INTRODUCTION AND REVIEW OF LITERATURE

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INTRODUCTION & REVIEW OF LITERATURE
Medical Mycology has emerged as an important branch of Microbiology due to increase in the isolation of opportunistic fungal pathogens especially in immunocompromised patients. Organisms once thought to be contaminants are now considered as pathogens in compromised patients. Fungal infections, however, are extremely common and some of them are very serious and even fatal. With the control of most bacterial infections in the developed countries, there is an increased incidence of fungal infections. Modern advances in treatment such as bone marrow and various organ transplantations, newer antibiotics, steroids and immunosuppressive agents have led to an increase in opportunistic fungal infections. Even though a given isolate is not a documented fungal pathogen, its isolation from a normal sterile site and its ability to grow at 37°C points to the fact that it may be considered a possible pathogen. With few exceptions, all the fungi that infect humans share the ability to grow at 37°C. The study of pathogenic fungi has received scanty attention in comparison with the study of other pathogens. This is probably due to the relatively benign nature of most of the common mycotic diseases and the techniques employed in mycology are more those of botanists than of bacteriologists.

The word “mycology” in fact, is derived from mykes, the Greek word for mushroom. Fungi were initially classified with the plants and much of the botanical influence is still seen, even though the organisms have been transferred to a separate kingdom on the basis of cell structure. Fungi are ubiquitous in nature. They are eukaryotic and cell wall containing chitin and/or cellulose, chemo- heterotrophic. They function as saprophytes and also as a decomposer in nature. Mycological identification can be frustrating because of the importance placed upon the morphology and certain structures and terms. The morphology and the clinical aspects of the fungi serve as a protocol for their identification. Clinicians, mycologist and
pathologists are essential for the diagnosis. Fungi are extremely successful organisms, as evidenced by their ubiquity in nature. They are an important component in energy, where they function as decomposers cycle. Of the estimated 25,000 species, less than 150 are known to be primary pathogens of humans. The infection of humans seems to be an accident of nature, since it represents a dead end for the fungus. Most fungal infections are not contagious but are acquired through exposure to a point source in nature, where the organism exists as a saprophyte.

Fungi reproduce by the formation of spores, which may be either asexual (involving mitosis only) or sexual (involving meiosis; preceded by the fusion of the protoplasm and the nuclei of two cells). One fungus can produce both sexual and asexual spores. Specialized structures (fruiting bodies) may be associated with either sexual or asexual spores and are helpful for identification. Asexual spores are of two general types: sporangiospores and conidia. Sporangiospores are characteristic of lower fungi, zygomycetes. Conidia are the asexual spores of higher fungi. They are represented by the classes Ascomycetes, Basidiomycetes, and Deuteromycetes. The sexual spores of Ascomycetes is the ascospore, basidiomycetes is the basidiospore. The Deuteromycetes (Fungi imperfecti) have no sexual spores.

One method of classifying mycoses is by geographical distribution. (Emmons C.W et al, 1970). This has some validity and usefulness. Actinomycosis, cryptococcosis, candidiasis, some dermatophytoses, certain mycetoma, nocardiosis, sporotrichosis, phycomycosis (mucormycosis), aspergillosis and histoplasmosis occur widely over temperate and tropical areas of the world. Chromoblastomycosis occurs all around the world; both north and south of the equator, but the predominant etiologic species vary in geographical areas. Certain mycetoma and agents causing subcutaneous mycosis are geographically limited in distribution. Some of these
mycoses appear to be permanently limited by soil or climatic conditions which are necessary for the growth and survival of the etiologic fungus in soil. These fungi are isolated from soil, many of them from specialized habitats characterized by elevated temperatures, high salinity, or enrichment of the substrates by excreta of birds and bats. In these special habitats the fungi grow as free living saprobes, permanent members of the flora and fauna of soil, apparently able to survive the competition of other micro-organisms without any necessity for reseeding of the substrate by an infected animal. Man, other animals and birds are accidental hosts, and periodic or cyclic parasitism of a host is not essential for the survival of the fungus in a suitable ecologic niche. Under these conditions of saprobic growth the pathogens produce enormous numbers of conidia which are resistant to unfavourable conditions. These conidia enter into the host either by penetrating wound or by splinters which implant them subcutaneously in the patients. The actual geographic distribution in soil may be much wider for the fungi which cause chromomycosis and mycetoma, than the relative frequencies of these mycoses in different parts of the world indicate. In these cases the socio-economic status of a country may influence the frequency of mycoses. Chromoblastomycosis and mycetoma occur most often on the feet and in persons who work in the fields without adequate protection of shoes. A topographic classification may be more important to the physician than geographical distribution. The mycetoma, chromomycosis and sporotrichosis are primarily (but not exclusively) cutaneous, sub cutaneous or lymphatic in distribution. They are often localized (but not exclusively) on the feet, legs and arms.

Infectious diseases are responsible for considerable morbidity and mortality in developing countries like India. Bacterial and viral diseases are largely under check due to skillful use of antibiotics and intensive prophylactic vaccination. Fungal
infections continue to be a cause of concern because of its chronic nature of infection and the fewer number of antifungal agents highly toxic to the ordinary tissues. Differential diagnosis is very difficult in subcutaneous fungal infections because of the clinical similarity with other subcutaneous skin infections like cutaneous tuberculosis, leishmaniasis, tertiary syphilis, and yaws. Diagnosis is often delayed because of the associated bacterial colonization which may be mistaken for the primary infectious agents. Accurate diagnosis is essential for treatment of fungal infections since antifungal agents are highly toxic and act directly on fungal agents. The other similar clinical conditions caused by bacterial, viral or protozoal have their own treatment profile.

The subcutaneous mycoses include a heterogeneous group of infections that involve the skin and subcutaneous tissue, generally without dissemination to other organs of the body. The agents causing subcutaneous infection may also produce dissimilated infection. The etiological agents are found in several unrelated fungal genera, all which may exist as saprophytes in nature. Humans and animals serve as accidental hosts after traumatic inoculation of the fungal spores into cutaneous and subcutaneous tissue. These mycoses are not opportunistic in the usual sense, since they occur in otherwise healthy people; they are chronic, evolving over a lengthy period, and may tend to be disfiguring. There is evidence of a causal relationship between the manner of acquisition of infection and pathologic process, particularly in view of the facts that in the few instances of primary cutaneous inoculation of some of the so called systemic fungi such as coccidioides and histoplasma, the ensuing disease processes have had a remarkable resemblance to those of the subcutaneous mycoses rather than to the ordinary course of events in systemic infection. These infections are characterized by the development of a lesion at the site of inoculation. Unlike the
systemic mycoses, whose primary mode of entry is usually pulmonary, these infections are the result of traumatic implantation of the fungus into the skin. In general the ensuing disease remains localized to a particular area or slowly spreads to the surrounding tissue. In some diseases slow extension via lymphatic channels is a frequent occurrence (sporotrichosis), and in others hematogenous and lymphatic dissemination is rarely recorded.

Subcutaneous mycoses can be classified into

- CHROMOBlastomycosis
- PHAEohypHomyCOses
- MYCetoma
- HYalohypHomyCosis
- SPorotrichosis
- Rhinosporidiosis
- Sub cutaneous phycomycoses
- Lobomycosis

**CHROMOBlastomycosis**

Chromoblastomycosis or verrucous dermatitis is caused by any of several morphologically related dematiaceous fungi. It is defined by Carrion A.L (1910) as chronic granulomatous diseases of the skin, confined most frequently to one of the lower extremities, but occurring also on other exposed areas such as the arm, head, neck or trunk and characterized clinically by the formation of warty cutaneous nodules or plaques which develop very slowly, ultimately forming prominent papillomatous vegetations which may or may not ulcerate. The infection is characterized by the development of a papule at the site of the traumatic insult that spread to form warty or tumor like lesions described as ‘cauliflower like’. The tissue
form, the sclerotic / muriform bodies are brown or copper colored, septate cells that appear to be dividing and are identical in all case of chromoblastomycosis. The presence of muriform bodies in cutaneous or sub cutaneous tissue is pathognomonic of chromoblastomycosis. The agents of chromoblastomycosis must be cultured because the appearance of the muriform bodies formed by all agents of chromoblastomycosis is similar, the fungus cannot be identified on the basis of tissue morphology.

The groups of fungi known to cause chromoblastomycosis are dematiaceous. All are slow growing and produce heaped up and slightly folded darkly pigmented colonies with a grayish – velvety appearance. The reverse side of the colony is jet black. The taxonomy of the organisms that causes chromoblastomycosis is complex. Their identification is based on distinct microscopic morphologic features. Three genera, Cladosporium, Phialophora, and Fonsecaea are known to cause chromoblastomycosis frequently.

The genus Cladosporium includes those species which produce long chains of conidia (blastoconidia) that have a dark septal scar.

The genus Phialophora includes those species that produce short, flask shaped or tubular phialides, usually with a well-developed collarette. Clusters of conidia are produced by the phialides through an apical pore.

The genus Fonsecaea includes the organisms which exhibits a mixed type of sporulation, that uniquely includes one celled primary conidia that are produced on either side of the conidiophores resembling a series of bent knees. Conidia are produced sympodially. The primary conidia gives rise to secondary conidia that appear to occur in loose heads. This is known as rhinocladiella type sporulation. *F.pedrosoi* and *F.compactum* are example for this type of sporulation.
The characteristic features of the three genera are summarized as follows

1. **Cladosporium**: Cladosporium type sporulation with long chains of elliptical conidia (2-3 μm x 4-5 μm) are born erect, tall branching conidiophore. The important species are *Cladosporium carrionii* and *C. bantianum*. Differentiation from the morphologically similar *C. carrionii* is made on the following basis:
   a) The *C. bantianum* generally grow slowly.
   b) There is a difference in spore size, distribution, *C. bantianum* having regular conidia which tend to be more elongate than those of *C. carrionii*.
   c) The maximum temperature for growth of *C. bantianum* is 42 to 43°C where as that of *C. carrionii* is 35 to 36°C.
   d) *C. carrionii* fail to induce brain abscess when injected into mice, whereas most strains of *C. bantianum* will do so.
   e) In *C. carrionii* long chains of conidia are seen. Pathogenic species may be differentiated from saprophytes of this genus on the basis of physiologic characters. The pathogen grow well at 21 to 25°C and 37°C and are slow growing, whereas the saprophytic forms are fast growing at 21 to 25°C but do not grow at 37°C.

2. **Phialophora** (*Phialophora verrucosa*)

   Tube-like or flask-like phialides each with a distinct collarette. Conidia are produced endogenously and occurs in clusters at the tip of the phialide. Examples are
   
   *P. verrucosa*
   
   *P. jeanselmei*

3. **Fonsecaea** (*F. pedrosoi* and *F. compactum*) conidial heads with sympodial arrangement of conidia, with primary conidia giving rise to secondary conidia. Cladosporium type of sporulation may occur and phialides with collarettes may also
be present. *F.pedrosoi* is differentiated from *F.compactum* by the production of loose heads in contrast to more compact heads produced by *F.compactum*.

The laboratory diagnosis of chromoblastomycosis is made easily. Biopsy was taken from the lesion for culture, direct mount using 10% KOH and for histopathologic examination. The presence of copper colored sclerotic/muriform bodies which appear rounded, brown and 4-10 μm in diameter resembling copper pennies is diagnostic.

**PHAEOHYPHOMYCOSIS**

Dematiaceous fungi are characterized by the presence of a brown to black color in the cell walls of their vegetative cells, conidia, or both that results in colonies ranging from olive or gray to black. The dark pigmentation of the majority of medically important fungi is caused by the deposition of dihydroxynaphthalene melanin formed via pentaketide metabolism. In chromoblastomycosis disease is characterized by the presence of muriform (sclerotic) bodies in infected tissue. Phaeohyphomycosis is characterized by the presence of dematiaceous yeast like cells, pseudohyphae, or any combination of these forms. The name phaeohyphomycosis is not restricted to hyphomycetes; it encompasses all fungi having dematiaceous cells in infected tissue, regardless of the taxonomic classification of the etiologic agents. The hyphae observed in clinical specimens may be regular and uniform in diameter or irregular in shape with many swollen cells and may be short or very long. Phaeohyphomycosis encompasses a spectrum of opportunistic entities that range from purely cosmetic conditions to fatal cerebral infections. As with chromoblastomycosis, the identities of etiologic agents of phaeohyphomycosis cannot be determined from microscopic examination of clinical specimens. These fungi must be grown in laboratory culture media before they can be identified. Masson-Fontana stain is used
for demonstrating the melanin pigment present in the cell wall of the fungi present in the tissue. The most common phaeohyphomycosis syndrome includes allergic fungal sinusitis, keratitis, and sub cutaneous infections. Subcutaneous infections commonly present are either a cyst or a diffuse lesion and are chronic, and usually remain localized.

**Medically important dematiaceous fungi causing Phaeohyphomycosis**

*Alternaria:* The important species are *A. alternata, A. tenuissima, A. chlamysopsora, A. longipes*

*Aureobasidium:* *A. pullulans*

*Bipolaris:* *B. spicifera, B. hawaiensis, B. australiensis*

*Chaetomium:* *C. globosum, C. strumarium, C. atrobrunnem*

*Cladosporium:* *C. cladosporioides*

*Cladophialophora:* *C. bantiana, C. emmonsii*

*Coniothyrium:* *C. fuckelii*

*Curvularia:* *C. lunata, C. senegalensis, C. verruculosa, C. clavata, C. geniculata*

*Dactylaria:* *D. constricta, D. gallopova*

*Exophiala:* *E. dermatitidis, E. jeanselmei, E. jeanselmei var. lecanii-corn*

*Exserohilum:* *E. rostratum, E. meginnisii*

*Fonsecaea:* *F. pedrosoi, F. compatum, Hormonema*

*Lasiodiplodia:* *L. theobromae*

*Lecythophora:* *L. hoffmannii, L. mutabilis*

*Nattrassia:* *N. mangiferae*

*Phaeoannellomyces:* *P. werneckii, P. elegans*

*Phaeococcomyces:* *P. exophilae*
Phialemonium: - *P. curvatun, P. obovatun*

Phaeosclera: - *P. dermatoides*

Phialophora: - *P. richardsiae*

Phialoacremonium: - *P. parasiticum, P. inflatipes, P. rubrigenum.*

Phiacremonium: - *P. rugrigenum*

Phoma: - *P. eupyrena, P. minutispora, P. oculo-hominis, P. sorghina.*

Rhinocladiella: - *R. aquaspersa, R. atrovirens, R.*

Ramichloridium: - *R. schulzeri, R. mackenzei, R. subulatum*

Scedosporium: - *S. apispermum, S. prolificans*

Scytalidium: - *S. dimidiatum, S. lignicola, S. hyalinum*

Sporothrix: - *S. schenckii, S. cyaneascens*

Wangiella: - *W. dermatitidis*

Xylohypha: - *X. bantiana, X. emmonsii*

**MYCETOMA**

Mycetoma (literally fungal tumor) is a chronic granulomatous infection that usually involves the lower extremities but may occur in any other part of the body. The disease was originally reported by Gill (1842) from Madurai, South India, and Carter (1860) established its fungal etiology. The infection is characterized by swelling, purplish discoloration and tumor like deformities of the subcutaneous tissue and multiple sinus tracts that drains pus containing yellow, white, red or black granules. The granules contain micro colonies of the causative agent. The infection gradually progresses to involve the bone muscle or other contagious tissue and ultimately requires amputation in most cases. There may be dissemination to other organs including the brain, however this type of infection is relatively uncommon. Mycetoma is common among persons who live in tropical and sub tropical regions of
the world, where outdoor occupation and failure to wear protective clothing predisposes the infections.

Two types of mycetoma are described – 1) Actinomycotic mycetoma, which is caused by species of aerobic and anaerobic actinomycetes including *Nocardia*, *Actinomadura*, and *Streptomyces* and 2) eumycotic mycetoma caused by heterogenous group of species having true septate hyphae.

**Geographical distribution:** Maduramycosis occurs most frequently in tropical and sub tropical zones where few people wear shoes and the feet come in direct contact with the soil. Instances have been reported from India, mainly Tamil Nadu, Africa, Europe, South America, Mexico, Canada and the United States. The source of infection is exogenous, and more than a half of the patients give a history of an injury, such as a minor scratch or a wound produced by a splinter. Of the organisms isolated from maduramycosis, most are thought to occur either as saprophytes in the soil or on plants.

Table 1. Organisms associated with maduramycosis

**Black granules:**

1. *Madurella mycetomii* (Laveraan) Brumpt, (1905)
2. *M. grisea* (MacKinnon), Ferrada and Montemayer, (1949)
4. *Leptosphaeria senegalensis* Baylet, Camain, and Segretain (1959)
5. *Phialophora jeanselmei* (Langeran) Emmons (1945)
6. *Curvularia lunata* (Wakker) Boedijn (1933)
7. *Corynespora lassicola*
8. *Curvularia geniculata*
9. *Exophiala jeanselmei*
10. *Plenodomus avramii*

11. *Pseudochaetosphaeronema larense*

12. *Pyrenochaeta mackinnonii*

13. *Pyrenochaeta romeroi*

**White to Yellow Granules:**

1. *Allescheria boydii.* Shear (1921)

2. *Monosporium apiospermum* Saccardo, (1911)

3. *Cephalosporium falciforme* Carrion (1951)

4. *Neotestudina rosatii,* Segretain and Destombes,(1961)

5. *Cephalosporium recifei,* Leao and Lobo.(1934)

6. *Acremonium falciforme*

7. *Acremonium.recifei*

8. *Aspergillus nidulans*

9. *Cylindrocarpon destructans*

10. *Fusarium moniliforme*

11. *Fusarium.solani*

12. *Polycytella hominis*

**Symptomatology:**

The mode of onset is neither characteristic nor uniform with or without a history of previous injury. The first detectable lesion may be (1) a small papule, (2) a small nodule which is deep seated and fixed, (3) and indurated area surrounded by a vesicle (4) and an abscess which ruptures with subsequent formation of a fistula. The disease progresses slowly and is at first characterized by periods of remissions and relapses. As many as 6 or 8 papules may form in succession, or as many as 12 abscesses may develop and disappear over a periods of months or years before the
entire foot becomes involved and presents the characteristic clinical picture. The classical picture of swellings and deformities may develop with in a period of months, but it usually takes much longer, sometimes as many as 10-15 years. As the infection extends deeper into the tissues, the muscles, bones, fascia and tendons may become involved and the foot or hand becomes club shaped or may develop into globose mass two or three times the normal size. The skin is discolored, with pitted scars, nodules and multiple sinuses develop. There is no loss of sensation in the skin. Nodules frequently develop around the openings of fistulas from which serosanguineous or oily fluid containing the diagnostic granules drains. The color of the granules varies depending upon the infecting organism. There is little systemic reaction unless the lesions are secondarily infected. Pain is present rarely even when the affected part is manipulated. The patient generally can walk until the disease has progressed to the stage where marked wastage of the leg muscles. The numerous fungi that have been isolated from cases of maduramycosis fall into two classes: Ascomycetes and Deuteromycetes (Fungi Imperfecti).

**HYALOHYPHOMYCOSIS**

(C.gleosporioides), Onychola, (O.canadensis) and Cheatomium, (C.globosum, C.atrobrunneum). Recently species of many other genera, viz Cylindrocarpon, Lecythophora and Philaemonium have been found to be responsible for severe infection in immunocompromised patients.

SPOROTRICHOSIS

Sporotrichosis is a chronic infection of world- wide distribution caused by the dimorphic fungus, Sporothrix schenckii, where natural habitat is living or dead vegetation. Sporotrichosis is typically a cutaneous to sub cutaneous chronic infection that may undergo lymphatic spread. Musculoskeletal involment and disseminated infection may occur rarely, and pulmonary infection following inhalation of the conidia has been documented. Human beings aquired infection through trauma (thorn prick or splinters) usually on the hand, arm or leg. More than one dozen species of sporothrix have been described. Sporothrix schenckii is the only documented pathogen. Howard A and Orr (1963) isolated sporothrix from soil and considered their isolation from nature to be a variants of S.schenckii and they were non pathogenic to human beings. Mackinnon (1969) and his associates found their isolates to be indistinguishable from S.schenckii in all respects. Sporothrix cyanescens, a recently described species that is distinctive for its purple blue diffusible pigment, can be recovered from clinical material, but animal studies have shown that it is not pathogenic by de Hoog and G.A.deVries (1973). Isolates of Sporothrix species that have been recovered from environmental sources lacks the dematiaceous thick walled conidia and are non virulent in mice. In order to identify a mold recovered from clinical material as Sporothrix schenckii, one must demonstrate its dimorphic capability, i.e. its ability to grow as both mold and stable yeast. To do so, isolates must be sub cultured on an enriched medium such as brain heart infusion broth.
containing 0.1% agar and incubated under 5% CO₂ at 37 °C, S.schenckii forms yeast phase and the color of S.schenckii transforms to a soft, cream colored to white, yeast like colony. The Primary lesion begins as a small non healing ulcer, commonly of the index finger or the back of the hand. The infection is characterized by the lymph nodes, skin or subcutaneous tissues of nodular lesions which soften and break down to form indolent ulcers. The disease becomes rarely disseminated and pulmonary infection may also be seen. The infection is an occupational hazard for farmers, gardeners, nursery workers and miners. So it is commonly known as "Rose Gardner’s Disease."

Sporothrix species are basidiomycetes. It is a dimorphic fungus which may appear in human tissues as cigar-shaped to oval, budding cells (3-5 μm in length), usually within the polymorphonuclear leukocytes, or in the form of an asteroid body (amorphous, radiating eosinophilic mass surrounding a cryptococcus- like yeast cell). However, it is extremely difficult, or usually impossible, to demonstrate the organism in pus or tissue sections from human lesions (an exception is pulmonary sporotrichosis, where lesions generally reveal large number of the yeast cells). Microscopically, the hyphae are delicate (1-2 μm thick) septate, exhibit branching and bear one celled conidia, 2-5 μm in diameter. These are borne bouquet like in clusters from the tips of single conidiophores by an individual delicate, thread like structure (denticle). As the culture ages, single celled, thick walled, black pigmented conidia, borne along the sides of the hyphae.

**RHINOSPORIDIOSIS**

Rhinosporidiosis is a chronic granulomatous disease characterized by the production of polyps as hyperplasia on mucus membrane. The etiologic agent is *Rhinosporidium seeberi*. Most of the early studies of rhinosporidiosis were made in
India and Ceylon where the disease occurs frequently. It is also reported from other parts of the world. The systematic position of *R.seeberi* is still uncertain. Most investigators consider it to be a fungus, though it has not been isolated in culture. Although rhinosporidiosis is most often seen in children and young adults, it occurs at any age group. Infections are seen most often in laborers and in those with frequent exposure to water in streams and pools. The disease is not contagious, and sources of infection are exogenous. Rhinosporidiosis was observed in workmen who lived under water to bring up sand in bucket, but not in their associates who carried the sand from the water’s edge. It has been suggested that water insects or fish may be the hosts of the fungus.

**Laboratory diagnosis** :- Direct examination of the surface of the polyp may reveal the subsurface position of sporangia which are white and large (up to 350 μm in diameter) that they can be seen with the naked eye. The mature sporangiums contain numerous endospores.

**SUBCUTANEOUS PHYCOMYCOSIS**

(Subcutaneous zygomycosis)

**CONIDIODOLOMYCOSIS** :- Is a chronic mycosis affecting the subcutaneous tissue. It originates in the nasal sinuses and spreads to the adjacent subcutaneous tissues of the face, causing disfigurement. The disease occurs mainly in the tropical rain forests of Africa, South and Central America and South and East Asia. *Conidiobolus coronatus* (*Entomophthora coronata*) lives as a saprophyte in soil humus and on decomposing materials in moist warm climates. It can parasite certain insects. The disease is most common among adult males particularly those working in tropical rain forests. Infection is acquired through inhalation of spores or through their introduction into the nasal cavities by soiled hands. Clinical manifestation of
Conidiobolous infection generally begins with unilateral involvement of the nasal mucosa. The most common symptoms is obstruction along with frequent nosebleed. Subcutaneous nodules then develop in the nasal and para nasal regions. The spread of infection is slow but relentless. The infection is usually confined to the face with the development of gross facial swelling involving the forehead, periorbital region, and upper lip is very distinctive. The lesions are firmly attached to the underlying tissue. Although the bone is spared, the skin remains intact. Spread to the lymph nodes has been reported.

**Diagnosis:**- Microscopic examination of smear or tissue from the nasal mucosa will reveal broad, non septate thin walled mycelial filaments.

**Culture:**- Cultures are difficult to obtain, and the specimen must be inoculated onto the largest possible number of media. The media should be incubated between 25 and 35 °C to enhance the growth of *Conidiobolus coronatus*. The colonies which grow rapidly are flat, cream colored, glabrous and become radially folded and covered by a fine powdery white surface mycelium and conidiphores. The colony becomes tan to brown with age.

**Microscopic morphology:**- Conidiophores are simple, forming solitary, terminal conidia that are spherical, 10 to 25 μm in diameter, single celled and have a prominent papilla. Conidia may also produce hair like appendages called villae. The histopathological examination shows fibroblastic proliferation and an inflammatory reaction with lymphocytes, plasma cells, histiocytes, eosinophils and giant cells. Broad, thin walled hyphae with occasional septa branched at right angles are seen.

**BASIDI BOLOMYCOSIS**

Is a chronic subcutaneous infection of the trunk and limbs. This disease is mainly seen in the tropical regions of East and West Africa, Indonesia and India. The
causative agent *Basidiobolus ranarum* is the sole agent causing the disease and that *Basidiobolus meristosporus* and *B. haptosporus* are only synonyms of the former. *B. ranarum* has been isolated from the guts of frogs, toads and lizards, ants and decaying plant matter. Inoculation through a thorn prick or an insect bite has been suggested. The disease is usually localized to the back of the shoulders and to the arms, but it may be found on the buttock and thigh. The initial swelling may be rapid or slow in onset and is hard and painless. The spread is slow and relentless, and a large mass that is attached to the skin but not the underlying tissue (unlike conidiobolous infection). This is a disfiguring infection, but the skin covering the lesion does not ulcerate. Lymphatic obstruction may occur and can result massive lymphoedema. The basidiobolomycosis closely resembles soft tissue sarcoma, mycetoma, bacterial cellulitis. All these conditions can be reliably distinguished from zygomycosis by biopsy and fungal culture of the lesion.

**LOBOMYCOSIS**

Lobomycosis is a chronic, localized, sub epidermal infection characterized by the presence of keloidal, verrucoid, nodular lesion or sometimes by vegetating crusty plaques and tumors. The lesions contain masses of the spheroidal yeast like organism tentatively referred to as *Lobo loboi*. There is no systemic spread. The disease has been found in man and dolphins. The disease was first described in 1931 by Jorge Lobo. The etiologic agent of lobo mycosis has not been isolated in culture. Its inability to be cultured in vitro and its clinical restriction to the cooler part of the body explain the organism is an obligate parasite of some lower animal forms.

Clinical disease:- The initial infection occurs at the site of some trauma to the skin. The lesion begins as small, hard nodules resembling keloids that are sharply defined, freely movable, and have a smooth surface. The color of the nodules may be slightly
brownish. The surrounding cutaneous area is normal and erythema is absent. The lesion are painless or slightly pruritic. The disease may be transferred to other area of the skin by subsequent abrasions and auto inoculation, in which case, groups of nodules may be formed on several different areas of the body. Lobomycosis causes little discomfort to the patients, and there are no generalized symptoms. The most successful treatment for the condition is wide surgical excision of the affected areas.

**MYCOLOGY HISTORICAL BACKGROUND**

The study of mycology started as early as 1677 when Hook constructed a magnifying lens. With this finding people became aware of microscopic organisms especially fungi. First human fungal infection was described by Mayer & Emmert, (1815) in a jay. Augustino Bassi (1773-1865) in 1815 observed that muscardine disease of the silk worms (Bombyx mori) was caused by a fungus called *Beauveria bassiana*. But the name aspergillus dates back to Michaeli (1729) who described the swollen vesicle of aspergillus. Fungal etiology of skin infection was first noticed by Remak (1937), Schoenlein (1839) established the pathogenic nature of a dermatomycosis (favus) after whom the pathogenic agent was named later as *Trichophyton schoenleinii*. After this scientists concentrated on various aspects of dermatomycosis.

The discipline of Medical Mycology attained recognition in the world sciences in 1910 when French dermatologist Raymond Jacques Sabouraud (1864-1936) published his monumental work on dematophytes, "Les Teignes". He has rightly been called the "Father of Medical Mycology". Similarly, P.A. Saccardo has played a significant role in the establishment in the field of Medical Mycology in earlier days. The other scientists who played an active role in the development of mycology are Schoenle, Norman Conant, Chester Emmons, David Gruby, Rippon J.W, Ajello L
and Kwon-Chung K.J. The research in the field of mycology was renewed in the later days of 19th century and beginning of 20th century Renon, (1897); Sabouraud, (1910). This may be due to the increasing incidence of various fungal infections, both superficial and deep, due to the increased use of antibiotics against bacterial infections. In 1918, Ernst cultured *Mucor* from sputum of a patient having pneumonitis. In 1952 Kligman demonstrated the development of *Candida albicans* infection after antibiotic treatment. It was noted by many researchers that debilitating conditions such as leukemia, diabetes and cancer predispose fungal infections Hausmann, (1958). Prolonged exposure to corticosteroids, antibiotics and immunosuppressive drugs also contribute to the predisposing factors to make one susceptible to fungal infection. Emmons et al. (1970).

Now nearly 24 well defined mycoses of man are recognized and about 150 saprobic fungi can adapt to parasitism in man. With a few exceptions the systemic, lymphatic, and sub cutaneous mycoses are caused by fungi which are essentially free living saprobes in nature. These mycoses are not contagious, and infection in man and animals follows inhalations or traumatic implantation of the fungi or its spore. In India diseases of mycotic origin were known from vedic period. Mycetoma was first described from India by Van Dyke Carter in 1860. Kanthaack in 1892 and Vincent in 1984 further defined the disease. Sporotrichosis was first reported from United States. In 1898 Schenck described a case and isolated the fungus *Sporotrix schenckii*. Pioneer workers in the field of mycology in India are Powel, Panja G, Gosh L.M and Day N.C. Most of the early studies of rhinosporidiosis were made in India and Ceylon where the disease occur frequently.

Contrary to what appears in most textbooks, chromoblastomycosis was first described by Max Rudolph in 1914 and not by Lane or Medlar in 1915. In 1987,
Castro and Castro reported that Max Rudolph, a German physician living in Brazil, published a preliminary communication where the first 6 cases of the disease were described. Rudolph was also able to isolate a dark-colored fungus from 4 of 6 patients; this fungus grew in culture as a dark grey-to-black-colored furlike colony. Rudolph believed this fungus to be a type of blastomycete, and he successfully inoculated the disease in 4 white rats and 2 monkeys. Surprisingly, he did not describe the histologic aspects of the disease or the pathognomonic sclerotic cells, which both Lane and Medlar described 1 year later. In 1908 Guiteras had observed 10 cases of a disease known as chapa in which the clinical aspects resembled those of chromoblastomycosis. Unfortunately, those cases were not published. *Torula bantianum* was first reported by Saccaro (1910).

In 1920, two Brazilian physicians, Pedroso and Gomes, published 4 cases that had been under observation for many years, the first one since 1911. According to them, all 4 cases were caused by *P. verrucosa*. Two years later, in 1922, Brumpt concluded that the agents isolated by Pedroso and Gomes could not be classified as *Phialophora* species, and he coined the denomination *Hormodendrum pedrosoi*, later renamed *F. pedrosoi* by Negroni in 1936. By 1930, new cases had been described outside the American continents in France, Sumatra, and Poland (Rippon, 1982). Four different genera are now widely accepted to cause chromoblastomycosis: *F. pedrosoi, P. verrucosa, C. carrionii*, and *F. compacta* (Lacaz, 1991). Rare cases of chromoblastomycosis caused by *Rhinocladiella aquaspersa* and *Exophiala* species have also been reported, allowing the inclusion of these species among those that cause the disease (South, 1981; Naka, 1986; Barba-Gómez, 1992; Queiroz-Telles, 1996; Padhye, 1996). Infection in animal as well as man due to dematiaceous fungi was reported first time by Kano K (1934). Emmons in Binford *et al.*, (1944).
Phialophora dermatitidis by Kano (1937). Carrion identified one of his case and named it Hormodendrum compactum. Simmon, (1946) studied Chromoblastomycosis in Australia, described Cladosporium carrionii Trejos.(1954). Phialophora gougerotii was first reported by Borelli (1955). One case of phaeosporotrichosis caused by P. richardsiae was reported by Schwartz and Emmons (1968).

Since its identification of chromoblastomycosis in the early 1910s, the name of the disease has been frequently misused to encompass other infections caused by dematiaceous fungi. More recently, the advent of immunosuppressive therapies and diseases brought more confusion because of the identification of new agents and clinical settings. With the introduction of the concept of phaeohyphomycosis by Ajello and colleague in 1975 and McGinnis in 1983, differentiation among these diseases became more obvious. The features of chromoblastomycosis are distinctive enough to be considered as an independent clinical entity. The infection should not be confused with mycoses, such as mycetoma or phaeohyphomycosis, caused by other dematiaceous fungi. Nowadays, the term chromoblastomycosis is restricted to the cases in which sclerotic cells are present in tissue. Sclerotic cells, also known as Medlar bodies, are globe-shaped, brown-colored, thick-walled structures that are 4-12 mm in diameter. Medlar first described them in 1915. These structures multiply by septation, and they induce a purulent and granulomatous inflammatory reaction in tissue. In 1935 chromoblastomycosis was contracted to chromomycosis as it was considered that the former term implied that the causal agents occurred as yeasts in tissues.

Chromoblastomycosis (CM) is a chronic granulomatous mycotic infection of the skin and subcutaneous tissue caused by pigmented fungi, the most being F. pedrosoi, Cathy P.M (1989). Other causative fungi are Phialophora verrucosa

Chromoblastomycosis caused by several species of dematiaceous fungi is usually confined to one of the lower extremities and affects only the skin and subcutaneous tissue, though the lymph glands draining the diseased focus, may participate in the pathological process Carrion et al (1933). Rajam et al (1958) studied a case which showed both yeast and mycelial phase in tissue and in culture. Rare cases have been reported affecting the hand, arm, face and buttocks, Bhaktaviziam C et al (1970). Mucous membrane is usually not involved, but invasion of the conjunctiva and nasal septum have been reported by Jakamitzu et al (1972) and Nagarkatti P.S et al (1972). The Chromoblastomycotic lesion may be verrucous with central scarring (tuberculoid), extremely scarred with a serpigenous border (syphiloid), scaly (psoriasiform) or indurated with fistula (mycetomatoid), Vollum D.I (1977). The diagnosis of chromoblastomycosis should be confirmed either by direct microscopy of the scarpings from the lesion in 20 % KOH when thick walled dark brown tissue form of the fungus (sclerotic bodies/muriform bodies/copper pennie body) are seen; or by histological examination of a biopsy specimen when the granulomatous reaction and spore are diagnostic; or by culture of scarpings or biopsy material, Vollum D.I et al (1977). Kotrajaras R and Chongsathien S, (1979) reported subcutaneous chromomycotic abscesses caused by Phialophora gougerotii in 50 year.
old woman characterized by subcutaneous abscesses adhering through fistulous tracts, rupturing and leaving black crusts over multiple sinuses mimicking mycetoma. Greer K.E etal (1979) reported cystic form of chromoblastomycosis due to *Wangiella dermatitidis* that developed following a nonpenetrating injury to the thumb.

Radhakrishnan K (1981) in his article Chromomycosis due to *Phialophora pedrosoi* (with dimorphism in tissue) reported three case of chromomycosis proved histopathologically. In one case *Phialophora pedrosoi* was grown in culture. The saprobic form of the fungus could also be seen in tissue. Dematiaceous fungi characteristically exhibit dimorphism ie parasitic tissue form and saprobic mycelial form. In all cases there was hyperplasia of epidermis. Dermis showed chronic inflammatory and giant cells. Characteristic sclerotic and septate dematiaceous mycelial forms were seen in H&E, PAS and Giemsa stains. In one case mycelia were also seen in PAS section. Morales L.A etal (1985) reported chromoblastomycosis in a renal transplant recepient with an asymptomatic mass in the right forearm. The infection was cured by aggressive diagnosis and surgical treatment. Jayalakshmi etal, (1990) reported nine cases of histologically diagnosed chromoblastomycosis. It was reported from Malaysia. All the patients were males and ranged in age from 56 to 65 years and duration of symptoms varies from 5 months to 13 years and all the lesions were noted in lower extremities.

Rubin H.A etal (1991) in his article pointed that the exact pathogenesis of chromoblastomycosis is unknown but direct percutaneous inoculation, inhalation and hematogenous dissemination have been implicated. They reported a case of chromoblastomycosis that followed a well-defined episode of penetrating trauma. The causative organism, *Fonsecaea pedrosoi*, was cultured from the patient’s lesions and from the tree branch responsible for trauma. This natural experiment supports the
contention that one cause of chromoblastomycosis is traumatic cutaneous implantation of the fungus. Sanjay Agarwal N et al (1991) presented a cystic type of subcutaneous fungal infection and the fungus isolated was *Phialophora*. This was the first reported case of cystic type of chromomycosis from India. Histopathology revealed clusters of pigmented sclerotic bodies (muriform bodies) surrounded by marked granulomatous inflammatory reaction and the presence of foreign body type giant cells. Woodgyer A.J et al 1992 reported four non-endemic New Zealand cases of chromoblastomycosis. All these cases were caused by *Fonsecaea pedrosoi*. Deshpande S et al (1993) reported two cases of chromomycosis during the period from 1980-1989. The isolates were identified as *Fonsecaea compactum*. Attapattu-M.C (1997) presented a study of the clinical and mycological features of 71 SriLankan patients suffering from chromoblastomycosis for the 16 year period from 1978 to 1993. Out of this 64 *Fonsecaea pedrosoi* (64), *Phialophora verrucosa* (3) and a fungus morphologically compatible to *F. compata* (2).

Tuffanelli-L et al (1990), reported the treatment of chromoblastomycosis was frequently difficult and unsatisfactory. Itraconazole, a triazole compound, is considered as the possible drug of choice. Queiroz-Telles-F et al (1992), in his article, itraconazole in the treatment of chromoblastomycosis due to *Fonsecaea pedrosoi* evaluated the efficacy and tolerability of itraconazole in chromoblastomycosis due to *Fonsecaea pedrosoi* in a non-comparative open clinical trial in 19 Brazilian patients with histopathologically and mycologically proven active chromoblastomycosis. Result of the study suggesting that itraconazole is an effective compound against chromoblastomycosis due to *Fonsecaea pedrosoi*. Successful treatment of chromoblastomycosis due to *Fonsecaea pedrosoi* by the combination of itraconazole and cryotherapy by Kullavanijaya-P and Rojanavanich (1995). In this
article they had tried itraconazole and cryotherapy. Itraconazole alone showing good response for chromoblastomycosis but it took as long as 18-30 months for lesion to heal. Itraconazole 200 to 400 mg/dl along with monthly liquid nitrogen therapy was tried in 10 cases. Result of the study showed that itraconazole along with cryotherapy was highly effective against chromoblastomycosis.

In a study conducted by De Bedout C, etal (1997) with different human isolates of *F.pedrosoi* in Brazil, it was found that 33 % were resistant to amphotericin B, 58 % to 5 fluorocystosine and 66 % to fluconazole. But none of the isolates proved resistant to itraconazole. Saperconazole, a newer drug showed best invitro activity against *F.pedrosoi* in experimental murine chromoblastomycosis. Chromoblastomycosis Combination therapy effective, in one case, presented at the 1998, Atlantic Dermatology Meeting combined azole and triazole antifungal with CO₂ laser therapy, by Robert Hayman and Zoila Flasher, to reduce lesions and manage fungal growth on the leg and foot of a man. Sevigny G.M and Ramos F.A (2000) reported chromoblastomycosis due to *Fonsecaea pedrosoi*, who was treated with 8 months of terbinafine 250 mg by orally daily with histologic and mycologic cure. Cutaneous chromomycosis, three cases reported by Mohan N etal (2002) from Bangalore and the culture yielded Cladosporium. Histologically all cases showed chronic granulomatous infiltration with microabscess formation; however no fungal elements were demonstrable. One case was successfully treated with itraconazole with no relapse. The second case failed to respond to itraconazole in spite of 600 mgs daily for 3 months. Two unusual case of chromo mycosis reported by Patra S etal (SIHAM 2002), one patient was from Tripura and the fungus isolated was *Fonsecaea pedrosoi*, the patient was treated by ketoconazole and diathermy cautery and the other patient from Mizoram, the isolated fungus was identified as *Cladosporium carrionii*. 
The patient was non responsive to treatment with ketoconazole, itraconazole, amphotericin B, potassium iodide and antituberculous drug.

Luiz G.M et al during the American Academy of Dermatology’s 56th Annual meeting, said that in recent years they have successfully treated a group of chromomycosis with cryosurgery with liquid nitrogen. The clinicians said that the surgical technique is a cost effective method that can be employed in low income population in developing countries, where chromomycosis is most prevalent and they also indicated that follow up itraconazole therapy is at times useful against these diseases. Agarwalla et al (2002) reported two cases of chromoblastomycosis from Nepal. The first case, a 67 year old male farmer, presented with itchy hyperkeratotic, scaly plaques with scarring and black dots on the lateral aspects of his left arm and dorsum of his left hand of 28 years duration. The second case, a 75 year old farmer presented with erythematous, crusted, scaly plaques on the dorsum of the left foot of 30 years duration. These two cases were the first reported case of chromoblastomycosis from Nepal. Brandt M.E and Warnock (2003) analyzed the epidemiology, clinical manifestation, and therapy of infections caused by dematiaceous fungi. Among the more important human pathogens are Alternaria spp, Bipolaris spp, Cladophialophora bantiana, Scedosporium prolificans, Scytalidium dimidiatum, and Wangiella dermatitidis. These infections are more common in tropical and subtropical climates. Disseminated infections are uncommon, but its incidence is increasing, particularly among immunocompromised individuals. Scedosporium prolificans is the most frequent cause. A number of dematiaceous fungi are neurotropic, including Cladophialophora bantiana, Ramichloridium mackenziei and Wangiella dermatitidis. Most forms of diseases caused by dematiaceous fungi require surgical and medical treatment. Itraconazole is the drug of choice for
chromoblastomycosis and phaeohyphomycosis, while ketoconazole is the drug of choice for mycetoma. Koga T etal (2003) discussed various therapeutic approaches of subcutaneous mycosis. Results of antifungal susceptibility test may provide valuable information for deciding the appropriate method of treatment. Development of new antifungal agents and combination therapies may result in improvement in the management of subcutaneous mycoses in the future.

Pang K.R etal (2004) discussed various subcutaneous mycosis and their mode of entry to the body. Sporotrichosis, mycetoma and chromoblastomycosis are the common subcutaneous mycoses than rhinosporidosis, zygomycosis, phaeohyphomycosis, and lobomycosis. Bonifaz A etal l (2004) Dermatology Service and Mycology Department Mexico described the treatment of chromoblastomycosis with systemic antifungal agents. At present there is no treatment of choice for chromoblastomycosis but rather, several treatment options, with low cure rates and many relapses. The choice of treatment should consider several conditions, such as the causal agent, extension of lesions, clinical topography and health status of the patient. Most oral and systemic antifungals have been used; the best results have been obtained with itraconazole and terbinafine at high doses, for a mean of 6-12 months. In extensive and refractory cases, chemotherapy with oral antifungals may be associated with thermotherapy (local heat/or cryosurgery). Limited or early cases may be managed with surgical methods with oral antifungal agents. It is also important to test the antifungal susceptibility to major casual agents.

Ajello L (1986) in his article hyalohyphomycosis and phaeohyphomycosis: two global disease entities of public health importance clearly defined both diseases. The term chromomycosis was unfortunately used (Mcginnis M.R, etal 1983) inappropriately for infections caused by a growing number of diverse dematiaceous
fungi from a number of different genera and species. This prompted Ajello L (1986) to introduce phaeohyphomycosis for those infections, which on the basis of clinical, pathological and mycological grounds, could be distinguished from chromoblastomycosis. In 1992, the International Society for Human and Animal Mycology (ISHAM) recommended that the best name to define the disease was chromoblastomycosis, which Terra et al coined in 1922. Therefore, widely or locally used terms, such as chromomycosis, verrucous dermatitis, dermatitis verrucosa chromoparasitaria, black blastomycosis, figueira, chapa, susna, sundam, and mossy foot, should be avoided whenever possible. In contrast to chromoblastomycosis, phaeohyphomycosis is characterized by the presence of dematiaceous yeast like cells, pseudohyphae, or any combination of these forms in the tissue.

Mariat et al (1967) proposed the term “phaesporotrichose” for infections caused by fungi with dematiaceous mycelial tissue forms when they were dealing with infections caused by Phialophora gougerotii. Emmons et al (1970) changed the term to “phaesporotrichosis” and included the infection caused by P.richardsiae. The suffix ‘sporotrichosis’ was later considered inappropriate since the Phialophora infections did not resemble sporotrichosis clinically or histopathologically. The term phaeohyphomycosis was proposed by Ajello L (1974), for cutaneous, subcutaneous and systemic disease of man and animals caused by pathogenic fungi which develop dark mycelial elements in the tissue of their hosts. Bennett J.E et al (1973) presented an excellent review of cerebral infections by dematiaceous fungi. The Cladosporium bantianum which cause cerebral infections was first reported by Banti G (1911) and the second case by Binford C.H, et al (1952).

Hironaga M and Watanabe S (1980) reported a rare mycotic infection in a 17 year old Japanese female who had cutaneous alternariosis of the face of nine years
duration but she died of a cerebral infection caused by *Cladosporium bantianum*. This is the first case reported in which two unusual and different mycoses have occurred successively. Peter E.Hohl, *etal* (1983), reported *Wangiella dermatitdis* in a subcutaneous knee infection in a diabetic patient with impaired T cell function and cutaneous anergy. It was the first documented case of infection due to this fungus in North America and ninth case documented world wide. McGinnis M.R; (1983). Kirlovc, S.M and Rhodes J.C of the Cincinnati VA Medical Center in Cincinnati, Ohio reported isolation of *Fonsecaea pedrosoi* from an orthopic Liver transplant patient causing Phaeohyphomycotic Osteomyelitis.

Michael R Mcginnis *etal* (1986) reclassified *Cladosporium bantianum* in the genus xylohypha. In this article they proposed dematiaceous hyphomycets *Cladosporium bantianum* into a new genus *Xylohypha bantiana*. This combination is necessary because *X.bantiana* produce conidiophores that are indistinguishable from its vegetative hypha and one celled smooth walled conidia which are borne in long infrequently branched chains. The blastoconidia do not possess darkly pigmented hila. In contrast, members of the genus Cladosporium produce erect, distinct conidiophores and one to four celled smooth to rough walled conidia that occur in short, frequently branched, fragile chains. The blastoconidia have darkly pigmented hila. Another distinguishing characteristic feature is *X.bantiana* can grow at temperature up to approximately $42$ to $43^\circ C$, where as *Cladosporium carrionii* can grow to a maximum of $35$ to $37^\circ C$. *X.bantiana* is an extremely important etiologic agent of cerebral phaeohyphomycosis. Appropriate management and early diagnosis of an infection caused by *X.bantiana* is vital. Even with antifungal chemotherapy and surgical management, mortality owing to this fungus is extremely high.

Padhye A.A *etal* (1988) reported first human phaeohyphomycotic infection
caused by *Xylohypha emmonsii* in an 83 year old woman. The biopsy tissue consists of thin or thick walled, oval to spherical, yeast like cells and septate hyphae. In culture, *X. emmonsii* grew moderately fast at 25°C, showed minimal growth at 37°C and failed to grow at 40°C. It produced acropetal chains of one celled (rarely two celled) conidia laterally and terminally directly from vegetative hyphal cells. However, recent work by de Hoog *etal* (1995) has demonstrated that this organism is nonspecific with another species that had been identified as *xylohypha bantiana* on the basis of rRNA sequencing studies and DNA/DNA reassociation. Furthermore, these authors addressed the cultural differences between these two presumably different species, pointing out that certain strains of *Xylohypha emmonsii*, like *X. bantiana*, could grow at 40°C, and with apparent differences in branching patterns, conidial shape, and pigmentation which could be altered by culture conditions. For these and other reasons, de Hoog *etal* (1995) established the species *C. bantiana* to include both organisms as well as those that had previously been designated *Torula bantiana, Cladosporium bantianum, Cladosporium trichoides, and Cladosporium trichoides var. chlamydosporum*. This organism known primarily for the intracerebral involment can rarely produce cutaneous and subcutaneous infection. Immune suppression should be suspected but it is not always clinically apparent. David L *etal* (1988) reported *P. richardsiae* as a rare cause of disease in humans.

James W. Patterson and *etal*, (1999) presented a case of cutaneous infection due to *Cladophialophora bantiana*, an agent of phaeohyphomycosis. This fungus was initially designated as *Xylohypha emmonsii* because of certain unique cultural characteristics, including its ability to grow at 40°C and the formation of short chains of curved blastoconidia. Romano C *etal* (1999) reported a case of cutaneous phaeohyphomycosis caused by *Cladosporium oxysporum*. This is the first reported
case of cutaneous phaeohyphomycosis due to *Cladosporium oxysporum*. During the past decades, phaeohyphomycoses has been attributed to more than 100 species and 60 genera of fungi in a variety of clinical syndromes, ranging from keratitis and solitary subcutaneous nodules to fulminant, rapidly fatal diseases. Most of the species are considered to be opportunistic pathogens, although some may be true pathogens. Matsumoto T *et al* (1994) and Renu Mathew *et al* (1999), reported a case of subcutaneous phaeohyphomycosis in the form of prepatellar bursitis due to *Fonsecaea pedrosoi* in a renal transplant recipient. *F.pedrosoi* usually recovered from chromoblastomycosis. An unusual cause of Phaeohyphomycosis in a liver transplant patient was reported at 98th general meeting of the American Academy of microbiology by S.M.Kralovic and J.C.Rhodes. A 29 year old orthopic liver transplant recipient who had presented with progressive mid thoracic back pain. MRI showed a tumorous mass occupying the majority of T-7 vertebral body. Biopsy from the mass showed the presence of brown, toruloid hyphae with sclerotic bodies, with a mild granulomatous inflammatory reaction of the surrounding tissue. Culture yielded *F.pedrosoi* and the clinician diagnosed the condition as deep seated phaeohyphomycosis.

Gugnani HC *et al* (2000) reported subcutaneous phaeohyphomycosis caused by *Cladosporium cladosporoides* in a 25 year old male. The clinical presentation was an elevated scaly suppurating lesion with sinuses on the right leg. The lesion healed completely with oral fluconazole therapy. This is the first record of subcutaneous infection due to *C.cladosporoides* from India. Chua JD *et al* (2001) reported *Exophiala jeaneselmei*, the most common cause of pheomycotic cyst/subcutaneous phaeohyphomycosis in the United States. A lung-transplant patient with relapsing and invasive Jeanselmei phaeohyphomycosis, who previously had a pheomycotic cyst
excised and treated with oral fluconazole. It was re-excised and the patient was subsequently treated with an eight month course of oral itraconazole. There was no relapse. Liou JM et al (2002) reported phaeohyphomycosis caused by exophilala species in three immunocompromised patients. Two of these were due to *E. jeaneselmei* and the one was *Exophiala (Wangiella) dermatitidis*.

Sharma NL et al (2002) reviewed subcutaneous phaeohyphomycosis in India and reported a case of subcutaneous phaeohyphomycosis in the lumbar region. In India 23 patients with subcutaneous phaeohyphomycosis have been reported, distributed throughout the country in a belt from north to south, sparing the eastern and western regions. The age of the patients ranged from 3 to 60 years, with a male to female ratio 1.3:1. A relatively early age of onset was observed. A history of prior injury was recalled by five patients. The lower extremities were involved in eight cases, upper extremities in five, gluteal region in two, lumbar area and submandibular area in one, face in two and disseminated disease was seen in four cases. Three of these cases died during follow up. Osteomyelitis was observed in two cases, hepatosplenomegaly in one, and lymph node involvement in two carcinomatous change developed in a long standing lesion of 33 years. Thirteen species from seven genera of dematiaceous fungi were isolated. *Phialophora dermatitidis* was the most common isolate. *Exophilala dermatitidis* seems to be associated with more fatalities. Treatment with newer azoles seems promising and excision alone or combined with azoles is a good therapeutic modality. Central Venous catheter as a risk factor for disseminated phaeohyphomycosis case reported by Anthony La Rocco Jr, etal (2002). *Wangiella dermatitidis* was isolated from the blood of a 61 year old woman receiving chemotherapy through a totally implanted venous device for metastatic breast cancer. The Central Venous Catheter was removed. The patient was treated with Amphotericin B and the patient recovered. There was no metastatic fungal involvement.
Severo L.C et al (1997) reviewed the literature and presented two cases of cutaneous scedosporiosis caused by \( S. \) \( apiospermum \). Both patients had lesion localized in the forearm, a solitary ulceration in one and a sporotrichoid- like lesion in the other. Ingo K. Mellinghoff, (2002) presented a case of 41 year old man with acute lymphoblastic leukemia, developed multiple \( Scedosporium \) \( apiospermum \) brain abscess. The infection progressed despite neurological drainage and treatment with itraconazole, amphotericin B, and ketoconazole, but the brain abscesses completely resolved after treatment with posaconazole alone. \( S.apiospermum \) is the asexual form of \( Pseudallescheria \) \( boydii \); a saprophytic fungus frequently isolated from soil and water and is usually associated with soft-tissue infection (madura foot). This report highlights the importance of performing a definitive fungal culture and standardized antifungal susceptibility testing. On the basis of their experiences, posaconazole would be a useful agent for treatment of central nervous system infections due to \( S.\) \( apiospermum \), \( P. \) \( boydii \) and other posaconazole susceptible molds, especially when options for surgical interventions are limited

Sanjay G Revankar (2004) reviewed 72 cases of disseminated phaeohyphomycosis. \( Scedosporium \) \( prolificans \) is far the most common cause. The presence of melanin in their cell wall may be a virulence factor for these fungi. The outcome of antifungal therapy remains poor with overall mortality rate of 79 % male patients accounted for 41 (57%) of 72 cases and female patients accounted for 31 (43%) of 72 cases. The mean patient age was 42 years (range 0-92). 75 % of all cases were reported during the years of 1992-2001. Of the 28 species isolated, \( Scedosporium \) \( prolificans \) accounted for 30 (42%) of 72 cases. The next common species was \( Bipolaris \) \( spicifera \) (six cases 8 %) followed by \( Wangiella \) \( dermatitidis \) five of 72 patients (7%).
Sub cutaneous phaeohyphomycosis due to *Exophiala jeanselmei* in renal transplant recipient, was reported by A.Chakrabartithi *etal* (2002) in a 53 year old renal transplant recipient. Central Venous catheter as a risk factor for disseminated phaeohyphomycosis. One case reported by Anthony La Rocco Jr; *etal* (2002). *Wangiella dermatitidis* was isolated from the blood of a 61 year old woman receiving chemotherapy through a totally implanted venous device for metastatic breast cancer. The Central Venous Catheter was removed and the patient was given amphotericin B and the patient recovered well. There was no metastatic fungal involvement. M.A. Barron *etal* (2003) reported an invasive mycotic infections caused by *Chaetomium perlucidum*, a new agents of cerebral hyphomycosis. This was the first case of cerebral hyphyomycosis caused by *Chaetomium perlucidum* and this fungus has the ability to disseminate beyond the central nervous system. The other Chaetomium species known to produce neurotropic diseases are *C.atrobrunneum* and *C.strumarium*

Jain SK *etal* (2003) from Gwalior, India, reported a patient suffering from subcutaneous phaeohyphomycosis caused by *Cladophialophora bantiana*. The face and upper site was involved with small, stellate, pyogranulomatous foci and low inflammation. The patient showed good response after amphotericin B and systemic corticosteroid. Kimura M *etal* (2003) reported an 85 year old woman with multifocal purulent subcutaneous nodules on the dorsal side of the right forearm and hand. Histopathologic examination revealed phaeomycotic cyst with faint brown septate hyphae and moniliform fungal elements were found in the granuloma. Culture yielded *Phialophora verrucosa*. This fungus is rarely reported in phaeohyphomycosis. Subcutaneous phaeohyphomycosis usually presents as a single lesion. This is the first report of multifocal subcutaneous phaeohyphomycosis caused by *P.verrucosa* and has responded well with oral itraconazole.
de Monbrison F et al (2004) reported two cases of phaeohyphomycosis due to Exophilala jeansemei, in cardiac transplant and renal transplant patients. Yehia M et al (2004) reviewed the literature of phaeohyphomycosis and described three cases of subcutaneous phaeohyphomycosis developing in the lower limb of renal transplant recipients shortly after transplantation. Each case presented with dark-colored nodules that subsequently ulcerated. Histopathologic examination revealed dematiaceous fungal hyphae with a surrounding granulomatous reaction. The fungi were subsequently identified as Alternaria alternatum in two cases and Phialophora richardisiae in one case. Prolonged course of itraconazole resolved the lesion in one case and combined medical and surgical treatment resulted in cure of the other two cases. Pandhye A.A et al (2004) presented subcutaneous phaeohyphomycotic abscess caused by Pleurophomopsis lignicola. A 41 year old man with past history of diabetes and AIDS complained with a painful swelling on his right arm. The pus was aspirated and culture was made on SDA agar. The growth was identified as Pleurophomopsis lignicola. Sutton D.A et al (2004) reported first US report of subcutaneous phaeohyphomycosis caused by Veronaea botryose which is a rare agent of human phaeohyphomycosis in heart transplant recipient and reviewed the literature.

Alan Woodgyer, Microbiological Diagnostic Unit, University of Melbourne, in his leading article described Chromoblastomycosis and phaeohyphomycosis as two separate entities and clearly defined the chromoblastomycosis and phaeohyphomycosis. The fungi, which cause both this diseases, are described as dematiaceous. The term dematiaceous is taken to mean that the fungi in culture produce melanin-like pigment in the walls of the hyphae and/or conidia. Fontana Masson Silver stains which specifically stain hyphae containing melanin and this can be used to confirm that the hyphae are dematiaceous.
Infection with the soil fungus *Sporothrix schenckii* is uncommon in human beings and results usually in a localized lymphocutaneous disease after direct inoculation of the fungus into the skin, reported by Werner A.H *et al* (1994). Epidemic cutaneous sporotrichosis by Campos-P *et al* (1994), reported first cases of epidemic sporotrichosis. They studied four members of two families who contracted sporotrichosis after sleeping in an old and rust stained camping tent. Result of the study showed all cases were presented with polymorphic lesions, three of them with multiple sites inoculation. The camping tent was shown to be the source of infection. In another work by Athol.J.Ware *et al* (1995) presented a disseminated sporotrichosis in a patient with AIDS. Usually sporotrichosis presents as a localized, lymphocutaneous infection that follows trauma, such as injury from a rose thorn. But in a patient having HIV, it may be widespread and disseminated and is a rare opportunistic infection that may affect these patients. Localised sporotrichosis is well respons to therapy but in immunocompromised patients it is life threatening. It is important that clinician be aware of the presentation of this unusual opportunistic infection and that they maintain close communication with pathology and clinical microbiology laboratory to ensure that proper stains and cultures are performed to avoid potential misdiagnosis.

A case of cutaneous sporotrichosis reported by Sumangala Bai *et al* (1998) from Pathanamthitta (Kerala), a 52 year old male working in a rubber plantation, presented with a case of chronic non healing plantar ulcer which failed to respond to anti tuberculous treatment. The culture yielded *Sporothrix schenckii* and was subsequently, successfully treated with itraconazole. Espinosa-Texis A *et al* (2001) studied 50 cases of sporotrichosis in Mexico and evaluated indirect immunofluorescence, hypersensitivity skin reaction, culture and histopathology
laboratory techniques. Metabolic antigen was used to elicit delayed hypersensitivity skin reaction in all patients. Result of the study showed that there was an increased frequency sporotrichosis in women (62%) followed by children and adolescents under 20 years of age (34%) and adults older than 50 years of age (28%). Disease was predominant in farmers (44%) followed by housewives (30%). Lymphagitic form accounted for 82% of cases and these were localized in upper limbs (54%). In 66% of cases, histopathology showed *S.schenckii* yeasts. Hypersensitivity skin reaction was positive in 76 % cases and culture was positive in 94 % cases. By indirect immunofluorescence, parasitic elements were demonstrated in all patients corresponding to both sensitivity and specificity 100 %. In this work indirect immunofluorescence was the most efficient diagnostic method followed by culture, hypersensitivity skin reaction and histopathology study.

Koc A..N *etal* (2001) presented a 48 year old man who had subcutaneous sporotrichosis, which is a rare disease in Turkey, and was successfully treated with short term itraconazole and potassium iodide. Ponnighaus M *etal* (2003) reported from Germany, a young man presented an ulcer on his lower leg which had developed over the past 9 weeks. Diagnosis confirmed by histopathologically as sporotrichosis. The patient was then treated with potassium iodide (KI). Bayles-M.A (1992), describes the common tropical subcutaneous and deep mycoses and the drug of choice for sporotrichosis infection as itraconazole. An enhanced efficacy by combining flucytosine and itraconazole was noticed in 3 out of 41 patients. In the present study itraconazole has an impressive safety profile, no side effects were noticed, no adverse reaction occurred and serum chemistry levels remained within the normal limits. Sandhuk and Gupta S (2003) reported a case of lymphocutaneous sporotrichosis that failed to respond to an adequate course of itraconazole yet responded dramatically to treatment with saturated solution of potassium iodide.
Alves S.H *etal* in (2004) reported that sporotrichosis is the most common mycosis observed in Brazil. A rare presentation of sporotrichosis noticed in a Caucasian male agricultural worker whose lesion occurred bilaterally and simultaneously on the upper limb. Coskun B *etal* (2004) reported that sporotrichosis was rare disease in Turkey. They have reviewed the literature and reported a 40 year old woman who had subcutaneous sporotrichosis caused by *S. schenckii* that was successfully treated with terbinafine (250 mg, twice a day) for a period of 6 months. She was also given saturated solution of potassium iodide (KI) orally for two months. So terbinafine and KI are suggested to be the choice treatment for sporotrichosis. Barros M.B *etal* (2004) analysed cat-transmitted sporotrichosis epidemic in Rio de Janeiro in Brazil, South America. The usual mode of infection is associated with traumatic implantation of the fungus. 178 cases of culture proven sporotrichosis had been diagnosed during 1998 to 2001. Female patients predominated, and the median age was 39 years. The most frequent clinical presentation was lymphocutaneous disease. Of the 178 patients, 156 reported domiciliary or professional contact with cats with sporotrichosis, and 97 of these patients had a history of receipt of a cat scratch or bite. This study suggests that feline transmission of sporotrichosis was associated with a large and long lasting outbreak of the disease in Brazil.

Geographical variation is very important for the occurrence of subcutaneous mycoses In India, mycetoma is prevalent in Tamilnadu where as in Kerala, it is rare. In Kerala dematiaceous fungi are reported as an important agent in subcutaneous mycosis. Pushpa Talwar *etal* (1979) described 60 cases of clinically suspected mycetoma by which 70% were due to actinomycetoma and 20% due to eumycetoma and another 20% were due to nocardia. The foot was the common site of infection. Patients of all age groups are susceptible for infection. The common age group
affected was 20-40. Actinomycetoma was the common type in South India. Dasgupta et al. (1974), Taralakshmi et al. (1977) and Murthi and Padmavathy (1963) have reported eumycetoma as the common type. Desai et al. (1970) found actinomycetoma more prevalent in Bombay while Mankodi & Kanavinde (1970) reported eumycetoma as the common infecting form. These studies indicated that the concept of preponderance in the incidence of certain species in different geographical regions is slowly fading. The etiological agents appear to be present ubiquitously as they await suitable opportunities to manifest themselves. There has been a uniform opinion concerning Madurella mycetomi as the most common etiological agent in eumycetoma in India.

Taralakshmi V. Venugopal et al. (1977) analysed 150 cases of clinically diagnosed mycetoma in Madras during 1964-1975, and found that the disease was predominantly seen in 21-40 age group. Men were more frequently affected than females and the commonest site of the lesion was foot. Actinomycotic mycetoma (68.9%) was more often found than the maduramycetoma type. Madurella mycetomi (27.8%) and Actinomadura madurae (26.7%) were the common casual agents. Nocardia spp. were the next most common (21.1%) followed by A. pelletieri (15.5%), S. somaliensis (5.6%) and Allescheria / Cephalosporium species from only 3 case of white grain mycetoma. Men were involved 5 times as often as women. This is probably because of their greater out door activities increasing the opportunities for trauma to the exposed surface of the body. Possibly the females may in addition have some protective mechanism against the entry or the proliferation of the fungus into the body. No site is exempt for mycetoma, though the foot is the main site (72%).

Stierstorfer M.B et al. (1998) reported a case of mycetoma affecting the foot of a 38 year old mentally retarded man from northern New England. The casual agent was
identified as *Pseudallescheria boydii*. The patient showed partial response to 8 month ketaconazole therapy.

Venugopal P.V and Venugopal TV (1990) reported Actinomycosis caused by *Actinomadura madurae* from Madras, India. Turiansky GW *et al* (1995) described *Phialophora verrucosa* a new agent causing mycetoma in a 29 year old Thai woman who had draining sinus tracts, tumefaction and granules on the plantar aspects of the foot. *P. verrucosa* is a major agent of chromoblastomycosis. This dematiaceous fungus has not been previously reported to cause mycetoma. McGinnis M.R (1996) in his article described the clinical details of mycetoma and *Madurella mycetomatis* as the important agent causing mycetoma. Combined medical and surgical management with ketaconazole resulted in the best outcome. Peizer K *et al* (2000) isolated both *Sporothrix schenckii* and *Nocardia asteroides* from a mycetoma of the forefoot. A combination of causative agents in mycetoma is rare, and the combination of *S. schenckii* and *N. asteroides* have not been reported earlier from one lesion. Kano R *et al* (2002) reported the first isolation of *Nocardia veterana* from a human mycetoma. It was identified by nucleotide sequence analysis of the 16S ribosomal DNA to reference strain of *N. veterana*.

Dieng M.T *et al* (2003) reported 130 cases of mycetoma in Senagal from 1983 to 2000. Clinical diagnosis of mycetoma was based on open tract sinuses, tumefaction or discharge of grain. Diagnosis was confirmed based on fungal culture and histology. They observed 76 actiniomycetoma and 54 eumycetoma (sex ratio M/F = 6.6; mean age = 34.7 +/- 14.8 years). Actinomycetoma was due to *Actinomadura pelletieri* (54 cases), *Actinomadura madurae* (17 cases) and *Streptomyces somaliensis* (5 cases). Eumycetoma was due to *Madurella mycetomatis* (38 cases), *Leptospharia senegalensis* (9 cases), *Pseudallescheria boydii* (6 cases) and *Rhinocladiella*
atrovirens (1 case). Clinical inflammatory features significantly associated with actinomyces ($p < 0.001$ or $= 2.64$) were predominant (85 cases). The geographical distribution of pathogenic mycetoma agents was determined by the annual rainfall. Distinction between eumycetoma and actinomycetoma is very important.

Fahal A.H (2004) reviewed various aspects of mycetoma, its geographical distribution, diagnosis and treatment of the eumycetomas. Foltz K.D and Fallat (2004) reviewed mycetoma and a case report of actinomycoses that was successfully treated with surgical resection and long term antibiotic therapy. Mycetoma are primarily found in tropical and subtropical areas of the world and are rare in United States. This case is unique because of the rarity of contracting this type infection in the United States. Ahmed A.O et al (2004) presented mycetoma caused by Madurella mycetomatis and review on developments in the clinical, epidemiological and diagnostic management of $M. mycetomatis$ eumycetoma. They described newly developed molecular diagnostic and gene typing procedures and their application for management of patients and environment research. A mouse model fungal susceptibility test was also developed.

Gordon M.A et al (1975) first reported a rare instance of infection of man and other animals by Phoma or Phoma like mold. The important species of phoma are $P. cava$, $P. glomerata$, $P. hominis$. Zaitz C et al (1997) reported a case of subcutaneous phaeohyphomycosis caused by Phoma cava and reviewed the literature. Oh C.K et al (1999) reported subcutaneous phaeohyphomycosis caused by Phoma species. Gordon M.Dickinson, et al (1983) reported the first case of subcutaneous phaeohyphomycosis caused by Scytalidium lignicola in a human. In this article he presented Scytalidium lignicola a dematiaceous hypomycetes associated with wood and soil as previously unknown agent of either human or animal disease. Many fungi once thought to be
laboratory contaminants are being documented as etiological agents of phaeohyphomycosis and other opportunistic mycotic infections. Subramanyam V.R etal (1993) reported the isolation of Curvularia species from a 21 year old man with chronic ulcer on the lower limb. This case was reported from Bhubaneswar, India.

Lobomycosis was first described by Jorge Lobo in 1931 from a patient from Amazon Valley and is characterised by the appearance of slowly developing keloid like ulcerated, or verrucous nodular or plaque like lesions, usually at the site of local trauma such as from a cut, insect bite, animal bite, or ray sting. The ulcerated lesions in which there are large numbers of spherical to lemon shaped fungus cells. Ciferri R etal (1956) described the fungal etiology of Lobos disease. Burns R.A etal (2000) described the first case of lobomycosis in United States. Sameer Elsayed etal (2004) reported a 42 year old woman with histologically confirmed lobomycosis as a chronic granulomatous infection of the skin and subcutaneous tissues caused by the fungus L.loboi.

Subcutaneous phycomycosis or subcutaneous zygomycosis caused by lower fungi was first reported by Drechsler in 1947. The fungus was identified as Basidiobolus ranarum by Emmons (Lie-Kian-joe etal 1956). Greer and Friedman (1966) identified two more species, B.haptosporus, B.meristosporus. In 1967 Srinivasan and Thrumalalchar concluded that the correct name was B.haptosporus, and that B.meristosporus is only a variety of B.haptosporus. Infection with Conidiobolus coronatus (Entomophthora coronata) was reported by Bras,G etal in (1967). Dasgupta L.R. etal (1976) reported four cases of subcutaneous phycomycosis diagnosed by isolating Basidiobolus meristosorus from the affected subcutaneous tissue. These were reported from Pondicherry. The first case of subcutaneous phycomycosis was reported by Mukerjee S etal (1962) as B.ranaram. Shah M.B. etal
(1970) reported 3 cases of *B. meristosporus*. Koshi *etal* (1972) reported three cases caused by *B. haptosporus*. Gugnani HC (1999) reviewed zygomycosis due to *Basidiobolus ranarum*. The laboratory diagnosis is based on histopathology and culture. The typical histopathology feature is the presence of thin-walled, broad often aseptate hyphae or hyphal fragments with an eosinophilic sheath, frequently phagocytised within giant cells.

Subcutaneous phycomycosis caused by *Basidiobolous species* a case report by Sujatha S *etal* from JIPMER Pondicherry, a 58 old male, agricultural labourer from south India presented with painless subcutaneous swellings on the left thigh of 4 year duration. The isolated fungus was *Basidiobolous species* and the patient was given potassium iodide over a 2 month period which resulted in subsidence of swelling rapidly. Ribes J.A *etal* (2000) reviewed zygomycetes in human disease. There are two order of zygomycetes that cause human diseases, the mucorales and entomophthorales. The important mucorales causing human infections are Mucor, Rhizopus, Rhizomucor, Absidia, Apophysomyces, Saksenaea, Cunninghamella, Cokeromyces, and Syncephalastrum species. Kalpadia S and Polenakovik H (2004) reported subcutaneous zygomycosis following attempted radial artery caused by rhizopus in a 70 year old man with cellulites of the left arm. A large bulla was found on the lateral aspect of the left wrist and aspirated fluid was cultured on SDA. Rhizopus was grown and the patient was started with amphotericin B. The patient died due to various other complications.

Choonhakaran C and Inthraburan K, (2004) reported concurrent subcutaneous and visceral basidiobolomycosis. A 55 year old female renal transplant recipient, who developed chronic hard nonpitting oedema of the right lower extremity and abdominal wall concurrent with infection from the same organism involving uterus, urinary
bladder and intra-abdominal lymph nodes. The patient responded successfully, both clinically and radiographically, to medical treatment without surgical resection. Bigliazzi C etal (2004), a young immunocompetent woman who had presented with eosinophilia and lung infiltrates. She died subsequently, and diagnosis of basidiobolomycosis was made on the basis of histological features at autopsy. Chiewchanvit S etal (2002) reviewed entomophthoromycosis in Maharaj Nakorn Chiang Mai Hospital, Thialand. Eight cases of entomophthoromycosis were found between 1988 and 1993, with five patients diagnosed as subcutaneous zygomycosis. Five patients were female with age group 7-77 years. They presented with painless subcutaneous mass, which was solitary or multiple and most commonly found on the extremities. The duration of the disease was 3 months to 5 years. Culture yielded the growth of Basidiobilous ranaram.

Gutierrez-Rodero F etal (1999) reported cutaneous hyalohyphomycosis caused by Paecilomyces lilacinus in an immunocompetent host which was successfully treated with itraconazole. This fungal pathogen is highly resistant to many antifungal agents. This case of sporadic cutaneous infection due to Paecilomyces lilacinus is believed to be reported first time in Europe and it was first histopathologically proven case successfully treated with itraconazole. Karam A etal (2003) presented a paper on subcutaneous mycosis due to Scopulariopsis brevicaulis in an aplastic patient. Anellospore group of hyphomycete class Scopulariopsis genera presently includes 16 species considered as opportunistic pathogens. The mycological and histological examinations are fundamental to confirm the diagnosis.

Kurzai O etal (2003) reported Paecilomyces lilacinus as an agent of subcutaneous infection in a patient with liver cirrhosis. Surgical treatment in combination with systemic amphotericin B led to complete recovery. Retrospectively
performed microdilution testing revealed dose dependent in vitro susceptibility of the isolate to voriconazole (MIC=2g/ml) and terbinafine (MIC=1 microg/ml). Guarro J et al 2003 reported two cases of subcutaneous infection due to *Phaeoacremonium species* from Brazil. The first case was caused by *Phaeoacremonium aleophilum* and the patient presented with a unique fistulated nodule on the left ankle. This is the first reported case of human infection caused by this fungus. The second reported case was caused by *Phaeoacremonium rubrigenum*. This patient presented with multiple nodules around the left ankle and foot. Dermatophytes are common pathogens of skin but rarely cause subcutaneous infections. Ran Nir-Paz, et al (2003) reported first time the isolation of *Trichophyton rubrum*, usually a skin pathogen, from a patient with multiple subcutaneous nodules on both legs. This patient was suffering from an autoimmune disease with liver, cardiac, and lung involvement. Biopsy of the nodules showed a granulomatous inflammatory reaction in the dermis and hypodermis composed of monocytes, macrophages, multinucleated giant cells and rare neutrophils. Septate hyphae were revealed by both PAS and GMS stains.

Bosma F et al (2003) reported two cases of *Scedosporium apiospermum* infection which successfully treated with voriconazole. This agent was considered as an opportunistic pathogen in an immunocompromised patient. Chaverio MA et al (2003) reported cutaneous infection due to *Scedosporium apiospermum* in an immunocompromised patient. It is an anamorphic form of *Pseudallescheria boydii*. The patient having rheumatoid arthritis and diabetes, who was submitted to long term therapy with cyclosporine and corticostroids. Posteraro P et al 2003 reported *Scedosporium apiospermum* infection in a 52 year old male heart transplant patient with a persistent localized subcutaneous infection with *Scedosporium apiospermum*. This patient showed multiple nodules on the right hand that were surgically removed.
and he received oral itraconazole, but the infection persisted for two years. Chade M.E et al (2003) reported post traumatic subcutaneous mycosis due to *Fusarium solani*. This case was a subcutaneous hyalohyphomycosis. A 24 year old man presented with ulcerative lesion in the right leg of approximately one year duration. It was caused by traumatic implantation of a yerba mate branch. Subcutaneous fungal infection due to *Eurotium herbariorum* presented by Shivani Vishnoi et al from R.D. University Jabalpur, M.P, the patient was 62 year old male, suffering from lichen planus, presented with patchy scaly lesions on neck, upperarm, anterior aspects of lower limb and waistline for the last 12 years. Diagnosis is based on histopathology and culture yielded *E. herbariorum*. Girard C et al (2004) reported subcutaneous phaeohyphomycosis due to *Pyrenochaeta romeroi* in patient with leprosy.

Penicillium species are the most common laboratory contaminants; unless it is accompanied by typical fungal elements in tissue specimens its pathologic role is uncertain. The only true pathogen among members of the genus is *Penicillium marneffei*. It is a dimorphic fungi and is common in Eastern Asia. Lis J.S et al (1991) reported three cases of disseminated penicilliosis in China. The clinical features were characterized by multiple organ involvement, multiple subcutaneous abscesses, inflammatory papules, nodules, pustules, enlargement of superficial lymph nodes with chill, anemia and leukocytosis. Infection caused by *P. marneffei* are usually disseminated, with multiple organ involment, manifesting lymphadinitis, subcutaneous abscesses, bone lesions, arthritis, enlarged spleen, or lung, liver, bowel lesions Kwon Chung K.J and Bennett J.E (1992). The potential risk of laboratory acquired infection was demonstrated by the individual who first described *P. marneffei*, who accidently punctured his right index finger while inoculating laboratory rodent. The fungus could be isolated from a small nodule that developed...
at the puncture site, Segretain G (1959). Successful treatment with nystatin was initiated since this fungus has been found to be sensitive to this antifungal.

There are only few cases of subcutaneous mycoses reported from Kerala. The earlier study was by Meenakshy and Ananthanarayanan (1961). Maheswariammam et al (1979) reported *Cladosporium bantianum* from a case of phaeohyphomycosis in Kerala. In this article, they presented *Cladosporium bantianum* from a case of phaeohyphomycosis. This was the first reported case in India; also this was the first known case of infection involving the foot caused by this fungus. The etiologic agents of phaeohyphomycosis are varied in number. At present 16 fungi belonging to 8 genera are recognized as agent of phaeohyphomycosis, one of which is *Cladosporium bantianum*. K.Pavithran (1991) from Kerala, presented a disseminated chromoblastomycosis and the fungi isolated was *Cladosporium carrionii*. K Pavithran (1992) from Kerala reported, chromoblastomycosis masquerading as tuberculoid leprosy (letter). Maheswariammam et al (1990) reported phaeohyphomycosis caused by *Phialophora dermatitidis* in Calicut from a case of subcutaneous lesion.

One of the most characteristic features of fungal infections is its refractoriness to treatment. Over the last decades, several different therapeutic schemes have been used, but most proved unsuccessful or of low efficacy. Surgical excision or electrodesiccation of lesions should be avoided because metastasis might ensue. The use of amphotericin B alone or with 5-flucytosine (5-FC) and ketoconazole is no longer indicated. Some physical therapies have produced noteworthy results. To date, two therapeutic approaches are accepted as the best choices: oral itraconazole (as monotherapy or with oral 5-FC) and cryosurgery with liquid nitrogen. Several authors indicated itraconazole as the best choice of therapy Restrepo, (1988); Graybill, (1992); Queiroz-Telles, (1992). Daily doses range from 200-400 mg, and results vary
greatly. Adverse effects are not common, but efficacy is not as high as one would desire. Severe cases should be treated for several years. The author's experience in treating more than 25 patients with varying degrees of severity for up to 5 years shows that itraconazole produces dramatic improvement after a few months of therapy; however, a complete cure is rarely reached, especially in severe cases. These results might be because of the predominantly fungistatic mechanism of action of the drug. In several cases, drug withdrawal led to relapse. Although few studies have been published, the association of itraconazole and 5-FC is promising, Pradinaud, (1991). As with 5-FC and amphotericin B, itraconazole and 5-FC produce a synergistic effect. Multidrug therapy for chromoblastomycosis seems to be an interesting approach and may also be used with cryosurgery.

In 1996, Esterre et al presented interesting results when using terbinafine to treat more than 100 patients in Madagascar. Similar to that of itraconazole, the drug presented below optimal results, it is expensive, and treatment lasts several months. To date, no reports on the association of terbinafine and itraconazole or terbinafine and 5-FC have appeared in the literature. Posaconazole, a new azole derivative, has been experimentally used to treat chromoblastomycosis, and the results of isolated cases suggest that outcomes may be slightly superior to those obtained by itraconazole or terbinafine (Unpublished data on file, Dr. Shikanai-Yasuda, Department of Infectious Diseases, Univ. São Paulo). Heat therapy is another treatment. Especially in Japan, the use of pocket warmers has proven successful in the treatment of a limited number of cases. Apparently, an increase in skin temperature somehow impairs fungal development (Kinbara, 1982).

Lidiane Meire Kohler et al (2004), studied thirty isolates of the yeast form of Sporothrix schenckii and their in vitro susceptibility to itraconazole and terbinafine by
the recommended NCCLS modified technique (M27-A2). The MICs of itraconazole obtained oscillated between 0.062 and 4.0 μg/ml, and those of terbinafine oscillated between 0.007-0.50 μg/ml; therefore, terbinafine showed greater invitro activity. Itraconazole is currently considered the treatment of choice to treat the diverse clinical manifestations of sporotrichosis, Koc A.N et al (2001). On the other hand terbinafine by virtue of its excellent invitro and invivo activity is under comparative evaluation for its therapeutic potential for a wide range of fungal infections, Hay R.J (1999). Promising invitro result by the technique of macrodilution in a liquid medium (NCCLS M27-A2) with terbinafine for both the fixed and lymphocutaneous forms of sporotrichosis due to S.schenckii (Hull P.R. and Vismer H.F 1992). Perez A. (1999) discussed the allylamine antifungals, of which terbinafine is most effective against chromoblastomycosis, phaeohyphomycosis, maduromycosis mucormycosis and various other fungal infections. Hay R.J (1999) discussed the therapeutic potential of terbinafine in subcutaneous and systemic mycosis

**IMPORTANCE OF THE STUDY**

**OBJECTIVE OF THE STUDY:**

**Main Objective:** To study the prevalent fungal pathogens responsible for subcutaneous mycosis in North Kerala.

The incidence of fungal infections is increasing at an alarming rate, presenting an enormous challenge to health care professionals. The higher incidence of fungal infections in the past 10 years has been attributed to the increased use of newer and more effective antibacterial agents, the AIDS pandemic, and the rapidly expanding number of chemically induced immunosuppressive patients, bone marrow, solid organ transplantation and oncology patients. As a result of improved management protocols, AIDS, cancer, and transplantation populations now survive longer and become highly
susceptible to life-threatening fungal infections. This increase is directly related to the growing population of immunocompromised individuals, resulting from changes in medical practice such as the use of intensive chemotherapy and immunosuppressive therapy.

After the skilful control of bacterial and viral infections by antibiotics and antiviral agents the incidence of fungal infection seems to be increasing. The increased number of diabetes patients also pose a greater challenge for fungal infections. The etiological agents of subcutaneous mycosis widely varies geographically. Some of them are geographically limited in distribution. Accurate diagnosis is essential for fungal infections because of the clinical similarity with other bacterial and parasitic infections like cutaneous tuberculosis, leishmaniasis, tertiary syphilis and yaws and each group has its own treatment profile. Few of the fungi causing subcutaneous mycosis are dangerous, so early diagnosis and treatment are very essential and failure to treat in time may be fatal.

Preliminary studies done by some workers (personal data) showed that disease chromoblastomycosis is highly prevalent in North Kerala exceptionally in hilly areas of Wynad, hence any study on the prevalence of subcutaneous mycoses and their sources of infection is supposed to yield fruitful results. The biopsy specimens collected from Dermatology and Surgery departments of Medical College, Calicut gives an accurate picture of the prevalence of subcutaneous mycosis in North Kerala.

At present we have a limited data regarding the prevalent fungal agents causing subcutaneous mycosis in this part of Kerala and more over only limited centre are available for the isolation and identification of fungal pathogens. Studies on the etiological agents of subcutaneous mycoses are rarely done in our area. Identification
of the etiologic agent by culture is essential for prognostic and management considerations, since some fungi are more frequently associated with dissemination and are dangerous and are often fatal. Hence the present study is mainly focused on the various subcutaneous mycoses prevalent in this area, its isolation, identification, along with source of infection. Moreover this study will have an added advantage to the health need of Kerala by bringing awareness on the prevalence of fungal disease among health care professionals.