Feline mycobacterial infections – part one: causes and clinical signs

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Categories: Vets

Date: March 10, 2014

DANIÈLLE GUNN-MOORE in the first part of an article, covers the epidemiology, pathogenesis, predisposition and clinical signs of feline tuberculosis, leprosy and NTM mycobacteriosis

Mycobacterial infections are a global health concern, both in humans and other animals. One third of all humans are infected with Mycobacterium tuberculosis (although only five per cent to 10 per cent develop disease). Several species cause disease in veterinary species, being either primary pathogens or becoming pathogenic under certain circumstances.

This is the first of two articles on feline mycobacterial infections. The second article will consider diagnosis and management.

Mycobacteria of feline importance

• Obligate pathogens, for example, the tuberculosis complex.

• Mycobacteria that are difficult to grow so their environmental niche cannot be determined, such as feline leprosy syndrome (FLS).

• Facultatively pathogenic saprophytes that can be divided into fast-growing and slow-growing opportunistic non-tuberculous mycobacteria (NTM).
As molecular techniques develop, the number of mycobacterial species identified in the latter two groups will increase, and the classification of these diseases may need to be altered.

All three syndromes (tuberculosis, FLS and NTM mycobacteriosis) are seen in the UK, with the majority of cases being cutaneous (Gunn-Moore et al, 2011). All three can present with nodules, draining tracts and/or ulceration. Disease can sometimes generalise secondary to skin inoculation, but only occasional cases present with primary systemic disease. Where systemic disease occurs, tuberculosis or *M. avium* infection is most likely, although other NTM may occasionally be responsible.

Most cases of feline mycobacteriosis result from percutaneous injury and/or soil contamination, and this tends to be reflected in the distribution of lesions (Greene and Gunn-Moore, 2012).

Little data is available on the prevalence of feline mycobacteriosis around the world. However, our recent studies revealed that in Great Britain these infections are far from rare, being reported in approximately one per cent of feline tissue samples submitted to diagnostic laboratories for routine histopathology (with approximately 0.3 per cent being Ziehl-Neelsen [ZN]-positive [Gunn-Moore et al, 2013]).

In addition, over a four-year period to December 2008, 339 ZN-positive feline samples were received by the AHVLA for culture; *M. microti* was identified in 19 per cent, *M. bovis* in 15 per cent, *M. avium* in seven per cent, *M. malmoense* in one per cent, unclassified mycobacterium in four per cent, and the samples failed to culture in 53 per cent (Table 1; Gunn-Moore et al, 2011). A positive culture was only gained in 47 per cent of samples, in part because the culture system used was optimised for *M. bovis*. That said, many NTM are very difficult to grow, even in optimised systems.

**Tuberculosis**

**Epidemiology and pathogenesis**

Tuberculosis is caused by a number of different, but closely related, bacteria. Relevant members of the tuberculosis complex include *M. tuberculosis*, *M. bovis* and *M. microti* (the vole bacillus).

*M. tuberculosis* causes more than 90 per cent of tuberculosis in man, but rarely infects other mammals, except for dogs. *M. bovis* is the main cause of tuberculosis in cattle, but it can also infect other mammals, including humans (where it causes only approximately one per cent of cases of tuberculosis), badgers, deer, dogs, cats, llamas and pigs, among others. *M. microti* causes tuberculosis in voles and cats (in the latter it was previously termed *M. microti*-like).

In cats, tuberculosis was historically quite common, caused by drinking tuberculous cow’s milk. With less cattle tuberculosis, and pasteurisation of milk, there has been a marked decline in this form of disease.
Currently, feline tuberculosis is recognised infrequently, but when it is diagnosed it is usually caused by either *M. microti* or *M. bovis*. Of a recent 115 cases, 55 per cent were caused by *M. microti* and 45 per cent by *M. bovis*, with these two infections accounting for 34 per cent of all cases of feline mycobacteriosis in Britain (Gunn-Moore et al, 2011). Infection with *M. tuberculosis* is very rare, probably because cats are naturally resistant to it.

The current epidemiology of feline tuberculosis is unclear.

Few cases are believed to result from drinking infected cow’s milk because intestinal disease is quite rare.

If we look at possible risk factors, we find most of the cats are keen hunters, regularly catching small rodents (Gunn-Moore et al, 1996). In the UK wild mice and voles can be infected with *M. microti* (Cavanagh et al, 2002; Burthe et al, 2008), and mice and voles, plus a wide range of other animals – for example, rats, stoats, foxes, deer and feral mink and ferrets – can be infected with *M. bovis* (Delahay et al, 2002 and 2007). It is most likely that cats become infected by hunting wild rodents. This accounts for the disease being mainly cutaneous, with lesions frequently affecting the face and legs (the areas most likely to be bitten when playing with prey), plus or minus associated lymphadenopathy (most typically affecting the submandibular lymph nodes). It is usually the chronic cases that have spread to the lungs (Gunn-Moore et al, 2011).

In some areas of Britain *M. bovis* is endemic in badgers (Gallagher and Clifton-Hadley, 2000). While cats and badgers rarely interact directly, there may be potential for cats to become infected via environmental contamination.

*M. bovis* can also be endemically present in many other species of free-ranging wildlife, so the risk of feline infection may vary in each country dependent on the likely interaction between these species and domestic cats.

A number of households have been identified where more than one cat is infected.

In most cases, the cats have little close contact and the infections appear to be unconnected; they result from hunting the same group of infected prey.

However, a small number of cases have occurred in cats that do not go outside, but are living with another cat (or in one case a dog) known to be infected and/or that does go outside to hunt. These cases appear to represent spread via close contact, particularly sleeping with and grooming an infected feline (or canine) companion (Isaac et al, 1983; Posthaus et al, 2011; Murray et al, in press and unpublished data).

In addition, there have now been a small number of nosocomial cases, where cats naturally infected with *M. bovis* have infected other cats via contamination within a veterinary practice during
routine neutering (Murray et al, in press and unpublished data).

All members of the tuberculosis complex pose potential zoonotic risks. However, to date, there is only one reported case where cats may have infected a human; however, the human involved was working with a colony of five cats and two possums with clinical *M. bovis*, when he became Mantoux test-positive, but never clinically ill (Isaac et al, 1983). By far the greatest risk to humans is spending time with infected humans or, much less frequently, handling infected cattle. *M. tuberculosis* and *M. bovis* can both cause reverse zoonoses and there have been a small number of unpublished cases where humans have infected their cats with *M. bovis*.

**Predisposition**

Disease is seen most commonly in adult male cats that have access outdoors. The median age for *M. bovis* is three years, for *M. microti* it is eight years. No evidence of classical immunosuppression has been found as cats tested for FIV and FeLV have usually been negative. However, we have shown these cats have low serum vitamin D concentrations, which may play a role in the effectiveness of their macrophages in fighting these infections (Lalor et al, 2012).

Infection typically occurs after protracted exposure, such as repeated exposure to infected small mammals, living on a farm housing tuberculous cattle, or living for prolonged periods with infected humans or poultry. However, when exposed to high doses of *M. bovis*, infection can be swift, with clinical disease being seen in less than a month (Francis, 1958; Isaac et al, 1983; Murray et al, in press and unpublished data).

In Great Britain, feline tuberculosis has a geographical distribution. *M. bovis*-infected cats are found in the southwest of England (coincident with the areas where cattle, badgers, mice and other small rodents are infected with *M. bovis*), while *M. microti* is found in south-east England, the north of England and southern Scotland (where *M. microti*-infected rodents have been detected; Figure 1).

**Clinical signs**

Depending on the route of infection, affected cats may present with clinical signs related to the alimentary and/or respiratory tracts, or with localised disease affecting the skin.

Currently, the most common presentation is the cutaneous form, with respiratory and particularly alimentary forms being seen less frequently.

Cutaneous disease probably arises from infected bite wounds, local spread, haematogenous dissemination to the skin or, occasionally, contaminated surgical wounds. The lesions often involve the face, extremities, tail base or perineum (“fight and bite” sites). Less frequently they involve the ventral thorax. They generally take the form of firm, raised, dermal nodules, ulceration, or non-healing wounds with draining sinus tracts. Extension of granulomatous tissue may involve the
subcutaneous structures, muscle and/or bone.

Skin lesions are commonly associated with either local or generalised lymphadenopathy. On occasion, submandibular or prescapular lymphadenopathy may be the only clinical finding.

In rare cases where the infection is acquired through inhalation, tubercles arise in the lungs and/or hilar lymph nodes and affected cats present with weight loss, anorexia, dyspnoea and coughing. However, pulmonary infection occurs more frequently secondary to haematogenous spread from cutaneous lesions so the infection is typically diffuse and interstitial (eventually spreading to bronchial) and the cats are dyspnoeic, sometimes with a soft cough.

In the alimentary form, tubercles arise in the intestines and/or mesenteric lymph nodes. Affected cats develop intestinal malabsorption and present with weight loss, anaemia, vomiting and diarrhoea. Occasionally, tubercles arise in the tonsils, resulting in signs of oropharangeal disease.

A range of clinical signs may be seen with disseminated disease. These include splenomegaly, hepatomegaly, pleural or pericardial effusions, generalised lymphadenopathy, weight loss and fever. Lameness may result from bone involvement. Granulomatous uveitis and signs referable to CNS involvement have been seen in some cases.

**Feline leprosy syndrome (FLS)**

**Epidemiology and pathogenesis**

Historically, feline leprosy was believed to be caused by *M lepraemurium*, which typically causes leprosy in rats. In cats, infection with *M lepraemurium* was largely assumed as bacteria could not be cultured using standard techniques.

However, FLS is actually caused by a number of different infections – molecular techniques have implicated *M lepraemurium*, *M visibile*, *Mycobacterium* species strain Tarwin, and some as yet unidentified mycobacterial species (Davies et al, 2006; Malik et al, 2013).

Initially, in Australia, FLS was described as taking two forms; with disease in younger cats (less than four years old) being caused by *M lepraemurium* – and having tuberculous pathology with few acid fast bacteria (AFB) – while in older cats it appeared to be caused by a novel, but as yet undefined, mycobacterial species (and had lepromatous changes and large numbers of AFB; Malik et al, 2002). However, both types of disease have now been seen in all ages of cat, and it is probably more the cat’s immune response that determines the nature of the pathology, than the species of mycobacteria involved per se (Davies et al, 2006).

Infection is believed to follow rodent bites. However, this is not proven and it is also possible infection is via soil contamination of cutaneous wounds. As yet, there is no known zoonotic
potential for these infections.

**Predisposition**

There is no breed predisposition, but adult male cats with access outdoors are more often affected. This is probably because of their tendency to hunt and fight. In Australia, it has been reported older cats may be immunosuppressed with FIV or chronic kidney disease (Malik et al, 2013). Prevalence is higher in temperate maritime climates, including Australia, New Zealand, Europe (UK, the Channel Islands, the Netherlands, France and Greece), western Canada and the US (especially California and Oregon).

**Clinical signs**

FLS is primarily a cutaneous disease presenting as single or multiple nodules, which may be haired, alopecic or ulcerated, and may be seen on the head, limbs and occasionally the trunk. They are non-painful and freely mobile. Rare cases affect the tongue, lips, nose or conjunctivae. Regional lymphadenopathy may be present.

While systemic disease is rare, some cases can have a progressive and aggressive course. In Australia, younger cats initially develop localised nodular, often ulcerated, lesions on the limbs, which progress rapidly, while older cats develop more generalised skin involvement with no ulceration and a slower clinical progression (Malik et al, 2002). However, with FLS overall, the severity of disease depends on the causal species, the size of the infective inoculum (s) and the immune response of the host (Malik et al, 2013).

**Disease caused by NTM**

**Epidemiology and pathogenesis**

This syndrome is caused by saprophytic, usually non-pathogenic, organisms, which are found in soil, water and decaying vegetation. Fast-growing NTM are most commonly implicated in causing disease. However, as our ability to recognise the implications of “bite site” lesions improves, along with our access to specialist laboratories, slow growing variants are being recognised more frequently. Since these bacteria are being detected by molecular techniques rather than culture they should perhaps be considered under FLS.

Many NTM have been implicated in causing this syndrome. *M avium* is most commonly cultured; being cultured from seven per cent of 339 cases of feline mycobacterial disease in Great Britain (Table 1; Gunn-Moore et al, 2011a). *M avium* is a member of the *M avium-intracellulare* complex (MAC), and it typically causes disease in birds. However, it can also infect humans (particularly when immunosuppressed), dogs and cats.
Other NTM found to cause disease in cats include *M chelonae-abscessus*, the *M fortuitum-peregrinum* group, *M smegmatis, M malmoense, M phlei, M genovense, M simiae, M thermoresistible, M flavescens, M xenopi, M alvei, M massiliense, M goodi, M mucogenicum, M septicum, M szulgai* and *M terrae* complex. These organisms typically cause disease through contamination of cutaneous wounds and are often more pathogenic if inoculated into adipose tissue. Entry through the gastrointestinal or respiratory tracts is rare.

**Predisposition**

In general, cats appear to be at greater risk of NTM infection than most other domestic species. Adult cats that hunt or fight are most likely to be affected. Certain breeds appear to be predisposed to MAC infection, including Siamese, Abyssinian and Somali breeds. Disease appears to be more common in tropical and subtropical areas of the world, although difficulties with diagnosis may influence its true prevalence.

Different species are seen more frequently in different countries: in Australia *M smegmatis* and *M fortuitum* are most common, while in the US *M fortuitum* and *M chelonae abscessus* predominate. Unlike the situation in humans, immunosuppression has only been found in a small number of infected cats.

**Clinical signs**

*M avium* is more pathogenic than other NTM. It has been associated with cutaneous lesions (which can look just like cutaneous tuberculosis or FLS), peripheral vestibular disease, generalised lymph node and pulmonary involvement, gastrointestinal disease, intracranial infection, and disseminated tuberculous disease (Baral et al, 2006).

NTM can produce a number of different clinical presentations. These include single or multiple cutaneous or subcutaneous nodules, granulomatous panniculitis, or disseminated disease, and some organisms (for example, *M fortuitum*) can cause all three presentations.

Single or multiple cutaneous or subcutaneous nodules, with or without ulceration, that look like FLS can be caused by fast-growing *M fortuitum, M chelonae, M smegmatis, M avium* and *M phlei*, and slow-growing *M xenopi, M ulcerans, M simiae* and *M visibilis*.

The definition of FLS was previously reserved for similar cutaneous infections, but where the bacteria could not be grown. The term is now starting to be used for this presentation in general, regardless of whether a causal organism can be cultured or only identified using molecular tests: this presentation can therefore be considered as part of the FLS.

Granulomatous panniculitis is seen where multiple punctate draining tracts occur associated with subcutaneous nodules and coalescence produces large areas of ulcerated, non-healing tissue.
Inguinal fat pads, flanks and tail base are affected most frequently; affected areas can be painful. Although systemic spread is rare, affected cats may show fever, anorexia and a reluctance to move. Organisms involved include fast-growing *M fortuitum, M smegmatis, M chelonae, M phlei, M alvei* and *M thermoresistible* and, occasionally, slow-growing *M xenopi* and *M ulcerans*.

Rarer disseminated disease has been seen with cases of primary pulmonary infection caused by *M avium, M fortuitum* or *M thermoresistible*; tracheal granuloma with an organism similar to *M xenopi*; cutaneous, ocular, lymph node and pulmonary involvement with *M visibilis* and *M simiae*; and lymphadenitis and peritonitis with *M xenopi*.

Références


Figure 1. Map of Great Britain showing the location of 326 feline samples from between January 2005 and December 2008, for which the AHVLA tried to culture mycobacteria. Successfully cultured samples were divided into the species isolated or grouped as unclassified mycobacteria. Also indicated is whether the position on the map is from a complete postcode (•) or the mean easting and northing of the postcode district (•). The coloured shaded areas correspond to predominance by one species and the coloured circles the spatial clusters identified by the SaTScan analysis. (Gunn-Moore et al, 2011).
*M. bovis* in an adult MN cat, few AFB.

IMAGE: Sally Mitchell.
*M. chelonae/abscessus* MN cat.

IMAGE: Stefano Bo.
Left: *M microti* in an adult FN cat, few AFB.

IMAGE: Philip Hanlon.
Below left: *M microti* in a young adult MN cat, few AFB.
IMAGE: Philip Hanlon.
Below: *M microti* in an adult MN cat, few AFB.

IMAGE: Daren Foster.
Ziehl Neelsen (ZN)-positive acid-fast bacteria (AFB), but failed to grow on culture; adult MN cat.

IMAGE: Joanna Aplin.
Many AFB, but failed to grow on culture; older MN cat.

IMAGE: Richard Malik.
Few AFB, but failed to grow on culture; adult FN cat.
Above: Many AFB, but failed to grow on culture; adult FN cat covered with many small lesions.
Below: Many AFB, but failed to grow on culture; adult FN cat covered with many small lesions, including a granuloma of the nictitating membrane.

IMAGE: Natasha Mitchell
### Table 1. Mycobacterial culture results

<table>
<thead>
<tr>
<th>Culture results</th>
<th>Number</th>
<th>Percentage (%) of total</th>
<th>Percentage (%) of cultured</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tuberculous mycobacteria: tuberculosis complex group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M. microti</td>
<td>63</td>
<td>39</td>
<td>40</td>
</tr>
<tr>
<td>M. bovis</td>
<td>52</td>
<td>15</td>
<td>33</td>
</tr>
<tr>
<td><strong>Non-tuberculous mycobacteria [NTM]</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M. avium</td>
<td>24</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>M. malmoense</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>M. fortuitum</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>M. celatum</td>
<td>1</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>M. intracellulare</td>
<td>1</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Unclassified</td>
<td>10</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td><strong>Cultured total</strong></td>
<td>159</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>No growth</td>
<td>180</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td><strong>Grand total</strong></td>
<td>339</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

The samples had histopathological changes indicative of mycobacterial infection and were submitted to the AHRLA for mycobacterial culture between January 2005 and December 2006 (Gunn-Moore et al., 2011).