

Demodicosis: A Dermatologist's Approach for Greater Success

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Canine demodicosis

Lifecycle

Demodex spp are mites that normally inhabit hair follicles and sebaceous glands. Each animal (including man) harbors its own species-specific mite species. Demodex rarely causes disease in horses, cattle or man. The entire life cycle (25-30 days) is completed on the host. Mites cannot persist free in the environment for more than an hour so. They feed on cellular debris within hair follicles.

There are four stages of the life cycle that are found on skin scrapings: spindle-shaped eggs, 6-legged larvae, 8-legged nymphs and 8-legged adults. It is important to be able to recognize the different life stages when monitoring treatment, as the continual presence of early life cycle mites may be an indication that treatment is not working.

Puppies typically become populated with mites within the first few weeks of life, with the dam as the source.

Pathogenesis

The pathogenesis of the disease states associated with the proliferation of demodex mites is not completely understood. Most animals harbor very low numbers, but in clinically affected animals, the mites proliferate in very large numbers within hair follicles. Whenever a normally benign resident organism becomes associated with disease, one must question the integrity of the immune system. Anti-lymphocyte serum given to very young puppies will cause them to get generalized demodex. The development of demodicosis in older dogs is typically associated with a condition that is causing suppression of the immune system, such as hyperadrenocorticism, hypothyroidism, or neoplasia. The tendency to develop generalized demodicosis is familial. Some bitches and sires will have litter after litter of affected pups. This is why it is recommended that all dogs with generalized demodex, even the ones that self-clear, be taken out of the breeding population. In most cases, canine demodex is not a contagious disease, although there are anecdotal reports of non-related housemates developing the disease at the same time.

Clinical features

There are 2 vastly different clinical forms, localized and generalized, and the prognosis and therapy varies for each condition.

Localized demodicosis

In localized demodicosis, the mites are typically limited to one body area. This condition usually occurs in young dogs under one year of age, and may be squamous or pustular in presentation. The squamous version typically presents as one to several patches of circumscribed, erythematous scaly alopecia that is usually affecting the head or extremities. Typically 90% of these cases will resolve on their own, with the remaining 10% becoming generalized, even if treated with shampoos, topicals or antibiotics. The pustular version of localized demodicosis often affects the face, especially the periorbital region, and typically a secondary bacterial folliculitis is present that needs to be appropriately treated with antibiotics. When any secondary infection is addressed properly, the pustular cases of localized demodex will improve without anti-miticidal therapy about 90% of the time. The differentials for localized demodex include bacterial folliculitis, puppy pyoderma (impetigo), dermatophytosis and juvenile cellulitis.

Diagnosis is made with deep skin scrapings. All obvious lesions should be scraped, as well as the head and paws, as these are common places for demodex mites to flourish, even though the patient may not be displaying clinical signs at these locations. The number of mites and life cycle stages of the mites should be recorded for future comparison, and it's important to note that the Shar Pei breed sometimes requires biopsy to find the parasites. A complete physical examination should be performed to make sure there is no condition that could be suppressing the dog's immune system, such as fecal parasitism. A familial history should also be obtained, if possible, to see if there is a history of demodex in the family, which may indicate that it is more likely to become generalized.

Therapy for localized demodex is typically not necessary except when antibiotics are needed for secondary bacterial folliculitis. It is not recommended to treat a localized case of demodex as if it was generalized with anti-mitocidals for several reasons, the first of which is the unnecessary use of medication that can have serious side effects. Furthermore, it is important to know which dogs develop generalized disease, as prognosis is different. Lastly, it is important to know if the disease is localized versus generalized so the proper recommendations for spaying/neutering the pet can be made.

The general recommendations for treatment of localized demodicosis includes resolution of any secondary bacterial folliculitis, use of benzoyl peroxide products for their antibacterial/follicular flushing effect, NEVER using glucocorticoids that can suppress the immune system and stimulate mite proliferation, and performing routine health maintenance and de-worming.

Generalized demodicosis

The line between localized and generalized demodex can be blurred, but one commonly followed definition for generalized demodex is the presence of five or more localized lesions, the involvement of an entire body region (e.g. face), or the complete involvement of 2 or more feet. Generalized demodicosis can present as squamous or pustular, with squamous typically demonstrating scaly, alopecic

patches that coalesce to form large areas of alopecia, erythema, +/- comedones. The pustular version often involves generalized hair loss and deep pyoderma. Generalized demodex comes in two forms, juvenile onset and adult onset.

Juvenile onset demodicosis typically occurs in dogs less than a year of age. This is a disease that is hereditary, and therefore dogs of both sexes should be neutered to prevent transmission to puppies, even if they are in the 40-50% of dogs that will self-cure.

Adult onset demodicosis typically occurs in dogs greater than 2 years of age and is usually secondary to a disease that is affecting the immune system, or glucocorticoid use. Common diseases that trigger adult onset demodex include Cushing's disease, hypothyroidism and neoplastic processes, although in many cases an underlying condition can't be appreciated and they are classified as idiopathic.

Diagnosis

Diagnosis is made with deep skin scrapings, until capillary oozing is achieved, because these are follicular mites. Sometimes in severely fibrotic skin, such as that associated with a lick granuloma or dogs with severe/fulminant pododemodosis, the mites can be difficult to find on skin scraping. The two breeds that the author has found occasionally difficult to find mites on scraping are the Shar Pei, Doberman and one Bull Terrier patient.

Treatment

Hundreds of treatments have been tried and many have been reported to work that don't, such as motor oil. This is due to the fact that 40-50% of the juvenile onset demodex dogs will self-cure, regardless of which treatment is employed. In these cases, they will often resolve once their secondary bacterial folliculitis is properly controlled.

If the generalized demodex patient is one of the 50-60% of juvenile cases that won't self-resolve, or is an adult onset dog whose mites don't resolve with control of the underlying disease, there are several treatment options.

Amitraz (mitaban and promeris)

These are the only approved treatments for canine demodicosis. Amitraz is a broad-spectrum miticide that is a member of the formamidine family, a monoamine oxidase inhibitor (MOI) and prostaglandin synthesis, and is a α_2 -adrenergic agonist.

In the USA, amitraz (Mitaban) is licensed as a 0.025% solution (1 vial/2 gallons of water, 250 ppm) every two weeks. If the dog is not responding to this treatment the dips can be administered off label at once weekly. To increase efficacy of this medication, dogs should be clipped prior to dipping, and bathing should be avoided between applications. Toy breeds seem more susceptible to lethargy, depression, and neurologic side effects, and sudden death has been reported in Chihuahuas. If used in toy breeds, ¼ -½ strength dips are recommended.

There are many safety concerns with this medication. Even if the dip is performed properly, side effects such as lethargy, depression, anorexia, vomiting, diarrhea, hypothermia, pruritus, bradycardia, ataxia, hyperglycemia and excessive sedation can occur. Yohimbine, at label doses, is the reversal agent for amitraz, and can be used if side effects are excessive. Because amitraz is a MOI, its use should be avoided when either the pet or owner is on a concurrent MOI (such as hydroxyzine, certain antidepressants, Parkinson's medications, and antihypertensive medications). Because it can cause hyperglycemia, it should be avoided in diabetic animals or if there is a diabetic human in the household. Do not use amitraz products in pregnant and lactating bitches and in puppies less than 12 weeks of age.

Promeris is a topical flea control product containing metaflumizone and amitraz that is now off the market and therefore extremely difficult to obtain. Because of its topical formulation, it is much easier to use than the dips. It has been found effective for treatment of demodicosis when administered at either every 2-week or 4-week intervals. A small number of dogs treated with this medication have developed pemphigus foliaceus-like reactions extending from the site of application.

Ivermectin (ivomec, merial)

Ivermectin is a member of the anti-parasitic avermectin family, and acts by potentiating the release and effect of the neurotransmitter GABA. In mammals, GABA is limited to the central nervous system (CNS), which is why this drug has a wide margin of safety when an intact blood brain barrier is present.

The dose recommended for treating canine demodex is 0.4-0.6 mg/kg once daily. The author commonly starts at the low end of the dose range and recommends slowly building up to the target dose to allow careful monitoring for side effects, often taking 10-14 days to reach maintenance.

Ivermectin should not be used in heartworm positive dogs, as animals with a high microfilaria load can have adverse, possible life threatening, reactions. The main side effects that need to be monitored for in a dog on ivermectin are neurological, including changes in pupil size, behavior, ataxia, seizures, coma and death. In a subpopulation of certain herding breeds (Collies, Shetland Sheepdogs, Border Collies, Australian Shepherds, Old English Sheepdogs), a homozygous mutation in the MDR1 gene exists that results in the production of abnormal P-glycoprotein proteins pumps in the blood brain barrier. This allows ivermectin to penetrate and remain within the CNS, and dogs with this gene mutation can experience life threatening neurological side effects. Dogs can be tested for their MDR1 genotype by submitting a cheek swab of DNA to the College of Veterinary Medicine Washington State University (<http://www.vetmed.wsu.edu/depts-VCPL/test.aspx>). Other drugs that utilize the P glycoprotein pump should be avoided when dogs

are on ivermectin, such as cyclosporine and certain chemotherapeutic drugs. Dogs of these specific breeds with negative MDR1 genotypes have still been reported to have neurological side effects when ivermectin was administered.

Milbemycin (interceptor novartis)

**At the time of note submission Interceptor is no longer available, but milbemycin is available from some compounding pharmacies. The current availability of this option will be discussed during the lecture.

Milbemycin is in a parasiticide family related to the avermectins that has the same effect on GABA, but appears to be safer and associated with fewer side effects, even in ivermectin sensitive breeds. Some anecdotal reports do exist, however, of some collies being sensitive to milbemycin at high doses. It is used at a dosage of 1.5-2mg/kg/day. Although potentially safer, the author recommends a gradual build up to maintenance dose as advised for ivermectin. When used at a dose of greater than 2.5mg/kg/day neurological side effects have been noted. The main drawback to this medication is its extreme expense.

Because both ivermectin and milbemycin are used off label and have serious potential side effects, it is advised to have the owners sign a consent form before using

Concurrent therapy

Benzoyl peroxide based shampoos are good adjunctive therapy due to their antibacterial and follicular flushing effect. One of the lynchpins of successfully treating a dog with demodex is identifying and properly treating secondary bacterial infections.

Therapy monitoring

Regardless of which treatment is utilized, patients need to remain on therapy until they have achieved three negative consecutive skin scrapings at 2-4 week intervals. The author typically scrapes dogs at 4-6 representative sites, trying to include the muzzle and at least one paw, each time they come in recheck. The mite counts and life stages should be monitored to help dictate treatment. For example, a dog with a copious amount of live mites and eggs several months into treatment needs an adjustment in therapy.

Feline demodex

Feline demodex is an uncommon to rare disease. There are two main species of demodex that affect cats, the follicular mite *Demodex cati* that is found on deep skin scrapings and is thought to be associated with an underlying immune suppression and *Demodex gatoi*. *Demodex gatoi* is found on superficial skin scrapings and is a stubby mite that is found in the stratum corneum and is contagious and commonly associated with pruritus. This parasite is fairly common in the gulf coast states of Texas and Louisiana.

Clinical signs

Alopecia, scaling, macules, erythema and hyperpigmentation can be associated with both forms of demodex in cats. A sparse hair coat and scaly skin will be present in some cats, and ceruminous demodectic otitis externa can occur. Cats with *Demodex gatoi* are typically very pruritic.

Diagnosis

Diagnosis is made via skin scraping, deep for *D. cati*, superficial for *D. gatoi*. Evaluation for underlying diseases, such as FELV/FIV, should be done in cats with *D. cati*. Because cats with *D. gatoi* are pruritic and typically groom excessively, these superficial mites can be difficult to find. It is recommended to scrape suspect cats in areas where their tongue can't reach easily, such as the dorsal neck and lateral antebrachium.

Therapy

The treatment of choice for *Demodex gatoi* is LymDyps weekly for 4-6 weeks, and all contact animals should be treated as well since it is a contagious disease. There have been reports of *Demodex cati* spontaneously resolving and responding to LymDip, which is hard to understand since it is a follicular mite. Ivermectin can be used with EXTREME caution off label at 300µg/kg once weekly for 4 consecutive treatment, although the author tries to avoid its use if at all possible in cats. Because amitraz can cause severe side effects such as anorexia, depression and diarrhea it is not recommended for use.