

# Actinomyces spp & Nocardia spp

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*Actinomyces* spp and *Nocardia* spp are members of class Actinobacteria, which can cause opportunistic infections in dogs, cats, and other species. Both can cause pyogranulomatous or suppurative disease that is often slowly progressing and challenging to diagnose; however, some differences in organism and characteristics exist (**Table 1**, next page). The incidence of disease caused by either is undefined and likely low.

## Actinomyces spp

Many different species are present, and taxonomy continues to change; some species previously known as *Actinomyces* have been reclassified in other genera, such as *Arcanobacterium* spp and *Trueperella* spp. Regardless, disease aspects remain unchanged. Commonly found as part of the oral, GI, and genital microbiotas,<sup>1-3</sup> *Actinomyces* spp and related genera are of limited virulence unless inoculated into tissue (eg, via bites, foreign bodies, or trauma).

- ▶ Four main types of infection can be encountered: cervicofacial, thoracic, abdominal, and subcutaneous.<sup>4-9</sup>
  - Clinical signs correspond to the tissues involved and the severity of disease.
  - Disease is often associated with firm and fibrous masses, persistent exudates (eg, pyothorax<sup>7,10</sup>), draining tracts, abscessation, and osteomyelitis.

## Nocardia spp

The *Nocardia* genus contains more than 30 saprophytic species that are widely, if not ubiquitously, disseminated in the environment. Disease occurs following inoculation of the bacterium into tissue or via inhalation.

- ▶ *Nocardia* spp are regionally variable, with higher rates of infection in dry, dusty, and windy regions (eg, southwestern United States, parts of Australia).
- ▶ Nocardiosis is classically divided into 3 clinical forms: pulmonary, disseminated (systemic), and cutaneous/subcutaneous.<sup>11-15</sup>
  - Clinical presentations are as would be expected with pulmonary, systemic, or cutaneous infections. Pulmonary or cutaneous disease can progress to disseminated disease.

## Diagnosis

Early diagnosis may be missed. These infections are often only considered in chronic cases.

- ▶ Neoplasia is sometimes suspected based on the types of lesions and failure to respond to empirical antimicrobials.
- ▶ Cytologic examination of aspirates or exudates, as well as histopathology, is critical for diagnosis because the filamentous nature of these bacteria is unlike typical pathogens.

- ▶ Acid-fast staining should be performed.
  - Presence of visible sulfur granules should prompt strong suspicion of *Actinomyces* spp infection.
- ▶ Isolation of other pathogens does not rule out these organisms; thus, reliance on culture as the first step is unwise.
  - *Actinomyces* spp often coaggregates with other bacteria and may be overlooked when a common, easily grown pathogen (eg, *Staphylococcus* spp) is isolated.

Isolation of *Actinomyces* spp and *Nocardia* spp can be difficult, as they are slow growing and may be overgrown by contaminants of coinfecting bacteria.

- ▶ Antimicrobial susceptibility testing is often not available because of the slow-growing nature of these organisms and lack of standard testing guidelines.

- ▶ Negative culture results do not rule out the presence of these bacteria.

**Treatment**

Optimal antimicrobial regimens have not been established, but differentiation between these similar pathogens is important, as empirical treatment recommendations differ (**Table 2**).

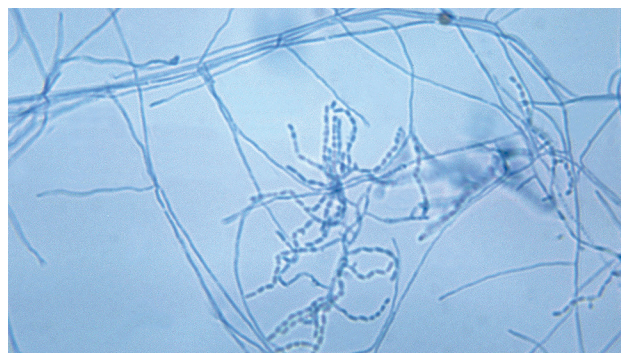
- ▶ Surgical resection of densely infected soft tissue may be beneficial or required.
- ▶ Accumulations of exudates (eg, pyothorax) should be removed.
- ▶ Underlying causes such as a penetrating foreign body should be part of the initial diagnostic and treatment plan.
  - For *Nocardia* spp infection, consideration of a possible underlying immunosuppressive disorder that could impact long-term prognosis is indicated.

TABLE 1

**COMPARISON OF ACTINOMYCES SPP & NOCARDIA SPP**

	<i>Actinomyces</i> spp	<i>Nocardia</i> spp
Cytology	<ul style="list-style-type: none"> <li>• Branched, filamentous, gram-positive</li> <li>• Often large sulfur granules</li> <li>• Pyogranulomatous/suppurative inflammation</li> </ul>	<ul style="list-style-type: none"> <li>• Branched, filamentous, gram-positive (<b>Figure</b>)</li> <li>• Occasionally smaller sulfur granules</li> <li>• Pyogranulomatous/suppurative inflammation</li> </ul>
Acid fast	No	Partially
Culture	<ul style="list-style-type: none"> <li>• May be difficult to culture because of slow growth</li> <li>• Facultative or obligate anaerobe</li> <li>• Often concurrent growth of other potential pathogens</li> </ul>	<ul style="list-style-type: none"> <li>• May be difficult to culture because of slow growth</li> <li>• Aerobe</li> </ul>
Sources of exposure	Oral, GI, and genital microbiotas	Environment (soil)
Spread	Direct spread via adjacent tissue	Direct and hematogenous spread
Coinfections	Common	Uncommon
Underlying immunosuppression	Uncommon	Common
High-risk animals	Large-breed dogs, hunting dogs, dogs at risk for penetrating wounds and foreign bodies	Male animals <2 years of age, animals in arid regions

- ▶ Duration of treatment is not well understood, but weeks to months of antimicrobial therapy are usually required, often with the approach of continuing for a few weeks after clinical resolution.
  - Many months of treatment may be required in patients with disseminated disease.
- ▶ Prognosis is variable and depends on severity and location of infection.
  - For *Actinomyces* spp infection, the prognosis is fair to good, particularly if affected tissue can be resected or if there is no extensive systemic involvement.
  - For *Nocardia* spp infection, the prognosis is guarded, especially in patients with disseminated or pulmonary disease.



▲ **FIGURE** Gram stain of *Nocardia asteroides*. Note the branching filamentous bacteria that may terminate in a rod and coccus shape. Image courtesy of US Centers for Disease Control and Prevention

### Zoonotic Potential

Although both pathogens can affect humans, there is little evidence that infected animals pose a zoonotic risk.

- ▶ Infected animals represent only one possible source of exposure.
- ▶ Basic infection control and hygiene practices to limit exposure (eg, hand hygiene, covering open wounds when handling an infected patient, safely handling sharps) should be taken, but specific measures are not indicated. ■

**There is little evidence that infected animals pose a zoonotic risk.**

**TABLE 2**

### COMMON TREATMENT OPTIONS FOR ACTINOMYCES SPP & NOCARDIA SPP INFECTIONS

	<i>Actinomyces</i> spp	<i>Nocardia</i> spp
First choice	Amoxicillin (20-40 mg/kg PO q6-8h)	Potentiated sulfonamides (15-30 mg/kg PO q12h)
Acid fast	No	Partially
Potential second-tier options	<ul style="list-style-type: none"> <li>• Erythromycin (10 mg/kg PO q12h)</li> <li>• Clindamycin (5-10 mg/kg q12h)</li> <li>• Doxycycline (5-10 mg/kg q12h)</li> <li>• Chloramphenicol (dogs, 40-50 mg/kg PO q8h; cats, 10-20 mg/kg PO q12h)</li> <li>• Third-generation cephalosporins</li> </ul>	<ul style="list-style-type: none"> <li>• Minocycline (5-7.5 mg/kg q12h)</li> <li>• Erythromycin (10 mg/kg PO q12h)</li> <li>• Doxycycline (5-10 mg/kg q12h)</li> </ul>

**References**

- Elliott DR, Wilson M, Buckley CM, Spratt DA. Cultivable oral microbiota of domestic dogs. *J Clin Microbiol.* 2005;43(11):5470-5476.
- Saphir DA, Carter GR. Gingival flora of the dog with special reference to bacteria associated with bites. *J Clin Microbiol.* 1976;3(3):344-349.
- Wunder JA, Briner WW, Calkins GP. Identification of the cultivable bacteria in dental plaque from the beagle dog. *J Dent Res.* 1976;55(6):1097-1102.
- Song RB, Vitullo CA, da Costa RC, Daniels JB. Long-term survival in a dog with meningoencephalitis and epidural abscessation due to *Actinomyces* species. *J Vet Diagn Invest.* 2015;27(4):552-557.
- Sherman A, Daniels JB, Wilkie DA, Lutz E. *Actinomyces bowdenii* ulcerative keratitis in a dog. *Vet Ophthalmol.* 2013;16(5):386-391.
- Barnes LD, Grahn BH. *Actinomyces* endophthalmitis and pneumonia in a dog. *Can Vet J.* 2007;48(11):1155-1158.
- Barrs VR, Allan GS, Martin P, Beatty JA, Malik R. Feline pyothorax: a retrospective study of 27 cases in Australia. *J Feline Med Surg.* 2005;7(4):211-222.
- Junius G, Bavegems V, Stalpaert M, Binst D, Schrauwen E. Mitral valve endocarditis in a Labrador retriever caused by an *Actinomyces* species identified as *Actinomyces turicensis*. *J Vet Intern Med.* 2004;18(6):899-901.
- Davies DR, Lucas J. *Actinomyces* infection in a dog with pulmonary carcinoma. *Aust Vet J.* 2003;81(3):132-135.
- Rooney MB, Monnet E. Medical and surgical treatment of pyothorax in dogs: 26 cases (1991-2001). *J Am Vet Med Assoc.* 2002;221(1):86-92.
- Eroksuz Y, Gursoy NC, Karapinar T, et al. Systemic nocardiosis in a dog caused by *Nocardia cyriacigeorgica*. *BMC Vet Res.* 2016;13:30.
- Uhde AK, Kilwinski J, Peters M, et al. Fatal nocardiosis in a dog caused by multiresistant *Nocardia veterana*. *Vet Microbiol.* 2016;183:78-84.
- Hilligas J, Van Wie E, Barr J, et al. Vertebral osteomyelitis and multiple cutaneous lesions in a dog caused by *Nocardia pseudobrasiliensis*. *J Vet Intern Med.* 2014;28(5):1621-1625.
- Siak MK, Burrows AK. Cutaneous nocardiosis in two dogs receiving ciclosporin therapy for the management of canine atopic dermatitis. *Vet Dermatol.* 2013;24(4):453-456, e102-e103.
- MacNeill AL, Steel JC, Dossin O, Hoi-en-Dalen PS, Maddox CW. Disseminated nocardiosis caused by *Nocardia abscessus* in a dog. *Vet Clin Pathol.* 2010;39(3):381-385.

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**Heartgard® Plus**  
(ivermectin/pyrantel)

**CHEWABLES**

**CAUTION:** Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

**INDICATIONS:** For use in dogs to prevent canine heartworm disease by eliminating the tissue stage of heartworm larvae (*Dirofilaria immitis*) for a month (30 days) after infection and for the treatment and control of ascarids (*Toxocara canis*, *Toxascaris leonina*) and hookworms (*Ancylostoma caninum*, *Uncinaria stenocephala*, *Ancylostoma braziliense*).

**DOSAGE:** HEARTGARD® Plus (ivermectin/pyrantel) should be administered orally at monthly intervals at the recommended minimum dose level of 6 mcg of ivermectin per kilogram (2.72 mcg/lb) and 5 mg of pyrantel (as pamoate salt) per kg (2.27 mg/lb) of body weight. The recommended dosing schedule for prevention of canine heartworm disease and for the treatment and control of ascarids and hookworms is as follows:

Dog Weight	Cheewables Per Month	Ivermectin Content	Pyrantel Content	Color Coding On Foil Backing and Carton
Up to 25 lb	1	68 mcg	57 mg	Blue
26 to 50 lb	1	136 mcg	114 mg	Green
51 to 100 lb	1	272 mcg	227 mg	Brown

HEARTGARD Plus is recommended for dogs 6 weeks of age and older.

For dogs over 100 lb use the appropriate combination of these chewables.

**ADMINISTRATION:** Remove only one chewable at a time from the foil-backed blister card. Return the card with the remaining chewables to its box to protect the product from light. Because most dogs find HEARTGARD Plus palatable, the product can be offered to the dog by hand. Alternatively, it may be added intact to a small amount of dog food. The chewable should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing. Chewables may be broken into pieces and fed to dogs that normally swallow treats whole.

Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes after administration to ensure that part of the dose is not lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

HEARTGARD Plus should be given at monthly intervals during the period of the year when mosquitoes (vectors), potentially carrying infective heartworm larvae, are active. The initial dose must be given within a month (30 days) after the dog's first exposure to mosquitoes. The final dose must be given within a month (30 days) after the dog's last exposure to mosquitoes.

When replacing another heartworm preventive product in a heartworm disease preventive program, the first dose of HEARTGARD Plus must be given within a month (30 days) of the last dose of the former medication.

If the interval between doses exceeds a month (30 days), the efficacy of ivermectin can be reduced. Therefore, for optimal performance, the chewable must be given once a month on or about the same day of the month. If treatment is delayed, whether by a few days or many, immediate treatment with HEARTGARD Plus and resumption of the recommended dosing regimen will minimize the opportunity for the development of adult heartworms.

Monthly treatment with HEARTGARD Plus also provides effective treatment and control of ascarids (*T. canis*, *T. leonina*) and hookworms (*A. caninum*, *U. stenocephala*, *A. braziliense*). Clients should be advised of measures to be taken to prevent reinfection with intestinal parasites.

**EFFICACY:** HEARTGARD Plus Chewables, given orally using the recommended dose and regimen, are effective against the tissue larval stage of *D. immitis* for a month (30 days) after infection and, as a result, prevent the development of the adult stage. HEARTGARD Plus Chewables are also effective against canine ascarids (*T. canis*, *T. leonina*) and hookworms (*A. caninum*, *U. stenocephala*, *A. braziliense*).

**ACCEPTABILITY:** In acceptability and field trials, HEARTGARD Plus was shown to be an acceptable oral dosage form that was consumed at first offering by the majority of dogs.

**PRECAUTIONS:** All dogs should be tested for existing heartworm infection before starting treatment with HEARTGARD Plus which is not effective against adult *D. immitis*. Infected dogs must be treated to remove adult heartworms and microfilariae before initiating a program with HEARTGARD Plus.

While some microfilariae may be killed by the ivermectin in HEARTGARD Plus at the recommended dose level, HEARTGARD Plus is not effective for microfilariae clearance. A mild hypersensitivity-type reaction, presumably due to dead or dying microfilariae and particularly involving a transient diarrhea, has been observed in clinical trials with ivermectin alone after treatment of some dogs that have circulating microfilariae.

**Keep this and all drugs out of the reach of children.**

In case of ingestion by humans, clients should be advised to contact a physician immediately. Physicians may contact a Poison Control Center for advice concerning cases of ingestion by humans.

Store between 68°F - 77°F (20°C - 25°C). Excursions between 59°F - 86°F (15°C - 30°C) are permitted. Protect product from light.

**ADVERSE REACTIONS:** In clinical field trials with HEARTGARD Plus, vomiting or diarrhea within 24 hours of dosing was rarely observed (1.1% of administered doses). The following adverse reactions have been reported following the use of HEARTGARD: Depression/lethargy, vomiting, anorexia, diarrhea, mydriasis, ataxia, staggering, convulsions and hypersalivation.

**SAFETY:** HEARTGARD Plus has been shown to be bioequivalent to HEARTGARD, with respect to the bioavailability of ivermectin. The dose regimens of HEARTGARD Plus and HEARTGARD are the same with regard to ivermectin (6 mcg/kg). Studies with ivermectin indicate that certain dogs of the Collie breed are more sensitive to the effects of ivermectin administered at elevated dose levels (more than 16 times the target use level) than dogs of other breeds. At elevated doses, sensitive dogs showed adverse reactions which included mydriasis, depression, ataxia, tremors, drooling, paresis, recumbency, excitability, stupor, coma and death. HEARTGARD demonstrated no signs of toxicity at 10 times the recommended dose (60 mcg/kg) in sensitive Collies. Results of these trials and bioequivalency studies, support the safety of HEARTGARD products in dogs, including Collies, when used as recommended.

HEARTGARD Plus has shown a wide margin of safety at the recommended dose level in dogs, including pregnant or breeding bitches, stud dogs and puppies aged 6 or more weeks. In clinical trials, many commonly used flea collars, dips, shampoos, anthelmintics, antibiotics, vaccines and steroid preparations have been administered with HEARTGARD Plus in a heartworm disease prevention program.

In one trial, where some pups had parvovirus, there was a marginal reduction in efficacy against intestinal nematodes, possibly due to a change in intestinal transit time.

**HOW SUPPLIED:** HEARTGARD Plus is available in three dosage strengths (See DOSAGE section) for dogs of different weights. Each strength comes in convenient cartons of 6 and 12 chewables.

For customer service, please contact Merial at 1-888-637-4251.



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