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Hot Topics in Feline Medicine Mini Series

Session 2: Infectious Diseases Old and New: What Do We Really Need to Know in Practice Today?

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Introduction

Unfortunately, in 2 hours we can't cover every important infectious disease in cats, so I have chosen some I hope are relevant and interesting. A good resource for further information is always the Journal of Feline Medicine and Surgery (which you receive as an ISFM member, see http://icatcare.org/isfm-membership) and the ABCD group website - http://www.abcdcatsvets.org/.

Feline Infectious Peritonitis – a diagnostic headache

Introduction

After being first described in the 1950s FIP continues to be a significant disease in feline medicine. In referral practice 1 in 200 cases seen are FIP (data from USA) and in general practice it continues to be a diagnostic challenge. Poor understanding of the disease amongst owners/breeders is often an issue taking much explaining by the vet managing the case. Often ending up with a situation where you are sure the cat has FIP, can't quite prove it and the owner is unhappy to have the cat put to sleep on this basis.

Feline coronavirus (FCoV) is a ubiquitous virus, i.e. it is commonly found in the environment and within the feline population. It is related to the canine enteric coronaviruses and TGE virus of pigs. It is a large RNA virus, with a few important things to be aware of: it has the largest RNA viral genome known and the genome encoded 4 structural proteins including: spike (S), matrix (M), nucleocapsid (N) and envelope (E), along with several non-structural proteins with an unknown role (including 3a, 3b. 3c, 7a, 7b). The S protein is used to attach to the target cell and may have a role in deciding which cells become infected. FCoV has a high mutation and recombination rate i.e. it is always changing during an infection.

In dry conditions FCoV is able to survive in the environment for 7 weeks but is easy killed with detergents/disinfectants.

There are 2 types of coronavirus; serotype I and serotype II. Type I is considered to be unique to cats, and type II is a recombination of type I and canine coronavirus. Importantly:

- Type I is the most prevalent worldwide
- Type I is very difficult (impossible) to propagate in the lab (in cell culture) but type II is easy to grow ***this creates big problems in researching this disease and most lab studies are about type II not type I***
- Various studies show different results regards ability of type I or II to cause FIP, with some just showing that depending on the area the most common type was more involved in FIP cases
- Infection with both types is possible

How does FCoV cause FIP?

FCoV is shed into the faeces 2 days after infection. The virus replicates in the gut wall cells (ICC junction in long term excretors). Some cats resist this infection, some (most) are transiently infected (2-3 months or so) and some become permanent carriers (who are interestingly unlikely to develop FIP). Stress increases shedding, and saliva only contains virus for a short amount of time. Faeces remain the main source of FCoV.

Most cats are infected via the oral route and up to 90% of a multicat household will seroconvert.

There are 4 possible outcomes to FCoV infection:

1. The cat is resistant to infection: 5-10%
2. A transient infection occurs: 70%
3. The cat becomes a persistent carrier: 13%
4. The cat develops FIP: 1-3%

How the differing outcomes occur is the subject of great debate and research.

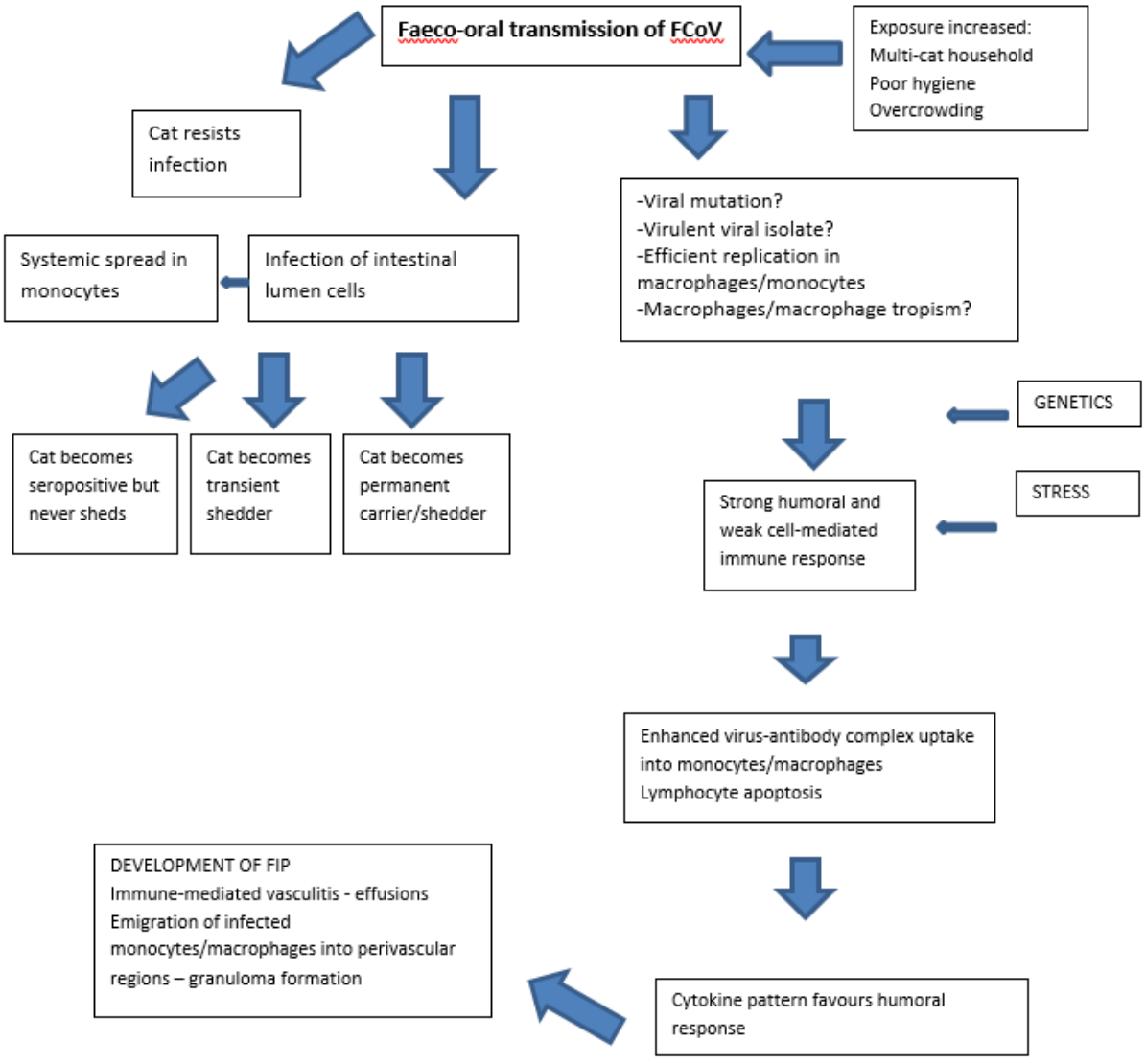
The majority of feline coronaviruses are the feline enteric coronaviruses (FECV) biotype, complicating the use of serology and PCR for diagnosis. The key difference between viruses causing FIP and those that don't is **the ability to replicate sustainably and in large volumes in macrophages**. This allows the virus to disseminate around the body and cause damage to the vascular endothelium and organs. Macrophage trophism is key to the development of FIP BUT is not the only feature of viruses causing FIP.

Key points:

- Cats can become viraemic WITHOUT developing FIP – 85% of FCoV-infected cats WITHOUT FIP had viral RNA in various haemolymphathic tissues (Kipar 2006)
- In cats that don't develop FIP, productive infection in the macrophages cannot be maintained
- The critical factor is NOT leaving the gut, it is leaving in macrophages and replicating efficiently within them

So for a cat to develop FIP you need: systemic infection with the virus, sustainable replication in monocytes and activation of the FIP infected monocytes. When FIPV spreads throughout the cat's body disseminated by monocytes, the virus targets specific tissues and organs which include the mesenteric lymph nodes, serosal surfaces of the gut, pleura and omentum. The infected monocytes mediate a granulomatous phlebitis and periphlebitis in these regions through interaction with endothelial cells. The cytokines and adhesion molecules produced by the activated macrophages cause systemic activation of the endothelium, which is thought to be only selectively responsive, explaining why FIP lesions appear only in specific organs, and in venules but not arterioles. There is currently no evidence to show that the virus itself attacks endothelial cells, instead it is the direct interaction between the macrophages and

endothelium which causes damage through the release of enzymes which can dissolve the vascular basement membrane, an apt demonstration of the immune-mediated nature of FIP pathology (Kipar 2014).



Clinical findings in FIP – the obvious and the subtle

The clinical signs of FIP are due to the immune-mediated processes occurring. Vasculitis is caused by the migration of monocytes/macrophages into perivascular areas and the resultant release of cytokines. The cytokine pattern also favours T lymphocyte apoptosis and will attract neutrophils and B lymphocytes into lesion areas perpetuating the inflammation.

'Feline infectious peritonitis' is a misnomer as not all cats develop peritonitis. Clearly effusive disease is obvious in some cases but remember the division into 'wet' and 'dry' FIP is usually not that simple. Effusive cats may only have small volume (difficult to detect) effusions and have granuloma lesions in organs. Cats with dry FIP may have on post-mortem small pockets of effusion. **Think of the 'wet' and 'dry' just being phases of the same disease.**

Cats with effusions seem to have more generalised vasculitis and therefore exhibit this as a main clinical signs whereas granulomas can occur anywhere and the clinical signs will depend on the organ affected.

General clinical signs of FIP

These are often vague, the usual sick cat signs of inappetance, weight loss, lethargy. Kittens may look like 'poor doers' that haven't grown as well as siblings. The mucous membranes may be slightly pale and they may be pyrexic (in some cases pyrexia is the only clinical signs). Icterus may be detected.

'*Effusive FIP'*: cats that classically fall into this group tend to develop clinical signs more quickly than cats with 'dry' FIP, perhaps because owners notice ascites or dyspnoea due to pleural effusion. If an effusion is noted in one cavity it is useful to look for it in the other as few diseases cause bicavitary effusions (diffuse neoplasia [carcinoma, mesothelioma, lymphoma], hypoalbuminaemia, congestive heart failure).

If you note an effusion in one cavity – look for it in the other and ALWAYS sample if possible.

Cats with '*dry' FIP* tend to present with the vague clinical signs noted above along with others you will detect on physical examination:

- Ocular signs of FIP: various ocular abnormalities are reported and so make sure you examine the eyes in any suspected cases. You may notice uveitis, iritis, retinal examination may show the classic perivascular cuffing or even granuloma. (Differentials here are limited: lymphoma, toxoplasmosis, myocbacteria).

- Neurological signs: 25-33% of cats without effusions have neurological signs including: forebrain signs such as seizures and depressed mental status, or if other areas are affected then other signs are observed; ataxia, tremor, vestibular signs, proprioceptive deficits and in spinal FIP paralysis/paresis may be noted. Visual deficits and cranial nerve abnormalities may be detected on neurological examination.
- Intestinal signs: GI disturbances are common due to lesion localisation in the gout, most commonly the large intestine or ileocaecocolic junction. Thorough palpation is important to detect these lesions on examination.
- Liver or kidney signs: jaundice, PU/PD depending on organ affected, and these organs may feel abnormal on palpation.
- Other signs/abnormalities: FIP affecting the skin is reported but uncommon, and reproductive failures and poor growth in kittens may occur in breeding colonies.

Making a diagnosis of FIP

This is often the difficult bit if the clinical signs are less than obvious. Some cases will be obvious (the 8 month old purebred cat with a large abdominal effusion) but others are subtle – the 2 year old DSH with inappetance for example.

Pre-mortem diagnosis of FIP – detective work

There is currently no test that will conclusively prove a pre-mortem diagnosis of FIP without obtaining tissue (pre- or post-mortem). Therefore, it is a matter of putting together the 'clues' and coming up with the most likely diagnosis. There is an evidence base for each step from research papers looking at prevalence and risk factors. **Definitive diagnosis of FIP can be achieved through use of direct immunofluorescence (DIF) performed on an effusion sample or histology coupled with immunohistochemistry (IHC) on a tissue sample.** (see later).

No one test is diagnostic for FIP – false positives with other inflammatory or neoplastic disease are common and must be excluded.

1. **Signalment**: Most cases of FIP seem to occur following a cat's first exposure to FCoV and therefore occur in cats < 1 year of age. There is a breed predisposition for purebred cats (the specific breeds at risk are different in different studies and different parts of the world, where it is likely genetics in breeds differ, so difficult to conclude). There is another small peak of infection in older cats – but this is unusual.

2. **History**: Multi-cat or breeding households are more at risk. A history of a stressful event such as neutering or re-homing may be reported. Clinical signs reported by owners (see above) are generally vague unless an obvious effusion is found.
3. **Physical examination**: get as many clues as possible from this examination ***if suspicion of FIP examine the eyes closely including the retina*** see above – lesions in the eyes can be highly suspicious of FIP. Make sure you take the temperature and palpate the abdomen carefully. Look for jaundice (can be subtle) and pallor.
4. **Blood tests:** some clues here BUT nothing definitive of course.

Haematology and biochemistry may be totally normal in a case of FIP

BIOCHEMISTRY:

- Elevated total protein and specifically globulins are seen in many cases (not all).
- Albumin:globulin ratio of <0.5 in serum has been proposed to make a diagnosis of FIP more likely but recent studies revealed a very poor positive predictive value (proportion of positive results that are truly positive) for A:G ratio <0.6 so this cannot be considered a particularly useful test, although if the ratio is high it may make FIP less likely.
- Elevated bilirubin is seen in some cases (often with liver involvement) along with various liver enzyme elevations and azotaemia if the kidneys are involved. Rarely haemolysis has been reported with FIP and this may also contribute to jaundice.

SERUM PROTEIN ELECTROPHORESIS:

has been used as a test for FIP but again is unreliable. Yes, cats with FIP often have increased α2 globulins and γ globulins but so do cats with many other disease and a monoclonal gammopathy has been described several times in cases of FIP. (Taylor 2010).

HAEMATOLOGY:

- Lymphopenia is often observed – a good clue! And may be profound in some cases and indicate a poor prognosis.
- Neutrophilia (with mild left shift)
- Anaemia of chronic disease (normocytic normochromic) – severe anaemia is reported but unusual (Norris et al 2005 – a paper where they noted severe immune mediated anaemias – this is from Australia)
- Reduced T lymphocytes

SEROLOGY

Serology on blood or effusions is usually no help at all. High levels will be seen in cats infected with FeCoV and this is likely most cats in multicat homes. Terminal cases can have negative serology. All in all it may add a piece of the jigsaw if a very high level, but is otherwise useless.

ACUTE PHASE PROTEIN ELEVATION:

- **Alpha-1 acid glycoprotein (AGP)** has been found to have a high sensitivity and specificity for FIP but it is worth noting again that false positives occur with other neoplastic and inflammatory diseases. As before it is another jigsaw piece but not specific alone.

PCR on blood is NOT useful in the diagnosis of FIP.

5. EFFUSION ANALYSIS

There is no doubt finding effusion is helpful – its presence and if you can sample it – look for it in every cavity and even getting a drop can help.

Start with basic effusion analysis – most are high protein, over 35g/l, with a moderate to low cellularity, so modified transudates or exudates. The cells are usually mixed, neutrophils and macrophages, small numbers of lymphocytes. The neutrophils are non-degenerate. This finding does not diagnose FIP but may exclude other causes of effusion such as bacterial peritonitis.

In summary:

- Gross examination: the effusion will be sticky, thick, straw coloured and froth when shaken (all indicators of high protein level)
- Chylous effusion is reported with FIP but is rare
- High specific gravity
- Protein analysis: a high protein content will be recorded
- A low albumin:globulin ratio (<0.45 is consistent with FIP [not diagnostic], >0.8 makes FIP unlikely) many cases come in the 0.5-0.8 range where FIP is still possible.
- Low cellularlity – mixed cells, mostly macrophages but some lymphocytes and neutrophils.
- Rivalta test: this test can be done in practice but a recent paper has shown a lower sensitivity/specificity than previously reported with false positives in several other diseases. The positive predictive value was only 58.4% (proportion of positive test results having FIP).

- Immunofluorescence staining: proving the presence of FCoV in macrophages in an effusion can be considered diagnostic for FIP BUT some effusions have too few cells to give a positive result so false negatives are possible (specificity 100% but reduced sensitivity). *note available at Liverpool University*
- Quantitative PCR may have some utility but is NOT diagnostic – see below.

6. **CSF testing**: in neuro FIP CSF is useful. It can show increased cells, particularly mixed and pyogranulomatous inflammation but it is most useful to exclude other causes of neuro signs such as lymphoma. See below for discussion of PCR.

7. **Diagnostic imaging:** this is very useful for diagnosis FIP, although as with all tests for FIP is just a further piece of the puzzle:
    - Radiograph may reveal effusions (particularly thoracic effusions when only abdominal effusions had been detected clinically)
    - Ultrasound may show lesions within organs: this is useful for the liver, kidneys etc. Renal ultrasound may show perirenal fluid which can be sampled. Generalised lymphadenopathy may be noted. Slivers of abdominal fluid may be obtained with ultrasound guidance.
    - Tru-cut biopsy samples may be obtained in an attempt more to exclude diseases such as lymphoma or submitted for immunohistochemistry or PCR (see below).
    - MRI/CT scanning: can be used to look for lesions in the CNS BUT results not pathognomic – CSF, biopsy etc required to exclude other conditions.

8. **Histopathology**: the gold standard for the diagnosis of FIP means obtaining tissue which on examination shows perivascular pyogranulomatous inflammation. There may be some plasma cells and neutrophils at the periphery of the lesion. Immunohistochemistry performed on the sample to demonstrate virus within a lesion is diagnostic. Again this is available from Liverpool, PCR on tissue may be useful but not diagnostic and does not replace immunohistochemistry at this time.

PCR in the diagnosis of FIP

This area has had some recent developments and laboratories are increasingly recommending this test. However, PCR is NOT at this point a definitive test for FIP due to conflicting work detailed below.

The IDEXX FIP Virus RealPCR test looks for virus that has a specific mutation in the spike protein of the FIP virus and in a study (Chang et al 2012) showed that 91% of FIP viruses had nucleotide substitutions in the spike protein (changing a methionine to a leucine, mutation M1058L). They also showed 4% of FIPVs had an alanine at 1060 instead of a serine found in all FECVs (mutation S1060A).

However, a more recent study from the University of Bristol (Porter et al 2014) showed that this mutation was found in the tissues of cats WITHOUT FIP (89%) and those with FIP (91%) and so this is a marker of systemic spread NOT FIP!

Currently Bristol University offer real time quantitative PCR tests for FIP on tissues, effusions and CSF – this test is not specific for FIP but high levels are found more often in cats with FIP than those without.

So PCR is not the answer we hoped it would be at this time – but further research is needed.

Definitive diagnosis

Definitive diagnosis of FIP can be achieved through the use of direct immunofluorescence (DIF) performed on an effusion sample or histology coupled with immunohistochemistry (IHC) on a tissue sample. DIF and IHC both detect FCoV antigens within macrophages and even though the antigens of FECV are indistinguishable from FIPV seen in FIP, it has been well established that only the virulent FIPV have mutations allowing sufficient replication within macrophages to be seen by DIF or IHC. Contact Liverpool university for this test if you are in the UK.

In conclusion – there is no one simple test to diagnose FIP – it remains a jigsaw to put together. In the talk we will cover the above to hopefully explain further how challenging cases can be diagnosed.

Treatment of FIP – anything new?

Ideally treatment of FIP would involve suppressing the excessive immune response and attempting to enhance cell mediated immunity using cytokines. However, currently there is little evidence for the efficacy of any drugs. Many studies that sound convincing have small case numbers and the diagnosis of FIP was not confirmed. Generally, options include:

- Prednisolone: as an immunosuppressive this may slow the progression of the disease but won't cure it. It is also toxic to lymphocytes which given the disease process is not desirable as cell mediated immunity is needed. Anti-inflammatory to immunosuppressive doses are used and help make affected cats feel better at least. Of course it is important to have a correct diagnosis and not miss something like a bacterial peritonitis/pyothorax and then immunosuppress the patient.
- Interferon (human or feline): has been shown to make no difference to survival or quality of life in a placebo controlled study BUT the cats in this study were also given prednisolone.
- Polyprenyl immunostimulant: a drug designed to simulate cytokine production, improve helper T cell production; prolonged survival times have been reported in dry FIP cases, further studies with larger numbers needed, conflicting results are reported, recent studies were less encouraging. This drug may have a role as an adjunctive treatment for dry FIP – note results for wet FIP are still described as 'abysmal'.

- Research is ongoing into compounds such as chloroquine, an anti-viral drug, to see if the virus can be treated directly.
- General attention to nutrition and analgesia is important of course.
- Surgical resection of granulomas in the GIT tract causing obstruction (but ? ethics of recovering a cat with FIP?)

Prevention of FIP

Given the fatal nature of FIP obviously avoiding it in the first place is desirable. People have attempted this in a few ways:

1. Breeding FCoV free kittens: this requires very strict hygiene measures – isolating the mother and weaning early to avoid the mother passing FCoV to the kittens (wean at 5 weeks). The problems with this are practical: it is very hard to prevent exposure to a ubiquitous virus, plus there is a chance that FCoV naive kittens may be MORE likely to develop FIP when they meet the virus (as they very likely will when re-homed), as first exposure seems more likely to result in FIP.
2. Removal of chronic shedders from a multi-cat environment. This technique requires faecal PCR testing and removal of cats shedding virus for >2 months or more. Again the issue is maintaining the low level of FCoV, strict rules on introduction of new cats etc etc are needed. Serology has been used for the same reason (high titres mean likely shedding) with isolation and removal of persistently infected cats or persistent shedders.
3. Vaccination: there is a vaccine available in the USA. It is intranasal, a temperature sensitive mutant. Its efficacy has been questioned although it does not seem to cause antibody dependant enhancement. No protection has been shown when seropositive cats are vaccinated. The vaccine is not given until 16 weeks anyway, and most cats have been exposed to FCoV by then.

In general, the risk of FIP is greatest in multi-cat home and so general advice on hygiene and stress avoidance is the best way to prevent FIP:

- Prevent overcrowding: this increases stress and the amount of FCoV in the environment
- Stable age similar groups should be maintained (not > 3-4 cats in each group)
- Litter tray hygiene: enough trays for all cats cleaned regularly, vacuuming around the tray often to avoid litter tracking. Food bowls away from litter trays.
- Breed lines may show higher numbers of FIP cases – avoid breeding from these lines again. UC Davis are attempting to find genes involved in sensitivity/resistance to FIP – see http://www.vetmed.ucdavis.edu/ccah/research/fip.cfm

Herpesvirus – does it make cats snotty?

There are many causes of chronic rhinitis in cats – so called chronic snufflers, but the most common is likely to be related to previous herpesvirus infection. Chronic rhinosinovitis can occur in cats of any age and can be a source of frustration to owners and vets. Although herpesvirus is often involved, it is a diagnosis of exclusion in many cases and other conditions such as neoplasia and foreign bodies should not be missed.

Ask the right questions:

- How long has it been going on for? Acute is more likely a foreign body, chronic progressive perhaps neoplasia.
- Does the cat have a history of cat flu?
- Has the discharge changed? Purulent becoming epistaxis warrants further work up for example.
- Is it unilateral (neoplasia, dental disease, FB) or bilateral (chronic rhinosinovitis).
- Does the cat also have signs of stridor or stertor? A pharyngeal polyp can cause obstruction, so can accumulated discharge or neoplasia.

Differential diagnoses for nasal discharge should be considered

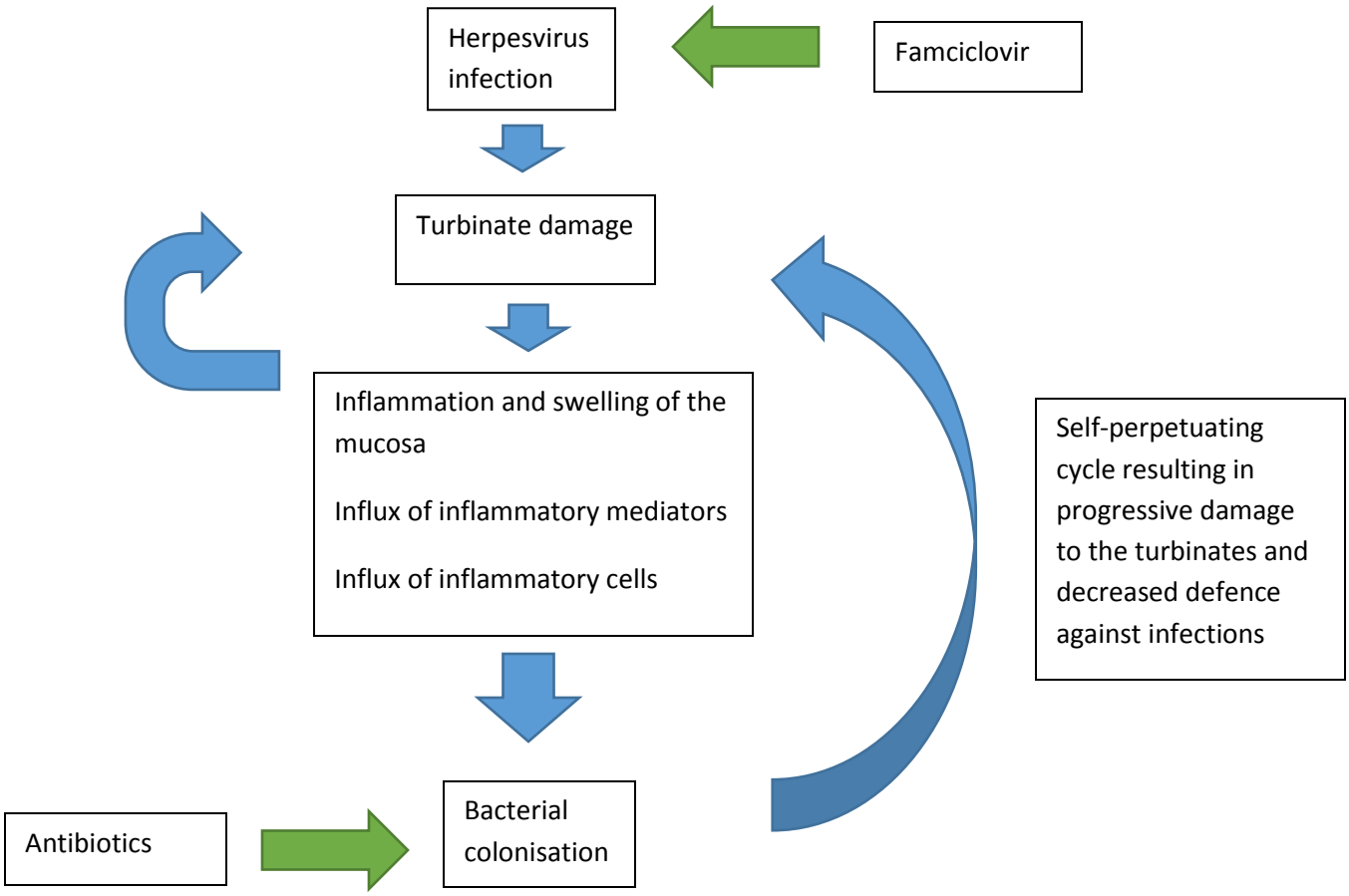
- Foreign body
- Nasal neoplasia
- Dental disease
- Polyps
- Nasopharyngeal stenosis
- Fungal rhinitis
- Chronic rhinitis
- Other: stenotic nares, cleft palate

So how does herpesvirus cause chronic rhinosinovitis?

Chronic rhinitis may result from an initial infection with herpesvirus. See the diagram below. We assume the herpes is the initiating factor and this starts the cycle of turbinate destruction, therefore swelling and inflammation, reduced defence against bacteria and recurrent infections that respond partially to antibiotics. Irreversible destruction of the turbinates may be the end result, and recurrent viral recrudesces may play a role. It is hard to determine at what stage the cat is in the disease at the time you see it.

Performing a PCR demonstrates the virus – but this may not be useful as it will be present in carrier cats anyway. In fact, 80% of infected cats are carriers of the virus, although it will be latent in many. A positive PCR really just shows viral DNA -not that it is active.

Bacteria are certainly involved in the pathogenesis of chronic rhinosinovitis. Mycoplasma species have been isolated from affected cats and may play a role. Taking a swab of the snot won't help – it will be full of contaminants. Culture of a biopsy will be more useful – or of material flushed from the nose.



Clinical assessment of the snotty cat

When presented with a cat with chronic rhinitis, ideally certain work-up is performed, although this will be dictated by the owner's finances and opinions. A clinical exam should be thorough and look for:

- Facial asymmetry – concern regards neoplasia (in some countries fungal infection) are raised if there is asymmetry, this is not typical of FHV related rhinitis.
- Pain on palpation of the facial bones?
- Exopthalmos
- Neuro examination e.g. Horner's
- Air flow – simply hold a slide to see which nares is patent
- Examination of the mouth – to do this thoroughly, requires anaesthesia, but depending on the cat the palate can be examined
- Examination of the fundus – to look for fungal disease and even lymphoma
- Examine the lymph nodes
- Otoscopic examination for evidence of polyps for example

Further diagnostics include:

- Bloods – not usually very helpful in the work up of nasal disease, although in certain circumstances it may be. For example, if the cat has epistaxis, is aspergillus or cryptococcus serology is indicated. A coagulation panel should be considered if the cat has epistaxis and biopsy or even just rhinoscopy is being considered. Depending on the patient's age pre-anaesthetic bloods may be indicated (+/- urinalysis). Retroviral serology is indicated.
- Viral swabs – issue with detection of vaccine strains, plus as mentioned – found in cats without clinical signs of disease, consider results carefully.
- Bacterial swabs - as mentioned culture of purulent discharge will be heavily contaminated. Culture (aerobic and anaerobic) of samples taken from deep inside the nose may be more indicative of the agents involved, flushing into the nose with a sterile catheter, or culture of material from the forced nasal flush (see below) may be useful. Mycoplasma culture can be requested and a PCR available – but as before may be found in normal cats.
- Examination under GA – check dental disease is not a cause of the nasal discharge – probe the teeth with the periodontal probe, depths should not exceed 0.5-1mm! Examine the soft palate, it can be gently retracted rostrally to examine behind – or a dental mirror plus light source used to check the area for foreign bodies, masses or strictures
- Imaging – in chronic rhinosinovitis radiographic findings are usually indicative of increased opacity due to exudate in the nares and possibly evidence of turbinate destruction. CT is a useful imaging modality, as is MRI.

- Rhinoscopy – retroflexed pharyngoscopy can be very useful to examine the caudal nasopharynx and choanae, anteriograde rhinoscopy with a rigid scope is challenging due to the small space in a cat's nose but may identify masses.
- Nasal flush – pack the pharynx after ensuring the ET tube s appropriately inflated or adequate size if non-cuffed (care with cuffing in all cats, count the swabs in and out) and using 3 x 10-20ml saline flush occlude the opposite nostril and flush. The swabs may collect samples, masses, foreign bodies and the flush maybe therapeutic as it removes inspissated pus for the nose.
- Biopsy – biopsies can be useful to confirm a diagnosis of rhinosinovitis and should be taken even is the mucosa looks normal. Risks include haemorrhage and care must be taken not to go too caudal with the forceps, so measure up to the medial canthus and mark the forceps.

Treatment of chronic rhinosinovitis

Manage owner's expectation – this condition can be recurrent and frustrating (and expensive) to manage. It is unlikely to be cured, but can be well managed.

Antibiotics

Many cases do respond to antibiotics and drugs should be used that penetrate bone e.g. amoxicillin-clavulanate, clindamycin for example. Drugs active against mycoplasma are sensible – such as doxycycline which may also have some immunomodulatory effect. Pradofloxacin should be reserved for cases with pseudomonas or culture results indicating the need for a fluoroquinolone. Antibiotic nasal drops are used in some cases. A long course may be needed, 4-6 weeks.

Antivirals

Recently the use of the antiviral famciclovir have increased. It has been shown to be effective in cats with FHV and many feline specialists are keen to recommend it. In some countries it is expensive to use. Doses of 30-40mg/kg TID are recommended and this can also be used in cats with herpetic dermatitis.

Anti-inflammatories

Could some of the self-perpetuating inflammation be arrested with immunosuppression? As most have lymphoplasmacytic rhinitis corticosteroids may have a place. However, viral recrudescence is a big concern. Certainly low doses and a rapid taper is indicated. NSAIDS may reduce pain and swelling and are more useful in the nose, hydration should be optimised.

Non-specific therapy

Nursing care is important – maintenance of hydration and nutrition. Nebulisation can be helpful, paediatric nebulisers can be purchased and the cat can learn to tolerate this, with them in a basket on in the small room. Saline drops into the nose have the same effect – to loosen the secretions and are available to

buy for children. Decongestants such as those found in nasal drops may be useful but poorly tolerated in some cases.

Calicivirus – to blame for chronic gingivostomatitis?

Feline gingivostomatitis is a serious, painful and frustrating disease resulting in lesions in the pharynx, buccal mucosa, tongue and gingiva. Clinical signs are oral pain, halitosis, dysphagia, anorexia, lethargy and weight loss. Treatments include extraction of all cheek teeth as well as anti-virals and immunosuppressants.

In some studies, up to 100% of cats with FCGS have feline calicivirus (FCV), however, attempts to induce the condition with calicivirus have not proved the link. One study considered palatoglossitis but not buccalstomatitis linked to calici. Case reports have shown cats that cease to shed calicivirus once clinical resolution of stomatitis occurred.

Affected cats seem to have a different cytokine profile than cats without the condition, so it may be an aberrant immune reaction to an infectious agent. Affected cats also seem to have lower levels of salivary IgA. Dowers et al (2009) showed that cats suffering from cat flu previously were more likely to develop FCGS, and the same study showed significantly more affected cats than control cats with FCV RNA present.

It is likely that there is a link but the condition has multifactorial causes – like FIP there is the role of the immune system as well as the virulence of the virus (another one prone to multiple mutations).

Hennet et al (2011) showed that treatment with feline interferon omega resulted in a significant improvement in lesion scores and decrease in pain scores when the cats were treated with interferon at a dose of 0.1MU daily. This effect was more than that seen in cats treated with prednisolone. Interferons are antiviral, antiproliferative and immunomodulatory.

Some dental specialists start with intralesional injection (i.e. at the time of extraction) (Lisa Milella personal communication) at 1MU/kg and follow with an oral dose – 10MU reconstituted with 100ml saline – frozen into 20ml aliquots (stable for 21 days). The dose is then 1ml orally daily alternating sides of the mouth. Continue for 3-6 months. This is AFTER extraction of the cheek teeth.

Regards corticosteroids, they should not be used for first line treatment and long term use is a concern. The cats tend to stop responding with continued use. They should be used for refractory cases as a last resort. Low dose can get some inflammation under control, but must be combined with other treatments such as extraction and plaque control.

Cyclosporine has also been used in the management of FCGS, but in one study it took 4-6 weeks for a response to be seen. Absorption and therapeutic levels can be an issue.

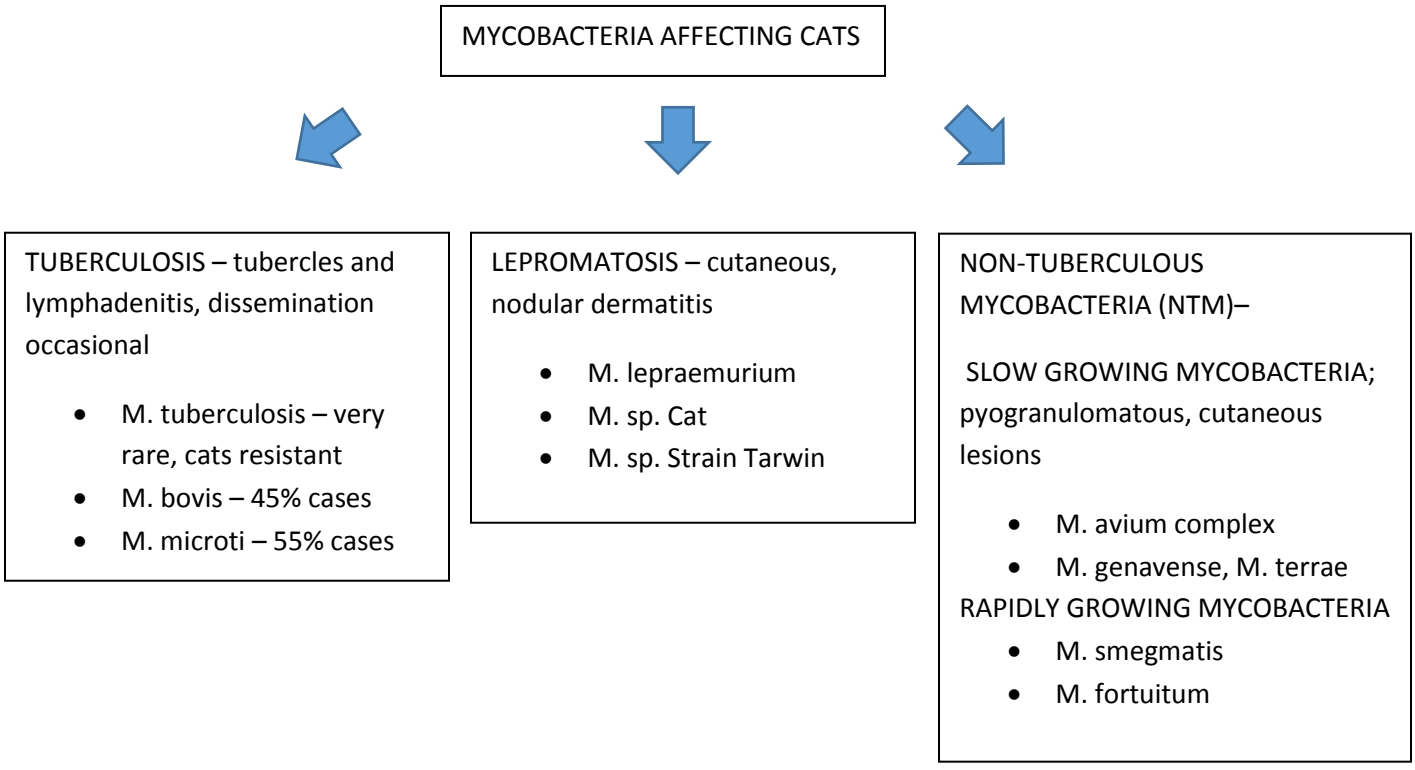
Feline mycobacterial infections: what do I need to know?

Infection with mycobacteria is something we are all aware of but the different organisms involved and the treatment can but confusing. In addition, the identification of the causative organism is not straightforward due to the difficulty culturing certain types of mycobacteria. In this talk I will try and make the definitions clearer and talk about the submission of samples as well as the treatment and prognosis. Cases of mycobacterial infection will be presented.

In cats (and dogs) there are 3 main subcategories of mycobacterial organism causing disease. Recently the VLA have published data on their culture results. Over 4 years up to 2008 the following were cultured from 339 cases:

- M. microti – 19%
- M. bovis – 15%
- M. avium – 7%
- Non-tuberculous (non-M. avium) – 6%
- No growth in 53%

Interestingly geographical location within the UK showed certain mycobacteria were much more common: south west England/wales – M. bovis, South eat – M. avium, South of London/South-west Scotland – M. microti.



1. **TUBERCULOSIS –** feline tuberculosis is caused by M. bovis or M. microti in the majority of cases. Cats seem to be inherently resistant to M. tuberculosis (unlike humans where 90% cases are due to M. tuberculosis and M. microti infection is rare). Historically infection with M. bovis was seen in farm cats drinking unpasteurised milk. With pasteurisation and the UK TB screening program in cattle this infection has become less common. Some people do lump M. avium into this group too but really it is non-tuberculous.

Source of infection

The main source of M. bovis and M. microti is likely to be hunting small rodents (mice and voles carry M. microti). This explains why lesions often begin on the face, or associated with small wounds (bites from prey whilst playing with them). Other wild animals may be infected, particularly with M. bovis (badgers, foxes, stoats etc) and although cats tend to stay out of the way of such predators they may be infected via the environment.

ZOONOTIC RISK FROM CATS

M. microti and M. bovis (and M. avium complex) are potentially zoonotic but no cases of infection from a cat to a human have been reported. However, cats can be infected by owners (reported with M. bovis). Certainly when mycobacterial infection is a differential material should be handled with gloves and immunocompromised people not allowed to handle the animal. M. bovis is a notifiable disease.

Clinical signs

Cats are infected via the skin, respiratory tract or alimentary tract. The cutaneous form is the most common resulting in nodules and non-healing, draining sinuses and tracts. Such lesions commonly affect the face, extremities of tail (sites of bites). Lymph nodes locally may be affected and invasion of local sift tissue or even bone is possible. Pulmonary infection causes a cough and dyspnoea. Intestinal lesions may form masses and obstructions, presenting with weight loss, GI signs and mesenteric lymphadenopathy. Disseminated disease can cause neurological signs, chorioretinitis, pyrexia, lameness, effusions and weight loss. The recent study (Gunn-Moore at al 2012) showed the following presenting signs:

- Single or multiple skin lesions – 74%
- Lesions on the head – 54%
- Lymph node involvement – 47% (typically submandibular)
- Systemic signs (inc. pulmonary) – 10-16%

Non-healing wounds, nodules, sinus tracts etc must be investigated with mycobacteria in mind.

Diagnosis

When a wound on a cat/or nodule etc raises suspicion of mycobacterial infection it is sensible to complete a work up for systemic infection at that point. This allows you on reaching a diagnosis (remember the culture will take a while) to have all the info you need to give the owner on which to base decisions. So taking a chest radiograph when the cat is under GA to biopsy a skin lesion makes sense, along with bloods to look for other organ involvement.

Bloods may show hypercalcaemia, non-regenerative anaemia, hyperglobulinaemia, neutrophilia for example.

Thoracic radiographic changes are variable and include: tracheobronchial lymphadenopathy, interstitial or miliary patterns, pleural or pericardial fluid or local pulmonary consolidation.

Abdominal imaging may show mesenteric and other lymphadenopathy, organomegaly, ascites or abdominal masses.

If bone lesions are present they can be seen on radiography as periostitis, boney lysis, sclerosis or discospondylitis. Polyarthropathy and osteoarthritis can be seen.

Specific tests for mycobacteria

Intradermal testing is not reliable in cats so further testing is always needed to confirm a diagnosis.

- Interferon-gamma test: this test shows promise and should be available from the VLA but is not currently when I contacted them in preparation for this talk.
- Biopsy material/effusions etc should be stained with a Ziehl Neelsen stain (ZN) for acid fast bacteria. Culture remains very important following the identification of acid fast bacteria to attempt to identify the species involved. The bacteria are often within macrophages. Note that the number of bacteria depends on the species of mycobacteria involved and the cat's immune response.
- Mycobacterial culture: samples positive on acid fast staining must be submitted for culture. This is however, not perfect: mycobacteria are very difficult to grow in culture and sometimes an acid fast positive sample will fail to grow anything. Stats on this were recently published with 53% of acid fast staining samples negative on culture. Conversely some positively cultured mycobacterium were negative on acid fast staining in a recent study (Gunn-Moore et al 2012).
- PCR testing – this is now available from laboratories such as the Leeds laboratory or possibly the Cardiff Mycobacteriology unit (addresses at bottom).

HANDLING BIOPSY MATERIAL CORRECTLY

It is important to think about mycobacteria when taking a biopsy from a suspicious lesion to avoid further surgery for the cat. SO FOR ALL CUTANEOUS/SUBCUTANEOUS LESIONS OF ENLARGED LYMPH NODES FROM A CAT DO THE FOLLOWING:

- Collect a biopsy and cut it into 4 pieces:
  1. Into formalin as standard for histopathology
  2. Place 2 bits in a sterile container and label and put in the freezer
  3. If suspecting bacterial infection put one into a plain tube for standard bacterial culture
- Then if ZN staining is positive one of the frozen bits is sent to the VLA (or other mycobacterial reference laboratory)
- The final piece stays in your freezer in case further investigation is needed (or sample is lost etc)

Treatment – to treat or not to treat

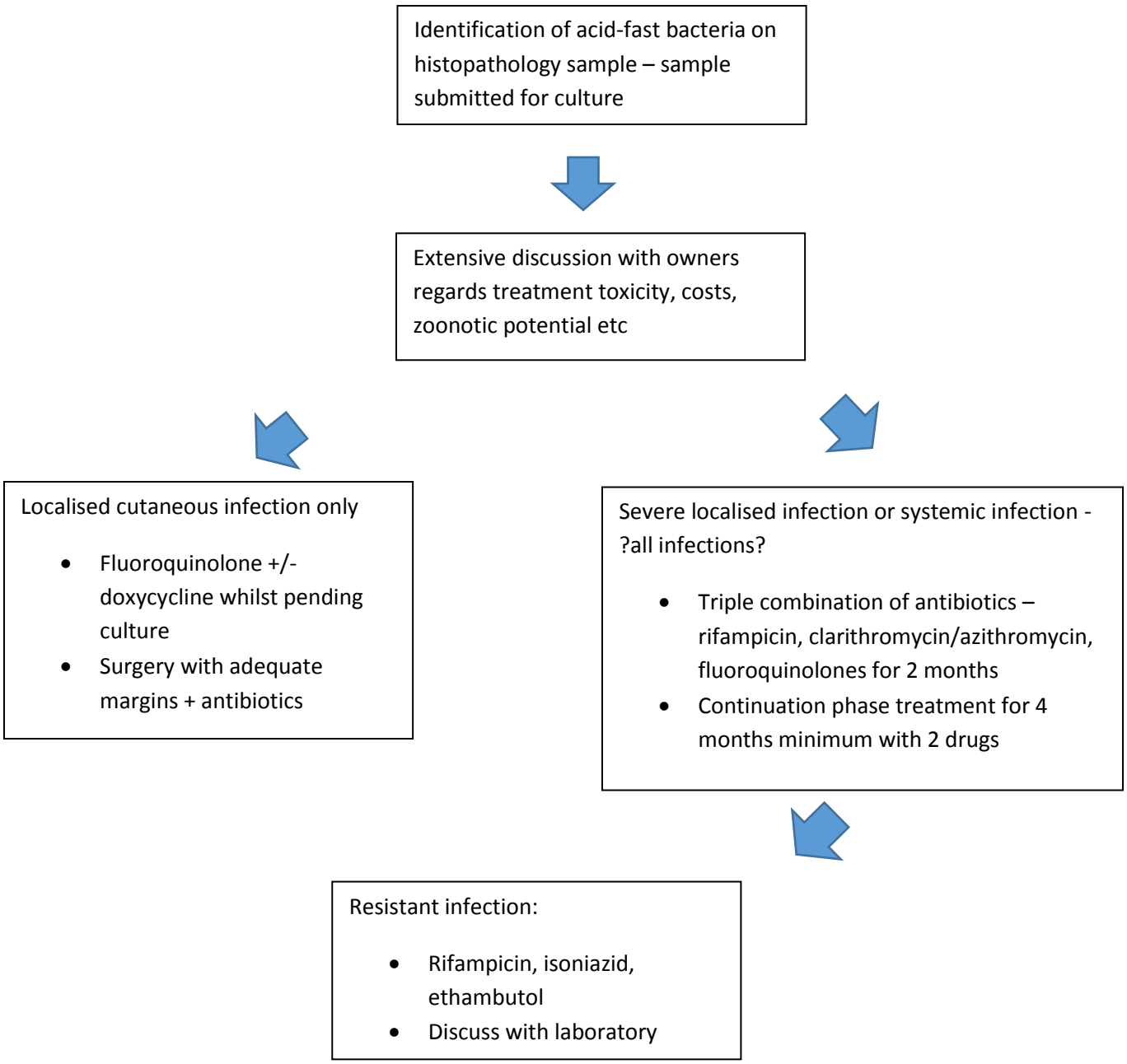
Before launching into treating a case of mycobacteria the following must be considered and discussed carefully with the owners:

- It is potentially zoonotic – ask if ANYONE the cat comes into contact with is immunocompromised (chemo patients, transplant patients, very elderly people, HIV patient). If so, then euthanasia must be advised. Note that even a negative culture does not exclude infection and therefore human health risk.
- The type of infection may be significant: cats may be an increased zoonotic risk if they have an exudative wound or a respiratory infection – this must be discussed with the owners. Also the systemically affected cats may be more difficult to treat than a simple cutaneous infection.
- The treatment is long term and expensive – establish finances now instead of running out of money later.
- Can they commit to pilling this cat for months?
- The treatment is potentially toxic – drugs may have to be altered if reactions are seen.

If the owner cannot commit to treatment it may be better to euthanase the cat unfortunately. It is not fair on the cat to start and the owner to then give up and the disease to relapse.

Surgical debulking is not generally recommended as this can result in a large non-healing wound.

The following plan is suggested if owners do want to treat:



Treatment ideally consists of an initial and continuation phase. The initial phase includes 3 drugs generally includes rifampicin, a fluoroquinolone and clarithromycin/azithromycin. This would be followed 2 months later by a continuation phase treatment of rifampicin and either a fluoroquinolone or clarithromycin for 4 months. Commonly rifampicin is not tolerated and in these cases it can be swapped for doxycycline.

To facilitate owner compliance:

- Chose liquid formulations
- Place all drugs into gelatine capsules so pilling is needed only once
- An oesophagostomy tube can be placed and left in place for liquid medications to be given

In cases where resistance is seen (or side effects necessitate discontinuation of a drug) ethambutol – isoniazid – rifampicin combinations can be considered. Dihydrostreptomycin or pyrazinamide can be substituted for ethambutol. **If M Bovis is cultured avoid pyrazinamide as it is resistant naturally*.*

Potential drug side effects: the drugs used will not be very familiar and some have considerable side effects including:

- Rifampicin: hepatotoxicity, discolouration of body fluids, generalised erythema and pruritus, poor palatability *monitoring of liver enzymes necessary* hospitalise for first treatment*
- Clarithromycin/azithromycin: pinnal or generalised erythema, ?hepatotoxicity
- Enrofloxacin: not recommended due to potential retinal toxicity
- Marbofloxacin: does not seem to cause same retinal toxicity
- Doxycycline: oesophagitis and GI signs **give with food or follow with food and water**
- Isoniazid: hepatotoxicity, peripheral neuritis, seizures, AKI
- Dihydrostreptomycin: ototoxicity
- Ethambutol: optic neuritis
- Pyrazinamide: hepatotoxicity

Prognosis

A recent study of mycobacteria infection in the UK produced the following results: 42% complete remission, but relapses were common (64%) and often followed by pulmonary and systemic spread. Short courses of medication may have contributed to this high rate of relapse.

2. Feline leprosy syndrome

Infection with *M. lepraemurium* is assumed as this mycobacterium cannot be cultured using standard techniques. However, recent PCR techniques have shown that more than one mycobacteria are involved with this condition. In Australia studies show young cats are affected with *M. lepraemurium* but older cats are affected by a novel mycobacteria called *Mycobacterium* spp cat. These cats are often immunosuppressed. Other mycobacteria have been cultured in other studies. Infection is likely via wounds and maybe from rodents but this is unproven.

Clinical signs include single or multiple nodules of the skin, often on the head, face, limbs or trunk. They are painless and soft. Overlying skin may ulcerate and in later stage disease local LN and even internal organs will be affected. Diagnosis is as for mycobacteria but culture is negative. PCR is effective at identifying the organism involved.

Feline leprosy has 2 clinical forms: lepromatous (poor cell mediated immunity, tubercules form containing pyogranulomatous inflammation and many mycobacteria)) and the tuberculoid form (pyogranulomatous dermatitis and panniculitis). Histology is the mainstay of diagnosis, with investigation as above for tuberculous mycobacteria.

Treatment

Initial management includes a fluoroquinolone whilst awaiting culture or PCR and surgical resection may be indicated for resection of small nodules. Other antibiotics considered (and used alongside surgery) include the combinations used for tuberculosis.

3. Mycobacterium avium complex

The M. avium complex (MAC) organisms are mycobacteria found in soil and water and are slow growing saprophytic mycobacteria. Other slow growing mycobacteria include *M. genavense, M. simiae, M. terrae, M. malmoense*. Generally, these infections come from soil/water contamination. MAC is found in large numbers in bird faeces. Immunosuppression may contribute to some infections.

Abyssinian, Somali and Siamese cats have been shown to be predisposed to disseminated MAC infection, possibly as young cats (< 5 years).

Clinical signs

Localised infections occur with regional lymphadenopathy. Subcutaneous swellings may be noted, especially around the head and face. Dissemination occurs to the lungs and other organs. In one paper 10 out of 12 cats had mesenteric lymphadenopathy.

Diagnosis

Diagnosis is as for tuberculous mycobacteria but the acid fast bacteria have a different appearance – they are smaller and often present in large numbers in infected cells. *MAC is zoonotic so care in sample handling should be taken**

Treatment

Treatment with combinations of doxycycline and clarithromycin have been effective, as have triple combinations. Surgery may be effective in conjunction but must be planned as for a neoplastic lesion. There is resistance shown by MAC infections to fluoroquinolones but more modern drugs may be effective (pradofloxacin). As these mycobacteria will grow in culture a sensitivity profile may be obtained.

4. Rapidly growing mycobacteria

These mycobacteria are ubiquitous in the environment and include *M. fortuitum, M. smegmatis and M. chelonae-abscessus*. These mycobacteria cause opportunistic infection in immunosuppressed and healthy cats. Localised wound infection is the most common as well as panniculitis. These bugs prefer areas rich in lipid so like the inguinal fat pads, especially after a fight or wound to the area. Wound breakdown often occurs prompting culture/histo.

Diagnosis is as for other mycobacteria and culture and sensitivity data should be sought. Combination antibacterial therapy is the best idea. IN the USA M. fortuitum is resistant to many drugs. Sensitivity in the UK is not well documented. Doxycycline and a fluoroquinolone may be the best combination to start with whilst awaiting sensitivity information. Surgical resection should be planned carefully to remove as much abnormal subcutaneous tissue as possible, with reconstruction required in many cases.

Prognosis is guarded.

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Gunn-Moore D, et al (2011) Mycobacterial disease in a population of 339 cats in Great Britain: II. Histopathology of 225 cases, and treatment and outcome of 184 cases. *JFMS* 13, 945-952

Useful contacts/addresses:

The VLA has merged with Animal Health to become the Animal Health and Veterinary Laboratories Agency. They are difficult to pin down regards submission forms etc and suggest they are contacted about every case individually.

https://www.gov.uk/government/organisations/animal-health-and-veterinary-laboratories-agency

AHVLA Corporate Office
Woodham Lane, New Haw
Addlestone
Surrey
KT15 3NB
T: 01932 341111
F: 01932 347046
E: corporate.centre@ahvla.gsi.gov.uk

National Mycobacterium Reference Laboratory (**NMRL**)
HPA National Mycobacterium Reference Laboratory
Abernethy Building
Institute of Cell and Molecular Science (ICMS)
2 Newark Street Tel: 020 7377 5895
London E1 2AT Fax: 020 7539 3459

Email nmrl@phe.gov.uk Telephone 020 7377 5895 Fax 020 7539 3459
Forms can be downloaded from the website using the link below:

https://www.gov.uk/government/collections/national-mycobacterium-reference-laboratory-nmrl

Where it is impossible to collect a sample for culture, it may be possible to confirm the presence of mycobacteria and whether or not the organism is a member of the tuberculosis complex by **PCR test** performed on formalin-fixed tissue (although a fresh unfixed tissue sample is always referred). Email the NMRL for more information. A PCR and culture is around £210 at the time of writing (2016).

Haemotrophic mycoplasmas – haemobartonella has a new look

Haemotrophic mycoplasmas are gram negative bacteria that have no cell wall and attach to the surface of red blood cells. The previously termed haemobartonella has been re-classified as a mycoplasma. Also recently discovered haemotrophic mycoplasma have been found and designated 'Candidatus'. This means in cats the species we need to think about are:

- Mycoplasma haemofelis
- Candidatus Mycoplasma haemominutum (Mhm)
- Candidatus Mycoplasma turicensis (Mt)

Species	**Mycoplasma haemofelis**	**Candidatus Mycoplasma haemominutum**	**Candidatus Mycoplasma turicensis**
Appearance and prevalence	Easier to see in blood smears UK study – 2% sick and 2% healthy cats infected	Rare to see in blood smears but the most common haemoplasma UK study – 20% sick cats, 8% healthy cats	Not seen on smears, identified on PCR UK study – 2.3% prevalence (sick and healthy)
Clinical disease?	Yes – anaemia and resultant clinical signs as well as fever, lymphadenopathy, icterus and hepatosplenomegaly	Not usually – cofactors may result in anaemia (immunosuppression)	Perhaps- cofactors may result in anaemia (immunosuppression) – has caused anaemia in experimental cats and acute infection may cause moderate to severe anaemia (more research needed)

They are not all equal regards disease causing ability as is summarised below (table adapted from Green's infectious diseases of the dog and cat 2012)

Note that mixed infections are also reported.

Transmission of infection

Flea transmission has been long considered the primary mode of infection BUT this has only been shown experimentally in a few cats. Iatrogenic infection is reported, along with maternal to kitten infection (not clear if transplacental, at nursing or at parturition). Outdoor cats have an increased risk of infection – adding evidence to the flea theory but also that fighting may be a method of transmission. Risk factors include: outdoor cats, FIV/FeLV positivity, lack of vaccinations, a cat bite abscess, and male sex.

The risk from blood transfusions

It has been shown that M.haemofelis and Mhm can survive in blood transfusions anti-coagulated with Citrate phosphate dextrose solution so blood transfusion is a risk for transmission of Haemotrophic mycoplasmas – should donors been screened?

Pathogenesis

Attachment of the organism causes erythrocyte membrane damage, reducing cell survival time. The damaged membranes can also then release previous hidden antigens and expose them to the immune system resulting in antibody production and a resultant immune-mediated haemolysis (type II and type III immune reaction). Macrophages in the spleen remove damaged and infected cells as well as those with antibodies attached. Even with appropriate treatment infection (PCR positivity) often remains, although bacteraemia is reduced. A carrier status can result, particularly with Mhm.

With M.haemofelis the parasitaemia associated with infection may wax and wane with corresponding peaks and troughs in PCV

Cats infected with M. haemofelis and Mt are more likely to be anaemic than those infected with Mhm and many consider Mhm non-pathogenic (this may be true in healthy cats but not cats with FeLV for example). Co infection with FeLV is associated with a more severe infection with H. haemofelis but infection with FIV does not seem to have the same effect although cats with FIV are more likely to be infected.

Combined infection with M. haemofelis and Mhm may result in a more severe anaemia.

Clinical signs

Clinical signs are those of an anaemic cat (pallor, lethargy, tachycardia, inappetance, weight loss, dehydration). Lymphadenopathy, pyrexia and hepatosplenomegaly may be noted on examination. Cats infected may also be asymptomatic. This is particularly true of Mhm which causes mild or absent clinical signs. Early evidence suggests that acute Mt infection can be pathogenic causing moderate to severe haemolytic anaemia.

Diagnosis

A CBC with smear examination and reticulocyte count is vital to confirm the nature of the anaemia (in the case of clinical haemoplasmosis it will be a regenerative anaemia). A Coombs' test will be positive in some cases (but a UK study actually found no association between Coomb's positivity and haemoplasma infection –so different from previous studies) and retroviral testing should be performed. Differentials for regenerative anaemia should be excluded (mainly haemorrhage).

Blood smear examination is not accurate for the detection of Haemoplasma infection. The parasitaemia is variable (false negatives), other cell surface abnormalities may give a false positive (stain debris, drying artefact, Howell-Jolly bodies, ribosome containing reticulocytes).

PCR is the test of choice due to its increased sensitivity. However, it may be negative if the cat is already on antibiotics and positivity does not confirm that the haemoplasma is the cause of the anaemia.

Treatment

Doxycycline 10mg/kg SID is effective. A course of 21 days is appropriate initially but a longer course may be needed to eradicate the infection. **side effects of doxycycline should be considered**. Enrofloxacin is also effective but rarely eliminates the infection, same for marbofloxacin. Pradofloxacin may offer a more effective long-term clearance of mycoplasma organisms. Concurrent prednisolone (starting at immunosuppressive doses is often suggested but in the authors experience with treatment for the mycoplasma lower doses – 1mg/kg can be used) may be needed to counter the immune mediated component of the condition and a transfusion may be needed in severe cases.

What's new in FeLV and FIV?

Feline immunodeficiency virus

Feline immunodeficiency virus (FIV) was once a death sentence for cats. However, publications including large numbers of cats have shown that cats with FIV live as long as cats without FIV and 80% are alive after 6 years. This means many cats with FIV have a normal life expectancy. Recent evidence shows that the end of the latent period and development of immunosuppression is due to the emergency of viruses with an altered receptor usage phenotype, this means that viral phenotyping may help 'stage' cats with FIV.

The prevalence of FIV depends on the population you test. Sick cats will have a higher prevalence, as will free roaming and feral cats. Across the world estimates of 1-14% and up to 44% in sick cats are reported.

As we now know infected cats can live without clinical signs for long periods – should we euthanase positive cats? Probably not – we should maximise their healthcare and keep seeing them in the clinic.

Vaccination of FIV positive cats is controversial – in early stages of infection they can mount a normal response that is protective – later in the disease they may not. Plus, immune-stimulation may cause

progression of FIV by promotion of virus production in lymphocytes. Benefits vs risks for the individual should be discussed.

Also see http://www.abcdcatsvets.org/feline-immunodeficiency/

Feline leukaemia virus

Feline leukaemia virus infections occur worldwide and consequences of infection include immune suppression, anaemia and lymphoma with the prognosis poor, quite different from the prognosis for cats with FIV. Young cats are more susceptible than older cats and transmission occurs through close contact such as mutual grooming.

The prevalence of FeLV has decreased dramatically over the last 20 years, and in some countries the prevalence in healthy cats is less than 1% due to vaccination and testing. As the prevalence of a disease falls remember that means more likely false positive tests – so positives should be confirmed before decisions are made. Positives in sick cats are more likely to be accurate.

Outcome of FeLV infection:

- 30-40% persistent viraemia
- 30-40% transient viraemia
- 20-30% seroconvert without becoming viraemic
- Minority (5%) show antigenaemia in the absence of viraemia – these cats may have a local focus of infections outside the bone marrow producing the p27 antigen, hence the antigen positive, PCR negative status of these cats

Cats overcoming infections may become latently infected, meaning proviral DNA remains present. For example, cells in the bone marrow. Re-activation is possible with immunosuppression. However, this is probably a rare event. These cats will test pro-virus positive, but p27 negative

Proviral DNA has been found in tumours (lymphoma) suggesting that the virus even in cats who have overcome the infection may be implicated in causing lymphoma. It is likely no cat ever totally overcomes the infection.

All positive tests in healthy cats should be confirmed. Ideally an FeLV PCR is performed AND if healthy the cats should be re tested in 6-8 weeks to see if they have overcome the infection. Note that this may take months. Cats clearing the infection will remain PCR positive, but proviral load will be much lower.

Positive results in sick cats with consistent clinical signs are more likely to be accurate but p27 tests should still be confirmed with PCR.

Vaccination does not prevent infection in all cases – but does protect against disease, long term monitoring of vaccinated cats after experimental challenge shows they still have proviral DNA in their blood but this should not be clinically significant.

Recent publications have shown that FeLV vaccination may last for 2 years or more. The ABCD recommends that cats over 3 years have a booster every 2-3 years.

Also see http://www.abcdcatsvets.org/feline-leukaemia-def/

Antiviral treatment

Antiviral treatment has been used in the management of FeLV and FIV with generally poor results. The side effects of most drugs has been unacceptable, limiting the use of human drugs in this species.

If cats with FIV or FeLV have no clinical signs no anti-viral should be given.

For cats FIV positive with stomatitis or recurring infections the antiviral AZT may be used (they may develop anaemia so check PCV) with improvements in clinical signs and viral load reported.

Another drug AMD3100 has also shown benefits in FIV positive cats regards viral load and clinical signs, more study is needed. Interferons (feline) did not show benefits in survival in one recent study.

In cats with FeLV interferon (feline) produced an improvement in clinical parameters and survival time, but this needs to be repeated in other studies, interferons may inhibit secondary infections rather than affect viral load. AZT in cats with FeLV has shown promise with improvements in clinical parameters, reduced viral load and improved survival. It may result in anaemia so should be used with care and PCV monitored as with cats with FIV.

The HIV integrase inhibitor raltegravir inhibits FeLV in vitro and vivo but not by enough to help the cat overcome the infection.

So in conclusion we do need to continue to worry about FeLV and FIV – but think carefully about interpreting results of blood tests and consider the altered prognosis for cats with FIV that are asymptomatic.

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Gunn-Moore D, et al (2011) Mycobacterial disease in a population of 339 cats in Great Britain: II. Histopathology of 225 cases, and treatment and outcome of 184 cases. *JFMS* 13, 945-952