

Conidiospores

Medical Mycology

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Conidiophore



Actinomyces & Nocardia

- Act. & Nocardia are Gram-positive rods with tree-like branching growth making them confused with fungi in the past.
- They are opportunists sometimes cause indolent diseases.
- A related genus is *Streptomyces*, an antibiotics - Producer & rarely cause infections.

structure

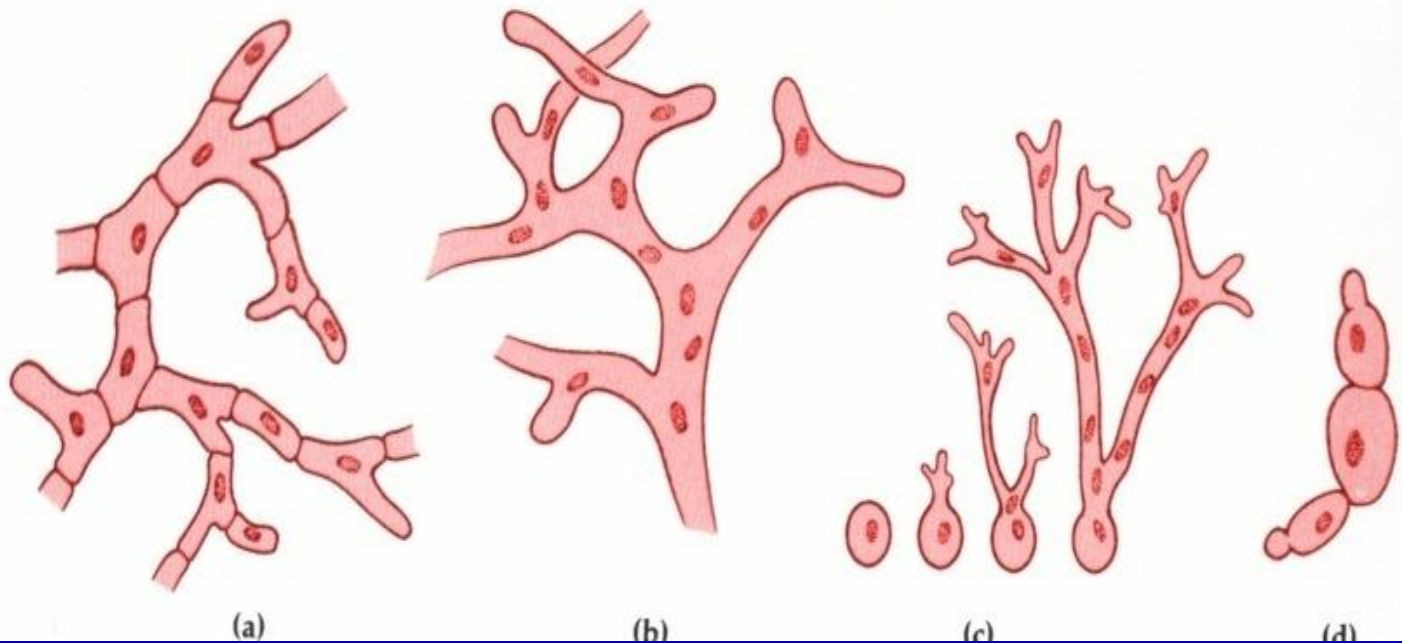
FIGURE 12.1

Vegetative structures of fungi. (a) Septate hyphae have crosswalls dividing the hyphae into cell-like units.

(b) Coenocytic hyphae lack crosswalls.

(c) Hyphae grow by elongating at the tips.

(d) Pseudohyphae are short chains of cells formed by some yeasts.



Actinomyces

- A Gram–positive bacilli that grow in 4-10 days but show irregular staining from sulfur granule (yellow-orange)
- They can be distinguished on the basis of:
Biochemical reactions, cultural features &
Cell wall composition.
- Actinomycosis is mainly due *A. israelii*.

Diagnosis

The etiologic diagnosis with certainty is difficult
Therefore a clinical diagnosis is usually adopted.

This is based on the nature of the lesion with a slow and progressive course and history of trauma.

The direct microscopic examination of large quantity of pus and biopsies for sulfur granules is essential.

Anaerobic growth period on the required media.

Treatment

-Penicillin G is the drug of choice

-Other antibiotics include:

Tetracycline, erythromycin and clidomycin

Nocardia

- Gram–positive rod-shaped with branches similar to *Actinomyces* but are shorter & more fragmented.
- Many strains take the Gram stain poorly hence appear beaded with alternating G+ & G – sections of the same filament.
- Human infections are mainly due to *N. asteroides* & *N. brasiliensis* which are weakly acid fast.

Nocardiosis

- Caused by *Nocardia spp*; mainly present in soil.
- It has two forms:
 - 1- The pulmonary form which is an acute bronchopneumonia. Usually occurs in patients with compromised immune systems.
 - 2- The cutaneous form produces localized pustules in areas of traumatic inoculation.

Diagnosis

- Nocardia infection is easier in diagnosis than Actinomyces because of their abundant presence in infected tissues
- Sputum and/or aspirates from skin or other purulent sites can be stained & searched for G + rods with primary or secondary branches.
- The acid-fastness is not strong as that of mycobacteria.
- Culture of Nocardia can be done on blood agar.

MYCOLOGY

- Fungi are eukaryotic organisms that do not contain chlorophyll, but have cell walls, filamentous structures, and produce spores.
- These organisms grow as saprophytes and decompose dead organic matter.
- They reproduce sexually or asexually.
- There are between 100,000 to 200,000 species depending on how they are classified, 300 species are currently known to be pathogenic to man.

Medically important fungi

1-Ascomycota - Sexual reproduction in a sack called an ascus with the production of ascospores (Fig 1).

2-Basidiomycota -Sexual reproduction in a sack called a basidium with the production of basidiospores (Fig 2).

3. Zygomycota - sexual reproduction by gametes and asexual reproduction with the formation of zygospores (Fig 3).

4. Mitosporic Fungi (Fungi Imperfect) - no recognizable form of sexual reproduction. Includes most pathogenic fungi.

***Fig.1: Chaetomium globosum* spores.**

***Chaetomium* is an ascomycete**

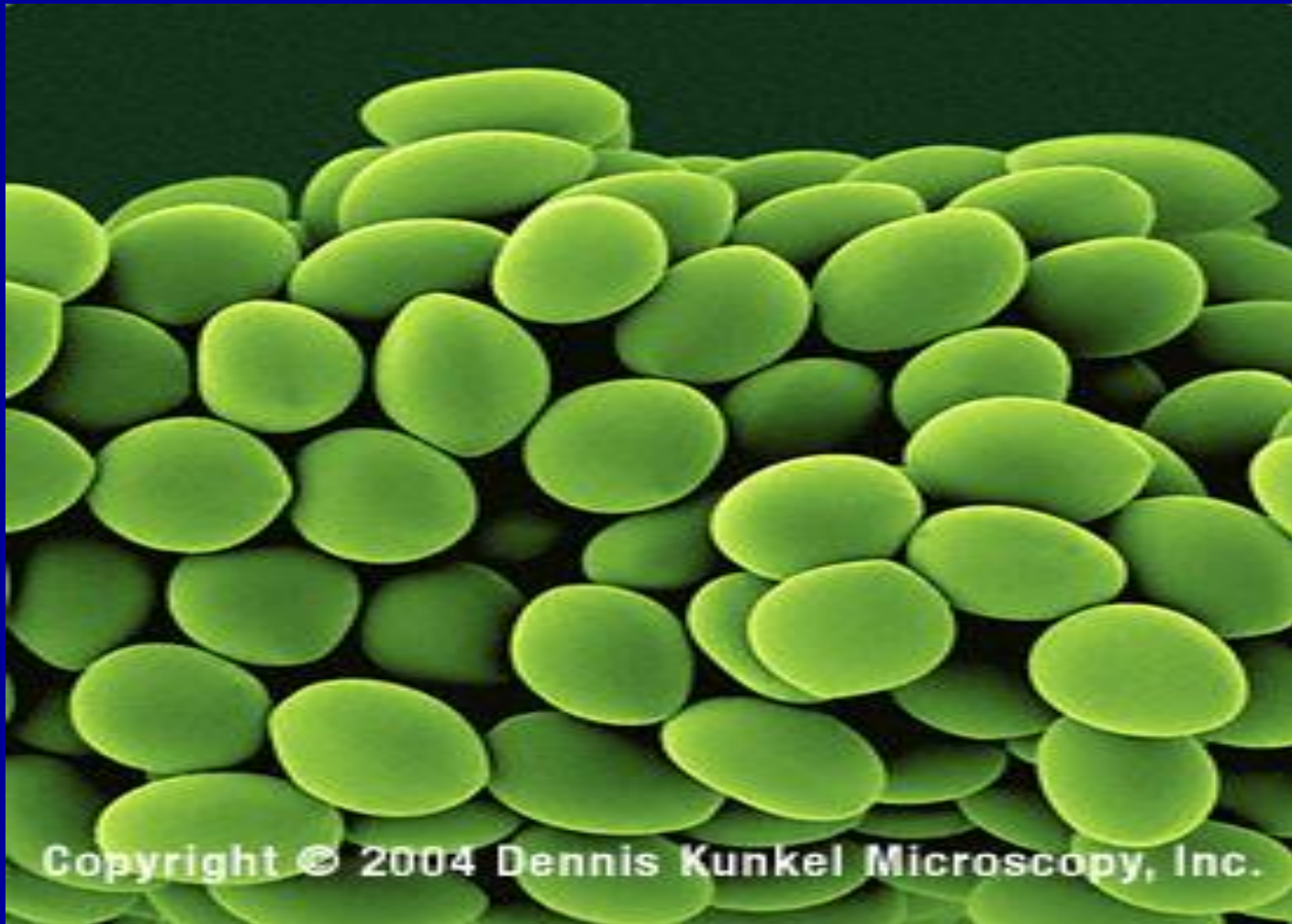
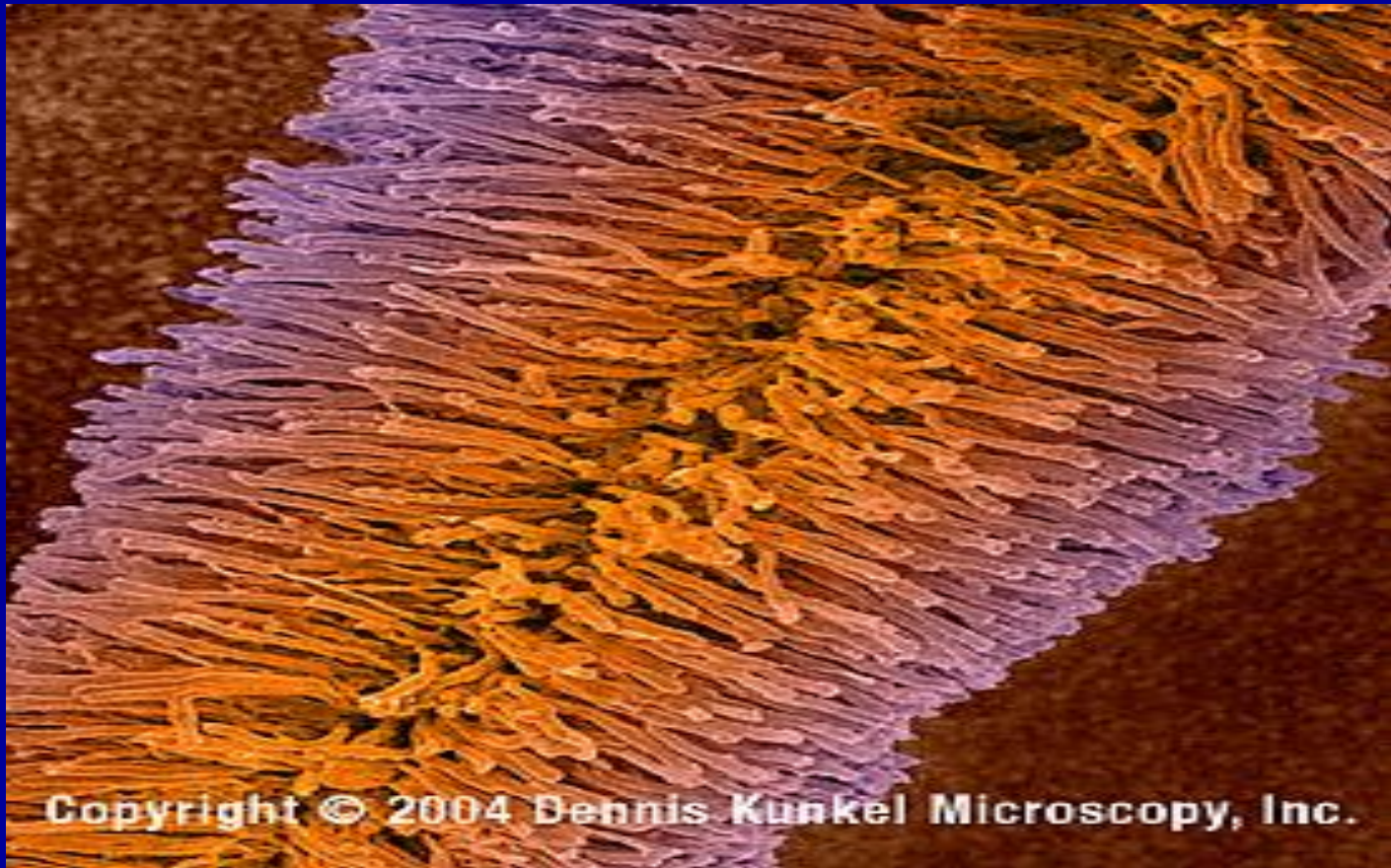


Fig. 2: Basidiomycota



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Mucor spp. fruiting structure



Cell wall Structure

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PART VII

Pathogen

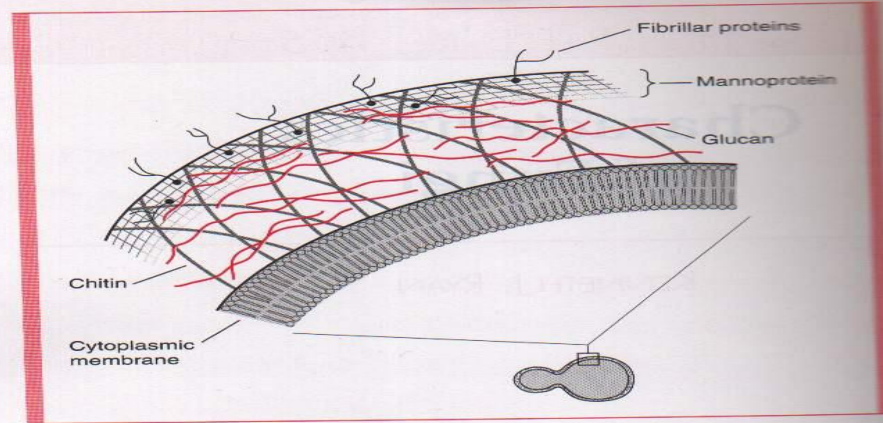


FIGURE 45-1
The fungal cell wall. The overlapping mannan, glucan, chitin, and protein elements are shown. Proteins complexed with the mannan (mannoproteins) extend beyond the cell wall.

Cell wall mannan linked to surface proteins

Chitin and glucans give rigidity to cell wall

Heterotrophic metabolism uses available organic matter

Photosynthetic mechanisms are lacking

Asexual reproduction forms conidia by mitosis

Meiosis forms sexual spores in specialized structures

Mannoproteins are mannose-based polymers (mannan) found on the surface and are a major component of the structural matrix of the cell wall, where they are linked to protein. They are major determinants of serologic specificity because of variations in the composition and length of the polymer side chains. Glucans are glucosyl polymers, some of which form dimers that increase the strength of the fungal cell wall, often in close association with chitin. Chitin is composed of long, unbranched chains of poly-*N*-acetylglucosamine. It is an insoluble, and rigid and provides structural support in a manner analogous to the chitin in crab shells or cellulose in plants. It is a major component of the cell wall of filamentous fungi. In yeasts, chitin appears to be of most importance in forming cross-bridges and the channels through which nuclei pass from mother to daughter cells during cell division.

METABOLISM

Fungal metabolism is heterotrophic, requiring exogenous carbon for growth. Metabolic diversity is great, but most fungi grow with only an organic carbon source and ammonia or nitrate ions as a nitrogen source. In nature, nutrients for free-living fungi are derived from decaying organic matter. A major difference between fungi and plants is that fungi lack photosynthetic energy-producing mechanisms. Most are strict aerobes, although some can grow under anaerobic conditions. None are strict anaerobes.

REPRODUCTION

Fungi may reproduce by either asexual or sexual processes. Reproductive elements produced asexually are termed **conidia**. Those produced sexually are termed **spores** (e.g., ascospores, zygospores, basidiospores). Asexual reproduction involves mitotic division of the haploid nucleus and is associated with production by budding spore-like conidia or separation of hyphal elements. In sexual reproduction, the haploid nuclei of donor and recipient cells fuse to form a diploid nucleus, which may then divide by classical meiosis. Some of the four resulting haploid nuclei may be genetic recombinants and may undergo further division by mitosis. Highly complex specialized structures may be involved. The study of this process in fungal species such as *Neurospora crassa* has been important in gaining an understanding of basic cellular genetic mechanisms.

Mycotic Diseases

- 1- Hypersensitivity: an allergic reaction to fungi antigens(molds and spores) •
- 2-Mycotoxicoses: poisoning by fungal toxins •
- 3- Mycetismus: the ingestion of preformed toxin (mushroom poisoning) •
- 4- Infection •

Skin Fungal Disease

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(a)



(b)

FIGURE 21.14 Dermatomycoses. (a) A severe case of ringworm on the side of a child's head (tinea capita). (b) Ringworm of the foot, or athlete's foot (tinea pedis). Moisture between the toes favors fungal infections.

Morphology

- Yeast & hypha are two forms for pathogenic fungi where Dimorphic ones can be in both forms.
- Yeasts are unicellular organisms reproduced by budding. They are of parasitic form OGT 37C
- Hyphae or mycelia or molds are frequently used interchangeably, these are multicellular saprophytic filamentous structures constituted by tubular cell.

Diagnosis

1- Skin scrapings suspected to contain dermatophytes or pus from a lesion can be mounted in KOH on a slide and examined directly under the microscope.

2. Skin testing (dermal hypersensitivity) used to be popular as a diagnostic tool, but this use is now discouraged because the skin test may interfere with serological studies by causing false positive results.

It may still be used to evaluate the patient's immunity as well as a population exposure index in epidemiological studies.

Diagnosis (cont.)

3. Serology may be helpful when it is applied to a specific fungal disease; there are no screening antigens for 'fungi' in general. The most common serological tests for fungi are based on latex agglutination, double immunodiffusion, complement fixation and EIA (enzyme immunoassays). Some EIA tests are being developed to detect both Immunoglobulin G (IgG) and IgM antibodies.

4. Direct fluorescent microscopy may be used for identification, even on non-viable cultures or on fixed tissue sections. The reagents for this test are difficult to obtain.

Antifungal Chemotherapy

- As compared with antibacterial agents:
 - 1- antifungal are less in number
 - 2- many of which approved to be unstable, toxic to humans , poorly diffused into tissues

The newly developed azol compounds have significantly higher therapeutic activity and lower toxicity than earlier antifungal drugs.

Fungal Treatment

Amphotericin B

A polyene antimycotic. It is usually the drug of choice for most systemic fungal infections. It has a greater affinity for ergosterol in the cell membranes of fungi than for the cholesterol in the host's cells; once bound to ergosterol, it causes disruption of the cell membrane and death of the fungal cell.

Azoles

The azoles (imidazoles and triazoles), including ketoconazole, fluconazole, and itraconazole, are being used for muco-cutaneous candidiasis, dermatophytosis, and for some systemic fungal infections. Fluconazole is presently essential for the maintenance of AIDS patients with cryptococcosis. Oral administration and reduced toxicity are distinct advantages.

Fungal Treatment

Griseofulvin

Griseofulvin is a very slow-acting drug which is used for severe skin and nail infections. Its effect depends on its accumulation in the stratum corneum where it is incorporated into the tissue and forms a barrier which stops further fungal penetration and growth. It is administered orally. The exact mechanism of action is unknown.

5-fluorocytosine

5-fluorocytosine (Flucytosine or 5-FC) inhibits RNA synthesis and has found its main application in cryptococcosis (to be discussed later). It is administered orally eg Caspofungin: good Vs Candida and aspergillus

Selection of Antifungals

-Selection of Antifungal Agents should be balancing the probable efficiency against Toxicity where the following factors are considered:

- 1- the threat of morbidity or mortality
- 2- the immune status of the patient.
- 3- the toxicity of the antifungal.
- 4- the probable activity of the antifungal.

Resistance to Antifungal Agents

- Measuring the susceptibility of AFAs is still under investigation, because of the diversity of growth rates & metabolic activity in various fungal species.
- The MICs performed in different types of fungal growth media can vary as much as 1000 folds.

Mechanism of Resistance

Alterations in the target of antifungal agent such as the production of cytochrome demethylases for Azoles.

- Resistance to both Azole & allylamine has been associated with overproduction of their target enzymes.
- The enzymatic inactivation(the most potent bacterial resistance) is not important to any antifungal agent in current use.