Histopathology of Fungal Infections

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Direct Microscopy / Histopathology

- Requires expertise and careful observation.
- Provides vital information and often a presumptive diagnosis, although not definitive identification of the organism.
- Histopathology is more about the disease process than identification of an individual fungus. Clinical information is also essential.
- Wet mounts in 10% KOH with Parker ink, India ink or Calcofluor White.
- Smears for Gram, Giemsa or PAS staining.
- Tissue sections for H&E, GMS and PAS staining.

Dimorphic Systemic Mycoses

These are fungal infections of the body caused by dimorphic fungal pathogens which can overcome the physiological and cellular defenses of the normal human host by changing their morphological form. They are geographically restricted, and the primary site of infection is usually pulmonary, following the inhalation of conidia.

Disease	Causative organism	Incidence
Histoplasmosis	*Histoplasma capsulatum*	Rare*
Talaromyces marneffei infection	*Talaromyces marneffei*	Rare*
Coccidioidomycosis	*Coccidioides immitis*	Rare*
Blastomycosis	*Blastomyces dermatitidis*	Rare*
Paracoccidioidomycosis	*Paracoccidioides brasiliensis*	Rare*

*more common in endemic areas

Histoplasmosis of the lower gum showing ulcer around base of the teeth.

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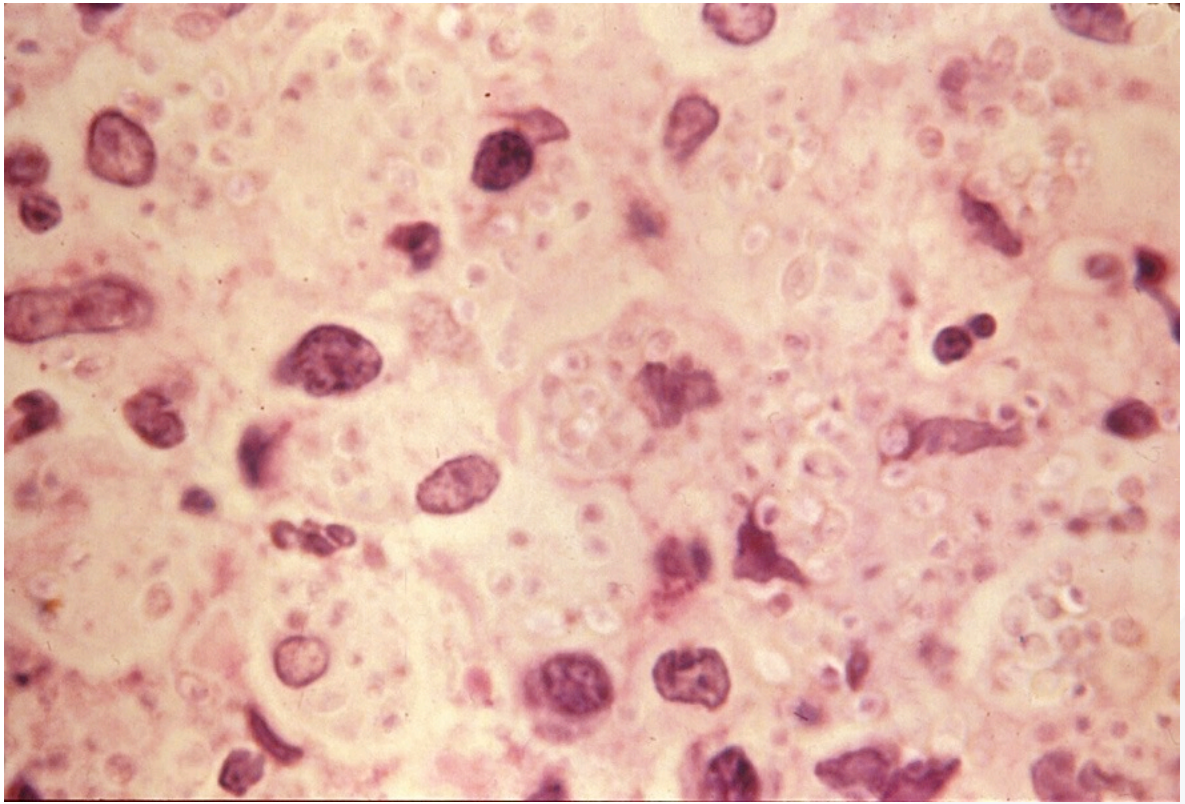
H&E showing macrophages containing numerous yeast cells of *Histoplasma capsulatum.* The basophilic cytoplasm of the fungal cells is retracted from the poorly stained cell wall, giving the false impression of a capsule.



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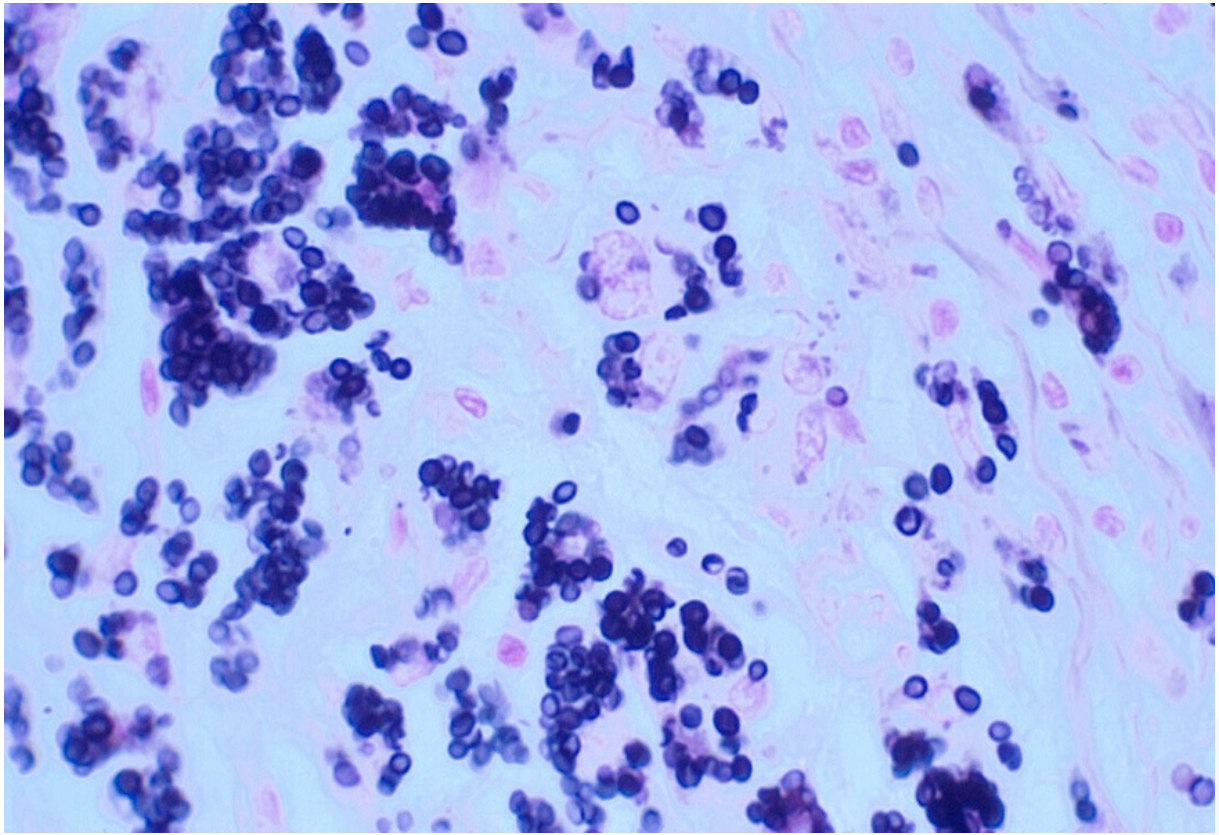
Grocott's methenamine silver (GMS) from a lung biopsy showing numerous yeast cells of *Histoplasma capsulatum* inside macrophages.



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Typical papules often with a central necrotic umbilication "Molluscum contagiosum" like lesions caused by *Talaromyces* (*Penicillium) marneffei* in an HIV+ patient.

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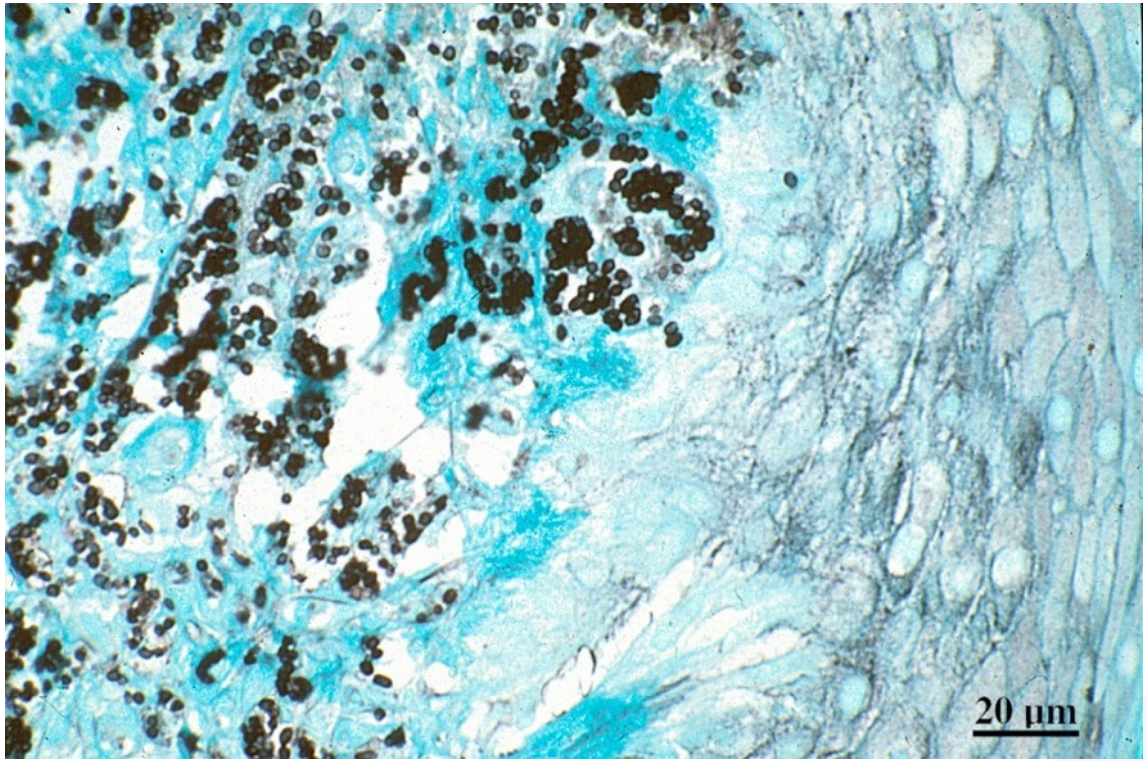
Grocott's methenamine silver (GMS) stained tissue section showing numerous small yeast-like cells of *Talaromyces marneffei* that closely resemble those seen in Histoplasmosis.



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A Giemsa stained touch smear showing the typical septate yeast-like cells of *Talaromyces marneffei.*

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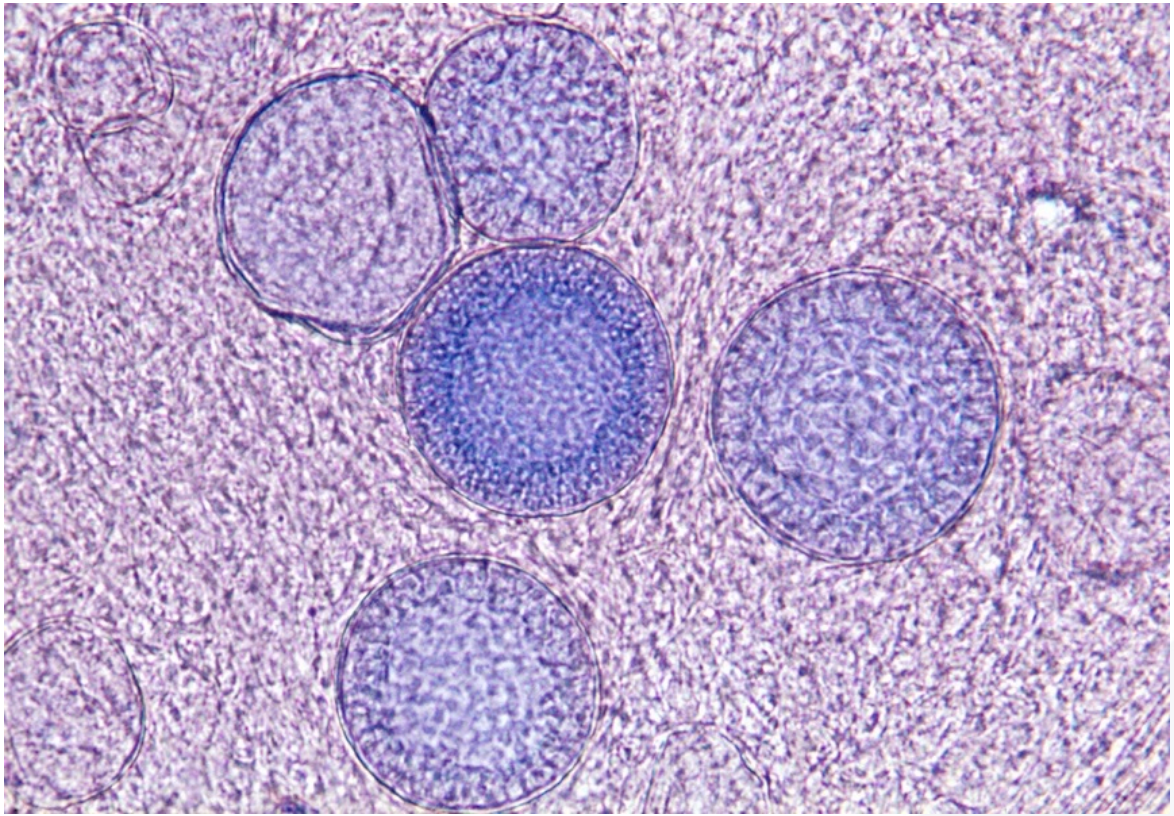
Coccidioidomycosis: Extension of pulmonary infection showing a large superficial, ulcerated plaque.

Direct microscopy of skin scrapings from a cutaneous lesion mounted in 10% KOH and Parker ink solution showing characteristic endosporulating spherules (sporangia) of *Coccidioides immitis*. The presence of spherules with endospores is diagnostic.



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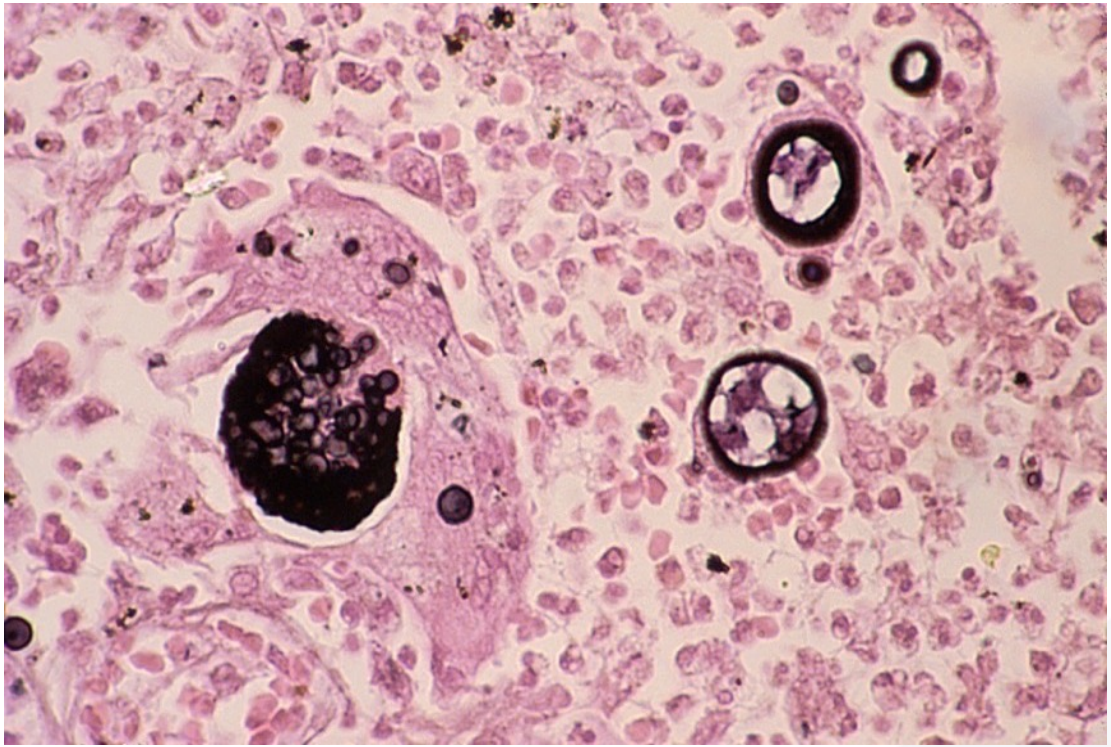
Periodic Acid-Schiff (PAS) stained tissue section showing typical endosporulating spherules of *Coccidioides immitis*. Young spherules have a clear centre with peripheral cytoplasm and a prominent thick wall. Endospores (sporangiospores) are later formed within the spherule by repeated cytoplasmic cleavage. Rupture of the spherule releases endospores into the surrounding tissue where they re-initiate the cycle of spherule development.



Blastomycosis: Ulcerated granuloma due to *Blastomyces dermatitidis*

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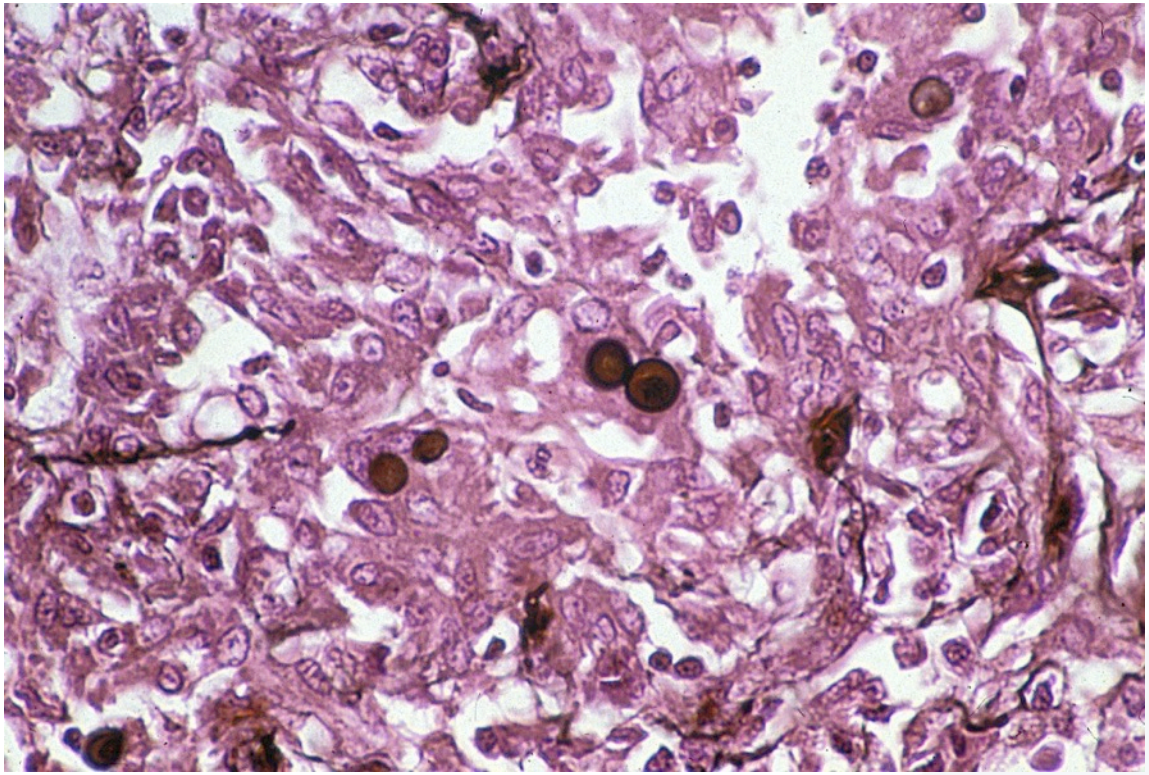
Blastomycosis: Tissue sections showing large, broad-base, unipolar budding yeast-like cells, 8-15m in diameter. Note: tissue sections need to be stained by Grocott's methenamine silver method to clearly see the yeast-like cells, which are often difficult to observe in Haematoxylin and eosin (H&E) stained preparations.



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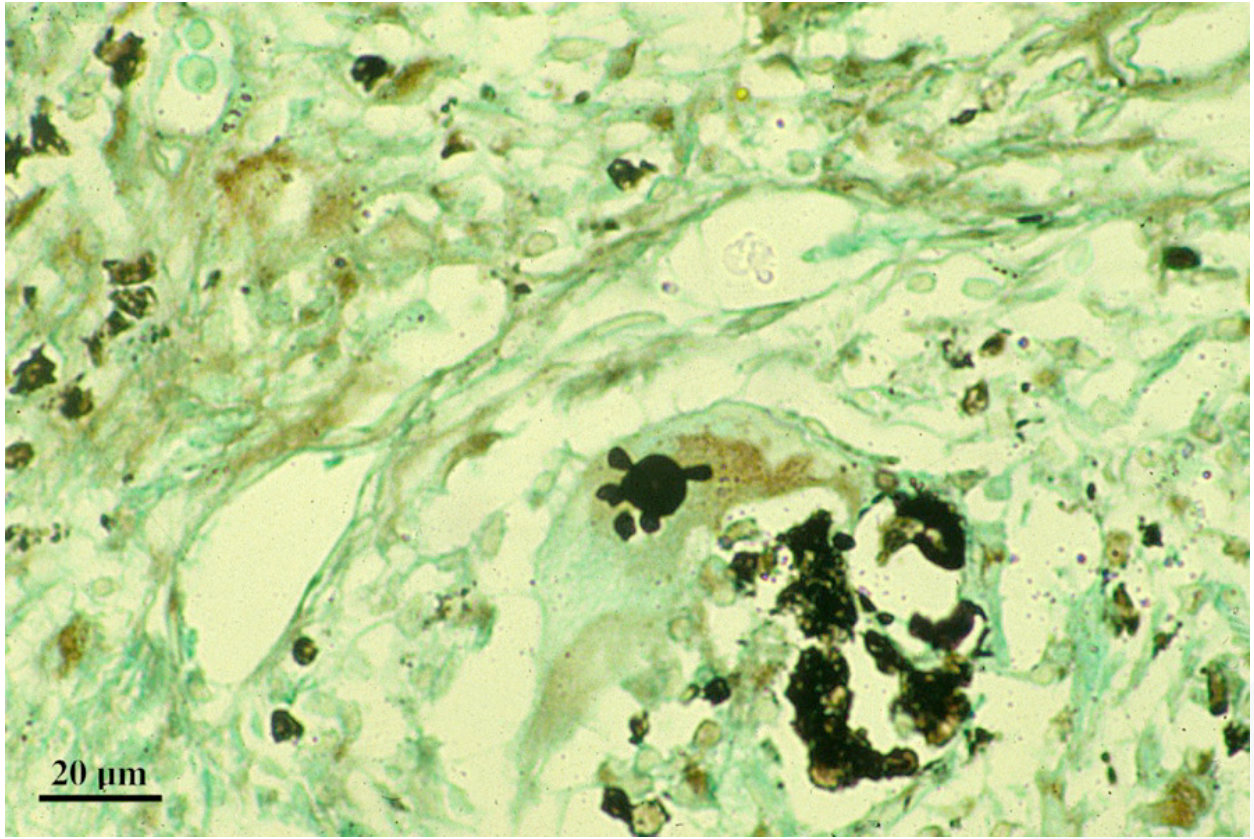
Mucocutaneous paracoccidioidomycosis showing extensive destruction of facial features.

Grocott's methenamine silver (GMS) stained lung tissue section showing multiple, narrow base, budding yeast cells "steering wheels" of *Paracoccidioides brasiliensis*.



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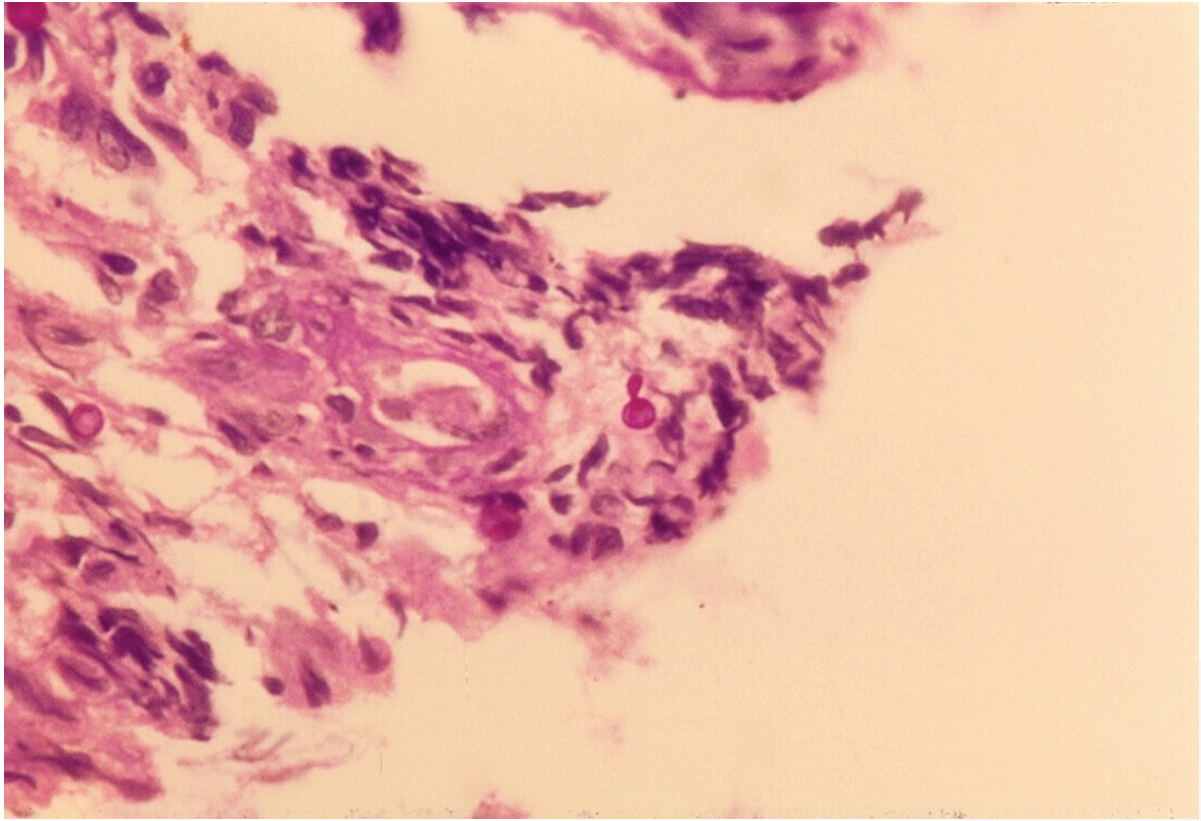
The Subcutaneous Mycoses

These are chronic, localized infections of the skin and subcutaneous tissue following the traumatic implantation of the aetiologic agent. The causative fungi are all soil saprophytes of regional epidemiology whose ability to adapt to the tissue environment and elicit disease is extremely variable.

Disease	Causative organism	Incidence
Sporotrichosis	*Sporothrix schenckii*	Rare
Chromoblastomycosis	*Fonsecaea, Phialophora, Cladosporium etc.*	Rare
Phaeohyphomycosis	*Cladophialophora, Exophiala, Curvularia, Exserohilum, etc*	Rare
Mycotic mycetoma	*Scedosporium, Madurella, Acremonium, Exophiala*	Rare
Subcutaneous zygomycosis (Entomophthoromycosis)	*Basidiobolus ranarum, Conidiobolus coronatus*	Rare
Subcutaneous zygomycosis (Mucormycosis)	*Rhizopus, Mucor, Rhizomucor, Lichtheimia, Saksenaea etc.*	Rare
Rhinosporidiosis	*Rhinosporidium seeberi*	Rare
Lobomycosis	*Loboa loboi*	Rare

Lymphocutaneous sporotrichosis showing typical elevated subcutaneous nodules developing along the regional lymphatics of the forearm.

Sporotrichosis: Section showing round Periodic Acid-Schiff (PAS) positive yeast-like cells, one with an elongated bud. *Sporothrix schenckii* is a dimorphic fungus and this is the typical parasitic or yeast-like form seen in tissue.



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Chronic verrucose chromoblastomycosis of the foot due to *Phialophora verrucosa*. Note tissue hyperplasia characterized by the formation of verrucoid, warty cutaneous nodules raised 1-3 cm above the skin surface.

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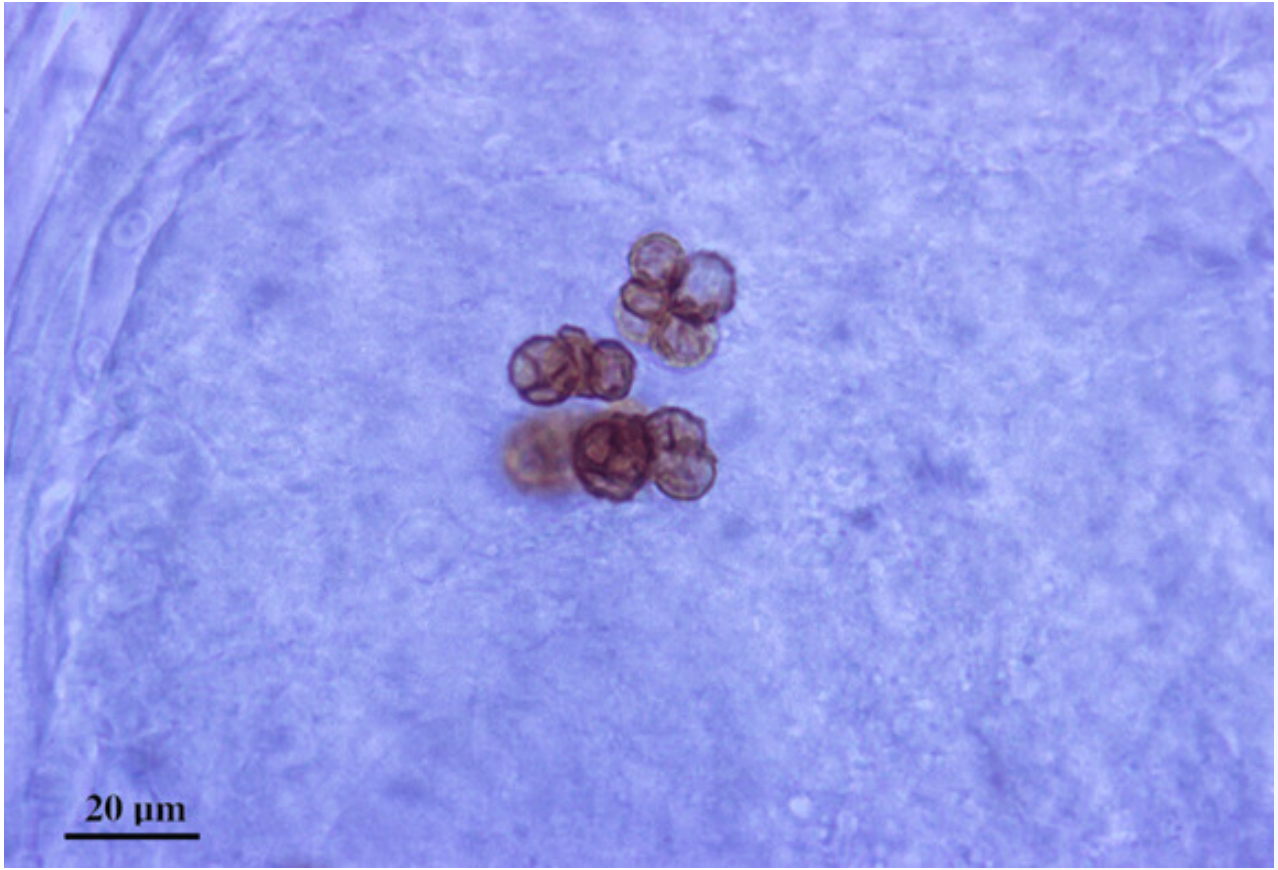
Skin scrapings from a patient with chromoblastomycosis mounted in 10% KOH and Parker ink solution showing characteristic brown pigmented, planate-dividing, rounded sclerotic bodies.



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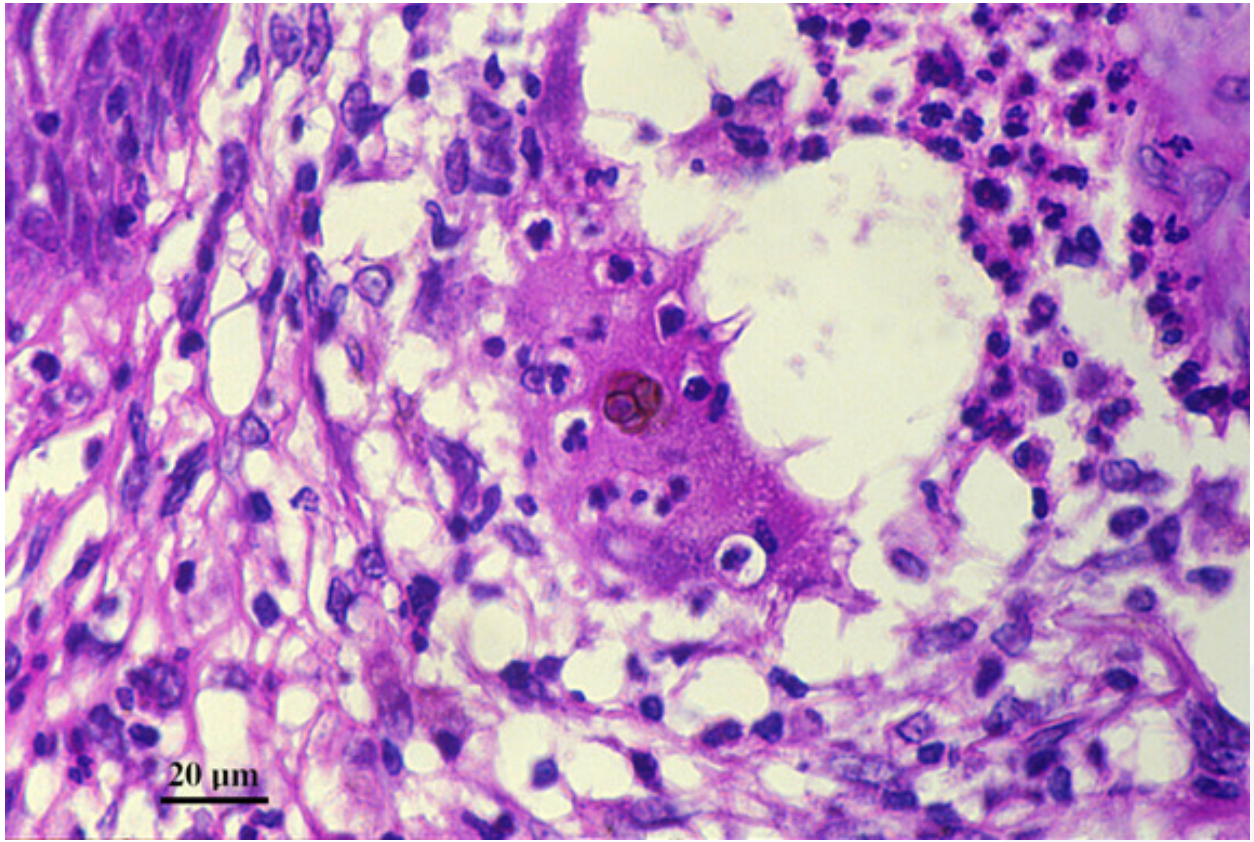
Chromoblastomycosis - Haematoxylin and eosin (H&E) stained sections showing characteristic dark brown sclerotic cells, which divide by binary fission and not by budding. Note all agents of chromoblastomycosis form these sclerotic bodies in tissue.



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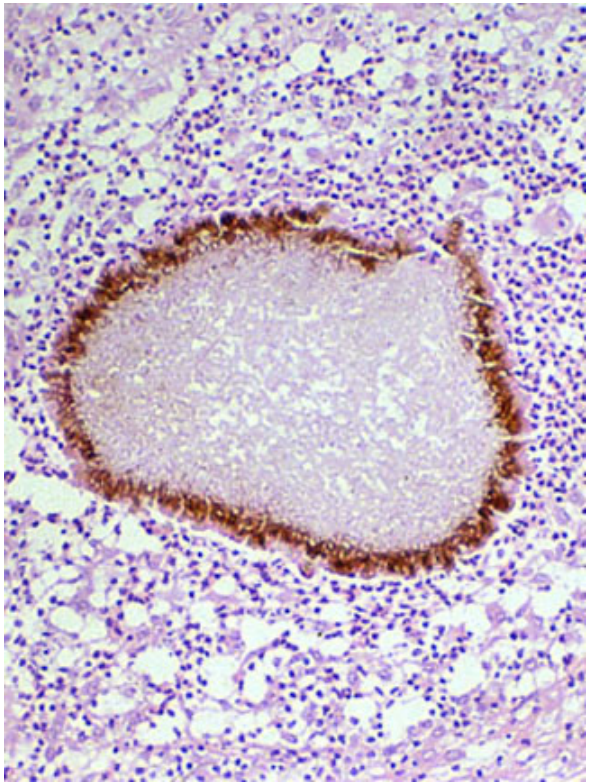
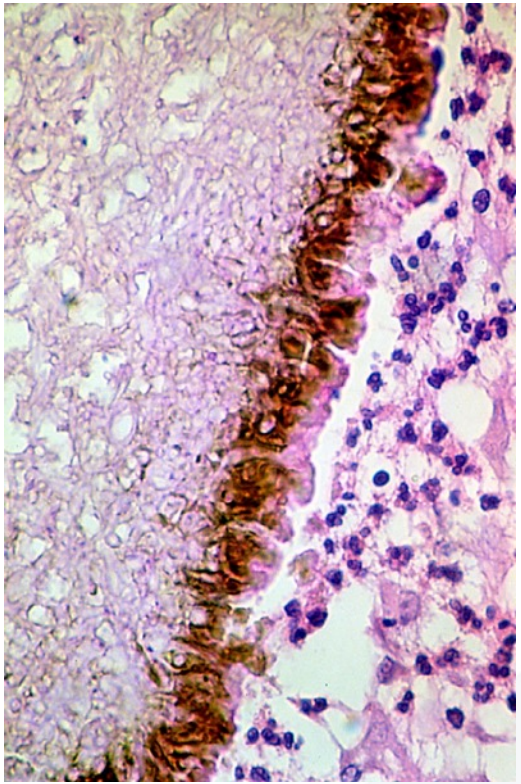
Mycetoma showing numerous draining sinuses. There is destruction of bone, distortion of the foot, and hyperplasia at the openings of the sinus tracts.

Haematoxylin and eosin (H&E) stained tissue section showing black grained eumycotic mycetoma caused by *Madurella mycetomatis*.





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Clinical slide of subcutaneous phaeohyphomycosis following a non-penetrating injury. The lesion, on the dorsum of the right thumb, was fluctuant, tender, blue-grey and had no connection to the surface. *Exophiala dermatitidis* was isolated.

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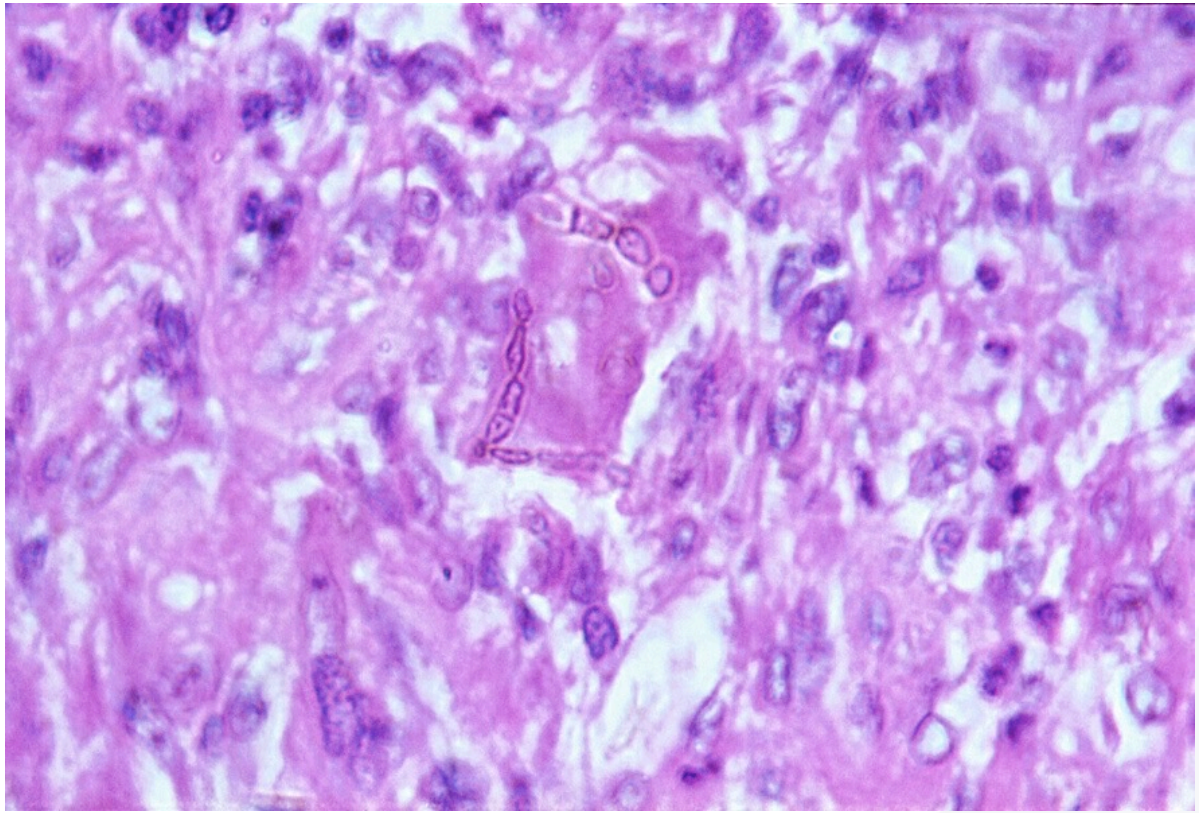
Phaeohyphomycosis - Haematoxylin and eosin (H&E) stained section showing characteristic, brown-pigmented, septate hyphal elements of *Exophiala jeanselmei*. The hyphae may be short to elongate, distorted or swollen, regularly shaped, or any combination of the above.



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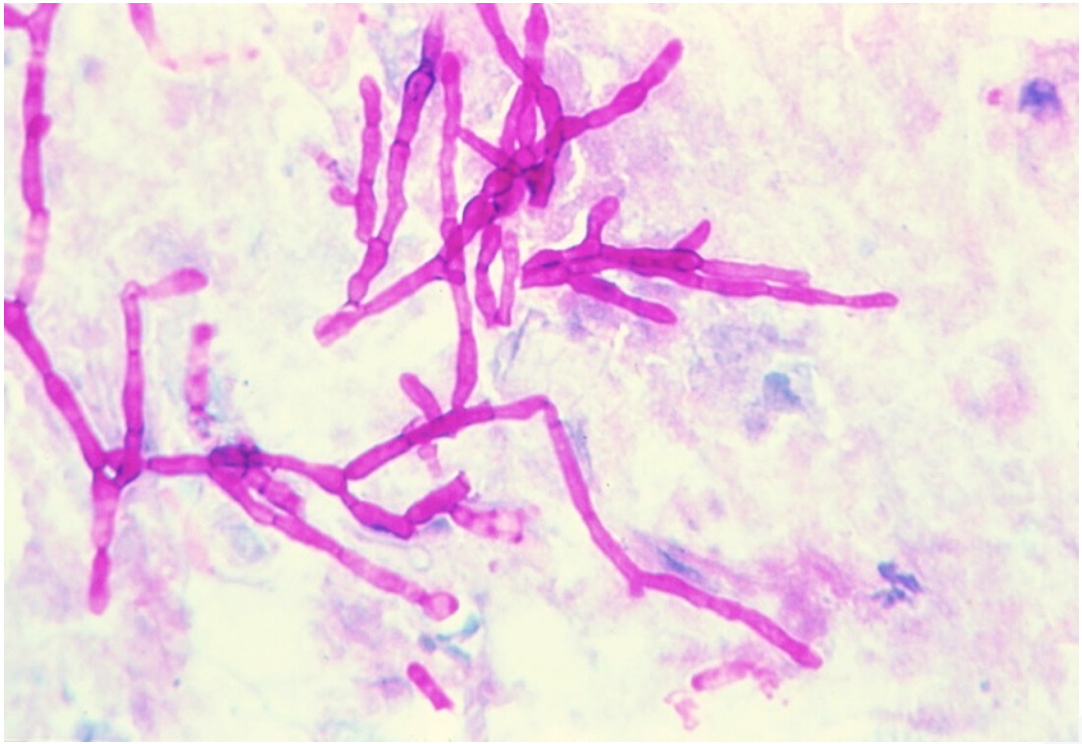
Phaeohyphomycosis - Periodic Acid-Schiff (PAS) stained smear of pus from a subcutaneous abscess of the toe showing septate hyphal elements of *Exophiala moniliae*.



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Entomophthoromycosis caused by *Basidiobolus ranarum* showing an ulcerated subcutaneous lesions on the abdomen of a young boy from Darwin.

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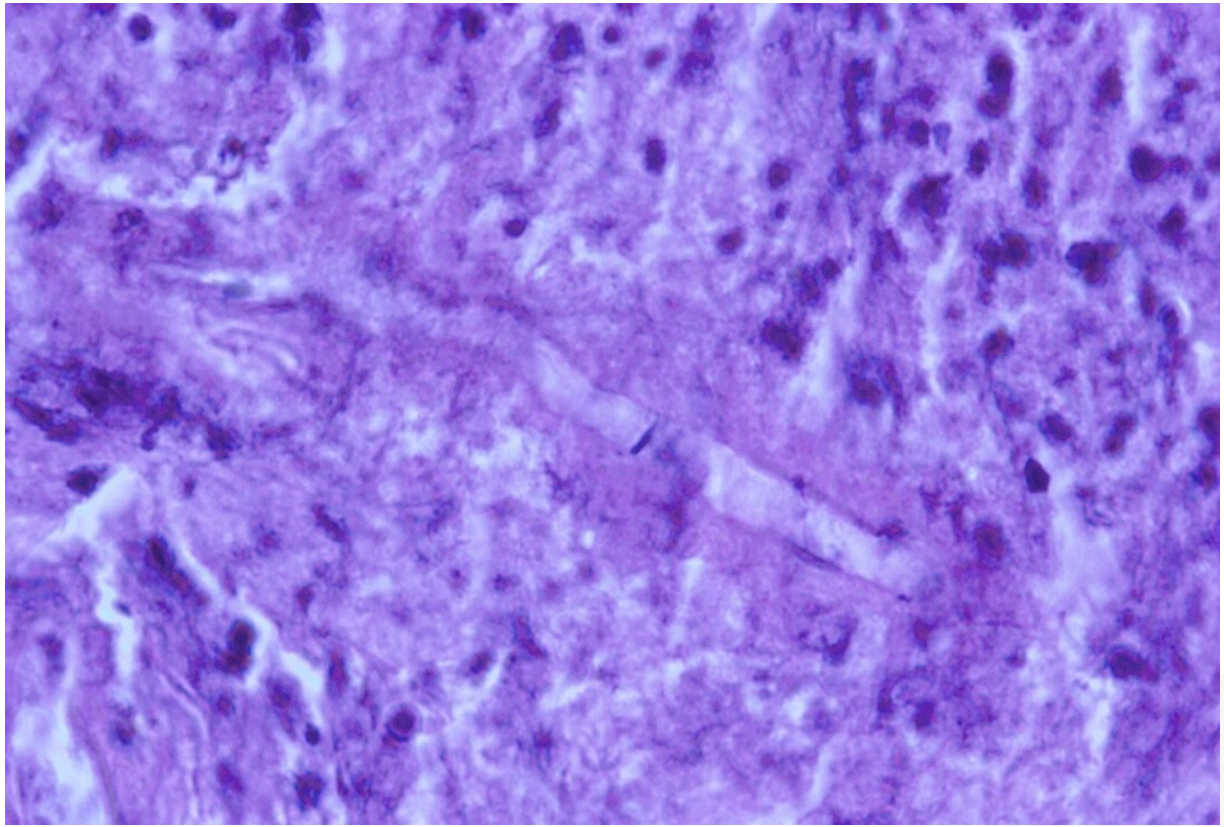
H&E stained section of tissue showing broad septate hyphae surrounded by an eosinophilic sheath (Splenodore-Hoeppli phenomenon) typical of Entomophthoromycosis.



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An ulcerated, erythematous plaque on a tattooed area of the left forearm of an otherwise healthy 25 year old male caused by S*aksenaea vasiformis*.

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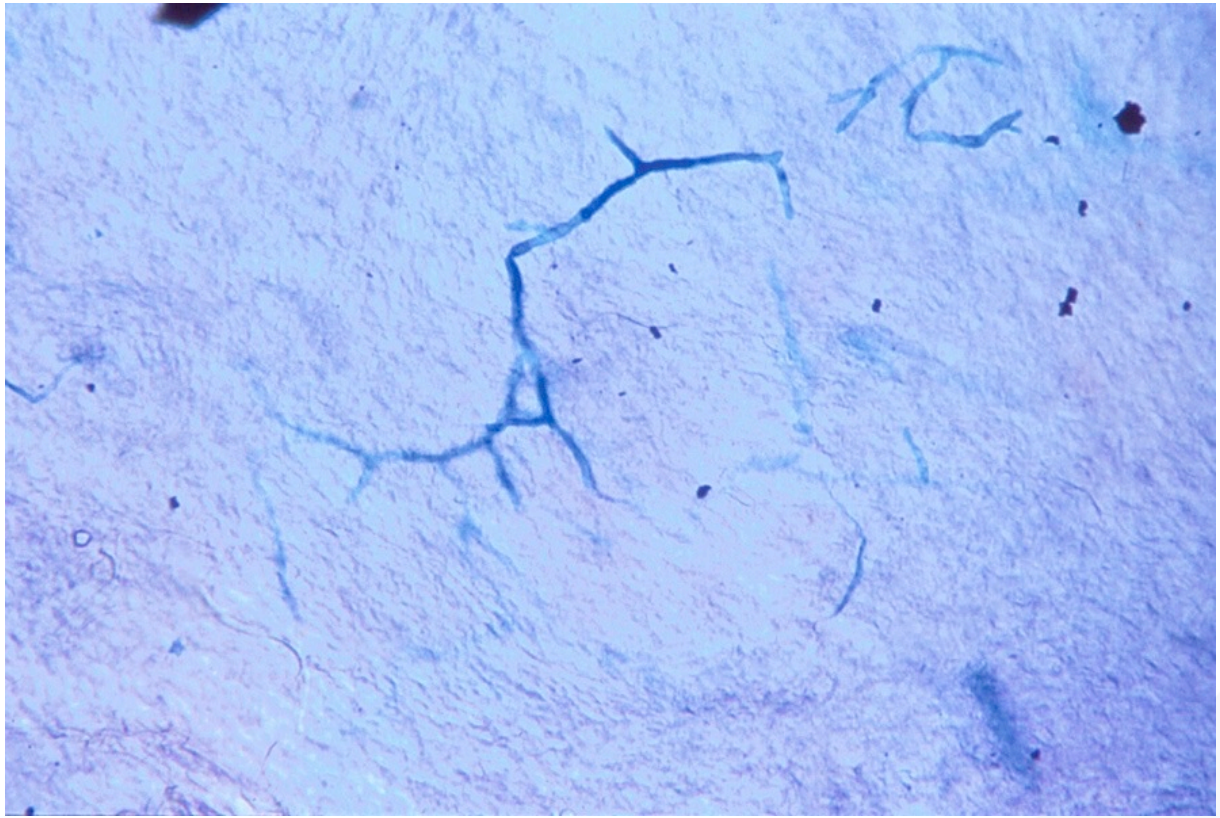
Direct microscopy of a skin scraping in 10% KOH and Parker ink solution showing broad, sparsely septate hyphae typical of a zygomycete.



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Direct microscopy of a skin scraping in KOH showing broad, sparsely septate hyphae with focal bulbous dilations typical of a zygomycete.

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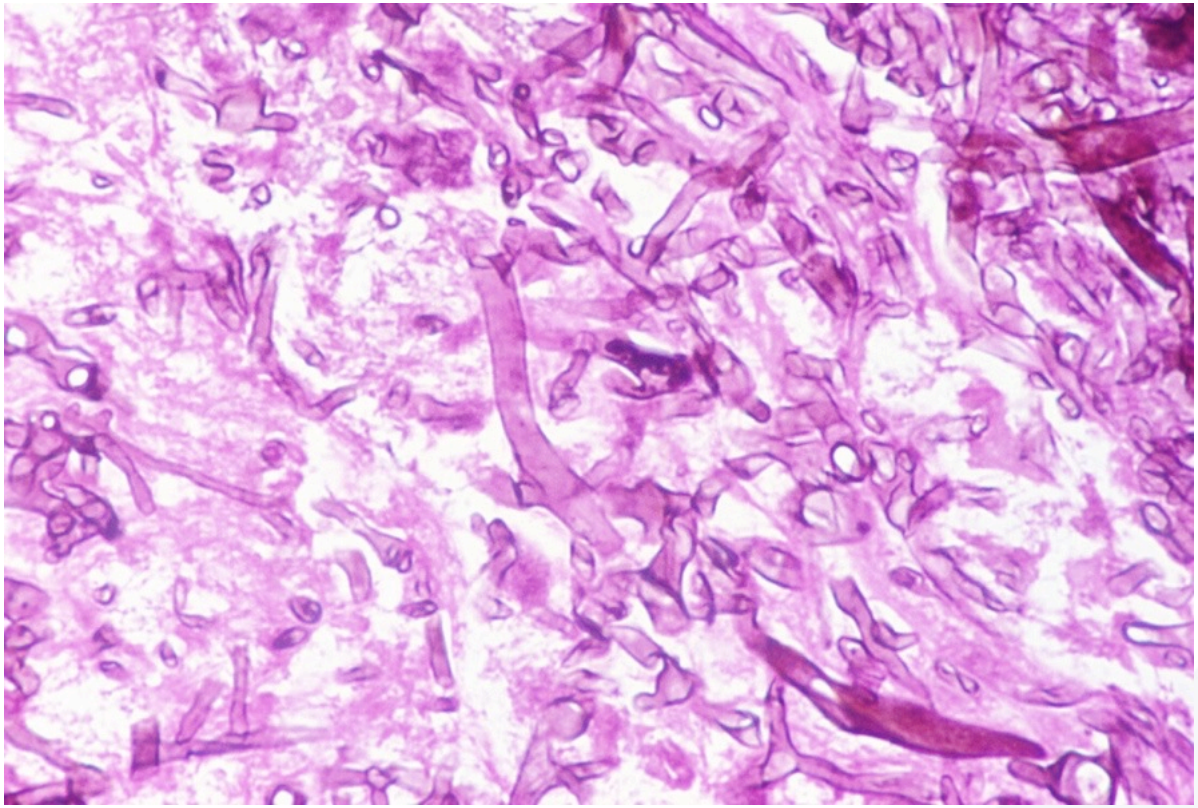
H&E stained section showing broad, infrequently septate, thin-walled hyphae with focal bulbous dilations and irregular, non-dichotomous, often right-angled, branching typical of a zygomycete.



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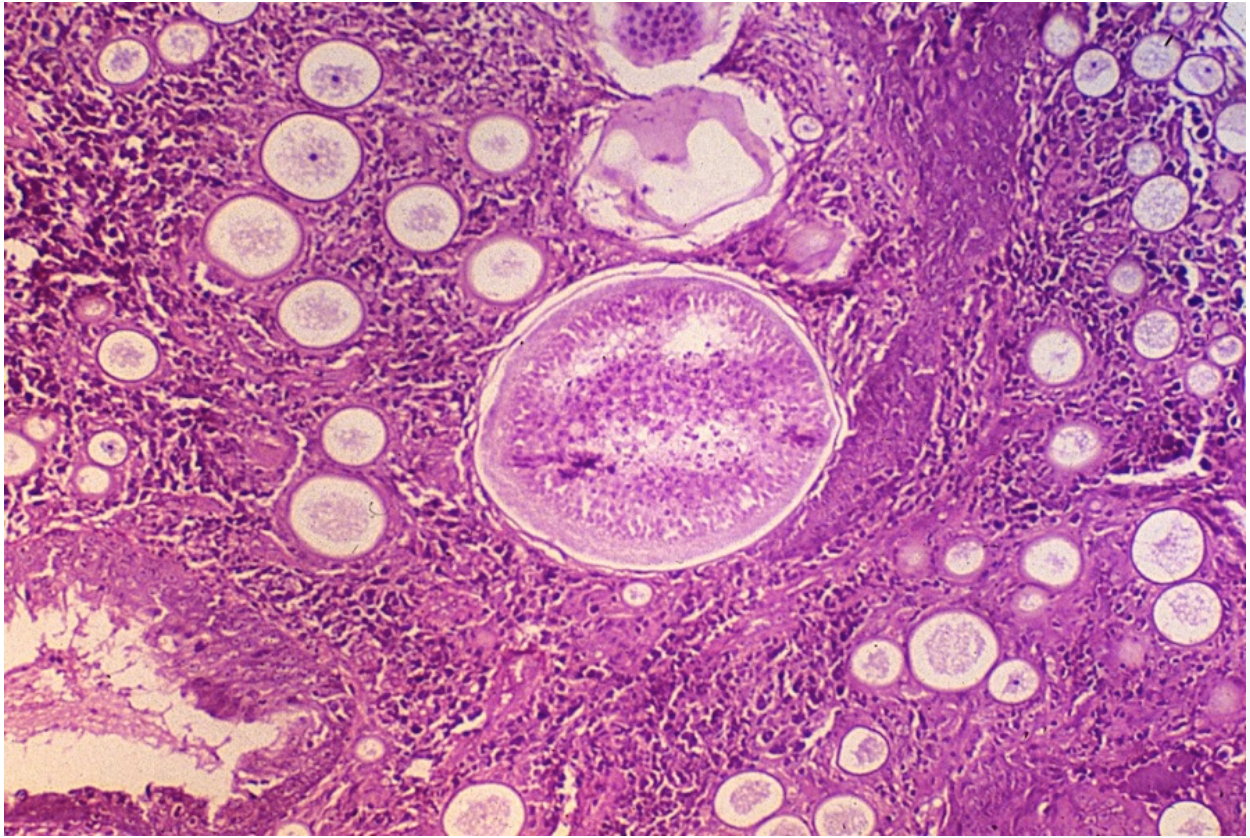
Rhinosporidiosis is a chronic granulomatous disease characterised by the production of large polyps, tumours, papillomas, or wart-like lesions.

Numerous spherules of varying sizes typical of rhinosporidiosis.



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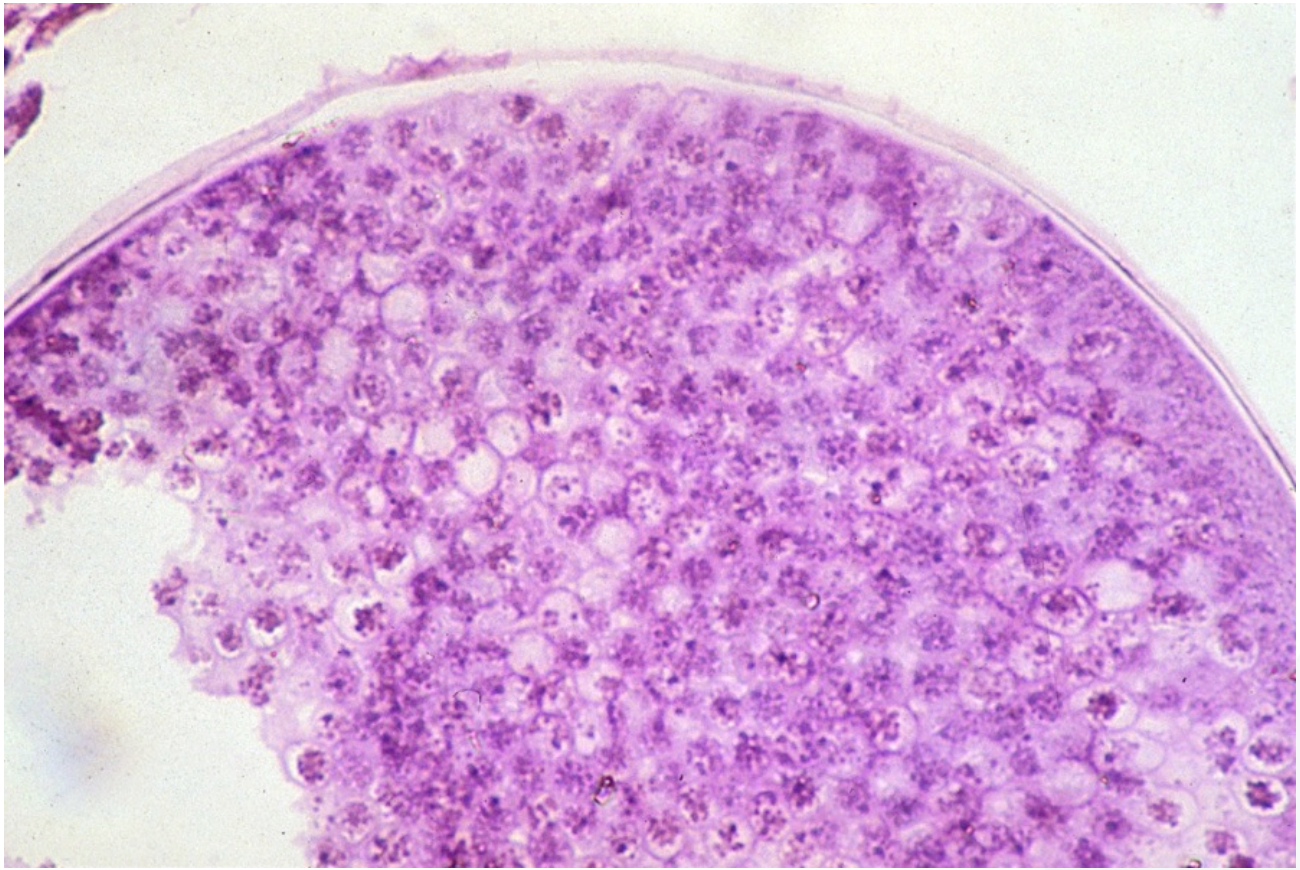
Mature spherule with endospores typical of rhinosporidiosis.



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Lobomycosis showing extensive verrucoid lesions on the legs. The lesions begin as small, hard nodules resembling keloids and may spread slowly in the dermis and continue to develop over a period of many years. Older lesions become verrucoid and may ulcerate. Lesions are usually found on the arms, legs, face or ears.

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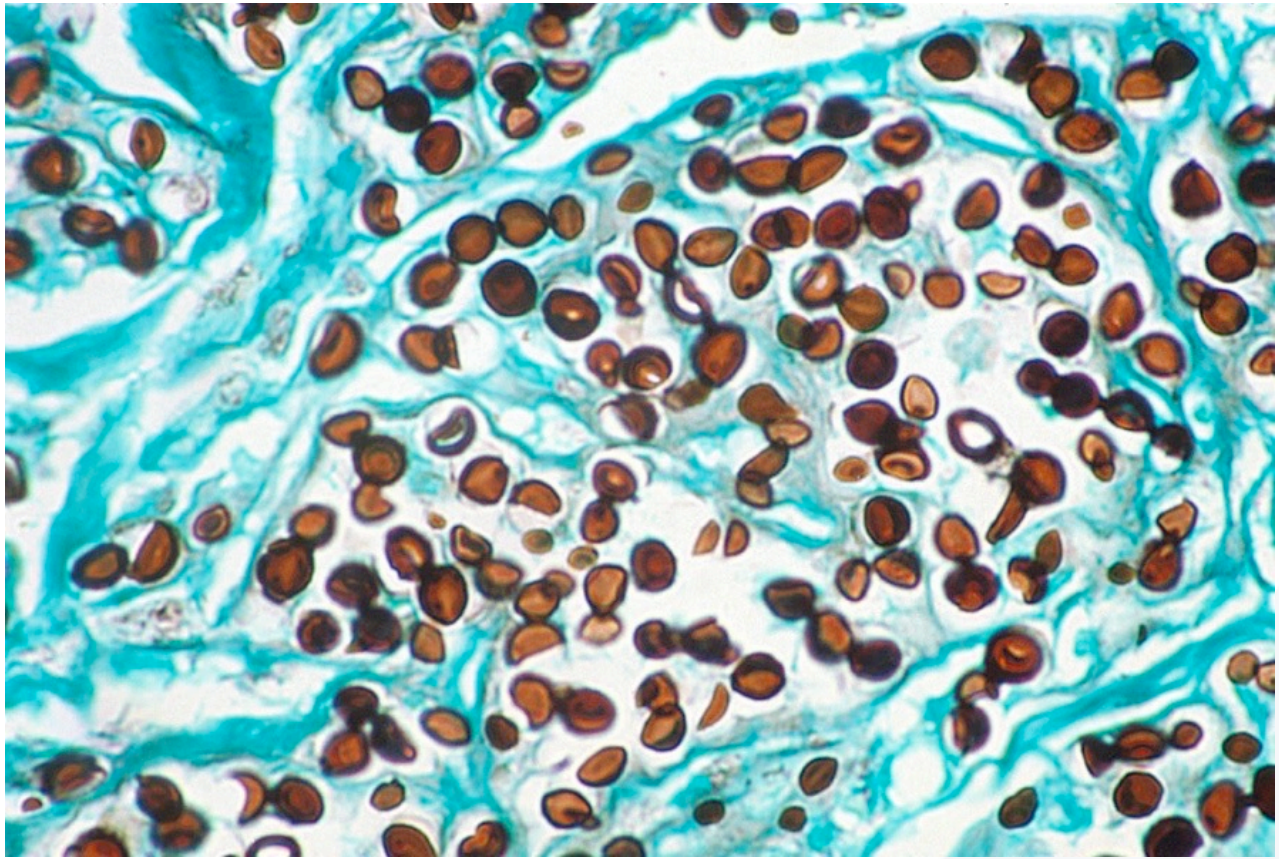
Grocott's methenamine silver (GMS) stained tissue section showing numerous darkly pigmented yeast-like cells, often in chains, 9-12 um in size typical of *Loboa loboi*.



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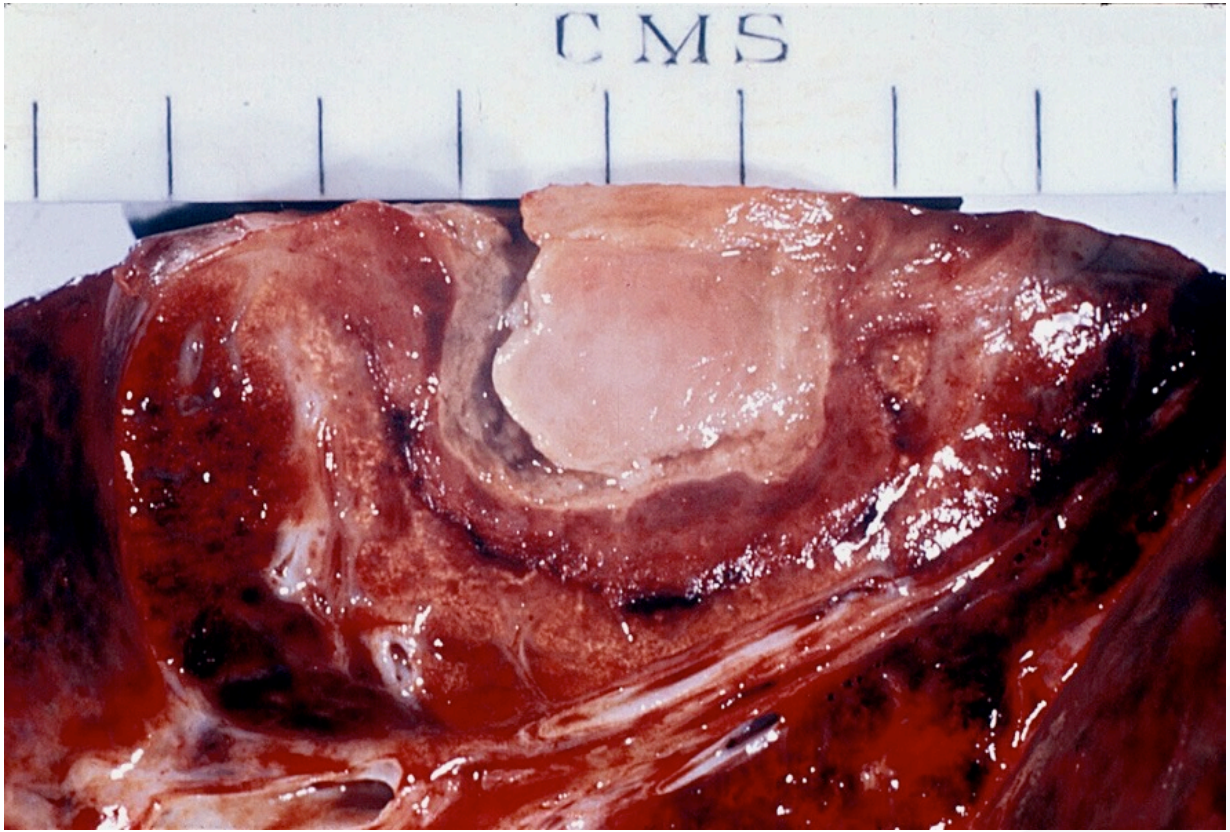
Opportunistic Systemic Mycoses

These are fungal infections of the body which occur almost exclusively in debilitated patients whose normal defence mechanisms are impaired. The organisms involved are cosmopolitan fungi which have a very low inherent virulence. The increased incidence of these infections and the diversity of fungi causing them, has parallelled the emergence of AIDS, more aggressive cancer and post-transplantation chemotherapy and the use of antibiotics, cytotoxins, immunosuppressives, corticosteroids and other macro disruptive procedures that result in lowered resistance of the host.

Disease	Causative organism	Incidence
Candidiasis	*Candida, Debaryomyces, Kluyveromyces, Meyerozyma, Pichia,* etc.	Common
Cryptococcosis	Cryptococcus spp. especially *C. neoformans* and *C. gattii.*	Rare/Common
Aspergillosis	*Aspergillus fumigatus* complex, *A. flavus*, complex, *A. terreus* complex etc.	Rare
Scedosporiosis (Pseudallescheriasis)	*Scedosporium* and *Lomentospora* sp.	Rare
Zygomycosis (Mucormycosis)	*Rhizopus, Mucor, Rhizomucor, Lichtheimia* etc.	Rare
Hyalohyphomycosis	*Penicillium, Paecilomyces, Beauveria, Fusarium, Scopulariopsis* etc.	Rare
Phaeohyphomycosis	*Cladophialophora, Exophiala, Bipolaris, Exserohilum* etc.	Rare

Aspergilloma found at post-mortem in the lung of a child with leukaemia. Note fungus ball occupying cavity.



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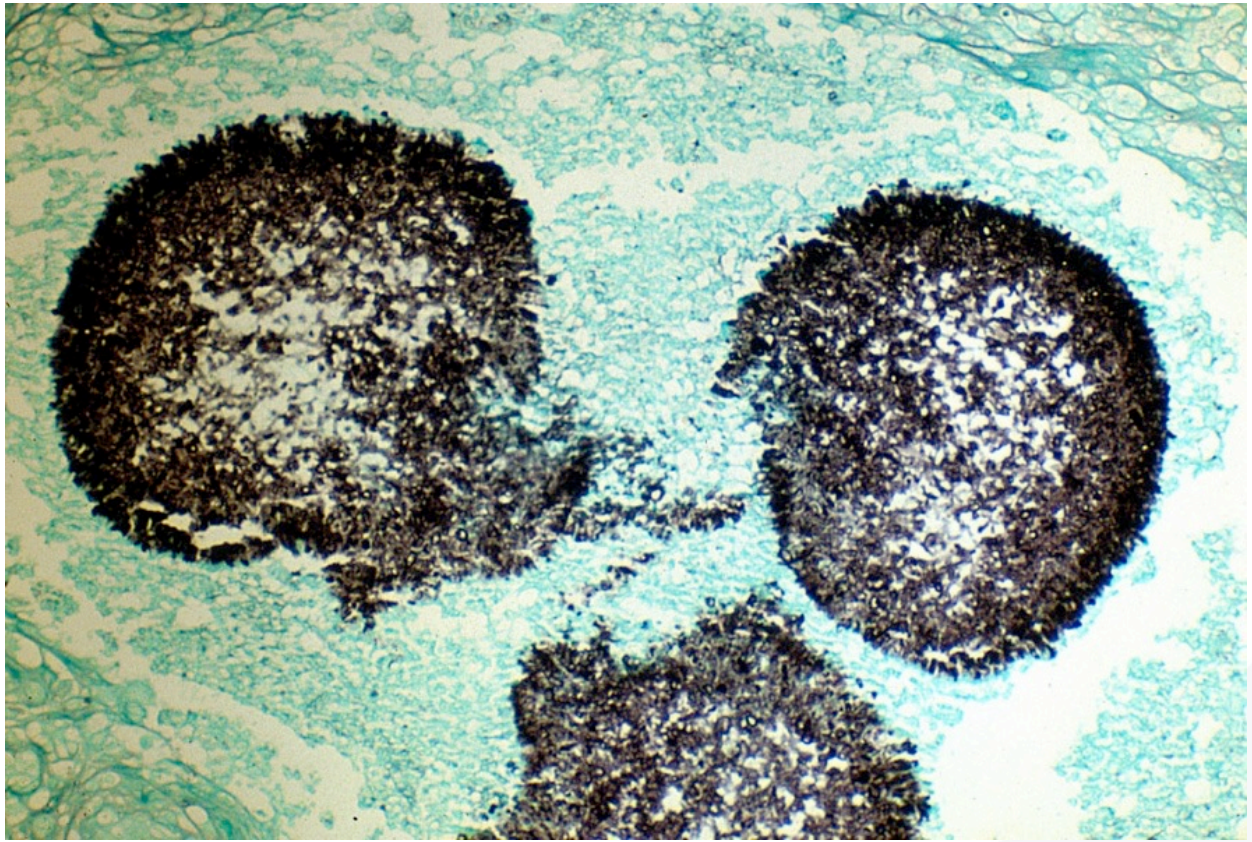
Grocott's methenamine silver (GMS) stained tissue section of lung showing fungal balls of hyphae of *Aspergillus fumigatus.*



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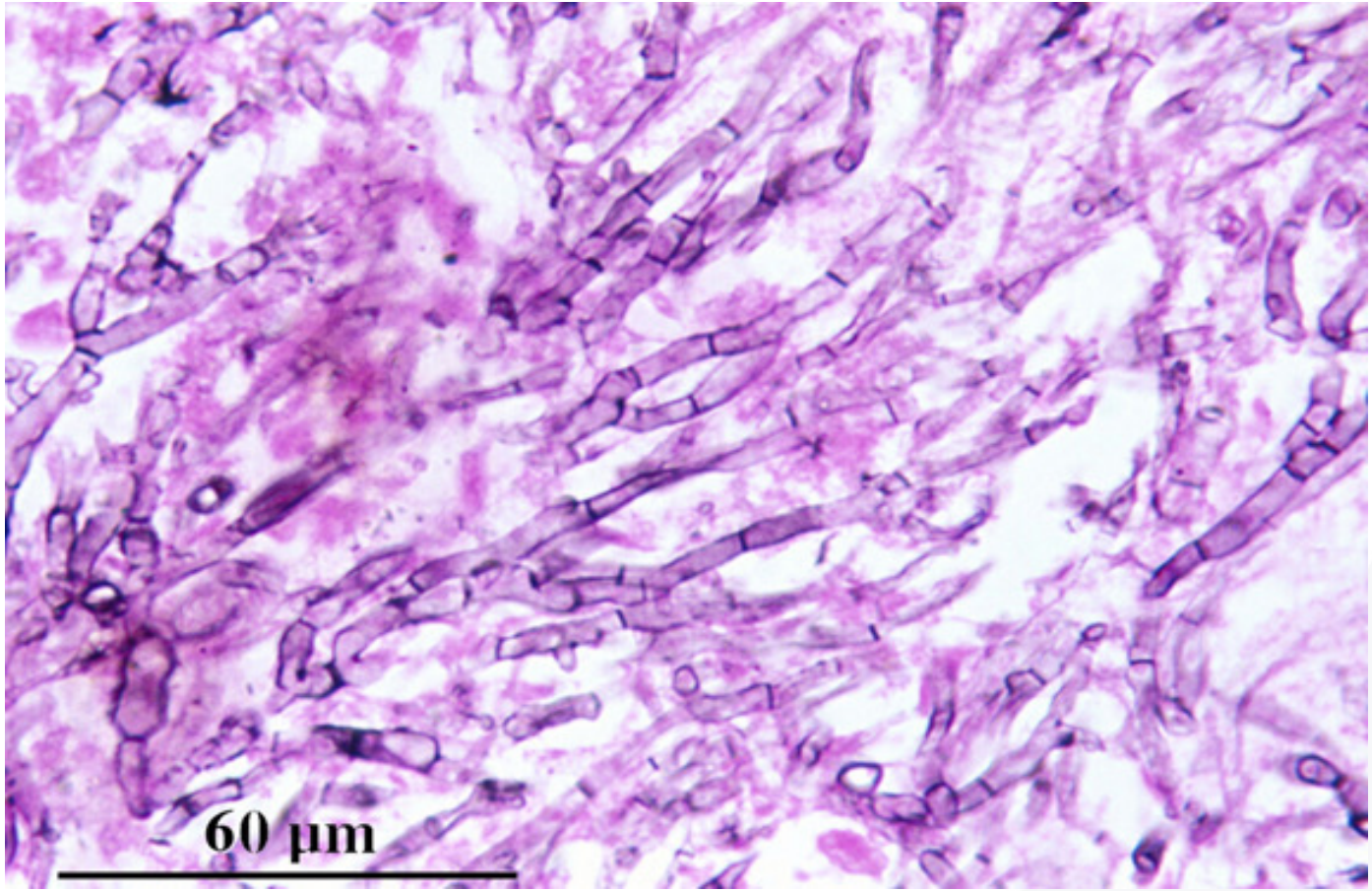
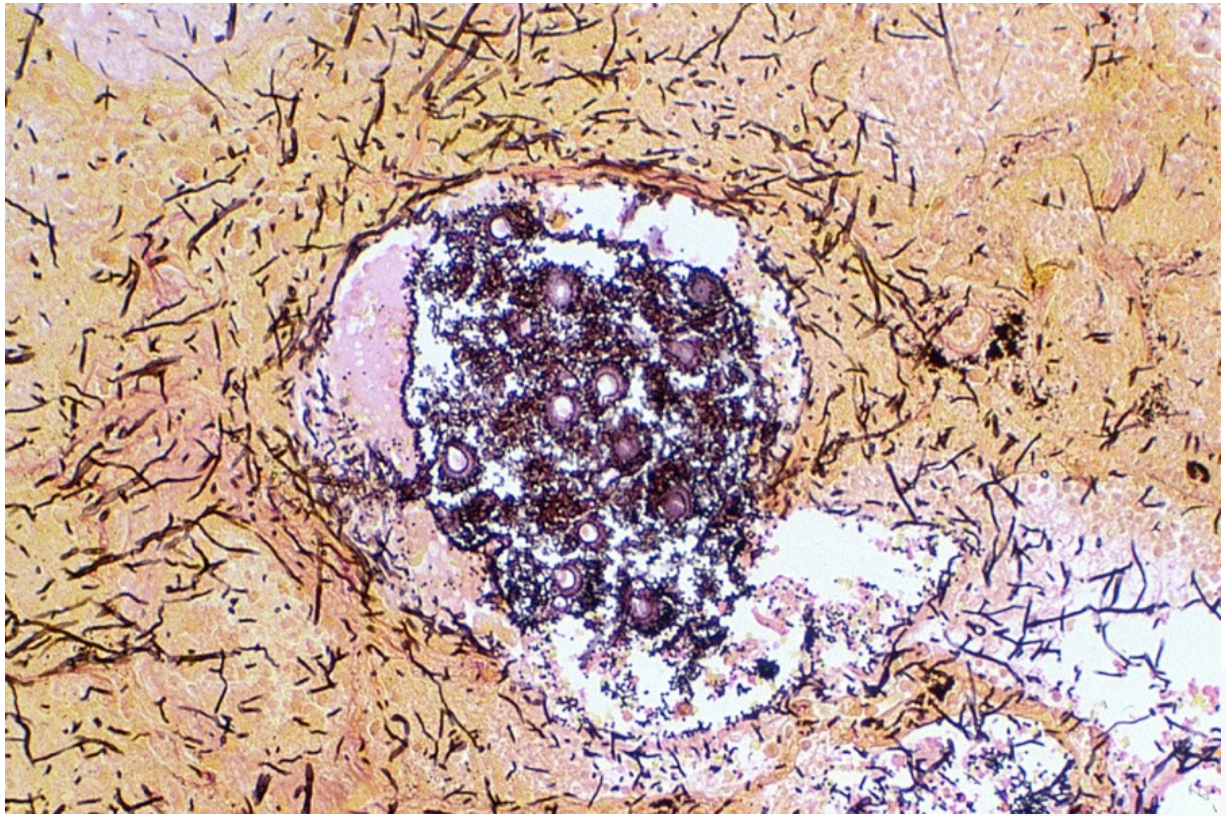
Aspergillosis of the lung. GMS stain showing dichotomously branched septate hyphae.



Grocott's methenamine silver (GMS) stained tissue sections showing *Aspergillus fumigatus* in lung tissue, note conidial heads forming in an alveolus.



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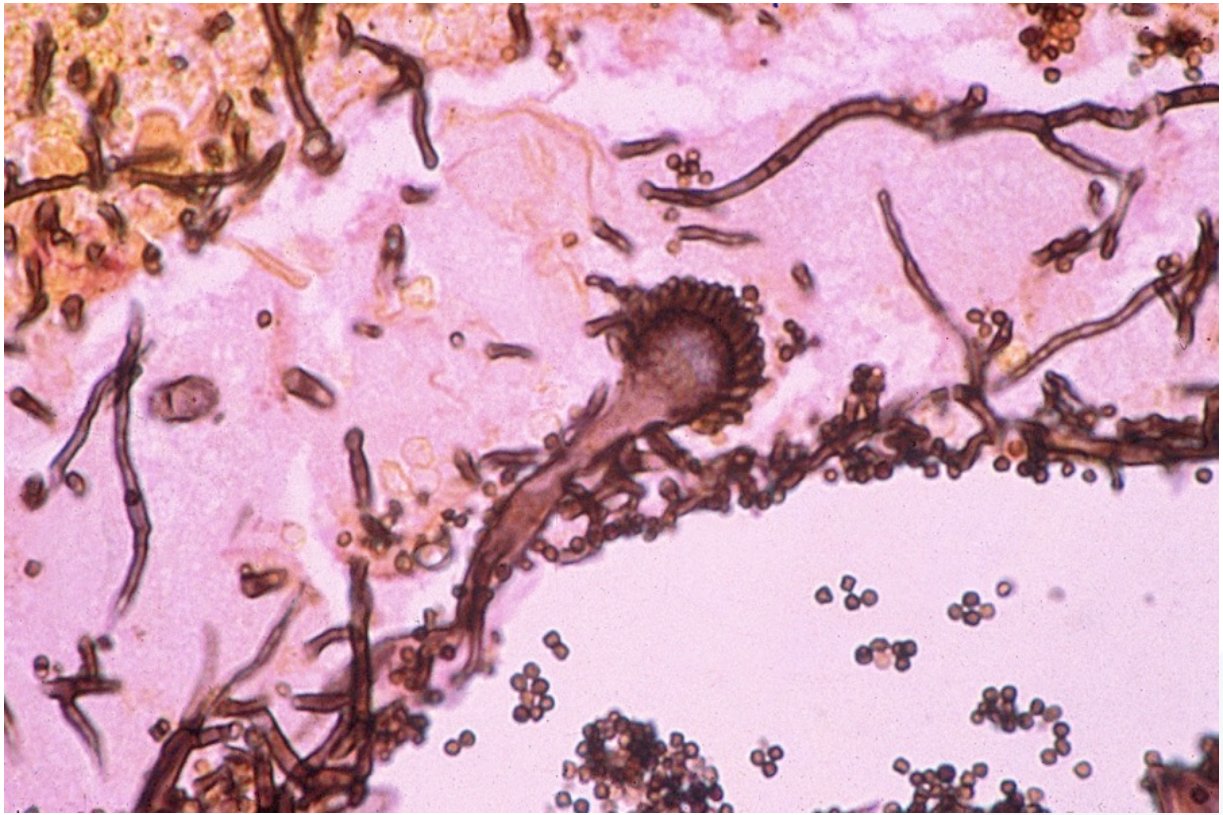

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Chronic oral candidiasis of the tongue and mouth corners (angular cheilitis) in an adult with an underlying immune deficiency. Note characteristic white pseudomembrane composed of cells and pseudohyphae of *C. albicans*.

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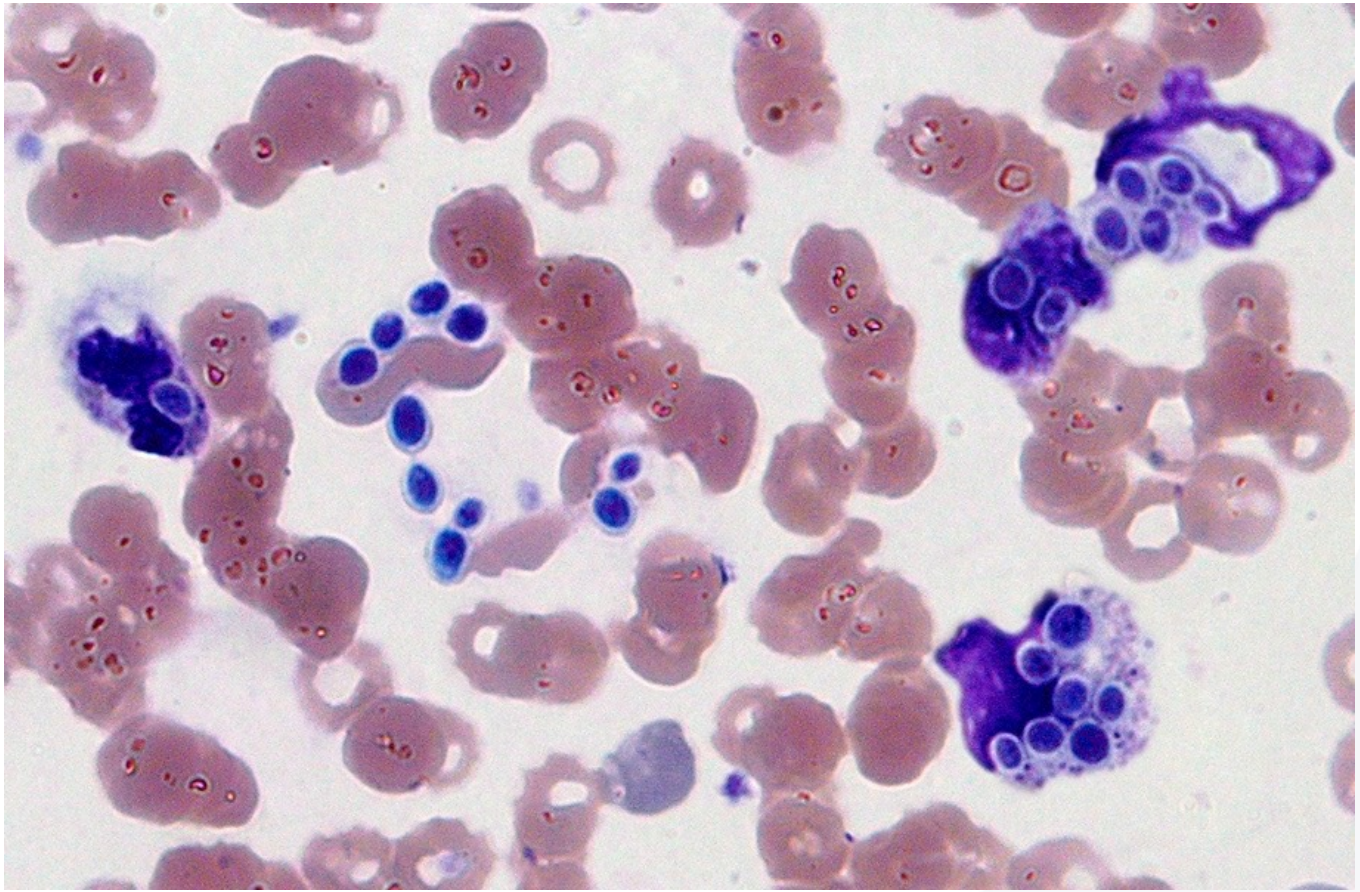
Candidemia: Giemsa stain showing *Candida* yeast cells.



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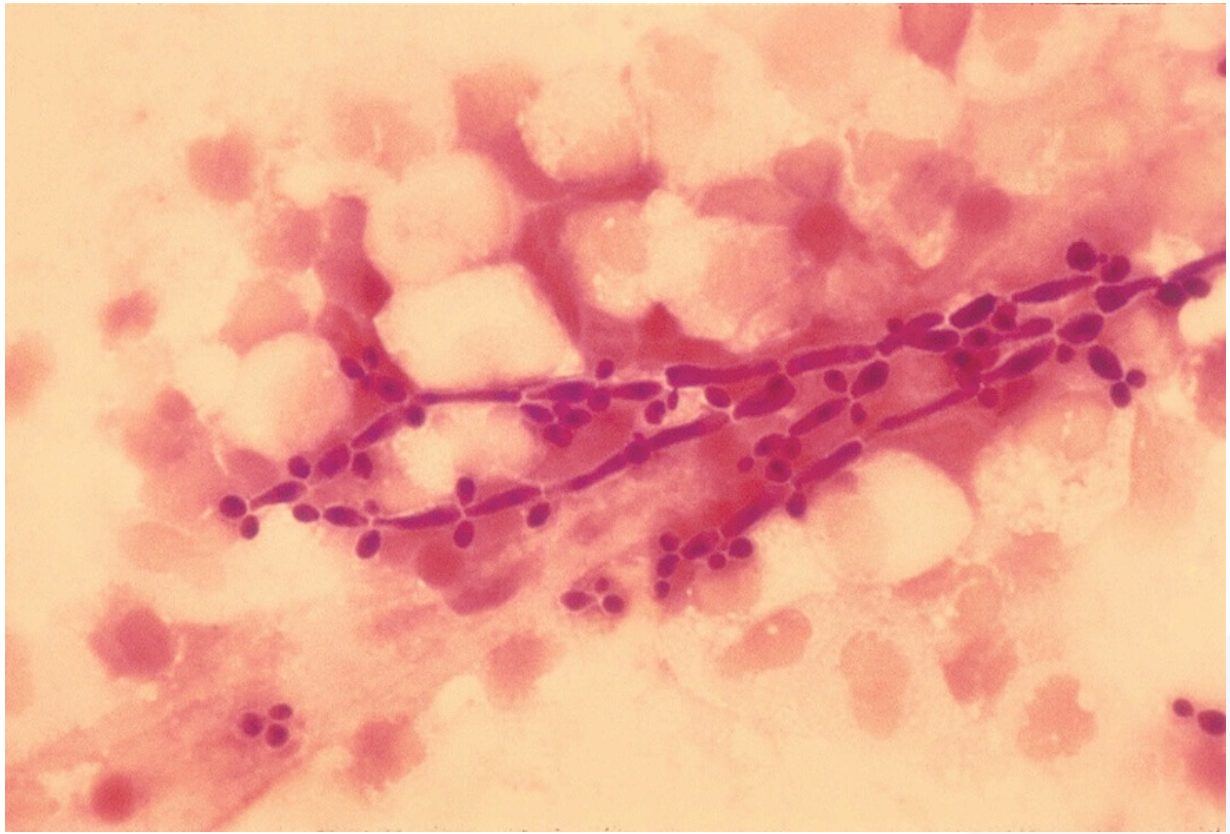
Direct smear of urine from a patient with candidiasis of the kidney showing *C. albicans* in mycelial or tissue phase with blastoconidia budding from the pseudohyphae.



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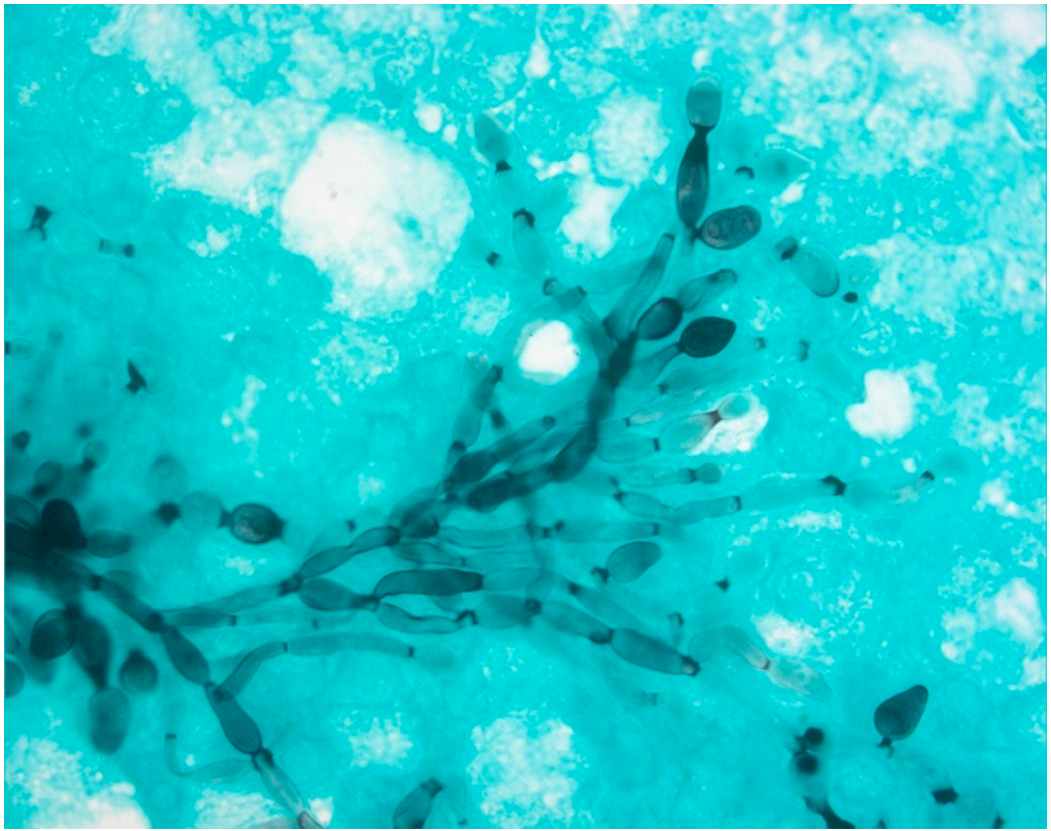
GMS – showing pseudohyphae (elongating yeast cells) of *Candida albicans.*



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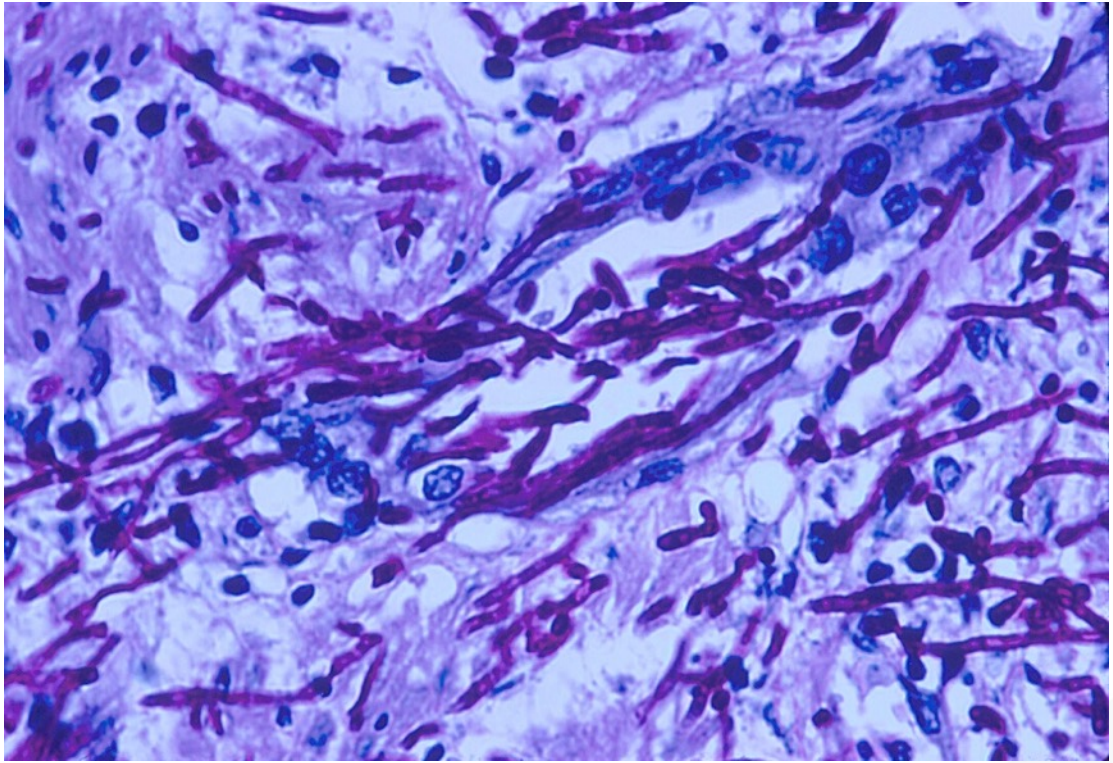
Periodic Acid-Schiff (PAS) stained section of post-mortem oesophagus showing invasion of blood vessel by *C. albicans*. Note blastoconidia and branched pseudohyphae**.**



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India ink preparation of CSF showing a budding yeast cell of *Cryptococcus neoformans* surrounded by a characteristic wide gelatinous capsule.

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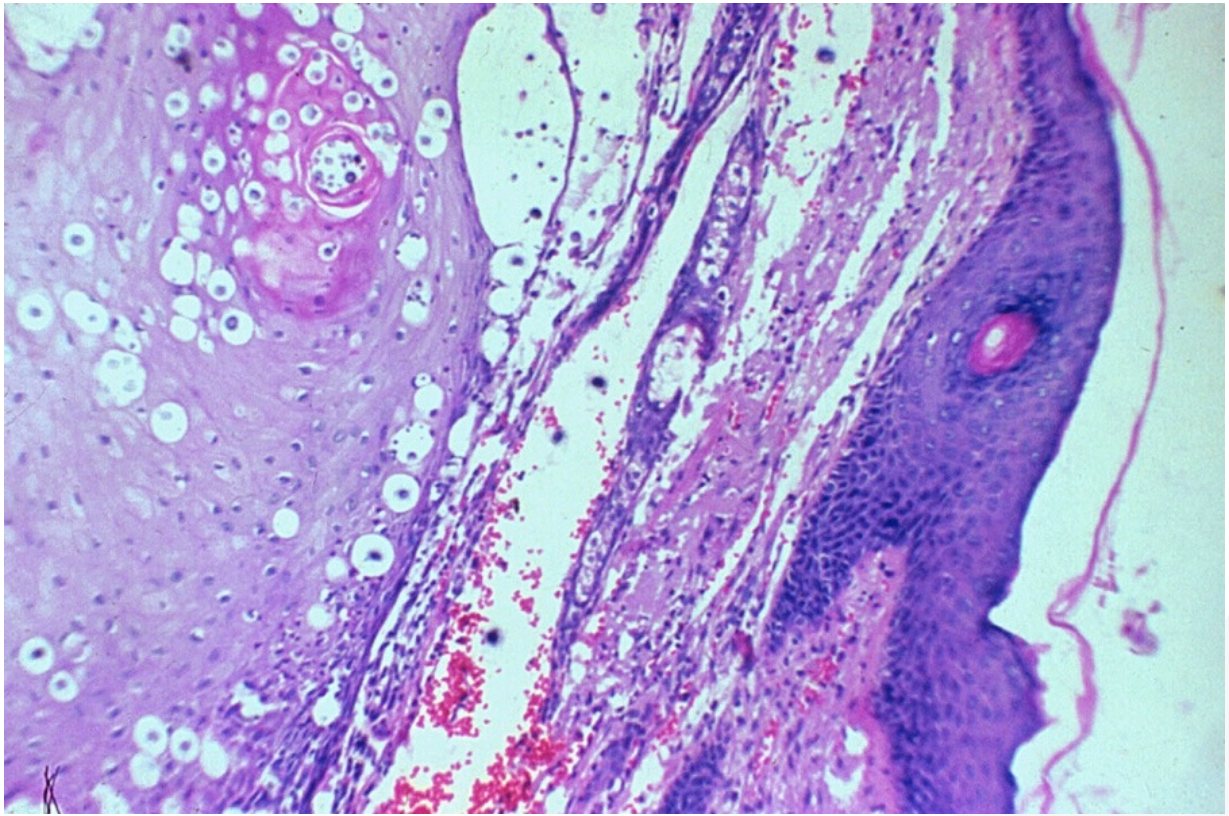
Tissue section stained by haematoxylin and eosin (H&E) showing numerous encapsulated yeast cells of *Cryptococcus neoformans*.



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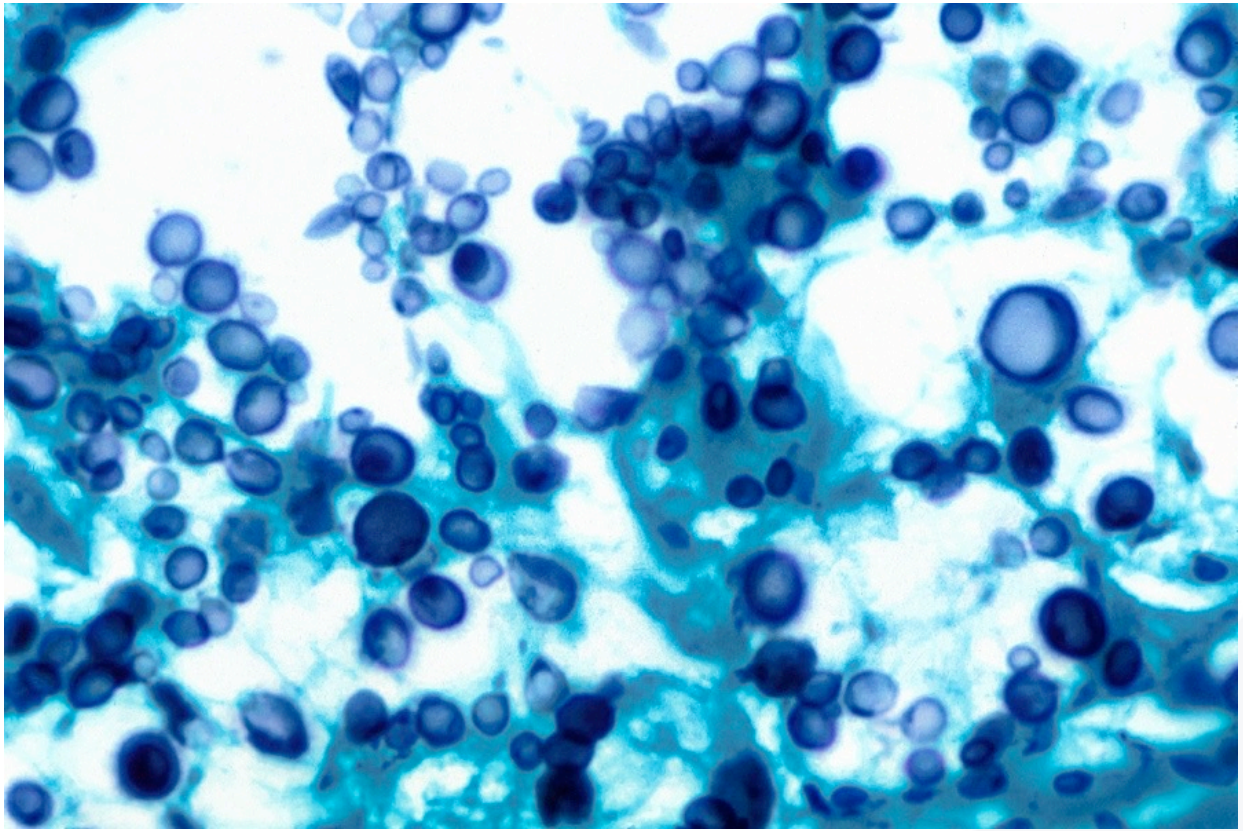
Grocott's methenamine silver (GMS) stained tissue section of lung showing typical encapsulated yeast cells of *C. neoformans.*



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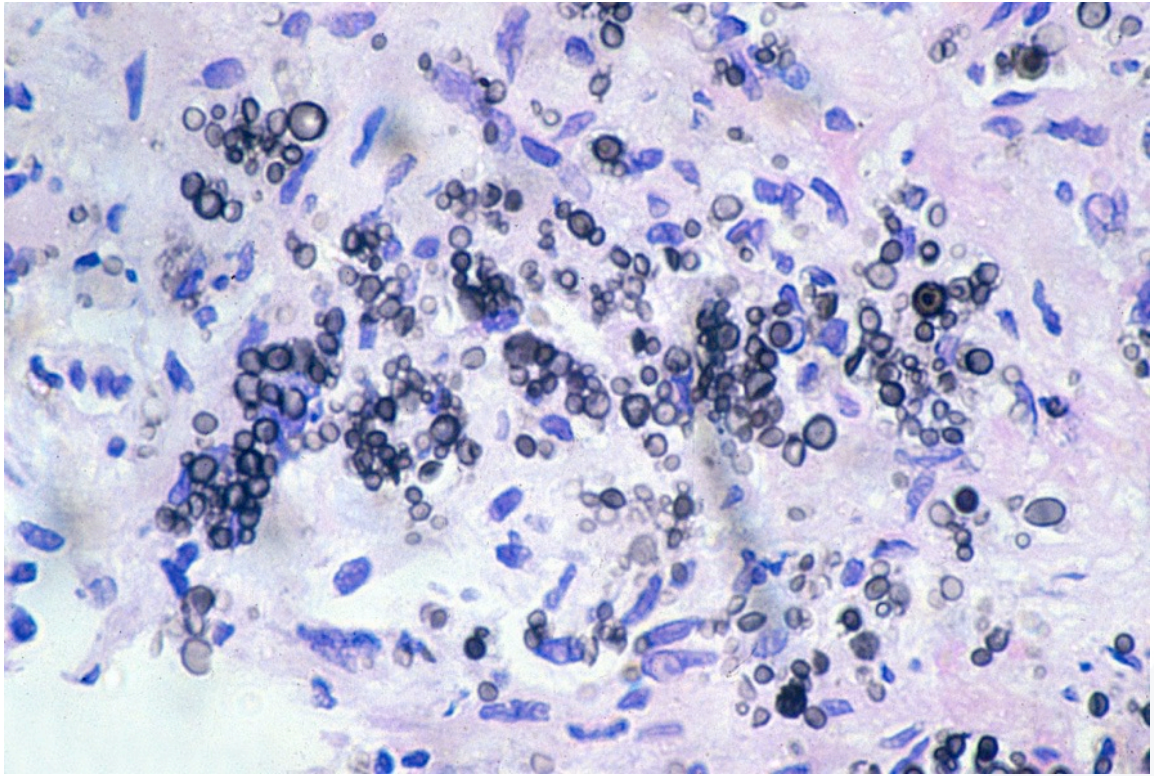
Grocott's methenamine silver (GMS) stained tissue section of lung showing atypical non-encapsulated yeast cells of *C. neoformans.*



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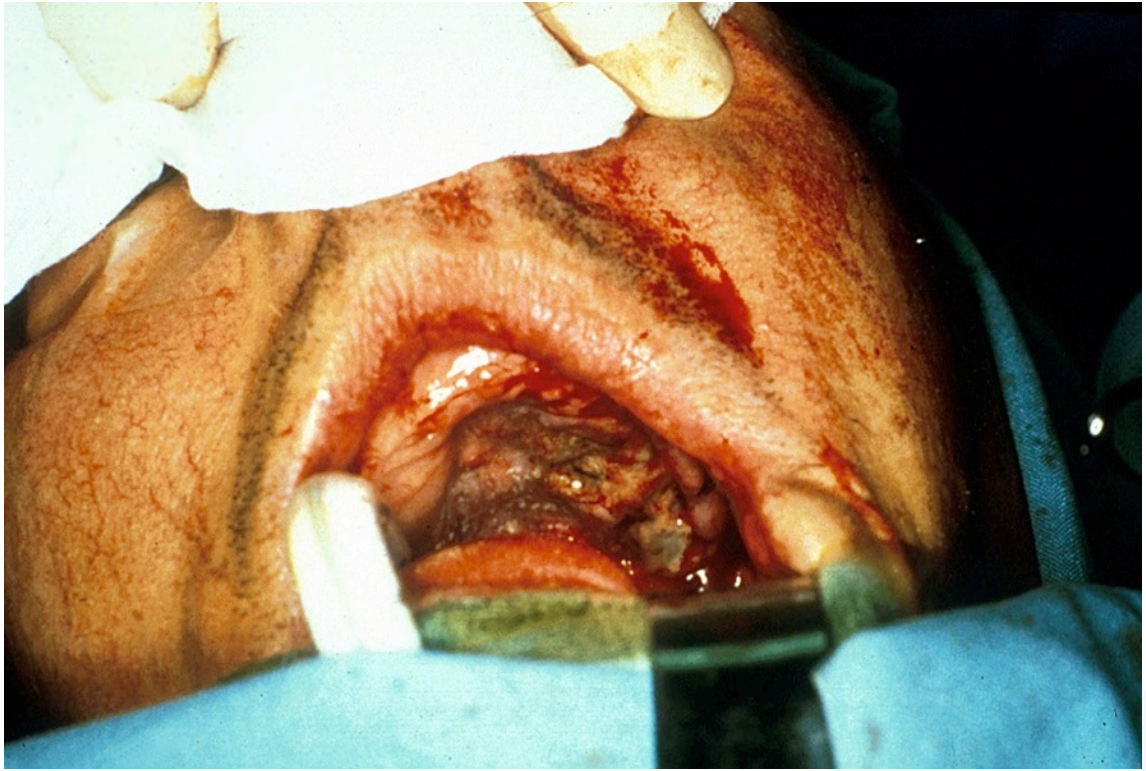
Rhinocerebral zygomycosis showing involvement of the palate caused by *Apophysomyces elegans*.



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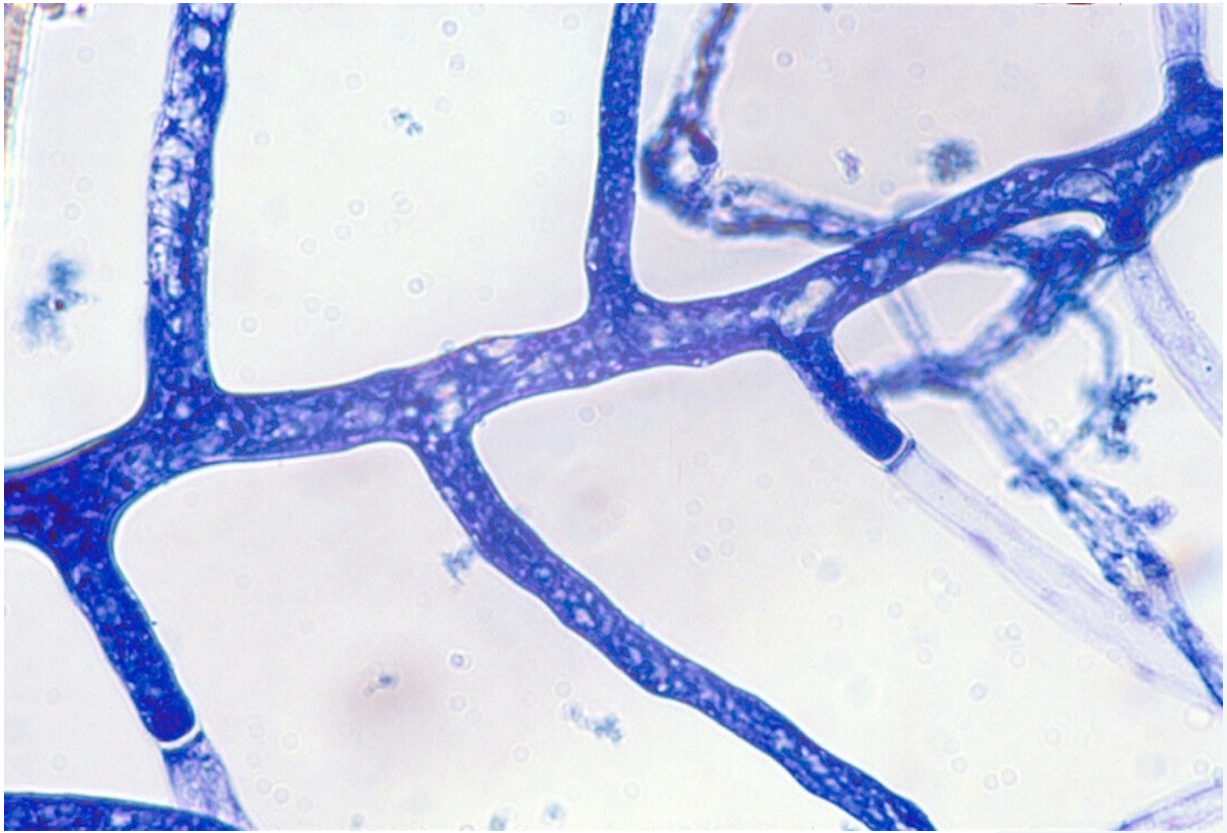
Microscopic morphology of *Saksenaea vasiformis* showing typical broad, sparsely septate (coenocytic) hyphae.



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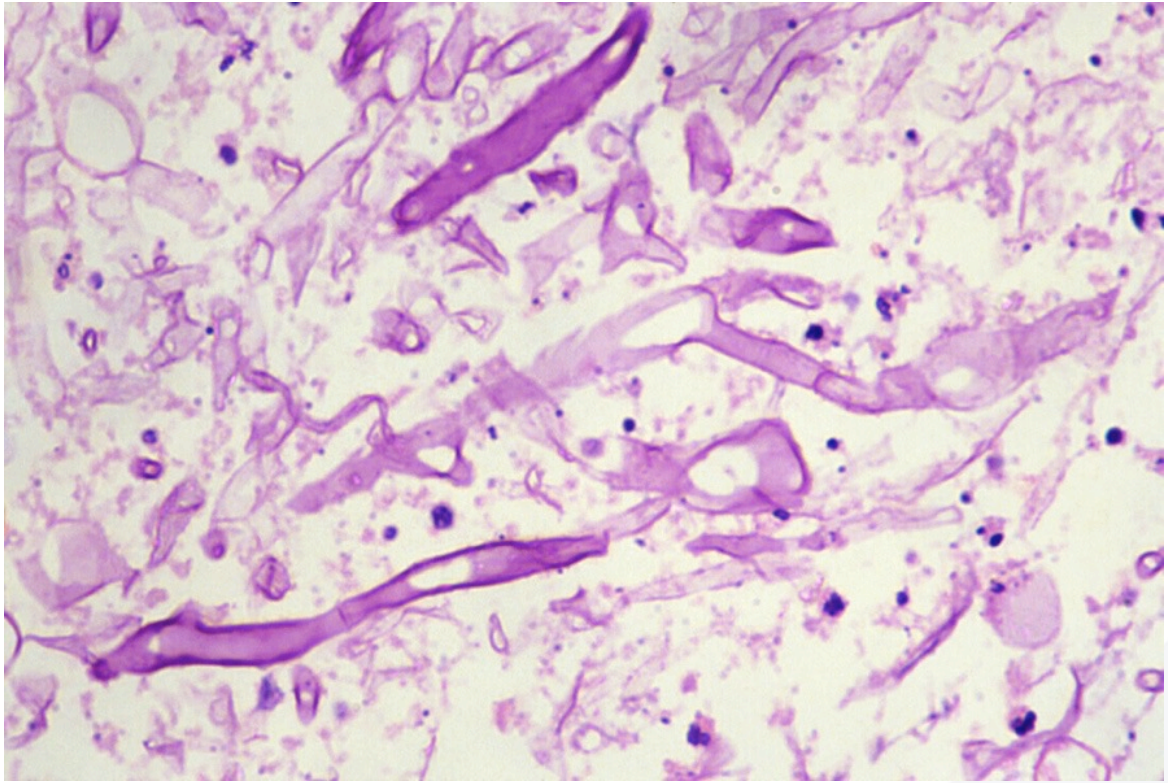
Haematoxylin and eosin (H&E) stained section of lung tissue showing the broad, infrequently septate, thin-walled hyphae of *Lichtheimia corymbifera*.



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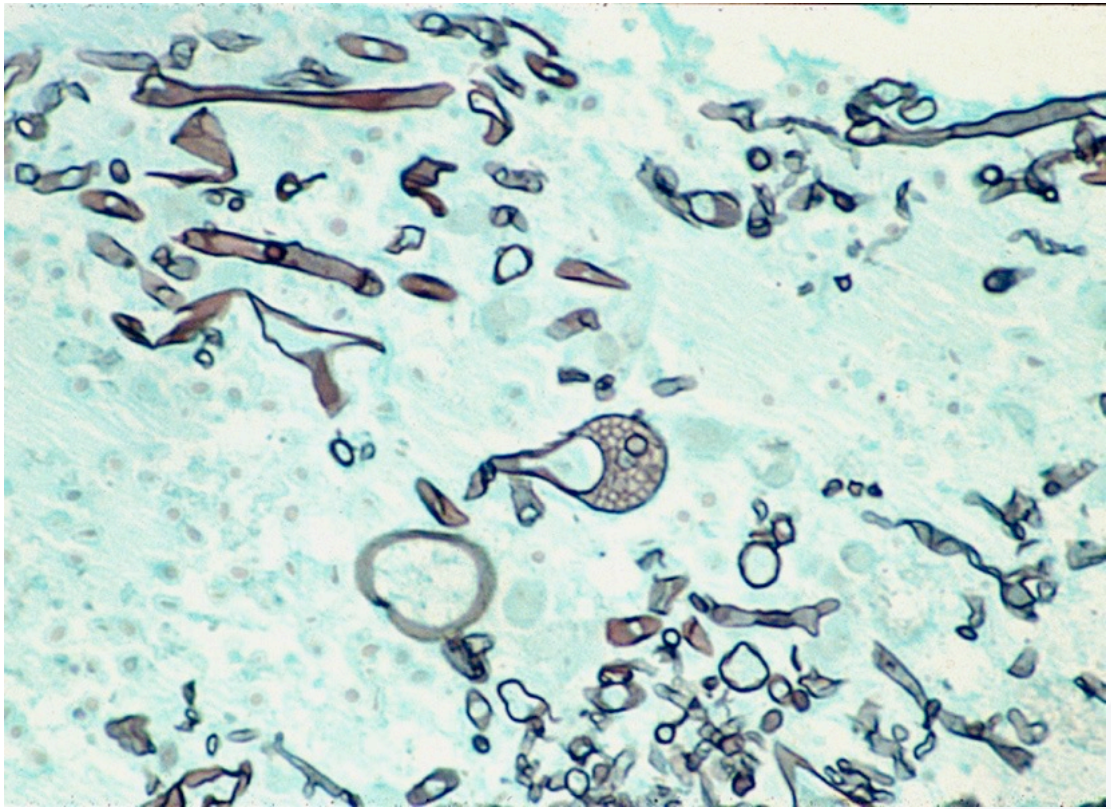
Grocott's methenamine silver (GMS) stained tissue section from a lung showing typical zygomycete hyphae and by chance a sporangium of *Lichtheimia corymbifera.*



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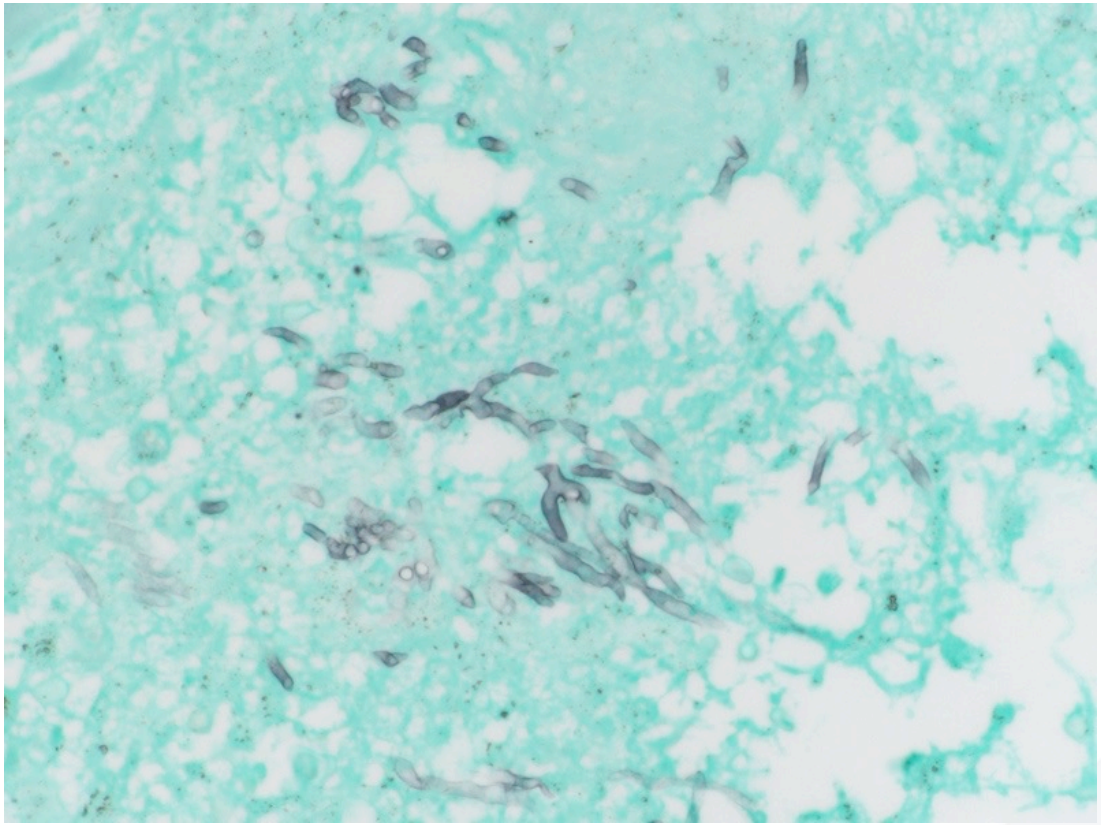
Question – is this *Aspergillus* or a Zygomycete?



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