Allergy Skin Testing of Children

William C. Deamer, MD
San Francisco, California

Skin tests are important aids in the management of patients with inhalant allergy. Their usefulness will be increased if these basic principles are kept in mind: (1) Scratch tests should be sufficiently deep, (2) Antigen extracts used for intradermal tests should be fresh enough to insure their activity, (3) Two control tests should be used each time tests are done, (4) Hydroxyzine and promethazine may diminish skin reactivity; therefore, negative skin tests should not be relied upon until repeated in the absence of such medication, and (5) Skin tests for food allergy are quite unreliable, whether positive or negative. Food allergy is best studied by means of elimination trial diets.

Allergy to inhalant substances is revealed by history and by skin tests. Since inhalants are the most frequent cause of respiratory tract allergy, it follows that skin tests for inhalants may play an important role in treating asthma, hay fever, and allergic rhinitis.

However, when respiratory tract allergy is due to food sensitivity, skin tests are of very little value. Their role is confined chiefly to allergens in the inhalant category – particularly pollens, house dust, mold spores, and animal epidermals. Knowing whether these four types of inhalants contribute to the etiology of a patient's symptoms can be crucial in planning his proper care.

Two types of skin tests are in common use – intradermal tests and scratch tests. The latter have several advantages over the former. They are relatively painless, and are quicker and easier to perform, especially on children who are apt to be needle-shy. There is also less tendency to nonspecific irritation with scratch tests.

Extracts used for scratch tests can be full strength. Dilution for safety reasons, as is usually done for intradermal tests, is seldom required. Scratch extracts usually contain 50 percent glycerin which helps to maintain their active shelf life for many months without refrigeration. Such a concentration of glycerin is irritating if injected and, therefore, is not used for intradermal tests. In the absence of glycerin, the shelf life of intradermal extracts is much shorter – only a few months – even with refrigeration.

Scratch tests are usually performed on the patient's back, the skin of which is a better test site than that of the upper arm, where intradermal tests are usually performed. While intradermal tests are more sensitive than scratch tests, the latter are sufficiently sensitive to reveal a patient's most important inhalant sensitivities in the majority of cases. Intradermal tests can then be reserved for occasions when they may help clarify questionable scratch tests, or provide a final opinion regarding pet sensitivity if the initial scratch test is negative. Intradermal tests are also useful when the history is in disagreement with a negative scratch test.

The purpose of skin testing is twofold. First, the results serve as a guide in deciding which environmental control measures are important. Second, they serve as a basis for selecting which antigens to use in the event hyposensitization is thought to be necessary.

Age Factors in Skin Testing

While skin tests may be performed at any time following birth, those done during infancy are of limited value. The sensitization process (which must always precede the establishment of clinical allergy) does not begin, *in the case of inhalant substances*, until after birth. It is unusual for an infant under one year of age to have become sensitized to an inhalant, although an occasional exception does occur. One infant in the author's experience was already pollen sensitive at nine months of age, another at 11 months.

Sensitization to food, on the other hand, can begin in utero, and may already be established at birth. Consequently, a skin test to milk, egg, or any food may be positive any time after birth. However, *only* the immediate-onset type of food allergy is indicated by such tests, and this limits the value of food tests in infancy. If the infant has the delayed-onset type of food allergy, which is more often the case, the skin tests will in all likelihood be negative.

Several years ago the occurrence of intrauterine sensitization was demonstrated in our clinic when a student scratch-tested a six-month-old infant

From the Department of Pediatrics, School of Medicine, University of California, San Francisco. Requests for reprints should be addressed to Dr. William C. Deamer, Director Pediatric Allergy Clinic Room 587-U, University of California Medical Center, San Francisco, Calif 94143.

Table 1. Grading of Skin Test Reactions

Recording		Criteria
Negative	o	No reaction
Questionable	±	Erythema only 2mm greater than either control.
One plus	+	Erythema 10 to 14 mm greater than either control.
Two plus	++	Erythema 14 to 20 mm and small wheal.
Three plus	+++	Wheal with beginning pseudopods and a large area of erythema. Itching.
Four plus	++++	Large wheal with marked pseudopods, large area of erythema and itching.

to milk, egg, wheat, and peanut. The only positive reaction was a three-plus test to peanut, something this infant had never ingested. The solution seemed clear when we discovered that the mother had developed the habit of eating a can of peanuts each day during most of her pregnancy.

A generalization may be made that clinical allergy during the first year of life is usually due to food (especially milk); in the second year, inhalant allergy becomes increasingly more frequent and from three on is the more common form of allergy. The persistence of an earlier food allergy, along with the establishment of an inhalant allergy, is quite common and is a possibility that must always be kept in mind.

A mother's positive skin tests are not transmitted to her infant. The skin test antibody (reagin, IgE) does not cross the placenta. Positive tests in an infant, therefore, indicate an independent, active sensitization.

Technique of Skin Testing

Scratch Tests

With the patient in the prone position, one to five rows of deep scratches are made on his back in rapid succession, each about 4 mm long and about 3 cm (more than one inch) apart. If necessary, 30 or 40 tests can be performed at one visit. The depth of the scratch, not its length, is the important factor. The ideal scratch test is one which penetrates the epidermis, reaches the dermis, but does not draw blood. It should be deep enough to be clearly visible. No preparation of the skin is needed. The sterile scarifier may be any instrument with a sharp point (Figure 1). If a scalpel is used, the blade should be dull enough to avoid accidentally cutting the patient, but the point should be sharp.

After placing the required number of scratches on the back, the two which are deepest or which have produced the most erythema are chosen as control tests and marked with a ball point pen. A drop of extract is then applied to each of the remaining scratches and gently rubbed in with the glass applicator which usually accompanies commercial scratch extracts. The tests should be read 20 to 25 minutes after application (Table 1), but it is best to observe them at five minute intervals as well to identify the most positive ones. These will begin to show erythema, itching, and possible wheal formation within a few minutes. One or more of the antigens in each row should be identified by marking the adjacent skin with a ball point pen instead of depending entirely on a routine sequence. Two control tests are desirable since they are most important to the testing. No other test can be considered positive until it surpasses both control tests in causing local erythema or wheal formation or both.

Technique of Intradermal Testing

A tuberculin-type syringe and a No. 27 needle are used. One tenth of a cc of the antigen solution is drawn into the syringe. This is more than the test requires, and allows for some leakage. With the skin of the upper arm drawn taut, enough extract is injected to produce a wheal 3 mm in diameter. The test is recorded in ten to 20 minutes in the same manner as the scratch test.

Interpretation of Skin Tests

False-Positive Tests

False-positive scratch tests occur frequently due to nonspecific irritation of the skin caused by the scratch or the needle, or because of dermographism. If the result of a skin test is equivocal, it should be repeated. Otherwise, it may be credited with immunological significance which it does not deserve. Actually, it would be advantageous if all one-plus tests were also repeated, especially when tests are performed by someone with limited experience in skin testing technique. If this advice were regularly followed, much disappointment in ultimate results would be avoided. Unfortunately, in the past a good deal of injection "therapy" has been given on the basis of skin tests which were quite unreliable. Injection therapy given on the basis of unreliable skin tests is, of course, equally unreliable therapy. Since injection therapy is time-consuming and costly, and benefit cannot be expected until maintenance dosage has been reached after 16 or more stepwise injections, it should not be undertaken unless there are firm indications for doing so, based on reliable, positive skin tests. Injection therapy should never be undertaken on a short-term "let's see what it can do" basis.

Even skin tests which are clearly reliable are not necessarily associated with clinical symptoms. Whitcomb[1] and others have shown that it is not uncommon for normal individuals without associated symptoms to have two-plus or greater skin reactions to a variety of allergenic extracts, including pollens and house dust. Thus, a patient may be pollen sensitive, but the amount of pollen he is exposed to may be insufficient to produce symptoms, even during pollen season. Treating such a patient by pollen injections is clearly unnecessary. Only symptoms should be treated, not skin tests alone.

Another example of positive skin test without clinical importance may be seen when a grass-pollen sensitive patient shows a positive reaction to wheat, corn, rice, oats, rye, or barley. These foods are the seeds of cultivated grasses. There is enough antigenic crossover between their seeds and the pollen of wild grasses to give a positive test. Most grass sensitive patients giving such a reaction to a grain can eat that grain with impunity, just as

they may eat honey containing grass pollen without trouble. Some clinical significance can be ascribed to the test, however, since such patients may have difficulty if they inhale flour, such as a baker is apt to do.

False-Negative Tests

Skin tests may be falsely negative as well as falsely positive. This may happen particularly if intradermal tests are done with extracts which are too diluted or which have lost their potency with age, or if scratch tests are too superficial.

Still another source of error is the use of extracts – either intradermally or by scratch – which, although fresh, lack adequate potency because of faulty extraction procedures. This happens most frequently with epidermal extracts, which are often difficult to extract. Where possible, each extract used should, therefore, be checked by the physician for activity on a patient known to be sensitive to the animal concerned. Cat and dog sensitivity is so common that it will usually be possible to do this without too much difficulty. Pollens and house dust, on the other hand, are easy to extract and can usually be assumed to be active when purchased.

Galant[2] and others have shown that the drug hydroxyzine (present in Marax and Atarax) is capable of inhibiting a skin test reaction for longer than 24 hours. Such inhibition must be taken into consideration when testing patients taking this drug. Promethazine (Phenergan) may also reduce the skin-test response.[3] The author requests his patients to avoid these medications in favor of some other modality for 48 hours prior to skin testing. Prednisone, aminophylline, and ephedrine do not interfere with skin testing. Other antihistaminic drugs may have a mild inhibitory effect but usually not enough to prohibit their use prior to testing.

Specific Kinds of Inhalant Skin Tests

Pollen Tests

All pollens are not equally important in causing allergy symptoms. In general, flowers and shrubs which are bright in color and fragrant are not likely to be allergenic. Their color and fragrance is for the purpose of attracting insects as a method of pollen

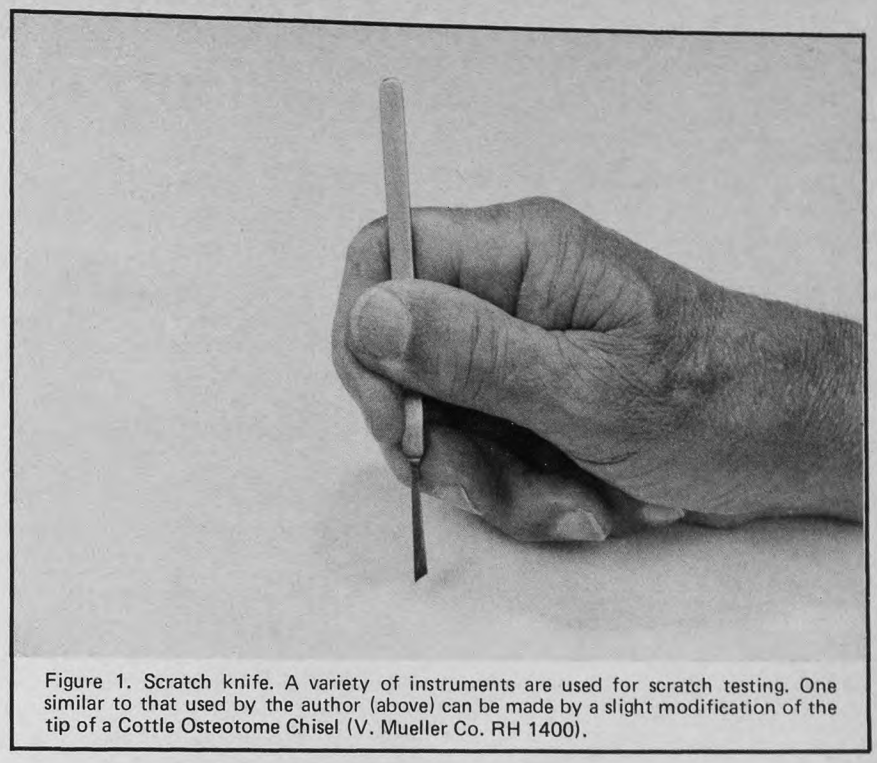


Figure 1. Scratch knife. A variety of instruments are used for scratch testing. One similar to that used by the author (above) can be made by a slight modification of the tip of a Cottle Osteotome Chisel (V. Mueller Co. RH 1400).

UNIVERSITY OF CALIFORNIA HOSPITALS
Pediatrics Department

Allergy Skin Tests

Name:

TREE POLLENS						WEED POLLENS					
Date						Date					
JUGLANS HINDSI (v) black walnut	4–5					Control					
OLEO SPECIES (v) olive	4–6					ARTEMISIA GROUP sages and mugwort	5–10†				
QUERCUS SPECIES (v) oak	3–5					PLANTAGO LANCEOLATA English plantain	4–8				
POPULUS SPECIES (v) cottonwood and poplar	2–3					RUMEX ACETOSELLA AND CRISPUS sheep sorrel and curly dock	4–9				
PLANTANUS SPECIES (v) sycamore and plane tree	2–4					FRANSERIA GROUP (v) false ragweed	5–10				
FRAXINUS (v) ash	3–4					XANTHIUM GROUP cocklebur	6–10				
ALNUS SPECIES alder	1–4					AMBROSIA PSILOSTACHYA western ragweed	6–10				
ULMUS SPECIES elm	2–3					AMARANTHUS GROUP (v) pigweed and tumbleweed	6–10				
JUGLANS REGIA English walnut	4–6					CHENOPODIUM GROUP lamb's quarters and goosefoot	4–10				
BETULA SPECIES birch	3–5					ATRIPLEX GROUP (v) saltbush and various "scales"	4–10				
ACER SPECIES maple and box-elder	3–4					SALSOLA KALI (v) Russian thistle	7–9				
ACACIA SPECIES	1–4 (1–12)					SALICORNIA AMBIGUA (v) pickle weed	6–9				
ALMOND	3–4					MEDICAGO SATIVA (v) alfalfa	5–9				
EUCALYPTUS SPECIES	3–5 (1–12)										
PINUS SPECIES pine	2–5					MIXED GRASS POLLENS					

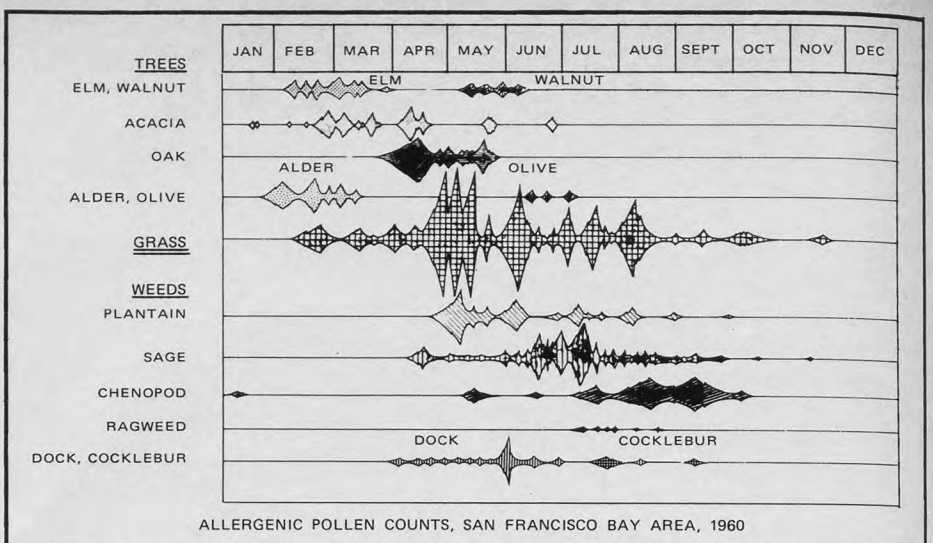
v. = important in hot interior valleys. †Pollinating months.

Figure 2. Pollen tests – North and Central California.

distribution. Pollen from such plants is seldom abundant, is usually not easily wind-borne, and for these reasons is not likely to be allergenic. Weeds, grasses and trees, on the other hand, do not usually have color and odor comparable to flowers and depend more on random wind distribution of their pollen, which therefore must be abundant. Such pollens are the usual causes of pollinosis (hay fever). There are occasional exceptions to this generalization. The acacia tree, for example, has a bright, showy blossom, but it produces abundant wind-borne pollen which is often allergenic. Although pine trees produce a huge amount of wind-borne pollen, it is seldom allergenic, possibly because the individual pollen grain has a large protective exine "shell" around its germinal center.

When testing for pollen allergy, one should test for all the allergically important pollens of the area where the patient lives. This does not mean that each variety of every species must be tested individually. A single variety or mixture of varieties should suffice. In Figure 2, it will be seen that at the University of California, San Francisco, Pediatric Allergy Clinic different varieties of sage and mugwort are grouped together in testing, since they are antigenically similar members of the *Artemisia* group. Similarly, the numerous varieties of olive and of oak are grouped under *Oleo species* and *Quercus species.* In this way, 26 tests suffice to test the average patient for weed and tree pollen sensitivity in our area. The total number of tests in the weed category might be even further reduced from 12 to 7 without too much sacrifice of accuracy if the three members of the ragweed family – false and Western ragweed and cocklebur (shown between the heavy lines, Figure 2) – were combined into a single test mixture, and the same were done in the pigweed-goosefoot family, which includes tumbleweed, lamb's-quarters, the various scales, and Russian thistle.

Grouping of *all* weed pollens into one test as "Mixed Weeds," however, is going too far and is not desirable since too much dilution of one group by other, unrelated groups could thus occur. Furthermore, if the test were positive, one would not be able to determine which pollen or pollens were responsible until additional, individual pollen tests were made.



ALLERGENIC POLLEN COUNTS, SAN FRANCISCO BAY AREA, 1960

Figure 3. Pollens identified at one station in San Francisco in 1960. A few additional tree and weed pollens were also identified but are not shown because of lack of space.

While some cross-reactivity within tree species does exist, it is not wise to mix all tree pollens together as a single "Tree Mix" for the same reason. The same argument, of course, applies to the use of a "Spring Mix" or "Fall Mix" for testing or injection therapy.*

The members of the grass family are antigenically so similar that a single test for grass sensitivity usually suffices. The "Mixed Grass" test is a mixture of pollens from several different varieties of grass (rye, brome, June, orchard, wild oats, velvet, red top, and Bermuda). Because Bermuda grass pollen displays some distinctive characteristics antigenically, in addition to those common to the entire family, twice as much Bermuda grass pollen is used in the mixture as of each of the other grasses.

Testing to numerous individual grasses is not only unnecessary but may, in a markedly grass-sensitive patient, cause an occasional constitutional reaction, since all such grass tests will be positive.

*It will be noted (Figure 2) that two separate walnut (Juglans) varieties appear under "Tree Pollens." This is not because we find them different antigenically, but because the duplication provides a type of control on skin-test technique. When one of the two walnut tests is positive and the other is negative, testing error is likely to be the reason. Pine pollen is also a check on our testing method. It is so rarely allergenic that a positive report suggests a testing error. Alfalfa (Medicago sativa) is a cultivated plant and should not be designated as a weed.

Each physician should be familiar with the antigenic pollens of his area and know in which months each is likely to be in the atmosphere. Graphs such as that shown in Figure 3 are helpful. Injection treatment with pollen extract is not logical unless the patient is symptomatic during pollen season. If the patient is symptomatic during pollen season but symptoms continue unabated or worsen at the end of the pollen season, one must also seek a cause other than pollen.

Injection therapy should not be undertaken on the basis of history alone, but should always be based on positive skin tests as well as history.

Scratch tests alone usually suffice to reveal pollen sensitivity, but if a pollen scratch test is doubtful or if it is negative in the face of a history suggesting pollinosis, intradermal testing should be undertaken.

Tests for Animal Danders

Allergy to a cat or dog is a frequent cause of asthma, allergic rhinitis, and atopic dermatitis. It is also one of the most difficult allergies to deal with. This is because the only really effective therapeutic measure is exclusion of the pet from the patient's home. Injection therapy, which is usually quite effective in pollen allergy, does not have comparable success in cat or dog sensitivity.[4,5]

Because success or failure to control a patient's symptoms may depend on recognition of pet sensitivity and

on how such sensitivity is handled, the physician should have firm evidence to support his position.

If a patient's scratch test to cat or dog dander is convincingly positive or if the intradermal test is markedly positive, the pet should not be in the house. By the same token, if both scratch and intradermal tests are negative, the physician is not justified in insisting on such an extreme measure. If the scratch test is negative and the intradermal test only one-plus, the best solution would still be exclusion of the pet, but a compromise may have to be reached in which the pet is never allowed in the patient's bedroom or playroom but is allowed to remain in other parts of the house on a trial basis.

A reliable history of symptoms such as sneezing or nasal itching, coughing, or wheezing closely following exposure on certain occasions to a household pet also constitutes a valid reason for its exclusion. The fact that at other times such exposure is not followed by symptoms should not alter this rule.

In some cases, a patient is so markedly sensitive that the lick of a cat or dog will cause local itching or redness, since saliva is antigenic as well as dander. This in itself constitutes a positive skin test and a high degree of allergy, and calls for removal of the pet. Unless this is done, it can safely be predicted that symptoms will continue. So long as the pet is indoors, the house becomes a reservoir of dander and dried saliva and provides a constant source of antigen. Contrary to what some pet owners would like to believe, there is little difference between one breed and another. A Chihuahua and a St. Bernard share a common antigen; the chief difference between them is one of size, not antigenicity. A frequent error is an owner's belief that only other cats or dogs are allergenic, but not his own. Dependence on the skin test in this important situation increases the need for reliable skin test extracts. As previously mentioned, each lot of dander extract should be of proven potency. The author has encountered relatively inactive commercial extracts more than once.

House Dust and House-Dust Mite Tests

House dust sensitivity is probably the most frequent type of inhalant allergy. It is usually associated with a clearly positive scratch test, not only to house dust but to the house-dust mite as well. This is a tiny mite that is found in, on, and under bedding and upholstered furniture and accounts for much, but not all, of the allergenicity of house dust. Mite extract is now available in this country. It is used increasingly for skin testing. Sometimes it is employed in combination with house dust in hyposensitizing injections. A positive skin test to house dust or the house-dust mite is indication for strict dust control in the bedroom, including allergen-proof encasings* for both mattresses and box springs if they contain cotton linters or kapok. Rubber or synthetic fiber (such as urethane foam) mattresses and box springs do not require encasings. Careful dust control in the bedroom alone often suffices to control house dust symptoms, but occasionally it may be needed in other rooms as well. After dust control measures have been carried out, injection therapy with house dust extract may not be necessary. In no case should injection therapy be undertaken until dust control in at least the bedroom has been implemented.[6]

Mold Allergy

Mold spore allergy has much in common with pollen allergy; however, since sources of mold are both inside the home and out, mold spores are even more difficult to avoid than pollen. Many varieties of mold can be cultivated from the air. Their clinical importance and cross-reactivity are, in many cases, still being investigated. While there is no uniform opinion on the importance of molds and mold therapy, there is general agreement that two of the most common and allergenic molds are Alternaria and Hormodendrum. These two are currently the only two *routinely* used in testing and in treatment by the author.

Allergy to Other Inhalants

Useful information can often be obtained by skin testing to feathers and the dander and/or hair of horses, cows, rabbits, hamsters, and guinea pigs. The list of additional allergens which might be mentioned is long indeed, and is beyond the scope of this article.

Food Tests

Skin tests for food allergy are largely a waste of time. There are two types of food allergy: (1) immediate reacting food allergy, and (2) delayed onset food allergy. Only in *immediate onset food allergy* are skin tests reliable. But they are usually not needed as the patient almost always knows that symptoms will promptly follow ingestion of the offending food and needs no skin test to verify it. This anaphylactic type of food allergy is dependent on specific IgE antibody, the presence of which is usually indicated by a markedly positive skin test.

In the totally different *delayed onset type of food allergy*, symptoms do not occur until several hours after ingestion. The patient is likely to have no clear idea of what food is responsible, or even that his symptoms are food related. In this instance, the mechanism cannot be shown to be IgE dependent and skin tests are negative. Neither the RAST test nor any other presently available laboratory test can be relied upon. One must resort to elimination trial diets.

This type of food allergy may be responsible for an amazing variety of symptoms, such as headache, stomachache, musculoskeletal discomfort ("growing pains"), fatigue, cranky behavior, and respiratory tract symptoms. But the possible role of food in causing such symptoms is easily overlooked by both physician and patient, largely because the skin tests are negative, but also because of the delay in appearance of symptoms following ingestion.

*Obtainable through Allergen-Proof Encasings, Inc, 1450 E 363rd St, Eastlake, Ohio 44094; in Canada, 325 Devonshire, Windsor, Ontario.

References

1. Whitcomb N: Incidence of positive skin tests among medical students. Ann Allergy 29:67-70, 1971
2. Galant SP, et al: The inhibitory effect of antiallergic drugs on allergen and histamine induced wheal and flare response. J Allergy & Clin Immunol 51:11-21, 1973
3. Bain WA, et al: Action of antihistamine antagonists. Lancet 2:964-969, 1948
4. Brown FR, Wolfe HI: Observations on animal dander hyposensitization. Ann Allergy 26:305-308, 1968
5. Deamer WC: Injection therapy for asthma and allergic rhinitis. Pediatr Clin North Am 16:243-255, 1969
6. Deamer WC: Techniques of desensitization therapy. Primary Care 1:87-108, 1974