ACTINOMYCES & NOCARDIA

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Actinomyces and Nocardia are Gram-positive rods characterized by filamentous, tree-like branching growth, which has caused them to be confused with fungi in the past. They are opportunists that can sometimes produce indolent, slowly progressive diseases.
**ACTINOMYCES**

- **Phylum**: Actinobacteria
- **Order**: Actinomycetales
- **Family**: Actinomycetaceae
- **Genus**: "Actinomyces"

- Most common recognized infections: oral and cervicofacial regions
- The thoracic region, abdominopelvic region, and the CNS also frequently can be involved.
- Most human actinomycosis is caused by *A. israelii*
- *A. naeslundii, A. odontolyticus, A. viscosus, A. meyeri* also cause human actinomycosis
Normal inhabitants of some areas of the GI tract of humans and animals from the oropharynx to the lower bowel.

- Grow slowly (4–10 days) under microaerophilic (6-10% ambient CO₂) or strictly anaerobic conditions.
- Actinomyces grow well in enriched media with brain-heart infusion. They grow best at 37°C. Colonies can appear at 3-7 days, but to ensure that no growth is missed, observe cultures for 21 days.
Agar plate culture of *Actinomyces* sp.
Actinomyces sp. Gram stain.
Typically appear as elongated Gram-positive rods that branch at acute angles

In pus, the most characteristic form is the sulfur granule: yellow–orange granule, named for its gross resemblance to sulfur.

Sulfur granule is a small colony (usually <0.3 mm) of intertwined branching Actinomyces filaments solidified with elements of tissue exudate.
Sulfur granule. The bacteria are clearly seen to be Gram-positive and branching only at the edge.
ACTINOMYCOSIS

- Def: chronic inflammatory condition originating in the tissues adjacent to mucosal surfaces
- Lesions: a slow burrowing course with induration and draining sinuses eventually opening through the skin
- Localized swelling with suppuration, abscess formation, tissue fibrosis, and draining sinuses characterize this disease.
- Human cases provide little evidence of immunity to Actinomyces
- Case-to-case transmission does not appear to occur
ACTINOMYCOSIS MANIFESTATIONS:

- Infection of the cervicofacial area, the most common site of actinomycosis is usually related to poor dental hygiene, tooth extraction, or some other trauma to the mouth or jaw.

- Lesions in the submandibular region and the angle of the jaw give the face a swollen, indurated appearance.

- Thoracic and abdominal actinomycoses are rare.

- The firm, fibrous masses are often initially mistaken for a malignancy.

- Pelvic involvement as an extension from other sites also occurs occasionally.
Cervicofacial actinomycosis. Note the “lumpy jaw” swelling and the draining sinuses at the angle of the jaw.
ACTINOMYCOSIS

DIAGNOSIS

- Based on the nature of the lesion, the slowly progressive course, and a history of trauma or of a condition predisposing to mucosal invasion by Actinomyces

- Difficult etiologic diagnosis: the organisms in pus may be few and concentrated in sulfur granule microcolonies deep in the indurated tissue

- Identification requires a variety of biochemical tests to differentiate Actinomyces from propionibacteria
ACTINOMYCOSIS

DIAGNOSIS

- Biopsies for culture and histopathology are useful, but it may be necessary to examine many sections and pieces of tissue before sulfur granule colonies of Actinomyces are found.

- With HE (hematoxylin and eosin), the edge of the granule shows amorphous eosinophilic “clubs” formed from the tissue elements and containing the branching actinomycotic filaments.
The sulfur granule (pink-purple) is surrounded by lymphocytes at periphery.
Treatment of choice: **Penicillin G**

Other antimicrobics (tetracycline, erythromycin, clindamycin) are active in vitro and have shown some clinical effectiveness.

High doses of penicillin must be used and therapy prolonged for 4 to 6 weeks or longer before any response is seen.
NOCARDIA

- Gram-positive, rod-shaped bacteria that show true branching both in culture and in stains from clinical lesions.
- Microscopic morphology is similar to that of Actinomyces.
- The species most common in human infection (N. asteroides and N. brasiliensis) are weakly acid fast.
- Nocardia species are ubiquitous in the environment, particularly in soil.
- Strict aerobes, Growth on blood agar after 2 to 3 days incubation.
- Colonies initially have a dry, wrinkled, chalk-like appearance, are adherent to the agar, and eventually develop white to orange pigment.
Nocardia in sputum. Note the filamentous bacteria forming treelike branches among the neutrophils.
Rough chalky-white colonies of *Nocardia brasiliensis* grown on Columbia blood agar
Nocardiosis occurs in two major forms:

- The pulmonary form is an acute bronchopneumonia with dyspnea, cough and sputum production.

- A cutaneous form produces localized pustules in areas of traumatic inoculation usually the exposed areas of the skin.

- The pulmonary form of disease follows inhalation of aerosolized bacteria.

- The cutaneous form follows injection by a thorn prick or similar accident.

- No case-to-case transmission.
Factors leading to disease following inhalation of Nocardia are poorly understood.

No specific virulence factors are known, but it is able to resist the microbicidal actions of phagocytes (may be related to disruption of phagosome acidification).

Primary lesions in the lung show acute inflammation, with suppuration and destruction of parenchyma.

Multiple, confluent abscesses may occur.

Unlike Actinomyces infections, there is little tendency toward fibrosis and localization.
Nocardiosis

Pathogenesis

- Dissemination to distant organs, particularly the brain, may occur. In the central nervous system (CNS), multifocal abscesses are often produced.
- The great majority of Nocardia pulmonary and brain infections are produced by N. asteroides.
- Skin infections follow direct inoculation of Nocardia (associated with minor trauma).
- The species is usually N. brasiliensis, which produces a superficial pustule at the site of inoculation.
If *Nocardia* gain access to the subcutaneous tissues, lesions resembling actinomycosis may be produced, complete with draining sinuses and sulfur granules.

This infection may occur with *Nocardia* species or related organisms.

T cell–mediated immunity is dominant in host defense against *Nocardia* infection.
Nocardiosis Manifestations

- Pulmonary infection: bronchopneumonia, including cough, dyspnea, and fever
- Production of cavities and extension to the pleura are common.
- The clinical signs of brain abscess depend on its exact location and size
- The combination of current or recent pneumonia and focal CNS signs is suggestive of Nocardia infection.
- Cutaneous infection: involves a pustule, fever, and tender lymphadenitis in the regional lymph nodes.
Nocardiosis Diagnosis

- Much easier than that of actinomycosis, because the organisms are present in greater numbers throughout the lesions.
- *Nocardia* can usually be found in sputum and in direct aspirates from skin or other purulent sites.
- **Culture:** easy
- **Acid-fast stain:** diagnostic of *N. Asteroides* or *N. brasiliensis.*
Nocardiosis

TREATMENT

- Susceptible to sulfonamide, but relatively resistant to penicillin
- The trimethoprim–sulfamethoxazole combination is the most widely used chemotherapeutic regimen.
- Susceptibility test: difficult → hampered the rational selection and study of other antimicrobics, but various reports support clinical activity of newer -lactams (imipenem, ceftriaxone), minocycline, and aminoglycosides.
- Antituberculous agents and antifungal agents such as amphotericin B have no activity against Nocardia.