

20 Subcutaneous Administration of Allergen Vaccines

Michael Radtke and Leslie C. Grammer

Division of Allergy-Immunology, Department of Medicine, the Ernest S. Bazley Asthma and Allergic Diseases Center of Northwestern Memorial Hospital, Northwestern University Feinberg School of Medicine, Chicago, Illinois, U.S.A.

INTRODUCTION

Subcutaneous allergen immunotherapy (SCIT) was first described in the United States by Noon and Freeman in 1911 (1) and has been used subsequently for the treatment of allergic symptoms due to inhalant allergens. In 1918, Dr. Robert Cooke suggested a mechanism of action for allergen injections as a "desensitization or hyposensitization." Prausnitz and Kustner elucidated the more specific immunologic basis for allergic disease, demonstrating that allergic sensitivity could be transferred by the serum of a sensitive person to the skin of a nonallergic person (2). SCIT is defined as the repeated administration of specific allergens to patients with IgE-mediated conditions for the purpose of providing protection against the allergic symptoms and inflammatory reactions associated with natural exposure to these allergens (3). The technique of SCIT differs from the process of desensitization, the term applied to the rapid, progressive administration of an allergenic substance, usually a drug, to render effector cells less reactive.

In the United States, SCIT with inhalant allergens most commonly consists of once or twice weekly subcutaneous aqueous allergen vaccine injections of increasing dose. Once the highest dose (i.e., the maintenance dose) is achieved, the interval between injections is increased up to four weeks (4–6). The timing and route of administration are the same in many other countries, but modified vaccines rather than aqueous vaccines are sometimes used. Numerous variations of inhalant immunotherapy are practiced relative to route of administration, timing, frequency, duration, and dosage.

ADMINISTRATION OF INHALANT VACCINES

General Considerations

SCIT for inhalant allergy is effective for allergic asthma and allergic rhinoconjunctivitis (SCIT for Hymenoptera hypersensitivity is reviewed in chap. 24). SCIT has not been proven effective for urticaria or food allergies (7). Limited data support its use in atopic dermatitis (8). SCIT with vaccines to a variety of pollen species, including grasses, ragweed, *Parietaria* species, and mountain cedar, is effective for allergic rhinitis due to these airborne pollen-producing plants. Vaccines with house-dust mite are effective treatment for both allergic asthma and allergic rhinitis (9). Limited data support that immunotherapy provides immunologic changes (10) or clinical efficacy (11) in patients allergic to cats. Likewise, efficacy data are limited for molds such as *Alternaria* (12) and *Cladosporium* species (13). Aeroallergens vary with geographic location; lists of pollen by geographic location and month are available in several standards texts (14–16). Familiarity with the significant aeroallergens in a physician's geographic location is critical to appropriately choose allergens for cutaneous testing and SCIT. Due to the mobility of today's population, one must also have a working knowledge of different geographic regions to effectively treat some patients (16). For example, Bermuda grass is an important allergen in the southern United States but is not present in northern climates. For a patient

living in Madison, Wisconsin, this may hold little importance. However, should this person spend the summer months in Florida, Bermuda grass becomes a potential allergen. The clinical relevance of an aeroallergen depends on certain key properties: (i) its allergenicity, (ii) its aerodynamic properties, (iii) whether it is produced in large enough quantities to be sampled, (iv) whether it is sufficiently buoyant to be carried long distances, and (v) whether the plant releasing the pollen is widely and abundantly prevalent in the region (3).

As outlined in the Allergen Immunotherapy Practice Parameter endorsed jointly by the American Academy of Allergy, Asthma, and Immunology (AAAAI) and the American College of Allergy, Asthma, and Immunology (ACAAI), SCIT should only be administered where adverse reactions can be appropriately managed (3). This includes proper training for physicians and staff in terms of reaction recognition and treatment. The Practice Parameter recommends that patients remain in the medical facility for 30 minutes after injections. It goes on to suggest which medical equipment and pharmaceuticals should be on hand in any setting in which immunotherapy is administered. A suggested listing of available equipment and medications is: a stethoscope, a sphygmomanometer, tourniquets, syringes/needles, epinephrine at 1:1000 (wt/vol), oxygen equipment, IV fluid setup, IV antihistamines, IV glucocorticosteroids, IV dopamine (or other pressor agents), and an intubation kit or oral airway as appropriate for the treating physician's skill with these devices.

Aqueous Vaccines

In the United States, aqueous vaccines are most commonly used for SCIT. Aqueous extracts are prepared by extracting proteins from fresh source material at physiologic pH and ionic strength and at low temperatures to delay proteolytic degradation and microorganism contamination. Some are standardized by cutaneous endpoint titration and quantified by either allergy units (AUs) (as in the case of dust mites), bioequivalent allergen units (BAUs) (as for grass pollen), or major allergen content (such as for ragweed and cat) (17). However, many extracts are labeled with protein nitrogen units (PNU) or as weight/volume (wt/vol). One PNU is approximately 10 ng of total protein nitrogen, and weight/volume refers to the weight (in grams) of the source material that is extracted in a given volume (in milliliters). Neither of these is reliably associated with allergenic potency (18). In other countries, different standard units are used to express allergenic potency. In Europe, especially in the Scandinavian countries, the biologic unit (BU), which is based on comparative histamine skin testing, is used (19). Allergen standards developed by the International Union of Immunologic Societies (IUIS) are quantified in international units (IUs) (20) (see chap. 20).

The starting SCIT dose is usually 1000-fold to 10,000-fold less than the maintenance dose and can even be lower for highly sensitized patients. The maintenance dose with standardized allergy vaccines is approximately 600 AU for dust mite or 4000 bioequivalent allergen units (BAU) for grass. For non-standardized vaccines, a suggested maintenance dose is 3000 to 5000 PNU or 0.5 mL of a 1:100 (wt/vol) dilution of manufacturer's extract. For vaccines with a known major allergen concentration, a recommended maintenance dose contains between 5 and 20 μ g of that major allergen (3).

Whenever possible, standardized extracts should be used to prepare vaccine treatment sets. Some commonly used allergens are standardized. As of 2007, these include cat hair, cat pelt, *Dermatophagoides pteronyssinus*, *D. farinae*, short ragweed, Bermuda grass, Kentucky bluegrass, perennial ryegrass, orchard grass, timothy grass, meadow fescue, red top, sweet vernal grass, and Hymenoptera venoms (yellow jacket, honeybee, wasp, yellow hornet, and white-faced hornet) (3). The following extracts are standardized but not commercially available: American elm, mountain cedar, paper birch, red alder, white oak, red oak, box elder, white ash, olive, cottonwood, mulberry, pecan, black walnut, sycamore, dog epithelium, German and American cockroaches, mugwort, Johnson grass, Bahia grass, and select molds (*Alternaria alternata*, *Cladosporium herbarum*, *C. cladosporioides*, *Penicillium chrysogenum*, *Aspergillus fumigatus*, *Epicoccum nigrum*, *Helminthosporium solani*).

Allergen extracts and vaccines should be maintained at recommended conditions until used for diagnostic tests or immunotherapy. Because extracts/vaccines lose their potency when stored at room temperature and with freezing and thawing, specific steps must be taken to avoid these conditions. Allergen extracts/vaccines should be kept at about 4°C. Dilutions of concentrated extracts/vaccines lose their potency more rapidly than the concentrates. Extracts

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that have questionable potency, such as those exposed to freezing and thawing, should be discarded (21) (see chap. 19).

Subcutaneous Immunotherapy

Administration of inhalant vaccines is usually by subcutaneous injection. In 1949, the first controlled study of the efficacy of SCIT with house dust was published (22). Numerous subsequent studies report the efficacy of SCIT with aqueous vaccines of tree (23,24), grass (25,26), and weed pollens (27,28); fungi (12,13); and house-dust mites (29,30). Early studies were inconclusive on SCIT efficacy for cat, but some data support its use (11). One study showed that the immunologic changes with cat SCIT are similar to those found with SCIT using other allergens (10). Dog SCIT alters skin prick testing and levels of dog-specific IgG4 but does not improve symptoms as described in available publications (31). High-dose perennial SCIT is the dose schedule resulting in the best efficacy (14–16). SCIT only during the pollen season (co-seasonal therapy), or only in the few months prior to the pollen season, (preseasonal therapy), are not recommended in the United States (15). These protocols are used in other countries.

When more than one inhalant allergen is required, the vaccines may be administered either individually or incorporated into a single vial. Since most patients would rather receive as few injections as possible, combined vials are preferable for comfort and convenience. Some data on house-dust mite and fungal extracts suggest the enzymes in those extracts might degrade proteins with which they are mixed in a combined vaccine (32). There are, however, no data on the efficacy of mixed versus individual allergen vaccines to clarify the clinical relevance of the protease content of component extracts in a vaccine (see chap. 19). The Allergy Immunotherapy Practice Parameter suggests that allergens with high protease activity (dust mite, mold, and cockroach) may be mixed with each other but should be kept separate from those with low protease activity (grass pollen, tree pollen, weed pollen, and animal allergens) (3). Ragweed may be combined with any of the other allergens. Occasionally, patients who are extremely sensitive to one inhalant allergen may benefit from administration of that allergen in a separate injection in order to limit local reactions and to allow optimal dose adjustments. The dosage schedule for that allergen likely would be more conservative than for other inhalant allergens administered.

Dosage Schedules

Three basic SCIT dosage schedules are proven to be beneficial for the treatment of inhalant allergy: standard weekly immunotherapy, cluster immunotherapy, and rush immunotherapy (6). A generally accepted principle of immunotherapy is that, within certain limits, the larger the cumulative dose, the greater the efficacy (27). The optimal dose is defined as the dose of allergen vaccine inducing a clinically relevant effect in the majority of patients without causing unacceptable side effects (33). Studies by investigators at Johns Hopkins reported that ragweed vaccines administered in annual cumulative doses of approximately 50 µg antigen E or *Amb a I* are likely to be effective (34). Effective cumulative doses for other vaccines are not as well defined; however, studies of cat vaccines standardized by *Fel d I* content (35), of mite vaccines standardized by *Der p I* content (36), and of pollen vaccines standardized by BUs (37) support the hypothesis that greater cumulative doses of inhalant allergen are more likely to result in amelioration of symptoms of aeroallergen allergy.

Conventional immunotherapy regimens. There are two phases of conventional SCIT administration: the initial buildup phase, when the dose and concentration of vaccine are slowly increased, and the maintenance phase, when the patient receives an optimal immunizing dose over a period of time (7). Perennial immunotherapy commonly follows a once or twice weekly dosage schedule (Table 1). If the vaccine is labeled in AU or BAU, the initial concentration is generally 0.1 to 1 AU/mL or BAU/mL, with an initial volume of 0.05 mL. In preparation for the buildup phase of immunotherapy, serial dilutions should be produced from each maintenance concentrate vaccine. Typically, these are 10-fold dilutions, although other dilutions are occasionally used. These vials should be labeled in terms of volume per volume to indicate that these are dilutions derived from the maintenance

Table 1 Illustrative Schedule for an Inhalant Allergen Vaccine

Dilution (vol/vol)	Volume (mL)
1:1000	0.05
	0.10
	0.20
	0.40
1:100	0.05
	0.10
	0.20
	0.30
	0.40
	0.50
1:10	0.05
	0.07
	0.10
	0.15
	0.25
	0.35
	0.40
	0.45
	0.50
Maintenance concentrate	0.05
	0.07
	0.10
	0.15
	0.20
	0.25
	0.30
	0.35
	0.40
	0.45
	0.50

concentrate. For example, serial 10-fold dilutions from the maintenance concentrate would be labeled as 1:10 (vol/vol), 1:100 (vol/vol), and so on (3). Injections during the buildup phase are commonly administered once or twice weekly; after reaching the maintenance dose, the interval generally increases to biweekly (every 2 weeks), triweekly, and finally monthly. The maintenance dose is usually administered at two- to four-week intervals provided that the injections are well tolerated and symptoms improve. If a systemic reaction or anaphylaxis occurs, the physician should review the patient's immunotherapy history and adjust the dose of immunotherapy accordingly. Though recommendations vary, the practice at Northwestern University is to decrease the vaccine dose by at least half after systemic reactions. Others reduce the dose by 10-fold. Subsequently, the dose is increased as tolerated at weekly or twice-weekly intervals. The maintenance vial is replaced with a newly prepared one every 6 to 12 months, reducing the dose of the first injection from a new vial by one-third to one-half due to the potentially greater potency of a fresher vaccine. The dose is subsequently increased weekly, biweekly, or monthly to the routine maintenance dose (21).

Rush immunotherapy regimens. Numerous schedules have been published for administration of allergen immunotherapy via a rush injection schedule. Initial doses are generally similar to those of more conventional schedules as listed in Table 1. A typical rush immunotherapy schedule entails multiple injections on the first day of treatment. On the second and third days, fewer injections are administered, with the proportional increases of allergen dose also declining with each successive injection. During the first few days, injections are given at intervals of 30 minutes to 2 hours. Patients reach a maintenance dose in 3 to 7 days.

Some rush protocols increase the dosages more rapidly than outlined in Table 1, some with increases of 50% to 100% per injection. The obvious advantage of a rush schedule is that the patient can attain the maintenance dose and associated symptom relief more quickly (38). Efficacy and immunologic changes have been reported to be similar to conventional SCIT with equivalent cumulative doses. The major disadvantage, though, is that rush immunotherapy is associated with a greater risk of systemic reaction than that reported in conventional weekly immunotherapy; this increased reaction rate appears to be particularly significant in children (39). Reported rates of systemic reactions have been as high as 36.8% of patients with select allergens (40). This type of protocol has been most extensively studied in Hymenoptera venom immunotherapy, with rates of systemic reactions in approximately 7% of patients in multiple studies (40). Premedication with prednisone and an H₁ histamine receptor antagonist, with or without an H₂ histamine receptor antagonist, has been reported to reduce the risk of systemic reactions (41,42). Omalizumab, a humanized monoclonal anti-IgE antibody, has been studied as pretreatment as well. It was found to decrease the rate of systemic reactions to venom rush immunotherapy from 25.6% to 5.6% per patient (43). In addition to the more typical rush schedules, studies have investigated more extreme protocols, often termed "ultra-rush." One publication reported only 8 systemic reactions in over 2000 injections. It is important to note, though, that a modified extract not available in the United States was used (44).

Cluster immunotherapy. In cluster SCIT protocols, starting doses are similar to those of conventional SCIT (45). As with conventional protocols, weekly visits are necessary. However, at each visit more than one injection is administered, with the interval between injections varying from 30 minutes to 2 hours. Once the maintenance dose has been achieved, the interval between visits is increased. The advantage of the cluster regimen is probably most obvious for the patient who must travel several hours in order to receive injections; receiving more than one injection per visit reduces overall travel time by reducing the number of visits. Efficacy and immunologic changes are likely similar to conventional SCIT with equivalent cumulative dose. The disadvantage to cluster SCIT is that the reaction rate is probably greater than with conventional schedules (45), though reaction rates in some studies are similar to conventional SCIT schedules with dust mite (46). Several alterations to the cluster protocol may increase its safety, including premedication with antihistamines, four or less injections per visit, and twice-weekly clusters (40).

Procedures for Subcutaneous Injection

Prior to administering inhalant immunotherapy, it is imperative that the patient, the immunotherapy vial(s) of the appropriate dilution, and the dosage schedule(s) be clearly identified. Error in dosage can cause serious systemic reactions to inhalant allergen injections (47). Several systems may be used to decrease the risk of errors, including color coding of vials, confirmation checks with a second member of the health care team, and dosing confirmation with the patient. Careful documentation of the administration of SCIT is extremely important. Information that should be noted in the medical record includes the concentration given, a record of the bottle's label and its contents, the volume of vaccine scheduled and given, which arm was used for the injection, peak expiratory flow before and 20 to 30 minutes after injection as indicated for high-risk patients, a history of reactions from previous injections, treatment of any reactions that occurred, and any adjustments from the standard schedule and the reasons for the changes (7). If a patient's asthma is not controlled, treatment should be provided before an injection is administered because of the potentially dangerous synergistic effects of asthma and anaphylaxis. In one survey-based study, 15 of 17 fatal reactions occurred in the setting of poorly controlled asthma (48). Injections should be administered with a 0.5 to 1 mL syringe to insure dosage measurement accuracy. The needle gauge should be greater than 25, and the injection should be subcutaneous and not intradermal, intramuscular, or intravenous. The subcutaneous adipose tissue in the mid-portion posterior aspect of the arm, typically at the junction of the deltoid and triceps muscle, is the most common site for injections (Fig. 1). Prior to vaccine injection, the syringe plunger should be withdrawn to insure that the needle tip is not intravenous. If blood appears in the syringe, it should be withdrawn, discarded, and replaced with a new needle and syringe. After injections of inhalant allergen vaccines, the

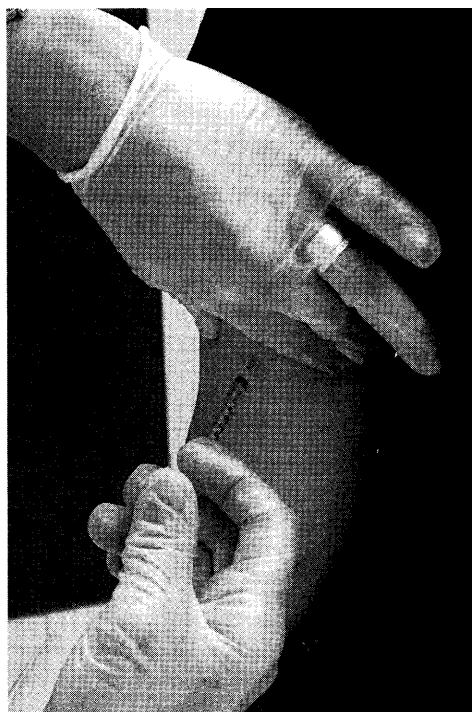


Figure 1 Proper technique for administration of an immunotherapy injection.

patient should be observed at least 30 minutes for reactions to injections and longer if he/she is considered to be at increased risk for a systemic reaction (3).

Reactions and Dosage Adjustment

Local reactions characterized by erythema and/or induration less than 2 cm and lasting less than 2 days are common and of no consequence. Large local reactions, defined as induration greater than 2 cm lasting more than 2 days, may result in the repetition or decrease of the next dose. Reactions greater than 2 cm in diameter may need to be treated with topical application of ice to reduce local blood flow, oral antihistamine therapy, and possibly topical corticosteroid therapy. These methods usually are sufficient, but rarely a large or biphasic local reaction may be so uncomfortable that a day or two of oral glucocorticosteroids may be beneficial. Oral antihistamines are often used in an effort to prevent local reactions. There appeared to be a trend favoring montelukast over loratidine for prevention of local reactions in one study (49), but the difference failed to reach statistical significance.

Most data do not correlate local reactions with risk for systemic responses but there are exceptions (50). One group analyzed the rates of systemic reactions under two different protocols: one that modified allergen vaccine doses based on local reactions and one that did not (51). Modification of dosing did not affect systemic reaction rates after analysis of nearly 8000 injection visits. These findings were confirmed by another group with a similar protocol design (52). Furthermore, the latter group found no increase in local reaction rates preceding systemic reactions. Changes in SCIT dosing schedules in response to local reactions, therefore, are unlikely to alter the risk of systemic reactions. However, they may offer some benefit at reducing subsequent local reactions and patient discomfort.

SCIT may result in systemic reactions or anaphylaxis manifested by urticaria, angioedema, generalized pruritus and erythema, laryngeal edema, headache, nausea, vomiting, bronchospasm, hypotension, shock, and even death. Most systemic reactions occur during the buildup phase or in highly allergic individuals, though anaphylaxis occurs in the maintenance phase as well. Physicians who administer allergen SCIT vaccines must be prepared to treat anaphylaxis. If a systemic reaction occurs, the subsequent SCIT dose should be reduced to one-half to one-tenth the dose that resulted in the systemic response, depending upon the severity of the symptoms. In patients who have experienced a systemic reaction, the

rate of increase in dosage may need to be reduced. After each systemic reaction, the risks and benefits of continuing immunotherapy generally should be reevaluated and discussed with the patient.

A common cause for dosage adjustment is a hiatus in therapy. Depending upon the patient's previous history of reactions and the length of the hiatus compared with the usual frequency of injections, the dosage may be repeated or reduced. If a patient has a pattern of being unable to comply with the injection schedule, particularly if the maintenance dose has not been achieved, the risks and benefits of continuing SCIT should be reevaluated.

When to Stop Immunotherapy

From our experience at Northwestern University, approximately 90% of properly selected SCIT-treated allergic patients will usually notice a reduction in symptoms and/or medications after receiving the maintenance dose for one year or more. Further, SCIT will not likely benefit and usually should be discontinued if maintenance therapy for over a year has not resulted in some improvement.

In a controlled study in which SCIT for grass pollen allergy was discontinued after three to four years of successful treatment, seasonal symptom scores and the use of rescue medication were decreased for three to four years after the discontinuation of SCIT. There was no significant clinical difference between patients who continued and those who discontinued SCIT (53). Evidence is not available to provide an absolute, optimal length of time to continue inhalant allergen vaccines. After two or three years of improvement, consideration of discontinuing SCIT is an option. In our experience, most patients whose inhalant allergen immunotherapy is discontinued at that time will continue to maintain their reduction of symptoms and/or medications. Several studies have demonstrated this, though most have been with few enrolled subjects (54). There is, however, a risk of relapse, and this should be discussed with the patient prior to stopping SCIT. In the setting of venom IT, there appear to be several factors associated with increased risk of recurrent reactivity: severity of sting reaction, systemic reaction to venom IT, allergy to honeybee, and immunotherapy duration less than five years (54) (see chap. 24).

Subcutaneous Immunotherapy in Pregnancy

Allergen SCIT is effective in the pregnant patient, and maintenance doses may be continued during pregnancy. When a woman receiving SCIT reports that she is pregnant, the dose of immunotherapy usually is not increased; rather, the patient is maintained on the dose she is receiving at the time of notification. Alternatively, some specialists slightly reduce the maintenance dose as an additional precaution. Allergen immunotherapy is usually not initiated during pregnancy because of the risks of systemic reaction and their treatment. These recommendations stem from the understanding that systemic reactions are more likely to occur during the build-up phase of immunotherapy. Possible obstetrical complications of anaphylaxis or its treatment include spontaneous abortion, premature labor, and fetal hypoxia. The initiation of immunotherapy may be considered during pregnancy for the pregnant patient with life-threatening Hymenoptera sensitivity (3).

Local Nasal Immunotherapy, Oral Immunotherapy, and Sublingual Immunotherapy

See chapters 23, 25 and 28.

Modified Extracts/Vaccines

Two major concerns exist despite the established efficacy of SCIT using conventional aqueous inhalant allergen vaccines. First, SCIT may induce systemic reactions that can be life-threatening. Second, the build-up phase of conventional SCIT generally requires 25 to 30 injections, each of which involves time and cost to the patient. Many investigators have attempted to modify inhalant allergen vaccines to reduce the risk of anaphylaxis or minimize the number of buildup injections (55). These modifications can be divided into three approaches: slowing absorption, inducing tolerance, and reducing allergenicity while retaining immunogenicity.

Alum-precipitated extracts are an example of the slow absorption approach (56). They are the only modified extracts available in the United States and are the most commonly used extracts in other countries (4). Ragweed, cat, and grass alum-precipitated vaccines have been studied and found to have equivalent efficacy when compared with aqueous vaccines. Systemic reactions are decreased, with rare prolonged local reactions the major side effect (21). To date, the FDA has not approved any modified extract other than those that are alum precipitated, and most immunotherapy outside of the United States employs alum and other modified extracts.

Experimental data demonstrate the potential to induce tolerance and enhance safety and efficacy of immunotherapy, though most of these data are from animal experiments. Possible modifications include addition of monophosphoryl lipid A, heat-killed bacteria, or CpG motifs (57). CpG motifs have been used in an effort to stimulate Toll-like receptors during immunotherapy, thereby inducing tolerance. In human studies with vaccines containing Toll-like stimulants, one group found improvement in allergic rhinitis symptom and quality-of-life scores, but failed to reach statistical significance on the primary endpoint of vascular permeability (58).

Aggregation or cross-linking of the proteins of an aqueous extract reduces the allergenicity while preserving the immunogenicity of the subsequent vaccine. Two methods of modification have accomplished this goal: polyethylene glycol-treated allergens and glutaraldehyde-treated allergens (polymerized allergen extracts). One study assessing the safety of these modifications found a rate of systemic reactions to be 1.31% per patient, or 0.12% per injection, using a protocol that required only four to six injections to reach maintenance (59). This compares favorably with published reaction rates of 0.8% per injection for aqueous vaccines used in conventional SCIT protocols (42). Direct comparison of modified to unmodified dust-mite allergen yielded one-third the number of systemic reactions in the modified group compared with the unmodified one (60). Furthermore, 10-fold higher allergen concentrations were tolerated in the modified allergen subjects. A double-blind, placebo-controlled trial of modified dust mite allergen immunotherapy showed a substantial improvement in bronchial provocation testing and symptom scores, with no systemic reactions (61). Similar findings have been published for recombinant grass pollen immunotherapy, with extracts produced via transfection of grass pollen cDNA into *Escherichia coli* (62).

Dosage Schedules

A variety of dosage schedules have been published for modified vaccines. An example of an efficacious protocol for glutaraldehyde-polymerized vaccines is shown in Table 2. Most modified vaccines require fewer than half the injections necessary with standard aqueous immunotherapy.

Techniques

Most modified vaccines are marketed for subcutaneous injection at weekly intervals. However, modified dosage schedules such as rush or cluster schedules have been published (63).

Table 2 Example of Dosage Schedule for Polymerized Ragweed Injections

Week	Amb a I ($\mu\text{g/mL}$)	Volume
1	25	0.10
2		0.25
3		0.50
4	250	0.10
5		0.25
6-15	250	0.50

Reactions and Dosage Adjustment

The package insert that accompanies modified vaccines generally advises physicians of the relative risk of reactions and dosage adjustment following reactions. For the most part, the reactions and dose adjustments are similar to those with unmodified aqueous vaccines.

When to Stop

For glutaraldehyde polymerized vaccines, 10 to 15 injections result in efficacy for up to six years (64). Most other modified vaccines have not been studied as to duration of efficacy after discontinuation of therapy. It should be noted that some forms of modification that reduce allergenicity can also denature the allergens. Therefore, modified vaccines, such as pyridine-extracted allergens, should only be used if clinical efficacy has been demonstrated by appropriately controlled clinical trials. In general, package inserts accompanying modified allergen vaccines include recommendations relative to a course of therapy.

SALIENT POINTS

- Allergen SCIT is defined as the repeated administration of specific allergens to patients with IgE-mediated conditions for the purpose of providing protection against the allergic symptoms and inflammatory reactions associated with natural exposure to these allergens.
- The most commonly used form of inhalant allergen immunotherapy in the United States is subcutaneous injection of aqueous vaccines (SCIT).
- While various low-dose immunotherapy regimens have been published, optimal efficacy results from a relatively high-dose immunotherapy schedule as illustrated in Table 1.
- Most systemic or anaphylactic reactions occur during the buildup phase and in highly allergic patients, especially those with poorly controlled asthma.
- Administering an incorrect dose can result in severe systemic reactions. To minimize risk, the patient, vial, dilution, and immunotherapy schedule must be individually identified prior to administration of an injection of inhalant allergen. If there was a significant reaction to the previous immunotherapy dose or if the time interval between injections is longer than designated, the dose will require adjustment.
- If a patient has been on SCIT maintenance doses for more than a year without improvement, the SCIT treatment should probably be discontinued. If improvement has occurred, the patient should be treated for two or three improved seasons or three years of more before consideration of discontinuation.
- Standardized, commercially available extracts as of 2007 include cat hair, cat pelt, *Dermatophagoides pteronyssinus*, *D. farinae*, short ragweed, Bermuda grass, Kentucky bluegrass, perennial ryegrass, orchard grass, timothy grass, meadow fescue, red top, sweet vernal grass, and Hymenoptera venoms (yellow jacket, honeybee, wasp, yellow hornet, and white-faced hornet).
- Allergen SCIT is effective in the pregnant patient and maintenance doses may be continued during pregnancy. Allergen immunotherapy is usually not initiated or advanced in dose or concentration during pregnancy because of risks associated with a potential systemic reaction and its treatment. Possible complications of systemic reactions include spontaneous abortion, premature labor, and fetal hypoxia.

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