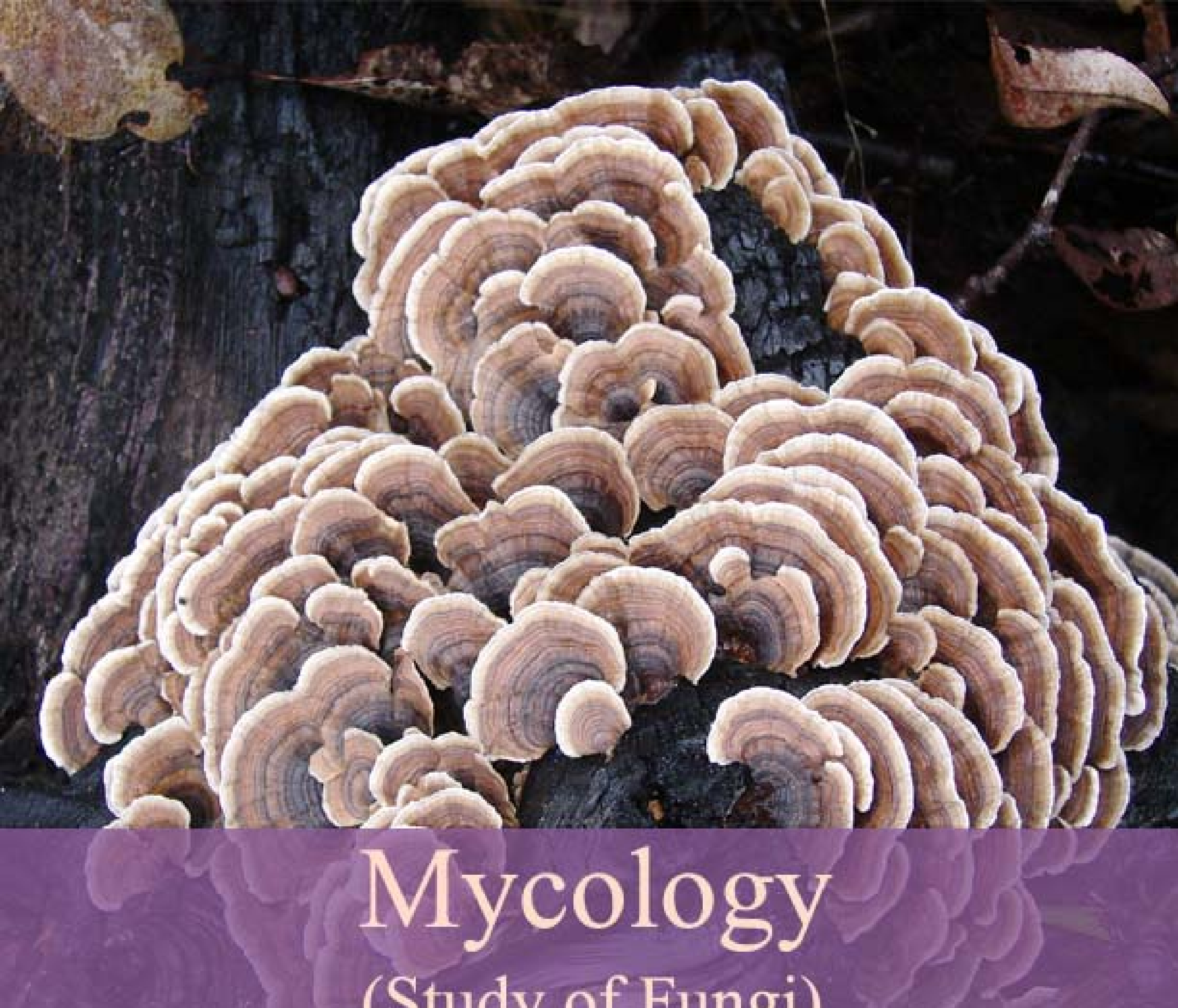

Mycology (Study of Fungi)

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Chapter- 1

Mycology

A mushroom is a reproductive structure of a fungus.

Mycology (from the Greek μύκης, mukēs, meaning "fungus") is the branch of biology concerned with the study of fungi, including their genetic and biochemical properties, their taxonomy and their use to humans as a source for tinder, medicinals (e.g., penicillin), food (e.g., beer, wine, cheese, edible mushrooms) and entheogens, as well as their dangers, such as poisoning or infection.

From mycology arose the field of phytopathology, the study of plant diseases, and the two disciplines remain closely related because the vast majority of plant pathogens are fungi. A biologist who studies mycology is called a **mycologist**.

Historically, mycology was a branch of botany (fungi are evolutionarily more closely related to animals than to plants but this was not recognized until a few decades ago). Pioneer *mycologists* included Elias Magnus Fries, Christian Hendrik Persoon, Anton de Bary and Lewis David von Schweinitz.

Today the most comprehensively studied and understood fungi are yeasts and eukaryotic model organisms *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe*.

Many fungi produce toxins, antibiotics and other secondary metabolites. For example the cosmopolitan (worldwide) genus *Fusarium* and their toxins associated with fatal outbreaks of alimentary toxic aleukia in humans were extensively studied by Abraham Joffe.

Fungi are fundamental for life on earth in their roles as symbionts, e.g. in the form of mycorrhizae, insect symbionts and lichens, potency in breaking down complex organic biomolecules such as lignin, the more durable component of wood, and by playing a role in xenobiotics, a critical step in the global carbon cycle.

Fungi and other organisms traditionally recognized as fungi, such as oomycetes and myxomycetes (slime molds), often are economically and socially important as some cause diseases of animals (such as histoplasmosis) as well as plants (such as Dutch elm disease and Rice blast).

Field meetings to find interesting species of fungi are known as 'forays', after the first such meeting organized by the Woolhope Naturalists' Field Club in 1868 and entitled "a foray among the fungi."

Some fungi can cause disease in humans or other organisms. The study of pathogenic fungi is referred to as medical mycology.

History

Humans probably started collecting mushrooms as food in Prehistoric times. Mushrooms were first written about in the works of Euripides (480-406 B.C.). The Greek philosopher Theophrastos of Eressos (371-288 B.C.) was perhaps the first to try to systematically classify plants; mushrooms were considered to be plants that were missing certain organs. It was later Pliny the elder (23–79 A.D.), who wrote about truffles in his encyclopedia Naturalis historia.

The Middle Ages saw little advancement in the body of knowledge about fungi. Rather, the invention of the printing press allowed some authors to disseminate superstitions and misconceptions about the fungi that had been perpetuated by the classical authors.

> “ ***Fungi and truffles are neither herbs, nor roots, nor flowers, nor seeds, but merely the superfluous moisture or earth, of trees, or rotten wood, and of other rotting things. This is plain from the fact that all fungi and truffles, especially those that are used for eating, grow most commonly in thundery and wet weather.*** ”
>
> —Jerome Bock (Hieronymus Tragus), 1552

The start of the modern age of mycology begins with Pier Antonio Micheli's 1737 publication of *Nova plantarum genera*. Published in Florence, this seminal work laid the foundations for the systematic classification of grasses, mosses and fungi. The term *mycology* and the complimentary *mycologist* were first used in 1836 by M.J. Berkeley.

Medicinal mycology

For centuries, certain mushrooms have been documented as a folk medicine in China, Japan, and Russia. Although the use of mushrooms in folk medicine is largely centered on the Asian continent, people in other parts of the world like the Middle East, Poland and Belarus have been documented using mushrooms for medicinal purposes. Certain mushrooms, especially polypores like Reishi were thought to be able to benefit a wide variety of health ailments. Medicinal mushroom research in the United States is currently active, with studies taking place at City of Hope National Medical Center, as well as the Memorial Sloan–Kettering Cancer Center.

Current research focuses on mushrooms that may have hypoglycemic activity, anti-cancer activity, anti-pathogenic activity, and immune system enhancing activity. Recent research has found that the oyster mushroom naturally contains the cholesterol-lowering drug lovastatin, mushrooms produce large amounts of vitamin D when exposed to UV light, and that certain fungi may be a future source of taxol. To date, penicillin, lovastatin, ciclosporin, griseofulvin, cephalosporin, ergometrine, and statins are the most famous pharmaceuticals which have been isolated from the fungi kingdom.

Chapter- 2

Fungus

Fungi Temporal range: Early Devonian–Recent	

Clockwise from top left: *Amanita muscaria*, a basidiomycete; *Sarcoscypha coccinea*, an ascomycete; bread covered in mold; a chytrid; a *Penicillium* conidiophore.

Scientific classification	
Domain:	Eukaryota
(unranked):	Opisthokonta
Kingdom:	**Fungi** (L., 1753) R.T. Moore, 1980

Subkingdoms/Phyla/Subphyla

Blastocladiomycota
Chytridiomycota

Glomeromycota
Microsporidia
Neocallimastigomycota

Dikarya (inc. Deuteromycota)

Ascomycota
Pezizomycotina
Saccharomycotina
Taphrinomycotina
Basidiomycota
Agaricomycotina
Pucciniomycotina
Ustilaginomycotina

Subphyla Incertae sedis

Entomophthoromycotina
Kickxellomycotina
Mucoromycotina
Zoopagomycotina

A **fungus** is a member of a large group of eukaryotic organisms that includes microorganisms such as yeasts and molds (British English: moulds), as well as the more familiar mushrooms. These organisms are classified as a kingdom, **Fungi**, which is separate from plants, animals, and bacteria. One major difference is that fungal cells have cell walls that contain chitin, unlike the cell walls of plants, which contain cellulose. These and other differences show that the fungi form a single group of related organisms, named the *Eumycota* (*true fungi* or *Eumycetes*), that share a common ancestor (a *monophyletic group*). This fungal group is distinct from the structurally similar myxomycetes (slime molds) and oomycetes (water molds). The discipline of biology devoted to the study of fungi is known as mycology, which is often regarded as a branch of botany, even though genetic studies have shown that fungi are more closely related to animals than to plants.

Abundant worldwide, most fungi are inconspicuous because of the small size of their structures, and their cryptic lifestyles in soil, on dead matter, and as symbionts of plants, animals, or other fungi. They may become noticeable when fruiting, either as mushrooms or molds. Fungi perform an essential role in the decomposition of organic matter and have fundamental roles in nutrient cycling and exchange. They have long been used as a direct source of food, such as mushrooms and truffles, as a leavening agent for bread, and in fermentation of various food products, such as wine, beer, and soy sauce. Since the 1940s, fungi have been used for the production of antibiotics, and, more recently, various enzymes produced by fungi are used industrially and in detergents. Fungi are also used as biological pesticides to control weeds, plant diseases and insect pests. Many species produce bioactive compounds called mycotoxins, such as alkaloids and polyketides, that are toxic to animals including humans. The fruiting structures of a few species contain psychotropic compounds and are consumed recreationally or in traditional spiritual ceremonies. Fungi can break down manufactured materials and buildings, and become significant pathogens of humans and other animals. Losses of crops due to fungal diseases (e.g. rice blast disease) or food spoilage can have a large impact on human food supplies and local economies.

The fungus kingdom encompasses an enormous diversity of taxa with varied ecologies, life cycle strategies, and morphologies ranging from single-celled aquatic chytrids to large mushrooms. However, little is known of the true biodiversity of Kingdom Fungi, which has been estimated at around 1.5 million species, with about 5% of these having been formally classified. Ever since the pioneering 18th and 19th century taxonomical works of Carl Linnaeus, Christian Hendrik Persoon, and Elias Magnus Fries, fungi have been classified according to their morphology (e.g., characteristics such as spore color or microscopic features) or physiology. Advances in molecular genetics have opened the way for DNA analysis to be incorporated into taxonomy, which has sometimes challenged the historical groupings based on morphology and other traits. Phylogenetic studies published in the last decade have helped reshape the classification of Kingdom Fungi, which is divided into one subkingdom, seven phyla, and ten subphyla.

Etymology

The English word *fungus* is directly adopted from the Latin *fungus* (mushroom), used in the writings of Horace and Pliny. This in turn is derived from the Greek word *sphongos*/σφογγος ("sponge"), which refers to the macroscopic structures and morphology of mushrooms and molds; the root is also used in other languages, such as the German *Schwamm* ("sponge"), *Schimmel* ("mold"), and the French *champignon* and the Spanish *champiñon* (which both mean "mushroom"). The use of the word *mycology*, which is derived from the Greek *mykes*/μύκης (mushroom) and *logos*/λόγος (discourse), to denote the scientific study of fungi is thought to have originated in 1836 with English naturalist Miles Joseph Berkeley's publication *The English Flora of Sir James Edward Smith, Vol. 5.*

Characteristics

Before the introduction of molecular methods for phylogenetic analysis, taxonomists considered fungi to be members of the Plant Kingdom because of similarities in lifestyle: both fungi and plants are mainly immobile, and have similarities in general morphology and growth habitat. Like plants, fungi often grow in soil, and in the case of mushrooms form conspicuous fruiting bodies, which sometimes bear resemblance to plants such as mosses. The fungi are now considered a separate kingdom, distinct from both plants and animals, from which they appear to have diverged around one billion years ago. Some morphological, biochemical, and genetic features are shared with other organisms, while others are unique to the fungi, clearly separating them from the other kingdoms:

Shared features:

- With other eukaryotes: As other eukaryotes, fungal cells contain membrane-bound nuclei with chromosomes that contain DNA with noncoding regions called introns and coding regions called exons. In addition, fungi possess membrane-bound cytoplasmic organelles such as mitochondria, sterol-containing membranes, and ribosomes of the 80S type. They have a characteristic range of soluble carbohydrates and storage compounds, including sugar alcohols (e.g., mannitol), disaccharides, (e.g., trehalose), and polysaccharides (e.g., glycogen, which is also found in animals).
- With animals: Fungi lack chloroplasts and are heterotrophic organisms, requiring preformed organic compounds as energy sources.
- With plants: Fungi possess a cell wall and vacuoles. They reproduce by both sexual and asexual means, and like basal plant groups (such as ferns and mosses) produce spores. Similar to mosses and algae, fungi typically have haploid nuclei.
- With euglenoids and bacteria: Higher fungi, euglenoids, and some bacteria produce the amino acid L-lysine in specific biosynthesis steps, called the α-aminoadipate pathway.
- The cells of most fungi grow as tubular, elongated, and thread-like (filamentous) structures and are called hyphae, which may contain multiple nuclei and extend at their tips. Each tip contains a set of aggregated vesicles—cellular structures consisting of proteins, lipids, and other organic molecules—called Spitzenkörper. Both fungi and oomycetes grow as filamentous hyphal cells. In contrast, similar-looking organisms, such as filamentous green algae, grow by repeated cell division within a chain of cells.
- In common with some plant and animal species, more than 60 fungal species display the phenomenon of bioluminescence.

Unique features:

- Some species grow as single-celled yeasts that reproduce by budding or binary fission. Dimorphic fungi can switch between a yeast phase and a hyphal phase in response to environmental conditions.
- The fungal cell wall is composed of glucans and chitin; while the former compounds are also found in plants and the latter in the exoskeleton of arthropods, fungi are the only organisms that combine these two structural molecules in their cell wall. In contrast to plants and the oomycetes, fungal cell walls do not contain cellulose.

Omphalotus nidiformis, a bioluminescent mushroom

Most fungi lack an efficient system for long-distance transport of water and nutrients, such as the xylem and phloem in many plants. To overcome these limitations, some fungi, such as *Armillaria*, form rhizomorphs, that resemble and perform functions similar to the roots of plants. Another characteristic shared with plants includes a biosynthetic pathway for producing terpenes that uses mevalonic acid and pyrophosphate as chemical building blocks. However, plants have an additional terpene pathway in their chloroplasts, a structure fungi do not possess. Fungi produce several secondary metabolites that are similar or identical in structure to those made by plants. Many of the plant and fungal enzymes that make these compounds differ from each other in sequence and other characteristics, which indicates separate origins and evolution of these enzymes in the fungi and plants.

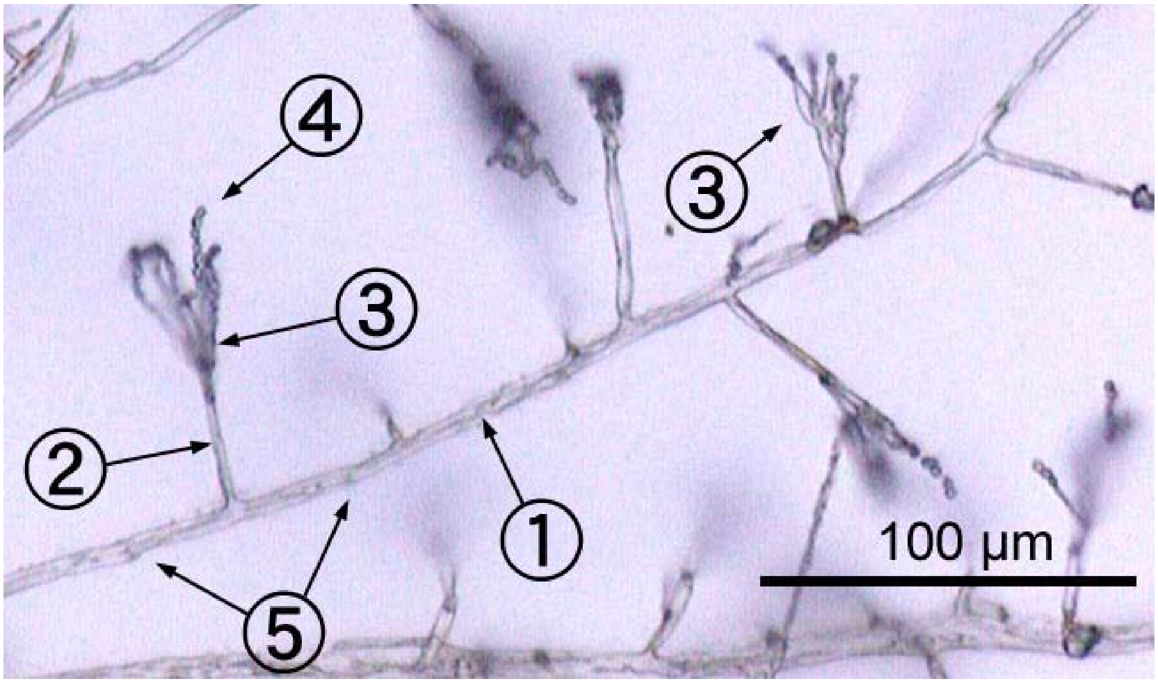
Diversity

Fungi have a worldwide distribution, and grow in a wide range of habitats, including extreme environments such as deserts or areas with high salt concentrations or ionizing radiation, as well as in deep sea sediments. Some can survive the intense UV and cosmic radiation encountered during space travel. Most grow in terrestrial environments, though several species live partly or solely in aquatic habitats, such as the chytrid fungus *Batrachochytrium dendrobatidis*, a parasite that has been responsible for a worldwide decline in amphibian populations. This organism spends part of its life cycle as a motile zoospore, enabling it to propel itself through water and enter its amphibian host. Other examples of aquatic fungi include those living in hydrothermal areas of the ocean.

Around 100,000 species of fungi have been formally described by taxonomists, but the global biodiversity of the fungus kingdom is not fully understood. On the basis of observations of the ratio of the number of fungal species to the number of plant species in selected environments, the fungal kingdom has been estimated to contain about 1.5 million species. In mycology, species have historically been distinguished by a variety of methods and concepts. Classification based on morphological characteristics, such as the size and shape of spores or fruiting structures, has traditionally dominated fungal taxonomy. Species may also be distinguished by their biochemical and physiological characteristics, such as their ability to metabolize certain biochemicals, or their reaction to chemical tests. The biological species concept discriminates species based on their ability to mate. The application of molecular tools, such as DNA sequencing and phylogenetic analysis, to study diversity has greatly enhanced the resolution and added robustness to estimates of genetic diversity within various taxonomic groups.

Morphology

Microscopic structures



An environmental isolate of *Penicillium*
1. hypha 2. conidiophore 3. phialide 4. conidia 5. septa

Most fungi grow as hyphae, which are cylindrical, thread-like structures 2–10 µm in diameter and up to several centimeters in length. Hyphae grow at their tips (apices); new hyphae are typically formed by emergence of new tips along existing hyphae by a process called *branching*, or occasionally growing hyphal tips bifurcate (fork) giving rise to two parallel-growing hyphae. The combination of apical growth and branching/forking leads to the development of a mycelium, an interconnected network of hyphae. Hyphae can be either septate or coenocytic: septate hyphae are divided into compartments separated by cross walls (internal cell walls, called septa, that are formed at right angles to the cell wall giving the hypha its shape), with each compartment containing one or more nuclei; coenocytic hyphae are not compartmentalized. Septa have pores that allow cytoplasm, organelles, and sometimes nuclei to pass through; an example is the dolipore septum in the fungi of the phylum Basidiomycota. Coenocytic hyphae are essentially multinucleate supercells.

Many species have developed specialized hyphal structures for nutrient uptake from living hosts; examples include haustoria in plant-parasitic species of most fungal phyla, and arbuscules of several mycorrhizal fungi, which penetrate into the host cells to consume nutrients.

Although fungi are opisthokonts—a grouping of evolutionarily related organisms broadly characterized by a single posterior flagellum—all phyla except for the chytrids have lost their posterior flagella. Fungi are unusual among the eukaryotes in having a cell wall that, in addition to glucans (e.g., β-1,3-glucan) and other typical components, also contains the biopolymer chitin.

Macroscopic structures

Armillaria ostoyae

Fungal mycelia can become visible to the naked eye, for example, on various surfaces and substrates, such as damp walls and on spoiled food, where they are commonly called molds. Mycelia grown on solid agar media in laboratory petri dishes are usually referred to as colonies. These colonies can exhibit growth shapes and colors (due to spores or pigmentation) that can be used as diagnostic features in the identification of species or groups. Some individual fungal colonies can reach extraordinary dimensions and ages as in the case of a clonal colony of *Armillaria ostoyae*, which extends over an area of more than 900 ha (3.5 square miles), with an estimated age of nearly 9,000 years.

The apothecium—a specialized structure important in sexual reproduction in the ascomycetes—is a cup-shaped fruiting body that holds the hymenium, a layer of tissue containing the spore-bearing cells. The fruiting bodies of the basidiomycetes (basidiocarps) and some ascomycetes can sometimes grow very large, and many are well-known as mushrooms.

Growth and physiology

The growth of fungi as hyphae on or in solid substrates or as single cells in aquatic environments is adapted for the efficient extraction of nutrients, because these growth forms have high surface area to volume ratios. Hyphae are specifically adapted for growth on solid surfaces, and to invade substrates and tissues. They can exert large penetrative mechanical forces; for example, the plant pathogen *Magnaporthe grisea* forms a structure called an appressorium which evolved to puncture plant tissues. The pressure generated by the appressorium, directed against the plant epidermis, can exceed 8 megapascals (1,200 psi). The filamentous fungus *Paecilomyces lilacinus* uses a similar structure to penetrate the eggs of nematodes.

Mold covering a decaying peach. The frames were taken approximately 12 hours apart over a period of six days.

The mechanical pressure exerted by the appressorium is generated from physiological processes that increase intracellular turgor by producing osmolytes such as glycerol. Morphological adaptations such as these are complemented by hydrolytic enzymes secreted into the environment to digest large organic molecules—such as polysaccharides, proteins, lipids, and other organic substrates—into smaller molecules that may then be absorbed as nutrients. The vast majority of filamentous fungi grow in a polar fashion—i.e., by extension into one direction—by elongation at the tip (apex) of the hypha. Alternative forms of fungal growth include intercalary extension (i.e., by longitudinal expansion of hyphal compartments that are below the apex) as in the case of some endophytic fungi, or growth by volume expansion during the development of mushroom stipes and other large organs. Growth of fungi as multicellular structures consisting of somatic and reproductive cells—a feature independently evolved in animals and plants—has several functions, including the development of fruiting bodies for dissemination of sexual spores (see above) and biofilms for substrate colonization and intercellular communication.

Traditionally, the fungi are considered heterotrophs, organisms that rely solely on carbon fixed by other organisms for metabolism. Fungi have evolved a high degree of metabolic versatility that allows them to use a diverse range of organic substrates for growth, including simple compounds such as nitrate, ammonia, acetate, or ethanol. For some species it has been shown that the pigment melanin may play a role in extracting energy from ionizing radiation, such as gamma radiation; however, this form of "radiotrophic" growth has only been described for a few species, the effects on growth rates are small, and the underlying biophysical and biochemical processes are not known. The authors speculate that this process might bear similarity to CO_2 fixation via visible light, but instead utilizing ionizing radiation as a source of energy.

Reproduction

Polyporus squamosus

Fungal reproduction is complex, reflecting the differences in lifestyles and genetic makeup within this kingdom of organisms. It is estimated that a third of all fungi reproduce by different modes of propagation; for example, reproduction may occur in two well-differentiated stages within the life cycle of a species, the teleomorph and the anamorph. Environmental conditions trigger genetically determined developmental states that lead to the creation of specialized structures for sexual or asexual reproduction. These structures aid reproduction by efficiently dispersing spores or spore-containing propagules.

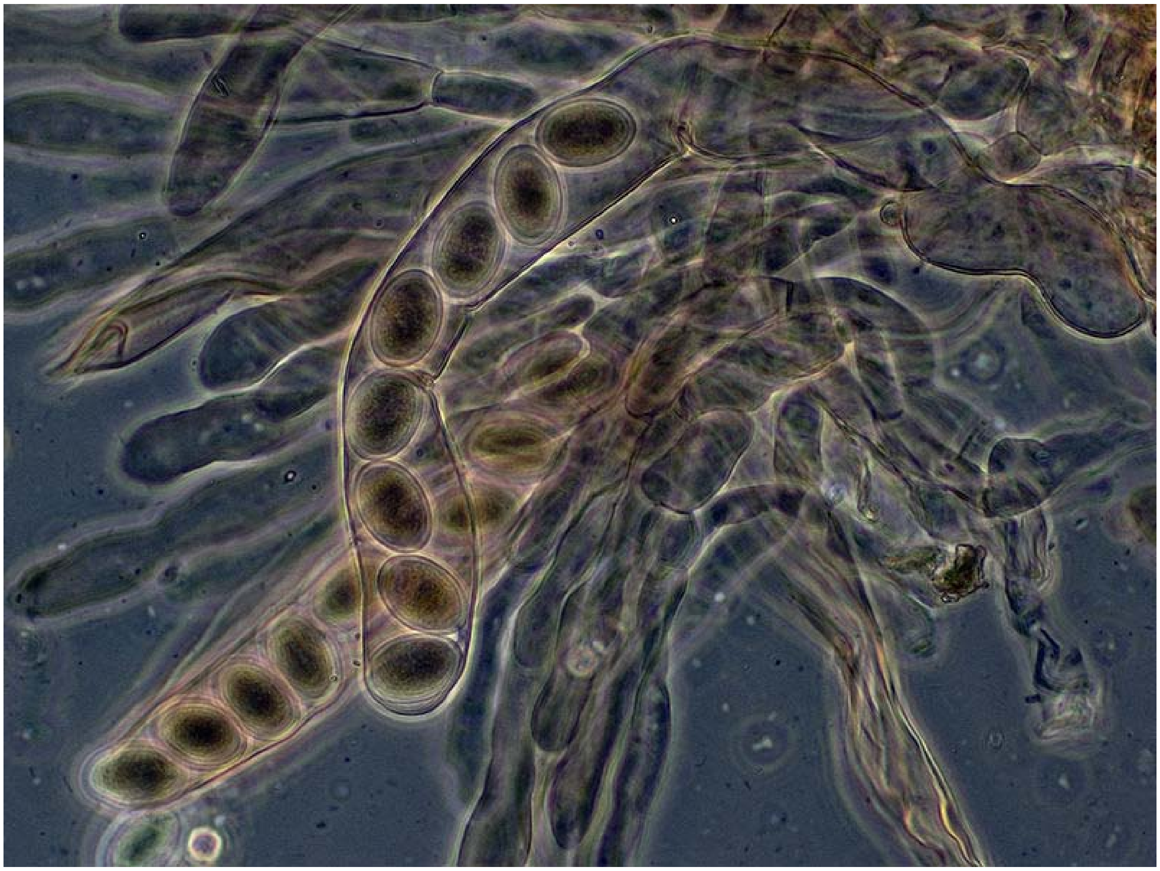
Asexual reproduction

Asexual reproduction via vegetative spores (conidia) or through mycelial fragmentation is common; it maintains clonal populations adapted to a specific niche, and allows more rapid dispersal than sexual reproduction. The "Fungi imperfecti" (fungi lacking the perfect or sexual stage) or Deuteromycota comprise all the species which lack an observable sexual cycle.

Sexual reproduction

Sexual reproduction with meiosis exists in all fungal phyla (with the exception of the Glomeromycota). It differs in many aspects from sexual reproduction in animals or plants. Differences also exist between fungal groups and can be used to discriminate species by morphological differences in sexual structures and reproductive strategies. Mating experiments between fungal isolates may identify species on the basis of biological species concepts. The major fungal groupings have initially been delineated based on the morphology of their sexual structures and spores; for example, the spore-containing structures, asci and basidia, can be used in the identification of ascomycetes and basidiomycetes, respectively. Some species may allow mating only between individuals of opposite mating type, while others can mate and sexually reproduce with any other individual or itself. Species of the former mating system are called heterothallic, and of the latter homothallic.

Most fungi have both an haploid and diploid stage in their life cycles. In sexually reproducing fungi, compatible individuals may combine by fusing their hyphae together into an interconnected network; this process, anastomosis, is required for the initiation of the sexual cycle. Ascomycetes and basidiomycetes go through a dikaryotic stage, in which the nuclei inherited from the two parents do not combine immediately after cell fusion, but remain separate in the hyphal cells.



The 8-spored asci of *Morchella elata*, viewed with phase contrast microscopy

In ascomycetes, dikaryotic hyphae of the hymenium (the spore-bearing tissue layer) form a characteristic *hook* at the hyphal septum. During cell division, formation of the hook ensures proper distribution of the newly divided nuclei into the apical and basal hyphal compartments. An ascus (plural *asci*) is then formed, in which karyogamy (nuclear fusion) occurs. Asci are embedded in an ascocarp, or fruiting body. Karyogamy in the asci is followed immediately by meiosis and the production of ascospores. After dispersal, the ascospores may germinate and form a new haploid mycelium.

Sexual reproduction in basidiomycetes is similar to that of the ascomycetes. Compatible haploid hyphae fuse to produce a dikaryotic mycelium. However, the dikaryotic phase is more extensive in the basidiomycetes, often also present in the vegetatively growing mycelium. A specialized anatomical structure, called a clamp connection, is formed at each hyphal septum. As with the structurally similar hook in the ascomycetes, the clamp connection in the basidiomycetes is required for controlled transfer of nuclei during cell division, to maintain the dikaryotic stage with two genetically different nuclei in each hyphal compartment. A basidiocarp is formed in which club-like structures known as basidia generate haploid basidiospores after karyogamy and meiosis. The most commonly known basidiocarps are mushrooms, but they may also take other forms.

In glomeromycetes (formerly zygomycetes), haploid hyphae of two individuals fuse, forming a gametangium, a specialized cell structure that becomes a fertile gamete-producing cell. The gametangium develops into a zygospore, a thick-walled spore formed by the union of gametes. When the zygospore germinates, it undergoes meiosis, generating new haploid hyphae, which may then form asexual sporangiospores. These sporangiospores allow the fungus to rapidly disperse and germinate into new genetically identical haploid fungal mycelia.

Spore dispersal

Both asexual and sexual spores or sporangiospores are often actively dispersed by forcible ejection from their reproductive structures. This ejection ensures exit of the spores from the reproductive structures as well as travelling through the air over long distances.

The bird's nest fungus *Cyathus stercoreus*

Specialized mechanical and physiological mechanisms, as well as spore surface structures (such as hydrophobins), enable efficient spore ejection. For example, the structure of the spore-bearing cells in some ascomycete species is such that the buildup of substances affecting cell volume and fluid balance enables the explosive discharge of spores into the air. The forcible discharge of single spores termed *ballistospores* involves formation of a small drop of water (Buller's drop), which upon contact with the spore leads to its projectile release with an initial acceleration of more than 10,000 g; the net result is that the spore is ejected 0.01–0.02 cm, sufficient distance for it to fall through the gills or pores into the air below. Other fungi, like the puffballs, rely on alternative mechanisms for spore release, such as external mechanical forces. The bird's nest fungi use the force of falling water drops to liberate the spores from cup-shaped fruiting bodies. Another strategy is seen in the stinkhorns, a group of fungi with lively colors and putrid odor that attract insects to disperse their spores.

Other sexual processes

Besides regular sexual reproduction with meiosis, certain fungi, such as those in the genera *Penicillium* and *Aspergillus*, may exchange genetic material via parasexual processes, initiated by anastomosis between hyphae and plasmogamy of fungal cells. The frequency and relative importance of parasexual events is unclear and may be lower than other sexual processes. It is known to play a role in intraspecific hybridization and is likely required for hybridization between species, which has been associated with major events in fungal evolution.

Evolution

In contrast to plants and animals, the early fossil record of the fungi is meager. Factors that likely contribute to the under-representation of fungal species among fossils include the nature of fungal fruiting bodies, which are soft, fleshy, and easily degradable tissues and the microscopic dimensions of most fungal structures, which therefore are not readily evident. Fungal fossils are difficult to distinguish from those of other microbes, and are most easily identified when they resemble extant fungi. Often recovered from a permineralized plant or animal host, these samples are typically studied by making thin-section preparations that can be examined with light microscopy or transmission electron microscopy. Compression fossils are studied by dissolving the surrounding matrix with acid and then using light or scanning electron microscopy to examine surface details.

The earliest fossils possessing features typical of fungi date to the Proterozoic eon, some 1,430 million years ago (Ma); these multicellular benthic organisms had filamentous structures with septa, and were capable of anastomosis. More recent studies (2009) estimate the arrival of fungal organisms at about 760–1060 Ma on the basis of comparisons of the rate of evolution in closely related groups. For much of the Paleozoic Era (542–251 Ma), the fungi appear to have been aquatic and consisted of organisms similar to the extant Chytrids in having flagellum-bearing spores. The evolutionary adaptation from an aquatic to a terrestrial lifestyle necessitated a diversification of ecological strategies for obtaining nutrients, including parasitism, saprobism, and the development of mutualistic relationships such as mycorrhiza and lichenization. Recent (2009) studies suggest that the ancestral ecological state of the Ascomycota was saprobism, and that independent lichenization events have occurred multiple times.

The fungi probably colonized the land during the Cambrian (542–488.3 Ma), long before land plants. Fossilized hyphae and spores recovered from the Ordovician of Wisconsin (460 Ma) resemble modern-day Glomerales, and existed at a time when the land flora likely consisted of only non-vascular bryophyte-like plants. Prototaxites, which was probably a fungus or lichen, would have been the tallest organism of the late Silurian. Fungal fossils do not become common and uncontroversial until the early Devonian (416–359.2 Ma), when they are abundant in the Rhynie chert, mostly as Zygomycota and Chytridiomycota. At about this same time, approximately 400 Ma, the Ascomycota and Basidiomycota diverged, and all modern classes of fungi were present by the Late Carboniferous (Pennsylvanian, 318.1–299 Ma).

Lichen-like fossils have been found in the Doushantuo Formation in southern China dating back to 635–551 Ma. Lichens were a component of the early terrestrial ecosystems, and the estimated age of the oldest terrestrial lichen fossil is 400 Ma; this date corresponds to the age of the oldest known sporocarp fossil, a *Paleopyrenomycites* species found in the Rhynie Chert. The oldest fossil with microscopic features resembling modern-day basidiomycetes is *Palaeoancistrus*, found permineralized with a fern from the Pennsylvanian. Rare in the fossil record are the homobasidiomycetes (a taxon roughly equivalent to the mushroom-producing species of the agaricomycetes). Two amber-preserved specimens provide evidence that the earliest known mushroom-forming fungi (the extinct species *Archaeomarasmius legletti*) appeared during the mid-Cretaceous, 90 Ma.

Some time after the Permian-Triassic extinction event (251.4 Ma), a fungal spike (originally thought to be an extraordinary abundance of fungal spores in sediments) formed, suggesting that fungi were the dominant life form at this time, representing nearly 100% of the available fossil record for this period. However, the relative proportion of fungal spores relative to spores formed by algal species is difficult to assess, the spike did not appear worldwide, and in many places it did not fall on the Permian-Triassic boundary.

Taxonomy

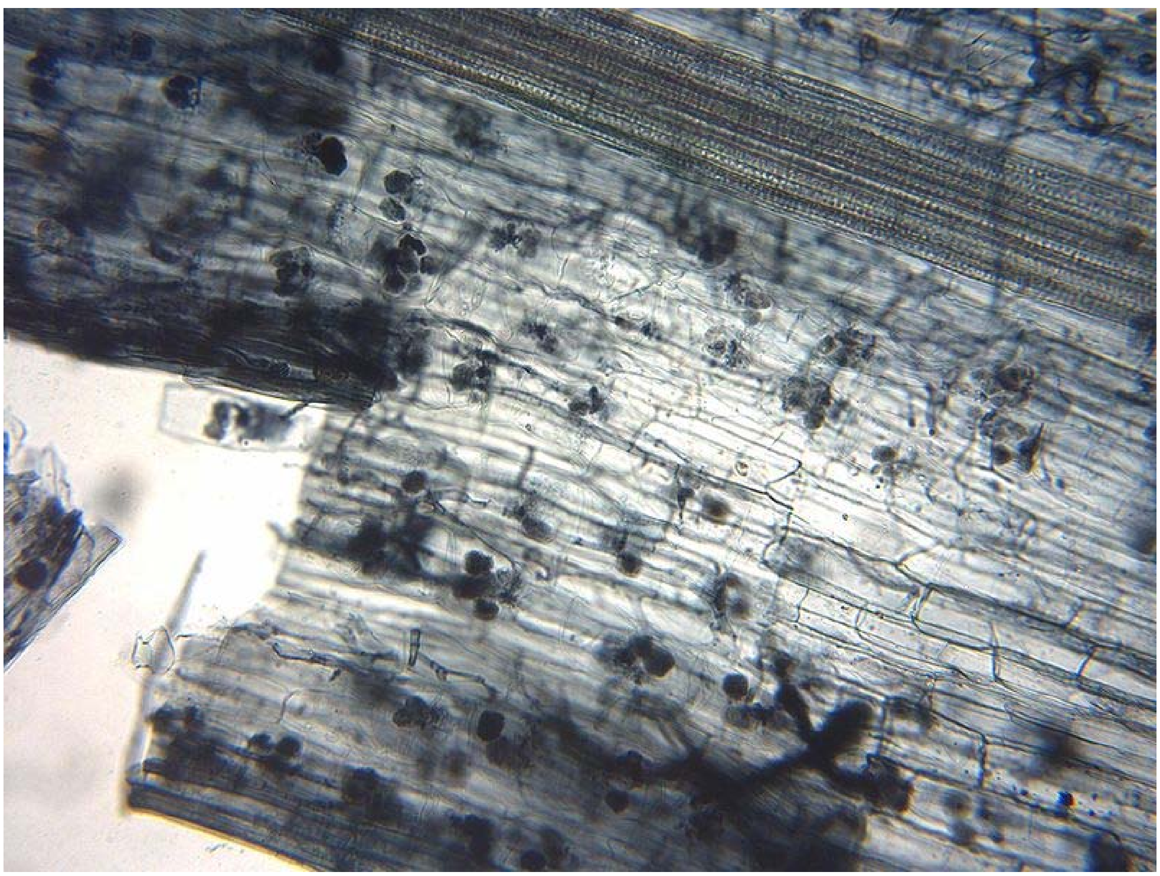
Even though traditionally included in many botany curricula and textbooks, fungi are now thought to be more closely related to animals than to plants and are placed with the animals in the monophyletic group of opisthokonts. Analyses using molecular phylogenetics support a monophyletic origin of the Fungi. The taxonomy of the Fungi is in a state of constant flux, especially due to recent research based on DNA comparisons. These current phylogenetic analyses often overturn classifications based on older and sometimes less discriminative methods based on morphological features and biological species concepts obtained from experimental matings.

There is no unique generally accepted system at the higher taxonomic levels and there are frequent name changes at every level, from species upwards. Efforts among researchers are now underway to establish and encourage usage of a unified and more consistent nomenclature. Fungal species can also have multiple scientific names depending on their life cycle and mode (sexual or asexual) of reproduction. Web sites such as Index Fungorum and ITIS list current names of fungal species (with cross-references to older synonyms).

The 2007 classification of Kingdom Fungi is the result of a large-scale collaborative research effort involving dozens of mycologists and other scientists working on fungal taxonomy. It recognizes seven phyla, two of which—the Ascomycota and the Basidiomycota—are contained within a branch representing subkingdom Dikarya. The below cladogram depicts the major fungal taxa and their relationship to opisthokont and unikont organisms. The lengths of the branches in this tree are not proportional to evolutionary distances.

Taxonomic groups

The major phyla (sometimes called divisions) of fungi have been classified mainly on the basis of characteristics of their sexual reproductive structures. Currently, seven phyla are proposed: Microsporidia, Chytridiomycota, Blastocladiomycota, Neocallimastigomycota, Glomeromycota, Ascomycota, and Basidiomycota.



Arbuscular mycorrhiza seen under microscope. Flax root cortical cells containing paired arbuscules.

Phylogenetic analysis has demonstrated that the Microsporidia, unicellular parasites of animals and protists, are fairly recent and highly derived endobiotic fungi (living within the tissue of another species). One 2006 study concludes that the Microsporidia are a sister group to the true fungi, that is, they are each other's closest evolutionary relative. Hibbett and colleagues suggest that this analysis does not clash with their classification of the Fungi, and although the Microsporidia are elevated to phylum status, it is acknowledged that further analysis is required to clarify evolutionary relationships within this group.

The Chytridiomycota are commonly known as chytrids. These fungi are distributed worldwide. Chytrids produce zoospores that are capable of active movement through aqueous phases with a single flagellum, leading early taxonomists to classify them as protists. Molecular phylogenies, inferred from rRNA sequences in ribosomes, suggest that the Chytrids are a basal group divergent from the other fungal phyla, consisting of four major clades with suggestive evidence for paraphyly or possibly polyphyly.

The Blastocladiomycota were previously considered a taxonomic clade within the Chytridiomycota. Recent molecular data and ultrastructural characteristics, however, place the Blastocladiomycota as a sister clade to the Zygomycota, Glomeromycota, and Dikarya (Ascomycota and Basidiomycota). The blastocladiomycetes are saprotrophs, feeding on decomposing organic matter, and they are parasites of all eukaryotic groups. Unlike their close relatives, the chytrids, which mostly exhibit zygotic meiosis, the blastocladiomycetes undergo sporic meiosis.

The Neocallimastigomycota were earlier placed in the phylum Chytridomycota. Members of this small phylum are anaerobic organisms, living in the digestive system of larger herbivorous mammals and possibly in other terrestrial and aquatic environments. They lack mitochondria but contain hydrogenosomes of mitochondrial origin. As the related chrytrids, neocallimastigomycetes form zoospores that are posteriorly uniflagellate or polyflagellate.

Members of the Glomeromycota form arbuscular mycorrhizae, a form of symbiosis where fungal hyphae invade plant root cells and both species benefit from the resulting increased supply of nutrients. All known Glomeromycota species reproduce asexually. The symbiotic association between the Glomeromycota and plants is ancient, with evidence dating to 400 million years ago. Formerly part of the Zygomycota (commonly known as 'sugar' and 'pin' molds), the Glomeromycota were elevated to phylum status in 2001 and now replace the older phylum Zygomycota. Fungi that were placed in the Zygomycota are now being reassigned to the Glomeromycota, or the subphyla incertae sedis Mucoromycotina, Kickxellomycotina, the Zoopagomycotina and the Entomophthoromycotina. Some well-known examples of fungi formerly in the Zygomycota include black bread mold (*Rhizopus stolonifer*), and *Pilobolus* species, capable of ejecting spores several meters through the air. Medically relevant genera include *Mucor*, *Rhizomucor*, and *Rhizopus*.

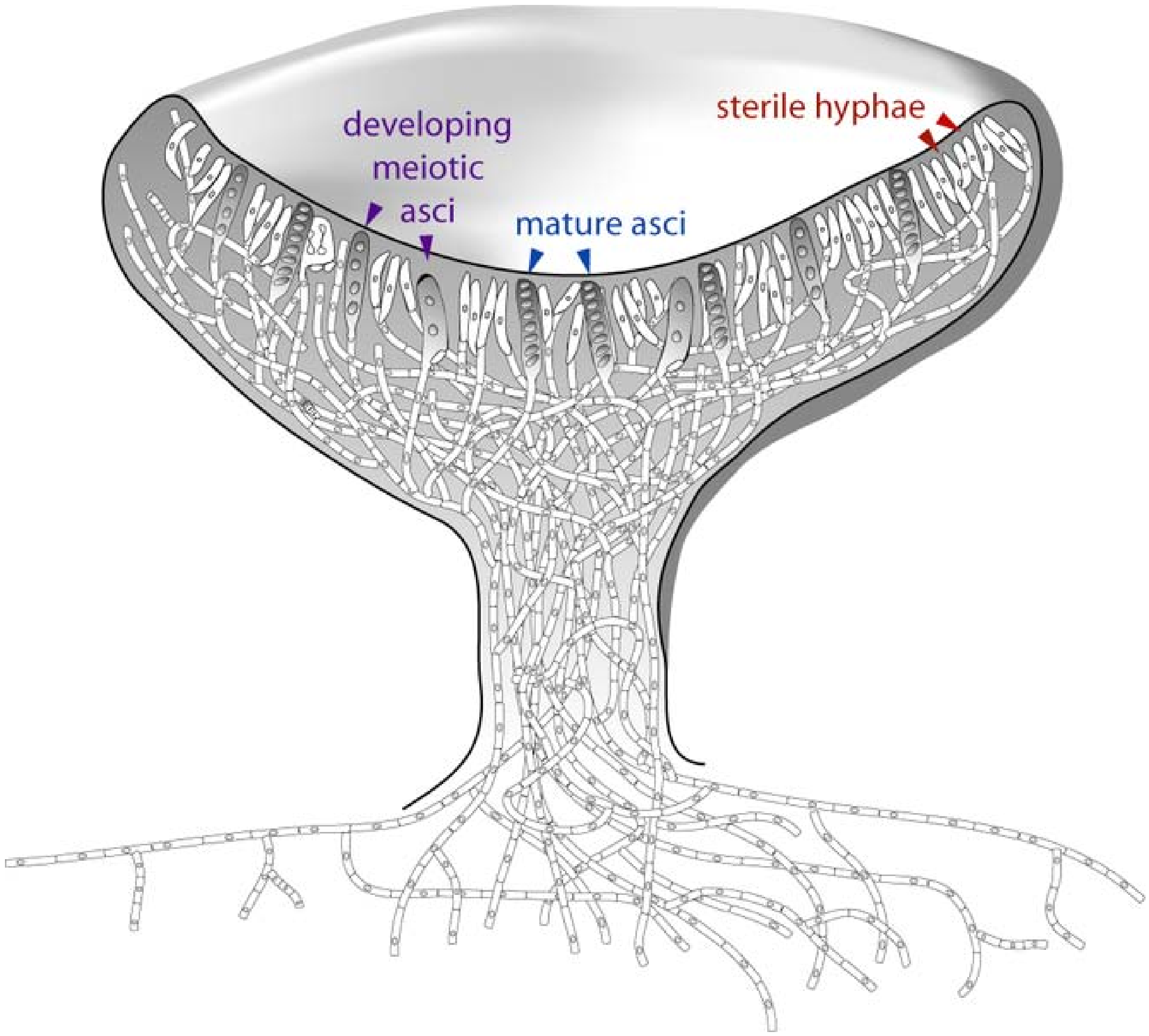


Diagram of an apothecium (the typical cup-like reproductive structure of Ascomycetes) showing sterile tissues as well as developing and mature asci.

The Ascomycota, commonly known as sac fungi or ascomycetes, constitute the largest taxonomic group within the Eumycota. These fungi form meiotic spores called ascospores, which are enclosed in a special sac-like structure called an ascus. This phylum includes morels, a few mushrooms and truffles, single-celled yeasts (e.g., of the genera *Saccharomyces*, *Kluyveromyces*, *Pichia*, and *Candida*), and many filamentous fungi living as saprotrophs, parasites, and mutualistic symbionts. Prominent and important genera of filamentous ascomycetes include *Aspergillus*, *Penicillium*, *Fusarium*, and *Claviceps*. Many ascomycete species have only been observed undergoing asexual reproduction (called anamorphic species), but analysis of molecular data has often been able to identify their closest teleomorphs in the Ascomycota. Because the products of meiosis are retained within the sac-like ascus, ascomycetes have been used for elucidating principles of genetics and heredity (e.g. *Neurospora crassa*).

Members of the Basidiomycota, commonly known as the club fungi or basidiomycetes, produce meiospores called basidiospores on club-like stalks called basidia. Most common mushrooms belong to this group, as well as rust and smut fungi, which are major pathogens of grains. Other important basidiomycetes include the maize pathogen *Ustilago maydis*, human commensal species of the genus *Malassezia*, and the opportunistic human pathogen, *Cryptococcus neoformans*.

Fungus-like organisms

Because of similarities in morphology and lifestyle, the slime molds (myxomycetes) and water molds (oomycetes) were formerly classified in the kingdom Fungi. Unlike true fungi the cell walls of these organisms contain cellulose and lack chitin. Myxomycetes are unikonts like fungi, but are grouped in the Amoebozoa. Oomycetes are diploid bikonts, grouped in the Chromalveolate kingdom. Neither water molds nor slime molds are closely related to the true fungi, and, therefore, taxonomists no longer group them in the kingdom Fungi. Nonetheless, studies of the oomycetes and myxomycetes are still often included in mycology textbooks and primary research literature.

The nucleariids, currently grouped in the Choanozoa, may be a sister group to the eumycete clade, and as such could be included in an expanded fungal kingdom.

Ecology

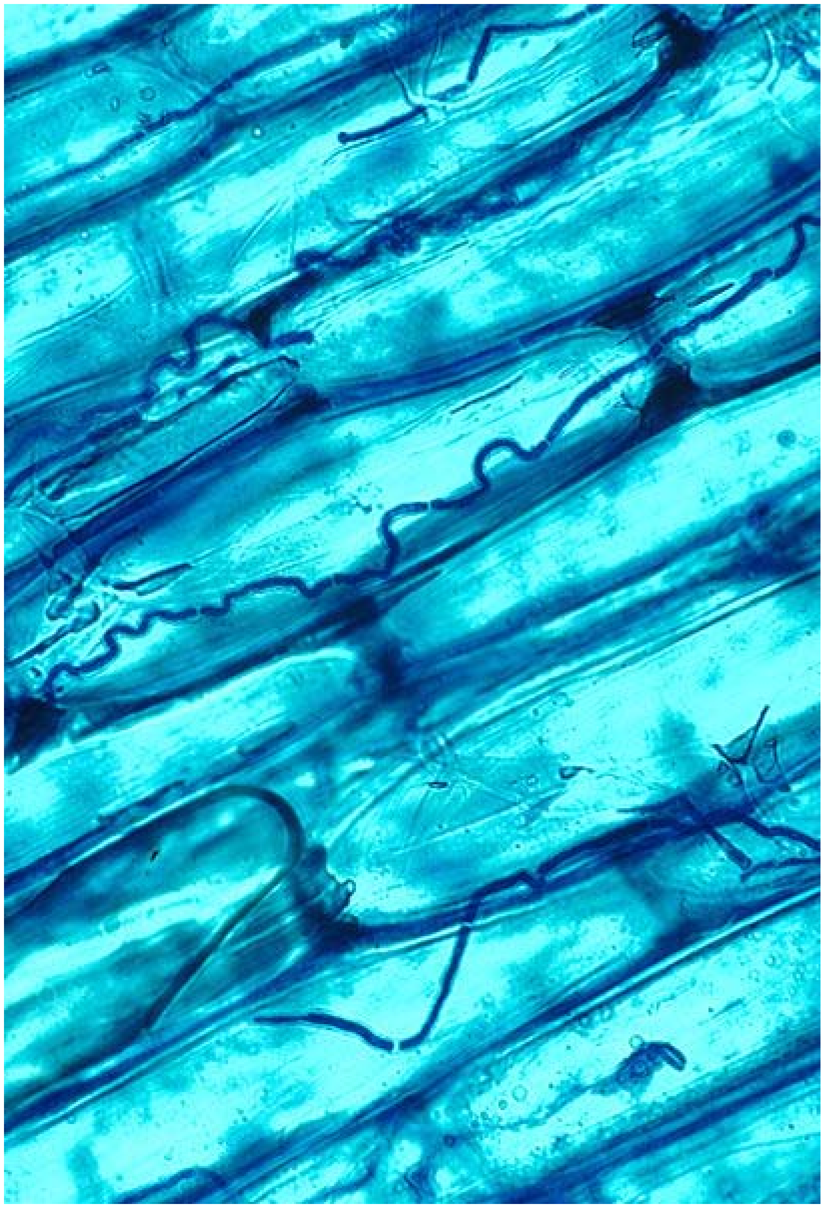
Although often inconspicuous, fungi occur in every environment on Earth and play very important roles in most ecosystems. Along with bacteria, fungi are the major decomposers in most terrestrial (and some aquatic) ecosystems, and therefore play a critical role in biogeochemical cycles and in many food webs. As decomposers, they play an essential role in nutrient cycling, especially as saprotrophs and symbionts, degrading organic matter to inorganic molecules, which can then re-enter anabolic metabolic pathways in plants or other organisms.

Symbiosis

Many fungi have important symbiotic relationships with organisms from most if not all Kingdoms. These interactions can be mutualistic or antagonistic in nature, or in the case of commensal fungi are of no apparent benefit or detriment to the host.

With plants

Mycorrhizal symbiosis between plants and fungi is one of the most well-known plant–fungus associations and is of significant importance for plant growth and persistence in many ecosystems; over 90% of all plant species engage in mycorrhizal relationships with fungi and are dependent upon this relationship for survival.



The dark filaments are hyphae of the endophytic fungus *Neotyphodium coenophialum* in the intercellular spaces of tall fescue leaf sheath tissue

The mycorrhizal symbiosis is ancient, dating to at least 400 million years ago. It often increases the plant's uptake of inorganic compounds, such as nitrate and phosphate from soils having low concentrations of these key plant nutrients. The fungal partners may also mediate plant-to-plant transfer of carbohydrates and other nutrients. Such mycorrhizal communities are called "common mycorrhizal networks". A special case of mycorrhiza is myco-heterotrophy, whereby the plant parasitizes the fungus, obtaining all of its nutrients from its fungal symbiont. Some fungal species inhabit the tissues inside roots, stems, and leaves, in which case they are called endophytes. Similar to mycorrhiza, endophytic colonization by fungi may benefit both symbionts; for example, endophytes of grasses impart to their host increased resistance to herbivores and other environmental stresses and receive food and shelter from the plant in return.

With algae and cyanobacteria

The lichen *Lobaria pulmonaria*, a symbiosis of fungal, algal, and cyanobacterial species

Lichens are formed by a symbiotic relationship between algae or cyanobacteria (referred to in lichen terminology as "photobionts") and fungi (mostly various species of ascomycetes and a few basidiomycetes), in which individual photobiont cells are embedded in a tissue formed by the fungus. Lichens occur in every ecosystem on all continents, play a key role in soil formation and the initiation of biological succession, and are the dominating life forms in extreme environments, including polar, alpine, and semiarid desert regions. They are able to grow on inhospitable surfaces, including bare soil, rocks, tree bark, wood, shells, barnacles and leaves. As in mycorrhizas, the photobiont provides sugars and other carbohydrates via photosynthesis, while the fungus provides minerals and water. The functions of both symbiotic organisms are so closely intertwined that they function almost as a single organism; in most cases the resulting organism differs greatly from the individual components. Lichenization is a common mode of nutrition; around 20% of fungi—between 17,500 and 20,000 described species—are lichenized. Characteristics common to most lichens include obtaining organic carbon by photosynthesis, slow growth, small size, long life, long-lasting (seasonal) vegetative reproductive structures, mineral nutrition obtained largely from airborne sources, and greater tolerance of desiccation than most other photosynthetic organisms in the same habitat.

With insects

Many insects also engage in mutualistic relationships with fungi. Several groups of ants cultivate fungi in the order Agaricales as their primary food source, while ambrosia beetles cultivate various species of fungi in the bark of trees that they infest. Similarly, females of several wood wasp species (genus *Sirex*) inject their eggs together with spores of the wood-rotting fungus *Amylostereum areolatum* into the sapwood of pine trees; the growth of the fungus provides ideal nutritional conditions for the development of the wasp larvae. Termites on the African savannah are also known to cultivate fungi, and yeasts of the genera *Candida* and *Lachancea* inhabit the gut of a wide range of insects, including neuropterans, beetles, and cockroaches; it is not known whether these fungi benefit their hosts.

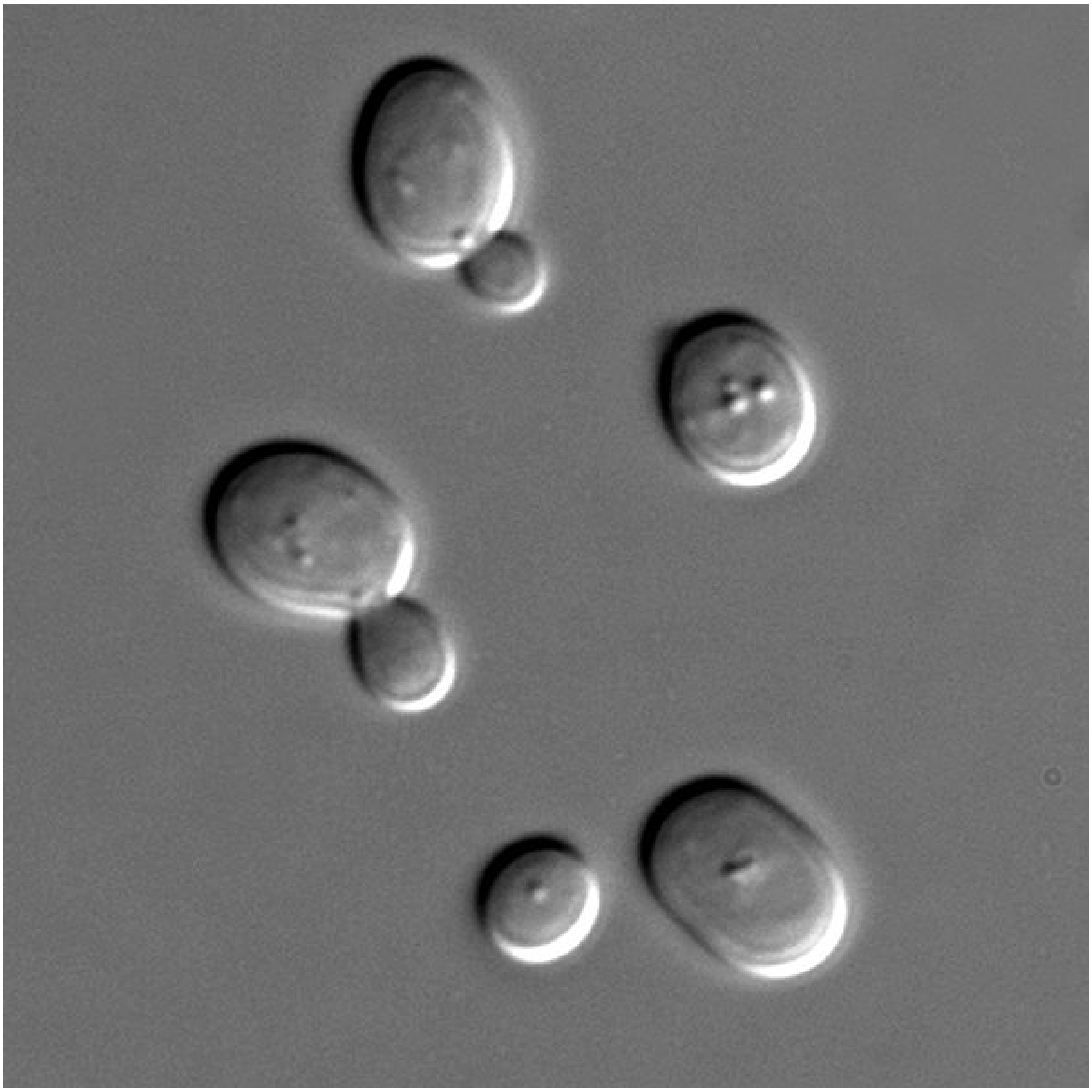
As pathogens and parasites

The plant pathogen *Aecidium magellanicum* causes calafate rust, seen here on a *Berberis* shrub in Chile.

Many fungi are parasites on plants, animals (including humans), and other fungi. Serious pathogens of many cultivated plants causing extensive damage and losses to agriculture and forestry include the rice blast fungus *Magnaporthe oryzae*, tree pathogens such as *Ophiostoma ulmi* and *Ophiostoma novo-ulmi* causing Dutch elm disease, and *Cryphonectria parasitica* responsible for chestnut blight, and plant pathogens in the genera *Fusarium*, *Ustilago*, *Alternaria*, and *Cochliobolus*. Some carnivorous fungi, like *Paecilomyces lilacinus*, are predators of nematodes, which they capture using an array of specialized structures such as constricting rings or adhesive nets.

Some fungi can cause serious diseases in humans, several of which may be fatal if untreated. These include aspergilloses, candidoses, coccidioidomycosis, cryptococcosis, histoplasmosis, mycetomas, and paracoccidioidomycosis. Furthermore, persons with immuno-deficiencies are particularly susceptible to disease by genera such as *Aspergillus*, *Candida*, *Cryptoccocus*, *Histoplasma*, and *Pneumocystis*. Other fungi can attack eyes, nails, hair, and especially skin, the so-called dermatophytic and keratinophilic fungi, and cause local infections such as ringworm and athlete's foot. Fungal spores are also a cause of allergies, and fungi from different taxonomic groups can evoke allergic reactions.

Human use



Saccharomyces cerevisiae cells shown with DIC microscopy.

The human use of fungi for food preparation or preservation and other purposes is extensive and has a long history. Mushroom farming and mushroom gathering are large industries in many countries. The study of the historical uses and sociological impact of fungi is known as ethnomycology. Because of the capacity of this group to produce an enormous range of natural products with antimicrobial or other biological activities, many species have long been used or are being developed for industrial production of antibiotics, vitamins, and anti-cancer and cholesterol-lowering drugs. More recently, methods have been developed for genetic engineering of fungi, enabling metabolic engineering of fungal species. For example, genetic modification of yeast species—which are easy to grow at fast rates in large fermentation vessels—has opened up ways of pharmaceutical production that are potentially more efficient than production by the original source organisms.

Drugs

Many species produce metabolites that are major sources of pharmacologically active drugs. Particularly important are the antibiotics, including the penicillins, a structurally related group of β-lactam antibiotics that are synthesized from small peptides. Although naturally occurring penicillins such as penicillin G (produced by *Penicillium chrysogenum*) have a relatively narrow spectrum of biological activity, a wide range of other penicillins can be produced by chemical modification of the natural penicillins. Modern penicillins are semisynthetic compounds, obtained initially from fermentation cultures, but then structurally altered for specific desirable properties. Other antibiotics produced by fungi include: ciclosporin, commonly used as an immunosuppressant during transplant surgery; and fusidic acid, used to help control infection from methicillin-resistant *Staphylococcus aureus* bacteria. Widespread use of these antibiotics for the treatment of bacterial diseases, such as tuberculosis, syphilis, leprosy, and many others began in the early 20th century and continues to play a major part in anti-bacterial chemotherapy. In nature, antibiotics of fungal or bacterial origin appear to play a dual role: at high concentrations they act as chemical defense against competition with other microorganisms in species-rich environments, such as the rhizosphere, and at low concentrations as quorum-sensing molecules for intra- or interspecies signaling.

Other drugs produced by fungi include griseofulvin isolated from *Penicillium griseofulvum*, used to treat fungal infections, and statins (HMG-CoA reductase inhibitors), used to inhibit cholesterol synthesis. Examples of statins found in fungi include mevastatin from *Penicillium citrinum* and lovastatin from *Aspergillus terreus* and the oyster mushroom.

Cultured foods

Baker's yeast or *Saccharomyces cerevisiae*, a single-celled fungus, is used to make bread and other wheat-based products, such as pizza dough and dumplings. Yeast species of the genus *Saccharomyces* are also used to produce alcoholic beverages through fermentation. Shoyu koji mold (*Aspergillus oryzae*) is an essential ingredient in brewing Shoyu (soy sauce) and sake, and the preparation of miso, while *Rhizopus* species are used for making tempeh. Several of these fungi are domesticated species that were bred or selected according to their capacity to ferment food without producing harmful mycotoxins (see below), which are produced by very closely related *Aspergilli*. Quorn, a meat substitute, is made from *Fusarium venenatum*.

Medicinal use

The medicinal fungi *Ganoderma lucidum* (Top) and *Cordyceps sinensis* (Bottom)

Certain mushrooms enjoy usage as therapeutics in folk medicines, such as Traditional Chinese medicine. Notable medicinal mushrooms with a well-documented history of use include *Agaricus subrufescens*, *Ganoderma lucidum*, and *Cordyceps sinensis*. Research has identified compounds produced by these and other fungi that have inhibitory biological effects against viruses and cancer cells. Specific metabolites, such as polysaccharide-K, ergotamine, and β-lactam antibiotics, are routinely used in clinical medicine. The shiitake mushroom is a source of lentinan, a clinical drug approved for use in cancer treatments in several countries, including Japan. In Europe and Japan, polysaccharide-K (brand name Krestin), a chemical derived from *Trametes versicolor*, is an approved adjuvant for cancer therapy.

Edible and poisonous species

Amanita phalloides accounts for the majority of fatal mushroom poisonings worldwide.

Edible mushrooms are well-known examples of fungi. Many are commercially raised, but others must be harvested from the wild. *Agaricus bisporus*, sold as button mushrooms when small or Portobello mushrooms when larger, is a commonly eaten species, used in salads, soups, and many other dishes. Many Asian fungi are commercially grown and have increased in popularity in the West. They are often available fresh in grocery stores and markets, including straw mushrooms (*Volvariella volvacea*), oyster mushrooms (*Pleurotus ostreatus*), shiitakes (*Lentinula edodes*), and enokitake (*Flammulina* spp.).

There are many more mushroom species that are harvested from the wild for personal consumption or commercial sale. Milk mushrooms, morels, chanterelles, truffles, black trumpets, and *porcini* mushrooms (*Boletus edulis*) (also known as king boletes) demand a high price on the market. They are often used in gourmet dishes.

Certain types of cheeses require inoculation of milk curds with fungal species that impart a unique flavor and texture to the cheese. Examples include the blue color in cheeses such as Stilton or Roquefort, which are made by inoculation with *Penicillium roqueforti*. Molds used in cheese production are non-toxic and are thus safe for human consumption; however, mycotoxins (e.g., aflatoxins, roquefortine C, patulin, or others) may accumulate because of growth of other fungi during cheese ripening or storage.

Stilton cheese veined with *Penicillium roqueforti*

Many mushroom species are poisonous to humans, with toxicities ranging from slight digestive problems or allergic reactions as well as hallucinations to severe organ failures and death. Genera with mushrooms containing deadly toxins include *Conocybe*, *Galerina*, *Lepiota*, and most infamously, *Amanita*. The latter genus includes the destroying angel *(A. virosa)* and the death cap *(A. phalloides)*, the most common cause of deadly mushroom poisoning. The false morel (*Gyromitra esculenta*) is occasionally considered a delicacy when cooked, yet can be highly toxic when eaten raw. *Tricholoma equestre* was considered edible until being implicated in serious poisonings causing rhabdomyolysis. Fly agaric mushrooms (*Amanita muscaria*) also cause occasional non-fatal poisonings, mostly as a result of ingestion for use as a recreational drug for its hallucinogenic properties. Historically, fly agaric was used by different peoples in Europe and Asia and its present usage for religious or shamanic purposes is reported from some ethnic groups such as the Koryak people of north-eastern Siberia.

As it is difficult to accurately identify a safe mushroom without proper training and knowledge, it is often advised to assume that a wild mushroom is poisonous and not to consume it.

Pest control

Grasshoppers killed by *Beauveria bassiana*

In agriculture, fungi may be useful if they actively compete for nutrients and space with pathogenic microorganisms such as bacteria or other fungi via the competitive exclusion principle, or if they are parasites of these pathogens. For example, certain species may be used to eliminate or suppress the growth of harmful plant pathogens, such as insects, mites, weeds, nematodes and other fungi that cause diseases of important crop plants. This has generated strong interest in practical applications that use these fungi in the biological control of these agricultural pests. Entomopathogenic fungi can be used as biopesticides, as they actively kill insects. Examples that have been used as biological insecticides are *Beauveria bassiana*, *Metarhizium* spp, *Hirsutella* spp, *Paecilomyces* (*Isaria*) spp, and *Lecanicillium lecanii*. Endophytic fungi of grasses of the genus *Neotyphodium*, such as *N. coenophialum*, produce alkaloids that are toxic to a range of invertebrate and vertebrate herbivores. These alkaloids protect grass plants from herbivory, but several endophyte alkaloids can poison grazing animals, such as cattle and sheep. Infecting cultivars of pasture or forage grasses with *Neotyphodium* endophytes is one approach being used in grass breeding programs; the fungal strains are selected for producing only alkaloids that increase resistance to herbivores such as insects, while being non-toxic to livestock.

Bioremediation

Certain fungi, in particular "white rot" fungi, can degrade insecticides, herbicides, pentachlorophenol, creosote, coal tars, and heavy fuels and turn them into carbon dioxide, water, and basic elements. Fungi have been shown to biomineralize uranium oxides, suggesting they may have application in the bioremediation of radioactively polluted sites.

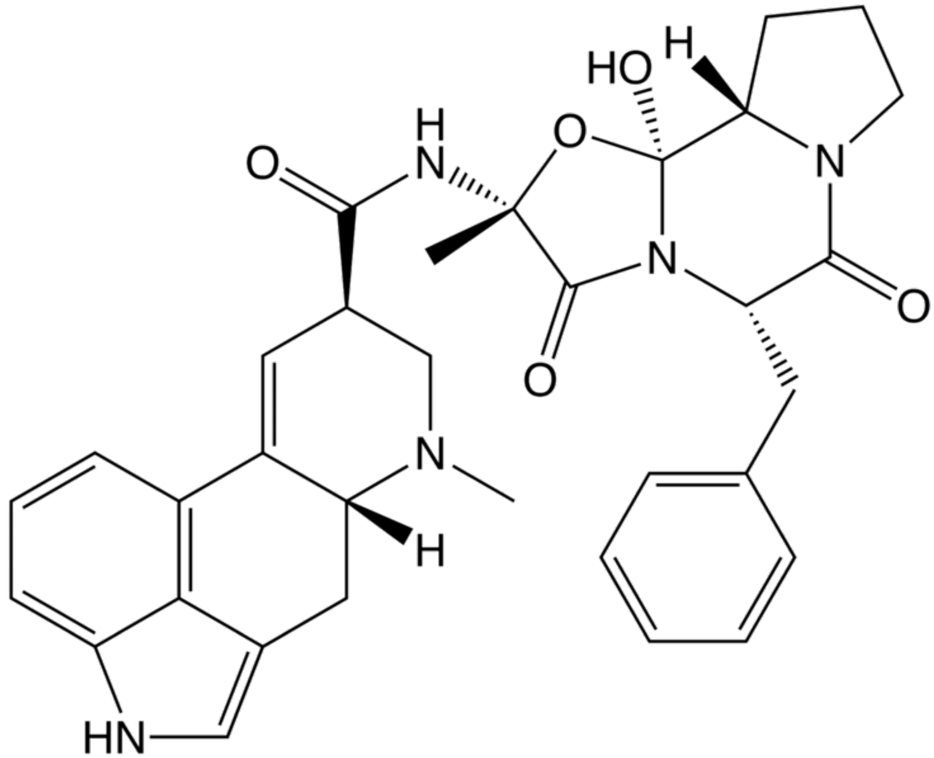
Model organisms

Several pivotal discoveries in biology were made by researchers using fungi as model organisms, that is, fungi that grow and sexually reproduce rapidly in the laboratory. For example, the one gene-one enzyme hypothesis was formulated by scientists who used the bread mold *Neurospora crassa* to test their biochemical theories. Other important model fungi are *Aspergillus nidulans* and the yeasts, *Saccaromyces cerevisiae* and *Schizosaccharomyces pombe*, each of which has a long history of use to investigate issues in eukaryotic cell biology and genetics, such as cell cycle regulation, chromatin structure, and gene regulation. Other fungal models have more recently emerged that each address specific biological questions relevant to medicine, plant pathology, and industrial uses; examples include *Candida albicans*, a dimorphic, opportunistic human pathogen, *Magnaporthe grisea*, a plant pathogen, and *Pichia pastoris*, a yeast widely used for eukaryotic protein expression.

Others

Fungi are used extensively to produce industrial chemicals like citric, gluconic, lactic, and malic acids, and industrial enzymes, such as lipases used in biological detergents, cellulases used in making cellulosic ethanol and stonewashed jeans, and amylases, invertases, proteases and xylanases. Several species, most notably *Psilocybin mushrooms* (colloquially known as *magic mushrooms*), are ingested for their psychedelic properties, both recreationally and religiously.

Mycotoxins



Ergotamine, a major mycotoxin produced by *Claviceps* species, which if ingested can cause gangrene, convulsions, and hallucinations

Many fungi produce biologically active compounds, several of which are toxic to animals or plants and are therefore called mycotoxins. Of particular relevance to humans are mycotoxins produced by molds causing food spoilage, and poisonous mushrooms (see above). Particularly infamous are the lethal amatoxins in some *Amanita* mushrooms, and ergot alkaloids, which have a long history of causing serious epidemics of ergotism (St Anthony's Fire) in people consuming rye or related cereals contaminated with sclerotia of the ergot fungus, *Claviceps purpurea*. Other notable mycotoxins include the aflatoxins, which are insidious liver toxins and highly carcinogenic metabolites produced by certain *Aspergillus* species often growing in or on grains and nuts consumed by humans, ochratoxins, patulin, and trichothecenes (e.g., T-2 mycotoxin) and fumonisins, which have significant impact on human food supplies or animal livestock.

Mycotoxins are secondary metabolites (or natural products), and research has established the existence of biochemical pathways solely for the purpose of producing mycotoxins and other natural products in fungi. Mycotoxins may provide fitness benefits in terms of physiological adaptation, competition with other microbes and fungi, and protection from consumption (fungivory).

Mycology

Mycology is the branch of biology concerned with the systematic study of fungi, including their genetic and biochemical properties, their taxonomy, and their use to humans as a source of medicine, food, and psychotropic substances consumed for religious purposes, as well as their dangers, such as poisoning or infection. The field of phytopathology, the study of plant diseases, is closely related because many plant pathogens are fungi.

Use of fungi by humans dates back to prehistory; Ötzi the Iceman, a well-preserved mummy of a 5,300 year old Neolithic man found frozen in the Austrian Alps, carried two species of polypore mushrooms that may have been used as tinder (*Fomes fomentarius*), or for medicinal purposes (*Piptoporus betulinus*). Ancient peoples have used fungi as food sources–often unknowingly–for millennia, in the preparation of leavened bread and fermented juices. Some of the oldest written records contain references to the destruction of crops that were probably caused by pathogenic fungi.

History

Mycology is a relatively new science that became systematic after the development of the microscope in the 16th century. Although fungal spores were first observed by Giambattista della Porta in 1588, the seminal work in the development of mycology is considered to be the publication of Pier Antonio Micheli's 1729 work *Nova plantarum genera*. Micheli not only observed spores, but showed that under the proper conditions, they could be induced into growing into the same species of fungi from which they originated. Extending the use of the binomial system of nomenclature introduced by Carl Linnaeus in his *Species plantarum* (1753), the Dutch Christian Hendrik Persoon (1761–1836) established the first classification of mushrooms with such skill so as to be considered a founder of modern mycology. Later, Elias Magnus Fries (1794–1878) further elaborated the classification of fungi, using spore color and various microscopic characteristics, methods still used by taxonomists today. Other notable early contributors to mycology in the 17th–19th and early 20th centuries include Miles Joseph Berkeley, August Carl Joseph Corda, Anton de Bary, the brothers Louis René and Charles Tulasne, Arthur H. R. Buller, Curtis G. Lloyd, and Pier Andrea Saccardo. The 20th century has seen a modernization of mycology that has come from advances in biochemistry, genetics, molecular biology, and biotechnology. The use of DNA sequencing technologies and phylogenetic analysis has provided new insights into fungal relationships and biodiversity, and has challenged traditional morphology-based groupings in fungal taxonomy.

Chapter- 3

Edible Mushroom

White mushrooms ready for cooking. While common, they are just one of the many types of mushrooms cultivated and eaten.

Picked edible mushrooms in a basket

Edible mushrooms are the fleshy and edible fruiting bodies of several species of fungi. They belong to the macrofungi, because their fruiting structures are large enough to be seen with the naked eye. They can appear either below ground (hypogeous) or above ground (epigous) where they may be picked by hand. Edibility may be defined by criteria that include absence of poisonous effects on humans and desirable taste and aroma. By some accounts, less than 10% of all mushrooms may be edible.

Edible mushrooms are consumed by humans for their nutritional and occasionally medicinal value as comestibles. Mushrooms consumed for health reasons are known as medicinal mushrooms. While hallucinogenic mushrooms (e.g. Psilocybin mushrooms) are occasionally consumed for recreational or religious purposes, they can produce severe nausea and disorientation, and are therefore not commonly considered edible mushrooms.

Edible mushrooms include many fungal species that are either harvested wild or cultivated. Easily cultivatable and common wild mushrooms are often available in markets, and those that are more difficult to obtain (such as the prized truffle and matsutake) may be collected on a smaller scale by private gatherers. Some preparations may render certain poisonous mushrooms fit for consumption.

Before assuming that any wild mushroom is edible, it should be identified. Proper identification of a species is the only safe way to ensure edibility. Some mushrooms that are edible for most people can cause allergic reactions in some individuals, and old or improperly stored specimens can cause food poisoning. Deadly poisonous mushrooms that are frequently confused with edible mushrooms and responsible for many fatal poisonings include several species of the *Amanita* genus, in particular, *Amanita phalloides*, the *death cap*.

History of mushroom use

Mycophagy, the act of consuming mushrooms, dates to ancient times. Edible mushroom species have been found in association with 13,000 year old ruins in Chile, but the first reliable evidence of mushroom consumption dates to several hundred years BC in China. The Chinese value mushrooms for medicinal properties as well as for food. Ancient Romans and Greeks ate mushrooms, particularly the upper class. The Roman Caesars would have a food taster taste the mushrooms before the Caesar to make sure they were safe.

Mushrooms are also easily preserved, and historically have provided additional nutrition over winter.

Many cultures around the world have either used or continue to use psilocybin mushrooms for spiritual purposes as well as medicinal mushrooms in folk medicine. Mushroom cultivation reached the United States in the late 1800s with imported spores from Mexico.

Current culinary use

A fraction of the many fungi consumed by humans are currently cultivated and sold commercially. Commercial cultivation is important ecologically, as there have been concerns of depletion of larger fungi such as chanterelles in Europe, possibly because the group has grown so popular yet remains a challenge to cultivate.

Commercially cultivated

Commercial cultivated Asian edible mushroom species. Clockwise from left, enokitake, buna-shimeji, bunapi-shimeji, king oyster mushroom and shiitake.

Mushroom cultivation has a long history, with over twenty species commercially cultivated. Mushrooms are cultivated in at least 60 countries with China, the United States, Netherlands, France and Poland being the top five producers in 2000.

Commercially harvested wild edibles

Chanterelles in the wild

A collection of Boletus edulis of varying ages

Hericium coralloides

Clitocybe nuda

Some species are difficult to cultivate; others (particularly mycorrhizal species) have not yet been successfully cultivated. Some of these species are harvested from the wild, and can be found in markets. When in season they can be purchased fresh, and many species are sold dried as well. The following species are commonly harvested from the wild:

- *Boletus edulis* or edible Boletus, native to Europe, known in Italian as Fungo Porcino (plural 'porcini') (Pig mushroom), in German as Steinpilz (Stone mushroom), in Russian as "white mushroom", in Albanian as (Wolf mushroom) and in French the *cep*. It also known as the king bolete, and is renowned for its delicious flavor. It is sought after worldwide, and can be found in a variety of culinary dishes.
- *Cantharellus cibarius* (The chanterelle), The yellow chanterelle is one of the best and most easily recognizable mushrooms, and can be found in Asia, Europe, North America and Australia. There are poisonous mushrooms which resemble it,

though these can be confidently distinguished if one is familiar with the chanterelle's identifying features.

- *Cantharellus tubaeformis*, the tube chanterelle or yellow-leg
- *Clitocybe nuda* - Blewit (or Blewitt)
- *Cortinarius caperatus* the Gypsy mushroom (recently moved from genus *Rozites*)
- *Craterellus cornucopioides* - Trompette du Mort or Horn of Plenty
- *Grifola frondosa*, known in Japan as *maitake* (also "hen of the woods" or "sheep's head"); a large, hearty mushroom commonly found on or near stumps and bases of oak trees, and believed to have Macrolepiota procera properties.
- *Gyromitra esculenta* this "False morel" is prized by the Finns. This mushroom is deadly poisonous if eaten raw, but highly regarded when parboiled (see below).
- *Hericium erinaceus*, a tooth fungus; also called "lion's mane mushroom."
- *Hydnum repandum* Sweet tooth fungus, hedgehog mushroom, urchin of the woods
- *Lactarius deliciosus* Saffron milk cap - Consumed around the world and prized in Russia
- *Morchella* species, (morel family), morels belong to the ascomycete grouping of fungi. They are usually found in open scrub, woodland or open ground in late spring. When collecting this fungus, care must be taken to distinguish it from the poisonous false morels, including *Gyromitra esculenta*.
    - *Morchella conica var. deliciosa*
    - *Morchella esculenta var. rotunda*
- *Tricholoma matsutake* the Matsutake, a mushroom highly prized in Japanese cuisine.
- *Tuber* species, (the truffle), Truffles have long eluded the modern techniques of domestication known as *trufficulture*. Although the field of trufficulture has greatly expanded since its inception in 1808, several species still remain uncultivated. Domesticated truffles include
    - *Tuber borchii*
    - *Tuber brumale*
    - *Tuber indicum* - Chinese black truffle
    - *Tuber macrosporum* - White truffle
    - *Tuber mesentericum* - The Bagnoli truffle
    - *Tuber uncinatum* - Black summer truffle

Other edible wild species

Many wild species are consumed around the world. The species which can be identified "in the field" (without use of special chemistry or a microscope) and therefore safely eaten vary widely from country to country, even from region to region. This list is a sampling of lesser-known species that are reportedly edible.

Lactarius salmonicolor

- *Amanita caesarea* (Caesar's Mushroom)
- *Armillaria mellea*
- *Boletus badius*
- *Boletus elegans*
- *Chroogomphus rutilus* (pine-spikes or spike-caps)
- *Calvatia gigantea* (Giant Puffball)
- *Clavariaceae* species (coral fungus family)
- *Clavulinaceae* species (coral fungus family)
- *Coprinus comatus*, the Shaggy mane. Must be cooked as soon as possible after harvesting or the caps will first turn dark and unappetizing, then deliquesce and turn to ink. Not found in markets for this reason.
- *Cortinarius variecolor*
- *Fistulina hepatica* (beefsteak polypore or the ox tongue)
- *Hygrophorus chrysodon*

Auricularia auricula-judae

- *Lactarius salmonicolor*
- *Lactarius subdulcis* (mild milkcap)
- *Lactarius volemus*
- *Laetiporous sulphureus* (Sulphur shelf). Also known by names such as the "chicken mushroom", "chicken fungus", sulphur shelf is a distinct bracket fungus popular among mushroom hunters.
- *Leccinum aurantiacum* (Red-capped scaber stalk)
- *Leccinum scabrum* (Birch bolete)
- *Lepiota procera*
- *Macrolepiota procera* Parasol Mushroom - Globally, it is widespread in temperate regions
- *Polyporus squamosus* (Dryad's saddle and Pheasant's back mushroom)
- *Polyporus sulphureus*
- *Polyporus mylittae*
- *Ramariaceae* species (coral fungus family)
- *Rhizopogon luteolus*
- *Russula*, some members of this genus are edible.
- *Sparassis crispa*. Also known as "cauliflower mushroom".
- *Suillus bovinus*
- *Suillus luteus*
- *Suillus tomentosus*
- *Tricholoma terreum*

Conditionally edible species

Amanita muscaria, a conditionally edible species

There are a number of fungi that are considered choice by some and toxic by others. In some cases, proper preparation can remove some or all of the toxins.

- *Amanita muscaria* is edible if parboiled to leach out toxins. Fresh mushrooms cause vomiting, twitching, drowsiness, and hallucinations due to the presence of ibotenic acid.
- *Coprinopsis atramentaria* is edible without special preparation. However, consumption with alcohol is toxic due to the presence of coprine. Some other *Coprinus* spp. share this property.
- *Gyromitra esculenta* is eaten by some after it has been parboiled; however, mycologists do not recommend it. Raw *Gyromitra* are toxic due to the presence of gyromitrin, and it is not known if all of the toxin can be removed by parboiling.
- *Lactarius spp.* - Apart from *Lactarius deliciosus* which is universally considered edible, other *Lactarius spp.* that are considered toxic elsewhere in the world are eaten in Russia after pickling or parboiling.
- *Verpa bohemica* - Considered choice by some, it even can be found for sale as a "morel", but cases of toxicity have been reported. Verpas contain toxins similar to gyromitrin and similar precautions apply.

Current medical use

The most well known "medicinal mushroom", Reishi

Many species of medicinal mushrooms have been used in folk medicine for thousands of years. The use of medicinal mushrooms in folk medicine is best documented in the East. Medicinal mushrooms are now the subject of study for many ethnobotanists and medical researchers. The ability of some mushrooms to inhibit tumor growth and enhance aspects of the immune system has been a subject of research for approximately 50 years. International mushroom research continues today, with a focus on mushrooms that may have hypoglycemic activity, anti-cancer activity, anti-pathogenic activity, and immune system enhancing activity. Recent research has found that the oyster mushroom naturally contains the cholesterol drug lovastatin, and that mushrooms produce large amounts of vitamin D when exposed to UV light, Below is a list of edible mushrooms that are best known for their medicinal properties.

- *Ganoderma* Mushrooms (Reishi)
- *Trametes versicolor* (Turkey tail)
- *Grifola frondosa* (Maitake)
- *Pleurotus ostreatus* (oyster mushroom)
- *Agaricus bisporus* (common mushroom)
- *Agaricus subrufescens* (*Agaricus blazei*)
- *Lentinula edodes* (Shiitake)
- *Inonotus obliquus* (chaga mushroom)

Preparing wild edibles

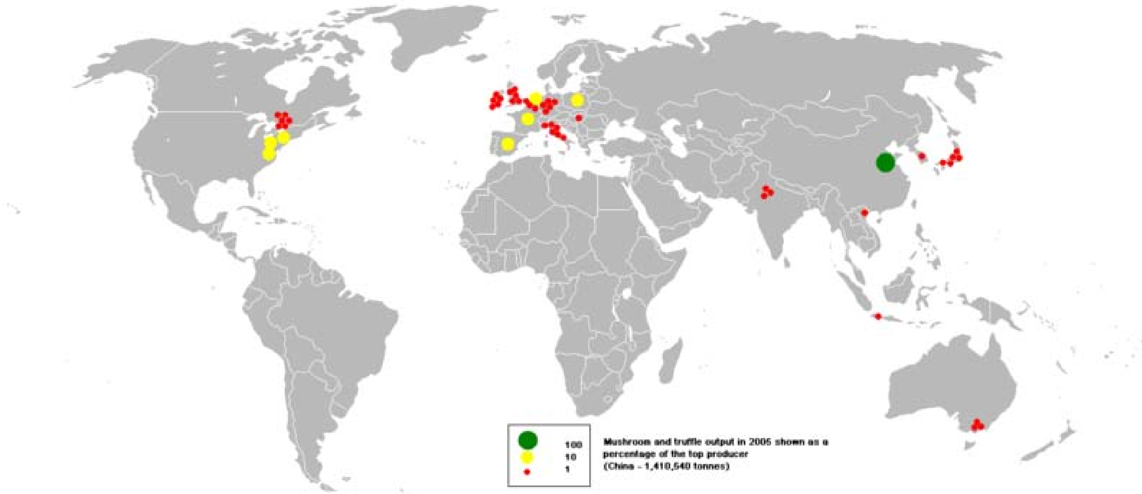
A collection of dried mushrooms

Some wild species are toxic, or at least indigestible, when raw. As a rule all wild mushroom species should be cooked thoroughly before eating. Many species can be dried and re-hydrated by pouring boiling water over the dried mushrooms and letting them steep for approximately 30 minutes. The soaking liquid can be used for cooking as well, provided that any dirt at the bottom of the container is discarded.

One recipe for Auricularia auricula-judae is to collect it while still soft, wash it thoroughly and cut it into thin slices. The prepared slices should be stewed in stock or milk for around three-quarters of an hour, and then served with plenty of pepper. The result is crispy and not unlike seaweed.

The difficult task of identifying mushrooms in the wild, for culinary or recreational purposes, can produce severe poisoning.

Production



Mushroom and Truffle output in 2005

Top ten mushroom and truffle producing countries in 2008

Country	Output in tonnes	Percentage of total world output
China	1,608,219	45.89
United States	363,560	10.40
Netherlands	240,000	6.86
Poland	180,000	5.15
France	150,450	4.30
Spain	131,974	3.77
Italy	100,000	2.86
Canada	86,946	2.49
Ireland	75,000	2.14
Japan	67,000	1.92
WORLD	3,497,290	100.00

Vitamin D

Mushrooms contain large amounts of vitamin D when exposed to UV light. Mushrooms that have been exposed to UV light are the only natural vegan food source of vitamin D.

Chapter- 4

Mycotoxin

A **mycotoxin** (from Greek μύκης (mykes, mukos) "fungus" and Latin (toxicum) "poison") is a toxic secondary metabolite produced by organisms of the fungus kingdom, commonly known as molds. The term 'mycotoxin' is usually reserved for the toxic chemical products produced by fungi that readily colonize crops. Most fungi are aerobic (use oxygen) and are found almost everywhere in extremely small quantities due to the minute size of their spores. They consume organic matter wherever humidity and temperature are sufficient. One mold species may produce many different mycotoxins and/or the same mycotoxin as another species.

Where conditions are right, fungi proliferate into colonies and mycotoxin levels become high. The reason for the production of mycotoxins is not yet known; they are neither necessary for growth nor the development of the fungi. Because mycotoxins weaken the receiving host, the fungus may use them as a strategy to better the environment for further fungal proliferation. The production of toxins depends on the surrounding intrinsic and extrinsic environments and the toxins vary greatly in their severity, depending on the organism infected and its susceptibility, metabolism, and defense mechanisms. Some of the health effects found in animals and humans include death, identifiable diseases or health problems, weakened immune systems without specificity to a toxin, and as allergens or irritants. Some mycotoxins are harmful to other micro-organisms such as other fungi or even bacteria; penicillin is one example.

Mycotoxins can appear in the food chain as a result of fungal infection of crops, either by being eaten directly by humans, or by being used as livestock feed. Mycotoxins greatly resist decomposition or being broken down in digestion, so they remain in the food chain in meat and dairy products. Even temperature treatments, such as cooking and freezing, do not destroy mycotoxins.

Although various wild mushrooms contain an assortment of poisons that are definitely fungal metabolites causing noteworthy health problems for humans, they are rather arbitrarily excluded from discussions of mycotoxicology. In such cases the distinction is based on the size of the producing fungus and human intention. Mycotoxin exposure is almost always accidental whereas with mushrooms improper identification and ingestion causing mushroom poisoning is commonly the case. Ingestion of misidentified mushrooms containing mycotoxins may result in hallucinations. The cyclopeptide-produced *Amanita phalloide* is well known for its toxic potential and is responsible for approximately 90% of all mushroom fatalities. The other primary mycotoxin groups found in mushrooms include: orellanine, monomethylhydrazine, disulfiram-like, hallucinogenic indoles, muscarinic, isoxazole, and gastrointestinal (GI)-specific irritants.

Many international agencies are trying to achieve universal standardization of regulatory limits for mycotoxins. Currently, over 100 countries have regulations regarding mycotoxins in the feed industry, in which 13 mycotoxins or groups of mycotoxins are of concern. The process of assessing a need for mycotoxin regulation includes a wide array of in-laboratory testing which includes extracting, clean-up and separation techniques. Most official regulations and control methods are based on high-performance liquid techniques (e.g., HPLC) through international bodies. It is implied that any regulations regarding these toxins will be in co-ordinance with any other countries with which a trade agreement exists. Many of the standards for the method performance analysis for mycotoxins is set by the European Committee for Standardization (CEN). However, one must take note that scientific risk assessment in commonly influenced by culture and politics which, in turn, will affect trade regulations of mycotoxins.

Food-based mycotoxins were studied extensively worldwide throughout the 20th century. In Europe, statutory levels of a range of mycotoxins permitted in food and animal feed are set by a range of European directives and Commission regulations. The U.S. Food and Drug Administration has regulated and enforced limits on concentrations of mycotoxins in foods and feed industries since 1985. It is through various compliance programs that the FDA monitors these industries to guarantee that mycotoxins are kept at a practical level. These compliance programs sample food products including peanuts and peanut products, tree nuts, corn and corn products, cottonseed, and milk. There is still a lack of sufficient surveillance data on some mycotoxins that occur in the U.S. which is largely due to the lack of reliable analytical methods.

Major groups

Aflatoxins are a type of mycotoxin produced by *Aspergillus* species of fungi, such as *A. flavus* and *A. parasiticus*. The umbrella term aflatoxin refers to four different types of mycotoxins produced, which are B1, B2, G1, and G2. Aflatoxin B_1, the most toxic, is a potent carcinogen and has been directly correlated to adverse health effects, such as liver cancer, in many animal species. Aflatoxins are largely associated with commodities produced in the tropics and subtropics, such as cotton, peanuts, spices, pistachios and maize.

Ochratoxin is a mycotoxin that comes in three secondary metabolite forms, A, B, and C. All are produced by *Penicillium* and *Aspergillus* species. The three forms differ in that Ochratoxin B (OTB) is a nonchlorinated form of Ochratoxin A (OTA) and that Ochratoxin C (OTC) is an ethyl ester form Ochatoxin A. *Aspergillus ochraceus* is found as a contaminant of a wide range of commodities including beverages such as beer and wine. *Aspergillus carbonarius* is the main species found on vine fruit, which releases its toxin during the juice making process. OTA has been labeled as a carcinogen and a nephrotoxin, and has been linked to tumors in the human urinary tract, although research in humans is limited by confounding factors.

Citrinin is a toxin that was first isolated from *Penicillium citrinum*, but has been identified in over a dozen species of *Penicillium* and several species of *Aspergillus*. Some of these species are used to produce human foodstuffs such as cheese (*Penicillium camemberti*), sake, miso, and soy sauce (*Aspergillus oryzae*). Citrinin is associated with yellow rice disease in Japan and acts as a nephrotoxin in all animal species tested. Although it is associated with many human foods (wheat, rice, corn, barley, oats, rye, and food colored with Monascus pigment) its full significance for human health is unknown. Citrinin can also act synergistically with Ochratoxin A to depress RNA synthesis in murine kidneys.

Ergot Alkaloids are compounds produced as a toxic mixture of alkaloids in the sclerotia of species of *Claviceps*, which are common pathogens of various grass species. The ingestion of ergot sclerotia from infected cereals, commonly in the form of bread produced from contaminated flour, cause ergotism the human disease historically known as St. Anthony's Fire. There are two forms of ergotism gangrenous affecting blood supply to extremities and convulsive which affects the central nervous system. Modern methods of grain cleaning have significantly reduced ergotism as a human disease, however it is still an important veterinarian problem. Ergot alkaloids have been used pharmaceutically.

Patulin is a toxin produced by the *P. expansum*, *Aspergillus*, *Penicillium*, and *Paecilomyces* fungal species. *P. expansum* is especially associated with a range of moldy fruits and vegetables, in particular rotting apples and figs. It is destroyed by the fermentation process and so is not found in apple beverages, such as cider. Although patulin has not been shown to be carcinogenic, it has been reported to damage the immune system in animals. In 2004, the European Community set limits to the concentrations of patulin in food products. They currently stand at 50 μg/kg in all fruit juice concentrations, at 25 μg/kg in solid apple products used for direct consumption, and at 10 μg/kg for children's apple products, including apple juice.

Fusarium toxins are produced by over 50 species of *Fusarium* and have a history of infecting the grain of developing cereals such as wheat and maize. They include a range of mycotoxins, such as: the **fumonisins**, which affect the nervous systems of horses and may cause cancer in rodents; the **trichothecenes**, which are most strongly associated with chronic and fatal toxic effects in animals and humans; and **zearalenone**, which is not correlated to any fatal toxic effects in animals or humans. Some of the other major types of *Fusarium* toxins include: beauvercin and enniatins, butenolide, equisetin, and fusarins.

Binding agents and deactivators

In the feed and food industry it has become common practice to add mycotoxin binding agents such as Montmorillonite or bentonite clay in order to affectively adsorb the mycotoxins. To reverse the adverse effects of mycotoxins, the following criteria are used to evaluate the functionality of any binding additive:

- Efficacy of active component verified by scientific data
- A low effective inclusion rate
- Stability over a wide pH range
- High capacity to adsorb high concentrations of mycotoxins
- High affinity to adsorb low concentrations of mycotoxins
- Affirmation of chemical interaction between mycotoxin and adsorbent
- Proven *in vivo* data with all major mycotoxins
- Non-toxic, environmentally friendly component

Since not all mycotoxins can be bound to such agents, the latest approach to mycotoxin control is mycotoxin deactivation. By means of enzymes (esterase, epoxidase), yeast (*Trichosporon mycotoxinvorans*) or bacterial strains (Eubacterium BBSH 797), mycotoxins can be reduced during pre-harvesting contamination. Other removal methods include physical separation, washing, milling, heat-treatment, radiation, extraction with solvents, and the use of chemical or biological agents. Irradiation methods have proven to be effective treatment against mold growth and toxin production.

In the indoor environment

Buildings are another source of mycotoxins and people living or working in areas with mold increase their chances of adverse health effects. Molds growing in buildings can be divided into three groups — Primary, Secondary, and Tertiary colonizers. Each group is categorized by the ability to grow at a certain water activity requirement. It has become difficult to identify mycotoxins production by indoor molds for many variables, such as (i) they may be masked as derivatives (ii) they are poorly documented and (iii) the fact that they are likely to produce different metabolites on building materials. Some of the mycotoxins in the indoor environment are produced by Alternaria, Aspergillus (multiple forms), Penicillium, and Stachybotrys. Stachybotrys chartarum contains a higher number of mycotoxins than other molds grown in the indoor environment and has been associated with allergies and respiratory inflammation. The infestation of S. chartarum in buildings containing gypsum board, as well as on ceiling tiles, is very common and has recently become a more recognized problem. When gypsum board has been repeatedly introduced to moisture S. chartarum grows readily on its cellulose face. This stresses the importance of moisture controls and ventilation within residential homes and other buildings. The negative health effects of mycotoxins are a function of the concentration, the duration of exposure and the subject's sensitivities. The concentrations experienced in a normal home, office or school are often too low to trigger a health response in occupants.

In the 1990s, public concern over mycotoxins increased following multi-million dollar toxic mold settlements. The lawsuits took place after the Center for Disease Control (CDC) did a study in Cleveland Ohio and claimed that there was an association between mycotoxins from *Stachybotrys* spores and pulmonary hemorrhage in infants. However in 2000, based on internal and external reviews of their data, the CDC concluded that because of flaws in their methods the association was not proven. *Stachybotrys* spores in animal studies have been shown to cause lung hemorrhaging but only at very high concentrations.

One study by the Center of Integrative Toxicology at Michigan State University investigated the causes of Damp Building Related Illness (DBRI). They found that *Stachybotrys* is possibly an important contributing factor to DBRI. So far animal models indicate that airway exposure to *S. chartarum* can evoke allergic sensitization, inflammation, and cytotoxicity in the upper and lower respiratory tracts. Trichothecene toxicity appears to be an underlying cause of many these adverse effects. Recent findings indicate that lower doses (studies usually involve high doses) can cause these symptoms.

Some toxicologists have used the Concentration of No Toxicological Concern (CoNTC) measure to represent the airborne concentration of mycotoxins that are expected to cause no hazard to humans (exposed continuously throughout a 70–yr lifetime). The resulting data of several studies have thus far demonstrated that common exposures to airborne mycotoxins in the built indoor environment are below the CoNTC, however agricultural environments have potential to produce levels greater than the CoNTC.

Human health effects

Mycotoxicoses is the term used for poisoning associated with exposures to mycotoxins. The symptoms of a mycotoxicosis depend on the type of mycotoxin; the concentration and length of exposure; as well as age, health, and sex of the exposed individual. The synergistic effects associated with several other factors such as genetics, diet, and interactions with other toxics have been poorly studied. Therefore it is possible that vitamin deficiency, caloric deprivation, alcohol abuse, and infectious disease status can all have compounded effects with mycotoxins. In turn, mycotoxins have the potential for both acute and chronic health effects via ingestion, skin contact, and inhalation. These toxins can enter the blood stream and lymphatic system, they inhibit protein synthesis, damage macrophage systems, inhibit particle clearance of the lung, and increase sensitivity to bacterial endotoxin.

Notably Severe Cases of Aflatoxin Ingestion: In 2004 in Kenya 125 people died and nearly 200 others were treated after eating aflatoxin contaminated maize. The deaths were mainly associated with homegrown maize that had not been treated with fungicides or properly dried before storage. Due to food shortages at the time, farmers may have been harvesting maize earlier than normal to prevent thefts from their fields, so that the grain had not fully matured and was more susceptible to infection.

Chapter- 5

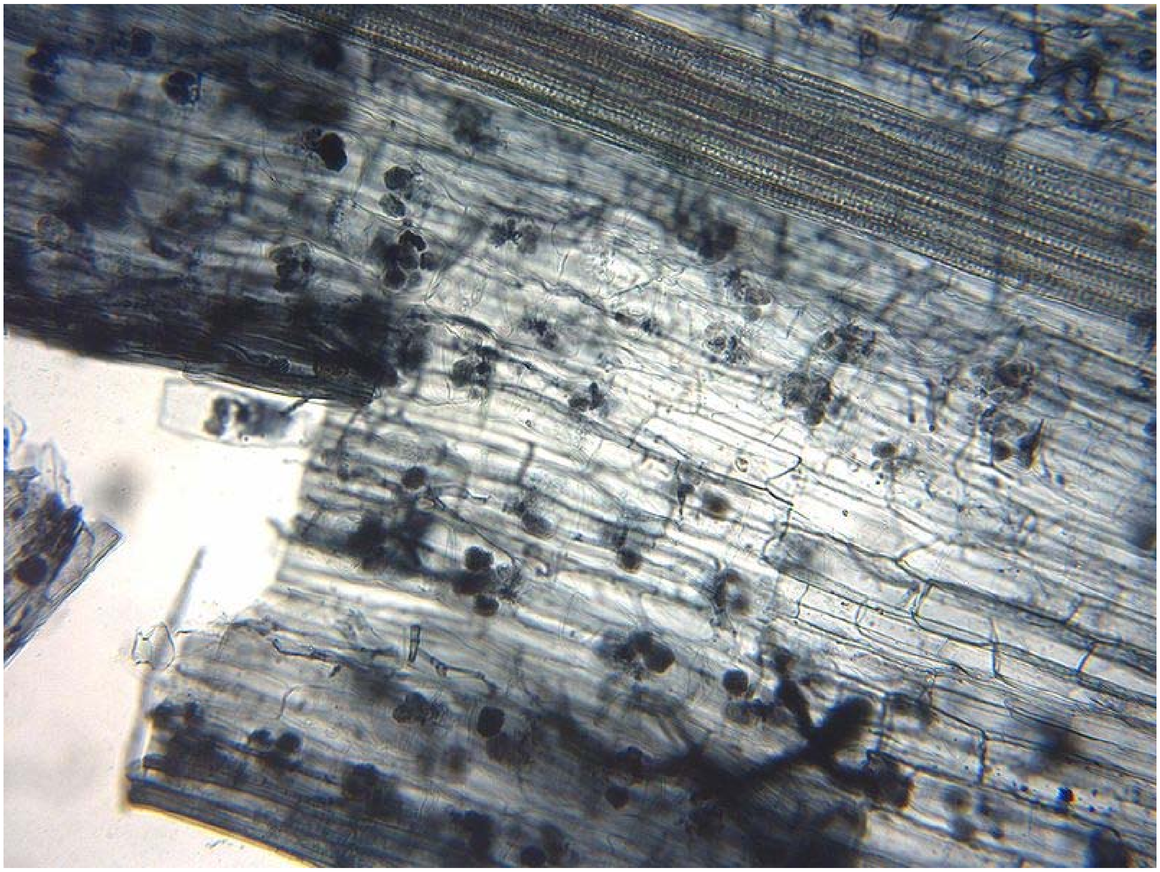
Arbuscular Mycorrhiza

An **arbuscular mycorrhiza** (plural **mycorrhizae** or **mycorrhizas**, aka *AM Fungi*) is a type of mycorrhiza in which the fungus penetrates the cortical cells of the roots of a vascular plant.

Arbuscular mycorrhizae (AMs) are characterized by the formation of unique structures such as arbuscules and vesicles by fungi of the phylum Glomeromycota (AM fungi). AM fungi (AMF) help plants to capture nutrients such as phosphorus and micronutrients from the soil. It is believed that the development of the arbuscular mycorrhizal symbiosis played a crucial role in the initial colonisation of land by plants and in the evolution of the vascular plants.

It has been said that it is quicker to list the plants that do not form mycorrhizae than those that do. This symbiosis is a highly evolved mutualistic relationship found between fungi and plants, the most prevalent plant symbiosis known, and AM is found in 80% of vascular plant families of today.

The tremendous advances in research on mycorrhizal physiology and ecology over the past 40 years have led to a greater understanding of the multiple roles of AMF in the ecosystem. This knowledge is applicable to human endeavors of ecosystem management, ecosystem restoration, and agriculture.



Flax root cortical cells containing paired arbuscules

Evolution of mycorrhizal symbiosis

Paleobiology

Both paleobiological and molecular evidence indicate that AM is an ancient symbiosis that originated at least 460 million years ago. AM symbiosis is ubiquitous among land plants, which suggests that mycorrhizae were present in the early ancestors of extant land plants. This positive association with plants may have facilitated the development of land plants.

The Rhynie chert of the lower Devonian has yielded fossils of the earliest land plants in which AM fungi have been observed. The fossilized plants containing mycorrhizal fungi were preserved in silica.

The Early Devonian saw the development of terrestrial flora. Plants of the Rhynie chert from the Lower Devonian (400 m.yrs ago) were found to contain structures resembling vesicles and spores of present *Glomus* species. Colonized fossil roots have been observed in *Aglaophyton major* and *Rhynia*, which are ancient plants possessing characteristics of vascular plants and bryophytes with primitive protostelic rhizomes.

Intraradical mycelium was observed in root intracellular spaces, and arbuscules were observed in the layer thin wall cells similar to palisade parenchyma. The fossil arbuscules appear very similar to those of existing AMF. The cells containing arbuscules have thickened walls, which are also observed in extant colonized cells.

Mycorrhizae from the Miocene exhibit a vesicular morphology closely resembling that of present *Glomerales*. The need for further evolution may have been lost due to the readily available food source provided by the plant host. However, it can be argued that the efficacy of signaling process is likely to have evolved, which could not be easily detected in the fossil record. A finetuning of the signaling processes would improve coordination and nutrient exchange between symbionts while increasing the fitness of both the fungi and the plant symbionts.

The nature of the relationship between plants and the ancestors of arbuscular mycorrhizal fungi is contentious. Two hypotheses are:

- Mycorrhizal symbiosis evolved from a parasitic interaction that developed in to a mutually beneficial relationship.
- Mycorrhizal fungi developed from saprobic fungi that became endosymbiotic.

Both saprotrophs and biotrophs were found in the Rhynie Chert, but there is little evidence to support either hypothesis.

There is some fossil evidence that suggests that the parasitic fungi did not kill the host cells immediately upon invasion, although a response to the invasion was observed in the host cells. This response may have evolved into the chemical signaling processes required for symbiosis.

In both cases, the symbiotic plant-fungi interaction is thought to have evolved from a relationship in which the fungi was taking nutrients from the plant into a symbiotic relationship where the plant and fungi exchange nutrients.

Molecular Evidence

Increased interest in mycorrhizal symbiosis and the rapid development of sophisticated molecular techniques has led to the rapid development of genetic evidence. Wang et al.performed an intensive investigation of three widely occurring plant genes that encode for a signal transduction cascade vital for communication with order Glomales fungal partners (DMI1, DMI3, IPD3). Sequences of these three genes were obtained from all major clades of modern land plants (including liverworts, the most basal group), and the maximum probability phylogeny of the three genes was in complete agreement with the current land plant phylogenies. These findings imply that the mycorrhizal genes must have been present in the common ancestor of land plants, and that these genes must have been vertically inherited since the colonization of land by plants.

Physiology

Presymbiosis

The development of AM fungi prior to root colonization, known as presymbiosis, consists of three stages: spore germination, hyphal growth, host recognition and appressorium formation.

Spores of the AM fungi are thick-walled multi-nucleate resting structures. The germination of the spore does not depend on the plant, as spores have been germinated under experimental conditions in the absence of plants both *in vitro* and in soil. However, the rate of germination can be increased by host root exudates. AM fungal spores germinate given suitable conditions of the soil matrix, temperature, carbon dioxide concentration, pH, and phosphorus concentration.

The growth of AM hyphae through the soil is controlled by host root exudates and the soil phosphorus concentration.

Low-phosphorus concentrations in the soil increase hyphal growth and branching as well as induce plant exudation of compounds that control hyphal branching intensity.

The branching of AM fungal hyphae grown in phosphorus media of 1 mM is significantly reduced, but the length of the germ tube and total hyphal growth were not affected. A concentration of 10 mM phosphorus inhibited both hyphal growth and branching. This phosphorus concentration occurs in natural soil conditions and could thus contribute to reduced mycorrhizal colonization.

Root exudates from AMF host plants grown in a liquid medium with and without phosphorus have been shown to effect hyphal growth. Pre-germinated surface-sterilized spores of *Gigaspora magarita* were grown in host plant exudates. The fungi grow in the exudates from roots starved of phosphorus had increased hyphal growth and produced tertiary branches compared to those grown in exudates from plants given adequate phosphorus. When the growth-promoting root exudates were added in low concentration, the AM fungi produced scattered long branches. As the concentration of exudates was increased, the fungi produced more tightly clustered branches. At the highest-concentration arbuscules, the AMF structures of phosphorus exchange were formed.

This chemotaxic fungal response to the host plants exudates is thought to increase the efficacy of host root colonization in low-phosphorus soils. It is an adaptation for fungi to efficiently explore the soil in search of a suitable plant host.

Further evidence that AM fungi exhibit host-specific chemotaxis: Spores of *Glomus mosseae* were separated from the roots of a host plant, nonhost plants, and dead host plant by a membrane permeable only to hyphae. In the treatment with the host plant, the fungi crossed the membrane and always emerged within 800 µm of the root. Whereas in the treatments with nonhost plants and dead plants, the hyphae did not cross the membrane to reach the roots. This demonstrates that arbuscular mycorrhizal fungi have chemotaxic abilities that enable hyphal growth toward the roots of a potential host plant.

Molecular techniques have been used to further understand the signaling pathways that occur between arbuscular mycorrhizae and the plant roots. In the presence of exudates from potential host plant roots, the AM undergoes physiological changes that allow it to colonize its host. AM fungal genes required for the respiration of spore carbon compounds are triggered and turned on by host plant root exudates. In experiments, there was an increase in the transcription rate of 10 genes half-hour after exposure and an even greater rate after 1 hour. A morphological growth response was observed 4 hours after exposure. The genes were isolated and found to be involved in mitochondrial activity and enzyme production. The fungal respiration rate was measured by O_2 consumption rate and increased by 30% 3 hours after exposure to root exudates. This indicates that AMF spore mitochondrial activity is positively stimulated by host plant root exudates. This may be part of a fungal regulatory mechanism that conserves spore energy for efficient growth and the hyphal branching upon receiving signals from a potential host plant.

When arbuscular mycorrhizal fungal hyphae encounter the root of a host plant, an apressorium (an infection structure) is formed on the root epidermis. The apressorium is the structure from which the hyphae can penetrate into the host's parenchyma cortex. The formation of apressoria does not require chemical signals from the plant. AM fungi could form apressoria on the cell walls of "ghost" cells in which the protoplast had been removed to eliminate signaling between the fungi and the plant host. However, the hyphae did not further penetrate the cells and grow in toward the root cortex, which indicates that signaling between symbionts is required for further growth once appresoria are formed.

Symbiosis

Once inside the parenchyma, the fungi forms highly branched structures for nutrient exchange with the plant called "arbuscules". These are the distinguishing structures of arbuscular mycorrhizal fungus. Arbuscules are the sites of exchange for phosphorus, carbon, water, and other nutrients. There are two forms: *Paris* type is characterized by the growth of hyphae from one cell to the next; and *Arum* type is characterized by the growth of hyphae in the space between plant cells. The choice between *Paris* type and *Arum* type is primarily determined by the host plant family, although some families or species are capable of either type.

The host plant exerts a control over the intercellular hyphal proliferation and arbuscule formation. There is a decondensation of the plant's chromatin, which indicates increased transcription of the plant's DNA in arbuscule-containing cells. Major modifications are required in the plant host cell to accommodate the arbuscules. The vacuoles shrink and other cellular organelles proliferate. The plant cell cytoskeleton is reorganized around the arbuscules.

There are two other types of hyphae that originate from the colonized host plant root. Once colonization has occurred, short-lived runner hyphae grow from the plant root into the soil. These are the hyphae that take up phosphorus and micronutrients, which are conferred to the plant. AM fungal hyphae have a high surface-to-volume ratio, making their absorptive ability greater than that of plant roots. AMF hyphae are also finer than roots and can enter into pores of the soil that are inaccessible to roots. The third type of AMF hyphae grows from the roots and colonizes other host plant roots. The three types of hyphae are morphologically distinct.

Nutrient uptake and exchange

AMF are obligate symbionts. They have limited saprobic ability and are dependent on the plant for their carbon nutrition. AM fungi take up the products of the plant host's photosynthesis as hexoses.

The transfer of carbon from the plant to the fungi may occur through the arbuscules or intraradical hyphae. Secondary synthesis from the hexoses by AM occurs in the intraradical mycelium. Inside the mycelium, hexose is converted to trehalose and glycogen. Trehalose and glycogen are carbon storage forms that can be rapidly synthesized and degraded and may buffer the intracellular sugar concentrations. The intraradical hexose enters the oxidative pentose phosphate pathway, which produces pentose for nucleic acids.

Lipid biosynthesis also occurs in the intraradical mycelium. Lipids are then stored or exported to extraradical hyphae where they may be stored or metabolized. The breakdown of lipids into hexoses, known as **gluconeogenesis**, occurs in the extraradical mycelium. Approximately 25% of the carbon translocated from the plant to the fungi is stored in the extraradical hyphae. Up to 20% of the host plant's photosynthate carbon may be transferred to the AM fungi. This represents a considerable carbon investment in mycorrhizal network by the host plant and contribution to the below-ground organic carbon pool.

An increase in the carbon supplied by the plant to the AM fungi increases the uptake of phosphorus and the transfer of phosphorus from fungi to plant (Bücking & Shachar-Hill 2005). Phosphorus uptake and transfer is also lowered when the photosynthate supplied to the fungi is decreased. Species of AMF differ in their abilities to supply the plant with phosphorus. In some cases, arbuscular mycorrhizae are poor symbionts, providing little phosphorus while taking relatively high amounts of carbon.

The benefit of mycorrhizae to plants is mainly attributed to increased uptake of nutrients, especially phosphorus. This increase in uptake may be due to increase surface area of soil contact, increased movement of nutrients into mycorrhizae, a modification of the root environment, and increased storage. Mycorrhizae can be much more efficient than plant roots at taking up phosphorus. Phosphorus travels to the root or via diffusion and hyphae reduce the distance required for diffusion, thus increasing uptake. The rate of inflow of phosphorus into mycorrhizae can be up to six times that of the root hairs. In some cases, the role of phosphorus uptake can be completely taken over by the mycorrhizal network, and all of the plant's phosphorus may be of hyphal origin.

The available phosphorus concentration in the root zone can be increased by mycorrhizal activity. Mycorrhizae lower the rhizosphere pH due to selective uptake of NH_4^+ (ammonium-ions) and release of H^+ ions. Decreased soil pH increases the solubility of phosphorus precipitates. The hyphal uptake of NH_4^+ also increases the flow of nitrogen to the plant as NH_4^+ is adsorbed to the soil's inner surfaces and must be taken up by diffusion.

Ecology

Habitat

Arbuscular mycorrhizal fungi are most frequent in plants growing on mineral soils. The populations of AM fungi is greatest in plant communities with high diversity such as tropical rainforests and temperate grasslands where they have many potential host plants and can take advantage of their ability to colonize a broad host range. There is a lower incidence of mycorrhizal colonization in very arid or nutrient-rich soils. Mycorrhizas have been observed in aquatic habitats; however, waterlogged soils have been shown to decrease colonization in some species.

Host range and specificity

The specificity, host range, and degree of colonization of mycorrhizal fungi are difficult to analyze in the field due to the complexity of interactions between the fungi within a root and within the system. There is no clear evidence to suggest that arbuscular mycorrhizal fungi exhibit specificity for colonization of potential AM host plant species as do fungal pathogens for their host plants. This may be due to the opposite selective pressure involved.

In parasitic relations, the host plant benefits from mutations that prevent colonization, whereas, in a symbiotic relationship, the plant benefits from mutation that allow for colonization by AMF. However, plant species differ in the extent and dependence on colonization by certain AM fungi, and some plants may be facultative mycotrophs, while others may be obligate mycotrophs.

The ability of the same AM fungi to colonize many species of plants has ecological implications. Plants of different species can be linked underground to a common mycelial network. One plant may provide the photosynthate carbon for the establishment of the mycelial network that another plant of a different species can utilize for mineral uptake. This implies that arbuscular mycorrhizae are able to balance below-ground intra–and interspecific plant interactions.

Rhizosphere ecology

The rhizosphere is the soil zone in the immediate vicinity of a root system.

Arbuscular mycorrhizal symbiosis affects the community and diversity of other organisms in the soil. This can be directly seen by the release of exudates, or indirectly by a change in the plant species and plant exudates type and amount.

Mycorrhizae diversity has been shown to increase plant species diversity as the potential number of associations increases. Dominant arbuscular mycorrhizal fungi can prevent the invasion of non-mycorrhizal plants on land where they have established symbiosis and promote their mycorrhizal host.

Recent research has shown that AM fungi release an unidentified diffusional factor, known as the **myc factor**, which activates the nodulation factor's inducible gene MtEnod11. This is the same gene involved in establishing symbiosis with the nitrogen fixing, rhizobial bacteria (Kosuta *et al.* 2003). When rhizobium bacteria are present in the soil, mycorrhizal colonization is increased due to an increase in the concentration of chemical signals involved in the establishment of symbiosis (Xie *et al.* 2003). Molecules similar to Nod factors were isolated from AM fungi and were shown to induce MtEnod11, lateral root formation and enhance mycorrhization. Effective mycorrhizal colonization can also increase the nodulations and symbiotic nitrogen fixation in mycorrhizal legumes.

The extent of arbuscular mycorrhizal colonization and species affects the bacterial population in the rhizosphere. Bacterial species differ in their abilities to compete for carbon compound root exudates. A change in the amount or composition of root exudates and fungal exudates due to the existing AM mycorrhizal colonization determines the diversity and abundance of the bacterial community in the rhizosphere.

The influence of AM fungi on plant root and shoot growth may also have indirect effect on the rhizosphere bacteria. AMF contributes a substantial amount of carbon to the rhizosphere through the growth and degeneration of the hyphal network. There is also evidence to suggest that AM fungi may play an important role on mediating the plant species' specific effect on the bacterial composition of the rhizosphere.

Phytoremediation

The use of arbuscular mycorrhizal fungi in ecological restoration projects has been shown to enable host plant establishment on degraded soil and improve soil quality and health (phytoremediation).

Disturbance of native plant communities in desertification-threatened areas is often followed by degradation of physical and biological soil properties, soil structure, nutrient availability, and organic matter.

When restoring disturbed land, it is essential to replace not only the above ground vegetation but also the biological and physical soil properties.

A relatively new approach to restoring land and protecting against desertification is to inoculate the soil with arbuscular mycorrhizal fungi with the reintroduction of vegetation. A long-term study demonstrated that a significantly greater long-term improvement in soils' quality parameters was attained when the soil was inoculated with a mixture of indigenous arbuscular mycorrhizal fungi species compared to the noninoculated soil and soil inoculated with a single exotic species of AM fungi (Figure 2). The benefits observed were an increased plant growth and soil nitrogen content, higher soil organic matter content, and soil aggregation. The improvements were attributed to the higher legume nodulation in the presence of AMF, better water infiltration, and soil aeration due to soil aggregation.

Inoculation with native AM fungi increased plant uptake of phosphorus, improving plant growth and health. The results support the use of AM fungi as a biological tool in the restoration of biotopes to self-sustaining ecosystems.

Agriculture

Many modern agronomic practices are disruptive to mycorrhizal symbiosis. There is great potential for low-input agriculture to manage the system in a way that promotes mycorrhizal symbiosis.

Conventional agriculture practices, such as tillage, heavy fertilizers and fungicides, poor crop rotations, and selection for plants that survive these conditions, hinder the ability of plants to form symbiosis with arbuscular mycorrhizal fungi.

Most agricultural crops can perform better and are more productive when well-colonized by AM fungi. AM symbiosis increases the phosphorus and micronutrient uptake and growth of their plant host (George *et al.* 1992).

Management of AM fungi is especially important for organic and low-input agriculture systems where soil phosphorus is, in general, low, although all agroecosystems can benefit by promoting arbuscular mycorrhizae establishment.

Some crops that are poor at seeking out nutrients in the soil are very dependent on AM fungi for phosphorus uptake. For example flax, which has poor chemotaxic ability, is highly dependent on AM-mediated phosphorus uptake at low and intermediate soil phosphorus concentrations (Thingstrup *et al.* 1998).

Proper management of AMF in the agroecosystems can improve the quality of the soil and the productivity of the land. Agricultural practices such as reduced tillage, low phosphorus fertilizer usage, and perennialized cropping systems promote functional mycorrhizal symbiosis.

Tillage

Tillage reduces the inoculation potential of the soil and the efficacy of mycorrhizaes by disrupting the extraradical hyphal network (Miller *et al.* 1995, McGonigle & Miller 1999, Mozafar *et al.* 2000).

By breaking apart the soil macro structure, the hyphal network is rendered non-infective (Miller *et al.* 1995, McGonigle & Miller 1999). The disruption of the hyphal network decreases the absorptive abilities of the mycorrhizae because the surface area spanned by the hyphae is greatly reduced. This, in turn, lowers the phosphorus input to the plants that are connected to the hyphal network (Figure 3, McGonigle & Miller 1999).

In reduced-tillage system, heavy phosphorus fertilizer input may not be required as compared to heavy-tillage systems. This is due to the increase in mycorrhizal network, which allows mycorrhizae to provide the plant with sufficient phosphorus (Miller *et al.* 1995).

Phosphorus fertilizer

The benefits of AMF are greatest in systems where inputs are low. Heavy usage of phosphorus fertilizer can inhibit mycorrhizal colonization and growth.

As the soil's phosphorus levels available to the plants increases, the amount of phosphorus also increases in the plant's tissues, and carbon drain on the plant by the AM fungi symbiosis become non-beneficial to the plant (Grant 2005).

A decrease in mycorrhizal colonization due to high soil-phosphorus levels can lead to plant deficiencies in other micronutrients that have mycorrhizal-mediated uptake such as copper (Timmer & Leyden 1980).

Perennialized cropping systems

Cover crops are grown in the fall, winter, and spring, covering the soil during periods when it would commonly be left without a cover of growing plants.

Mycorrhizal cover crops can be used to improve the mycorrhizal inoculum potential and hyphal network (Kabir and Koide 2000, Boswell *et al.*1998, Sorensen et al. 2005).

Since AM fungi are biotrophic, they are dependent on plants for the growth of their hyphal networks. Growing a cover crop extends the time for AM growth into the autumn, winter, and spring. Promotion of hyphal growth creates a more extensive hyphal network. The mycorrhizal colonization increase found in cover crops systems may be largely attributed to an increase in the extraradical hyphal network that can colonize the roots of the new crop (Boswell *et al.* 1998). The extraradical mycelia are able to survive the winter, providing rapid spring colonization and early season symbiosis (McGonigle and Miller 1999). This early symbiosis allows plants to tap into the well-established hyphal network and be supplied with adequate phosphorus nutrition during early growth, which greatly improves the crop yield.

Soil quality

Restoration of native AM fungi increases the success of ecological restoration project and the rapidity of soil recovery. There is evidence to suggest that this enhancement of soil aggregate stability is due to the production of a soil protein known as glomalin.

Glomalin-related soil proteins (GRSP) have been identified using a monoclonal antibody (Mab32B11) raised against crushed AMF spores. It is defined by its extraction conditions and reaction with the antibody Mab32B11.

There is other circumstantial evidence to show that glomalin is of AM fungal origin. When AM fungi are eliminated from soil through incubation of soil without host plants, the concentration of GRSP declines. A similar decline in GRSP has also been observed in incubated soils from forested, afforested, and agricultural land and grasslands treated with fungicide.

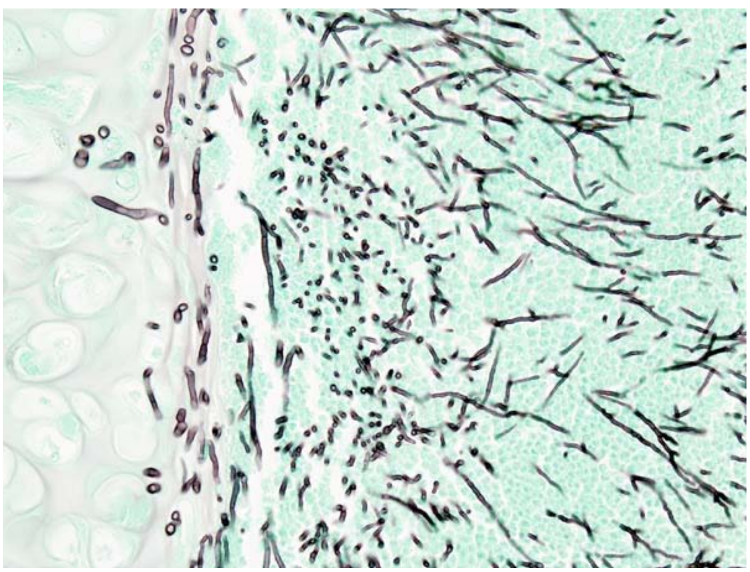
Glomalin is hypothesized to improve soil aggregate water stability and decrease soil erosion. A strong correlation has been found between GRSP and soil aggregate water stability in a wide variety of soils where organic material is the main binding agent, although the mechanism is not known. The protein glomalin has not yet been isolated and described, and the link between glomalin, GRSP, and arbuscular mycorrhizal fungi is not yet clear.

Chapter- 6

Fungal Diseases

Aspergillosis

Aspergillosis	



Histopathologic image of pulmonary invasive aspergillosis in a patient with interstitial pneumonia. Autopsy material. Grocott's methenamine silver stain.

ICD-10	B44.
ICD-9	117.3
MedlinePlus	001326
eMedicine	med/174

MeSH D001228

Aspergillosis is the name given to a wide variety of diseases caused by fungi of the genus *Aspergillus*. The most common forms are allergic bronchopulmonary aspergillosis, pulmonary aspergilloma and invasive aspergillosis. Most humans inhale *Aspergillus* spores every day. Aspergillosis develops mainly in individuals who are immunocompromised, either from disease or from immunosuppressive drugs, and is a leading cause of death in acute leukemia and hematopoietic stem cell transplantation. Conversely, it may also develop as an allergic response. The most common cause is *Aspergillus fumigatus*.

Symptoms

A fungus ball in the lungs may cause no symptoms and may be discovered only with a chest x-ray. Or it may cause repeated coughing up of blood and occasionally severe, even fatal, bleeding. A rapidly invasive *Aspergillus* infection in the lungs often causes cough, fever, chest pain, and difficulty breathing.

Aspergillosis affecting the deeper tissues makes a person very ill. Symptoms include fever, chills, shock, delirium, and blood clots. The person may develop kidney failure, liver failure (causing jaundice), and breathing difficulties. Death can occur quickly.

Aspergillosis of the ear canal causes itching and occasionally pain. Fluid draining overnight from the ear may leave a stain on the pillow. Aspergillosis of the sinuses causes a feeling of congestion and sometimes pain or discharge.

In addition to the symptoms, an x-ray or computerised tomography (CT) scan of the infected area provides clues for making the diagnosis. Whenever possible, a doctor sends a sample of infected material to a laboratory to confirm identification of the fungus.

Diagnosis

On chest X-ray and computed tomography pulmonary aspergillosis classically manifests as an air crescent sign. In hematologic patients with invasive aspergillosis the galactomannan test can make the diagnosis in a noninvasive way.

On microscopy, Aspergillus species are reliably demonstrated by silver stains, eg, Gridley stain or Gomori methenamine-silver. These give the fungal walls a gray-black colour. The hyphae of Aspergillus species range in diameter from 2.5 to 4.5 µm. They have septate hyphae, but these are not always apparent, and in such cases they may be mistaken for Zygomyces. Aspergillus hyphae tend to have dichotomous branching that is progressive and primarily at acute angles of approximately 45°.

Treatment

The favored treatment with the fewest side effects, such as nephrotoxicity, is voriconazole. Newer findings suggest use of mild oral steroids for a longer period of time, preferably for 6-9 months in Aspergillosis in pulmonary segment.

Other drugs used such as amphotericin B, caspofungin, flucytosine, itraconazole are used to treat this fungal infection. For severe cases of invasive aspergillosis a combination therapy of voriconazole and caspofungin is suggested as a first line treatment.

Infections in animals

Albeit relatively rare in humans, aspergillosis is a common and dangerous infection in birds, particularly in pet parrots. Mallards and other ducks are particularly susceptible as they will often resort to poor food sources during bad weather. Captive raptors such as falcons and hawks are susceptible to this disease if they are kept in poor conditions and especially if they are fed pigeons, which are often carriers of "asper".

Aspergillosis has been the culprit in several recent rapid die-offs among waterfowl. From 8 December until 14 December 2006 over 2,000 Mallards died in the Burley, Idaho area, an agricultural community approximately 150 miles southeast of Boise. Moldy waste grain from the farmland and feedlots in the area is the suspected source. A similar aspergillosis outbreak caused by moldy grain killed 500 Mallards in Iowa in 2005.

While there is no connection between aspergillosis and the H5N1 strain of Avian Influenza (commonly called "bird flu"), rapid die-offs caused by aspergillosis can spark fears of bird flu outbreaks. Laboratory analysis is the only way to distinguish bird flu and aspergillosis.

Athlete's foot

Athlete's Foot

Pale, flaky & split skin of athlete's foot in a toe

ICD-10	B35.3
ICD-9	110.4
DiseasesDB	13122
MedlinePlus	000875
eMedicine	derm/470
MeSH	D014008

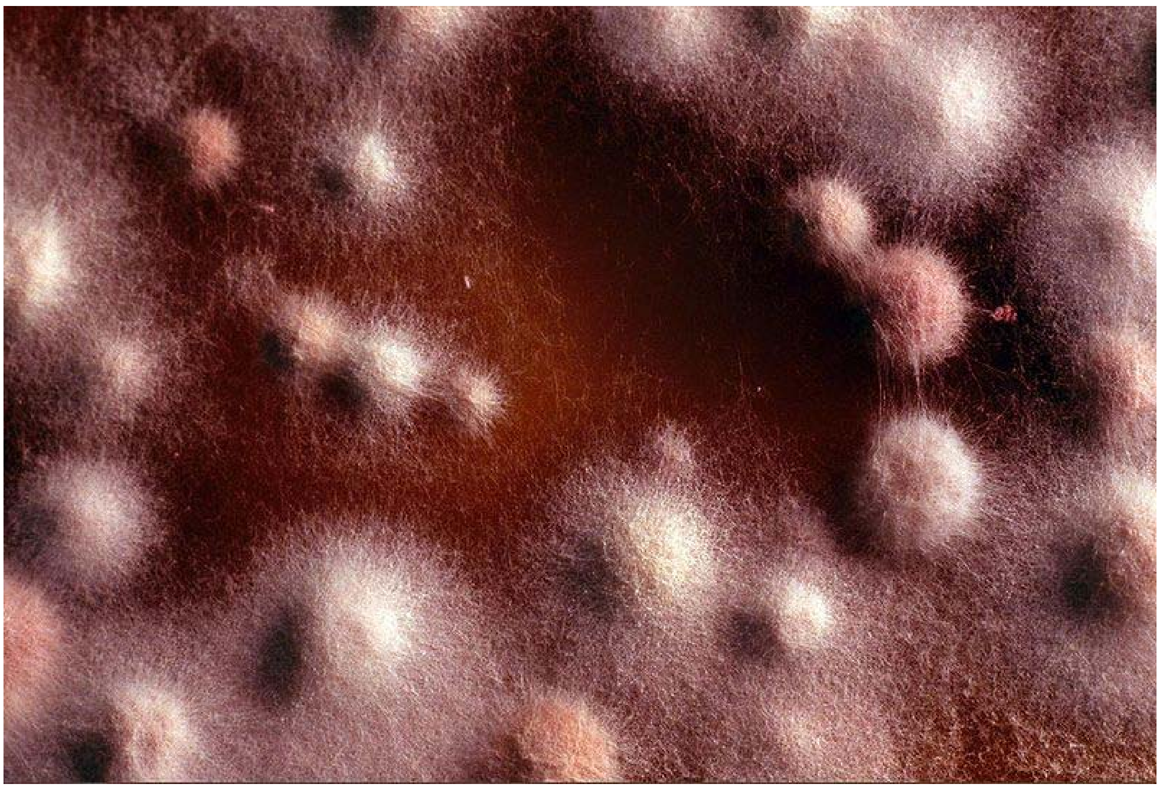
Athlete's foot (also known as **ringworm of the foot** and **tinea pedis**, and also **Hong Kong foot** (simplified Chinese: 香港脚; traditional Chinese: 香港腳) in the Chinese world) is a fungal infection of the skin that causes scaling, flaking, and itch of affected areas. It is caused by fungi in the genus *Trichophyton* and is typically transmitted in moist areas where people walk barefoot, such as showers or bathhouses. Although the condition typically affects the feet, it can spread to other areas of the body, including the groin. Athlete's foot can be treated by a number of pharmaceutical and other treatments.

Etymology

Hong Kong foot

The name "Hong Kong foot" originated from the stationing of the British army in Hong Kong. After the Qing Dynasty of China lost in the First Opium War, they ceded Hong Kong to the United Kingdom. Because the British were used to life in less humid climates of Europe, when they came to Hong Kong, which has a hot and moist climate, they were still wearing their military boots without good ventilation resulting in many British soldiers catching an unknown skin disease with many tiny boils. Some were swollen red with pus, and it was very itchy. Yet, at that time the European physicians had never seen this kind of disease, so they thought it was an epidemic in Hong Kong, so they called it "Hong Kong foot".

Signs and symptoms



Microscopic view of athlete's foot fungus

Athlete's foot causes scaling, flaking, and itching of the affected skin. Blisters and cracked skin may also occur, leading to exposed raw tissue, pain, swelling, and inflammation. Secondary bacterial infection can accompany the fungal infection, sometimes requiring a course of oral antibiotics.

The infection can be spread to other areas of the body, such as the groin, and usually is called by a different name once it spreads, such as tinea corporis on the body or limbs and tinea cruris (jock itch or dhobi itch) for an infection of the groin. Tinea pedis most often manifests between the toes, with the space between the fourth and fifth digits most commonly afflicted.

Some individuals may experience an allergic response to the fungus called an "id reaction" in which blisters or vesicles can appear in areas such as the hands, chest and arms. Treatment of the fungus usually results in resolution of the id reaction.

Diagnosis

Athlete's foot can usually be diagnosed by visual inspection of the skin, but where the diagnosis is in doubt direct microscopy of a potassium hydroxide preparation (known as a KOH test) may help rule out other possible causes, such as eczema or psoriasis. A KOH preparation is performed on skin scrapings from the affected area. The KOH preparation has an excellent positive predictive value, but occasionally false negative results may be obtained, especially if treatment with an anti-fungal medication has already begun.

If the above diagnoses are inconclusive or if a treatment regimen has already been started, a biopsy of the affected skin (i.e. a sample of the living skin tissue) can be taken for histological examination.

A Wood's lamp, although useful in diagnosing fungal infections of the hair (Tinea capitis), is not usually helpful in diagnosing tinea pedis since the common dermatophytes that cause this disease do not fluoresce under ultraviolet light. However, it can be useful for determining if the disease is due to a non-fungal afflictor.

Transmission

From person to person

Athlete's foot is a communicable disease caused by a parasitic fungus in the genus Trichophyton, either *Trichophyton rubrum* or *Trichophyton mentagrophytes*. It is typically transmitted in moist environments where people walk barefoot, such as showers, bath houses, and locker rooms. It can also be transmitted by sharing footwear with an infected person, or less commonly, by sharing towels with an infected person.

To other parts of the body

The various parasitic fungi that cause athlete's foot can also cause skin infections on other areas of the body, most often under toenails (onychomycosis) or on the groin (tinea cruris).

Prevention

The fungi that cause athlete's foot can live on shower floors, wet towels, and footwear, and can spread from person to person from shared contact with showers, towels, etc.

Hygiene, therefore, plays an important role in managing an athlete's foot infection. Since fungi thrive in moist environments, keeping feet and footwear as dry as possible, and avoiding sharing towels, etc., aids prevention of primary infection.

Treatments

There are many conventional medications (over-the-counter and prescription) as well as alternative treatments for fungal skin infections, including athlete's foot. Important with any treatment plan is the practice of good hygiene. Several placebo controlled studies report that good foot hygiene alone can cure athlete's foot even without medication in 30-40% of the cases. However, placebo-controlled trials of allylamines and azoles for athlete’s foot consistently produce much higher percentages of cure than placebo.

Medication

Conventional treatment typically involves daily or twice daily application of a topical medication in conjunction with hygiene measures outlined in the above section on prevention. Keeping feet dry and practicing good hygiene is crucial to preventing reinfection. Severe or prolonged fungal skin infections may require treatment with oral anti-fungal medication. Zinc oxide based diaper rash ointment may be used; talcum powder can be used to absorb moisture to kill off the infection.

Topical

The fungal infection is often treated with topical antifungal agents, which can take the form of a spray, powder, cream, or gel. The most common ingredients in over-the-counter products are miconazole nitrate (2% typical concentration in the United States) and tolnaftate (1% typ. in the U.S.). Terbinafine is another common over-the-counter drug. There exists a large number of prescription antifungal drugs, from several different drug families. These include ketaconazole, itraconazole, naftifine, nystatin,

Some topical applications such as carbol fuchsin (also known in the U.S. as Castellani's paint), often used for intertrigo, work well but in small selected areas. This red dye, used in this treatment like many other vital stains, is a fungicide. Nonetheless, good hygiene is the most important in curing athlete's foot.

The time-line for cure may be long, often 45 days or longer. The recommended course of treatment is to *continue to use the topical treatment for four weeks after the symptoms have subsided* to ensure that the fungus has been completely eliminated. However, because the itching associated with the infection subsides quickly, patients may not complete the courses of therapy prescribed.

Anti-itch creams are *not* recommended as they will alleviate the symptoms but will exacerbate the fungus; this is due to the fact that anti-itch creams typically enhance the moisture content of the skin and encourage fungal growth. For the same reason, some drug manufacturers are using a gel instead of a cream for application of topical drugs (for example, naftin and Lamisil). Novartis, maker of Lamisil, claims that a gel penetrates the skin more quickly than cream.

If the fungal invader is not a dermatophyte but a yeast, other medications such as fluconazole may be used. Typically fluconazole is used for candidal vaginal infections moniliasis but has been shown to be of benefit for those with cutaneous yeast infections as well. The most common of these infections occur in the web spaces (intertriginous) of the toes and at the base of the fingernail or toenail. The hall mark of these infections is a cherry red color surrounding the lesion and a yellow thick pus.

Oral

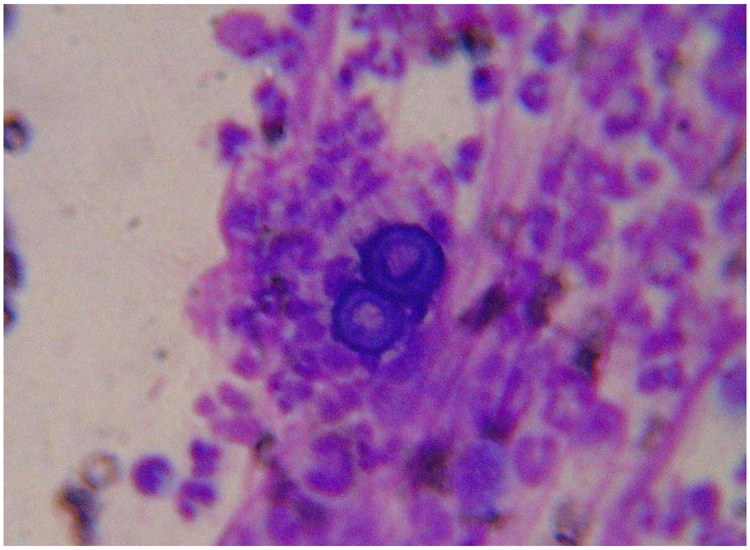
Oral treatment with griseofulvin was begun early in the 1950s. Because of the tendency to cause liver problems and to provoke aplastic anemia the drugs were used cautiously and sparingly. Over time it was found that those problems were due to the size of the crystal in the manufacturing process and microsize and now ultramicrosize crystals are available with few of the original side effects.

For severe cases, the current preferred oral agent in the UK is the more effective terbinafine. Other prescription oral antifungals include itraconazole and fluconazole.

Alternative treatments

Tea tree oil may improve the symptoms but does not cure the underlying fungal infection. Ajoene, a compound found in garlic, is sometimes used to treat athlete's foot.

Blastomycosis

Blastomycosis	
	
Blastomyces dermatitidis, the causative agent of blastomycosis.	
ICD-10	B40.
ICD-9	116.0
DiseasesDB	1439
MedlinePlus	000102
eMedicine	med/231 ped/254
MeSH	D001759

Blastomycosis (also known as "North American blastomycosis," "Blastomycetic dermatitis," and "Gilchrist's disease") is a fungal infection caused by the organism *Blastomyces dermatitidis*. Endemic to portions of North America, blastomycosis causes clinical symptoms similar to histoplasmosis.

Signs and symptoms

Blastomycosis of skin

Blastomycosis can present in one of the following ways:

- a flu-like illness with fever, chills, myalgia, headache, and a nonproductive cough which resolves within days.
- an acute illness resembling bacterial pneumonia, with symptoms of high fever, chills, a productive cough, and pleuritic chest pain.
- a chronic illness that mimics tuberculosis or lung cancer, with symptoms of low-grade fever, a productive cough, night sweats, and weight loss.
- a fast, progressive, and severe disease that manifests as ARDS, with fever, shortness of breath, tachypnea, hypoxemia, and diffuse pulmonary infiltrates.
- skin lesions, usually asymptomatic, appear as ulcerated lesions with small pustules at the margins
- bone lytic lesions can cause bone or joint pain.
- prostatitis may be asymptomatic or may cause pain on urinating.
- laryngeal involvement causes hoarseness.

Cause

Infection occurs by inhalation of the fungus from its natural soil habitat. Once inhaled in the lungs, they multiply and may disseminate through the blood and lymphatics to other organs, including the skin, bone, genitourinary tract, and brain. The incubation period is 30 to 100 days, although infection can be asymptomatic.

Diagnosis

Once suspected, the diagnosis of **blastomycosis** can usually be confirmed by demonstration of the characteristic broad based budding organisms in sputum or tissues by KOH prep, cytology, or histology. Tissue biopsy of skin or other organs may be required in order to diagnose extra-pulmonary disease. Commercially available urine antigen testing appears to be quite sensitive in suggesting the diagnosis in cases where the organism is not readily detected. While culture of the organism remains the definitive diagnostic standard, its slow growing nature can lead to delays in treatment of up to several weeks.

However, sometimes blood and sputum cultures may not detect blastomycosis; lung biopsy is another option, and results will be shown promptly.

Treatment

Itraconazole given orally is the treatment of choice for most forms of the disease. Ketoconazole may also be used. Cure rates are high, and the treatment over a period of months is usually well tolerated. Amphotericin B is considerably more toxic, and is usually reserved for immunocompromised patients who are critically ill and those with central nervous system disease. Fluconazole has also been tested on patients in Canada.

Prognosis

Mortality rate in treated cases

- 0-2% in treated cases among immunocompetent patients
- 29% in immunocompromised patients
- 40% in the subgroup of patients with AIDS
- 68% in patients presenting as acute respiratory distress syndrome (ARDS)

Epidemiology

In the United States, blastomycosis is endemic in the Mississippi river and Ohio river basins and around the Great Lakes. The annual incidence is less than 1 case per 100,000 people in Mississippi, Louisiana, Kentucky, and Arkansas. The cases are greater in northern states such as Wisconsin, where from 1986 to 1995 there were 1.4 cases per 100,000 people. It also frequently affects hunting dogs in northern Wisconsin and the upper Mississippi and Wisconsin Rivers.

In Canada, most cases of blastomycosis occur in Northwestern Ontario, particularly around the Kenora area. The moist, acidic soil in the surrounding woodland harbors the fungus.

Blastomycosis is distributed internationally; cases are sometimes reported from Africa.

History

Blastomycosis was first described by Thomas Casper Gilchrist in 1894 and sometimes goes by the eponym *Gilchrist's disease*. It is also sometimes referred to as Chicago Disease.

Candidiasis

Candidiasis	
	
Agar plate culture of *Candida albicans*	
ICD-10	B37.
ICD-9	112
DiseasesDB	1929
MedlinePlus	001511
eMedicine	med/264 emerg/76 ped/312 derm/67
MeSH	D002177

Candidiasis or **thrush** is a fungal infection (mycosis) of any of the *Candida* species (all yeasts), of which *Candida albicans* is the most common. Also commonly referred to as a **yeast infection**, candidiasis is also technically known as **candidosis**, **moniliasis**, and **oidiomycosis**.

Candidiasis encompasses infections that range from superficial, such as oral thrush and vaginitis, to systemic and potentially life-threatening diseases. *Candida* infections of the latter category are also referred to as candidemia and are usually confined to severely immunocompromised persons, such as cancer, transplant, and AIDS patients as well as non-trauma emergency surgery patients.

Superficial infections of skin and mucosal membranes by *Candida* causing local inflammation and discomfort are common in many human populations. While clearly attributable to the presence of the opportunistic pathogens of the genus *Candida*, candidiasis describes a number of different disease syndromes that often differ in their causes and outcomes.

Classification

Candidiasis may be divided into the following types:

- Oral candidiasis (Thrush)
- Perlèche (Angular cheilitis)
- Candidal vulvovaginitis
- Candidal intertrigo
- Diaper candidiasis
- Congenital cutaneous candidiasis
- Perianal candidiasis
- Candidal paronychia
- Erosio interdigitalis blastomycetica
- Chronic mucocutaneous candidiasis
- Systemic candidiasis
- Candidid
- Antibiotic candidiasis (Iatrogenic candidiasis)

Signs and symptoms

Most candidial infections are treatable and result in minimal complications such as redness, itching and discomfort, though complication may be severe or fatal if left untreated in certain populations. In immunocompetent persons, candidiasis is usually a very localized infection of the skin or mucosal membranes, including the oral cavity (thrush), the pharynx or esophagus, the gastrointestinal tract, the urinary bladder, or the genitalia (vagina, penis).

Candidiasis is a very common cause of vaginal irritation, or vaginitis, and can also occur on the male genitals. In immunocompromised patients, *Candida* infections can affect the esophagus with the potential of becoming systemic, causing a much more serious condition, a fungemia called candidemia.

Children, mostly between the ages of three and nine years of age, can be affected by chronic mouth yeast infections, normally seen around the mouth as white patches. However, this is not a common condition.

Symptoms of candidiasis may vary depending on the area affected. Infection of the vagina or vulva may cause severe itching, burning, soreness, irritation, and a whitish or whitish-gray cottage cheese-like discharge, often with a curd-like appearance. These symptoms are also present in the more common bacterial vaginosis. In a 2002 study published in the *Journal of Obstetrics and Gynecology*, only 33 percent of women who were self-treating for a yeast infection actually had a yeast infection, while most had either bacterial vaginosis or a mixed-type infection. Symptoms of infection of the male genitalia include red patchy sores near the head of the penis or on the foreskin, severe itching, or a burning sensation. Candidiasis of the penis can also have a white discharge, although uncommon. However, having no symptoms at all is common, and a more severe form of the symptoms may emerge later, even up to three months of initial contact.

Causes

Candida yeasts are commonly present in humans, and their growth is normally limited by the human immune system and by other microorganisms, such as bacteria occupying the same locations (niches) in the human body.

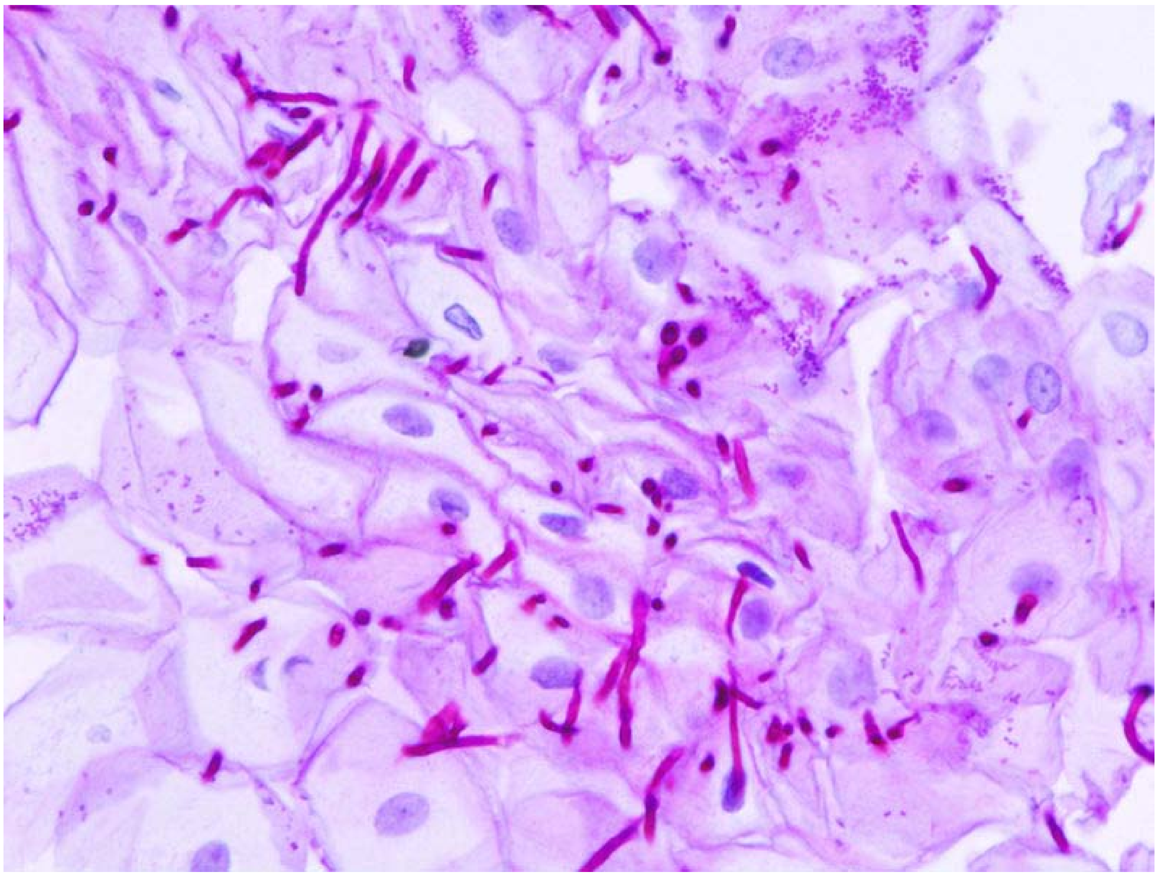
C. albicans was isolated from the vaginas of 19% of apparently healthy women, i.e., those that experienced few or no symptoms of infection. External use of detergents or douches or internal disturbances (hormonal or physiological) can perturb the normal vaginal flora, consisting of lactic acid bacteria, such as lactobacilli, and result in an overgrowth of *Candida* cells causing symptoms of infection, such as local inflammation. Pregnancy and the use of oral contraceptives have been reported as risk factors, while the roles of engaging in vaginal sex immediately and without cleansing after anal sex and using lubricants containing glycerin remain controversial. Diabetes mellitus and the use of anti-bacterial antibiotics are also linked to an increased incidence of yeast infections. Diet has been found to affect rates of symptomatic Candidiases in some animal infection models, and hormone replacement therapy and infertility treatments may also be predisposing factors. Wearing wet swimwear for long periods of time is also believed to be a risk factor.

A weakened or undeveloped immune system or metabolic illnesses such as diabetes are significant predisposing factors of candidiasis. Diseases or conditions linked to candidiasis include HIV/AIDS, mononucleosis, cancer treatments, steroids, stress, and nutrient deficiency. Almost 15% of people with weakened immune systems develop a systemic illness caused by *Candida* species. In extreme cases, these superficial infections of the skin or mucous membranes may enter into the bloodstream and cause systemic *Candida* infections.

In penile candidiasis, the causes include sexual intercourse with an infected individual, low immunity, antibiotics, and diabetes. Male genital yeast infection is less common, and incidence of infection is only a fraction of that in women; however, yeast infection on the penis from direct contact via sexual intercourse with an infected partner is not uncommon.

Candida species are frequently part of the human body's normal oral and intestinal flora. Treatment with antibiotics can lead to eliminating the yeast's natural competitors for resources, and increase the severity of the condition. In the western hemisphere approximately 75% of females are affected at some time in their life.

Diagnosis



Micrograph of esophageal candidiasis. Biopsy specimen; PAS stain.

Diagnosis of a yeast infection is done either via microscopic examination or culturing.

For identification by light microscopy, a scraping or swab of the affected area is placed on a microscope slide. A single drop of 10% potassium hydroxide (KOH) solution is then added to the specimen. The KOH dissolves the skin cells but leaves the *Candida* cells intact, permitting visualization of pseudohyphae and budding yeast cells typical of many *Candida* species.

For the culturing method, a sterile swab is rubbed on the infected skin surface. The swab is then streaked on a culture medium. The culture is incubated at 37 °C for several days, to allow development of yeast or bacterial colonies. The characteristics (such as morphology and colour) of the colonies may allow initial diagnosis of the organism that is causing disease symptoms.

Treatment

In clinical settings, candidiasis is commonly treated with antimycotics—the antifungal drugs commonly used to treat candidiasis are topical clotrimazole, topical nystatin, fluconazole, and topical ketoconazole.

For example, a one-time dose of fluconazole (150-mg tablet taken orally) has been reported as being 90% effective in treating a vaginal yeast infection. This dose is only effective for vaginal yeast infections, and other types of yeast infections may require different dosing. In severe infections amphotericin B, caspofungin, or voriconazole may be used. Local treatment may include vaginal suppositories or medicated douches. Gentian violet can be used for breastfeeding thrush, but when used in large quantities it can cause mouth and throat ulcerations in nursing babies, and has been linked to mouth cancer in humans and to cancer in the digestive tract of other animals.

Chlorhexidine gluconate oral rinse is not recommended to treat candidiasis but is effective as prophylaxis; chlorine dioxide rinse was found to have similar in vitro effectiveness against *candida*.

C. albicans can develop resistance to antimycotic drugs, recurring infections may be treatable with other anti-fungal drugs, but resistance to these alternative agents may also develop.

History

The genus *Candida* and species *C. albicans* was described by botanist Christine Marie Berkhout in her doctoral thesis at the University of Utrecht in 1923. Over the years, the classification of the genera and species has evolved. Obsolete names for this genus include *Mycotorula* and *Torulopsis*. The species has also been known in the past as *Monilia albicans* and *Oidium albicans*. The current classification is *nomen conservandum*, which means the name is authorized for use by the International Botanical Congress (IBC).

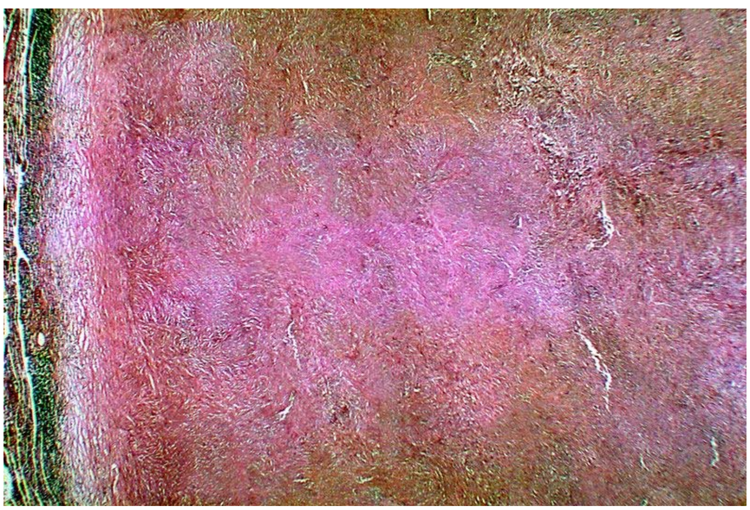
The genus *Candida* includes about 150 different species, however, only a few are known to cause human infections: *C. albicans* is the most significant pathogenic species. Other *Candida* species pathogenic in humans include *C. tropicalis*, *C. glabrata*, *C. krusei*, *C. parapsilosis*, *C. dubliniensis*, and *C. lusitaniae*.

Society and culture

Some alternative medicine proponents postulate a widespread occurrence of "systemic candidiasis" (or candida hypersensitivity syndrome, yeast allergy, or gastrointestinal candida overgrowth). The view was most widely promoted in a book published by Dr. William Crook, which hypothesized that a variety of common symptoms such as fatigue, PMS, sexual dysfunction, asthma, psoriasis, digestive and urinary problems, multiple sclerosis, and muscle pain, could be caused by subclinical infections of *Candida albicans*. Crook suggested a variety of remedies to treat these symptoms, ranging from dietary modification, prescription antifungals, to colonic irrigation. With the exception of the few dietary studies in the urinary tract infection section conventional medicine has not used most of these alternatives, since there is limited scientific evidence to prove their effectiveness, or that subclinical "systemic candidiasis" is a viable diagnosis.

Coccidioidomycosis

Coccidioidomycosis



Histopathological changes in a case of coccidioidomycosis of the lung showing a large fibrocaseous nodule.

ICD-10	B38.
ICD-9	114
MedlinePlus	001322
eMedicine	med/103 ped/423
MeSH	D003047

Coccidioidomycosis (also known as "**California disease**", "**Desert rheumatism**", "**San Joaquin valley fever**", and "**Valley fever**") is a fungal disease caused by *Coccidioides immitis* or *C. posadasii*. It is endemic in certain parts of Arizona, California, Nevada, New Mexico, Texas, Utah and northwestern Mexico.

C. immitis resides in the soil in certain parts of the southwestern United States, northern Mexico, and parts of Central and South America. It is dormant during long dry spells, then develops as a mold with long filaments that break off into airborne spores when the rains come. The spores, known as arthroconidia, are swept into the air by disruption of the soil, such as during construction, farming, or an earthquake. Infection is caused by inhalation of the particles. The disease is not transmitted from person to person. *C. immitis* is a dimorphic saprophytic organism that grows as a mycelium in the soil and produces a spherule form in the host organism.

Presentation

The disease is usually mild, with flu-like symptoms and rashes. The Mayo Clinic estimates that half the population in some affected areas have suffered from the disease. On occasion, those particularly susceptible may develop a serious or even fatal illness from valley fever. Serious complications include severe pneumonia, lung nodules, and disseminated disease, where the fungus spreads throughout the body. The disseminated form of valley fever can devastate the body, causing skin ulcers, abscesses, bone lesions, severe joint pain, heart inflammation, urinary tract problems, meningitis, and often death. In order of decreasing risk, people of Filipino, African, Native American, Hispanic, and Asian descent are susceptible to the disseminated form of the disease. Men and pregnant women, and people with weakened immune systems (as from AIDS) are more susceptible than non-pregnant women.

It has been known to infect humans, cattle, deer, dogs, elk, fish, mules, livestock, apes, kangaroos, wallabies, tigers, bears, badgers, otters and marine mammals.

Symptomatic infection (40% of cases) usually presents as an influenza-like illness with fever, cough, headaches, rash, and myalgia (muscle pain). Some patients fail to recover and develop chronic pulmonary infection or widespread disseminated infection (affecting meninges, soft tissues, joints, and bone). Severe pulmonary disease may develop in HIV-infected persons.

An additional risk is that health care providers who are unfamiliar with it or are unaware that the patient has been exposed to it may misdiagnose it as cancer and subject the patient to unnecessary surgery.

Geographic distribution of coccidioidomycosis

Types

Coccidioidomycosis may be divided into the following types:

- Primary pulmonary coccidioidomycosis
- Disseminated coccidioidomycosis
- Primary cutaneous coccidioidomycosis

Incidence (North America)

California state prisons, as far back as 1919, have been particularly affected by Coccidioidomycosis. In 2005 and 2006, the Pleasant Valley State Prison near Coalinga and Avenal State Prison near Avenal on the western side of the San Joaquin Valley had the highest incidence in 2005, of at least 3,000 per 100,000.

Incidence varies widely across the west and southwest. In Arizona, for instance, in 2007, there were 3,450 cases in Maricopa County, which in 2007 had an estimated population of 3,880,181 for an incidence of approximately 1 in 1,125. In contrast, though southern New Mexico is considered an endemic region, there were 35 cases in the entire state in 2008, and 23 in 2007, in a region that had an estimated 2008 population of 1,984,356 for an incidence of approximately 1 in 56,695. Infection rates vary greatly by county, and although population density is important, so are other factors that have not been proven yet. Greater construction activity may disturb spores in the soil. In addition, the effect of altitude on fungi growth and morphology has not been studied, and altitude can range from sea level to 10,000 feet or higher across California, Arizona, Texas and New Mexico.

In California from 2000 to 2007, there were 16,970 reported cases (5.9 per 100,000 people) and 752 deaths (0.26 per 100,000 people) with the highest incidence in the San Joaquin Valley (44.1 per 100,000).

Biological warfare

C. immitis was investigated by the United States during the 1950s and 1960s as a potential biological weapon. The Cash strain received the military symbol OC, and original hopes were for its use as an incapacitant. As medical epidemiology later made clear, OC would have lethal effects on several segments of the population, so it was later considered a lethal agent. It was never standardized, and beyond a few field trials, it was never weaponized. Most military work on OC was on vaccines by the mid-1960s. It is still on the CDC's list of select agents however.

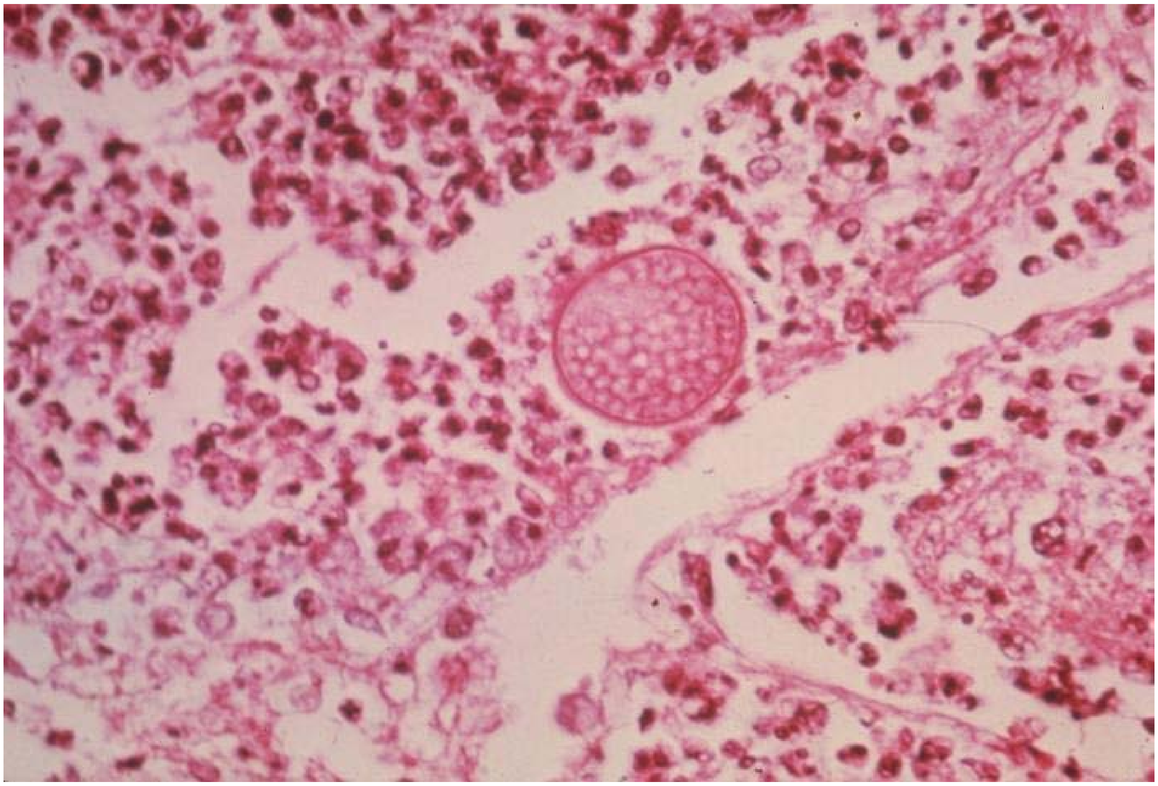
Diagnostic test

The fungal infection can be demonstrated by microscopic detection of diagnostic cells in body fluids, exudates, sputum and biopsy-tissue. With specific nucleotide primers *C.immitis* DNA can be amplified by PCR. It can also be detected in culture by morphological identification or by using molecular probes that hybridize with *C.immitis* RNA. An indirect demonstration of fungal infection can be achieved also by serologic analysis detecting fungal antigen or host antibody produced against the fungus.

Treatment

There are no published prospective studies that examine optimal antifungal therapy for coccidioidomycosis. Mild cases often do not require treatment. Oral Fluconazole and intravenous Amphotericin B are used in progressive or disseminated disease, or in which patients are immunocompromised. Alternatively, itraconazole or ketoconazole may be used. Posaconazole and voriconazole have also been used.

Additional images



Chapter- 7

Fungal Morphology and Anatomy

Agaric

The agaric *Amanita muscaria*, late August, Norway

An **agaric** is a type of fungal fruiting body characterized by the presence of a pileus (cap) that is clearly differentiated from the stipe (stalk), with lamellae (gills) on the underside of the pileus. "Agaric" can also refer to a basidiomycete species characterized by an agaric-type fruiting body. An archaic usage of the word agaric meant 'tree-fungus' (after Latin *agaricum*); however, that meaning was superseded by the Linnaean interpretation in 1753 when Linnaeus used the generic name *Agaricus* for gilled mushrooms.

Most species of agarics are classified in the Agaricales, however, this type of fruiting body is thought to have evolved several times independently, hence the Russulales, Boletales, Hymenochaetales, and several other groups of basidiomycetes also contain agaric species. Older systems of classification place all agarics in the Agaricales, and some (mostly older) sources still use "agarics" as a common name for the Agaricales. Contemporary sources now tend to use the term **euagarics** when referring only to members of the Agaricales. "Agaric" is also sometimes used as a common name for members of the genus *Agaricus*, as well as for members of other genera, for example, *Amanita muscaria* is sometimes called "fly agaric".

Amadou

Fomes fomentarius

Romanian cap made from amadou

Amadou is a spongy, flammable substance prepared from bracket fungi. The species generally used is *Fomes fomentarius* (formerly *Ungulina fomentaria* or *Polyporus fomentarius*) which in English is also called horse's hoof fungus or tinder fungus. The amadou layer can be found on top of the fungus just below the outer skin and above the pores. It is used as tinder (especially after being pounded flat, and boiled or soaked in a solution of nitre) and also used when smouldering as a portable firelighter.

It is also used in fly fishing for drying out artificial flies. It is sometimes also used to form a felt-like fabric used in the making of hats and other items. It has great water-absorbing abilities. Amadou for dry flies can be prepared by soaking the amadou layer in washing soda for a week beating it gently from time to time. After that it has to be dried and when dry it has to be pounded with a blunt object to soften it up and flatten it out.

Amadou was a precious resource to ancient people, allowing them to start a fire by catching sparks from flint struck against iron pyrites. Remarkable evidence for this is provided by the discovery of the 5000-year-old remains of "Ötzi the Iceman", who carried it on a cross-alpine excursion before his murder and subsequent ice-entombment.

Ascocarp

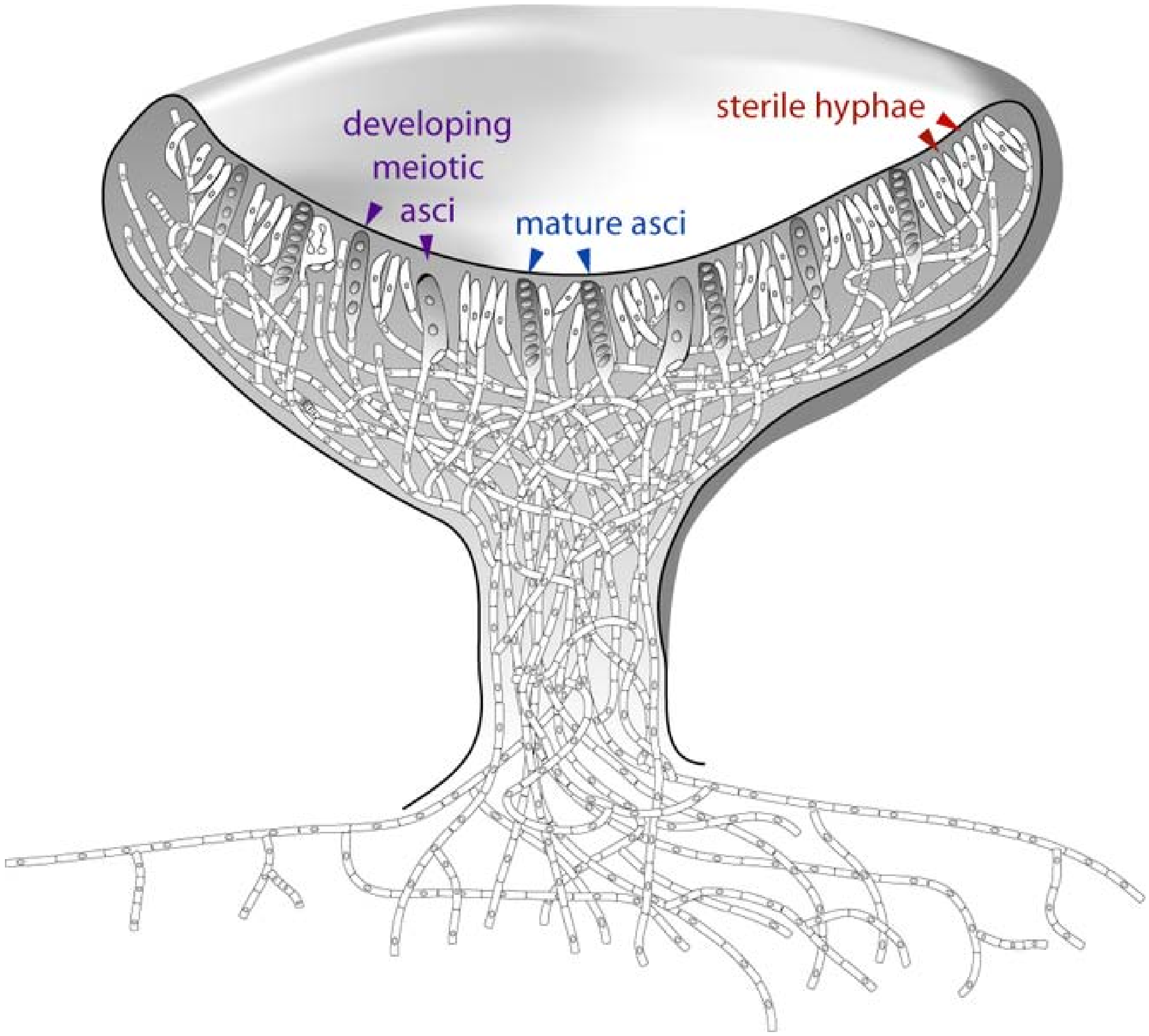


Diagram of an apothecium showing sterile tissues as well as developing and mature asci.

An **ascocarp**, or **ascoma** (plural: **ascomata**), is the fruiting body (sporocarp) of an ascomycete fungus. It consists of very tightly interwoven hyphae and may contain millions of asci, each of which typically contains eight ascospores. Ascocarps are most commonly bowl-shaped, but may take on a number of other forms.

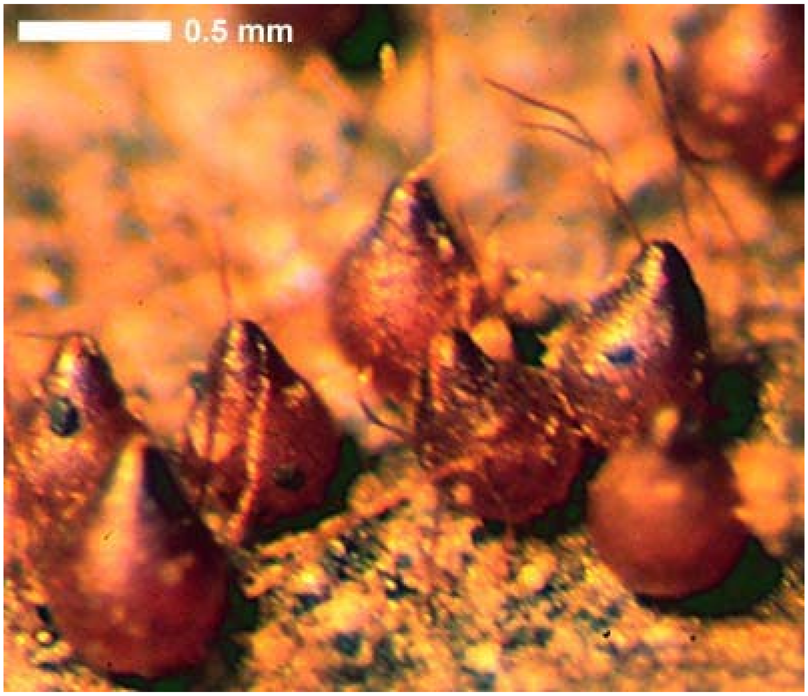
Classification of ascocarps

The ascocarp is classified according to its placement (in ways not fundamental to the basic taxonomy). It is called **epigeous** if it grows above ground, as with the morels, whilst underground ascocarps, such as truffles are **hypogeous**.

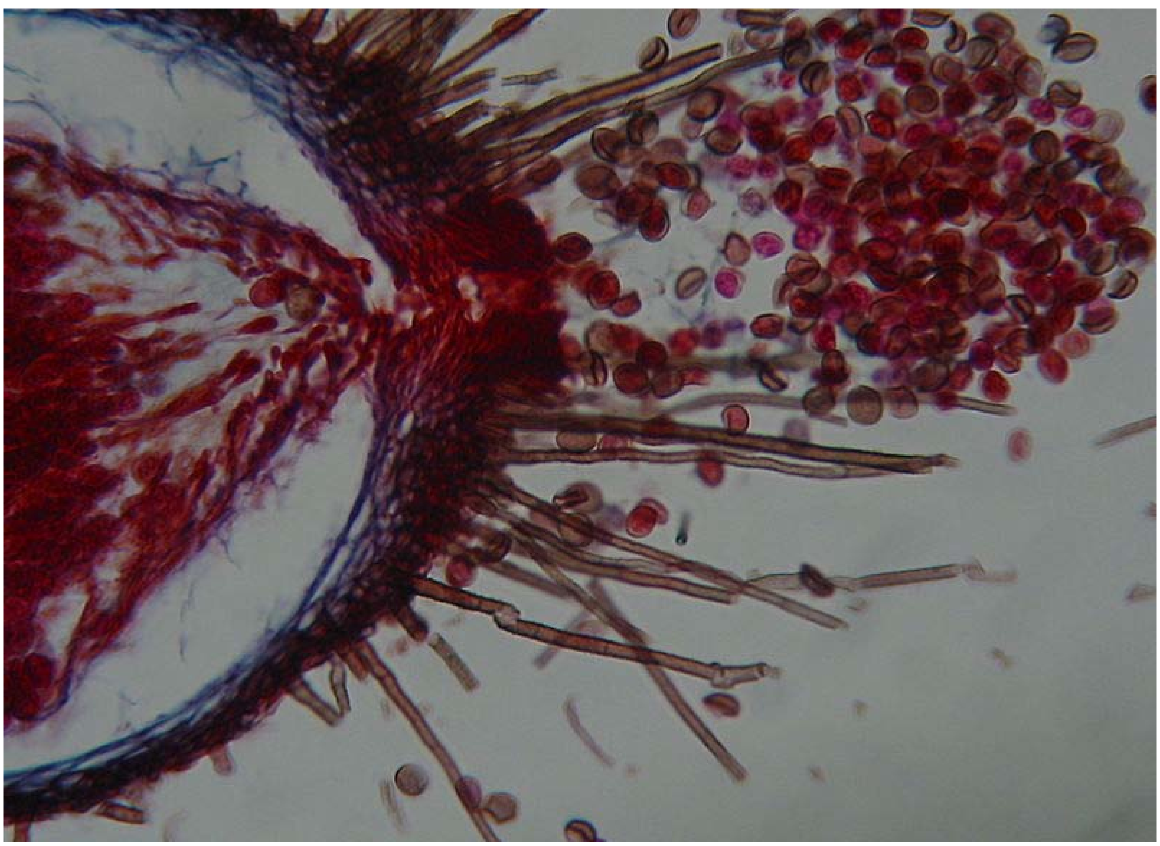
The form of the hymenium is divided into the following types (which *are* important for classification). Apothecia can be relatively large and fleshy, whereas the others are microscopic — about the size of flecks of ground pepper.

- **Apothecium**: here the ascocarp is open above like a cup. The fertile layer is free, so that many spores can be dispersed simultaneously. The morel, *Morchella*, an edible ascocarp, not a mushroom, favored by gourmets, is a mass of apothecia fused together in a single large structure or cap. The genera *Helvella* and *Gyromitra* are similar.

The ascocarp of a morel contains numerous apothecia



Perithecia of *Nectria*



Rupturing cleistothecium

- **Cleistothecium**: in this case the ascocarp is round with the hymenium enclosed, so the spores do not automatically get released, and fungi with cleistothecia have had to develop new strategies to disseminate their spores. The truffles, for instance, have solved this problem by attracting animals such as wild boars, which break open the tasty ascocarps and spread the spores over a wide area. Cleistothecia are found mostly in fungi that have little room available for their ascocarps, for instance those that live under tree bark, or underground like truffles. Also, the dermatophyte *Arthroderma* forms cleistothecia.

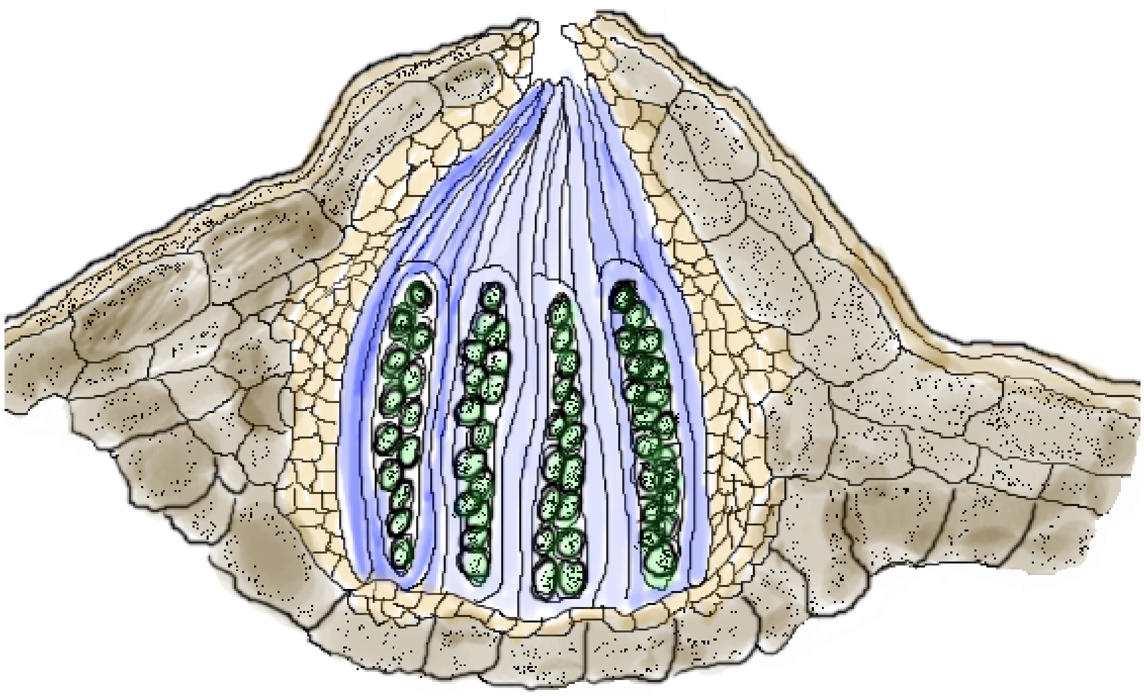
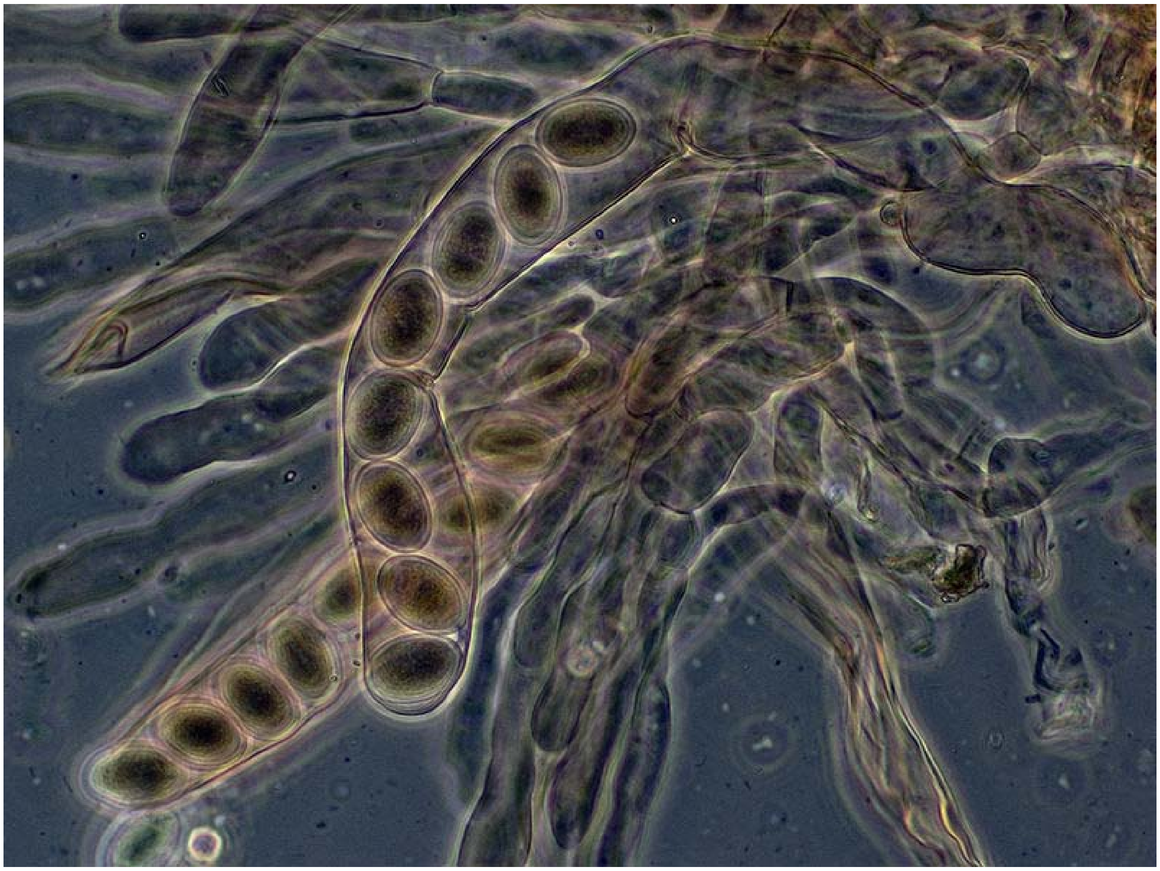


Diagram of a perithecium. The ascospores (green) are in 8 pairs in each ascus.

- **Perithecium**: this has the shape of a skittle or a ball. Its distinguishing feature is that on top it has a small pore, the **ostiole**, through which the spores are released one by one when ripe (in contrast to apothecia where they are released together). Perithecia are found for example on *Xylaria* (Dead Man's Fingers, Candle Snuff) and *Nectria*.

- **Pseudothecium**: this is similar to a perithecium, but the asci are not regularly organised into a hymenium and they are **bitunicate**, having a double wall that expands when it takes up water and shoots the enclosed spores out suddenly to disperse them. Example species are Apple scab (*Venturia inaequalis*) and the horse chestnut disease *Guignardia aesculi*.

Ascospore



Asci of *Morchella elata*, containing ascospores

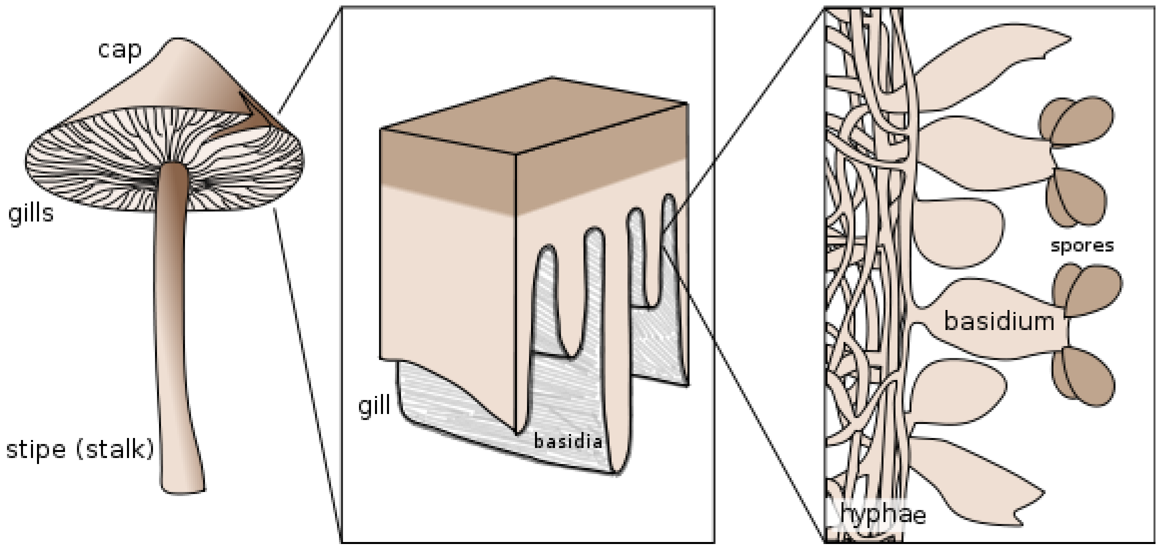
An **ascospore** is a spore contained in an ascus or that was produced inside an ascus. This kind of spore is specific to fungi classified as ascomycetes (Ascomycota).

Typically, a single ascus will contain eight ascospores. The eight spores are produced by a combination of a meiotic division followed by a mitotic division. The meiosis division turns the original diploid zygote nucleus into four haploid ones. That is, the single original cell from which the whole process begins contains two complete sets of chromosomes. In preparation for meiosis, all the DNA of both sets is duplicated, to make a total of four sets. The nucleus that contains the four sets divides in two stages, separating into four new nuclei – each of which has one complete set of chromosomes. Following this process, each of the four new nuclei duplicates its DNA and undergoes a division by mitosis. As a result, the ascus will contain four pairs of spores.

The Fungi Saccharomyces produces ascospores when grown on V-8 medium, acetate ascospor agar, or Gorodkowa medium. These ascospores are globose and located in asci. Each ascus contains one to four ascospores. The asci do not rupture at maturity.

Ascospores are stained with Kinyoun stain and ascospore stain. When stained with Gram stain, ascospores are gram-negative while vegetative cells are gram-positive.

Basidiocarp



Schematic of a typical basidiocarp, showing fruiting body, hymenium and basidia.

In fungi, a **basidiocarp**, **basidiome** or **basidioma** (plural: **basidiomata**), is the sporocarp of a basidiomycete, the multi-cellular structure on which the spore-producing hymenium is borne. Basidiocarps are characteristic of the hymenomycetes; rusts and smuts do not produce such structures. As with other sporocarps, epigeous (above-ground) basidiocarps that are visible to the naked eye (especially those with a more or less agaricoid morphology) are commonly referred to as mushrooms, while hypogeous (underground) basidiocarps are usually called false truffles.

Structure

All basidiocarps serve as the structure on which the hymenium is produced. Basidia are found on the surface of the hymenium, and the basidia ultimately produce spores. In its simplest form, a basidiocarp consists of an undifferentiated fruiting structure with a hymenium on the surface; such a structure is characteristic of many simple jelly and club fungi. In more complex basidiocarps, there is differentiation into a stipe, a pileus, and/or various types of hymenophores.

Types

Basidiocarps of *Amanita muscaria*, an agaric

Basidiocarps of *Ramaria rugosa*, a coral fungus

Basidiocarps of *Craterellus tubaeformis*, a cantharelloid fungus

Basidiocarps are classified into various types of growth forms based on the degree of differentiation into a stipe, pileus, and hymenophore, as well as the type of hymenophore, if present.

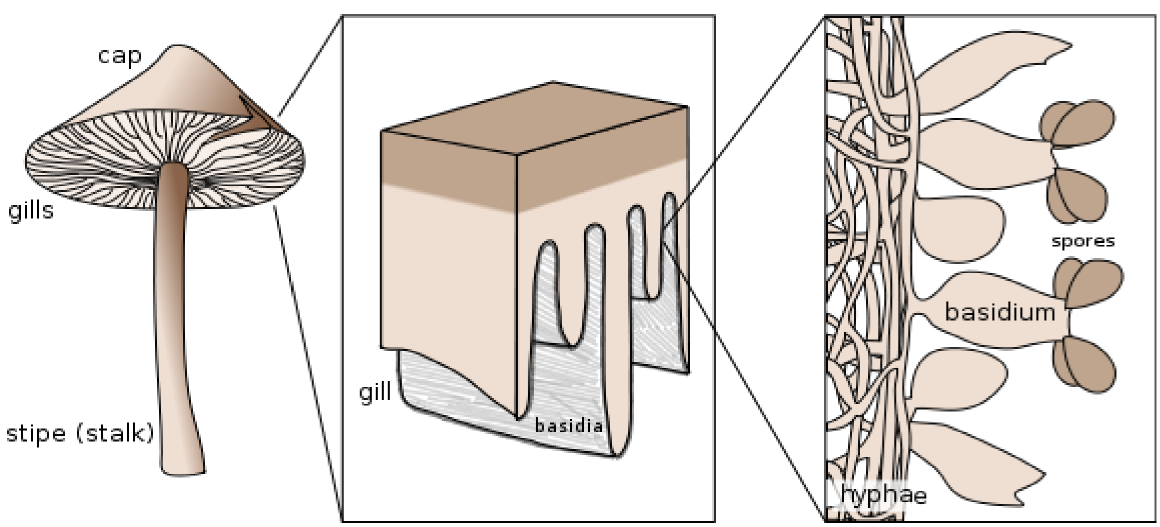
Growth forms include:

- jelly fungus – fruiting body is an undifferentiated mass of jelly-like tissue.
- club fungus and coral fungus – erect fruiting body without a distinct stipe and pileus, either unbranched (club fungus) or profusely branched (coral fungus).
- polypore – fruiting body is hard, woody, and perennial, and often grows shelf-like on the side of a tree or log. Polypores have a pileus, and usually (but not always) tubes and no stipe.

- cantharelloid fungus – fruiting body with shallow fold-like lamellae running over most of the lower surface of the fruiting body and not much differentiation between the stipe and pileus.
- tooth fungus or "hydnoid fungus" – fruiting body with tooth-like hymenophores.
- gasteromycete or "gastroid fungus" – fruiting body has a ball-like shape and in which the hymenophore has become entirely enclosed on the inside of the fruiting body.
- false truffle – like a gasteromycete, however, but with a hypogeous (underground) fruiting body.
- secotioid fungus – like a gasteromycete, but with stipe. Though to be an evolutionarily intermediate stage between a gasteromycete and an agaric.
- agaric or "agaricoid fungus" – fruiting body with a pileus, lamellae, and (usually) a stipe.
- bolete – fruiting body with a pileus, a stipe, and tubes.

Basic divisions of Agaricomycotina were formerly based entirely upon the growth form of the mushroom. Molecular phylogenetic investigation (as well as supporting evidence from micromorphology and chemotaxonomy) has since demonstrated that similar types of basidiomycete growth form are often examples of convergent evolution and do not always reflect a close relationship between different groups of fungi. For example, agarics have arisen independently in the Agaricales, the Boletales, the Russulales, and other groups, while secotioid fungi and false truffles have arisen independently many times just within the Agaricales.

Basidium



Schematic showing a basidiomycete mushroom, gill structure, and spore-bearing basidia on the gill margins.

A **basidium** (pl., **basidia**) is a microscopic, spore-producing structure found on the hymenophore of fruiting bodies of basidiomycete fungi. The presence of basidia is one of the main characteristic features of the Basidiomycota. A basidium usually bears four sexual spores called basidiospores; occasionally the number may be two or even eight. In a typical basidium, each basidiospore is borne at the tip of a narrow prong or horn called a **sterigma** (pl. sterigmata), and is forcibly discharged upon maturity.

The word *basidium* literally means *little pedestal*, from the way in which the basidium supports the spores. However, some biologists suggest that the structure more closely resembles a club. An immature basidium is known as a **basidiole**.

Basidium structure

Most basidiomycetes have single celled basidia (**holobasidia**), but in some groups basidia can be multicellular (a **phragmobasidia**). For instance, rust fungi in the order *Uredinales* have four-celled phragmobasidia that are transversely septate; some jelly fungi in the order Tremellales have four-celled phragmobasidia that are cruciately septate. Sometimes the basidium (metabasidium) develops from a **probasidium**, which is a specialized cell which is not elongated like a typical hypha. The basidium may be stalked or sessile.

Mechanism of basidiospore discharge

In most basidiomycetes, the basidiospores are **ballistospores**--they are forcibly discharged. The propulsive force is derived from a sudden change in the center of gravity of the discharged spore. Important factors in forcible discharge include **Buller's drop**, a droplet of fluid that can be observed to accumulate at the proximal tip (**hilar appendage**) of each basidiospore; the offset attachment of the spore to the subtending sterigma, and the presence of hygroscopic regions on the basidiospore surface.

Upon maturity of a basidiospore, sugars present in the cell wall begin to serve as condensation loci for water vapor in the air. Two separate regions of condensation are critical. At the pointed tip of the spore (the hilum) closest to the supporting basidium, Buller's drop accumulates as a large, almost spherical water droplet. At the same time, condensation occurs in thin film on the adaxial face of the spore. When these two bodies of water coalesce, the release of surface tension and the sudden change in the center of mass leads to sudden discharge of the basidiospore. Remarkably, Money (1998) has estimated the initial acceleration of the spore to be about 10,000 g.

Successful basidiospore discharge can only occur when there is sufficient water vapor available to condense on the spore.

Evolutionary loss of forcible discharge

Some basidiomycetes lack forcible discharge, although they still form basidiospores. In each of these groups, spore dispersal occurs through other discharge mechanisms. For example, members of the order Phallales (stinkhorns) rely on insect vectors for dispersal;

the dry spores of the Lycoperdales (puffballs) and Sclerodermataceae (earth balls and kin) are dispersed when the basidiocarps are disturbed; and species of the Nidulariales (bird's nest fungi) use a splash cup mechanism. In these cases the basidiospore typically lacks a hilar appendage, and no forcible discharge occurs. Each example is thought to represent an independent evolutionary loss of the forcible discharge mechanism ancestral to all basidiomycetes.

Clamp connection

A **clamp connection** is a structure formed by growing hyphal cells of certain fungi. It is created to ensure each septum, or segment of hypha separated by crossed walls, receives a set of differing nuclei, which are obtained through mating of hyphae of differing sexual types. It is used to create genetic variation within the hypha much like the mechanisms found in crozier during sexual reproduction.

Figure 1: *Cantharellus* clamp connection

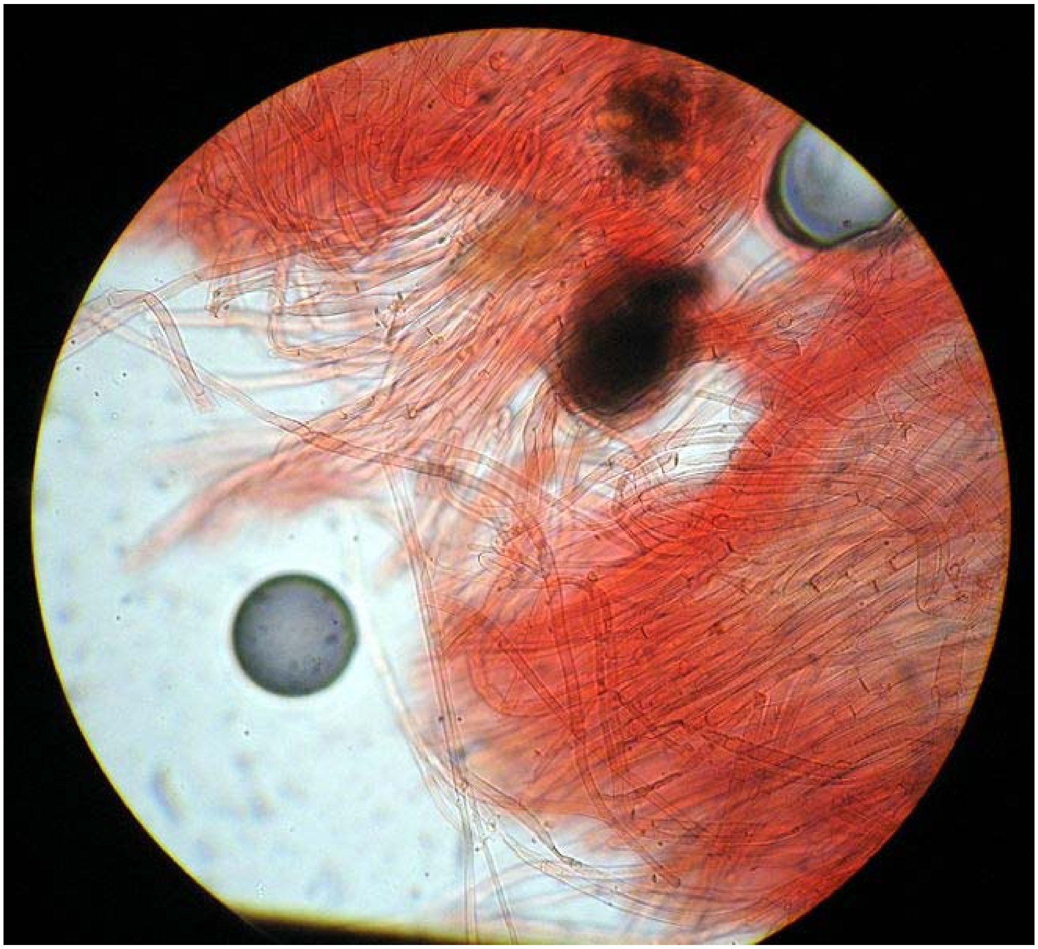


Figure 2: Clamp connections in mushroom hypha

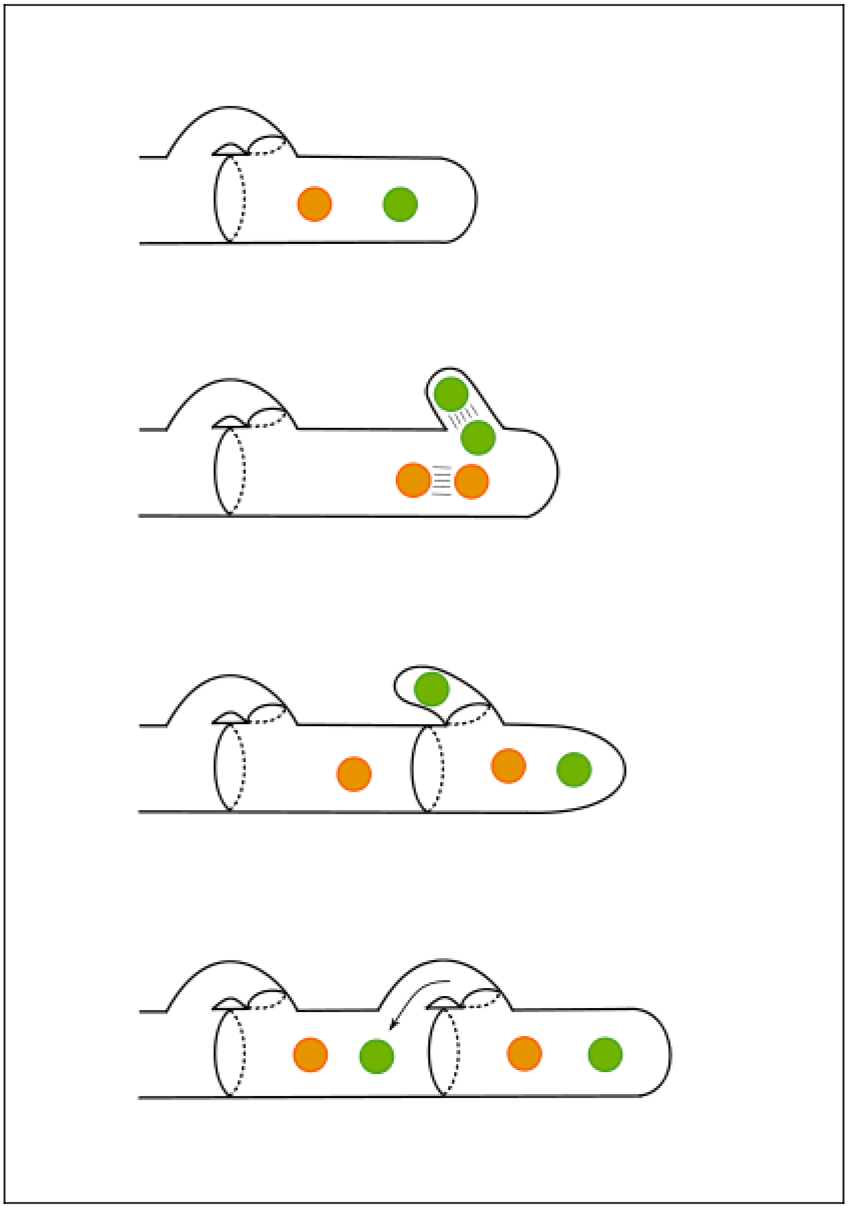


Figure 3: Clamp connection formation

Formation

Clamp connections are formed by the terminal hypha during elongation. Before the clamp connection is formed this terminal septa contains two nuclei (depicted as green and orange circles in Figure 3). Once the terminal septa is long enough it begins to form the clamp connection. At the same time each nuclei undergoes mitotic division to produce two daughter cells. As the clamp continues to develop it uptakes one of the daughter (green circle) cells produced and separates it from its sister cell. While this is occurring the remaining nuclei (orange circles) begin to migrate from one another to opposite ends of the cell. Once all these steps have occurred a septum forms, separating each set of nuclei.

Use in classification

Clamp connections are structures unique to the phylum Basidiomycota. Many fungi from this phylum produce spores in basidiocarps (fruit bodies, that is the mushrooms), above ground. Though clamp connections are exclusive to this phylum, not all species Basidiomycota possess these structures. As such, the presence or absences of clamp connections has been a tool in categorizing genera and species.

Conidiomata

Conidiomata are blister-like fruiting structures produced by a specific type of fungus called Coelomycetes. They are formed as a means of dispersing asexual spores call conidia, which they accomplish by creating the blister-like formations which then rupture to release the contained spores.

Structure

Conidiomata mainly consist of a mass of densely packed hypha which develops below the surface of the host cuticle, and the fungus may or may not use some of the host's own tissue to construct the structure. Development of these structures can either occur just below the cuticle or below the epidermal layer of the tissue. Formation on the differing levels is dependent upon the type of conidiomata being formed. Four types of conidiomata have been found and are classified as acervuli, pycnidia, sporodochia, synnemata.

Types

Avervuli

Acervuli is one of the two major groups of conidiomata (the other being pycnidia). Conidiomata of this type form just below the cuticle of host tissue and produce massive blisters which protrude fairly far into the outside environment. Acervuli also have a large opening at the top from which the conidia are released. *Colletotrichum* and *Pestaloptiopsis* are examples of genera which produce these structures.

Pycnidia

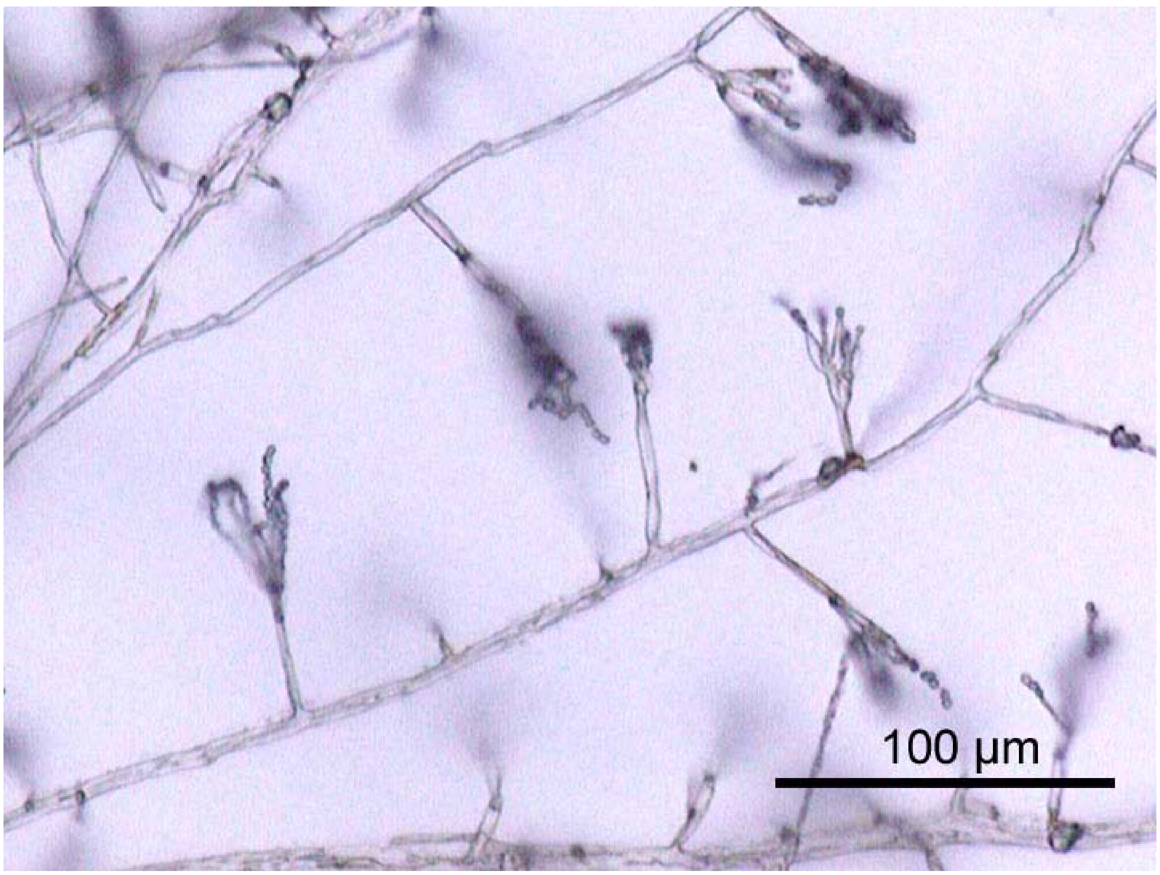
Pycnidia, the other major group of conidiomata, forms beneath the epithelial layer of host tissue. The structure resembles that of ascospores, and a pear-shaped structure produced entirely below the surface. This formations leaves the cuticle with only a minor bulge on the outside surface rather that a massive blister which was seen with Acervuli. Genera which produce this type of structure include Phomopsis, *Botryodiplodia*, and *Phoma*

Sporodochia and Synnmata

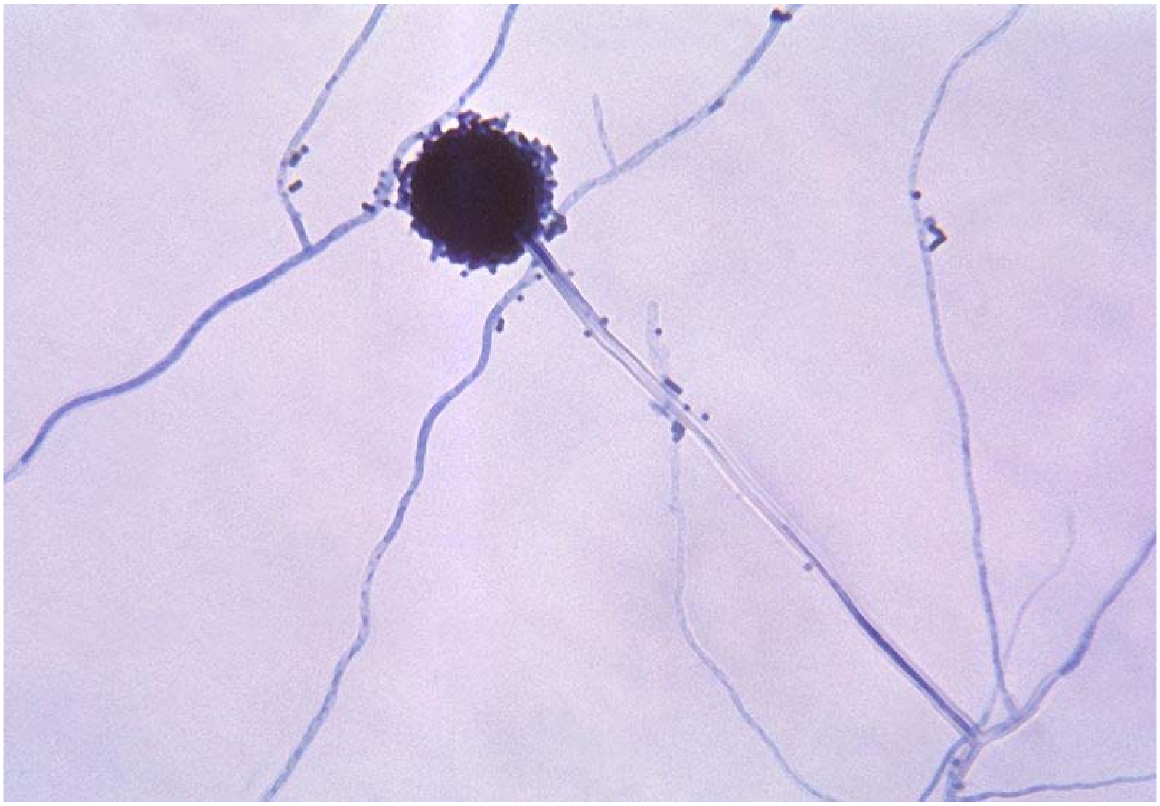
Sporodochia are small, compact, slightly raised circles which form on host. *Deuteromycota* and *Hyphomycetes* produce these types of structures.

Synnemata are large, fused conidiophores which form a strand resembling a stalk of wheat, with spores lining the outside of the structure. Genera which produce synnemata include *Doratomyces*.

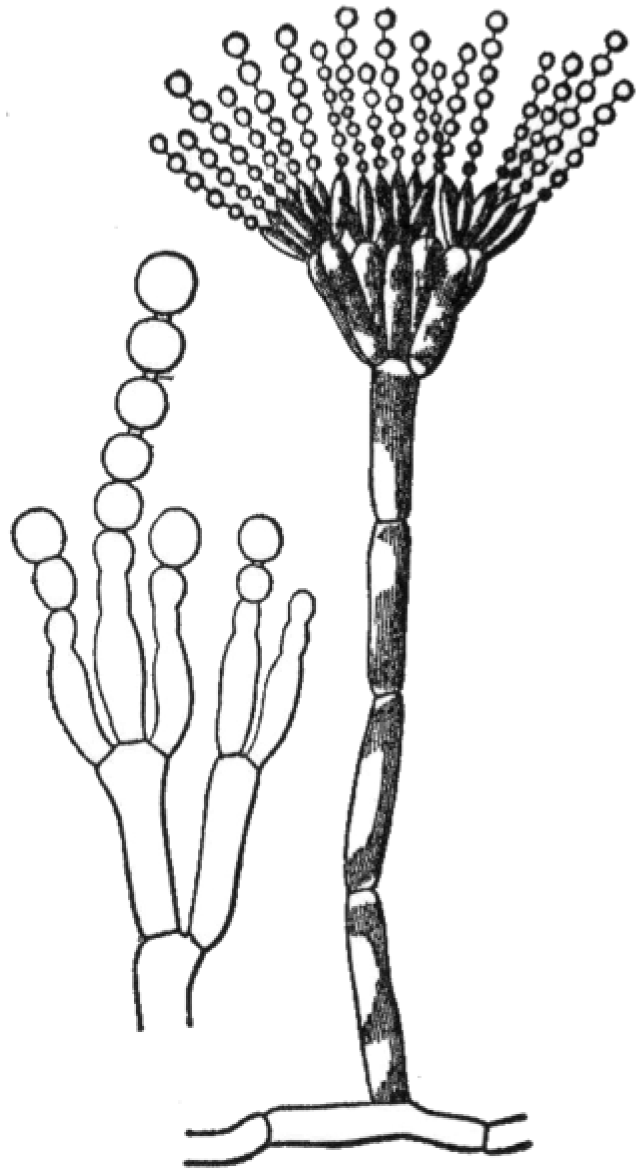
Hypha



Hyphae of Penicillium



Aspergillus niger



Conidia on conidiophores

A **hypha** (plural **hyphae**) is a long, branching filamentous structure of a fungus, and also of unrelated Actinobacteria. In most fungi, hyphae are the main mode of vegetative growth, and are collectively called a mycelium; yeasts are unicellular fungi that do not grow as hyphae.

Structure

A hypha consists of one or more cells surrounded by a tubular cell wall. In most fungi, hyphae are divided into cells by internal cross-walls called "septa" (singular septum). Septa are usually perforated by pores large enough for ribosomes, mitochondria and sometimes nuclei to flow between cells. The major structural polymer in fungal cell walls is typically chitin, in contrast to plants that have cellulosic cell walls. Some fungi have aseptate hyphae, meaning their hyphae are not partitioned by septa.

Growth

Hyphae grow at their tips. During tip growth, cell walls are extended by the external assembly and polymerization of cell wall components, and the internal production of new cell membrane. The spitzenkörper is an intracellular organelle associated with tip growth. It is composed of an aggregation of membrane-bound vesicles containing cell wall components. The spitzenkörper is part of the endomembrane system of fungi, holding and releasing vesicles it receives from the Golgi apparatus. These vesicles travel to the cell membrane via the cytoskeleton and release their contents outside the cell by the process of exocytosis, where it can then be transported to where it is needed. Vesicle membranes contribute to growth of the cell membrane while their contents form new cell wall. The spitzenkörper moves along the apex of the hyphal strand and generates apical growth and branching; the apical growth rate of the hyphal strand parallels and is regulated by the movement of the spitzenkörper.

As a hypha extends, septa may be formed behind the growing tip to partition each hypha into individual cells. Hyphae can branch through the bifurcation of a growing tip, or by the emergence of a new tip from an established hypha.

Modifications

Hyphae may be modified in many different ways to serve specific functions. Some parasitic fungi form haustoria that function in absorption within the host cells. The arbuscules of mutualistic mycorrhizal fungi serve a similar function in nutrient exchange, so are important in assisting nutrient and water absorption by plants. Hyphae are found enveloping the gonidia in lichens, making up a large part of their structure. In nematode-trapping fungi, hyphae may be modified into trapping structures such as constricting rings and adhesive nets. Mycelial cords can be formed to transfer nutrients over larger distances.

Types

Classification based on cell division

- Septate (with septa)
  - *Aspergillus* and many other species have septate hyphae.

- Aseptate or coenocytic (without septa)
  - Non-septate hyphae are associated with Mucor, some zygomycetes, and other fungi.

- "Pseudohyphae" are distinguished from true hyphae by their method of growth, relative frailty and lack of cytoplasmic connection between the cells.

- Yeast can form pseudohyphae. They are the result of a sort of incomplete budding where the cells remain attached after division.

Classification based on cell wall and overall form

Characteristics of hyphae can be important in fungal classification. In basidiomycete taxonomy, hyphae that comprise the fruiting body can be identified as generative, skeletal, or binding hyphae.

- **Generative** hyphae are relatively undifferentiated and can develop reproductive structures. They are typically thin-walled, occasionally developing slightly thickened walls, usually have frequent septa, and may or may not have clamp connections. They may be embedded in mucilage or gelatinized materials.
- **Skeletal** hyphae are of two basic types. The classical form is thick-walled and very long in comparison to the frequently septate generative hyphae, which are unbranched or rarely branched, with little cell content. They have few septa and lack clamp connections. Fusiform skeletal hyphae are the second form of skeletal hyphae. Unlike typical skeletal hyphae these are swollen centrally and often exceedingly broad, hence giving the hypha a fusiform shape.
- **Binding** hyphae are thick-walled and frequent branched. Often they resemble deer antlers or defoliated trees because of the many tapering branches.

Based on the generative, skeletal and binding hyphal types, in 1932 E. J. H. Corner applied the terms monomitic, dimitic, and trimitic to hyphal systems, in order to improve the classification of polypores.

- Every fungus must contain generative hyphae. A fungus which only contains this type, as do fleshy mushrooms such as agarics, is referred to as **monomitic**.

- Skeletal and binding hyphae give leathery and woody fungi such as polypores their tough consistency. If a fungus contains all three types (example: *Trametes*), it is called **trimitic**.

- If a fungus contains generative hyphae and just one of the other two types, it is called **dimitic**. In fact dimitic fungi almost always contain generative and skeletal hyphae; there is one exceptional genus, *Laetiporus* that includes only generative and binding hyphae.

Fungi that form fusiform skeletal hyphae bound by generative hyphae are said to have **sarcodimitic** hyphal systems. A few fungi form fusiform skeletal hyphae, generative hyphae, and binding hyphae, and these are said to have **sarcotrimitic** hyphal systems. These terms were introduced as a later refinement by E. J. H. Corner in 1966.

Classification based on refractive appearance

Hyphae are described as "gloeoplerous" ("gloeohyphae") if their high refractive index gives them an oily or granular appearance under the microscope. These cells may be yellowish or clear (hyaline). They can sometimes selectively be coloured by sulphovanillin or other reagents. The specialized cells termed cystidia can also be gloeoplerous.

Chapter- 8

Medicinal Mushrooms

Medicinal mushrooms are mushrooms or extracts from mushrooms that are used or studied as possible treatments for diseases. Some mushroom materials, including polysaccharides, glycoproteins and proteoglycans, modulate immune system responses and inhibit tumor growth. Some medicinal mushroom isolates that have been identified also show promising cardiovascular, antiviral, antibacterial, antiparasitic, anti-inflammatory, and antidiabetic properties. Currently, several extracts have widespread use in Japan, Korea and China, as adjuncts to radiation treatments and chemotherapy.

Historically, mushrooms have long had medicinal uses, especially in traditional Chinese medicine. Mushrooms have been a subject of modern medical research since the 1960s, where most modern medical studies concern the use of mushroom extracts, rather than whole mushrooms. Only a few specifc mushroom extracts have been extensively tested for efficacy. Polysaccharide-K and lentinan are among the mushroom extracts with the firmest evidence. The available results for most other extracts are *in vitro* data, effects on isolated cells in a lab dish, animal models like mice, or underpowered clinical human trials. Studies show that glucan-containing mushroom extracts primarily change the function of the innate and adaptive immune systems, functioning as bioresponse modulators, rather than by directly killing bacteria, viruses, or cancer cells as cytocidal agents. In some countries, extracts like polysaccharide-K, schizophyllan, polysaccharide peptide, and lentinan, are government-registered adjuvant cancer therapies.

Fungi that do not produce mushrooms, especially molds and yeasts, are the original source of some notable drugs including lovastatin, ciclosporin, as well as the antifungal griseofulvin, and the antibiotics penicillin and cephalosporin.

History

Man holding *ganoderma* mushroom (artist Chen Hongshou 1598-1652)

For close to 5,000 years, mushrooms have been consumed for medicinal purposes. The concept of a medicinal mushroom is most established in China, Japan, Korea, Russia, and Eastern European and Baltic countries. Medicinal use of shiitake mushrooms dates back to 100 AD in China. In ancient Japan, *Grifola frondosa* was thought to be medicinal, and was traded for it's weight in silver.

In the hadith, Muhammad said, "Truffles are 'manna' which Allah, sent to the people of Israel through Moses, and its juice is a medicine for the eyes". The ancient Egyptians considered mushrooms food for royalty. Hippocrates wrote that *Fomes fomentarius* was used as an ointment for the skin. *Fomes fomentarius* was used in Europe during the 18th and 19th centuries as an ointment for wounds. Ötzi the Iceman, a mummified human from 3300 BC, was found carrying two polypore mushrooms *Fomes fomentarius* and *Piptoporus betulinus*. Researchers have noted *Piptoporus betulinus* was probably used medicinally, considering Ötzi was infected with *Trichuris trichiura*.

Although mushrooms are sometimes incorrectly considered vegetables, they are far more closely related to animals than to plants.

Research

A 2008 review by Borchers stated that although there was "no scientific basis" for using mushrooms or their extracts in treating humans at this time, "there is significant potential for rigorous research to understand the potential of mushrooms in human disease". A 2010 review by Ferreira stated, "mushrooms comprise a vast and yet largely untapped source of powerful new pharmaceutical products. In particular, and most importantly for modern medicine, they represent an unlimited source of compounds which are modulators of tumour cell growth".

Mushroom polysaccharides, the immune system, and cancer

Tremella fuciformis

A diverse class of polysaccharides (typically beta-glucans) found in medicinal mushrooms may alter immune responses. The effect of these compounds on the immune system was discovered in the 1960s.

The potential anticancer and cancer preventative effects of medicinal mushrooms are thought to be due to altering immune function, rather than by directly killing or inhibiting cancer cells. For example, the mushroom compound polysaccharide-K (PSK) "significantly enhanced" the number and activity of immune system cells in most patients treated with the extract, with relatively few side effects and no undesirable interference with conventional cancer treatments. Altogether, extracts from six different mushrooms have been studied for use against cancer in humans.

Although the cancer drug paclitaxel was discovered in a tree, and is now made synthetically, the fungus *nodulisporium sylviforme* can create it.

Effect on blood sugar

Coprinus comatus

Animal research and limited clinical data has shown that some medicinal mushrooms have potential to lower elevated blood sugar levels. Mushrooms noted for this ability include *Tremella fuciformis*, *Poria cocos*, reishi, *Auricularia auricula-judae*, *Agaricus* *campestris*, *Agaricus blazei*, chaga, *Hericium erinaceus*, *Agrocybe aegerita*, *Coprinus comatus*, and cordyceps. Explanation for this effect is limited, with the exception of the maitake mushroom; its ability to lower blood sugar levels has been explained by the fact that the mushroom naturally contains an alpha-glucosidase inhibitor.

Effect on cholesterol

Auricularia auricula-judae

Some mushrooms like *Tremella fuciformis*, *Auricularia auricula-judae*, *Agaricus blazei*, maitake, and reishi have been shown to be able to have an inhibitory effect on cholesterol levels. Shiitake mushrooms contain the anticholesterol compound eritadenine.

Different varieties of fungi are known to produce zaragozic acids, compounds known to inhibit cholesterol synthesis by inhibiting the enzyme farnesyl-diphosphate farnesyltransferase.

Fungal statins

Statins are a class of drugs used to treat high cholesterol by inhibiting the enzyme HMG-CoA reductase. The first statin ever discovered was mevastatin, a compound produced by the fungus *Penicillium citrinum*.

Oyster mushrooms have been found to naturally contain the statin lovastatin. Tests have shown the oyster mushroom contains up to 2.8% lovastatin on a dry weight basis.

Red yeast rice is made from the growth of the fungus *Monascus purpureus* on rice. This fermented food has a long history in Asian cuisine and medicine. Red yeast rice is known to contain lovastatin. Using the *Aspergillus terreus* fungus, scientists created the statin simvastatin.

Vitamin D_2 and conjugated linoleic acid (CLA)

Mushrooms are rare vegan sources of vitamin D and conjugated linoleic acid (CLA). Portobello (*Agaricus bisporus*) and shiitake mushrooms are known to contain large amounts of vitamin D_2 after brief UV light exposure. Portobello and *Agaricus blazei* mushrooms contain conjugated linoleic acid (CLA).

In vitro antiviral, antibacterial, antifungal, and antimicrobial activities

Cantharellus cibarius

Laetiporus sulphureus

Fungi produce various antiviral, antibacterial, antifungal, and antimicrobial compounds to survive in the wild against competing or pathogenic agents. The fungus *Penicillium chrysogenum* produces the famous antibiotic penicillin, while the antifungal drug griseofulvin, is produced from the fungus *Penicillium griseofulvum*. Research has reported that *in vitro*, some mushrooms have activity against certain viruses, bacteria, fungi, and microorganisms. A review by The University of Mississippi stated of an "evaluation of over 200 mushroom species, more than 75% of screened polypores showed strong antimicrobial activity."

Agaricus subrufescens (**agaricus blazei**) - Activity against poliovirus and the western equine encephalitis virus. *Agrocybe aegerita* (**pioppino**) - Activity against the tobacco mosaic virus. *Boletus edulis* (**porcini**) - Activity against HIV and the tobacco mosaic virus. *Cantharellus cibarius* (**chanterelle**) - Activity against certain microbes, bacteria, and fungi. *Cordyceps* (**cordyceps**)- Activity against *Bipolaris maydis*, *Mycosphaerella arachidicola*, *Rhizoctonia solani*, *Candida albicans* and HIV. *Fistulina hepatica* (**beefsteak fungus**) - Antibacterial activity. *Ganoderma applanatum* (**artist's conk**) - Activity against the vaccinia virus, *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas syringae*. *Ganoderma lucidum* (**reishi**) - Activity against *Plasmodium*, *Botrytis cinerea*, *Fusarium oxysporum*, HSV-1, HSV-2, influenza virus, and *vesicular stomatitis*. *Grifola frondosa* (**maitake**) - Activity against HSV-1, and hepatitis B virus. *Hypsizygus tessellatus* (**beech mushroom**) - Activity against the Epstein-Barr virus. *Kuehneromyces mutabilis* (**sheathed woodtuft**) - Activity against the influenza virus. *Laetiporus sulphureus* (**chicken of the woods**) - Activity against methicillin-resistant

Staphylococcus aureus (MRSA) and glycopeptide-resistant *Leuconostoc mesenteroides*. *Lentinula edodes* (**shiitake**) - Activity against HSV-1 and HIV. *Piptoporus betulinus* (**birch polypore**) - Activity against the vaccinia virus, *staphylococcus aureus*, *enterococcus faecalis*, *bacillus subtilis*, *escherichia coli*, *rhodotorula rubra*, *kluyveromyces marxianus*, *candida albicans*, *sporobolomyces salmonicolor*, and *penicillium notatum*. *Pleurotus eryngii* (**king oyster mushroom**)- Activity against the tobacco mosaic virus. *Pleurotus pulmonarius* (**indian oyster**) - Nematicidal activity. *Polyporus umbellatus* (**zhu-ling**) - Activity against *Chlamydia trachomatis*. *Poria cocos* (**fu-ling**) - Activity against *Chlamydia trachomatis*. *Sparassis crispa* (**cauliflower mushroom**) - Antifungal activity and activity against HIV. *Terfezia* (**desert truffle**) - Activity against *Bacillus subtilis* and *Staphylococcus aureus*. *Ustilago maydis* (**huitlacoche**) - Contains the antibiotic ustilagic acid.

The following mushrooms inhibited the HIV virus *in vitro*, *Hericium erinaceum* (**lion's mane mushroom**), *Flammulina velutipes* (**enokitake**), *Lactarius camphoratus* (**candy cap**), *Inonotus obliquus* (**chaga**), *Pleurotus ostreatus* (**oyster mushroom**), *Pleurotus pulmonarius* (**indian oyster**), *Trametes versicolor* (**turkey tail mushroom**), *Poria cocos* (**hoelen**), and *Umbilicaria esculenta* (**stone ear**).

Effect on cognition

Hericium erinaceus

Polyozellus multiplex

Hericium erinaceus (lion's mane mushroom, pom pom blanc, yamabushitake) has been researched for possible antidementia activity. *In vitro* experiments with *Hericium erinaceus* have demonstrated its ability to stimulate rat nerve cells, stimulate nerve growth factor, and stimulate myelination. In 2009, a double-blind, parallel-group, placebo-controlled trial showed that supplementation with *Hericium erinaceus* improved cognitive ability.

Polyozellus multiplex (blue chanterelle) contains the compound polyozellin, a chemical which inhibits prolyl endopeptidase, an enzyme that may be involved in Alzheimer's disease.

Many *psilocybin* mushrooms contain the hallucinogens psilocybin, psilocin, and baeocystin. *Amanita muscaria* (fly agaric) contains the semi-toxic hallucinogens muscimol and ibotenic acid. Using *Claviceps purpurea* (ergot), scientists created pergolide and cabergoline, two drugs used for Parkinson's disease. Using *Claviceps purpurea*, Albert Hofmann created lysergic acid diethylamide (LSD).

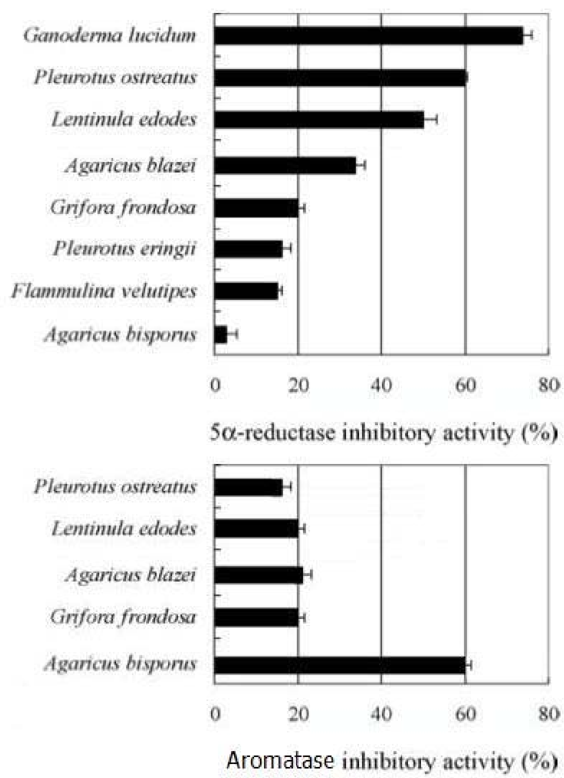
Antioxidant activity

Mushrooms are known to contain various types of antioxidant compounds. Chemical analysis has shown that a specific antioxidant found in some mushrooms like *Flammulina velutipes* and *Agaricus bisporus* is ergothioneine.

Anti-inflammatory activity

Animals studies noted extracts of *Phellinus linteus*, *Ganoderma lucidum*, and the *Inonotus obliquus* may reduce inflammation. An *in vitro* experiment showed extracts of *Grifola frondosa* may inhibit the enzyme cyclooxygenase. *Agrocybe aegerita* may partially inhibit the enzyme cyclooxygenase. *Piptoporus betulinus* demonstrated *in vitro* anti-inflammatory properties.

In vitro antihormone activity



In vitro assay of mushrooms impact on aromatase and 5-alpha reductase activity

Mushrooms may be able to influence the production of certain human hormones, based on evidence from enzyme assay analysis. *Agaricus bisporus* may be able to partially inhibit the activity of aromatase, the enzyme responsible for producing estrogen. Reishi mushrooms have been shown to be able to partially inhibit the activity of 5-alpha reductase *in vitro*, the enzyme responsible for producing dihydrotestosterone.

Epidemiological research

Research in Japan found enokitake mushroom producers had lower cancer rates than the rest of the population. A case-control study published by the *International Journal of Cancer* in 2009, compared the diets of 1009 women who had been diagnosed with breast cancer with 1009 healthy women. Compared to nonconsumers of mushrooms, women who consumed at least 10 grams of fresh mushrooms per day had a breast cancer risk of only 36%. The risk for those who consumed at least 4 grams of dried mushrooms per day was 53%. A similar case-control study involving 362 women with breast cancer also found a strong association between mushroom consumption and decreased risk of breast cancer in postmenopausal, but not premenopausal, women. Researchers at the City of Hope National Medical Center have noted this possible inhibition of breast cancer is due to the fact mushrooms may reduce estrogen production by inhibiting the enzyme aromatase.

Edible species

Agaricus bisporus (Portobello, crimini, white button, champignon mushroom)

Agaricus bisporus

Agaricus bisporus (portobello, crimini, white button, champignon mushroom) is the world's most popular edible mushroom. Research *in vitro* suggested that the mushroom may inhibit the enzyme aromatase, which is used by the body to create estrogen. The FDA and the National Cancer Institute have also shown interest in investigating this mushroom's relation to breast cancer development. Mouse studies have reported potential immune system regulation, while an *in vitro* study reported activity against various cancer cell lines.

Agaricus subrufescens (Agaricus blazei, almond mushroom)

Agaricus subrufescens

Agaricus subrufescens (*Agaricus blazei*, *Agaricus brasiliensis*, *Agaricus sylvaticus*, almond mushroom, himematsutake) is an almond-scented mushroom that was commercially grown in the United States during the 19th century.

In Japan, *Agaricus subrufescens* is the most popular complementary and alternative medicine used by cancer patients, with usage estimated at 500,000. There is some evidence for using Agaricus extracts in patients with certain cancers, such as colorectal cancer and and gynaecological cancers.

Animal research showed *Agaricus subrufescens* may promote vaccination.

Agrocybe aegerita (Pioppino mushroom)

Agrocybe aegerita

Agrocybe aegerita (pioppino mushroom, chestnut mushroom) may have anticancer and immune modulating activities.

***Flammulina velutipes* (Enokitake, winter mushroom)**

Flammulina velutipes

Flammulina velutipes (enokitake, winter mushroom) contains compounds with antitumor activity, and epidemiological studies in Japan have associated the mushroom with lower cancer rates. Animal research showed the mushroom may inhibit cancer development.

***Grifola frondosa* (Maitake, hen-of-the-woods)**

Grifola frondosa

Grifola frondosa is an edible mushroom revered in Asian folk medicine. In ancient Japan, the mushroom was worth its weight in silver. No well-designed randomized controlled trials have been conducted, although some researchers advocate investigating maitake's possible effects on cancer, diabetes, and immune system activity.

Lentinula edodes (Shiitake)

Lentinula edodes

Shiitake (*Lentinula edodes*) is the world's second most popular mushroom. Modern research has indicated that shiitake mushroom may stimulate the immune system, possess antibacterial properties, reduce platelet aggregation, have antiviral properties, and may have chemicals that act as proteinase inhibitors.

Lentinan, an isolate of Shiitake mushrooms, is used as an intravenous anticancer agent in some countries. Studies have demonstrated lentinan possesses antitumor properties, and human clinical studies have associated lentinan with a higher survival rate, higher quality of life, and lower recurrence of cancer. Clinical research with lentinan includes studies with 78 hepatocellular carcinoma patients, 32 gastric cancer patients, a multi-institutional study of lentinan and gastric cancer, a meta-analysis of lentinan and gastric cancer, 80 colorectal cancer patients, 20 gastric cancer patients, 36 hepatocellular carcinoma patients, and 29 pancreatic cancer patients.

Active Hexose Correlated Compound (AHCC), an isolate of Shiitake mushrooms, is an alternative medicine used by Japanese cancer patients, and current research is examining its use as an adjunctive treatment for people with hepatocellular cancer. Animal research suggests AHCC can help prevent influenza and the West Nile virus.

Pleurotus eryngii (King oyster mushroom)

Pleurotus eryngii

Cellular research showed *Pleurotus eryngii* (king oyster mushroom) may stimulate immune function.

Pleurotus ostreatus (Oyster mushroom)

Pleurotus ostreatus

The oyster mushroom (hiratake, píng gū) naturally contains the statin lovastatin, which, in its purified or synthetic form, is used to lower elevated cholesterol. Research with *Pleurotus ostreatus* demonstrated activity against various cancer cell lines and animals studies have shown an anticancer effect.

Sparassis crispa (Cauliflower mushroom)

Sparassis crispa

Animal studies have shown *Sparassis crispa* (cauliflower mushroom, hanabiratake) has potential anticancer and immune enhancing activities.

Tremella mesenterica (Golden jelly fungus)

Tremella mesenterica

Tremella mesenterica may have immuno-modulatory and anticancer activity.

Species used by tea or extraction

Antrodia camphorata

Antrodia camphorata is a medicinal mushroom of Taiwan. A review from 2009, noted the mushroom may have immuno-modulatory and anticancer activity.

***Cordyceps sinensis*, *Cordyceps militaris* (Caterpillar fungus)**

Cordyceps militaris

Cordyceps mushrooms (*C. sinensis*, *C. militaris*, *C. pruinosa*, *C. ophioglossoides*) are a Chinese herbal remedy with 2000 years of history. These mushrooms have traditionally been used for a variety of ailments, including cancer. Extracts from both mycelium and fruiting bodies of *C. sinensis*, *C. militaris* showed significant anticancer activities. Some polysaccharide components including cordycepin (3'-deoxyadenosine), have been isolated from *C. sinensis* and *C. militaris*.

Limited clinical data supports the use of cordyceps for fatigue, bronchitis and coughs. Cordyceps may improve exercise performance in healthy older subjects.

Ganoderma lucidum (Língzhī. reishi)

Ganoderma lucidum

Ganoderma lucidum (língzhī, reishi, mannentake) mushrooms have a long and very well established history in traditional Asian medicine. *Ganoderma* is the most famous medicinal mushroom in Asia and can be found in many herbal remedies. *Ganoderma* teas are described in Shennong Ben Cao Jing and Bencao Gangmu. The *Ganoderma* mushroom is occasionally seen in Chinese artwork.

Cellular and animal research has shown *Ganoderma* may contain anticancer and immune system enhancing properties. Researchers have noted *Ganoderma* appears to have antibacterial, antiviral, and antifungal properties. Animal studies have noted *Ganoderma* may protect the liver and protect against radiation. A randomized clinical study noted *Ganoderma* improved urinary tract symptoms in men. Research has shown that *Ganoderma* contains compounds that may act as ACE inhibitors, inihibit blood platelets, and fibrosis. Many of these possible effects, including anticancer potential, have not been validated with clinical trials.

Inonotus obliquus (Chaga mushroom)

Inonotus obliquus

Inonotus obliquus or Chaga is a mushroom that has been used medicinally in Russia, Poland, and Belarus. In Russia, befungin an extract of Chaga, is considered a medicine. A review from 2010, stated, "as early as in the sixteenth century, Chaga was used as an effective folk medicine in Russia and Northern Europe to treat several human malicious tumors and other diseases in the absence of any unacceptable toxic side effects." In *Cancer Ward*, a novel by Aleksandr Solzhenitsyn, Dr. Maslennikov believes tea made from the chaga mushroom inhibits cancer.

The mushroom has anticancer properties and may be able to stimulate the immune system. In one experiment, mice implanted with melanoma showed a 4-fold increase in survival rate when given an extract of Chaga mushroom. The Chaga mushroom contains betulin, which can be converted to betulinic acid. Betulinic acid is known as a potent anticancer compound.

Peziza vesiculosa

Studies with mice have shown *Peziza vesiculosa* may have anticancer activity.

Phellinus linteus (Mesima)

Phellinus linteus is a medicinal mushroom known in Korea. A 2008 review from Beth Israel Deaconess Medical Center reported that *Phellinus linteus* is a possible anticancer agent.

Piptoporus betulinus (Birch polypore mushroom)

Piptoporus betulinus

Piptoporus betulinus (birch polypore mushroom, birch bracket mushroom, kanbatake) may have anticancer properties. Ötzi the Iceman, a mummified human from 3300 BC, was found carrying *Piptoporus betulinus* wrapped in a leather string. Researchers have noted the mushroom was probably used for medicinal properties, considering Ötzi was found to be infected with the parasite *Trichuris trichiura*.

***Polyporus umbellatus* (Zhu-ling)**

Polyporus umbellatus

Polyporus umbellatus may have immuno-modulatory and anticancer activity.

***Poria cocos* (Fu-ling, hoelen)**

Poria cocos (*Wolfiporia extensa*, hoelen, fu-ling) is another medicinal mushroom used in folk medicine. A 2009 review noted the mushroom may have immuno-modulatory and anticancer activity.

Trametes versicolor (Turkey tail mushroom)

Trametes versicolor

Trametes versicolor (turkey tail mushroom, *Coriolus versicolor*, kawaratake, yun-zhi) is a medicinal mushroom known for producing polysaccharide-K and polysaccharide peptide. Polysaccharide-K is used in some countries as a therapy for patients undergoing chemotherapy for cancer. Polysaccharide-K is intended to counteract the negative effect that many chemotherapeutic agents have on the immune system. A detailed scientific review of polysaccharide-K by the MD Anderson Cancer Center, reported 40 clinical and 55 animal studies have been conducted on this mushroom isolate. Polysaccharide-K remains a best selling anticancer medicine in Japan, and it is commonly used as a supplement to surgery, radiation, and chemotherapy.