

Aspergillosis

- Aspergillosis comprises a broad spectrum of diseases caused by members of the genus *Aspergillus* . Exposure to *Aspergillus* in the environment may cause allergic reactions in hypersensitized hosts or destructive, invasive, pulmonary, and disseminated disease in highly immunosuppressed individuals.

- *A. fumigatus*
- *A. flavus*
- *A. niger*
- *A. terreus*

Diseases Caused by *Aspergillus*

Allergic Reactions

Nasal cavity
Paranasal sinuses
Lower respiratory tract

Colonization

Obstructed paranasal sinuses
Bronchi
Preformed pulmonary cavities

Superficial Cutaneous Infections

Wounds
Catheter sites

Limited Invasive Infections

Mildly immunodeficient patients
Bronchi
Pulmonary parenchyma

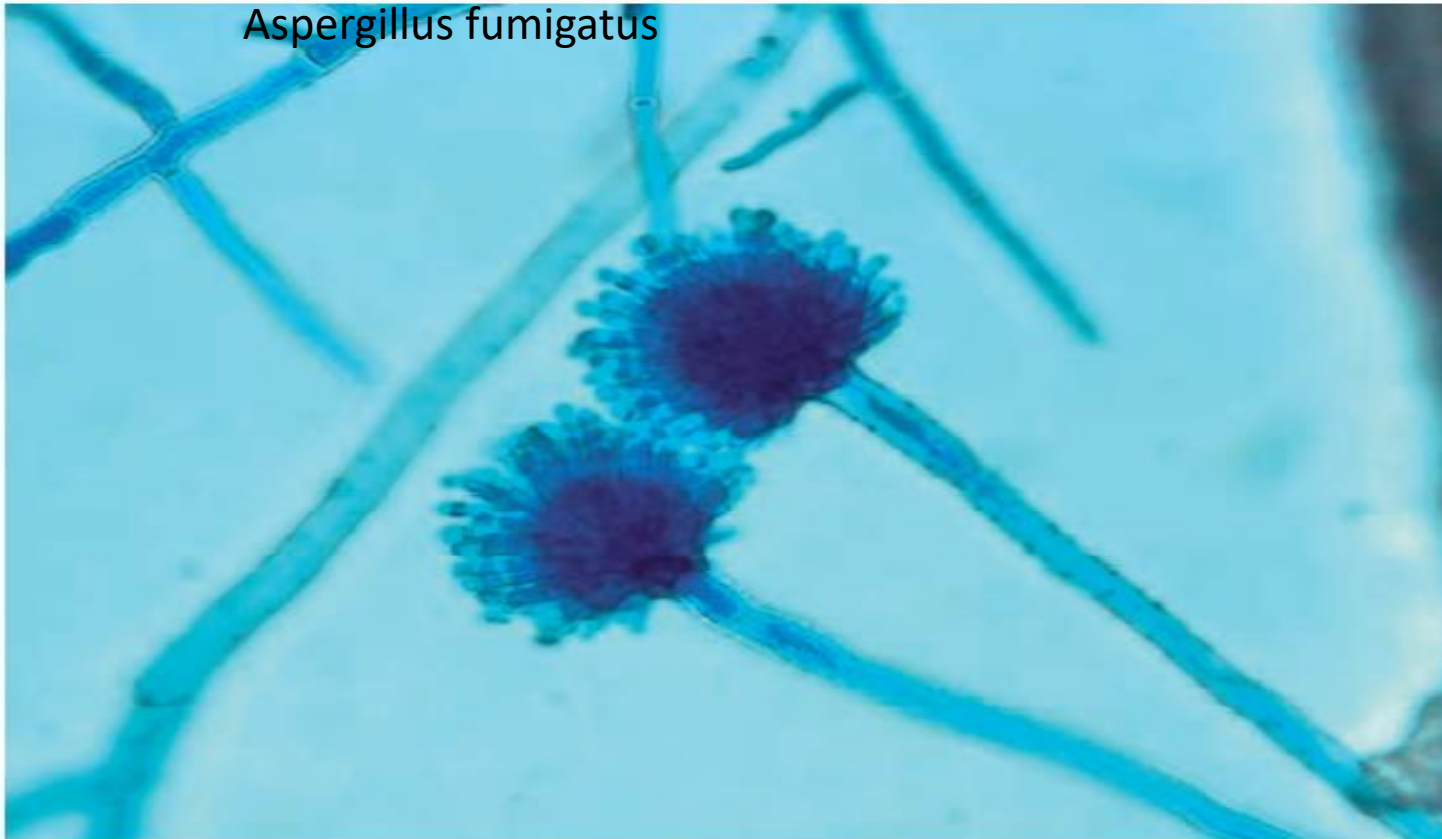
Frankly Invasive Pulmonary Infection

Severely immunodeficient patients
Pulmonary vasculature and parenchyma
Systemic dissemination
Death

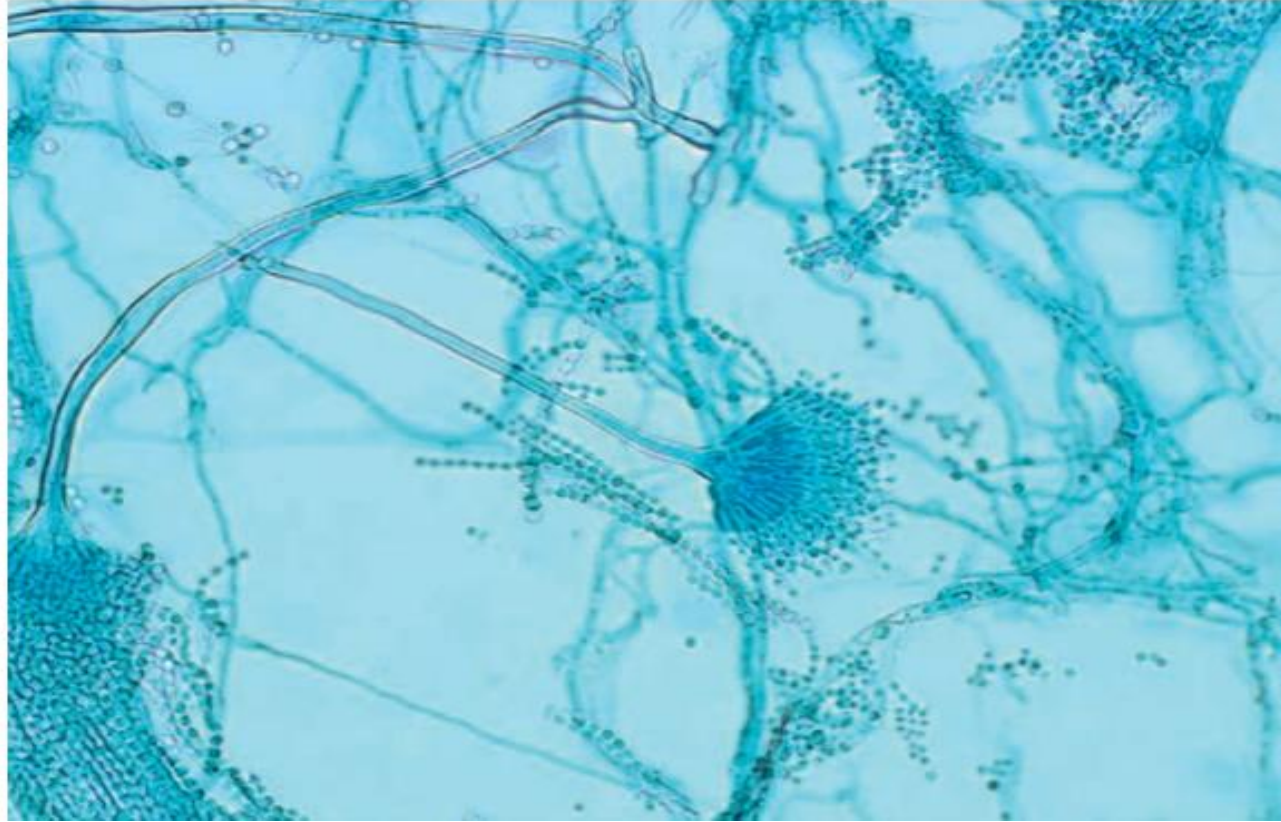
Morphology

- Aspergillus spp. grow in culture as hyaline molds. On a gross level, the colonies of Aspergillus may be black, brown, green, yellow, white, or other colors, depending upon the species and the growth conditions.
- Aspergilli grow as branched septate hyphae that produce conidial heads when exposed to air in culture and tissue. A conidial head consists of a conidiophore with a terminal vesicle, on which are borne one or two layers of phialides, or sterigmata.
- The elongated phialides in turn produce columns of spherical conidia, which are the infectious propagules from which the mycelial phase of the fungus develops.
- The hyphae are homogeneous, uniform in width (3 to 6 μm), with parallel contours, regular septations, and a progressive treelike pattern of branching.
- The branches are dichotomous and usually arise at acute (≈ 45 -degree) angles. The hyphae may be seen within blood vessels (angioinvasion), causing thrombosis.
- The important species *A. terreus* can be identified in tissue by its spherical or oval aleurioconidia that develop from the lateral walls of the mycelium

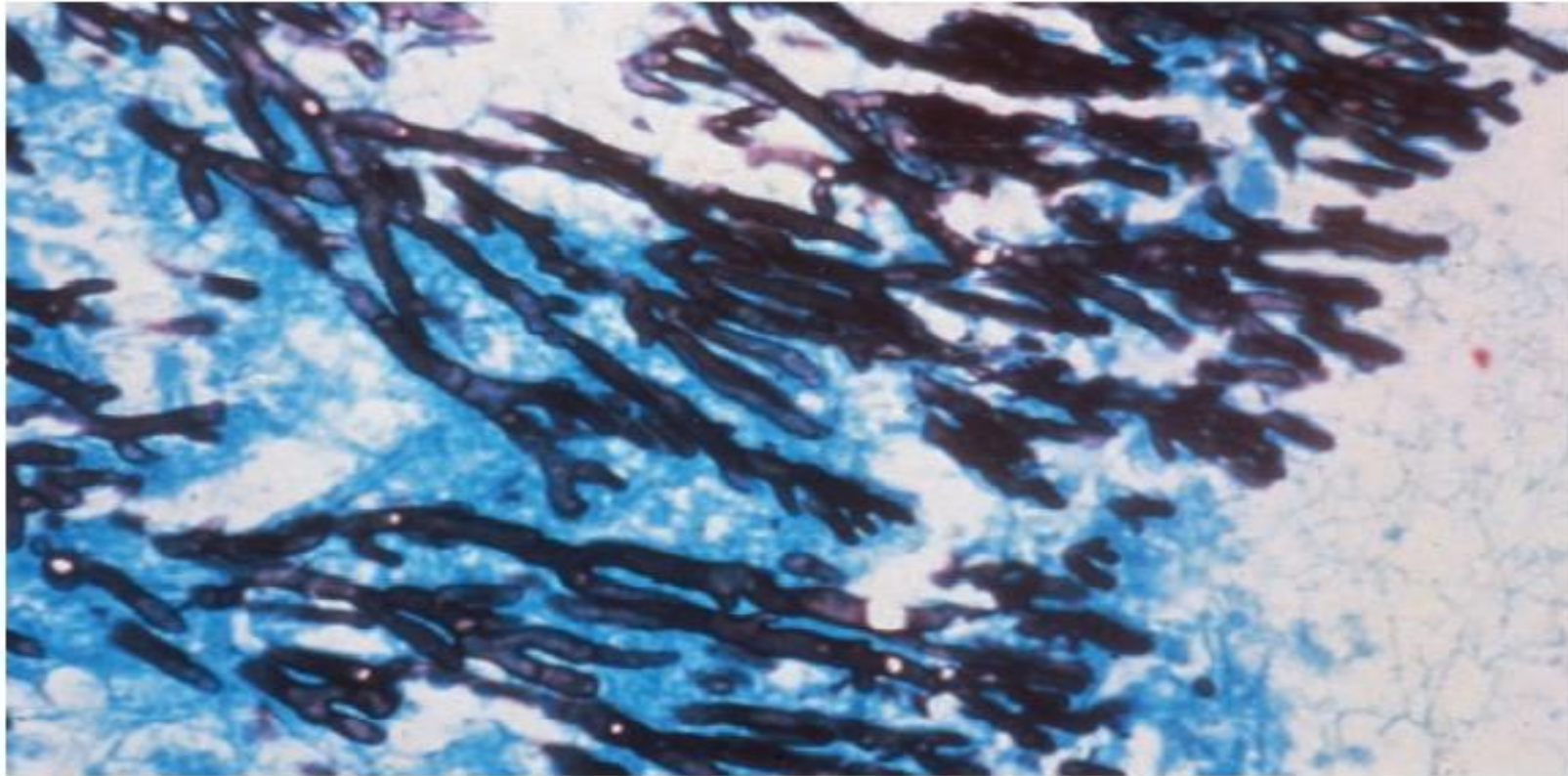
Aspergillus fumigatus



A. terreus



Aspergillus in tissue showing acute-angle branching, septate hyphae



Epidemiology

Aspergillus spp. are common throughout the world. Their conidia are ubiquitous in air, soil, and decaying matter. Within the hospital environment, *Aspergillus* spp. may be found in air, showerheads, hospital water storage tanks, and potted plants. As a result, the conidia are constantly being inhaled.

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The respiratory tract is the most frequent and most important portal of entry.

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Clinical Syndromes

1. ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS

- The allergic manifestations of aspergillosis constitute a spectrum of presentations based on the degree of hypersensitivity to *Aspergillus* antigens.
- In the bronchopulmonary form, asthma, pulmonary infiltrates, peripheral eosinophilia, elevated serum immunoglobulin (Ig)E, and evidence of hypersensitivity to *Aspergillus* antigens (skin test) may be seen.
- Allergic sinusitis shows laboratory evidence of hypersensitivity to go along with upper respiratory symptoms of nasal obstruction and discharge, headache, and facial pain.

- Both the paranasal sinuses and the lower airways may become colonized with *Aspergillus* spp., resulting in obstructive bronchial aspergillosis and true aspergilloma (“fungus ball”).
- Obstructive bronchial aspergillosis usually occurs in the setting of underlying pulmonary disease such as cystic fibrosis, chronic bronchitis, or bronchiectasis. The condition is marked by formation of bronchial casts or plugs composed of hyphal elements and mucinous material.

2. INTRA CAVITY ASPERGILLOSIS

- An aspergilloma can form either in the paranasal sinuses or in a preformed pulmonary cavity secondary to old tuberculosis or other chronic cavity lung disease.
- In the event of pulmonary hemorrhage, which may be severe and life threatening, surgical excision of the cavity and fungus ball is indicated.

3. INVASIVE ASPERGILLOSIS

- Forms of invasive aspergillosis run the gamut from superficially invasive disease that may occur in the setting of mild immunosuppression (e.g., low-dose steroid therapy, collagen vascular disease, or diabetes) to destructive, locally invasive pulmonary or disseminated aspergillosis.
- The more limited forms of invasion generally include necrotizing pseudomembranous bronchial aspergillosis and chronic necrotizing pulmonary aspergillosis.
- Bronchial aspergillosis may cause wheezing, dyspnea, and hemoptysis. Most patients with chronic necrotizing pulmonary aspergillosis have underlying structural pulmonary disease, which may be treated with low-dose corticosteroids. This is a chronic infection that may be locally destructive, with the development of infiltrates and fungus balls.

4.ENDOCARDITIS

5.SUPERFICIAL INFECTION

- Sinusitis
- Otomycosis
- Mycotic keratitis
- The mortality of this infection despite specific antifungal therapy is quite high, usually exceeding 70% .
- Hematogenous dissemination of infection to extrapulmonary sites is common because of the angioinvasive nature of the fungus. Sites most often involved include brain, heart, kidneys, GI tract, liver, and spleen

Laboratory Diagnosis

- 1. Direct microscopy
- 2. Isolation
 - Aspergillosis grow readily on routine mycologic media lacking cycloheximide.
 - Species level identification of the major human pathogens can be made by observing cultural and microscopic characteristics from growth on potato dextrose agar.
 - Microscopic morphology (conidiophores, vesicles, phialides, conidia) is best observed with a slide culture and is necessary for species identification.
 - *A. terreus*, among all species of *Aspergillus*, has been shown to cause true aspergillemia in which yeastlike spores (aleurioconidia) are formed in tissue and are more likely to be detected in blood obtained for culture.
- 3. Serology
 - Rapid diagnosis of invasive aspergillosis has been advanced by the development of immunoassays for the *Aspergillus* galactomannan antigen in serum.
- 4. PCR-based assays have proven to be both sensitive and specific for the diagnosis of invasive aspergillosis.
- 5. Skin test

Treatment and Prevention

- Prevention of aspergillosis in high-risk patients is paramount. Neutropenic and other high-risk patients are generally housed in facilities where the air is filtered to minimize exposure to *Aspergillus* conidia.
- administration of voriconazole or one of the lipid formulations of amphotericin B.
- combination therapy with voriconazole plus anidulafungin
- surgical resection of involved areas is recommended if possible