Medical Mycology

The kingdom fungi is composed of **unicellular** or **multicellular**, **eukaryotic**, **heterotrophic** microbes. Each fungal cell contains a full array of organelles and is bound by a rigid cell wall containing **chitin**, **glucan**, and/or **cellulose**.

Table 1. Comparison of structure/function of bacterial and fungal Organelles.

Organelles	Bacteria	Fungi
Cell Wall	Murein=peptidoglycan	Glucan, Mannan, Chitin
Cell membrane	No sterols	Ergosterol
Metabolism	Aerobic or anaerobic	Aerobic
Energy Transduction	Cell membrane	Mitochondria
Cytoplasm	proteins	Glycoproteins, actin, tubulin, mitotic spindle, Golgi
Gene structure	Operons, no introns	Single gene, introns, repetitive DNA
Nuclear material	Prokaryotic: a single chromosome; no nuclear membrane	Eukaryotic: multiple chromosomes contained in a nucleus bounded by a nuclear membrane; for example *Candida albicans* has 8 chromosomes
Ribosome	30S + 50S= 70S	40S + 60S = 80S
Extrachromosomal DNA	plasmids	Mitochondrial DNA, dsRNA
Capsular polysaccharide	Several agents of meningitis	One agent of meningitis: *Cryptococcus neoformans*

Of the thousands of fungal species that are free-living in nature or are pathogenic for plants, only a small group are known to be pathogenic for humans and animals. It is also true that **any fungus capable of growing at 37° C is a potential pathogen in a debilitated or immunocompromised host**.

Some fungi are primary pathogens (e.g., *Coccidiodes* species) and can cause disease in immune-normal persons. Severity of a fungal disease is related to host factors (immune status, general health status) and the number of infectious propagules (conidia or spores) inhaled, ingested, or injected. Persons who are

immunocompromised, or otherwise debilitated, are prone to develop more serious disease and to be susceptible to opportunistic fungi against which immune-normal persons have level of resistance.

What is Medical Mycology?

Medical mycology is a distinct discipline of medical microbiology concerned with all aspects of diseases in humans and lower animals caused by pathogenic fungi.

Mycoses are diseases of humans and lower animals caused by pathogenic fungi. There is a broad spectrum of mycoses ranging from superficial skin diseases to deep-seated, multisystem disseminated diseases.

Rationale for Fungal identification

Why do we need to identify fungi? When dealing with microbes causing disease in humans there are important reasons to identify the causal agent.

1- **Developing the treatment plan:** knowledge of the pathogen will increase chances for successful therapy because the pathogenesis of most mycoses is well studied. That will influence the choice of diagnostic tests, medical and surgical procedures, and antifungal therapy.

2- **Investigating Outbreaks:**

- **The Hospital Setting.** The source of infection may be in the environment, including construction or renovation near patient wards, faulty HVAC systems affecting airflow in operating rooms or patient wards, contaminated hospital injectable solutions, indwelling medical devices, substandard hand-washing procedures, or other factors implicated in the healthcare environment.
- **The Community Setting.** An outbreak of fungal disease in the community typically requires an investigation of the causal agent.

3- **Determining the Susceptibility to Antifungal Agents:** Because different fungi are susceptible to different antifungal agents it is important to:

- Identify the causal agent in order to select the most appropriate antifungal agent.
- Determine its in vitro killing effectiveness. Susceptibility in vitro does not uniformly predict clinical success in vivo because host factors play a critical role in determining clinical outcome. Resistance in vitro, however, will often, but not always, correlate with treatment failure.
- Monitor the therapeutic response of the patient. Additional diagnostic tests and/or surgical intervention may be necessary.

4- **Estimating the Significance of Fungi Generally Considered to be Opportunists or Saprobes:** the physician should consider the immunocompetence of the patient, among other risk factors, to assess whether a fungus generally considered a saprobe may be the cause of disease.

5- **Types of Vegetative Growth: what are the major forms of microscopic fungi?** The microscopic fungi are classified by the type of vegetative growth as either yeasts or molds.

Sporulation

Vegetative growth is necessary but is not sufficient to perpetuate fungi and a variety of reproductive propagules are formed for dispersal with the aid of air currents or in water. Fungal propagules are different types of spores, a means of asexual reproduction. The method of sporulation used by fungi is the major character with which clinical laboratory scientists use to identify fungi in the clinical laboratory.

Dimorphism

Dimorphism (definition: two forms) is an important characteristic of certain fungal pathogens. Dimorphism is morphogenesis that allows growth to occur in either the mycelium or yeast forms, (mycelium to yeast, or yeast to mycelium conversion); for example, *Histoplasma capsulatum* is a dimorphic fungus. Fungi

causing primary systemic infections are typically filamentous soil-dwelling molds. The infectious propagules most frequently are conidia that are inhaled, along with hyphal fragments. Morphogenesis to the yeast form occurs during infection of tissues, usually in the lungs. This conversion in temperature sensitive, with the yeast form developing at 37° C. in the laboratory, growth at 35-37° C on an **enriched medium** may be used to help identify the fungus by this form change also known as "**morphogenesis**".

There are notable exceptions to the mold –to-yeast dimorphism. The primary systemic pathogens *Coccidioides immitis* and *C. posadasii* grow as a mold form in the environment. The mold form fragments into **arthroconidia**, which are the infectious propagules. Once inhaled, arthroconidia convert to **spherules**, enlarge, and segment into endospores. **Melanized** molds (e.g., *Fonsecaea pedrosoi, Cladophialophora carrionii*), the causative agents of chromoblastomycosis, grow as molds in the environment but in the cutaneous and subcutaneous tissues convert to **muriform** cells – round cells that do not bud but enlarge and divide by internal septation. Growth by enlargement in all directions is called **isotropic**.

Dimorphism and Pathogenesis

As an adaptation to the host environment, dimorphism improves a fungus's ability as a pathogen; for example, *Histoplasma capsulatum* yeast forms survive after phagocytosis within alveolar macrophages and travel from the lunges via the bloodstream into the spleen and liver. Spherules produced by during infection by *Coccidioides* species produce many endospores, which spread the infection within the lung and to other body sites.

Although true of the primary systemic fungal pathogens, not all fungi that produce disease in humans are dimorphic. The opportunistic fungi may or may not be dimorphic. Monomorphic yeasts in culture and in host tissues, for example, *Candida glabrata* and *Cryptococcus neoformans*. Many opportunistic pathogens are monomorphic molds, for example, *Aspergillus* species or members of the **Mucorales**. They exhibt only the mold form in diseased tissue.