

ROLE OF ENVIRONMENTAL ALLERGENS IN RHINITIS

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Allergic rhinitis affects 15% to 20% of the general population with environmental allergens commonly implicated.⁵⁵ In 1880, Charles Blackley was the first person to implicate pollens in hay fever by performing skin tests and measuring pollen counts.¹¹ Since his pioneer work, many other allergens have been discovered and further insight has been gained into the role of allergens in rhinitis. Allergens are proteins or glycoproteins that are capable of eliciting IgE-mediated reactions. Although there are many potential allergenic proteins in the environment, few are clinically important, and even fewer have been isolated and characterized. A given allergen is considered major when there is IgE binding by radioimmuno-electrophoresis in 50% or more individuals sensitive to that allergen and minor if the IgE binding is present in less than 50% of allergic individuals.³⁹ Most aeroallergens have molecular weights between 10 and 40 kD and are carried on particles (e.g., pollen grain and house dust) between 2 and 60 μm in size. The particle size largely determines the location of deposition of the allergen once it reaches the human respiratory tract. Studies have shown that particles of greater than 10 μm will generally only be deposited in the upper airways; those of 5 μm in size, will reach the lower airways 20% of the time, and those less than 2 μm in size will reach the lower airways 100% of the time.^{21, 76}

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It is convenient to divide the various allergens into those that exist in the outdoor environment, and those that exist in the indoor environment. In the outdoors, pollens of trees, grasses, weeds, and certain fungi (e.g., *Alternaria* and *Cladosporium*) represent the most common allergens that provoke rhinitis symptoms. Pollen-sensitive individuals typically experience seasonal rhinitis symptoms in predictable time intervals from one season to the next. Although fungi are more ubiquitous in nature and do not have distinct seasons like pollens, outdoor and indoor fungi thrive in a moist environment. Therefore, in temperate climates, fungi counts start to rise in spring with a peak in mid to late summer. Indoor allergens include fungi, animals, cockroaches, and dust mites. Unlike the outdoor allergens, which typically produce seasonal symptoms, indoor allergens often produce symptoms perennially; however, the symptoms are less drastic in nature, often making diagnosis more difficult.

AEROALLERGEN SAMPLING

Numerous methods of allergen identification and quantification are available, each with its own advantages and limitations. Outdoor pollen and fungal spores are quantitated commonly by light microscopy following collection with samplers. Although daily pollen and spore counts are widely published in the media, often with the perception among the public of a direct relationship between the counts and severity of allergy symptoms, the clinician must recognize limitations of such assumptions and educate patients accordingly. With regard to symptoms of allergic rhinitis and aeroallergen counts, neither threshold levels nor dose response effects of allergens have been established.⁶⁰ Published counts on a given day reflect levels of the previous day because most sampling is performed over a 24-hour period. Measured aeroallergen counts may not truly reflect actual human exposure because most aeroallergen samplers are placed on the rooftops, where counts may be different than on the ground because of different aerodynamic characteristics. Despite its limitations, aeroallergen sampling can provide an excellent means of following the general trends of allergen exposures.

Gravitational samplers (e.g., Durham sampler) were the first devices used to analyze aeroallergens. In the gravitational sampling method, a stained microscope slide is exposed for 24 hours in a standard housing. Following exposure, the contents are identified by light microscopy. It is a simple and inexpensive method. Although the volume of air sampled is not known and the collection depends on wind speed and direction, it only provides qualitative data and commonly is not used today.

In contrast, in volumetric sampling, the volume of air is known in the recovery of the sample, and provides quantitative data expressed in particles per unit volume of air. There are two types of volumetric samplers available: impactors and suction devices. Rotating impaction samplers (e.g., Rotorod Sampler [Fig. 1]) are most commonly used for

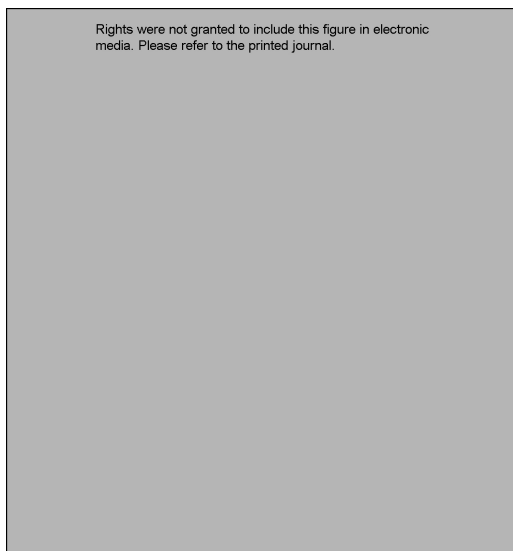


Figure 1. Rotating impaction sampler: Rotorod Sampler Model 40 (Sampling Technologies, Minnetonka, MN). (Courtesy of Medical Media Services, William S. Middleton Memorial Veterans Hospital, Madison, WI.)

pollen measurement, whereas suction samplers are more suitable for sampling smaller particles such as fungal spores. In impaction sampling, an adhesive-coated surface onto which airborne particles adhere rotates in a circular path through air at a known speed. The speed of rotation is up to several thousand revolutions per minute and is nearly independent of wind velocity. These samplers usually are run intermittently for 20 to 60 seconds every 10 minutes to reduce overloading. With this sampling method, there is predilection for collection of larger particles such as pollen grains. The Rotorod sampler has been shown to be over 90% efficient at capturing pollen particles of approximately 20 μm in diameter.

Suction samplers (e.g., Burkard, Burkard Manufacturing, Rickmansworth, Hertfordshire, England) employ a vacuum pump to draw the air sample into the device. Unlike impaction samplers, the collection efficiency in suction samplers depends on the orientation of the device with the wind direction. For example, if the wind velocity is less than that generated by the sampler, smaller particles are collected in greater concentrations than exist in the ambient air and vice versa. The Hirst spore trap is an inertial suction sampler with a clock mechanism that moves a coated slide at a set rate along an intake orifice. In the Burkard modification of the spore trap, particles are collected on an adhesive-coated drum that takes 1 week to make a full revolution around an intake orifice. These spore traps are designed to measure nonviable material. Spore traps are the most flexible devices for sampling particles over a wide range of sizes.

The Andersen sampler (Andersen Samplers, Atlanta, GA) is another suction device, but it is unique in its adaptability for enumerating viable fungal spores. Air passes through a series of sieve-like plates, each containing 400 holes. Although the air moves from plate to plate, the diameter of the holes decrease. The larger particles are retained by the upper plates and the smaller ones by successive lower plates. A Petri dish containing growth medium is placed beneath each sieve plate, and the spores that pass through the holes fall onto the agar and form colonies. This method has value for identifying fungi whose spore morphologic features do not permit microscopic identification. In general, however, nonviable volumetric collection is more accurate in reflecting the actual spore prevalence than volumetric culture methods.¹⁵

Fungal culture techniques often are necessary for fungal identification because many spores lack distinct morphologic characteristics. Most commonly, Petri dishes with appropriate nutrient agar are exposed to the air; following incubation, the plates are grossly and microscopically inspected for the number and types of colonies. It is important to use a broad spectrum growth medium (e.g., malt extract agar) to support growth of a variety of fungi.¹ Conversely, specialized media such as Czapek agar may be used to promote growth of specific fungi such as *Aspergillus* or *Penicillium*. In general, the culture plate method grossly underestimates the spore count in comparison with the nonviable methods. The combined use of an Anderson sampler and fungal culture can enhance the overall yield.

Immunoassays are other major means of identifying and quantitating allergens, especially from indoor amorphous materials of mites, cockroaches, and animal dander. Samples for immunochemical analysis are obtained either with entrapment of airborne particles by suction samplers or directly from reservoirs such as dust obtained by vacuuming. Various techniques including ELISA, radioimmunoassays (RIA), and radioallergosorbent tests (RAST) may be used to quantitate various allergens. These methods are all highly specific and sensitive. Currently, immunochemical assays to quantify the major house dust mite allergens (Der p I, Der f I) and the major cat allergen (Fel d I) are commercially available.^{18, 19} Although certain pollens also can be identified with immunoassays, it is cost-effective to use the physical count method under microscopy for the clinical assessment of exposure to these allergens.

POLLENS

Pollen allergens, which typically use pollen grains as vectors, must achieve high enough concentrations in the environment to be clinically significant. The concentration of the allergen in the environment depends on numerous factors, including the amount of allergen production, weather variables, and the aerodynamic characteristics of the allergens. Pollen production of the most important allergenic flowering plants (e.g., trees, grasses, and weeds) occurs in predictable yearly time intervals in

temperate climates of North America. Although the clinical consequences of pollen exposure are generally more severe with increased production, threshold levels above which symptoms of pollinosis occur have not been determined. Studies with grass and ragweed pollen have suggested elicitation of rhinitis symptoms in most sensitive individuals at levels of 20 grains/m³ for grass²³ and between 50 to 80 grains/m³ for ragweed.⁶² The difficulty in obtaining the exact clinical threshold levels of various allergens is, in part, because of the influences of other factors that modify the response to an allergen. These factors include the priming effect (an increase in sensitivity to allergens after repeated exposure), weather, respiratory infections, and simultaneous exposure to airborne irritants.⁵⁹

Weather conditions play a significant role in the airborne concentration of allergens. The role of sunlight in pollen release is one example of the importance of weather factors in the overall pollen concentration in the environment. Farnham and others have shown that increased concentrations of oak, birch, ragweed, and grass pollens occur within 60 to 90 minutes following sunrise.²⁷⁻²⁹ The sunrise is accompanied by increasing temperatures, which further enhances pollen release. Relative humidity, which usually falls with sunrise, also has important implications in pollen production. Lower relative humidity promotes pollination, as evident by studies of oak and ragweed pollens, which show that the anthers of these pollens remain closed if the relative humidity is greater than 45% and 80%, respectively, during pollination.³⁰ The calmer and cooler conditions of evenings generally cause descent of air and the accompanying pollen towards the ground, thereby increasing exposure. Pollen concentration commonly increases as wind speed rises to 13 to 17 mph; however, above this range, pollens usually are swept into the upper atmosphere, thus diminishing ground exposure.⁵⁹ With regard to rainfall, a brief downpour in which large droplets predominate causes little pollen capture and levels usually are unaffected. With prolonged rainfall, small droplets scour these particles, and there is a decrease in the particle levels.⁵⁹

The aerodynamic characteristics of allergens also can contribute significantly to their concentrations in the environment. Under normal wind conditions, smaller particles tend to remain airborne longer than larger particles, allowing a longer period of contact time with the respiratory mucosa. With increasing winds, the larger particles do not settle to the ground as rapidly as in normal wind conditions. Smaller particles also can be deposited more readily in the lower respiratory mucosa, whereas larger particles tend to remain in the upper airway. Most pollens are greater than 10 μ m in size, and remain in the upper airways, causing mainly rhinoconjunctivitis symptoms.

Pollination in higher plants is the transfer of the male gametophyte to the nearby female gametophyte. The pollen-producing plants belong in the Spermatophyta division, which is divided into two major classes: Gymnospermae and Angiospermae (Fig. 2). The class Gymnospermae contains the conifers, and although there are exceptions, trees in this

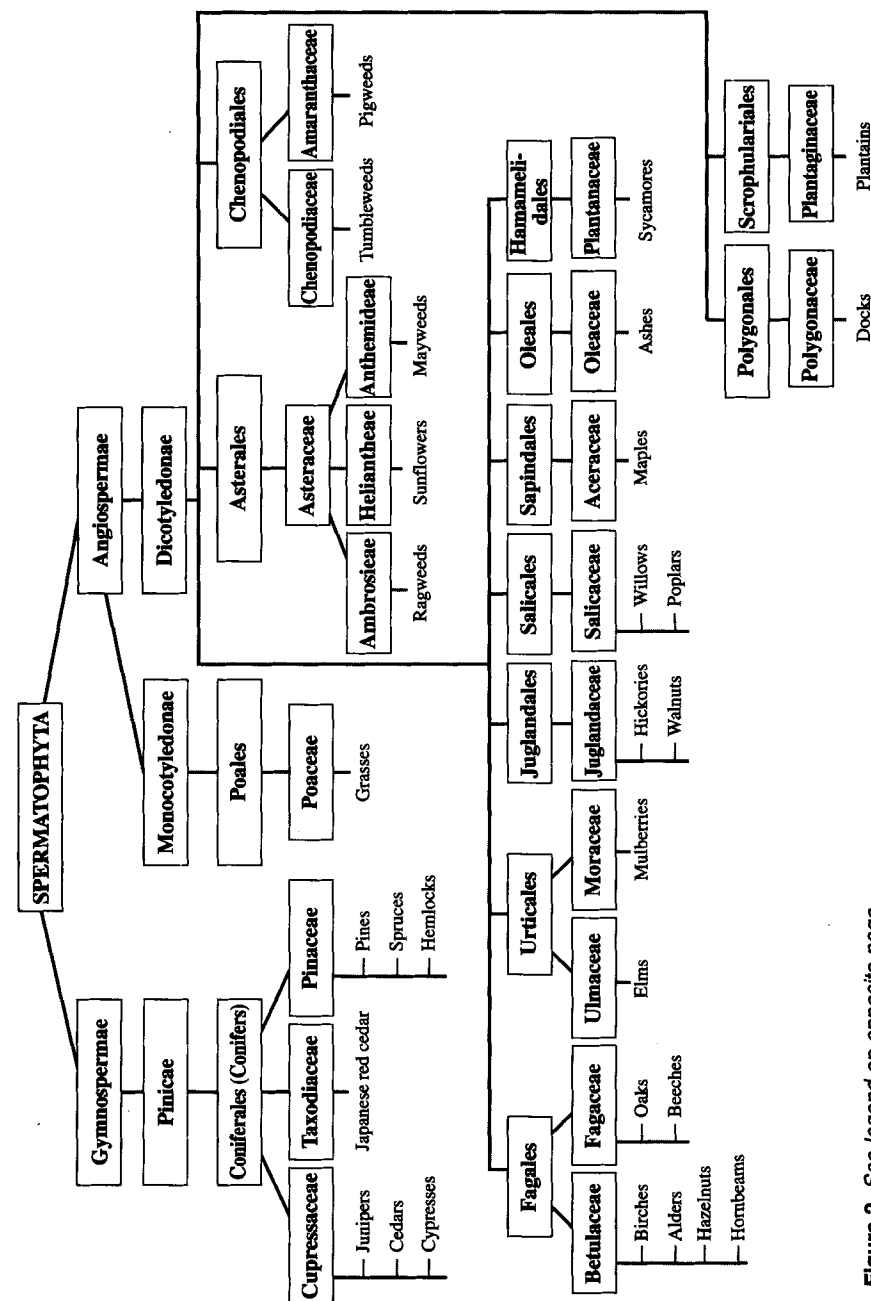


Figure 2. See legend on opposite page

class are clinically insignificant from an allergic standpoint. Conversely, the flowering plants in the class Angiospermae, which include trees, grasses, and weeds, play a significant role in allergic rhinitis. The tree in grass, and weed species belong in two major subclasses (Monocotyledonae, Dicotyledonae) of the class Angiospermae. The grasses belong in the subclass Monocotyledonae, and the trees and weeds belong in the subclass Dicotyledonae.

Flowering plants may be divided into entomophilous, which rely on animal vectors (e.g., insects) for pollination, and anemophilous, which depend on the wind for pollination. In general, only the anemophilous plants, which include trees, grasses, and weeds, are important from an allergic standpoint. Wind-borne pollen grains are usually spheroidal, 20 to 60 μm in size, and comprise an outer exine layer and an inner intine layer. The exine layer further is divided into the external sexine, containing numerous pores and substructures that provide access to the outside environment, and the internal nexine. Because pollination of trees, grasses, and weeds occurs in predictable yearly intervals, especially in temperate climates, it is important for the clinician to be aware of the local botany and the respective pollination periods (Fig. 3). It is also important to be familiar with some representative allergens of trees, grasses, and weeds (Table 1).

Trees

In many parts of North America, tree pollination in spring marks the onset of allergy season. It begins as early as mid-January in the Southwest region to early April in the Northeast, and terminates from early to late May (see Fig. 3). Although the flowering plants in the class Angiospermae are implicated most often in allergic rhinitis, two families in another class, Gymnospermae, also may cause significant pollinosis. These are the Cupressaceae family (e.g., junipers, cedars, cypresses) and the Taxodiaceae family (e.g., Japanese red cedar) of the order Coniferales (conifers). For example, in central and western Texas, mountain cedar (a juniper) is highly prevalent, and a leading cause of pollinosis and the Japanese red cedar is a common cause of hay fever in Japan.⁸¹ Another family in the class Gymnospermae, the Pinaceae family (e.g., pines,

Figure 2. Classification system of pollen-producing plants. The hierarchical system (with the characteristic endings): division (-phyta) $\rightarrow$ class (-ae) $\rightarrow$ subclass (-ae) $\rightarrow$ order (-ales) $\rightarrow$ family (-aceae) $\rightarrow$ tribe (-eae) $\rightarrow$ genus (no characteristic ending) $\rightarrow$ species. The trees of the Gymnospermae class are of lesser allergenic significance than those of the Angiospermae class. The Angiospermae class is divided into two subclasses: Monocotyledonae (containing the grasses) and Dicotyledonae (containing trees and weeds). With the exception of the Japanese red cedar, all listings below the family boxes are common genus names. Only members (and their corresponding hierarchy) of allergenic importance are listed in each class. Subfamilies and tribes of the grasses are not listed.

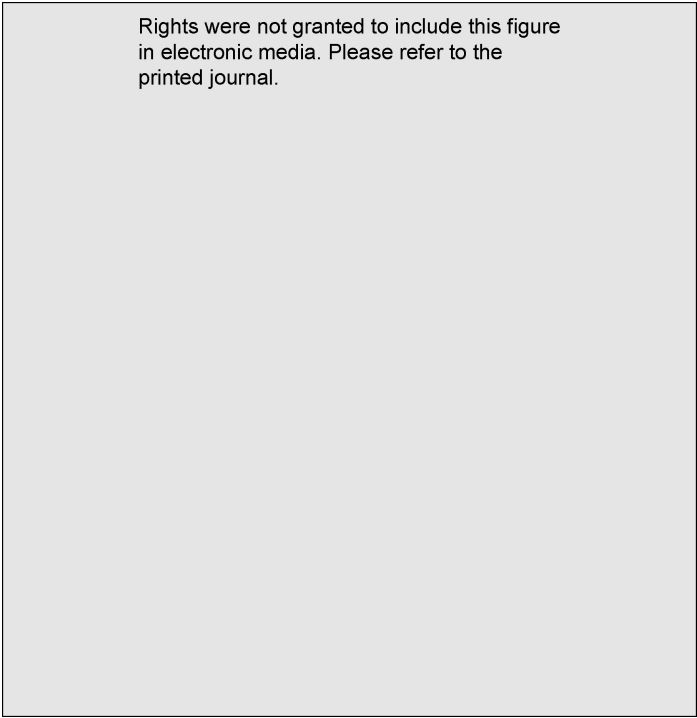


Figure 3. Pollen seasons by region in the continental United States. (From Sicherer SH, Eggleston PA: Environmental allergens. In Lieberman P, Anderson JA (eds): Allergic Disease: Diagnosis and Management. Totowa, NJ, Humana Press, 1997, p 40; with permission.)

Table 1. MAJOR POLLEN ALLERGENS

Common Name	Taxonomic Name	Allergen	Molecular Weight (kD)
Trees			
Birch	<i>Betula verrucosa</i>	Bet v I	17
Hazel	<i>Corylus avellana</i>	Cor a I	17
Alder	<i>Alnus glutinosa</i>	Aln g I	17
Hornbeam	<i>Carbinus betulus</i>	Car b I	17
Japanese cedar	<i>Cryptomeria japonica</i>	Cry j I	41–45
Grasses			
Ryegrass	<i>Lolium perene</i>	Lol p I, Lol p V	34, 25–28
Timothy grass	<i>Phleum pratense</i>	Phl p I, Phl p V	34, 29–31
Weeds			
Short ragweed	<i>Ambrosia artemisiifolia</i>	Amb a I, Amb a II	38
Giant ragweed	<i>Ambrosia trifida</i>	Amb t V	5

spruces, hemlocks), although capable of producing large quantities of pollen, seldom causes allergic rhinitis symptoms.³⁶

Most of the allergenic trees are contained in the subclass Dicotyledonae of the class Angiospermae (see Fig. 2). Some important families in various orders of this class are Betulaceae (e.g., birches, alders, hazelnuts, hornbeams); Fagaceae (e.g., oaks, beeches); Ulmaceae (e.g., elms); Moraceae (e.g., mulberries); Juglandaceae (e.g., hickories, pecans, walnuts); Salicaceae (e.g., willows, poplars); Aceraceae (e.g., maples); Oleaceae (e.g., ashes); and Plantanaceae (e.g., sycamores). The families Betulaceae and Fagaceae, belonging to the order Fagales, are the most potent tree allergens and can cause significant allergic symptoms. Birches are distributed widely in North America and produce abundant pollen that is highly allergenic. Alders are more important west of the Rockies and are predominant producers of tree pollinosis in the Pacific Northwest.⁶⁰ Oaks and beeches produce abundant pollen and the former causes a great deal of tree pollinosis in areas where they are numerous.

Approximately 20 species of elms are in the Northern Hemisphere, mainly distributed east of the Rockies. They produce large amounts of allergenic pollen and continue to be a major cause of tree pollinosis despite the almost total elimination of the American elm by Dutch elm disease. Numerous mulberries are recognized as sources of pollinosis. One in particular, the white mulberry, is especially a major source of hay fever in the state of Arizona.

Hickories are found primarily in the eastern United States. Pecan trees are important in the origin of allergic rhinitis where they grow or are cultivated. Walnut trees are implicated less often than pecan trees in rhinitis. In the Salicaceae family, willows are mainly insect-pollinated, and are not considered allergenic. Conversely, poplars are wind-pollinated, and some are of considerable allergenic importance.

There are more than 100 species of maple, many of which are important in allergy. Box elder (e.g., ash-leaf maple) is particularly important because of its wide distribution, its prevalence, and the amount of pollen it sheds. Over a dozen species of ashes are present in North America, most of which are important regionally (e.g., Oregon, Arizona). Finally, *P. acerfolia* (a sycamore) commonly is planted in urban areas, and represents the most common exposure to the sycamores. Skin reactivity to this pollen is especially prevalent in large eastern cities of the United States.

The allergenic fractions of trees have not been studied as extensively as ragweed and grasses.¹⁰ There seems to be a higher degree of specificity to skin testing with individual tree pollen extracts compared with grass pollens because pollens of individual tree species may contain unique allergens. Most tree pollen characterization has been done using birch (e.g., *Betula verrucosa*); alder (e.g., *Alnus glutinosa*); hazel (e.g., *Corylus avellana*); hornbeam (e.g., *Carbinus betulus*); and Japanese red cedar (e.g., *Cryptomeria japonica*). The tree allergens have been divided into two groups, the group I (major) allergens and group II (minor) allergens. Birch pollen allergen, Bet v I, was one of the first tree pollen allergens

to be cloned molecularly (Fig. 4).¹² The deduced amino acid sequence derived from birch allergen showed homology with similar proteins from hazel, alder, and hornbeam. Major allergens of hazel, alder, and hornbeam are Cor a I, Aln g I, and Car b I, respectively. Bet v II is a minor allergen that has been isolated from birch. Using the combination of recombinant Bet v I and Bet v II in immunoassays, virtually 100% of birch pollen-allergic individuals can be identified.⁶⁸ The birch allergen is known to cross-react with allergens of apple, pear, celery, carrot, and potato; therefore, individuals sensitive to these foods may have a positive skin test to the birch pollen and vice versa.⁶⁸ Finally, Cry j I is the major allergen isolated from the Japanese cedar.

Grasses

Grass pollen, with its worldwide distribution, is a significant source of allergen exposure and a major cause of allergic rhinitis in sensitive individuals. The pollen grains of grasses are spheroidal, uniform, and range in size from 20 to 25 μm (Fig. 5). Grasses belong to the class Angiospermae, subclass Monocotyledonae, order Poales, and family Poaceae (see Fig. 2). In this family are several subfamilies that contain a number of tribes to which the thousands of grass species belong. Some grasses are self-pollinated or insect-pollinated and noncontributory to allergies. Of the more than 1000 wind-pollinated species in North America, only a few are significant in producing allergic symptoms. Most grass species that cause allergic rhinitis are those that are cultivated

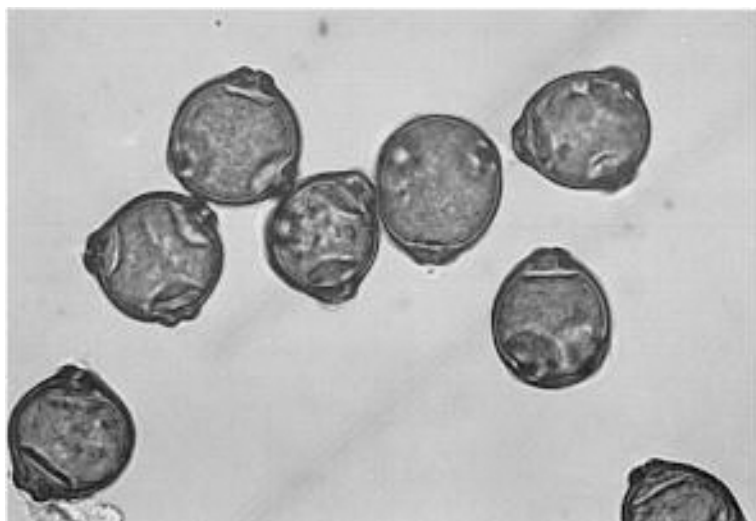


Figure 4. Birch pollens (original magnification $\times 40$). Average diameter is 20 to 30 μm . Pollen grains have three pores and a smooth exine. (Courtesy of R. Vrtis, BS, Madison, WI.)

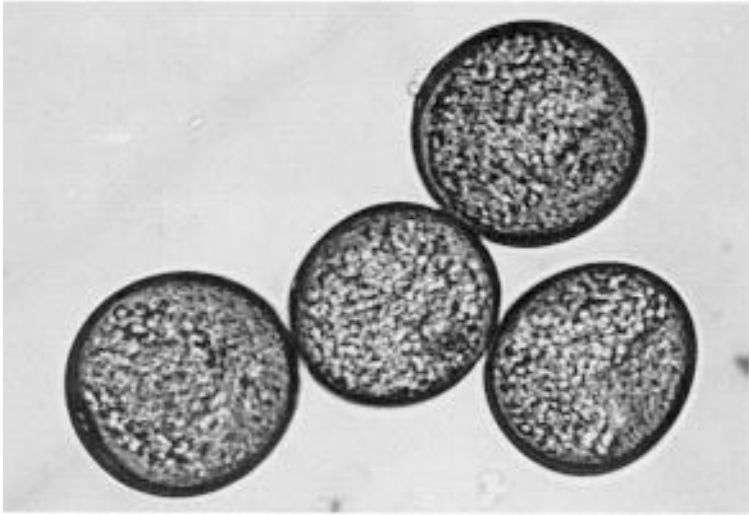


Figure 5. Pollen grains of grasses (original magnification $\times 40$). They are spheroid and range in diameter from 20 to 25 μm . Note the characteristic granular texture and the single germ pore. (Courtesy of R. Vrtis, BS, Madison, WI.)

and are most prevalent where people live. The geographic area is the main determinate of the timing of grass pollination. In frost-free areas of North America, grass pollen may be present year round whereas in temperate climates, the major grass pollen peak is seen between mid-May to mid-July (see Fig. 3.) In general, grass pollination is of short duration and occurs at certain times of the day. The peak time of grass pollination is between early and late morning.

The grasses are occasionally broken into two groups, those found primarily in temperate areas and those with a more tropical and subtropical distribution. The temperate grasses include rye grass (*Lolium perenne*), timothy grass (*Phleum pratense*), Kentucky blue grass or June grass (*Poa pratensis*), and orchard or cocksfoot grass (*Dactylis glomerata*). The more subtropical and tropical include Bermuda grass (*Cynodon dactylon*) and Johnson grass (*Sorghum halepense*). In the northeastern United States and Canada, important contributors of grass pollen allergy are blue, timothy, and orchard grasses. Bermuda grass is used extensively in the southern United States and the Pacific Coast.

Allergens from grass pollens have been divided into eight groups based on their physiochemical and immunochemical similarities. Unlike ragweed and tree pollen allergens, grass pollen allergens show extensive cross-reactivity among different species and individuals are generally sensitive to many of these species. Of the eight groups (I, II, III, IV, V, IX, X, XI), major grass allergens are found in group I and group V. Rye and timothy grass have been studied most extensively.³⁸ Major allergens of rye grass and timothy grass from group I are Lol p I and Phl p I,

respectively. The group I allergens are located in the outer wall and cytoplasm of the pollen grains and around the starch granules.⁶³ These small granules are readily released on contact with water. Group V allergens have been sequenced and cloned from various grasses, including Kentucky blue, rye, timothy, orchard, and fescue. Among the group V allergens, the most work has been done with the timothy grass allergen Phl p V. The allergens of rye grass, Lol p V, are localized to starch granules of the pollen. There is a paucity of data regarding groups II, III, and IV grass allergens, and sensitivity to these grasses are less extensive than that of groups I and V allergens. On skin testing with group I allergens, 90% to 95% of grass pollen-allergic individuals show reactivity. Groups II and III show significant but lesser degrees of reaction, varying between 60% and 70% of individuals.³³

Weeds

There are numerous loosely related families of weeds that exist in North America. In temperate climates, weed pollination characteristically begins in mid-August, peaks in early September, and terminates in October with the first frost (see Fig. 3). In southern states along the Gulf coast, however, ragweed pollinosis may be present perennially. The Asteraceae (Compositae) family, containing the tribe Ambrosieae (ragweed), is perhaps the most important allergenic weed group (see Fig. 2). *Ambrosia trifida*, giant ragweed, with broad leaves and three to five lobes, may grow to a height of 15 ft. Short ragweed grows to a height of 4 ft, with more slender leaves and two pinnae on each side of a central axis. Other significant ragweed species are southern, western, and false ragweed. Southern ragweed is confined to the central United States; western ragweed commonly grows on the Pacific coast and in the south/southwest states, and false ragweed is found mainly in the southwest and Colorado. The other two tribes in the Asteraceae family are Heliantheae (e.g., sunflowers) and Anthemideae (e.g., mayweeds). The flowers of the Heliantheae tribe cause pollinosis mainly among those who handle them. Some species in the Anthemideae tribe, however, are important allergenic weeds.

The Chenopodiaceae (goosefoot) and Amaranthaceae (amaranth) are two closely related weed families implicated in rhinitis. The most significant member of the Chenopodiaceae family is one of the tumbleweeds known as Russian thistle. The main concentration of the Russian thistle in North America is in the Great Plains and Great Basin. Lamb's quarters is another member of the Chenopodiaceae family; however, with its low pollen production it is not considered as significant as the Russian thistle. The redroot pigweed is the best known amaranth, and can be a prolific pollen producer in certain areas.

The English plantain in the Plantaginaceae family is the only member of this family that is important. This weed can produce copious

amounts of pollen and cause potent rhinitis symptoms. It sheds pollen mainly in May and June, and may be confused with grass pollination.

The docks, comprising the genus *Rumex*, are the only allergenic members of the Polygonaceae family. *Rumex acetosella* (sheep sorrel), *Rumex crispus* (curly dock), and *Rumex obtusifolius* (bitter dock) are the most important species. In the whole spectrum of pollen allergy, however, the docks are of minor significance.

Of all the weed pollens, ragweed pollen has been studied most extensively (Fig. 6). Short ragweed has been best studied molecularly. It contains the major allergens Amb a I and II and minor allergens Amb a III through Amb a VII and cystatin.³⁵ Amb a I, which constitutes 90% of the allergenic activity of ragweed pollen, consists of fragments A and B, and is primarily contained in the intine of the pollen grain.⁴¹ Approximately 90% to 95% of ragweed-sensitive individuals demonstrate skin test reactivity to Amb a I and Amb a II allergens. There is lesser degree of reactivity with the minor ragweed allergens. Amb a I and Amb a II share significant homologies with each other and also with other ragweed species. Cross-reactivity between ragweed and certain foods, such as melons,²⁵ cucumber, and squash, also have been reported. In addition to the short ragweed allergens, an allergen from giant ragweed, Amb t V, has been identified.⁵¹

FUNGI

The role of fungi in allergic rhinitis and other respiratory allergies is well established. With the exception of a few fungal species, however,

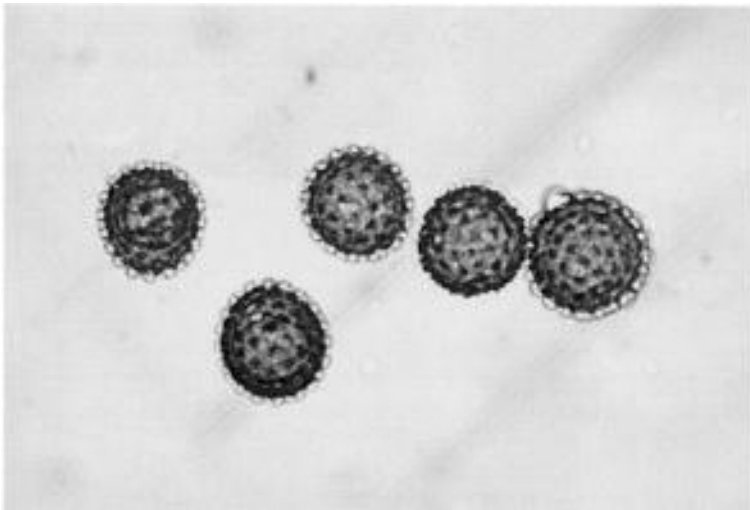


Figure 6. Short ragweed (*Ambrosia artemisiifolia*) (original magnification $\times 40$). Average diameter is 20 μm . Pollen grains have spicules on the surface. (Courtesy of R. Vrtis, BS, Madison, WI.)

a clear causal relationship between exposure and allergic symptoms has not been established. Although there are hundreds of fungal species in the environment that are capable of causing allergic symptoms, major allergens from only a few fungi have been identified. The ubiquitous nature of the fungi has made it difficult to collect, identify, and prepare reliable fungal extracts for diagnostic and therapeutic purposes. Often, assumptive associations are made between symptoms and possible exposure to fungi and positive skin tests. Estimating the extent to which a sensitive person's rhinitis symptoms can be attributed to fungal allergy is a major clinical problem because exposure to fungi, like exposure to house dust mites, is continuous, usually without definite seasonal endpoints.

Fungal spores can be quantified roughly in the air by the use of spore traps. Atmospheric fungal spore counts frequently are 1000-fold greater than pollen counts,¹⁷ and exposure to indoor spores can occur throughout the year.⁶¹ Exposure to fungi is in contrast to pollen exposure, which have distinct seasons, and to animal dander, for which a definitive history of exposure usually can be obtained. Such a history is sometimes possible for fungal exposure (e.g., raking leaves or being in a barn with moldy hay), but these exposures are not common for many individuals. Some species do show distinctive seasons; nevertheless, during any season, and especially during winter, the number and types of spores a patient inhales on a given day is purely conjectural.

Fungi are found outdoors and indoors and cause seasonal and perennial rhinitis. Most allergenic activity of fungi has been associated with the spores; however, other particles, such as mycelial fragments and allergens absorbed onto dust particles, may contain relevant activity. Although airborne fungal spores may be present year round, significant seasonal variation occurs in spore levels of indoor and outdoor fungi. Throughout the year under normal conditions, the indoor fungal spore concentration is less than half that of outdoors, unless an indoor source of contamination is present.³⁰ Although fungi are able to survive in extreme temperatures and humidity, most require adequate moisture for growth. Dry spores, however, typically produced by common outdoor fungi such as *Alternaria* (Fig. 7) and *Cladosporium* (Fig. 8), are most prevalent during hot, dry, and windy days (e.g., late summer). In the outdoors, fungi commonly grow on leaves, soil, plant litter, and on moist surfaces; therefore, in temperate climates, fungal spore levels increase with local plant growth, and decrease with the first snow cover. Of spores that thrive on humidity, spore discharge is highest in early morning, before sunrise when the relative humidity is highest. In contrast, discharge from dry spores is highest in late afternoon, when it is driest and windiest.

Fungi are identified mainly on their morphologic characteristics, and although there are numerous classes of fungi, three classes are important from an allergic standpoint: Zygomycetes (e.g., *Rhizopus*, *Mucor*), Basidiomycetes (e.g., rust, smut, *Ganoderma*), and Ascomycetes (e.g., *Cladosporium*, *Penicillium*, *Aspergillus*, *Alternaria*, *Epicoccum*). Many spe-



Figure 7. *Alternaria* spores ($\sim 45 \mu\text{m}$) (original magnification $\times 40$). Spores are snowshoe-shaped and contain horizontal and vertical septae with pores. (From Smith EG: Sampling and Identifying Allergenic Pollens and Molds, vol 2. San Antonio, Blewstone Press, 1986, p 59; with permission.)

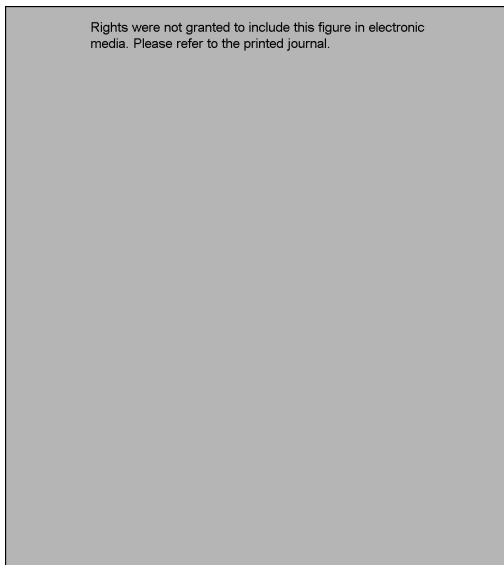


Figure 8. Spore cluster of *Cladosporium* species (original magnification $\times 60$). (From Smith EG: Sampling and Identifying Allergenic Pollens and Molds, vol 2. San Antonio, Blewstone Press, 1986, p 61; with permission.)

cies in the Ascomycetes class, which includes most allergic species, also are classified as Deuteromycetes or fungi imperfecti. These represent the asexual stage of Ascomycetes. Among the common outdoor fungi, *Cladosporium* and *Alternaria* are the most abundant. The exception is the Pacific Northwest, where the prevalence of *Alternaria* is much less than in other areas of the United States. Although *Cladosporium* counts are usually much higher than those of *Alternaria*, it is not as antigenic as *Alternaria*. Numerous skin test studies with fungal antigens also have shown that sensitivity to *Alternaria* is most prevalent.⁵⁰ These fungi are *field fungi*, and thrive on plants in the field and decaying plant parts in the soil. Outdoor activities such as lawn mowing, leaf raking, and farming can cause tremendous increases in exposure of these fungi and in rhinitis symptoms. Among the *Alternaria* species, *A. alternata* has been the subject of the most research. The major allergenic fraction, Alt a I, has been obtained by several biochemical methods²² and recently a second major allergen, Alt a II, has been identified (Table 2).¹⁶ Two *Cladosporium* species, *Cladosporium cladosporoides* and *Cladosporium herbarum*, have been studied in detail. As a result, two major (Cla h I, Cla h II), 10 intermediate, and at least 25 minor allergens have been identified.⁷

Indoor fungi consist of those that grow indoors and those that have entered from outdoors. An example of the outdoor type is *Alternaria*, which has been found in house dust samples in the indoor environment.⁹ More so than the outdoor fungi, it has been difficult to study the relationship of exposure and allergic symptoms with the indoor fungi because of the ubiquitous nature of the fungi and limitations of the sampling techniques. The spectrum of indoor airborne mold spores, such as in homes, offices, and other workplaces, differs from place to place because of the influx of spores from outdoor air through ventilation and air exchangers.⁷¹

Of the indoor fungi, which include *Penicillium*, *Aspergillus*, *Rhizopus*, and *Cladosporium*, the first two usually are considered the major indoor fungi and are found most commonly in houses, especially in basements, crawl spaces, and bedding. *Aspergillus* (Fig. 9) and *Penicillium* (Fig. 10) sometimes are called *storage fungi* because they are common causes of rot in stored grain, fruits, and vegetables. *Aspergillus* thrives on substrates with low moisture content (12%–16%) and *Penicillium* is the green "mildew" often seen on articles stored in basements. Finally, *Rhizopus*

Table 2. REPRESENTATIVE FUNGAL ALLERGENS

Taxonomic Name	Allergen	Molecular Weight (kD)
<i>Alternaria alternata</i>	Alt a I, Alt a II	28–31, 25
<i>Cladosporium herbarum</i>	Cla h I, Cla h II	13, 23
<i>Aspergillus fumigatus</i>	Asp f I, Asp f II, Asp f VI	18, 34, 27

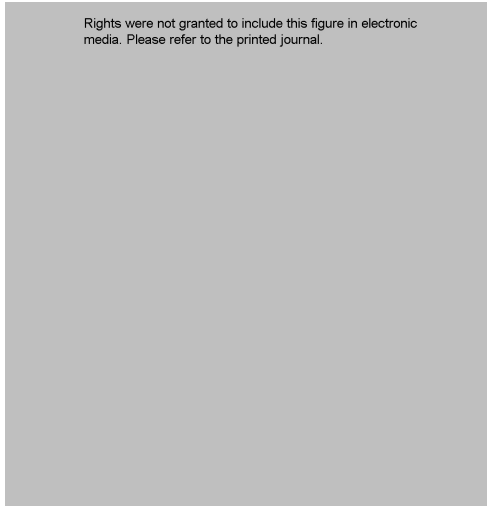


Figure 9. *Aspergillus niger* showing characteristic bulbous enlargement of terminal conidiophore (specialized hyphae) into vesicle (original magnification $\times 40$). (From Smith EG: Sampling and Identifying Allergenic Pollens and Molds, vol 2. San Antonio, Blewstone Press, 1986, p 63; with permission.)

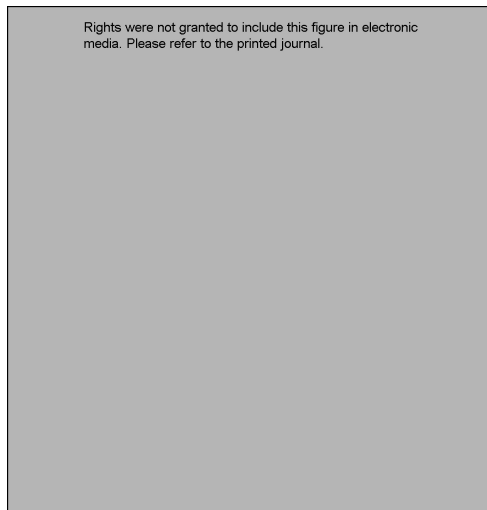


Figure 10. Spores of *Penicillium* species forming on broom-shaped heads (original magnification $\times 40$). (From Smith EG: Sampling and Identifying Allergenic Pollens and Molds, vol 2. San Antonio, Blewstone Press, 1986, p 59; with permission.)

causes black, moldy bread and proliferates on home vegetables, especially onions.

Contrary to common belief, indoor plantings are associated with only a slight increase in the number of indoor fungal spores. These are from the genera *Cladosporium*, *Penicillium*, *Alternaria*, and *Epicoccum*. Greenhouses do show an increased number of spores, particularly when plants are agitated by watering or fanning.¹³ Similar studies in laboratory animal care units fail to show excessive numbers of fungal spores.¹⁴

There are few data available on the characterization of allergens from indoor fungi. Out of the group, several major allergens from *Aspergillus* have been identified, including Asp f I (see Table 2).⁴² The gene encoding for this protein is found in *A. fumigatus* and *A. restrictus*, but has not been found in *A. flavus*, *A. niger*, *A. terreus*, or *A. nidulans*.⁵

DUST MITES

Dust mites are a common cause of allergic rhinitis in the indoor environment, and are the most important source of allergens in house dust. Mites are free-living organisms whose natural food sources include human skin scales, fungi, and other high protein substances in the environment. Dust mites, ubiquitous in most environments, are microscopic (~0.33 mm long), eight-legged animals belonging to the subclass of arachnids that constitute several orders of Acarina (Fig. 11). The family Pyroglyphidae contains most of the mites important in house dust allergy, but other families, such as Glycyphagidae, Acaridae, and Echymyopodidae, may be important in certain geographic areas. *Dermatophagoides pteronyssinus*, *D. farinae*, *Euroglyphus maynei*, and *Blomia tropicalis* are some of the important members of the Pyroglyphidae family. Although there is a significant overlap, the most dominant mites in North American and European homes are *D. farinae* and *D. pteronyssinus*, respectively. Mites found in houses are called domestic mites, but the term *house dust mite* is reserved for the Pyroglyphidae family of mites.⁴³ Storage mites are found primarily in grain, hay, barns,³² and occasionally in homes.⁷⁴ The family Tyroglyphidae, among others, contains many of the important storage mites, including *Acarus siro*, *Tyrophagus putrescentiae*, *Lepidoglyphus* (*Glycyphagus*) *domesticus*, and *Lepidoglyphus destructor*. The predisposing factors for developing allergic reactions to storage mites are occupation, damp homes, and possibly the type of bedding used for household pets.⁷⁹

Seasonal and geographic variation in the number of house dust mites in house dust have been observed. In North America, sharp peaks of mite growth have been observed in the summer months.⁴⁵ The major factors governing mite propagation are temperature and humidity, with optimal temperature being 77°F to 86°F (25°C–30°C) and relative humidity approximately 70% to 90%. When the relative humidity falls below 40% to 50%, mites are unable to survive beyond 11 days because of lack of hydration.³ The larval form (protonymph) of *D. farinae*, however, may



Figure 11. *Dermatophagoides farinae*, or house dust mite (original magnification $\times 200$). (Courtesy of L. G. Arlian, PhD, Dayton, OH.)

survive the heating season because it is resistant to desiccation. At higher altitudes, the absolute humidity of the outdoor air decreases sharply, reducing indoor humidity and therefore mite growth. Environmental conditions influence not only mite growth but also the species of mite found. *D. farinae* tend to predominate where there are prolonged periods of dry weather, whereas *D. pteronyssinus* usually favors humid conditions. *B. tropicalis* has been found in significant numbers in the southeastern United States and in tropical and subtropical countries.

Deeper dust of mattresses, pillows, blankets, and furred toys containing higher levels of humidity as opposed to surface dust from clothing, furniture, and closets, contains the highest concentration of mites. Meticulous housekeeping or the presence of household pets does not necessarily influence the mite load. Levels of Der p I (a major dust

mite allergen) greater than 10 $\mu\text{g/g}$ of dust often are associated with allergic rhinitis and asthmatic symptoms, whereas levels less than 1 $\mu\text{g/g}$ are not associated with allergic symptoms.⁴ Although these levels cannot be translated directly into dust mite counts, 10 $\mu\text{g/g}$ of Der p I is approximately equivalent to 200 mites/g of dust. The fecal particles of mites, approximately 10 to 35 μm in diameter, contain most of the allergenic activity of dust mites and are the main source of dust mite allergen extracts.⁶⁷ A high percentage of dust mite-sensitive individuals are skin test-positive to *D. farinae* and *D. pteronyssinus*, as evidenced by studies with crossed radioimmuno-electrophoresis (CRIE) and crossed immuno-electrophoresis (CIE), which demonstrate that *D. farinae* and *D. pteronyssinus* extracts contain numerous cross-reacting antigens and allergens. Fecal extracts of both species also contain unique, species-specific antigens and allergens.⁴

At least seven groups of house dust mite allergens have been described, with representatives of each isolated, purified, and partially sequenced (Table 3). The group I allergens are among the most extensively studied allergens of any origin, and are recognized by most mite-sensitive individuals. These allergens are found in whole body, fecal, and gut extracts from the various mite species. Examples of group I allergens include Der p I, Der f I, Der m I, and Eur m I. Amino acid sequences of these allergens reveal 80% to 85% homology among the mite species, with moderate levels of antigenic cross-reactivity as measured by IgE antibodies.⁶⁵ The group II allergens, which include Der p II and Der f II, also are considered major allergens in most individuals sensitive to house dust mites. These allergens differ from the group I members in that they are resistant to denaturation by heat and pH variations.

The group III allergens, Der p III and Der f III, are found primarily in fecal material from the house dust mites and so far only Der p III has been identified as a major allergen. With the exception of some group V and VII allergens, which have shown IgE binding in approximately 50% to 70% of sera from house dust mite-allergic individuals,⁶⁴ all other allergens in groups IV through VII are considered minor and have not been studied extensively.

Studies from mite feces show that 90% to 95% of the allergen content is Der p I. The high concentration of allergen is believed to be clinically significant in that it could cause an intense local inflammatory response when inhaled into the respiratory mucosa. As many as 75% of the serum antibodies to mites are directed against the Der p I allergen⁶⁷ and in some subjects, IgE antibody to Der p I constitutes 9% to 21% of the total IgE.²⁰ Removal of allergic children from environmental exposure to house dust mite antigen reduces specific IgE antibodies to *D. pteronyssinus* and total IgE levels.⁷⁰

ANIMALS

Emanations including hair, dander, feathers, saliva, and urine are important sources of animal allergens that can cause allergic rhinitis.

The total pet population is estimated to be 100 million in the United States, with over one third to one half of homes having a pet.⁵⁶ Animals are major sources of exposure for many sensitive individuals, especially given the fact that most individuals are reluctant to get rid of their pets despite being allergic to them. Dogs and cats are the most popular pets; however, many homes also contain other potentially allergenic pets, such as hamsters, gerbils, guinea pigs, rabbits, rats, and mice. Occupational exposure of farmers, veterinarians, and laboratory workers to animals also contributes significantly to the overall prevalence of animal allergy. The prevalence of laboratory animal allergy is estimated to be 11% to 44% among laboratory workers who are in contact with animals.⁵⁷ Rat and mice most often are implicated in laboratory animal allergy because of their widespread use in medical research.

Cat

Cats are popular pets in the Western civilization, and it is estimated that 28% of homes in the United States contain at least one cat.⁴⁰ Approximately 2% to 30% of atopic subjects are determined to be allergic to cats, as determined by skin testing or in vitro specific IgE measurement.⁵³ Cats seemingly produce the most dramatic symptoms in sensitive individuals, particularly in those who are exposed intermittently. Whether the dramatic symptoms are caused by the concentration of allergens in the cat's environs or by the potency of the allergens is unknown. The major cat allergen, recognized by over 80% of cat-sensitive individuals, is Fel d I (Table 3).⁴⁴ Fel d I is produced mainly in cat saliva, but is also in the sebaceous glands of the skin, the sublingual glands, and brain.^{8, 75} Although all breeds of cats, including long and short hair, produce

Table 3. REPRESENTATIVE DUST MITE AND ANIMAL ALLERGENS

Common Name	Taxonomic Name	Allergen	Molecular Weight (kD)
Dust mites	<i>Dermatophagoides farinae</i>	Der f I, II	24, 15
	<i>Dermatophagoides pteronyssinus</i>	Der p I, II, III, V	24, 15, 30, 15
	<i>Dermatophagoides microceras</i>	Der m I	24
	<i>Euroglyphus maynei</i>	Eur m I	24
	<i>Blomia tropicalis</i>	Blo t V	15
Cat	<i>Felis domesticus</i>	Fel d I	17
Dog	<i>Canis familiaris</i>	Can f I	25
Rat	<i>Rattus norvegicus</i>	Ran n I	20
Mouse	<i>Mus musculus</i>	Mus m I	17
Guinea pig	<i>Cavia porcellus</i>	Cav p I, II	25, 25
Rabbit	<i>Oryctolagus cuniculus</i>	Ory c I	17
Cockroach	<i>Blattella germanica</i>	Bla g I, II	25, 36
	<i>Periplaneta americana</i>	Per a I	25
Horse	<i>Equus caballus</i>	Equ c I, II	19, 51

Fel d I, the males produce greater quantities than females and it may be detected in the urine of male but not female cats. Studies with individual cats show that some cats are high producers of allergens and others are not. These factors may explain why some individuals are more allergic to certain cats than to others.⁸ Allergens other than Fel d I in some sensitive individuals also have been detected in cat serum and urine, but these are minor allergens.⁹

Morphologic room sampling shows abundant squamous cell fragments smaller than 5 μm in size, enabling cat allergen to remain airborne in undisturbed conditions for extended periods.⁴⁰ The "sticky" nature of the cat protein causes it to adhere to reservoirs such as carpets, walls, mattresses, and soft furnishings. Serial dust samples collected in the study of 15 homes after removal of the cats have shown a decrease in the levels of Fel d I to those of control homes after 20 to 24 weeks.⁷⁷ Cat allergen has been found in places where cats have never been present, suggesting passive transport of the allergen from clothing of people exposed to cats.²⁶ Based on this evidence, it is prudent to advise patients that it might take up to 6 months after removal of a cat for the bulk of the cat allergens to disappear from the home.

Dog

Like cats, dogs are common domestic pets; however, the prevalence of dog allergy is not as great as that of cat. The fact that dogs tend to spend more time outdoors and are bathed more frequently may explain their decreased importance as an allergen source relative to cats. Dog allergens have been identified in dander, saliva, urine, and serum, with major sources being dander and saliva. The major dog allergen, Can f I, has been described and can be assayed, although most skin tests and RAST use dander for diagnostic purposes. Danders of all breeds are allergenic; however, differences between breeds occur in the number and amount of antigens. Only 20% or fewer of individuals clinically allergic to dogs showed positive results on RAST or prick tests to dog serum albumin.³⁷ There is individual variation in the positivity of skin test results to different breeds, but in one study, these variations did not correlate with the individual's perception of specific breed allergy.

Rodents

Exposure to rodents, such as rats, mice, rabbits, and guinea pigs, not only causes allergies in individuals who keep these animals as pets in their homes, but is a significant occupational health hazard to those individuals who are in contact with these animals on a regular basis. Estimates of the prevalence of laboratory animal allergy have ranged from 11% to 44%, in part because of different methods used for evaluation. Allergic rhinoconjunctivitis is the most common manifestation of

laboratory animal allergy, occurring in 80% of symptomatic workers.⁵⁴ Air sampling techniques for rat allergens have shown that feeding and cleaning produce the highest airborne concentrations of the prealbumin protein Rat n I, whereas injection and handling produce somewhat less allergen exposure. Although many studies have shown that atopic individuals are more likely to develop laboratory animal allergy than nonatopic individuals, other studies have not confirmed this finding, and currently there are no recommendations to exclude these individuals from employment based on pre-employment screening. Not all atopic individuals develop laboratory animal allergy and nonatopic individuals may become allergic to animals in the workplace if exposed to sufficient allergen loads.^{47, 58}

In rats, mice, and guinea pigs, the major allergens are in the urine, whereas saliva and fur provide the major source in rabbits. In mouse-sensitive individuals, a major urinary protein, Mus m I, seems to be the primary allergen. It is the prominent member of a family of allergenic murine proteins collectively known as the major urinary proteins.³¹ Mus m I protein is synthesized in the liver, and its synthesis is stimulated by androgen, accounting for fourfold higher concentrations in male mice than in females. The two predominant rat urinary allergens are Rat n I and Rat n II. Workers with intense exposure to rats develop IgG antibodies to rat urinary protein, but in the absence of IgE to these proteins, they are asymptomatic. Of the three layers of rat pelt, the outermost fur is most allergenic, probably because of contamination with body fluids. The two important allergens of guinea pig are Cav p I and Cav p II⁷² and that of rabbit is Ory c I.⁷³

Cockroach

Although cockroach sensitization was first reported in the 1960s, its role in respiratory allergy has only been recognized in the last 10 years. The prevalence of cockroach hypersensitivity, which is related inversely to socioeconomic status, is more common in urban than suburban areas and is encountered frequently in crowded, multifamily dwellings with heavy infestation.⁶⁶ Sensitization to the cockroach allergen may occur by way of inhalation, ingestion, and dermal contact. Potential sources of relevant cockroach allergens in the environment include whole bodies, cast skins, secretions, egg casings, and fecal material.³⁴ Aerosolized particles containing allergens of cockroaches rapidly are being recognized as significant indoor allergens, second only to the house dust mites.³⁴ Common rhinoconjunctivitis symptoms associated with cockroach allergy include sneezing, rhinorrhea, and pruritus.

Of the over 50 species of cockroach described, only eight are regarded as indoor pests. Allergens from the two most common species, *Blattella germanica* (German cockroach) and *Periplaneta americana* (American cockroach), have been studied. Much less is known about *Blattella orientalis* (Oriental cockroach), which is more predominant in the United

Kingdom. The German cockroach allergen, Bla g I, shows skin test reactivity in approximately 30% of cockroach-allergic individuals, whereas Bla g II, a major allergen, shows skin test reactivity in approximately 58% of cockroach-allergic individuals.⁶ Other minor German cockroach allergens that have been identified include Bla g IV, Bla g V and Bla g VI. One allergen from the American cockroach, Per a I, has been cloned molecularly,⁸⁰ and has some cross-reactivity with Bla g I.

Other Animals

Allergic rhinitis secondary to numerous other animals, including horses, cows, sheep, and birds, also may occur. Although allergies to many of these animals are occupation-related (e.g., farming), many individuals keep one or more of these animals as pets. There are few epidemiologic or immunologic data available on most of these potential allergens. On exposure, horses can cause explosive symptoms in sensitive individuals, but this clinical situation is less common, primarily because of the absence of horse dander in the home. Horse hair has been used in the manufacture of some mattresses, furniture, and rug pads; however, this practice is not used currently. Although hypersensitivity pneumonitis is the most common manifestation of bird allergy, IgE-mediated hypersensitivity to bird feathers also has been described.⁶⁹

ENVIRONMENTAL CONTROL MEASURES

Outdoors

Although outdoor pollen and fungal spore avoidance may be difficult because of its widespread distribution, certain common sense measures can be taken to reduce exposure. Outdoor activities should be limited or avoided completely during times of the day when pollen and spore counts are at their peaks. As mentioned previously, pollen counts peak in the early morning to mid-afternoon. Fungal spores have a binodal peak consisting of early morning and late afternoon (for the so-called dry spores). When inside a house or an automobile, windows should be closed and the air conditioner should be turned on because pollen and spores readily can gain excess if the windows are open. During pollen season, studies have shown the presence of pollens in house dust samples.⁴⁶ Wearing a mask while mowing the lawn may be helpful in grass- or fungal-sensitive individuals. Limiting activities, such as leaf raking, lawn mowing, and farming, can reduce outdoor fungal exposure. Although somewhat drastic, traveling abroad or on cruise ships during a peak pollen season is an effective avoidance measure.

Indoors

Studies within the last 10 years have shown that continuous exposure to indoor allergens, such as dust mites, cats, and cockroaches, can lead to acute asthma attacks and sensitization. For example, Platts-Mills et al in 1991 showed that exposure to Der p I at levels of greater than 2 $\mu\text{g/g}$ of house dust leads to sensitization and greater than 10 $\mu\text{g/g}$ increases the risk of asthma.⁴⁸ Another study of inner-city children implicated cockroach exposure in causing acute asthma attacks.⁵² Avoidance measures taken to reduce exposure to these indoor allergens may play a significant role in reducing the morbidity and mortality of asthma. There are few data on the value of environmental control measures for dust mite and cockroach allergens in reducing rhinitis symptoms, which is not the case with animals because there is little doubt that decreasing exposure clearly decreases allergic symptoms in sensitive individuals. Although further studies are needed to clarify the role of avoidance measures in rhinitis, given the fact that many environmental control measures are simple, inexpensive, and much safer than medical therapy, they should be a standard part of the treatment plan of allergic rhinitis.

Dust Mites

Dust mite exposure can be reduced by several methods, including removing sources of mite growth, application of barriers between mites and sensitive individuals, and killing or denaturing the allergens (see list below).

DUST MITE ENVIRONMENTAL CONTROLS

1. Remove carpets (especially in bedroom and basement)
2. Remove upholstered furniture and stuffed toys (especially in bedroom)
3. Replace fabric drapes with vinyl or metal blinds (especially in bedroom)
4. Encase mattress, box spring, and pillows in allergen-proof covers
5. Keep relative humidity less than 50%
6. Wash all bedding in hot cycle ($>130^{\circ}\text{F}$ [55°C]) every 1 to 2 weeks
7. Vacuum weekly
8. Use tannic acid or acaricides on carpets and upholstered furniture

Common sources of mite growth are mattresses, pillows, down comforters, carpeting, upholstered furniture, stuffed toys, and fabric drapes. One of the most important dust mite control measure is regulating the humidity level. Because dust mites require at least 50% humidity to survive, decreasing levels below 50% by use of an air conditioner or a dehumidifier is an excellent method of controlling dust mite populations. Proper ventilation helps also to reduce the humidity level. Otherwise, the bedroom should be the major area of concentration for dust

mite control because most indoor time is spent there. Removal of mattresses and pillows is impractical and unnecessary; instead these items should be encased with special covers that form an impermeable barrier between the skin-feeding dust mites and the individual. In addition, all the bedding should be washed in a hot cycle ($>130^{\circ}\text{F}$ [55°C]) every 1 to 2 weeks.

Removing carpeting or fabric drapes from the entire house may be impractical; therefore, removal from at least the bedroom and other areas of the house where significant time is spent may be a reasonable option for sensitive individuals. If carpeting is left in place, it should be vacuumed once a week to avoid excessive dust build-up. Because vacuuming removes only little dust mite allergen, the best option is removal. Chemical treatments of carpets and furniture with agents that kill (acaricides [e.g., benzyl benzoate]) or denature (tannic acid) dust mites are also available. Although both types of agents have been shown to reduce the dust mite levels by 70% to 90%,⁷⁸ their clinical efficacy has not been studied. Carpeting should never be placed directly on a concrete slab because condensation can form on the surface of the concrete. The condensation can dampen the carpet, providing an excellent medium for dust mite and fungal growth.

Animals

Complete avoidance of the animal to which a person is allergic is the best treatment of animal allergy; however, most people are reluctant to rid of their favorite pet. Efforts should be focused on limiting exposure to the allergen (see list below).

ANIMAL ENVIRONMENTAL CONTROLS*

1. Remove the animal
2. If animal cannot be removed:
 - Prohibit access in the bedroom
 - Remove reservoir (e.g., carpets and upholstered furniture)
 - Maintain proper ventilation
 - Wash animal weekly
 - Use of high-efficiency particulate air (HEPA) filter may be beneficial

Keeping the cat out of the bedroom or only outside can decrease allergen exposure; however, because of the "sticky" nature of the cat allergen, it easily can be brought into the house or bedroom by passive transfer. Studies have shown the presence of Fel d I in areas where a cat has never been present. There is some evidence that washing cats can reduce airborne allergen levels, but to be effective, the procedure should be performed regularly.²⁴ Reducing reservoirs for cat allergen, such as

*Based on cat studies. Data unavailable for other animals.

carpets, sofas, and drapes, and increasing ventilation can decrease exposure to the allergen significantly.

The small particles of cat allergen make it possible for the allergen to be distributed easily in the environment. For this reason, the use of HEPA filters has been shown to be beneficial in removing these particles from the environment.²⁴ This study also showed that the combination of air filtration, regular washing of the cat, vacuum cleaning, and removal of allergen reservoirs, such as the carpet, may reduce the airborne cat allergen dramatically.²⁴ It may take up to 4 to 6 months after removal of the cat from the home to no longer detect cat allergen levels. Aggressive cleaning measures, such as washing the walls, steam cleaning the carpet, and increasing ventilation, may cause a more rapid decline of the cat allergens.

Avoidance measures for a dog follow the same general principles as those for a cat. Unlike the cat, the lack of standardization of dog allergen has hampered the study of dog allergy and avoidance measures. There are also a lack of studies on avoidance measures for cockroaches and most other animals. Although extermination of cockroaches may be attempted, reinfestation is common in inner-city homes because of poor living conditions. Good housekeeping and proper storage of foods can be helpful in reducing the cockroach population. With regard to rodents, it is important to avoid contact with bedding contaminated with urine during cage cleaning because the urine is a major source of allergens of many rodents.

Fungi

Important indoor fungal avoidance measures include dehumidification, proper ventilation, fungicide use on contaminated areas, and removal of sources of fungi growth. Common sites of fungal growth in the home are basements, crawl spaces, bathroom walls, garbage containers, food storage areas (especially vegetables and bread), humidifiers, and bedding.

SUMMARY

This article discusses the role of environmental allergens in allergic rhinitis. Although any foreign protein in the environment can be a potential allergen, few are clinically important. The most important allergens involved in allergic rhinitis are pollens, fungi, dust mites, and animals. Various aspects of these allergens are discussed, including various sampling techniques, important survival and allergenic factors (e.g., proper weather conditions), environmental distribution, seasonal patterns, and sources of exposure. Molecular biology of aeroallergens also is discussed, with emphasis on the most relevant major and minor allergens. Lastly, principles of environmental control of outdoor and indoor allergens are outlined.

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