British Veterinary Dermatology StudyGroup

SPRING MEETING • APRIL 2020

Feline Dermatology

International Convention Centre (ICC), Birmingham
Wednesday 1st April 2020

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A message from the President

Dear Friends and Colleagues

The British Veterinary Dermatology Study Group (BVDSG) would like to welcome you to their Spring Meeting 2020 entitled "Feline Dermatology".

The meeting will once again be held at the ICC Birmingham where we will have full use of one of the most spacious and sophisticated rooms in the centre – hall 4. Both the location and the exceptional facilities make this venue easy to reach and ideal for relaxed and productive meetings as well as social gatherings.

This year, by popular demand, we will be covering the wonderful yet challenging topic of Feline Dermatological disease. We welcome world expert speakers including Silvia Colombo, Stephen Shaw, Angela Fadda, Simone Kirby and Nicola Swales, who between them, will be covering topics such as feline allergy, feline viral skin disease, dermatophytosis, feline parasites, neurological skin disease, dental disease relevant to dermatologists, feline autoimmune disease and behavioural aspects of feline skin disease.

We would like to thank our Sponsors for their continued and valued support, and our members for their regular attendance and commitment, both of whom make it possible for us to hold these high quality educational events.

We look forward to welcoming you to Birmingham!

Sarah Warren, BVetMed MSc (Clin. Onc.) CertVD MRCVS
RCVS Advanced Practitioner in Veterinary Dermatology
BVDSG President

BVDSG Spring Meeting – April 2020

Feline Dermatology

Programme & Contents

Wednesday 1st April

Feline Allergy

Silvia Colombo
DR, MED. VET, DIP. ECVD

Dr. Colombo was born in 1966 in Legnano (MI), Italy, and graduated in Veterinary Medicine in 1992 at the Faculty of Veterinary Medicine of Milan (Italy). She completed a Research Doctorate in Small Animal Internal Medicine at the Medicine Department of the Faculty of Veterinary Medicine of Milan (Italy) from November 1993 to November 1996 and a Post-Doctorate from October 1998 to October 2000. She completed a Senior Clinical Scholarship in Veterinary Dermatology (residency in Veterinary Dermatology) at the Department of Clinical Veterinary Studies, The University of Edinburgh in September 2003 and worked at the Department of Clinical Veterinary Science, University of Bristol, as a Temporary Clinical Fellow in Veterinary Dermatology from November 2003 to June 2004. Dr. Colombo passed the Diploma Exam of the European College of Veterinary Dermatology (ECVD) in 2004. She has been a Full Member of the ESVD (European Society of Veterinary Dermatology) since 1996. Dr. Colombo is president of SIDEV (Italian Society of Veterinary Dermatology), member of the ECVD Board and Chair of the ECVD Credentials Committee. Currently, Dr. Colombo is seeing referral cases as a private practitioner in various practices in Northern Italy.

INTRODUCTION

Feline allergic diseases are far less understood than their canine counterparts. For this reason, in cats, the terms "atopy", "atopic dermatitis" and "feline-atopic-like dermatitis" should not be used. Recently ICADA (International Committee on Allergic Diseases of Animals) proposed the term "feline atopic syndrome" (FAS), which includes environmental causes of allergy and some manifestations of cutaneous adverse food reactions (CAFR) and of asthma, which can occur in the same cat.[1] According to this definition, flea-bite hypersensitivity (FBH) is a distinct entity, while "immunologic" CAFR may be a manifestation of FAS. CAFR include food hypersensitivity and food intolerance. Since we cannot distinguish between a true immunological reaction (hypersensitivity) and a non-immunological one (intolerance) on a clinical basis, in veterinary medicine CAFR is the most accurate term. FBH is common in cats, however it can be easily diagnosed/ruled out with good flea prevention,

which is also part of the diagnostic approach to the allergic cat. This presentation will concentrate on FAS and CAFR.

PATHOGENESIS

Feline atopic syndrome (FAS) is thought to be similar to human and canine atopic dermatitis, being characterized by an "abnormal" response of the immune system to substances which do not induce any reaction in a healthy individual. However, we do not have enough information to consider the feline disease the same as the canine and human one. We know that pruritus and self-trauma are a clinical hallmark of FAS, that cats have IgE and that microscopic features of lesional FAS skin and of atopy patch test sites after tape-stripping are similar to the ones of canine atopic dermatitis. On the other hand, we only have one case report of FAS occurring in related cats, we do not know whether the route of allergen penetration in cats is epicutaneous and whether FAS cats have skin barrier defects.

A recent study contributed to our knowledge by showing that intradermal injection of anti-IgE antibodies in healthy cats induced an immediate wheal reaction as well as a late-phase reaction, with microscopic and immunohistochemical features similar to the natural disease.[2] Two recent studies on the bacterial and fungal populations of the feline skin compared healthy and allergic cats, showing in the latter group both bacterial and fungal dysbiosis, with more abundance of *Staphylococcus* bacteria.[3,4]

Very little is known on the pathogenesis of CAFR in cats, with most information being extrapolated from what is known in people and dogs.[5,6] Food hypersensitivity in cats is due to an exaggerated immune response to food antigens, causing most commonly diarrhoea and/or various 'cutaneous reaction patterns'.[5] The most common antigens in cats are beef, chicken and fish.[7]

CLINICAL FEATURES

Pruritus is always present in allergic cats, it is usually moderate to severe and can be seasonal in FAS or year-round in both FAS and CAFR. However, a cat may suffer from different allergies, and a CAFR affected cat may show seasonal variation of pruritus if FBH or FAS are present as well.

Cats may manifest pruritus in different ways such as scratching, licking, biting off their fur or shaking the head in case of auricular pruritus. Scratching in cats is part of the normal behaviour, however when it is excessive and causes lesions it can be easily recognized by the owner. Cats scratch with their hind paws, and this is usually the main clinical manifestation when pruritus involves the head and the neck. Licking is also a normal grooming behavior and in this case the owner may be unaware of the fact that the cat licks excessively, either because he/she considers it "normal" or because the cat hides to do it. Alopecia due to excessive grooming can affect any area of the body reachable by a cat's tongue.

Feline pruritus is frequently expressed with clinical patterns, regardless of the etiology. The most common clinical patterns are head and neck pruritus, self-induced alopecia, miliary dermatitis and eosinophilic dermatitis (including eosinophilic granuloma, eosinophilic plaque, lip ulcer). Two or more patterns can be present in the same cat. In a recent study, head and neck involvement was more frequent in CAFR than in FAS due to environmental allergy, although the difference was not statistically significant, and this pattern was also seen in 55%

of cats with non-allergic diseases.[8] In another study on a small number of cats with CAFR, the head and face were involved in 14/17 cases.[9] Less common patterns are pododermatitis, exfoliation (due to mural folliculitis or other histopathological patterns), facial erythema and pruritus without lesions.

Papular eosinophilic/mastocytic dermatitis, also known as urticaria pigmentosa-like dermatitis, may also be a clinical pattern in Devon rex and Sphynx cats. It is important to remember that none of these clinical patterns is pathognomonic of FAS or CAFR. Non-dermatological signs such as conjunctivitis, sneezing/coughing, and otitis externa or media may also be noted in FAS.[10] CAFR cats may have gastrointestinal signs such as vomiting, flatulence, soft stools, increased defecation or diarrhoea in up to 21% of cases.[8] However, on clinical grounds, this must be interpreted with caution, especially if many dietary changes have already been tried. Any food change may cause gastrointestinal signs.

In the study by Hobi et al., the mean age at onset of CAFR was 4 years-old, compared to 3 years-old for environmental FAS. CAFR may also affect older cats: 26% of CAFR cats started after 6 years of age, compared to 12% of cats affected by environmental FAS.[8]

Secondary infections such as superficial pyoderma and *Malassezia* overgrowth are uncommon in allergic cats. In a recent retrospective study on 52 cases of feline superficial pyoderma collected over 10 years, an underlying allergic disease was identified in 60% of the cases.[11] Bacterial or *Malassezia* otitis externa is also uncommon, however a recent cytological study showed that bacterial and yeast numbers in the ear canals of allergic cats are higher compared to healthy cats and cats with systemic diseases.[12]

DIAGNOSTIC APPROACH

The diagnosis of feline allergies is, first of all, a diagnosis of exclusion. Clinical diagnostic criteria for FAS have recently been developed as an aid to the clinician, however a thorough diagnostic investigation must be carried out in all cases.[13]

The first step is ruling out ectoparasitic diseases, with particular attention to fleas, which can induce flea-bite hypersensitivity (FBH), the most common allergic disease in cats. If secondary skin infections or otitis are suspected, a cytological examination is mandatory. A fungal culture should also be performed to rule out dermatophytosis. Other diagnostic tests may be necessary, depending on the clinical presentation (e.g. biopsy in a cat with head and neck pruritus may be required to diagnose/rule out herpesvirus dermatitis).

If all tests are negative or pruritus persists after treating the infections, an elimination diet trial should be carried out to investigate CAFR. At present, no serological test or gastroscopic food sensitivity test has been shown to be reliable for the diagnosis of CAFR, and the food trial is the only recommended test available to veterinarians.[1,14] Performing a food trial in cats is important because CAFR can be managed by avoidance. On the other hand, if CAFR is ruled out by performing a good food trial, the remaining diagnosis in a non-seasonally pruritic cat is FAS due to environmental allergens.

The elimination diet should be fed exclusively for at least 8 weeks, and may be prolonged if necessary up to 12-13 weeks.[15] If the cat improves on the elimination diet, CAFR must be confirmed by challenging with the previous diet. At least 50% improvement or more must be observed before challenge.[15] The challenge involves feeding the old food (dry and/or canned) mixed with the elimination diet in a proportion of approximately 20%, to prevent

gastrointestinal adverse effects. Pruritus relapse or worsening may occur soon after re-feeding the previous food or may take up to two weeks. If pruritus worsens, the cat should be fed again the elimination diet only and improvement must be observed within three weeks. At this point, a diagnosis of CAFR is confirmed. If no worsening of pruritus is observed after two weeks, CAFR can be ruled out and environmental FAS is the likely diagnosis.

Environmental allergens are difficult to investigate in the cat, and testing should be only proposed if the owner is willing to try allergen-specific immunotherapy (ASIT). Intradermal testing is not easy to perform, due to the thin and hard skin of the cat and the poor quality of the wheal. The interpretation may be improved by injecting fluorescein intravenously before starting performing the test.[16] A recent study investigated percutaneous testing in cats, showing that allergens applied percutaneously were not irritant in healthy cats and concluded that percutaneous testing was simple to perform.[17] Serological testing is also available, and the most widely used and studied is an ELISA test based on the IgE high affinity receptor.

However, a recent study showed that the test is only reliable to diagnose FBH, because IgE production in cats is strongly influenced by age, flea control, presence of endoparasites and way of life.[18] A screening assay, which tests groups of allergens, is also commercially available and has been show to reliably predict the results of the complete test, with the advantage of being less expensive.[19] Performing the screening test first and the full test only if positive results are found on the screening test may be a reasonable and cost-effective approach. Since non-allergic cats may also have positive results, these tests must always correlate to the cat's history and life environment, and should only be used to select relevant allergens for ASIT.

THERAPEUTIC OPTIONS

If CAFR is diagnosed, identifying the responsible protein/s is important because the disease can be controlled by simple avoidance of the offending food. While continuing the elimination diet as the main food, a single ingredient should be added every two weeks, starting with the proteins mostly fed in the past. The owner should be instructed to keep a diary and to go back to the elimination diet for three weeks if the cat shows a reaction. This will also help finding a maintenance diet that the cat can tolerate, to be fed long-term. Some owners refuse to go through this long and difficult process, and choose to feed the elimination diet forever. If the food trial was performed with a home-cooked diet, a non-flavoured supplement must be added to avoid nutritional deficiencies.
Treatment options for FAS include symptomatic therapy, aimed at controlling pruritus and improving the cat's quality of life, and ASIT.

ASIT is theoretically the best option in cats as it is in dogs, however it is much less frequently chosen due to the previously described diagnostic problems. When positive results of IDT or serological testing are available and correlate well to the cat's environment and history, subcutaneous or sublingual ASIT may be implemented. Whatever the protocol chosen, adverse effects of ASIT in cats are rare. Reported effectiveness of subcutaneous ASIT in cats varies between 50 and 75%, however there are no controlled studies.[20] A recent retrospective study on 45 cats indicated a 57% success rate.[21] ASIT protocols are the same used in dogs, with the additional option of a "rush" protocol which allows to complete the induction phase of ASIT in eight hours. The cat needs to be hospitalized and pre-medicated with glucocorticoids and antihistamines.[22] There are no published studies on sublingual ASIT in the feline species.

Systemic glucocorticoids, particularly prednisolone and methylprednisolone, are widely used to treat FAS. They represent the best option to treat seasonal FAS with clinical signs lasting up to four months, however they are not ideal for cats with perennial pruritus, due to potentially severe adverse effects. Systemic glucocorticoids are also very useful at the beginning of the elimination diet, to control pruritus and resolve clinical signs, and may also help to convince the cat to eat the diet. Glucocorticoids must be discontinued in the second half of the diet period, in order to evaluate recurrence of pruritus. Long term administration and/or high doses may cause polyuria, polydipsia, diabetes mellitus, urinary tract infections, congestive heart failure, skin atrophy and iatrogenic hyperadrenocorticism with acquired skin fragility syndrome.

Doses required to control the clinical signs are reportedly higher, compared to the dog. A recent study suggested a mean daily dose of 1.41 mg/kg of methylprednisolone as the induction dose.[23] The induction dose is continued until clinical signs are controlled and then the dose is tapered, aiming at every other day administration. Difficult cats may be treated with injectable methylprednisolone acetate, however the risk of severe adverse effect with repeated injections is high. Once daily topical application of hydrocortisone aceponate has also been reported as effective and safe in a small pilot study on 10 allergic cats.[24]

Systemic ciclosporin is currently the best treatment option for FAS when clinical signs are year-round and continuous treatment is necessary. It is available as a liquid formulation to be administered at 7 mg/kg once daily for two months, and then it can be tapered to every other day administration in most cats and to twice weekly administration in a few patients. Ciclosporin has been shown to be as effective as oral prednisolone in a controlled study.[25] It is generally well-tolerated, although some cats may refuse to eat it or salivate excessively after administration. Reported adverse effects include vomiting, diarrhoea and decreased appetite in the first weeks of treatment and weight loss and gingival hyperplasia in the long term.[26]

As ciclosporin may suppress the activity of the immune system, opportunistic infections may occur. It is recommended to test cats for FIV and FeLV before starting treatment and to avoid feeding raw meat or let the cat go out and hunt, to prevent toxoplasmosis. Ciclosporin is metabolized in the liver by the cytochrome P-450 enzymes and is both a substrate and an inhibitor of P-glycoprotein. If administered concurrently with other drugs, interactions are possible.

Antihistamines and essential fatty acids (EFAs) have been reported to be useful in allergic cats, both administered alone and in combination. However, all the published studies were open and often included very small numbers of cats. There is only one controlled study on the efficacy of cetirizine in FAS cats, and no statistically significant difference was observed for cetirizine compared to placebo.[27] EFAs may help by improving the skin and hair coat quality, even if we do not know if FAS cats have a defective skin barrier. Both antihistamines and EFAs are very safe and may be tried in mildly affected cats. Palmitoylethanolamide (PEA) is a natural substance whose main activity is inhibition of mast cell degranulation. Recently, a product containing ultra-micronized PEA (PEA-um) with improved bioavailability was used in a study to investigate its glucocorticoid sparing effect, and was able to prolong the effect of methylprednisolone in treated cats.[28]

Maropitant is a neurokinin-1 receptor antagonist, able to block the interaction of substance P, a pruritogenic neurokinin, to its receptor. Maropitant is marketed as an antiemetic for dogs. In an open pilot study, it was reported to be effective and safe against pruritus and lesions in 11/12 allergic cats when administered at 2 mg/kg once daily.[29]

Oclacitinib, although not registered for cats, when used at a higher than recommended dose (0.7-1.2 mg/kg twice daily for 28 days), was effective and safe in controlling pruritus and lesions in 15/20 cats.[30]

In cats presenting with indolent ulcer or eosinophilic plaque, resolution of the clinical lesions may be obtained with amoxicillin-clavulanic acid.[31]

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Feline Viral Skin Disease

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Steve qualified in 1987 from the Royal Veterinary College. After 4 years in practice he joined the Animal Health Trust where he completed his RCVS Certificate in Small Animal Dermatology and PhD in canine atopic dermatitis. In 2006, Steve left the Animal Health Trust and after a period of further study completed his RCVS Diploma in Veterinary Dermatology achieving RCVS Specialist Status. Steve has been involved in undergraduate and post-graduate education for many years, working for pharmaceutical companies, the University of Nottingham, and the University of Liverpool. Steve is currently co-editor for the journal 'Veterinary Dermatology'. Most recently he has published work describing atopic dermatitis in large populations considering both behavioural and environmental aspects of the disease as part of the Nottingham 'itchy-dog' project. In the past Steve has been President and treasurer of the BVDSG and an RCVS examiner.

INTRODUCTION

Viral skin disease in the cat is uncommon, but important for clinicians, both in dermatology and oncology. The over-representation of allergy as the cause of skin lesions in cats including all the four feline cutaneous reaction patterns often results in early and in cases of viral disease potentially harmful use of steroids which is to be avoided. We will cover the common viral skin diseases of cats including the Herpesvirus, Calcivirus, FeLV, FIV, Parapox (cowpox) virus and papillomaviruses.

COWPOX VIRUS

Cowpox virus is a DNA virus of the Orthopoxvirus genus similar to smallpox. Although originally associated with cattle, rodents, particularly voles (Kurth et al., 2008) are the natural host and cats, zoo animals, and humans, are accidental hosts. It has been reported rarely in dogs (Von Bomhard et al., 2011). Cowpox has not been isolated from cattle for several decades. The virus is non-enveloped and is resistant to chemical disinfection and in particular dry scabs and crusts may remain viable for long periods. Alcohol, of particular note in the clinical setting with the wide use of gels, is ineffective. In the home, bleach is the most available disinfectant. The virus is a zoonosis and has been fatal in immunocompromised people (Czerny et al., 1991).

CLINICAL SIGNS

The disease is almost exclusively seen in hunting cats and often in more rural settings, but has also been reported in zoo animals fed laboratory rats. Infection in the late summer is more common. Infection usually occurs around the head. Virus is innoculated by a bite or scratch from the prey and then replicates locally in the epidermis forming a crusted ulcerated area with central ulceration and a distinctive crater-edge in some. Secondary infection of the lesions can cause increased signs of general ill-health. Viral multiplication results in secondary papular crusting eruption at other sites in 7-14 days. Most cats recover spontaneously in around 4-5 weeks, but in immunocompromised animals replication in the chest can cause severe signs including pneumonia and exudative pleuritis. Generalised cowpox infections may be fatal in young kittens and in cats treated with corticosteroids. Following infection there is strong immunity and further infection will not be seen. The typical history and clinical signs are not always present and in four cases in the literature less typical signs indicate that a higher index of suspicion for pox in other circumstances is justified (Godfrey et al., 2004).

DIAGNOSIS AND DETECTION OF POX VIRUS

Diagnosis may be made by history and clinical signs. The onset of a single crusted ulcerated lesion followed by smaller lesions is consistent with the disease, but this might be confused with allergic skin disease, Herpes and calicivirus or trauma initially. To confirm, biopsy from the edge of the lesion, avoiding the ulcerated centre of the lesion for histopathology and/or PCR and/or Poxvirus isolation can be used. Sellotape or direct impression smear cytology should be taken to assess for secondary infection, but gently as the lesions are painful.

TREATMENT

Specific treatment is not available and the cat should receive supportive therapy and steroids must not be used. In cats, with respiratory disease the prognosis is poor and various treatments have been attempted. In cases with concurrent respiratory disease (e.g. feline herpesvirus, Bordetella bronchiseptica ± Mycoplasma infection) specific treatments for those diseases may be helpful and secondary bacterial infection should be addressed. Recombinant interferon-omega (Virbagen Omega [Virbac] 1 MU/kg IV q24h) has been used as a non-specific agent in some cases, but its role in improving the prognosis is unclear (McInerney et al., 2016). Death is not an inevitable consequence and notably a cat with combined Poxvirus and FeLV treated conservatively with fluids and antibiotics survived (Johnson et al., 2009).

MANAGEMENT AT HOME

Direct cat to cat transmission can occur as well as transmission to people. Owners may need to isolate the cat from other animals in the house, wear gloves for handling and use suitable disinfectants for food bowls and shared equipment. General environmental disinfection with a suitably rated product is recommended.

PAPILLOMAVIRUS

Papillomaviruses are double stranded circular DNA viruses. The genome contains five or six early (E) genes and two late (L) genes. They are usually species specific and can be limited to certain locations on the body (e.g. oral hyperplasia in lions). There are around 300 different papilloma viruses divided into 35 genera. The majority have been found in man, but over 30% have been shown in other species including mammals, reptiles, and birds.

SITE OF REPLICATION

Papillomaviruses (PV) replicate in the basal cells of the epithelium of stratified squamous epithelium. As this is not accessible in normal circumstances, some form of cutaneous damage is needed for infection to occur. The virus can remain in the skin chronically, and it is only when an infected cell commits to terminal differentiation that viral replication takes place. Virion assembly occurs as the cell reach the stratum granulosum (or equivalent in mucous membranes) so that viral particles are released during desquamation.

IMMUNITY

Papilloma viruses do not invade the skin beyond the epidermis and do not cause necrosis and so the immune response is usually mild. Destructive surgery such as laser or cryosurgery may increase 'danger signals' or DAMPS leading to a more effective immune response. Cell-mediated immunity is the key arm of the immune response. This response can be variable and sometimes delayed resulting in florid infections or neoplastic transformation. Serum antibodies (IgG) are usually produced in low concentrations and are considered only protective for papillomaviruses of the same type. Vaccines have been used in people to effectively prevent HPV (multivalent vaccines having types 6, 11, 16, and 18 with up to 5 others) associated with genital warts, cervical cancer and some mouth and throat cancers. In addition, such vaccines are used as an adjuvant therapy in precancerous and dysplastic lesions due to HPV. Currently no PV vaccine is available for dogs and cats in the United Kingdom, although previously some clinicians have reported obtaining these from the US.

Immunosuppression can delay clinical cure in the case of overt disease and may otherwise also predispose the patient to PV induced neoplasia and multiple papillomas have been reported in both naturally and iatrogenically immunosuppressed dogs.

CONSEQUENCES OF INFECTION

Viral replication is often slow and subclinical both in people and most animal species and some PVs are found in many normal animals and possibly acquired from birth in some cases (e.g. HPV-11). When rapid replication occurs, it results in a marked increase in basal cell replication and terminal differentiation resulting in a typical papilloma or wart. PVs have also been implicated in cancer development and alpha-papilloma viruses have been shown to cause more than 5% of all human cancers including most cervical squamous cell carcinomas. In domestic animals, the role of PVs in cancer is less well established, but demonstrated in sarcoids in horses, bladder and gastrointestinal tumours in cattle and cutaneous neoplasia in dogs.

DETECTION OF PAPILLOMAVIRUSES

The methods available to demonstrate papillomavirus in tissue are shown in Table 1

Table 1: Detection methods for papilloma virus

Method	Notes	Findings	Sensitivity
Histopathology	Standard H&E	Expanded greyish blue, slightly granular cytoplasm Dark shrunken nuclei surrounded by a clear cytoplasmic halo (koilocytes) Clumping of keratohyaline granules Eosinophilic Intranuclear inclusions	Although present in many cases, these findings are not universal
Immunohistochemistry	Antibodies for L1 antigen	Positive signal in the upper layers of the epidermis	Need active viral replication to see L1 proteins, so not useful for latent or slow growing regions Virions are not formed in neoplastic lesions
Molecular methods	PCR In situ hybridisation Consensus (all PV) and individual primers available	PCR: Positive results do not indicate the position of the viral DNA ISH: Location revealed	Detect DNA rather than the product of DNA expression, they can detect PV in lesions where there is no viral replication Since PVs can be present subclinically, it is difficult to determine the significance of intralesional PV DNA

CLINICAL DISEASE IN THE CAT

Cats are not often not considered to be affected with clinical disease associated with papillomavirus as viral warts are very uncommon. However, there is growing evidence that suggests that papillomaviruses are associated with a number of clinical syndromes. These include cutaneous papillomas, viral plaques, Bowenoid in situ carcinoma (BISC), feline squamous cell carcinoma and feline sarcoids. The individual PV types associated with the various clinical syndromes are shown in Table 2.

Table 2: Types of papillomavirus causing disease in cats (adapted from Munday et al, 2017)

Genus	Papilloma type	Typical lesions
Lambda	FcaPV-1	Oral papilloma
Dyotheta	FcaPV-2	Viral plaques / BISC Cutaneous squamous cell carcinoma
Unclassified	FcaPV-3 and 4	Viral plaques / BISC Basal cell carcinoma
Delta	BPV-14	Feline sarcoids

Note: Cutaneous warts are very rare in cats and this has not allowed identification of the papillomavirus. One case was reported to be human papillomavirus 9.

CUTANEOUS PAPILLOMA

Unlike dogs, feline cutaneous papilloma (viral warts) are very uncommon. There are few reports in the literature. In both cases there was surgical or disease-mediated damage (actinic keratosis). Both reported cases in the literature were cured by surgical excision. (Munday et al., 2007 & Carpenter et al., 1992).

VIRAL PLAQUES

Viral plaques are also uncommon in the cats, although it is likely that these are under-reported. The plaques are alopecic, small slightly raised lesions covered with a keratin crust. They are variable pigmented. These can be found in many different areas of the body.

Microscopically the lesions have a sharply demarcated focus of mildly thickened epidermis having prominent viral cytopathology on histology(see Table 1). These plaques are usually associated with FcaPV-2, but there is a report of FcaPV-1. A huge difficulty arises in that around 50% of normal cats when swabbed for virus isolation, FcaPV-2 is found. This suggests that other factors may be involved in this rare cutaneous lesion, with immunosuppression due to naturally occurring or iatrogenic disease being most important. Although some plaques will spontaneously resolve, others will transform to Bowenoid in-situ carcinoma. Surgical excision is curative.

BOWENOID IN SITU CARCINOMA (BISC)

These tumours are commonly seen in middle aged to older cats and the more hairless breeds may be predisposed. Lesions appear as crusted to ulcerated plaques and are usually mulifocal, although solitary lesions are also seen. The face, neck and limbs are predisposed. The presence of these lesions in haired and pigmented lesions suggests that UV light is not essential, but the reported over-representation of BISC in hairless cats suggests a role. It is not known if BISC are preceded by viral plaques in all cases.

Microscopically, the lesions demonstrate a well-demarcated area of epidermal thickening and dysplasia within all levels of the epidermis and extending into hair follicles, but remaining confined by the basement membrane. The dysplastic cells can show a distinct pattern of elongated nuclei called the 'windblown' appearance. PV antigen can be detected in up to 45% of tumours in immunohistochemistry. PCR is positive in between 24 and 61% of tumours in 2 studies using consensus primers. FcaPV-2 was most commonly detected when tested. However, other PVs have been found including human PVs. Using an alternative PV antigen (p16), all plaques and BISC were positive on immunohistochemistry in one study comparing the two lesions.

Progression of BISC can be variable with some lesions remaining quiescent for long periods, others spreading rapidly and others progressing to squamous cell carcinoma.

Treatment is by observation and surgical excision. Imiquimod a TLR-7 agonist, causes local cytokines (IL-6, interferon-a, and TNF-a) to be upregulated and causes Langerhan cell activation (Miao et al., 2012). This human preparation (used for genital warts and BISC), has been associated with some adverse effects including anorexia and vomiting, erythema, neutropenia, and elevated liver enzymes in about half the cats treated. The individual tumours were helped, but this did not stop the appearance of other masses during or after treatment, suggesting that imiquimod did not stimulate a protective immunity or that such immunity was too late in the progression of the new lesions.

FELINE SCC

Cutaneous squamous cell carcinoma are common in cats and appear as flat, ulcerated masses with tissue destruction and loss being obvious when affecting the nose and pinnal margins. These masses are commonly associated with non-haired and non-pigmented areas such as the ears, nose and eyelids, but this is not always the case. FcaPV-2 is found in SCC more than in normal skin, but this could represent an area of damaged, more 'permissive' environment. However, if this was the case you would expect SCCs to have similar FcaPV-2 regardless of the site. However, 76% of haired/pigmented area SCCs were PV positive compared to 42% at non-pigmented/hairless sites. Despite these findings and others, doubt remained regarding the role of PV in SCC in cats.

Borrowing from human medicine cats were examined for cellular dysregulation consistent with tumorigenesis. An absence of p53 and pRb combined with an increase in p16 are considered reliable IHC markers and in cats such changes were seen in 100% (15/15) of viral plaques and BISCs. In addition, increased p16 staining was noted in both UV-protected (86%) and UV-exposed (40%) SCCs. These findings do open the possibility of vaccination, but the epidemiology of PV transmission is poorly understood.

FELINE SARCOIDS (CUTANEOUS FIBROPAPILLOMA)

Feline sarcoid is a rare tumour of cats seen in young to middle aged cats in rural areas. The nose, upper lips and digits are most involved and microscopically they are similar to equine sarcoids with a disorganised expansive dermis under a hyperplastic epidermis. Ulceration is not uncommon. Local recurrence after surgical excision is noted in 30–50% of cases. Metastasis has not been reported. The papillomavirus involved (FeSarPV) appears to be of bovine origin, but is not bovine PV-1 or PV-2 as found in equine sarcoids. FeSarPV has been identified in normal bovine skin.

CALICIVIRUS

BACKGROUND

Feline calicivirus (FCV) is a small non-enveloped, single stranded RNA virus that affects domestic cats and other Felidae. As an RNA virus genetic variation can occur rapidly leading to many different strains with varying antigenicity and pathogenicity. However, there is sufficient cross-reactivity to group them into a single serotype with some cross-protection being afforded.

INFECTION

FCV is contracted from respiratory secretions from infected cats by direct cat to cat contact, droplets over less than 1.5m and though indirect contact particularly of oral, nasal and ocular secretions. Calicivirus is stable in the environment for up to 28 days, longer in cold temperatures. Disinfection requires bleach, chloride dioxide and potassium peroxymonosulfate. Alcohol hand sanitisers and quaternary ammonium disinfectants may be ineffective. Animals will shed for around 30 days and some go onto be chronic shedders. Around 10% of healthy cats will shed FCV at arrival at the shelter.

CLINICAL SIGNS

Clinical signs are usually respiratory with upper repiratory, ocular and oral signs being common. Ulcers in the mouth due to rupture of viral vesicles often make cats very inappetant. Highly pathogenic strains have caused sporadic outbreaks of FCV-associated virulent systemic disease (VSD) in which pyrexia, cutaneous oedema, ulcerative dermatitis, anorexia and jaundice, with up to 50% of cats dying or being euthanased in extremis. Interestingly adult cats are more severely affected than kittens and field vaccination does not appear to be protective. These outbreaks have been described in the USA and rarely in Europe (e.g. Reynolds et al 2008). Clinical signs reported by Pasavento et al., (2004) are shown in Table 3.

Table 3: Clinical signs in VSD calcivirus infections

Area	Signs
Oral cavity	Ulcers affecting the dorsum of the tongue, with smaller ulcers on the hard palate and gingiva
Feet	One or more feet were affected with circumferential hyperemia at the pad junction to sloughing of the entire footpad
Limbs and ventrum	Alopecia with subcutaneous oedema of the limbs
Face	Subcutaneous oedema
Conjunctiva	Red and swollen, with crusting discharge at the medial canthus
Chest cavity	Pulmonary edema of variable severity, and some cats had blood-tinged pleural effusion.
Abdominal cavity	Multiple, small, discrete foci of peripancreatic and omental fat necrosis were present in some cats.

Cutaneous signs are seen as part of VSD, but calicivirus has also caused a syndrome typified by ventral abdominal skin signs following clipping and surgical intervention in 2 cats in Belgium. Pustules were described affecting the clipped areas for surgery. Histologically the skin showed a panepidermal pustulosis and necrotising dermatitis. In the first, a full recovery was made despite the use of steroids, whereas in the other despite supportive therapy the animal was euthanased (DeClerq, 2005). Using steroids in viral disease appears contradictory, but FCV ulcers appear to heal more quickly when they are used.

DIAGNOSIS

In the face of clinical signs, virus isolation from oropharyngeal swabs in VTM should be submitted for virus isolation, but it should be remembered that shedding in apparently normal animals is not unlikely. Immunohistochemistry using monoclonal antibody anti-feline calici virus CV8-1A is described on formalin fixed tissue with antigen retrieval which would confirm the diagnosis in cases with cutaneous signs.

TREATMENT

See below for Herpesvirus

HERPESVIRUS

BACKGROUND

Felid herpesvirus type 1 (FHV-1) [Varicellovirus genus] is an enveloped DNA virus characterised by latent infections. The virus is common and associated with upper respiratory disease, ocular disease and occasionally dermatitis.

IMMUNITY AND LATENCY

Vaccines are licensed to reduce the clinical signs caused by infection feline herpes virus type 1 (FHV) rather than provide full protection. Latent infection will occur in around 30% of cats that are infected and recrudescence is common with stress or immunosuppression or concurrent illness. The virus is neurotropic and resides in the trigeminal ganglion and in recrudescence the distribution of lesions usually follows the distribution pattern of this nerve.

CLINICAL SIGNS

Cutaneous disease (Herpes dermatitis) due to FHV-1 is almost always seen affecting the face including the lips, periocular skin and nose and is typically seen as crusted vesicular lesions which appear to coalesce and ulcerate, resulting in alopecia. Ulcerative stomatitis is less common than in calicivirus. A recent case report showed only pinnal dermatitis (Porcellato et al., 2018) and previously two cats were reported with lesions on the trunk without any facial signs (Sanchez et al., 2012). The usual (rostral) distribution of the signs mean that mosquito-bite hypersensitivity, eosinophilic granuloma complex, pox virus and squamous cell carcinoma as well as allergic dermatitis are all differential diagnoses.

Histopathology reveals a necrotising eosinophilic dermatitis that often results in ulceration. The inflammatory infiltrate that may contain many eosinophils leading to confusion with EGC and parasitic lesions. The intranuclear inclusion bodies characteristic of herpesvirus can be difficult to find and immunohistochemistry or PCR on tissue biopsy samples may be needed. Confirmation of the diagnosis is important because immunosuppressive drugs can worsen this condition.

TREATMENT OF CALICIVIRUS AND HERPESVIRUS

The focus of treatment for animals with respiratory disease is supportive care. Fluids, and nutritional support are often needed and appetite stimulants such as mirtazapine are suggested by some authors. Steam inhalation may assist decongestion and topical ocular medications are often needed in FHV-1 to treat pain and ulceration and include antivirals such as trifluidine, lubricants and antibiotics.

Specific antiviral therapy may be useful in FHV-1. Famciclovir has been used and more recently the dose recommendation has increased to 90 mg/kg BID PO (previously 40mg/kg BID PO) (Sebbagg et al., 2016) and some authors have reported improved outcomes. In addition, one paper has described the successful use of famciclovir in 2 cats with Calicivirus (Cervone & Bensignor, 2016). Lysine administration for FHV-1, although initially thought of as promising appears ineffective in the face of Herpes disease (Bol et al., 2015). Feline

interferon omega (by injection 3 times a week or orally every 24 hours) has been used for FHV-1, but there is controversy as to whether this is of clinical benefit. Whatever the treatment herpesvirus dermatitis is guarded because the viral infection will persist and recrudescence is common.

FIV

Feline Immunodeficiency Virus–Related Dermatitis. Cats with either feline immunodeficiency virus (FIV) or feline leukemia virus may get skin disease related to immunosuppression. FIV-related skin problems include abscesses, skin and ear bacterial infections, demodicosis (D. cati) and mycotic infections. Some cats with FIV develop nonpruritic, generalized, papulocrustous lesions with concurrent alopecia and scaling, which are most severe on the head and limbs. On histopathology, FIV-related dermatitis demonstrates hydropic interface dermatitis and giant keratinocytes. To date, treatment options for this skin disease have not been successful.

FeLV

FeLV is a retrovirus with oncogenic and immunosuppressive properties. It is an enveloped RNA virus that is not viable in the environment. FeLV infected cats are at increased risk of cutaneous infections including pyoderma, paronychia, poor wound healing, seborrhoea, exfoliative dermatitis and pruritus. In addition, such cats have increased susceptibility to ringworm, demodicosis, Malassezia dermatitis and BISC.
Two specific cutaneous syndromes are described. The first is cutaneous horns and the second is giant cell dermatosis.

CUTANEOUS HORNS

These are not pathognomic for FeLV, and a similar clinical appearance may be seen in a variety of tumours. Affected cats have warty hyperkeratotic lesions affecting the paw pad most commonly. Histologically these are distinct from non-FeLV associated cutaneous horns and show parakeratotic hyperkeratosis, apoptosis and multinuceate epithelial giant cells. Surgical excision or benign neglect are the treatment options.

GIANT CELL DERMATOSIS

This is a rare disease characterised by severe crusting and scaling in the cases described by Gross et al., (1993) and less severe signs in a single case report by Favrot et al., (2005). In this latter case ulcerative skin lesions were noted affecting the head, legs and feet. In all but one case, in the earlier series, the formation of epithelial syncytial cells was the key histopathological finding.

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Selected Zoonoses: Dermatophytosis and Mycobacterial Infections in Cats

Steve Shaw

DERMATOPHYTOSIS

INTRODUCTION

Ringworm is common in cats, but much less common in dogs. Although rarely seen in people, cats provide a consistent source of infection with *Microsporum canis* and potentially other less common *Trichophyton species*. The most common cause of ringworm in people is *Trichophyton rubrum* and causes onychomycosis most often, as well as athlete's foot (also *Trichophyton mentagrophytes and Epidermophyton floccosum*). Interestingly, the prevalence of *T. mentagrophytes* is much higher in athletes with athlete's foot indicating a different epidemiology. When ringworm affects people different syndromes are seen. These historically have been described by their location e.g. Tinea capitis affecting the scalp. Similar to veterinary infections, non-inflamed alopecia, through to more inflamed skin and kerion are seen.

PREVALENCE AND RISK FACTORS

An accurate assessment of the prevalence of dermatophytosis in small animals is not available. Hill et al., (2006) reported 2/154 cases in a survey of the prevalence of dermatological disease in dogs and cats in small animal practice in the UK. The prevalence in cat shelters is considered higher, but in a shelter study in Canada in which 400 cats were tested by culture using the Mackenzie toothbrush method for sample collection on entry, no cats were shown to be positive over a 4 month period. However, experience has shown that dermatophytosis can be a considerable problem in some catteries and shelters. FeLV and FIV infection in themselves do not increase the risk of dermatophytosis, but young kittens and immunosuppressed cats have more severe clinical signs and Persians cats are predisposed to dermatophilic pseudomycetoma due to *Microsporum canis*. Long-haired cats were more likely to be infected in one study (Patel et al., 2005) Inapparent carriage is commonly considered to be a problem, but was rare in a UK survey (Patel et al., 2005).

CLINICAL SIGNS

In many cats, dermatophytes cause mild disease with scale and associated alopecia in a limited area. The alopecia is often circular and on the head. There may be an erythematous margin and the typical size is around 4-6 cm. Lesions may affect other sites and are often multifocal, becoming confluent in severe cases. Except in young cats where the bridge of the nose and ear tips are often involved, lesions are non-symmetrical. Pruritus is often absent. Generally, the cat is well. Less commonly miliary dermatitis has been reported as a clinical sign, but this speaker has never seen this form. In immunosuppression, bacterial secondary

infection occurs making lesions more severe. In many cats, self-cure will occur within 20 weeks or before.

Pseudomycetoma is a subcutaneous form of dermatophytosis usually seen in the Persian cat (Nuttall et al., 2008) and has exceptionally been associated with intra-abdominal masses in infected animals that have undergone surgery (Black et al., 2001)

DIAGNOSIS

Clinicians will often be highly suspicious of dermatophytosis based on the animal's circumstances and clinical signs and although there is no definitive test for dermatophytosis, fungal culture and increasingly qPCR are highly sensitive and can both identify the species in many cases. The approach, based on trying to achieve at least a tentative diagnosis early in the work-up, should include:

1.) Microscopic examination of hairs taken from the lesion or identified by Wood's Lamp examination and possibly aided by dermascopy.

2.) Wood's lamp examination of the animal or possibly of samples collected by toothbrush

3.) Fungal culture and/or qPCR.

In a recent study, qPCR was positive in the majority of cases for a genus level identification, but was less able to determine the species. Based on this study, fungal culture remains the most useful test in that it was more sensitive and the species was determined in all cases (Moriello & Leutenegger, 2018).

In cases of nodular dermatophytic disease, biopsy is needed for diagnosis and in the case of small numbers of masses excisional biopsy can be very useful to debulk the lesions prior to treatment. In addition, many cats with dermatophytic pseudomycetoma are culture positive on coat brushings.

Monitoring treatment success uses a combination of clinical signs, the Wood's lamp method and fungal culture. Cats should be retested every 1-2 weeks. When considering the culture results, the number of colony forming units is useful in monitoring treatment response. qPCR will provide positive results when fungi are dead, and ultimately, clinical cure is defined as negative qPCR in a treated cat, or negative fungal culture in a cat with no lesions. Wood's lamp testing may reveal positive glowing hair tips in such cured cases.

TOPICAL AGENTS

The role of topical therapy is to aid in obtaining clinical cure and in reducing infectivity and contamination of the environment. Clipping to remove infected material is controversial. Clipping removes large amounts of contaminated hair, allows easy application of topicals, but can result in further areas becoming infected demonstrated in 3/9 studies (Moriello et al, 2017).

Twice weekly lime sulphur dips or miconazole/chlorhexidine shampoos are recommended for the topical therapy of dermatophytosis. However, chlorhexidine as a sole agent is poorly effective. Enilconazole has been used in the cat, but is not licensed and carries the risk of

hyper-salivation, idiopathic muscle weakness and elevated serum ALT. For local therapy clotrimazole and miconazole creams and ointments have been used as adjuvant therapies.

SYSTEMIC TREATMENTS

Systemic therapy is the principle mode of therapy. The registered treatment in the UK is itraconazole (Itrafungol, ELANCO) that is used daily for one week on and one week off (5mg/kg/day for 3 alternate periods of 7 consecutive days) and is highly effective. Terbinifine is also considered efficacious but is not licenced in the UK. Lufenuron was considered a possible therapy for dermatophytosis, but this has no in vitro efficacy against ringworm, does not change the clinical course of the disease and should not be used.

ENVIRONMENTAL DISINFECTION

Dermatophytosis spores can remain in the environment for long periods and may lead to infection in people or cats especially in multi-cat environments as well as confusing monitoring fungal cultures during treatment. Infection from the environment alone is considered rare (Moriello et al., 2017). Ringworm in people is treatable and can be cured, but prolonged treatment times may be required in immunocompromised people. Vets may be at risk of complaint in cases of zoonosis when identification of dermatophytosis is slow or incorrect and should be careful to inform clients of ways of decontaminating their homes and avoiding infection. Clipping of hair from affected areas (possibly the whole cat), topical treatments and routine cleaning are useful in reducing spores.

Routine cleaning is required: vacuum cleaning, surface wiping and hot machine washing of animal bedding are required. All of the common disinfectant types, for instance bleach, chloride dioxide, quaternary ammonium compounds, and accelerated hydrogen peroxide products are effective against dermatophytes. In addition, enilconazole (Imaverol, ELANCO) can be used for the environment. Cat flaps should be thoroughly cleaned as a common narrow route for all cats in the house. Isolation of animals during treatment may be useful, but welfare, and possible behaviour effects need to be considered. In multi-cat shelters, isolation may be an essential to achieve dermatophyte-free status.

MYCOBACTERIAL DISEASE

INTRODUCTION

Mycobacterial infections in the cat are rare, and in many cases are not zoonotic. This group of infections could fill several lectures and so today we will deal with diagnosis, so that in the face of possible disease you are equipped to make a definitive diagnosis and protect yourself, staff and owners from potential zoonotic disease. Treatment will not be discussed.

Mycobacteria are a broad group of organisms and possible organisms are shown in Table 1. In many cases, cat will be presented with subcutaneous nodules and at referral, if otherwise well will be investigated within dermatology and oncology clinics.

Table 1: Species of Mycobacteria

Mycobacterium	Route of infection	Zoonosis
M. microti	Small rodents (voles) - also seen in llamas	Human infection from rodents and llamas reported (1)
M. bovis	Environmental contamination from cattle (± badgers)	Yes
Mycobacterium lepraemurium	Small rodents	No
Non-tuberculous mycobacteria (NTM) M. fortuitum, M. avium-intracellulare and others	Soil and plants	No

(1) Xavier Emmanuel et al., 2007).

PREVALENCE AND RISK FACTORS

Most cases of mycobacterial disease are introduced by inoculation of the skin by trauma, particularly when hunting or fighting although gastrointestinal infections in cats fed a raw venison food has recently been reported, similar to that seen from milk before TB eradication and pasteurisation. Geographic differences are seen in the prevalence of some organisms with M. bovis in the southwest, Wales and Welsh borders, M. microti south of London and south-west Scotland and M. avium in the east of England. Immunocompromise, due to breed factors (e.g. Abyssinians), FeLV and FIV or immunosuppressive treatments are important determinants of the severity of the tuberculoid disease.

CLINICAL SIGNS

The clinical signs of the zoonotic and non-zoonotic mycobacterial infections are very similar and these are summarised in Table 2. Systemic disease is more common in infections with M. bovis and M. microti.

Table 2: Common cutaneous clinical signs of Mycobacterial infections in cats

Organism (s)	Clinical signs	Notes
Slow growing organisms		
M. bovis M. microti	Single or multiple ulcers, abscesses, plaques and nodules	Most common on the head, neck and limbs Commonly associated with systemic signs (including lymphadenopathy)
M. avium complex M. avium avium M. avium hominissus M. avium partuberculosis	Single or multiple nodular skin lesions	Lymphadenopathy is common, but generalised disease is usually only seen in immunocompromised animals
M. lepraemurium	Focal mass comprising a subcutaeous granuloma, which rapidly develops into a more widespread pattern of nodular disease. Ulceration and fistulae may follow. Lesions are common on the head and limbs and are occasionally seen on the nasal planum, lips and tongue	Usually seen in young adult male cats or cats that are immunocompromised
M. visibile	Feline multisystemic granulomatous mycobacteriosis Diffuse subcutaneous disease and widespread disseminated disease	Seen in older cats in the US
Novel Mycobacterial sp, with genetitic similarity to M. leprae, M haemophilium and M malmoense	Slow (months to years) development of nodular disease which does not ulcerate	Older cats in Australia
Mycobacterium sp strain Tarwin	Both M. lepraemurium like disease and M. visible-like disease	In both young and old cats
Rapidly growing organisms		
M. fortuitum group (incl. M. fortuitum & M. perigrinum) M. chelonae group (incl. M. chelonae and M. abscessus) M. smegmatis group (incl. M. smegmatis ss, M. goodii & M. wolinskyi Other species	Following a penetrating wound cat bite abscess like lesions or plaques and/or nodules appear There is often skin thinning and then discharge from small fistulae Lesions are common in the inguinal fat and over the lumbar region	Signs are most severe in immunocompromised cats 1 case in literature with Mycobacterium and Nocardia resulted in significant hyperglycaemia of granulomatous disease

DIAGNOSTIC TESTING

The primary tool in considering the potential presence of mycobacterial infection is cytology. A granulomatous or pyogranulomatous pattern should be seen. In addition, giant cells are often observed. Mycobacteria are not stained by Romanowsky staining, but negative staining in which non-stained rods are seen against the stained back-ground will sometimes be seen. In cases where there is a suspicion of mycobacterial involvement fixing cytology slides for 1 hour in 95% ethanol will make the slide safer for handling and this should be performed for all slides leaving the practice for cytology.

In the university department or larger hospital the slide can be stained immediately using Ziehl–Neelsen stain which may give a rapid result in some cases. PCR can then be used to identify the organism in positive cases or provide a second stage check.

Biopsy for histopathology is useful and will be essential in some cases, but in M. microti and others ZN staining may be very insensitive. In view of this a fresh tissue sample can be kept for culture, although some organisms will not grow in vitro.

Comprehensive mycobacterial culture, susceptibility and identification services are available at APHA Weybridge. In addition, the Leeds Medical Microbiology Labs offer both MTB Complex and non-TB Complex Mycobacterium spp PCR. Their address is Department of Microbiology, Old Medical School, Leeds General Infirmary, Thorseby Place, Leeds. LS1 3EX. Please contact the labs before submitting any samples!

When M. bovis is suspected or confirmed in a cat or dog post mortem or confirmed in a living patient, the disease is notifiable. However, the suspicion of infection in a living animal is not. Notification should be to APHA England (Veterinary Head of Field Delivery (VHoFD)) (TB legislation 2006). The TBOS team can be contacted on CSC.TBOS@apha.gov.uk and the e-mail should be copied to PRESTONAH.DUTYVET@apha.gov.uk for information. In the event of an animal being euthanased with ZN positive tissue identified on cytology or histology, or strong suspicion of mycobacterial disease, the owner should be encouraged to submit the animal for post mortem at the APHA.

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Parasites Relevant to Feline Skin Disease

Silvia Colombo

INTRODUCTION

Ectoparasitic diseases in owned cats are becoming less common in the western world. The recent introduction on the market of new wide spectrum parasiticidal drugs, effective in prevention of flea and tick infestations and with acaricidal and insecticidal activity are making ectoparasite control much easier. For some diseases, however, there are no registered products and/or standardized protocols for the feline species.

Diseases still seen in cats by general practitioners and dermatologists are flea infestation or hypersensitivity, otodectic mange and, in season, trombiculosis. Cheyletiellosis, notoedric mange, pediculosis and demodicosis are uncommon in everyday practice. Some of these diseases can be seen in specific situations, such as colonies of stray cats, breeding facilities or catteries.[1-3]

This presentation will give a brief update on common and uncommon diseases, including their prevalence. Flea infestation/hypersensitivity will not be addressed in this lecture.

OTODECTIC MANGE

Prevalence in stray cats: 19.3-25% USA; 15.8% Greece[1-3]

Otodectic mange (OM) is a parasitic disease of the external ear canal caused by the mite *Otodectes cynotis*. The mite is not species-specific and found all over the world. It is responsible for 50-80% of cases of otitis externa in the cat. The life cycle is completed in three weeks, with adults surviving for up to two months on the host and 12 days off the host in ideal conditions. OM is very contagious and typically seen in kittens or, less frequently, in adult cats coming from colonies, catteries or pet shops.[4,5]

Many topical and systemic active ingredients are available to treat OM. Before treatment, cleaning the ear canals with a cerumenolytic product in order to mechanically remove the parasites and the excess of cerumen is recommended. Topical therapy involves using acaricidals or non-acaricidals, which are also effective in killing the mites, possibly because they cannot move and/or breathe due to the product.[6] It is important to treat for a minimum of three weeks to cover all life stages of the mite, and to treat all in contact animals. Systemic therapy is more practical for the owners and increases the compliance.[6] Among the newer products containing isoxazolines, the only one registered for the treatment of otodectic mange in cats is selamectin-sarolaner spot on, effective as a single treatment.[7-11]

TROMBICULOSIS

Prevalence in stray cats: 0.02% USA[1]

Trombiculosis (TR) is a parasitic skin disease caused by larvae of mites belonging to the Trombiculidae family. In Europe it is caused by *Neotrombicula autumnalis*. The disease is also called "harvest mites", because it is usually seen in late summer or fall. Only the larval stage is parasitic (transient parasitism) while nymphae and adult mites live in the environment.[4,5] *Neotrombicula autumnalis* larvae are oval, six-legged and red-orange in color. They climb on grass and wait for the host, on which they feed for 3-15 days. The life cycle of this mite is strongly influenced by the season, lasts for 50-70 days and more than one life cycle can be completed in one year. [4,5] Cats get infested when wandering in the countryside and woods, and pruritus and lesions are extremely variable in severity, possibly due to a hypersensitivity reaction. There is currently no registered treatment for TR and although the disease is not difficult treat, re-infestation is possible. Fipronil spray, selamectin and imidacloprid-moxidectin spot on[12-14] have been successfully used with a single application and seem to protect against environmental re-infestations.

CHEYLETIELLOSIS

Prevalence in stray cats: 0.02-0.9% USA; 2% Greece[1-3]

Cheyletiellosis (CB) is a parasitic skin disease caused by mites belonging to the genus *Cheyletiella*. The species adapted to the cat is *Cheyletiella blakei*, but these mites are not species-specific and infestation with the other two species - *Cheyletiella yasguri* in dogs and *Cheyletiella parasitivorax* in rabbits - is possible.[4,5] These are large-sized mites, spend their entire life on the host and the life cycle lasts for 14-21 days. Adult female mites can survive up to 10 days off the host and despite being mainly transmitted by direct contact, environmental transmission may occur. CB is more commonly observed in kittens coming from pet shops or colonies, although it can also be seen in systemically ill adult animals. Clinical presentation in cats may vary from mild exfoliative dermatitis to self-induced alopecia or miliary dermatitis, and pruritus may be of any intensity from absent to severe.[4,5] There are many diagnostic tests which may be useful to diagnose CB, however mites can be difficult to find. The most widely recommended tests are microscopic examination of samples obtained with clear tape and superficial skin scrapings. In some cases, a therapeutic trial is required to confirm the diagnosis.

There is no registered active ingredient to treat CB in cats. Topical (fipronil spray, fipronil spot-on as a single treatment) or systemic (selamectin spot on, three applications with one-month interval or ivermectin, 0.2-0.3 mg/kg subcutaneously once every two weeks) products have been reported to be effective.[15-18]

NOTOEDRIC MANGE

Prevalence in stray cats: 0.002% USA; 2.35% Greece[1,3]

Notoedric mange (NM), also known as feline scabies, is a pruritic, contagious disease caused by the mite *Notoedres cati*. The mite may affect other mammals, including man, and exceptionally the dog. The disease prevalence is unknown; it is thought to be rare, however epidemics are still reported in some European countries.[4-5] Kittens are more prone to the disease compared to adult cats.

After mating on the skin surface, female mites burrow tunnels within the stratum corneum, where they lay 2-3 eggs a day. The life-cycle lasts 14-21 days, in favorable environmental conditions.

NM is extremely contagious and transmitted by direct contact: cats living in breeding facilities, catteries or colonies are predisposed. Notoedric mange is a zoonotic disease and man can transiently be infested. Typical lesions are grey-yellow thick crusts, affecting the pinnae, face and neck in the initial stages of the disease. Lesions may become generalized and pruritus is severe, with self-trauma contributing to the clinical presentation.[4,5] Diagnosis is usually achieved with superficial skin scrapings and mites are not difficult to find. Recently, diagnosis of notoedric mange by microscopic examination of samples collected by using clear tape has been reported, with sensitivity comparable to skin scrapings.[19]

Registered products for treatment of NM include a spot-on formulation containing eprinomectin, fipronil, (S)-methoprene and praziquantel and a spot-on containing moxidectin and imidacloprid, both applied once or twice at one-month intervals. Other protocols involving active ingredients not registered for the disease involve the use of selamectin spot-on (applied twice at 14 or 30 days interval), ivermectin (0.2-0.3 mg/kg subcutaneously at 14 days interval) and doramectin (0.2-0.3 mg/kg subcutaneously once).[18,20-24] The new family of isoxazolines has been shown to be effective in other diseases caused by mites. There are no specific studies on feline notoedric mange, but isoxazolines are likely to be effective. All in contact cats must be treated to avoid re-infestations.

PEDICULOSIS

Prevalence in stray cats: 1% USA; 0.59% Greece[2,3]

Pediculosis is a lice infestation. Lice are small, wingless insects, with legs carrying strong claws to attach to the hair shafts. They spend their whole life on the host, are highly host-specific and many species have preferred body locations. *Felicola subrostrata* is the only louse infesting cats. The whole cycle requires 2-3 weeks and lice cannot survive for more than 1-2 days off the host. The most severe cases are seen in malnourished cats or cats living in poor hygienic conditions. Lice can infest the whole body with preferred localization on the head, neck and dorso-lumbar region, and pruritus is usually absent to moderate. Self-traumatic secondary lesions (excoriations, crusts), self-induced alopecia or miliary dermatitis can be observed. Lice and their eggs are easily identified by close observation or using a magnifying lens, with microscopic examination of hair shafts and samples collected with clear tape confirming the diagnosis.[4,5] Lice are susceptible to the majority of insecticides on the market. Currently, registered active ingredients to treat feline pediculosis include fipronil (spot on and spray) and selamectin spot on, recently made available also in association with sarolaner. A single treatment is recommended with all these products, however eggs are resistant to the majority of insecticides. It is advisable to repeat the treatment after 14 days and treat all in-contact cats.[25-26]

DEMODICOSIS

Feline demodicosis is an uncommon disease caused by mites belonging to the genus *Demodex*. Currently, three species have been identified in cats: *Demodex cati, Demodex gatoi* and a third unnamed species. *Demodex* spp are host-specific mites and the disease is not zoonotic. Infestation with different *Demodex* species in the same cat has been reported.[27-29]

DEMODEX CATI

Demodex cati is very similar to *Demodex canis*, with minimal taxonomic differences. The body is elongated and cigar-shaped. *Demodex cati* lives in the hair follicle, often located close to the exit of the sebaceous gland duct, with its head directed downwards. The way of transmission of *Demodex cati* is unknown and it is hypothesized that it is passed from the queen to kittens soon after birth. Clinically, the localized form involves the head and neck, particularly the periorbital and perilabial regions and the chin. Lesions are erythema, alopecia, scales and crusts with mild to absent pruritus. The disease can also cause bilateral ceruminous otitis, often reported in feline immunodeficiency virus (FIV)-positive cats.[30] A localized form has also been reported in cats affected by asthma and chronically treated with glucocorticoids administered with aerosol.[31]

The generalized form causes similar lesions but more severe and extensive, involving the muzzle, neck, trunk and limbs or the whole body and often associated with immunosuppressive therapies or concurrent systemic diseases (diabetes mellitus, xanthomas, toxoplasmosis, systemic lupus erythematosus, hypercortisolism, retroviral infections, Bowenoid *in situ* carcinoma).[5,30]

Since *Demodex cati* lives in the hair follicle, the preferred diagnostic method is the deep skin scraping, followed by microscopic examination of hair pluckings.

DEMODEX GATOI

Demodex gatoi is smaller and stubbier than *Demodex cati* and morphologically similar to *Demodex criceti*, the hamster's parasite. *Demodex gatoi* lives in the stratum corneum and seems to be contagious among cats living together. In *Demodex gatoi* infestation, the most common clinical sign is variable pruritus (absent to severe). Cats may show self-induced alopecia involving the trunk, abdomen, flanks or limbs or self-traumatic lesions such as alopecia, excoriations, ulcers and crusts or papular and crusting dermatitis (miliary dermatitis). This type of demodicosis is not associated with immunosuppression. To diagnose *Demodex gatoi*, a superficially located species, the suggested methods are superficial skin scrapings or microscopic examination of samples obtained by clear tape. In overgrooming cats, the observation of *Demodex gatoi* may be difficult and some authors suggest a fecal examination with flotation.[5,30,32]

UNNAMED *DEMODEX*

The third, still unnamed *Demodex* species is of intermediate size, with a body shorter and stubbier than *Demodex cati* but longer and more tapered than *Demodex gatoi*. Its way of transmission and environment are unknown, but it has been recently demonstrated to be a distinct species using PCR.[28] It has been described both with *Demodex cati* infestation and on its own, causing severe pruritus, erythema and alopecia in six cats living in a shelter.[33-34]

TREATMENT

There is no registered product for feline demodicosis and no standardized protocols. An evidence-based review recommended the use of weekly rinses with 2% calcium sulphur, however this product is not available in many countries. Moderate evidence of effectiveness for both *Demodex* species was reported for once or twice weekly amitraz rinses (0.0125% to 0.025%), which may be toxic in felines, and for macrocyclic lactones.[35] Ivermectin may be administered both orally and subcutaneously and is effective in both species, however failures have been reported in *Demodex gatoi* cases. Doramectin (600 µg/kg subcutaneously once weekly for two to three weeks) is effective to treat *Demodex cati.* Milbemycin oxime has been shown to be effective against *Demodex cati* at 1-1.5 mg/kg orally once daily for two to seven months,[35] and once weekly topical imidacloprid/moxidectin for eight applications is effective against *Demodex gatoi*.[36]

Recently, single treatment with oral fluralarer has been reported to be effective for both *Demodex* species.[37-38] *Demodex gatoi* is contagious and treatment of all in-contact cats is recommended.

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Feline Neurology meets Dermatology

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Angela graduated in Italy at the University of Parma. After dedicating some years working in general practice and in various small animal hospitals in Italy, she moved to Switzerland, where she completed a residency training programme in Neurology at the University of Bern before successfully sitting the examination for the European College of Veterinary Neurologists. She has worked as Senior Training in Veterinary Neurology and Neurosurgery at the veterinary teaching hospital of the same institution, where she has also carried out a research project focused on infectious disease of the nervous system obtaining a PhD in the field of Neuroscience. Angela moved to the United Kingdom in 2017 and she has worked at the referral hospital Lumbry Park Veterinary Specialists running the neurology and neurosurgery service. She has then joined Langford Veterinary Services, part of the University of Bristol, as a Senior neurologist, having primary responsibility for neurological cases referred to the hospital and supervising residents, interns and students. Angela's main focuses are infectious diseases of the central nervous system, neuroimaging and neurosurgery.

NEUROLOGICAL CONSEQUENCES OF OTITIS MEDIA/INTERNA (OMI) IN CATS

Vestibular signs, deafness, facial nerve paralysis and Horner's Syndrome may occur as a complication of otitis media/interna (OMI). Rare but potentially deadly complications of OMI are otogenic brain abscesses and meningoencephalomyelitis, which are more frequently reported in the feline species[1] [2] than in dogs. Clinical signs of otogenic brain abscesses and meningoencephalomyelitis arising from otological complications match signs from other structural brain diseases such as intracranial tumours, non-otogenic brain abscesses, infectious or immune mediated meningoencephalitis and cerebrovascular accidents. Clinical history and progression of signs should ideally aid the formulation of an appropriate list of differential diagnoses. Vestibular signs associated with OMI can occur without concurrent evidence of otitis externa, leading to delayed diagnosis and treatment.

A critical step in the management of feline patients with onset of vestibular signs is therefore to localize the lesion within the vestibular system. This latter covers a broad neuroanatomical territory and lesion localization is possible only by systematic evaluation of mental status, gait, postural reactions and cranial nerve function. Vestibular signs include head tilt, vestibular ataxia, leaning, falling towards one side, circling, positional strabismus and nystagmus[3]. Head tilt, ataxia and falling or circling occur toward the side of the lesion as a

result of decreased muscular (extensor) tone ipsilaterally. The extensor tone is increased on the side contralateral to the lesion. On elevating the head of these patients the eye globe on the side of the lesion is rotated ventrally and laterally (positional strabismus). Physiological nystagmus results from an intact oculocephalic reflex when the head of the cat is rotated towards one side; it consists of a slow movement of the eyeball opposite to the direction of head rotation and a fast phase in the direction of head rotation. Pathological nystagmus is called spontaneous if it occurs when the head is held in a normal position or positional, when the cat is placed upside down on its back. The fast phase of spontaneous nystagmus identifies its nature (horizontal, vertical, rotatory) and direction (left or right). In peripheral lesions the fast phase is always away from the lesion [4]. Affected cats may vomit (motion sickness) due to unbalanced input to the reticular formation[4].

Facial nerve axons travel through the temporal bone running beside the middle ear. Similarly, the sympathetic supply of the eye runs along the middle ear as its post ganglionic axons travel between the petrous temporal bone and the tympanic bulla. Facial paralysis and Horner's syndrome may accompany vestibular signs when lesions localize within the peripheral vestibular system.

Bilateral vestibular peripheral signs are rare but more frequently observed in cats. In such cases head tilt and nystagmus are not a feature, while a head excursion from side to side and a serpentine gait is observed. Physiological nystagmus is absent in these cats, but the eyes move to follow objects.

On neurological examination differentiation between central and peripheral vestibular syndrome is made on the presence/absence of signs of dysfunction of the pons and medulla oblongata. As a rule, the absence of these signs supports the suspicion of peripheral vestibular syndrome. An abnormally dull mentation associated with vestibular signs may indicate a central lesion with involvement of the ascending reticular formation. Lesions affecting the UMN system in the brainstem of cats may affect the gait resulting in hemi or tetraparesis with varying degrees of ataxia. Postural reaction deficits may occur ipsilaterally to the lesion due to disruption of the ascending general proprioceptive pathways. Due to the close anatomical location of their emergence, multiple cranial nerve deficits may be observed in central vestibular syndrome (whilst only facial and sympathetic deficits occur for a peripheral lesion).

Spontaneous nystagmus may present in any direction; vertical pathological nystagmus and fast phase changing direction nystagmus are typically reported for central lesions[43]. Advanced diagnostics (CT and/or MRI) should be always considered if central vestibular disease is suspected. Nevertheless, central vestibular lesions without obvious signs of brainstem involvement are possible and care should be taken to provide reasonable expectations from our neurological exam to owners. Recent work recognized the low efficiency of neurological examination in attributing signs to peripheral lesions, claiming that advanced imaging should be recommended in dogs with persistent signs which have been localized at the peripheral vestibular system.[5] CT and/or MRI allow visualization of the middle and internal ear.

While CT scan represents an option to delineate the extent of inflammation of bony structures and to exclude destructive processes at these levels (i.e. soft tissue tumours, carcinoma, osteomyelitis) MRI enables investigation of brain parenchyma and meninges, cranial nerves, presence/absence of intra-labirinthine fluid and provides more important information on the causes of neurological dysfunction. Cerebrospinal fluid analysis (CSF) can identify the spread of infection to meninges and CNS. Rarely CSF culture may be supportive of bacterial meningitis in cats.

Deafness associated with OMI is reported in cats as a direct consequence of inner ear infection (conductive deafness) and/or secondary to ototoxicity (sensorineural deafness) following aminoglycoside antibiotics and local antiseptic administration (chlorhexidine). [6] Conductive deafness may improve over weeks if appropriate treatment is established. Sensorineural deafness is, in most cases, irreversible. Brainstem auditory evoked potentials (BAEP) testing should be considered to detect hearing loss in these cats.

HYPERAESTHESIA AND SUSPECTED NEUROLOGICAL DISORDERS ASSOCIATED WITH ITCH IN THE FELINE SPECIES

PERIPHERAL AND CENTRAL SENSITIZATION OF ITCH AND PAIN

Itch is an irritant sensation which cause a motor response aiming to provide temporary relief[7]. This motor response consists mainly of scratching, rubbing and overgrooming. In more chronic and severe cases self-induced skin lesions may occur as a result of these motor responses.

In people, acute itch is defined as the sensation experienced when itch-inducing stimuli contact the skin, and is usually relieved by pain (including scratch) in the surrounding area[7,8]. In the setting of itch, scratch and self-inflicted skin wounds may alleviate this and are therefore perceived as pleasurable. Chronic itch is the persistent sensation that results from various causes in which pain does not relieve itch, and may actually be perceived as itch. [8]

Chronic itch shares similarities with a particular form of chronic pain called neuropathic pain, which is thought to arise due to a lesion or disease in the nervous system, however chronic conditions occurring elsewhere in the body (i.e. chronic osteoarthritis, cystitis) are known to result in neuropathic like pain in several species including the feline[9,10]. Neuropathic pain consists of a range of abnormal sensations ranging from discomfort, paraesthesia, hyperaesthesia and allodynia (painful sensation in response to non-painful stimuli as touch, warm) to hyperalgesia.

Comparable symptoms are observed in people with chronic pruritus. Itch is indeed a complex process which include cells, mediators and receptors in the peripheral skin, spinal cord, and brain[8]. Alloknesis, comparably to allodynia, is itch augmented by light touch/ brushing of the skin around an itching source. Hyperknesis, similarly to hyperalgesia is uncontrollable itch that is enhanced when prick is applied to the same surrounding skin area.[8,7,11]

The underlying mechanisms of neuropathic pain and chronic pruritus are not yet deciphered in small animals[11,12] however it is acknowledged that an initial peripheral sensitization (prolonged chronic stimulation/inflammation of sensory nerve end terminal, pain/itch receptors) followed by central sensitization (an abnormal processing of the nociceptive information resulting in amplification and facilitation of the painful/itchy sensation) occurring in the cord and superior centres play a role in its development [10,9].

Itch and pain similarities have led to consider chronic itch as a subthreshold form of pain in people in the past[7,11]. Current experimental studies however, suggest that itch and pain are different sensory modalities but that pain- and itch-related cord and brain activation overlap in their development [8]. The phenomena of chronic itch and its central sensitization remain

yet undeciphered in cats but should ideally be considered for novel therapeutic strategies in this species.

FELINE HYPERAESTHESIA SYNDROME (FHS)

Feline hyperaesthesia syndrome (FHS) is a syndrome characterised by tail chasing; biting or licking the lumbar area, flank, or tail, skin rippling and muscle spasms of the dorsal lumbar area, which may be spontaneous or elicited by only a light touch. These episodes may be prevented in many cats by not stimulating this area[3]. Other clinical signs include excessive and unusual vocalisations, episodes of apparently wild and uncontrolled jumping and running, hallucination and behaviours that mimic signs of oestrus.[13] Many of these cats also lick at the air or chew at their paws during the episodes[3]

FHS is a poorly understood disorder which has been associated with behavioural, dermatological, orthopaedic and neurological conditions. Among these, lumbar intervertebral disc disease and myopathy of lumbar muscles have been reported[3]. It has been reported that FHS may result from an excessive sensory stimulation of the prosencephalon resulting in focal seizures in cats with an especially low seizure threshold[3].

In a recent case series of seven cats submitted to extensive work up, including neurological, dermatological and behavioural assessment definitive final diagnosis was not reached, although hypersensitivity dermatitis was suspected in two cats[14]. In this study no evidence of intra- or extracranial causes of seizures was identified in cats with an MRI scan of the head and cerebrospinal fluid analysis. However, this does not exclude that FHS could represent a form of idiopathic epilepsy; the poor response to anti-epileptic drugs conventionally used in this species (Phenobarbital, Diazepam) make this hypothesis less likely. On the contrary the response of some cases to gabapentin and topiramate, which are indeed antiepileptic drugs with effects on neuropathic pain in small animals may indicate that neuropathic itch/ pain play a role in the development of this condition in cats.[14]

FELINE IDIOPATHIC ULCERATIVE DERMATOSIS

Idiopathic ulcerative dermatosis **(**IUD) is a rare condition in cats characterized by ulcerative lesions located between the shoulder blades or at the base of the neck, associated with scratching and self-inflicted trauma. Lesions heal spontaneously as soon as the cat is prevented from self-mutilating with an Elizabethan collar or bandages but affected cats are subjected to frequent relapses.[15] Moreover, this condition is refractory to medications and surgical treatment unattainable making its prognosis guarded to poor. [15],[16]

Few publications have focused on this condition. One case of a cat improving with topiramate 5 mg/kg PO q12h has been reported. During a 30 months follow-up the clinical signs were controlled by this drug, although two recurrences following two attempts to stop this medication occurred. In the same cat treatment with gabapentin, pregabalin and phenobarbital failed to improve the clinical signs[16]. Response to topiramate, an antiepileptic drug with beneficial effects in the treatment of obsessive-compulsive disorders and self-mutilation in humans may suggests a form of neuropathic itch syndrome, leading to the hypothesis that feline IUD has a neurological aetiology.

Other successful treatments reported include steroids[17], although relapses are reported after a few weeks of treatment, and anecdotally gabapentin, ciclosporine, or oclacitinib[18].

A recent publication claims that IUD is a purely behavioural disorder resulting from poor cat welfare and that environmental modifications lead to successful healing in all cases.[15] However, in agreement with the theory of peripheral and central sensitization of itch, in the author's opinion it is not excluded that IUD represents a form of psychogenic pruritus in which chronic damage of itch receptors is established by sustained scratching.

FELINE OROFACIAL PAIN SYNDROME

Feline orofacial pain syndrome (FOPS) consists of episodes of exaggerated licking, chewing, and facial pawing frequently associated with self-induced trauma to the face and tongue. Burmese cats are overrepresented which may indicate some hereditary component for this disorder. Cats may be affected at any age, but signs can frequently start during teeth eruption around 6 months of age. However, in most cases, dermatological and dental work up, MRI and CSF evaluations have yielded normal results. It has been suggested that affected cats may have a genetically based lowered threshold for seizure development where the increased activity of the general somatic afferent system is sufficient to elicit a focal seizure[3]. An initial facial or oral lesion, (such as the eruption of permanent teeth) may be the initial trigger for the episodes.

In a retrospective study on 113 cases[19] antiepileptic drugs (phenobarbital, diazepam, gabapentin and carbamazepine) were more effective than opioids or anti-inflammatory drugs (including corticosteroids) in reducing clinical manifestations, which seems to validate the previous hypothesis of this condition being focal seizures. However, striking similarities have been found in this study between clinical manifestation of FOPS in cats and trigeminal neuralgia/glossodynia in people, a sensory disorder affecting trigeminal information associated with excruciating neuropathic pain/allodynia. In both species dental/oral lesions may trigger the condition by sensitization/damage of the trigeminal nerve endings[19] and antiepileptic drugs with analgesic effects have beneficial effects in relieving pain and discomfort.

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Straight from the Cat's Mouth...
Dental Diseases Relevant for Dermatologists

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Simone graduated from Berlin University (Freie Universitaet Berlin) and moved to the UK soon after graduation. Her interest in veterinary dentistry early emerged early in her career. This led to becoming a member of the British Veterinary Dental Association and of the European Veterinary Dental Society. Simone did her residency at the University of Pennsylvania in Philadelphia, USA.

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In this talk disease conditions that are relevant to both disciplines in a direct or indirect context will be presented.

Conditions with the potential to cause systemic effects or localised cutaneous infections, for example through oral contaminated discharges.

- Periodontal disease
- Feline Chronic Gingivo-stomatitis

We will briefly consider the diagnostic and treatment approaches for these dental conditions, and the feline oral microbiome in healthy cats versus periodontally diseased cats will be discussed in more detail.

Conditions with a more direct overlap with dermatology: Eosinophilic granuloma complex.

- Indolent ulcer
- Eosinophilic plaque
- Eosinophilic granuloma

A case of eosinophilic stomatitis and glossitis will be presented, with emphasis on the dentistry-specific diagnostic and treatment aspects which had to be considered in addition to the cutaneous EGC treatment approach.

NOTES:

Feline Autoimmune Skin Disease

Silvia Colombo

INTRODUCTION

Autoimmune skin diseases are characterized by reactions of the immune system against "self" antigens (https://pathology.jhu.edu/autoimmune/definitions) and are uncommon to rare diseases in both general and referral practice.[1] In felines, among antibody-mediated autoimmune diseases pemphigus foliaceus is the most common, while pemphigus vulgaris, paraneoplastic pemphigus and autoimmune subepidermal blistering diseases are extremely rare. Cell-mediated autoimmune diseases is represented by lupus erythematosus. A few cases of systemic lupus erythematosus have been described in cats, while there is debate about the existence of discoid (cutaneous, nasal) lupus erythematosus. The pathogenetic mechanism behind vitiligo is currently unknown, and both anti-melanocyte antibodies and cell-mediated immunity may be involved.

PEMPHIGUS FOLIACEUS

Pemphigus foliaceus (PF) is the most common autoimmune skin disease in cats, although it only represents 1% of cases seen by veterinary dermatologists.[1] Pemphigus foliaceus is an antibody-mediated autoimmune skin disease, with autoantibodies disrupting the integrity of the desmososmes, as in dogs. The target autoantigen, identified in humans (desmoglein-1) and dogs (desmocollin-1), is unknown in the feline species. A recent study identified circulating anti-keratinocyte IgG in 77% of cats affected by PF and postulated that the target autoantigen is likely to be different from the one identified in dogs.[2] Pemphigus foliaceus in cats may be spontaneous or, in some cases, a drug-induced or drug-triggered pemphigus has been suspected. Two feline cases associated with thymoma and one case associated with feline leishmaniosis have also been reported.

CLINICAL FEATURES

There is no apparent breed predisposition, and the median age of onset is 6 years. The female to male ratio is 1.5, and the average time between onset of disease and diagnosis is three months[3-5]

The primary lesion is a large subcorneal pustule, spanning multiple hair follicles, however, this lesion is easily ruptured and cannot often be appreciated. The most common lesions identified are superficial erosions and honey-coloured, often coalescing crusts. The most commonly involved body sites are the nasal planum, muzzle, eyelids, pinnae and footpads. The area surrounding the nipples is a peculiar location in the cat, although the most distinctive localization of PF in cats is the claw fold. A thick, yellowish, caseous exudate can be expressed from the claw folds. In the majority of cases, the disease involves two or more body sites, however localized lesions have been reported in 19% of cases. Lesions are symmetrical in over 80% of cases, and 30% of affected cats also have otitis externa. Pruritus is common and the cat may be systemically ill with anorexia, lethargy and hyperthermia, enlarged lymph nodes and lameness, if pedal lesions are severe. Clinicopathological

abnormalities include leukocytosis and neutrophilia. Differential diagnoses include pustular dermatophytosis, adverse drug reaction, leishmaniosis and superficial pyoderma.[3-5]

DIAGNOSIS

Despite the difficulty of identifying an intact pustule in cats, useful samples for cytological examination can be obtained from the underneath of a crust of from the claw folds. Cytology shows large numbers of neutrophils and acantholytic cells which may be in rafts. A bacterial/fungal infection should be ruled out and bacterial and fungal cultures should be performed. Bacterial infection as a complicating factor has been reported in 63% of cases, and *Malassezia* overgrowth in 19% of cases on cytological examination. Secondary infections should be treated before taking biopsy samples for histopathological examination. The confirmative diagnostic test is histopathology from skin biopsy samples and crusts, which may show subcorneal pustules containing neutrophils and acantholytic cells, sometimes admixed with eosinophils.[6] The diagnosis may be difficult due to the lack of intact pustules in the sample, and the observation of ghost acantholytic cells in the crusts supports the diagnosis. Direct/indirect immunofluorescence is not commercially available.

TREATMENT

In general, cats affected by PF respond well to treatment, achieving remission in three to four weeks on average. Glucocorticoid monotherapy is the first treatment, and the majority of cats do not require an additional immunosuppressive drug. Recommended induction doses are 2-3 mg/kg/day when using prednisolone, 0.1-0.2 mg/kg/day when using dexamethasone, or 0.3-0.5 mg/kg when using triamcinolone. The dosage is gradually reduced when the disease is in remission and a reduction of 20-25% every two to four weeks is recommended.[3-5] A recent study on 37 cats reported complete remission within 8 weeks in 97% of cats with a median induction dose of 2 mg/kg prednisolone daily. The median maintenance dose in the study was 1.2 mg/kg/week.[7] In some cases, glucocorticoids are not effective in maintaining remission at an adequate dose or cause adverse effects. Other immunosuppressive drugs can be added, such as ciclosporin (5-10 mg/kg) or chlorambucil (0.1-0.2 mg/kg/day).[8] Azathioprine is not recommended in cats due to the high risk of bone marrow suppression.

Long term remission with discontinuation of all drugs is not uncommon in cats (approximately 15% of cases). The majority of cats require long term treatment with glucocorticoids, ciclosporin or chlorambucil, alone or in combination. Other suggested treatments, in older papers, include doxycycline, gold salts and megestrol acetate.

PEMPHIGUS VULGARIS (PV)

PV has been rarely reported in cats, and most descriptions of this disease are anecdotal or have been published in the 80s, when the modern diagnostic techniques were not available. The antigen targeted in cats is unknown. Lesions affect the oral cavity, nasal planum, mucocutaneous junctions, and less commonly haired skin and footpads, and are characterized by vesicles, erosions and crusting. The affected cat is usually systemically ill. Diagnosis requires histopathology and rule out of other diseases causing erosions, because vesicles are very fragile and rupture easily. Apparently, the disease responds to immunosuppressive doses of glucocorticoids.[9,10]

RARE ANTIBODY-MEDIATED AUTOIMMUNE SUBEPIDERMAL BLISTERING DISEASES

Only two cases of mucous membrane pemphigoid and one case of bullous pemphigoid have been reported in cats so far.[11,12] Both diseases target antigens of the dermoepidermal junction, such as BPAG2 (BP180), the transmembrane type XVII collagen in both diseases and laminin 332 (laminin 5) in mucous membrane pemphigoid.

VITILIGO

Vitiligo is uncommon in cats. The target cells in this disease are the melanocytes of the skin, mucocutaneous junctions and oral cavity. The pathogenesis of vitiligo in animals is currently unknown and in human medicine various theories have been proposed to explain the destruction of melanocytes. It is an autoimmune disease and both anti-melanocyte antibodies and cell-mediated immunity may be involved. In humans, the disease has a genetic component and interestingly it seem to affect preferably young adult Siamese cats. Non-inflammatory depigmentation is observed on the nasal planum, eyelids and footpads.

Histopathologically, loss of melanocytes from the epidermis and/or the hair follicles is the main feature of the disease. Lymphocytes can be seen in the basal layer of the epidermis, close to apoptotic melanocytes, in the active phase of the disease. There is minimal dermal inflammation, with melanophages full of melanosomes lost by the dying melanocytes. Vitiligo is a cosmetic disease, and spontaneous remission may occur. Various treatments have been tried in dogs, however reports are anecdotal and involve too small a number of dogs to draw any conclusion on efficacy.[13]

RARE CELL-MEDIATED AISD

Discoid (cutaneous, nasal) lupus erythematosus has been reported only twice, in 1990 and 1991, in a total of five cats.[14,15] There is debate about the existence of the disease in the cat, and the authors of the dermatopathology book "Skin Diseases in the Dog and Cat" do not believe that DLE has been diagnosed convincingly in the cat.[6] Systemic lupus erythematosus fulfilling the criteria of the American Rheumatism Association criteria has been described only in one cat so far.[16]

RARE ANTIBODY- AND CELL-MEDIATED AUTOIMMUNE DISEASES

One case of putative paraneoplastic pemphigus has been described in an eight-year-old female spayed Himalayan cat with lymphocytic thymoma and myasthenia gravis.[17]

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Behavioural Aspects of Feline Skin Disease

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Nicola graduated from the University of Bristol in 2015 with a degree in Veterinary Nursing and Bioveterinary Science. Since then she has been working as the sole dermatology nurse at Langford Vets, supporting the dermatology service and student teaching. She is currently working towards a Masters degree in clinical veterinary research at the University of Bristol, looking at the role of stress as a flare factor for cats with allergic skin disease.

The only recognised skin condition in cats that has an underlying behavioural cause is psychogenic alopecia. This is a very uncommon, likely over-diagnosed condition for which Siamese, Burmese, Himalayan and Abyssinian cats are predisposed. Treatments for this condition involve identification of known triggers of stress and removal of these triggers or desensitisation to these triggers, alongside psychoactive drugs such as clomipramine (Clomicalm®). The diagnosis of this disease is one of exclusion, whereby all other causes of pruritus or alopecia, including allergic skin disease, parasites, endocrine disorders and disorders of the hair or hair follicle must be ruled out. Taking a history from the owner may reveal specific behavioural signs of stress or known triggers of chronic stress, such as living in a multicat household or a lack of outside access.

Stress has been found to be an underlying cause or a trigger in other diseases in cats, including idiopathic cystitis, infectious peritonitis and idiopathic ulcerative dermatitis. In humans, it is well-established that stress and mental health problems such as depression can be a trigger and aggravating factor in atopic dermatitis. Research into this area has shown that the skin expresses the same receptors to various neurotransmitters and neuropeptides, such as serotonin and substance P, as the cells of CNS. Stress also causes a shift from a Th1 response, involving cellular immunity (NK cells, cytotoxic $CD8^+$ T cells etc) to a Th2 response, where IL-4, IL-10 and IL-13 become upregulated. These pro-inflammatory cytokines lead to B cell differentiation into effector cells, class switching to IgE, and activation and degranulation of both eosinophils and mast cells, all of which are mediators of

human and feline allergic skin disease. Atopic dogs have been shown to have raised hair cortisol levels compared to unaffected controls. One study of dogs with atopy also showed a link between allergies and stress, with more affected dogs showing signs of stress-induced 'problematic' behaviours, such as chewing, hyperactivity, coprophagia, begging, stealing food, attention-seeking, excitability and reduced trainability. While this study did not evaluate whether stress is a cause or trigger for atopy in these dogs, there is a clear link between allergic skin disease and stress.

There is plenty of research being carried out regarding stress in human atopic patients and only a little in canine patients, despite the similarities between the diseases in both species. There is even less evidence available in cats. Cats are notoriously difficult to treat for allergic skin disease and both the disease and its diagnosis and treatment can impact on their quality of life quite significantly. Because of this, any additional resource to help treat allergic cats would be greatly appreciated by a lot of vets and cat owners alike, but first we need to know if stress is a trigger for feline allergic skin disease.

To do that we designed a case-control study using a questionnaire about cats' signalment, early life, health, household, lifestyle and husbandry, based upon a similar questionnaire used for investigating the role of stress in FIC (Seawright, 2009). The control questionnaire had all mentions of skin disease removed for the unaffected cats. Case and control cats were matched by age category rather than exact age as the exact age of many rescue cats is unknown. The questionnaire was disseminated to clients of Langford Vets who had had cats referred to the dermatology service that fit the recruitment criteria. Case numbers were increased by placing advertisements in The Veterinary Record and on social media and by approaching other referral dermatology specialists. Healthy control cats were recruited from clients who had visited the orthopaedic referral service at Langford vets but were no longer being treated for the condition e.g. fracture repair. Examination of the veterinary records of these cats revealed no evidence of skin disease.

The recruitment criteria for case cats was that they had been diagnosed with allergic skin disease, either cutaneous adverse food reaction (CAFR) or non-flea, non-food induced hypersensitivity dermatitis (NFNFIHD) or with an undetermined allergy. Flea allergic dermatitis (FAD) had to have been ruled out either by a veterinary surgeon or by using prescription ectoparasite control at manufacturer-recommended doses for at least six months. Because of this, the lower age range for inclusion was six months of age. Control cats were eligible if they too were over six months of age and had had no prior signs of skin disease.

Table 1 – Variables

Simple variables:	Complex variables – computed from more than one simple variable:
Age **Sex** **Neuter status** **Presence of children** **Presence of dogs in the household** **How busy the household was** **Moving to a new house** **Outside access or house cat** **Recent decrease in outside access** **Multicat household** **Cats receiving medication** **Percentage success with medicating** **Cattery visits in the last year**	**Source** - cats who were bred by the owner or bought from a breeder or pet shop, rescue centre or cattery, those that were found, farm cats and those whose owners selected 'other source' were combined. **Illness or injury** - fleas, worms, cat flu, coughing or wheezing, urinary problems, skin or ear problems, eye problems, dental problems, lameness, heart problems, vomiting, diarrhoea, being 'off colour', reduced appetite, increased appetite, increased thirst, weight loss and 'other' **Fear of:** the owner; visitors to the house visits to the veterinary practice; wearing a buster collar medications; dogs **When cats showed one or more 'fearful' behaviours:** running away; hiding vocalising or hissing; aggression freezing; increased breathing rate crouching/lowering the head; tail swishing or twitching pupil dilation/widening of the eyes; flattened ears flattened whiskers; urine spraying **Conflict between cats** in the household used these options plus whether the owners had seen visible signs of conflict: chasing or being chased blocking access to resources/having access blocked having wounds from fighting **Owners trying to prevent scratching and overgrooming** - use of a buster collar etc, distracting their cat from itching, description of the distraction methods and whether the cat exhibited negative behavioural signs to the distraction technique **Sharing resources** - number of cats in the household and the number of food bowls, water bowls, water fountains, toys, litter trays and puzzle feeders available

RESULTS

Owners of 219 cats responded to the questionnaires, with 108 case cats and 111 controls. Because of incomplete questionnaires, inadequate ectoparasite control or cats being under six months old, 24 case cats were excluded from analysis. All case cats were neutered so entire control cats were also excluded. Control cat numbers were reduced to 98 to match 84 case cats. Matching was by age category; under six years, seven to ten years and over 11 years.

Spearman correlation was performed on all the variables that were biologically significant and had high enough numbers to make sure none were significantly correlated with each other. There were no significant correlations ($p<0.5$) between the selected variables that could not be explained by other factors, such as multicat households being more likely to have evidence of inter-cat conflict, compared to single cat households. Univariable analysis was performed to determine which were to be taken forward to the multivariable analysis. Six variables were significant in the univariable analysis ($P<0.2$) and one was borderline and was also included in the multivariable analysis due to the weight of literature suggesting that decrease in outside access is a potential stressor in cats.

Table 2 – Univariable analysis results

Variable to be included	*P* value	Included in multivariable analysis?
Sex	0.018*	Yes
Source	0.380	No
Illness/injury in last 12 months	0.189*	Yes
Presence of children	0.092*	Yes
Busy household	0.553	No
Moved to a new house	0.471	No
Cattery visits	0.352	No
Outside access	0.397	No
Decrease in outside access	0.287*	Yes §
Signs of fear/conflict with cats	0.049*	Yes
Multicat household	0.196*	Yes
Fear of owner	0.454	No
Fear of visitors	0.600	No
Fear of noises	0.152*	Yes

A Hosmer and Lemeshow test for goodness of fit had a χ^2 value of 3.825 and a significance of $p<0.01$ indicating that the model was able to distinguish between cats with and without skin disease. The model explained between 13.3% (Cox and Snell R Square) and 17.8% (Nagelkerke R Square) of the variance and correctly classified 64.8% of the cases (with a specificity of 70.4% and a sensitivity of 58.3%).

Five variables made a statistically significant contribution to the model:
- the cat's sex
- whether there was conflict with other cats in the household
- whether it was a multicat household
- fear of loud noises
- presence of illness or injury in the previous 12 months

Female cats were 2.5 times more likely to have skin disease than male cats and cats that exhibited negative behavioural signs with other cats in the household were 2.3 times more likely to have skin disease than those that appear to be part of the same social group as other cats in the household (exhibited no negative behavioural signs). Because of this distinction, simply being part of a multicat household was not a significant predictor for skin disease, with the odds of being in a multicat household being 56.4% lower in cases than controls.

We are not sure of the reason for the female predisposition; a hormonal component is unlikely due to all cats in the study being neutered. There could be a sex-linked genetic difference that predisposes female cats to skin disease.

The fact that simply being in a multicat household does not predispose cats to allergic skin disease is interesting. It shows that cats can live peacefully together if they see each other as the same social or family group, or if they are given a suitable environment within which to co-exist. The chronic stress of conflict with other cats however does contribute, compared to the acute stress of loud noises etc.

Stress can be caused by many things, for example:

- Inter-cat conflict
- A barren environment
- Poor human-cat relationship with inappropriate handling or punishment
- Environmental change – a perceived sense of unpredictability and lack of control
- Competition for resources
- Lack of access to outside

But these all depend on the personality of the cat in question. We should start adding questions related to stress into our dermatology history taking with client's e.g.

- Is the cat a generally outgoing or nervous/fear-aggressive cat?
- Is it a multicat household or are there any other pets in the household?
- Do the other pets in the household get on?
    - Do the cats groom each other?
    - Do they sleep on the same bed while touching?
    - Do they rub against each other?
- Are there enough resources in the house for one per cat plus one?
- Do the cats exhibit any typical signs of stress for any reason?
    - running away
    - hiding
    - vocalising or hissing
    - aggression
    - freezing
    - increased breathing rate
    - crouching/lowering the head
    - tail swishing or twitching
    - pupil dilation/widening of the eyes
    - flattened ears
    - flattened whiskers
    - urine spraying/inappropriate toileting

Stress can be hard for owners to notice because cats try their hardest to always appear fine, even when they're not. It's not enough that the cats will share the same bed or share the same food and water bowl. Sometimes cats who are not in the same social group will establish 'time-share' routines to prevent contact with other cats in the household. Even if cats don't exhibit overt signs like hissing or fighting, if one cat is intimidated by another they will not attempt to use resources like food, water and litter trays while another cat is present which can lead to inappropriate elimination in the home. Some may also show redirected

aggression as a coping mechanism, where they become aggressive and attack a different stimulus to the one that is causing frustration. Feigned resting and hypervigilance can also be difficult to detect as the cats may appear to be sleeping but are actually consistently on guard and surveying their surroundings.

If you can establish that there are signs and causes of stress in the household of your patients there are things you can recommend to help with this. Multimodal Environmental Modification (MEMO) has been shown to be efficacious in reducing the clinical signs of FIC and may therefore be helpful in cases of allergic skin disease also. Referral to a Certified Clinical Animal Behaviourist or Veterinary Behaviourist may be required and can be helpful to help with a multimodal approach to skin disease.

MEMO is something that owners can easily implement in the home that can really help with reducing stress, especially in multicat households.

It involves:

- Proper litter tray etiquette! Cats enjoy having a clean litter tray and often prefer certain types of litter over others. Offering more than one litter tray per cat (n+1 rule) is important but trying out different substrates to find which one the cat prefers can be helpful. It can also help to place the litter trays in quiet or more private areas of the house to make the cat more comfortable. Making sure to clean the tray after every use is also very important.

- Resources – as well as litter trays, the n+1 rule applies to all resources including food and water bowls, beds and toys. Each resource should be in a separate area of the house to allow the cats to choose which they use and to prevent the blocking of access by other cats

- Appropriate handling from owner – if the cat does not enjoy being picked up or stroked, the owner should try and stop doing this. 'Scruffing' the cat should never be used as a method of restraint, either in the home or at the veterinary practice. Allowing the cat to choose when to have human contact on their terms helps to reduce feelings of a lack of control. Owners should also try to not shout or raise their voice at the cat, as well as any other form of punishment as the cat will likely not associate the punishment with the perceived 'bad behaviour'

- Appropriate play – cats can sometimes become frustrated when playing with toys such as 'fishing rods' and laser pointers, where they are prevented from actually catching the toy or light. Rewarding the cat with a treat at the end of a play session allows them to feel like they have had a successful hunt

- Outside access – this is a contentious issue because of many reasons, including road safety, theft of pedigree breeds, communicable diseases and hunting behaviour. Some cats do not mind being confined and are happy to stay as inside cats however preventing a cat that wants to be outside from having access can impact their quality of life substantially. Some owners may be happy to cat-proof their garden or provide an outdoor pen for their cat to have safe access to the outside world

- Safe places to hide and sleep – cats prefer secluded areas to rest where they can't be disturbed. These could be various types of beds and boxes, or a cat tree with multiple levels to allow them to escape unwanted attention. Owners should be encouraged to leave their cats alone while they are sleeping and not disturb them

- Vertical space – cats often prefer vertical space to allow them to survey their surroundings. Installations such as 'cat shelves', walk-ways and cat trees can allow cats to traverse a room without being in contact with people and other cats when they wish to be left alone

- Feline facial pheromone – these are available as sprays and diffusers and can be useful in some situations to reduce stress

- Cat-friendly medications – avoiding having to restrain and forcibly administer medications can be very helpful, especially as most allergic cats will be receiving medications of some sort. Liquids on food, palatable tablets or 'pill pockets' are available and should be recommended to owners as alternatives

In summary, stress may be an important flare factor for cats with allergic skin disease. Treatment of this disease needs to be holistic and multimodal, to include medications and environmental and behavioural modification. More research should be performed to look at the link between stress and allergic skin disease and whether there is a true predisposition in female cats. Studies should also look at whether MEMO is clinically effective at reducing the signs of the disease.

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