CPSC Staff Statement on Toxicology Excellence for Risk Assessment (TERA) Report "Review of the Health Risks of Mold, Basic Mold Characteristics"[1]

June 2015

The report titled, "Review of the Health Risks of Mold, Basic Mold Characteristics," presents basic mold characteristics and was performed by TERA under Contract CPSC-D-12-0001, Task Order 0013. A second report, "Review of the Health Risk of Mold, Health Effects of Molds and Mycotoxins," can be found under a separate cover. Consumer exposure to mold on a product may be more frequent and direct than exposures that might occur in a building setting, making remediation even more important for products with mold contamination. Therefore, this contract was initiated for staff to gain a better understanding of these hazards and new information developed over the past several years on mold characteristics and toxicity.

First, TERA provides general information on mold classification schemes (taxonomy). Next, TERA provides the growth characteristics of mold, including indoor and outdoor mold presence, growth on materials, prevention of mold growth, and remediation. This report concludes with a discussion of general effects of medically important molds, such as *Alternaria*, *Aspergillus*, *Penicillium*, and *Stachybotrys*, and some terminology, by detailing the taxonomy, physical characteristics, and medical importance of each mold.

Based on this report, of the approximately 100,000 named fungal species, 500 are commonly associated with human or animal disease, and 50 of those are known to be infectious in healthy humans. Fungi are chemoheterotrophs[2]; therefore, they absorb their nutrients from their environment. Because of these unique characteristics, they are able to grow on substrates, such as bathroom walls, shoe leather, and paper. Some of the key factors associated with mold growth include: moisture, presence of organic material, age of the material, meteorological conditions, presence of air conditioning systems, and pH.[3]

A fungal infection is called a mycosis. Generally, fungal infections can be classified as: systemic (whole body), cutaneous (skin), subcutaneous (under the skin), superficial (on a surface), or opportunistic (secondary to another infection, often a bacterial infection). Exposure to some of these molds may cause adverse health effects, including: asthma, allergic reactions, lung infections, infections in wounds, psoriasis, eczema, endocarditis,[4] and inflammation of the abdomen, eye, or esophagus.

[1] This statement was prepared by the CPSC staff, and the attached report was produced by TERA for CPSC staff. The statement and report have not been reviewed or approved by, and do not necessarily represent the views of, the Commission.

[2] An organism deriving energy by ingesting intermediates or building blocks that it is incapable of creating on its own, *i.e.*, obtains its energy from the oxidation of organic compounds.

[3] A measure of the acidity or alkalinity of a substance.

[4] An inflammation of the inner layer of the heart, the endocardium. It usually involves the heart valves.

Review of the Health Risks of Mold

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Basic Mold Characteristics

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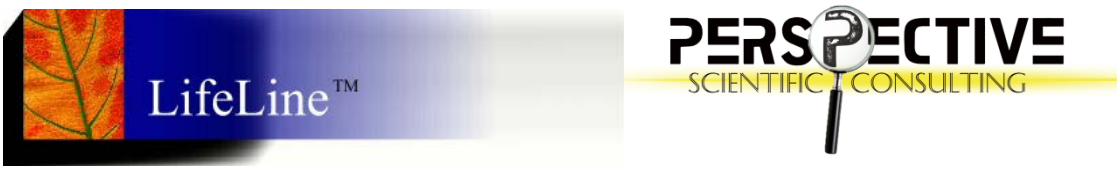

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1 Basic Mold Characteristics

1.1 General Information

1.1.1 Mold Classification Schemes (Taxonomy)

There are approximately 100,000 named fungal species, 500 of which are commonly associated with human or animal disease, and 50 of those are known to be infectious in healthy humans (Brandt and Warnock, 2011). Fungi are heterotrophic, meaning that they require organic carbon for nutrition, and this requirement is met by embedding into their food source via enzymes.

Fungi are broken into two categories based on physical appearance of colony characteristics and reproductive spores (Tortora et al., 2010). Yeasts are nonfilamentous, unicellular fungi. Yeasts sometimes appear as white powdery coatings on fruits and leaves and are mistakenly identified as a mold. Molds consist of long filaments of cells (hyphae) that can grow to immense proportions. Vegetative hyphae obtain the nutrients (attach to nutrient source) and aerial hyphae act as a reproductive structure. When environmental conditions are right and enough hyphae are formed, the colony becomes visible to the naked eye, and the mass is called a mycelium.

Fungi can undergo asexual (anamorph) and sexual (teleomorph) reproduction, which means that naming fungi can be a challenge and sometimes confusing. In a laboratory, molds generally produce asexual spores and, therefore, clinical identification is based on asexual spores. There are two types of asexual spores; conidiospore (or conidium) or sporangiospores. Conidiospores are borne externally in chains on aerial hypha called a conidiophore. Sporangiospores are produced inside a sac-like structure known as a sporangium. Spores can be disseminated by air, water, animals, or objects and will germinate when conditions are right. Sexual spores (ascospores and zygospores) are also a possible means of reproduction, but they are not very common. A single organism can frequently have several names depending on what reproductive stage was observed and recorded.

Molds can sometimes be identified based on the differences in the macroscopic physical characteristics, such as colonial form, surface color, pigmentation, and growth rate (Brandt and Warnock, 2011). Identification by macromorphology characteristics (those characteristics that can be observed with the naked eye), even to the Genus level, is difficult, even for mycologists (those who study molds).

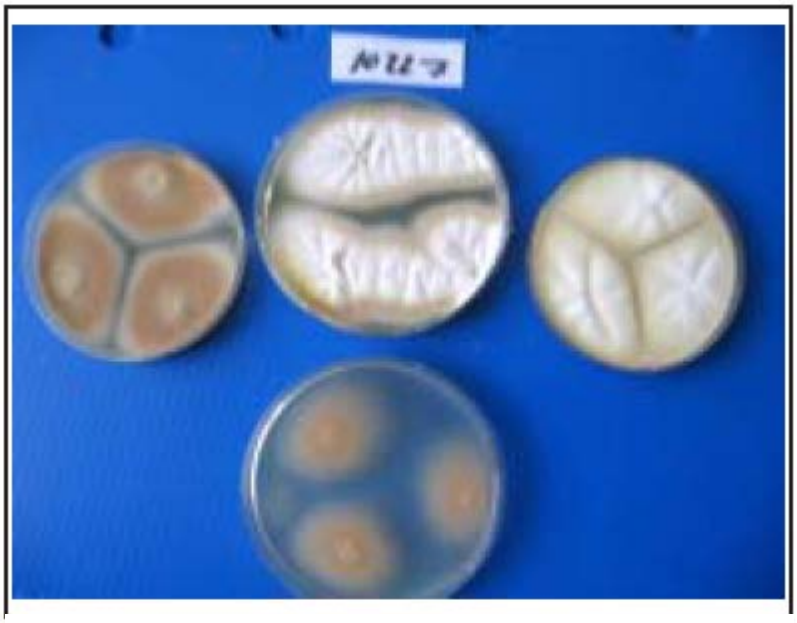

Figure 1. Illustration of different growth appearances of *Aspergillus tereus* on four different growth media (Figure 1 from Diba et al., 2007).

Differing media (nutrient sources), temperature, light cycles, and other growth conditions can dramatically alter the appearance of a mold (Visagie et al., 2014). For example, Figure 1 illustrates the possible differences for *Aspergillus tereus* after growth on four differential media (Diba et al., 2007). Micromorphology and genetic characteristics are used more often, and even with this level of scrutiny, it is still a challenge to identify molds without targeted strategies. The addition of DNA sequence analysis has improved isolate identification and is part of the normal routine protocol for fungal identification in many laboratories. The most useful, practical and cost-effective approach for identification employs both morphological and genotypic aspects.

Table 1 provides the current taxonomic classification for the molds presented in this report. It is important to note that in the past several years several taxonomic reorganizations have occurred due to the advent of genomic methods; therefore, some of this information may differ from what is presented in older references and textbooks. Because of the continual practice of taxonomical-updating based on new and developing scientific techniques cross-confirming and cross-referencing is strongly encouraged.

Table 1. Taxonomic Classification from Catalogue of Life: 2014 Annual Checklist

Phylum	Class	Order	Family	Genus
Ascomycota	Dothideomycetes	Capnodiales	Davidiellaceae	Cladosporium
		Pleosporales	Pleosporaceae	Alternaria
				Epicoccum
			Not assigned	Phoma
	Eurotiomycetes	Eurotiales	Trichocomaceae	Aspergillus
				Penicillium
	Sordariomycetes	Hypocreales	Not assigned	Stachybotrys
		Sordariales	Chaetomiaceae	Chaetomium
		Xylariales	Xylariaceae	Dicyma
Basidiomycota	Not assigned	Malasseziales	Not assigned	Malassezia
Zygomycota	Zygomycetes	Mucorales	Mucoraceae	Rhizopus
				Mucor
		Entomorphthorales	Ancylistaceae	Conidiobolus
			Basidiobolaceae	Basidiobolus

Table 2 provides additional information on the species level and is an attempt at aligning current species of interest and obsolete names to aid in tracking current and historical information for the given fungi. Generally speaking, the common species or species of interest are the most studied because they have either health (medical) or economic impacts that affect humans. As noted from Table 2, there are many more identified species in each genus than can be reviewed in this

document. Likewise, it is important to remember that only fungi that grow in a laboratory environment can be morphologically characterized; therefore, the known and reported information about fungi is biased towards those characteristics observed in the laboratory. For some fungi, identification may be possible using molecular techniques when growth in a laboratory may not be successful.

Table 2. Summary of Taxonomic Information

Genus	Phylum	# of species[a]	Common species / Species of Interest	Previous classification
Alternaria	Ascomycota (ITIS)[a]	461	*A. alternata*	None found.
Aspergillus	Ascomycota (ITIS)	362	*A. fumigatus; A. flavus; A. niger; A. clavatus, A. glaucus, A. nidulans, A. oryzae, A. terreus, A. ustus, A. versicolor*	*Sterigmatocystis*
Chaetomium	Ascomycota (COL)[b]	239	*C. globosum, C. atrobrunneum, C. perlucidum, C. strumarium*	None found.
Cladosporium	Ascomycota (COL)	258	*C. cladosporidides*	*Dermatium herbarum, Acladium herbarum*
Dicyma	Ascomycota (COL)	9	*Ascotricha chartarum Berk* (anamorph)	*Hansfordia Ramichloridium*
Epicoccum	Ascomycota (COL)	41	*E. nigrum*	None found.
Malassezia	Basidiomycota (COL)	17	*M. globosa, M. furfur*	*Pityrosporum*
Penicillium	Ascomycota (COL)	352	*P. marneffei*	None found.
Phoma	Ascomycota (COL)	980	*P. glomerata*	*Deuterophoma tracheiphila*
Stachybotrys	Ascomycota (COL)	69	*S. chartarum*	*S. alternans* and *S. atra*
Rhizopus[c]	Zygomycota	73	*R. delemar, R. oryzae, R. rhizopodiformis*	None found.
Mucor[c]	Zygomycota	277	*M. circinelloides*	None found.
Conidiobolus[c]	Zygomycota	68	*C. coronatus*	None found.
Basidiobolus[c]	Zygomycota	8	*B. ranarum*	None found.

[a] Integrated Taxonomic Information System (http://www.itis.gov/)
[b] Catalogue of Life: 2014 Annual Checklist
[c] Specific genera of the taxonomic class “Zygomycetes”

1.2 Growth Characteristics

Fungi are chemoheterotrophs, therefore, they absorb their nutrients from their environment. Because of their unique characteristics they are able to grow on substrates, such as bathroom walls, shoe leather, and paper. Below are some general nutritional and growth characteristics of fungi (Tortora et al., 2010):

- Most fungi grow in an acidic environment, with a pH of about 5.
- Most molds are aerobic whereas yeasts are facultative anaerobes.
- Fungi are generally resistant to osmotic pressure and, therefore, can grow in relatively high sugar or salt concentrations.
- Fungi can grow on substrates with very low moisture content (but favor high moisture environments).
- Nitrogen is less of a requirement for growth relative to bacteria.
- Fungi are capable of metabolizing complex carbohydrates (e.g., lignin – a component of wood).

1.2.1 Indoor vs. Outdoor Mold Presence

Indoor and building-associated molds are frequently isolated from air and surface samples worldwide. Not surprisingly, the molds found indoors are generally consistent with those present in the outdoor environment (Burge, 2002). The list of the most commonly isolated indoor and outdoor organisms is consistent across geographic locations, and includes genera, such as *Penicillium, Aspergillus, Chaetomium, Ulocladium, Stachybotrys, Cladosporium, Acremonium, Mucor, Paecilomyces, Alternaria, Verticillium and Trichoderma*, many of which are addressed in this report (Verhoeff et al., 1992; Wickman et al., 1992; Gravesen et al., 1999; Koch et al., 2000; Burge, 2002; Shelton et al., 2002; Chew et al., 2003; Baxter et al., 2005; Vesper et al., 2011). Mold spores are much smaller than pollen grains and, therefore, are generally not geographically specific. However, some genera may promote higher outdoor air spore concentrations in some regions due to specific environmental conditions (Vesper et al., 2011; Aggarwal and Chakrabarti, 2013). It is estimated that 2 quadrillion microorganisms are transferred globally with the over 2 billion metric tons of desert dust that is transported in Earth's atmosphere each year (Shinn et al., 2003). The mold spores that are transported are able to survive the transoceanic transport and exposure to ultraviolet radiation; therefore, they may be more capable of withstanding extreme conditions than the native species. This "survival of the fittest" concept provides some insight into possible reasons why mold occurrence and control is changing over time (Shinn et al., 2003).

Some molds, however, are more prominent indoors or outdoors. There are sometimes clear differences between indoor and outdoor concentrations and species (Verhoeff et al., 1992). For example, *Alternaria* and *Cladosporium* are predominantly outdoor molds that are commonly also detected indoors, whereas *Penicillium* and *Aspergillus* are predominantly indoor molds (Aggarwal and Chakrabarti, 2013).

In 2002, an extensive study evaluated 9,619 indoor and 2,407 outdoor air samples from 1,717 buildings across the United States between 1996 and 1998 (Shelton et al., 2002). Samples were submitted by building investigators, and building types included hospitals, schools, and office

buildings (residential and industrial). The reasons the investigators submitted a sample were due to odors, health complaints, visual growth, known water damage, and proactive sampling. Table 3 provides the results of the percentages of buildings that had mold species detected, with the top 4, plus *Stachybotrys*, being shown.

Table 3. Summary of top 4 molds, plus *Stachybotrys* from Shelton et al., 2002

Species	INDOOR		OUTDOOR	
	% of building with species detected	Median Concentration (CFU/m^3)[a] (95% CI)[b]	% of building with species detected	Median Concentration (CFU/m^3) (95%CI)
Cladosporium	86	40 (12 – 480)	92	200 (18 – 1,849)
Penicillium	80	30 (12 – 570)	77	50 (12 – 377)
Nonsporulating fungi	80	30 (12 – 204)	92	100 (12 – 901)
Aspergillus	62	20 (12 – 373)	49	20 (12 – 170)
Stachybotrys	6	12 (12 – 118)	1	12 (4 – 318)

[a] Colony Forming Unit/cubic meter
[b] 95% Confidence Interval

Median outdoor and indoor fungal concentrations varied by region and were highest in the Southwest, Far West, and Southeast and lowest in the Northwest (see Figure 2 for the definitions of the regions as defined by the study authors) (Shelton et al., 2002). Fungal counts were highest in samples submitted because of visible fungal growth, and the next highest counts were for those from which health complaints were noted. Both indoor and outdoor fungal counts varied significantly by season.

Figure 2. Regions of the United States for the Shelton et al. (2002) study (Figure 1 in Shelton et al., 2002; n = number of samples). Copyright 2002 by American Society for Microbiology.

Baxter et al. (2005) sampled 625 buildings and outdoor locations in San Diego, comparing coastal and inland locations, and found that the means and confidence intervals (by Genus) for mold levels were essentially identical. Baxter et al. (2005) developed evaluation criteria for buildings in Southern California, proposing acceptable levels of total spores, *Aspergillus/*

Penicillium counts and Asco/Basidospores counts, per cubic meter. For a residential building, air sampling resulting in total spores greater than 1,300 counts/m^3 is considered "moldy". For a commercial building the air sampling result for total spores must be greater than 1,000 counts/m^3 to be considered "moldy". The criteria for "moldy" specifically for *Aspergillus/Penicillium* are air samples returning greater than 900 counts/m^3 for both residential and commercial buildings. For Asco/Basidospores, the counts criteria are greater than 1,300 counts/m^3 for residential buildings and greater than 1,100 counts/m^3 for commercial buildings.

After not being able to show a statistical difference between mold species by geographical region, Vesper et al. (2011) utilized mapping techniques to draw regional conclusions. The 36 molds included in their survey were classified into two groups. Group 1 molds (*Aspergillus, Penicillium, Cladosporium and Stachybotrys* and others) are often associated with water-associated phenomena (humidity or precipitation) and were scattered throughout the United States, indicating that water problems are national in scope. The authors associated group 2 molds (*Alternaria, Aspergillus, Cladosporium, Penicillium, Epicoccum, Mucor, Rhizopus*, and others) with outdoor conditions, such as the type of soil and vegetation; these also did not show clear regional differences. The only observed difference was in the desert southwest and southeast, where Group 2 molds appeared to be less abundant.

In 2003, Chew et al. reported that indoor air fungal levels in Boston, MA may be predicted by the type of housing (apartment or house) and the presence of carpeting. Chew et al. (2003) also compared dust samples to air samples. Generally speaking, apartments did not have fungi concentrations as high as in houses, possibility because outdoor fungi are removed during walking through the apartment building. Apartments are also warmer and drier than homes. Carpeted floors contained higher fungal loads than non-carpeted floors.

1.2.2 Growth on Materials

There have been several investigations on the key factors associated with mold growth on various materials.

1.2.2.1 *Moisture*

Water is the primary determinant of fungal growth (Gravesen et al., 1999; Burge, 2002; Zalar, 2011). Burge (2002) specifies that it is water within the materials that is important, not necessarily relative humidity, which is often the parameter that is measured. Condensation is particularly problematic, especially if occurring in places with improperly installed vapor barriers. For example, in cold climates, warm moist indoor air diffuses through walls and contacts cold vapor barriers, which leads to condensation and fungal growth.

Gravesen et al. (1999) reported that water activity (water available to microorganisms; defined as the vapor pressure in substrate/vapor pressure of pure water at the same temperature) was the most important factor for mold growth. A difference in water activity of only 0.02 resulted in a significance difference in mold growth on gypsum boards. Fungal species can be classified depending on the amount of moisture needed for growth and the associated water activity (Johansson et al., 2012):

- Hydrophilic fungi = minimum of 0.9
- Moderately xerophilic = 0.80 – 0.89
- Slightly xerophilic fungi = 0.75 – 0.79
- Extreme xerophiles = 0.75

However, Johansson et al. (2012) did not specify which genera fall into each of their categories. A wood surface moisture content of about 20% is needed to support mold growth (Vlosky and Shupe, 2004).

Relative humidity is the current vapor content in relation to the vapor content at saturation, and it is temperature dependent. Materials in the environment either absorb or release moisture until an equilibrium is reached. The relationship between materials and relative humidity is complex; some materials can tolerate high relative humidity without mold growth, while others grow mold in as low as 75% relative humidity (Johansson et al., 2012). Many factors affect the moisture level, growth and characterization of mold growth. Some of the major factors are temperature, relative humidity, incubation time, mold species and assessment criteria. A relative humidity of 86% was required for mold growth on gypsum board (Nielsen et al., 2004). For materials that are wood, wood composites and starch-containing materials, the necessary relative humidity was 78% (Nielsen et al., 2004). In a controlled study of temperature and relative humidity, the most susceptible materials to mold growth were pine sapwood and plywood, chipboard, thin hardboard, plaster boards and asphalt paper. The most resistant, where no growth was observed, was glass fiber board, cement-based board, or extruded polystyrene boards (Johansson et al., 2012). Relative humidity also appears to have an impact on the quantity of metabolites produced by molds. Metabolites and mycotoxin quantities produced by *Penicillium*, *Aspergillus*, and *Eurotium* decreased with lower relative humidity (Nielsen et al., 2004).

1.2.2.2 *Presence of Cellulose (Organic Material)*

Material can be classified as organic or inorganic depending on the amount of biodegradable components present. The presence of cellulose seems to increase the presence of mold (Gravesen et al., 1999; Vlosky and Supe, 2004). Generally speaking, inorganic material (concrete, glass, or plastics) do not support the growth of *Penicillium*, *Cladosporium* and *Stachybotrys* species, but growth may occur if nutrients are present on the surface (Burge, 2002; Vlosky and Shupe, 2004). *Stachybotrys* has a particular affinity to cellulose (Kuhn and Ghannoum, 2003), but it is usually a tertiary colonizer, arriving after *Penicillium* and *Cladosporium*.

1.2.2.3 *Age of Material*

Because mold spores are ubiquitous in the environment, the age of the material is important for growth. Older material generally has experienced more surface damage, which exposes unprotected surfaces of the item material to spores. In addition, as the degradation process naturally occurs, mold spores may have an increased opportunity to grow (Gravesen et al., 1999).

1.2.2.4 *Meteorological Conditions*

It appears there may be a species-specific relationship between meteorological conditions (e.g., temperature, humidity, distribution of rainfall, and surge in extreme weather events) and the

presence of mold spores (Katial et al., 1997; Aggarwal and Chakrabarti, 2013). Specifically, *Cladosporium, Alternaria* and *Epicoccum* were studied over 8 years (1989-1994) in Denver, Colorado, in an attempt to find a correlation between meteorological parameters and spore counts. Outdoor air samples revealed a consistent peak of *total spore* counts (sum of all three genera) from the third week in July to the third week in September (Katial et al., 1997). *Cladosporium* was positively associated with average temperature and humidity, and negatively associated with precipitation. However, *Alternaria and Epicoccum* as individual genera were not found to be statistically correlated with the meteorological variables.

1.2.2.5 *Air-Conditioning*

The use of an air-conditioner reduces circulation of fresh air and increases thermal gradients that can create localized cool and moist areas conducive to mold growth (Shinn et al., 2003). Air conditioning ductwork also serves as a favorable place for microbe growth.

1.2.2.6 *pH*

pH affects the growth of some molds. Zalar et al. (2011) tested dishwashers (measured at an alkaline pH) and found *Aspergillus, Candida, Penicillium, Magnusiomyces, Fusarium* and *Rhodotorula* present. Other molds, such as *Chaetomium* and *Epicoccum*, prefer acidic conditions (Fogle et al., 2008; Rizzo-Longo et al., 2009).

1.2.3 Prevention

To increase material durability (capacity of a structure to give a required performance during an intended service period under the influence of degradation mechanisms), mold growth must remain in check and be minimized (Isaksson et al., 2010). There is a significant body of research regarding prevention methods, and information on prevention is available from the Environmental Protection Agency, National Institute of Occupational Safety and Health, Centers for Disease Control and Prevention, and the Occupational Safety and Health Administration. Guidance documents have also been developed by the American Conference of Governmental Industrial Hygienists, American Industrial Hygiene Association, and the Institute of Inspection Cleaning and Restoration. Generally speaking, prevention of mold growth is a function of controlling air moisture levels and condensation potential. Proper site drainage, vapor retarders, insulation and ventilation are required and must be adjusted to meet ambient environmental conditions (Vlosky and Shupe, 2004). Adequate ventilation, along with appropriate solutions (i.e., baking soda, vinegar or bleach) have been shown to provide effective control (Weir, 2000).

1.2.4 Remediation

If prevention fails, mold can be removed with commercial cleaners. If contamination is severe enough, the material may need to be destroyed. Specific remediation strategies are beyond the scope of this review, but guidance can be found from governmental agencies such as the Environmental Protection Agency, National Institute of Occupational Safety and Health, Centers for Disease Control and Prevention, and the Occupational Safety and Health Administration. Useful references include publications from the American Conference of Governmental Industrial Hygienists and the Institute of Inspection Cleaning and Restoration (ACGIH, 1999; BSR-IICRC, 2015).

1.3 General Effects of Medically Important Molds and Terminology

The remainder of this chapter provides general information on each of the genera (and the one class – *Zygomycetes)* addressed in this report. Brief information on the medical importance of each group is presented here, but more information is provided in Chapter 3. Chapter 5 provides an overall summary of the molds addressed in this report, and their health effects, including health effects of their toxins.

A fungal infection is called a mycosis. Frank pathogens are those organisms that are known to cause disease in a host considered "healthy", in contrast with an opportunistic pathogen which will not cause disease in a "healthy" person, but will cause disease in an immunocompromised host. In some cases, when the fungi grow very slowly, infections may be long-lasting and the resulting signs and symptoms may not attract immediate attention. For example, a low-grade fever or slow-growing mass caused by a fungal infection may not be recognized or detected for a longer period of time. This concept is relative and may be contrasted with a high-fever or a more immediate local redness and inflammation characteristic of some bacterial infections.

Generally speaking, fungal infections can be classified as:

- Systemic: infections that have crossed the boundary of some portal of entry and are not necessarily restricted to any particular region but can affect a number of tissues and organs
- Subcutaneous: infections beneath the skin
- Cutaneous (dermatomycoses): infections of the epidermis, hair and nails
- Superficial: localized along hair shafts and surface epidermal cells
- Opportunistic: generally harmless mold but becomes pathogenic when host is immunocompromised (e.g., immune system disorder or certain pre-existing illnesses).

1.3.1 Alternaria

Alternaria is a genus with over 400 species that are commonly isolated from plants, soil, food, and the indoor environment. *A. alternata* is the most commonly reported isolate associated with human infections. However, it is not clear if that name is better associated with a species-complex (i.e., a group of species) rather than a single species of mold (Woudenberg et al., 2013).

Alternaria species are known to cause disease in plants (Figure 3) but are also considered opportunistic pathogens to humans, in addition to causing allergic disease (Aggarwal and Chakrabarti, 2013). The plant-pathogen variants produce host-selective toxins that cause disease on specific plants (Gat et al., 2012). Known plant diseases are Alternaria blotch of apple, brown spot of citrus, black spot of Japanese pear, Alternaria black spot of strawberry, brown spot of tobacco, stem canker

Figure 3. *Alternaria brassicicola* on broccoli. http://www.picsearch.com/alternaria-fungi-pictures.html Copyright 2015 by Picsearch Services AB.

of tomato, and black spot disease of pomegranate (Gat et al., 2012). *Alternaria* also can cause seed diseases. For example, *Alternaria* was isolated in association with inhibited seminal root elongation and seedling rot in tomato seeds (Nishikawa, 2006).

1.3.1.1 *Taxonomy*

Kingdom:	Fungi
Phylum:	Ascomycota
Class:	Euascomycetes
Order:	Pleosporales
Family:	Pleosporaceae
Genus:	Alternaria
Species:	461

Telemorphic genera are *Clathrospora* and *Leptosphaeria*.

1.3.1.2 *Physical Characteristics*

A defining characteristic of *Alternaria* is the production of a melanin pigment (Kimura and Tsuge, 1993). The melanin is important for the survival and longevity of fungal propagules (spores) and may be involved in pathogenicity. *Alternaria* colonies are commonly observed as dark colored spots.

Alternaria spores are common throughout the world, and the magnitude of exposure is determined primarily by spore counts outdoors where most exposures occur. In the UK, a study demonstrated a seasonal increase in spore counts (June – October), along with a positive correlation with monthly rainfall and temperature (Corden and Millington, 2001). A similar study in Italy also observed seasonal variation in *Alternaria* spore counts in outdoor air (Rizzi-Longo et al., 2009).

A study focused on indoor exposures in U.S. homes via the National Survey of Lead and Allergens in Housing (conducted by U.S. Department of Housing and Urban Development, 1998 – 1999). This study reported nationally representative estimates of dustborne *A. alternata* antigen levels and identified independent predictors of antigen concentrations in U.S. homes. Samples were collected in 831 housing units that permit children as occupants in all 50 states and the District of Columbia. Surface dust samples were collected from a bed, sofa or chair, and from bedroom, living room and kitchen floors. More than 95% of the dust samples had detectable levels of *Alternaria* antigens (detection limit = 0.14 µg/g sieved dust). Higher concentrations were present in older homes, homes in the Midwest and South census regions, non-urban homes, single family homes, owner-occupied homes, homes in impoverished census areas, homes inhabited by white individuals, and homes inhabited by individual with less education (Table 5). The presence of children and the number of occupants were not associated with higher levels of *Alternaria* (Table 4). Additional considerations associated with higher antigen levels included homes that used forced air heating systems or radiators where mold or moisture-related problems were observed. Higher antigen levels were also seen in homes that had a musty or mildew odor, used a dehumidifier, had cats or dogs, or where smoking occurred (Table 5).

Table 4. Geometric means of *Alternaria* concentrations by demographic characteristics (Table 1 in Salo et al., 2005). NIH Open Access.

Geometric means of *Alternaria* concentrations (house index[*]) by demographic characteristics

Characteristic	Number of homes	GM (SE)[†] (µg/g)	p-value[‡]
Total	822	4.88 (0.13)	--
Construction year			<0.001
1978-1998	216	4.21 (0.17)	
1977 or earlier	606	5.22 (0.17)	
Census region			<0.001
Northeast	151	4.59 (0.46)	
Midwest	195	5.42 (0.30)	
South	276	5.21 (0.22)	
West	200	4.06 (0.19)	
Urbanization			<0.001
MSA[§]	684	4.53 (0.14)	
Non-MSA	138	6.16 (0.20)	
Housing unit type			<0.001
Multi-family	124	4.01 (0.24)	
Single family	698	5.04 (0.15)	
Tenure			0.036
Renter occupied	282	4.58 (0.17)	
Owner occupied	537	5.01 (0.16)	
Number of persons in the household			0.870
1-3	543	4.89 (0.14)	
4-9	279	4.85 (0.24)	
Children (< 18 years)			0.188
No	423	4.97 (0.16)	
Yes	396	4.74 (0.16)	
Census poverty			0.002
No	643	4.76 (0.16)	
Yes	136	5.67 (0.26)	
Race			<0.001
White	603	5.10 (0.16)	
Other	219	4.11 (0.16)	
Education			0.008
Above high school	553	4.67 (0.17)	
High school or less	255	5.38 (0.19)	

[*] House index is the mean of the sample location concentrations

[†] GM indicates geometric mean, (SE) standard error of the mean

[‡] Wald F-test on difference of means across levels of the characteristic

[§] Metropolitan Statistical Area

Table 5. Geometric means of *Alternaria* concentrations by allergen-related housing and behavioral characteristics (Table 2 in Salo et al., 2005). NIH Open Access.

Geometric means of *Alternaria* concentrations (house index) by allergen-related housing and behavioral characteristics

Characteristic	Number of homes	GM (SE)* (µg/g)	p-value†
Total	822	4.88 (0.13)	--
Main heating source			0.003
Gas/Electric forced air	556	4.68 (0.15)	
Radiator	74	4.77 (0.56)	
Other	189	5.64 (0.24)	
Air filtration device used			0.547
No	702	4.87 (0.15)	
Yes	101	5.04 (0.27)	
Mold or moisture problems‡			<0.001
No	398	4.43 (0.15)	
Yes	424	5.38 (0.18)	
Dehumidifier in the home			0.001
No	676	4.70 (0.15)	
Yes	130	5.87 (0.34)	
Cats or dogs currently			0.016
No	455	4.66 (0.18)	
Yes	359	5.17 (0.15)	
Windows/doors kept open in the past month			0.920
No	132	4.91 (0.23)	
Yes	685	4.88 (0.14)	
Season			0.682
Summer	285	4.90 (0.26)	
Fall	344	4.75 (0.23)	
Winter	193	5.05 (0.28)	
Smoking inside the home			0.027
No smoking indoors	536	4.61(0.19)	
Light smoking§	75	4.89 (0.34)	
Heavy smoking‖	208	5.60 (0.28)	

*GM indicates geometric mean, (SE) standard error of the mean

†Wald F-test on difference of means across levels of the characteristic

‡Assessed by observation (occupants, field team)

§Tobacco products smoked indoors < 4 times a day

‖Tobacco products smoked indoors 4 or more times a day

1.3.1.3 *Medical Importance*

Exposure to *Alternaria* has been linked to asthma (Halonen et al., 1997), and it is also an opportunistic pathogen (Morrison and Weisdorf, 1993).

1.3.2 Aspergillus

The genus *Aspergillus* was first defined in 1809, and the 69 species were organized into 13 groups with a few outliers (Christensen and Tuthill, 1985). As various culture-techniques and agar were developed or improved, additional species were identified and added to the list. In 1965, Raper and Fennell published detailed descriptions of 132 species classified into 18 groups. From 1965 to current times, the identification and classification of species continues to evolve, and it appears there are approximately 360 named species to date (COL, 2014). The taxonomy of *Aspergillus* has been in flux, due to large-subunit ribosomal DNA analysis, and currently consists of seven subgenera: *Aspergillus, Fumigati, Ornati, Clavati, Nidulantes, Circumdati* and *Stilbothamnium.* *Aspergillus* species are identified on the basis of phenotypic characteristics of the anamorph.

Figure 4. *Aspergillus* on a ear of corn. http://www.picsearch.com/index.cgi?q=aspergillus. Copyright 2015 by Picsearch Services AB.

Aspergillus are ubiquitous in nature, found worldwide, and are commonly isolated from soil, plant debris, water, food (Figure 4), and the indoor air environment. Generally *Apergillus* grows very rapidly on environmental media, and dry conidia are easily dispersed in the air (Balajee and Brandt 2011). *Aspergillus* is observed to be powdery white, green, yellowish, brownish, or black colonies.

Aspergillus fumigatus accounts for most cases of aspergillosis (human infections caused by members of the genus). *A. flavus* and *A. niger* are also common pathogenic species. Two newer species are being increasingly reported and recognized as human pathogens: *A. terreus* and *A. lentulus.*

1.3.2.1 *Taxonomy*

Kingdom:	Fungi
Phylum:	Ascomycota
Class:	Eurotiomucetes
Order:	Eurotiales
Family:	Trichocomaceae
Genus:	Aspergillus
Species:	362

1.3.2.2 *Physical Characteristics*

Aspergillus are in the phylum Ascomyota and produce conidiospores. This genus grows rapidly and produces powdery white, green, yellowish, brown, or black colonies (Balajee and Brandt 2011). Experts report that essential features for morphologically identifying *Aspergillus* are (Figure 5): spore color, head shape, length and unusual features of conidiophores, orientation

and dimensions of metulae (secondary braches of conidiophore), phialide (flask-shaped projection beyond metulae) density per metula, and size, shape and wall texture of conidia (Christensen and Tuthill, 1985). Growth rate and thermotolerance may also be identifying factors to differentiate between *Aspergillus* species (Rhodes, 2006).

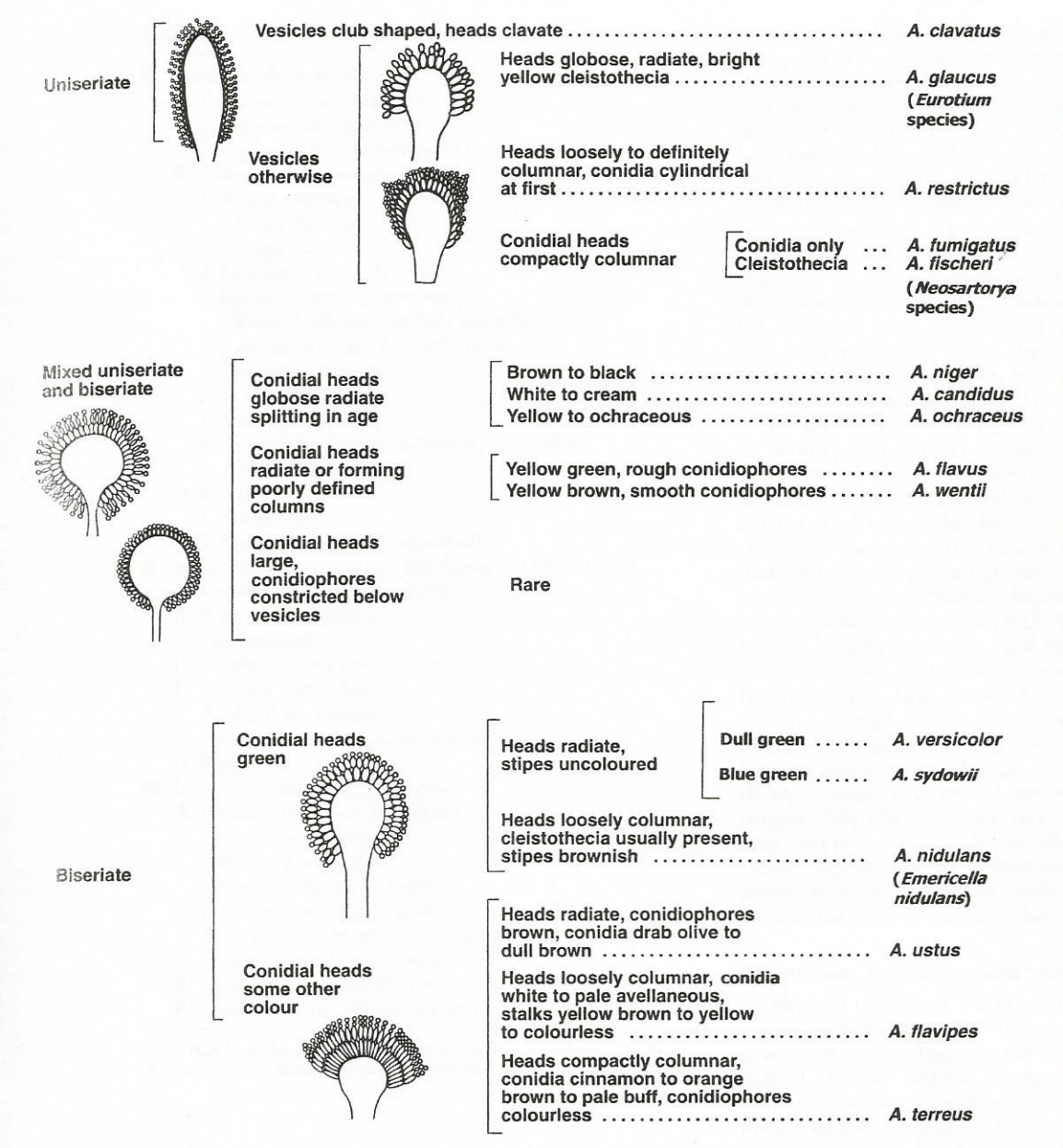

Figure 5. Representative species from *Aspergillus* (Balajee and Brandt, 2011).

Diba et al. (2007) compared *Aspergillus* growth on four different culture media. Sabouraud Glucose Agar 4% was used to identify to the genus level, and then czapek dox agar, czapek yeast agar, malt extract agar, and czapek yeast 20% sucrose agar were evaluated for speciation. Over 18-months, 205 clinical and environmental specimens were collected at three Iranian teaching hospitals. Clinical specimens were from nail scrapings, sinus discharge, ear exudates, sputum

specimens and biopsy material. Environmental samples were from the air and surfaces of the hospital gardens and floors, walls, beds and the air conditioners at the hospitals. The authors found that *A. flavus* (55%), *A. niger* (31.7%) and *A. fumigatus* (8.7%) were the most commonly isolated species from both the clinical and the environmental samples.

Table 6. (Table II from Diba et al. 2007) Microscopic characteristics used for identification of Aspergillus isolates

Aspergillus Species	*Size*	*Stipes Color*	*Surface*	*Vesicle Serration*	*Metula Covering*	*Shape*	*Conidia Surface*
A.flavus	400-800	pale brown roughened	quietly spherical	biseriate	3/4	glubose ellipsoid	smooth finely roughened
A.niger	400-3000	slightly brown	smooth walled	biseriate large size	entirely	glubose	very rough irregular
A.fumigatus	200-400	grayish near apex	smooth walled	uniseriate pyriform	upper 2/3	glubose small in columns	smooth or spinose
A.nidulans	70-150	brown in age	smooth walled	Biseriate spatulate	upper 1/2	spherical	smooth slightly rough
A.tereus	100-250	unclored	smooth walled	biseriate spherical	upper 1/2 to 3/4	glubose	Smooth walled
A. parasiticus	250-500	colorless	finely roughened	uniseriate spherical	1/2	glubose	distinctly rough
A.oryzae	500-2500	uncolored	rough	uniseriate	1/2 or more	glubose	smooth
A.tamarii	600-1500	uncolored	rough walled	biseriate spatulate	entirely	spherical	smooth
A.ochraceus	300-1700	yellowish pale brown	coarsely rough	biseriate globose elongate	entirely	spherical small	smooth finely rough
A.sojae	300-900	uncolored	rough	predominantly uniseriate	------	spherical rough walled	rough walled
A.niveus	100-500	uncolored	smooth	biseriate	upper 2/3	glubose	smooth walled

1.3.2.3 *Medical Importance*

Thermotolerance, nutritional versatility and the ability to produce many small spores (2 -3 micron) allow *Aspergillus* to effectively grow and spread (Rhodes, 2006). When growth of *Aspergillus* occurs in human tissue, it is referred to as aspergillosis (EPA, 1997). Most patients who experience aspergillosis are immunocompromised, and, therefore, susceptible to an otherwise harmless microorganism. The most common species to cause aspergillosis are *A. fumigatus* and *A. niger*. When the organism colonizes the lung, a ball of hyphae may form in the bronchi and obstruct air flow.

Alternative to a lung infection, *A. niger* has been observed growing on the ceruman (ear wax) and desquamated debris (dead skin) of the external auditory canal (ear) (EPA 1997), a condition known as otomycosis.

Aspergillus infections can also result in disease caused by toxicosis due to mycotoxins or other metabolites.

Aspergillus and its antigens can also cause allergic reactions (Bennett, 1980; EPA, 1997).

A risk assessment by the Environmental Protection Agency (EPA) concluded that *A. niger*, specifically, has a history of safe use and that most isolates are not documented to be a serious concern to humans. While specific strains may elicit an allergic response, these instances are limited (EPA, 1997).

1.3.3 Chaetomium

Integrated biological control of plant pathogens using *Chaetomium* has been successfully utilized in China, Philippines, Russia, Thailand and Vietnam using several *Chaetomium* species, because the genus has antagonistic activity against various soil microorganisms (Soytong et al., 2001). The genus is commonly found in soil and plant debris, where they are effective at cellulose degradation (Abbott et al., 1995). The most clinically relevant species are *C. globosum, C. atrobrunneum,* and *C. perlucidum* (Guarro and de Hoog, 2011; Sutton and Brandt, 2011).

1.3.3.1 *Taxonomy*

Kingdom:	Fungi
Phylum:	Ascomycota
Class:	Sordariomycetes
Order:	Sordariales
Family:	Chaetomiaceae
Genus:	*Chaetomium*
Species:	239

1.3.3.2 *Physical Characteristics*

Chaetomium produce brown, lemon-shaped to fusiform ascospores within ascomata that are ornamented with hairs (or setae), especially around the upper part near the opening (Sutton and Brandt, 2011; Najafzadeh et al., 2014). Anamorph sporulation is absent or insignificant (Najafzadeh et al. 2014).

C. globosum is the species commonly isolated from water-damaged buildings (Fogle et al., 2008). Laboratory studies have been performed to determine the nutritional requirements and pH that results in the greatest growth and mycotoxin (chaetoglobosins A and C) production (Fogle et al., 2008). It was found that growth can occur on potato dextrose agar ranging from pH 4.3 to 9.4 (Figure 6), and maximum mycotoxin production was at a neutral pH. An acidic environment favored sporulation.

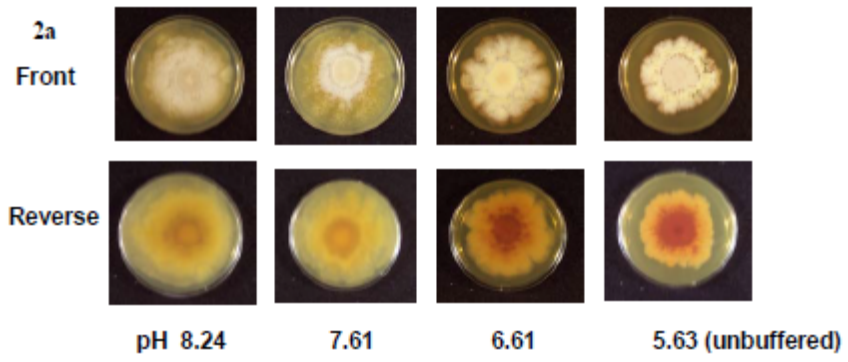

Figure 6. Growth on potato dextrose agar (Figure 2 in Fogle et al. 2008). Copyright 2008 by MDPI.

1.3.3.3 *Medical Importance*

Chaetomium species are opportunistic pathogens and can cause phaeohyphomycosis (general term for infections caused by filamentous fungi that contain melanin in their cell walls) (Najafzadeh et al., 2014).

1.3.4 Cladosporium

In 1794 *Cladosporium herbarum* was introduced as *Dematium herbarum* and later was reclassified as *Acladium herbarum* in 1809 (Crous et al., 2007; Schubert et al., 2007). It is one of the most common environmental fungi isolated worldwide. It is commonly found on fading or dead leaves, in soil, foodstuffs, paints, and on textiles and humans (Schubert et al., 2007).

The genus is also isolated from dairies, bakeries, barns, and greenhouses (Haligur et al., 2010). Schubert et al. (2007) offers a detailed review of the *C. herbarum* complex (which includes five species), with extensive phylogenetic trees, morphological identification keys and light and scanning electron microscopy photographs. *Studies in Mycology* dedicated an entire volume to *Cladosporium* (Crous et al., 2007).

Cladosporium has also been associated with seedborne disease in eggplant seeds that suppressed germination (Nishikawa et al., 2006).

1.3.4.1 *Taxonomy*

Kingdom:	Fungi
Phylum:	Ascomycota
Class:	Dothideomycetes
Order:	Capnodiales
Family:	Davidiellaceae
Genus:	*Cladosporium*
Species	258

Synonyms for *Cladosporium trichoides* are C*ladosporium bantianum* and *Xylohypha bantianum* (Kwon-Chung et al., 1989).

Telemorphs are *Davidiella* (Schubert et al., 2007).

Figure 7. *Cladosporium*. www.moldlibrary.ca Copyright 2015 by Mold Busters.

1.3.4.2 *Physical Characteristics*

Cladosporium species are considered to be halophilic and halotolerant and are, therefore, isolated from hypersaline environments worldwide (Zalar et al., 2007). Some species, such as *C. sphaerospermum*, are capable of growth at very low water activities (0.816). *Cladosporium* colonies are olive-green to black with a velvet-to-powdery appearance (Figure 7).

Cladosporium spores tend to clump, and therefore, the method used for sampling will affect the measured colony count (Chew et al., 2003). For example, air sampling using direct impaction

onto agar plates may result in a single colony, while suspending the clump in solution prior to plating would break the clump into individual cells/spores, and thus result in a higher count.

1.3.4.3 *Medical Importance*

Similar to *Alternaria*. *Cladosporium* is implicated in phaeohyphomycosis. *Cladosporium* can also cause allergic reactions, infections in wounds, and other opportunistic infections.

1.3.5 Dicyma

Exposure to *Dicyma* may increase as it is being found to be an effective biocontrol agent. Mello et al. (2008) demonstrated that *D. pulvinata* was a potential biocontrol agent for South American leaf blight of the *Hevea* rubber plant, which is one of the world's top five most threatening plant diseases. In 2009, *Dicyma pulvinata* was identified as an effective biocontrol agent of another fungus that infects orchardgrass and causes choke (Alderman et al., 2009). Orchardgrass seed production is focused in the Willamette Valley, Oregon, and there was no effective chemical or other control previously for choke in orchardgrass.

1.3.5.1 *Taxonomy*

Kingdom:	Fungi
Phylum:	Ascomycota
Class:	Sordariomycetes
Order:	Xylariales
Family:	Xylariaceae
Genus:	Dicyma
Species	9

The teleomorph (sexual stage) is named *Ascotricha chartarum*.

At one time this genus was also known as *Hansfordia*.

Molecular characterization has been performed by Tavares et al., (2004).

1.3.5.2 *Physical Characteristics*

Very little information is available regarding the physical characteristics of *Dicyma*. When grown on Potato Dextrose Agar it is reported to be gray- to olivaceaous grey-white with abundant conidial production (Alderman et al., 2009). Some micrographs are also posted on the internet, but there were no macro-characteristic pictures from a reputable source.

In support of *Dicyma* as a biocontrol agent, Melo and Mello (2009) investigated ideal conditions for conidia mass production by evaluating the impact on growth of substrate, container, temperature, and light regime. Substrates included parboiled rice, common rice, maize, chipped maize, wheat and rice husk in either poly-propylene bags, Erlenmeyer flasks or trays. Temperatures evaluated were 19, 22, 25, 28, and 31^{o}C. Light regimes included continuous darkness, 6 hours of light/darkness, 12 hours of light/darkness and continuous light. Growth was observed on all substrates, with spore production being highest on parboiled rice and lowest on the rice husk. Spore production did not differ statistically among containers. Growth occurred at

all the temperatures except 31°C, and less mycelia growth was observed at 28°C. Sporulation varied with temperature; lower temperatures were associated with significantly higher sporulation. Growth was favored the most under conditions of continuous darkness and 6 hours of light/dark, while continuous light favored sporulation.

1.3.5.3 *Medical Importance*

Data on health effects associated with *Dicyma* are very limited, but in 1996 the first case of successfully treated maxillary sinusitis caused by what was reported as *Ascotricha chartarum* was reported (Singh et al., 1996).

1.3.6 Epicoccum

Epicoccum is associated with the primary decomposition of plant material and has been found to be an effective biocontrol agent. Its effectiveness as a biocontrol agent has been demonstrated in control of sunflower head rot (Burge, 2002; Favaro et al., 2011), *Monilinia* (fungal pathogen in fruit) species on peaches and nectarines (Favaro et al., 2011) and *Pythium* (an oomycete or water mold) on cotton (Favaro et al., 2011).

On the other hand, *Epicoccum* is known to be a plant pathogen to cucumber, tomato, apple, cantaloupe, and pear, causing decay with a red coloration (Figure 8) (Bruton et al., 1993).

1.3.6.1 *Taxonomy*

Kingdom: Fungi
Phylum: Ascomycota
Class: Dothideomycetes
Order: Pleosporales
Family: Leptosphaeriaceae
Genus: *Epicoccum*
Species: 41

At one time there were over 70 species described, but reclassification reduced that number to 41 species. Many of the species are now captured in the variable *E. nigrum* (Favaro et al., 2011).

Figure 8. *Epicoccum*. http://mold-pro.com/Glossimages/epicoccum.htm No Copyright, on Mold-Pro Inspections, LLC website.

1.3.6.2 *Physical Characteristics*

Typically *Epicoccum* presents conidia that are darkly pigmented and multi-septate on short conidiophores (Figure 9). Morphological differences are sometimes misinterpreted to represent different species, but the differences are simply expression of interspecific variation (Figure 10; Favaro et al., 2011). Even isolates with similar geographical origins show high variability (Arenal et al., 1999). These differences were observed by Foppen and Gribanovski-Sassu (1968) when they investigated the effect of light and temperature on *E. nigrum*. They observed that production of carotenoids (red and orange pigments) at 24^{o}C was inhibited at higher light intensities, but at 28^{o}C, the production increased with higher light intensities.

In culture, clay minerals (i.e., montmorillonite) and quartz accelerated biomass formation, glucose consumption and nitrogen assimilation (Filip et al., 1972).

Growth occurred between -3ºC and 45ºC, with optimum growth at 23-28ºC at pH 3 – 4.5. Minimum available water requirement is between 0.86 and 0.90 (Rizzi-Longo et al., 2009).

1.3.6.3 *Medical Importance*

Epicoccum is associated with skin disease (Weber, 2006), but not systemic infection.

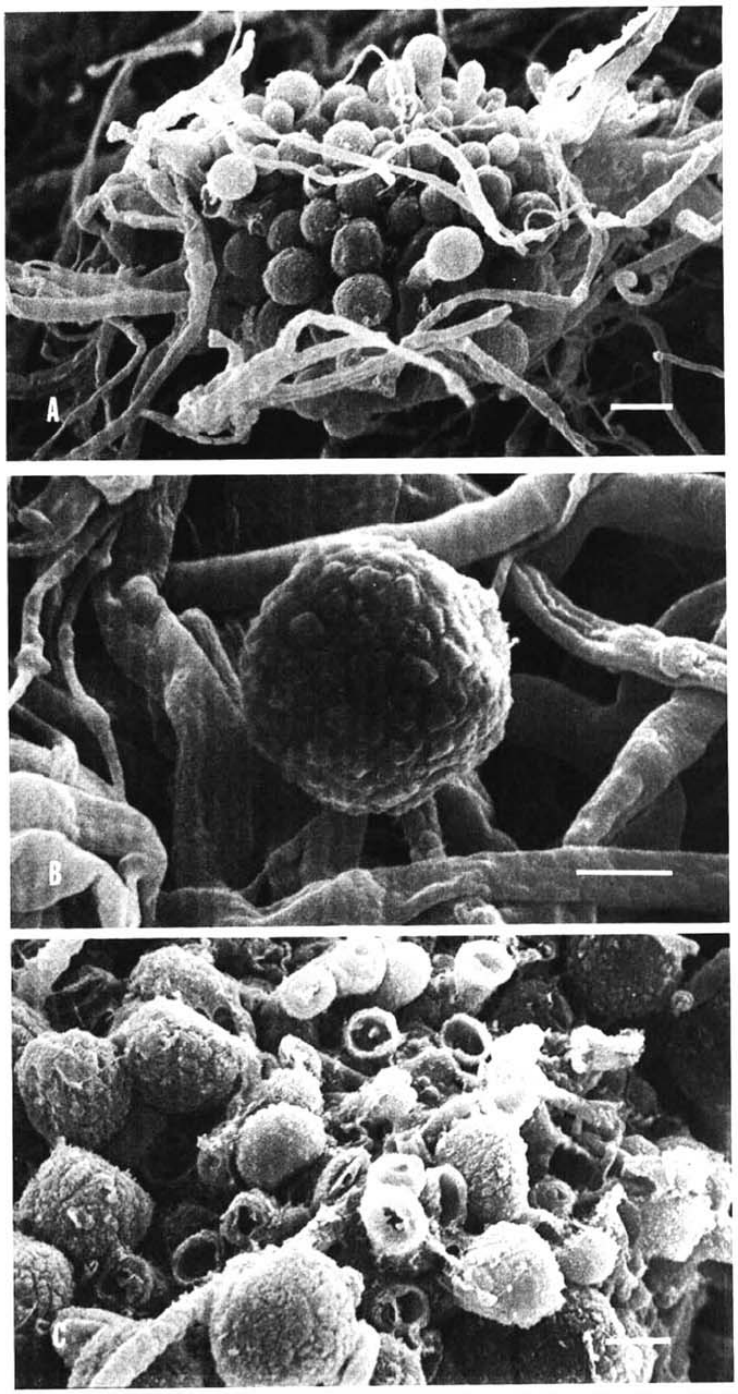

Figure 9. *Epicoccum nigrum* (Figure 1 in Bruton et al. 1993). Public domain per American Phytopathological Society, 1993.

Figure 10. Top view of colonies of 5 *Epicoccum* strains from sugarcane after growth in different culture medium. PDA = Potato Dextrose Agar; CM = Complete Medium (Figure 1 in Favaro et al. 2011). Copyright 2011 by Favaro et al.

1.3.7 Malassezia

Malassezia are the only basidiomycete considered in this report. Basidomycete is an informal term used to describe all members of the phylum *Basidiomycota*. Basidomycetes are a diverse group of organisms including molds, rusts, and stinkhorns (mushrooms commonly found in urban settings) (Brandt, 2013). *Malassezia* is considered a yeast (nonfilamentous) and differs from the (filamentous) molds reviewed in this report.

Malassezia is normally present as part of the cutaneous commensal microflora of both healthy and diseased people. Until recently it was believed that this genus of fungi had a special niche associated with mammalian skin, but it is now known that the genus is environmentally diverse and can be found even in marine environments (Amend, 2014).

1.3.7.1 *Taxonomy*

Kingdom:	Fungi
Phylum:	Basidiomycota
Class:	Not assigned
Order:	Malasseziales
Family:	Not assigned
Genus:	Malassezia
Species	17

Due to dimorphic characteristics of yeast, taxonomy has been confusing. The yeast phase was classified as *Pityrosporum* and the mycelial phase as *Malassezia*. In 1986, both phases were united into *Malassezia* (Prohic, 2012).

1.3.7.2 *Physical Characteristics*

The members of the genus *Malassezia* are lypophilic and/or lipid dependent with a thick cell wall. The cells range from 1.5 to 10 micron in size and are usually ovoid in shape. However, different species may be round or cylindrical in shape. Colonies are raised, dull, creamy yellow and have a brittle texture (Figure 11. Prohic, 2012). The yeast form usually dominates in culture and is the form associated with human skin.

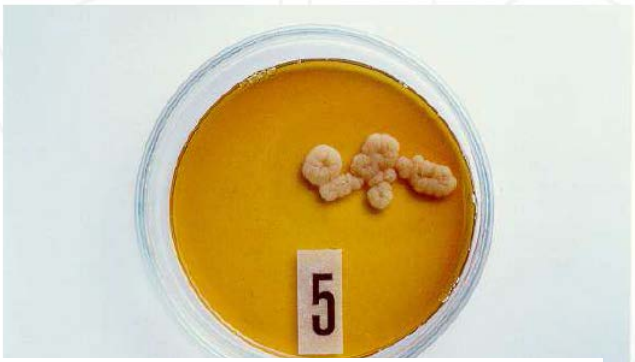

Figure 11. *Malassezia* species on modified Dixon agar (Figure 2 in Prohic, 2012). Copyright 2004 – 2015 by InTech.

For differentiation of *Malassezia* species, Lemming and Notman agar or Dixon agar should be used (Prohic, 2012). The exception is *M. pachydermatis*, which grows only on Sabouraud agar (Prohic, 2012).

Molecular characterization is reviewed in Cafarchia et al. (2011).

1.3.7.3 *Medical Importance*

Because of the association with skin, conditions, such as psoriasis, dandruff and eczema, have been associated with this genus (Cafarchia et al., 2011; Amend. 2014).

1.3.8 Penicillium

In 1809, the generic name *Penicillium* was introduced (Hawksworth, 1985) for three species. Since then, the genus has grown to include over 350 species (COL, 2014), but the naming of the species has undergone many revisions (Visagie et al., 2014). It is very difficult to identify species of this genus using conventional microbiological methods; identification by macro- and micro-morphological features may not provide definitive results (Kozlovskii et al., 2013; Visagie et al., 2014). However, the possibility of species-specific identification based on biologically active compounds produced by the fungus is promising (Kozlovskii et al., 2013), and the recent paper by Visagie et al. (2014) strives to offer a stabilizing review of the taxonomy, identification, and nomenclature for the genus.

Penicillium is a very common fungus with a worldwide distribution and large economic impact on human life, due to its main functions of decomposition.and use in food production. For example, *Penicillium* can cause devastating rots, can act as a pathogen on food crops, and produces mycotoxins. Conversely, *Penicillium* is used in food production (e.g., Camembert of Roquefort cheeses and fermented sausages) and in the production of penicillin (Figure 12) (Visagie et al., 2014).

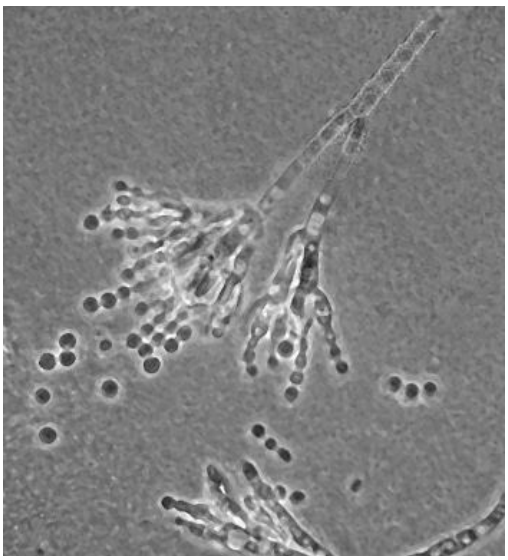

Figure 12. *Penicillium chrysogenum* (also known as *P. notatum*), the source for penicillin. http://botit.botany.wisc.edu/toms_fungi/nov2003.html. Copyright 1995 – 2010 by Tom Volk.

1.3.8.1 *Taxonomy*

Kingdom:	Fungi
Phylum:	Ascomycota
Class:	Euascomycetes
Order:	Eurotiales
Family:	Trichomaceae
Genus:	*Penicillium*
Species:	352

Teleomorphs include *Eupenicillium, Talaromyces, Hamigera*, and *Trichocoma*.

1.3.8.2 *Physical Characteristics*

Penicillium's macromorphological characteristics vary greatly depending on growth conditions. Important characteristics that are used for identification after 7 – 10 days of growth are: colony texture, degree of sporulation, color of conidia, the abundance, texture and color of mycelia, and observation of any pigments or exudates. However, it is commonly observed to be white-green and "fluffy".

Czapek Yeast Autolysate agar and Malt Extract Agar are the recommended standard growth media for identification by morphology (Visagie et al., 2014). The conidiophore of *Penicillium* resembles a paintbrush (Figures 12 and 13; penicillus is the Latin word for paintbrush). Visagie et al. (2014) reported on the importance of the media used and its impact on characterization and identification, even down to the manufacturer of the same media (for example Oxoid vs Difco formulations of Malt Extract Agar). Differences in nutrients, temperature, lighting and humidity can also make strain identification based on morphology very complicated.

As show in Figure 13, the characteristics of the conidiophores are very useful for identification purposes, but identification is not an exact science. Wall texture also aids in the identification.

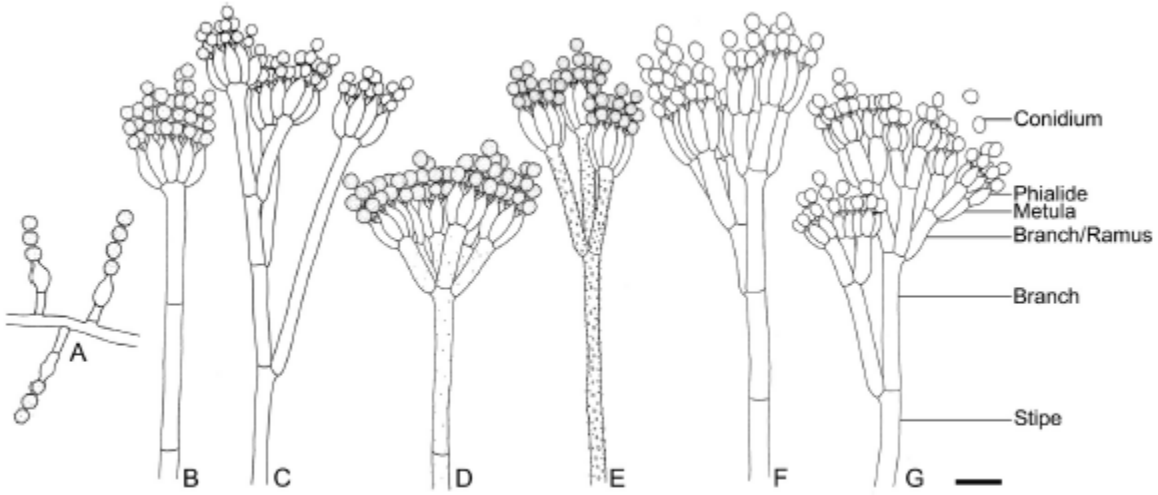

Fig. 2. Conidiophore branching patterns observed in *Penicillium*. A. Conidiophores with solitary phialides. B. Monoverticillate. C. Divaricate. D, E. Biverticillate. F. Terverticillate. G. Quaterverticillate, terms used for describing parts of conidiophores are given. Scale bar = 10 µm.

Figure 13. (Figure 2 from Visagie et al. 2014), illustrating conidiophore branching patterns. Copyright 2014 by CBS-KNAW Fungal Biodiversity Center.

1.3.8.3 *Medical Importance*

Probably the most commonly reported, medically important species is *P. marneffei*, which causes an opportunistic infection in HIV-infected patients in Southeast Asia (Duong, 1996; Sirisanthana, 2001; Cao et al., 2011). However, there are some reports of other cases of invasive disease caused by species other than *P. marneffei*.

In a review of non-*P. marneffei* cases since 1951, there were 31 cases of invasive disease including 12 cases of pulmonary infection (six in non-immunocompromised patients), four cases of prosthetic valve endocarditis, six cases of continuous ambulatory peritoneal dialysis (CAPD) peritonitis (inflammation of the peritoneum, the lining of the abdomen), and five cases of endophthalmitis (inflammation of the entire eye). Single cases of fungemia (fungi in blood) and oesophagitis (inflammation of the esophagus) in HIV/AIDS patients and a case each of upper urinary tract infection and intracranial infection (immune status not specified) (Lyratzopoulos,

2002) were also noted. Trauma, surgery (e.g., heart valve replacement for prosthetic valve endocarditis), and prosthetic material are the common causes in non-pulmonary cases.

Another case report was published of a 56-year-old female Chinese gardener with a history of type 2 diabetes who had fever, fatigue, and a productive cough. A ball of *P. capsulatum* hyphae was removed from her lung;. She recovered after surgery and anti-fungal treatment, (Chen et al., 2013).

1.3.9 Phoma

Members of the genus *Phoma* can be found worldwide. The genus consists of many harmless species but also includes human and plant pathogens. Because some species can infect economically important crops, some *Phoma* species are of quarantine significance (Aveskamp et al., 2008). The most important pathogens that are associated with Black Leg (disease of cruciferous vegetables, cabbages, and mustard plants) are *P. lingam* and a *Phoma* anamorph of *Leptosphaeria biglobosa*.

Ubiquitous species that have been found on inorganic materials, such as asbestos, cement, oil-paint, plaster, and crockery, include *P. herbarum, P. glomerata, P. pomorum, and P. eupyrena* (Aveskamp et al., 2008).

Effective biocontrol has also been demonstrated by *P. herbarum, P. exigua, and P. macrostoma* against broadleaf weeds (e.g., dandelion) and chickweed (Aveskamp et al., 2008).

1.3.9.1 *Taxonomy*

	Catalog of Life, 2014	EFSA 2014
Kingdom:	Fungi	Fungi
Phylum:	Ascomycota	Ascomycota
Class:	Dothideromycetes	Dothideomycetes
Order:	Pleosporales	Pleosporales
Family:	Not assigned	Leptosphaeriaceae
Genus:	*Phoma*	*Plenodomus*
Species:	1,866	33

Synonyms for *Phoma tracheiphila* are (EFSA 2014):

Plenodomus tracheiphilus
Deuterophoma tracheiphila
Bakerophoma tracheiphila .

Teleomorph states are in the genera *Didymella, Leptosphaeria, Pleospora* and *Mycosphaerlla* (de Gruyter et al. 2009).

1.3.9.2 *Physical Characteristics*

Phoma are observed to be flat and white-to-grey in color with brown pigment (Figure 14).

Figure 14. http://mold-pro.com/Glossimages/phoma.htm No Copyright, on Mold-Pro Inspections, LLC website.

Species in *Phoma* are pycnidial coelomycetes. This group of organisms bears the conidia within semi-enclosed (acervuli) or enclosed (pycnidia) structures. Because of their conidial strategy (being enclosed), they are not considered ubiquitous airborne organisms; therefore, infection is usually the result of traumatic implantation (Sutton, 1999; Aveskamp et al., 2008).

1.3.9.3 *Medical Importance*

Phoma species are known to infect humans, cattle, fish (salmon and trout), arthropods and nematodes (Aveskamp et al. 2008). Diseases associated with *Phoma* species include skin infections, bovine mycotic mastitis and fish-mycosis.

1.3.10 Stachybotrys

In the 1990's S*tachybotrys* was thrust into the limelight by the media as the cause of morbidity and mortality related to contaminated indoor home or work environments (e.g., Cleveland infant pulmonary hemosiderosis (iron overload); Weir, 2000; Kuhn and Ghannoum, 2003). However, when compared to other commonly found molds, *Stachybotrys* is generally less common and is rarely found in isolation (Kuhn and Ghannoum, 2003; Pestka et al., 2008). This is important because other species that are often co-located with *Stachybotrys* are capable of producing mycotoxins and, therefore, the observed effects have not been definitively attributed to *Stachybotrys*.

This genus is found worldwide in soil and cellulose-rich media (e.g, hay, straw, grain, hemp, plant debris, dead roots, wood pulp, cotton, fabric, paper, book binding glue and plant fiber-processing plants) (Kuhn and Ghannoum, 2003).

1.3.10.1 *Taxonomy*

Kingdom:	Fungi
Phylum:	Ascomycota
Class:	Sordariomycetes
Order:	Hypocreales
Family:	Not assigned
Genus:	*Stachybotrys*
Species	69

Commonly called "black mold" or "toxic black mold" (Figure 15).

Figure 15. *Stachybotrys.* www.biotopia.net.au Copyright 1999 – 2009 by Parallels.

This genus was first described in 1837 after isolation from domestic wallpaper in Prague. Li and Yang (2005) investigated several organisms identified as *Stachybotrys chartarum* and concluded that the species is not as well-delineated as originally believed and that additional morphological and phylogenetic analyses are needed to differentiate closely related organisms.

S. alternans and *S. atra* are obsolete species names and were replaced with *S. chartarum.*

All species can produce simple trichothecenes. A third of the species can produce macrocyclic trichothecenes (satratoxins). The other two-thirds can produce less-toxic atranones. A species that can make both satratoxins and atranones has not been observed (Semeiks et al., 2014).

1.3.10.2 *Physical Characteristics*

While most molds thrive in relative humidity as low as 75%, the requirement of *Stachybotrys* is much higher, around 93% at 25°C (Kuhn and Ghannoum, 2003). It can survive in a wide range of temperatures and dies only at temperatures greater than 60ºC. The fungal spores can survive winter temperatures and remain viable for decades. Conidia retain viability even after passage through the gastrointestinal tract (Kuhn and Ghannoum, 2003).

Stachybotrys has a particular affinity to cellulose (Kuhn and Ghannoum, 2003), but it is usually a tertiary colonizer, arriving after *Penicillium* and *Cladosporium*. It has also been found growing on pipe insulation, gypsum, fiberglass wallpaper and aluminum foil. Studies on plasterboard of differing composition showed that a statistically significant difference in growth and spore characteristics could be observed depending on the modifications of the plasterboard (Murtoniemi et al., 2003). Growth was reduced when plasterboard was treated with 1% Parmetol DF 17 (a fungicide), the starch was removed, or desulfurization gypsum (DSG) was used in the core. Cytotoxicity of spores was also affected by the plasterboard components; spores from board with DSG were less cytotoxic than spores from a reference board.

In non-cellulose based media and materials, the growth of *Stachybotrys* is slower than other genera, leading to overgrowth by other molds (Kuhn and Ghannoum, 2003). However, when the substrate is cellulose-based, *Stachybotrys* will proliferate much better.

1.3.10.3 *Medical Importance*

It does not appear that *Stachybotrys* is a pathogen, but instead health effects are a direct function of the toxins that it produces. In the late 1800's and early 1900's, it was noticed that horses, cattle and humans would experience disease that was associated with the presence of the mold, but Koch's postulates have not been fulfilled (Kuhn and Ghannoum, 2003; Pestka et al., 2008; Semeiks et al., 2014). Weir (2000) suggested non-infectious causes of health effects may be immune-mediated (hyper-sensitivity pneumonitis), toxic (mucosal irritation), and carcinogenic (aflatoxin) mechanisms.

Potentially beneficial compounds produced by *Stachybotrys* include antiviral stachyflins and the immunosuppressant cyclosporin (Semeiks et al., 2014).

1.3.11 Zygomycetes

Zygomycetes is a class name, and this large group of organisms was first associated with human disease in the 1800's. It was through tissue samples that the mold was identified, rather than via culture-based methods. The presence of "coenocytic angioinvasive hyphae" (Figure 16; angioinvasive means "causing infiltration in blood vessels") suggested the presence of what was a member of the genus *Mucor*. Some of the members of the genus *Mucor* have since been reassigned to other genera such as *Rhizopus*, *Absidia*, *Rhizomucor*, *Aphphysomyces*, *Saksenaea*, *Cunninghamella, Cokeromyces, and Syncephalastrum* (Ribes et al., 2000).

1.3.11.1 *Taxonomy*

Kingdom:	Fungi
Phylum:	Zygomycota
Class:	Zygomycetes
Order:	Mucorales or Entomophthorales
Family:	Mucoraceae, Cunninghamellaceae, or Ancylistaceae
Genus:	See Figure 18
Species:	over 450

In 2012 it was proposed that some of the members of the phylum Zygomycota be moved into a new phylum, Glomeromycota (Kwon-Chung, 2012). Zygomycetes belong to two orders (Entomophthorales and Mucorales; Figure 17), and the members of the orders produce clinical diseases with distinct order-associated patterns (Kwon-Chung, 2012).

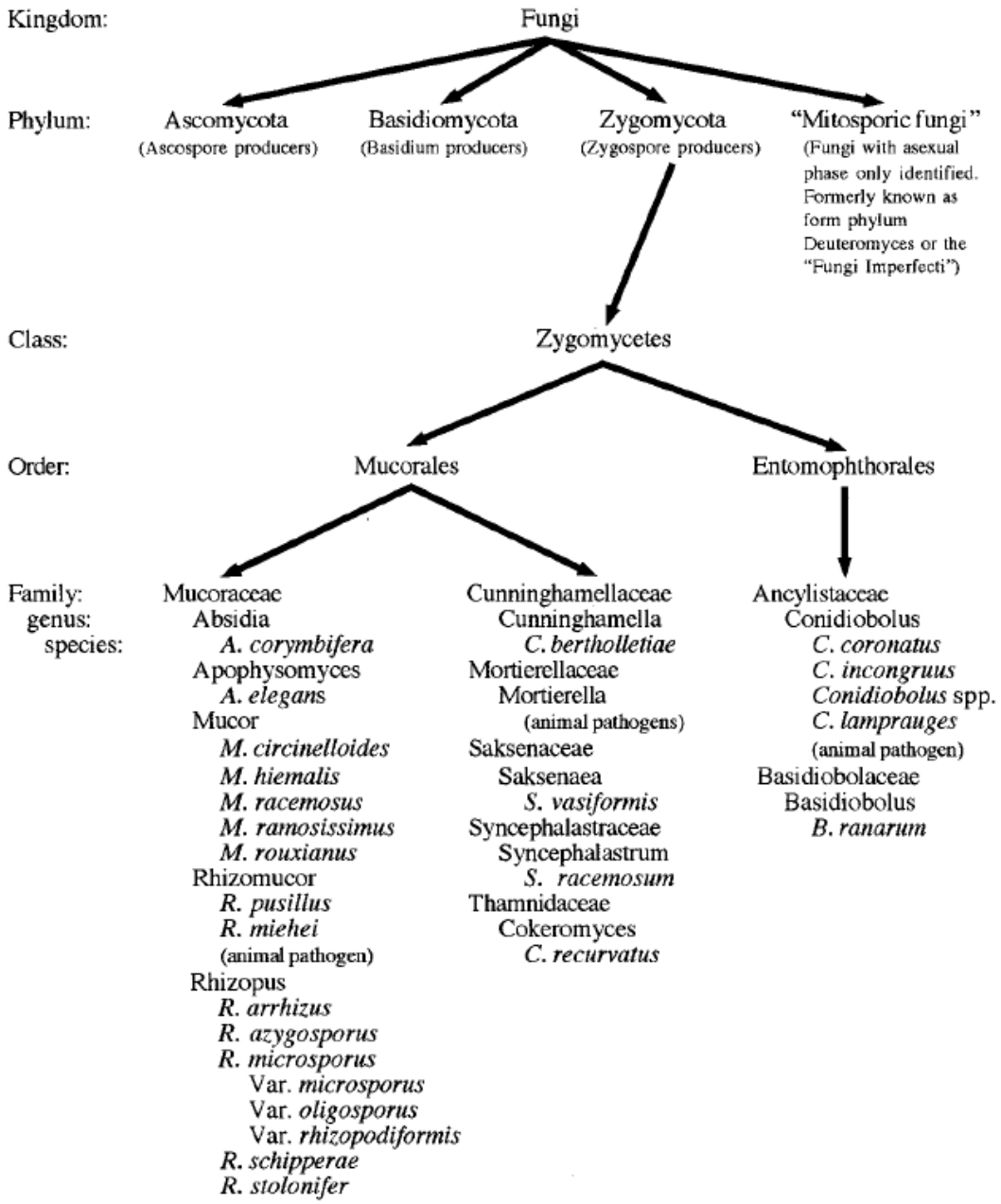

Figure 17. Taxonomic organization of zygomycetes (Ribes et al., 2000). Copyright 2000 by American Society for Microbiology.

1.3.11.2 *Physical Characteristics*

Zygomycetes grow rapidly and form grey-white, brown, or grey-brown "cottony" or "wooly" colonies (Figure 18).

Under the microscope, Zygomycetes appear as wide ribbon-like coenocytic hyphae. They differ from other molds because their spores (asexual reproduction) produce sporangiospores in sack-like structures. It is the formation of a zygosporangium (sexual reproduction) that accounts for the characteristic coloration and surface ornamentation of each isolate (Ribes et al., 2000).

Zygomycetes are easily confused with *Aspergillus* species. A defining feature for differentiation is the hyphal type: aseptate (lack cross-walls) in Zygomycetes and septate (have cross walls) in *Aspergillus*. The width of the hyphae also differs: 6 – 16 microns wide in zygomycetes and only 2 – 3 microns wide for *Aspergillus* (Ribes et al. 2000). Zygomycetes have a high-affinity iron permease gene (RFTR I) that has been proposed as a tool for the molecular identification of Zygomycete species (Symeonidis, 2009). Other genetic markers are also being targeted to assist with identification of Zygomycetes (Walsh et al., 2012).

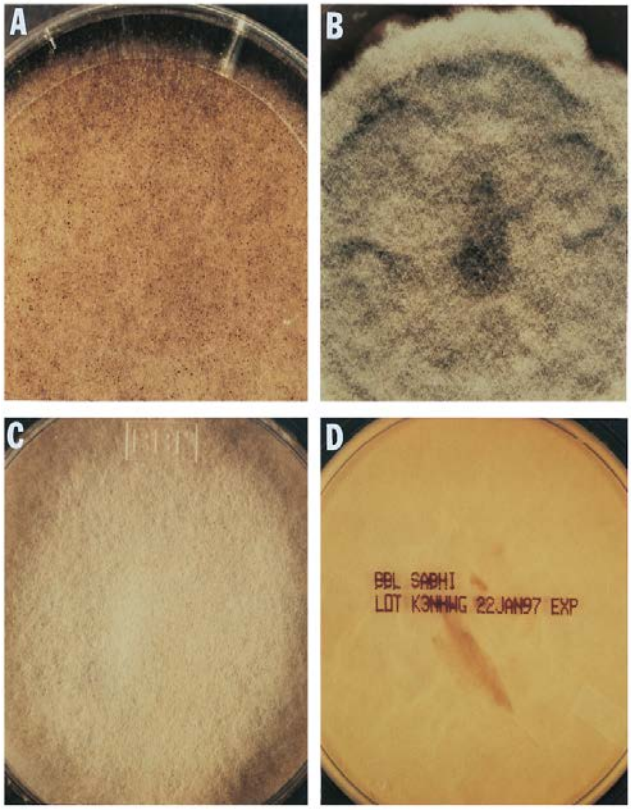

Figure 18. Macromorphology of A) *Rhizopus* B) *Mucor* and C) *Absidia*. D) is the reverse of the *Absidia* plate showing the lack of dark pigment. (Figure 4 in Ribes et al. 2000). Copyright 2000 by American Society for Microbiology.

1.3.11.3 *Medical Importance*

Zygomycosis is a "catch all" term that describes a variety of infections caused by members of the Zygomycetes. The most prominent and well-studied/characterized genera associated with human disease (rhinocerebral, pulmonary, allergic reaction, cutaneous effects) are *Rhizopus* and *Mucor* (Ribes et al., 2000). Other genera with pathogenic members include *Basidiobolus* and *Conidiobolus*. Fungal infections caused by Zygomycetes are considered emerging infections in intensive care units (Paramythiotou et al., 2014) where patients are critically ill and susceptible to infections for a variety of reasons.

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