Allergy Specific Immunotherapy-How to Maximize the Results

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Allergen specific immunotherapy (desensitization or "allergy shots") has been one of the mainstays of care in specialized dermatology practice for years. In the mid 1980s serology (RAST) testing was marketed to veterinarians, and since then numerous companies have developed their own RAST or ELISA tests. Intradermal allergy testing (skin testing) is the traditional test performed by most veterinary dermatologist. The number, purity, and specificity of extracts available for skin testing and immunotherapy have improved over the years. The diagnosis of atopy should be made based on history, clinical presentation and the ruling out of other hypersensitivities such as parasite and food allergy and not based on any type of allergy test.

Allergen specific immunotherapy is most definitely not a "one size fits all" program. If a veterinarian wants to become proficient at administering immunotherapy, she or he should first become familiar with the regional pollen producing plants, when they bloom, how long they bloom, and how prevalent the plant (and allergen) is in the area. An awareness of the prevalence of indoor, potentially year round allergens, such as house and storage mites, mold spores, animal and human dander and insect particles is also necessary. This knowledge will enable the veterinarian to more effectively determine or prioritize what each individual patient should be desensitized to. The first critical step in achieving success with immunotherapy is determining accurately and completely what the patient is allergic to. In our practice we utilize intradermal skin testing almost exclusively for defining what an atopic patient is allergic to. We find we get the most specific and sensitive results from intradermal testing. This also allows us to customize the list for which we are testing based on specific location, not just region. Does it really make sense to lump Southern Arizona in the same region as northern Montana when considering what allergens to test for? Intradermal allergy testing is expensive to set up and maintain, and requires practice and skill interpreting results and is therefore mostly performed only in a specialty setting. If intradermal testing is not available, then serology testing must be utilized.

It should be emphasized that the only reason to perform any type of allergy (blood or skin) testing is to follow up with immunotherapy. Once allergy test results are obtained, these results should always be critically analyzed to insure that the results are consistent with the patients' pruritus history. This determination will include historical information regarding seasonality. If allergy testing reveals positive reactions only to seasonal pollens in a patient which is pruritic year-round, then something is being missed! Choosing the allergens to be included in the extract is something the veterinarian should personally direct based on the specifics of each individual patient. This is where knowledge of the regional allergens is necessary. For the outdoor working dog that is pruritic only in the summer and fall, then positive reactions to grasses and weeds should be present, and they need to be emphasized or prioritized when formulating the extract. For the indoor Chihuahua which sleeps under the covers at night and who is pruritic year round, then indoor allergens such as dander, mold spores, house dust and house mites need a higher priority in the extract recipe. Yet another factor to consider when developing the "correct" mix or recipe is how long particular pollen is present. In our practice Bermuda grass is one of the dominant pollens, and Bermuda will bloom for over six months in our area. Most tree pollens are present for 2-6 weeks. Does it make sense to put equal levels of a tree pollen and Bermuda grass? Or equal levels of house mites and Ash tree pollen in the patient pruritic year round? One should not assume that the allergens in a vial all have to be equal quantity or volume. If Oak is a significant reaction in a dog living in central California who is the most pruritic in spring, why not double (or more) the quantity of Oak pollen compared to some of the other ingredients. Our current skin test panel includes 70 different allergens.

A number of our patients will have significantly strong skin test reactions to over twenty different positive allergens and some will have over 50 significantly positive reactions. In such cases we will often utilize two different vials of allergen to more fully incorporate all the allergens into the immunotherapy program. Another reason to utilize two different vials of allergens is when significant reactions to mold spores occur. Some molds may have proteolytic enzymes which have the potential to degrade pollen proteins when mixed in the same vial. In such cases, placing the molds in a second, separate vial can alleviate this concern.

The volume, concentration, and frequency of the allergen injections are additional variables which will affect the success of the immunotherapy program. At Dermatology for Animals we have utilized a "rush protocol" in over 5,000 patients over 20 years. With this schedule, patients receive therapeutically effective levels of allergen (10,000 pnu) within two weeks. We find patients respond more quickly to this program, which can be important for the suffering patient and impatient owner. Yet each patient will respond differently to immunotherapy so there is no "set in stone" protocol. Determining the most effective volume and frequency of injections requires close observations by the owners and the ability of the clinician to make proper adjustments of the protocol. Finding the minimum effective volume with the maximum duration of effect is our goal when administering immunotherapy. For patients under 20 pounds, we are especially careful as we increase the quantity of protein given, and will usually limit the maximum amount of protein to 10,000 pnu.

Occasionally during the course of immunotherapy, owners will observe a flare of pruritus after exposure to certain allergens such as a walk in the park, or a trip to the mountains. Such observations by the owner can be helpful in "fine tuning" the extract contents. For these patients we will make slight or moderate adjustments in the contents of the extract to specifically address the cause of the

flare. For example, when an owner reports the patient flares after going outside and walking on the lawn, increasing the grass content in the extract of that particular grass would be indicated.

Immunotherapy continues to improve partly due to advances in allergen purification as well as isolation of specific allergen isotypes. We also continue to have additional allergens available for testing and treatment. Significant additions in the last several years include Malassezia allergen, human dander and storage mites.

Keep in mind that immunotherapy will never be effective if the wrong diagnosis has been made, or if additional concurrent allergies are present but not identified or treated. We find many of our atopic patients to have a concurrent food allergy or parasite (flea) allergy. It is not uncommon to have to repeat food trials, or reinstitute parasite control if or when immunotherapy has failed to help after an "adequate" amount of time. Many of our patients will respond favorably to the ASIT program within the first 2-5 months of starting injections, yet we recognize the occasional patient which requires over 18 months before improvement is seen. Obviously in such cases it is imperative that the diagnosis be accurate and complete.

Because ASIT requires some time before efficacy is seen, and because there is only partial improvement for some patients receiving ASIT, it is often appropriate to treat an atopic patient with concurrent medication, especially in the induction phase of the immunotherapy program. Fortunately there is no evidence that medications such as corticosteroids or cyclosporine interfere with ASIT. Therefore ASIT is rarely utilized as the single therapy for atopic dermatitis initially. Once the positive effects of ASIT are seen, the concurrent therapies are often reduced and then eliminated.

Management of adverse events or reactions to ASIT is also occasionally necessary. In our practice less than one percent of patients undergoing immunotherapy need to have the program discontinued do to adverse reactions. Potential adverse reactions include pain or swelling at the injection site, lethargy or increased pruritus immediately after an injection. More serious events include urticaria or hives after the injection. Signs of anaphylaxis or collapse are rare but could occur. Owners are instructed to always monitor the patient for at least one hour after an injection is given. If mild adverse events are observed, we simply reduce the volume of the injection to the previous, well tolerated level. If a serious event occurs, this is not an indication to discontinue the program, but closer monitoring is necessary. In these cases we will hospitalize the patient on the day the injection is due, and pretreat with diphenhydramine (2 mg/kg) orally 1-2 hours before the injection is given. We will administer 50% less volume of the quantity which triggered a reaction, and observe the patient for the day before discharging later that afternoon. Once a quantity of allergen is found which is tolerated by the patient we will not exceed that level. It may be necessary to adjust the frequency of the injections if it is determined the effects are "wearing off" before the next injection is due. Our clinical impression is these patients often time do very well with the ASIT program, which is why patients who have adverse events need their program modified, not discontinued.

For many atopic patients, immunotherapy is one of the more safe, cost effective and medically effective options for managing their disease. In general it is easy for most owners to administer. It is an excellent choice in large and or young patients where the long term lower maintenance costs are best realized. It is also an excellent choice for the non-seasonal patient where treatment with corticosteroids or cyclosporin on a long-term basis would have medical or financial drawbacks. Consequently it is not as good a choice for the geriatric patient, or patient with short-term seasonal disease. Immunotherapy does not lend itself to starting and stopping (using as needed) unlike the other medical options.

Below is an example of a one vial and two vial induction schedule which we would use for a patient in our office.

Immunotherapy: Induction schedule

It is very important that all injections be given subcutaneously (SQ) and that they be given on schedule. Side effects are rare but may include hives, difficulty breathing, vomiting and weakness. Animals should be watched closely for 1 to 2 hours after each injection. If any adverse reactions (side effects) occur, they should be treated as a potential emergency. Our office and your regular veterinarian should be notified immediately. If a reaction does occur, it does not necessarily mean that desensitization must be stopped, although a change in the dose may be required and the next infection should be given under the direct supervision and observation of a veterinarian. Occasionally, a small lump may occur at the site of the injection. Since this is normal and will slowly resolve, it can be ignored unless it is warm or painful to your pet. If the animal develops recurring painful lumps, then our office should be notified.

Please keep allergens refrigerated at all times. Injections are given only once during the week and a new syringe and needle need to be used each time.

Week volume injected date given comments

1	0.25 cc
2	0.50 cc
3	0.75 cc
4	1.00 cc
5	SKIP
6	1.0 cc
7	SKIP
8	SKIP
9	1.0 cc
10	SKIP
11	SKIP
12	1.0 cc
13	SKIP
14	SKIP
15	SKIP
16	1.0 cc

Booster injections of 1.0 cc are then given every 3-4 weeks although this can vary with each patient.

When you have finished the above schedule, please call for an appointment so that we may reevaluate your pet so that a maintenance program may be started. This usually involves a booster injection every 2 to 6 weeks, depending on the response of your animal. It occasionally requires over 12 months of desensitization before a good response is seen**.**

Immunotherapy: Induction schedule for 2 vial set

It is very important that all injections be given subcutaneously (SQ) and that they be given on schedule. Side effects are rare but may include hives, difficulty breathing, vomiting and weakness. Animals should be watched closely for 1 to 2 hours after each injection. If any adverse reactions (side effects) occur, they should be treated as a potential emergency. Our office and your regular veterinarian should be notified immediately. If a reaction does occur, it does not necessarily mean that desensitization must be stopped, although a change in the dose may be required and the next injection should be given under the direct supervision and observation of a veterinarian.

Occasionally, a small lump may occur at the site of the injection. Since this is normal and will slowly resolve, it can be ignored unless it is warm or painful to your pet. If the animal develops recurring painful lumps, then our office should be notified**.**

Please keep allergens refrigerated at all times

Injections are given only once during the week and a new syringe and needle need to be used each time.

WEEK	VIAL	VOLUME INJECTED	DATE	COMMENTS
1	A & B	0.10 CC EACH		
2	A & B	0.20 CC EACH		
3	A & B	0.40 CC EACH		
4	A	0.60 CC		
6	B	0.60 CC		
8	A	0.80 CC		
10	B	0.80 CC		
12	A	1.00 CC		
14	B	1.00 CC		
16	A	1.00 CC		
18	B	1.00 CC		

Booster injections of 1.00 cc are then given every 2 weeks by alternating between vial A & B although this can vary with each patient.

When you have finished the above schedule, please call for an appointment so that we may reevaluate your pet so that a maintenance program may be started. It occasionally requires over 12 months of desensitization before a good response is seen.