Actinomycosis and nocardiosis are bacterial diseases that can affect both cats and dogs. The causative organisms of both diseases are gram-positive, filamentous bacteria that can be visualized directly on cytology from affected animals. The challenges of managing these infections are diagnosing and differentiating between the two causal bacteria and prescribing appropriate treatment for the infected animal.

Actinomycosis is caused by bacteria from the genus *Actinomyces*, which are either facultative or obligate anaerobic bacteria. These bacteria are found in the normal bacterial flora of mammalian mucous membranes, making inoculation into bite wounds a possible route of infection. However, the most common source of actinomycetic infection is the ingestion of grass florets or awns that have passed through and become contaminated by *Actinomyces* organisms within the oral cavity. These florets or awns then become entrenched within the body and serve as a nidus of infection. Classically, animals affected by actinomycosis present with chronic infections characterized by pleural and peritoneal exudates, dense fibrous masses, frank abscesses, and fistulous draining tracts. It is important to note that actinomycetic infections are caused by *Actinomyces* organisms in concert with other associated bacteria found in the oral cavity (i.e., these are mixed infections).

Nocardiosis is caused by bacteria from the genus *Nocardia*. These bacteria are aerobic, gram-positive bacteria that are present throughout the environment in soil, straw, grasses, decaying plant matter, and stagnant water. As part of their growth cycle, nocardial filaments fragment into small unicellular cells (similar to fungal spores) that are found in the environment. *Nocardia* organisms are not part of the normal mammalian flora but can be carried on the skin of the distal extremities in normal animals. Animals may become infected when they receive penetrating wounds carrying nocardial organisms into their body or through inhalation of the small nocardial sporelike cells from the environment. Classically, animals affected by *Nocardia* infection have clinical signs referable to the lungs and respiratory system with the possibility of systemic involvement of organ systems such as the skin, subcutaneous tissues, spleen, lymph nodes, central nervous system (CNS), bone, or joints. Unlike *Actinomyces* spp, *Nocardia* spp usually cause disease without the presence of other associated bacterial species.

### DIAGNOSTIC CRITERIA

#### Historical Information

**Gender Predisposition**

**Actinomycosis**
- Overall, male dogs are affected more commonly.
- Among hunting dogs, males and females are affected equally.
- Cats are infrequently affected.

**Nocardiosis**
- Male dogs are affected three times more often than females.
- Male cats are affected four times more often than females.
- Historically, dogs have been noted to be infected more commonly with nocardiosis than cats. However, in a recent retrospective study from Australia, 17 cats were found to be infected, but no dogs were.

**Age Predisposition**

**Actinomycosis**
- Young adult to middle-aged dogs.
- Cats are infrequently affected.

**Nocardiosis**
- Young dogs are primarily affected.
- There is no age predisposition in cats.

**Breed Predisposition**

**Actinomycosis**: Hunting dogs and large-breed dogs are most commonly affected.

**Nocardiosis**: No breed predisposition is noted.

#### Owner Observations

For both diseases, clinical signs vary depending on the organ system affected.
**Actinomycosis**

- **Cervicofacial**: Soft tissue swelling in the head and neck.
- **Thoracic or abdominal cavity**: Weight loss (often severe), fever, lethargy, decreased or absent appetite, paroxysmal cough, tachypnea, dyspnea, abdominal distension.
- **Retroperitoneal**: Thoracolumbar discomfort; paraparesis or tetraparesis; soft mass in the caudal thorax or flank, often with a draining sinus.
- **Cutaneous–subcutaneous**: Soft to firm mass with or without a draining sinus from the mass. The mass is typically located in the head or neck, lateral thoracic wall, or flank region.

**Nocardiosis**

- **Pulmonary**: Difficulty breathing, hemoptysis, collapse, sudden death, chronic weight loss, hyporexia, mucopurulent nasal discharge, paroxysmal cough, diarrhea (large or small bowel).
- **Systemic (disseminated)**: This form is typically a combination of the pulmonary form with a second organ system also affected. Therefore, the clinical signs are the same as noted above plus firm swellings with or without fistulous draining tracts (cutaneous or subcutaneous involvement), generalized seizures (CNS involvement), or mono- or multifocal joint effusion or lameness (joint involvement).
- **Solitary extrapulmonary**: Firm, painful swelling that may or may not rupture and drain (abscess); other firm swelling on the body (tumorlike growth).

**Other Historical Considerations/Predispositions**

**Actinomycosis**

- Dogs housed outside or that frequently participate in outdoor activities, such as hunting, are commonly affected.
- Dogs may contract actinomycosis in any of the localizations (cervicofacial, thoracic or abdominal cavity, retroperitoneal, or cutaneous–subcutaneous). There does not seem to be a predilection for dogs to contract disease with greater frequency at any particular location.
- Cats are most commonly affected by the thoracic cavity form (pyothorax) or cutaneous–subcutaneous form (abscesses).

**Nocardiosis**

- Approximately 27% of dogs have a concurrent underlying medical condition (e.g., canine distemper virus).
- Dogs are most commonly affected by the pulmonary form of disease.

**Public Health Considerations**

*Actinomyces and Nocardia infections cannot be transmitted from direct physical contact from clinically affected animals to people or from handling samples infected with either bacterium. However, Actinomyces spp can be transmitted to people through a bite wound from an animal, and Nocardia spp can be transmitted to people from the scratch or bite of an animal.*

- Cats are commonly affected by wounds or abscesses (solitary extrapulmonary form).
- The owner often reports that a nonhealing wound is present at the site of a previous standard bacterial abscess repair.

**Physical Examination Findings**

See Table 1.

**Laboratory Findings**

**Complete Blood Count**

- **Actinomycosis**: Results vary with the degree of systemic involvement of disease. In patients with localized disease, often no changes are noted in the complete blood count (CBC).
- **Disseminated or chronic disease**:
  - Mild to moderate nonregenerative anemia.
  - Neutrophilic leukocytosis with an elevated band neutrophil count and monocytosis.

- **Nocardiosis**: Nonregenerative anemia.

**Serum Chemistry**

- **Actinomycosis**: Localized disease: There are often no significant abnormalities.
- **Disseminated or chronic disease**: Hypoalbuminemia, hyperglobulinemia (can be marked), or hypoglycemia in cases with body cavity effusions.

- **Nocardiosis**: Hyperproteinemia characterized by hyperglobulinemia.
- Ionized hypercalcemia (associated with granulomatous disease).
- Specific changes indicating concurrent disease (e.g., azotemia with isosthenuria when the patient is in renal failure).
Urinalysis

- No specific findings.
- In cases with concurrent renal failure, isosthenuric specific gravity.

Other Diagnostic Findings

Thoracic Radiography

- Pulmonary abscesses or consolidation may sometimes be aspirated with a needle.
- Patients with diffuse airway disease are candidates for bronchoalveolar lavage or transtracheal wash so a sample for cytology can be obtained.

Abdominal Radiography or Abdominal Ultrasonography

- The spleen, liver, and other abdominal organs should be examined for abscess formation and aspirated if possible.
- Any free abdominal fluid should be located and sampled for cytologic examination.
If present, enlarged organs may be aspirated for cytologic examination.

Any solitary mass lesions within the abdomen should be recognized and aspirated.

**Echocardiography**

- In rare cases of endocarditis, a vegetative lesion is present on the mitral valve.

**Cytology**

Cytology of masses, draining lesions, and body cavity effusions should be done (Table 2). Ziehl-Niessen staining is the preferred method for determining if organisms are acid fast.

**Actinomycosis**

- Neutrophils with or without macrophages noted (suppurative to pyogranulomatous inflammation): Aspirates of firm masses may not display any inflammation.
- Mixed bacterial population with rods and cocci.
- *Actinomyces* organisms appear singly or in dense aggregates (macroscopic sulfur granules):
  - Gram positive, non–acid-fast filamentous organisms.
  - Occasionally, branched, nonbeaded filaments.
  - Aggregates are visible sulfur granules.

**Nocardiosis**

- Associated inflammation is less likely than with actinomycosis. Neutrophils with or without monocytes may be seen (suppurative to pyogranulomatous inflammation).
- Samples are rarely mixed bacterial populations.
- *Nocardia* organisms are usually found singly.
  - Gram-positive, partially or weakly acid-fast organisms.
  - Beaded and rarely branched filamentous organisms.
  — Although uncommon, when present, macroaggregates (sulfur granules) can be seen in the sample without microscopic examination.

**Culture and Sensitivity Testing**

- Samples for *Actinomyces* spp are anaerobic and grow on blood agar or enriched thioglycolate media. It is difficult to grow these organisms, but some species are facultative anaerobes that can be grown in aerobic conditions. Practitioners should expect at least three other bacterial species to grow from the same sample because actinomycosis is a mixed bacterial infection.
- *Nocardia* organisms are aerobic and grow on blood agar or other growth media at room temperature. The organisms are readily cultured. Rarely, a mixed bacterial infection is present.

**Histopathology of Tissue Samples**

**Actinomycosis**

- A core of neutrophils is seen encapsulated by fibrosing granulation tissue (macrophages, plasma cells, lymphocytes in a dense fibrous tissue matrix).
- Difficult-to-find, centrally located actinomycetic granules: The granules are round, oval, or scalloped amphophilic solid masses with outer basophilic bands. The granules are 30 to 3,000 μm in diameter.
- Visible gram-positive or -negative nonfilamentous bacteria may also be present.

**Nocardiosis**

- A central region of necrosis and neutrophils surrounded by macrophages, lymphocytes, and plasma cells is seen.
- The fibrous tissue is poorly structured, causing incomplete encapsulation of the lesion.
- Abundant nocardial organisms may be noted in the tissue individually or in loose aggregates.

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**TABLE 2**

**Summary of Cytologic Findings**

<table>
<thead>
<tr>
<th><strong>Actinomyces spp</strong></th>
<th><strong>Nocardia spp</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive and non–acid-fast organisms</td>
<td>Gram-positive and partially acid-fast organisms</td>
</tr>
<tr>
<td>Anaerobic or facultatively anaerobic organisms</td>
<td>Aerobic organisms</td>
</tr>
<tr>
<td>Staining rarely produces beading in organisms</td>
<td>Staining commonly produces beading in organisms</td>
</tr>
<tr>
<td>Suppurative to pyogranulomatous inflammation</td>
<td>Suppurative to pyogranulomatous inflammation</td>
</tr>
<tr>
<td>Mixed bacterial population (three to five associated organisms)</td>
<td>Rarely, other bacteria are noted</td>
</tr>
<tr>
<td>Long filamentous bacteria</td>
<td>Long filamentous bacteria</td>
</tr>
<tr>
<td>Macroscopic and microscopic dense mats of bacteria are common (sulfur granules)</td>
<td>Commonly present singly or in loose aggregates (rarely found in dense mats, e.g., sulfur granules)</td>
</tr>
</tbody>
</table>
Summary of Diagnostic Criteria

- Young male dogs are predominantly affected.
- A mass with a draining tract is commonly present and is often associated with chronic and nonspecific (e.g., anorexia, weight loss) or no clinical signs.
- Filamentous bacteria may be noted on cytology, often with associated supplicative to pyogranulomatous inflammation. It may be possible, especially in the case of actinomycosis, to see visible sulfur granules in the cytologic samples. The granules appear grossly as yellow, variably shaped particulate matter.
- Culture may be used to confirm the diagnosis. (Both aerobic and anaerobic cultures are recommended.)

Diagnostic Differentials

- Fungal infections (e.g., aspergillosis, blastomycosis) are ruled out with the presence of fungus on cytologic aspirates or histopathology, serum titers for fungal diseases, lesion distribution on the body, and patient history.
- Bacterial pneumonia is ruled out with radiography, bronchoalveolar lavage or transtracheal wash, and patient history.
- Mycobacterium, Rhodococcus, Corynebacterium, or Dermatophilus infection causing pyogranulomatous inflammation is ruled out with culturing and RNA sequencing for mycobacteria. Mycobacterial panniculitis in cats includes lesions that are grossly indistinguishable from subcutaneous or cutaneous nocardial disease.
- Other bacterial abscesses are ruled out with cytology (nonfilamentous bacteria; only rods and cocci).
- Diskospondylitis and intervertebral disk disease are ruled out with spinal radiography, myelography, or computed tomography (CT). Diskospondylitis lesions are typically found on the vertebral end plates rather than the ventral aspect of the vertebrae as with Actinomyces spp.
- Brain tumors, intracranial vascular lesions, and infectious or inflammatory brain diseases are ruled out with spinal fluid analysis or CT scanning or magnetic resonance imaging of the brain.

Treatment Recommendations

Initial Treatment

- If possible, exudate (e.g., pyothorax, subcutaneous abscess) should be drained and lavaged.
  - For cats with pyothorax, chest tubes should be placed for lavage, continuous suction, and removal of material. Chest tubes should be removed when purulent exudate becomes serosanguineous (4–10 days).
  - For dogs with pyothorax, recommendations include surgical exploration and chest lavage before chest tube placement rather than non-surgical management with chest tubes.
- Subcutaneous abscesses should be lanced and the purulent material lavaged.
- Other antibiotics within the same antibiotic family should not be substituted; only the antibiotics specified on the following list should be used to treat these infections.

Actinomycosis

- Penicillin is the antibiotic of choice. After drainage of any free fluid, abscesses, and so on, the patient should be started on antibiotic therapy. Prolonged therapy is necessary for penetration of dense granulomatous tissues. Parenteral therapy should not be started unless the patient is unable to tolerate oral therapy because of vomiting or inappetence. It is acceptable to start oral therapy immediately. Oral medication should be given 1 hour before or 2 hours after feeding. (Food reduces the absorption of penicillins.) The patient should be treated for weeks to months after resolution of clinical signs.
  - Penicillin G: 100,000 U/kg IV, IM, or SC q6–8h. Practitioners should be sure to carefully look at the penicillin formulation for the appropriate concentration. Veterinary formulations include:
    - Procaine penicillin G: 300,000–500,000 U/ml (IM injection).
    - Benzathine penicillin G: 300,000 U/ml (parenteral).
    - Procaine and benzathine combination product: 300,000–600,000 U/ml.
  - For IV usage, the entire daily patient dosage of aqueous penicillin should be infused over 24 hours in the patient’s daily fluids. For example, a 10-kg dog may receive 6,000,000–8,000,000 U of penicillin (100,000 U/kg q6–8h) in 600 ml (60 ml/kg/day) of crystalloid fluids over 24 hours (if receiving maintenance IV fluids).
  - For IM or SC usage, 100,000 U/mL concentration should be administered. No more than 10 ml of procaine or benzathine penicillin should be administered in any one location intramuscularly.
    - Penicillin G (benzyl penicillin) or penicillin V (phenoxyethyl penicillin): 40 mg/kg q8h PO.
- Other antibiotics:
  - Clindamycin: 5 mg/kg SC q12h.
  - Erythromycin: 10 mg/kg PO q8h.
  - Chloramphenicol: 50 mg/kg PO, IV, IM, or SC q8h for dogs and q12h for cats.
  - Rifampin: 10 mg/kg PO q12h for dogs.
— Minocycline: 5–25 mg/kg IV PO q12h.
— Ampicillin (amoxicillin): 20–40 mg/kg IM, SC, or PO q6h.

Nocardiosis
- Antibiotic therapy is recommended for extended periods (1 to 3 months for cutaneous infections, 6 months for pulmonary infections, and 12 months or longer for systemic infections or if the patient is immunocompromised). $–$$
- Use of combinations of drugs (sulfonamide plus another drug) is only necessary in severely ill patients, immunocompromised patients, and patients with another underlying condition. $–$$
- Sulfonamides (including trimethoprim-sulfamethoxazole) are drugs of choice and should be used in addition to drainage of exudates or abscesses. Patients may hypersalivate, vomit, or refuse to eat while taking oral medications. Myelosuppression or keratoconjunctivitis sicca may develop from long-term use of sulfa drugs (see Treatment Contraindications). $–$$
  — Triple sulfa no. 4: 120 mg/kg IV initially and then 60 mg/kg IV q12h. This drug is most useful when patients are anorexic or debilitated and unable to take oral dosing. It can be used in patients exhibiting signs of vomiting or inappetence.
  — Trimethoprim–sulfadiazine: 15–30 mg/kg q12h.
  — Sulfadiazine: 80 mg/kg PO q8h.
  — Sulisoxazole: 50 mg/kg PO q8h.
- Other antibiotics: (usefulness may vary with the exact species of Nocardia because some species are resistant):  
  — Amikacin: 8–12 mg/kg IV, IM, or SC q8h. $–$$
  — Imipenem–cilastatin: 2–5 mg/kg IV q8h. $–$$–$$
  — Cefotaxime: 20–80 mg/kg IV or IM q6h. $–$$–$$
  — Minocycline: 5–25 mg/kg IV or PO q12h. $–$$
  — Erythromycin: 10 mg/kg PO q8h. $–$$
  — Ampicillin: 20–40 mg/kg IV, IM, SC, or PO q6h. $–$$
  — Linezolid: 8–20 mg/kg PO q24h. $–$$–$$

Alternative/Optional Treatments/Therapy
- In some cases, granulomatous disease cannot be cured with antibiotic therapy alone. Pulmonary abscesses often require exploratory thoracotomy and lung lobectomy. $–$$–$$
- In cases of solitary masses involving the walls of the thoracic and abdominal cavities, radical excision may be required to remove disease. Excision should always be done after several weeks of antibiotic therapy in an attempt to reduce the size of these masses before surgery. $–$$–$$

Supportive Treatment
- Oxygen therapy should be provided if necessary (i.e., with pulmonary involvement). $–$$
- IV fluid therapy should be provided for patients with dehydration or hypovolemia. $–$$
- A feeding tube should be used if necessary. $–$$
- If the patient has had any sort of thoracic or abdominal surgery, hospitalization with analgesic medications, postoperative monitoring, and IV fluid therapy is needed. $–$$–$$

Patient Monitoring
- Thoracic radiography should be performed if pulmonary or pleural space disease is present. The patient should be monitored for resolution of pleural fluid and resolution of pulmonary disease (e.g., abscesses, lobar consolidation, pulmonary parenchymal disease). $–$$
- Abdominal ultrasonography (with or without abdominal radiography) should be repeated to monitor resolution of abdominal abscesses, organomegaly, and free abdominal fluid. $–$$

ON THE NEWS FRONT
- The physician-based literature is riddled with reports of nocardial infections in immunosuppressed patients (e.g., patients with human immunodeficiency virus, organ transplant recipients, and persons with immune-mediated disease). At this time, the veterinary literature has a few case reports of animals receiving immunosuppressive drugs and contracting Nocardia infections. Based on this information, it is prudent to keep actinomycosis and nocardiosis on the differential diagnosis list when an animal is immunosuppressed for other reasons (including feline renal transplant patients).

- The physician-based literature also points out some relatively unusual fomites for actinomycotic infection, including intrauterine contraceptive devices in women. As veterinary medicine expands its armament of implants used in animals, there is a possibility that similar unusual fomites will be found to transmit Actinomyces spp to veterinary patients.

- In cases of actinomycosis, whenever surgery is required, an attempt should be made to find the grass floret or awn that is the persistent source of infection. $–$$–$$
- Antibiotic therapy is required before, during, and after surgery. $–$$

ON THE NEWS FRONT
• All subcutaneous masses should be measured and palpated to ensure that they are decreasing in size with treatment.
• Serial physical examinations should be done to monitor the patient’s clinical response to therapy.

**Home Management**
• The owner should continue administering the animal’s antibiotic therapy until directed to stop by a veterinarian.
• Any palpable masses should be monitored at home for resolution.
• Any other underlying or concurrent disease should be treated with the indicated treatment. (As noted previously, up to 27% of nocardial infections are found with other concurrent diseases).

**Milestones/Recovery Time Frames**
• Resolution of respiratory distress or increased inspiratory effort.
• Resolution of any subcutaneous masses.
• Improved appetite and weight gain.
• Treatment should continue for 2 to 3 weeks after all visible signs of disease are gone. If the patient is immunocompromised, then treatment should continue for months after visible signs of disease have resolved.

**Treatment Contraindications**
• If surgical resection indicated, the practitioner should try to minimize the amount of resection. Actinomycetic granulomas are often highly vascularized and can bleed profusely during and after surgery.
• To maximize the patient’s outcome, the patient should be stable before being anesthetized.
• Long-term sulfonamide drug therapy for nocardiosis can lead to a variety of side effects.
  — Cats may experience severe anorexia, vomiting, or weight loss while on sulfonamide drug therapy. Suggestions to combat these side effects include compounding sulfonamide drugs into gelatin capsules that can be given to patients or treating with other alternative antibiotics alone or in combination (guided by culture and sensitivity results). There are some indications that multiple-drug therapy may be best when sulfonamide drugs are not being used because in vitro culture results do not always predict in vivo results.
  — Myelosuppression (anemia and leukopenia): It is important to monitor serial CBCs during treatment.
  — Keratoconjunctivitis sicca: Serial Schirmer tear tests should be performed.
  — Hepatotoxicity: Blood work and clinical signs (anorexia, depression, icterus) should be monitored.
  — Immune-mediated disease, including polyarthritis, retinitis, glomerulonephritis, vasculitis, and various skin disorders: Serial physical examinations should be performed.
  — Cutaneous drug eruptions causing skin disease ranging from dermatitis to toxic epidermal necrolysis: Serial physical examinations should be performed.
  — Renal failure (especially in cats): Renal values, urine specific gravity, and the patient’s clinical signs should be monitored.
  — Dogs may develop hypothyroidism after long-term usage of sulfonamide drugs.

**PROGNOSIS**

**Favorable Criteria**
• Highly localized disease without systemic involvement.
• Cutaneous or subcutaneous localization.
• Fast initial response to antibiotics.
• No other underlying or concurrent disease, especially those causing immunosuppression.

**Unfavorable Criteria**
• Concurrent immunosuppressive disease.
• Systemic or disseminated disease.
• Severely debilitated patient at time of diagnosis.
• In a study of 17 cats with nocardiosis, only three cats were cured, and four cats relapsed several months after apparent cure.

**RECOMMENDED READING**


