

DERMATOLOGY CLINIC FOR ANIMALS LAS VEGAS

Las Vegas Animal Emergency Clinic
5231 W. Charleston Blvd.
Las Vegas, NV 89146

Phone: (702) 821-1002 Fax: (702) 821-1007

Two Locations:

Animal Emergency Center
3340 E. Patrick Lane
Las Vegas, NV 89120

Phone: (702) 434 - 1002 Fax: (702) 434 - 1058

Visit us on the Web at www.dermvetvegas.com

The Pros and Cons of Cyclosporin in the Treatment of Atopy

One of the most frequent questions we receive from referring veterinarians and clients at our office is "what do you think of cyclosporin, and does it work for the treatment of atopy?" We have been using cyclosporin for the treatment of refractory atopic cases since 1996. Like all of our therapeutic options for atopy, it has both pros and cons.

Cyclosporin is a fat-soluble cyclic polypeptide derived from the fungus *Tolypocladium inflatum* gams. It was originally developed for the prevention of organ transplant rejection. Its use, however, has been expanded in both human and veterinary medicine. It affects primarily T cell activity and interleukin production. The drug is absorbed best when in a microemulsified formulation. It is now available and approved for veterinary use under the brand name Atopica (Novartis Animal Health). The human counterpart drug is Neoral or the generic product Gengraft.

When used for atopic patients, we generally expect to see a favorable response within the first two weeks, although some patients are reported to require four to six weeks to respond. It has a relatively low

toxicity, but the most common side effect that we see is gastrointestinal upset, especially vomiting. The drug has maximum absorption when given on an empty stomach, although giving the drug with food may decrease the incidence of vomiting. Less common side effects which are reported and which we have seen include gingival hyperplasia and papillomatous (wart-like) growths on the skin. The starting dose is 5 mg/kg orally daily. If improvement in clinical signs is seen, the dose may be decreased to every other day usage or less. Although reported, we do not



often find patients whose symptoms are able to be adequately controlled at a cyclosporin dose of less than 5 mg/kg every other day. We also do not, in general, add other drugs such as ketoconazole to increase blood levels of cyclosporin due to our concerns of increased liver toxicity. In addition to ketoconazole,

other drugs reported to decrease the metabolism of cyclosporin (and thereby increase its blood levels) include itraconazole, fluoroquinolone antibiotics, calcium channel blockers, erythromycin, metoclopramide and others.

When deciding on appropriate therapy for an atopic patient there are many factors which should be considered. The severity of the disease, the duration (short-term sea-

sonal vs. year round) and the age of the patient are some of the important variables. When treating atopic dermatitis, we consider basic supportive care to include frequent baths (which wash allergens off the coat and so reduce percutaneous absorption), antipruritic sprays or conditioners, antihistamines and essential fatty acid supplementation. Unfortunately, there are many patients for which this approach is inadequate in controlling pruritus. In those cases, the remaining treatment options are systemic corticosteroids, allergen specific immunotherapy (desensitization) and cyclosporin. Steroids offer the fastest and least expensive relief but obviously have the most long-term side effects, which are well known. Allergen-specific immunotherapy is the safest long-term option but often requires several months before improvement is seen. This approach has a greater upfront cost because of the expense of allergy testing, but maintenance therapy is less costly. Cyclosporin is less toxic than steroids, but there are reports of cases of systemic infections such as fa-

tal toxoplasmosis and atypical mycobacteriosis in cats treated with cyclosporin. Additionally, chronic immunosuppressive therapy such as cyclosporin may predispose patients to development of neoplasia due to suppression of immunosurveillance. Long-term therapy with cyclosporin remains the most expensive medical option for atopy.

In our practice, our philosophy is to consider cyclosporin to be a temporary therapy in most patients. We like the fact that this is one of the few drugs which can control pruritus without interfering with results of intradermal allergy testing. We often will use cyclosporin during the corticosteroid withdrawal time prior to this test. In addition, we can use the drug during the induction phase of immunotherapy until the positive effects of desensitization are seen. Some patients are on

cyclosporin and steroids together, so that a steroid-sparing effect may be seen. We will also occasionally use this drug in patients judged too old in which to perform intradermal allergy testing, or which do not respond to allergy desensitization. And finally, we will use cyclosporin long term in cases of refractory pruritus. Our concern is for animals inaccurately diagnosed as having "refractory atopy" which are treated with cyclosporin life-long when, in fact, they had food hypersensitivity, scabies, cheyletiella, dermatophytosis,



bacterial pyoderma and/or Malassezia infections. We have seen examples of all of these cases, and long-term cyclosporin would have been an inappropriate, expensive and potentially

harmful choice. In appropriately selected patients, however, cyclosporin is a welcome medical option for the treatment of atopy in both the dog and cat.

Bibliography

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