What is the best way to approach atopic dermatitis?
Atopic dermatitis cannot be cured, but it can be managed! Each allergy patient is different, and therapy is most successful when it can be tailored to the individual’s needs. Additionally for success, it is important to remember to treat both the atopic dermatitis and the secondary infections that accompany the disorder.

SUBLINGUAL IMMUNOTHERAPY – Not just for clients with needle phobia!
Allergen immunotherapy – either traditional subcutaneous or the newer sublingual form – is an excellent treatment option for atopic dermatitis because it has the potential to “normalize” the patient’s immune response to inciting allergens. Therefore, instead of suppressing symptoms of allergy, as occurs with other treatments for atopy, immunotherapy modifies the underlying immunologic abnormalities of atopic dermatitis. Subcutaneous (injectable) immunotherapy (SCIT) has been the mainstay of allergen immunotherapy in veterinary medicine, but sublingual immunotherapy (SLIT) has recently been evaluated and has become increasingly available.

First, a few important things to know about allergen immunotherapy, whether using SCIT or SLIT:
1. The main goal of allergen immunotherapy is to obtain LONG TERM control of allergy symptoms; it is not an appropriate choice for immediate relief of symptoms. It is important to relay this to clients so they have realistic expectations for the benefits of immunotherapy.

So, when should you recommend allergen immunotherapy for an atopic patient? Although potentially all atopic patients could benefit from immunotherapy, it is particularly useful for those with:

a. severe seasonal symptoms that are not well-controlled with symptomatic therapy
b. year-round symptoms requiring chronic glucocorticoid or cyclosporine for symptom control
c. year-round symptoms not adequately controlled with glucocorticoid or cyclosporine therapy
d. chronic, recurrent skin and ear infections (particularly if antibiotic-resistance is occurring)

2. Allergen immunotherapy should be formulated based on results from intradermal or serologic allergy testing, combined with the patient’s history of allergen exposure and seasonality of symptoms. Response to immunotherapy is believed to be better when allergen-specific immunotherapy is formulated rather than selecting allergens based solely on environmental exposure (regional allergen selection).

3. The strength of the allergen formulation may vary based on the dermatologist or laboratory providing the therapy – this is true for both injectable and sublingual immunotherapy. Due to
the differences in concentration of the allergen immunotherapy, schedules for immunotherapy administration also vary. In general, lower concentrations of allergen immunotherapy need to be given more frequently, whereas higher concentrations may be given less frequently.

4. If serologic testing is performed, the reference laboratory providing the testing is often very helpful in identify pertinent allergens for inclusion in allergen immunotherapy. Additionally, they provide an injection schedule for the client to follow, and are a good resource during allergen immunotherapy if patients require adjustments in their dose (strength or frequency).

5. There are a lot of misconceptions about the success of allergen immunotherapy. On average, there is a 60% response rate (reports vary from 50-80%) for good to excellent results. An easy way to explain patient immunotherapy response to clients, is to give an estimate of 30% of patients have an excellent response, 30% have a moderate response, and 30% have poor to no response.

The success rate of immunotherapy can be increased! It is critical to tailor the therapy to each individual patient. Too often, clients discontinue allergen immunotherapy early in the course of treatment because of exacerbation in allergy symptoms. Ways to improve success include:

a. Maintain good communication with the client.

b. Adjust the dose and frequency of administration based on patient response.
   • For example, with SCIT, if a patient is itchier within the first 1-2 days after the injection is given, consider lowering the dosage. If a patient is itchier 1-2 days before the next injection is given, consider increasing the frequency of administration.
   • For example with SLIT, if a patient’s oral cavity is itchier with administration, consider temporarily decreasing the frequency of administration and/or lowering the dosage.

c. Maintain control of secondary bacterial and yeast dermatitis and otitis.

d. Give anti-inflammatory medications along with allergen immunotherapy.

e. Ask the owner to commit to giving the allergen immunotherapy for at least 1 full year.

**How does administering SLIT different from using SCIT?**

1. Subcutaneous immunotherapy is traditionally administered with a 1.0ml syringe and 27 gauge needle. Owners are typically taught how to administer SC injections at home. The frequency and dose of administration vary. In general treatment begins with an induction phase, during which the concentration and dose of allergen immunotherapy is gradually increased. Once the target concentration and dose is achieved, the maintenance phase begins. In the maintenance phase the same dose of immunotherapy is given every 7-30 days long-term.

2. Sublingual immunotherapy is given with a metered dispensing pump bottle. Usually 1-2 pumps (drops) are administered by mouth two to three times a day. Similar to SCIT, there is often an induction phase in which the concentration of the allergen immunotherapy is “stepped up”. The difference with SLIT is that the dose and frequency the owner administers remains the same (i.e.
2 pumps BID) – the concentration is increased when the client starts their 2nd bottle, and often increased again when they start the 3rd bottle. Usually the 2nd or 3rd bottle is their maintenance concentration, and this is continued long-term.

**What are some advantages of SLIT over SCIT?**

1. SLIT is great for the client who prefers not to administer injections.

2. SLIT generally has an easier dosing schedule, which may increase client compliance – SCIT schedules can be confusing for some owners. Additionally, some owners find it difficult to remember to administer SCIT every “X” days – the routine of BID dosing can be easier to maintain.

3. Some patients respond faster to SLIT than to SCIT – with notable improvement within 6 months.

4. SLIT generally has lower risks of side effects, particularly anaphylaxis. May see an increase in itchiness of the oral cavity, or less commonly increased generalized pruritus.

5. Some patients who failed to respond to SCIT have benefitted from SLIT.

6. Allergen formulation may vary, but SLIT may allow inclusion of a greater number of allergens in the therapy. Additionally, molds can be added to the SLIT formulation without risk of mold proteases degrading pollens, as can be a concern in SCIT formulation.

**MODIFIED-CYCLOSPORINE**

Modified-cyclosporine (CSA) is not a brand new therapy, but is an important medication to consider for management of atopic dermatitis.

**When should CSA be used in patients with atopic dermatitis?**

1. To help control allergy symptoms, while withdrawing patients from other medications in preparation for allergy testing; intradermal and serologic allergy testing can be performed while a patient is receiving CSA.

2. For control of atopic dermatitis while waiting for the benefits of allergen immunotherapy.

3. When patients cannot receive allergen immunotherapy due to owner constraints.

4. When immunotherapy isn’t practical – for example, advanced patient age can be a reason to forgo allergy testing and immunotherapy, since allergen immunotherapy can take 6-12 months to provide benefits.

5. For patients who did not respond optimally to at least 1 year of allergen immunotherapy.
6. When an alternative to steroid therapy is desired, potentially because of unacceptable side effects or a concurrent disease that is complicated by steroid use. Some owners are also very sensitive to the potential side effects of steroid therapy and prefer alternative treatments.

7. For short-term control of seasonal symptoms, or long-term control of year-round allergic dermatitis when other therapies are not effective or have too many side effects.

**Is there a time when glucocorticoids may be preferable to CSA?**
There are several reasons that glucocorticoids may be used instead of CSA. One scenario is the allergic patient with an acute flare in symptoms for which immediate relief is desired – steroid therapy is more likely than CSA to provide fast and noticeable benefits to the patient. A second reason for using glucocorticoid therapy is the relatively low cost in comparison to CSA, which can be cost-prohibitive for some owners with large breed dogs.

**Can a generic form of modified-cyclosporine be used instead of Atopica®?**
Atopica® may be more effective in some animals than generic forms of modified-cyclosporine. Therefore, it is best to start with the brand name product and assess response to therapy. If there is a good response, then potentially consider changing to the generic form and monitor for changes in overall control of the symptoms. If the patient is not as stable with the generic form, it is best to use the brand name. As a side-note, non-modified CSA (i.e. Sandimmune®) is often less expensive than modified-CSA, but should not be used due to significantly lower bioavailability of the product.

**How do you combine CSA and ketoconazole to effectively lower the dose of CSA?**
The combination of CSA and ketoconazole can lead to less predictable blood levels of CSA. Common protocols are modified cyclosporine 2.5-3.0 mg/kg once a day and ketoconazole 2.5-5.0 mg/kg once a day. In some instances the ketoconazole is given a few hours prior to the CSA.

**Helpful hints for managing vomiting after CSA administration:**
Vomiting after CSA dosing is more common in the initial phases of therapy – approximately 1/3 of patients will experience this side effect.

1. Although CSA has higher bioavailability if given 2 hours before/after a meal, many dogs tolerate the medication better when it is given with food, and clinically still have a good response to the medication. Therefore, it is worthwhile to try giving it with food.

2. Decrease the dose by 50% for 1-2 weeks, and then return back to normal dosing regimen.

3. Administer with an antiemetic such as metoclopramide(Reglan®) 0.2 – 0.4 mg/kg q. 12 hours or maripotent (Cerenia®) 2 mg/kg once a day for 4 days.
Once the desired response is achieved, CSA dosing can be tapered for many atopic patients. Start with modified-cyclosporine 5mg/kg (canine) or 7mg/kg (feline) daily for a minimum of 30 days. If well-controlled can:

1. Give the same dose of CSA every other day, then try every 3 days... or even taper to 2 days a week.

2. Give 50% of the daily dose of CSA once a day, and then try to taper to every other day dosing.

What kind of monitoring is suggested when a patient receives long term therapy?
Generally baseline CBC, chemistry, and urinalysis are recommended; FeLV and FIV status should be evaluated for feline patients. A CBC, biochemistry and urinalysis with urine culture are recommended every 6 -12 months for chronic therapy.

Blood levels of CSA are generally not indicated in dogs. Exceptions are patients that are not responding optimally, patients experiencing adverse effects, or patients receiving higher than normal CSA doses. In these instances, a trough level can be obtained (12 hours post-pill if BID dosing, 24 hours post-pill if once daily dosing). In some patients, a peak level (2 hours post-pill) may be helpful as well. Blood levels should be evaluated 2 weeks after initiation of the medication to allow the levels to stabilize.

Some cats may be “super-absorbers” and can achieve very high blood levels of CSA. It is worthwhile to perform CSA blood levels for cats to determine whether they are achieving higher than the target levels. Animals with significantly elevated blood CSA levels may be more prone to infection – notably, in cats, toxoplasmosis has been a concern for naïve pets. Cats receiving CSA should be kept indoors and fed cooked meat.

**OCLACITINIB (APOQUEL®)**
This new drug has a unique mechanism of action – it is a janus kinase inhibitor (specifically JAK-1), which inhibits cytokines (IL-2, IL-4, IL-6, IL-13, IL-31) that are associated with itch and inflammation. To date, oclacitinib has only been approved for use in dogs.

**How is oclacitinib dosed?**
Oclacitinib is dosed at 0.4-0.6mg/kg twice a day for 2 weeks, then once a day. The medication is supplied in tablet form, and can be given with or without food (food does not affect bioavailability).

**Age matters**
Oclacitinib should be given to patients greater than 1 year of age. When administered to puppies under 1 year of age, signs of immune suppression were seen. Specifically, young dogs receiving oclacitinib are at greater risk of developing demodicosis (this was not seen in adult dogs), and possibly pneumonia.
Good to know...

1. Rapid onset of action: oclacitinib starts to provide relief to patients within one hour of dosing.

2. Minimum inhibition of canine CYP450 enzymes at recommended doses.

3. At this time, it appears that oclacitinib does not interfere with intradermal allergy testing.

4. No contraindications for vaccination while receiving oclacitinib.

Precautions / side effects for oclacitinib

1. Possible increased risk of infection (interdigital furunculosis, papillomas, demodex).

2. May exacerbate neoplasia. This is based on a theory that decreased immune surveillance may lead to lack of protection against tumors.

3. Should not be used in patients under 1 year of age; or in breeding, pregnant or lactating dogs.

4. Vomiting / diarrhea

5. Increased risk of interdigital furunculosis.

6. Early clinical pathology changes appear to normalize over time. There can be a mild dose-related decrease in hemoglobin, hematocrit and reticulocyte counts. Additionally there may be a decrease in lymphocytes, eosinophils and basophils. Total protein can be decreased over time as well.