

Mycobacterial infections in cats (*Felis catus*) as a potential threat to humans – a review 2014-2023

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Summary

Mycobacteria infections in cats include tuberculosis (caused by *Mycobacterium bovis* and *Mycobacterium microti*) and mycobacteriosis caused by non-tuberculous mycobacteria (NTM). The aim of the paper is to present the latest reports on mycobacterial infections in cats and place emphasis on their impact on the health of their owners. The reviewers looked for papers about mycobacterial infections in cats in PubMed and Google Scholar from any date from January 2014 to June 2023. The search used the following keywords: cat, feline, tuberculosis, and mycobacteria. Papers were evaluated for their value to science and their applicability. Papers published in recent years have shown that mycobacterial infections in cats should still be considered in a differential diagnosis when many clinical signs present and they are mainly skin and ocular symptoms. An epidemiological investigation of these infections is highly important because cases were reported also in low-risk regions. Mycobacterial infections pose a risk to humans. The degree of risk depends on many factors, such as the species of mycobacteria, the closeness of animal-owner contact, and the immune status of the owner. The greatest risk are still believed to be *M. bovis* infections; however, NTM infections should also raise a concern, especially in high-risk groups.

Keywords: cat, feline, *Mycobacterium*, tuberculosis, mycobacteriosis, public health

Mycobacteria infections in cats include tuberculosis (mainly caused by *Mycobacterium bovis* and *Mycobacterium microti*) and mycobacteriosis caused by non-tuberculous mycobacteria (NTM). Mycobacterial infections are the subject of research in both wild felids (12, 13, 25) and domestic ones (24). From a public health point of view, infections in domestic cats are the main concern. Both diagnosis and treatment of feline mycobacterial infections can be challenging (20).

In 339 UK cases of mycobacterial diseases in cats, 19% were caused by *M. microti*, 15% by *M. bovis*, 7% were caused by *Mycobacterium avium* complex (MAC) bacteria, 6% by other NTM, and in 53% the mycobacteria were not identified (15). Tuberculosis mycobacteria may pose a risk to animal owners because of their zoonotic potential (33, 34, 43). Recently, increasing attention has been paid to atypical mycobacteria in the context of the threat to immunocompromised people (17).

For these reasons, a presentation of the latest reports on mycobacterial infections in cats is justified. Such is the purpose of this review, which places particular emphasis on the impact of these infections on the health of the suffering cats' owners. As the last large review concerning feline mycobacterial infections is from 2014 (14), the aim of this paper was to update it with current research.

Review methods

The PubMed and Google Scholar sites were searched for studies on mycobacterial infections in cats. For continuity from the last review, the inclusion period started from January 2014. The most recent investigations in this review's scope were from June 2023. The following keywords were used for the search strategy: cat, feline, tuberculosis, and mycobacteria. To identify additional articles, references from the studies found on PubMed and Google Scholar were also analysed. There was no formal meta-analysis or statistical analysis.

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Tuberculosis

Tuberculosis in cats is mainly caused by *M. bovis* and *M. microti*, and rarely by *Mycobacterium tuberculosis*. *Mycobacterium bovis* infections are usually associated with consuming infected cow's milk products or raw meat (16), while *M. microti* infections are related to consuming small rodents (3). Before the wide-scale pasteurisation of milk, the most common form of tuberculosis in cats was alimentary tract disease (16), while now lymphadenopathy and cutaneous disease are the most common forms (40). Although cat tuberculosis prevalence has been falling because of the common pasteurisation of milk and the general lower prevalence of bovine tuberculosis (44), case series or case reports from several countries were still numerous enough for them to be reported and reviewed in 2014 by Pesciaroli et al. (33). Since then, TB cases have been confirmed in cats and the disease is still afflicting these animals (Fig. 1).

Reports from the last 10 years have shown that it is possible to find *M. bovis* infection in unlikely regions. Cases of *M. bovis* were confirmed in two house cats in the same home in Houston (Texas, USA), where bovine tuberculosis is not endemic (39), and they transpired to be associated with an *M. bovis*-infected owner. An interview with the owner revealed that the family had been consuming dairy products made with unpasteurised milk. This case draws attention to the need for conducting an in-depth interview and observation or diagnosis of the pets of people with confirmed tuberculosis. The diagnostic innovation resulting from the Houston study was successfully using serological tests to assist treatment monitoring (39). Another recent case of *M. bovis* in two cats was reported in Buenos Aires, Argentina, where bovine tuberculosis is endemic (1). The authors suggested that the source of infection might have been raw bovine viscera fed to the cats. In one case the spoligotype isolated was SB0140, which is the most frequent pattern in Argentina and is also sometimes confirmed in humans, but the second noted spoligotype – SB1058 – is less frequent (1). The causation of diseases which are consequences of feeding cats raw bovine meat products is an emerging problem. In two UK households *M. bovis* was confirmed in young pedigree cats. As those cats had been fed commercial raw food, the authors of the investigation urged veterinarians to be aware of the likelihood of tuberculosis in young cats which may have been given a raw food diet, even if there is no history of outdoor access (29, 31). This is a concern which may not be ignored, and raw food for pets should be better investigated. Some authors suggested avoiding the feeding of raw offal to any companion animal (31). Subsequent studies by



Fig. 1. Map showing reviewed cases of tuberculosis in cats: 2014 to 2023 (designed by Layerace/Freepik)

these authors showed more cases in cats likely to be associated with them having been fed a commercial raw food diet. The five cases in those studies with positive cultures were spread throughout England and Scotland in regions with minimal risk of endemic bovine tuberculosis. Epidemiological investigation revealed that the commercial raw diet of the affected cats was the likely route of infection (31, 33). Another study suggesting an oral route of infection because of the involvement of submandibular lymph nodes was on a case of systemic tuberculosis (granulomatous inflammation in the lungs, liver, lymph nodes and kidneys) in a cat in Turkey (7).

In Italy, an outbreak was described of *M. bovis* infection in a cattery of Abyssinians after the importation of kittens from Russia. Five cats developed tuberculous interstitial pneumonia (5). A less typical course of tuberculosis in cats is also sometimes noted. Recently, a series of tuberculosis joint infections in cats were described for the first time. The cats were 2-6 years old and immunocompetent. Two of the described cases were caused by *M. bovis*, and another two of them by *M. microti*. Osteolysis, periosteal response, and concomitant soft-tissue swelling were all detected in radiological examinations (19). This case study emphasised the significance of taking mycobacterial disease into account as a differential diagnosis for joint disease in cats.

The zoonotic potential of *M. bovis* raises the importance of testing owners, breeders and veterinarians to critical if they have been in contact with cats suspected of being infected with this pathogen. This is borne out by two recently described cases of confirmed cat-to-human *M. bovis* transmission in the United Kingdom (28). According to World Health Organisation the most common symptoms in humans include prolonged cough, chest pain, weakness, fatigue, weight loss, fever, night sweats. Even though it is a curable and preventable disease, multidrug-resistant strains remains a public health threat.

Research from Switzerland pointed out that *M. microti* is not just a coincidental pathogen in felines by

describing eleven independent cases of infection in domestic cats. In this study, the authors also showed that an adapted feline interferon-gamma release assay (IGRA) is a promising tool for the diagnosis of tuberculosis in cats (37).

Atypical mycobacteria

Non-tuberculous mycobacteria are a group of pathogenic opportunistic saprophytes from soil, water and vegetation (8). They can cause disease in many species, including cats and humans, especially those with immunodeficiencies (26, 38). Most cases of disease caused by atypical mycobacteria in cats have nodules in the skin and tracts, lymphadenopathies, and ulceration as the clinical signs or lesions, fewer cases exhibiting systemic dissemination (20, 47). Recently, a new strain of a *Mycobacterium* sp., MFM001, was confirmed in an immunocompromised cat with disseminated mycobacteriosis, and the isolate was not associated with MAC (18).

Disseminated mycobacteriosis is not always associated with immunodeficiencies in cats, which is proved by three cases described by Pekkarinen et al. (35). All affected cats were immunocompetent. Disseminated mycobacteriosis caused by *Mycobacterium malmoeense*, *Mycobacterium branderi/shimoidei* and *M. avium* was confirmed. The authors suggested that cats can be considered potential environmental mycobacteria reservoirs because of the possible presence of mycobacteria in secretions (35). Another systemic disease in two related cats was caused by *Mycobacterium kansasii*, which are potentially zoonotic mycobacteria. In these cases, both cats made a full recovery after antimicrobial therapy with rifampicin, azithromycin and pradofloxacin (4). Disseminated mycobacteriosis has also been described in cats in California. While it had aetiology in a few cases in rapid-growing mycobacterial (RGM) infections, in California, such being with the most prevalent RGM species of *M. smegmatis* and *M. fortuitum*, the non-RGM *M. avium* was the more common aetiological agent of the disseminated form of mycobacteriosis. The most prevalent species of RGM in this region were *M. smegmatis* and *M. fortuitum* (26).

Recently several cases of mycobacterial infections with atypical courses in cats have been described. One of them was meningoencephalitis in a 33-month-old, neutered female Abyssinian cat caused by *Mycobacterium avium* subsp. *hominissuis*. In the description of this case, it was suggested that *M. avium* subsp. *hominissuis* infections and the zoonotic aspect of the pathogen should be considered in cats with neurological signs (21). Another mycobacterium with zoonotic potential – *Mycobacterium kansasii* – was isolated from a diseased indoor cat in Japan (9).

More typical cases of mycobacteriosis manifested by skin lesions in cats were caused by *Mycobacterium thermoresistibile* (26, 46), *Mycobacterium porcinum* (6), and *Mycobacterium goodii* (49). However, many

cases of skin infection probably remain undiagnosed in cats, so it is difficult to determine the real prevalence and importance of mycobacteriosis in cats. There are many undiagnosed skin diseases as recently described three cases of idiopathic sterile pyogranuloma in domestic cats (11). Another fairly common site for mycobacterium infection in cats are the eyes, and the primary site of lesion development is usually the choroid (23, 42). Mycobacterial ocular infections are considered to be underestimated causes of morbidity in domestic cats (23).

New reports have also been noted in the context of feline leprosy syndrome (FLS) (45). An unusual presentation of FLS caused by *Mycobacterium lepraemurium* was confirmed in the Alpine region (10). The clinical symptoms included ulcerative and non-ulcerative nodules in the periocular area, sclera, at the base of the ears, and on the tongue, and a progressive ulcerative skin nodule on the tail was also observed (10). The clinical and molecular characterisation of over 30 cases was presented by O'Brien et al. (41). In this study three leporid disease agents were presented: “*Candidatus* *Mycobacterium tarwinense*”, *Mycobacterium lepraemurium*, and “*Candidatus* *Mycobacterium lepraefelis*”.

Diagnosis remains a challenge in learning the true prevalence of mycobacterial infections in cats. Culture is the gold standard; however, some mycobacteria, e.g. *M. microti*, grow very slowly (44). Cases of mycobacterial infection can appear very similar, whether their causative pathogens are the same or different. However, identification of the infecting *Mycobacterium* species is crucial, because mycobacteria have different responses to antibiotics and pose different zoonotic risks. Recently, the feline gamma-interferon release assay is being improved (24, 37), and will facilitate diagnosis of mycobacterial infections. Also, diagnostic imaging (22) and biomarker (cytokine and chemokine concentrations) measurement (32) seem to be promising additional diagnostic tools.

It is not recommended to continue treatment in cats with *M. tuberculosis* infection or disseminated *M. bovis* infection. In the case of potential feline mycobacteriosis, it is highly challenging and should be undertaken with great caution in tuberculosis-endemic areas (15). Owners should be informed about a potential zoonotic risk. To treat or not to treat the infection should be considered particularly if there are respiratory clinical signs, because of the possibility of transmission to humans. Another consequential aspect is that treatment might generate drug-resistant bacteria. Treatment is usually long-term and may be difficult to maintain by pet owners. Besides treatment duration, another possibly difficult aspect for owners of cats with *M. tuberculosis* or disseminated *M. bovis* infection who must administer treatment is the multiplicity of drugs likely to be used. Gunn-Moore (14) reviewed potential drugs for the treatment of feline mycobacterial diseases and

listed marbofloxacin, pradofloxacin, moxifloxacin, clarithromycin, azithromycin, dihydrostreptomycin, pyrazinamide, ethambutol, clofazimine, doxycycline, amikacin, and cefovecin (15). Multidrug regimens are recommended and new regimens are being tested, which include cefovecin and clofazimine (2, 48). This research should be continued for better care and protection of both animal and human health.

Summary

The real prevalence of mycobacterial infections in cats remains unknown. This review of recent research has shown that mycobacterial infections should be considered in a differential diagnosis in cats with therapy-resistant lymphadenopathy and skin nodules. Even in tuberculosis-free areas and in indoor cats, tuberculosis should not be excluded from a differential diagnosis. Repeat culture and testing should be performed when mycobacterial infection is persistent. An important issue regarding the spread of tuberculosis in cats, highlighted by the research in the United Kingdom, is the feeding of cats with raw mycobacteria-infected food (33). Noteworthy is the fact that cases of transmission of tuberculosis from cats to humans have been confirmed in recent years. Also human cases of NTM transmission by the same route have been reported (50); owners of cats who are immunocompromised are threatened by mycobacteriosis to a presently underestimated extent. Further epidemiological studies and sensitisation of clinicians to this problem are necessary. The degree of risk to human health depends on many factors, such as the species of mycobacteria, the closeness of contact between animal and owner, and the immune status of the owner. The greatest risk is still believed to be *Mycobacterium tuberculosis* complex infections; however, NTM infections should also raise a concern, especially in higher-risk groups. Special attention should be paid in the case of HIV-positive people, pregnant women, children under five years of age, or cancer patients.

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