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Feline Immunotherapy

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Feline allergen specific immunotherapy (ASIT) is considered to be a safe and effective treatment for feline atopy. ASIT is defined as the practice of administering gradually increasing quantities of an allergen extract to an allergic subject. The purpose of which is to reduce or eliminate the symptoms associated with subsequent exposures to the causative allergen. ASIT offers an effective and safe treatment option for cats. Reported success rates range for 60 to 78% in feline atopic patients. Additionally, the reported incidence of side effects in feline atopic patients undergoing ASIT is very low and mainly anecdotal. Clin Tech Small Anim Pract 21:157-161 © 2006 Elsevier Inc. All rights reserved.

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Feline allergen specific immunotherapy (ASIT) is considered to be a safe and effective treatment for feline atopy. However, ASIT is often confusing and frustrating for both the clinician and owner as often very subtle changes in dosing and frequency may dramatically alter the level of success achieved with this therapeutic option. Often times ASIT is discontinued because of a lack of information, unrealistic expectations, or improper interpretation of persistent or worsening symptoms.

What is ASIT and How Does it Work?

ASIT is defined as the practice of administering gradually increasing quantities of an allergen extract to an allergic patient; the purpose of which is to reduce or eliminate the symptoms associated with subsequent exposures to the causative allergen.¹ Multiple clinical studies have shown ASIT to be a safe and effective treatment for humans and dogs with atopic dermatitis. In contrast, fewer studies have been performed in feline atopic patients and most information on ASIT in cats is anecdotal. Although the mechanism of action of ASIT in both the canine and feline atopic patient has not been fully elucidated, it is thought to be similar to that seen in human patients. A number of immunologic changes have been documented in humans undergoing ASIT. These include alterations in the quantities and types of inflammatory cells; modifications in the secretion of inflammatory mediators; changes in the types and concentrations of allergen-

specific immunoglobulins; and modulations of T-cell function and cytokine production.^{1,2}

Explaining ASIT to Clients

One of the most difficult tasks is explaining to owners why ASIT would be a beneficial treatment option for their cat. The proposed theory behind ASIT is complex and difficult to comprehend for most owners. Often a simple explanation may help them to understand what ASIT is meant to accomplish. One may start out by explaining that the patient's allergy is an overreaction of the immune system to something in the environment that it perceives as harmful to itself. Whereas allergies in people lead to runny eyes and stuffy noses, allergies in cats lead to increases in grooming behaviors, licking, scratching, skin sores, and ear infections. Such a comparison helps make an abstract concept more concrete. Often cat owners are concerned about shortening their pet's life expectancy with drugs. Explaining that ASIT is a more specific therapeutic option that targets the cells in the body responsible for causing the clinical signs they are seeing and induces tolerance to the offending allergens relieves some of their fears.

Benefits versus Drawbacks of Using ASIT

ASIT offers an effective and safe treatment option for cats. Reported success rates range from 60 to 78% in feline atopic patients.^{3,4} Additionally, the reported incidence of side effects in feline atopic patients undergoing ASIT is very low. A thorough literature search failed to reveal any documented cases of systemic ASIT reactions in feline patients. Anecdotally, reported reactions in cats are rare and primarily consist

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of increased pruritus; although anaphylaxis has been reported in a few cases. It has been reported anecdotally that one cat developed localized pruritus, vomiting, and diarrhea after an injection of 0.3 mL of approximately 20,000 PNU/mL. The cat was taken to an emergency clinic and responded well to treatment. Respiratory distress and gastrointestinal signs have also been anecdotally reported in another cat within 3 hours of an injection. Anaphylaxis appears to be a rare event; although must be considered a theoretical possibility. A pilot study investigating the use of a rush induction protocol reported the development of a localized injection site reaction in 2 of the 4 cats involved in the study.⁵

The initial costs of ASIT may be substantial (ie, allergy testing, initial allergy serum), but once maintenance therapy has been established the costs to the client are minimal. When one compares the costs of other therapeutic options and the monitoring required to maintain these therapies, ASIT is typically less expensive in the long term.

Once the choice is made to begin immunotherapy the clinician or a technician must follow up frequently with the client. Often times a response is not seen for several months once therapy begins and clients are tempted to stop prematurely before the therapy has had time to be effective. Additionally, some owners may notice side effects from the injections and fail to notify the clinician. In such cases the owner may just need a bit of encouragement that they are doing the right thing for their pet. Thus the decision to offer ASIT as a therapeutic option to a client is not to be entered into without thorough evaluation of the client's and clinician's long term commitment to follow through. ASIT requires continual communication with the client and follow up visits. Failure to follow through after beginning ASIT may lead to further frustration on the client's part and cause the clinician to lose a patient.

Use of ASIT in Feline Atopy

Patient Selection

Feline dermatitis that responded to ASIT was first reported in 1982⁶ and since then ASIT has been shown to be an effective treatment for a myriad of clinical syndromes associated with feline atopy. Pruritus, miliary dermatitis, noninflammatory



Figure 1 Atopic cat demonstrating pruritus by rubbing head on owner's sweatshirt. Note the barbed alopecia on lateral thorax lumbar area that has resulted from excessive self grooming. (Color version of figure is available online.)



Figure 2 Atopic cat with barbed alopecia on the caudal thigh, another common location for pruritus in atopic cats. (Color version of figure is available online.)

alopecia, eosinophilic granuloma complex, otitis, pyoderma, and asthma are all commonly recognized clinical syndromes associated with feline atopy.^{3,4,6} Cats may present with one or a combination of clinical syndromes (Figs. 1-4). It must be noted that the above clinical signs are suggestive of but not pathognomonic for feline atopy as there are multiple potential causes for these clinical signs besides atopy, and neither intradermal skin allergy testing nor serum allergy testing are diagnostic for atopy. Proper diagnostics (including cytology, skin scrapes, fungal cultures, and possibly skin biopsies) along with a thorough history are critical to the diagnosis of feline atopy.

Choosing Allergens

Specific allergens should be identified for each individual patient based on a positive allergy test score. Either intradermal or serum allergy testing may be used to identify allergens. Although intradermal skin testing (IDST) is considered the gold standard by many dermatologists for canine atopic patients, IDST in the feline atopic patient is wrought with difficulty. Cats may have very subtle reactions creating a higher incidence of false negative reactions. In feline patients, IDST is difficult to perform and interpret, and some dermatologists report that it has been associated with a higher incidence of anaphylaxis when compared with the canine.³ Additionally, cats must be sedated with minimal stress to permit IDST. Stress responses in cats may be so overwhelming that IDST will be completely negative. In light of these facts, there are multiple veterinary dermatologists that perform solely serum allergy testing in cats and use these tests as a basis for ASIT. Nevertheless the practitioner should be aware that multiple companies offer serum allergy testing and none have published studies that permit one to evaluate their true accuracy levels in feline patients.



Figure 3 Face and head pruritus is also common in feline atopic dermatitis. This photo shows atopic cat with alopecia and excoriations on the face and head. (Color version of figure is available online.)

Regardless of the testing method used, only allergens with positive scores on either IDST or serum allergy testing should be included in the allergy treatment serum. Each testing method provides a guideline as to what constitutes a positive score. In general, the higher the test score the more likely that the allergen should be included in the mixture. Moreover, the clinician should evaluate the patient's environment and history and make sure that the positive scores on the allergy test correlate with this information. For example, if the cat's strongest positive is to dog dander and the owners do not have a dog, or the cat is not exposed to dogs from kenneling or grooming, the test results do not correlate well to the history and the patient should be re-evaluated. Even some strictly indoor cats may have seasonal pollen allergies. Allergens can be transferred into the home on owner's clothing, on



Figure 4 Generalized pruritus may occur and excessive licking may result in erythematous skin and barbered alopecia. (Color version of figure is available online.)



Figure 5 Instructing owners how to administer injections. (Color version of figure is available online.)

other animals, or even through the air conditioner or open windows.

Beginning ASIT

Once the allergens have been chosen and the serum mixed the owner should schedule an appointment to come into the hospital so either the clinician or technician can spend time going over in detail the injection schedule, how to administer the injections and possible side effects (Fig. 5). Such an appointment is critical to the success of treatment and the client relationship because some owners will spend the money to allergy test and purchase the allergy serum and then fail to begin the injections because they do not feel adequately prepared or understand how to follow the schedule. Given the proper guidance and treat incentives, very few owners and their cats cannot manage to administer the injections at home.

Before starting the injections, having the owners practice at home may make the journey more successful. Often times sending home a syringe and telling owners to practice daily for a week by putting the cat on their lap or a table or counter top, giving the cat its favorite treat, then touching the capped syringe to the back of its neck and then giving it a follow up treat will train the cat to like or accept getting the shots. Also allowing the allergen solution to come to room temperature before giving the injection will make the injection less objectionable for many cats.

Owners are instructed to monitor the cat for at least 2 hours after an injection. A written list of side effects to watch for is sent home with each owner but these are discussed in detail verbally as well. Although anaphylaxis is rare owners are told that vomiting, diarrhea, sudden collapse, or difficulty breathing represent an emergency situation and immediate treatment is necessary. More common is an increase in pruritus and if this is exhibited after a shot then the owners are instructed to call before administering another injection. Monitoring the injection site for localized swelling, warmth or hair loss is also important.

Of the various companies that prepare allergy treatment serums, each one proposes a slightly modified version of the injection schedule shown in Table 1. The schedule shows a gradually increasing amount of allergen over a period of several weeks followed by gradually decreasing the frequency of

Table 1 ASIT Schedule

Day	Volume
Vial #1	
1	0.1
3	0.2
5	0.3
7	0.4
9	0.6
11	0.8
13	1.0
Vial #2	
15	0.1
17	0.2
19	0.3
21	0.4
23	0.5
25	0.5
Five day interval	
30	0.5
35	0.5
40	0.5
Seven day interval	
47	0.5
54	0.5
61	0.5
68	0.5
Ten day interval	
78	0.5
88	0.5
98	0.5
108	0.5
118	0.5

injections but leaving the amount of allergen constant. To ensure success, it is important that owners score the cat's level of pruritus before and after each injection throughout the treatment period. Pruritus may be scored on a scale of 0 to 10 with 10 representing the cat's itchiest times. This helps to monitor progress and provides a scale that owners can follow to see that although the cat may still be pruritic it has decreased in intensity. It also aids in adjusting treatment along the way. One can also have owners keep track of whether or not the cat was on additional medications during certain times that they were also on ASIT.

Generally 7 to 10 days after initiating ASIT the owners are contacted to make sure that they are not having any problems administering the injections. Multiple phone calls are made along the way to make sure that the cat is not experiencing any adverse reactions and that the owners are continuing to administer the injections and follow the schedule correctly. A follow up examination is typically scheduled 6 to 8 weeks and then repeated 4 months after beginning ASIT. These are rough guidelines and each client and patient will require varying amounts of monitoring along the way.

It is important to note that the veterinarian must carefully manage and consider client expectations. Unrealistic expectations on the client's part often lead to premature discontinuation of ASIT. Clients must understand that ASIT is not a quick fix to all of their cat's problems. It must be clear that ASIT is a safer, but longer term approach to therapy as opposed to glucocorticoids and other therapies that work

quickly but may have more side effects. Whereas 60 to 78% of cats respond to ASIT, a portion of the cats that improve with ASIT still require additional medications on an intermittent or continual basis. Some feline patients may improve with allergy shots within a month but others may show no improvement for ten months or more. This variable guideline is frustrating and there is no way to be able to predict which cats will respond quickly. Thus, the veterinarian should discuss these issues during the pretreatment conference and prepare the client for the possibility that in some cases this is a life long therapy or at minimum owners should expect to have their cats on ASIT for at least 1 year.

Adjusting ASIT

Adjusting ASIT customizes it for the individual patient and often times makes the therapy more successful. However, making adjustments to immunotherapy is frustrating for many clinicians. There is no strict set of guidelines to follow and each patient may present a new set of challenges. Additionally, even among experts there is some disagreement when adjusting ASIT. Table 2 gives examples of common adjustments that may need to be made during ASIT.

Discontinuing ASIT

There is no absolute answer as to when ASIT should be discontinued. This is true regardless of whether the patient is responding or whether the patient is not showing any improvement. Current recommendations are to encourage owners to continue ASIT for at least 1 year before discontinuing therapy. Improvement may be monitored by the dose and frequency required of additional medications, and the pruritus scores that owners have assigned to their pet during the course of therapy. Thus, even in cats that are not exhibiting marked improvement one can compare the amount of medication or the number of ear infections or sores that the cat had the previous year and if less then there has been some response to ASIT.

In cats that exhibit only minimal to moderate amounts of improvement during the first year of ASIT, the clinician and owner have to decide whether or not continuing ASIT provides therapeutic benefit to the patient. Many of these patients require lower dosages of other medications that may have more side effects while they are undergoing ASIT. In

Table 2 ASIT Adjustment Scenarios

Scenario	Adjustment
Injections every 10 days Itches around day 7	Change injections to every 7 days
Injections every 14 days (0.5mls) Itches after injection for 24 hours	Decrease the amount of injection
Injections every 7 days Itches after injection for 24 hours and begins itching again 5 days after injection	First decrease the amount of injection then increase frequency of injections to every 5 days
Injections every 14 days No break through itching	Change injections to every 21 days

these cats if the injections are not a problem for the owner or the patient, then the recommendation would be to continue ASIT. Those patients that show minimal to moderate improvement on ASIT after 1 year and either the patient or owner have difficulties with the injections should discontinue ASIT.

In patients that exhibit good to excellent response to ASIT after 6 months to 1 year, the recommendation would be to gradually decrease the frequency of the injections over the subsequent year. For example, if the cat's allergies are controlled and it is receiving an injection once every 3 weeks, then the recommendation would be to reduce the frequency of the injections to once every 4 weeks for several months. If the cat's allergies were still controlled for 1 year with no clinical signs attributable to allergy or need for other medications, then the recommendation would be to discontinue the injections and monitor the patient for recurrence of clinical signs.

Concurrent Use of Medications

The use of concurrent medications during both the induction and maintenance of ASIT is controversial. There is no published data on the effect of concurrent medications on the success of ASIT in feline or canine patients. Many patients are uncomfortable and require concurrent medications to maintain a good quality of life during the initial months of ASIT. In these cases the clinician may attempt to taper the medications required each month to assess the effects of ASIT on the patient. Concurrent medications may include antihistamines, corticosteroids, or cyclosporine. The author prefers to use oral as opposed to injectable corticosteroids in these cases as oral corticosteroids are much easier to adjust as they have less residual effect. It is also important to emphasize the need of treating secondary bacterial infections. The use of appropriate antibiotics can often provide the initial relief necessary to make the cat more comfortable without the addition of other therapy.

Rush Allergen Specific Immunotherapy

Rush allergen specific immunotherapy (RIT) is a technique of advancing an allergic patient to a maintenance dose of

an extract over a shorter period of time than that required for the traditional induction period. Typically, this is an 8 hour period as opposed to the 25 days that usually comprises an induction. An effective and safe protocol for RIT has been reported for the canine and human. Additionally, RIT in the canine is associated with a higher success rate than conventional ASIT. A pilot study reported and evaluated the safety of a RIT protocol for 4 feline atopic patients.⁵ RIT is an exciting alternative for the feline patient as successful completion of the prolonged induction period associated with traditional ASIT requires both client and patient compliance. Clients may give up during the induction period because of frustration and cats may object to the injections when they are more frequent. Although the true impact of missed injections on the overall success rate of ASIT is unknown, missed injections may increase the failure rate and the incidence of adverse reactions. Although this study showed that RIT is a feasible alternative in the feline patient, the true incidence of adverse reaction has not been established.⁷

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