.9 μg/g concentrated Der p 1. The amount of allergen recovered from the 6 μm and 2 μm fabrics reflects the lower limit of the assay. The control was a used cotton sheet (laboratory control).

THE ENIGMA OF DOWN VERSUS SYNTHETIC PILLOWS

Feathers are in general an excellent growth medium for mites; indeed, the name *Dermatophagoides pteronyssinus* means skin eating, feather loving (*pteron* is Greek for a feather or a wing). Thus, although it had been clearly shown that synthetic pillows could have a large concentration of mites, it was generally assumed that down pillows were worse and should not be used by allergic individuals. Thus it was a surprise when a large population survey in England suggested that individuals sleeping on synthetic pillows had a higher risk of asthma than those who reported sleeping on down pillows.[31,32] The first guess was that synthetic pillows gave off volatile organics but direct testing established that this was not true. By contrast, the direct experiment of measuring mite allergen demonstrated that synthetic pillows had up to five times more group 1 mite allergen than down pillows did.[33,34] Although the explanation for this is not certain, the most probable answer is that down pillows are covered with better quality (ie, tighter woven) fabrics that not only prevent feathers coming out but also prevent entry of mites into the pillow. The importance of this is that it suggests that covering a new pillow with a finely woven fabric is the correct approach to controlling mite growth close to the patient's head. In addition, knowing that synthetic pillows contain more mites than down pillows, the epidemiologic evidence that synthetic pillows increase the risk of asthma provides further evidence that exposure plays an important role in the disease.[31,32]

WASHING AND DRYING

Soon after mites were discovered it became obvious that simply washing blankets, jerseys, etc, would not remove mites. Indeed, the cool wash detergents had just been introduced and it was found that even weekly washing at 100°F did not reduce mite populations. Most studies found that washing at ≥130°F was necessary to kill mites. Subsequently, MacDonald and Tovey[35] in Sydney reported detailed studies showing that the presence of detergent actually protects the mites (probably because of the salt content of detergents). The problem with hot washing is that hot water is a risk for infants and the American Academy of Pediatrics recommends that families maintain water temperature at or below 120°F. (Certainly 130°F is the maximum temperature that should be recommended for the water in a house.) In Europe most washing machines heat the water and can be set to a desired temperature. Similarly, all laundromats should be required to offer the option of hot water washing (ie, ≥140°F).

Alternatives to hot washing include drying outside in the sun, which is very effective at killing mites, or drying in a tumble drier at 130°F for at least 20 minutes.[36,37] Dry cleaning blankets and duvets generally kills mites but is less effective at removing allergen.[38]

CARPETS: A MAJOR MANAGEMENT PROBLEM

Carpets represent both a very large nest for mites and a reservoir for all allergens. In many houses they are

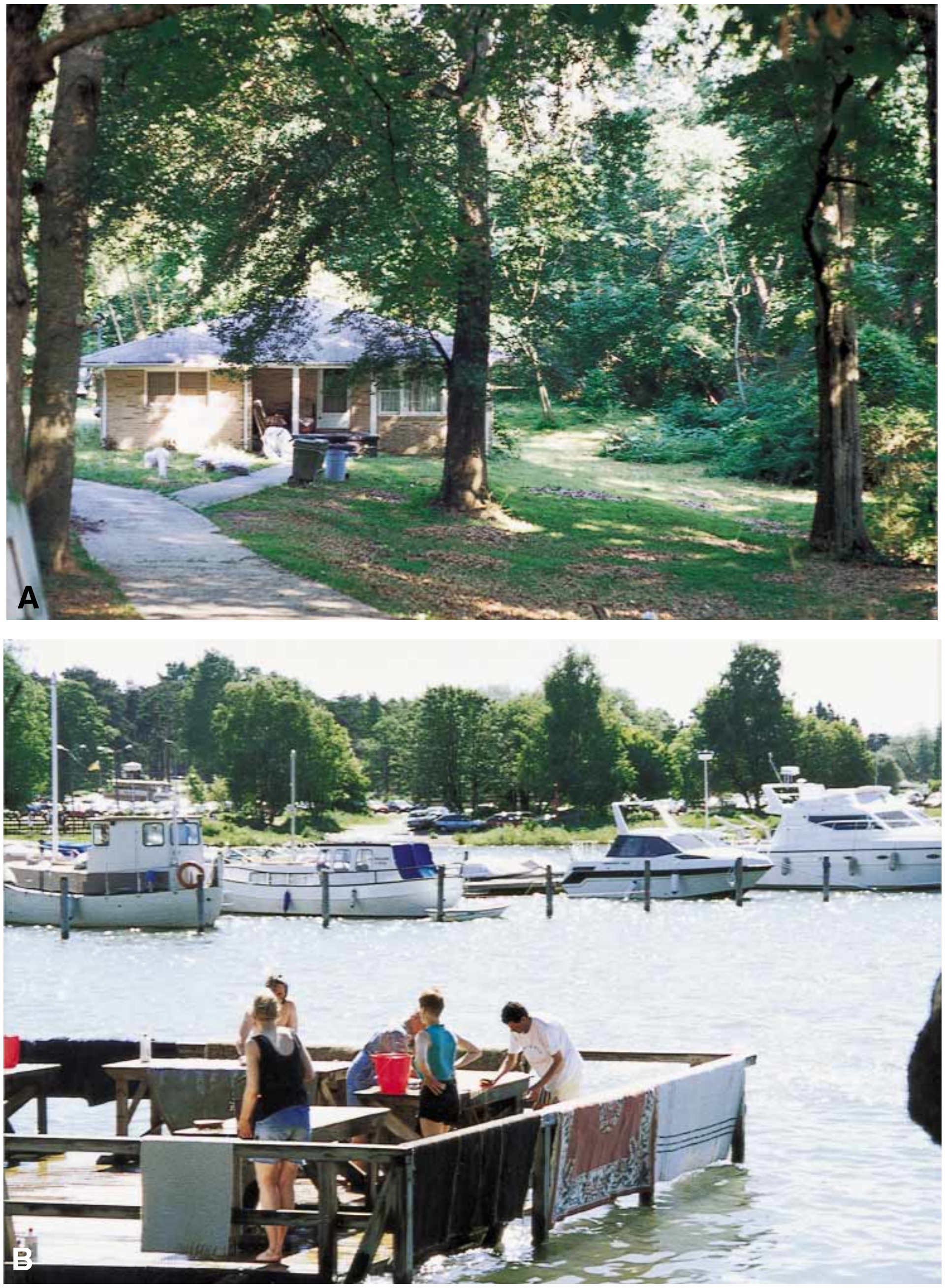

FIG 3. A, Single family home in a low income area of Atlanta, Ga. In these houses windows are typically left open, and most houses are without carpeting and contain high levels of cockroach and dust mite allergens. **B,** A platform in Helsinki, Finland, provided by the government for citizens to wash their carpets in salt water.

fixed and the underflooring is plywood so that cleaning of carpets can only be carried out in situ. It is important to recognize that in most societies taking up carpets to clean them or store them (during the summer) was considered to be an important part of household management. Thus in Finland carpets are washed in the summer and put out in the snow in the winter (Fig 3). In North Africa, the Middle East, and India carpets are put out in the sun; closer to home, in the United States putting carpets into storage and beating them were normal practices until ~1935.[39] Wall-to-wall or fitted carpets represent a challenge because they accumulate large quantities of human debris, which provides food for mites, as well as preventing cleaning. The decision to leave carpets down was based on the claim of the vacuum cleaner manufacturers that carpets could be cleaned without removal from the floor.[40] It is important to remember that without vacuum cleaners it is completely impossible to keep a carpet on the floor clean. Thus in modern houses vacuum cleaners are absolutely essential although they also create problems of their own.

In most houses human skin scales provide an excellent food source for mites, and the temperature is maintained within the range that is optimal for mite growth (ie, 65°F to 75°F.[41,42] Under these conditions the primary variable that determines mite growth is humidity. Mites absorb water by secreting from their supracoxal glands a hygroscopic fluid that flows forward to the oral cavity.[43] Absorption of water from the air is the only method that mites have to obtain water and they are totally dependent on ambient humidity.[43-45] The optimum humidity depends on the temperature but is in the range of 55% to 75% relative humidity. This is in complete contrast to insects such as cockroaches, which can move around a house to find a water supply and can survive extremely low humidity (ie, relative humidity [RH] ≤ 20%). In humid climates mite growth can occur anywhere in the house (ie, clothing, drapes, and all upholstered furniture), as well as bedding and carpets. In temperate climates mite growth may be strongly seasonal and growth can be dramatically higher in parts of the house that maintain humidity (eg, carpets laid on a concrete slab or sofas).[45,46] In dry climates (eg, the upper Midwest, the Mountain States, the southwestern United States, or northern areas of Scandinavia), mite growth in homes will be minimal unless steps are taken to humidify the house.[47-49]

Controlling humidity in the home is an important measure in reducing both mite and mold growth. Thus dehumidifiers in the basement and air conditioners (A/Cs) may play an important role. However, the benefits of standard A/C have been reduced by recent advances in A/C control. The newer systems only cool the air just below the required temperature and thus only remove the minimum amount of water. The older systems cooled the air further, which removed large quantities of water and resulted in a lower RH once the air was rewarmed. Recently it has been demonstrated that a whole house dehumidifier can produce highly significant decreases in mite growth in a temperate climate.[50] Thus it is possible to control humidity sufficiently to decrease mite growth, but this requires a central unit that is specifically designed for dehumidification.[50] Units of this kind are expensive (ie, $4000-$6000) but would not be prohibitive in the cost of a new building. Dehumidification has not been tested in truly humid climates (ie, Florida or Georgia). Most statements about housing depend to some degree on the climate; however, the effects of heating and opening windows can be opposite in different climates. In brick-built carpeted houses in England heating the house to 75°F cannot dry out the house and will simply improve mite growth.[51] By contrast, in New England or the Midwest heating in the winter will make a house sufficiently dry to kill all mites. Opening windows for 1 hour per day is a very effective method of controlling mite growth in Scandanavia because the outdoor air is dry.[52,53] In the southern states of the United States opening windows simply increases the quantity of water in the house.

CHEMICAL AGENTS

Over the last 30 years hundreds of different chemicals have been tested for their ability to kill mites in culture. A few of these chemicals have been tested in houses for their ability to decrease allergen and, in addition, one denaturing agent has been investigated. It is always important to remember that mites are not insects and that many excellent insecticides do not kill mites at the concentration that is used in houses.[54] Chemicals have been recommended for treating carpets, upholstered furniture, and mattresses (Table II). However, the results on thickly padded materials have not been encouraging. The agents tested include some potent insecticides such as pirimiphos methyl and ivermectin (Arlian, personal communication)[55,56] as well as agents acting in other ways, such as common salt, which can kill mites by dehydration; liquid nitrogen, which kills mites very effectively but has to be applied professionally[57]; the antifungal natamycin, which interferes with mite reproduction; and eucalyptus oil. There are, however, only two agents that have been used on any scale: these are the acaricide benzyl benzoate and the denaturing agent tannic acid (TA).

Benzyl benzoate

Benzyl benzoate was developed as a powder by Bischoff in Germany as a combined carpet cleaning agent and acaricide. The great advantage of benzyl benzoate is that it is nontoxic. It is widely used as a preservative in human food, it is a potent scabicide and is licensed to be painted on the skin of children, and it has not produced any reports of toxicity despite widespread use in homes.[58-60] Benzyl benzoate is a potent acaricide in laboratory cultures of house dust mites; however, the key problem is how to achieve effective concentrations for killing mites living within sofas or especially carpets, which have a large accumulation of human debris.[60] Several attempts have been made to develop a better method of delivery. Of these, the foam form of benzyl benzoate appears to be completely ineffective. By contrast, some finer powders may be more effective. The acarosan "moist powder" should be left on overnight and brushed into the carpet twice to be effective.[60] Opinion about whether carpet powders should be recommended as part of an avoidance regimen is mixed, but some authors consider that it is not possible to attain effective doses of benzyl benzoate in heavy pile or dirty carpets.[11,21,38]

There are several reasons why more potent acaricides have not become popular or marketed. The first concern has been the potential toxicity to children; however, more realistically, both pirimphos methyl and ivermectin have an enormous agricultural market and the companies concerned (ICI and Merck) would not risk marketing for domestic use because of the potential or perceived risk. The problems of marketing an agent to the public have recently become very obvious with the events surrounding the launch of AllerCare (SCJ). This product contained benzyl benzoate and a widely used commercial perfume. The reported reactions to the powder were not consistent with the known toxicity of either agent, yet the reactions led to public concern and the product was voluntarily withdrawn by the company.

Tannic acid

The role of TA as a denaturing agent or protein-stabilizing agent has been known for centuries. This process is the basis for tanning leather, using the bark of oak trees as the source of TA.[61] TA is present in tea and is consumed in large quantities, establishing that it has very low oral toxicity. TA has been used clinically to help form an eschar over an extensive burn and as part of a barium enema solution. However, both uses gave rise to occasional cases of hepatotoxicity, and it is no longer used in ways that could facilitate rapid absorption. Estimates of the molar ratio of TA to protein suggest that denaturing a molecule of Der p 1 would require 6 to 10 molecules of TA. TA was first recommended for treating carpets to decrease mite allergen by Green et al[62,63] in Sydney; they also introduced the combination of TA and benzyl benzoate. The denaturing action is not protein specific, that is, it also binds to Fel d 1 and Bla g 2 and presumably to most proteins. Consequently, the presence of other proteins in carpet or dust samples will decrease the denaturing effect of TA.[64,65] When dust samples are analyzed after a carpet has been treated with TA, it is important to block further action of the acid. With use of ferric chloride, which turns blue in the presence of TA, it is easy to demonstrate residual active TA in carpet dust samples.[65] The practical implication is that any material should be cleaned to remove excess dust, including proteins, before TA is added. In a house with a cat the sheer quantity of protein from the animal will make it difficult to denature mite or other allergens. At present, there is only limited enthusiasm for routine use of this agent. However, it has been used in at least two successful controlled trials.[25,66]

VACUUM CLEANERS

It was only the introduction of the vacuum cleaner around 1935 that persuaded housekeepers to leave carpets down. The problem is that, however powerful the machines and compelling their advertising, they cannot remove live mites from a carpet, and they will still allow debris to accumulate.[39,40] Indeed, in the carpet industry it is well recognized that carpets become progressively heavier for several years after they are laid. There is a good case for arguing that current carpet management is not successful and that polished floors should be the objective for allergic patients. There is a stronger case for saying that concrete slab or unventilated floors should have a primary flooring other than carpet (ie, polished wood, vinyl, or tile). The objective is to design the house so that carpets can be removed if there is a symptomatic individual in the house.

There are two elements to carpet cleaning: first, whether the cleaner removes dust from the carpet and, second, how much allergen/dust becomes airborne while the cleaner is in use. There are various approaches used by manufacturers for testing the efficiency of removing dust from the carpet (Asbury G., personal communication, 2000). The design of the beater or front of the cleaner can dramatically alter the efficiency of removing dust from a standard carpet. The question that is of more direct concern to allergic individuals is how much allergen becomes airborne. From experiments in houses and in the laboratory it appears that the major source is from leakage of dust in the airflow coming out of the cleaner, rather than that generated by disturbance as a result of the brush's beating action. The factors that influence leakage are connection sites integral to the machine's design, the quality of the paper bag used, and the filtration system (Fig 4).[67-70] Vacuum cleaner manufacturers have often tested leakage with use of a particle counter. However, these data are meaningless: first, because there are very large numbers of small particles (ie, <1 µm in diameter) that do not carry significant allergen and, second, because the engine of the vacuum cleaner is an important source of allergen-free small particles.[70] Most of the particles coming out of the engine are carbon from the "brushes." In our calculations we assume that there is a maximum concentration of allergen that can be present on any particle, which is approximately 10 mg/mL. Given this concentration, a mite fecal particle or a pollen grain can (and does) carry approximately 0.2 ng of allergen. By contrast, particles of 0.2 µm could not carry more than one millionth of a nanogram. Thus most of the particles that are counted with a particle counter are too small to carry significant allergen, and most of them are inert (ie, do not carry allergen at all). We believe that testing of cleaners recommended for allergic patients should evaluate whether the cleaner leaks allergen. This requires testing samples obtained from the air using sensitive assays for mite or cat allergen.[69,71] In homes, cat allergen is often airborne so that the effect of a cleaner will be to increase (or decrease) existing levels.[69] By contrast, mite allergen is not airborne without disturbance of dust in the reservoir, so that in theory the effect of a vacuum cleaner on airborne mite allergen should be easier to evaluate.[72] However, the average particle size of cat allergen (dander, etc) is smaller than that of mite (feces), so that Fel d 1 is a better test of the filtration system.

TABLE II. Chemicals for controlling house dust mite and cockroach allergens

Mites	Cockroach
Benzyl benzoate*	Boric acid
Pirimiphos methyl	Pyrethroids
Natamycin	Cypermethrin
Avermectin	Permethrin
Tannic acid*	α-Methrin
	λ-Cyhalothrin
	Fenvalerate
	Hydromethylnon
	Fipronil
	Avermectin
	Methylcarbamate

*Only benzylbenzoate is currently marketed for killing mites. Tannic acid is marketed as an allergen-denaturing agent.

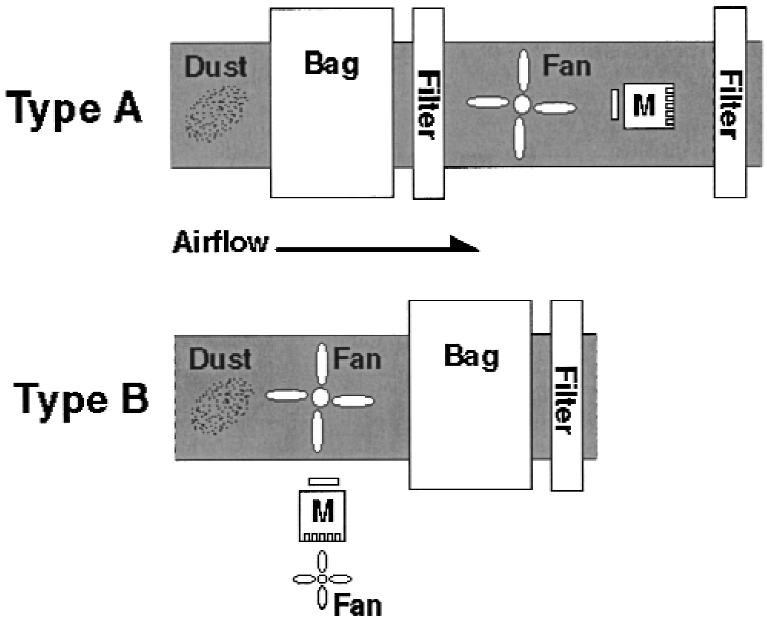

FIG 4. Two predominant designs used by vacuum cleaner manufacturers. Both designs allow airborne particles to pass through the bag and a filter leading out of the machine. In design *A* airflow passes around the motor before exiting through the exhaust filter. In design *B* the motor is located outside the flow of air through the machine, and particles emitted from the motor are driven into the environment by the fan used to cool the motor. *M,* Motor.

In our initial studies on vacuum cleaners we identified a dramatic problem with some water trap cleaners.[69] When collecting dust-containing cat allergen, they generate a fine spray of allergen on particles of ~2 μm diameter. We theorized that these particles would work efficiently as a bronchial provocation, and the results illustrated the importance of testing these machines. In 1994 we published the results of a series of experiments establishing the significance of filters, bags, and the connection sites in vacuum cleaners.[67] When we tested several models in 1998 the overall quality of the machine design was much improved but the bags still showed a very wide range of leakage (Tables III and IV).[70] Those studies used the technique for testing materials that had been used on barrier fabrics (Table I). The results reinforce the conclusion that two or more layers are generally necessary in a paper bag.[67,70,73,74] There are several conclusions about cleaner design:

1. Junctions within the cleaner need to be tight so that air does not leak.
2. The paper bags should be double thickness or specially designed nonwoven synthetic materials (Fig 5). The number of layers does not guarantee full filtration (Table IV).
3. The final filter can control leakage completely, especially if it is a true or modified HEPA filter; however, it is only essential if the bag leaks.[67,69,70,73,74]

A standard test of cleaners would be very helpful; however, attempts to establish such a test have not been successful. The problems include (1) the manufacturers are interested in counting all emitted particles, which include those not relevant to allergic disease, (2) testing requires a sensitive assay of airborne cat (or other small particle) allergen, and (3) the rate of change of models is too rapid. Many manufacturers produce two or three new models per year and change the details of other models without changing the model description. In addition, new approaches to filtration or cleaning are developed. The recent introduction of cyclone cleaners, which do not incorporate a dust bag, is a good example. These machines are very popular and have not yet been tested for allergen leakage.

AIR CLEANING

The idea of cleaning the air we breathe is obvious and inherently attractive. Filters are used for many purposes; in the home they are commonly an integral feature of the air handling system, vacuum cleaners, and personal or room air cleaners.[75,76] The filter requirements for these situations are different, but resistance to airflow, efficiency of filtration, and maintenance are all relevant. We are primarily concerned with the ability of filters to remove particles carrying allergens. However, it is important to remember that both allergic and nonallergic individuals may derive symptomatic benefit from removing irritant particles such as tobacco smoke from the air. Air filters work by forcing air to pass through a mesh of fibers that capture particles. There are hundreds of different types, which are used extensively for (1) central air condition-

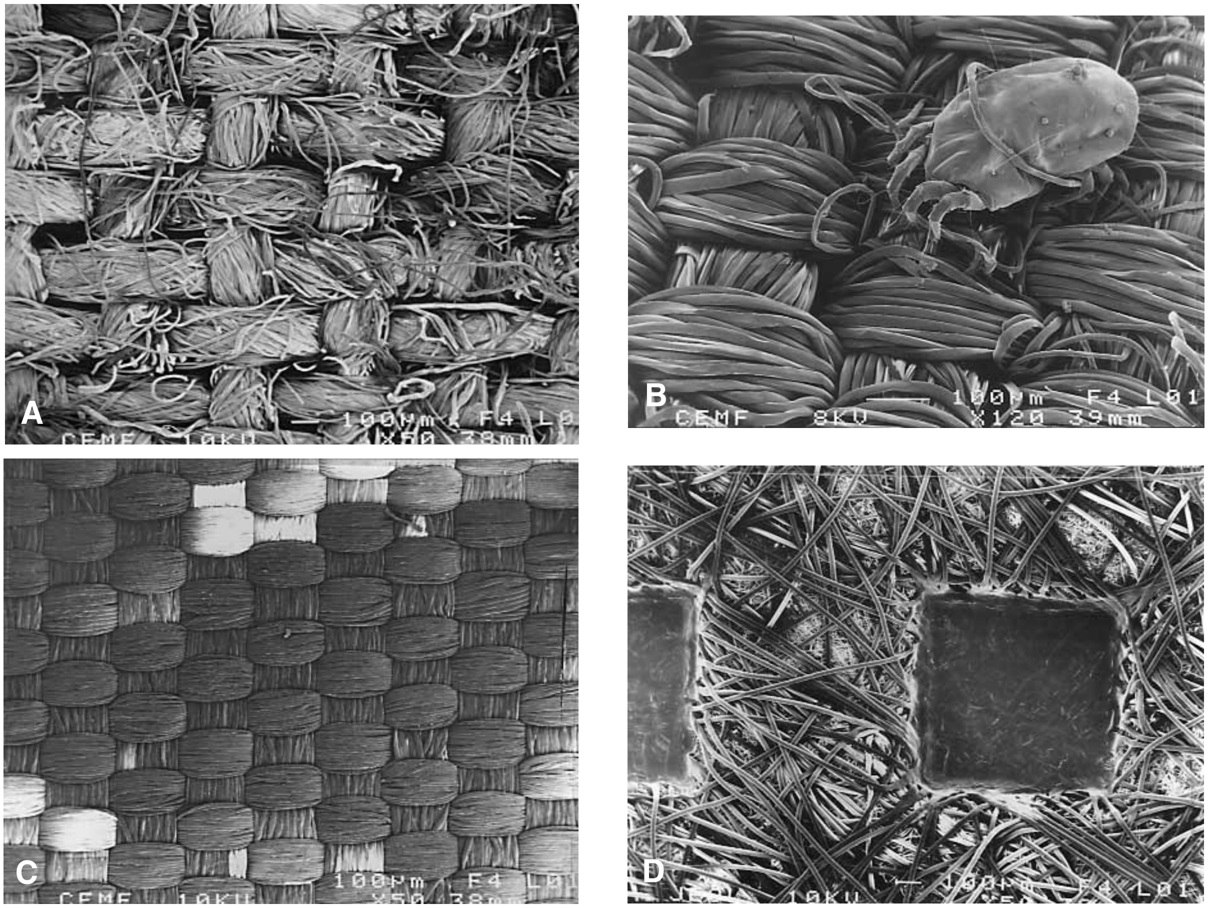

FIG 5. Scanning electron microscope pictures of four fabrics: **(A)** cotton sheet with large pores (laboratory control), **(B)** dust mite on fine woven fabric (Pristine, 6 µm fabric), **(C)** very tightly woven (2 µm) fabric used for surgical gowns, and **(D)** nonwoven material showing heat welding (Softek, Medibed) (see Table I for details).

TABLE III. Quantitative measurement of cat allergen leakage from selected vacuum cleaner testing

Vacuum cleaner	Filters	Background readings*†	Fel d 1 recovered with dust added to bag*	Overall performance
Oreck-XL	‡	0.37	0.42	+
Eureka EnviroVac	§‖	0.34	0.52	+
Miele White Pearl	§‖	0.73	0.67	+
Kenmore Upright	‡§	0.76	0.69	+
Miele Air Clean Plus	‡§	0.67	0.87	+
Eureka Excalibur	§‖	0.52	2.06	±
Hoover Dimension Supreme		0.44	4.04	–
Kenmore 4.3 (used)¶	§	10.4	43.1	–

Performance ratings: +, good; ±, adequate; –, poor. Data from Vaughan JW, Woodfolk JA, Platts-Mills TAE. Assessment of vacuum cleaners and vacuum cleaner bags recommended for allergic subjects. J Allergy Clin Immunol 1999;104:1079-83.
*Fel d 1 recovered in nanograms per cubic millimeter ± SE.
†Background readings taken with empty vacuum cleaner running inside laboratory room for 30 minutes.
‡Exhaust filter.
§Prefilter leading to fan.
‖HEPA exhaust filter.
¶Control, 36 g of dust added containing 41 mg of Fel d 1.

ing, (2) room air cleaners, (3) vacuum cleaners, and (4) filters on central air vents. The simplest filters are loosely packed coarse fibers that have very little ability to trap any particles of ≤10 µm in diameter.[76,77] These filters are commonly used on central air or heating units. By packing the fibers closer and making them finer, the efficiency of the filters can be increased. The American Society of Heating, Refrigerating, and Air Conditioning Engi-

TABLE IV. Testing materials used for vacuum cleaner bags

Vacuum cleaner bag	Layers	Vacuum	Airflow (L/min)	Fel d 1 recovered (ng)*
3M Filtrete (n = 3)	3		20.7	0.53
Hoover Microfiltration (n = 2)	2	Hoover Dimension Supreme	19.5	0.93
Kenmore Microfiltration Bag (n = 2)	2	Kenmore Upright	19.6	2.79
Dirt Devil—Microfiltration (n = 2)	2		20.4	13.5
Kenmore Vacuum Cleaner Bag (n = 3)	1	Kenmore 4.3 (used)	18.1	268
Miele (n = 4)	2	Miele White Pearl, Miele Air Clean Plus	20.1	720
Oreck-XL (n = 2)	1	Oreck-XL	16.3	1910
Eureka (n = 2)	2	Eureka EnviroVac, Eureka Excalibur	19.2	2450
American Fare (n = 2)	1		18	2640

From Vaughan JW, Woodfolk JA, Platts-Mills TAE. Assessment of vacuum cleaners and vacuum cleaner bags recommended for allergic subjects. J Allergy Clin Immunol 1999;104:1079-83.
*1.0 g of dust added containing 1.32 mg/g Fel d 1.

neers has standards that rate filters by their efficiency at removing particulates, so filters can be rated as 40%, 60%, or 95% efficent. However, many of these filters are very inefficient at removing particles of 0.3 µm. More efficient filters can be made by using fibers in the form of a paper or by spot welding the nonwoven fibers (Fig 5, *D*).[76,77] The disadvantage of efficient filters is that their resistance progressively increases. However, pleating of a paper filter can dramatically increase the surface area and thus reduce the resistance.

The most efficient filters are HEPA filters. These filters are defined by their filtration efficiency (ie, 99.97% of all airborne particles of 0.3 µm must be removed from the air pressing through them). In most cases they are made from a microfine glass paper that is folded in a minipleated form of 66 or 124 µm deep. In general, HEPA filters have too high a resistance for central air but may be suitable for room air cleaners, the air supply to special clean rooms, and vacuum cleaners. In addition, most HEPA filters define the total number of hours for which they should be used.

The third group of filters depend on applying an "electrostatic" charge to particles in the airflow so that particles will then adhere either to plates in the filter, to duct walls, or to the walls of the building. Electrostatic filters may be up to 90% effective and have the advantage that they have very low resistance to airflow. The disadvantages of these filters are that it is more difficult to test their efficiency, they can generate significant ozone, and they generally do not have defined efficiency for different particle sizes or the number of hours for which they will work effectively. Nonetheless, some electrostatic filters may work efficiency for heating and A/C or room air cleaners. At present, we recommend HEPA filters for room air cleaners, nonwoven fiber filters for heating and A/C, and good-quality 2-layered "paper" bags for vacuum cleaners.

In testing room air cleaners under artificial conditions it is simple to demonstrate that a HEPA filter removes all detectable allergen (eg, Fel d 1 from cat) from the air passing through it. However, many room air filters have airflow of 200 L/min and this flow can produce a disturbance of other allergen in the room.[67,68] Thus an "effective" air filter placed on a carpet in a house with a cat may not decrease airborne allergen if the airflow coming out of the filter disturbs as much allergen as the filter removes. In our experience, room air cleaners are more effective at controlling airborne cat allergen if combined with removal of carpets and cleaning.[68,76,78] The role of air filters in controlling mite allergen exposure is not clear. In general, mite allergen only becomes airborne during disturbance and falls rapidly; thus there is little opportunity for air filtration to exert an effect.[51,69,79] However, the respiratory tract of allergic individuals is usually nonspecifically sensitive, and these individuals may have symptomatic improvement with reduction of particles in the air that are not carrying relevant allergens.

SPECIAL PROBLEMS OF DOMESTIC ANIMALS

Domestic animals are present in up to 60% of homes and are an extraordinarily prolific source of proteins that can act as sensitizers. The main source of allergen may be urine from rodents and rabbits or dander from cats and dogs. Direct measurement of cat or dog allergen in dust has demonstrated that the levels can be higher than those for dust mite or cockroach. However, these measurements may underestimate real exposure because the particles carrying cat or dog allergen that become airborne have very different characteristics compared with those carrying mite (or cockroach) allergens. The particles of cat allergen are not very well defined; however, they consistently remain airborne without disturbance, and as judged by their passage through fabrics, are physically smaller.[29,30] Cat dander particles also "stick" to all surfaces (eg, clothing, furniture, and walls). As a result, the allergen is tranferred to other houses, schools, and public buildings.[47,80-82] This has many consequences.

Many cat-allergic patients are exposed to allergen in their own houses and should receive advice about avoidance even if they do not have a cat. Children who do not have a cat may become sensitized to cat allergen from exposure occurring at school, in other children's houses, or in their own house from passively transferred aller-

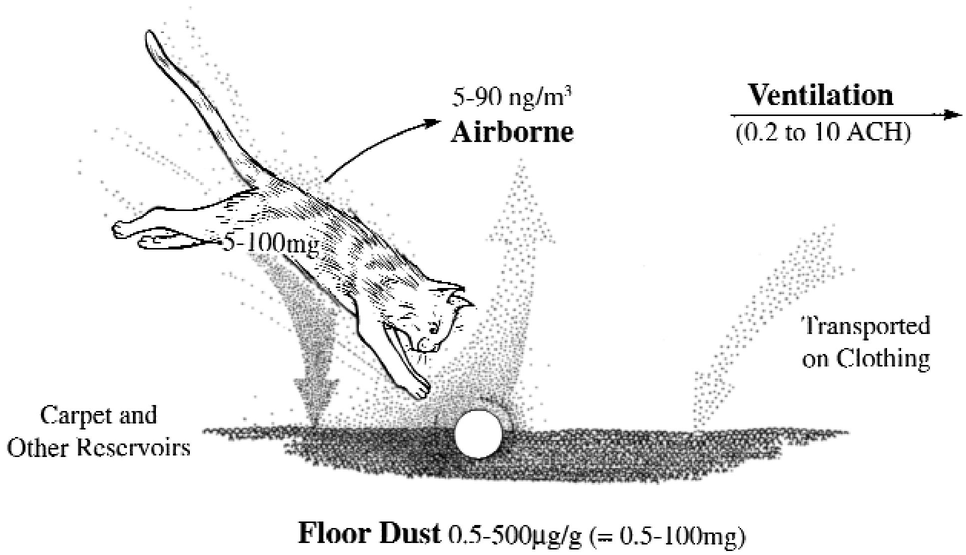

FIG 6. Dynamics of cat allergen (Fel d 1) in a house. The quantity of cat allergen in carpet dust and airborne is dependent on several factors. Cat allergen accumulates to high levels in carpets (up to 500 µg/g dust), representing total allergen levels within a carpet of up to 100 mg. Owing to passive transfer of allergen on clothing, it is not uncommon to measure cat allergen in carpet dust from houses without a cat. The cat is also a major reservoir of allergen and the quantity of allergen on the cat, along with levels in floor dust, ventilation rates, and the degree of disturbance of carpet dust, contribute to the total amount of airborne Fel d 1. Low ventilation rates (fewer than three air changes per hour *[ACH]*) increase airborne Fel d 1 levels.

gen.[47,81,83] It is important to remember that a large proportion of day care occurs in domestic homes, so young children may spend many hours per day in another house. Recent evidence suggests that children living in a house with "moderate" levels of cat allergen (ie, 4 to 20 µg of Fel d 1 per gram of dust) are more likely to become allergic to cats than those exposed to ≥20 µg of Fel d 1 per gram of dust.[84-87] Indeed, it appears that high-dose exposure to cat allergen can induce a form of immunologic tolerance. This response, which includes IgG and IgG4 antibodies to Fel d 1 without IgE antibodies or skin sensitization to cat allergens, should be regarded as a modified T_H2 response.[88] The important conclusion is that primary avoidance of cat allergens by removing the cat from the home of one family within a community where many families have cats might achieve the opposite of the intended effect.

Controlling exposure to cat allergen in a house with a cat requires controlling all the sites where cat allergen accumulates, as well as the source.

Washing and wiping cats

Some cats enjoy being washed and even enter showers voluntarily. In addition, there are plenty of individual testimonials to the beneficial effects of regular washing. By contrast, washing a cat that is not used to it may be very difficult and the experimental results have not been consistent. Most domestic cats carry a large quantity of allergen (Fig 6), and clearly they are the primary reservoir. Initially, it was reported that the major source of allergen was saliva. However, detailed experiments on shaved areas of skin established that allergen comes from glands in the skin.[89] After the accumulation of allergen in an experimental room over 2 months, we estimated that the cat was producing ~5 mg per day.[68] A house with a cat may contain at least 100 mg of Fel d 1 in the carpets and furniture, in addition to the allergen on the animal. Washing is designed to achieve two effects: (1) removing allergen from the cat that would otherwise accumulate in the house and (2) decreasing the quantity becoming airborne from the cat.[68,90] Provided an adequate quantity of water is applied, washing can remove 2 to 3 mg from the cat, and after washing very little allergen will become airborne. However, contrary to our initial result, this decrease usually only lasts a few days.[90,91] This suggests that washing would have to be repeated twice a week.[90] Strikingly, the same conclusion has been reached from studies on dogs.[92] Washing dogs is normal practice in many areas, particularly where dogs run outside, and it is generally not difficult. A more practical approach may be wiping cats with a wet cloth or hand towel, although this does not remove as much allergen as washing does.[93] However, it has not yet been proved that regular washing or wiping of cats decreases accumulation of allergen in the house.

Allergic patients who are living in a house should be educated on ways in which allergen accumulates in the house and should be advised about measures that would be required to control airborne allergen. Obviously, this is very demanding; however, some families are willing to do it and do succeed. It is important to remember that patients become very attached to their pets, and it is a mistake to advise them to get rid of their cats without first giving them other options. An alternative approach is keeping the animal outside or in a garage. Keeping an animal restricted to one part of the house has not been shown to be effective and would not be expected to help because allergen is transferred around the house. Treating cat-allergic patients is always a challenge but the key is education. The patients will make much better choices about how to handle the situation if they understand the ways in which allergen accumulates in the house and becomes airborne, the steps that are necessary to control exposure, and the reasons why we believe decreasing exposure would improve allergic symptoms.

SPECIAL PROBLEMS IN CITIES

Life in cities has many special features that can influence allergic disease both positively and negatively. These can be broadly divided into the effects of (1) multiple family buildings and (2) poverty. Multiple family buildings or apartment blocks have several effects: first, the higher the living space in the building, the lower the humidity and consequently the lower the mite growth. This effect can be dramatic in northern areas of Europe (such as Denmark) or in northeastern towns in the United States.[53] Recent studies in Boston have shown that the mite concentration in dust from apartments is on average 10-fold lower than in single family homes.[94] As we discussed before, this effect will not be the same in areas where the climate is different. In the southern states of the United States, in England, or in Brazil there is sufficient humidity to allow mite growth to occur in apartments regardless of their level in the building.[95-97]

The second major consequence of multiple family dwellings is that it is easier for insect or rodent pests to survive and spread from one apartment to the next. Thus cockroaches are a major problem in all our cities, although they are unusual in single-family houses in northern areas of the United States or Europe. Cockroaches, despite their eponyms, are tropical in origin and can only live outside in areas where it is continuously warm for many months of the year. In areas where the outdoor temperature is below 50°F at night, even in the summer, cockroaches cannot move from one house to another and are generally not a problem in single-family homes. Mice and rats are also far more of a problem in multiple dwellings. Controlling all these pests requires a consistent policy on the part of the families and the building management. For both rats and cockroaches, the primary method of control is to deny them an attractive food supply. All food must be encased and waste should never be stored in the building. Large buildings are hospitable to cockroaches because one badly infected site will provide a source for recolonizing the building. Such sites include an apartment, a basement with waste storage, or a waste disposal chute. In addition, the temperature of many apartment buildings and hospitals is maintained sufficiently hot for cockroaches to flourish. Thus the simple physical circumstances provide an explanation for many of the differences in allergens that are found in different housing types and areas of the country.

Cockroaches as a specific problem for low-income housing

From many studies over the last 20 years it has been established that the German cockroach is an important allergen among families living in poverty in American cities.[98-103] In most of these studies the population affected has been predominantly African American, and some authors have implied that there might be genetic or special immunologic features of this allergen source relative to this population. However, it is more likely that the importance of the German cockroach reflects the actual concentrations of these allergens in the homes and that this results from a combination of housing conditions (and lifestyle). Several different factors contribute to the pattern of sensitization seen among children with asthma in the American cities studied by the National Inner City Cooperative Asthma Study[49]:

1. Apartments in the North and Northeast are very dry because of climate, structural features of apartment buildings, and overheating. This low humidity strongly or completely inhibits mite growth.
2. Most low-income housing units do not allow the occupants to keep domestic pets, and in addition many families do not like cats inside their homes. This means that cat allergen levels are usually very low (ie, ≤0.6 µg Fel d 1/g dust) and that this allergen is not a significant cause of sensitization.[49,102,103] In addition, outdoor cats will eat cockroaches and the striking dissociation between these two allergens suggests that domestic cats may be able to control cockroach infestation sufficiently to prevent accumulation of their allergens in houses.[102]
3. Heated apartment buildings allow cockroach colonization and make full eradication difficult. In addition, many families living in poverty are under considerable social stress and this often leads to poor housekeeping. It has been suggested that housekeeping standards in general have deteriorated in the United States.[104] However, the evidence that this could have contributed to allergen concentrations or quantities airborne is not clear. The important conclusion is that under conditions where cockroaches are almost inevitable (ie, heated apartment buildings), poor housekeeping will lead rapidly to heavy infestation.

Although there is extensive information in the entomologic literature about techniques for killing cockroaches,[105,106] effective control of these insects in apartments or houses presents a considerable challenge. The allergen in a house is very unevenly distributed and can accumulate to create a large reservoir that will persist for years, even after the cockroaches have been exterminated.[105] Thus controlling cockroaches is a complex task that involves both killing the insects and removing accumulated allergen. It is perhaps not a surprise that the first generation of studies on controlling cockroach allergen in the treatment of asthma were not very successful.[66,107,108] Cockroaches are remarkably well adapted to breed in small cracks, within walls, behind pictures, or within upholstered furniture. Thus, as with dust mites, it is difficult to apply insecticides to the sites where cockroaches breed. Hundreds of different chemicals have been tested for their ability to kill cockroaches and dozens are (or have been) marketed for this purpose (Table II). When insecticides are sprayed inside a house, it is not unusual for allergic patients to have a marked exacerbation of their symptoms. For this reason bait is recommended as the primary method of control. Bait-containing chemicals can be applied as a "bait station" or as paste. A major problem with bait is achieving access to sites where cockroaches reside. Cockroaches generally track around the corners of a room. If bait is used in the form of a paste, professional exterminators apply bait to many sites in a room: under furniture, in cracks, behind paintings, etc. Surprisingly, the chemical sprays used for killing insects, which can be extremely irritating to the respiratory tract of allergic patients, have never been questionned by the Environmental Protection Agency, perhaps because they are marketed solely for the purpose of killing cockroaches and not as a method of helping allergic patients. Cockroaches, along with many other insects, have shown themselves adept at developing resistance to insecticides, so there is considerable interest in alternative control techniques.

Three other approaches to controlling these insects should be mentioned:

1. The traditional use of boric acid is moderately effective. It can be made up as a paste together with flour, milk, and chopped onions. The action of boric acid is to damage the foregut so that the insect dies of starvation.[109]
2. "Obsessional" caulking to prevent re-entry of insects and to reduce the number of sites available for breeding can be helpful, but it is hard work.
3. The traps or "roach motels" that are widely available will have little effect on the population of roaches. However, there have been attempts to design a better trap. This includes a pheromone to attract insects and a specially designed shape that fits into a corner in such a way that it covers the normal pathways of roaches. And finally, these traps are designed with a super-sticky floor area surrounded by a plastic surface that prevents the roaches pulling themselves out of the glue.

Although it is well recognized that cockroaches can develop resistance to chemical insecticides, there is an interesting secondary effect of this response. One of the major allergens of the German cockroach is a glutathione transferase (Bla g 5).[110] This inducible enzyme is an important component of mechanisms used by cockroaches to protect themselves from toxins. Thus in theory an insecticide could increase allergen production in cockroaches that survive.

RELEVANCE OF AVOIDANCE TO PRIMARY SENSITIZATION

The protocols recommended for decreasing mite, domestic animal, or cockroach allergen in houses can decrease allergen, and they can play an important role in the management of allergic patients. Because sensitization to mite and cockroach allergens is strongly associated with exposure, it is logical to ask whether decreasing exposure to these allergens would decrease the onset of asthma. Indeed, several large studies are currently under way. The problem is that sensitization and asthma develop progressively in the first 5 years of life and the full relationship between the two may not be clear until as late as age 10 years.[111-113] Thus it is not clear when avoidance needs to be started, nor whether it needs to be continued. It has been suggested that the response to inhalants starts in utero.[114,115] However, the only evidence supporting that idea comes from cord blood T-cell responses in vitro. Our analysis of these data indicates that there is no evidence that the responses are related to exposure of the mother and no evidence that the responses predict outcome.[116] Given the high background on cord blood T-cell responses, it seems that most if not all the cord blood data should be regarded as in vitro artifact. Certainly, the evidence is not sufficient to conclude that the infants have made an immune response in utero. Specific objective evidence for a response to dust mite is unusual below the age of 2 years.[111] Thus currently we cannot answer when primary avoidance needs to start, how long it should continue, or whether it is relevant to allergens other than mite or cockroach.

The major trials of allergen avoidance that are under way in the world are focused on mite avoidance (Marks et al, Sydney; Chan Yeung et al, Canada; Brunekeef et al, Holland; and Custovic et al[117]). None have yet answered the central question positively, perhaps because it is too early to judge the results or because there are other major changes that have contributed to increasing asthma and still are increasing the risk of allergic disease, particularly asthma.

It is important to recognize that the whole argument about primary avoidance depends on there being a simple dose-response relationship between exposure and sensitization. The currently available evidence for cat allergens shows clearly that this is not so.[84-87] The evidence about cat allergen can be summarized into three areas.

First, in many studies the presence of an animal in the house is associated with a decreased risk of sensitization and a decreased risk of asthma.[84-87] In those studies where this effect is not seen, it appears that the concentration of cat allergen in houses is less than 20 µg/g.

Second, the maximum prevalence of cat sensitization (at 10%-15%) in studies from Europe, New Zealand, and the United States is consistently lower than the prevalence of sensitization to mite (ie, 20%-30%) although

TABLE V. Patient education: house dust mite allergen avoidance

____	Patient's home environment assessed
____	House dust mites (HDM) described (microscopic insect, sloughed skin is food source)
____	Optimal HDM growth conditions described (>50% relative humidity, 65°F-75°F)
____	Locations of highest HDM infestation (pillows, mattress, box spring, carpet, soft upholstered furniture, draperies, stuffed animals/toys)
Avoidance: priorities	
____	Encase mattress and all pillows in allergen-proof cover (vinyl or 6 µm microdenier, or fabric backed with vinyl or urethane membrane)
____	Wash bed linens weekly in hot water (130°F) and damp wipe the mattress cover weekly
____	Encase box spring in vinyl plastic
____	Reduce clutter/toys/other collections in bedroom
____	Vacuum or dust weekly (wear mask and leave area for 20 minutes after cleaning) (Vacuum cleaners that incorporate a double-thickness bag and HEPA filter leak little allergen*)
____	Use Filtrete (3M) or "microclean" (DuPont) filters to reduce allergen leakage from vacuum cleaner
____	Place stuffed animals in freezer overnight, or hot water wash weekly
____	Hang bulky comforter/bedspread outside in dry, subzero weather
____	Clean or replace heat/air conditioner filter as per manufacturer's instructions†
Avoidance: long-term modifications	
____	Reduce indoor relative humidity with air conditioning or dehumidifier (30%-45% RH). Humidity can also be controlled by increasing ventilation if the outdoor conditions are cold and/or dry.
____	Replace carpet with polished flooring (wood, vinyl, linoleum, tile)
____	Replace upholstered furniture with leather, vinyl, wood, plastic
____	Replace drapery with wipable shades/blind or washable curtains
____	Avoid living in basement or in room with cement slab floor. Bedrooms should be upstairs.

*Allergy clinics should provide patients with details regarding which product brands are recommended.
†Pleated 1-inch paper filters are more effective than loosely packed fiber filters. However, HEPA filters are not suitable for central air conditioning systems because their resistance to airflow is too high.

TABLE VI. Patient education: pet allergen avoidance

Pet you are allergic to:______________________________	
____	Source of pet allergen discussed
____	Cat and dog allergens suspended in air for long periods
____	Allergen passively transferred on clothing
____	Allergen present in places where there has never been a pet (ie, school, library)
____	Suggested pets: reptiles, tropical fish, hermit crabs
Avoidance	
A. Priority	
____	Remove pet from home or keep outdoors
B. Additional measures	
____	If indoors, confine the animal to a room with polished floor, wipable furniture
____	Keep the animal out of the bedroom; bedroom door should be closed; keep air vents closed
____	Wash thoroughly and change clothes after contact with pet
____	Use a HEPA room air cleaner if cat or dog is indoors; keep the HEPA cleaner off the floor
____	Bathe animal frequently in warm water
____	Encase mattress, pillow, and box spring
____	Wash bed linens weekly

exposure as measured in micrograms of the major allergen appears to be much higher.

Third, children aged ~12 years old raised in a house with ≥20 µg/g Fel d 1 have a high prevalence of IgG and IgG4 antibodies without sensitization.

What is clear is that the IgE antibody response to cat allergens does not show a simple dose response; thus measures that decreased exposure in early childhood from high exposure to moderate exposure would not be expected to decrease sensitization or asthma.

Overall, it is clear that the rationale for primary avoidance has to be considered separately from the evidence about the use of avoidance as part of the treatment of established allergic disease.

CONCLUSIONS

Controlling exposure to allergens in houses is an effective treatment for patients who are allergic and who are seen for help in controlling their symptoms. The

TABLE VII. Patient education: mold/mildew/fungal allergen avoidance

____	High humidity and organic material needed for growth
____	Outdoor locations (plant material, soil, mulch, leaves, compost pile, barn)
____	Indoor locations (basement; bathroom shower tub and curtain; toilet bowl and tank; kitchen; house plants; antique shop; plant nursery)
Avoidance	
____	Outdoor: avoid mowing grass, moving mulch, raking leaves, working with plant materials and hay, cleaning barn
____	Indoor
____	Dehumidify with air conditioner or dehumidifier (30%-45% RH)
____	Clean moldy areas with fungicide or 10% chlorine bleach solution (1 part chlorine bleach to 9 parts water: test for color fastness)
____	Clean refrigerator, dehumidifier, and humidifier drip pans with bleach
____	Discard moldy belongings
____	Thoroughly dry clothing before storing in closet
____	Keep light on in closet to reduce dampness
____	Repair structural leaks; drain runoff away from house
____	Run vent over stove when cooking
____	Run vent in bathroom when showering or bathing
____	Limit number of houseplants and exclude from bedroom
____	Avoid living in basement

alternatives of long-term pharmacologic treatment, immunotherapy, or simply waiting for sensitization to spontaneously resolve are clearly second best. Furthermore, extensive experience suggests that both drug treatment and immunotherapy are more effective if patients also decrease exposure. The approach to avoidance is to identify the allergen source (or sources) to which the patient is allergic and to educate patients extensively. Education should be achieved by a combination of discussion, with written and audiovisual material, and should include information about both the biology of the source and methods of decreasing exposure (Tables V-VII). This education is an important part of treatment and should be designed to demistify the disease and convince patients that they can play an important role in controlling their symptoms.

Understanding the biology of dust mites, domestic animals, and cockroaches has helped enormously in designing avoidance measures. For dust mite the relevant measures are well defined and can certainly be accomplished by any motivated family. By contrast, the measures that are necessary to control cat allergens with a cat in the house are more demanding and have not been established effectively in a controlled trial. The measures necessary to clean a house once the animal has left the house are well defined. Cockroach control appears to be at the stage we were at with mites 15 years ago (ie, we understand what needs to be done but an effective protocol has not yet been established).

Studies on houses in different geographic regions of the United States emphasize how much variation there is in exposure without intervention. It is well recognized that patients moving from one part of the United States to another may enter an area where indoor allergen exposure is completely different (eg, moving from the suburbs of Atlanta to Colorado). Not only are there very few mites at that altitude, but any mites in the patient's furniture will die within about 1 year. It is less well recognized that moving from an apartment block to a suburban house in Chicago dramatically reduces the risk of cockroach infestation, or that moving from a house to an apartment in Boston may be a very effective dust mite avoidance strategy. Given the number of times families move (particularly in the United States), providing information about the regional and structural influences on house dust should be part of their education so that they can make sensible choices.

The primary objective of intervention is to decrease symptoms; however, the best defined outcome in asthma management has been decreased BHR. Achieving this objective on a consistent basis is still an important goal. However, the decrease in exposure to dust mite, cat, or cockroach allergen in a sanatorium or hospital room is greater than the decreases that have been reported in most controlled trials of avoidance. Thus avoidance that results in consistent decreases in BHR will require significant effort on the part of the family. In addition, it is important to remember that moving patients to a sanatorium or hospital involves many other changes in their normal regimen. In our experience, patients in "allergen-free" conditions improve sufficiently within a week to allow more physical activity and less use of β_2-agonist, as well as dietary changes. In addition, the "allergen-free" conditions also include decreased fungal and bacterial contamination. Thus sorting out which of these changes are most important in decreasing BHR is a continuing challenge in the management of asthma.

It is easy to jump intellectually from secondary avoidance to primary avoidance. At a practical level the evidence is not clear. The time in childhood when exposure needs to be controlled to prevent the onset of sensitization is not well defined; decreasing exposure to any allergen for a period of up to 5 years in a controlled trial is a real challenge, and for some allergens (particularly cat) it is not clear that there is a simple dose-response relationship between exposure and the probability of sensitization. In addition, we do not know what happens to atopic children if their exposure to dust mites is delayed by 3 years or more. Whether in the long term we will choose to modify the ways in which we live is an open question. At present, the message about allergen avoidance should be kept simple and restricted to patients who are allergic and who have symptoms that are likely to be caused by current exposure. For these patients avoidance can achieve benefits that are just as effective as pharmacologic treatment; the difference is that they are much cheaper, do not require daily treatment, and allow the patients an important role in controlling their own disease.

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