

THE MITEY MENACE OF MANGE

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An army of treatments is being employed against the threats of sarcoptic and demodectic mange

Nothing is more frustrating for either an owner or a veterinarian than a dog that is suffering from a chronic skin condition. And since skin can only respond to disease causing agents in a few selected ways, the appearance of many skin illnesses will be similar. These responses are redness, blistering, ulcerating, oozing, (either serum or oils), thickening, scaliness and increased pigmentation. Consequently, many diseases, including allergies hypothyroidism, fungal infections, bacterial infections and other skin parasites besides the mites that cause demodectic and sarcoptic mange may have similar appearances on the medical examination table. Consequently, a veterinarian's complete dermatologic examination will include several diagnostic tests.

The first is generally the examination of hairs under a fluorescent light, because the most common form of ringworm, the skin fungus *Microsporum canis*, will frequently glow green. Next, a deep skin scraping for parasitic mites, particularly *Demodex* and *Sarcoptes*, will be performed and the material examined under a microscope. Additional tests on the scrapings can reveal bacteria, yeast, non-fluorescing species of ringworm or other species of parasitic arthropods (insects or mites). Finally, fungal and bacterial cultures as well as biopsies may be needed to reveal the cause of an animal's skin disease.

Unfortunately, sarcoptic mange cases are successfully diagnosed with these tests less than 50 percent of the time because only a small number of mites need to be present to cause a dog severe discomfort. This frequently misdiagnosed disease is common and contagious, yet completely treatable. Its hallmark sign is unremitting itchiness, particularly on the ears. Indeed, many veterinarians ignore negative skin scrapings, treating for scabies anyway, if a hind limb scratch reflex is stimulated by vigorous rubbing of the inside of the ear with fingernails. This response is very specific for dogs with sarcoptic mange, because even itchy dogs with chronically thickened, red, raw skin and extensive hair loss due to long-term food, pollen or flea allergies will not respond this way. Yet, a dog with an early case of sarcoptic mange, one with no crusting changes or hair loss yet visible on the ears, will kick with the hind leg when the inside of the ear is scratched as described.

WHAT CAUSES SARCOPTIC MANGE?

What is this irritating creature? Briefly, the *Sarcoptes scabiei* (variety *canis*) mite is a microscopic, eight legged arthropod that both burrows into the superficial layers of the skin and crawls along its surface. After mating, females dig through the skin to lay their eggs,

the resultant larval and nymph stages travel in these burrows as well as break through the skin to the exterior. It is believed that the extreme itchiness experienced by scabies sufferers is not only due to the high level of activity and migration of the mites, but to an intense, almost allergic-like reaction of the patient that may persist for variable periods of time after the mites are killed, and the skin appears healing.

The mites, which require cool temperatures and high humidity to survive off their canine host, generally die in the environment within one to two days under typical room conditions. Nevertheless, cages in animal shelter or boarding kennels with a high dog population turnover can be sources of infection. Moreover, mites may survive as long as 19 days under conditions of 97 percent humidity and a temperature of roughly 10 degrees Celsius, but this is difficult to reproduce except in moist winter barns.

On the dog, however, mites may live four to five weeks, moving easily onto a new host if available. For this reason, all contact dogs must be treated once a diagnosis has been made, whether this was by skin scrapes or by a satisfactory response to specific, anti-mange therapy. This is particularly important because some researchers believe that carrier dogs do exist. These animals, impeccably groomed and receiving excellent nutrition, may show little or no itchiness. Those that do scratch constantly have been called cases of "scabies incognito"; they are itchy but the dog is bathed so frequently that the mite population on the surface of the skin is kept very low and no typical hair loss or crusty exudate develops. Proper therapy resolves the signs of discomfort for the dog.

Ultimately then, a dog must get this disease from another dog. Exceptions might include free-roaming dogs that kill feral foxes, since sarcoptic mange is endemic in many fox populations. However, such a dog is as likely to be visiting another dog with mange than to be killing wild animals, and since the incubation period can be as short as 10 days to as long as eight weeks, it is often hard to guess where a dog initially contracted sarcoptic mange.

The mite is capable of infecting animals besides the dog, but only rarely can females successfully lay eggs and complete the life cycle on a different host. Unusual cases in cats, pigs, guinea pigs, rabbits and humans have been reported, but generally the mites eventually die without any specific treatment. Nevertheless, many veterinarians will recommend treating all contact cats, if possible, when sarcoptic mange is diagnosed. Precautions must similarly be made for any possible human infections. In a household, owners may develop a red, raised, papular rash as early as 24 hours after handling a dog with scabies, but if the dog is successfully treated, most affected family members will be normal within 14 days. It is believed that as many as 30 percent of canine cases will cause human infections, and some of these will require a physician's attention.

FIGHTING SARCOPTIC MANGE

Without proper treatment, canine scabies will progress from the dog's ears and elbows to include other lightly haired areas, particularly the hocks, abdomen and chest. Eventually, it may generalize to the sides and back of the dog and become further complicated by a secondary bacterial infection. Rarely, an affected dog can become severely debilitated and even die. In fact, debility and death from sarcoptic mange is considered one of the major diseases controlling the wild fox population in many states

Fortunately, proper treatment is nearly always successful, and if completed early in the course of the disease, scarring or permanent hair loss is unlikely. However, over the years, these mites have developed resistances to many of the chemicals previously shown to be effective. These resistances are not uniform across the nation, and inadequate treatment is possible if resistance has occurred. Three different topical dips may be prescribed for sarcoptic mange, but each has shown case failures in certain geographic regions. It is important to work with your veterinarian if you are battling this disease, because he or she is most likely to be aware of resistance problems in your specific area. All dips must be preceded by a thorough bath to remove scabs, crusts and dandruff; generally, a medicated, anti-seborrheic shampoo is necessary.

The oldest acaricidal dip was initially developed as an orchard spray against mites affecting apples. Lime sulfur solution (LymDyp®, DVM Pharmaceuticals, Inc.) is still effective in most parts of the country, and more importantly, it is extremely safe, even for puppies, elderly dogs or those with other illnesses. This makes the product invaluable for treating contact animals who may not show any skin problems but need to be treated to prevent recurrence of disease in the household. Owners may safely do the baths and dips at home without any concern for the dog's or their own toxic exposure. The only negative result is the significant sulfide smell (similar to rotten eggs) and the yellow staining properties of the product.

The second topical product most commonly employed is the organophosphate called phosmet (Paramite®, Vet-Kem Division of Zoecon Corp.). This product is also effective against fleas, but for sarcoptic mange it must be applied at twice the flea-killing concentration. Such high concentrations make it unsafe for cats, and possibly puppies, elderly dogs or those individuals known to be sensitive to organophosphate flea control products. It also cannot be used if a dog is wearing an organophosphate flea and tick collar or if the dog is receiving prescription systematic flea control products such as Proban® pills or Pro-Spot® liquid (Bayer Inc.) from a veterinarian. The additional burden of phosmet can cause signs of organophosphate poisoning such as drooling, vomiting, diarrhea, muscle tremors, seizures and even coma or death. Finally, the common, non-prescription availability of many other organophosphate chemicals for flea control has made chemical resistance of sarcoptic mange mites to phosmet common in many areas of the country.

The third product, another orchard spray, has its greatest veterinary use as an approved, prescription treatment against demodectic mange. While not approved as an acaricide against *Sarcoptes*, amitraz (Mitaban®, Upjohn Company) has proven effective against both species of mites, but not in all geographic areas. This formamidine pesticide's precise mechanism of mite control is not fully understood, but in mammals it can have several pharmacologic effects. Its predominate effect is to inhibit the enzyme monoamine oxidase (MAO). Consequently, systematic effects of amitraz on treated dogs can include low body temperature, depression and increased blood sugar concentrations. Thus, it cannot be used on diabetic animals, cats or sick dogs. Recently the drug yohimbine (Yobine®, Lloyd Laboratories) has been identified, however, which can reverse some of the depression, if necessary, in a dog that shows a severe reaction to amitraz dip.

Due to the toxic nature of this chemical, it is available only by prescription through licensed veterinarians. Furthermore, many veterinarians advise against home dipping

with this product, both for the dog's and the owner's safety, recommending instead that all treatments be done at the veterinary hospital. If owners insist on doing the dips at home, it is important that they themselves are not taking any MAO inhibitors by prescription from their doctor. Such patients can succumb to the cumulative effects of excessive MAO inhibition simply by inhaling the amitraz fumes during the dipping process, even if they are covering their skin with protective clothing. For sarcoptic mange, three dips given on alternate weeks are usually successful, but again, resistance to this product by sarcoptic mites has been demonstrated in certain regions of the country.

THE IMPORTANCE OF AVERMECTINS

Probably one of the greatest advances in the treatment of all parasitic diseases, both internal and external types, was the discovery and development of avermectins and the structurally similar milbemycins in the 1980's.. First isolated as potential macrolide-type antibiotics from various species of soil Streptomyces bacteria, these compounds were shown to be chemically similar to many other macrolide antibiotics, yet these had no antibacterial activity. Instead, they were toxic to higher organisms such as nematode worms. Since their discovery, avermectins and milbemycins have become a mainstay against worm parasites, and we recognize ivermectin (Heartguard-30®, Merck AgVet Division) and milbemycin (Interceptor®, Ciba Animal Health) as today's two most effective preventatives against heartworm infection. Additional research over the past decade has shown that these chemicals are also effective against arthropods such as mange mites, if dosed appropriately. Indeed, no resistance of sarcoptic mange mites to ivermectin has yet been demonstrated in the United States, assuming the patient has been adequately treated at the correct dosage for a sufficient number of treatments and has no other health problems that could lower its resistance to disease.

Ivermectin, federally approved to milbemycin for heartworm prevention, has been frequently prescribed for dogs with sarcoptic mange. This drug alone has proven an effective cure for Sarcoptes in shelter and kennel situations, as well as for dogs who cannot be bathed. However, since most dogs heal faster if given medicated baths and dips, these are usually prescribed for pet dogs along with the ivermectin treatment. Nevertheless, doses here are roughly 60 times that necessary to prevent heartworm disease, and at that level the drug must be administered by a veterinarian; the dogs must also have a negative blood test for heartworm. Generally, the first dose will be given in the hospital. If no untoward reactions occur, subsequent doses (two or three at two week intervals) may be given on an outpatient visit.

The avermectins cause a flaccid paralysis in worms and arthropods by blocking the conduction of nerve impulses in certain specialized nerves that depend on GABA (rather than the usual acetylcholine) for interneuron communication. Mammals are more resistant to toxicity because GABA dependent nerves are found only in the central nervous system, which is protected from many chemicals by specialized membranes and processes called the "blood-brain barrier." At high ivermectin doses, or in certain sensitive breeds such as Collies, Shetland Sheepdogs and Old English Sheepdogs, penetration of this barrier can occur and toxicity may result. Signs include dilated pupils, drooling, weakness, depression, possible coma and even death. The susceptibility of

certain breeds is believed to be linked to greater permeability of the blood brain barrier. In other words, ivermectin enters the brain and central nervous system of these dogs to a greater extent than it does in other breeds. Milbemycin, however, does not penetrate the blood-brain barrier of these breeds as easily, so toxicity is rarely a problem.

Since ivermectin is such a successful systemic treatment for sarcoptic mange, adequate dosages of milbemycin for this condition have not been established. Experimental work, however, suggests that this drug could be effectively used in ivermectin-sensitive dogs who have sarcoptic mange and have not responded to any of the topical baths and dips described above. More importantly, milbemycin has been actively researched as a treatment for resistant cases of demodectic mange, and the doses for this condition have been recently published in several veterinary journals by different researchers.

THE DEMODECTIC MITE

Demodex canis is the cause of "red mange," and the organism, while also an eight-legged mite, is very different than the sarcoptic mange mite. More important than the striking difference in appearance is the difference in life cycle. While the sarcoptic mite is a true parasite, the demodectic mite is not. *Demodex canis* is a normal commensal organism that can be isolated by skin scrapings from a majority of normal dogs. When a dog develops "the red mange," it represents an imbalance between the mite and the dog's immune system. *Demodex canis* does not cause disease in most dogs who have the organism living in their hair follicles, and it is not considered to be contagious between dogs or between dogs and other species of animals, including humans. Except for afflicted Shar-Pei dogs, this disease is easy to diagnose by your veterinarian with a skin scraping because disease occurs only when the organism is multiplying rapidly. Large numbers of mites will be present.

Small numbers of *Demodex* mites inhabit the hair follicles and skin glands of most dogs. They move from the skin around the bitch's nipples to a puppy's face in the first 72 hours of life during nursing. The life cycle takes 20 to 35 days, and the organism never leaves the dog. In fact, transmission among dogs after puppyhood is very difficult since mites die rapidly on the skin surface under typical room conditions. It is not considered a contagious disease, so contact dogs do not require treatment.

Clinical illness from *Demodex* depends more on the age and the health status of the dog than on the activity of the mites. Consequently, demodicosis is classified as juvenile vs. adult-onset as well as localized vs. generalized. While a single, small patch of hair loss with redness and scaling on the face of a young pup is not unusual, it would be on a dog older than 2 years of age. Similarly, one spot may not be cause for alarm, but multiple areas, particularly on the feet, toes and nail beds, could indicate serious disease. Whenever demodicosis appears on a mature dog, it is cause for concern. Generally speaking, such dogs have some other medical problem that has lowered their resistance and depressed their immune system, allowing mites that have lived there harmlessly for years to suddenly multiply out of control and cause inflammation. These dogs may have a depression of their immune system from a hormonal imbalance such as Cushing's disease, or be debilitated from a severe case of other parasites such as hookworm,

whipworm or heartworm. When treated, the demodicosis may resolve.

Juvenile-onset demodicosis is more commonly seen, but the course of the localized and the generalized forms are radically different. The localized form is characterized by only a few patches of scaly, reddish spots that do not itch. A deep skin scraping, with the skin pinched to help extrude mites from hair follicles, will reveal many mites and often eggs and larvae as well. Lesions generally appear on the head, neck and fore limbs. Ninety percent of such pups will self-cure with maturity, although lotions that slow the multiplication rates are sometimes prescribed to speed the healing process.

Unfortunately, 10 percent of these same pups will progress to the generalized form, and the definition of "generalized" extends to those pups that have several feet involved, even if the rest of the body is free of lesions. Indeed, some clinical researchers consider this a third form -- called "podo demodicosis" -- because it is frequently very difficult to eradicate the organisms from toes and nail beds. Owners of such dogs are often given a guarded prognosis for cure.

Thirty to 50 percent of juvenile generalized demodicosis cases will actually self-cure without any specific anti-Demodex therapy, usually around 1 year of age. However, secondary bacterial infections must be controlled, often requiring both medicated shampoos and systemic antibiotics, for healing to occur. The remaining generalized cases, either because the mite populations are so high that bacterial infection cannot be prevented or because the dogs do not self-cure by 12 to 18 months of age, must receive anti-Demodex therapy. Finally, a very small number of these cases even prove to be refractory to currently approved and experimental methods of treatment.

THE QUESTION OF BREED

While generalized demodicosis can develop in any breed, including mixed breeds, certain breeds seem to be predisposed. These include a preponderance of short-haired breeds (Beagle, Pointer, Chinese Shar-Pei, Pug, Boxer, Chihuahua, Dalmation, Great Dane, English Bulldog, Doberman Pinscher, Dachshund, Staffordshire Terrier and Boston Terrier), although other breeds are certainly well-represented (Old English Sheepdog, Collie, Afghan Hound, German Shepherd and Cocker Spaniel). It is best not to think of this disease as breed-specific, but rather line-specific. In 1983, the American Academy of Veterinary Dermatology passed a resolution that all dogs with generalized demodicosis be neutered.

Many breed associations and breeders have gone beyond this recommendation, urging all the parents and siblings of generalized demodicosis patients to be neutered as well. Breeders of the Chinese Shar-Pei have been very aggressive in eradicating demodicosis from their breeding programs. This is perhaps because 1.) the disease often develops before puberty, and 2.) in the Shar-Pei, diagnosis can be difficult due to the unusual characteristics of their skin.

Unlike other breeds, surgical skin biopsies, rather than simple skin scrapings, are often required for a diagnosis. Rigorous and disciplined elimination (no exceptions) of all affected and carrier dogs (both parents and all siblings) from a breeding program can markedly reduce the incidence of this disease from a breeding line.

The heritability of this disease is not in question, but the exact nature of the inadequacies in the immune system that would allow this normally commensal mite to multiply excessively remain to be solved. Much research has been done on localized cases, early generalized cases and severely affected cases as well on non-affected siblings and parents. Certain deficiencies have been demonstrated before disease occurs, and other types develop only when large numbers of mites are present in severe, chronic cases. This latter immune deficiency resolves after successful treatment, suggesting that the mites themselves secrete a substance that depresses the immune system. However, other researchers point out that such dogs have severe bacterial infection as well as high mite population. They believe that the bacterial infection depresses the immune system. Clearly, much more work needs to be done in this area.

TREATING DEMODECTIC MANGE

Regardless of the cause for profound illness, hair loss and severe skin disease of these patients, treatment demands eradication of the mites as well as antibiotics if secondary skin infection is present. Medicated baths and soaks are crucial, both to remove bacteria-laden crusts as well as to open the pores and follicles where the mites live. Hot soaks combined with a follicular-flushing, anti-bacterial shampoo are necessary before the specific anti-mite therapy can be applied. Benzoyl peroxide (OxyDex, DVM Pharmaceuticals, Inc.) has been shown to be the most effective product to prepare the skin and best expose the mites to the anti-Demodex dip.

Amitraz dip (Mitaban®, Upjohn Company) is the only product licensed for treatment of generalized demodicosis. As mentioned earlier, this miticide has broad systemic effects, and as a monoamine oxidase inhibitor, it also can affect humans applying the dip if they are taking other monoamine oxidase inhibitors under prescription by their doctors. The fumes alone can affect such individuals, even if they are wearing protective clothing that adequately shields against skin contact. For this reason, many veterinarians urge that amitraz dips be performed by hospital personnel, not at home. However, since most dogs with generalized demodicosis require an average of 10 to 12 treatments, therapy is unquestionably expensive.

All affected dogs with thick hair should be shaved to allow good penetration. Of both the benzoyl peroxide medicated shampoo as well as the amitraz dip. Continued monitoring with repeated skin scrapings by the attending veterinarian during therapy is vital because many cases require higher concentrations of dip or more frequent applications than are allowed on the label. Generally speaking, when a dog is started on amitraz therapy, the approximate number of mites per microscopic field from a skin scraping has already been recorded on the patient's medical record. More importantly, the vitality and physical activity of the mites as well as the relative proportion of eggs and larvae to adults is noted. The more active the mites and the greater the percentage of immature forms seen, the more serious is the disease.

Treatments then begin on alternate weeks. On the morning of the third scheduled treatment, a skin scrape is repeated, and if the population of mites is significantly decreased or if only dead mites are found, then treatments continue at this level until

three consecutive skin scrapes are completely negative. This may take as few as six treatments, but usually more are necessary. Ten to 12 treatments is not unusual.

If there has been no improvement, and if the dog has shown no signs of depression or illness from the treatment, then the concentration of the amitraz is doubled. After two or three more treatments, the scrape is repeated. If there is still no improvement, the treatment at this higher concentration is performed weekly rather than on alternate weeks. Generally speaking, a dog who fails to respond to this regimen may not respond to any amitraz therapy, although some researchers report that refractory cases may respond if half the body is treated every day with a concentration that is five times the recommended dosage.

However, many dogs cannot tolerate these higher doses of amitraz. As many as 9 percent of dogs, subjected only to the lower, approved doses of amitraz, will exhibit significant itchiness, high blood sugar levels and/or sedation as long as three days after treatment. This makes the product unsuitable for diabetic dogs, elderly dogs and others with certain medical problems. A very small number of individuals could potentially develop a profoundly low body temperature, seizures or even death. Fortunately, an antidote (Yobine, Lloyd Laboratories) has been discovered that can reverse some of these side effects, particularly deep sedation, if given intravenously by the attending veterinarian.

If months of effort prove fruitless, many owners decide to let their dogs live with the disease if a schedule dips can be found that keeps the mite population to a comfortable level. This is often only once every three to four weeks. On the other hand, many owners are willing to pursue a complete cure through various experimental protocols. Additionally, disabled owners or ones whose dogs violently resist baths and dips may want to try an experimental therapy that does not require topical treatments. For these owners, recent research has shown that ivermectin and milbemycin, if dosed appropriately, can cure many dogs whose case resist amitraz therapy.

THE RESISTANCE OF MITES

As we have seen, three amitraz treatments will often cure a case of sarcoptic mange, but 10 or more dips are generally needed to cure Demodex. The resistant capabilities of these mites are further demonstrated by a look at the necessary dosages milbemycin and ivermectin. Milbemycin oxime (Interceptor/Ciba Animal Health) must be given at roughly twice the heartworm-preventative dose every day for treatment to be successful, and this usually takes at least three months. At this dosage ivermectin-sensitive Collies and other breeds might show an adverse drug reaction, but these seem to be mild. For ivermectin (Heartgard 30/Merck AgVet Division) to be effective against Demodex, it must be administered at roughly 180 times the heartworm preventative dosage or three times the sarcoptic mange dosage every day. When one recall that ivermectin is effective against sarcoptic mange when given only three times on alternate weeks, it is obvious that demodectic mites are well-shielded in the follicles and glands of the skin.

It is important to realize that the use of ivermectin and milbemycin for dogs with generalized Demodex is still considered to be in the research phase. It should be reserved for those dogs who do not respond to or who cannot tolerate amitraz, the approved drug

for this condition. Most importantly, it is necessary to be patient with Demodicosis. Many generalized juvenile patients have the potential to self-cure around 1 year of age, provided that secondary bacterial infections are kept in check. If amitraz has already been initiated in a young dog with poor results, it still might be better to stick with amitraz than to try other drugs if the dog is less than 1 year of age. That dog's Immune system may simply need a few extra months of growth and development before any drug will be successful.

Owners work closely with your veterinarian if you have a dog with generalized demodectic mange, and don't hesitate to seek a second opinion from a diplomate of American Academy of Veterinary Dermatology. These veterinarians are associated with every veterinary college and veterinary research and clinical center in the country. Moreover, many of these specialists have their own practices, although these will generally be found only near major metropolitan centers. In any case, just knowing about this disease and these new advances may help you deal with the frustrations and expense of demodicosis.

Finally, remember that dogs with generalized demodicosis, as well as their close relatives, should not be used for breeding. It has been demonstrated clearly that conscientious breeders can largely eliminate this condition from affected pedigree lines, and everyone should follow their lead. Do not breed siblings or parents of generalized Demodex cases, and certainly do not breed any affected individual. Do not risk condemning another dog and another owner to this disease because it is considered to be based in a deficit of that dog's own immune system. Moreover, not all dogs respond even to these new, experimental therapies, and every treatment therapies, and every treatment takes many months and much expense to effect a cure when finally achieved.