



scivac

SOCIETÀ CULTURALE ITALIANA
VETERINARI PER ANIMALI DA COMPAGNIA
SOCIETÀ FEDERATA ANMVI

in collaborazione con



Close window to return to IVIS



RICHIESTO ACCREDITAMENTO

scivac

56th INTERNATIONAL CONGRESS

organizzato da  certificata ISO 9001:2000 

RIMINI 1st-3rd June 2007
PALACONGRESSI DELLA RIVIERA DI RIMINI

INFORMATION
SCIVAC Secretary

Palazzo Trecchi, via Trecchi 20 Cremona
Tel. (0039) 0372-403504 - Fax (0039) 0372-457091
commscientifica@scivac.it www.scivac.it





In: 50° Congresso Nazionale Multisala SCIVAC, 2005 – Rimini, Italia

Immunosuppressive therapy – Art or Science

Dr.med.vet.Dr.med.vet.habil. Ralf S. Mueller, DipACVD, FACVSc
Ludwig-Maximilians-University, Munich, Germany

First we will cover the more benign ways of downregulating the immune system:

- *Vitamin E* is an antioxidant and as free radicals are thought to play a role in many types of immune-mediated inflammation and vitamin E successfully deals with these radicals, it has been used in a number of inflammatory diseases. It is administered at 400 to 800 Units daily.
- Scott and Miller reported essential fatty acid supplementation with *omega 3/omega 6 fatty acids* as an alternative to vitamin E for dogs with DLE. I have only few dogs with immune-mediated skin disease that seem to benefit from fatty acid supplementation.
- A combination of *tetracycline and niacinamide* (vitamin B3) at 250 (if the patient is <15kg) -500mg (if the dog is >15kg) q 8 hours has been reported to treat a number of immune-mediated diseases such as lupus erythematosus, bullous pemphigoid or sterile granulomatous disease. We use trial therapy with this combination for 6-8 weeks. We have reasonable success with that combination in about half of our patients with discoid lupus erythematosus, patients with pemphigus foliaceus have a much lower success rate (approximately 30%). If this combination works, we usually try to replace it with doxycycline at 5 mg/kg once to twice daily for convenience reasons.
- *Topical steroids* (typically in the form of a roll-on containing a steroid and DMSO) is used in dogs with nonulcerated skin and focal disease. The drugs are absorbed extremely quickly and if the dog does not lick the area for 5-10 minutes, sufficient absorption has occurred. Feeding or walking the dog directly after application of the roll-on may be beneficial. The disadvantage with topical steroids is the thinning of skin seen after chronic use. In these patients, trauma leads rapidly to bleeding and wound healing is suppressed in these areas.
- *Tacrolimus* is a newer drug absorbed through intact epithelium. In dogs, we use it most commonly for the treatment of localized immune-mediated disease, particularly discoid or cutaneous lupus erythematosus, and for the treatment of anal and perianal fistulae. The topical is very expensive, but needs to be applied in very small amounts only once to twice daily.

Now we come to the more extreme suppression of the immune system:

- Before you think about immunosuppressive therapy you must be sure about your diagnosis. It can be very dangerous for your patient to start immunosuppressive drugs just because history and clinical examination lead you to the diagnosis of pemphigus. If the animal has an infectious disease (fungal, bacterial or parasitic), it can rapidly deteriorate and even die. **There is no place for trial therapy in immune-mediated disease** (!) (except may be in the case of a patient facing euthanasia otherwise).
- The second pitfall is a possible secondary infection. I regularly see patients with diagnosed pemphigus foliaceus and concurrent bacterial or even fungal infection. These patients need to be recognized and treated for both conditions.
- Another problem with immunosuppressive therapy is the fact that is impossible to give you a good general purpose recipe. Every dog or cat reacts differently to each of the drugs mentioned below. Immunosuppression is an art requiring instinct, sensitivity and experience as well as the theoretical knowledge.

Glucocorticoids

- All of my patients with uncomplicated pemphigus receive prednisolone as the first agent. This drug is inexpensive, relatively safe, has a fast onset of action and is easy to monitor. Thus expensive laboratory monitoring is usually not necessary.
- Induction dose is 1 - 2 mg/kg twice daily. After two weeks, the patient needs to be reexamined. If significant to full remission is not achieved within that time, it is unlikely that the animal will do well on glucocorticoids alone and other drugs have to be added. About 30 - 40% of the patients with pemphigus will respond to glucocorticoid treatment.
- Once remission is achieved, the dose is tapered down slowly (over about 10-20 weeks) to a minimal maintenance dose. The lower the dose the slower the tapering should be.
- Semi-yearly to yearly monitoring with blood samples and urine cultures as well as occasional ACTH response tests are performed to monitor side effects such as urinary tract infections (subclinical UTI's were present in 40% of canine patients treated with long-term corticosteroids independent of the dose in an American study), adrenocortical suppression etc.

Azathioprine

- Azathioprine competes with purin in the synthesis of nucleic acids leading to nonfunctional nucleic acid strands that prevent the proliferation of dividing cell populations. It also inhibits T lymphocyte-dependent antibody synthesis and cyclo-oxygenase as well (and thus production of proinflammatory prostaglandins).
- The use of azathioprine in cats is not recommended.
- The canine dose is 50 mg/m² or 2 mg/kg once daily initially. Once remission is achieved, you can give the medication every other day for 4-6 weeks and then taper in small steps, keeping the patient on each dose for 1-2 months. As with all cytotoxic drugs frequently used in veterinary dermatology, there is a lag period (the period from start of therapy to first signs of improvement) of up to several weeks. For this reason azathioprine is commonly used in conjunction with prednisolone for the first weeks or months.
- Haematological and gastrointestinal side effects are most common. Vomiting and diarrhoea can often be avoided by giving the drug with food or lowering the dose. Hepatotoxicosis can be severe and of acute onset (within the first 10 days of treatment) in individual patients. Initial chemistry screens may be performed before and after 1, 2 and 4 weeks of therapy. Easier to overlook, but as serious is the bone marrow suppression which occurs in some patients on treatment. I evaluate complete blood counts (including platelet counts) for leukopenia, anemia and thrombocytopenia before treatment, after week 1, 2, 4, 8, 12 and every 3 months thereafter.
- Another possible side effect is an increased susceptibility to infections due to the immunosuppression. If a patient previously in remission suddenly shows clinical signs of disease, evaluate the possibility of demodicosis (skin scrapings), bacterial or fungal infections (cytological samples, Wood's light examination, cultures). Not always is a relapse due to insufficient immunosuppression! Sometimes, additional biopsies may be needed.

Chlorambucil

- Chlorambucil is an alkylating agent, which forms covalent bonds with nucleic acids thus crosslinking or breaking DNA strands. It suppresses antibody production.
- Chlorambucil is used alone or more commonly in conjunction with other drugs. It is one of the safest cytotoxic drugs, but its lag period is longer than that of azathioprine (up to 8 weeks).
- It is given at 0.1-0.2 mg/kg daily until the patient is in remission. Then it is administered every other day and tapered in a similar fashion to azathioprine.
- Side effects are gastrointestinal upset and bone marrow suppression. Monitoring is similar to azathioprine. Hepatotoxicosis is not of major concern. Seizures can occur rarely due to chlorambucil therapy.

Aurothioglucose

- Parenteral gold compounds are absorbed rapidly and reach peak levels at 4-6h. Rising serum values are noted for up to 12 weeks, the half life is about 6 days.
- Parenteral gold accumulates at highest concentrations in the reticuloendothelial system (bone marrow, liver, spleen) and in the kidneys and adrenal glands. It is excreted by the kidneys.
- Aurothioglucose reduces the release of inflammatory mediators (lysosomal enzymes, prostaglandines, histamine) and inhibits a number of enzymes (esp. lysosomal enzymes). It interferes

with antibody-synthesizing cells. Gold also has an inhibitory effect on DNA- RNA- and protein synthesis *in vitro*. However, the exact mechanisms of action in immunosuppressive therapy are unclear.

- Diarrhea, bone marrow suppression and kidney failure are the most common side effects.
- Some specialists recommend a test dose of 1-5 mg IM, thereafter 1mg/kg is given weekly until remission. Then fortnightly and later monthly injections can be used. The lag effect is up to 12-15 weeks.
- Some dogs with pemphigus will have seasonal relapses (sun-induced?, allergy-induced?).
-

This manuscript is reproduced in the IVIS website with the permission of the Congress Organizing Committee

Leading the way in providing veterinary information

