

## Allergic and Atopic Dermatitis What's New, What Works

### Dr Rob Hilton

*BVSc (Hons) MACVSc (Canine  
Medicine) Cert.VD MRCVS*

[www.skinvet.org](http://www.skinvet.org)

Mob. 0433-853560

[rob@skinvet.org](mailto:rob@skinvet.org)



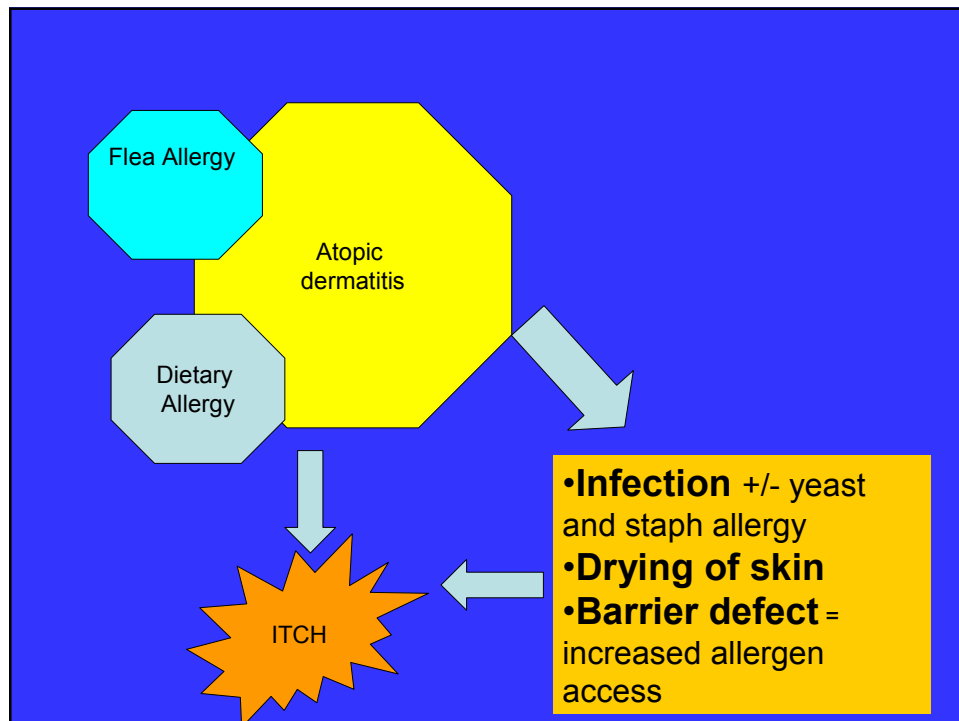
## Chronic Pruritus Problem and Opportunity

- In chronic or relapsing cases, your next dose of "pred" will be less effective than your predecessor
- "Just pred" approach is MAJOR source of client loss
- No dermatologist can do these cases in < one hour. Don't try
- Be systematic
  - History
  - Tape and scrape every case
  - Protocol based. Don't vary for individuals
  - Have and explain plan A and B



## What is Atopic Dermatitis

- *Genetically predisposed T cell disease*
- *Inappropriate response to environmental allergens*
- *Primary or secondary barrier defect.*
- *Most common veterinary disease in Australia*



## Diagnosis of Atopic Dermatitis

1. Typical Signs
2. Exclusion of other diseases
  - Fleas
  - Food
  - Sarcoptes
  - Infection
  - CATS – Ringworm and psychogenic

Presentation and signs are often clinically indistinguishable from “DIETARY ALLERGY”.  
Alternative or concurrent diagnosis

## Criteria for the diagnosis of atopic dermatitis Favrot 2009

1. Onset of signs under 3 years of age
2. Mostly indoors
3. Glucocorticoid-responsive pruritus
4. Pruritus without lesions at onset
5. Affected front feet
6. Affected ear pinnae
7. Non-affected ear margins
8. Non-affected dorso-lumbar area

Five satisfied criteria sensitivity of 85% specificity of 79%  
Six criteria sensitivity 89% Specificity 58%  
Exclusion of ectoparasites increases specificity



Flea bite allergy



Sarcoptes

## Cutaneous adverse food reactions “Food allergy”



## Cats - Atopic Dermatitis



- Miliary Dermatitis
- Allergic Alopecia – Pruritus
- Eosinophilic plaque
- Eosinophilic Granuloma Complex
- "Head and Neck Pruritus"
- Urticaria Pigmentosa
- Persian facial dermatitis?

All have similar etiologies  
Similar diagnostic strategy  
Similar therapeutics

Hnilica 2009

## Caution

- Atopic dermatitis (or dietary allergy) may present as otitis without other symptoms and occasionally unilateral!
- Hydrolysed diet trials will miss up to 25% of food allergies
- In cats, dermatophytosis may present as a pruritic dermatitis. Only 50% of *M. canis* strains are Wood's Light positive.



Don't get caught  
Toothbrush test  
all suspect cats

## Five + 1/2 Pillars Approach to Atopic Dermatitis



### 1. Symptomatic immunosuppressive drugs

- Corticosteroids
- Cyclosporine

### 2. Allergen specific immunotherapy (ASIT) "Desensitization"

### 3. Infection control

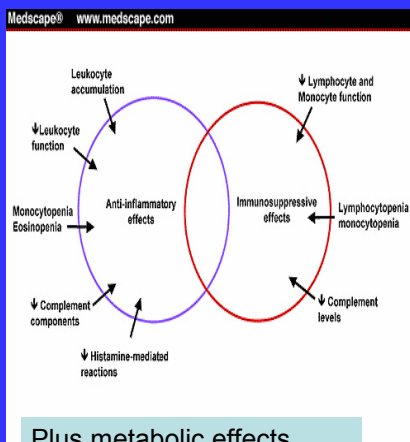
### 4. Skin hydration and barrier repair. Moisturizing

### 5. Control other allergies (diet , fleas)

### 5&1/2.

- Essential fatty acid therapy
- Allergen avoidance
- Antihistamines ??

## Corticosteroids



Plus metabolic effects through receptors on most tissues

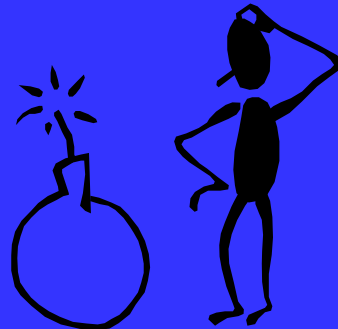


## Corticosteroids



- Highly effective
- Failure to respond to corticosteroids usually indicates that either:
  1. The diagnosis of atopic dermatitis is not correct
  2. The atopic dermatitis is complicated by secondary infection

- There is no “safe” dose of prednisolone but dogs maintained on 0.25-0.5 mg/kg twice weekly have a reduced risk of side effects
- The cheap cost of prednisolone may soon be overtaken by the cost of it's side effects



## Hemodynamic effects of methylprednisolone acetate in cats.

Ployngam T et al , (2006)

- 5mg/mg methylprednisolone acetate (MPA)
- Substantial increase in serum glucose concentration at 3 to 6 days after administration.
- Plasma volume increased substantially (> 40% in 3 cats)
- Analogous to the plasma volume expansion that accompanies uncontrolled diabetes mellitus in humans.

**MYTH** – That Cats are resistant to corticosteroid side effects

They just need higher doses to suppress allergy!

## Do Not Use !!!

- Dexamethasone to begin an anti-inflammatory course of prednisolone. No significant difference in onset of action.
- Depot corticosteroid injections of any sort in dogs.
  - Immunosuppressive
  - Cant be withdrawn







## Corticosteroid Sprays

- Hydrocortisone aceponate 0.584 mg/ml (Cortavance®)
- Triamcinolone acetonide 0.015% (US-Genesis®) or compounded
- **Compounded 0.025% budesonide in moisturizer**
- Good efficiency
- Issues with dry or broken skin
- NOT a cure-all!
- NOT a free ride



## Creams, ointments and Lotions

- Particularly with potent corticosteroids, risk of skin thinning and systemic absorption.
- Lower potency hydrocortisone preparations during maintenance



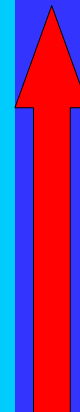
Colbetasol propionate 0.05% -0.1%

Mometasone 0.1% (Elcon) , Betamethasone dipropionate (Diprosone)

Betametasone valerate (Celestone, Betnovate)

Triamcinolone (Panolog Aristocort)

Hydrocortisone

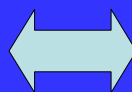
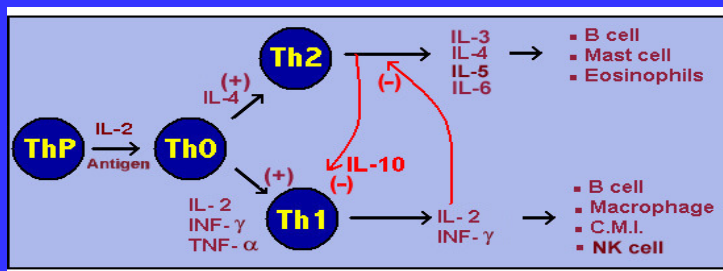


# Cyclosporine

- Lag period of about 2-3 weeks
- 75-85% of cases get 75-85% better within 6 weeks

- Hepato/nephrotoxic side effects generally not recognized in dogs.
- Reversible gingival or cutaneous papilloma (more commonly bacterial, occasionally viral)
- Hirsutism
- Non interference with intradermal allergen testing
- Significant minority may go into remission if suspended.
- Used clinically in diabetic dogs

## Cyclosporine inhibits cytokine production, especially interleukin-2



## •Cyclosporine and Canine Atopic Dermatitis

### • Perceived failures?



- Trialed for < 6 weeks
- Infection
- Owner expectations and compliance
- Tapering failures. 2 days on and 1 day off for 4 weeks BEFORE trying EOD**
- Something other than atopic dermatitis
- One of the 25% that don't respond

## Vomiting and Cyclosporine

1. Give initially with food
  2. If vomits, freeze capsule
  3. If still vomits, ½ dose for 3 days and give metacloprimide 30 mins before.
  4. Discontinue metocloprimide after 14 days
- Metocloprimide moderately increases cyclosporine blood levels and the food does not decrease clinical efficacy

## Interactions with other drugs

### Cytochrome P450 3a

- Catalyses metabolism of many drugs

### P-Glycoprotein

- Active transport pump
- Gut, brain, kidney, liver

#### Ketoconazole

50-70% dose decrease  
@ 10mg/kg KTZ

#### Ivermectin group

Death risk

•Phenobarbitone induces hepatic Cyt P450 3a Decreases levels of Cs-A = increase dose Cs-A by 25%

## Cyclosporine in Cats for Atopic Dermatitis

- FIV/FelV negative
- No evidence of systemic disease
- Rule out of other pruritic diseases:
  - ✓ Flea allergy
  - ✓ Mites
  - ✓ Pyoderma & Malassezia
  - ✓ Food reactions
  - ✓ Dermatophytes
  - ✓ Pemphigus
  - ✓ Psychogenic
  - ✓ Neoplasia

- Very good response rate
- 25mg/cat daily for 1-2 months => every 2-3 days
- Monitor for infectious disease
- Widely used off label
- Much lower rate of serious side effects than corticosteroids (Diabetes, Heart Failure)
- Main reported side effects = GI disturbances and wt loss. Most cases not severe enough to stop usage

## Cyclosporine and Feline Toxoplasmosis



- Uncommon complication
- New infections more important than re-activation of latent.
- Sero-negative cats at higher risk
- No evidence of re-shedding of oocysts. Only shed for a few weeks
- Cats that hyper-absorb cyclosporine at higher risk

### •Prevent new infections

Cook meat  
Stop hunting  
Eliminate rodents

### •30 day CsA blood level

EDTA sample whole blood  
24 hours post pill  
Should be 200-500ng/ml and not in 1000's

## When do I use ?

### Prednisolone

- **Short term** to break itch scratch cycle
- **Pulse 3-5 days** for flares
- < 2x week in combo if **NOTHING else works**
- **Never alone**

### Cyclosporine

- When **prednisolone reliant**
- **Severe cases awaiting allergen test**
- **Never alone.** Always part of combo

## Results of allergen-specific immunotherapy in 117 dogs with atopic dermatitis. [Schwab](#)

[J, Bennett JE, Dow K, Nielsen DL, Vet Rec.](#)  
2006 Jan 21;158(3):81-5.



“The success of the treatment of 117 dogs with atopic dermatitis with allergen-specific immunotherapy for up to 48 months was assessed. An excellent response (remission with exclusive immunotherapy) was recorded in 18 of the dogs, **a good response** (more than 50 per cent reduction in medication and improvement of clinical signs) was recorded in 57, a moderate response was recorded in 24 and a poor response in 18.”

## Atopic dermatitis and atopic-like dermatitis

- Not all dogs “atopic” dogs have demonstrated IgE against common environmental allergens

Prelaud 2007

- Food allergy excluded
- Typical signs
- Two negative intradermal tests
- Negative serological test

## Allergen Specific Immunotherapy ASIT

Set the goal posts:  
2/3 get 50%+ better !

- The majority of cases will BENEFIT from ASIT BUT MAY require adjunct symptomatic therapy, including corticosteroids, for at least part of the year.
- Low cost means of long term control with minimal risks of side effects.
- Some cases may go into spontaneous remission



## Infection Control- Vital !



- Infection significantly adds to the pruritus induced by allergy.
- In some cases, good infection control may be sufficient to keep the patient below the pruritic threshold.
- Atopic patients suffer from reoccurring infections because:
  - Increased bacterial adhesion
  - Altered local defense compounds and structure
  - Defective cell mediated immunity
  - Side effects of corticosteroids and cyclosporine(??)
  - Self trauma

# Infections

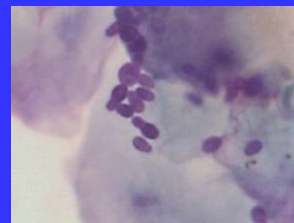
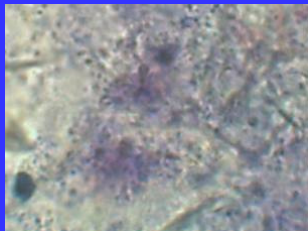


Always scrape and tape

Every case  
Be systematic



# Infections





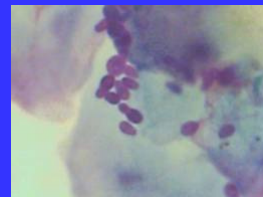
## Tips for infection control



1. Treat any superficial bacterial/Malassezia infections systemically for at least 3 weeks or 10 days beyond clinical cure.
2. If bacterial infections re-occur straight away after systemic therapy, the duration of therapy may not have been long enough.
3. Reoccurrence 2-4 times a year best managed by repeated full course of antibiotics and topical therapy. More frequently re-occurring cases can be managed by weekend therapy

## Options for Malassezia treatment and control

- Topical miconazole (Daktarin ®), Hydrozole ® clotrimazole and hydrocortisone. Daily to treat, 2-3x week to hold
- Itraconazole (Sporonox ® ) 5-7mg/kg 2 consecutive days/week for 4 weeks
- Ketoconazole or Fluconazole 5-7mg/kg daily for 4 weeks
- 2% acetic acid wipes or footbaths



### Malassezia hypersensitivity

- Demonstrated by ID test
- Immunotherapy

# Systemic antibiotics for Pyoderma

## First generation cephalosporins (e.g. cephalexin)

Spectrum= gram positive bacteria, many anaerobes and a some gram -v's

In Australia, low resistance *S. pseudintermedius*. Expect resistance to rise!

The **dermatology** dose rate of cephalexin is 25mg/kg+ BID. Limited evidence 30mg/kg SID

Moderately good intracellular penetration.

About 5% of dogs will vomit on cephalexin.

## Third generation cephalosporins Cefovecin (Convenia®)

**Wider activity against gram negative bacteria**

**Blood levels above the MIC90 for cephalosporin susceptible stains of *S. pseudintermedius* for 14 days (in dogs and cats only) at the label dose.**



## Amoxicillin clavulanate

More costly.  
For ceph vomiting

## Potentiated sulphonamides

Previous high resistance  
Drug reactions (esp. Doberman).  
Renewed role in treating resistant staphylococci?

## Lincosamides (lincomycin clindamycin) Macrolides

(clarithromycin azithromycin)  
75% staphylococci sensitive.  
Good intracellular levels  
Bacteriostatic and resistance can develop quickly

## Tetracyclines

Bacteriostatic  
Poor penetration into skin.  
Moderate resistance  
Mildly immunosuppressant.

## Fluoroquinolones

- Resistance is rising.
- Ineffective against anaerobes and streptococci.
- Good penetration into skin
- Concentrated intracellularly.
- Activity related to peak blood levels, so don't divide the dose.
- Joint damage in growing dogs.
- Reserved for resistant cases where indicated by culture and sensitivity.

## Hydration and restoring the epidermal barrier



Major cornerstone of managing human atopic dermatitis



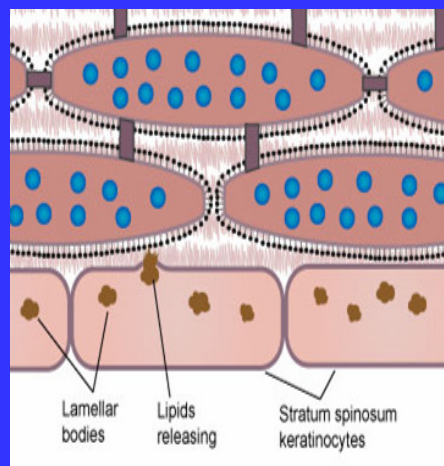
## Bricks and Mortar model of the Epidermis



- Surface hydrophobic film
- Keratinocytes in a “sea” of lipids
- Tight junctions between keratinocytes



- Adhesion and proliferation of microorganisms
- Ingress of allergens
- Drying via increased transepidermal water loss



## Epidermal barrier defects: Primary or secondary ?



### Genetics

- Fifty-four genes differentially expressed in canine AD.

### Atopic dog skin has:

- Decreased ceramide levels
- Increased cholesterol
- Disturbed extrusion of lamellar bodies by keratinocytes
- Increased trans-epidermal water loss
- Altered defensins

## Stratum Corneum Lipids

- 20% of volume of SC is lipid
- Sphingolipids 50%
- Cholesterol 25%
- Free fatty acids 10-20%

### Phytosphingosine

- Mainly found in plants
- Occur in mammalian cells
- Similar properties (?)

Ceramides

Ceramidases

Sphingosines

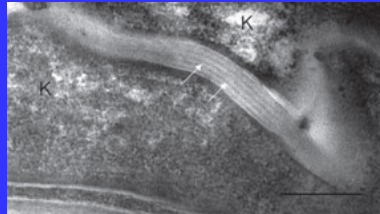
Recycling

### Sphingosine properties

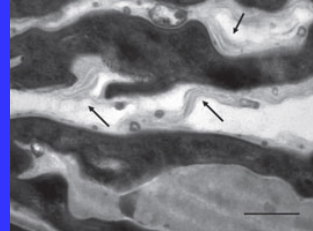
- Antimicrobial
- Barrier
- Immunomodulatory

## Lipid Lamellae Stratum Corneum

Marsalla 2010



Normal dog non  
lesional stratum  
corneum.



Atopic dog non  
lesional stratum  
corneum.

**Abnormal structure exacerbated  
by allergen challenge**

## Moisturizers

### Hygroscopic ((humectant) agents

- Attract water into stratum corneum.
- Urea, glycerin, lactic acid and propylene glycol.

### Emollients (Paraffin/mineral oil)

- Decrease epidermal water loss
- Form a barrier between skin and potential allergens.



### Moisturizers

#### •Paws NutriDerm 1:2 spray

•Propylene glycol 25-33% spray

•Sorbolene (glycerin and paraffin oil + additives)

•Alpha Keri bath oil 1:50 spray

### Bathing and wetting the skin

Benefit or harm (?)

Emollients may be MORE effective without bathing



## Spingolipid moisturizers

Some studies in humans to indicate superiority

Optimal lipid balance yet to be determined in humans & dog.

Veterinary placebo controlled studies lacking

Good clinical results



Add 200ml tube to 400ml water.

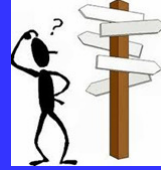
## 0.025% BUDESONIDE Spray

- Active steroid in Rhinocort spray
- Reduced systemic absorption ?
- In 30% propylene glycol and 10% glycerin base
- Compounded
- Initial results = 1x week can maintain



## Barrier Repair Therapy - Conclusions

- Topical and oral lipid complexes alter diseased skin structure and composition resulting in improved barrier function
  - Decreased doses of corticosteroids and cyclosporine
  - Increased immunotherapy efficiency
  - Decreased number of infections
  - Cost effective
  - Low toxicity
  - Not a monotherapy “cure”



## Ancillary Therapy - Antihistamines

- Some dogs may respond to different antihistamines. Several may need to be trialed (individually) for 10-14 days.
- In the author's experience, <10% of dogs show some response to antihistamines.
- Trial anti-histamines as a drug sparing agent once a base-line of control has been achieved with drug therapy and while awaiting the benefits of immunotherapy.



## Ancillary Therapy – Essential fatty acids



- Optimal 3:6 ratio unknown
- Omega 6 improve barrier, Omega 3 anti-inflammatory
- Lower doses of drugs = decreased risk of side effects

- Don't expect control with fatty acid therapy alone.
- A lag period of 6-12 weeks
- Synergism between fatty acid and antihistamines ?

### The “Neo-classical” Roadmap Repeated courses of steroids Now NOT on pred. Signs fit Favot criteria

- Elimination trial for fleas and sarcoptes
- Treat secondary infections.
- No topical or systemic steroids
- Moisturize
- Begin food trial



**Allergen test within 2 - 3 weeks.**

- 6-8 week food trial with RE-CHALLENGE
- Steroids can be used intermittently but stop 10-14 days before re-challenge

**Diagnosis of atopic dermatitis.  
Make vaccine as part of treatment.**



## Thank you and any questions

- ✓ References available on request

