Feline demodicosis - a literature review

There are three Demodex species known to be able to cause feline demodicosis, *Demodex cati*, *Demodex gatoi* and a third unnamed species, unofficially named *Demodex felis*. The disease can be localized or generalized and the clinical presentation differs depending on the Demodex species, as well as the localisation of lesions. Pruritus and alopecia are characteristic symptoms of feline demodicosis but it can be asymptomatic in some cases. Skin scrapings and microscopic evaluation is the primary diagnostic procedure but recently a fecal flotation method and PCR methods have shown to be successful. Regardless of the mite species, lime sulfur dips have, until now, been the treatment of choice for feline demodicosis. In a recent study a topical solution containing 10 % imidacloprid/1 % moxidectin was found to be effective in treating *D. gatoi i*nfestations and one case report suggest that demodicosis caused by *D. cati* can be treated successfully with oral fluralaner.

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Introduction

Feline demodicosis is considered to be a rare parasitic skin disease. Three species of Demodex mites have been described in cats. *Demodex cati*, *D. gatoi* and a third, as yet unnamed species (7, 14, 16). The unnamed species has been referred to as *D. felis* (9, 27). *D. cati* is thought to be part of the normal skin fauna of cats and demodicosis caused by this species is associated with systemic illness and immunosuppression (1, 9). Whether the other two species could be a part of the cat's normal skin fauna is unconfirmed (21, 25). *D. gatoi* mites are transmissible to other cats through casual contact and is regarded as highly contagious (1, 25). Concurrent infestations of *D. cati* and *D. gatoi* (4, 7, 16) as well as *D. cati* and the unnamed species have been reported (7, 16). The aim of this literature review is to describe the mites causing demodicosis in cats, its pathogenesis, the clinical presentation, diagnostic workup, treatment and prognosis.

Demodex mites described in the cat

Demodex mites on cats were first recognized in 1859 by Leydig. The species was named *D. cati* in 1919 by Hirst and a full description of the parasite was published 1979 by Desch and Nutting (5). *D. gatoi* was discovered in 1982 by Conroy and others, but it was not named and fully described until 1999 by Desch and Stewart. They also mentioned two mites, which resembled *D. gatoi* but differed in shape and size. It was suggested they represent a new third Demodex species (7). Since then there have been several reports about a Demodex mite morphologically different to *D. cati* and *D. gatoi* (14, 16, 21). It was confirmed, in 2015, that this is a genetically distinct species and not simply a morphological variant of the other two mite species. Several of the cats in the that study were also found to harbor non-feline Demodex species (*D. canis*, *D. folliculorum* and *D. brevis*) (9).


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Morphology

Demodex mites belong to the parasite class Arachnida. The adult mites of the Demodex genus share similar features; an elongated body composed of a gnathosoma, podosoma with four sets of stumpy legs and an opisthosoma (5, 24, 30).

The body length of *D. cati* is reported as 181.7 ± 17.9 µm for males and 219 ± 27.4 µm for females. *D. gatoi* has a shorter and broader appearance than *D. cati* and the body length measures 90,6 ± 4,8 µm in males and 108,3 ± 4,4 µm in females. The third, unnamed, species is described as longer than *D. gatoi* but shorter than *D. cati* (7, 9, 14, 16, 21, 25).

Life cycle

Little is known about the life cycle of feline Demodex species, but the following has been described. The eggs give rise to hexapod larvae which moults to produce a protonymph, also with three pair of legs. This is followed by a larger octopod nymph and finally the adult form (5, 30). The length of the life cycle is unknown (5).

Prevalence
Feline demodicosis has been reported in many countries around the world (5). *D. gatoi* seems to be one of the three mite species that most frequently causes demodicosis in cats (1). In the U.S.A., there are enzootic areas in the southern and south-eastern parts of the country (1, 14, 19, 25). Knowledge about the unnamed feline Demodex species is still very limited (27). Recently PCR techniques have indicated that the presence of Demodex mites can be far more frequent than previously suspected (9, 11, 27). In one study where 74 cats were tested for prevalence of DNA from Demodex species, 26% were positive for Demodex DNA. *D. cati* was detected in 4% of these cats, 15% were positive for *D. canis* and 6% were positive for *D. folliculorum* DNA. This also suggests that cats can harbor a variety of Demodex species in their skin (9).

Pathogenesis
D. cati is thought to be transferred from mother to offspring during nursing and is considered a harmless resident of cats in most cases (9, 25). The mite lives in the hair follicles and sebaceous glands. Demodicosis caused by this species is often associated with a compromised immunity. It has been reported in cats with diabetes mellitus, feline immunodeficiency virus (FIV) infection, feline leukemia virus (FeLV) infection, hyperadrenocorticism, systemic lupus erythematosus, chronic upper respiratory tract infection and toxoplasmosis (5, 16, 18, 24, 32). Demodicosis caused by *D. cati* has also been confirmed in cats with multicentric squamous cell carcinoma in situ. The infestation was confined to the site of the lesions and it is possible that the local cutaneous immunodeficiency plays a part in the multiplication of *D. cati* locally (13).

D. gatoi dwells superficially, in the stratum corneum (24). Because of its location on the skin *D. gatoi* can be removed by grooming (1). *D. gatoi* is unique compared to other Demodex species in the sense that it is a primary pathogenic skin parasite that tends to be contagious, causing severe pruritus in otherwise healthy cats of all ages (1, 25). Most cases of *D. gatoi* are not linked to immunosuppression, but the mite has been reported in a cat with feline immunodeficiency virus infection (24). Although many of the reported cases of *D. gatoi* infestations have a history of glucocorticoid administration, this seems to be a result of the pruritus and not a cause of the infestation (1). Hypersensitivity reaction to *D. gatoi* has been suspected in some cases. There is also a possibility that some cats can possess an unsuitable microenvironment for mites, or may be able to clear the infestation by excessive grooming or through their immune responses (1, 25).

Predisposition
The feline Demodex species have been found in both short and longhaired cats of both sexes. Feline demodicosis does not seem to have a certain age predisposition, it has been diagnosed in cats of a wide variety of ages (5, 9, 18).

A recent study suggests that purebred cats might be more susceptible to *D. gatoi* infestations than domestic shorthair cats. There is a suspicion that cornish rex cats might be predisposed to this type of demodicosis. In the study, five out of ten cats belonged to the breed cornish rex, and the special structure and character of the fur may be the cause (25). In another recent case report a cornish rex cat presented with pruritus and alopecia while the other cat in the same household, a thai, showed no clinical signs. However, *D. gatoi* was detected in both of these cats (28).

Clinical signs
The clinical presentation may differ with the causative mite. Since more than one Demodex species can affect the same individual, this may influence the clinical presentation (7, 16). The disease is characterized by a varying degree of pruritus and alopecia but some cats may be asymptomatic (5, 24). The affected areas may be alopecic with or without crusting, scaling and hyperpigmentation. Seborrhoea, papules, comedones, miliary dermatitis and ulceration have also been described (1, 15, 19).

Feline demodicosis may be localized or generalized (19). Generalized disease caused by *D. cati* can usually involve the head, neck, flank and distal portions of the limbs. The lesions can be multifocal, patchy, regional or symmetrical. Pruritus is variable (15, 19). The generalized form is rare and associated with systemic illnesses or immunosuppression, either endogenous or iatrogenic (2, 29).

Localized disease caused by *D. cati* tend to involve the head area. Lesions are most common around the eyes, on the head or on the neck (1, 5, 16, 19, 24). *D. cati* also has been associated with a ceruminous otitis externa (31). Localized demodicosis caused by *D. cati* has also been found in cats treated with inhalant glucocorticoids. The lesions where localized exclusively to the site covered by the inhaler mask (3).

Generalized demodicosis caused by *D. gatoi* differs from *D. cati* in the sense that *D. gatoi* can cause severe pruritic disease in otherwise healthy cats (25). Skin lesions caused by *D. gatoi* can affect any area.

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However, the ventral abdomen, inner thighs, flanks and forelimbs appear to be most commonly affected. The main clinical signs associated with *D. gatoi* infestation is pruritus and self-inflicted lesions and a cat can be severely pruritic even if only a small number of mites are present (1). Alopecia is common and can be accompanied by scaling and erythema (1, 24). A localized form of *D. gatoi* has been described in a cat with lesions only located on the head (33).

Clinical signs associated with the third Demodex species have been described with a varying degree of pruritus and alopecia associated with easily epilated hair and a varying degree of erythema (9, 21).

Diagnosis

It is recommended to do broad, superficial scrapings as well as concentrated, deep scrapings of the skin to maximize chances of recovering both *D. gatoi* and *D. cati* (21, 24). Clipping the fur before scraping the skin might be beneficial to prevent the scraped material from being lost in the surrounding fur (24). *D. cati* resides in the hair follicles and sebaceous glands so scrapings need to be deep enough to cause capillary bleeding (1, 30). *D. gatoi* mites are more superficially located than *D. cati* (24). Due to its location, the mite is often removed with grooming, so it is important to scrape even non-alopecic areas that the cat has trouble reaching (1, 25). The samples obtained by deep and superficial skin scrapings should be evaluated microscopically by using a x10 objective (1, 24). *D. gatoi* is smaller and more translucent than *D. cati* and therefore can be missed if the contrast of the microscope is not increased adequately (24).

Tape strips and trichograms may also be useful in the diagnosis. In areas where the skin is inflamed and ulcerated, biopsies have been shown to be successful in several cases caused either by *D. cati* or *D. gatoi* (1, 25).

A study in 2013 detected *D. gatoi* with a fecal flotation method and was shown to be more reliable than skin scrapings and cellophane taping in both of the cases presented. The mites will be taken up continuously with grooming and then passed through the gut (28). *D. gatoi* mites have also been detected in the feces six months after start of treatment and two months after skin material showed negative results (27).

In recent years, the presence of feline Demodex species using PCR techniques has been successful in several studies, both in showing the frequency of and identification of the different species of mites (2, 9, 11, 28). The assay detects DNA fragments of Demodex and allows the species to be determined by sequencing the amplified product (9). There are now commercial tissue kits available for detecting feline Demodex mites (2). The presence of mites does not necessarily implicate demodicosis, as *D. cati* belongs to the normal skin fauna.

In cases of suspected *D. gatoi* infestation, where the parasite cannot be detected, a diagnostic treatment trial is recommended with lime sulfur dips (1, 22). All cats that have been in contact with infected cats should be treated (1).

Differential Diagnosis

Differential diagnosis depends on the clinical signs presented, but the main ones include dermatophytosis, bacterial folliculitis, hypersensitivity reactions (e.g. food, atopy, flea bite) and other ectoparasites such as *Cheyletiella*, *Otodectes*, *Sarcoptes scabiei* and *Notoedres cati*. In the case of otodemodicosis other causes of otitis externa need to be considered (1, 14, 19, 25).

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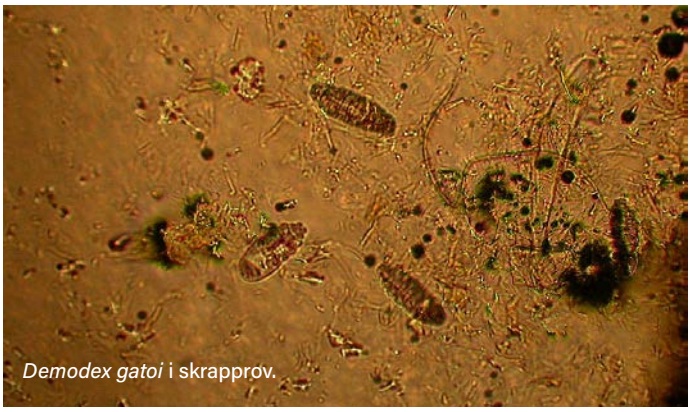
Rex-katt med självinducerad päls på buken till följd av klåda orsakad av *Demodex gatoi.*



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Demodex gatoi i skrapprov.

Treatment and prognosis

There are a number of different treatment options for feline demodicosis, depending on its location on the body and the species of mite. Environmental treatment is not necessary (1). In case of *D. gatoi* infection, all in contact cats should also be treated (1, 13, 19). Localized demodicosis caused by *D. cati* may resolve spontaneously without any treatment (13, 19).

The prognosis for localized demodicosis is good. The prognosis for generalized demodicosis caused by *D. cati* is considered to be good to guarded, depending on whether the underlying immunosuppressing disorder can be resolved (19).

Lime sulfur

The exact miticidal mechanism of lime sulfur is unknown but it is believed to be a combination of its keratolytic properties and formation of miticidal products (12). Lime sulfur dips are the

treatment of choice in cases of *D. gatoi* infestations (1, 12). The dip is performed by immersing the whole cat in the solution or by sponging it on for 5-10 minutes and then letting it dry. Contact with eyes, mouth and nose should be avoided (1). Weekly dips for a minimum of 6 weeks are recommended. The concentration of the solution should be approximately 2% (1, 12). Studies have shown that using a weaker solution, below 1%, is ineffective (23). Gastrointestinal signs, oral ulcerations and drying of the cat´s skin are potential side effects of this treatment. Oral and gastrointestinal signs can be prevented by using an Elizabethan collar and use of a moisturizing shampoo before the dip may minimize dry and irritated skin (12, 23). Lime sulfur treatment has also been shown to be effective in treating some cases of generalized demodicosis caused by *D. cati*, even though it is a follicular mite (12, 19, 23).

Imidacloprid/Moxidectin

A recent study showed great success in treating *D. gatoi* infestation with a topical solution of 10% imidacloprid/1% moxidectin (Advantage Multi for Cats Topical Solution; Bayer HealthCare, Shawnee Mission, USA). The dose was according to the manufacturer´s recommendation based on body weight. The solution was applied to the skin of each cat weekly. In the study, there were 13 cats in the household, of which eight were symptomatic. After eight weeks of treatment none of the cats showed any clinical signs of demodicosis and skin scrapings following the therapy were negative (26). Earlier reports regarding this treatment for feline demodicosis have shown unreliable results (1, 25, 26).

Ivermectin

Ivermectin has not been uniformly successful when used orally 0,2-0,3 mg per kg at 24, 48h or weekly intervals for *D. gatoi* infestation. (1, 12). Although in a report by Saari -09, oral ivermectin 1 mg every other day for 10 weeks was effective in one household (25).

Ivermectin has also been reported effective in the treatment of demodicosis due to *D. cati*, when used orally at 0,3 mg per kg daily (1). There is one case reported of otitis externa caused by *D. cati* that was treated successfully with a 1 % injectable formulation of ivermectin. Three drops of the solution were administered in both ear canals once daily (31). In a report regarding a mixed infestation of *D. cati* and the unnamed feline Demodex species, ivermectin cleared the infestation of *D. cati* but it was ineffective against the unnamed species. The use of ivermectin was associated with serious side effects resulting from neurotoxicity (16).

Doramectin

Doramectin may be effective in the case of generalized demodicosis caused by *D. cati*. The recommended dose is 0,6 mg per kg administered subcutaneously weekly (1, 19, 23). Doramectin has been used in a reported case with mixed infestation of *D. cati* and the unnamed feline Demodex species, where the drug was ineffective (16).

Amitraz

Amitraz dips have been reported as a successful treatment of both *D. cati* and *D. gatoi* infestations. The dose described is a concentration of 0,0125-0,025% applied twice weekly to every other week. (1, 12, 23). Amitraz is not recommended as a first option treatment because of the risk of toxicosis in cats and humans (1, 8, 12). Toxicosis in humans may occur by skin contact, inhalation or ingestion of amitraz and it is metabolised rapidly within the body. The main clinical signs in humans is altered sensorium, hyperglycemia, bradycardia, vomiting and respiratory depression. Amitraz is also considered possibly carcinogenic in humans (8). Reported side effects in cats include anorexia, diarrhea and hypersalivation (6, 12).

Rotenone

Rotenone is a compound similar to pyrethrins and is produced from the root of the Derris plant (20). In the case of localized lesions of feline demodicosis, topical use of Rotenone as an ointment or powder has been described with variable results (4, 23, 31). In one study, a cat with mixed *D. cati* and *D. gatoi* infestation was treated with a rotenone and methylated spirit solution, shortly after the cat became anorexic and died. It is uncertain if the treatment with rotenone was the cause of death (4).

Fluralaner

A novel group of antiparasitic drugs, isoxazolines, has shown success in treating generalized demodicosis in dogs (10). A recent case report, involving one cat suffering from generalized demodicosis caused by *D. cati*, that it was successfully treated with fluralaner. A single dose of 28 mg/kg fluralaner was administered orally and no side effects were observed (17).

Discussion

Three distinct Demodex species have been described in cats (9). However, the clinical presentation may differ depending on the infesting species. Pruritus and alopecia are the main clinical signs for feline demodicosis (5). In general *D. gatoi* causes more intense pruritus than *D. cati*, although not all cats with *D. gatoi* infestation are pruritic (22).

D. cati is usually associated with an underlying immunosuppression (15) and in several cases of *D. cati* infestations demodicosis could not be controlled without concurrent control of the primary disease (12, 21). *D. gatoi*, in contrast to *D. cati*, is usually unconnected to immunosuppressive disease but has been associated with the use of immunosuppressive drugs. It remains unclear whether it is the actual cause of the infestation or not (1, 4, 32).

D. gatoi is easily transmitted between cats and the emergence of *D. gatoi* can be correlated with the time frame over which international cat shows and breeding catteries became more common (24). To prevent further spreading of *D. gatoi* it is important that affected cats are free from infestation before going to exhibitions, shows and breeding facilities and that they should have no contact with other cats until proven free from infestation.

For demonstrating the presence of feline Demodex species skin scrapings and microscopic evaluation of the material obtained are recommended (1, 5, 22) even though it has been proven to be less sensitive compared to the use of PCR techniques (2, 9, 11, 27) and fecal flotation methods. (27). Fecal flotation is non-invasive and a fairly low cost method that should be considered as part of the diagnostic process as well as for monitoring treatment success.

There are a number of different protocols described in regards to treating feline demodicosis. Several parameters must be considered; such as, method of administration, owner compliance, possible side effects for the cat and risks for the person handling the medication.

Lime sulfur dips have a large margin of safety and have been

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reported effective. However, owner compliance can be an issue. Dipping is often difficult to carry out for the owner, especially in a multicat household. Many cats protest aggressively when being immersed in a fluid. The owner must be made aware of the foul odour, often described as 'rotten eggs', and the potential for the solution to stain (1, 12, 23).

Amitraz dips, doramectin and ivermectin should only be used as a last option, since there are potentially serious side effects with these treatments (1, 12). Amitraz also carries a risk of toxicosis for the person administering it, most commonly due to oral or percutaneous exposure (8, 12). The risk can be reduced by wearing gloves, protective clothing and being used in a room well ventilated.

There are two recent publications, both of which reported successful results in treating feline demodicosis. The first described the use of a topical solution of 10% imidacloprid/1% moxidectin (25) and the second, orally administered fluralaner (17). Both treatments have the potential to be used more frequently in the future, since they are considered safe for both patient and owner, cost effective and comparatively simple to administer. A spot-on solution with fluralaner is registered for cats but, to the author´s knowledge, there is no publications regarding its effectiveness in treating feline demodicosis.

Feline demodicosis is considered a rare parasitic condition, but recent studies using new diagnostic techniques indicate that the Demodex species affecting cats could be more frequent than previously suspected. Colonization of both feline and non-feline Demodex mites have been observed in healthy cats, but it is still uncertain what causes colonization and whether the mites colonize in a permanent or temporary way. Further studies are needed about feline demodicosis, particular regarding host-parasite relationships as well as treatment and prevention of the disease. •

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