

# 199 Nocardiosis

Gregory A. Filice

*Nocardia*, a genus of saprophytic aerobic actinomycetes that are common worldwide, resides in soil, contributing to the decay of organic matter. Nearly 100 species have been identified, mostly on the basis of 16S rRNA gene sequences. Nocardiae are relatively inactive in standard biochemical tests, and speciation is difficult without molecular phylogenetic techniques. Historically, the majority of isolates associated with pneumonia and systemic disease were identified as *Nocardia asteroides*, but the lineage of the type strain was muddled, and it is now clear that human disease is associated with several species. Most clinical laboratories cannot speciate isolates accurately and may identify them simply as *N. asteroides* or *Nocardia* species.

Nine species or species complexes are commonly associated with human disease (Table 199-1). Most systemic disease involves *Nocardia cyriacigeorgica*, *Nocardia farcinica*, *Nocardia pseudobrasiliensis*, and species in the *Nocardia transvalensis* and *Nocardia nova* complexes.

**TABLE 199-1** *NOCARDIA* SPECIES MOST COMMONLY ASSOCIATED WITH HUMAN DISEASE AND THEIR IN VITRO SUSCEPTIBILITY PATTERNS

Species	Susceptible to	Resistant to
<i>N. abscessus</i>	Amikacin, amoxicillin/clavulanic acid, ampicillin, ceftriaxone, gentamicin, linezolid, minocycline, TMP-SMX	Ciprofloxacin, clarithromycin, erythromycin, imipenem (v) <sup>a</sup>
<i>N. brevicatena/paucivorans</i> complex ( <i>N. brevicatena</i> , <i>N. paucivorans</i> , <i>N. carnea</i> , others)	Amikacin, amoxicillin/clavulanic acid, ampicillin, ceftriaxone, ciprofloxacin, linezolid, minocycline (v), moxifloxacin, tobramycin, TMP-SMX	Ciprofloxacin, clarithromycin, erythromycin, gentamicin, imipenem (v)
<i>N. nova</i> complex ( <i>N. nova</i> , <i>N. veterana</i> , <i>N. africana</i> , <i>N. kruczakiae</i> , <i>N. elegans</i> , others)	Amikacin, ampicillin, ceftriaxone, clarithromycin, erythromycin, imipenem, linezolid, minocycline, TMP-SMX	Amoxicillin/clavulanic acid, ciprofloxacin, gentamicin, tobramycin
<i>N. transvalensis</i> complex ( <i>N. blacklockiae</i> , <i>N. wallacei</i> , others)	Amoxicillin/clavulanic acid (v), ceftriaxone (v), ciprofloxacin, linezolid, minocycline (v), TMP-SMX	Amikacin, ampicillin, clarithromycin, erythromycin, gentamicin, imipenem (v)
<i>N. farcinica</i>	Amikacin, amoxicillin/clavulanic acid, imipenem (v), linezolid, minocycline (v), TMP-SMX	Ampicillin, ceftriaxone, ciprofloxacin, clarithromycin, erythromycin, gentamicin, tobramycin
<i>N. cyriacigeorgica</i>	Amikacin, ceftriaxone (v), imipenem, linezolid, minocycline (v), TMP-SMX	Amoxicillin/clavulanic acid, ampicillin (v), ciprofloxacin, erythromycin, gentamicin
<i>N. brasiliensis</i>	Amikacin, amoxicillin/clavulanic acid, minocycline, moxifloxacin, TMP-SMX	Ampicillin, ceftriaxone, ciprofloxacin, clarithromycin, imipenem
<i>N. pseudobrasiliensis</i>	Amikacin, ceftriaxone (v), ciprofloxacin, clarithromycin, TMP-SMX	Amoxicillin/clavulanic acid, ampicillin, imipenem, minocycline
<i>N. otitidiscaviarum</i> complex	Amikacin, ciprofloxacin, gentamicin, TMP-SMX	Amoxicillin/clavulanic acid, ampicillin, ceftriaxone, imipenem

<sup>a</sup>Variable.

**Abbreviation:** TMP-SMX, trimethoprim-sulfamethoxazole.

**Source:** Adapted from multiple sources.

*Nocardia brasiliensis* is usually associated with disease limited to the skin. Actinomycetoma—an indolent, slowly progressive disease of skin and underlying tissues with nodular swellings and draining sinuses—is often associated with *N. brasiliensis*, *Nocardia otitidiscaviarum*, *N. transvalensis* complex strains, or other actinomycetes.

## EPIDEMIOLOGY



Nocardiosis occurs worldwide. The annual incidence, estimated on three continents (North America, Europe, and Australia), is ~0.375 cases per 100,000 persons and may be increasing. The disease is more common among adults than among children and more common among males than among females. Nearly all cases are sporadic, but outbreaks have been associated with contamination of the hospital environment, cosmetic procedures, and parenteral illicit drug use. Person-to-person spread is not well documented. There is no known seasonality.

The majority of cases of pulmonary or disseminated disease occur in people with a host defense defect. Most have deficient cell-mediated immunity, especially that associated with lymphoma, transplantation, glucocorticoid therapy, or AIDS. The incidence is ~140-fold greater among patients with AIDS and ~340-fold greater among bone marrow transplant recipients than in general populations. In AIDS, nocardiosis usually affects persons with <250 CD4+ T lymphocytes/μL. Nocardiosis has also been associated with pulmonary alveolar proteinosis, tuberculosis and other mycobacterial diseases, chronic granulomatous disease, interleukin 12 deficiency, and treatment with monoclonal antibodies that interfere with tumor necrosis factor. Any child with nocardiosis and no known cause of immunosuppression should undergo tests to determine the adequacy of the phagocytic respiratory burst.

Cases of actinomycetoma occur mainly in tropical and subtropical regions, especially those of Mexico, Central and South America, Africa, and India. The most important risk factor is frequent contact with soil or vegetable matter, especially in laborers.

## PATHOLOGY AND PATHOGENESIS

Pneumonia and disseminated disease are both thought to follow inhalation of fragmented bacterial mycelia. The characteristic histologic feature of nocardiosis is an abscess with extensive neutrophil infiltration and prominent necrosis. Granulation tissue usually surrounds the lesions, but extensive fibrosis or encapsulation is uncommon.

Actinomycetoma is characterized by suppurative inflammation with sinus tract formation. Granules—microcolonies composed of dense masses of bacterial filaments extending radially from a central core—are occasionally observed in histologic preparations. The granules are frequently found in discharges from lesions of actinomycetoma but almost never in discharges from lesions in other forms of nocardiosis.

Nocardiae have evolved a number of properties that enable them to survive within phagocytes, including neutralization of oxidants, prevention of phagosome-lysosome fusion, and prevention of phagosome acidification. Neutrophils phagocytose the organisms and limit their growth but do not kill them efficiently. Cell-mediated immunity is important for definitive control and elimination of nocardiae.

## CLINICAL MANIFESTATIONS

**Respiratory Tract Disease** Pneumonia, the most common form of nocardial disease in the respiratory tract, is typically subacute; symptoms have usually been present for days or weeks at presentation. The onset is occasionally more acute in immunosuppressed patients. Cough is prominent and produces small amounts of thick, purulent sputum that is not malodorous. Fever, anorexia, weight loss, and malaise are common; dyspnea, pleuritic pain, and hemoptysis are less common. Remissions and exacerbations over several weeks are frequent. Roentgenographic patterns vary, but some are highly suggestive of