CP/Clinic

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CATS PROTECTION

Mycobacterial disease – underdiagnosed, increasingly recognised and potentially zoonotic. Find out more on page 4

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Meet the team

Lucinda Alderton-Sell, Field Vet Officer East of England

How long have you worked for CP? I did a maternity cover at the National Cat Adoption Centre (NCAC) clinic and have been in my current role for a year.

What did you do before working for CP? I worked for the PDSA for over six years.

What is your role within CP? I am a Field Veterinary Officer for the East of England. I provide veterinary advice for adoption centres and branches in my area and liaise with vets working with CP. I help develop new CP policies and protocols and deliver feline welfare and shelter medicine talks and workshops.

What do you like most about your job? I love my job and enjoy the variety it offers, and that I get to travel meeting lots of gorgeous cats!

What is your most memorable CP moment? While working in the NCAC clinic one of my all-time favourite cats finally found his forever home.

Do you/did you have a pet/pets? I have a handsome rescue cat and a beautiful Jack Russell Terrier (of course I am very biased!).

What are your hobbies/other interests? I love tennis and other sports as well as art/creating things, and regularly attend a jewellery-making class.

Where is your favourite place to visit? The beach (with a cup of tea and some chips!).

If I wasn't doing this, I'd probably… Be somewhere wishing I could be doing this!

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Mycobacterial diseases in cats

Jordan Mitchell, Conor O'Halloran and Danièlle Gunn-Moore

explore these often underdiagnosed, but increasingly recognised, potentially zoonotic infections.

Feline mycobacterial infections have been recognised for over 100 years, yet it remains challenging to recognise their clinical signs, diagnose cases and provide appropriate treatment. The gross appearance of lesions cannot be used to differentiate between mycobacterial species and different infectious agents require different antimicrobials. Diverse mycobacterial species carry varying prognoses and some pose a small, yet real, zoonotic risk.

Aetiology and epidemiology

There are over 150 species of mycobacteria and broadly speaking, they are categorised into two groups: the *Mycobacterium tuberculosis*-complex (MTBC) and the non-tuberculous mycobacteria (NTM). Currently, there are 10 members of the MTBC, causing tuberculosis (TB) in many species. TB in cats is caused by *M. microti* and *M. bovis*. Thankfully, *M. tuberculosis*, the main cause of human TB, does not appear to cause clinical disease in cats. Among NTM, some species are identified as causing 'feline leprosy syndrome' (FLS) and others for causing 'atypical mycobacteriosis', but the distinction between these disease entities is narrowing as molecular diagnostics improve. In the UK, *M. avium* is the most common NTM of cats.

Approximately 1% of all feline biopsy samples submitted for histopathology in the UK show signs consistent with mycobacterial infection, and of these one-third are positive on Ziehl-Neelsen (ZN) staining for acid-fast bacilli (AFB; confirming the presence of Mycobacteria). Male cats with outdoor access, and cats that hunt were identified as being at greatest risk of becoming infected. Obesity is a risk factor for NTM infections with lipophilic species, which usually contaminate wounds occurring in fat pads, especially the 'apron fat'. Most cats with mycobacterial infection are FeLV and FIV negative and some breeds (Siamese, Abyssinian) appear to be over-represented for *M. avium* infections.

Clinical signs

Mycobacterial infections can result in a myriad of clinical signs. However, the most common is localised, nodular, cutaneous disease. Lesions can vary in size, they may be ulcerated (Fig 1) and/or have discharging sinus tracts. There may be associated lymphadenopathy; sometimes this is the only clinical sign. Lesions tend to be in 'fight and bite' sites ie the face, limbs, perineum and tail base and are thought to be associated with injuries when hunting and/or playing with rodent prey.

Occasionally, cats with cutaneous disease may develop secondary pulmonary involvement. This is thought to occur via haematogenous spread of bacteria resulting in diffuse interstitial pulmonary disease and if left to progress dyspnoea and a soft cough may develop. Primary respiratory TB in cats is uncommon.

Historically, ingestion of *M. bovis*-infected milk resulted in gastrointestinal TB, resulting in non-specific clinical signs including vomiting, diarrhoea and weight loss. This form of the disease has become rare since the routine pasteurisation of milk.

As mentioned above, some lipophilic NTM species result in panniculitis, often in the inguinal region, with lesions having a 'salt-and-pepper shaker' appearance, with multiple punctate draining tracts and areas of ulceration (Fig 2). Lesions can coalesce to form larger areas of non-healing tissue. These can be painful and cats may present lethargic and reluctant to move.

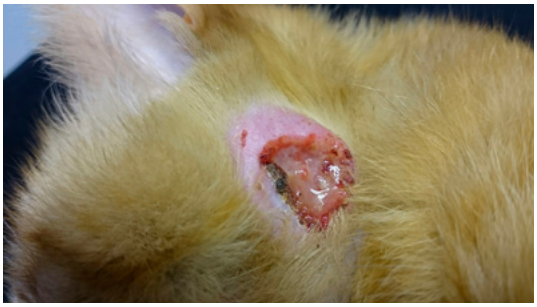

Fig 1: An ulcerative, nodular skin lesion on the head of a cat. This is a typical presentation of feline TB. (credit Conor O'Halloran and Jayne Hope)

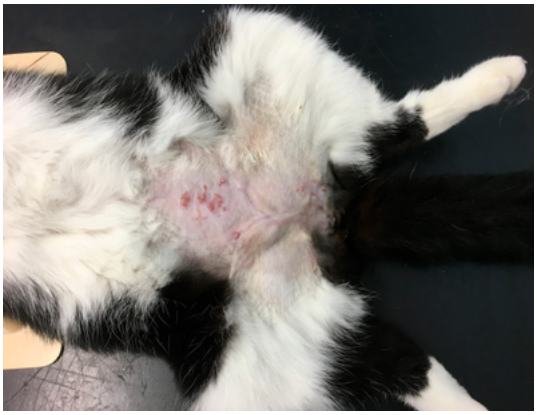

Fig 2: Lipophilic NTM often infect the fatty apron of tissue in the inguinal region, resulting in this classical appearance of granulomatous panniculitis. This cat also had enlarged inguinal lymph nodes and evidence of pulmonic involvement on radiography. (credit Paul Saunders).

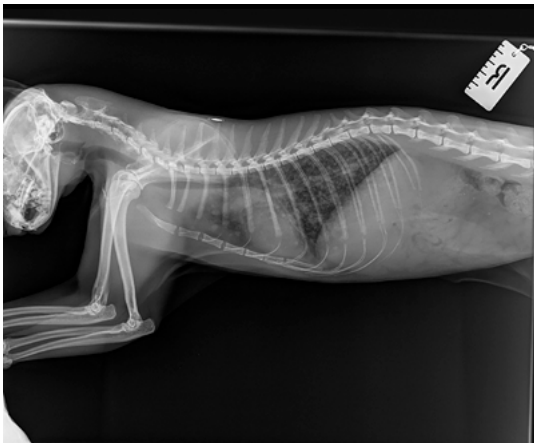

Fig 3: Right lateral thoracic radiograph showing a diffuse interstitial pulmonary pattern in a five-year-old, neutered male exotic shorthair. A diagnosis of M. microti was made on IGRA. (credit Gillian McLeod).

Any site can become involved in mycobacterial infections. Frequently reported cases include the eyes, the central nervous system and joints, resulting in blindness, neurological deficits, lameness and soft tissue swelling over joints. Disease may progress to become disseminated, affecting a multitude of organ systems, resulting in hepatosplenomegaly, generalised lymphadenopathy and/or the development of pericardial, pleural or abdominal effusions.

Diagnostics

Although all mycobacterial infections can present with similar clinical signs, it is important to try to obtain a definitive diagnosis as this will influence treatment protocols, prognosis and there may also be other factors to consider, such as zoonotic risk.

Routine haematology and serum biochemistry should be assessed as standard. Although there may be no or non-specific changes, values provide a baseline before starting anti-mycobacterial treatment. Hypercalcaemia may be identified which is a poor prognostic indicator.

Radiographic assessment for pulmonary involvement should be performed early, with an interstitial pattern indicating pulmonary spread. This may become bronchial if disease progresses, while follow-up radiographs are useful to determine whether lesions are resolving (Figs 3A and 3B). Depending on the presentation, imaging of other body regions may be indicated, and FeLV/FIV screening is recommended.

A standardised approach to nodular cutaneous disease can help identify potential cases at an early stage. In-house cytology can exclude neoplasia and unstained cytological smears from mycobacterial infections can be stored for further testing by PCR.

Biopsies from skin lesions are the most frequent method of obtaining a diagnosis. Biopsies should be bisected, with half formalin-fixed for histopathology and the other retained and frozen for further testing if required.

Histopathology reveals granulomatous inflammation, dominated by macrophages, with frequent neutrophils and necrosis. Discrete granulomas may be seen in some cases, whereas other samples may show more unstructured, expansive inflammatory change. Macrophage morphology varies from epithelioid to large and vacuolated. ZN staining may identify intra- or

extracellular AFB (Fig 4), however a negative ZN stain does not rule out mycobacterial disease.

Histology cannot differentiate which species of mycobacteria is present. While bacterial culture can identify the exact mycobacteria causing disease, it only has 50% sensitivity and takes on average three months. A negative culture cannot be used to rule out mycobacteriosis and if awaiting culture results, empirical treatment should be started given the slow-growing nature of many species.

The interferon gamma (IFN-γ) release assay (IGRA) is available through Biobest Laboratories. For this test, leucocytes are isolated from heparinised blood and stimulated to release IFN-γ, which is then measured. It can distinguish between TB and non-TB infections and can identify, or infer, infection with either *M. microti* or *M. bovis*. It has a more rapid turnaround time than culture, but is limited in its ability to speciate NTM infections.

PCR diagnostics are increasingly available. Unstained cytological smears and fresh tissue provide better chances of getting a result than formalin-fixed tissue.

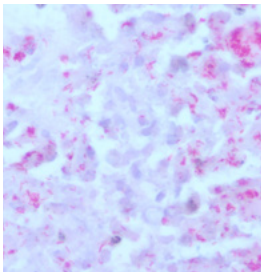

Fig 4: ZN stain showing vast numbers of intracellular AFB in a cutaneous lesion from a case of feline TB (x400 magnification). Numbers of ZN-positive AFB cannot be used to determine the underlying species or differentiate TB from NTM infection.

Treatment and prognosis

Deciding to treat a case of mycobacterial disease requires good communication with the owners as *M. bovis*, if present, is potentially zoonotic, antimicrobial protocols are lengthy, some drugs have potentially serious side effects, patient compliance is essential and treatment can be costly. While long-term remission has been reported in 40% of cases, many cases in that paper were treated sub-optimally (monotherapy and/or inadequate duration of treatment) and a success rate of 70-80% has been seen, including cases of TB with pulmonary involvement (DGM/COH, unpublished data).

No antimicrobials are licensed for the treatment feline mycobacterial infections and human anti-TB protocols cannot be directly transposed, due to the severe toxicity associated with some of these drugs (isoniazid, ethambutol), or the ineffectiveness (pyrazinamide) against *M. bovis*.

Recommended treatment of feline TB is triple therapy comprising rifampicin, pradofloxacin and azithromycin. This allows for once daily dosing with all three drugs given together. Treatment should be given for four to six months, depending on the extent of disease, and at least two months post-resolution of clinical signs, including pulmonary radiographic changes. An oesophagostomy tube can be placed to facilitate treatment and improve patient compliance.

Rifampicin is an excellent anti-mycobacterial drug, even showing efficacy against non-replicating intracellular bacteria. However, it can be hepatotoxic as well as causing nausea, pruritus, muscle twitching and even seizures. Consequently, patients should be carefully monitored with serum biochemistry performed at the onset of treatment and then monthly afterwards, or sooner if the cat presents unwell. Rifampicin should never be used as monotherapy due to the risk of resistance developing against this drug.

Protocols for NTM infections vary due to differences in resistance and susceptibility profiles between and within mycobacterial species. Clarithromycin and doxycycline may be used in place of azithromycin and pradofloxacin, respectively, especially in cases of *M. avium* infection which is notoriously difficult to treat.

Surgical removal of small, discrete nodules may be curative in some infections. Spontaneous resolution has been reported in some cases of FLS and other NTM infections, but this has not been seen in cases of TB. If there is evidence of disseminated *M. bovis* infection with multiple lesions and/or patients are systemically unwell, euthanasia may be advised.

Zoonotic risk

Public health bodies deem the risk of humans becoming infected with *M. bovis,* the most zoonotic mycobacteria encountered in cats, to be very low, but there are some aspects to consider. Discharging lesions are more likely to result in spread of infection than non-draining granulomas, so wear gloves when handling cats with purulent lesions or open wounds. Good hygiene can also reduce the risk of nosocomial spread.

M. bovis accounts for 1% of cases of human TB in the UK and a handful of these have reportedly been due to infection from a cat. Only 27 cases of *M. microti* infection in humans have been documented worldwide, and while *M. avium*-complex disease occurs more frequently in humans, there have been no reported cases involving transmission of either infection from cats to humans.

Individual risk factors associated with an increased risk of becoming infected with mycobacteria includes: malnourishment, HIV infection, diabetes, kidney disease, smoking, substance abuse, organ transplantation, chemo- or radiotherapy and immunomodulatory medications.

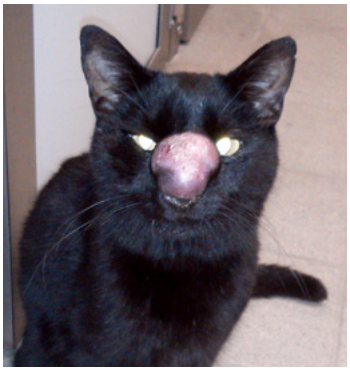

Fig 5A: A large, non-ulcerative lesion arising just caudal to the nasal planum. Empirical treatment and culture had been unsuccessful. IGRA suggested M. microti infection and triple therapy was commenced. (credit Danièlle Gunn-Moore)

Fig 5B: Two months post commencing treatment the lesion had grossly resolved and the cat eventually made a full recovery. (credit owner, Ms. Dunlop)

Summary

Mycobacterial disease in cats is underdiagnosed, but it is increasingly recognised by veterinary surgeons. Nodular cutaneous disease is the most common clinical presentation of mycobacterial disease in the cat and it should be considered as a differential diagnosis when evaluating any dermatological case not responding to conventional therapy (Figs 5A and 5B).

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Jordan graduated with distinction from the University of Edinburgh in 2015 before working in small animal general practice, developing interests in feline medicine, anatomic pathology and cytology. He returned to Edinburgh in October 2017 to start a PhD looking into the immunopathology and diagnostics of feline tuberculosis.

Ureteral obstruction – an underdiagnosed problem?

***Sheila Wills** highlights this condition that is often grossly under-recognised in our feline patients*

Ureteral obstruction (UO) is an increasingly diagnosed problem in cats but is still likely to be grossly under-recognised in veterinary practice. The prevalence of this problem in cats is still largely unknown but with increasing awareness and more routine screening of cats for ureteral obstruction, a better understanding of the epidemiology, pathogenesis and management of this condition can be achieved.

Ureteral obstructions are most typically caused by calculi (~80%), with a smaller proportion caused by ureteral strictures (~20%). In cats >92% of these calculi are calcium oxalate stones and the remaining ~8% are calcium phosphate, magnesium ammonium phosphate (struvite) or dried solidified blood (DSB)/ inflammatory debris calculi (eg purulent material associated with pyelonephritis). There does not appear to be any gender predisposition to ureteral calculi in cats but the DSH and DLH are the most commonly affected breeds. Most cats tend to be middle-aged to older at the time of presentation but this condition can be seen at any age so this should not preclude screening of younger cats with a suspicion of UO.

Pathogenesis

UO leads to a rapid build-up of uraemic toxins and progressive renal damage. The presence of azotaemia depends on the contralateral kidney function, the number of ureters affected and the severity and duration of the obstruction. UO can result in life-threatening azotaemia especially if a bilateral obstruction (~15%) is present or if the cat has concurrent pre-existing renal insufficiency (>70-95%). UO is a challenging disorder requiring knowledge of the condition, an index of suspicion to assess for UO and often highly sophisticated therapeutic aids and specialist surgical/interventional skills to manage the condition.

Most cats with UO present for medical care with advanced disease, however a significant proportion of cats may only show subtle clinical signs in the early stages of unilateral obstruction/ partial obstruction which may go undetected. The mechanical obstruction is aggravated by secondary local inflammation and spasm. Local ureteral damage (eg stricture or rupture) is a potential complication of UO but increased intra-ureteral hydraulic pressure and decreased renal blood flow are more common consequences. The increased hydraulic pressure results in increased pressure within the renal tubules and Bowman's space causing direct nephron damage and a precipitous decline in GFR. If the contralateral renal function is preserved, clinical signs if present, are pain-related and often overlooked, thus the episode may go unnoticed. If the obstruction is dynamic, it may also

Abdominal palpation may reveal renal/ abdominal pain and asymmetric kidneys – this should ring alarm bells for a possible ureteric obstruction

resolve spontaneously. The progressive damage to the obstructed kidney is determined by the severity of obstruction (partial vs. complete) and the chronicity of this obstruction. Limited work has been performed assessing the timing of renal insult in cats but this has been more extensively reviewed in dogs. If the canine kidney is completely obstructed renal blood flow decreases to 40% of normal within 24hrs and to 20% of normal by two weeks. As a result, GFR permanently declines to 54% after 14 days and to 100% after 40 days indicating the need for urgent intervention in patients with complete UO. It is also worth noting that the canine models above had no evidence of pre-existing renal disease and hence we can conclude that a worse outcome would be expected in our feline patients with complete UO. In contrast, partial UO appears to result in less severe nephron destruction and in one dog model, GFR returned to normal with intervention after a partial obstruction had been present for four weeks. Many of our feline patients present with suspected chronic partial UO and it may be questioned if intervention is truly required if the cat is "coping" with the partial obstruction. However, the above models indicate that improvement in renal function is possible even after chronic partial obstructions are identified hence treatment should be pursued in these patients.

'Big kidney-little kidney syndrome'

If a unilateral obstruction resolves (the cat may not even be presented to the veterinary practice due to subtle signs), the affected kidney may have residual damage or normal function. If a complete UO does not resolve, renal fibrosis of the ipsilateral kidney and compensatory hypertrophy of the contralateral kidney occurs. This results in the finding of 'big kidney-little kidney syndrome' which can be detected on abdominal palpation. At this stage of the disease process, cats may be free of uraemic signs as the compensatory hypertrophy allows steady state renal function and hence a degree of suspicion is again very important if the 'big kidney-little kidney' syndrome is to be detected (with or without azotaemia these cats need to be investigated urgently). Prompt intervention will reduce the degree of nephron damage.

An acute uraemia will develop following obstruction of the hypertrophied kidney. The severity of the clinical signs depends on the degree of UO and the function of the contralateral kidney. Unfortunately, this is the stage that many cats typically present in practice and this can easily be diagnosed as 'simple' chronic kidney disease (CKD) and treatment implemented for that alone (acute on chronic kidney injury). If only one ureter is obstructed and the cat is azotaemic, this is a clear indication of reduced function in the contralateral kidney but again these cats are often diagnosed as CKD and the ureteric obstruction can be missed at this crucial early phase. Thus, if a cat presents with acute onset azotaemia or apparent rapid progression of pre-existing CKD, possible ureteral obstruction should be urgently investigated.

Clinical signs

Cats with ureteral obstructions can present with varying signs ranging from no or very subtle signs (inappetance and lethargy) to signs associated with severe azotaemia and pain. The pain associated with ureteral obstruction is the result of direct ureteral stimulation at the site of obstruction and stretch of the collecting system and the renal capsule.

Clinical signs are usually non-specific including inappetance and lethargy but may progress to more marked signs on development of azotaemia and uraemic signs such as vomiting, polyuria (PU) and polydipsia (PD), weight loss, haematuria and renal pain. With complete bilateral obstruction more advanced signs of acute kidney injury (eg oliguria/anuria, bradycardia, vomiting, severe depression/obtundation) will be seen. Abdominal palpation may reveal renal/abdominal pain and asymmetric kidneys – this should ring alarm bells for a possible ureteric obstruction especially if one kidney is small and irregular and the other is large and painful. If renal pain is detected this should prompt investigation for a ureteric obstruction as many cats may present with only vague clinical signs and unremarkable blood results.

Diagnosis of partial and complete ureteric obstructions

1) Physical examination findings

Abdominal palpation may reveal signs of abdominal or renal pain. Findings of the 'big-kidney, little-kidney' syndrome should also prompt investigation. Detection of pyrexia may be associated with pain but may also be indicative of pyelonephritis.

2) Blood and urine tests

Serum biochemistry in affected cats can range from being completely unremarkable (for example in unilateral ureteric obstruction with normal function of the contralateral kidney) through to changes consistent with severe CKD or acute kidney injury (eg severe azotaemia, hyperphosphataemia, hyperkalaemia and anaemia of inflammatory disease). USG is often <1.035 and pyuria, proteinuria and crystalluria may also be detected. Urine culture should be performed in all cases, as pyelonephritis can be an exacerbating problem and a UTI is found in approximately 30% of cats with ureteric obstruction. It should be noted that >75% of cats are azotaemic with a unilateral obstruction, indicating contralateral renal insufficiency.

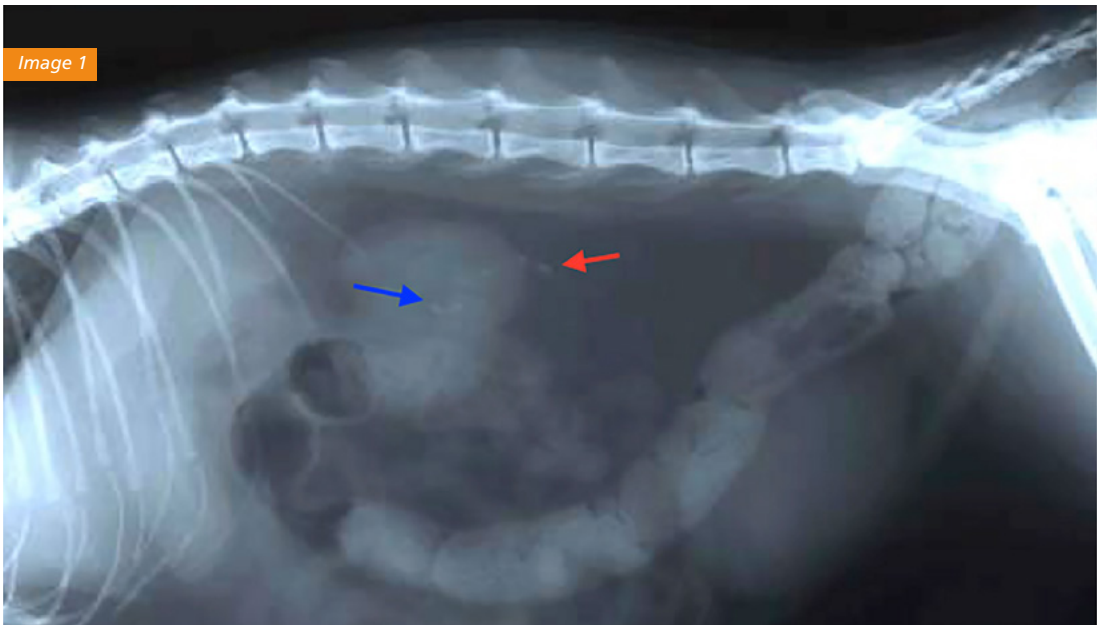
3) Imaging

Radiography and ultrasound: the combination of abdominal radiography and ultrasound has been demonstrated to be the most sensitive, readily available diagnostic tool for detection of ureterolithiasis in general practice. More advanced techniques such as intravenous pyelography, antegrade pyelography and computed tomography (CT-IVP) have been found to be inconsistent in diagnosis of UO and may offer very little additional clinical information. The use of intravenous contrast agents and additional anaesthesia should also be questioned in these renally compromised patients.

Radiography: the retroperitoneal space should be carefully scrutinised for any mineral opacities (Image 1.). Ureteroliths can be obscured by gas in the gastrointestinal tract during ultrasound assessment hence, the combination of ultrasound with radiographs increases the sensitivity of detecting UO. Renal size and shape should also be assessed together with the renal pelvic area for nephroliths (commonly found with ureteroliths). Plain abdominal radiographs can readily be performed in practice and are crucial for reaching an early diagnosis of ureterolithiasis allowing intervention at the earliest possible stage with the aim of preventing further nephron damage. An enema is highly recommended prior to performance of radiography to ensure ureteroliths are not obscured by faecal material.

Image 1. Right lateral abdominal radiograph indicating ureteroliths (red arrows) and renoliths (blue arrows). *(Please note the volume of faeces identified in this radiograph may have obscured other ureteroliths hence the importance of other ureteroliths hence the importance performing an enema!)*

Abdominal ultrasound: DSB calculi, strictures (20% of cats with UO) or inflammatory debris obstructing the ureter (eg pyelonephritis) may not be observed on plain radiographs. Abdominal



ultrasound is a sensitive imaging modality for detection of hydronephrosis and/or hydroureter and can be valuable in cases where ureteroliths are not observed on plain radiographs. Hydronephrosis (Image 2.) is usually readily detectable on renal ultrasound however detection of hydroureter (Images 3. & 4.) can be more challenging and is dependent on the quality of the ultrasound machine/probe and the skill of the veterinarian performing the procedure. Renal pelvic mineralisation may also be noted during ultrasound examination (Image 5.) and radiography (Image 1.). Dilation of the ureter and/or renal pelvis is usually apparent ultrasonographically within three to four days of obstruction. Although there is significant discussion of renal pelvic size as an indicator of UO, the presence of renal pelvic dilation (>1.5-2mm) with concurrent hydroureter raises concern for UO until proven otherwise. Observation of the above with a ureteric obstruction (stone, DSB, inflammatory debris) is of course diagnostic and should prompt immediate intervention to decompress the renal pelvis and allow return of renal function. It is possible that no structural obstruction will be observed despite a very strong suspicion for UO. This is usually due to either a ureteric stricture or DSB calculi that do not shadow on ultrasound or are not radiopaque on radiographs. In this instance, antegrade pyelography may be helpful to more clearly define the ureteric obstruction however the clinician should also consider if this will provide any additional benefit to the patient in terms of management (if there is a strong index of suspicion of UO).

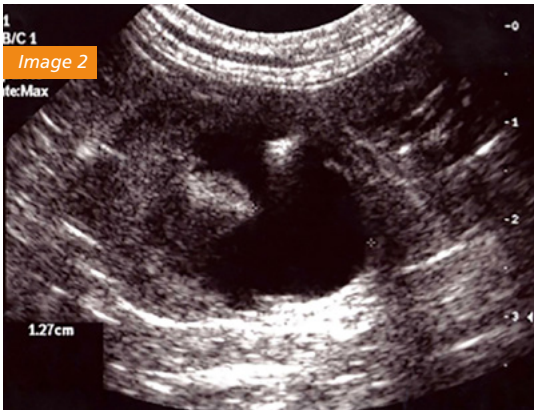


Image 2. Ultrasound image of right feline kidney with severe renal pelvic dilation (1.27cm).

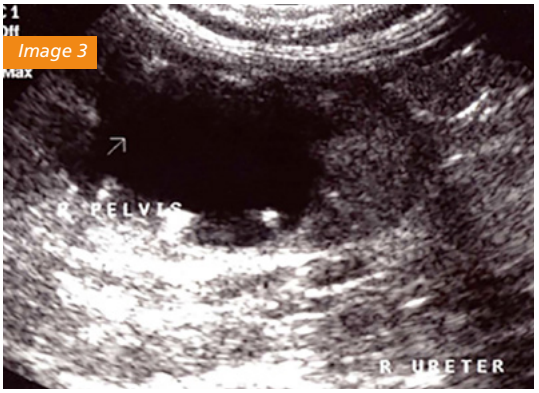


Image 3. Ultrasound image of the same right feline kidney (as noted in image 2) with evidence of dilated right ureter

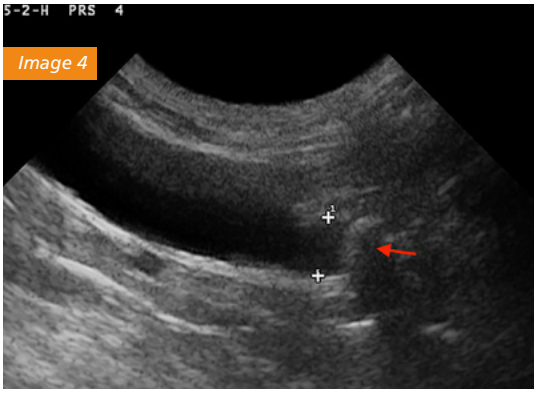


Image 4. Ultrasound image of a severely dilated feline ureter (5.3mm) and shadowing caused by a ureterolith (red arrow). (Image courtesy of Monica Merlo)

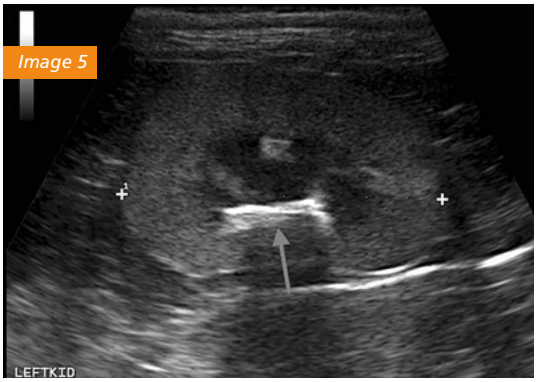


Image 5. Ultrasound image of feline kidney demonstrating renal pelvic mineralisation (grey arrow). (Image courtesy of Monica Merlo)

Treatment

Most cases of feline ureteral obstructive disease will require referral to a specialist centre with the skills and expertise to deal with this challenging condition. This includes pre-operative, intra-operative and post-operative care all of which require an intensive care facility. The cat may remain hospitalised for approximately five to 10 days depending on the complexity of surgery, any pre-existing renal disease and/or complications encountered.

If referral is not consider an option due to financial reasons or the owners wishes, medical management may be considered for three to five days providing the cat is not oliguric, anuric, hyperkalaemic or overhydrated. Clinical evidence suggests that resolution of ureteral obstruction occurs in approximately 8-13% of cats that are medically managed.

1) Medical management

Ureteral obstruction is incredibly painful so effective **analgesia** (typically opioids) must be provided at all times until the obstruction has been relieved and the patient is more comfortable.

Medical management of UO involves judicious fluid therapy with or without diuretics (furosemide or mannitol with the aim that the diuretic increases glomerular filtration rate and raises the intraureteral luminal pressure thus pushing the ureteroliths/DSB into the urinary bladder where it can be either more easily removed or voided). These patients are at a higher risk of volume overload and increased pressure on the renal pelvis if a total UO is present. In addition to fluid therapy to try and restore renal perfusion and correct dehydration, supportive care for uraemic consequences should also be considered (antacids, antiemetics etc). Many specialists in this area consider that as soon as the cat is stabilised, surgery should be performed to minimise further nephron damage caused by the combination of the complete obstruction and excessive fluid therapy. As a general rule cats that have shown no response to diuresis after 24-48 hours should undergo surgical intervention where possible. When referral for surgery is not an option and the cat is not hyperkalaemic, anuric or volume overloaded (generally cats with unilateral obstruction or partial obstructions) then medical management can be trialed for three to five days.

Prazosin (α1-antagonist) is also a potent smooth muscle relaxant and α1-antagonists are considered the standard of care for inducing human ureteral dilation. Again limited studies are available to assess the efficacy of this class of drug in treating feline ureteral spasm but it may be of benefit in those patients that can only be treated using medical management. The dose range varies from 0.25-0.5mg/cat q12-24hrs. Blood pressure must be assessed prior to starting the drug and closely monitored for the first few days after initiation of treatment to ensure there is not development of or pre-exisiting hypotension. Consideration should also be given to treatment of any UTI that is detected on urine culture.

If medical management fails to encourage stone passage (monitored by ultrasound and radiography), immediate resolution of the obstruction at a referral centre should be considered as detailed below. It is also important to note that 20% of feline UOs are caused by ureteral strictures (most of which are in the proximal ureter) for which medical management will not be effective. Consideration should also be given to the fact that a proportion of ureteric stones will be embedded in the ureteric mucosa hence passage of the stone will be unlikely.

1) Surgical management

From the description below for all three surgical options, it is clear that these procedures are complex and require considerable experience and specialist equipment as well a highly skilled team providing intensive care. They are described here for information only so that an informed discussion can be had with the owner regarding possible options and complications prior to considering referral (this will also be discussed at length by the specialist team at the referral appointment).

a) Traditional techniques *(now largely superseded by the more sophisticated and successful procedures listed below)*

Surgery to directly remove the ureterolith(s) has traditionally been performed by coeliotomy however due to high mortality (20%) and complication (33%) rates compared to the other more sophisticated procedures detailed below, this form of surgery is now rarely performed.

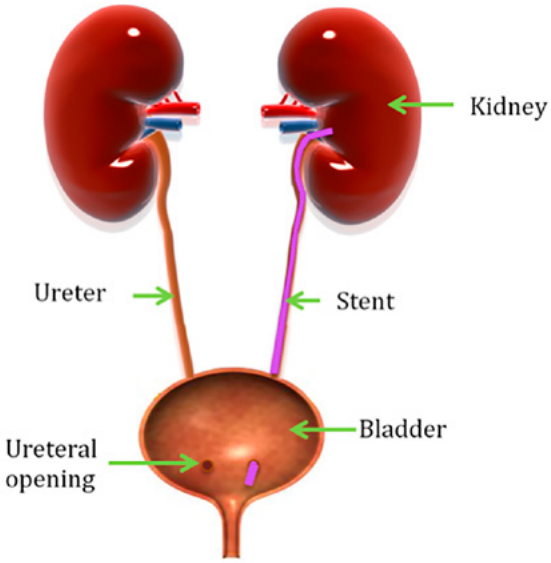
When performed, a full examination of the urinary tract should be completed as multiple ureteroliths may be present (note also the bladder and kidneys should have been assessed with imaging for uroliths). A recent large study revealed that cats had a median of four ureteroliths and 86% of cats also had ipsilateral renoliths. If the ureterolith(s) is in the proximal ureter it may be flushed back to the renal pelvis by performing a cystotomy and catheterising the ureter. The ureterolith is then removed via a pyelotomy which is technically easier and less likely to result in ureteral inflammation/spasm/stenosis/stricture. Distal ureteric obstructions can be managed by ureterectomy of the affected portion of ureter and re-implantation of the remaining ureter into the apex of the bladder (neoureterocystotomy). Ureteronephrectomy is not a viable treatment option in these cases as >75% of cats are azotaemic at the time of presentation, implying dysfunction of the contralateral kidney hence renal function needs to be preserved as much as possible in these cases.

Mortality rates are approximately 20% for cats undergoing traditional surgical management of ureteroliths. It should be noted that survival rates for surgery are better than those receiving medical management alone (33% mortality rate), with 91% of cats who survived the first month following diagnosis alive after 12 months compared to 66% of cats who received medical management alone. Complications are seen in approximately one third of cats and include oedema/inflammation at the ureterovesical junction, ureteral stricture, uroabdomen and persistent obstruction. Urine leakage is the most common problem and occurs in approximately 16% of cases. 40% of cats have a further ureteral obstruction most likely due to previously undetected nephroliths.

b) Stents *(becoming less commonly performed in the UK)*

Stents are polyurethane tubes containing multiple fenestrations that are inserted into the ureter. The stent has a pigtail at either end with one end secured in the renal pelvis and the other secured at the ureteric opening into the bladder trigone (Figure (1)). The stent provides passive ureteric dilatation and urine is able to flow either through or around it. Stents can be very challenging to place and surgical times can be prolonged. There may also be a high rate of dysuria because of the position of the pigtail in the bladder trigone area. Peri-operative mortality rates after stent surgery are significantly lower (7.5%) than traditional surgical techniques (20%).

Figure (1): Basic schematic of ureteral stent placement



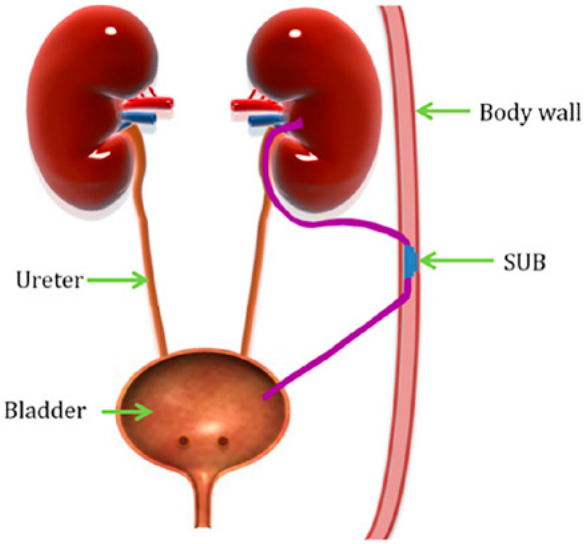
With the more recent advances in surgical management of ureteroliths (eg SUB and stents), mortality rates are significantly lower (6-7%) than those receiving medical management alone

c) Subcutaneous Ureteral Bypass *(SUB) system (more commonly performed in the UK and now considered the treatment of choice by highly experienced specialists at the Animal Medical Centre, New York)*

This is a tube that completely bypasses the obstructed ureter, effectively creating a false ureter. The SUB was developed as an alternative to ureteral stents when either a stricture was present (which resulted in >50% stent occlusion) or when a stent could not be successfully placed due to excessive stones, a narrow ureteric lumen or patient stability. A pigtail catheter is inserted into the renal pelvis and connected to a subcutaneous access port. A separate pigtail catheter is also inserted into the bladder (note via this technique, the pigtail catheter is not near the bladder trigone area) and this tube is also connected to the subcutaneous access port (Figure (2)). This procedure has been shown to be highly successful for the treatment of all causes of feline UO (strictures, stones, tumours, obstructive pyelonephritis). This surgical procedure is technically simpler with a shorter surgery time (45-60 minutes with experienced specialists). In terms of long-term patient comfort and complications, SUBs were found to be superior to stents in a recent study (less dysuria and stent occlusion). Perioperative mortality rate after surgery was 6.2% in a recent study, which compares well to traditional surgery (20%) and stenting (7.5%). Post-operative complications were rare and included urine leakage (4%), kinking of the catheter (5%) and blockage of the system with either blood clots (8%), debris, purulent material or mineralisation (24%). Dysuria is rarely seen with SUBs (6%) compared to ureteral stents (38%).

Appropriate post-operative management of these patients is essential for a good outcome. Post-obstructive diuresis is common in these patients, hence this needs to be appropriately managed with fluid therapy. Intensive monitoring is essential to avoid fluid overload which can lead to congestive heart failure. This is one of the main post-operative complications associated with management of ureterolithiasis (despite normal echocardiogram in most cats). Abdominal palpation should also be avoided for 2 weeks post-operatively and cystocentesis should not be performed in these patients. Urine culture should be performed on a urine sample obtained from the SUB port at the time of routine flushing (which is typically performed every 3-6 months at the referral centre).

Figure (2): Basic schematic of SUB placement



In terms of long-term patient comfort and complications, SUBs were found to be superior to stents

2) Nephrostomy tube

A nephrostomy tube can be placed to immediately relieve the intra-ureteric/pelvic pressure with the aim of rapidly resolving azotaemia. This may be performed as an emergency procedure on arrival to the referral centre to minimise further nephron damage while stabilising the cat prior to surgery. A locking loop pigtail catheter is surgically placed with fluoroscopic guidance. The locking loop pigtail mechanism has resulted in a significant reduction in complications associated with this tube placement (previously due to premature removal/displacement of the tube, urine leakage and poor drainage). Some specialists with considerable UO experience will now progress straight to SUB placement as the time taken for this procedure is similar to nephrostomy tube placement (approximately 45-60 minutes with experience) and also negates the need for two anaesthetics in a renally-compromised patient.

3) Lithotripsy

This treatment has been used successfully in dogs but the feline kidney is more sensitive to shock wave-induced injury. Also note that the intraluminal diameter of the feline ureter is incredibly small measuring only 0.4mm and along with technical challenges due to the size of the ureter, structural damage can occur due to inciting an inflammatory response at the site of lithotripsy and subsequent ureteral strictures.

Prognosis

The main factor that affects the outcome of these cases is the severity of the kidney disease as a result of the obstruction. The earlier UO is detected (ideally prior to complete obstruction and secondary renal damage) the more likely a good outcome will be achieved. Cats with IRIS stage 1 or 2 CKD have a good long-term outcome. The author hopes that this article will highlight the likely higher incidence of this under-recognised condition. Any cat that has apparent rapidly advancing CKD (ie an increase in IRIS renal stage over a short time period) or 'big kidney-little kidney' should be urgently investigated for a UO. If both veterinary and owner awareness of this condition can be increased, earlier detection and intervention can be sought resulting in a much more favourable outcome.

(References available on request)

Sheila Wills

BVetMed CertSAM DipECVIM-CA MRCVS

After graduating from the Royal Veterinary College in London in 1998, Sheila spent five years in small animal practice before undertaking a FAB Residency in Feline Medicine at the University of Bristol, which she completed in 2006. Sheila then worked as a small animal medicine consultant for 11 years before joining the European School of Veterinary Postgraduate Studies (ESVPS) as their Director in July 2017. She is a senior tutor for Sydney University's distance education course in Feline Medicine. She is an EBVS® European Veterinary Specialist in Small Animal Internal Medicine and a RCVS Specialist in Feline Medicine. Sheila enjoys all aspects of feline medicine with a specialist interest in feline renal and ureteric disease.

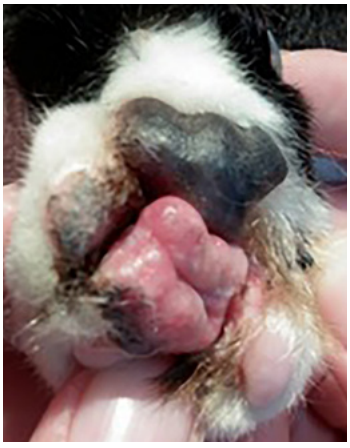
Feline plasma cell pododermatitis – a pathologist's eye view

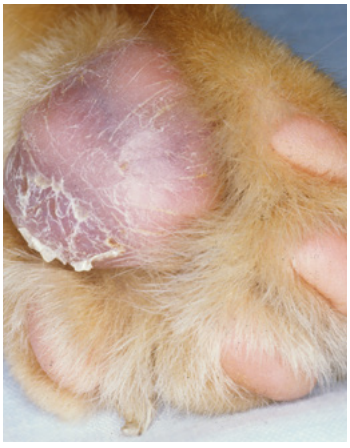
Melanie Dobromylskyj *BSc (Hons), BVSc, PhD, FRCPath, MRCVS*
Diagnostic Histopathologist, Finn Pathologists, UK

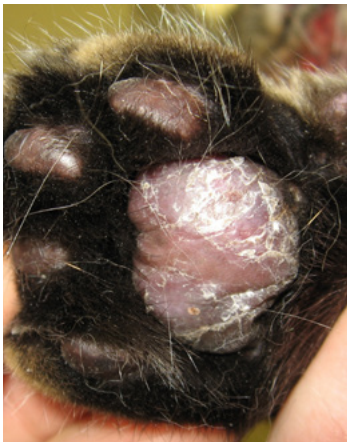
Plasma cell pododermatitis is an uncommon but well-recognised condition in cats, described in all standard textbooks. Yet the aetiology is poorly understood and a search of the published literature shows a relative lack of information on this fascinating disease.

Affected cats will present with purple, spongy swelling of one or multiple pads, typically the metacarpal and/or metatarsal pads, often criss-crossed by linear striations giving a typical gross appearance. Lesions may then progress to ulceration with secondary superficial bacterial infection. The presence of pain and lameness appears to vary between cases, and some may have involvement of the nasal planum. A classic entry on the histopathology submission form – 'the foot pad has exploded!'

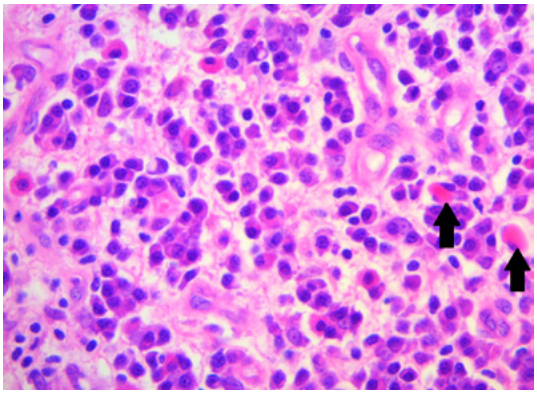
The histological diagnosis is not usually a challenge; there is an intense inflammatory infiltrate expanding the soft tissues of the pad, mostly comprised of well-differentiated plasma cells, including Mott cells. Mott cells are plasma cells that have spherical inclusions within their cytoplasm, called Russell bodies, which correspond to accumulations of immunoglobulins (antibodies). Small numbers of other cells, including lymphocytes and neutrophils, are usually present too, and the epidermis can be hyperplastic and/or ulcerated. The diagnosis based on the clinical history, the gross and histological appearances is fairly easy in these cases, but determining the underlying causes of this disease is apparently far more complex!



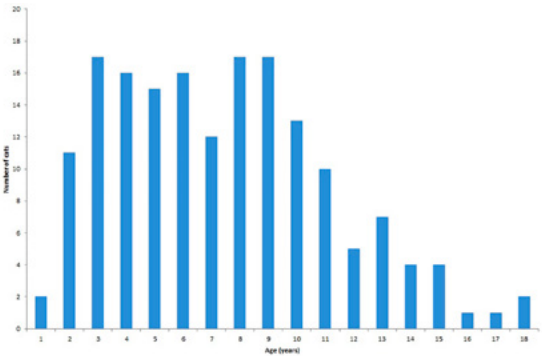




Affected paw pads may be purple with spongy swelling and the condition is sometimes referred to as 'mushy pad disease'. One or more pads may be affected, most often the metacarpal and metatarsal pads. These pads are often criss-crossed by linear striations. Photographs of affected pads kindly supplied by Ildiko Plaganyi (a) and Richard Malik (b & c).



Histological appearance of a biopsy taken from an affected foot pad: the soft tissues contain an intense inflammatory cell infiltrate composed mostly of well-differentiated plasma cells, including Mott cells (black arrows).



Graph showing the age distribution of cats diagnosed with plasma cell pododermatitis, based on 170 cases submitted to the laboratory between 2006 and 2013.

A search of our laboratory's records for samples of plasma cell pododermatitis revealed that 186 cases were diagnosed between 2006 and 2013. These cases were primarily from first opinion practices and most were from UK-based practices (Dobromylskyj 2017).

Of the 176 cases for which the cat's gender was recorded on the submission form, 70 were female and 106 were male. This gender imbalance was also seen in some smaller studies (Guaguere et al. 2004; Scarampella and Ordeix 2004; Bettenay et al. 2003). In our 176 cases, this gender imbalance was statistically significant (p=0.0085). Age was recorded for 170 of our cases, with a median of six years and range from nine months to 17 years; there was a tendency for this condition to affect young to middle-aged cats, although there was a huge variation in the ages affected; again these findings agree with those in other studies (Bettenay et al. 2003; Dias Pereira and Faustino 2003; Scarampella and Ordeix 2004; Guaguere et al. 2004).

Of the 176 cases for which the cat's gender was recorded on the submission form, 70 were female and 106 were male

For those cats in our records where the breed was noted (180 cases), all bar 11 were domestic short-haired, domestic long-haired, 'domestic cat' or 'cross-breed' (93.9%). The 11 pedigree cats included five Siamese, and one each of Bengal, Ragdoll, Burmese, British short-hair, Persian and Abyssinian. The breed prevalence of the background feline population (based on laboratory submissions) was 88.6% non-pedigree (domestic short-haired, domestic long-haired, 'domestic cat' or 'cross-breed').

Analysis according to the month the biopsy was submitted did not reveal any apparent seasonal distribution, although the length of time the lesion has been present prior to biopsy may vary considerably between cases and this may have obscured any seasonal pattern in this data.

Sadly, no clinical history or indication of biopsy site(s) were included for 28 of our samples. For the remainder, 83 cases appeared to have two, three or four affected feet, with 24 cases specifying all four feet were affected to some degree. Seventy-five cases involved one foot only, although it is possible single-foot cases are over-represented in our population; clinicians would presumably be more likely to biopsy if only single pad was abnormal, due to concern about a possible underlying tumour for example. Two cases in our cohort had apparent involvement of the nasal planum.

In terms of concurrent diseases (based on biopsies submitted) five cases had plasmacytic stomatitis/gingivitis, and two had eosinophilic granuloma-type lesions in the oral cavity – since these are both

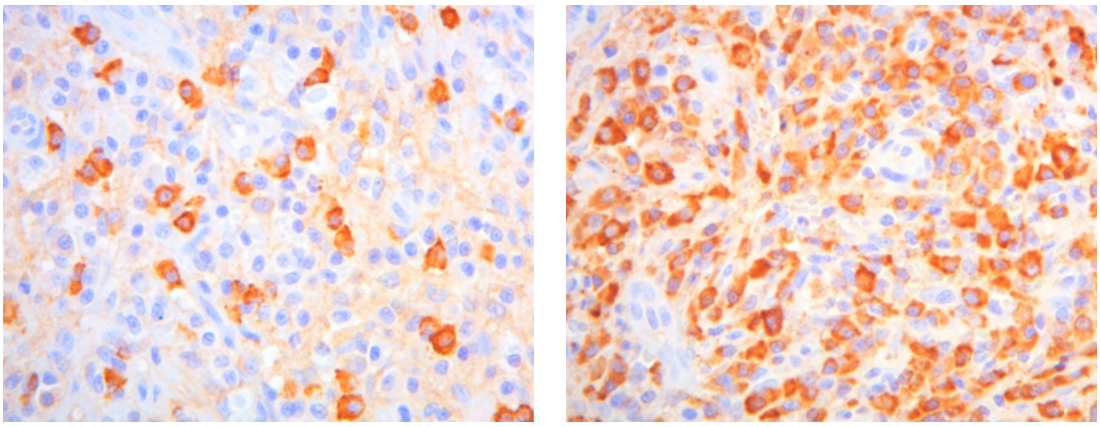
common conditions within the cat population, this could just be co-incidental.

Previous studies have produced interesting but variable findings including spontaneous regression, seasonality, responses to treatments such as steroids, doxycycline or surgical excision, variable but persistent hypergammaglobulinaemia and concurrent conditions including feline immunodeficiency virus (FIV) infection, feline leukaemia virus (FeLV) infection, glomerulonephritis and plasmacytic stomatitis. Whether plasma cell pododermatitis is a purely immune-mediated condition or whether there is an underlying infectious agent is still a matter for debate – studies searching for infectious agents within the pad have not yet yielded any conclusive evidence, despite looking for a variety of organisms including *Bartonella, Ehrlichia, Anaplasma, Chlamydophila felis, Mycoplasma, Toxoplasma gondii, feline herpesvirus 1*.....

Since doxycycline is both an antibiotic and an immunomodulatory drug, the response to doxycycline therapy could indicate one of two things (or possibly both) – either there is some bacterial involvement not yet found, and/or this is an abnormal immune response involving primarily plasma cells and localised to the foot pad (and nasal planum).

The potential link with FIV infection is interesting; although obviously many cats with plasma cell pododermatitis do not have FIV, it is feasible that a disease altering the immune function could produce errant B-lymphocyte and plasma cell behaviour. In a paper describing six experimentally infected cats (Simon et al. 1993), four had evidence of plasma cell pododermatitis, and in one case immunohistochemical (IHC) staining found FIV-immunoreactive cells in situ. Scarampella and Ordeix (2004) reported four out of nine cases were FIV-positive, while Guaguere et al. (2004) had 16 FIV-positive cats out of 26 cases, together with one FeLV-positive cat. In humans infected with human immunodeficiency virus, B-lymphocytes show signs of phenotypic and functional alterations, such as polyclonal B-cell activation, loss of B-cell memory and hypergammaglobulinemia; it is interesting to speculate whether FIV produces similar effects in feline B-lymphocytes, leading to accumulation of functionally abnormal plasma cells within tissues, as well as the hypergammaglobulinemia described by Scarampella and Ordeix (2004).

We know that the plasma cells within these pads are not neoplastic, using IHC-stains; each plasma cell can only produce a single kind of antibody isotype. Furthermore, of the two types of light chain that exist as part of an antibody (kappa and lambda chains) each individual plasma cell can only produce one. Therefore a inflammatory population of plasma cells will contain a roughly equal mixture of cells producing either kappa or lambda light chain, while a neoplastic plasma cell population (derived from a single malignant cell) will produce only one type, either kappa OR lambda.



Immunohistochemcial staining is positive (golden brown) for kappa (left) and lambda (right) light chains. Note that both types of light chain are present, indicating a non-neoplastic cell population proliferating within the pad.

One study (Kyriazidou et al. 1989) looked at the antibody isotypes produced (IgG, IgA, IgM, IgD and IgE); for neoplastic plasma cell populations a single isotype would be expected as cells are monoclonal, but inflammatory lesions would contain several isotypes due to polyclonal expansion. This study looked for IgG, IgA and IgM and found that the five other inflammatory lesions produced none, one, two or all three of these isotypes. The four plasma cell pododermatitis cases were all positive for IgG, with only one case positive for IgA and none for IgM. Although this is only a small number of cases, it suggests a relatively restricted set of B-cells and plasma cells are being expanded, could these represent 'auto-reactive' clones? PARR testing of these pads would be interesting, to see whether this is a relatively oligoclonal (few clones) or truly polyclonal (many clones) cell population. An oligoclonal expansion of plasma cells might suggest an auto-immune pathogenesis, although whether and what triggers are potentially involved would still remain a question...

PARR testing of these pads would be interesting, to see whether this is a relatively oligoclonal (few clones) or truly polyclonal (many clones) cell population

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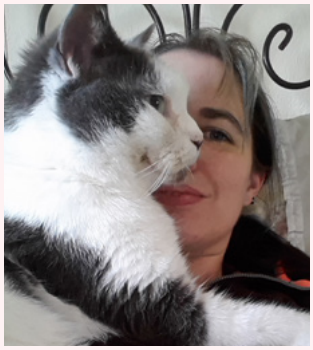

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Dr Dobromylskyj qualified from Bristol in 2004, also intercalating a Veterinary Pathology BSc at the RVC. Following a small animal internship at the AHT, she completed her immunology PhD at IAH and University of Cambridge in 2009, studying NK cells. She started her pathology training at Glasgow University before joining Finn Pathologists and a part-time residency at the RVC in 2012. She gained her FRCPath qualification in 2014 and became honorary lecturer at the RVC in 2015.

All the latest news from Cats Protection

Must you scruff

MDC (manufacturers of humane animal handling equipment) are urging feline welfare, behaviour, grooming, training and veterinary organisations to join them in warning of the possible dangers of using unnecessary scruffing techniques to restrain cats.

Techniques include applying physical restraint to inhibit the natural behaviour of the cat such as fight and flight and may take place during examinations, grooming, anaesthesia induction, euthanasia and blood taking procedures. It can include the use neck clips, pinning down and scruffing to restrict the cat's ability to move.

Increasingly, MDC are being made aware that scruffing and restraint techniques and equipment is being used 'as standard' to reduce the likelihood of injury to the operator during handling, but believe the use of such techniques may compromise the welfare of cats unnecessarily. In reality, gentle handling is more likely to result in greater safety for both handler and patient.

MDC Director, Melvyn Driver said: "We have been alerted to the issue by those who appear to have been instructed to take every precaution to prevent personal injury during animal handling. There is a perception that scruffing must be done in all instances to prevent the handler from being injured. We have over 50 years' experience handling and trapping cats and know that scruffing often makes things much more stressful for both the cat and handler. We want to challenge the idea that scruffing (in the first instance) is the normal or acceptable thing to do. We believe that scruffing should only ever be used as a last resort or in an emergency."

MDC are asking others to join forces to voice their concerns about scruffing through their 'Must You Scruff?' campaign. Numerous feline groups and other animal welfare organisations, including Cats Protection, have given their backing to the campaign and will be sharing the message that scruffing is often unnecessary and can be physically and emotionally harmful to the cat.

For more information, please contact Miranda Luck RVN (**miranda@mdcexports.co.uk**)

Speaking up for cats

Campaign for air gun licensing in England and Wales

In December 2017 the Government announced a consultation into the licensing of air weapons in England and Wales.

Thank you to the more than 50,000 people who sent an email to the Government calling for air weapons to be licensed in England and Wales. This built on our online petition which has over 90,000 signatures. Our petition is still live as it is helpful to continue to get as many signatures as possible. You can sign the petition at **www.cats.org.uk/airgunpetition**

We had a tremendous response in a very short space of time both from the public and our colleagues in the animal welfare sector, including the British Veterinary Association who sent a submission to the Government about sad cases of cat shootings and injuries treated by their members. The air weapons consultation is now closed and we are waiting for the Government to announce its next steps. However, as a result of our campaign we have secured a meeting with the Home Office to discuss the issues we have raised. We are also due to meet the responsible officers for gun crime in the police.

We will continue to keep you up to date about what the Government says and any further action or support you can give.

We can only bring about change to the laws on air weapons in England and Wales with your help. Thank you so much for taking the time to get behind our campaign.

New All-Party Parliamentary Group puts cat welfare on the political agenda at Westminster

On the 6 March the first All-Party Parliamentary Group (APPG) dedicated to improving feline welfare was launched at Westminster.

The group is made up of MPs and Peers with the support of Cats Protection and Battersea Dogs & Cats Home.

The APPG on Cats (APGOCATS) will discuss feline welfare and how to tackle key cat issues both in parliament and in society more widely. The group will be looking to propose solutions to a range of problems facing cats, such as toxins contained in antifreeze and laws on air guns, as well as highlighting the benefits of owning a cat to combat loneliness.

Maria Caulfield MP, who was elected Chair at the meeting, said: "As a cat owner myself, I'm very pleased to have been elected Chair of a group which recognises the important role cats play in many people's lives, and which will work to better protect the needs of both cats and their owners."

As a cat owner myself, I'm very pleased to have been elected Chair of a group which recognises the important role cats play in many people's lives

Everton Cat Watch

Everton has a community of stray cats. You can help Cats Protection to give better care for cats in your community. Everton is one of the first places in the country to be doing this. Let's stay in control of the area – by keeping tabs on strays and making sure they are looked after.

Snap a Moggy

We're trying to record every single stray in Everton. We're asking you to take a picture of a stray cat if you see one, using the Cat Watch app. Uploading a photo will help Cats Protection know how many strays there are so we can help control numbers.

Download the app for free now from the Google Play store or the App store. Search for 'Cat Watch' it really is quick and easy.

Find out more and other ways to report strays

Talk to us about cats in Everton and find out how you can get involved.

1. **Drop in and talk to us**
   Where? The Breckfield and North Everton Community Centre, Breckfield Road North, Everton, Liverpool, L5 4QT
   When? From 11am – 1pm each Wednesday
2. **Follow us on social media**
   Facebook: Everton Cat Watch
3. **Look out** for our Everton Cat Watch free events and activities through Autumn

For further info please get in touch with Rachele Follini, Cats Protection Community Neutering Officer.

T: 07583 365 630
E: rachele.follini@cats.org.uk
W: www.cats.org.uk/cat-watch

Reg Charity 203644 (England and Wales) and SC037711 (Scotland)

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