Clinical approach to the pruritic cat

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When dealing with cats with skin disease, it is important to understand that cats are not small dogs. The same cause may elicit different reaction patterns in different cats.

As Hobi et al (2011) in a large multi-country study of 502 pruritic cats concluded ***"many diagnoses presented with similar lesional patterns, a thorough clinical workup is required for establishment of a specific diagnosis."***

Cats are often difficult to pill, resent bathing, fail to eat elimination diets, hunt and steal food and love to remove topical medication by licking as soon as it is put on.

The principal causes of feline pruritus are listed below:

Common

Allergies and ectoparasites
- Flea bite allergy
- Food allergy (and on rare occasions, non immune-mediated adverse food) reactions
- Atopic dermatitis
- Mosquito hypersensitivity
- Reactions to mites (*Otodectes, Cheyletiella, Notoedres, Sarcoptes*)

Infections
- Bacterial pyoderma (almost always secondary)
- Dermatophytosis
- Feline Herpes infection (especially nose and face)
- Malassezia (especially Rex and Sphinx)

Less Common

Ectoparasites
- Feline demodecosis The contagious short-bodied *D. gatoi* is commonly recognised in Europe and North America. This mite is uncommon in Australia but individual case reports do exist
- Lice
- Infestation with *Trombicula* spp

Immune mediated disease
- Pemphigus foliaceus
- Drug reactions
- Sebaceous adenitis
- Lymphocytic mural folliculitis

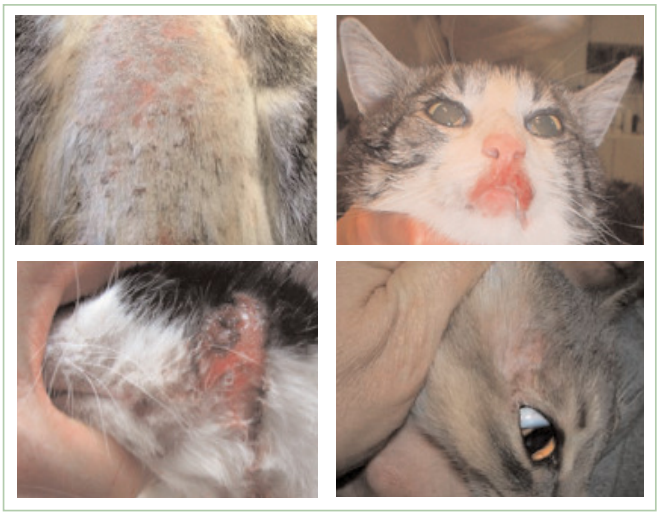
Neoplasia
- Epitheliotropic lymphoma
- Squamous cell carcinoma (common neoplasm, uncommonly pruritic)
- Feline mast cell tumours/Mastocytosis

Idiopathic
- Psychological pruritus
- Feline idiopathic ulcerative dermatitis

(Adapted from Noli and Scarampella (2004)

Milliary dermatitis presents as multiple small crusted papules on any part of the body. **Eosinophilic plaque** may be the result of coalescence of these papules into red eroded hairless raised lesions. **Eosinophilic granuloma** is a nodular lesion that needs to be differentiated from an infectious granuloma or a neoplasm. **Urticaria pigmentosa** is a mast cell rich nodular lesion identified in Sphinx and Rex cats.

In cats, is particularly important to realise that **dermatophytosis** (ringworm) can be a pruritic disease and that every pruritic cat should be checked by toothbrush culture. A negative Wood's light examination does not rule out dermatophytosis as only 50 per cent of *Microsporum canis* strains will fluoresce.



Same aetiology **Same protocol** **Same treatment**

Manifestations of feline allergic disease. Any one or more of the following:

Milliary dermatitis	Eosinophilic plaque
Eosinophilic granuloma	Linear plaque/granuloma
Over grooming syndrome	Head and neck pruritus
Urticaria pigmentosa	Rodent ulcer
Bilateral otitis	Facial dermatitis of Persian cats

Psychological pruritus is a vastly over diagnosed disease, and in the author's experience, is uncommon. There is a history of stress in the life almost every cat. A recent study from a behaviour and dermatology referral practice has shown that the majority of cats referred for behavioural or psycho-dermatitis were fact suffering from a more common dermatological disease. A diagnosis of psychodermatitis should only be made after all dermatological causes have been eliminated and a lack of response to a therapeutic trial of corticosteroids (prednisolone 2 mg per kilogram daily for 10 to 14 days).

Pemphigus foliaceus in cats is uncommon but by no means rare. The presence of yellow crusts particularly on the medial pinna and/or cheesy exudate in the nail beds raises the suspicion of pemphigus foliaceus. The presence of acantholytic cells on cytology and typical histopathology confirms the diagnosis.

Herpes virus dermatitis typically involves the nasal plan and/or facial areas. The diagnosis of herpes virus dermatitis can be quite difficult because on histopathology inclusion bodies are not always seen and the reaction to the virus may involve significant numbers of eosinophils. PCR has both false negatives and false positives and is best done on tissue cores rather than surface samples. Immunohistochemistry can be used to detect the presence of the virus in biopsy samples. This disease will get worse if corticosteroids are administered and will respond well to high doses of **famciclovir**. Unfortunately in some cases, where tissue samples have not been diagnostic, we are left with no alternative but therapeutic trial. Off label doses range from 40 mg/kg - 90 mg/kg 2-3 times a day with data suggesting the higher dose and frequency giving faster and better clinical results.

Mosquito bite allergy typically involves the nose and ears. The characteristic lesions consist of papules with a small black necrotic centre. These may coalesce to form areas of plaque or ulceration. The condition responds well to corticosteroids and resolution of the problem by confinement of the cat away from mosquitoes confirms the diagnosis.

***Malassezia* dermatitis** is recognised in particularly Sphinx and Rex cats and in the Abyssinian. A greasy dark exudate on the skin and a brown coating on the nails is regarded as characteristic. Sticky tape cytology or examination of scrapings from the nails yields significant numbers of characteristic yeast bodies. It is not clear to what extent cases of *Malassezia* dermatitis in these particular breeds resents a genetic predisposition and/or a secondary overgrowth in reaction to allergy. *Malassezia* dermatitis responds to itraconazole, 5 to 7 mg per kilogram given daily for a week on/ week off basis for 6 weeks (three cycles). Topical treatment and control of the underlying allergic disease will further enhance clinical recovery.

Eosinophilic granuloma is just another reaction pattern in the cat, most commonly to allergy. Eosinophilic granuloma needs to be differentiated from tumours, infectious granulomas and Herpes virus infection and a biopsy is often

required. Like other eosinophilic diseases of cats, eosinophilic granuloma will respond to immunosuppressive therapy and identification and elimination of the primary cause. An exception sometimes is the ulcerated lesions opposite the canine teeth on the upper lips. Some of these cases will respond better to antibiotics to corticosteroids. **Linear granuloma** is a variation of feline eosinophilic granuloma, which as the name suggests, has raised striped-like appearance.

Feline acne is not an allergic disease. Feline acne is a keratinization defect of hair follicles under the chin. This leads to black keratin plugging (comedones) and secondary infection. Pruritus is usually related to the secondary infection.

Feline idiopathic ulcerative dermatosis is an uncommon disease affecting the interscapular and neck area of the cat. (see Figure 11). It has different histological findings to those seen in allergic cases (neutrophilic vs eosinophilic). Treatment protocols have involved combinations of antibiotics, silver sulphadiazine, corticosteroids, cyclosporine, toprimate and maropitant. It can be a very difficult condition to control long term as the aetiology(s) are unknown.

Clinical approach to the allergic cat – a 3 step process

STEP 1 - eliminate ectoparasites, bacterial infections and dermatophytes

- Obtain a full clinical history. No shortcuts.
- Full dermatological examination including skin scrapings, impression smear cytology and Wood's light examination.
- Submit a toothbrush sample over at the least a one minute and submit the whole brush for fungal culture. If the suspicion of ringworm is high, it is rational to begin treatment in anticipation of the fungal culture results.
- If there is clinical or cytological evidence of pyoderma, treat for at least three weeks with oral doses of cephalexin (25 mg per kilogram twice a day), amoxicillin clavulanate (12 to 15 mg per kilogram twice a day) or 1 to 2 courses of cefovecin (Convenia) every two weeks.
- If there is furious pruritus, particularly of the head and neck, this needs to be stopped. Elizabethan collars, bandaging and, if needed, 7 to 14 days of prednisolone at 2 mg per kilogram daily. In cats that severely mutilate the neck area , the severe pruritus is compounded by deep infection which needs to be treated.
- Selamectin (Revolution) every 2-3 weeks is effective against surface and burrowing mites but is not effective against Demodex species.
- A full flea elimination trial is absolutely indispensable. Fleas need to be killed fast so they inject the minimum amount of saliva into the skin. Many spot on preparations take too long to kill the flea and hence are not suitable for diagnostic trials.
- For rapid flea elimination, the gold standard is nitenpyram (Capstar) DAILY. Compliance is assisted by using the large dog tablets divided into approximate quarters. Most other products display a decreased speed of kill after the third week of administration. Alternatives that give rapid and sustained kill include indoxacarb (Activyl) or spinosad (Comfortis) given every 3 weeks on an offlabel basis. Fluralaner spot-on is undergoing registration and shows promise as a 12 weekly topical treatment for cats. At this point, the off label use of canine oral isoxazalines (sarolaner, fluralaner and afoxalaner) in cats is not backed by any reliable data and is not encouraged.
- In cases where cats are using their claws to mutilate themselves, the use of corticosteroids is unavoidable however they need to be stopped at least two weeks before assessing the results of the parasite or diet elimination programme.

STEP 2 – diet elimination and ensuring that none of the less common causes of pruritus are present. If there has been a failure to respond to parasite pathogen elimination, we are left with a diagnosis of diet related pruritus, feline atopic dermatitis or one of the rarer diseases listed previously. If one of the rarer conditions is suspected, skin biopsies indicated. If, based on history and previous response to treatment, allergic skin disease is highly likely, we need to proceed to a diet elimination trial. The gold standard for this is a minimum of eight weeks on a diet of a normal protein. Kangaroo or rabbit meat of human consumption standard is suitable. Hydrolysed low allergen diets are regarded by most dermatologists as the next best if the owner is unprepared or unable to feed a normal protein diet. In a study when current hydrolysed low allergen cat diets were fed to cats later proven to have a food-related allergy, hydrolysed diets FAILED to identify over 50 per cent of food-related allergy.

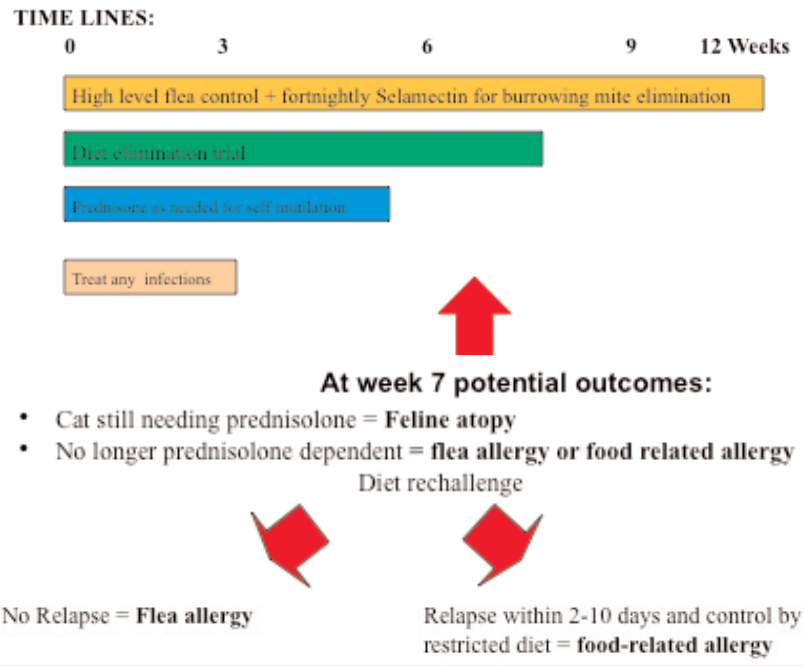
A recent product using hydrolysed feather protein (Royal Canin Analergenic for cats) may be potentially more useful pending controlled independent studies. Some cats just will not eat the elimination diet no matter what or will steal food/hunt. In this cases, it is just not possible to establish a diagnosis of food related dermatitis and we must proceed with the management of the cat as if it were atopic.

Serum tests for food allergy are of no significant value in determining if a cat has a food-related allergy or what the offending foods are.

During the food trial, the use of corticosteroids is not contraindicated provided they are withdrawn at least two weeks before the diet rechallenge phase. A diet trial without rechallenge is an incomplete diet trial. Food allergic animals will relapse within 10 days of diet rechallenge (most commonly within 1 to 2 days).

It is quite acceptable, particularly in cases where parasites or parasite allergy is less likely, to begin the food elimination trial concurrently with the parasite elimination trial. It is imperative not to cease a test diet at the same time as ceasing to parasite elimination medication. The author's method is to continue the high level flea control (daily nitenpyram or 3 weekly indoxacarb or spinosad) after the diet rechallenge has been done. In this way it is possible to differentiate any response and establish an accurate diagnosis.

A model diagnostic protocol to diagnose flea allergy, food-related allergy and atopic dermatis in the cat with a single trial period



Important notes – clinical judgement and assessment

1. There are cases that have multiple allergy types
2. Very occasionally a diet or flea control trial will require longer than 7 weeks
3. Bacterial superficial pyoderma is common in cats and pustules are uncommon and transient. Treatment with cefovecin (Convenia) and topical short term offlabel fucidic acid/betamethasone ointment (Isaderm) are the author's preferred modalities. The diagnosis is based on tape cytology.

STEP 3 – Management of atopic dermatitis in cats

Atopic dermatitis is a clinical diagnosis, made after exclusion of the other possibilities. In all likelihood, atopic dermatitis will never be cured and will be need lifelong management. In owner must be made aware of this. A corticosteroid only approach is highly likely to lead to serious side-effects and failure.

Corticosteroids in cats

It is a common myth that cats are resistant to the side-effects of corticosteroids. It is true that cats require higher doses of corticosteroids to reduce pruritus or to treat immune mediated disease (roughly twice the doses used in dogs). The initial dose of prednisolone often needed to suppress pruritus is of the order of 2mg/kg once daily, that is to say half of 20 mg prednisolone tablet daily for an average sized cat. This can often be reduced to 1mg/kg as control of pruritus is established.

Many veterinary dermatologists recognise a subset of pruritic cats that will not respond to prednisolone. A proportion of these cats will respond to oral dexamethasone at a dose rate of 0.1-0.25 mg/kg every 24-48 hours. This is off label use and benefits must be weighed against the risk of diabetes and feline Cushing's disease

Cats however, are not resistant to the side-effects of corticosteroids. Corticosteroid induced diabetes (type II) and heart failure due to plasma volume expansion wellrecognised side-effects in the cat. Typically, corticosteroid doses are reduced by 25 per cent every 10 days until an absolute minimum dose is found that is needed to maintain the cat. The author,

Figure 1. Lesions suggestive of flea allergy dermatitis. A treatment response trial would confirm the diagnosis

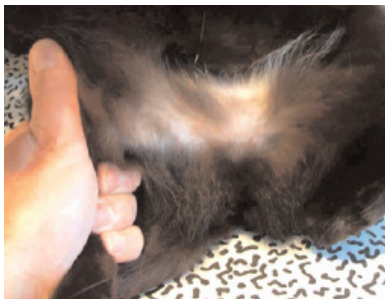


Figure 2. Alopecia from over grooming. Allergic skin disease is far more likely than psychological dermatitis

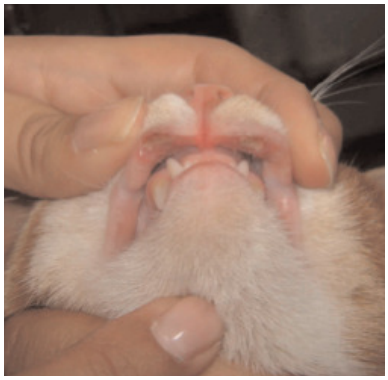


Figure 3. Rodent ulcer. Some cases will respond better to antibiotics than corticosteroids. *Dr V Balazs*

Figure 4. A biopsy, possible PCR and immuno-histochemisty would be required to diagnose space this ulcerative lesion. Differentials include squamous cell carcinoma, feline herpes dermatitisatypical infections and eosinophilic granuloma. The final diagnosis was feline herpes

however, rarely relies on systemic corticosteroids long term in the cat beyond occasional 3-5 day pulses for flare-ups or a maximum of 1mg/kg prednisolone twice weekly.

Depot corticosteroids should be used only as a last resort in cats that absolutely refuse oral medication (including oral prednisolone suspension). If a cat were to require no more than 2-3 depot methyprednisolone acetate injections over a 12 month period, this could be considered as reasonable management. However, with each injection, rises in blood glucose and plasma volume analogous to uncontrolled human Type II diabetes mellitus have been demonstrated.

The more potent topical corticosteroids, particularly those containing mometasone or betamethasone are effective in local lesions and reduce the dependence on systemic corticosteroids. Cat's licking will remove medication and result in increased systemic levels. Prolonged use of high potency topical corticosteroids will result in severe skin atrophy.

The use of antihistamines combined with a omega-3/6 essential fatty acids in cats may further reduce the doses and dependence on corticosteroids. Antihistamines and fatty acid supplements often are not effective alone in controlling the signs of atopic dermatitis. If they reduce the amount of immunosuppressive drugs needed, and they are worthwhile. Clinicians, however, need to consider carefully the benefits of antihistamines versus compliance if another medication is brought into the regime. The only antihistamine registered for feline use in Australia is chlorpheniramine. A report of the successful use of cetirizine at 1mg/kg daily in a proportion of cats conflicts with more recent placebo controlled study to that cetirizine in the cat was not effective in controlling pruritus.

Megesterol acetate has been used in the past to treat pruritus in cats and provoked many cases of diabetes. The pseudo-disease described prior to 1980 as "feline endocrine alopecia" is in fact over-grooming due to allergy. If hair is examined under a microscope the distal ends are barbered to a square cut-off shape by the tongue rather than rounded end typical of endocrine disease. In the last 30 years, the author has not used megesterol acetate in a cat and would only do so if the only alternative were to be euthanasia.

Cyclosporine in cats

In the past, cyclosporine has become a widely used and effective off-label medication for the management of atopic dermatitis in cats. Many cats with manifestations of feline atopic disease could be maintained long-term with 25mg of cyclosporine every 2 to 4 days. Since 2013, cyclosporine is registered for feline use as a 100mg/ml oral liquid (Atopica for cats) at a dose rate of 5-7mg/kg daily.

Cyclosporine has:

- Much lower rate of metabolic effects than corticosteroids (diabetes, heart failure). Post transplantation diabetes is recognised in humans but it's incidence in domestic pets is unclear.
- Main reported side effects are gastro-intestinal disturbances and weight loss. Most cases not severe enough to stop usage.
- Predisposition, through immunosuppression, to opportunistic infections.
- A much slower onset of actions. Owners need to be aware that will take at least three weeks for any benefit whatsoever to become apparent. Corticosteroids can be used during this lag phase to prevent serious selfmutilation.

Cyclosporine and feline toxoplasmosis

- Uncommon complication, cases reported in the literature and the author has personally recorded two cases.
- Both new infections and re-activation of latent infections are possible. New infections are regarded as important, placing sero-negative cats are at risk.

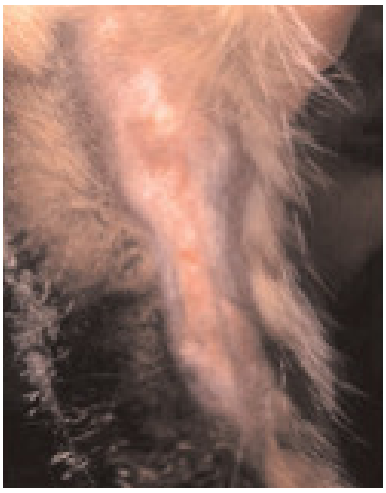


Figure 5. Linear granuloma. A variant of eosinophilic granuloma

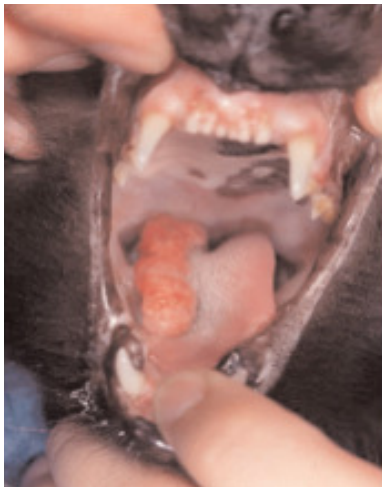


Figure 6. Oral eosinophilic granuloma may occur on the tongue, palette or at the fauces. *Dr Candace Sousa*

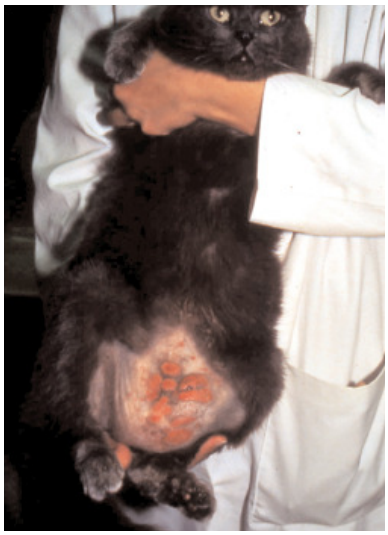


Figure 7. Eosinophilc plaque, most commonly reaction pattern to allergy. *Dr. Michelle Rosebaum*

Candidate cats for cyclosporine treatment
- FIV/FeLV negative
- No evidence of systemic disease
- Owners consent to off label use
- Rule out of other pruritic diseases: or
  - ✓ Flea allergy
  - ✓ Mites
  - ✓ Pyoderma & Malassezia
  - ✓ Adverse food reactions
  - ✓ Dermatophytes
  - ✓ Pemphigus
  - ✓ Psychogenic

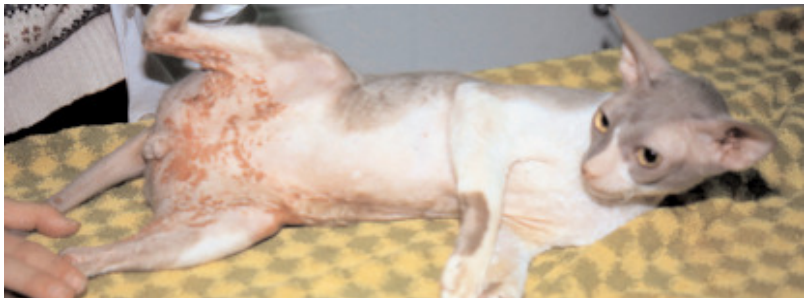


Figure 8. Urticaria pigmentosa occurs in Sphinx or Rex cats as a reaction pattern to allergy. The clinical appearance is that of erythema nodules and plaque. ***Dr M Rosebaum***

• To prevent new infections, client should be advised to cook all meat and to prevent hunting of rodents etc.
• No evidence of re-shedding of oocysts.
• Cats that hyper-absorb cyclosporine are potentially at higher risk. Normally, only about 25-30 per cent of orally administered cyclosporine is absorbed by the cat.

Author's protocol
• Atopic dermatitis is FIRST confirmed by appropriate elimination trials.
• The owner is advised of the risks of opportunist infections, especially toxoplasmosis and its signs.
• The cat is determined to be FIV negative and have no evidence of systemic disease.
• Cyclosporine is begun at a more conservative dose of 5mg/kg daily, independent of feeding time. If after 4-5 weeks, of treatment there is no response a 24-hour post-pill trough cyclosporine blood level test (EDTA sample) should return levels of 200 to 500 ng per ml. Cats with levels at below 100 ng per ml may require increased doses. If there is a response to cyclosporine, the dose is lowered to two days on and one day off for three weeks then progressively to a target dose of every 2nd or 3rd day (if possible). A 24 hour post pill sample is submitted when a stable dose is achieved. Cats with levels into the high hundreds or thousands are considered to be hyper absorbers and are at increased risk of toxoplasmosis. Hyper absorbing cats should have the dose rates rapidly reduced and further trough levels evaluated.
• Daily cyclosporine should be continued for 30 days or until significant clinical improvement is noted. In some cases, the full benefit of cyclosporine may not be apparent for up to 6 weeks. If there is no benefit after 6 weeks of administration than the drug should be abandoned or the diagnosis of feline atopic dermatitis reassessed.

Off label anti-pruritic agents in the cat
Maropitant
Maropitant (Cerenia) is a neurokinin-1 (NK-1) receptor antagonist and inhibits binding of substance P to NK-1 receptors. Substance P is a neuropeptide which may play a significant role in the induction and maintenance of pruritus. The NK-1 receptor, is abundantly expressed in the skin and CNS. Maropitant is registered for acute vomiting in the cat at a dose of 1mg/kg and has a half-life of the order of 13-17 hours. There are reports of its longer term use in cats on an off-label basis for the control of chronic vomiting in cases of renal failure and data to suggest doses of up to 5mg/kg are tolerated medium term. In humans, the use of NK-1 receptor antagonists has been reported for the successful management of refractory chronic pruritus.

In a study of experiential asthma in cats, maropitant at 2mg/kg was not effective in treating the clinical signs. The author and some colleagues have unpublished data to show that maropitant at 2mg/kg once daily for 13 out of 14 days is effective in a high percentage of cases of non flea induced feline pruritus where there as been a failure or intolerance to cyclosporine and the patients have been dependent on toxic or potentially toxic doses of corticosteroids. In these cases, patient dependence on corticosteroids has been significantly reduced. This is off label use and dosing and requires informed owner consent. Further studies are needed to elicit the optimum dose and the long term safety of maropitant for the symptomatic management of refractory feline pruritus.

Oclacitinib in cats
Oclacitinib (Apoquel) has been a major advance in the symptomatic management of canine pruritus. In the cat, there has been little published as to its efficacy and dosing. A single published pilot study of 12 cats treated with oclacitinib, 0.4-0.6 mg/kg orally twice daily for 2 weeks, then once daily for an additional 14 days. Dermatologist assessed lesion and pruritus scores showed good improvement in 5/12 cases. Other anecdotal reports show variable to poor results with doses up to 1mg/kg twice daily. The author's experience with oclacitinib in cats has been poor, particularly in cyclosporine refractory cats (1 out of 5 cases with a good response).

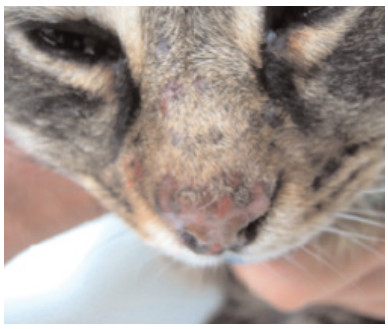


Figure 9. Clinical appearance of focal lesions that suggest mosquito hypersensitivity

Further studies are needed to determine what dose regimes (if any) are required for cats and their medium to long term safety. The reasons for oclacitinib being less effective in the cat are not clear and may be related to the kinetics of the drug in cats or pruritus in the cat being significantly mediated by mechanisms other than the JAKSTAT pathway.

Immunotherapy in atopic cats
Immunotherapy in dogs has been shown to produce significant benefits in about 70 per cent of cases. In cats, there is a lack of formal large-scale studies. However, most dermatologists agree that cats benefit from immunotherapy at least as well, if not better, than dogs. House dust mites are the most common allergen identified but significant numbers of cats will react to one or more plant pollen.

The problem lies in the testing. Serum IgE tests are available however studies have shown that both normal and atopic cats of and have similar levels of IgE to common allergens; in particular dust mites. Intradermal testing in cats is limited by the weak and transient nature of some of the skin reactions, resulting in a significant number of false negative results. This may be due to the characteristics and structure of feline skin and potentially the need for higher testing allergen concentrations in the cat. To assist in interpretation, some dermatologists interpret the test both with and without an injection of intravenous fluoroscein and reading the size of the reactions with a UV light.

The author's opinion is that intradermal testing is still worthwhile because those cats that react positively will often show very good responses to immunotherapy.

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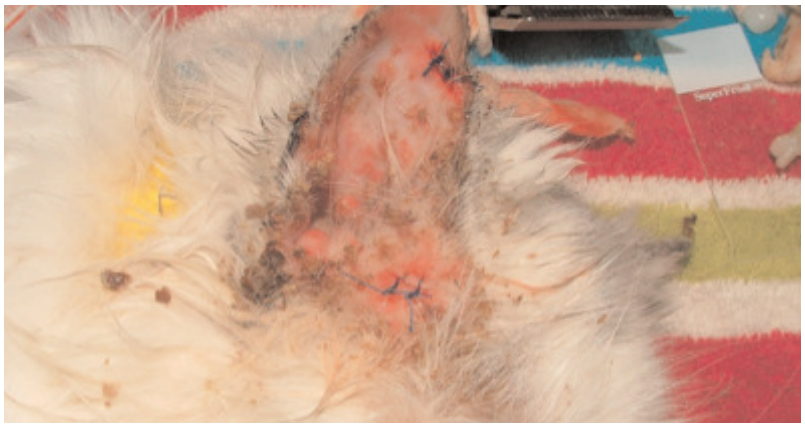

Figure 10. Yellow crusts and pustules that suggest pemphigus foliaceus. Cytology and a biopsy confirm the diagnosis

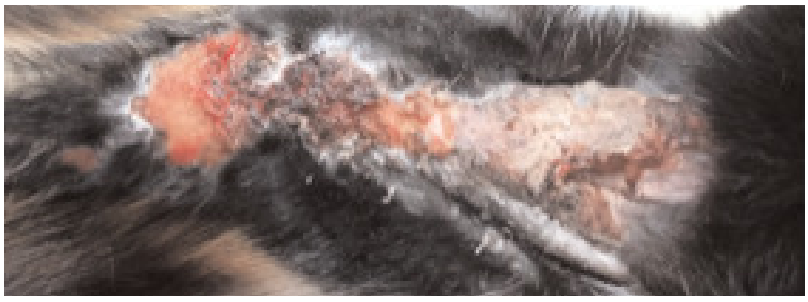

Figure 11. Feline indiopathic ulcerative dermatosis