with nocardial pneumonia, a careful history should be obtained and a thorough physical examination performed. Suggestive symptoms or signs should be pursued with further diagnostic tests. Computed tomography (CT) or magnetic resonance imaging (MRI) of the head, with and without contrast material, should be undertaken if signs or symptoms suggest brain involvement. Some authorities recommend brain imaging in all cases of pulmonary or disseminated disease. When clinically indicated, CSF or urine should be concentrated and then cultured. Actinomycetoma, eumycetoma (cases involving fungi; **Chap. 243**), and botryomycosis (cases involving cocci or bacilli, often *Staphylococcus aureus*) are difficult to distinguish clinically but are readily distinguished with microbiologic testing or biopsy. Granules should be sought in any discharge. Suspect particles should be washed in saline, examined microscopically, and cultured. Granules in actinomycetoma cases are usually white, pale yellow, pink, or red. Viewed microscopically, they consist of tight masses of fine filaments (0.5–1 μm wide) radiating outward from a central core (Fig. 199-5). Granules from eumycetoma cases are white, yellow, brown, black, or green. Under the microscope, they appear as masses of broader filaments (2–5 μm wide) encased in a matrix. Granules of botryomycosis consist of loose masses of cocci or bacilli. Organisms can also be seen in wound discharge or histologic specimens. The most reliable way to differentiate among the various organisms associated with mycetoma is by culture.

Isolation of nocardiae from sputum or blood occasionally represents colonization, transient infection, or contamination. In typical cases of respiratory tract colonization, Gram-stained specimens are negative and cultures are only intermittently positive. A positive sputum culture in an immunosuppressed patient usually reflects disease. When nocardiae are isolated from sputum of an immunocompetent patient without apparent nocardial disease, the patient should be observed carefully without treatment. A patient with a host-defense defect that increases the risk of nocardiosis should usually receive antimicrobial treatment.

TREATMENT NOCARDIOSIS

For mild or moderate cases, therapy with drugs known to be effective against most isolates is usually adequate. For severe cases or cases that do not respond promptly to antimicrobial therapy, isolates should be sent to a laboratory experienced with *Nocardia* for identification and susceptibility testing. Identification of an isolate to the species level is accomplished with molecular testing, and susceptibility is assessed with a Clinical Laboratory Standards Institute (CLSI)–approved broth dilution test. Nocardial growth is slower than the growth of most clinically important bacteria, and nocardiae tend to clump in suspension so that susceptibility test endpoints are unusual; thus experience is necessary for reliable results. Because nocardiosis is uncommon, data on the relation between susceptibility test results for specific drugs and clinical outcomes in patients treated with these drugs are meager. Careful clinical monitoring is essential, and consultation with clinicians who have experience with nocardiosis is often needed.

Sulfonamides are the drugs of choice **(Tables** 199-1 and **199-2)**. The combination of sulfamethoxazole (SMX) and trimethoprim (TMP) is at least equivalent to a sulfonamide alone and may be slightly more effective, but the combination also poses a modestly greater risk of hematologic toxicity. At the outset, 10–20 mg/kg of TMP and 50–100 mg/kg of SMX are given each day in two divided doses. Later, daily doses can be decreased to as little as 5 mg/kg and 25 mg/kg, respectively. In persons with sulfonamide allergies, desensitization usually allows continuation of therapy with these effective and inexpensive drugs.

Sulfonamide susceptibility testing is difficult. The CLSI standard methodology includes a technique for TMP-SMX but not for a sulfonamide alone. Reported rates of sulfonamide susceptibility have varied widely, and controversy has ensued about the reliability of sulfonamides for therapy. However, clinical responses to appropriate sulfonamide treatment are nearly always satisfactory. Sulfonamides remain the drugs of choice in nearly all cases.

TABLE 199-2 TREATMENT DURATION FOR NOCARDIOSIS

Disease	Duration
Pulmonary or systemic	
Intact host defenses	6–12 months
Deficient host defenses	12 months[a]
CNS disease	12 months[b]
Cellulitis, lymphocutaneous syndrome	2 months
Osteomyelitis, arthritis, laryngitis, sinusitis	4 months
Actinomycetoma	6–12 months after clinical cure
Keratitis	Topical: until apparent cure
	Systemic: until 2–4 months after apparent cure

[a]In some patients with AIDS and CD4+ T lymphocyte counts of <200/μL or with chronic granulomatous disease, therapy for pulmonary or systemic disease must be continued indefinitely. [b]If all apparent CNS disease has been excised, the duration of therapy may be reduced to 6 months.

Clinical experience with other oral drugs is limited. Minocycline (100–200 mg twice a day) is often effective; other tetracyclines are usually less effective. Linezolid is active against all species in vitro and in vivo, but adverse effects are common with long-term use. Tigecycline appears to be active in vitro against some species, but little clinical experience has been reported. Amoxicillin (875 mg) combined with clavulanic acid (125 mg), given twice a day, has been effective but should be avoided in cases involving strains of the *N. nova* complex, in which clavulanate induces β-lactamase production. Among the quinolones, moxifloxacin and gemifloxacin appear to be most active.

Amikacin, the best-established parenteral drug except in cases involving the *N. transvalensis* complex, is given in doses of 5–7.5 mg/kg every 12 h or 15 mg/kg every 24 h. Serum drug levels should be monitored during prolonged therapy in patients with diminished renal function and in the elderly. Ceftriaxone and imipenem are usually effective except as indicated in Table 199-1.

Patients with severe disease are initially treated with a combination including TMP-SMX, amikacin, and ceftriaxone or imipenem. Clinical improvement is usually noticeable after 1–2 weeks of therapy but may take longer, especially with CNS disease. After definite clinical improvement, therapy can be continued with a single oral drug, usually TMP-SMX. Some experts use two or more drugs for the entire course of therapy, but whether multiple drugs are better than a single agent is not known, and additional drugs increase the risk of toxicity. In patients with nocardiosis who need immunosuppressive therapy for an underlying disease or prevention of transplant rejection, immunosuppressive therapy should be continued.

Use of SMX and TMP in high-risk populations to prevent *Pneumocystis* disease or urinary tract infections appears to reduce but not eliminate the risk of nocardiosis. The incidence of nocardiosis is low enough that prophylaxis solely to prevent this disease is not recommended.

Surgical management of nocardial disease is similar to that of other bacterial diseases. Brain abscesses should be aspirated, drained, or excised if the diagnosis is unclear, if an abscess is large and accessible, or if an abscess fails to respond to chemotherapy. Small or inaccessible brain abscesses should be treated medically; clinical improvement should be noticeable within 1–2 weeks. Brain imaging should be repeated to document the resolution of lesions, although abatement on images often lags behind clinical improvement.

Antimicrobial therapy usually suffices for nocardial actinomycetoma. In deep or extensive cases, drainage or excision of heavily involved tissue may facilitate healing, but structure and function should be preserved whenever possible. Keratitis is treated with topical sulfonamide or amikacin drops plus a sulfonamide or an alternative drug given by mouth.