Canine demodicosis is a common inflammatory parasitic skin disease believed to be associated with a genetic or immunologic disorder. This disease allows mites from the normal cutaneous biota to proliferate in the hair follicles and sebaceous glands, leading to alopecia, erythema, scaling, hair casting, pustules, furunculosis, and secondary infections.1-3 The face and forelegs to the entire body surface of the dog may be affected.1-3

Three morphologically different types of *Demodex* mites exist in dogs:

1. *Demodex canis*: The most common form of *Demodex* (Figure 1)
2. *D cornei*: A short-body form, likely a morphological variant of *D canis*4 (Figure 2, page 78)
3. *D injai*: A long-body form1-3 (Figure 3, page 78)

Published studies indicate similar efficacy of treatment regardless of the type of mite.1,2

**THERAPEUTIC APPROACH**

Effective treatment of generalized demodicosis requires a multimodal approach.1,2 In order to establish prognosis and provide a successful treatment, it is very important to evaluate the:

- Age of onset
- Extent and location of skin lesions
- Presence of secondary infections
- General health of the dog.1,3,5

Independent of age, it is important to identify and treat any predisposing or contributing factors in order to achieve a successful outcome.1-3
AGE OF ONSET

Juvenile-Onset

Demodicosis may occur in dogs 18 months of age or younger as a result of an immunocompromised state associated with endoparasitism, malnutrition, or health debilitation. Puppies may also develop demodicosis due to an immature immune system or mite-specific immunoincompetency.1 The increased prevalence in certain breeds indicates a hereditary basis for juvenile-onset demodicosis, particularly for the generalized form.3

Adult-Onset

In dogs older than 18 months of age, demodicosis may occur as a result of immunosuppression due to drugs (eg, glucocorticoids, ciclosporin, oclacitinib maleate, chemotherapy) or systemic disease (eg, hyperadrenocorticism, hypothyroidism, neoplasia, malnutrition, parasitism).1,3 Therefore, dogs with adult-onset demodicosis should have a detailed physical examination and full diagnostic workup (Table 1) performed to identify underlying diseases.

Evidence has indicated that successful treatment of an underlying disease may contribute to remission of demodicosis.1,3 However, up to 56% of dogs with adult-onset canine demodicosis have been reported to have no detectable underlying disease.2

EXTENT & LOCATION OF LESIONS

Localized Form1

- Four skin lesions or fewer
- Lesion diameter ≤ 2.5 cm

Prognosis for localized demodicosis is good, as most lesions resolve spontaneously within 6 to 8 weeks.1,3 Topical therapy with benzoyl peroxide shampoo or gel may be recommended.1,3

Generalized Form1

- More than 4 skin lesions
- Lesion diameter > 2.5 cm (Figures 4 and 5)
- And/or feet are affected

TABLE 1 Demodicosis: Diagnostic Analysis

<table>
<thead>
<tr>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count</td>
</tr>
<tr>
<td>Serum biochemical profile</td>
</tr>
<tr>
<td>Urinalysis</td>
</tr>
<tr>
<td>Heartworm and fecal tests</td>
</tr>
<tr>
<td>Lymph node aspirates</td>
</tr>
<tr>
<td>Thyroid and adrenal testing</td>
</tr>
<tr>
<td>Abdominal ultrasound</td>
</tr>
<tr>
<td>Chest radiographs</td>
</tr>
</tbody>
</table>
Overall prognosis for resolution of skin lesions is good (Figure 6), but prognosis depends on the patient's health status and underlying conditions or presence of immunosuppression.1,3

Spontaneous remission in a subset of young dogs has been reported to be 30% to 50%; however, the true incidence of spontaneous resolution of generalized demodicosis is unknown.

Relapses of generalized demodicosis are not uncommon.1 Dogs may be euthanized as owners may be unable to afford cost of therapy or commit to the necessary intense management.1-3 In some patients with refractory or noncurable demodicosis, treatment may be lifelong.1,2

**PRESENCE OF SECONDARY INFECTIONS**

Secondary bacterial and yeast skin and ear infections are common problems associated with canine demodicosis, which aggravate the skin disease and cause or contribute to pruritus.1,3 Identifying and treating these secondary infections is very important to the successful treatment of demodicosis.1,3

Topical and/or oral antibiotics may be prescribed according to clinical signs and cytology. Bacterial culture and susceptibility testing should be performed in patients that do not respond to antibiotic therapy or have a history of multiple antibiotic courses, in an attempt to identify and treat resistant bacteria.

Most dogs benefit from weekly antimicrobial baths with benzoyl peroxide or chlorhexidine shampoos.1,3

**MITICIDAL THERAPIES**

Multiple conventional and newer therapeutic options currently exist for generalized demodicosis (Table 2, page 80);1,3,6 however, most of these therapies are extralabel, can be difficult to administer, and may lead to adverse effects. Miticidal therapy may need to be adjusted according to the dog's response and tolerance.
### TABLE 2 Canine Generalized Demodicosis: Acaricidal Treatment Options

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DOSAGE</th>
<th>ADVERSE EFFECTS</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LABELED FOR CANINE DEMODICOSIS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Amitraz  
(Mitaban, zoetisus.com) | 0.025%–0.06% topical rinses weekly to every 2 weeks | Hyperglycemia, bradycardia, depression, lethargy, polydipsia, polyuria, vomiting, diarrhea, transitory pruritus, sedation | • Good evidence for use  
• Labeled at 0.125% Q 2 weeks  
• Dogs > 4 months of age  
• Avoid other sedating agents, such as GABA agonists (eg, benzodiazepines), alpha-adrenergic agonists (eg, xylazine), and heterocyclic antidepressants (eg, amitriptyline) |
| **EXTRALABEL USE FOR CANINE DEMODICOSIS IN THE U.S.** | | | |
| Afoxolaner  
(Nexgard, merial.us) | 1 tablet PO Q 2–4 weeks | Vomiting, diarrhea, lethargy, dry/flaky skin | • Further studies needed to establish protocol, efficacy, and safety  
• Dogs ≥ 8 weeks of age  
• Use with caution in dogs with history of seizures  
• Safety has not been evaluated in breeding, pregnant, or lactating dogs |
| Doramectin  
(Dectomax, zoetisus.com; Doramec, agrovetmarket.com) | 0.6 mg/kg PO or SC weekly or twice weekly | Lethargy; neurologic signs, such as tremors, mydriasis, ataxia, coma, death | • Some evidence for use  
• 0.3 mg/kg twice weekly may reduce adverse effects  
• Do not use in herding breeds and their crosses or dogs with confirmed ABCB1-1Delta (MDR-1) gene mutation |
| Fluralaner  
(Bravecto, merck.com) | 1 tablet PO Q 12 weeks | Vomiting, diarrhea, anorexia, flatulence, lethargy | • Further studies needed to establish protocol, efficacy, and safety  
• Dogs ≥ 6 months of age  
• Safe for use in breeding, pregnant, and lactating dogs  
• Safe for use in dogs with ABCB1-1Delta (MDR-1) gene mutation, such as collies |
| Ivermectin  
(Ivomec 1%, merial.us; Ivermax 1%, aspenveterinaryresources.com) | 0.3–0.6 mg/kg PO Q 24 H | Lethargy; vomiting; neurologic signs, such as tremors, mydriasis, ataxia, coma, death | • Good evidence for use  
• Do not use in herding breeds and their crosses or dogs with confirmed ABCB1-1Delta (MDR-1) gene mutation  
• Do not use concurrently with spinosad (Comfortis and Trifexis, elanco.us) due to resulting severe neurologic adverse effects |
| Milbemycin oxime  
(Interceptor, elanco.us) | 1–2 mg/kg PO Q 24 H | Lethargy; vomiting; neurologic signs, such as tremors and ataxia | • Good evidence for use  
• Use with caution in herding breeds and their crosses or dogs with confirmed ABCB1-1Delta (MDR-1) gene mutation |
| Moxidectin  
(Cydectin, bi-vetmedica.com) | 0.2–0.5 mg/kg PO Q 24 H | Lethargy; neurologic signs, such as tremors, mydriasis, ataxia, lethargy, coma, death | • Good evidence for use  
• Do not use in herding breeds and their crosses or dogs with confirmed ABCB1-1Delta (MDR-1) gene mutation  
• Do not use in dogs with confirmed ABCB1-1Delta (MDR-1) gene mutation |
| Moxidectin + Imidacloprid  
(Advantage Multi for Dogs, bayerdvm.com; known as Advocate in Europe) | 1 tube/dog topical spot-on weekly | Local cutaneous inflammation or irritation, pruritus, lethargy, reduced appetite, and hyperactivity | • Good evidence for use  
• Dogs ≥ 7 weeks of age  
• Do not use, or use with caution, in herding breeds and their crosses or dogs with confirmed ABCB1-1Delta (MDR-1) gene mutation  
• Further studies needed to establish protocol, efficacy, and safety  
• Dogs ≥ 6 months of age  
• Safety has not been evaluated in breeding, pregnant, or lactating dogs |
| Sarolaner  
(Simparica, zoetisus.com) | 1 tablet PO Q 4 weeks | Vomiting, diarrhea, lethargy; may cause neurologic signs, such as tremors, ataxia, and seizures | • Good evidence for use  
• Dogs ≥ 8 weeks of age  
• Use with caution in dogs with history of seizures  
• Safety has not been evaluated in breeding, pregnant, or lactating dogs |
Amitraz Therapy

Amitraz (Mitaban, zoetisus.com) is a monoamine oxidase inhibitor approved by the FDA for treatment of generalized demodicosis in dogs older than 4 months of age.5

There is good evidence to recommend weekly amitraz rinses for the treatment of canine demodicosis.1,5 However, based on published reports, amitraz seems to be less efficacious in adult-onset demodicosis.1

Recommended concentrations range from 0.025% to 0.06% once weekly to every other week,1,3,5,6 but other protocols have been reported (Table 3). Clinical efficacy increases with increased concentration and shorter treatment intervals.1 Dogs should be treated in well-ventilated areas. For heavily infested dogs, or dogs with medium or long coats, clipping the hair coat is advisable.1,3

Transitory sedation and depression, pruritus, lethargy, hyperglycemia, bradycardia, polydipsia, polyuria, vomiting, and diarrhea may occur.3,6 Marked ataxia and lethargy are rare.3 Amitraz use should be avoided in Chihuahuas and toy breeds as they are reportedly sensitive to amitraz.2

Macrocyclic Lactone Therapy

While macrocyclic lactones are not licensed in the United States for treatment of canine demodicosis, they are widely used by veterinarians due to their known efficacy.

Certain precautions should be taken when using macrocyclic lactones:

- Macroyclic lactones should not be administered to herding breeds and their crosses, including collies, Shetland sheepdogs, Old English sheepdogs, border collies, bearded collies, and Australian shepherds.
- These dogs have a higher risk of depression, ataxia, coma, and death due to their predisposition to the ABCB1-1Δ (MDR-1) gene mutation.5,6
- Prior to prescribing macrocyclic lactones in these breeds, it is recommended that evaluation for the ABCB1-1Δ genotype be performed or alternative treatment pursued.
- A polymerase chain reaction test is available from Washington State University (vcpl.vetmed.wsu.edu).
- In dogs without the ABCB1-1Δ mutation, including puppies, use of lower doses or gradual dose increase of macrocyclic lactones—on a daily or weekly basis—is usually recommended due to possible drug neurotoxicity.1,3,7
- Do not implement macrocyclic lactone therapy in patients without up-to-date negative heartworm tests or in those with heartworm disease.6 Other heartworm preventives should be discontinued during treatment.6

Milbemycin oxime (Interceptor, elanco.us) is licensed in the U.S. as a heartworm and intestinal parasite preventive in dogs older than 4 weeks of age. There is good evidence to recommend milbemycin (1–2 mg/kg PO Q 24 H) for treatment of canine demodicosis.1,5 Milbemycin is better tolerated by dogs compared with other macrocyclic lactones, and may have a higher margin of safety. However, it should be used carefully in dogs with the ABCB1-1Δ gene mutation due to reports of neurologic side effects in these dogs.1

<table>
<thead>
<tr>
<th>Table 3 Demodicosis: Amitraz Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild to moderate cases</strong></td>
</tr>
<tr>
<td><strong>Severe or unresponsive cases</strong></td>
</tr>
<tr>
<td><strong>Pododemodicosis</strong></td>
</tr>
<tr>
<td><strong>Otodemodicosis</strong></td>
</tr>
</tbody>
</table>
Ivermectin use (0.3–0.6 mg/kg PO Q 24 H) for treatment of canine demodicosis is supported by good evidence. To mask its bitter taste, ivermectin may be mixed with fruit sauce or ice cream. Do not use concurrently with spinosad (ie, Comfortis and Trifexis [elanco.us]) due to a drug interaction, which results in severe neurologic adverse effects.

Doramectin use (0.6 mg/kg PO or SC weekly or twice weekly) for treatment of canine generalized demodicosis is supported by some evidence. A recent retrospective study, which included 232 dogs, demonstrated that weekly SC injections of doramectin was a useful and well tolerated treatment for canine generalized demodicosis; remission was reported in 94.8% of the dogs.

Moxidectin use (0.2–0.5 mg/kg PO Q 24 H) for treatment of canine demodicosis is supported by good evidence. Moxidectin 2.5% + imidacloprid 10% (Advantage Multi, bayerdvm.com) is a spot-on medication approved for prevention of fleas, heartworm, and intestinal parasites in dogs of at least 7 weeks of age. This product:

- Has good evidence supporting its use as a weekly treatment for dogs with juvenile-onset demodicosis or mild forms of the disease, or those that cannot receive or tolerate amitraz or macrocyclic lactones
- Seems to be well tolerated without the potential toxicity associated with other avermectin products, and is safe for dogs with the ABCB1-1Δ gene mutation
- Was shown to have a much higher success rate when administered weekly or every 2 weeks versus monthly in mildly affected, juvenile-onset patients compared with moderately or severely affected dogs.

In dogs prone to recurrent demodicosis, I recommend use of Advantage Multi Q 4 weeks to help prevent relapses.

Isoxazoline Therapy

The following isoxazolines are flavored, chewable tablets newly available as veterinary prescriptions and labeled for the prevention and treatment of flea and tick infestations in dogs:

- Fluralaner (Bravecto, merck.com)
- Afoxolaner (Nexgard, merial.us)
- Sarolaner (Simparica, zoetisus.com).

These medications can be used in young dogs of at least 6 months (fluralaner and sarolaner) and 8 weeks (afoxolaner) of age.

Mechanism of Action. Fluralaner, afoxolaner, and sarolaner have similar mechanisms of action, antagonistically binding primarily to the arthropod gamma-aminobutyric acid and glutamate receptor regulated chloride channel and inhibiting the arthropod nervous system, causing paralysis and death. They possess potent, fast, and long-lasting insecticide and acaricide effects, offering 4 (afoxolaner and sarolaner) and 12 (fluralaner) weeks of protection.

Adverse Effects. These products are generally quite safe. The most frequently reported adverse effects include vomiting, diarrhea, anorexia, lethargy, and flatulence. Specific considerations include:

- Afoxolaner should be used with caution in dogs that have a history of seizures.
- Sarolaner may cause neurologic signs, including tremors, ataxia, and seizures.
- Fluralaner is labeled as safe for use in breeding, pregnant, and lactating dogs, as well as in dogs with the ABCB1-1Δ gene mutation.

Use in Demodicosis. Recently, these medications have been anecdotally suggested as an alternative efficacious treatment for canine demodicosis. To date, 3 studies investigating the use of this new class of parasiticide for the treatment of canine demodicosis have been published. Note, in the following studies, that Advocate is the European version of Advantage Multi.

One open study compared the effect of Bravecto (fluralaner; single dose) with Advocate (moxidectin + imidacloprid; applied Q 28 days) in 16 dogs with generalized demodicosis. Dogs treated with fluralaner had lower mean mite counts after treatment (99.8% on day 28, and 100% on days 56 and 84) compared to those treated with moxidectin/imidacloprid (98% on day 28, 96.5% on day 56, and 94.7% on day 84). Statistically, on days 56 and 84, significantly fewer
mites were found on dogs treated with fluralaner compared with those treated with moxidectin/imidacloprid. Reduction of mite counts was consistent with reduction in clinical signs in both groups.

A similar study compared the efficacy of Nexgard (afoxolaner) with Advocate (moxidectin + imidacloprid), both administered biweekly on days 0, 14, 28, and 56, in 8 dogs with generalized demodicosis. Dogs treated with afoxolaner had lower mite counts after treatment (99.2%, 99.9%, and 100% on days 28, 56, and 84, respectively) compared with those treated with moxidectin/imidacloprid (89.8%, 85.2%, and 86.6% on days 28, 56, and 84 respectively). On days 28, 56, and 84, mite reductions were significantly higher in dogs treated with afoxolaner; skin condition in these dogs also improved significantly from day 28 to day 84.

Another recent study investigated the efficacy of Simparica (sarolaner; doses on days 0, 30, and 60) compared with Advocate (moxidectin + imidacloprid; weekly applications from days 0 to 81) for the treatment of 16 dogs with generalized demodicosis for 91 days. The study demonstrated that dogs treated with sarolaner had significant mite count reduction after the first dose (97.1% and 99.8% at days 14 and 29, respectively), with no live mites detected at 44 days and thereafter. Dogs treated with moxidectin/imidacloprid experience mite count reduction of 84.4% and 95.6% at days 14 and 29, respectively, with no mites detected at 74 days and thereafter. All dogs in both groups showed marked improvement in clinical signs.

The results of these studies are encouraging because this new treatment modality offers the potential to provide effective and safe control of canine demodicosis, with low administration frequency, while helping prevent and control fleas and ticks.

**SUPPORTIVE THERAPY**

It is extremely important to improve nutrition by feeding a balanced, age-appropriate diet and treating intestinal parasites or other stress factors, particularly in puppies, stray or rescued, and sick dogs.

Most dogs with demodicosis are treated on an outpatient basis; however, dogs with severe generalized demodicosis, pododermatitis, deep pyoderma, sepsis, pain, fever, dehydration, and complications from underlying diseases may require hospitalization for supportive care. Fluids, systemic antibiotics, and pain medications may be required.

**MONITORING & DURATION OF TREATMENT**

One of the most common reasons for treatment failure is ending therapy too soon. Clinical resolution usually occurs 0.5 to 6 months sooner than parasitologic cure. Therefore, it is important to rely on length of therapy, rather than clinical appearance, to finalize treatment since clinically improved dogs may still harbor mites.

**Therapies Lacking Evidence of Efficacy**

According to evidence-based studies, there is currently insufficient evidence to recommend treatment of canine demodicosis with amitraz collars, closantel, deltamethrin, vitamin E, muramyl dipeptide, phoxime, and herbal and homeopathic products. There is current evidence against use of weekly pour-on or injectable ivermectin, lufenuron, roben, oral selamectin, and levamisole.

**Dogs Affected by Demodicosis: Therapeutic Precautions**

Avoid glucocorticoids, progestogens, ciclosporin (Atopica, novartis.com), and oclacitinib maleate (Apoquel, zoetisus.com) due to their immunosuppressive effects. These agents may inhibit the host immune response, preventing resolution of Demodex infection or inducing relapses. Apoquel is contraindicated in patients with demodicosis or a history of demodicosis.

Avoid use of other P-glycoprotein inhibitors when administering avermectins, such as azole antifungals and ciclosporin, due to potential synergistic toxicosis.

Do not administer macrocyclic lactone medications to herding breeds and their crosses, including collies, Shetland sheepdogs, Old English sheepdogs, border collies, bearded collies, and Australian shepherds, as there is a higher risk of depression, ataxia, coma, and death due to their predisposition to the ABCB1-1Delta gene mutation.

Relapses may occur at times of stress, such as estrus, pregnancy, lactation, and systemic diseases.
1. Perform recheck visits and skin scrapings every 4 weeks to monitor response.

2. Continue treatment until 2 consecutive negative skin scrapings are obtained. A minimum of 4 to 6 skin scraping sites should be negative. Usually, at least 3 to 4 months of treatment are needed.

3. If there is no reduction in mite numbers after several skin scrapings, especially if active mite reproduction is seen (eggs, larvae, and nymphs), reinvestigate for the presence of underlying causes or consider an alternative treatment.

4. Monitor patients for 12 months after treatment is discontinued, with rechecks and skin scrapings performed every 3 to 4 months to monitor for relapses. Relapses were reported in 10% to 45% of patients. One study demonstrated that the largest percentage of recurrence of disease occurred within the first few months after treatment discontinuation. Interestingly, the same study also demonstrated that older dogs were more sensitive to side effects of therapy but were generally clear of mites more quickly than younger dogs.

5. Consider life-long therapy in dogs that respond to therapy clinically but do not have negative skin scrapings and in those with frequent relapses despite proper treatment duration. Based on recently published guidelines for the treatment of demodicosis, Demodex resistance to acaricidal therapy has not been reported.

Remember, during monitoring, the presence of any live, dead, and/or fragments of Demodex mites on skin scrapings should be considered positive, indicating the need for continued treatment.

**CLIENT EDUCATION**

Client education is extremely important. Clients should know and understand the following:

- Dogs with adult-onset demodicosis need a complete workup for possible underlying conditions.
- About 10% of dogs with localized demodicosis may progress to generalized form.
- Treatment of generalized demodicosis may be lengthy and costly.
- Clinical signs often improve before parasitologic cure; therefore, frequent rechecks and skin scrapings are important to achieve treatment success.
- There is a possibility of recurrence after treatment discontinuation, especially if therapy is ended prematurely, leading to disease relapse.
• Some dogs can be controlled but not cured, particularly those treated with immunosuppressive drugs that cannot be discontinued or with unidentified, uncontrolled, or noncurable underlying conditions.

• According to current evidence-based guidelines, dogs with demodicosis requiring parasiticidal therapy should not be bred due to potential heredity. 1

In addition, the pros, cons, and contraindications of various treatment options should be explained to clients.

IN SUMMARY

In most dogs, demodicosis has a good prognosis for cure as long as underlying diseases are identified and treated properly. Treatment should be monitored monthly with multiple skin scrapings and extended beyond clinical and microscopic cure to minimize recurrences. Canine demodicosis can be a challenge to treat; however, the future is brighter with multiple therapeutic options available and the advancement of new, potentially safer, efficacious, and easier-to-administer therapies, such as the isoxazolines. TVP

References


Sandra Koch
Sandra Koch, DVM, MS, DACVD, is an associate professor of veterinary dermatology at University of Minnesota College of Veterinary Medicine. She is primarily involved with clinical service and teaching, and her special interests include allergic and infectious skin diseases, particularly multidrug- and methicillin-resistant Staphylococcus skin and ear infections and dermatologic therapies. She is the primary author of Canine and Feline Dermatology Drug Handbook.