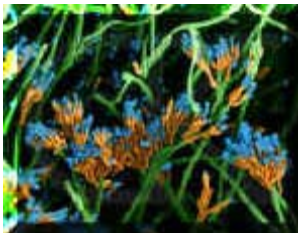
MYCOLOGY
真菌学



Dr. Arthur Di Salvo

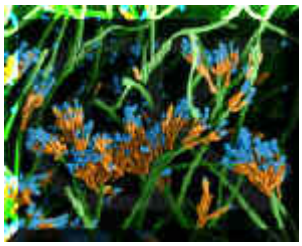
（孙长贵　　制作整理）

二00四年十月十六日

目　　录

MYCOLOGY（真菌学）

Dr. Arthur Di Salvo



MYCOLOGY - CHAPTER ONE （真菌学----第一章）

INTRODUCTION TO MYCOLOGY （真菌学概述）

INTRODUCTION（概述）

A. CLASSIFICATION（分类）

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. There are between 100,000 to 200,000 species depending on how they are classified. About 300 species are presently known to be pathogenic for man.

There are five kingdoms of living things. The fungi are in the Kingdom Fungi.

KINGDOM	CHARACTERISTIC	EXAMPLE
Monera	Prokaryocyte	Bacteria Actinomycetes
Protista	Eukaryocyte	Protozoa
Fungi	Eukaryocyte *	Fungi
Plantae	Eukaryocyte	Plants, Moss
Animalia	Eukaryocyte *	Arthropods Mammals Man

*This common characteristic is responsible for the therapeutic dilemma in anti-mycotic therapy.

The taxonomy of the Kingdom Fungi is evolving and is controversial. Formerly based on gross and light microscopic morphology, studies of ultra structure, biochemistry and molecular biology provide new evidence on which to base taxonomic positions. Medically important fungi are in four phyla:

1. Ascomycota - Sexual reproduction in a sack called an ascus with the production of ascopspores.

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

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

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

B. MORPHOLOGY

Pathogenic fungi can exist as yeasts or as hyphae. A mass of hyphae is called mycelia. Yeasts are unicellular organisms and mycelia are multicellular filamentous structures, constituted by tubular cells with cell walls. The yeasts reproduce by budding. The mycelial forms branch and the pattern of branching is an aid to the morphological identification. If the mycelia do not have SEPTA, they are called coenocytic (nonseptate). The terms "hypha" and "mycelium" are frequently used interchangeably. Some fungi occur in both the yeast and mycelial forms. These are called dimorphic fungi.

Dimorphic fungi

The dimorphic fungi have two forms (figure 1):

1. YEAST - (parasitic or pathogenic form). This is the form usually seen in tissue, in exudates, or if cultured in an incubator at 37 degrees C.

2. MYCELIUM - (saprophytic form). The form observed in nature or when cultured at 25 degrees C. Conversion to the yeast form appears to be essential for pathogenicity. In the dimorphic fungi. Fungi are identified by several morphological or biochemical characteristics, including the appearance of their fruiting bodies. The asexual spores may be large (macroconidia, chlamydospores) or small (microconidia, blastospores, arthroconidia).

There are four types of mycotic diseases:

1. Hypersensitivity - an allergic reaction to molds and spores.

2. Mycotoxicoses - poisoning of man and animals by feeds and food products contaminated by fungi which produce toxins from the grain substrate.

3. Mycetismus- the ingestion of toxin (mushroom poisoning).

4. Infection

We shall be concerned only with the last type; pathogenic fungi which cause infections. Most common pathogenic fungi do not produce toxins but they do show physiologic modifications during a parasitic infection (e.g., increased metabolic rate, modified metabolic pathways and modified cell wall structure). The mechanisms which cause these modifications as well as their significance as a pathogenic mechanism are just being described. Most pathogenic fungi are also thermotolerant, and can resist the effects of the active oxygen radicals released during the respiratory burst of phagocytes. Thus, fungi are able to withstand many host defenses. Fungi are ubiquitous in nature and most people are exposed to them. The establishment of a mycotic infection usually depends on the size of the inoculum and on the resistance of the host. The severity of the infection seems to depend mostly on the immunologic status of the host. Thus, the demonstration of fungi, for example, in blood drawn from an intravenous catheter can correspond to colonization of the catheter, to transient fungemia (i.e., dissemination of fungi through the blood stream), or to a true infection. The physician must decide which is the clinical status of the patient based on clinical parameters, general status of the patient, laboratory results, etc. The decision is not trivial, since treatment of systemic fungal infections requires the aggressive use of drugs with considerable toxicity. Most mycotic agents are soil saprophytes and mycotic diseases are generally not communicable from person-to-person (occasional exceptions: Candida and some dermatophytes). Outbreaks of disease may occur, but these are due to a common environmental exposure, not communicability. Most of the fungi which cause systemic infections have a peculiar, characteristic ecologic niche in nature. This habitat is specific for several fungi which will be discussed later. In this environment, the normally saprophytic organisms proliferate and develop. This habitat is also the source of fungal elements and/or spores, where man and animals, incidental hosts, are exposed to the infectious particles. It is important to be aware of these associations to diagnose mycotic diseases. The physician must be able to elicit a complete history from the patient including occupation, avocation and travel history. This information is frequently required to raise, or confirm, your differential diagnosis. The incidence of mycotic infections is currently increasing dramatically, due to an increased population of susceptibles. Examples are patients with AIDS, patients on immunosuppressive therapy, and the use of more invasive diagnostic and surgical procedures (prosthetic implants). Fungal diseases are non-contagious and non-reportable diseases in the national public health statistics. However, in South Carolina most of the important mycotic (fungal) diseases were notifiable to the public health authorities until 1994.

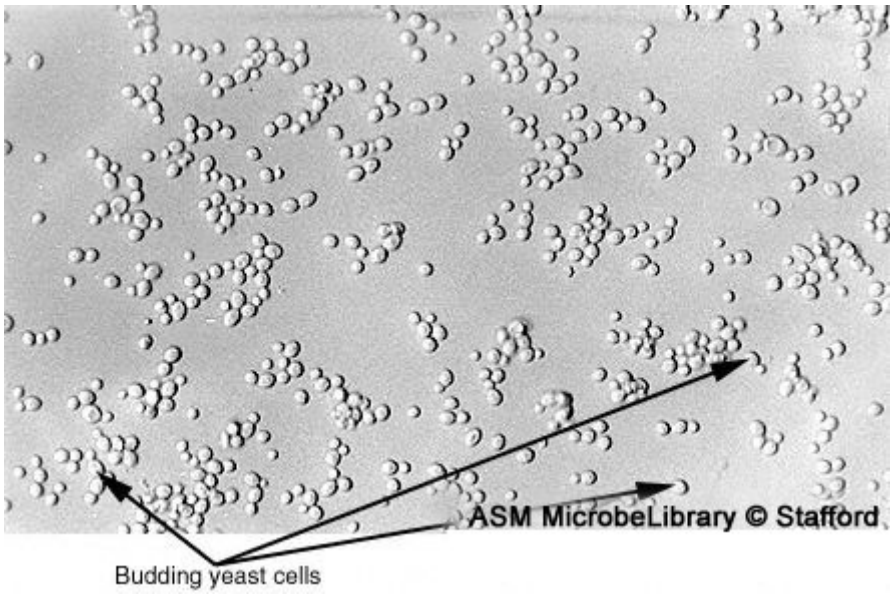
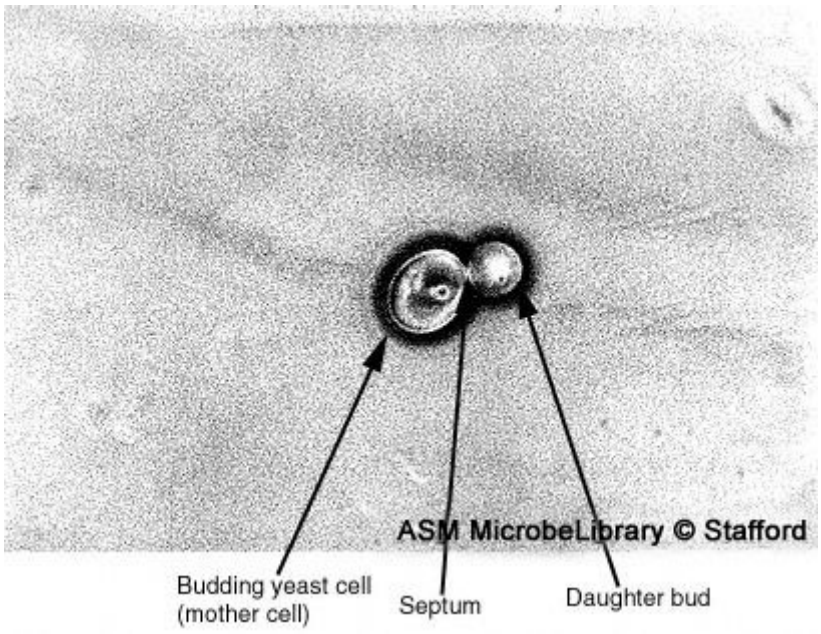
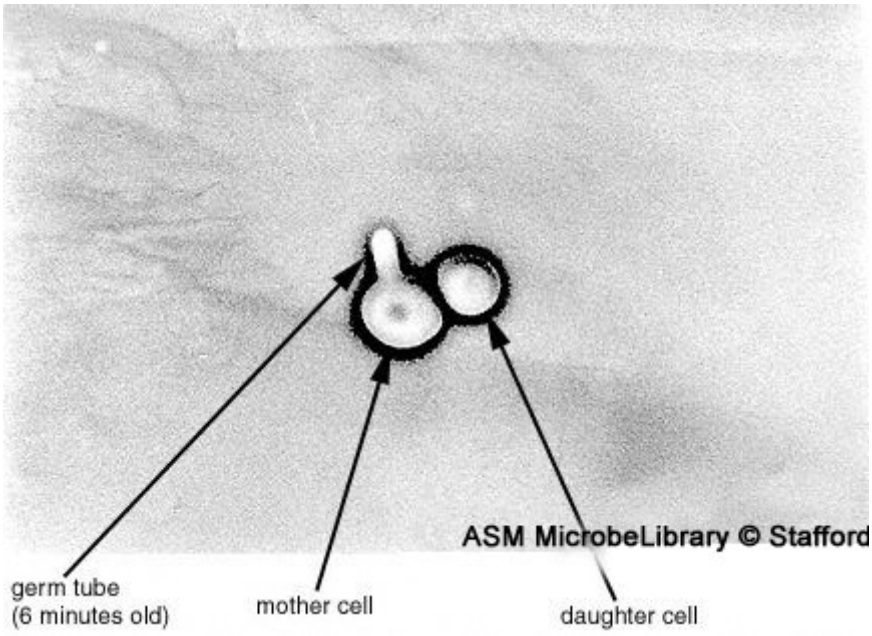


Figure 1A

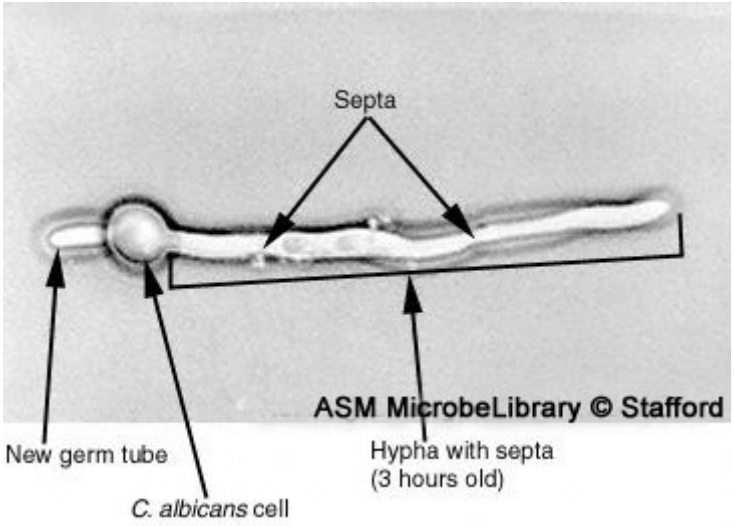
Candida albicans is a dimorphic fungus in that it grows as a unicellular yeast under some environmental conditions and as a filamentous fungus under other conditions. Budding yeast cells. C. albicans was grown at 37°C with aeration for 3 h in yeast-peptone-dextrose (YPD) medium. In this image, unstained cells are magnified x400. The image was taken with phase- contrast microscopy.



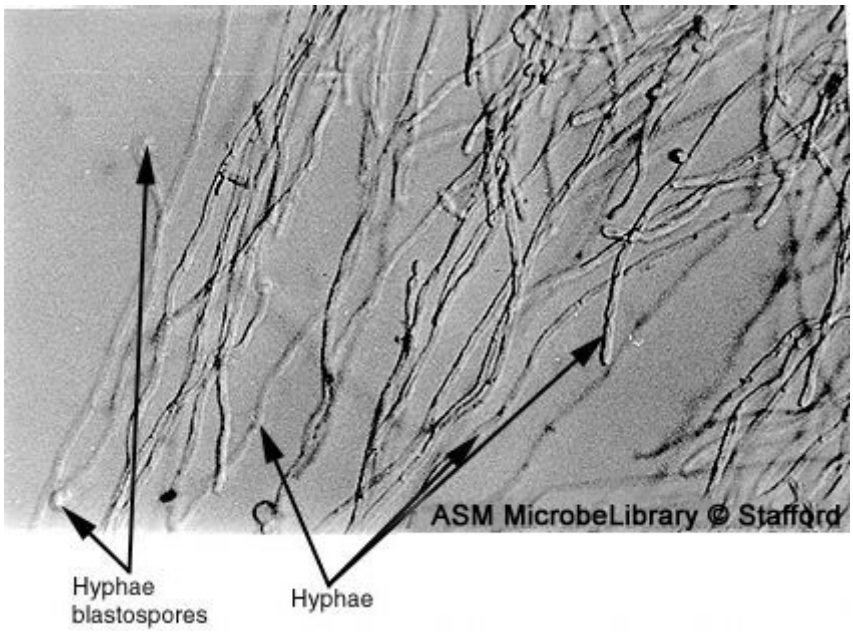
B. Budding yeast with septum. The septum has formed between the daughter bud and the mother cell, but separation of the two has not occurred. This image is from a culture of cells grown at 37° C for 3 h in YPD medium. The unstained cell is magnified x1,000 using phase- contrast microscopy.



C. Candida albicans mother and daughter cells. Cells were grown under conditions that induced hypha formation for 30 min. The daughter cell is on the right; the mother cell is on the left. The daughter cell has not reached a threshold volume and therefore has not yet formed a hypha. The mother cell has passed the threshold volume and has started forming a germ tube which will become a hypha. The germ tube seen here is 6 min old. A septum between the germ tube and the mother cell has not yet formed. The unstained cells are magnified x1,000 using phase-contrast microscopy.



D. C. albicans cell at 3 h. Three hours after the appearance of the germ tube, the hypha has septa. A new germ tube at the distal pole of the cell is also evident at this time. The unstained cells are magnified x1,000 using phase-contrast microscopy.



E. C. albicans hyphal cells at 5 h. After 5 h in hypha-inducing medium, many hyphae are evident. Clumping of the hyphae is also apparent, and hyphae are beginning to form hypha blastospores, which are new budding cells.

Figure 1 A-E © Phillip Stafford Dartmouth Medical School Hanover, New Hampshire and The MicrobeLibrary

C. 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.

3. Serology may be helpful when it is applied to a specific fungal disease; there are no screening antigens for 'fungi' in general. Because fungi are poor antigens, the efficacy of serology varies with different fungal infections. The serologic tests will be discussed under each mycosis. The most common serological tests for fungi are based on latex agglutination, double immunodiffusion, complement fixation and enzyme immunoassays. While latex agglutination may favor the detection of IgM antibodies, double immunodiffusion and complement fixation usually detect IgG antibodies. Some EIA tests are being developed to detect both IgG and IgM antibodies. There are some tests which can detect specific fungal antigens, but they are just coming into general use.

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.

5. Biopsy and histopathology. A biopsy may be very useful for the identification and as a source of the of tissue-invading fungi. Usually the Gomori methenamine silver (GMS) stain is used to reveal the organisms which stain black against a green background. The H&E stain does not always tint the organism, but it will stain the inflammatory cells.

6. Culture. A definitive diagnosis requires a culture and identification. Pathogenic fungi are usually grown on Sabouraud dextrose agar. It has a slightly acidic pH (~5.6); cyclohexamide, penicillin, streptomycin or other inhibitory antibiotics are often added to prevent bacterial contamination and overgrowth. Two cultures are inoculated and incubated separately at 25 degrees C and 37 degrees C to reveal dimorphism. The cultures are examined macroscopically and microscopically. They are not considered negative for growth until after 4 weeks of incubation.

D. TREATMENT

Mammalian cells do not contain the enzymes which will degrade the cell wall polysaccharides of fungi. Therefore, these pathogens are difficult to eradicate by the animal host defense mechanisms. Because mammals and fungi are both eukaryotic, the cellular milieu is biochemically similar in both. The cell membranes of all eukaryotic cells contain sterols; ergosterol in the fungal cell membrane and cholesterol in the mammalian cell membrane. Thus, most substances which may impair the invading fungus will usually have serious side effects on the host. Although one of the first chemotherapeutic agents (oral iodides) was an anti-mycotic used in 1903, the further development of such agents has been left far behind the development of anti-bacterial agents. The selective toxicity necessary to inhibit the invading organism with minimal damage to the host has been difficult to establish within eukaryotic cells.

The primary antifungal agents are:

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. Amphotericin B is usually administered intravenously (patient usually needs to be hospitalized), often for 2-3 months. The drug is rather toxic; thrombo-phlebitis, nephrotoxicity, fever, chills and anemia frequently occur during administration.

Azoles

The azoles (imidazoles and triazoles), including ketoconazole, fluconazole, and itraconozole, 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. The general mechanism of action of the azoles is the inhibition of ergosterol synthesis. Oral administration and reduced toxicity are distinct advantages.

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 p.o.

. CLINICAL CLASSIFICATION OF THE MYCOSES

Fungal diseases may be discussed in a variety of ways. The most practical method for medical students is the clinical taxonomy which divides the fungi into:

a. Superficial mycoses

b. Subcutaneous mycoses

c. Systemic mycoses

d. Opportunistic mycoses

The Superficial mycoses (or cutaneous mycoses) are fungal diseases that are confined to the outer layers of the skin, nail, or hair, (keratinized layers) rarely invading the deeper tissue or viscera. The fungi involved are called dermatophytes. The Subcutaneous mycoses are confined to the subcutaneous tissue and only rarely spread systemically. They usually form deep, ulcerated skin lesions or fungating masses, most commonly involving the lower extremities. The causative organisms are soil saprophytes which are introduced through trauma to the feet or legs. The Systemic mycoses may involve deep viscera and become widely disseminated. Each fungus type has its own predilection for various organs which will be described as we discuss the individual diseases.
The Opportunistic mycoses are infections due to fungi with low inherent virulence. The etiologic agents are organisms which are common in all environments.

MYCOLOGY - CHAPTER TWO （真菌学----第二章）

ACTINOMYCETES （放线菌）

In this section, we shall discuss three genera of actinomycetes: Actinomyces, Nocardia, and Streptomyces. These organisms have been shown to be higher bacteria, but they were thought to be fungi for many years because they have filamentous forms, 0.5 to 0.8 microns in diameter, which appear to branch. Some species form aerial mycelia in culture. The clinical manifestations of infection are similar to those of a systemic fungal infection. It is now clear that they are not fungi but are closely related to the mycobacteria. Some facts that you should know about these

genera are that:

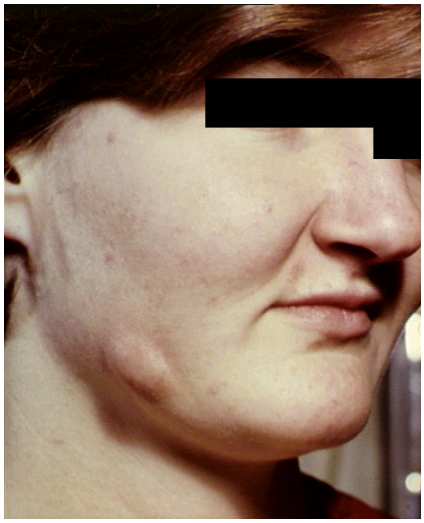
Actinomyces are anaerobic, while Nocardia and Streptomyces are aerobic.

Nocardia stain partially acid-fast, Actinomyces and Streptomyces are not acid-fast.

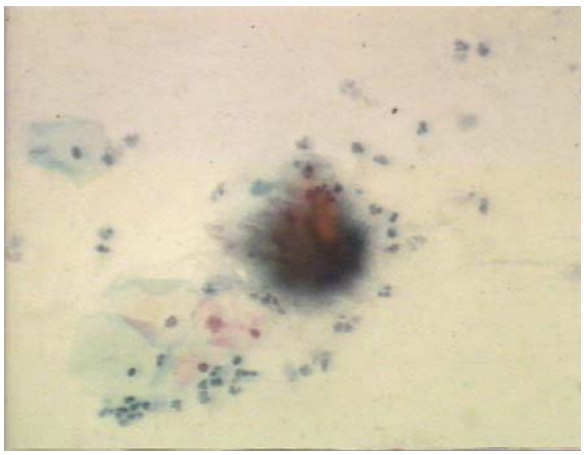
Actinomyces produce granules. Most actinomycetes in tissue do not stain with the H & E stain commonly used for general histopathology. All genera may produce granules; Actinomyces almost always produce granules.

A. ACTINOMYCOSIS

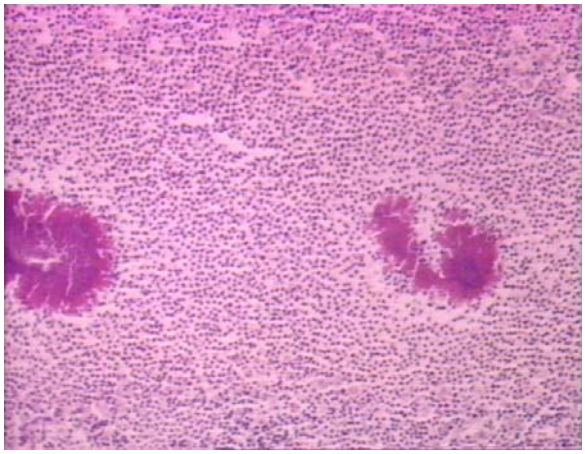
The most common cause of actinomycosis is the organism *Actinomyces israelii* which infects both man and animals. In cattle, the disease is called "lumpy jaw" because of the huge abscess formed in the angle of the jaw. In man, *A. israelii* is an endogenous organism that can be isolated from the mouths of healthy people. Frequently, the infected patient has a tooth abscess or a tooth extraction and the endogenous organism becomes established in the traumatized tissue and causes a suppurative infection. These abscesses are not confined to the jaw and may also be found in the thoracic area and abdomen. The patient usually presents with a pus-draining lesion, so the pus will be the clinical material you send to the laboratory. This diagnosis can be made on the hospital floor. If you rotate the vial of pus, the yellow sulfur granules, characteristic of this organism, can be seen with the naked eye. You can also see these granules by running sterile water over the gauze used to cover the lesion. The water washes away the purulent material leaving the golden granules on the gauze. This organism, which occurs worldwide, can be seen histologically as "sulfur granules" surrounded by polymorphonuclear cells (PMN) forming the purulent tissue reaction. The organism is a gram positive rod that frequently branches. The laboratory must specifically be instructed to culture for this anaerobic organism. These lesions must be surgically drained prior to antibiotic therapy and the drug of choice is large doses of penicillin (2 million units q 6 h).



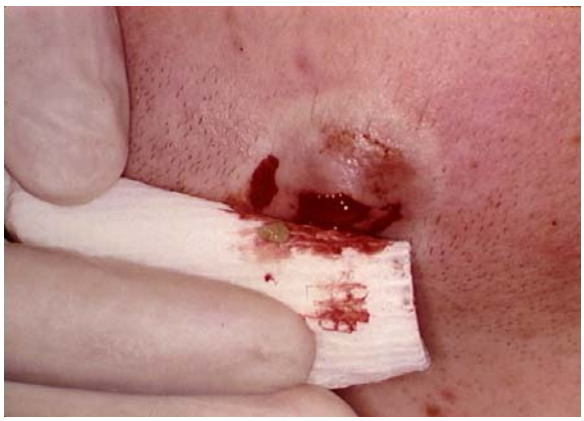
Actinomycosis, Cervicofacial © Bristol Biomedical Image Archive. Used with permission



Actinomyces: histological stain © Bristol Biomedical Image Archive. Used with permission



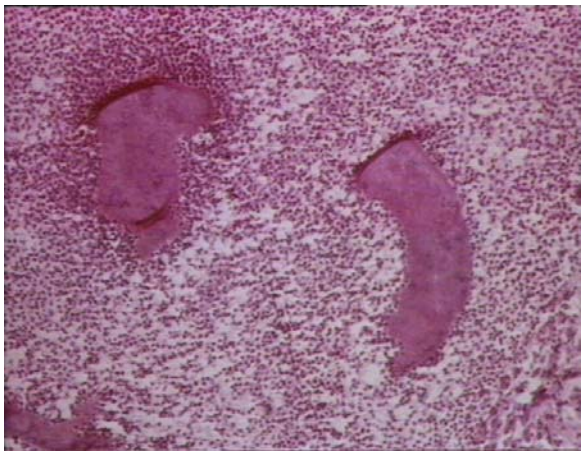
Actinomyces colonies from lung abscess © Bristol Biomedical Image Archive. Used with permission



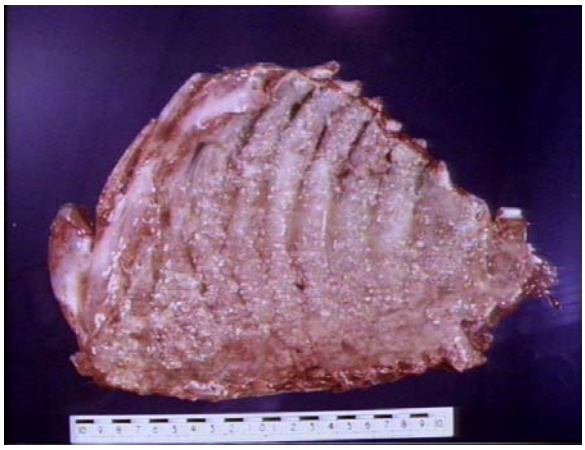
Sulphur granules in actinomycosis © Bristol Biomedical Image Archive. Used with permission

B. NOCARDIOSIS

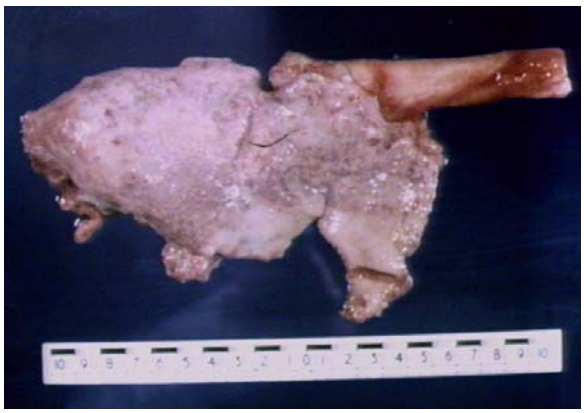
The most common species of Nocardia which cause disease in human beings are *N. brasiliensis* and *N. asteroides*. These are soil organisms which can also be found endogenously in the sputum of apparently healthy people. Nocardiosis primarily presents as a pulmonary disease in the U.S. In Latin America, it is more frequently seen as the cause of a subcutaneous infection, with or without draining abscesses. It can even present as a lesion in the chest wall that drains onto the surface of the body similar to actinomycosis. Brain abscesses are frequent secondary lesions. N. asteroides is usually the etiologic agent of pulmonary nocardiosis while *N. brasiliensis* is frequently the cause of sub-cutaneous lesions. The material sent to the lab, depending on the presentation of the disease, is sputum, pus, or biopsy material. These organisms rarely form granules. The Nocardia are aerobic, gram-positive rods and stain partially acid-fast (i.e., the acid-fast staining is not uniform). There are no serological tests, and the drug of choice is Sulfa drugs (Trimethoprim). The nocardia grow readily on most bacteriologic and TB media. The geographic distribution of these organisms is worldwide.



Pleurisy due to nocardiosis



Pleurisy in thoracic wall due to nocardiosis



Lung: pleurisy due to nocardiosis © Bristol Biomedical Image Archive. Used with permission

C. STREPTOMYCETES

The streptomyces species usually cause the disease entity known as mycetoma (fungus tumor). These infections are usually subcutaneous, but they can penetrate deeper and invade the bone. Some species produce a protease which inhibits macrophages. Material sent to the lab is pus or skin biopsy. The streptomycetes are aerobic like Nocardia, and can grow on both bacterial and fungal (Sabouraud) media. They produce a chalky aerial mycelium with much branching. It is important to let the lab know the organism you suspect because most bacterial pathogens will grow out overnight, but the actinomycetes take longer to be visible on the culture plates (48-72 hours). The various species of streptomyces produce granules of different size, texture and color. These granules along with colonial growth and biochemical tests allow the bacteriologist or mycologist to identify each species. The organisms are found world-wide. There are no serological tests, and the drugs of choice are the combination of sulfamethoxazole/trimethoprim or amphotericin B. In the tropics this disease may go undiagnosed or untreated for so long that surgical amputation may be the only effective treatment.

MYCOLOGY - CHAPTER THREE （真菌学----第三章）

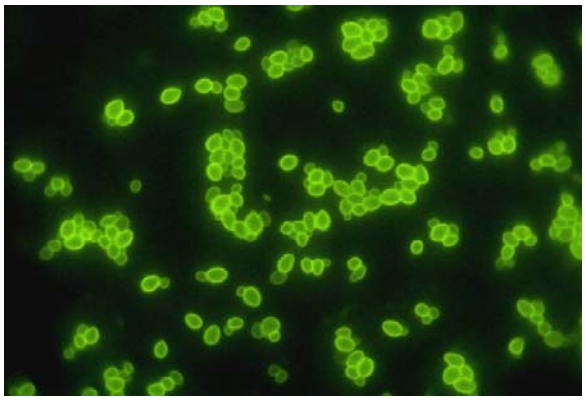
YEASTS （酵母菌）

Yeasts are single-celled budding organisms. They do not produce mycelia. The colonies are usually visible on the plates in 24-48 hours. Their soft, moist colonies resemble bacterial cultures rather than molds. There are many species of yeasts which can be pathogenic for humans. We will discuss only the two most significant species: *Candida albicans* and *Cryptococcus neoformans*

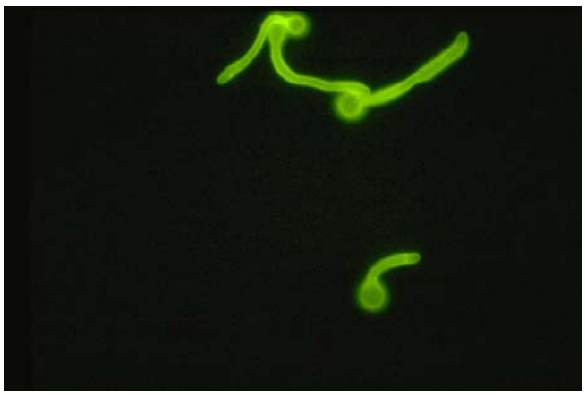
A. CANDIDIASIS *(Candida albicans)*

There are many species of the genus Candida that cause disease. The infections caused by all species of Candida are called candidiasis. *Candida albicans* is an endogenous organism. It can be

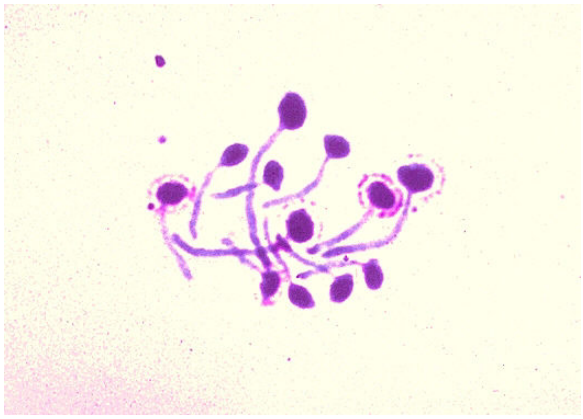
found in 40-80% of normal human beings. It is present in the mouth, gut, and vagina. It may be present as a commensal or a pathogenic organism. Infections with Candida usually occur when a patient has some alteration in cellular immunity, normal flora or normal physiology. Patients with decreased cellular immunity have decreased resistance to fungal infections. Prolonged antibiotic or steroid therapy destroys the balance of normal flora in the intestine allowing the endogenous Candida to overcome the host. Invasive procedures, such as cardiac surgery and indwelling catheters, produce alterations in host physiology and some of these patients develop Candida infections. Although it most frequently infects the skin and mucosae, Candida can cause pneumonia, septicemia or endocarditis in the immuno-compromised patient. The establishment of infection with Candida species appears to be a property of the host - not the organism. The more debilitated the host, the more invasive the disease. The clinical material to be sent to the lab depends on the presentation of the disease: blood cultures, vaginal discharge, urine, feces, nail clippings or material from cutaneous or mucocutaneous lesions. Candida is a polymorphic yeast, i.e., yeast cells, hyphae and pseudohyphae are produced. It has been shown that Candida needs a transcription repressor to maintain the yeast form. This ability to assume various forms may be related to the pathogenicity of this organism. The yeast form is 10-12 microns in diameter, gram positive, and it grows overnight on most bacterial and fungal media. It also produces germ tubes, and pseudohyphae may be formed from budding yeast cells that remain attached to each other. Spores may be formed on the pseudomycelium. These are called chlamydospores and they can be used to identify different species of Candida. Some mycologists think that the pseudomycelial form represents a more invasive form of the organism. The species are identified by biochemical reactions. The organism occurs world-wide. The drugs of choice for systemic infection are itraconazole and fluconazole. If an artificial heart valve or in-dwelling catheter becomes infected, it must be replaced. Drug therapy alone will not suppress the organism if the foreign body remains in the host. This resistance is due to biofilms which we will discuss later.



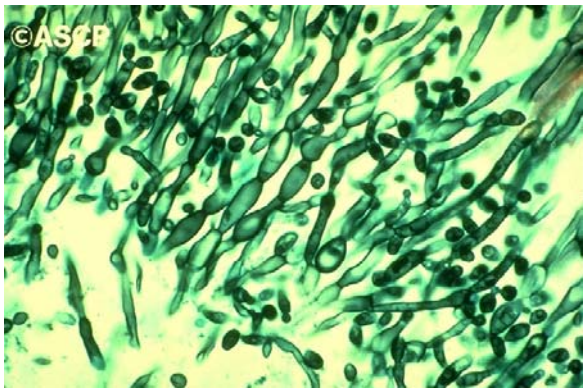
Oval budding yeast cells of Candida albicans. Fluorescent antibody stain.
CDC/Maxine Jalbert, Dr. Leo Kaufman. lek1@cdc.gov



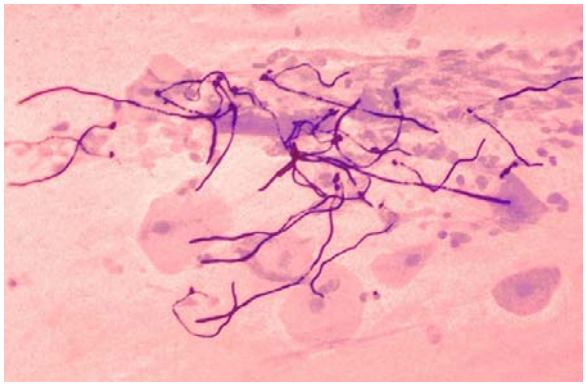
Candida albicans showing germ tubes. Calcofluor white stain in peptone medium. Germ tube production is a diagnostic feature of C. albicans. CDC/Mercy Hospital, Toledo, OH/Dr. Brian Harrington



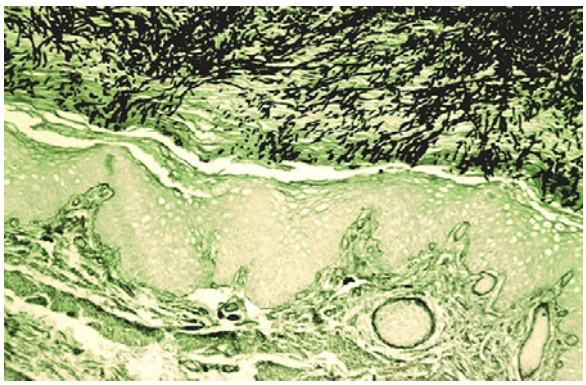
Candida albicans showing germ tube production in serum. Gram stain. CDC/Dr. Lucille K. Georg



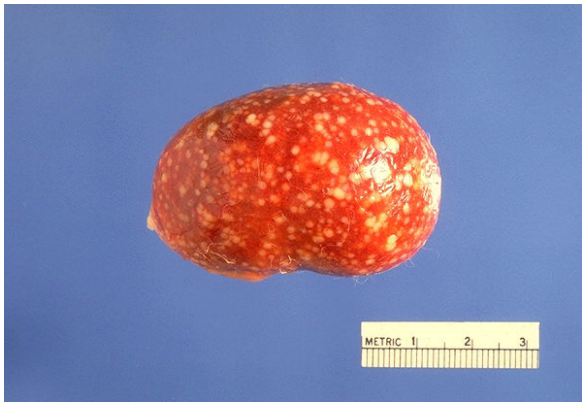
Histopathology of Candida albicans infection. Methenamine silver stain. Pseudohyphae and true hyphae. ASCP



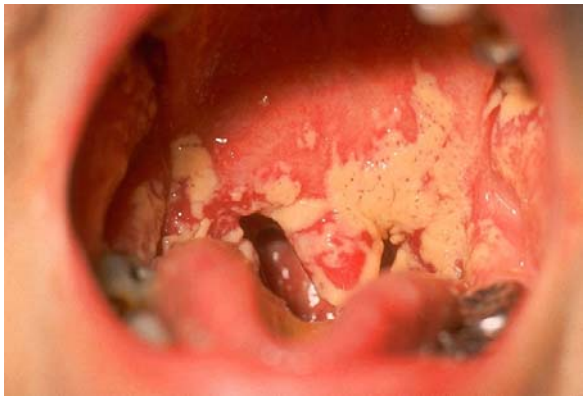
Sputum smear from patient with pulmonary candidiasis. Gram stain. CDC



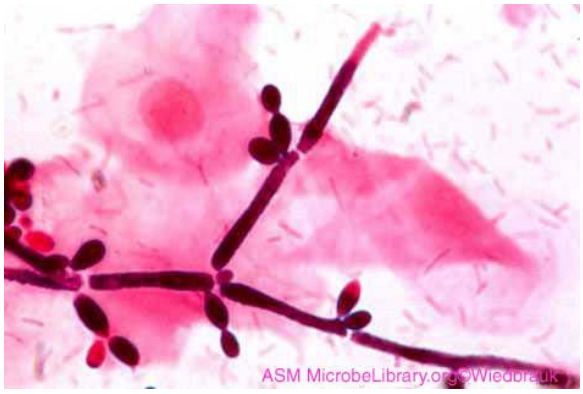
Histopathology of Candida esophagitis. Methenamine silver stain (digitally colorized). CDC



Gross pathology of rabbit kidney lesions due to experimental Candida albicans infection. Rabbit was cortisone-treated. CDC



Oral thrush. CDC

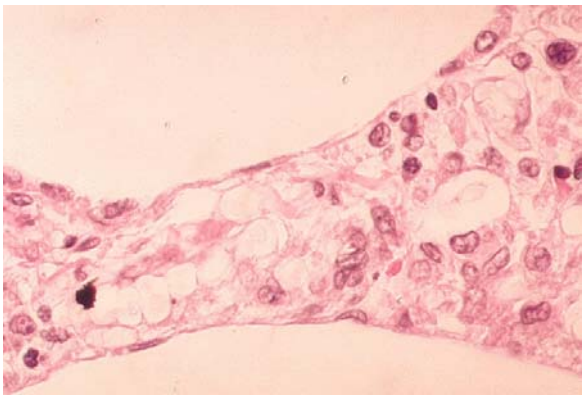


Gram-stain of vaginal smear showing Candida albicans epithelial cells and many gram-negative rods. (1,000X oil) © Danny L. Wiedbrauk, Warde Medical Laboratories, Ann Arbor, Michigan and The MicrobeLibrary

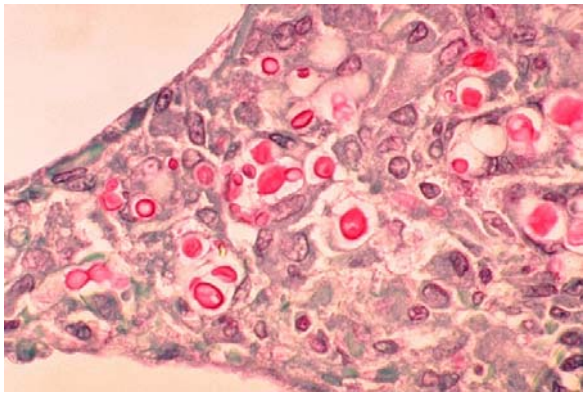
B. CRYPTOCOCCOSIS *(Cryptococcus neoformans)*

Cryptococcosis manifests itself most commonly as meningitis but in recent years many cases of pulmonary disease have been recognized. *C. neoformans* is a very distinctive yeast. The cells which are spherical and 3-7 microns in diameter, produce buds which characteristically are narrow-based and the organism is surrounded by a polysaccharide capsule. There is evidence that the capsule may suppress T-cell function and can be considered a virulence factor. *C. neoformans* also produces an enzyme called phenoloxidase which appears to be another virulence factor. The ecological niche of *C. neoformans* is pigeon and chicken droppings. However, although this organism can be easily recovered from pigeon droppings, a direct epidemiological link has yet to be established between exposure to pigeon droppings and a specific human infection. Infection and disease production is probably a property of the host--not the organism. The source of human infection is not clear. This organism is ubiquitous, especially in areas like abandoned buildings contaminated with pigeon droppings. The portal of entry is the respiratory system. Evidence is developing which indicates that the initial exposure may be many years prior to the manifestation of disease. The organism can be sequestered for this time. Infection may be subacute or chronic. The highly fatal meningoencephalitis caused by *C. neoformans* has a prolonged evolution of several months. The patients symptoms may begin with vision problems and headache, which then progress to delirium, nuchal rigidity leading to coma and death unless the physician is thinking about cryptococcus and does a spinal tap for diagnosis and institutes aggressive therapy. The CSF is examined for its characteristic chemistry

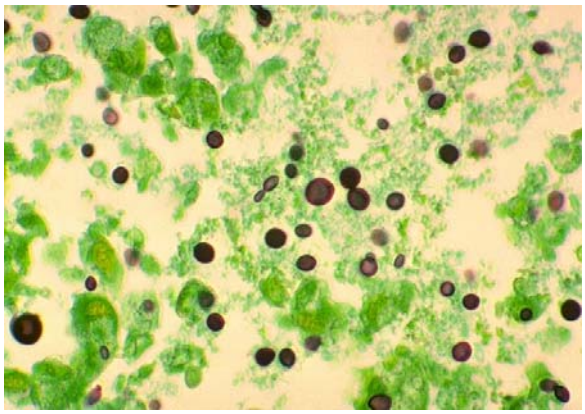
(elevated protein and decreased glucose), cells (usually monocytes), and evidence of the organism. The latter is measured by the visual demonstration of the organism (India Ink preparation) or by a serologic assay for the antigen of *C. neoformans*. The India Ink test, which demonstrates the capsule of this yeast, is supplemented by the latex agglutination test for antigen which is more sensitive and more specific. The Latex Agglutination test measures antigen, NOT antibody. A decreasing titer indicates a good prognosis, while an increasing titer has a poor prognosis. When you consider Cryptococcosis, think of Capsules and CNS disease. In addition to causing meningitis, *C. neoformans* may also infect lungs and skin. The disease in the lungs and skin is characterized by the formation of a granulomatous reaction with giant cells. As with other fungal diseases, there has been an increase in the recognition of pulmonary infection. The yeast may also form a mass in the mediastinum called a cryptococcoma. The geographical distribution of this organism is world-wide. The clinical material sent to the lab is CSF, biopsy material, and urine (for some unexplained reason the organism can be isolated from the urine in both the CNS and systemic infections). This organism will grow overnight on bacterial or fungal media at 37 C. but growth is a little slower at room temperature. In culture the organism grows as creamy, white, mucoid (because of the capsule) colonies. Growth in culture is usually visible in 24 to 48 hours. As the culture ages, it turns brown due to a melanin produced by the phenoloxidase. The organism is a round, single cell, yeast surrounded by a capsule. Identification is based on physiological reactions. Pathologists use a mucicarmine stain, which stains the capsule, to identify the organism in tissue sections. There is usually little or no inflammatory response. The Direct Fluorescent Antibody test identifies the organism in culture or tissue section specifically, by causing the yeast cell wall to stain green. To test the patient's serum there are 3 serologic tests: The Indirect Fluorescent Antibody test, the Tube Agglutination test for antibody, and the Latex Agglutination test for antigen. The latex agglutination test can be used as a prognostic test. As the patient improves, the serum antigen titer will also decrease. The drugs of choice to treat cryptococcus infection are amphotericin B and 5-Fluorocytosine (5-FC). 5-FC is an oral drug. If it is given as the only treatment, there are relapses so most physicians use both drugs simultaneously. Actually, these two drugs are synergistic, and thus, their association is advantageous.



Cryptococcosis of lung in patient with AIDS. Histopathology of lung shows widened alveolar septum containing a few inflammatory cells and numerous yeasts of *Cryptococcus neoformans* CDC/Dr. Edwin P. Ewing, Jr. epe1@cdc.gov



Cryptococcosis of lung in patient with AIDS. Mucicarmine stain. Histopathology of lung shows widened alveolar septum containing a few inflammatory cells and numerous yeasts of *Cryptococcus neoformans.* The inner layer of the yeast capsule stains red. CDC/Dr. Edwin P. Ewing, Jr. epe1@cdc.gov



Cryptococcosis of lung in patient with AIDS. Methenamine silver stain. Histopathology of lung shows numerous extracellular yeasts of *Cryptococcus neoformans* within analveolar space. Yeasts show narrow-base budding and characteristic variation in size. CDC/Dr. Edwin P. Ewing, Jr. epe1@cdc.gov

MYCOLOGY - CHAPTER FOUR （真菌学----第四章）

SUPERFICIAL MYCOSES （浅部真菌病）

The superficial (cutaneous) mycoses are usually confined to the outer layers of skin, hair, and nails, and do not invade living tissues. The fungi are called dermatophytes. Dermatophytes, or more properly, keratinophilic fungi, produce extracellular enzymes (keratinases) which are capable of hydrolyzing keratin.

A. CLINICAL MANIFESTATIONS

Tinea means "ringworm" or "moth-like". Dermatologists use the term to refer to a variety of lesions of the skin or scalp.

Tinea corporis - small lesions occurring anywhere on the body.

Tinea pedis - "athlete's foot". Infection of toe webs and soles of feet.

Tinea unguium (onychomycosis) - nails. Clipped and used for culture (figure 1).

Tinea capitis - head. Frequently found in children.

Tinea cruris - "jock itch". Infection of the groin, perineum or perianal area.

Tinea barbae - ringworm of the bearded areas of the face and neck.

Tinea versicolor - Characterized by a blotchy discoloration of skin which may itch. Up to 25% of the general population may have this lesion at any one time. Diagnosis is usually possible by direct microscopic examination of KOH-treated skin scrapings which show a typical aspect of mycelia and spores described as "spaghetti and meatballs." Caused by *Malassezia furfur* (figure 2)

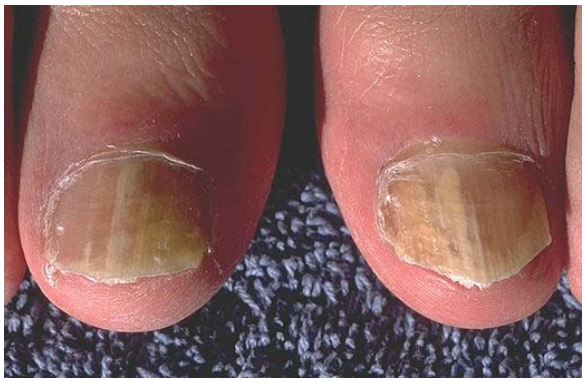


Figure 1 Onychomycosis due to *Trychophyton rubrum*, right and left great toe. Tinea unguium. CDC/Dr. Edwin P. Ewing

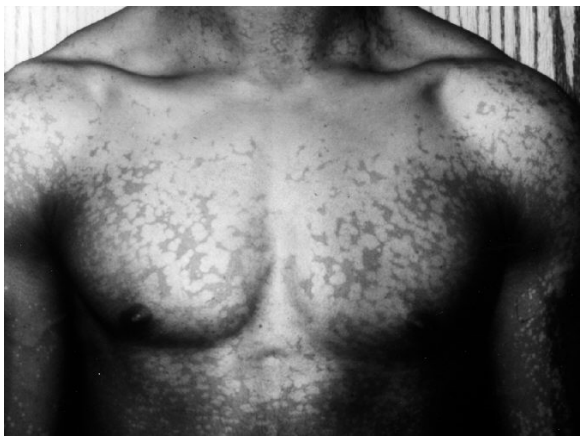


Figure 2 Tinea Versicolor on chest. CDC/Dr. Gavin Hart

B. ECOLOGY

The dermatophytes (skin plants) causing human infections may have different natural sources and modes of transmission:

anthropophilic - usually associated with humans only; transmission from man to man by close contact or through contaminated objects.

zoophilic - usually associated with animals; transmission to man by close contact with animals (cats, dogs, cows) or with contaminated products.

geophilic - usually found in the soil, transmitted to man by direct exposure. Knowledge of the species of dermatophyte and source of infection are important for proper treatment of the patient and control of the source.

Invasion by zoophilic or geophilic organisms may cause inflammatory disease in man.
Geographic distribution: Dermatophytes occur worldwide, but some species have geographically limited distribution.

C. ETIOLOGIC AGENTS

There are three genera of dermatophytes:

1. *Trichophyton* species (19 species) Figure 3.

These infect skin, hair and nails. Rarely can cause subcutaneous infections, in immunocompromised individuals. Take 2-3 weeks to grow in culture. The conidia are large (macroconidia), smooth, thin-wall, septate (0-10 septa), and pencil-shaped; colonies a re a loose aerial mycelium which grow in a variety of colors. Identification requires special biochemical and morphological techniques (figure 4). Trichophyton rubrum is presently the most common cause of tinea in South Carolina.

2. *Microsporum* species (13 species). These may infect skin and hair, rarely nails. Its prevalence has decreased significantly. When prevalent (15-20 years ago), this organism could be easily identified on the scalp because infected hairs fluoresce a bright green color when illuminated with a UV-emitting Wood's light. The loose, cottony mycelia produce macroconidia (figure 5) which are thick-walled, spindle-shaped, multicellular, and echinulate (spiny). Microsporum canis is one of the most common dermatophyte species infecting humans.

3. *Epidermophyton floccosum*. These infect skin and nails and rarely hair. They form yellow-colored, cottony cultures and are usually readily identified by the thick, bifurcated hyphae with multiple smooth, club-shaped macroconidia.

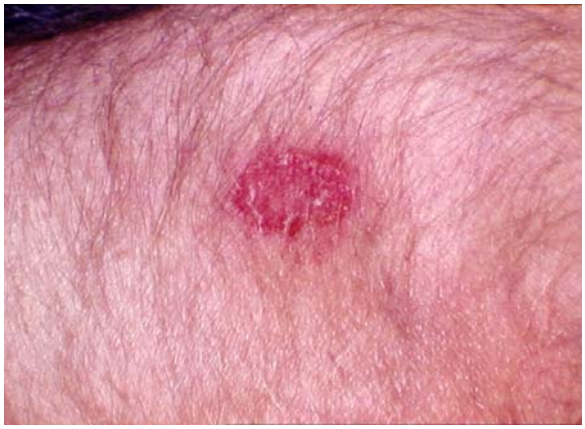


Figure 3 Trichophyton mentagrophytes contracted from a dog © Bristol Biomedical Image Archive. Used with permission

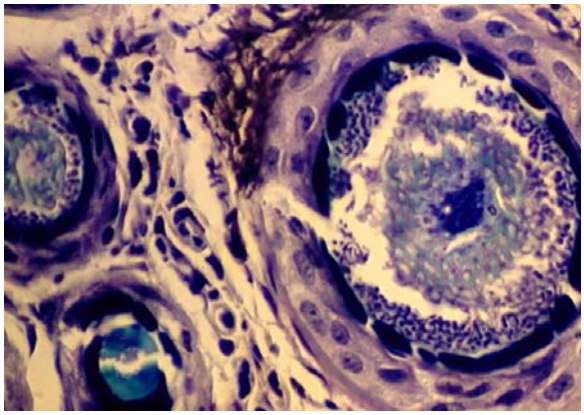


Figure 4 Dermatomycosis (ringworm) of hair follicles © Bristol Biomedical Image Archive. Used with permission

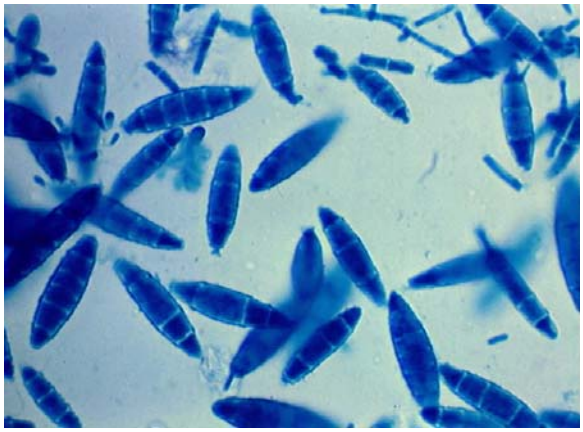
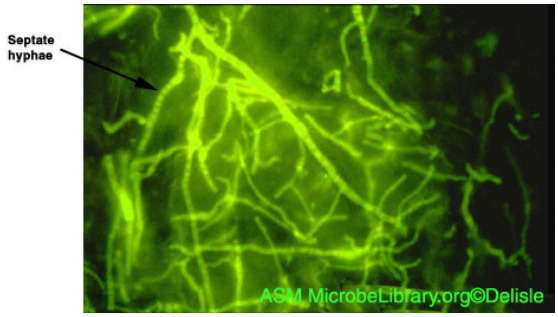
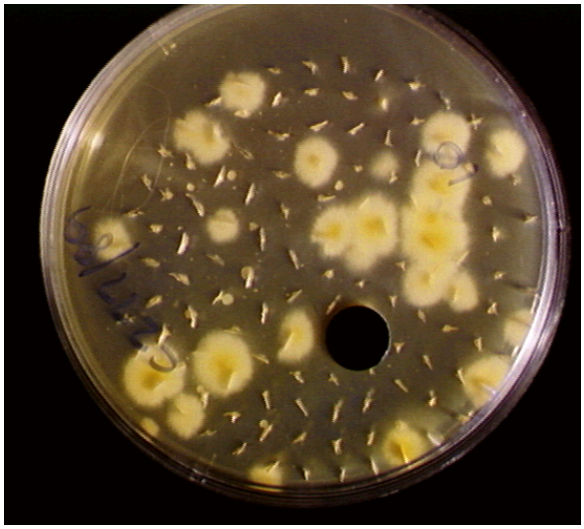


Figure 5 Ringworm, stained preparation, macroconidia of Microsporum canis © Bristol Biomedical Image Archive. Used with permission



Microsporum canis obtained from a skin scraping of a patient with ringworm on the neck acquired from her infected cat. The fungus is identified as a dermatophyte by this calcofluor stain of the skin scrapings viewed at 500X magnification. The calcofluor dye binds to the chitin in the fungus and fluoresces under a fluorescent light. © Gloria J. Delisle, Lewis Tomalty, Queens University Ontario and The MicrobeLibrary



Ringworm caused by Microsporum gypseum, culture plate with Sabouraud's dextrose agar © Bristol Biomedical Image Archive. Used with permission

D. THERAPY

Skin infections can be treated (more or less successfully) with a variety of drugs, such as:

Tolfnatate (Tinactin) available over the counter - Topical

Clotrimazole - Topical

Miconazole - Topical.

Ketoconazole seems to be most effective for tinea versicolor and other dermatophytes.

Itraconazole - oral

Terbinifine (Lamisil) - oral, topical.

For skin and Nail infections.

Morpholines - oral

For infections involving the scalp and particularly the nails, griseofulvin is commonly used. This antimycotic must be incorporated into the newly produced keratin layer to form a barrier against further invasion by the fungus. This is a very slow process requiring oral administration of the drug for long periods - up to 6 to 9 months for fingernail infections and 12 to18 months for toenail infections.

Itraconazole and terbinafine are the drugs of choice for onychomycoses.

E. THE ID REACTION

Patients infected with a dermatophyte may show a lesion, often on the hands, from which no fungi can be recovered or demonstrated. It is believed that these lesions, which often occur on the dominant hand (i.e. right-handed or left-handed), are secondary to immunological sensitization to a primary (and often unnoticed) infection located somewhere else (e.g. feet). These secondary lesions will not respond to topical treatment but will resolve if the primary infection is successfully treated.

MYCOLOGY - CHAPTER FIVE （真菌学----第五章）

FILAMENTOUS FUNGI （丝状真菌）

A. CHROMOBLASTOMYCOSIS （着色真菌病）

A chronic, localized infection infection of subcutaneous tissues caused by several species of dematiaceous fungi. The 3 most common agents are:

1. *Fonsecaea pedrosoi*

2. *Cladosporium carrionii*

3. *Phialophora verrucosa*

These fungi, recognized by a variety of names, are saprobes located in soil and decaying vegetation. The route of entry is usually by trauma. The lesions are sub-cutaneous and the surface can be flat or verrucous. The lesions take several years to develop. These organisms are called dematiaceous fungi, because they have a black color in the mycelium cell wall (in culture and in tissue). In tissue these fungi form sclerotic bodies which are the reproductive forms dividing by fission. These organisms induce a granulomatous reaction. The etiologic agents of chromoblastomycosis are septate, mold-like, branching, darkly pigmented which produce asexual fruits called conidia. We identify these fungi in culture by the shape and formation of the conidia. The fungi have a world-wide distribution especially in warmer climates like the tropics or the southern U.S. The melanin in the pigment may be a virulence factor. These organisms are distributed world-wide. There is no really successful therapy. Excision

and local heat have been used with some success. Flucytosine (5-FC), thiabendazole and itraconazole have also been used to treat (or control) this disease. There are no serological tests to aid in the diagnosis.

B. MYCETOMA (Maduromycosis)

Mycetomas (fungous tumors) are also chronic, subcutaneous infections. These are called eumycotic mycetoma (tumors caused by the TRUE fungi as opposed to those caused by actinomycetes). These tumors frequently invade contiguous tissue, particularly the bone. A diagnosis of the etiologic agent is essential for patient management because the prognosis and therapy differs. Mycetoma characteristics:

1. tumefaction - swelling

2. granules - a variety of colors (white, brown, yellow, black)

3. draining sinus tracts

The three most common etiologic agents are:

1. *Madurella mycetomatis*

2. **Exophiala jeanselmei*

3. **Pseudallescheria boydii*

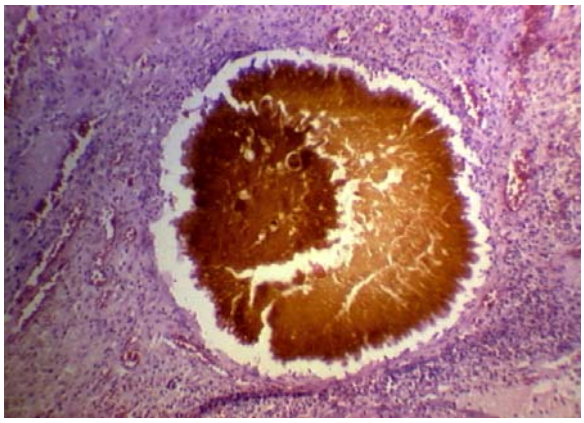
*The most common in the US. These organisms are associated with the soil, thus you see many infections in the feet and legs.

Clinical specimens for diagnosis:

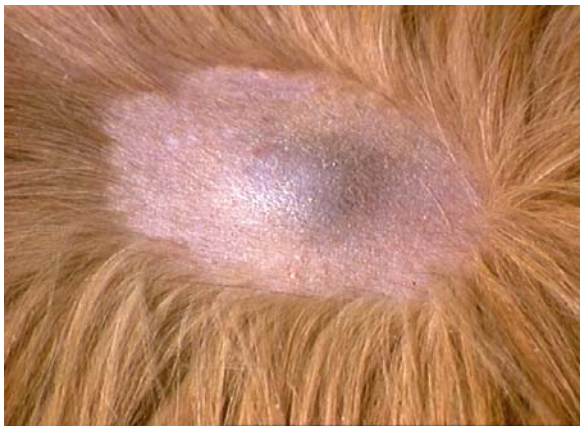
1. pus - with granules

2. tissue - for histological examination

The color, size and texture of the granules are an aid in the diagnosis of mycetomas. The agents of mycetoma are all filamentous fungi which require 7-10 days for visible growth on the culture media and then another several days for specific identification. These fungi are identified by the colonial morphology, conidia formation and biochemical reactions. The species of fungi cannot be distinguished in histopathological tissue sections.Treatment is very difficult, but ketoconazole and itraconazole have been used with some success.



Black grain mycetoma: subcutaneous nodule due to Madurella Mycetomatis, magnified x 100



Mycetoma with presence of geotrichum

C. ZYGOMYCOSIS

Also known as mucormycosis and phycomycosis. Zygomycosis is an acute inflammation of soft tissue, usually with fungal invasion of the blood vessels. This rapidly fatal disease is caused by several different species in this class. The zygomycetes, like the Candida species, are ubiquitous and rarely cause disease in an immunocompetent host. Some characteristic underlying conditions which cause susceptibility are: diabetes, severe burns, immunosuppression or intravenous drug use.

The three most common genera causing this clinical entity are:

1. Rhizopus species

2. Mucor species

3. Absidia species

Characteristics: world-wide distribution, commonly in soil, food, organic debris, seen on decaying vegetables in the refrigerator and on moldy bread. Rhinocerebral infections are common. This disease is frequently seen in the uncontrolled diabetic. Typical case: An uncontrolled diabetic patient comes to

ER (may be comatose depending on the state of diabetes) and a cotton-like growth is observed on the roof of the mouth or in the nose. These are the hyphae of the organism. If untreated, the patient will die within a few hours or days. What do you do to help this patient first? Controlling the diabetic state is most important before administering amphotericin.
These fungi have a tendency to invade blood vessels (particularly arteries) and enter the brain via the blood vessels and by direct extension through the cribiform plate. This is why they cause death so quickly.
Culture: A rapid growing, loose, white mold which is visible in 24 to 48 hours. With age, and the formation of sporangia, the colony becomes dark gray. The sporangia contain the dark spores. The mycelium is, wide (10-15 microns), ribbon-like and non-septate (coenocytic). This same appearance is clear in tissue sections. The species are identified by the morphology in culture.
Treatment consists of debridement and amphotericin
There is an immunodiffusion test available, but the physician cannot wait for these results before instituting rapid, vigorous intervention. The diagnosis and treatment must be immediate and based primarily on clinical observations.

D. ASPERGILLOSIS

Aspergilli produce a wide variety of diseases. Like the zygomycetes, they are ubiquitous in nature and play a significant role in the degradation of plant material as in composting. Similar to Candida and the Zygomycetes, they rarely infect a normal host. The organism is distributed world-wide and is commonly found in soil, food, paint, air vents. They can even grow in disinfectant. There are more than one hundred species of aspergilli The most common etiologic agents of aspergillosis in the United States:

1. Aspergillus fumigatus

2. A. niger

3. A. flavus

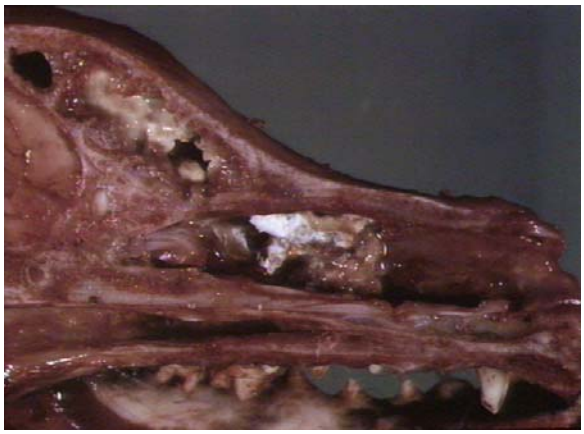
There are three clinical types of pulmonary aspergillosis:

1. Allergic - hypersensitivity to the organism. Symptoms may vary from mild respiratory distress to alveolar fibrosis.

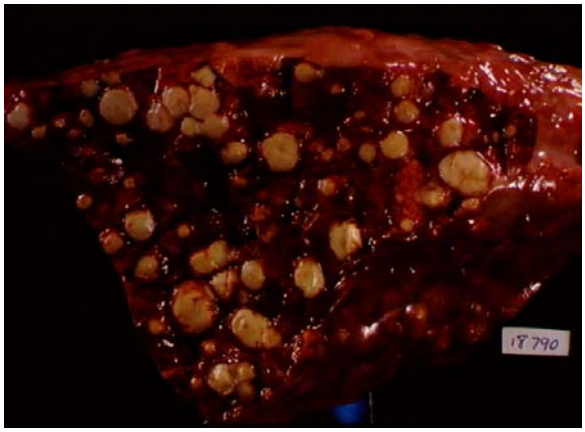
2. Aggressive tissue invasion. Primarily a pulmonary disease, but the aspergilli may disseminate to any organ. They may cause endocarditis, osteomyelitis, otomycosis and cutaneous lesions.

3. Fungus ball which is characteristically seen in the old cavities of TB patients. This is easily recognized by x-ray, because the lesion (actually a colony of mold growing in the cavity) is shaped like a half-moon (semi-lunar growth). The patients may cough up the fungus elements because the organism frequently invades the bronchus. Chains of conidia can sometimes be seen in the sputum.

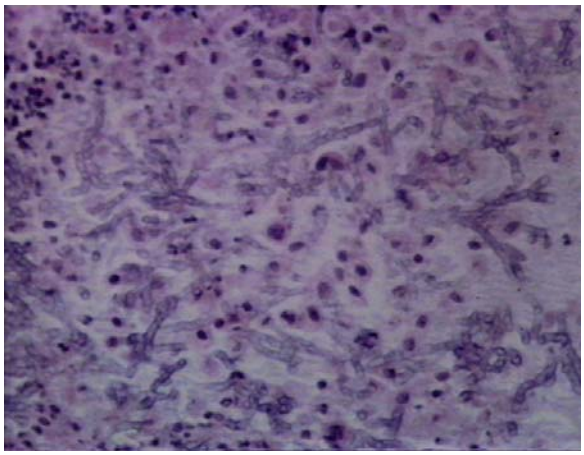
Culture: Aspergilli require 1-3 weeks for growth. the colony begins as a dense white mycelium which later assumes a variety of colors, according to species, based on the color of the conidia. The hyphae are branching and septate. Species differentiation is based on the formation of spores as well as their color, shape and texture.
Histopathology: The septate hyphae are wide and form dichotomous branching, i.e., a single hypha branches into two even hyphae, and then the mycelium continues branching in this fashion.
Serology: There is an excellent serological test for aspergillosis which is an Immunodiffusion test. There may be 1 to 5 precipitin bands. Three or more bands usually indicate increasingly severity of the disease. i.e., tissue invasion.
Treatment: Itraconazole and Amphotericin B.



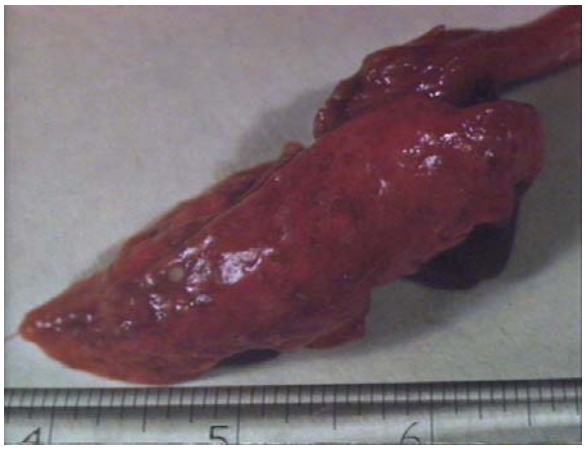
Nasal aspergillosis



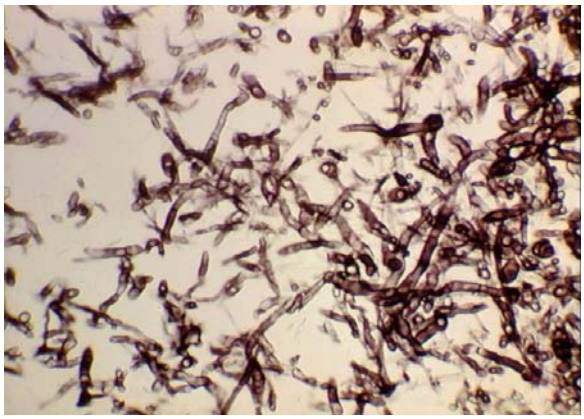
Aspergillus pneumonia in lung of deer



Lung: Aspergillus hyphae in fungal pneumonia



Fungal granulomas in lung caused by Aspergillus fumigatus



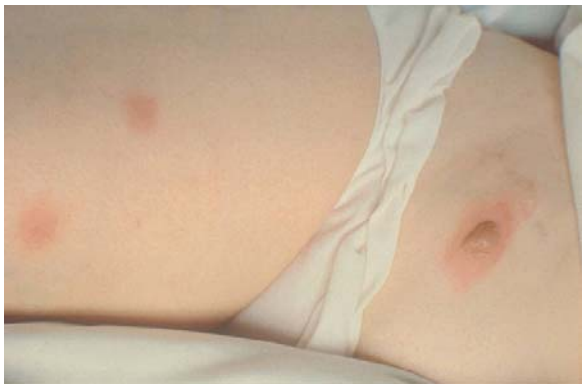
Aspergillosis. Human mouth. Gomori's silver methenamine stain

MYCOLOGY - CHAPTER SIX （真菌学----第六章）

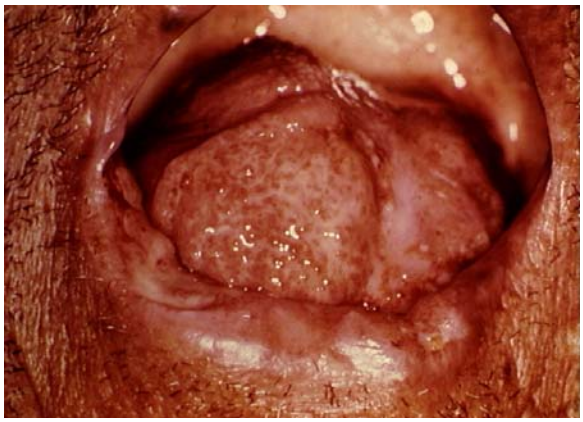
DIMORPHIC FUNGI （双相真菌）

A. BLASTOMYCOSIS (*Blastomyces dermatitidis*)

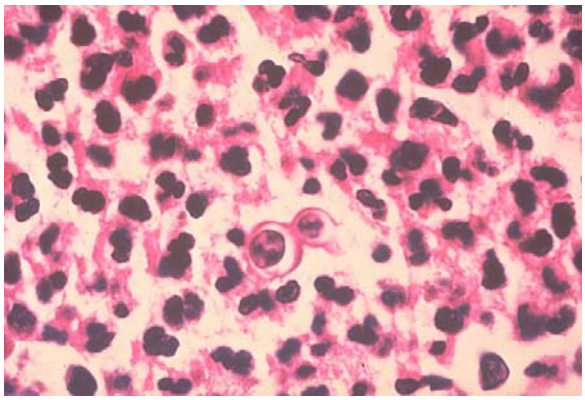
Most of the systemic fungi have a specific niche in nature where they are commonly found. *Blastomyces dermatitidis* survives in soil that contains organic debris (rotting wood, animal droppings, plant material) and infects people collecting firewood, tearing down old buildings or engaged in other outdoor activities which disrupt the soil. In addition to an ecological niche, most fungi that cause systemic infections have a limited geographic distribution where they occur most frequently. Blastomycosis occurs in eastern North America and Africa. The vast majority of patients with blastomycosis in South Carolina are infected in the northern part of the state, above the Fall Line (Augusta, GA, Aiken, Columbia, Cheraw, Raleigh, NC).



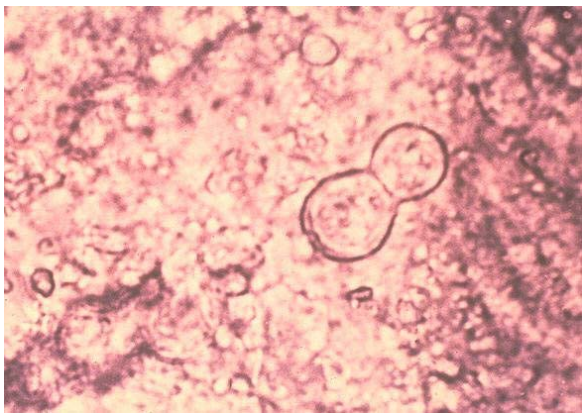
Nodular skin lesions of blastomycosis, one of which is a bullous lesion on top of a nodule. CDC



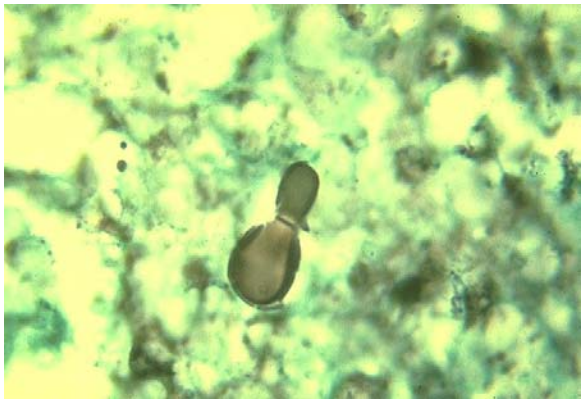
South American Blastomycosis. Paracoccidioidomycosis: Mouth Mucosa in man



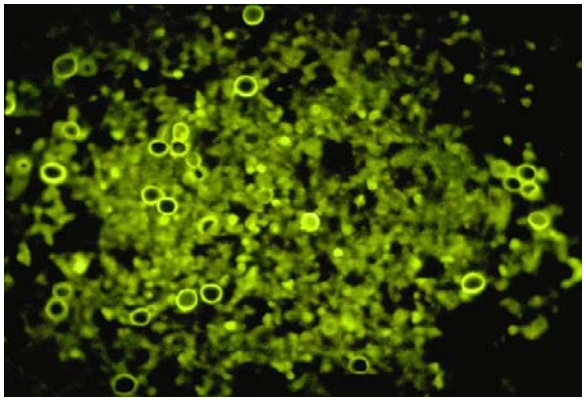
Histopathology of blastomycosis of skin. Budding cell of Blastomyces dermatitidis surrounded by neutrophils. Multiple nuclei are visible. CDC



Smear from foot lesion of blastomycosis showing Blastomyces dermatitidis yeast cell undergoing broad-base budding. ASCP/Atlas of Clinical Mycology II / CDC



Histopathology of blastomycosis. Yeast cell of Blastomyces dermatitidis undergoing broad-base budding. Methenamine silver stain. African case. CDC



Histopathology of blastomycosis, lung of wolf. Yeast cells of Blastomyces dermatitidis. FA stain. CDC/Dr. Leo Kaufman

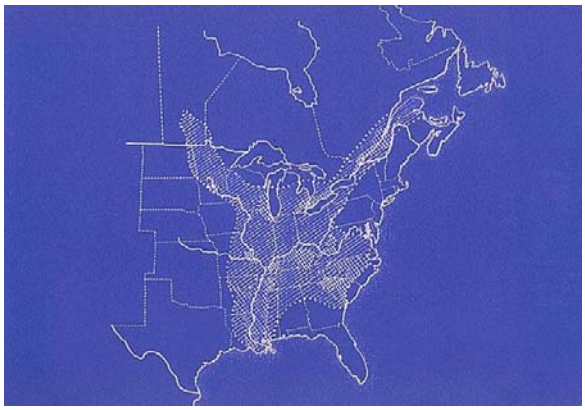
Blastomycosis is a chronic granulomatous disease which means that it progresses slowly. Although the pulmonary and skin involvement is the most common, *B. dermatitidis* frequently affects bone, prostate and other organs. More frequently blastomycosis presents as a cutaneous or a respiratory disease. The cutaneous lesions may be primary (usually self-limiting) or secondary (a manifestation of systemic disease). The patient who presents with a complaint of respiratory symptoms will frequently remark about loss of appetite, loss of weight, fever, productive cough, and night sweats. While these symptoms resemble those of TB, it is not this disease. The X-ray shows obvious pulmonary disease. To make the specific diagnosis, the physician must be aware of blastomycosis. Sputum sent to the lab for "culture" will not grow the organism. The lab must be alerted to look for fungal organisms or to look specifically for blastomyces. Some patients have a sub-clinical or "flu-like" response to infection. *B. dermatitidis* can frequently be demonstrated in a KOH preparation of pus from a skin lesion. A typical cutaneous lesion shows central healing with microabscesses at the periphery. A pus specimen may be obtained by nicking the top of a microabscess with a scalpel, obtaining the purulent material and making the diagnosis in 5 min. by microscopic examination with KOH. This organism has a characteristic appearance of a double contoured wall with a single bud on a wide base. There are no specific virulence factors for *B. dermatitidis.* Laboratory specimens depend on the manifestation of the disease: If there are skin lesions, send skin scrapings or pus. If there is pulmonary involvement, send sputum. Other specimens include biopsy material and urine. Occasionally, the organism can be isolated from urine as it often infects the prostate.

Mycology

If you request a fungus culture from the microbiology lab, they will incubate the cultures at 37 degrees C and at 25 degrees C because most of the significant pathogenic fungi are dimorphic.

A culture of *B. dermatitidis* takes 2 to 3 weeks to grow at 25 degrees C. It appears as a white, cottony mold (mycelium) on Sabouraud dextrose agar. Most specimens for fungus culture are plated on Sabouraud's dextrose agar. Microscopically, the mycelia and the fruiting bodies are evident. However, the mold cannot be identified by its fruiting bodies. The fruiting bodies are called microconidia, but they are not distinctive. Other fungal saprophytes and pathogens have similar conidia. At 37 degrees C the yeast form grows in about 7-10 days. It appears as a buttery-like, soft colony with a tan color. Microscopically, we see the typical yeast form of a thick wall and a single bud with a WIDE BASE. This wide base is characteristic of *B. dermatitidis*, and it is important to be able to recognize this. The cells are 12-15 microns in diameter. The yeast will convert to the mycelial form when incubated at 25 degrees C, taking from 3 to 4 days up to a few weeks. Similarly, the mycelial growth can be converted

to yeast form when incubated at 37 degrees C.In the past, the only way to identify the dimorphic fungi was to convert from one form to the other, but now it is possible to take the mycelial growth (which is the easiest to grow), and confirm the isolate with a DNA probe in a matter of hours.



Map of eastern United States and Canada showing distribution of reported cases of blastomycosis. CDC

Histopathology

B. dermatitidis produces both a granulomatous and suppurative tissue reaction

Serology

There are three serological tests used for blastomycosis:

1. Immunodiffusion test (precipitin). This requires 2 to 3 weeks to become positive. This test is positive in about 80% of the patients with blastomycosis. When it is positive, there is close to 100% specificity.

2. Complement fixation (CF) test. This test requires 2 to 3 months after the onset of disease to develop detectable antibody. Besides the long delay before there is measurable antibody, another disadvantage of the C-F is that it cross reacts with other fungal infections (coccidioidomycosis and histoplasmosis). The advantage is that it is a quantitative test. The physician can follow the patient's response to the disease by monitoring the antibody titer.

3. Enzyme Immunoassay (EIA). The latter test has met with mixed acceptance by mycologists. However it is easy to perform and antibody is detected early in the disease process.

Amphotericin B remains is the drug of choice (DOC) although it is very toxic and must be administered intravenously for several weeks. Ketoconazole is also being used in mild cases.

B. HISTOPLASMOSIS (*Histoplasma capsulatum*)

Histoplasmosis is a systemic disease, mostly of the reticuloendothelial system, manifesting itself in the bone marrow, lungs, liver, and the spleen. In fact, hepatosplenomegaly is the primary sign in children, while in adults, histoplasmosis more commonly appears as pulmonary disease. This is one of the most common fungal infections, occurring frequently in South Carolina, particularly the northwestern portion of the state. The ecological niche of *H. capsulatum* is in blackbird roosts, chicken houses and bat guano. Typically, a patient will have spread chicken manure around his garden and 3 weeks later will develop pulmonary infection. There have been several outbreaks in South Carolina where workers have cleared canebrakes which served as blackbird roosts with bulldozers. All who were exposed, workers and bystanders, contracted histoplasmosis. Histoplasmosis is a significant occupational disease in bat caves in Mexico when workers harvest the guano for fertilizer. In the endemic area the majority of patients who develop histoplasmosis (95%) are asymptomatic. The diagnosis is made from their history, serologic testing or skin test. In the patients who are clinically ill, histoplasmosis generally occurs in one of three forms: acute pulmonary, chronic pulmonary or disseminated. There is generally complete recovery from the acute pulmonary form (another "flu-like" illness). However, if untreated, the disseminated form of disease is usually fatal. Patients will first notice shortness of breath and a cough which becomes productive. The sputum may be purulent or bloody. Patients will become anorexic and lose weight. They have night sweats. This again sounds like tuberculosis, and the lung x- ray also looks like tuberculosis, but today radiologists can distinguish between these diseases on the chest film (histoplasmosis usually appears as bilateral interstitial infiltrates). Histoplasmosis is prevalent primarily in the eastern U.S. In S.C., a histoplasmin skin test survey of lifetime, one county residents, white males, 17 to 21 years old, was performed on Navy recruits. The greatest number of positive skin tests appeared in the northwestern part of the state. A similar study of medical students conducted at Medical University of South Carolina, about 25 years ago, bore the same distribution (Goodman and Ever, J.S.C.M.A. 67:53-55, 1971).The skin test is NOT used for diagnostic purposes, because it interferes with serological tests. Skin tests are used for epidemiological surveys.

Clinical specimens sent to the lab depend on the presentation of the disease: Sputum or Bronchial alveolar lavage, if it is pulmonary disease, or Biopsy material from the diseased organ. Bone marrow is an excellent source of the fungus, which tends to grow in the reticulo-endothelial system. Peripheral blood is also a source of visualizing the organism histologically. The yeast is usually found in monocytes or in PMN's. Many times an astute medical technologist performing a white blood cell count will be the first one to make the diagnosis of histoplasmosis. In peripheral blood, *H. capsulatum* appears as a small yeast about 5-6 microns in diameter. (Blastomyces is 12 to 15 microns). Gastric washings are also a source of *H. capsulatum* as people with pulmonary disease produce sputum and frequently swallow their sputum.

Mycology

When it is grown on Sabouraud dextrose agar at 25 degrees C, it appears as a white, cottony mycelium after 2 to 3 weeks. As the colony ages, it becomes tan. In the mold form, Histoplasma has a very distinct spore called a tuberculate macroconidium. The tubercles are diagnostic, however there are some non-pathogens which appear similar. A medical mycologist will be able to distinguish them. Grown at 37 degrees, C the yeast form appears. It is a white to tan colony. The yeast cell is 5-6 microns in diameter and slightly oval in shape. This is not diagnostic. To confirm the diagnosis, one must convert the organism from yeast to mycelium or vice-versa or use the DNA probe.

Serology for histoplasmosis is a little more complicated than for other mycoses, but it provides more information than blastomycosis serology.

There are 4 tests:

1. Latex agglutination

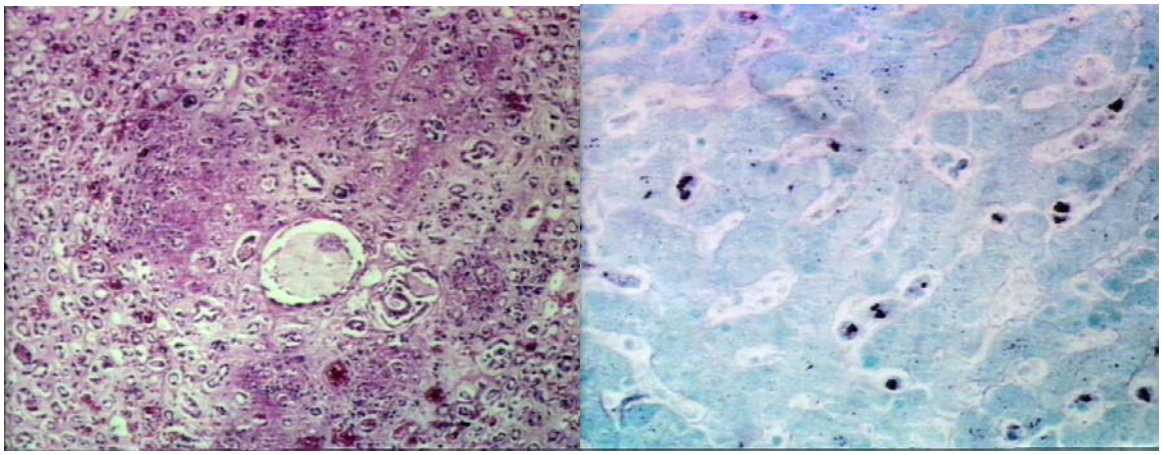
2. Complement Fixation

3. Immunodiffusion

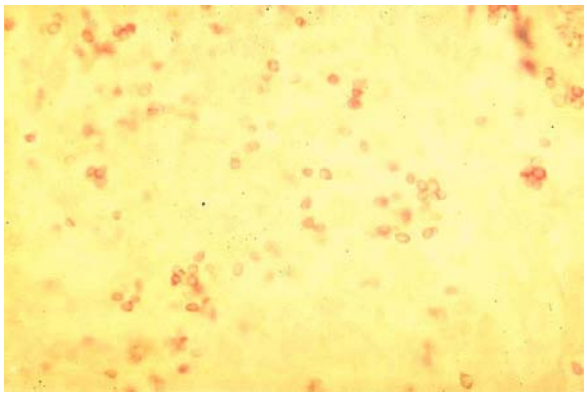
4. EIA

Each of these serological tests has different characteristics that make them useful. The latex agglutination test is a very simple test involving agglutination in a test tube. The Ab is fairly specific and rises early in the disease (in the first 2 weeks), and disappears in about 3 months. The complement fixation test is like the one for blastomycosis, except there are 2 antigens, one to the yeast form of the organism and the other to the mycelial form. Some patients react to one form and not the other, while some individuals react to both. The reason for the different responses is not clear. One disadvantage is that complement fixing antibody develops late in the disease, about 2 to 3 months after onset. A second disadvantage is that it cross reacts with other mycotic infections. An advantage of the C-F test is that it is quantitative, so the physician can follow the course of the disease by observing the titer of several samples. The interpretation of the immunodiffusion test is a little more complicated than with blastomycosis because there are two bands which may appear. An H band indicates active disease and will appear in 2 to 3 weeks. An M band can indicate past or present disease, or result from a skin test. This is one reason why skin tests are not used for diagnosis because they can interfere with other tests. Skin tests will also affect the complement fixation test.

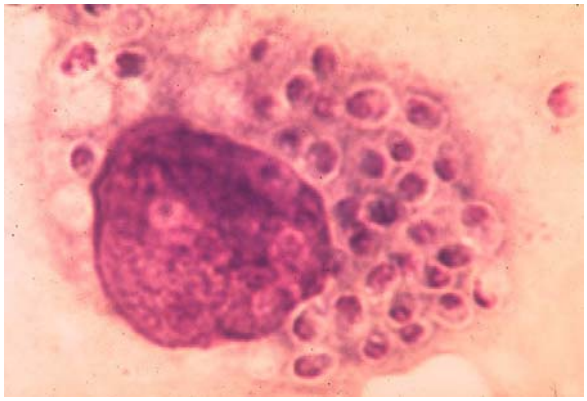
Recently, a radioimmunoassay for histoplasma polysaccharide antigen has been developed. This is a proprietary test so the evaluation of the results have been questioned. The drug of choice (DOC) is amphotericin B, with all its side effects. Itraconazole is now also being used.



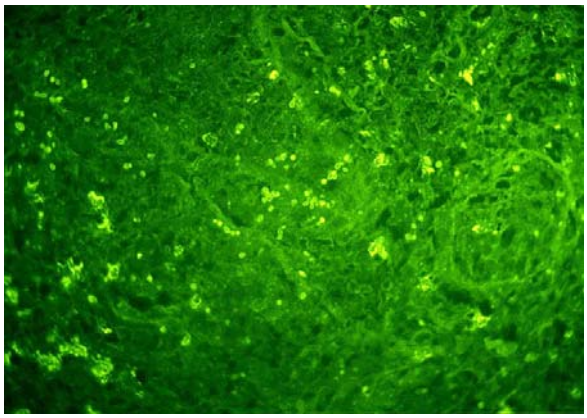
Histoplasmosis



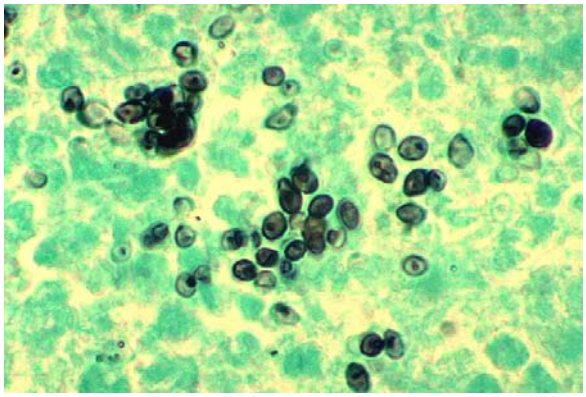
Histopathology of histoplasmosis showing yeast forms of Histoplasma capsulatum. This fungus shows thermal dimorphism: mold form at 25°C and yeast form at 37°C. CDC



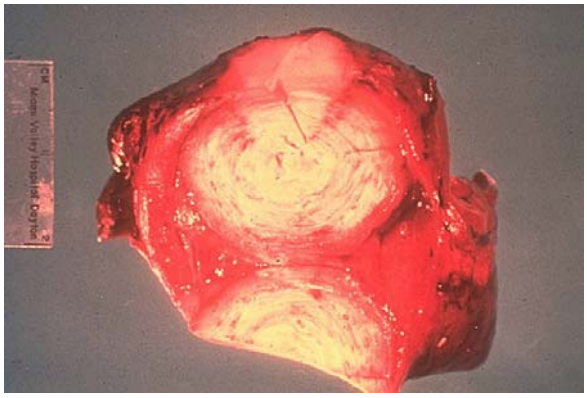
Histiocyte containing numerous yeast cells of Histoplasma capsulatum. Dr. D. T. McClenan / CDC



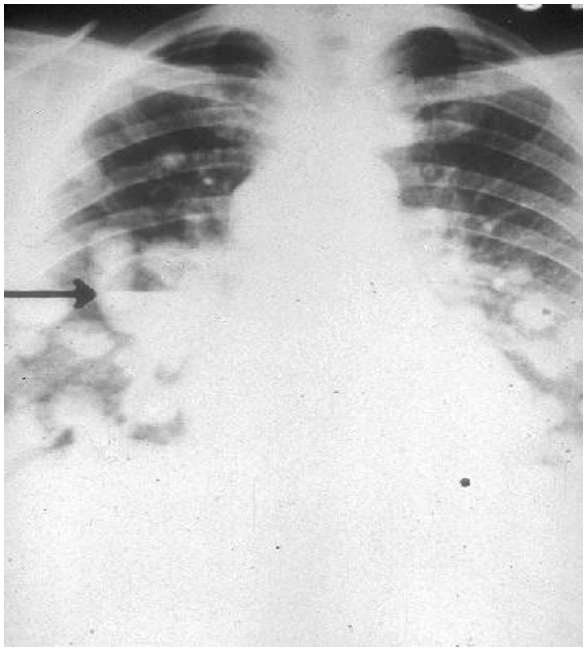
Histopathology of histoplasmosis in open lung biopsy. FA stain reveals numerous yeast cells of Histoplasma capsulatum. CDC/Dr. Leo Kaufman, Maxine Jalbert lek1@cdc.gov



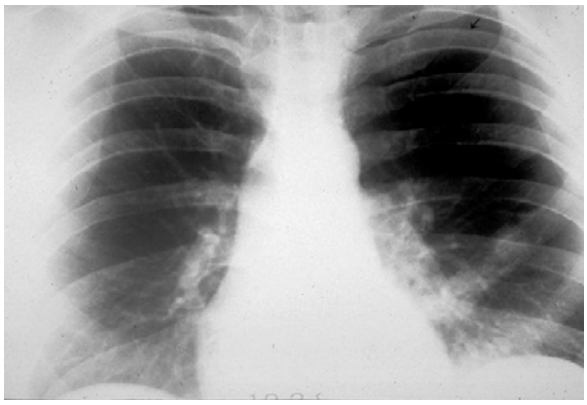
Methenamine silver stain reveals Histoplasma capsulatum fungi. CDC/Dr. Edwin P. Ewing, Jr. epe1@cdc.gov



Gross pathology specimen of lung showing cut surface of fibrocaseous nodule due to Histoplasma capsulatum.
ASCP Atlas of Clinical Mycology II / CDC

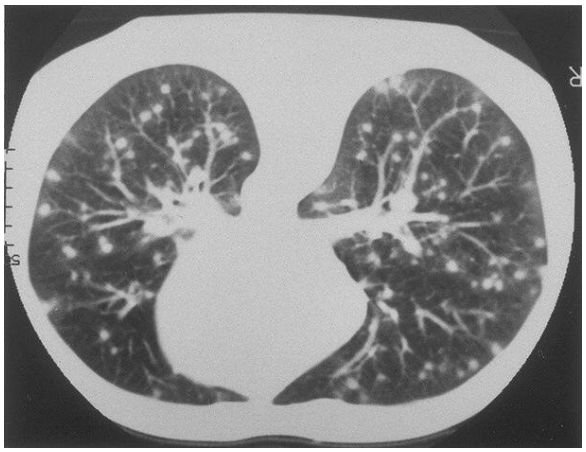


Chest radiograph showing miliary densities in both lung fields plus thin-walled cavity with fluid level. Histoplasmosis. ASCP Atlas of Clinical Mycology II /CDC

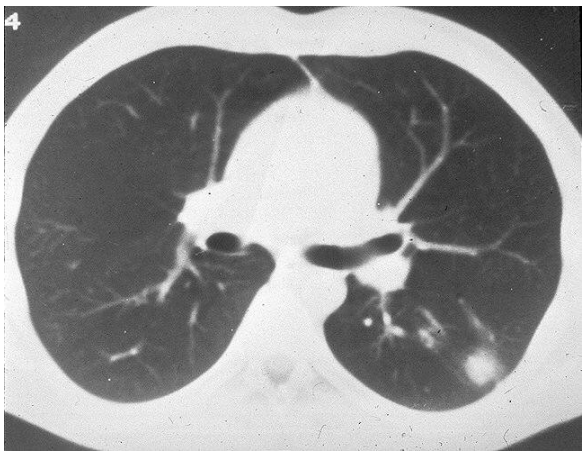


Chest radiograph showing single pulmonary nodule of histoplasmosis.

Case 49-03. Mass Gen Hosp Case Records. CDC



Computed tomography scan of lungs showing classic snowstorm appearance of acute histoplasmosis CDC



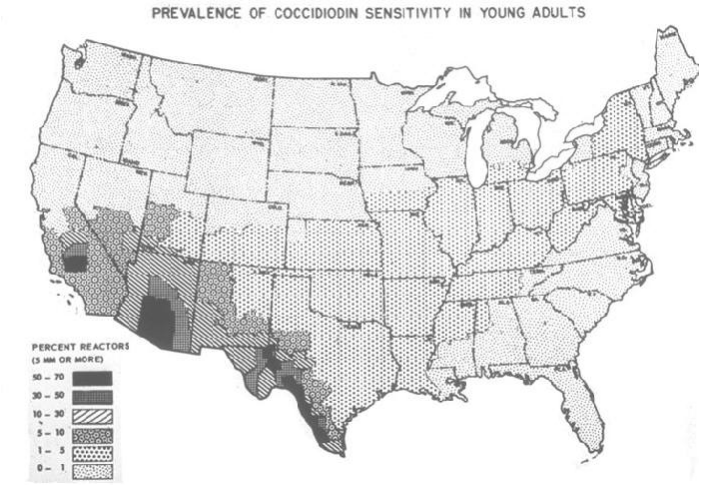
Computed tomography scan showing single pulmonary nodule of histoplasmosis. Case 49-01. Mass Gen Hosp Case Records. CDC

C. COCCIDIOIDOMYCOSIS (*Coccidioides immitis*)

Coccidioidomycosis is primarily a pulmonary disease. About 60 % of the infections in the endemic area are asymptomatic. About 25 % suffer a "flu-like" illness and recover without therapy. This disease exhibits the typical symptoms of a pulmonary fungal disease: anorexia, weight loss, cough,

hemoptysis, and resembles TB. CNS infection with *C. immitis* is more common while it is less frequent with the other fungal diseases. The ecological niche of *C. immitis* is the Sonoran desert, which includes the deserts of the Southwest (California, Arizona, New Mexico and Texas) and northern Mexico. It is also found in small foci in Central and South America.

Desert soil, pottery, archaeological middens, cotton, and rodent burrows all harbor *C. immitis*. *C. immitis* is a dimorphic fungus with 2 life cycles. The organism follows the SAPROPHYTIC cycle in the soil and the PARASITIC cycle in man or animals. The saprophytic cycle starts in the soil with spores (arthroconidia) that develop into mycelium. The mycelium then matures and forms alternating spores within itself. The arthroconidia are then released, and germinate back into mycelia. The parasitic cycle involves the inhalation of the arthroconidia by animals which then form spherules filled with endospores. The ambient temperature and availability of oxygen appear to govern the pathway The organism can be carried by the wind and therefore spread hundreds of miles in storms so the distribution is quite wide. In 1978, cases were seen in Sacramento 500 miles north of the endemic area, from a dust storm in Southern California. The spores of the organism are readily airborne. The cases that occur in South Carolina are usually in patients who have visited an endemic area and brought back pottery, or blankets purchase from a dusty roadside stand, or in Navy and Air Force personnel who were exposed when they were stationed in the endemic area. The disease manifests itself after they are transferred to a base in South Carolina. A few interesting cases occurred in cotton mills in Burlington and Charlotte, N.C. The cotton, grown in the desert of the Southwest, was contaminated with the fungus and the mill workers inhaled the spores while handling the raw cotton and developed coccidioidomycosis.

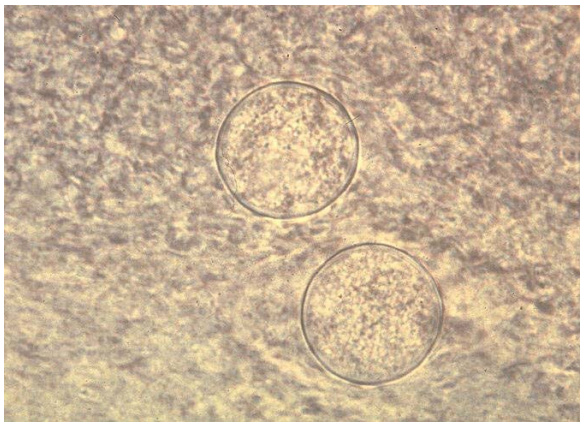


Map of United States showing geographic variation in the prevalence of coccidioidin sensitivity in young adults CDC

Clinical Specimens

Clinical specimens include sputum, pus from skin lesions, gastric washings, CSF, and biopsy material from skin lesions.Mycology*C. immitis* is a dimorphic fungus. Cultured on Sabouraud's agar at 25 degrees C it grows as a mold in 2 to 3 weeks. Characteristically, the mycelia develop arthroconidia. ("By their fruits ye shall know them"). It is a barrel-shaped (smaller at the edges, wider at the middle) asexual spore. Typically, the arthroconidia alternate with non spore-forming cells in the mycelium.

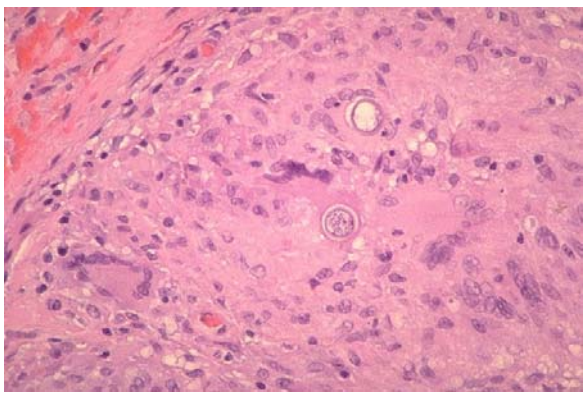
When grown *in vitro* at 37 degrees C, there is no yeast form!! *C. immitis* is a dimorphic fungus; *in vivo*, (pus or tissue) one sees the pathogenic or invasive form B which is a spherule. The organism develops into spherules (30-60 microns) that are filled with endospores which are 3 to 5 microns in diameter (see figure above). A spherule will develop endospores within, then break apart, releasing the endospores. This is the tissue form seen in pus or histological sections: spherules and loose endospores. They can also be seen in a KOH preparation of sputum. It is pathognomonic for coccidioidomycosis.



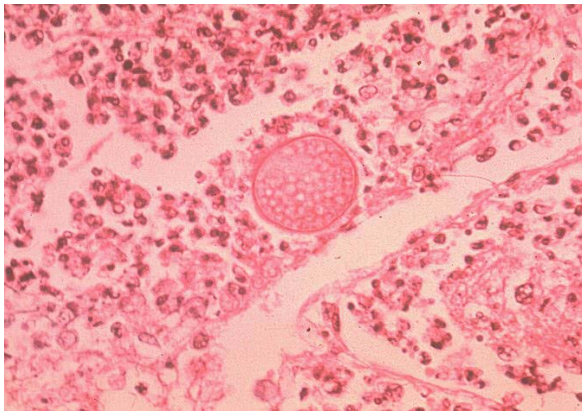
Smear of exudate showing spherules of Coccidioides immitis. Experimental infection of mouse with soil sample. CDC

Histopathology

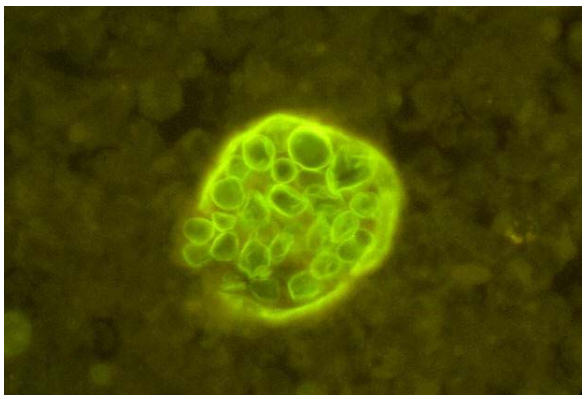
The inflammatory reaction is both purulent and granulomatous. Recently released endospores incite a polymorphonuclear response. As the endospores mature into spherules, the acute reaction is replaced by lymphocytes, plasma cells, epithelioid cells and giant cells.



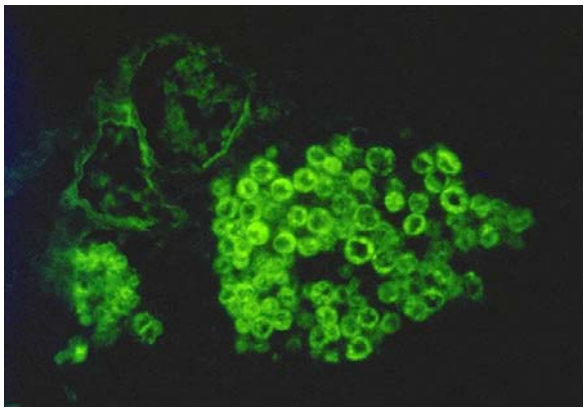
Histopathology of coccidioidomycosis, retroperitoneal area. Coccidioides immitis fungi are visible within granuloma. CDC/Dr. Edwin P. Ewing, Jr. epe1@cdc.gov



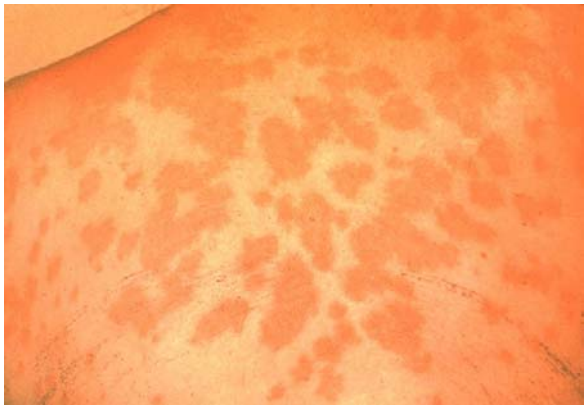
Histopathology of coccidioidomycosis of lung. Mature spherule with endospores of Coccidioides immitis, intense infiltrate of neutrophils. CDC/Dr. Lucille K. Georg



Histopathology of coccidioidomycosis. Spherule of Coccidioides immitis with endospores. Mercy Hosp Toledo OH/Brian J. Harrington



Histopathology of coccidioidomycosis of lung showing spherule with endospores of Coccidioides immitis. FA stain. Endospores, not spherule wall, are stained. CDC



Erythema nodosum lesions on skin of back due to hypersensitivity to antigens of Coccidioides immitis CDC/Dr. Lucille K. Georg

Serology

There are four tests for diagnosis:

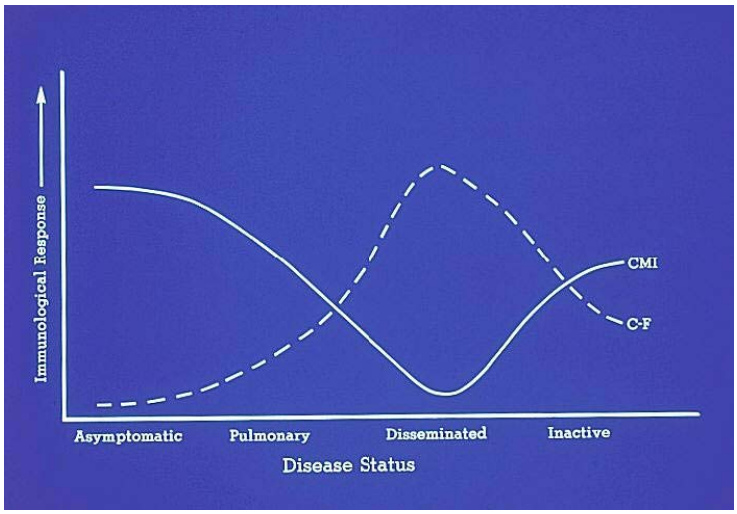
1. Complement-Fixation

2. Slide agglutination

3. Immunodiffusion

4. EIAC-F antibody is slow to rise and develop in about 1 month. This test is excellent for coccidioidomycosis because it is quantitative. However, these antibodies cross-react with some other fungi (Blastomyces and Histoplasma). The C-F test is also a PROGNOSTIC test. If the titer keeps rising, then the patient is responding poorly and the course may be fatal. If the C-F titer is dropping then the prognosis for that patient is favorable. A titer of greater than 1:128 usually indicates extensive dissemination. Life-long immunity usually follows infection with *C. immitis.* There is a much greater mortality rate in dark-skinned people (Mexicans, Filipinos, and Blacks). They are 25 times more likely to develop progressive disease and death. The reason for this is obscure.

Amphotericin B, fluconazole and itraconazole are the drugs of choice.



Immune responses during coccidioidomycosis. Line graph showing immunologists' concept of the interplay between humoral and cell-mediated immune responses during coccidioidomycosis. TX State Chest Hosp/Dr. Rebecca A. Cox

D. PARACOCCIDIOIDOMYCOSIS (*Paracoccidioides brasiliensis*)

This is a chronic granulomatous disease of mucous membranes, skin, and pulmonary system. This disease occurs from the middle of Mexico (North America) to Central and South America. Most cases are reported from Brazil. The ecological niche of this organism is probably the soil. A common triad of symptoms that are seen in Latin America is pulmonary lesions, edentulous mouth, and cervical lymphadenopathy. Prior to the recognition of this disease, patients in Latin America with paracoccidioidomycosis were often sent to TB sanitariums, just as patients with histoplasmosis were in the U.S. The organisms invade the mucous membranes of the mouth causing the teeth to fall out. White plaques are also found in the buccal mucosa, and this along with the triad are now used to clinically differentiate between TB and. This disease has a long latency period. 10-20 years may pass between infection and manifestation of the infection in the non-endemic areas of the world. Typically, a case of paracoccidioidomycosis seen in the U.S. occurs in someone who worked in South America for some period of time and then they return to the U.S. and years later, develop this disease. The patient does not realize the importance of this past history. Almost all diagnoses of fungal diseases depend upon careful questioning and a probing history.The clinical material which should be sent to the lab for examination is sputum, biopsy material, pus, and crust from the lesions. Examination of sputum or crust from one of the lesions with KOH reveals a yeast because this is a dimorphic fungus. In contrast to the other yeasts, particularly Blastomyces, Paracoccidioides has multiple buds, a thin cell wall, and a narrow base. At 25 degrees C, the colony is a dense, white mycelium, not loose and cottony like the others. On Sabouraud's agar it takes 2-3 weeks to grow. When cultured at 37 degrees C, it is slow growing with a white-tan, thick colony. Microscopically, these yeasts appear as described above ranging in size from 5 to 15 microns.

Histopathology

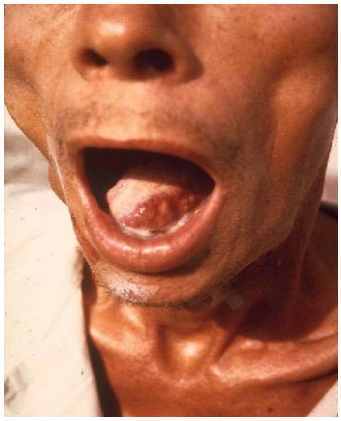
Histologically, one sees multiple buds forming a "Captain's wheel." This is diagnostic of paracoccidioidomycosis. In this case, the mother cell is 40-50 microns in diameter and the buds are 2-5 microns in size.

Serology

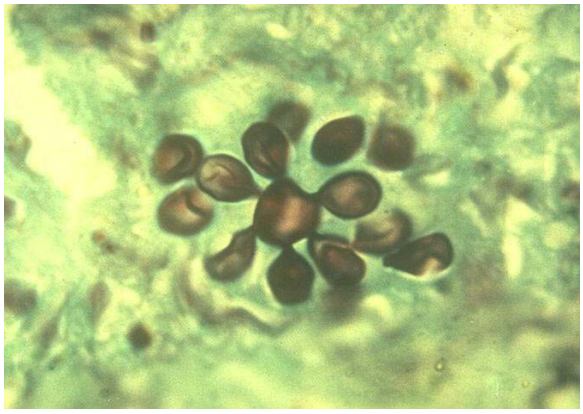
The best serological test for paracoccidioidomycosis is the immunodiffusion test. It is better than 99% specific and almost 85% sensitive.

Therapy

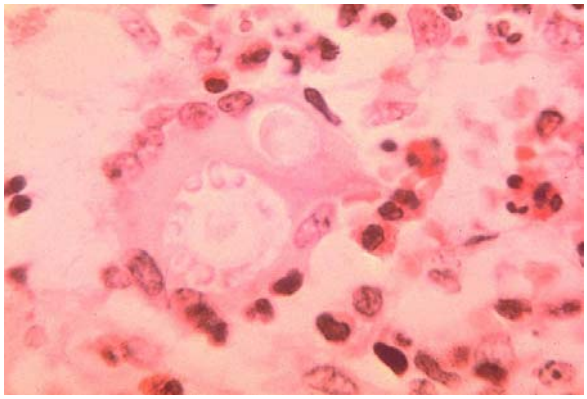
The D.O.C. is amphotericin B. Sulphonamide-trimethoprim and ketoconazole have also been used. Presently Itraconazole appear to provide the best recovery.



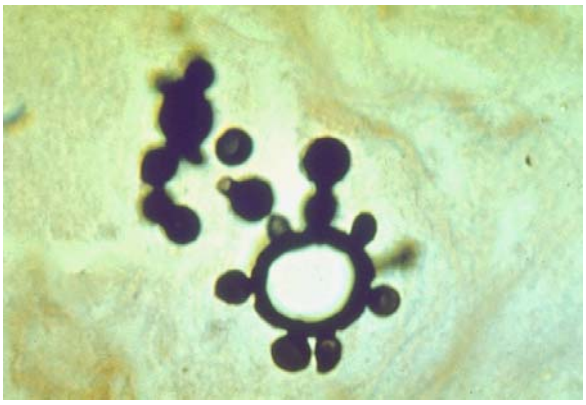
Tongue lesion of paracoccidioidomycosis. CDC/Dr. Lucille K. Georg



Histopathology of paracoccidioidomycosis. Budding cell of Paracoccidioides brasiliensis. Methenamine silver stain. CDC



Histopathology of paracoccidioidomycosis, skin. Budding cell of Paracoccidioides brasiliensis within multinucleated giant cell. CDC/Dr. Lucille K. Georg



Histopathology of paracoccidioidomycosis. Budding cells of Paracoccidioides brasiliensis. Methenamine silver stain.
CDC/Dr. Lucille K. Georg

E. SPOROTRICHOSIS (*Sporothrix schenckii*)

Sporotrichosis is usually a chronic infection of the cutaneous or subcutaneous tissue which tends to suppurate, ulcerate and drain. In recent years, a pulmonary disease has been seen more frequently. Occasionally, infection with *S. schenckii* may result in a mycetoma. Sporotrichosis is caused by another dimorphic fungus. The infection is also known as "rose growers disease." The ecologic niche for this organism is rose thorns, sphagnum moss, timbers and soil. A study on the occupational distribution of sporotrichosis showed that forest employees accounted for 17% of the cases, gardeners and florists, 10%; and other soil-related occupations another 16%. Sporotrichosis occurs worldwide. Every aspect of this disease (clinical, pathology, mycology, ecology) was investigated during an epidemic of 3,000 patients in a gold mine in South Africa during the 1940's. Patient history is very important in this disease also. It is often seen in gardeners and begins with a thorn prick on the thumb. A pustule develops and ulcerates. It infects the lymphatic system and then the disease progresses up the arm with ulceration, abscess formation, break down of the abscess with large amounts of pus followed by healing. Progression usually stops at the axilla. Clinical material to be sent to the lab may be pus, biopsy material, or sputum from pulmonary patients. The yeast form of this fungus in tissue or in culture, can be round (6-8 *u*m) or fusiform. The fusiform shape is not the usual form but if a cigar-shaped yeast is observed in tissue, it is usually diagnostic of sporotrichosis. *S. schenckii* does not stain with the usual histopathological stains. If sporotrichosis is suspected, the pathologist must be informed so he can use special stains. Histologically asteroid bodies, a tissue reaction (also known as Splendori reaction) may be seen around the yeast cell. At 25 degrees C, this colony is white-cream and very membranous, but as it ages for 2-3 weeks it becomes black and leathery. Microscopically, the mycelium is branching, septate and very delicate, 2-3 um in diameter. The pyriform conidia, 2-4 um form a typical arrangement in groups at the end of a conidiophore called "daisies." Serologic tests are not commercially available.The drug of choice for the cutaneous form is saturated iodides (e.g., potassium iodide) administered orally. The patient begins with 2-3 drops, 3-4/days until tolerance to the drug is built up, then the dose is increased. Potassium iodide may interact with the host immune system. For the systemic form the drug of choice is itraconazole or amphotericin B.

MYCOLOGY - CHAPTER SEVEN （真菌学----第七章）

OPPORTUNISTIC MYCOSES （机会真菌病）

Opportunistic mycoses are infections due to fungi with low inherent virulence which means that these pathogens constitute an almost limitless number of fungi. These organisms are common in all environments.

The disease equation:

$$\frac{\text{Number of organisms} \times \text{Virulence}}{\text{Host resistance}} = \text{Disease}$$

is tilted in favor of "disease" because resistance is lowered when the host is immunocompromised. In fact, for the immunocompromised host, there is no such thing as a non-pathogenic fungus.

The fungi most frequently isolated from immunocompromised patients are saprophytic (i.e. from the environment) or endogenous (a commensal). The most common species are *Candida* species, *Aspergillus*, and zygomycetes.

The upward trend in the diagnoses of opportunistic mycoses reflects increasing clinical awareness by physicians, improved clinical diagnostic procedures and better laboratory identification techniques. Another important factor contributing to the increasing incidence of infections by fungi that have not been previously known to be pathogenic has been the rise in the number of immunocompromised patients who are susceptible hosts for the most uncommon agents. Patients with *primary* immunodeficiencies are susceptible to mycotic infections particularly when cell-mediated immunity is compromised. In addition, several types of *secondary* immunodeficiencies may be associated with an increased frequency of fungal infections.

When a fungus is isolated from an immunocompromised patient, the attending physician has to distinguish between:

- Colonization (which is of no major concern)
- Transient fungemia (often involving *C. albicans*)
- Systemic infection.

A great deal of clinical judgment is required to reach these conclusions, which imply important therapeutic decisions.

The diagnosis of opportunistic infections requires a high index of suspicion. Without this curiosity, the clinician may not consider mycotic infections in the compromised patient because:

- Patients present with atypical signs and symptoms

- The etiological agent may be considered a saprophyte or contaminant
- The systemic mycoses may occur outside the known endemic area

Causes of immunodeficiency commonly encountered are:

- Malignancies. (Leukemias, lymphomas, Hodgkin's Disease). In one study of cancer patients, fungal septicemia and pneumonias accounted for almost a third of deaths.
- Drug therapies. Anti-neoplastic substances, steroids, immunosuppressive drugs.
- Antibiotics. Over-use or inappropriate use of antibiotics can also contribute to the development of fungal infections by altering the normal flora of the host and facilitating fungal overgrowth or by selecting for resistant organisms.

Therapeutic procedures can predispose for fungal infections:

- Solid Organ and Bone Marrow transplantation
- Open heart surgery
- Indwelling catheters (urinary, I.V. drugs or parenteral hyperalimentation). In cases of fungemia, the contaminated catheter must be removed before starting anti-fungal therapy.
- Artificial heart valves can be colonized by a variety of infectious agents, including *Candida* species. In a case of Candida infection of an artificial heart valve, antifungal treatment is only efficient if the infected valve is replaced.
- Radiation therapy.

Other factors associated with increased frequency of mycotic infections are:

- Severe burns
- Diabetes
- Tuberculosis
- I.V. drug use
- AIDS. Virtually all AIDS patients will have a fungal infection sometime during the course of disease.

Certain fungi may be frequently associated with some of the predisposing factors listed above. However, any one of the ubiquitous saprophytes (most of which do not cause disease in immunocompetent hosts) as well as occasional pathogens may cause disease in these patients.

Biofilm Formation

It has long been recognized that in patients with a microbial infection, any artificial device such as an indwelling catheter or prosthetic valve, must be removed prior to initiating antibiotic therapy. The foreign body will act as a nidus, seeding the infection if it remains present. The exact mechanism is not clear. A biofilm is a microcolony of organisms which adhere to a surface (catheter, implant, or dead tissue) and which resist removal by fluid movement and have a decreased susceptibility to antimicrobials. This biofilm phenomenon, which occurs on the rocks in a stream, was first recognized as a public health problem in water pipes and was regarded as a source of coliform contamination of drinking water. Recent work in clinical

microbiology has shown that these organisms develop a resistance to therapy because they are contained in a matrix which acts like a tissue to and becomes a barrier to antibodies and antimicrobial agents.

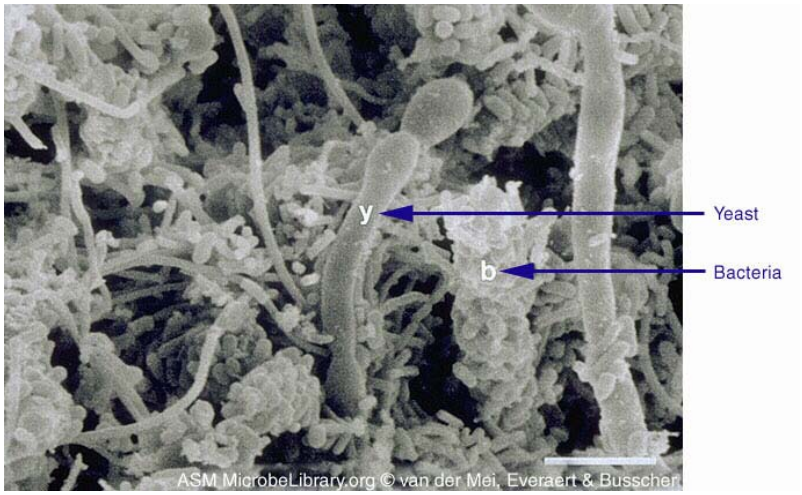
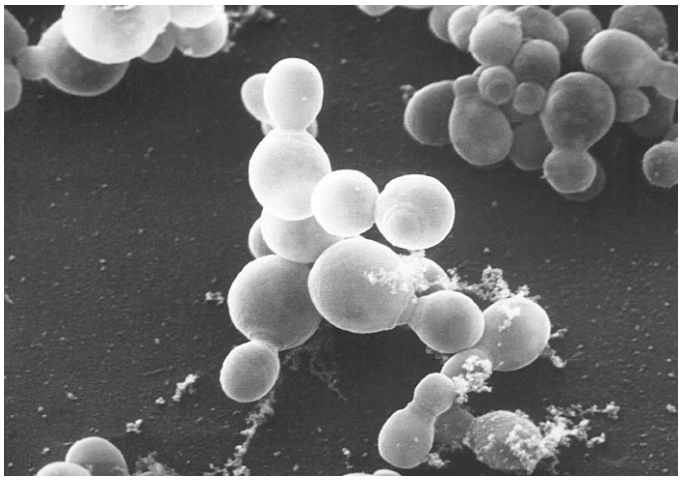


Figure A biofilm consisting of various bacteria (b) and yeast (y) strains colonizing an indwelling, silicone rubber voice prothesis after being placed for 3 to 4 months in a laryngectomized patient. The image was taken by scanning electron microscopy. Scale bar: 5 μm. © Henny C. van der Mei, E.P.J.M. Everaert, H. J. Busscher. University of Groningen and the MicrobeLibrary

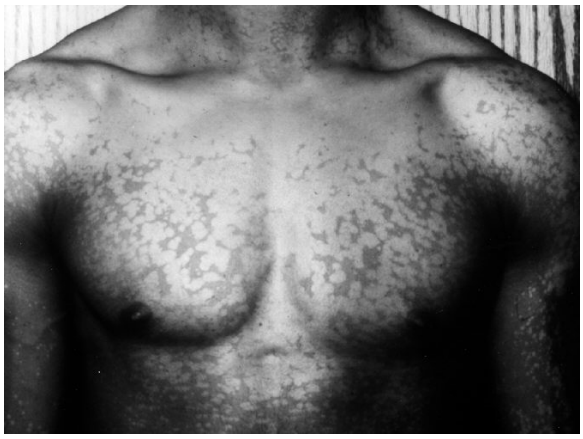


Scanning Electron Micrograph of *Malassezia furfur* CDC/Janice Carr

CLINICAL PRESENTATION

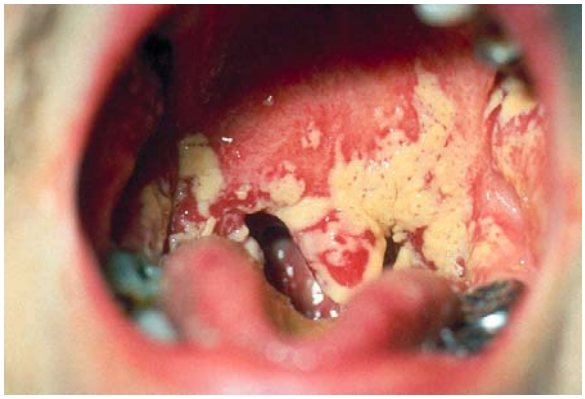
In immunosuppressed patients, common fungal infections may have an unusual presentation because of:

1. Atypical signs and lesions.
   Malassezia furfur usually causes a rather benign and self-limited disease in normal hosts (Tinea versicolor), but in immunocompromised patients may show a rash with disseminated disease and sepsis. This organism requires long-chain fatty acids for growth. Patients receiving parenteral fat emulsions for nutrition become a walking petri plate.



Tinea Versicolor on chest. CDC/Dr. Gavin Hart

2. Unusual Organ affinity.
   Candida may invade liver, heart valves; Oral thrush occurs in people who are relatively immunocompetent while esophageal candidiasis occurs in those patients who are immunologically compromised. Cryptococcus may cause pulmonary and cutaneous infections.



Oral thrush. Aphthae. *Candida albicans*. CDC

3. Infections with systemic dimorphic fungi occurring outside endemic areas. These factors complicate the diagnosis and management of these diseases.

4. Unusual Histopathology.

Even the inflammatory reaction may be different in biopsy specimens. The normal host reaction to fungal invasion is usually pyogenic or granulomatous. In the immunodeficient host, the reaction is necrotic.

Some examples of variations from standard fungal clinical presentation, diagnosis and treatment.

- Cryptococcosis

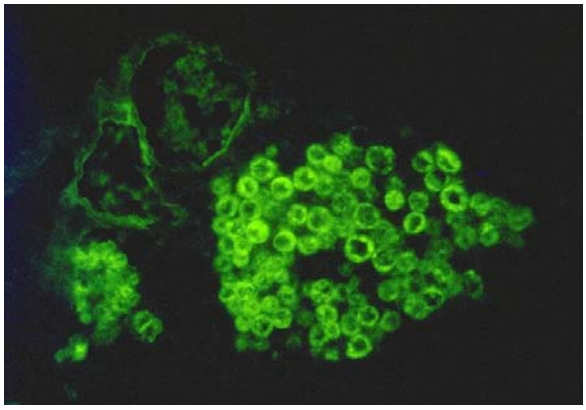
Studies show that from 10 % to 30 % of AIDS patients have cryptococcal meningitis and they will require maintenance therapy with fluconazole for the remainder of their life. Fluconazole penetrates the

cerebro-spinal fluid

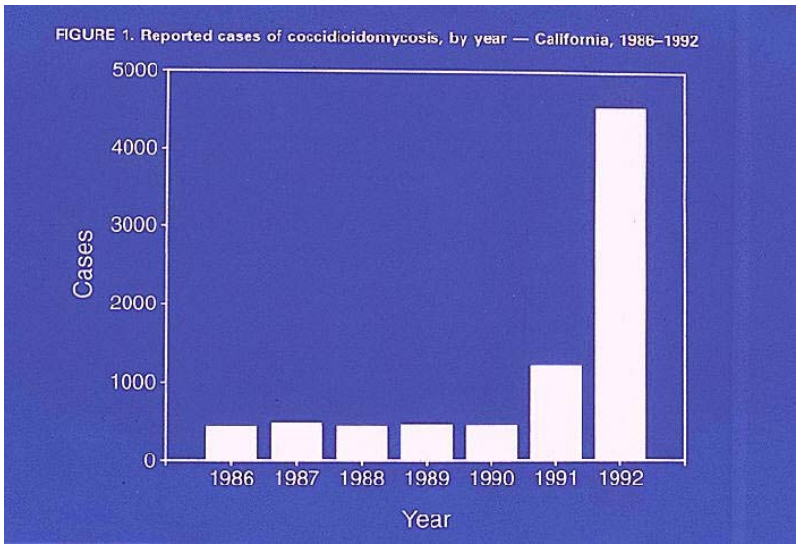
Mortality: Without treatment 100%
With treatment 20%

Relapse : Non-AIDS patients15-20%
AIDS patients 50%

With relapse there is 60% mortality



Histopathology of coccidioidomycosis of lung showing spherule with endospores of Coccidioides immitis. FA stain. Endospores, not spherule wall, are stained CDC



Bar graph showing reported cases of coccidioidomycosis in California by year, 1986-1992. Epidemiology, surveillance. CDC

- Sporotrichosis

  Co-infection with other fungi is frequent

- Coccidioidomycosis

Mycelial forms seen in tissue. Occurs in patients outside the endemic area. Patients require fluconazole or itraconazole maintenance therapy.

- Histoplasmosis

  All cases are disseminated.
  Relapse rate is > 50% and the infection is rapidly fatal in 10% of patients. It occurs in patients outside the endemic area and they require fluconazole or itraconazole maintenance therapy

- Blastomycosis

  More frequently disseminated. All patients have done very poorly.

There has been one report on 15 cases of blastomycosis in AIDS patients. Six patients (40%) had CNS involvement. Usually CNS disease only occurs in 3-10% of the patients.

- Aspergillosis

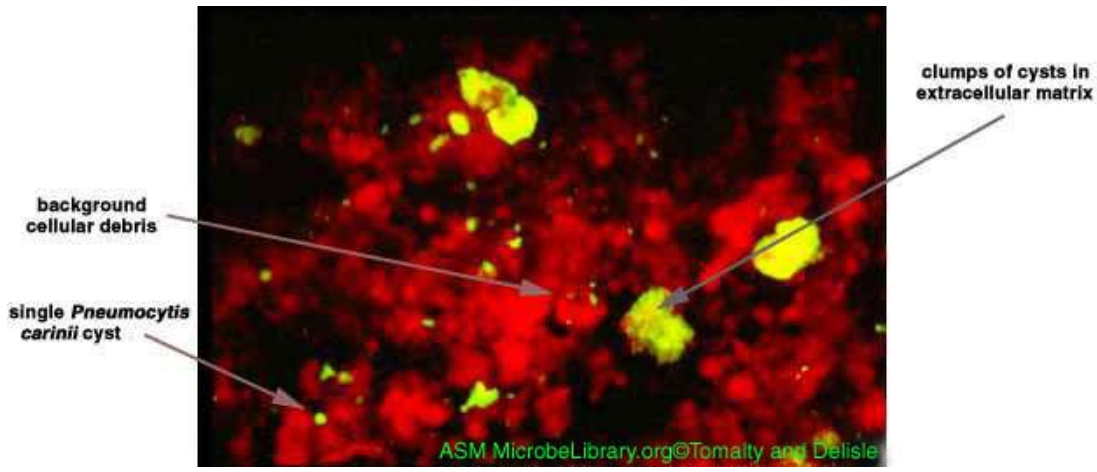
  Mortality: With amphotericin B 72%
  Without amphotericin B 90%

- Penicillium marneffei

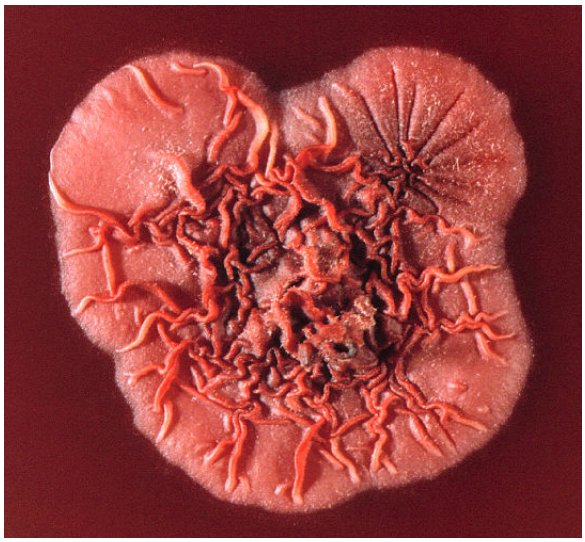
  This is a dimorphic fungus that produces a red pigment and reproduces by fission. It requires amphotericin B therapy and oral itraconazole maintenance.

- Pneumocystis carinii

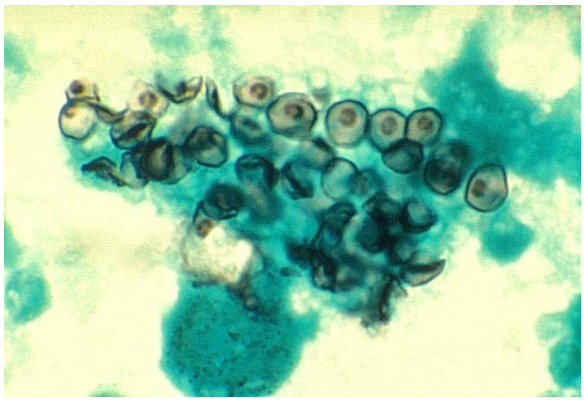
  This wasformerly thought to be a protozoan. Presently it is believed to be a fungus.



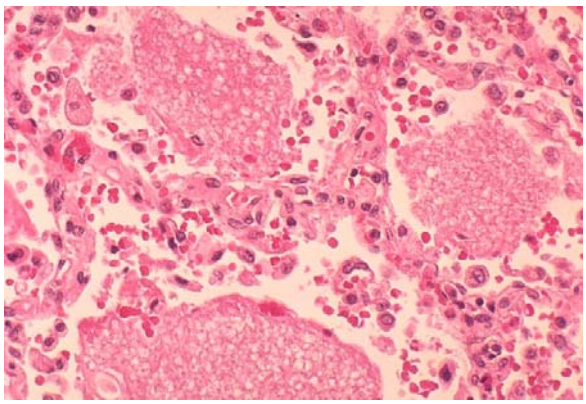
Pneumocystis carinii is an important cause of opportunistic respiratory tract infections in immunocompromised patients, particularly AIDS patients. This
image depicts P. carinii from bronchial washings of an AIDS patient. Mouse monoclonal antibodies against P. carinii are labeled with a fluorescent tag. The labeled Pneumocystis organisms fluoresce bright apple green against a red background.



P. marneffei is endemic to Southeast Asia, where it is one of the more common HIV-related opportunistic infections.
James Gathany/CDC



Cysts of Pneumocystis carinii in smear from bronchoalveolar lavage. Methenamine silver stain.
Dr. Russell K. Brynes/CDC



Histopathology of lung shows alveolar spaces containing exudates characteristic of infection with Pneumocystis carinii CDC/Dr. Edwin P. Ewing, Jr.

Some common associations between fungal organisms and disease conditions				
Cryptococcus neoformans	*Candida albicans*	*Candida (Torulopsis) glabrata*	*Zygomycetes*	*Aspergillus species*
Diabetes mellitus	Prolonged antibiotic therapy	Cytotoxic drugs	Diabetes mellitus	Leukemias
Tuberculosis	Prolonged intravenous catheters	Immunosuppression	Leukemias	Corticosteroid therapy
Lymphoma	Prolonged urinary catheters	Diabetes mellitus	Corticosteroid therapy	Tuberculosis
Hodgkin's disease	Corticosteroid therapy	Hyperalimentation	Intravenous therapy	Immunosuppression
Corticosteroid therapy	Diabetes mellitus	Intravenous catheters	Severe burns	I.V. drug abuse
Immunosuppression	Hyperalimentation			
	Immunosuppression			

SUMMARY

"Only the prepared mind can help the impaired host." Dr. Libero Ajello, Opportunistic Fungal Infections. Proceedings of the Second International Conference. Charles C.Thomas, 1975. P. 31-35.

CHAPTER EIGHT （第八章）

MEDICAL MYCOLOGY GLOSSARY （医学真菌学词汇）

ACTIDIONE - Trademark name for cycloheximide, a selective antifungal agent.

AERIAL - mycelium: Hyphal units above the colony agar interface.

ANAMORPH - A somatic or reproductive structure that originates without nuclear recombination (asexual reproduction). Cf. Teleomorph.

ANTHROPOPHILIC - A fungus (dermatophyte) that preferentially grows on man rather than other animals or

the soil.

ARTHROCONIDIUM - (pl. arthroconidia) A thallic conidium released by the fragmentation or lysis of hypha. It is not notably larger than the hypha from which it was produced, and separation occurs at a septum.

ARTHROSPORE - See arthroconidium.

ASTEROID BODY -(Splendore-Hoeppli phenomenon) An eosinophilic substance which forms a covering of approximately 10 microns thick around a basophilic yeast especially in sporotrichosis.

BASE - The junction of a bud and the mother cell of a yeast.

BIOFILM – Microcolonies of organisms which adhere to a surface (catheter, implant, waterpipe, blood vessel) and which resist removal by fluid movement and have a decreased susceptibility to anti-microbials.

BUD - A type of asexual reproduction commonly found in yeasts.

CAPSULE - A hyaline mucopolysaccharide covering around the cell body of certain yeasts (Cryptococcus, Rhodotorula) and some spores and conidia.

CHLAMYDOSPORE - Thick-walled resistant resting spore, especially in Histoplasma capsulatum. See macroconidium.

COENOCYTIC - Without septa.

COLONIZATION - growth of an organism in a host without tissue invasion.

COLUMELLA - A sterile invagination of a sporangium, as in the Zygomycetes.

COMMENSALISM - A symbiotic relationship in which there is no damage to either participant.

COMPLEMENT FIXATION - A serologic procedure to determine antibody to fungus infections. Cross reacts with other systemic fungi but is a quantitative test.

CONIDIOGENOUS CELL - The cell that gives rise to a conidium.

CONIDIUM (pl. conidia) - A reproductive propagule produced in the absence of nuclear recombination, thus representing anamorphic or asexual reproduction.

CONIDIOPHORE - A specialized hypha that gives rise to, or bears a conidium.

CYCLOHEXIMIDE - See Actidione.

DERMATOMYCOSIS - An infection of hair, skin and nails caused by the keratinophilic fungi of the genera Trichophyton, Microsporum and Epidermophyton which infect hair, skin and nails.

DERMATOPHYTE - Infection of hair, skin and nails caused by fungi other than dermatophytes.

DEMATIACEOUS - A fungus having brown or black melanotic pigment in the cell wall.

DICHOTOMOUS - A type of branching of hyphae that is repetitious without pattern; the branches are approximately equal in size and equal the stem from which they originated.

DIMORPHIC - Having two forms.

ECHINULATE - Covered with delicate spines.

ECOLOGY - The science of organisms as affected by the factors of their environment.

ECTOENDOTHRIX - Arthroconidia formed on the outside and inside of a hair shaft.

ECTOTHRIX - Forming a sheath of arthroconidia on the outside of a hair shaft. The cuticle of the hair is destroyed.

EDENTULOUS - The absence of teeth.

ENDOGENOUS - From within.

ENDEMIC - A disease which occurs in a limited geographic area.

ENDOSPORE - A spore formed within some other unit, such as in a spherule. (Typical of Coccidioidomycosis).

ENDOTHRIX - Arthroconidia formed inside a hair shaft. The cuticle of the hair remains intact.

EXOGENOUS - From without. The source of most mycotic infections is exogenous, i.e. outside the body (the environment).

FLOCCOSE - Cottony or wooly.

FOMITE - A substance other than food that may harbor and transmit infections organisms.

FRUITING BODY - Reproductive structures of fungi. (Spores).

FUNGEMIA - Presence of fungi in the blood.

GMS - Gomori methenamine-silver. An excellent stain for visualizing fungi. The cell wall stains black and the background is green. Advantage: stains all fungi. Disadvantage: the tissue reaction is not visible.

GEOPHILIC - Soil-seeking, having a soil reservoir.

GERM TUBE - Initial hypha from a sprouting conidia, spore or yeast.

GLABROUS - Smooth.

H & E - Hemotoxylin and Eosin. A stain used routinely for general pathology. Most fungi are visible, but not distinctive. Fungal walls usually stain blue or purple. Other cells stain pink. Advantage: the tissue reaction is visible.

HYALO - Colorless; also hyaline.

HYPHA (pl. hyphae) - A vegetative filament of a fungus.

HYPHOMYCETE - An fungus that produces mycelium with or without discernible dark pigment in the cell walls. If the hypha is pigmented, it is called dematiaceous; if colorless, hyaline.

IMMUNODIFFUSION - A serologic test to determine the presence of antibody by double diffusion precipitation in auger.

INCIDENCE - The number of new cases of a disease occurring during a specific period.

INCUBATION PERIOD - The time between an infectious agent entering the body and the onset of clinical symptoms.

INDURATED - Hard.

INTERCALARY - Formed within a hyphal unit.

INVASIVE - The entrance and growth of an organism in tissue.

LATEX AGGLUTINATION - A simple serologic procedure to detect antibody by the clumping of antigen coated particles.

MACROCONIDIUM - The larger of two types of conidia produced in the same manner by the same fungus.

MICROCONIDIUM (pl. microconidia) - The smaller of two types of conidia produced in the same manner by the same fungus.

MOLD - See Mycelium.

MURIFORM - Like a wall; multicellular, with transverse and longitudinal septations.

MYCELIUM - The mass of hyphae making up a fungus colony.

MYCOLOGY - The study of fungi.

ORGANOTROPISM - The predilection of a fungus to invade a particular organ.

PHAEO - Darkly pigmented

PREVALENCE - The total number of cases of a disease in existence at a certain time in a designated area.

PROBE – A specific nucleic acid sequence (known) used to detect a complimentary sequence in an unknown fungus.

PSEUDOHYPHA (pl. pseudohyphae) - A fragile string of cells that result from the budding of blastoconidia that have remained attached to each other. The septa separating the cells are complete and there is no cytoplasmic connection, as is found in most true septate hypha.

RHIZOID - A root like structure. Used in the identification of some Zygomycetes.

RESERVOIR - A permanent host or carrier from which infection is spread.

SAPROBE - An organism which requires organic material as a source of energy.

SAPROPHYTE - See Saprobe.

SCLEROTIC BODY - (sclerotic cell). The tissue form (yeast-like) of most agents of chromomycosis. Dark brown, single or in short chains, occasionally septate, 5 - 15 microns in diameter.

SENSITIVITY - The ability to detect all patients with a specific disease.

SEPTUM (pl. septa) - A cross wall.

SEROLOGY - The study of antigens or antibodies in peripheral blood to support, confirm or rule out certain diseases.

SOURCE - The clinical specimen most likely to yield the etiologic agent. ALSO The ecologic niche or natural nidus of the etiolgic agent.

SPECIFICITY - The capacity to identify a disease correctly.

SPINOSE - Covered with small spines.

SPORANGIOPHORE - A specialized hypha that gives rise to a sporangium.

SPORANGIOSPORE - A reproductive unit formed in a sporangium.

SPORANGIUM - A cell within which spores are borne by progressive cleavage.

SPORE - A reproductive propagule produced internally by "free cell" formation, as in the ascomycete, i.e., complete spores formed all at once around the nuclei available or by "progressive cleavage," as in a sporangium.

STOLON - Hypha from which rhizoids and sporangiophores are produced, as in the genus Rhizopus.

SYNONYM - Another (especially a later or illegitimate) name for a species or taxonomic group.

TELEOMORPH - The sexual state of a fungus.

TERMINAL - Formed at the end of a structure.

TINEA - Literally "moth". A clinical term meaning "ringworm".

THERMOTOLERANT - Ability to grow at high temperatures (usually above 42 C).

TUBERCULATE - Spines or finger-like projections on macroconidia, characteristic of Histoplasma capsulatum.

VESICLE - A swollen or bladder-like cell.

VIRULENCE - Degree of pathogenicity; the disease producing capacity of an organism.

YEAST - A unicellular fungus, usually round or ovoid, that reproduces by budding.

ZOOPHILIC - Infecting lower animals rather than man.

The glossary was derived from several sources including: Rippon, Medical Mycology, Third Edition; Emmons, Binford, Utz, and Kwon-Chung, Medical Mycology, third Edition; Ainsworth & Bisby's Dictionary of the Fungi, Seventh Edition; and other keen authorities.