Chapter 47

Basic Mycology

Structure and Growth

-- **Fungi are eukaryotes** whereas **bacteria are prokaryotes** so they differ significantly.

-- Two fungal structures are of medical importance, **cell wall** and **cell membrane**.

Cell wall

-- The fungal cell wall consists primarily of **chitin (not peptidoglycan)** so fungi are **insensitive to antibiotics that inhibit peptidoglycan synthesis.**

-- Chitin is a **polysaccharide** composed of long chains of **N-acetylglucosamine**.

-- The cell wall contains other polysaccharides as well, most importantly **β-glucan**, a long polymer of D-glucose.

-- It is site of action of antifungal drug **caspofungin**.

Cell membrane

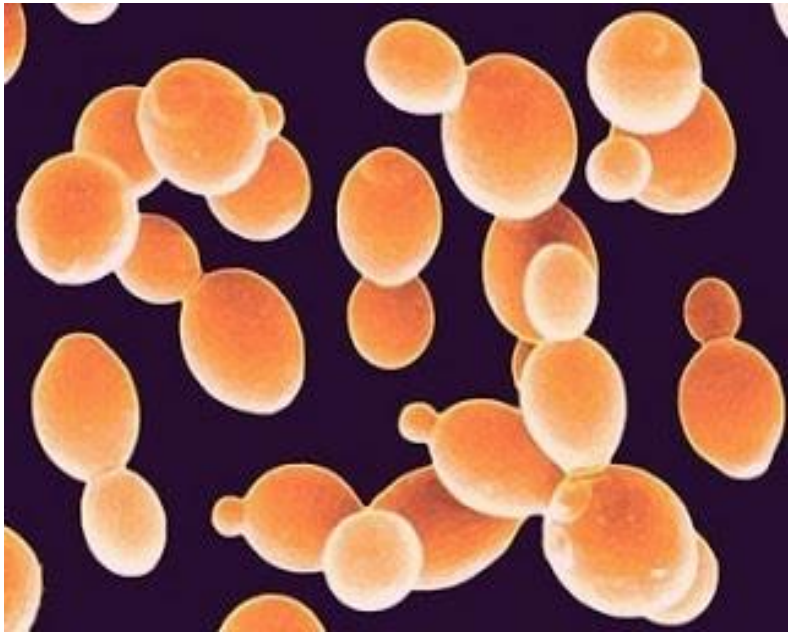
-- The fungal cell membrane contains **ergosterol**, in contrast to the human cell membrane which contains **cholesterol**.

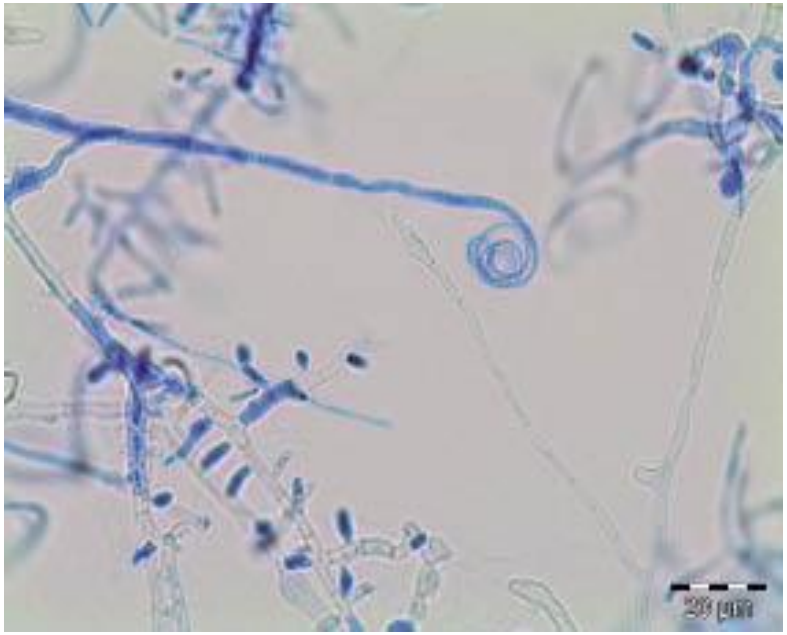
-- The **selective action** of amphotericin B and azole drugs, such as fluconazole and ketoconazole on fungi is **based on this sterol difference**.

There are **two** types of fungi: **yeasts** and **mold**

Yeasts grow as **single cells** that reproduce by **asexual budding**.

Molds grow as **long filaments (hyphae)** and form a **mat (mycelium).**

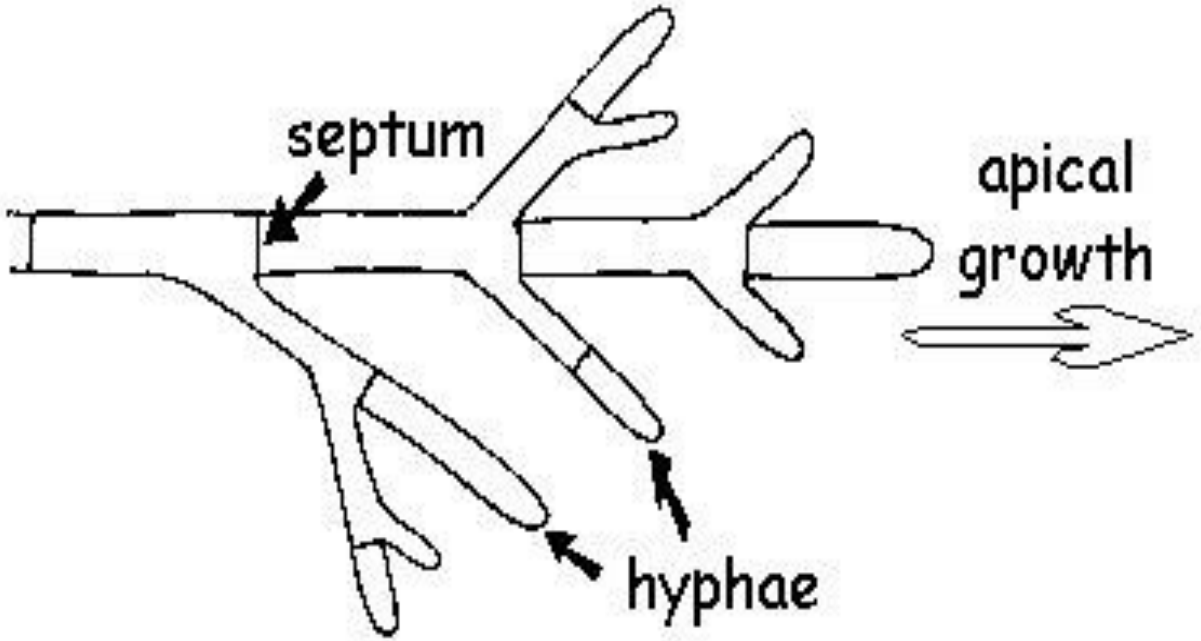




Some hyphae form **transverse walls (septate hyphae)** whereas others do not (non septate hyphae).

Non septate hyphae are **multinucleated (coenocytic).**

The **growth** of hyphae occurs by **extension of tip**, **not by cell division** all along the filament.



-- Several fungi of medical importance are **thermally dimorphic**, i.e., they form different structures at different temperatures.

-- They exist as **molds at ambient temperature** but as **yeasts at 37°C**.

-- Most fungi are **obligate aerobes**, some are facultative anaerobes but **none are obligate anaerobes**.

-- All fungi require a **preformed organic source of carbon**, the reason why they like **decaying matter**.

-- So their natural habitat is **environment**.

-- ***Candida albicans*** is an exception being **part of normal human flora**.

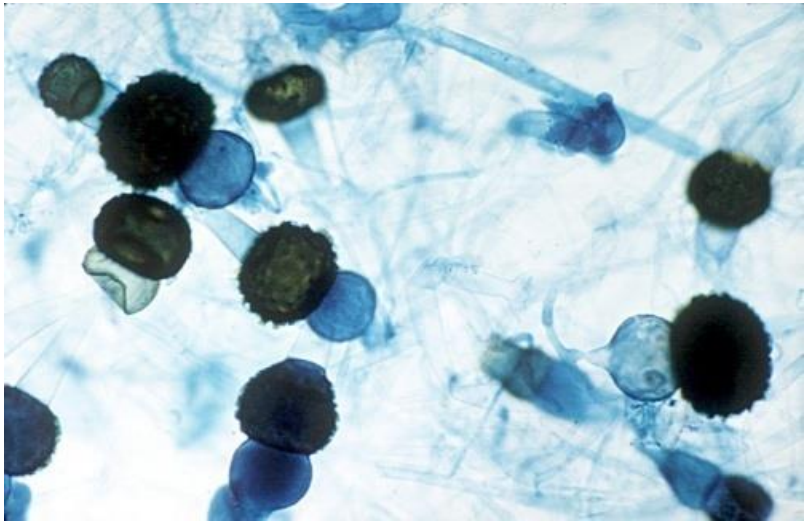
-- Some fungi **reproduce sexually** by mating and **forming sexual spores (zygospores, ascospore and basidiospores).**

-- **Zygospores** are **large single spores with thick walls**.

-- **Ascospores** are formed in a **sac called ascus**.

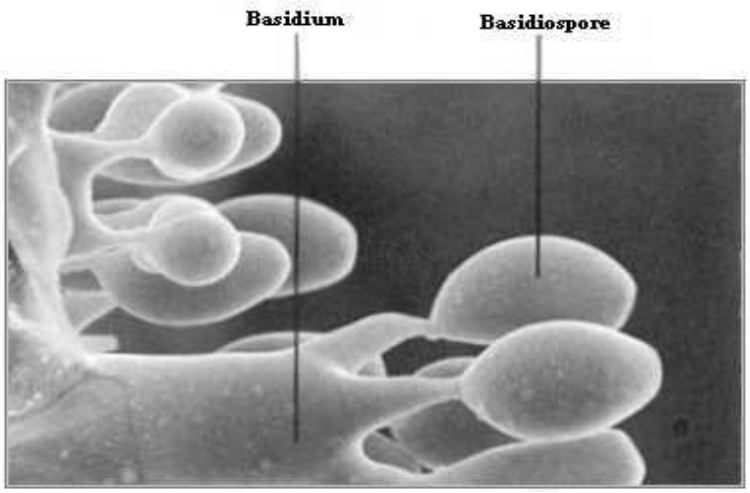
-- **Basidiospores** are formed **externally on the tip of a pedestal called basidium**.

-- Classification of these fungi is based on their sexual spores.



Zygospores

Ascospores



Basidiospores

-- Fungi that **do not form sexual spores** are called **fungi imperfecti**.

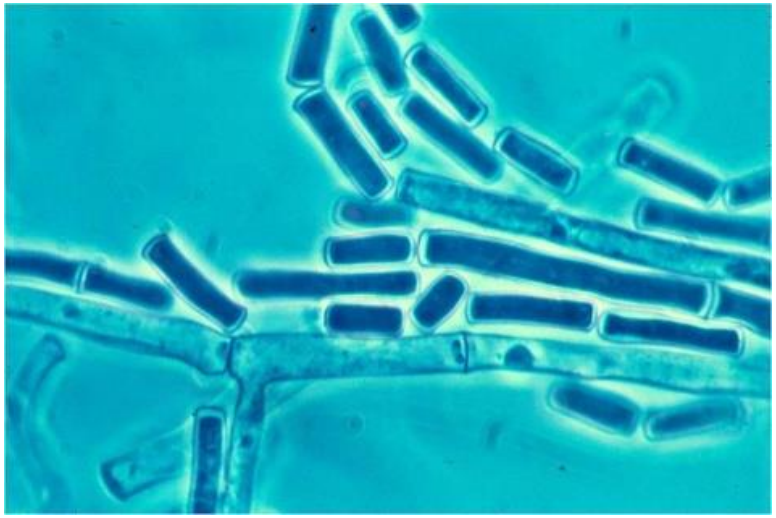
-- Most fungi of **medical importance** form **asexual spores called conidia**.

-- Their **shape**, **color** and **arrangement** aid in **identification**.

Asexual spores are of different types:

Arthrospores: These arise **by fragmentation of ends of hyphae**, e.g., in ***Coccidioides immitis***.

Chlamydospores: These are **rounded, thick walled and quite resistant**, e.g., in ***Candida albicans***.



Arthroconidia

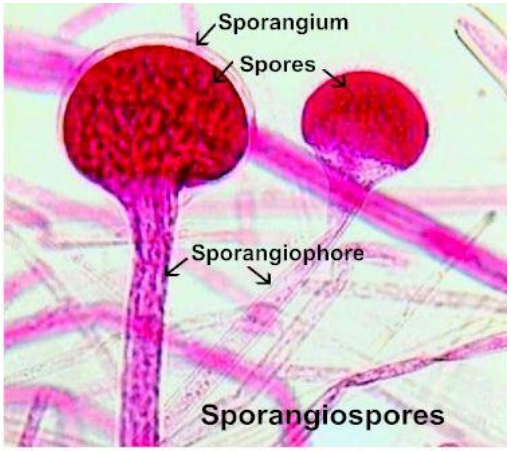
Chlamydoconidia

Blastospores: These are formed by **budding process** by which yeasts reproduce asexually.

Some yeasts such as ***Candida albicans*** can form **multiple buds** that do not detach thus producing sausage like chains called **pseudohyphae.**

Sporangiospores: These are formed **within a sac (sporangium) on a stalk** by molds such as ***Rhizopus*** and ***Mucor***.

Blastospores



Sporangiospores

Pathogenesis

-- Fungi cause **formation of granulomas** which are produced in **major systemic diseases**.

-- Granuloma formation is related to **cell mediated immunity**.

-- **Acute suppuration**, characterized by the presence of **neutrophils in the exudates** also occurs in certain fungal diseases such as **aspergillosis** and **sporotrichosis**.

-- Fungi **do not have endotoxin** in their cell walls, nor they produce **bacteria like exotoxins**.

-- Activation of cell mediated immune response results in a **delayed hypersensitivity skin test** response to certain fungal antigens injected intradermally.

-- A **positive** skin test **only indicates exposure** whether past or present.

-- **Negative** test means **no exposure** except in immunocompromised persons.

-- To check the status of **CMI**, ***Candida*** antigens can be used as **positive control** because ***Candida*** is part of normal flora.

-- **Fatty acids in the skin inhibit dermatophyte growth.**

-- Some hormones have **similar effect**.

-- The normal flora of the skin and mucous membrane **suppress fungi**.

-- Its **inhibition by antibiotics** may result in **fungal overgrowth**, e.g., ***Candida albicans***.

-- In the respiratory tract, the important host defenses are the **mucous membranes of the nasopharynx** which trap inhaled fungal spores and **alveolar macrophages**.

-- Circulating **IgM** and **IgG** are also produced but their role is uncertain.

-- **CMI is protective** and its suppression may lead to reactivation and dissemination of asymptomatic fungal infections and to disease caused by **opportunistic fungi**.

Fungal toxins and allergies

-- In addition to **mycotic** infections, there are two other types of fungal diseases **mycotoxicosis** caused by ingested toxins and **allergies** to fungal spores.

-- An example of **mycotoxicosis** is that caused by eating of ***Amanita*** **mushrooms** which produce two of the most potent hepatotoxins, **amanatin** and **phallaoidin**.

-- **Amanatin** inhibits **mRNA synthesis**.

-- Another common example is production of **aflatoxins** by ***Aspergillus flavus*** which cause liver damage and tumors in animals and are suspected of causing **hepatic carcinoma in humans**.

-- These are ingested with **spoiled grains and peanuts** and are metabolized by the liver to epoxide, a potent carcinogen.

-- **Aflatoxin B1** induces a mutation in the **p53 tumor suppressor gene**, leading to a **loss of p53 protein** and consequent **loss of growth control** in the hepatocyte.

-- **Allergies** to fungal spores, particularly those of ***Aspergillus***, are manifested primarily by an **asthmatic reaction** (rapid bronchoconstricition mediated by IgE), **eosinophilia**, and a **"wheal and flare"** skin test reaction.

-- These clinical findings are due to **immediate hypersensitivity response** to the fungal spores.

Laboratory diagnosis

There are **four** approaches:

1. Direct **microscopic** examination
2. **Culture** of organisms
3. **DNA probe** tests
4. **Serologic** tests

Direct microscopic examination

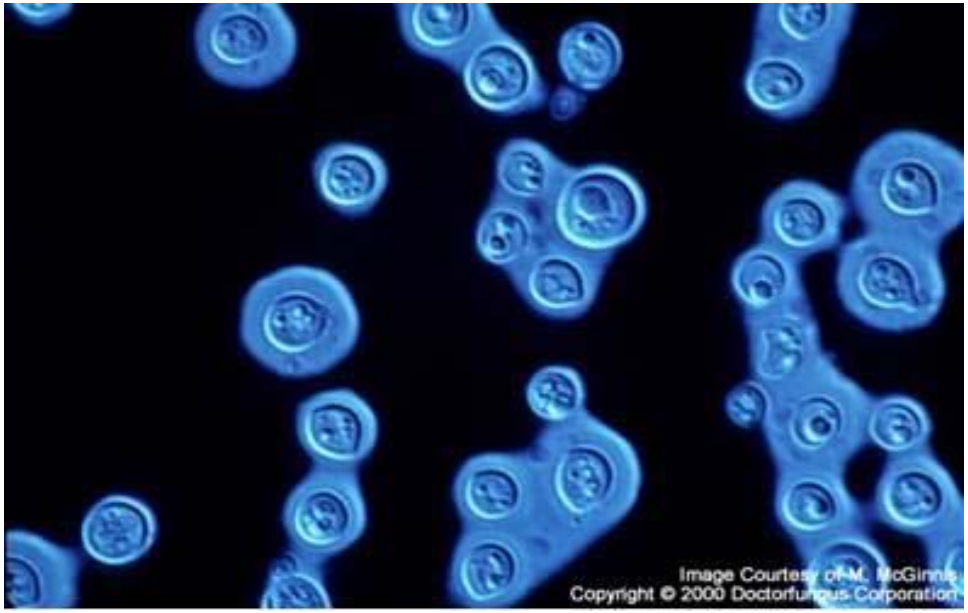
-- Direct microscopic examination of **sputum, lung biopsy material**, and **skin scrapings** depends on finding **characteristic asexual spores, hyphae or yeasts** in the **light microscope**.

-- The specimen is either **treated with 10% KOH** to dissolve tissue material, leaving alkali resistant fungi intact, or **stained with special fungal stains**.

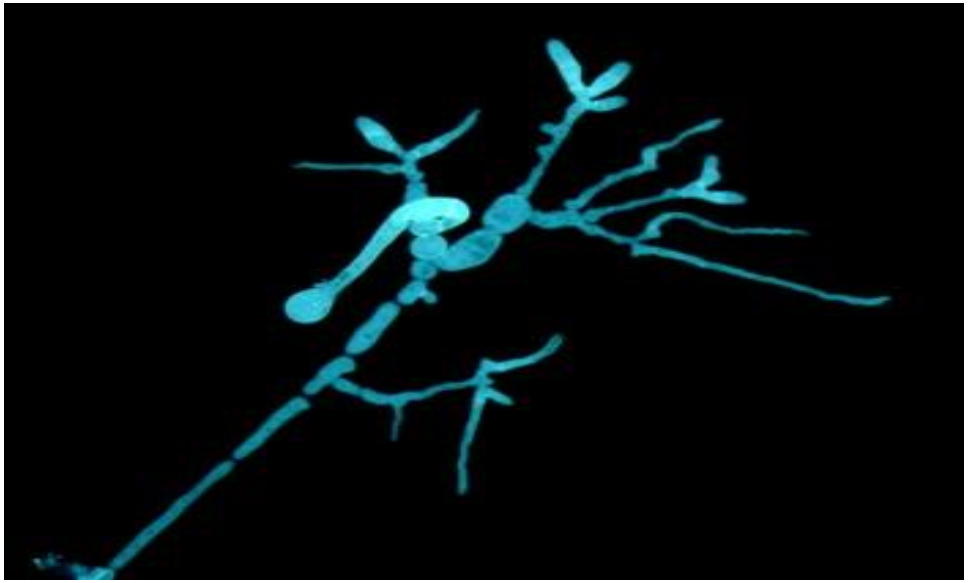
-- It can be especially useful for detecting spherules of ***Coc. immitis*** and wide capsule of ***Crypt. neoformans*** in India ink preparations.

-- **Calcofluor white** is a **fluorescent dye** that binds to fungal cell walls and is useful in the identification of fungi in tissue samples.

-- **Mathanamine silver stain** is also useful in the microscopic diagnosis of fungi in tissue.



***Crypt. neoformans in* India ink**



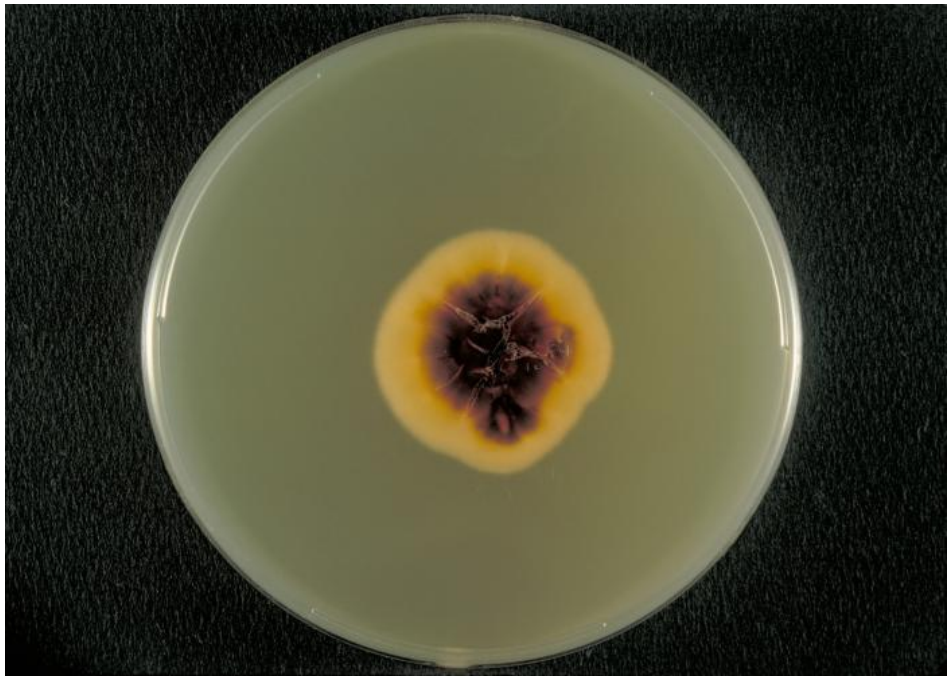
Calcofluor white fungal staining

Culture

-- Fungi are frequently cultured on **Sabouraud's agar** which facilitates the appearance of the slow growing fungi by inhibiting bacterial growth.

-- This inhibition is due to **low pH** and presence of **chloramphenicol** and **cycloheximide**.

-- The **appearance of the mycelium** and **nature of asexual spores** are **usually sufficient for diagnosis**.



Molecular methods

-- Molecular methods are available for the diagnosis of ***Coccidiodes, Histoplasma, Blastomyces*** and ***Cryptococcus***.

Serologic tests

-- Serologic tests are useful for diagnosis of **systemic mycosis**.

-- A **significant rise in titer** must be observed.

-- The **complement fixation test** is most commonly used in suspected cases of **coccidioidomycosis**, **histoplasmosis,** and **blastomycosis**.

-- In **cryptococcal meningitis**, the presence of polysaccharide capsular antigens of ***Cry. neoformans*** in the spinal fluid can be detected by the **latex agglutination test**.

Antifungal therapy

-- **Antibacterial drugs have no effect on fungi.**

-- Cell wall structure is different so all bacterial antibiotics which act on cell walls are of no use.

-- The **most effective** antifungal drugs target **ergosterol** in fungal membrane.

-- **Amphotericin B** disrupts fungal **membranes where ergosterol is present** and **azole drugs inhibit its synthesis.**

-- Another antifungal drug, **caspofungin inhibits the synthesis of β-glucan** which is found in fungal but not bacterial cell walls.

-- **Clinically significant resistance to antifungal drugs is uncommon.**

Chapter 48

Cutaneous and subcutaneous mycoses

Medical mycoses can be divided into **four** categories:

1. **Cutaneous**
2. **Subcutaneous**
3. **Systemic**
4. **Opportunistic**

Cutaneous mycoses

Dermatophytoses

-- **Dermatophytoses** are caused by **fungi (dermatophytes)** that infect **only superficial keratinized structures** (skin, hair, and nails) **not deeper tissues**.

-- The **most important** dermatophytes are classified in three genera ***Epidermophyton***, ***Trichophyton***, and ***Microsporum***.

-- They are spread by **direct contact**.

-- ***Microsporum*** is also spread from **animals** such as dogs and cats.

-- So to prevent reinfection, animal must be treated also.

-- **Dermatophytoses (tinea, ringworm)** are **chronic infections** often located in the **warm, humid areas** of the body (**athlete's foot** and **jock itch**).

-- **Typical ringworm lesions** have an **inflamed circular border containing papules and vesicles surrounding a clear area of relatively normal skin.**

-- The lesions are **typically pruritic**.

-- **Broken hairs** and **thickened broken nails** are often seen.

Tinea capitis

Tinea corporis

Tinea pedis

Favus

-- In some infected persons, **hypersensitivity causes dermatophytid reactions**, e.g., vesicles on fingers.

-- These lesions are a **response to circulating fungal antigens** and **do not contain hyphae**.

-- Patients with **tinea infections** show **positive skin tests** with **fungal extracts**, e.g., trichophytin.

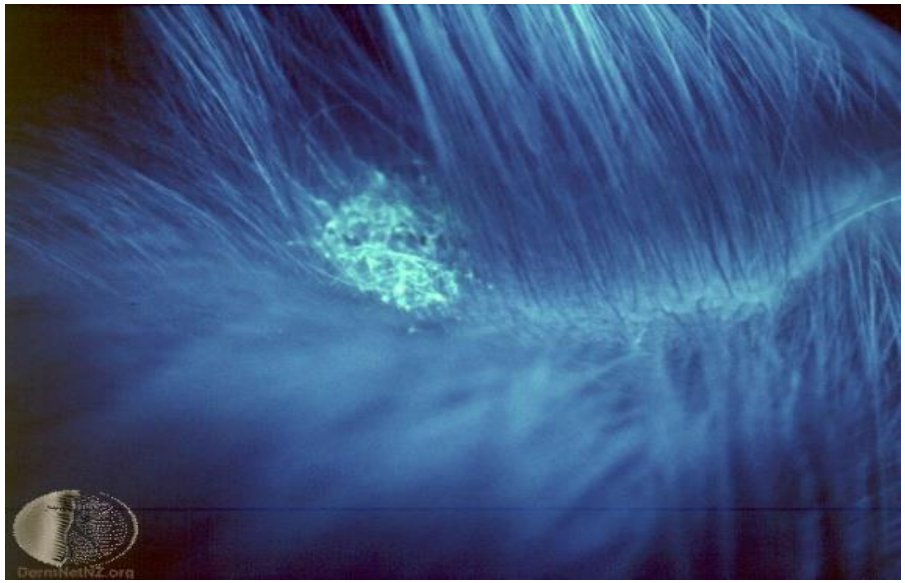
-- **Skin and nail scrapings** treated with **10% KOH** show **septate hyphae** under microscope.

Cultures on **Sabouraud's agar** at RT develop **typical hyphae and conidia**.

Tinea capitis lesions caused by ***Microsporum*** species can be detected by seeing **fluorescenc**e when the lesions are exposed to **UV light** from Wood's lamp.

Treatment involves **local antifungal creams** such as terbinafine (Lamisil) or oral griseofulvin.

Prevention centers on keeping **skin dry and cool**.



Tinea versicolor

Tinea versicolor is a superficial skin infection caused by ***Molassezia furfur***.

The lesions are usually noticed as **hypopigmented** areas esp. on tanned skin in the summer, more frequently in hot humid weather.

Lesions contain **budding yeast cells** as well as **hyphae**.

Miconzole subsides the lesions but they tend to recur.

Tinea nigra

Tinea nigra is an infection of the **keratinized layers** of the skin.

It appears as a **brownish spot** caused by melanin like pigment in the hyphae.

The causative agent ***Cladosporium werneckii*** is found in soil and transmitted during injury.

Diagnosis is made by **microscopic examination** and **cultures of skin scrapings**.

Infections are treated with a **topical keratolytic agent** (e.g., salicylic acid).

Subcutaneous mycosis

These are caused by **fungi** in soil and on vegetables which **enter the skin through a trauma.**

Sporotrichosis

-- ***Sporothrix schenkii*** is a **dimorphic** fungus.

-- The **mold form lives on plants** and the **yeast form occurs in human tissues**.

-- Spores when introduced into skin causes a **local pustule or ulcer with nodules along the draining lymphatics.**

Lesions are painless and there is little systemic involvement however **disseminated disease** may occur in **immuncocompromised patients.**

Untreated lesions may **increase and decrease in size and persist for years**.

In laboratory **round or cigar-shaped budding yeasts** are seen in tissue specimens.

In culture at RT, **hyphae occur bearing oval conidia in clusters at the tip of slender condiophores**.

Drug of choice is **itraconazole**.

Chromomycosis

-- This is a **slowly progressive granulomatous infection** caused by several soil fungi when introduced in the skin by trauma.

-- These fungi are collectively called **dematiaceous fungi** because their **hyphae or conidia are dark colored** either gray or black.

-- These include ***Phialophora*** and ***Cladosporium*** species.

Wart like lesions with crusting abscesses extend along the lymphatics.

It is **tropical disease** and usually **bare feet and legs** are affected.

In the laboratory, **dark brown, round fungal cells** are seen in leukocytes or giant cells.

The disease is treated with **oral flucytosine or thiabendazole plus local surgery**.

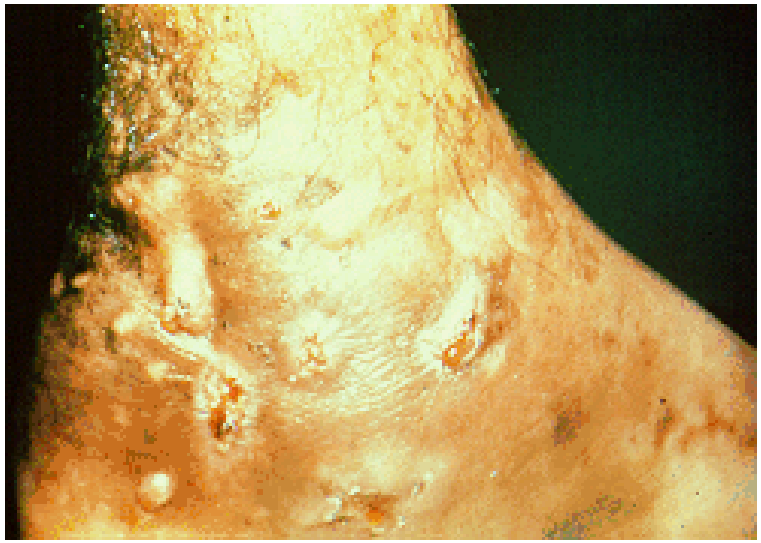
Mycetoma

Soil fungi (***Petriellidium, Madurella***) enter through **wounds on the feet, hands, or back** and cause **abscesses**, with pus discharged through sinuses.

The pus contains **compact colored granules**.

Actinomycetes such as ***Nocardia*** can cause similar lesions which **can be cured by sulphonamides**.

There is **no effective drug against fungal form** and **surgical excision is recommended**.

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