The hypha is the basic morphologic element of multicellular fungi in the vegetative phase. It is a multi-branched tubular structure subdivided by transverse septa. These structures form a network known as a mycelium. The unicellular hyphae are oval to round, but often adhere together in the form of hypha-like chains (pseudo-hyphae). Most of the fungi that cause disease in humans have only slight pathogenic potential and can only invade tissue in an immunocompromised host or after destruction of competing bacterial flora. These are known as opportunistic pathogens. Tissue destruction by mycotic pathogens is partially attributable to toxic fungal products that cause disease by mechanisms that are not always well understood. It is also partially attributable to abnormal immune reactions. Antigens of the fungus capsule stimulate a population of B lymphocytes to form antibodies. This leads to precipitating and complement-binding antibodies, whose presence aids in diagnosing these disorders.

- The spores of saprophytic fungi such as Aspergillus, Candida, Coccidioides, and Penicillium cause allergic hypersensitivity reactions in predisposed patients and lead to mycotic allergies. A cell-mediated type IV hypersensitivity reaction also plays a decisive role in combating mycotic infections, as does uncompromised granulocyte function.
- Histologic findings of a “ruthlessly proliferative” mycelium that does not respect tissue septa, organ capsules, or vascular walls are common to all infectious diseases caused by mycelium-forming fungi (mycoses). The mycelium grows through these structures and typically exhibits a ring-like or spherical pattern of proliferation.

**Skin Mycoses (Superficial Mycoses)**

Pathogenesis: Forms of mycosis are differentiated according to the pathogen and depth of penetration in the tissue.

- **Superficial epidermal mycosis** is infestation of the horny layer of the epidermis with fungus organisms (not dermatophytes or fungi that produce deeper types of mycosis).
- **Cutaneous mycosis** refers to infestation of the entire epidermis and/or hair with fungal organisms (primarily dermatophytes, which cause dermatophytosis, and Candida, which causes candidosis).

**Dermatophytes**

Pathogens (dermatophytes): They only infect tissue containing large amounts of keratin such as the epidermis (Epidermophyton floccosum), hair (Trichophyton rubrum), and nails (Trichophyton mentagrophytes).

Pathogenesis: Dermatophytes are the only fungal infections that are spread by human-to-human or animal-to-human contact.

Pathogen identification: All dermatophytes are hyphomycetes and form septated hyphae in the skin lesions they create. These hyphae will be positive in a periodic acid-Schiff reaction (PAS).

**Clinical presentation and morphology:**

**Dermatomycoses** (skin mycoses) are caused by variety of pathogens that produce morphologically similar cutaneous lesions (referred to as a tinea and further specified according to location). These tineas consist of round or oval erythematous rashes that are often concentric (A).

**Onychomycosis** (nail mycosis) is an infection of the nails of the fingers or toes causing yellowish-white opacification and flaking of the nail (B). The disorder begins as distal unguinal, proximal unguinal, or superficial onychomycosis and later progresses to dystrophic onychomycosis.

**Deep trichophytosis** is dermatophytosis with bacterial superinfection that results in a suppurative abscess-forming inflammation with mycelium at the depth of the hair follicles.

**Subcutaneous and Mucosal Mycoses**

**General pathogenesis:** Fungi grow beyond the epidermis and penetrate into deeper layers of subcutaneous connective tissue through skin wounds. This results in a focal chronic inflammatory reaction around the mycelium (C2); granulomatous inflammatory reactions (C1) may occur in patients with stronger immune systems.

**Organ and Systemic Mycoses**

**General pathogenesis:** Fungal penetration may occur by several mechanisms.

- **Aerogenic penetration** leads to fungal bronchitis (D1) with invasion of the bronchial wall (D2) progressing to invasion of surrounding pulmonary tissue.
- **Latrogenic penetration** of fungi present in the oral flora can occur during endoscopic retrograde cholangiopancreatography (ERCP).
- **Hematogenous penetration** can occur in vascular invasion, which may successively lead to fungal vasculitis (E), fungemia (fungal sepsis), and fungal colonization of organs such as the liver (F).

**Note:** The general principle of mycosis due to mycelium-forming fungi involves these elements:

- Relentless invasion of tissue septa, organ capsules, and vessel walls;
- Organ invasion → spherical pattern;
- Skin invasion → circular pattern.
A Dermatomycosis

B Onychomycosis in a black patient

C Granulomatous fungal inflammation (PAS) x 15

D Aerogenic fungal infection (fungal bronchitis) (Grocott-silver stain) x 25

E Hematogenous fungal infection (vasculitis) (Grocott-silver stain) x 25

F Hematogenous fungal infection (fungal sepsis in the liver; PAS) x 75