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Practice Parameter

Environmental assessment and exposure control: a practice parameter—furry animals

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This parameter was developed by the Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma and Immunology, the American College of Allergy, Asthma and Immunology, and the Joint Council of Allergy, Asthma and Immunology.

The American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) have jointly accepted responsibility for establishing "Environmental Assessment and Remediation: A Practice Parameter." This is a complete and comprehensive document at the current time. The medical environment is a changing environment, and not all recommendations will be appropriate for all patients. Because this document incorporated the efforts of many participants, no single individual, including those who served on the Joint Task Force, is authorized to provide an official AAAAI or ACAAI interpretation of these practice parameters. Any request for information about or an interpretation of these practice parameters by the AAAAI or ACAAI should be directed to the executive offices of the AAAAI, the ACAAI, and the Joint Council of Allergy, Asthma and Immunology. These parameters are not designed for use by pharmaceutical companies in drug promotion.

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Disclosures: The following is a summary of interests disclosed on Work Group members' Conflict of Interest Disclosure Statements (not including information concerning family member interests). Completed Conflict of Interest Disclosure Statements are available on request. Dr. Sublett is the owner of AllergyZone. Dr. Portnoy is a speaker and consultant for ThermoFisher (Phadia). Dr. Barnes is a consultant for and has received research funding from Clorox Corporation. Mr. Grimes is the owner of Healthy Habitats LLC. Dr. Matsui is speaker for Indoor BioTechnologies. Dr. Miller is the owner of Mission:Allergy Inc. Dr. Seltzer is the President of James M. Seltzer, Assoc. The other Work Group members have no conflicts to disclose. The Joint Task Force recognizes that experts in a field are likely to have interests that could come into conflict with development of a completely unbiased and objective practice parameter. To take advantage of that expertise, a process has been developed to prevent potential conflicts from influencing the final document in a negative way.

At the work group level, members who have a potential conflict of interest either do not participate in discussions concerning topics related to the potential conflict or, if they write a section on that topic, the work group completely rewrites it without their involvement to remove potential bias. In addition, the entire document is reviewed by the Joint Task Force, and any apparent bias is removed at that level. Finally, the practice parameter is sent for review both by invited reviewers and by anyone with an interest in the topic by posting the document on the websites of the ACAAI and the AAAAI.

In particular, the 2 owners of companies that produce products discussed in this practice parameter are Jeffrey D. Miller, MD, and James Sublett, MD. Dr Miller wrote an initial section on mattress encasings. This section was then completely rewritten by other members of the work group without his participation. Dr Sublett wrote a preliminary draft of the section on air filtration. That section was also subsequently rewritten by other members of the work group without his participation. Neither participant provided subsequent input into those sections.

The Joint Task Force has made a concerted effort to acknowledge all contributors to this parameter. If any contributors have been excluded inadvertently, the Task Force will ensure that appropriate recognition of such contributions is made subsequently.

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Classification of recommendations and evidence

Category of evidence

Ia Evidence from meta-analysis of randomized controlled trials
Ib Evidence from at least 1 randomized controlled trial
IIa Evidence from at least 1 controlled study without randomization
IIb Evidence from at least 1 other type of quasiexperimental study
III Evidence from nonexperimental descriptive studies, such as comparative studies
IV Evidence from expert committee reports or opinions or clinical experience of respected authorities or both

Strength of evidence supporting recommendation

A Directly based on category I evidence
B Directly based on category II evidence or extrapolated recommendation from category I evidence
C Directly based on category III evidence or extrapolated recommendation from category I or II evidence
D Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence
LB Laboratory based
NR Not rated

How this practice parameter was developed

The joint task force on practice parameters

The Joint Task Force on Practice Parameters (JTF) is a 13-member task force that consists of 6 representatives assigned by the American Academy of Allergy, Asthma & Immunology, 6 by the American College of Allergy, Asthma & Immunology, and 1 by the Joint Council of Allergy and Immunology. This task force oversees the development of practice parameters, selects the work group chair(s), and reviews drafts of the parameters for accuracy, practicality, clarity, and broad utility of the recommendations for clinical practice.

The environment practice parameter work group

The Environment Practice Parameter Work Group was commissioned by the JTF to develop practice parameters that address environmental assessment and remediation. The cochairs (James Sublett, MD, and Kevin Kennedy, MPH) invited work group members to participate in the parameter development who are considered to be experts in the field of environmental assessment and contaminant reduction. Work group members have been vetted for financial conflicts of interest by the JTF, and their conflicts of interest have been listed in this document and are posted on the JTF website at http://www.allergyparameters.org. Where a potential conflict of interest is present, the potentially conflicted work group member was excluded from discussing relevant issues.

The charge to the work group was to use a systematic literature review, in conjunction with consensus expert opinion and work group–identified supplementary documents to develop practice parameters that provide a comprehensive approach for identifying and managing environmental exposures and their health effects based on the current state of the science.

Protocol for finding evidence

A search of the medical literature was performed for a variety of terms that were considered to be relevant to this practice parameter. Literature searches were performed on PubMed and the Cochrane Database of Systematic Reviews. All reference types were included in the results. References identified as being relevant were searched for relevant references, and those references also were searched for relevant references. In addition, members of the work group were asked for references that were missed by this initial search. Although the ideal type of reference would consist of a randomized, double-blind, placebo-controlled study, the topic of this practice parameter is represented by few such studies. Consequently, it was necessary to draw on a number of observational studies along with basic laboratory reports and regulatory requirements to develop a complete document that addresses most of the issues involved in the topic.

Glossary

Terms related to evaluation of exposures

Allergen is a molecule that induces an IgE response in humans.

Assessment is an appraisal based on careful analytical evaluation.

Contaminant is any physical, chemical, biological, or radioactive substance that can have an adverse effect on air, water, or soil or on any interior or exterior surface and that has the potential to cause harm to a building's occupants. Contaminants can be allergens, irritants, or other types of substances, including biologically active ones.

Reservoirs are contained spaces or microenvironments in which contaminants can accumulate for subsequent release into the environment. Examples include carpeting, bedding, and contaminated building materials.

Source of contaminant is a mechanism for the production of contaminants. For allergens this usually would consist of biologic organisms, such as fungi, rodents, dust mites, furry animals, and insects. Nonallergen sources include chemical reactions, combustion, and microbial organisms that produce substances, such as endotoxin and volatile organic compounds. Production of contaminants from sources can be augmented by facilitating factors.

Terms related to interventions

Abatement is defined as a diminution in amount, degree, or intensity. Abatement includes removing, treating, or isolating reservoirs of contaminants using interventions such as air filtration, vacuuming, or removal of carpeting, denaturing chemicals, and removal of contaminated building materials. The term *abatement* is often used in the context of removal of asbestos. Because there are no facilitative factors or sources of ongoing asbestos production, asbestos can be considered to be entirely composed of a reservoir, which is why the term *abatement* is appropriate.

Environmental control refers to the use of one or more interventions to reduce the amount of contaminant in the environment. To be effective, environmental control generally requires the use of one or more interventions, including source control and abatement.

Exposure reduction is an attempt to block pathways to contaminants or reduce their prevalence, with the goal of reducing occupant exposure. The goal is to keep contaminant exposure below the threshold where adverse health effects can occur.

Source control is the process of reducing or eliminating sources of allergens or irritants. If the source of the allergen is removed, then exposure will decrease over time as the previously released contaminants are removed from the environment.

Terms related to health effects of exposure

Sensitization is the development of IgE antibodies to a particular allergen.

Sensitivity is the tendency of a person to develop symptoms on exposure to a substance to which they are sensitized.

Preface

Environmental assessment and exposure control is different from other practice parameters developed by the Joint Task Force on Practice Parameters in a number of important ways. Previous

practice parameters generally describe a medical condition in terms of diagnosis and treatment with the implicit assumption that the diseases are somehow intrinsic to the patient. Although environmental factors may influence the severity and course of a disorder, the assumption is that if a patient does not have the disease to begin with, the environmental factors would not be relevant. Yet increasing evidence suggests that exposure to environmental factors can contribute to the genesis of certain disorders, such as allergic rhinitis and asthma. The process begins with development of specific IgE antibodies, referred to as sensitization, which occurs as a consequence of exposure to certain environmental factors in individuals with the appropriate genetic background. If the exposure persists, then predisposed individuals may progress to develop an allergic disease. Subsequent exposure will trigger symptoms in individuals who have progressed through this sequence of events.

The treatment of allergic diseases therefore includes the use of 3 different types of intervention. Exposure control can be used to prevent sensitization, disease progression, or triggering of symptoms, either allergic or nonallergic. Medications are used to alleviate and control symptoms once the disease has developed. For selected patients, specific allergen immunotherapy can be used to reduce sensitization. Although all 3 types of intervention are important, for many reasons exposure control is particularly so. For most allergists, exposure control consists of a group of measures that are used to reduce exposure to allergens. Historically, many common recommendations for achieving this reduction are not based on substantial scientific data or evidence-based clinical trials. As we better understand the effect of both the characteristics of housing stock (the dwellings) and occupant activities (the dwellers) on the indoor living environment, more effective means are being identified for reducing exposure to triggers of allergic diseases, referred to in this practice parameter as *contaminants*. As one would expect, exposure reduction usually includes modification of the dwellers' habits but also can require source control (removal of organisms that produce the triggers), abatement (which refers to reduction of reservoirs), and elimination of facilitative factors. Containment of contaminants by blocking pathways from sources to occupants would, in the context of this practice parameter, simply mean that a pet is kept out of a bedroom.

From a health perspective, exposure control is a model for implementing the 3 types of prevention. Primary prevention consists of avoidance measures directed at preventing the clinical manifestations of atopy by suppressing or delaying the onset of sensitization. Primary prevention begins before birth, continues during pregnancy, and extends into the first few months of life.

Secondary prevention is directed at reducing or removing triggers, especially of allergens, in the environment that lead to the development of allergic disease in a sensitized individual. One major drawback in many secondary prevention studies to date has been the focus on a single allergen (eg, dust mites) or intervention (eg, air filtration for cat or dog allergy). In fact, most allergic individuals, once they become sensitized, have polysensitivity. Other important allergen exposures that could play a role in the early induction and subsequent trigger of allergies and asthma include pollen, mold, mouse, and cockroach. Environmental Control is therefore more likely to be beneficial if approached from a comprehensive and multi-faceted fashion that targets multiple triggers where possible and individual triggers when appropriate.

Tertiary prevention, or what is commonly called treatment, consists of avoiding triggers for individuals who are sensitized and who already have developed an allergic disease. A barrier to proof of effectiveness from avoidance measures is the complexity of the gene-host-environment interactions. Our expectations have been tainted by the fact that short-term drug studies of only a few months can show statistical effectiveness. However, despite major advances in the drugs available for the treatment of allergy and asthma, none have been shown to permanently arrest disease progression. Improved understanding of what contaminants to avoid and how to avoid them would be expected to have this benefit. Observational epidemiology has already led to the recognition of a wide range of triggers, from dust mite to diesel exhaust particulates. Further applied epidemiologic studies are helpful in understanding targeted avoidance and prevention of disease progression.

The challenge for the practicing allergist is to identify through interaction with his/her patient potential environmental exposures that may be causing symptoms, building stock issues that may be the underlying cause of the exposures, and then helping the patient correct the underlying problems.

The influences and causes of allergy, asthma, and immunologic health effects on occupants by the built environment is complex and requires the correlation of building health data with human health data. The physician needs to be aware of the possibility of environmental effects and which medical conditions are relevant for developing an assessment hypothesis and prescribing a home assessment. The home assessment should be comprehensive to provide an accurate representation of the home to the physician. Once a home assessment is completed, the physician can correlate the building assessment data with the human health data to form his/her diagnosis. To do so, the physician requires assessment data that are representative, credible, and reported in a consistent format. The treating physician becomes a primary participant with a team of professionals involved with the care and management of buildings, occupants, and the medical interactions.

Environmental Assessment and Exposure Control: A Practice Parameter (Furry Animals) describes methods for both source control and abatement. We define exposure control as the use of methods to reduce occupant exposure to a contaminant in their environment when the source of the exposure is likely to persist, such as with a pet cat or dog. Source control involves the complete removal of the furry animal. Finally, abatement involves removing contaminated materials that serve as reservoirs from the home.

The choice of methods for reducing exposure depends on the contaminant to be avoided. Families are generally reluctant to get rid of a favored pet so the common practice of summarily instructing them to get rid of the pet is unlikely to be followed. For that reason, control methods are used so that the pet can remain. Obviously, bait traps and biocides are not appropriate for eliminating dog and cat exposure because such animals are invited into the home and do not enter surreptitiously. In this situation, identification of a family to adopt the pet may be an appropriate form of source control. On the other hand, source control generally is appropriate for other furry animals, such as rodents (with the possible exception of a pet rat). It is better to eliminate such sources completely than to perform avoidance measures designed to allow the home owner to live in harmony with them.

Because of the complexity of the topic, Environmental Assessment and Exposure Control: A Practice Parameter has been divided into a number of separate "stand-alone" practice parameters. The first series will deal with specific environmental exposures, such as furry animals, rodents, dust mites, cockroaches, fungi, and nonallergic irritants. Each of these topics is believed to be extensive and important enough to merit its own practice parameter. After the individual exposures, a series of practice parameters will be developed that deal with specific avoidance and remediation measures along with building science, how to design and build a healthy home, and how to do a home assessment. Finally, the contents of an effective environmental report will be discussed along with recommendations about how to interpret the results. Although these sections are all important, they are not completely independent, so there will be some overlap. To keep the parameters relatively short,

whenever possible, details of a section will be referred to a different section if it has already been discussed.

Executive summary: furry animals

The domestic house cat (*Felis domesticus*) is a small, furry, domesticated, carnivorous mammal that is valued for its companionship and for its ability to hunt rodents. Cats have been associated with humans for at least 9500 years and are currently the most popular pet in the world.[1] Because of their close association with humans, cats are now found almost everywhere on Earth. Allergies to furry animals other than cats and dogs have been extensively reviewed elsewhere and are not the topic of this practice parameter.[2,3]

According to the American Pet Products Manufacturers Association survey from 2010, it is estimated that there are 93.6 million cat owners in the United States.[4] The same survey shows that 33% of US households (or 38.2 million) own at least 1 cat, and 56% of those own more than 1 cat.

The dog (*Canis lupus familiaris*) is a domesticated form of the gray wolf. Members of the Canidae family of the order Carnivora, dogs are the most widely kept companion animals in human history. The 2010 American Pet Products Manufacturers Association survey estimates that there are 77.5 million dog owners in the United States.[4] The same survey shows that nearly 40% of American households own at least 1 dog, of which 67% own just 1 dog, 25% own 2 dogs, and nearly 9% own 3 or more dogs.

Both cats and dogs have a number of identified allergens with a variety of biologic and immunologic properties. These allergens are present throughout the indoor environment of homes, with animals living in them and in other buildings, such as schools and workplaces, regardless of whether the animals are present. For that reason, some degree of exposure to cat and dog allergens is inevitable. It is recommended that cats and dogs be removed from the environment or at least kept out of the bedroom to reduce exposure to these allergens. In addition, the length of hair does not correspond with the allergenicity of a cat or dog, and there is no evidence of the existence of a completely nonallergenic furry animal. Because carpeting and bedding serve as significant reservoirs, frequent vacuuming or ideally carpet removal should be considered.

The health effects of furry animal exposure include development of allergen specific IgE (defined as sensitization) in susceptible individuals, often leading to manifestations of diseases, such as asthma and rhinitis, if the exposure persists. Once a sensitized individual develops an allergic disease, continued exposure to the allergens is likely to exacerbate symptoms and lead to poorer outcomes. It is with this background in mind that identification of exposure sources and their removal can be used as a form of treatment.

There are a few considerations with this model that may seem counterintuitive. In particular, there is evidence that early exposure (ie, within the first 3 months of life) to animal allergens may have a protective effect in some individuals in the form of prevention of sensitization and possibly even prevention of disease development in individuals who already are sensitized, although the evidence is not strong enough to recommend getting a furry animal for the purpose of prevention. Thresholds of exposure have even been proposed for this effect, although such thresholds appear to be somewhat arbitrary on close inspection of the underlying evidence for them.

Exposure control involves a variety of interventions that are designed to reduce exposure to specific allergens. A variety of control measures are discussed in this parameter, although the evidence of their effectiveness at improving health tends to be somewhat circumstantial. It is often possible to demonstrate that a particular intervention, such as use of high-efficiency particulate air (HEPA) filters, vacuuming, chemical treatment of carpeting, and use of mattress encasements, are able to reduce environmental exposure. It is another matter to demonstrate that such reduction improves health. The difficulty is that animal allergens are present throughout the environment, making it virtually impossible to avoid all exposure. How much avoidance is necessary to improve outcomes is unknown, although this is an area of active study.

Clearly, one should not get a pet purely with the intent to modify allergic sensitization. On the other hand, considerations such as a desire for companionship often override the medically prudent advice to avoid exposure to dogs and cats for a sensitized person. The bottom line is that patients love their pets. They are part of the family, providing companionship and love to millions of pet owners. Because pet ownership is likely to persist, allergists need to be able to advise their patients how to live with the pet while remaining as healthy as possible. This practice parameter will help in that endeavor.

The clinical evaluation of a potentially pet-sensitive patient includes obtaining a history of pet exposure along with skin or in vitro tests for pet specific IgE to assess sensitization status. Treatment includes removal of the pet when feasible along with interventions targeted at reducing exposure to reservoirs and blocking pathways from reservoirs to home occupants. Because individual interventions generally are not effective, allergen exposure reduction requires a combination of interventions, including regular washing of the pet, use of denaturants for reservoirs, HEPA air filtration, and regular vacuuming. The goal is to improve the health of furry animal-allergic individuals using environmental interventions.

Major cat allergens

The currently identified significant cat allergens are Fel d 1 (secretoglobulin), Fel d 2 (albumin), Fel d 3 (cystatin), Fel d 4 (lipocalin), Fel d 5 (IgA), Fel d 6 (IgM), Fel d 7 (lipocalin-Von Ebner's gland protein), and Fel d 8 (latherin). All cats produce detectable amounts of clinically significant allergens.

Fel d 1 (Secretoglobulin)

Fel d 1 is considered to be the major cat allergen because up to 90% of cat-allergic individuals are sensitized to it. Although some of the other allergens are considered minor allergens, this does not mean that they are clinically irrelevant. Fel d 1 appears to be a unique marker for the presence of cats.[5]

All natural breeds of cat produce Fel d 1, with males producing a larger amount than females. Cat hair extracted for 3 minutes with tap water or pet shampoo for 3 minutes can remove a mean of 200 μg of Fel d 1 per gram of hair. The quantity of Fel d 1 on samples of cat hair can range from 1 μg/g to more than 1770 μg/g, with the highest concentrations being found on hair from the neck. Estimates of the total Fel d 1 content on a typical cat range from 3 to 142 mg, with a mean of 67 mg.[6]

Fel d 1 is primarily found in cat skin and hair follicles and is produced in sebaceous, anal, and salivary glands. Cat fur has demonstrated that Fel d 1 concentrations are higher at the root than at the tip. It also is found in epithelial squamous cells, within the epidermis and hair follicles. It is stored mainly on the surface of the epidermis and fur.[7]

Fel d 2 (Cat Albumin)

Fel d 2 is cat albumin. All cats have this allergen. In a study of 117 cat-allergic patients, 22% had specific IgE to cat albumin. Total IgE binding to cat extract was inhibited by 15% using cat albumin, which indicates that, although cat albumin is an allergen, there are other important allergens in cat extract as well.[8] Cross-reactivity between cat and pork albumin may be responsible for reports of allergic reactions after ingestion of pork in cat-allergic individuals.

Fel d 3 (Cystatin)

Fel d 3 is a cysteine protease inhibitor. The protein was sequenced using a cat skin complementary DNA library. The resulting allergen showed 79% and 75% homology with bovine and human cystatin A, respectively. Cat cystatin has a conserved cysteine protease inhibitor structure and 2 of 3 lipocalin motifs. Between 60% and 90% of serum samples from cat-allergic individuals have IgE to Fel d 3.[9]

Fel d 4 (Lipocalin)

Fel d 4 is found primarily in cat saliva. It is an important cause of allergic sensitization in part because of extensive allergen cross-reactivity with horse (Equ c 1), mouse (MUP1), rat (Rat n 1), and dog (Can f 2).[10] Cross-reactivity of Fel d 4 with dog allergen suggests a role in cosensitization between cat- and dog-allergic patients. In one study, 68 of 109 patients with animal allergy had specific IgE to both cat and dog allergens.[11] Fel d 4 and 7 and Can f 2 and 6 are lipocalins that also cross-react with each other.[5]

Fel d 5 (IgA) and Fel d 6 (IgM)

The main source of cat IgA is saliva. In a study of 81 cat-sensitized patients, 38% had specific IgE to cat IgA and a similar amount to cat IgM. In addition, deglycosylated IgA had little IgE-binding capacity.[12] This IgE-binding epitope appears to be the carbohydrate galactose-α-1,3-galactose or α-gal.[13]

Fel d 7 (Another Cat Lipocalin)

Fel d 7 has substantial similarity to Fel d 4.

Exposure to cat allergen

1. **Removal of cats is recommended to decrease overall exposure; however, complete removal of all cats is necessary to minimize cat allergen exposure in a home. (C)**
2. **Cat characteristics, such as length of hair, sex, reproductive status, and time spent indoors, are not associated with levels of Fel d 1 in the environment. Therefore, interventions related to these factors cannot be recommended. (C)**
3. **Data about the effect of neutering a dog or cat are inconsistent, so no specific recommendations can be made at this time about performing such a procedure to reduce allergen exposure. (D)**

Dog and cat allergens are widespread, having been found in homes and public places that do not have pets. Clinically, cat allergen is the most ubiquitous of the pet allergens, frequently appearing in dust samples where a cat does not live,[14] such as schools and childcare centers.[15,16] Airborne levels of Fel d 1 can be detected in virtually all houses with cats, although low concentrations also can be found in approximately 30% of houses without a cat.[17]

Cat allergen–containing particles produced by cats range in size from 1 to more than 20 μm. In a survey of British homes, up to 50% of airborne Fel d 1 was found to be associated with particles greater than 10 μm in diameter, whereas 25% was associated with respirable particles smaller than 5 μm. Approximately 60% of airborne Fel d 1 settles out within 2 days of disturbance, leaving smaller particles that can remain airborne for up to 14 days or longer.[17,18]

Cat allergen levels increase with increasing numbers of cats in the home. The most important factor contributing to the amount of cat allergen in a house is the presence of a cat. In a cohort study in the Detroit, Michigan area, cat allergen concentrations in house dust were found to increase with increasing numbers of cats in the home. Other characteristics of cats, such as length of cat hair, cat sex, reproductive status, and time spent indoors, were not associated with levels of Fel d 1.[19] The presence of a cat can increase airborne Fel d 1 within 30 minutes. Factors that lead to increased airborne Fel d 1 concentrations include low ventilation rate and the presence of upholstered furnishings. In addition, carpeting is a substantially greater reservoir for Fel d 1 than a polished floor.[20]

There are conflicting data about allergy production in dogs and cats that have been neutered. One study documented an increased production of Fel d 1 in cats and Can f 1 in dogs from neutered animals,[18] whereas another study documented reduced amounts of Fel d 1 production in neutered cats that could be increased by treatment with testosterone.[19] Given this uncertainty, the decision to neuter a cat or dog should be made based on considerations other than a desire to alter allergen production.

Hypoallergenic cats

4. **Because 1 or more cat allergens are present in all cats, patients should not be advised that it is safe to obtain a nonallergenic cat. (C)**

Although there are reports of cats that have been genetically engineered to not produce Fel d 1, such cats, if they exist, would still be potentially allergenic because they are likely to produce other cat allergens. At the very least, all cats have cat albumin, IgA, and IgM, each of which is a significant allergen to some individuals. Despite claims that there are hypoallergenic cats, there have not been any studies to conclusively confirm these claims. In addition, whether a cat is hypoallergenic depends on which allergens a particular patient is sensitized to and which allergens the alleged hypoallergenic cat produces. No studies have shown conclusively that cats can be hypoallergenic.

Reservoirs for pet allergens in homes with pets

5. **Measurement of cat allergens in settled dust should not be used as a surrogate for airborne exposure. (C)**

The relationship between airborne and settled dust concentrations of cat allergen is not well defined. Carpets are the major reservoir for pet allergens in homes with pets, whereas the allergens are more uniformly distributed in homes without pets.[21] Most homes with pets and many homes without pets have dog and cat allergens on smooth floors and on finished furniture. Other reservoirs include upholstered furniture and bedding.[17] Floor cover type and last time floor was vacuumed are also important determinants of exposure.[14] Cat allergen can be detected on the surfaces of walls.[22] The concentrations of cat and dog allergens in both air and dust tend to vary widely within the same house and between different homes. In addition, allergen concentrations tend to be higher in the fall, although one study found cat allergens to also peak in the spring.[23] Little correlation was found between airborne and dust concentrations of cat allergen in one study using a 24-hour air sampling regimen.[24] In another study of settled dust vs airborne mouse allergen Mus m 1 (mentioned as a proxy marker for allergen exposure) in 150 homes in which air samples were collected during a 3- to 7-day duration, a moderate correlation was found between airborne and, in this study, settled dust Mus m 1. The different conclusions of these studies illustrate the differences that sampling methods can introduce into the measurements of airborne allergens.[25] Although mouse and cat allergens might behave differently, these are the best markers that have been studied for differences between airborne and settled dust allergens. Therefore, the relationship between airborne and settled dust concentrations of cat allergen is not well defined.

Dust from living rooms contains significantly higher concentrations of both Fel d 1 and Can f 1 than dust from bathrooms, kitchens, and bedrooms, although the beds may contain even higher concentrations of Fel d 1.[23] Allergen concentrations tend to be higher in homes with poor ventilation and in homes with wall-to-wall carpets. Higher numbers of airborne particles are found in homes with high humidity.[26] On the other hand, dust levels of Fel d 1 are inversely related to relative humidity in houses without cats.[27]

6. To reduce transport of cat allergen, people should consider changing their clothes when traveling from a high cat allergen environment to a low cat allergen environment. (C)

One reason that cat allergen is so ubiquitous is that it is transported from low cat allergen environments with high cat allergen concentrations. In one study, cat allergen was present in 38 of 40 homes that did not have a cat.[28] Another study found dog and cat allergen in dust samples from public places, including schools, hotels, cinemas, buses, and trains.[29] Multiple studies have shown that pet owner's clothing is an important source of allergen dispersal.[30,31] In particular, clothing that is less frequently washed tends to carry more cat allergen. Clothing worn by non–cat owners in a workplace tended to accumulate cat allergen throughout the day if cat owners are around.[31]

Cat allergen also appears to be spread through clothing from homes with cats to classrooms where the allergen is dispersed in air and contaminates the clothes of children who don't have cats. Consequently, allergen levels in homes without cats correlate with exposure to cat allergen at school.[30] Classrooms with carpeting tend to have higher concentrations of cat allergen than those with bare floors.[15]

It is uncertain whether cat allergy is more common than dog allergy. In a study of 1238 children, symptoms after exposure to cats and positive skin test results from cat hair extract were significantly more frequent than symptoms after exposure to dogs or reactions to dog hair extract. This greater frequency of cat sensitivity was not caused by more exposure to cats in homes. It was suggested that it may be due to increased intimacy of exposure to cats rather than to the potency of cat allergen.[32] Alternatively, these studies relied on skin test extracts, which create a bias, because dog allergen extracts are more difficult to manufacturer and may lack potency. Another study using specific IgE measurements indicate that sensitization to dog and cat allergens are approximately equal.[33]

Major dog allergens

The major dog allergens are Can f 1 (lipocalin), Can f 2 (lipocalin), Can f 3 (albumin), Can f 4 (odorant binding/prostatic kallikrein lipocalin), Can f 5 (trypsinlike protease), and Can f 6 (lipocalin). Can f 2 has extensive cross-reactivity with cat allergen Fel d 4.

Can f 1 (Lipocalin)

Can f 1 is largely secreted from canine sebaceous glands. It also is found in dog hair, dander, and saliva. Approximately 52% of dog-allergic people produce Can f 1 specific IgE, which is mostly directed to an 18-kD lipocalin component. Recombinant Can f 1 that binds to IgE from dog-allergic humans has been produced.[34] Airborne levels and particle size distribution of Can f 1 are similar to that of cat allergen. The small particles of cat and dog allergen can scatter easily in the air and adhere to clothing for further dispersal.

Can f 2 (Lipocalin)

Can f 2 is nearly identical with the aeroallergens Equ c 1 and Mus m 1 from mouse, horse Equ c 1, cow Bos d 2, and rat Rat n 1. IgE cross-reactivity was demonstrated between Can f 2 and the cat allergen Fel d 4, although they share less than 22% sequence identity. This is likely to contribute to the frequently observed cosensitization to cats and dogs in some individuals.[10] Various milk proteins, such as β-lactoglobulin (Bos d 5), and lipocalins from cockroach (Bla g 4) may also be cross-reactive.

Can f 3 (Albumin)

Can f 3 is dog albumin. Albumin seems to be a common cross-sensitizing allergenic component. It is obviously found in all dogs, which therefore makes it impossible for there to be a completely nonallergenic dog. In one study of 117 patients sensitized to cat, 22% had IgE to cat albumin and 41% of those also were sensitized to dog and horse albumin.[8]

Can f 4 (Odorant Binding)

Can f 4 is a lipid-carrying, odorant-binding protein that was purified from dog dander extract. Recombinant Can f 4 has been produced in *Escherichia coli*. Recombinant Can f 4 is similar to purified natural Can f 4 and in one study bound to IgE in 13 of 37 serum samples (35%) from dog-allergic patients. Can f 4 reactive sera has IgE that binds to a 23-kD protein that is present in cow dander extract. The molecule is related to a family of odorant-binding proteins. The dog and cow proteins shared 37% sequence identity, and their cross-reactivity was demonstrated by IgE inhibition experiments.[35]

Can f 5 (Arginine Esterase/Prostatic Kallikrein)

Can f 5 is an arginine esterase similar to prostatic kallikrein. As such, cross-reactivity to Can f 5 may be a culprit in the development of IgE-mediated vaginal reactions to semen.[36] Can f 5 is a common allergen from a number of different sources that has defined effects on allergen penetration and immunologic responses. Its presence may be why dog extracts are not particularly stable.

Can f 6 (Lipocalin)

Can f 6 is another lipocalin from dogs, but data distinguishing it from other lipocalins are not yet available.

Exposure to dog allergen

7. Because 1 or more dog allergens are present in all dogs, patients should not be advised that it is safe to obtain a nonallergenic dog. (C)

Although there has been a great deal of public interest in the possibility of hypoallergenic dogs, it makes sense that at least 1 or more dog allergens are present in all dogs. A recent study examined dust samples from homes with dog breeds reported to be hypoallergenic and those of homes with regular dogs. The concentrations of dog allergen in homes with hypoallergenic dogs did not differ from other homes, leading the authors to conclude that currently available so-called hypoallergenic dogs were no less allergenic than regular breeds.[37]

8. Dogs should be excluded from rooms in which reduced exposure is desired. (C)

In houses with dogs, approximately 45% of Can f 1 is associated with large particles greater than 9 μm, whereas particles less than 5 μm in diameter comprise approximately 20% of the total airborne allergen load. Airborne Can f 1 is detectable in undisturbed conditions in all homes with dogs and in almost one-third of the homes without dogs. The smaller particles tend to remain airborne for long periods and, when inhaled, can penetrate into the lower airways and trigger asthma symptoms.[38]

Homes with dogs tend to have higher levels of dog allergen than those without dogs; however, the number of dogs in the home is not related to dog allergen levels. Homes with outdoor dogs have higher dog allergen levels than homes without any dogs but lower levels than homes with indoor dogs. Rooms in which a dog is allowed have higher Can f 1 levels than rooms from which the dog is excluded. The length of hair does not determine the amount of dog allergy shedding.[39]

Can f 1 can be found in almost all homes with a dog and in approximately 15% of homes without a dog. Most homes with pets and many homes without pets have Can f 1 and Fel d 1 allergens on walls, smooth floors, and finished furniture. Carpets also appear to be the major reservoir for dog allergen in homes with dogs.[21] In an environment with little dust mite or cockroach, such as Los Alamos, New Mexico, concentrations of dog and cat allergens are elevated in

almost all houses that have pets, although they also are high in many houses without pets. People who have increased bronchial hyperresponsiveness also tend to have IgE to dog and cat, suggesting that sensitization to cat and dog allergen is strongly associated with asthma in such dry environments.[40]

Upholstered chairs in hospitals are an important reservoir of cat and dog allergen. Inhalation of airborne allergen in patients being evaluated in the hospital can exacerbate asthma in those highly allergic to cats or dogs. Three-times-weekly vacuuming can significantly reduce dog and cat allergen levels in upholstered hospital chairs.[41]

Special daycare centers with children who don't have dogs or cats have lower concentrations of both dog and cat allergen than daycare centers with children who live with a dog or cat.[42]

Health effects

The most desirable strategy for treatment of furry animal allergy is to prevent it from occurring in the first place. This type of strategy can be divided into primary, secondary, and tertiary prevention.[43,44] The US Preventative Services Task Forces' *Guide to Clinical Preventive Services*[45] defines primary prevention measures as "those provided to individuals to prevent the onset of a targeted condition." This would include prevention of IgE sensitization to an allergen. Secondary prevention measures are those that "identify and treat asymptomatic persons who have already developed risk factors or preclinical disease but in whom the condition is not clinically apparent."[45] Avoidance of allergy exposure in already sensitized individuals to prevent development of respiratory illness, such as asthma, is a type of secondary prevention. Tertiary prevention involves the care of persons with established disease, which usually is considered to be treatment rather than prevention. Allergen avoidance in sensitized individuals who have allergic disease is a type of tertiary prevention.

Primary prevention to avoid ige sensitization

9. **Although exposure to elevated cat allergen Fel d 1 concentrations before 3 months of age may reduce the likelihood of developing cat sensitization, the risk reduction is not sufficient to justify a decision to get a cat to avoid IgE sensitization. (C)**
10. **Although exposure to elevated dog allergen Can f 1 concentrations before 3 months of age may reduce the likelihood of developing dog sensitization, the risk reduction is not sufficient to justify a decision to get a dog to avoid IgE sensitization. (C)**

There is controversy about whether early dog and cat exposure can reduce the risk of development of sensitization to a furry animal. The difficulty that studies designed to evaluate this question face is that it is not practical to randomly assign individuals either to live with or without exposure to dog and/or cat allergen prospectively for long periods. For that reason, studies of early exposure tend to have either cross-sectional or cohort designs. Because the evidence for primary prevention is largely observational, it should be interpreted with caution. Furthermore, in these observational studies, results may be biased because of the potential that less atopic families may be more likely to have furry pets than more atopic families. This means that any perceived protective effect of early pet exposure may actually occur as a result of a nonatopic genetic background.

A protective effect seems to occur when exposure to the animal takes place during infancy, leading to reduced prevalence of a variety of allergic outcomes, including allergic sensitization later in childhood.[46-49] In addition, living with both a cat and dog appears to reduce the risk of developing sensitization to either one more than living with one or the other.[46]

The concept of a specific threshold amount of exposure required for this effect has been discussed; however, a wide range of values have been reported. Determination of a specific threshold (such as 8 μg/g of dust) is problematic because new standards for the assays used to measure exposure have been developed over time such that older studies may state erroneous values for exposure. In addition, use of a specific threshold is probably misleading in part because it requires a log difference in exposure to be clinically important.[50]

In one large, prospective birth cohort study of healthy, full-term infants, the prevalence of atopy, defined as at least 1 positive skin test result to a panel of aeroallergens, at 6 to 7 years of age was 33.6% with no dog or cat exposure in the first year of life, 34.3% with exposure to 1 dog or cat, and 15.4% with exposure to 2 or more dogs or cats. This study was able to demonstrate a dose effect and suggests that exposure to 2 or more dogs or cats in the first year of life may reduce subsequent risk of allergic sensitization to multiple allergens during childhood.[48] This study did not find, however, that the protective effect was specific to either cat or dog sensitization. These results seem to have been confirmed by the German Multicentre Allergy Study in which 66 infants exposed to the highest levels of cat allergen (Fel d 1) had decreased cat specific IgE levels and high IgG levels with corresponding low risk phenotype for wheeze.

On the other hand, another study of 332 children found that the prevalence and degree of sensitization to cat in atopic children was not associated with increasing domestic concentrations of these allergens.[51] In another study, exposure to cat allergen measured during the child's first 3 months of life and sensitization to cat and asthma outcomes at 6 years of age showed a dose-dependent relationship up to a plateau of 1 μg of Fel d 1 per gram of dust. Analysis of a high-risk subgroup demonstrated an even greater association with asthma diagnosis at 6 years. This association is corroborated by previously published data.[52,53] To further complicate things, there might be a nonlinear relationship of exposure with sensitivity and subsequent development of asthma.[50,54]

To help clarify this situation, a recent systematic review of studies from 2000 to 2009 looking at dog and cat exposure and sensitization concluded that the relationship between exposures and clinical responses are contradictory. A review of 17 cat exposure and 13 dog exposure birth cohort studies found that dog exposure during infancy protected children from developing sensitization to dog.[55]

The protective effect of early exposure to dog and cat may be modulated by the genetic background of the patient. In particular, although loss-of-function variants in the gene encoding filaggrin have been shown to increase the likelihood of developing eczema in young children, early exposure to cats has been shown to reduce this likelihood. In 2 longitudinal studies, that protective effect was reduced in patients who had the filaggrin mutation vs those with the wild-type gene.[56]

A follow-up study looking at the association between lifetime dog and cat exposure and allergic sensitization at 18 years of age found that males with an indoor dog during the first year of life had half the risk of being sensitized to dogs. In addition, teens with an indoor cat in the first year of life had a decreased risk of being sensitized to cats. This provides increased evidence that the first year of life is a critical period when indoor exposure to dogs or cats influences sensitization to these animals.[57]

Secondary prevention to avoid disease in IgE sensitized individuals

11. **Cat exposure should be minimized in cat sensitized individuals to reduce the likelihood of developing asthma. (C)**
12. **Dog exposure should be minimized in dog sensitized individuals to reduce the likelihood of developing asthma. (C)**

Once sensitization to a furry animal has occurred, exposure is associated with significantly poorer lung function in early life, particularly among young children with a parental history of asthma, suggesting that secondary prevention might be effective at stopping progression of disease.[58] Data from the Asthma Multicentre Infant Cohort Study[59-61] strongly suggested that cat allergen exposure is associated with the development of sensitivity and subsequent asthma. In some reports, exposure to pet allergens resulted in a dose-dependent increase in production of specific IgE and also in the development of allergic diseases, such as rhinitis and asthma. This finding suggests that the presence of specific IgE could be used as a marker for exposure to pet allergens in addition to mere sensitization.[62] Other studies demonstrated a similar prevalence of sensitivity in children who live with a cat and those who do not.[63]

A systematic review of studies from 2000 to 2009 found that cat or dog exposure in early life had no protective effect on the development of asthma or wheezing symptoms if sensitization already was present. In addition, an inverse association was found between cat exposure and development of asthma and wheezing. Clearly, the decision of whether to keep a cat or a dog in the family should be based on arguments other than the concern of developing asthma and allergy.[55]

In another systematic review, reduction of exposure to multiple allergens, including animal allergens, was found to decrease the likelihood of asthma development in sensitized children. In addition, for young children who were at risk of developing asthma, multiple allergen reduction and multifaceted environmental control were found to reduce asthma prevalence by half, given a number needed to treat of 17.[64] However, avoidance of only one allergen, such as cat alone, did not yield such promising results. In addition, studies evaluating the effect of eliminating exposure to a single allergen source, such as cat, often simultaneously affect exposure to other allergens, making it hard to interpret the results. It is likely, therefore, that most studies that document reduced exposure to one measured allergen are likely overlooking similar changes in other, often unmeasured, allergens.

Similar to cat, once a child is sensitized to dog, subsequent exposure to dog allergen has been hypothesized to increase the likelihood of developing asthma and its severity. In a prospective study of children from birth to 3 years, specific airway resistance and skin prick test results were measured along with data on cat and dog ownership. The investigators also measured allergen concentrations in dust from their homes. They found that sensitized children exposed to high levels of allergen had significantly poorer lung function than children who either were not sensitized or were sensitized but not exposed. This finding suggests that in already sensitized but nonasthmatic individuals, animal allergens are problematic and can cause airway hyperresponsiveness and increase asthma severity in those who do develop asthma.[58] A recent meta-analysis[65] noted a slightly decreased, statistically significant relative risk of asthma in cat but not dog owners, not taking into account allergic sensitization. This finding suggests that although sensitization increases the risk of developing asthma, mere exposure regardless of sensitization is also associated with increased risk. Other birth cohort studies have found no such association, so this conclusion remains uncertain for now until further data can be collected.

As with primary prevention to avoid sensitization, exposure to a cat or to Fel d 1 concentrations of at least 8 μg/g of dust before 3 months of age has been reported to be associated with a reduced risk of wheezing between the ages of 1 and 5 years, although the caveat about using a specific threshold for exposure applies here as it did for sensitization. On the other hand, a maternal history of asthma was found to be associated with a slightly increased risk of wheezing by 3 years of age regardless of early exposure.[66] Although the evidence for this seems to be better for cats, there are fewer data for dog exposure and allergic outcomes, including IgE sensitization. In addition, it is possible that other allergens will behave differently, making an overall generalization difficult to prove. Families with a history of animal allergy should not be counseled to get furry animals solely to prevent sensitization.

A number of hypotheses have been proposed to explain development of tolerance to furry animals. The presence of a cat in the home is associated with what has been described as a "modified T_H2 response" in young children, characterized by predominant development of Fel d 1 specific IgG1 and IgG4 antibodies but not IgE immune responses. The presence of cat specific IgG4 is not associated with the development of asthma or cat specific IgE.[67] A detailed analysis of T-cell responses to Fel d 1 suggests that the structure of the molecule induces high levels of interleukin 10 production, which differs from responses to dust mite and cockroach allergens.[68]

Tertiary prevention to treat furry animal allergy

13. Exposure to cat allergens should be minimized to reduce the likelihood of an asthma exacerbation in cat sensitized schoolchildren and adults who already have asthma. (A)

14. Exposure to dog allergens should be minimized to reduce the likelihood of an asthma exacerbation in dog sensitized schoolchildren and adults who already have asthma. (A)

The evidence for the development of disease once sensitization has occurred consists of both observational studies and prospective cohort and interventional studies. It seems clear that exposure to cat and dog allergens is associated with the development of asthma in schoolchildren once sensitization has taken place.[40] In areas of the country with low dust mite allergen exposure, dog and cat tend to be the major allergens to which asthmatic children become sensitized. Under those circumstances, a combination of sensitization and increased exposure levels for either dog or cat strongly correlates with development of asthma.

In a study of 112 adolescents and adults sensitized to cat, patients with a cat at home had lower skin sensitivity than patients without a cat, although cat specific IgE did not differ between the 2 groups. In addition, specific IgG4 was associated with the presence of cat at home.[69] IgE antibody to both mite and cat were strongly associated with wheezing; however, among sensitized children, cat ownership was associated with a lower prevalence of IgE antibody to cat.[70] In another study of 546 inner-city adolescents enrolled in the Asthma Control Evaluation study, investigators found that elevated specific IgE levels were associated with increased exposure and sensitization to cat and that this was associated with increased asthma severity.[63] There also is evidence that long-term exposure to 8 μg/g or more of Fel d 1 in cat-sensitized adult women is associated with asthma manifestations, such as steroid use and wheezing in the absence of a cold.[71]

In a prospective study of patients with asthma who were sensitized to furry animals, some elected to find their pet a new home and others chose to keep it. After 1 year, there was a substantial and significant improvement in airway hyperresponsiveness and reduction in inhaled corticosteroid use in the pet removal group compared with the pet keeping group.[72] In a study of 374 schoolchildren, higher exhaled nitric oxide levels were found in cat-sensitized children with a cat at home compared with children without pets, suggesting that pet exposure is associated with increased asthmatic inflammation.[73] This type of response may explain anecdotal observations that children living with a cat who go to college tend to develop worse asthma when they return.

Asthma symptoms in children with cat allergy may be affected by indirect cat exposure at school. A study of 410 cat-allergic children who attended classes with more than 18% of cat owners

reported significantly increased asthma symptoms and medication use as opposed to those in classes with fewer cat owners. The children in classes with many cat owners had a 9-fold increased risk of exacerbated asthma after school start compared with children in classes with few cat owners.[74]

Clinical evaluation

15. Patients should be asked whether there is a dog or cat in the house because an affirmative answer is associated with greater exposure to dog or cat allergens. (C)

Clinical evaluation of potentially cat- or dog-allergic individuals should begin with a pertinent medical history that focuses on whether there is an association between development of symptoms and exposure to dog or cat allergens. If the association is clear, such as a patient reporting symptoms immediately on entering an environment with a furry animal, the likelihood of clinically important allergy is high. In many cases, such as when a patient lives with a pet, symptoms are persistent and the association between exposure and symptoms is less clear.

Because environmental allergen measurements are not widely available, it usually is necessary to rely on patient reports of the presence or absence of cats. Fortunately, such reports appear to correlate with the concentrations of cat allergen and can be used as a surrogate for actual exposure measurements.[75] On the other hand, given the ubiquitous nature of many cat allergens, a negative report of cat exposure in the house might not accurately reflect a true lack of exposure even if a cat does not live in the house. Absence of a pet in the home, therefore, does not exclude clinically relevant exposure. Common sites of potentially clinically relevant exposure to ask about include the workplace, schools, daycare centers, friends' and relatives' homes, and other indoor environments.

16. Patients with allergic disorders should be evaluated for sensitization to cat and dog allergens by skin prick testing or in vitro testing for cat and dog specific IgE. (C)

Diagnostic allergy tests, such as skin tests and in vitro tests, can help to determine whether symptoms are allergic in origin. The decision to perform diagnostic testing must rely on clinical judgment to select patients who would benefit most from determining their allergic status while minimizing unnecessary testing. Patients with a low probability of allergic sensitization should not be tested for specific IgE because of the increased likelihood of a false-positive test result.[76] The use of diagnostic tests to identify the presence of sensitization in clinical practice has been described in detail in Allergy Diagnostic Testing: An Updated Practice Parameter.[77]

Currently available extracts for skin testing include cat epithelia and hair and dog epithelia and hair. In vitro tests are available for measurement of specific IgE to cat and dog dander, and component testing is available for cat Fel d 1 and Fel d 2 and dog Can f 1, Can f 2, and Can f 3. Dog allergens in epithelia and dander extracts are relatively stable over a range of temperatures; however, their activities may be compromised when mixed with fungal or insect extracts due to protease activity. In particular, dog Can f 3 exhibited degradation into discrete fragments though these retained IgE binding activity.[78] Cat Fel d 1 was more stable when incubated with protease-containing extracts, retaining most of its activity.[79] Both dog and cat extracts are more stable when stored in 50% glycerin than in aqueous form.

An unpublished report of 2 cat extracts indicated that extracts derived from cat hair had 40 to 80 μg/mL of Fel d 1 and 30 to 100 μg/mL of Fel d 2 (cat albumin). Extracts derived from cat pelt, on the other hand, had the same concentration of Fel d 1 but 400 to 2,000 μg/mL of Fel d 2 (Robert Esch, PhD, Greer Laboratories, Lenoir, North Carolina, personal communication). This finding suggests that patients who are sensitized to cat albumin are likely to respond better if they are diagnosed and treated with cat pelt as opposed to those who are exclusively Fel d 1 sensitized. In addition, the total biologic activity of cat extracts correlates well with in vitro measurements of Fel d 1, making it a suitable marker for cat extract potency.[80]

Table 1
Performance Characteristics of Skin and In Vitro Tests for Cat Sensitivity

Characteristic	Skin test	In vitro test
Sensitivity	0.88	0.46
Specificity	0.83	1.00
PPV	0.92	1.00
NPV	0.74	0.27
LR+	5.15	ND
LR−	0.14	0.54

Abbreviations: ND, not determined; LR+, likelihood ratio for a positive test results; LR−, likelihood ratio for a negative test result; NPV, negative predictive value; PPV, positive predictive value.[84]

Up to 90% of cat-allergic patients have specific IgE to Fel d 1, and 15% to 40% of patients are sensitized to Fel d 2. Because Fel d 2 is cat albumin, specific IgE directed at this component tends to cross-react with other mammalian albumins, including dog Can f 3.[81] In a study of 776 polysensitized atopic children who underwent diagnostic allergy testing, 87% were sensitized to dog and 74% were sensitized to cat, indicating how common it is for patients to be sensitized both to cats and dogs.[82]

In terms of sensitization to dog components, 50% to 90% of patients are sensitized to Can f 1, 20% to 33% to Can f 2, and 70% are sensitized to Can f 5.[81] Can f 4 is another species-specific allergen component for dog.[35] This variation in IgE responses might explain why some individuals can tolerate some breeds of dog but react to others. Additional research will be needed to determine the spectrum of the dog allergen components among various breeds of dog.

In one study of sensitivity to a variety of aeroallergens, including dog and cat, allergen specific IgE (Phadebas RAST, modified RAST, and Pharmacia CAP System) were compared to skin tests in 198 patients. An experienced allergist also rated the likelihood of clinical sensitivity to each inhalant. The 3 in vitro tests correlated well with each other and generally agreed with physician assessments and skin test results. Analysis of receiver operating characteristic curves showed that sensitivity of the 3 assays when compared at the 95% level of specificity did not differ.[83]

In another study, 120 patients were challenged with a well-characterized cat exposure model after evaluation by history, skin prick tests, and in vitro tests. Skin test results were positive in 81 patients, and in vitro test results were positive in 45 of 51 patients with a positive skin test result and were negative in all patients with a negative skin test result. Positive challenge results were seen in 38 of 41 patients with a positive skin test result and in 10 of 39 patients with a negative skin test result. Challenges were also positive in 27 of 27 patients with a positive in vitro test result and in 12 of 44 patients with a negative test result. The performance characteristics for skin testing and in vitro testing as determined by this study are given in Table 1.[84]

In one study of 564 young adults in a general risk cohort, allergen specific IgE was measured for dog and cat. Patients also were asked about dog- and cat-related symptoms. The investigators identified 0.12 kU/L for cat and 0.2 kU/L for dog as optimal cut points for determining sensitivity. These results were confirmed in 2 validation populations.[85]

Avoidance

17. Avoidance is the most effective way to manage cat and dog allergy. Patients should be advised to consider removing the cat or dog from the environment, if present, to improve respiratory health. (A)

18. To reduce exposure to cat allergens with the cat still living in the house, a combination of measures, such as removing

reservoirs, keeping the cat out of the bedroom, washing the cat, air cleaning with a HEPA room air cleaner, improving ventilation, and mattress and pillow covers, may be helpful. (C)

Although primary and secondary prevention strategies of cat allergy are preferable, once allergic diseases have developed it is important to avoid exposure. Complete avoidance of cat exposure is difficult because Fel d 1 is widely distributed in schools, other public buildings, and even in homes without a cat.[86] Even within the home, controlling cat exposure can be difficult. In a longitudinal study, the effect of cat removal on Fel d 1 content in the home was determined by collecting serial house dust samples from 15 homes during a 9- to 43-week period after the cat was removed. Baseline Fe1 d 1 content ranged from 7.8 to 436.7 U/g of dust. By 20 to 24 weeks, 8 of 15 homes reached Fel d 1 levels consistent with those found in control homes without cats. Fel d 1 levels decreased more rapidly after aggressive environmental control measures were undertaken in 2 of the homes. Three homes had little decrease in Fel d 1 even though the cat was gone.[53]

Many pet-allergic patients with asthma simply refuse to remove the pet to which they are sensitized from their home. For that reason, control of exposure to cat allergens with the cat still living in the environment is necessary. This process often requires aggressive measures, such as removing reservoirs, washing the cat, and air cleaning.[87] Fel d 1 is very pervasive in indoor spaces. Approximately 60% of airborne Fel d 1 settles out within 2 days of disturbance, leaving smaller particles that can remain airborne for up to 14 days or longer.[17] This duration can be reduced using HEPA filtration.[17,88] Airborne cat Fel d 1 levels and particle size distributions are not significantly influenced by ventilation.[89]

Dry dusting with a sticky dust cloth is an effective cleaning method for removing Fel d 1 from hard smooth surfaces, but fabric and carpet can represent significant reservoirs.[19,21] When compared with high-efficiency vacuum cleaning alone, the addition of HEPA filters significantly improved asthma symptoms after 12 months in cat-allergic individuals who were living with a cat but showed no change in reservoir or airborne Fel d 1 levels.[90] A combination of a HEPA room air cleaner, mattress and pillow covers, and cat exclusion from the bedroom was shown to reduce airborne cat Fel d 1 levels, although this was not associated with clinical improvement in one controlled study.[91] Washing cats by immersion for 3 minutes at weekly intervals for a 1-month period produced a mean decrease in airborne allergen of 79%. However, after repeated washing, the airborne levels before the next wash were not consistently decreased.[6]

Chemical treatments

19. **Chemical treatments, such as tannic acid, can be applied to carpet to give short-term reduction of cat allergen, but this is not sustained and there is no evidence that it improves respiratory health. (C)**
20. **Use of hypochlorite bleach to denature indoor allergens can reduce allergen exposure, improve quality of life, and reduce the likelihood of developing atopy, but it can also lead to increased respiratory symptoms in individuals using it. (C)**

Chemical treatments are used to denature, oxidize, or otherwise modify allergens so that they no longer cause symptoms when sensitized individuals are exposed to them. Because the source of the allergen is not removed, chemical treatments represent temporary measures at best because the allergen will reaccumulate after the treatment is applied. Chemicals in the home need to be used with caution because some agents are volatile and can trigger symptoms in sensitized individuals. They also can stain or modify dyes on furniture, carpets, drapes, and other items commonly found in homes, so all chemicals should be first applied to an inconspicuous location to determine whether this will be a problem before widespread use.

Sodium hypochlorite bleach (0.05% solution) is capable of inactivating allergens, including cat, dog,[92] mouse,[93] and dust mite, and it can reduce exposure to bacteria, fungi, and protein allergens.[94] Chlorine bleach (1.8% solution) also has been shown to denature Fel d 1 under controlled circumstances.[95] It can lead to improved quality of life for asthmatic persons in the home, and there are indications that its domestic use may reduce the risk of developing allergies in children. In a study of 3626 participants of the European Community Respiratory Health Survey II, specific IgE was measured for 4 aeroallergens. The use of bleach for a mean of 8.9 years was associated with less atopic sensitization to cat and grass. Respiratory symptoms were more common among those using bleach 4 or more days per week, suggesting that the bleach may have contributed to those symptoms.[96]

In another European study, house cleaning with chlorine bleach appeared to protect children from the risks of asthma and sensitization to indoor allergens while increasing the risk of recurrent bronchitis apparently through an interaction with parental smoking.[97]

Tannic acid applied to carpet in one study led to short-term reductions of cat allergen, but this was not sustained. As a result, repeated applications were necessary to provide a significant reduction in exposure. When allergen levels were followed for several weeks after 2 carpet treatments with tannic acid, the study did not show a significant reduction in cat allergen levels.[98] This intervention alone has therefore not been shown to reduce health effects of cat exposure. Another study of 52 families with allergic children and no pets found that tannic acid initially reduced Fel d 1 by 30% and Can f 1 by 10%, but only for 2 week.[99]

Tannic acid solution can denature cat allergen in vitro, but its short-term effects on cat allergen in carpet are less than initially thought and are insignificant at the high allergen levels often found in the homes of patients allergic to and living with cats.[100] The concern is that certain carpet treatments can interfere with immunoassay measurement of allergens, which raises questions about the validity of studies that used this outcome measure. In particular, the presence of tannic acid or other protein denaturants used in the study can interfere with commercial assays used to measure Fel d 1, so it is not clear whether this study really supports the recommendation.

In one study, 9 cleaning solutions and 5 chemical detergents were tested for their ability to denature cat and dust mite allergens. Soft soap, guanidine hydrochloride, and sodium lauryl sulphate were most likely to denature the allergens, although even they were unable to destroy all of the allergenic activities even when used up to 10 times the recommended concentrations.[101]

In one study, several substances commonly found in dust (carpet fresheners, powdered pesticides, and table salt) were shown to affect immunoassays of purified standard allergens, including Der p 1, Der f 1, and Fel d 1, and a monoclonal/polyclonal assay for Bla g 1. The carpet fresheners tended to decrease Der p 1, increase Der f 1, and produce little change in Fel d 1. For each of the 4 allergens, the largest effects of dust additives occurred when secondary antibody binding was altered.[102]

Washing cats and dogs

21. **Washing cats or dogs at least weekly can reduce airborne cat Fel d 1 or dog Can f 1; however, the clinical benefit is yet to be proven and the effect of washing is not sustained. (B)**

Regular washing of a furry animal to reduce allergen exposure is a strategy that has been evaluated in a number of studies. The idea of washing is to remove pet allergens from fur before it can spread into the environment. Because pets will continue to produce aller-

gens, washing is clearly a temporary measure that needs to be repeated regularly to be effective. The main questions about washing are how frequently the pet needs to be washed, what solution to wash with, and how much of a reduction in environmental can be obtained as a result of washing.

Washing cats can reduce airborne Fel d 1 3 hours later. Cats that were washed weekly for 5 weeks produced a mean decrease of 44% in airborne Fel d 1, whereas washing by immersion for 3 minutes at weekly intervals for 1 month reduced airborne allergen by 79%, although this decrease was not maintained after 1 week.[6] Another study of cat washing found that the amount of Fel d 1 collected in the wash water decreased progressively during 4 weeks. Most of the reduction in Fel d 1 in the air before cat washing occurred with the first wash, whereas little or no change was observed in the last 3 washes. Airborne Fel d 1 measured after washing was low throughout the study, although a greater decrease was seen in particles smaller than 2.5 μm than in larger ones.[20]

Although washing may briefly reduce the amount of cat allergen on the cat's body, it does not change the overall rate of shedding. In a study of 6 female cats that underwent weekly washings, high shedders and low shedders of Fel d 1 stayed the way they were before they were washed.[103] A study in which 10 cats were bathed monthly for 9 months showed a consistent decrease of Fel d 1 in filtered bath water, although 2 cats continued to shed more than 1,000 μg of Fel d 1 per cat.[104]

In a study that examined the effect of regular washing, 25 dogs, which had not been washed for at least the previous 3 weeks, were washed with a handheld shower and proprietary shampoo. Can f 1 was measured from hair clippings, and air sampling was performed in 5 of the homes in which the dogs lived. Washing reduced Can f 1 in clippings by 84%, from 73 to 12 μg/g, and by a similar amount from dander samples. This reduction persisted for the first 2 days after washing and then increased on days 3 to 7. Airborne Can f 1 levels decreased for 3 days and then it too increased on days 4 to 7. The investigators concluded that Can f 1 allergen exposure can be reduced by washing but that a dog needs to be washed at least twice a week to maintain the reduction in recoverable Can f 1.[105]

To determine what solution to use for washing, some cats were washed with soap and warm water for 60 seconds; another group was washed by immersion in warm tap water for 3 minutes while the pelt was massaged; and a third group was washed as in group 2 but rinsed for an additional 3 minutes. The authors observed an increased amount of allergen in the bathwater with each additional intervention; however, it was not clear that the 3 methods resulted in different amounts of allergen shed into the environment. Their conclusion was that cats should be washed for 3 minutes with pet shampoo and rinsed after that.[6]

Few of these studies specify the sex and neutered status of the cats, an important factor when considering Fel d 1 concentrations. Dust and air collection techniques varied widely among studies, as did the Fel d 1 results. Only one of the publications[106] reported the clinical response of the cat-sensitive patients, and descriptions of dust collection techniques and control groups, if present, are often sparse. Currently, we can only conclude that washing an indoor cat at least weekly, and possibly less often during a longer period, can reduce airborne and catborne Fel d 1, that the amount of Fel d 1 on a given cat and the amount recovered after cat washing are highly variable, and that the clinical benefit of cat washing has yet to be proven.

Mattress encasings

22. Some woven microfiber bed encasings, generally those with a mean pore size of 6 μm or less, block cat allergen from penetrating the fabric though the respiratory health benefit from their use is unclear. (C)

23. Nonwoven microfiber encasings collect allergen on their surface over time, including cat and mite allergens. Because they cannot be washed, they are unsuitable for allergen avoidance. (C)

There is no reason or evidence to suggest that allergen-impermeable encasings placed on a pillow and mattress will decrease cat allergen exposure of an individual living with a cat that is allowed on the bed. However, in cases where a cat has been removed from the home, or at least from the bedroom, the mattress can act as a reservoir of cat allergen that could persist for years. It would therefore seem desirable to decrease exposure to that allergen reservoir.[107,108]

Commercially available woven barrier fabrics vary considerably in the tightness of their weave. In general, woven microfiber fabrics with a mean pore size less than 10 μm block Der p 1, but only those with a mean pore size less than 6 μm block Fel d 1. As a result, many commercially available woven microfiber encasings block Der p 1 but not Fel d 1.[109]

In contrast to woven barrier fabrics, nonwoven fabrics are manufactured by fusing a mass of overlain short filaments to each other with heat, glue, and pressure. Although nonwoven microfiber fabrics block Fel d 1 passage, recent information indicates that the interstices between the randomly crisscrossing fibers of nonwoven encasings is deep enough to accumulate allergens, including Der p 1, Der f 1, and Fel d 1, over time, so that the patient is eventually sleeping on a layer of allergen. This is not the case with the smooth surface of woven encasings. Ironically, in contrast to woven encasings, the nonwoven encasings—the ones that accumulate allergen—are not washable. These findings suggest that nonwoven microfibers do not succeed in reducing allergen exposure and should not be used for allergen avoidance.[110]

Vacuum cleaners

24. Long-term regular use of high-efficiency or central vacuum cleaners is associated with reduced exposure to Fel d 1 and Can f 1 in homes with cats or dogs living in them, although the health effects are uncertain. (B)

A potential method for reducing environmental exposure to cat allergens such as Fel d 1 is with vacuuming. The benefits from vacuuming have proven to be difficult to demonstrate in part because Fel d 1 is known to be sticky and difficult to remove from carpeting and fabrics. One laboratory study tested the ability of a commercially available vacuum cleaner to remove Fel d 1 from rectangles of cotton fabric. After spiking test rectangles with cat allergen by having cats lay on them for a week, the investigators attempted to clean them by vacuuming them for 15 minutes each. After extracting the cotton material, an assay for Fel d 1 failed to demonstrate a reduction in the amount of cat allergen recovered.[111] This finding confirmed the stickiness of Fel d 1 and suggests that vacuuming alone is not sufficient to remove it from fabrics.

A variety of avoidance combinations have been evaluated for their ability to reduce exposure to cat (Fel d 1) and dog (Can f 1) in house dust. In one study, 52 families with allergic children and no pets were divided into 5 different groups. Central, microfilter, and HEPA filter vacuum cleaners did not reduce Fel d 1 or Can f 1.[99] In another study of 60 homes, British investigators tested high-efficiency and standard vacuum cleaners for their ability to remove Fel d 1 and Can f 1. After 12 months of using the high-efficiency cleaners, Fel d 1 and Can f 1 concentrations were reduced. Patients in the high-efficiency group showed improvements in peak flow and bronchodilator use.[112]

If frequent vacuuming is capable of removing Fel d 1, a concern with such vacuuming is that it may stir up settled allergens from carpeting and furniture, leading to increased exposure by the allergic occupants. One solution would be with a vacuum that sends collected dust to a different location, such as a central vacuum. For

that reason, central vacuum cleaners have been studied as a way possibly to avoid this problem. In one study, 12 houses that were equipped with a central vacuum cleaning system were used to compare airborne Fel d 1 concentrations between the central system and a regular cleaner. Surprisingly, the investigators did not find a difference in airborne Fel d 1 between conventional and central vacuum cleaners either during or after use. This means that it is not useful to advise patients to get a central vacuum system to reduce exposure to Fel d 1.[113] On the other hand, another study of the short-term effect of vacuum cleaning with 2 different types of cleaners was performed in 10 homes with cats living in them. A vacuum that exhausted to the outside was associated with smaller amounts of airborne cat allergen than a traditional canister model.[114]

Although high-efficiency vacuums may fail to reduce exposure during acute vacuuming, long-term use of such vacuums can lead to decreased overall exposure. In another study, 60 homes were studied to compare the effects of high-efficiency and standard vacuum cleaners on Der p 1 (house dust mite), Fel d 1 (cat), and Can f 1 (dog) allergens. After 12 months of regular use, the investigators found a significant reduction in Fel d 1 in dust samples from the living room, bedroom, mattress, and living room sofa with the high-efficiency cleaners compared with the standard units. Can f 1 also was reduced in the mattress but not at other sites. In addition, cat-sensitive asthmatic patients living in these homes experienced improvements in lung function associated with the reduced exposure to Fel d 1.[112]

Vacuum cleaners may increase the level of airborne allergens by leakage through the cleaners or by disturbance of floor dust by the exhaust air produced. To prevent leakage of allergens from vacuum cleaners, high-efficiency microfiltration bags have been developed that are claimed to capture 99.9% of particles 0.3 μm or larger. Several such cleaners were tested in a laboratory room with dust containing high levels of Fel d 1. The investigators found that vacuum cleaners with double or triple layer bags leaked less Fel d 1 than single-layer bags. The investigators also noted that there was substantial variability in capture efficiency among different manufacturers of the same type of bag.[115]

Vacuum cleaners with double-thickness bags and HEPA filters theoretically should lead to reduced airborne allergen levels and therefore are commonly recommended to allergic patients. On one study, HEPA vacuum cleaners were compared with non-HEPA cleaners in 5 homes that had cats residing in them. During the vacuuming, a significant increase was found in airborne cat Fel d 1 allergen with both. The investigators found no difference between the 2 types of vacuum cleaners.[116]

In another study, 5 different vacuums were evaluated under laboratory conditions and in an apartment with cats. The vacuums tested included 1 with a HEPA filter, 1 with a water impingement and HEPA filter, 1 with a cleaner with a foam fabric filter, and 2 standard models. The investigators found that the HEPA and water impinge models did not lead to an increase in airborne Fel d 1, whereas the others did. In addition, all of the vacuums were associated with short-term increases in airborne Fel d 1, primarily carried by particles larger than 5 μm in diameter.[117]

Finally, another study compared 9 different models that were loaded with dust containing 50 mg of Fel d 1 and run for 15 minutes in a laboratory room. The cleaners using a double-thickness dust bag either did not leak or had minor leakage. On the other hand, those with single-thickness paper bags leaked more. Water-filter cleaners each emitted significant cat allergen on particles larger than 2.5 μm in diameter, although this could be controlled by taping electrostatic filter paper over the air outlet.[118]

Air filtration

25. HEPA air cleaners run continuously over time can reduce exposure to dog and cat allergen concentrations, but the clinical benefits are unknown. (B)

There have been conflicting reports regarding the potential benefit of air cleaners with respect to reducing exposure to dog allergens and subsequent development of asthma. In a randomized trial of 36 asthmatic children sensitized and exposed to cat and/or dog, HEPA cleaners placed in the living room and bedroom failed to provide a significant change in bronchial hyperresponsiveness or allergen exposure.[119]

In a crossover study of 20 asthmatic children sensitized and exposed to dog and/or cat allergens (Fel d 1 and Can f 1), air cleaners placed in the living room and bedroom for 3 months decreased airway hyperresponsiveness, although no differences were found in symptom scores or medication use. Interestingly, although substantial amounts of airborne cat Fel d 1 and dog Can f 1 were captured by the cleaners, allergen levels in floor dust were not changed.[120]

In a systematic review of 10 randomized controlled trials evaluating the effects of air filtration systems on patients with asthma, 2 studies reported a decrease in airway responsiveness and lower symptom scores, although medication use was not affected.[93]

A Cochrane review of the clinical efficacy of pet allergen control in homes with pet-sensitized people with asthma identified only 2 studies that met the inclusion criteria for analysis. Both trials were too small to provide evidence for or against the use of air filtration to reduce allergen levels in the management of pet-allergic asthma.[121]

In a randomized controlled trial of 35 cat-allergic patients who were living with one or more cats, bedrooms were equipped with an active or placebo air cleaner for 3 months. The active-filter group had a significantly decreased airborne exposure to Fel d 1 compared with the placebo group; however, no differences were detected in settled-dust allergen levels. In addition, asthma symptoms were not improved with this intervention alone even though the HEPA room air cleaner, mattress and pillow covers, and cat exclusion reduced airborne Fel d 1 cat allergen levels.[91]

Another study of adult asthma patients sensitized and exposed to cats and/or dogs evaluated the effect of placing air cleaners in the living room and bedroom for 12 months and using HEPA filter vacuum cleaners compared with using these vacuum cleaners alone. Clinical improvement was observed in 67% of the active group compared with 20% of the control group.[90]

Duct cleaning

26. Duct cleaning has not been proven to reduce exposure to furry animal allergens. Ducts should not be cleaned specifically to reduce exposure to dog and cat allergens. (D)

Duct cleaning is performed under standards set forth by the National Air Duct Cleaners Association with their ACR (Assessment, Cleaning, and Restoration) 2006 standard[122] and the Air Conditioning Contractors Association (ACCA) with their American National Standards Institute–ACCA 6 cleaning and restoration standard.[123] Homeowners who are considering having the ducts of their homes cleaned should select a duct cleaning company with training from a national professional organization with objective training criteria. Because no studies have examined the effect of duct cleaning on exposure to furry animal allergens, ducts should not be cleaned specifically to reduce such exposure. Duct cleaning for furry animal allergen avoidance is an unproven procedure.

Use of dry heat

27. Dog and cat allergens are relatively stable to dry heat so dry heat should not be used specifically to reduce exposure. (C)

Allergens tend to be more stable when they are dry, particularly when they are heated. In a study that evaluated the effect of dry heat on dust mite, dog, and cat, the cat and dog allergens showed greater resistance to heat than did mite allergens. Therefore, although dry heating methods may be useful for killing mites and removal of mite allergens, the greater stability of Fel d 1 and Can f 1 suggests that it may not be appropriate for removal of pet allergens.[124]

Combination measures

28. Sufficient control of exposure to cat allergens to improve health requires a combination of measures, such as removing reservoirs, keeping the cat out of the bedroom, washing the cat, air cleaning with a HEPA room air cleaner, improving ventilation, and mattress and pillow covers. (C)

Although primary prevention of sensitization to cats is preferable, once sensitization has occurred, exposure to cat allergen is associated with significantly poorer lung function in early life.[58] Control of exposure to cat allergens with the cat still living in the environment requires aggressive measures, such as removing reservoirs, washing the cat, and air cleaning.[87]

One combination study demonstrated that 11 months of biweekly cat washing, use of mattress and pillow encasings, weekly washing of encasings at 60°C, excluding the cat from the bedroom, and application of tannic acid led to reductions of Fel d 1 concentration in house dust by 91.4% in an active intervention group but not in a control group.[125]

In another study, 9 cat-sensitive, asthmatic patients were evaluated before and after a combined intervention. Five cats were washed weekly for 4 months, along with the use of a HEPA air cleaner and vacuum cleaner, mattress covers, and reduced carpet. At the end of the study, clinical and medication scores improved, and nonspecific bronchial hyperreactivity and airborne Fel d 1 concentrations were significantly reduced at the end of 4 months in the treatment group compared with baseline values. Although this combined intervention appears to have had some clinical benefit, the study was not designed to determine which interventions, alone or in combination, were responsible for the benefit.[106]

Another controlled study evaluated a combination of HEPA room air cleaner, mattress and pillow covers, and cat exclusion from the bedroom. This intervention also reduced airborne Fel d 1 cat allergen levels, although this was not associated with clinical improvement.[91] Dry dusting with a sticky dust cloth is an effective cleaning method for removing cat allergen from hard smooth surfaces.[21]

Although a combination of environmental interventions seems to be effective in reducing the allergen load in homes, they also appear to lead to reduced symptoms. Such intervention combinations, involving both mechanical methods for allergen reduction and educational efforts of asthmatic children and their parents, appear to be necessary to reduce exposure to asthma triggers and improved health outcomes for asthmatic children.[126]

29. Adherence with avoidance measures can be enhanced with education and monitoring. (C)

Adherence with measures designed to reduce exposure is necessary for the interventions to work. In one study of high-risk children, families were randomized to receive environmental education or usual care. The education group was more likely to use mattress covers, keep pets outside, and avoid smoke exposure; however, little adherence improvement was found for regular cleaning, avoidance of carpeting, improved ventilation, and pet removal. This led to reduced exposure to mite, cat, and dog allergens on the mattresses and in the living room.[127]

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