Dissecting Demodicosis

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Objectives

1. To understand the pathogenesis, diagnosis, and clinical presentation of demodicosis in dogs and cats using a case-based approach.
2. Updates regarding current treatment strategies:
    a. Extra-label use in dogs and cats.
    b. Extra-label use in other species.
3. Discuss combination preventives on the horizon and the potential uses in demodicosis therapy.

Overview

Demodex mites are present in every mammalian species and are considered a normal part of the fauna typically acquired shortly after birth; however, overgrowth of these mites and associated clinical signs are still encountered quite commonly in small animal practice and are often referred to as demodectic mange.

Demodex spp. are incredibly host specific, and are not of zoonotic risk from pets to their human counterparts.

Pathogenesis

Majority of *Demodex* spp. reside within the lumen of the hair follicles or sebaceous glands. A few species, such as *D. gatoi* and *D. cornei*, dwell more superficially in the stratum corneum. It typically takes 3–5 weeks for development from the egg to adult stage, and all stages reside on the host.

In the absence of mite overgrowth, animals harbor their infestations without developing any clinical signs; However, if mite proliferation occurs, clinical signs may develop and may eventually become so severe that the animal is no longer able to compensate.

The mechanisms surrounding the development of demodicosis are not yet fully understood; however, it seems that immune compromise is a common predisposing factor.

Clinical Presentation

Since mites are a part of the normal fauna, most animals handle their infestations without ever developing clinical signs. However, when mite overgrowth is present, animals may suffer from mild alopecia and erythema to severe dermatitis with secondary bacterial or fungal infections.

In dogs, there are two clinical presentations for demodicosis: (1) localized and (2) generalized. Either form may be seen regardless of the age of the dog.

(1) Localized demodicosis

- This form of demodicosis is sometimes referred to as juvenile demodicosis as most cases are seen in puppies less than 6 months of age.

- Lesions are typically mild in nature (patchy alopecia, no pruritus) and present in only one or a couple of small areas (head or limbs).
- These cases may resolve without treatment.

(2) Generalized demodicosis

- Lesions are typically moderate to severe (large areas of alopecia, erythema, pyoderma, crusting and scabbing) and may be present in several areas or across a large portion of the body.
- Pruritus is common if a secondary bacterial infection is present.
- Underlying immune defects often play a role (improper nutrition, stress, systemic disease, etc.).
- Treatment is required to reduce the mite infestation and to address the cause of the immune deficiency.

Demodicosis in cats may be localized or generalized as well. The localized form typically involves alopecia and crusts. Most lesions are along the face or neck. Scaling and hyperpigmentation are also possible. Extensive lesions and underlying immune deficiency are characteristic of generalized demodicosis in cats.

Unlike most follicular *Demodex* infestations, presence of superficial species (e.g. *Demodex gatoi*) OFTEN causes pruritus and can be considered contagious between cats.

Diagnosis

Signalment and history are often helpful for initially recognizing a case of demodicosis. Most animals will have a history of being stray or feral, or a pet that has not been routinely receiving prevention products for fleas, ticks, and/or heartworms or a proper plane of nutrition. Animals experiencing concurrent disease or receiving immunosuppressive drugs may also break with clinical demodicosis.

Recovery of mites via deep skin scraping (with skin pinching) followed by visualization with a microscope is recommended, as many of the *Demodex* spp. live within the hair follicles. Scraping from a primary lesion, such as a papule or pustule, is best. Plucking of hairs for microscopic examination (trichography) may also lead to recovery of mites. For the species that live in the stratum corneum, a hair sample, superficial scrape, or tape impression is more likely to yield recovery of mites. It is not uncommon to find these mites present in a fecal flotation from an animal with lesions that can be physically groomed by the host, and if mites are not recovered via skin techniques, attempts to visualize them in a fecal float is recommended. Mites can also be identified in biopsy specimens. In the last several years, PCR techniques have been developed to identify *Demodex* mites in the skin of dogs and cats; however, this technique may not provide much clinical relevance or diagnostic power given the prevalence rates of *Demodex* in the populations tested. This technique is a very sensitive methodology, and a positive sample cannot confirm diagnosis since 100% of dogs carry *Demodex canis.* Reliance upon history, physical exam, clinical signs, and deep skin scraping are more predicative of true disease. This methodology may be more useful for demodicosis caused by *D. cornei* or *D. gatoi* since these species are present in fewer numbers during clinical disease; however, more research is needed to determine prevalence rates in normal and diseased animals, and to determine the positive and negative predictive values of this test.

Identification of *Demodex* mites is often simple compared to identification of other mite species. Larval, nymphal, and adult stages are all elongate (cigar-shaped), with overall adult length ranging from ~80 µm to 370 µm, depending on which particular species is present in dogs or cats.

Treatment/Prevention

Most cases of localized demodicosis resolve without treatment. Generalized cases, however, require a more rigorous course of action including three key components: (1) miticidal therapy, (2) address secondary infections with appropriate medication, and (3) address the underlying condition contributing to the immune deficiency.

(1) Miticidal options continue to improve regarding safety and route of administration.

- **Amitraz** dips (Mitaban®)—the only approved option in the United States for treating demodicosis in dogs; production **<u>discontinued</u>** Summer 2018.

- **High-dose macrocyclic lactones**—many practitioners would use a compounded formulation of ivermectin orally at elevated doses (working up to 600 µg/kg daily for dogs; 300 µg/kg weekly for cats) for several weeks or injectable doramectin weekly for dogs (600 µg/kg). Increased frequency of dosing with products such as moxidectin + imidacloprid (topical) or oral milbemycin oxime-containing heartworm prevention products has also been shown effective.

  *High-dose macrocyclic lactones must be used with caution in dogs that may possess the MDR1 gene mutation.

- **Isoxazolines**—these products (which are labeled in the U.S. for treatment and control of flea and tick infestations) have all been shown effective at treating demodicosis when given at the frequency approved on the label (Table 1).
  - Afoxolaner (NexGard®)
  - Fluralaner (Bravecto®)
  - Lotilaner (Credelio®)
  - Sarolaner (Simparica®)

  *concern regarding MDR1 gene mutations is not of concern with these products.
  *some of these products have also been shown efficacious at treating additional mite species (*Otodectes cynotis*, *Sarcoptes scabiei*, *Cheyletiella* sp., and *Lynxacarus* sp.) in dogs and cats, as well as effective at treating mite infestations in poultry, rabbits, hedgehogs, and wildlife.

With the advent of routinely used canine and feline preventive products that have extra-label efficacy against *Demodex* mites (e.g. isoxazolines), most animals experiencing either localized or generalized demodicosis are started on one of the many available products that will reduce the mite burden to tolerable levels resulting in the resolution of clinical signs. Several months of treatment may be required; it is imperative that consistent treatment be continued for 1 to 2 months after mites are no longer detected by skin scrape.

(2) If secondary bacterial or fungal infection is present, appropriate use of antimicrobials or antifungals and any adjunct therapies should be instituted.

(3) Diagnostics to determine any underlying cause of immunosuppression should be performed accordingly, and any causes of immunosuppression addressed. Animals should also be provided a proper plane of nutrition, receive appropriate shelter, and be spayed or neutered to eliminate the stresses associated with mating and reproduction and to eliminate the potential for any hereditary traits that may be associated with the development of demodicosis from being passed on.

Table 1: Isoxazoline compound FDA-approved label indications

Drug	Trade Name	Route of Administration	Species	Age and Weight	Frequency of dosing	Arthropods Covered	Precautions
Afoxolaner	Nexgard® (Boehringer Ingelheim)	Oral chewable tablet, artificially flavored	Dog	8 weeks >4 pounds	Monthly	Fleas, black-legged (deer) tick, American dog tick, lone star tick, brown dog tick	Caution with underlying neurological disease
Fluralaner	Bravecto® (Merck)	Oral chewable tablet, hydrolyzed pork liver flavored OR Topical solution	Dog	6 months >4.4 pounds	8 weeks: Lone star ticks 12 weeks: fleas and other ticks	Fleas, lone star tick, black-legged (deer) tick, American dog tick, brown dog tick	Caution with underlying neurological disease
Fluralaner	Bravecto® (Merck)	Topical solution	Cat	6 months >2.6 pounds	8 weeks: American dog tick 12 weeks: fleas and black-legged (deer) tick	Fleas, lone star tick, black-legged (deer) tick, American dog tick, brown dog tick	Caution with underlying neurological disease
Lotilaner	Credelio® (Elanco)	Oral chewable tablet, beef flavored	Dog	8 weeks >4.4 pounds	Monthly	Fleas; lone star tick, black-legged (deer) tick, American dog tick, brown dog tick	Caution with underlying neurological disease
Sarolaner	Simparica® (Zoetis)	Oral chewable tablet, pork flavored	Dog	6 months >2.8 pounds	Monthly	Fleas; lone star tick, Gulf Coast tick, American dog tick, black-legged (deer) tick, brown dog tick	Caution with underlying neurological disease

References:

1. Mueller RS, 2012. An update on the therapy of canine demodicosis. Compend Contin Educ Vet. 34:E1–4.
2. Beale K, 2012. Feline demodicosis: a consideration in the itchy or overgrooming cat. J Feline Med Surg. 14:209–213.
3. Duangkaew L, Hoffman H, 2018. Efficacy of oral fluralaner for the treatment of *Demodex gatoi* in two shelter cats. Vet Dermatol. 29:262.
4. Short J, Gram D, 2016. Successful treatment of *Demodex gatoi* with 10% imidacloprid/1% moxidectin. J Am Anim Hosp Assoc. 52:68–72.
5. Snyder DE, Wiseman S, Liebenberg JE, 2017. Efficacy of lotilaner (Credelio™), a novel oral isoxazoline against naturally occurring mange mite infestation in dogs caused by *Demodex* spp. Parasit Vectors. 10:532.
6. Six RH, Becskei C, Mazaleski MM, Fourie JJ, Mahabir SP, Myers MR, Slootmans N, 2016. Efficacy of sarolaner, a novel oral isoxazoline, against two common mite infestations in dogs: *Demodex* spp. and *Otodectes cynotis*. Vet Parasitol. 222:62–66.
7. Paterson TE, Halliwell RE, Fields PH, Louw ML, Ball G, Louw J, Pinckney R, 2014. Canine generalized demodicosis treated with varying doses of a 2.5% moxidectin + 10% imidacloprid spot-on and oral ivermectin: parasiticidal effects and long-term treatment outcomes. Vet Parasitol. 205(3–4):687–696.
8. Beugnet F, Halos L, Larsen D, de Vos C, 2016. Efficacy of oral afoxolaner for the treatment of canine generalized demodicosis. Parasite. 23:14.
9. Ferrer L, Ravera I, Silbermayr K, 2014. Immunology and pathogenesis of canine demodicosis. Vet Dermatol. 25:427–e65.
10. Milley C, Dryden M, Rosenkrantz W, Griffin J, Reeder C, 2017. Comparison of parasitic mite retrieval methods in a population of community cats. J Feline Med Surg. 19:657–664.
11. Fourie JJ, Liebenberg JE, Horak IG, Taenzler J, Heckeroth AR, Frénais R, 2015. Efficacy of orally administered fluralaner (Bravecto™) or topically applied imidacloprid/moxidectin (Advocate®) against generalized demodicosis in dogs. Parasit Vectors. 8:187.
12. Churgin SM, Lee FK, Groenvold K, Kovi RC, Cheung KY, Martelli PR, Zoo C, 2018. Successful treatment of generalized demodicosis in red-handed tamarins (*Saguinus midas*) using a single administration of oral fluralaner. J Zoo Wildl Med. 49:470–474.
13. Hinkle NC, Jirjis F, Szewczyk E, Sun F, Flochlay-Sigognault A, 2018. Efficacy and safety assessment of a water-soluble formulation of fluralaner for treatment of natural *Ornithonyssus sylviarum* infestations in laying hens. Parasit Vectors. 11:99.
14. Romero C, Sheinberg Waisburd G, Pineda J, Heredia R, Yarto E, Cordero AM, 2017. Fluralaner as a single dose oral treatment for *Caparinia tripilis* in a pygmy African hedgehog. Vet Dermatol. 28:622–e152.
15. Sheinberg G, Romero C, Heredia R, Capulin M, Yarto E, Carpio J, 2017. Use of oral fluralaner for the treatment of *Psoroptes cuniculi* in 15 naturally infested rabbits. Vet Dermatol. 28:393–e91.