**L.14 –Biotechnology Mycology D.Ibtihal Muiz**

**Fungal Pathology**

**Introduction**   
 Fungi can be helpful and not helpful, but they all are important. Fungi are one of the earth's big recyclers. Without them we could not live, and sometimes humans die because of them.   
There are more than a million species of fungi, but only about 400 cause diseases relevant to man, animals, or plants. The majority of the pathogenic species are classified within the Phyla Zygomycota, Basidiomycota, Ascomycota, or the form group Fungi Imperfecti. Fungi (the singular form is ‘fungus'), including those pathogenic to humans and animals, are eukaryotic microorganisms.   
Classically, there are two broad groups of fungi: yeasts and moulds. Mould spores germinate to produce the branching filaments known as hyphae. Yeasts, on the Other hand, are solitary rounded forms. These rounded forms are the actively dividing, growing, and metabolizing form of the fungus. Reproduction occurs via budding (or fission) and the colonies are typically moist and mucoid.   
Typical mould produce interwoven filamentous forms known as hyphae. The mass of hyphae is called a mycelium. The hyphae grow by elongation at their tips. At the ends of some of these hyphae are rounded forms that 6ould be confused with yeast, but that are instead called conidia or spores. These rounded fungal forms are relatively metabolically inactive. They can be likened to seeds--they are alive, but they’re not doing much. Rather, they are looking for a good place to live.   
As an important contrast, the actinomycetes are prokaryotic gram positive filamentous bacteria. Historically, because of their microscopic morphology, some actinomyceles have been studied by medical mycologists. However, they are quite different from fungi. The actinomycetes serve as a host to bacteriophages, whereas fungi cannot serve as their host. These organisms are sensitive antibacterial agents such as penicillin but not to antimycotic agents such as amphotericin B, the opposite is true for fungi. A number of diseases of humans and animals are caused by mould and yeast-like fungi. Diseases caused by fungi are known as mycoses (singular = mycosis). Over 50 different fungi from among the bread molds (Zygomycota), cup fungi (Ascomycota) and the imperfect fungi (related to the cup fungi) have been reported to infect humans. The number of people infected by fungi is increasing. There more people in the population with weak immune systems, due to chemotherapy, or having undergone an organ transplant, for example. It is ironic that cyclosporin, a fungal drug that reduces the risk of rejection in organ transplants, weakens the immune system so that other fungi may infect the patient. Increased exposure may contribute to the increase in fungal infections. Adding insulation to a house, for example, restricts air exchange with the outside, and one effect of this may be increased dampness, a condition that encourages mold growth.

**Allergies and Asthma**   
 Some a1lergits now think that a very high percentage of the chronic year-round allergies may be caused by fungal spores. The number of people affected is increasing, probably due to increased awareness and changes in building construction. New homes are ‘tighter’ so air is not mixed with outside air as often as in older homes. Many molds grow on damp walls, etc. and the number of spores can reach very high levels in air-tight homes. One study estimates that about F/o of homes in the USA contain toxic molds. The molds involved include *Aspergillus* and *Penicillium,* The "gorilla fungus”, *Stachybotrys atra,* has recently received a lot of attention in the press because it been linked to infant deaths and headaches, nose bleeds and sinus problems in adults.   
Fungus irritates the nose and causes allergies. Over 37 million people have allergies and many of them are caused by fungus. Buildings can also et sick. Buildings can get some fungi known as Penicillium and Stachybotrys. They float in the air and can cause watery eyes and breathing problems.

**Mycoses**   
 Several fungi can occur on living tissues and cause serious ease and even death. Many such organisms are known only from individuals who have low disease resistance, due to prior infection, AIDS, old age, or other factors. Most commonly, infections by these fungi occur when the normal bacterial populations of the body are eliminated by the use of antibiotic. Without competition from bacteria these fungi occupy the tissues and grow rapidly, off en causing considerable damage.   
Other fungi attack healthy living tissues without the aid of antibiotics, causing more localized but very serious infections. Histoplasmosis, a disease with symptoms similar to those of tuberculosis, is caused by *Histoplasma capsulatum,* a mould associated with bird nests in nature. It is frequently reported in perfectly healthy people who have been exposed to the dust from nesting materials, such as while tearing down old barns.   
Most commonly, fungi cause something to happen on the skin of animals or people. This is sometimes called Ringworm (superficial mycoses caused by keratinophilic Hyphomycetes), but there is no worm involved Ringworm can also be called Tinea or Dermatomycosis. TlNEA —a general name for ringworm is resemble a superficial infection caused by dermatophytes.   
Ringworm can be found all over the world. It mostly forms on the foot and scalp. Some Ringworm is Anthropophilic. Anthropophilic means human (anthro- think of anthropology) loving (-philic), and you catch - this fungus from other people. Ringworm can also be Zoophilic or Geophilic. Zoophilic means animal (zoo- just think of going to a real zoo) loving, and this is a fungus you may catch from your pet. Geophilic means earth (geo- as in geology, or the earth) loving, of course you get this one from the soil.

**DERMATOPHYTES** Dermatophytes- anamorphs of some Onygenales (Ascomycetes), which live on keratin and can cause skin disease in humans, the cause of a number of skin diseases such as ringworm and athletes foot a known only from this habitat and are quite specialized. The fungus grows on the outermost layer of skin causing reddening of the surrounding tissues (zoophilic types) and sometimes scaliness (anthropophilic types Dermatophytes may attack deeper tissues; the symptoms are usually due to an allergic reaction. Because of their essentially non-parasitic nature dermatophytes are usually easy to grow in the laboratory. Many closely related species occur on substances similar to human skin, such as leather, feathers, hair, and horn, and are unable to grow on living animals or an. Probably the most commonly isolated dermatophytes are species of *Microsporum Trichophyton,* and *Epidermophyton.*To cure things such as Ringworm, mycologists use a drug from one of these families of drugs: Allylamines, antimetabolites, azoles, glucan synthesis inhibitors, polyenes,

and others. Fungal infections can be classified according to the type of tissues they infect and the extent of their infection:   
1-Dermatomycosis, infections of the epidermis (surface of the skin).   
2-Deep mycoses those infecting tissues below the epidermis, and internal organs

**Dermatomycoses:**   
Infections of the epidermis.   
 Infections of the epidermis are the most common and widespread mycoses. The fungi causing dermatomycoses are common soil fungi. which colonize hair, skin, and feathers These structures all contain keratin a tough fibrous protein. Their biology in the soil enable these fungi to also invade and absorb nutrients from the keratinized areas of the body. They also attack scales, and even the lens of the eye, because they, too, contain keratin. Dermatologists often call dermatomycosis “tineas” because these diseases resemble infections that are caused by parasitic worms burrowing beneath the skin. Each mycosis was given a Latin binomial (two part name) based on where the infection occurs: *Tinea capitis* (on the head). *Tinea* ***corporis*** (on the body), *Tinea pedis* (on the foot). Common names for these infections include “athletes foot”(irritation of the skin between the toes caused by dermatophytes-conidial anamorphs of the Arthrodermataceae, Onygenales: Ascomycetes), “ringworm”, and “jock itch.” The most common genera of fungi causing dermatomycoses are *Microsporum, Epidermophyton,* and *Trichophyton.*The name ringworm has been in use at least from the sixteenth century and was coined to describe the circular lesion produced by dermatophytes on the skin or scalp.

**Taxonomic classification**   
Kingdom: Fungi   
Phylum: Ascomycota   
Order: Onygenales   
Family: Arthrodermataceae   
Genus: Arthroderma (includes Nannizia, Microsporum, Epidermophyton,   
Trichophyton)

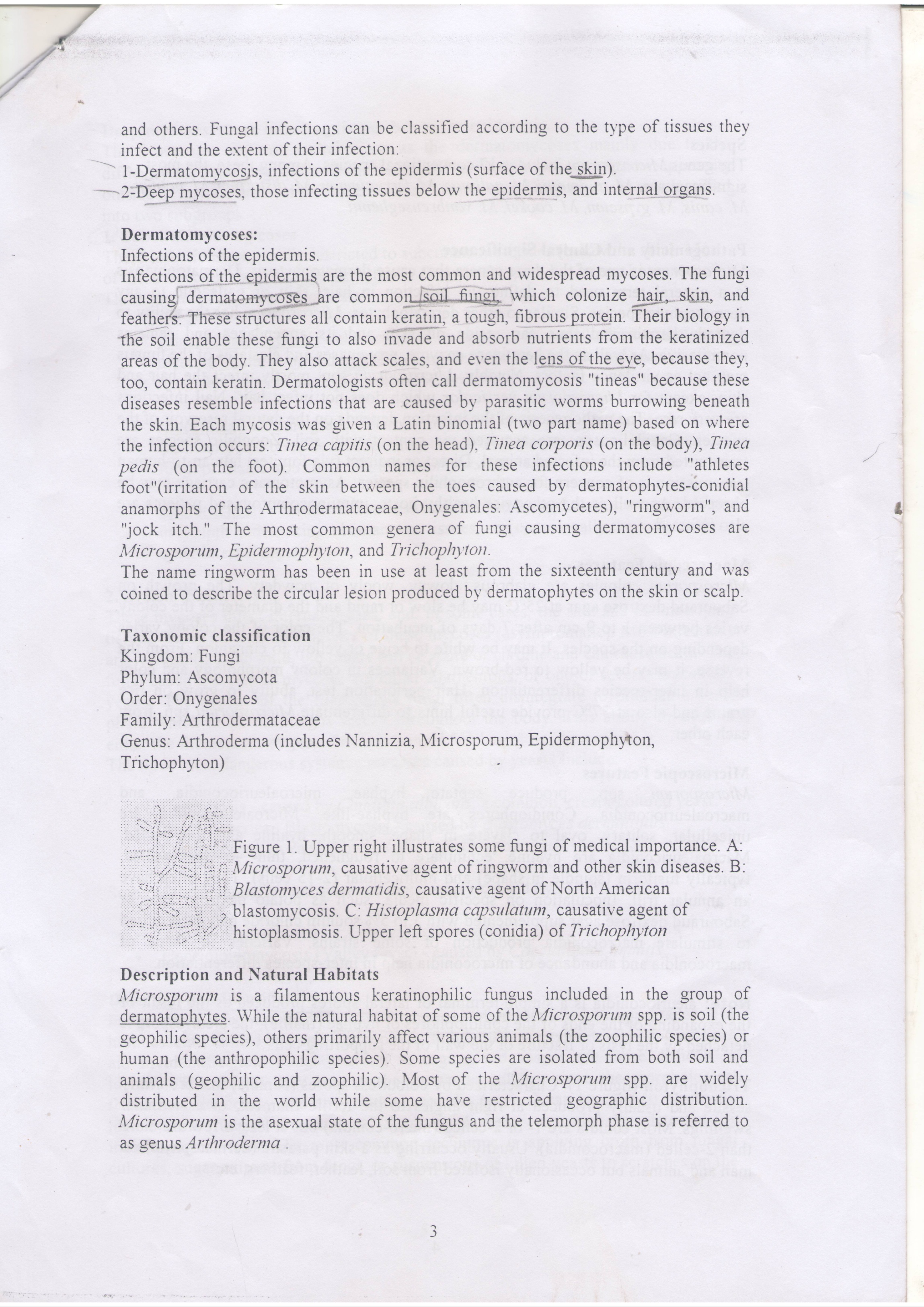


Figure 1 Upper right illustrates some fungi of medical importance. A:   
M*icrosporum,* causative agent of ringworm and other skin diseases. B:

*Blastomyces dermatidis ,* causative agent of North American   
 blastomycosis C: *Histoplasma capsulatum,* causative agent of histoplasmosis. Upper left spores (conidia) of *Trichophyton.*

**Description and Natural Habitats**   
 *Microsporum* is a filamentous keratinophilic fungus included in the group of dermatophytes. While the natural habitat of some of the *Microsporum* spp. is soil (the geophilic species), others primarily affect various animals (the zoophilic species) or human (the anthropophilic species). Some species are isolated from both soil and animals (geophilic and zoophilic) Most of the *Microsporum* spp. are widely distributed in the world while some have restricted geographic distribution. *Microsporum* is the asexual state of the fungus and the telemorph phase is referred to as genus *Arthroderma*

**Species**   
 The *genus Microsporum* includes 17 conventional species. Among these, the most   
significant are: M. *audouinii, M. gallinae, M. Ferrugineum, M distortum, M. nanum, M. canis, M. gypseum, M. cookei, M.vanbreuseghemii.*

**Pathogenicity and Clinical Significance**   
 *Microsporum* is one of the three genera that cause dermatophytosis. Dermatophytosis is a general term used to define the infection in hair, skin or nails due to any dermatophyte species. Similar to other dermatophytes, *Microsporum* has the ability to degrade keratin and thus can reside on skin and its appendages and remains noninvasive. As well as the keratinase enzyme, proteinases and elastases of the fungus may act as virulence factors. Notably, *Microsporum* spp. mostly infect the hair and skin, except for *Microsporum persicolor* which does not infect hair. Nail infections are very rare. The pathogenesis of the infection depends on the natural reservoir of the species. Geophilic spp. are acquired via contact with soil. Zoophilic species are transmitted from the infected animal. Direct or indirect (via fomites) human-to-human transmission is of concern for anthropophilic species. Asymptomatic carriage *may* be observed. As well as the otherwise healthy hosts, immunocompromised patients are also infected.

**Macroscopic Features**   
 *Microsporum* colonies are glabrous, downy, wooly or powdery. The growth on Sabouraud dextrose agar at 25°C may be slow or rapid and the diameter of the colony varies between I to 9 cm after 7 days of incubation. The color of the colony varies depending on the species. It may be white to beige or yellow to cinnamon. From the reverse, it may be yellow to red-brown. Variances in colony morphology and color help in inter-species differentiation. Hair perforation test, ability to grow on rice grains and also at 37°C provide usel hints to differentiate *Microsporum* spp. from each other.

**Microscopic Features** *Microsporuni* spp. produce septate hyphae, microaleurioconidia, and macroaleurioconidia. Conidiophores are hyphae-like. Microaleuriconidia are unicellular, solitary, oval to clavate in shape, smooth, hyaline and thin-walled. Macroaleuriconidia are hyaline, echinulate to roughened, thin- to thick-walled, typically fiusiform (spindle in shape) and multicellular (2-15 cells). They often have an annular frill, Inoculation on specific media, such as potato dextrose agar or Sabouraud dextrose agar supplemented with 3 to 5% sodium chloride may be required to stimulate macroconidia production of some strains. Varieties in shape of macroconidia and abundance of microconidia help in inter-species differentiation.

**Note:** aleurioconidia is a simple terminal or lateral spores produced as the result of the expanding of the ends of the conidiophores or hyphae (thallic), the aleuriospore is detached by the lysis or fracture of the wall of the supporting cell.

**Trichophyton** (figure 1): Characterized by colourless spores (conidia) that are nearly sessile and usually produced at right angles to the fertile filament, or as terminal swellings. Most conidia are 1- or 2-celled (micro-conidia) but at least a few are more than 2-celled (macroconidia). Usually occurring as a skin parasite (dermatophyte) on man and animals but occasionally isolated from soil, leather, feathers, etc.

**Deep mycoses, those infecting tissues below the epidermis.**   
 These mycoses are not as infectious as the dermatomycoses mainly due to the difficulty of dispersing spores from within tissue. Deep mycoses are now appearing outside of historic areas of infection because of air travel. Deep mycoses are classified into two subgroups;

**1. Subcutaneous mycoses** These infections are usually restricted to subcutaneous tissues (below the skin). Most of these infections start in skin lacerations. They rarely spread to internal organs Three mycoses of this subgroup are:   
• Chromoblastomycosis - characterized by warty or tumor-like lesions that may ulcerate on the arms and legs. The fungi include dark pigmented species of the imperfect genera *Cladosporium* and *A lternaria.*• Mycetoma - chronic granulomatous infections of the jaw, feet, or hands. Deformity and bone destruction may result. These mycoses may be caused by fungi or filamentous bacteria, *(Streptomyces* species).   
• Sporotrichosis - chronic infections characterized by nodular lesions and ulcers in lympth nodes, skin, subcutaneous tissues, and occasionally the lungs and other internal organs.

**2. Systemic mycoses** These mycoses infect internal organs, and, in some cases, the skin and its underlying tissues. There may be no evidence of these mycoses (asymptomatic). Most infections are self-limiting and mild, but others can be acute or chronic and can cause death. The fungi causing systemic mycoses are either filamentous, or one of several unicellular yeasts. The hyphae of the filamentous fungi often disintegrate to produce a yeast phase which helps the fungus spread throughout the body. This ability to exist in either the filamentous or yeast forms is termed “diphasic” or “dimorphic’.   
The three most dangerous systemic mycoses caused by yeasts include:   
• Candidiasis - caused by *Candidia albicans,* a common, cream-colored yeast.   
• North American Blastomycosis - caused by *Blas tomyces* ***dermatitidis.***• Cryptococcosis - caused by *Cryptococcus neofrmans.*Some of the potentially fatal systemic mycoses are caused by:   
• Aspergillosis- caused by *Aspergilius fumigatus.*• Coccidioidomycosis (Valley fever) - caused by *Coccidioides immitis.*

**Detection and Identification** Fungi which infect the skin (dermatophytes) are often identified by appearance. The luminescence emited by some dermophytic fungi under ultraviolet light *(366* nm) can aid in identification. Fungi growing in organs and tissues are more difficult to identify. The fungus may have to be grown in culture, since the morphological features of the colony and any resulting conidia (spores) can be used to positivitly identify the fungus. Presence of fungi in humans can also by detected by immunological tests. The most common technique is applying broth from fungal cultures, sugar extracts from fungi, or suspensions of killed yeasts to scratches on the skin. Immunological tests are not always reliable, as the telltale reaction may occur only when material from the correct life stage of the fungus is used.   
Biopsy may also be used. Thin sections of infected tissue are stained and examined under a microscope for hyphae and the spore producing structures necessary for species identification.

**Treatment** Treatment of fungal infections is difficult, since the physiology of fungi is very similar to humans. If a drug controls fungi by s2ping cell division so that the fungus cannot spread, it may also affect cell division in humans. Many of the earlier fungal antibiotics produced serious side effects, including sensitivity to light and liver toxicity. The newer antibiotics stop fungal growth by suppressing chitin synthesis. Chitin is a major component in fungal cell walls, but not in human cells, so drug side effects have been reduced.

**Miscellanous Syndromes** These diseases are a little harder to classify as some of them are caused by one of several different fungi. Thus, even though they have a fungal-sounding name (e.g., *Tinea barbae),* you can't always expect to find a corresponding fungus named *Tinea barbosa!*Chromoblastomycosis   
Eye Infections   
Lobomycosis   
Mycetoma   
Nail, Hair, and Skin disease   
• Onychomycosis (Tinea ungujum)   
• Piedra   
• Pityriasis versicolor   
• Tinea barbae   
• Tinea capitis   
• Tinea corporis   
• Tinea cruris   
• Tinea favosa   
• Tinea *nigra*• Tinea pedis   
Otomycosis   
Phaeohyphomycosis   
Rhinosporidiosis