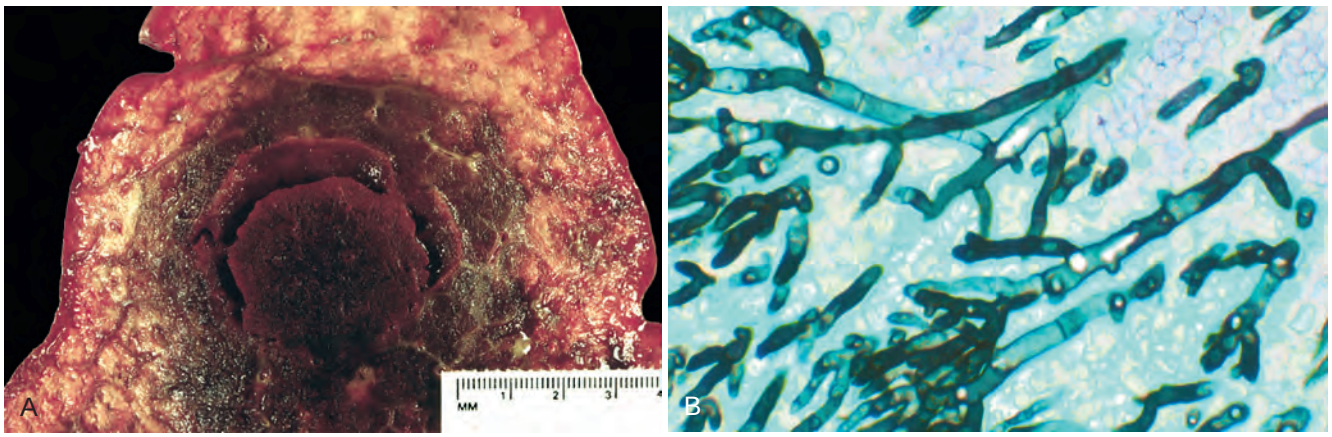


**Figure 8-44** *Aspergillus* infection. **A,** Invasive aspergillosis of the lung in a bone marrow transplant patient. **B,** Gomori methenamine-silver (GMS) stain shows septate hyphae with acute-angle branching, consistent with *Aspergillus*.

The pulmonary lesions take the form of necrotizing pneumonia with sharply delineated, rounded, gray foci and hemorrhagic borders; they are often referred to as target lesions (Fig. 8-44*A*). ***Aspergillus* forms fruiting bodies (usually in lung cavities) and septate filaments, 5 to 10 μm thick, branching at acute angles (40 degrees)** (Fig. 8-44*B*). *Aspergillus* hyphae cannot be distinguished from *Pseudallescheria boydii* and *Fusarium* species by morphology alone. *Aspergillus* has a tendency to invade blood vessels, therefore areas of hemorrhage and infarction are usually superimposed on the necrotizing, inflammatory tissue reactions. Rhinocerebral *Aspergillus* infection in immunosuppressed individuals resembles that caused by Mucormycoses (e.g., *Mucor*, *Rhizopus*).

### *Zygomycosis (Mucormycosis)*

**Mucormycotina are widely distributed in nature and cause no harm to immunocompetent individuals, but they infect immunosuppressed people, causing mucormycosis.** Mucormycosis (formerly zygomycosis) is an opportunistic infection caused by bread mold fungi, including *Mucor, Rhizopus, Lichtheimia (formerly Absidia),* and *Cunninghamella*, which belong to the family Mucormycetes. Major predisposing factors are neutropenia, corticosteroid use, diabetes mellitus, iron overload, and breakdown of the cutaneous barrier (e.g., as a result of burns, surgical wounds, or trauma).

***Pathogenesis.*** Immune responses to Mucormycotina differ from other fungi and the organisms have variable natural resistance. As with *Aspergillus*, Mucormycotina are transmitted by airborne asexual spores. Inhaled spores commonly produce infection in the sinuses and the lungs, but percutaneous exposure or ingestion can also lead to infection. Macrophages provide the initial defense by phagocytosis and non-oxidative killing of germinating sporangiospores. Mucormycotina hyphal components are recognized by TLR2, which results in a pro-inflammatory cascade of cytokines including IL-6 and TNF-α. Neutrophils have a key role in killing hyphae after germination by directly damaging hyphae walls. If the macrophages or neutrophils are compromised in numbers or function, the probability of an established and then invasive infection is greatly increased. There is natural variation in resistance to both phagocytosis of spores and neutrophil damage to hyphae depending on the species of Mucormycotina causing infection; thus, some infections can appear more aggressive than others despite a similar host milieu. Lastly, the availability of free iron (a promoter of Mucormycotina growth) increases probability of infection, as seen in people with diabetes (increased free iron due to ketoacidosis and/or glycosylation-induced poor iron affinity) and patients on chronic iron chelation treatment (where deferoxamine acts as a siderophore within the fungi).

## MORPHOLOGY

**Mucormycetes form nonseptate hyphae of variable width (6-50 μm) with frequent right angle branching, distinct from *Aspergillus* hyphae,** that are readily demonstrated by hematoxylin and eosin or special fungal stains (Fig. 8-45). The three primary sites of invasion are the nasal sinuses, lungs, and gastrointestinal tract, depending on whether the spores (which are widespread in dust and air) are inhaled or ingested. Most commonly in individuals with diabetes, the fungus may spread from nasal sinuses to the orbit and brain, giving rise to **rhinocerebral mucormycosis**. The Mucormycotina cause local tissue necrosis, invade arterial walls, and penetrate the periorbital tissues and cranial vault. Meningoencephalitis follows,

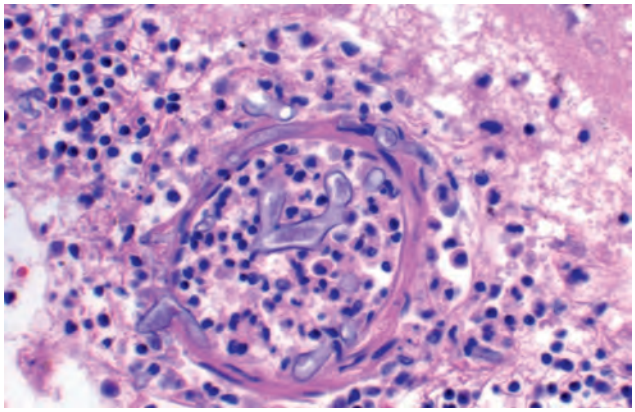

**Figure 8-45** Meningeal blood vessels with angioinvasive *Mucor* species. Note the irregular width and near right-angle branching of the hyphae. Compare with Aspergillus, Fig. 8-44.