SUBCUTANEOUS MYCOSES

- These are chronic infections of the skin and subcutaneous tissue following the traumatic implantation of the aetiologic agent.

- Most of the causative fungi are saprophytes found in soil, on thorns, decaying vegetation etc

DISEASE	CAUSATIVE AGENT
Sporotrichosis	*Sporothrix* spp.
Chromoblastomycosis	*Fonsecaea, Phialophora, Cladophialophora carionni* etc.
Phaeohyphomycosis	*Exophiala, Bipolaris,Exserohilum Cladosporium, Exophiala, Wangiella, etc*
Mycotic mycetoma	*Scedosporium, Madurella, Trematosphaeria, Acremonium, Exophiala etc.*
Lobomycosis	*Loboa loboi*
Rhinosporidiosis	*Rhinosporidium seeberi*
Subcutaneous zygomycosis (Entomophthoromycosis)	*Basidiobolus ranarum* *Conidiobolus coronatus*
Subcutaneous zygomycosis (Mucormycosis)	*Rhizopus, Mucor, Rhizomucor, Lichtheimia, Saksenaea* etc.

1. MYCETOMA (Madura Foot)

"Madura foot" referring to the first case seen in "Madura" region of India which was in the foot of that patient.

- Caused by fungi (Eumycetoma) or filamentous bacteria Actinomycotic mycetoma …actinomycetoma).

…mycetoma

- A mycotic infection of humans and animals caused by a number of different fungi and bacteria and is characterized by draining sinuses and granules
- The disease results from the traumatic implantation of the aetiologic agent from vegetation, plant debris, soil..
    - Not contagious
- Usually involves the cutaneous and subcutaneous tissue, fascia and bone of the foot or hand.

…mycetoma

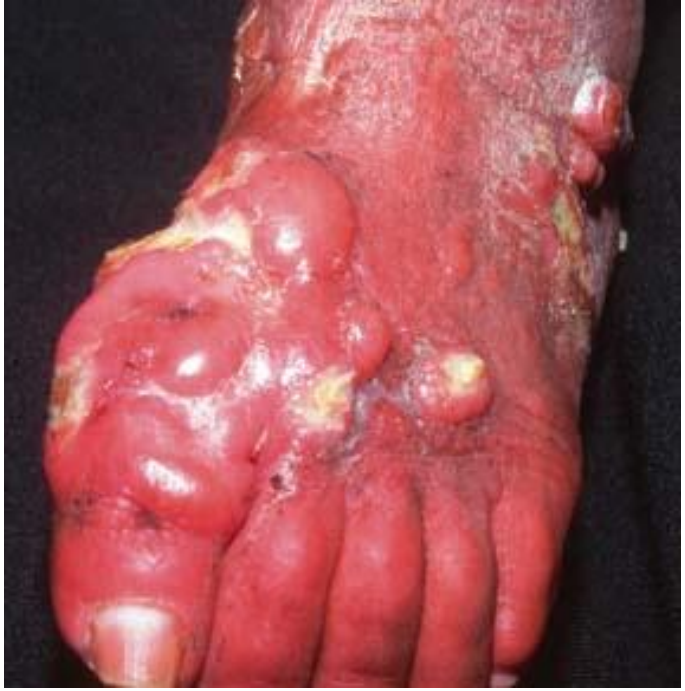
- World-wide distribution but most common in bare-footed populations living in tropical or subtropical regions.

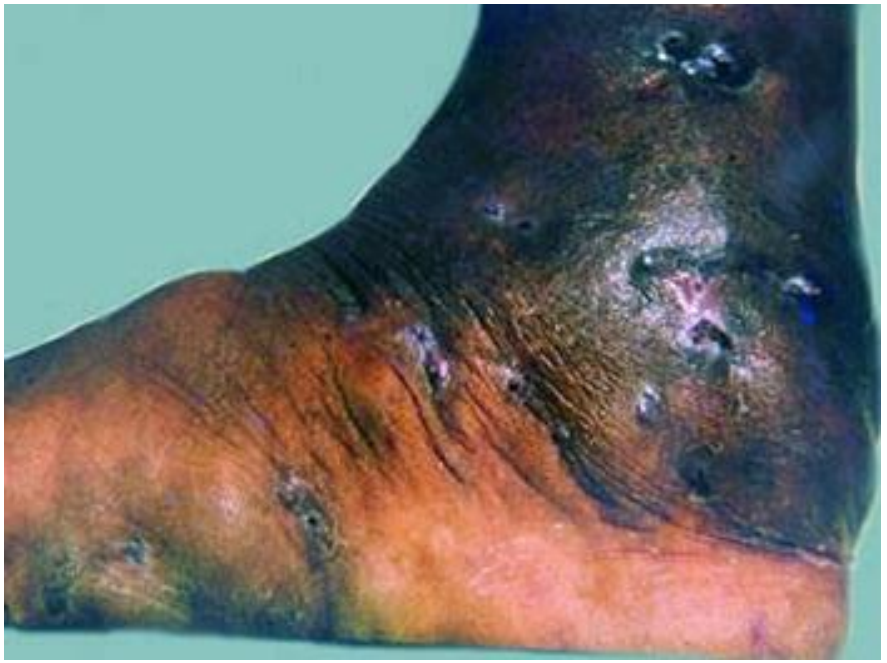
- Aetiological agents include *Madurella, Acremonium, Pseudallescheria, Exophiala, Leptosphaeria, Curvularia, Fusarium*

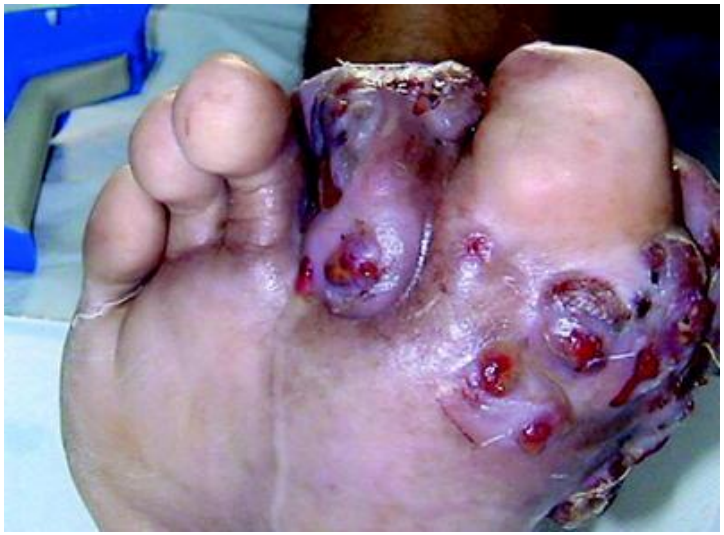
…mycetoma clinical manifestations:

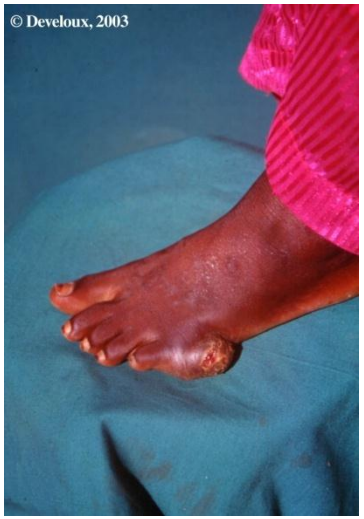
- The clinical features are fairly uniform, regardless of the organism involved.
- The feet are the most common site for infection. Other sites - lower legs, hands, head, neck, chest, shoulder and arms.
- Most cases start out as a small hard painless nodule which over time begins to soften on the surface and. ulcerate to discharge a viscous, purulent fluid containing grains

- The infection slowly spreads to adjacent tissue, including bone, often causing considerable deformity.
- Sinuses continue to discharge fluid containing the granules which vary in size, colour and degree of hardness, depending on the aetiologic species.
- These grains are the hallmark of mycetoma…





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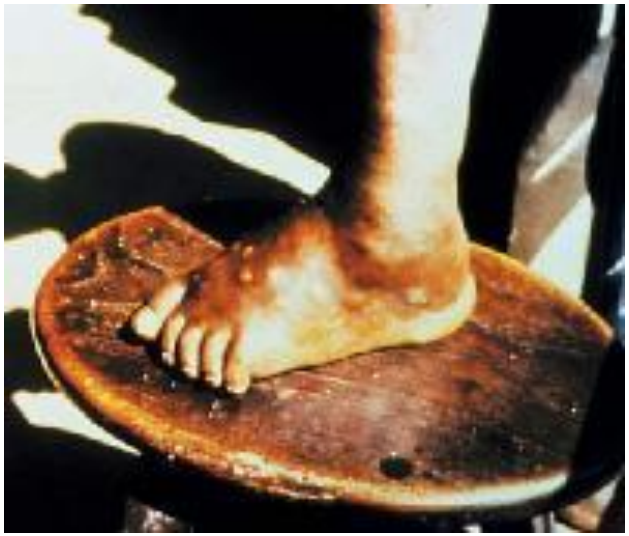
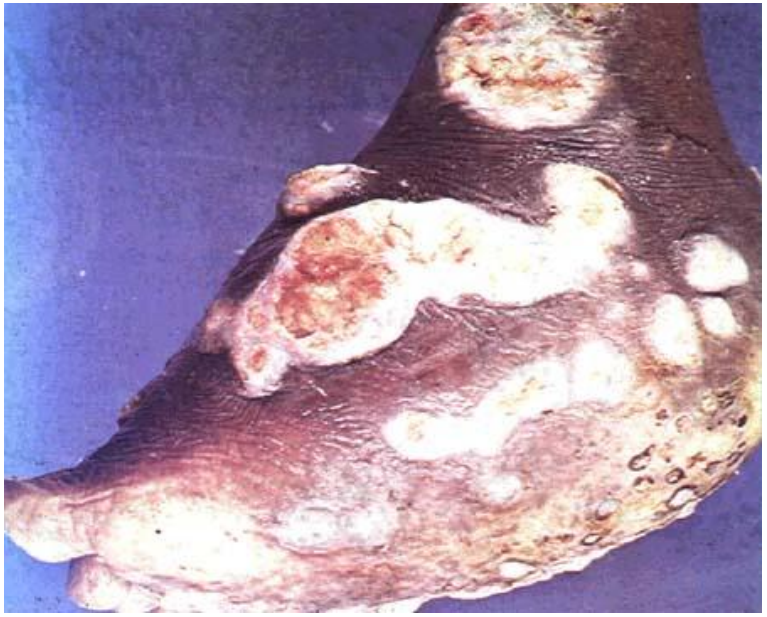
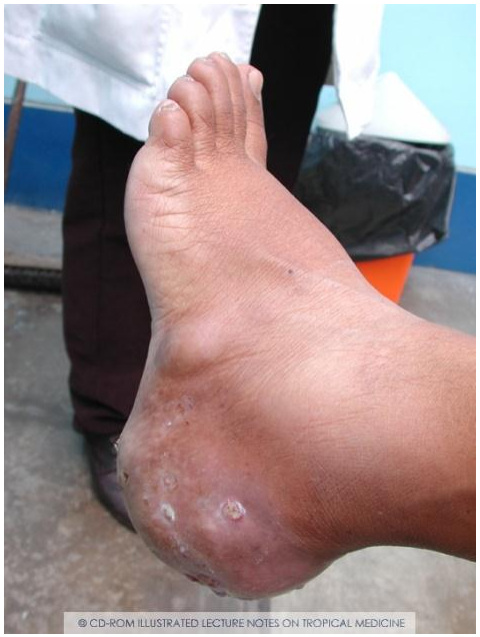
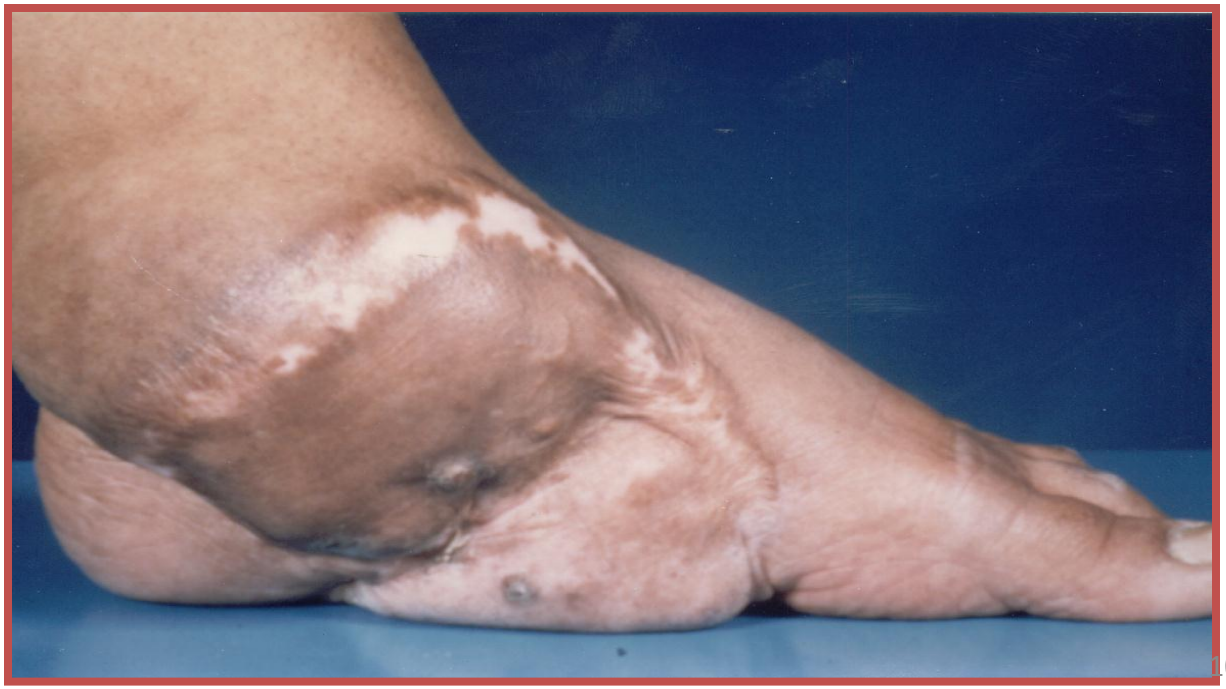
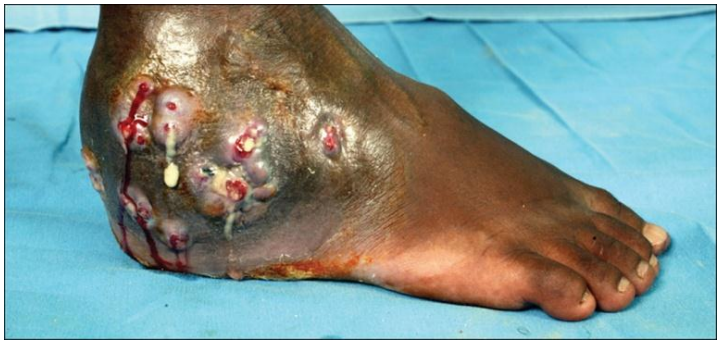




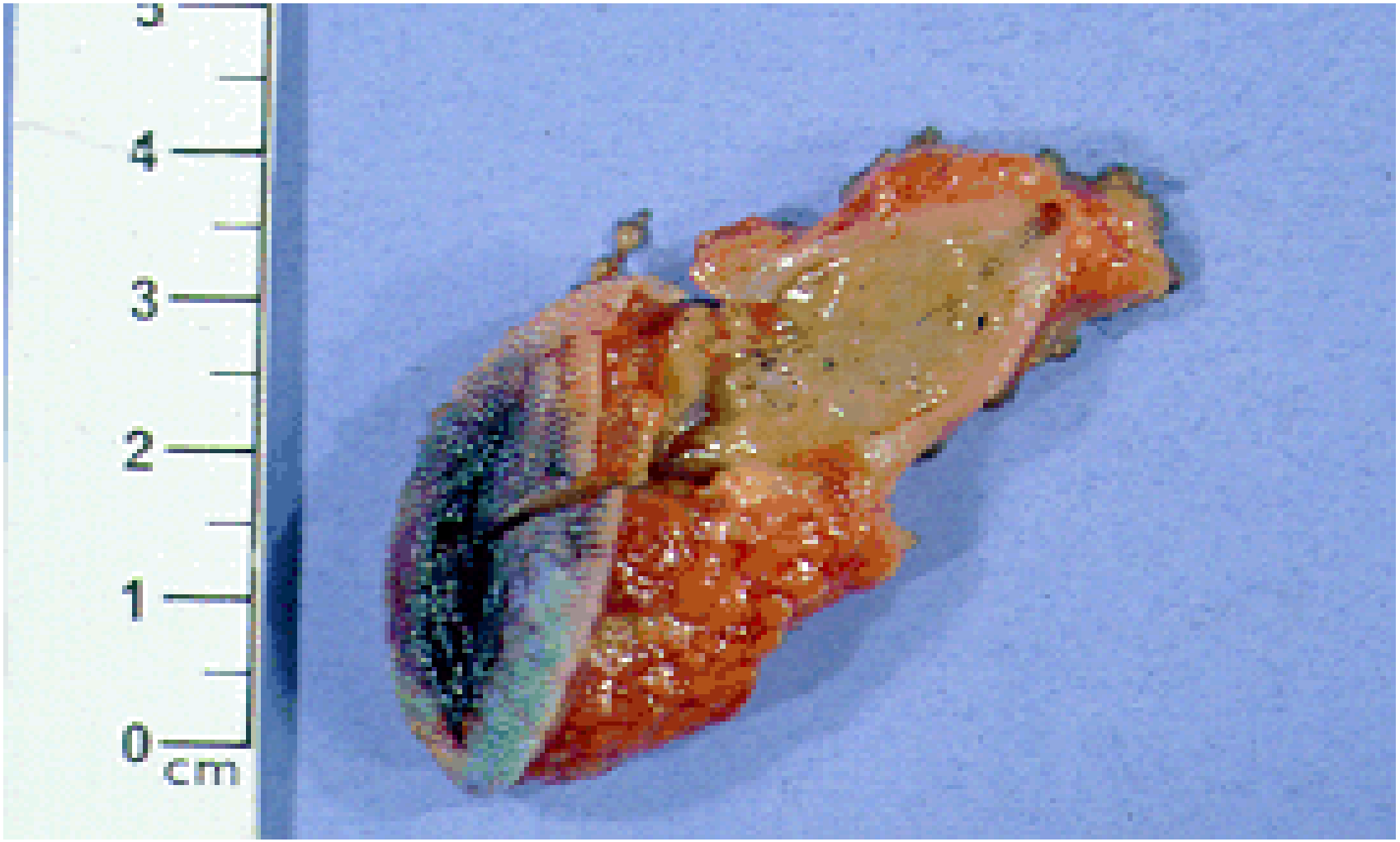

© CD-ROM ILLUSTRATED LECTURE NOTES ON TROPICAL MEDICINE





lesions present with multiple abscesses, formation of sinuses that drain pus to the surface of the skin, and presence of grains.

- **Eumycetoma**: caused by several mold fungi.
  - The color of grains in this type of mycetoma is black or grey.
  - **Fungi include:** *Madurella*, *Pseudallescheria*, *Acremonium*, *Leptosphaeria*
    - *Madurella mycetomatis* causes the majority of the cases with black grains.
    - *Madurella grisea* …grey grains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- **Actinomycetoma:**

  - Main etiologies:
    - *Streptomyces somaliensis*- causes the majority of the cases – color of grains yellow to yellow-brown.
    - *Actinomadura madurae* – white or yellow grains.
    - *Actinomadura pelletieri* – pinkish-red grains
    - *Nocardia brasiliensis* – white grains.
    - *N. asteroides*, *N. caviae*, *N.coeliaca* – white or yellow grains.

Laboratory Diagnosis:

1. **Clinical Material:**
   Tissue biopsy (not skin pinch), or Pus Aspirate from sinus tracts containing the granules

2. **Direct Microscopy:**
   Pus containing the granules should be examined using either 10% KOH and Parker ink or calcofluor white mounts, and tissue sections should be stained using H&E, PAS digest, and Grocott's methenamine silver (GMS).

   Interpretation:

   The presence of black pigmented grains, from a patient with supporting clinical symptoms should be considered significant. Direct microscopy or histopathology does not offer a specific identification of the causative agent.

3. **Culture:**
   Clinical specimens should be inoculated onto primary isolation media eg SDA

4. **Serology:**
   There are currently no commercially available serological procedures for the diagnosis of mycetoma.

6. **Causative agents:**
   Madurella, Acremonium, Pseudallescheria, Exophiala, Leptosphaeria, Curvularia, Fusarium

- **Management:** Usually actinomycetoma respond better to than eumycetoma.
  - Generally if bone is infected the response to treatment is poor.

- Actinomycetoma:
  - Trimethoprim – Sulfamethoxazole
  - Penicillin G
- Eumycetoma:
  - Azole derivatives eg Ketoconazole

- Surgical intervention: Debride tissue, Limb amputation if there's deformity in the bone

❖ Treatment duration is long

2. PHAEOHYPHOMYCOSIS

- A mycotic infection of humans and animals caused by a number of dematiaceous (brown-pigmented) fungi where the tissue morphology of the causative organism is mycelial.
- This separates it from other clinical types of disease involving pigmented fungi where the tissue morphology of the organism is a grain (mycotic mycetoma) or sclerotic body (chromoblastomycosis).

(pigmented filamentous fungi which contain melanin in their cell walls…melanin in cell walls may be a virulence factor)

…**phaeohyphomycosis**

The etiological agents include various dematiaceous moulds especially species of *Phialophora, Bipolaris, Exserohilum, Exophiala, Cladophialophora, Verruconis, Aureobasidium, Cladosporium, Curvularia* , *Alternaria*….

***Ajello (1986) listed 71 species from 39 genera as causative agents of phaeohyphomycosis.

…Clinical Manifestations:

- Clinical forms of phaeohyphomycosis range from localized superficial infections of the stratum corneum to subcutaneous cysts (phaeomycotic cyst) to invasion of the brain.
- Clinical signs consist of nodules underneath the skin, abscesses or cysts. In immunosuppressed patients, deep infections within the eyes, bones, heart and central nervous system.

- Current antifungal agents: posaconazole and voriconazole

1. Subcutaneous phaeohyphomycosis:

- Subcutaneous infections occur after traumatic implantation of fungal elements from contaminated soil, thorns or wood splinters.
- *Exophiala jeanselmei* and *Wangiella dermatitidis* are the most common agents
- Cystic lesions

2. Paranasal sinus phaeohyphomycosis:

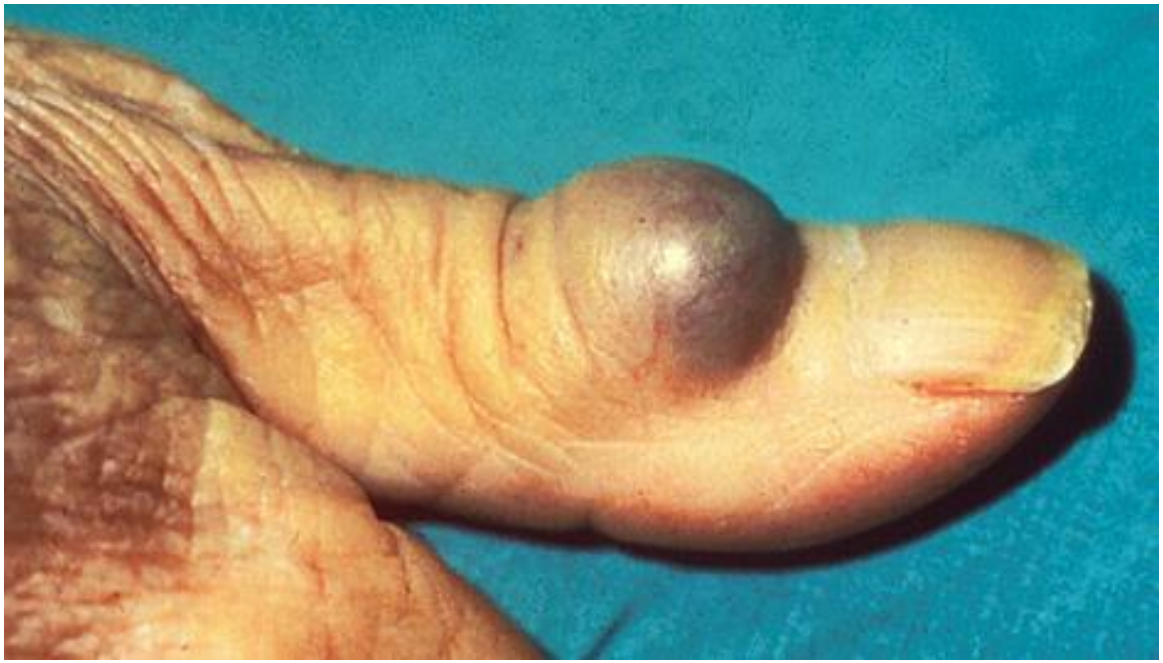
Sinusitis caused by dematiaceous fungi, especially species of *Bipolaris,Exserohilum,Curvularia* and *Alternaria* in pts with a history of allergic rhinitis

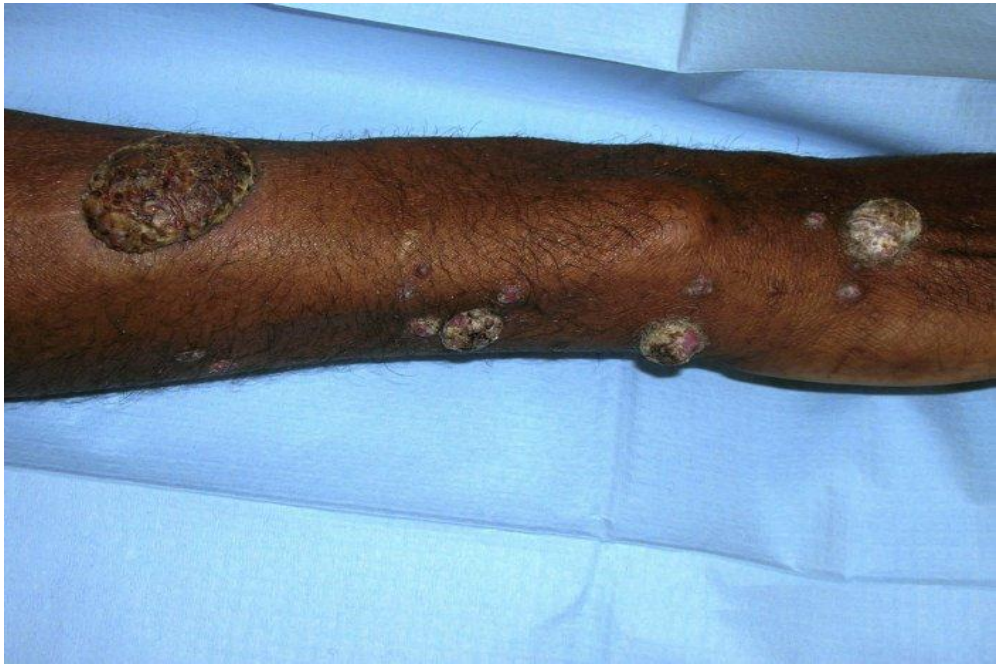
3. Cerebral phaeohyphomycosis:

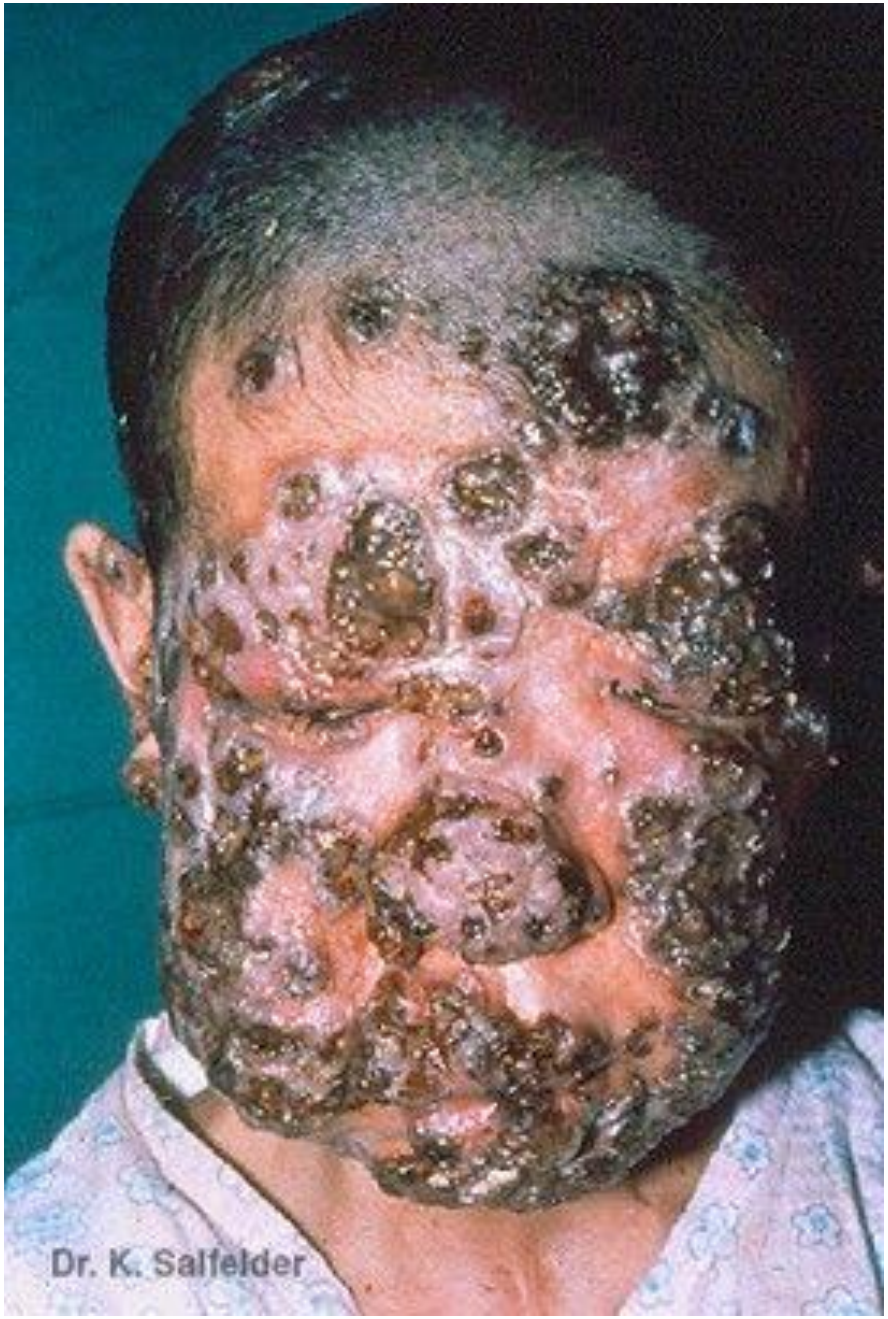
A rare infection, mostly in immunosuppressed patients following the inhalation of conidia.

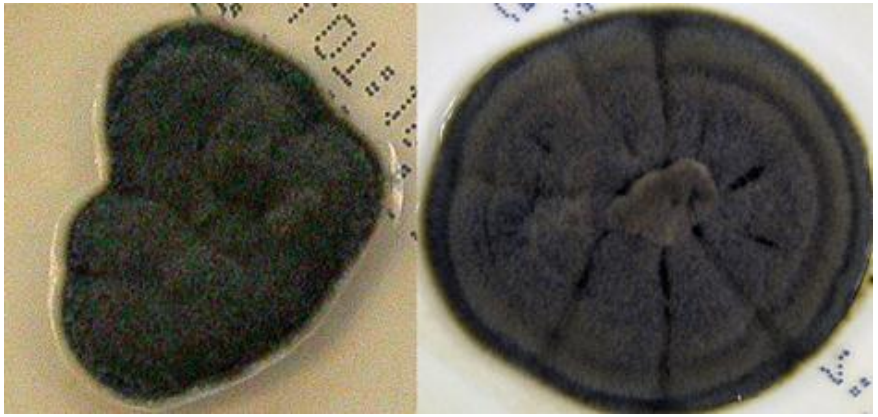
However, cerebral infections caused by *Cladophialophora bantiana* have been reported in a number of patients without any obvious predisposing factors.

This fungus is neurotropic and dissemination to sites other than the CNS is rare.






Dr. K. Salfelder



Laboratory Diagnosis:

1. Clinical Material:

Skin scrapings and/or tissue biopsies, aspirates, cerebrospinal fluid…etc

2. Direct Microscopy:

(a) Skin scrapingsaspirates should be examined using 10% KOH and Parker ink or calcofluor white mounts;

(b) Exudates and body fluids should be centrifuged and the sediment examined using either 10% KOH and Parker ink or calcofluor white mounts

(c) Tissue sections should be stained using H&E, PAS digest, and Grocott's methenamine silver (GMS).

Interpretation:

The presence of brown pigmented, branching septate hyphae in any specimen, from a patient with supporting clinical symptoms should be considered significant.

- **Note:**
  Direct microscopy of tissue is necessary to differentiate between chromoblastomycosis which is characterized by the presence in tissue of brown pigmented, rounded sclerotic bodies and phaeohyphomycosis where the tissue morphology of the causative organism is mycelial.

3. Culture:

Clinical specimens should be inoculated onto primary isolation media, like Sabouraud's dextrose agar.. very slow growing black or grey colonies

Interpretation:

Organisims involved are well recognized as common environmental airborne contaminants, therefore a positive culture from a non-sterile specimen eg skin must supported by direct microscopic evidence in order to be considered significant

Culture identification is the only reliable means of distinguishing these fungi.

4. Serology:

There are currently no commercially available serological procedures for the diagnosis of any of the infections classified under the term phaeohyphomycosis.

5. Identification:

Culture characteristics and microscopic morphology are important, especially conidial morphology, the arrangement of conidia on the conidiogenous cell

Causative agents:

Alternaria sp., *Aureobasidium pullulans*, *Bipolaris* sp., *Cladophialophora bantiana*, *Verruconis gallopava*, *Curvularia* sp., *Exophiala* sp., *Exserohilum* sp., *Phialophora verrucosa, Wangiella,*

3. CHROMOBLASTOMYCOSIS

(Chromomycosis, Fonseca's disease)

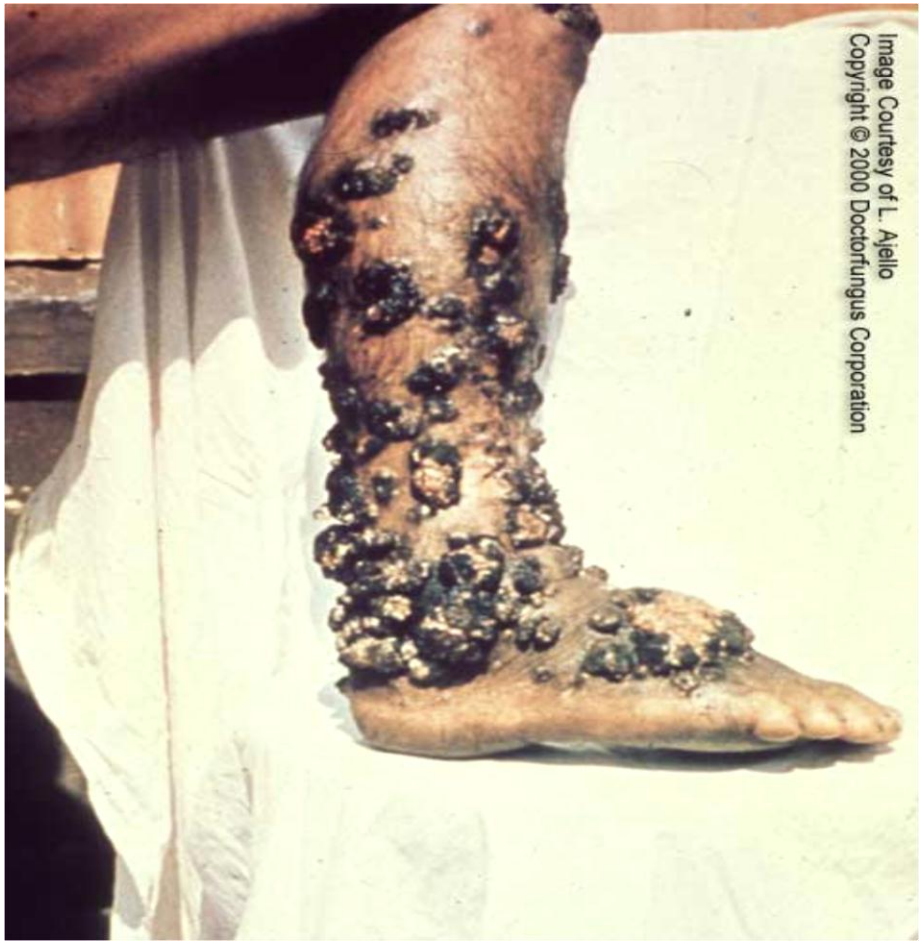
- A mycotic infection of the cutaneous and subcutaneous tissues characterized by the development in tissue of dematiaceous (brown-pigmented), planate-dividing, rounded sclerotic bodies.
- Infections are caused by the traumatic implantation of fungal elements into the skin and are chronic
- Tissue proliferation usually occurs around the area of inoculation producing crusted wart-like lesions.
- World-wide distribution but more common in bare footed populations living in tropical regions.
- Aetiological agents include *Phialophora verrucosa, Fonsecaea* spp., and *Cladophialophora carrionii.*

..Clinical Manifestations:

- Lesions of chromoblastomycosis are most often found on exposed parts of the body
- Infection site has a small red papule which is painless but may be itchy.
- Infection slowly spreads to the surrounding tissue through lymph vessels, producing metastatic lesions at distant sites.

- Secondary infection with bacteria may lead to lymph stasis

- In long standing infections, lesions may become tumorous/cauliflower-like in appearance.
- Other prominent features include epithelial hyperplasia, fibrosis and microabscess formation in the epidermis.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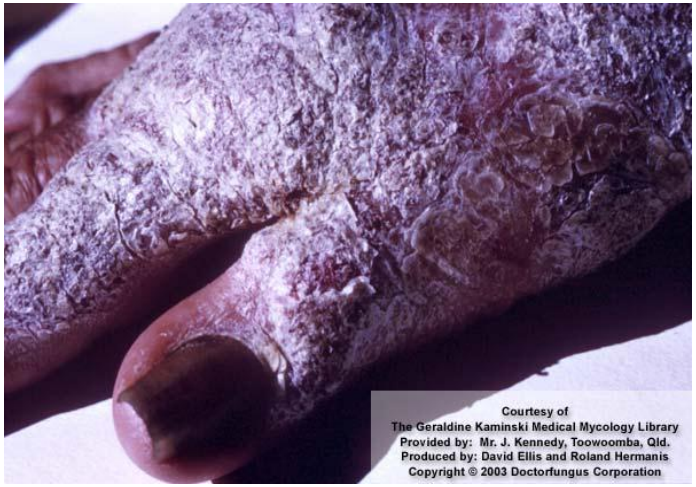
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Laboratory Diagnosis:

1. Clinical Material:

Skin scrapings and/or biopsy.

2. Direct Microscopy:

(a) Skin scrapings should be examined using 10% KOH and Parker ink or calcofluor white mounts

(b) Tissue sections should be stained using H&E, PAS digest, and Grocott's methenamine silver (GMS).

Interpretation:

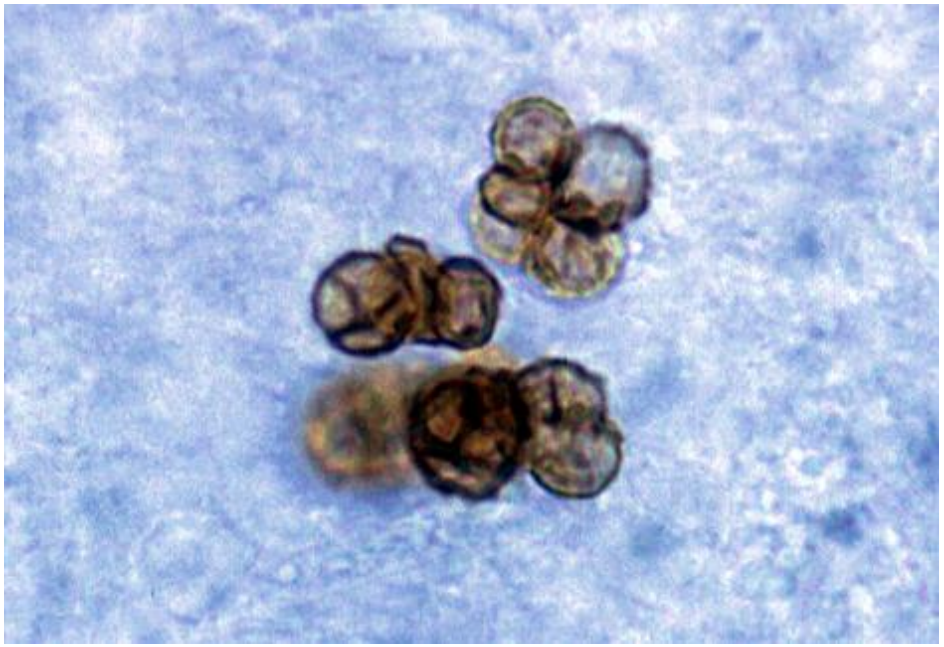
The presence in tissue of brown pigmented, planate-dividing, rounded sclerotic bodies from a patient with supporting clinical symptoms should be considered significant. Remember direct microscopy or histopathology does not offer a specific identification of the causative agent.

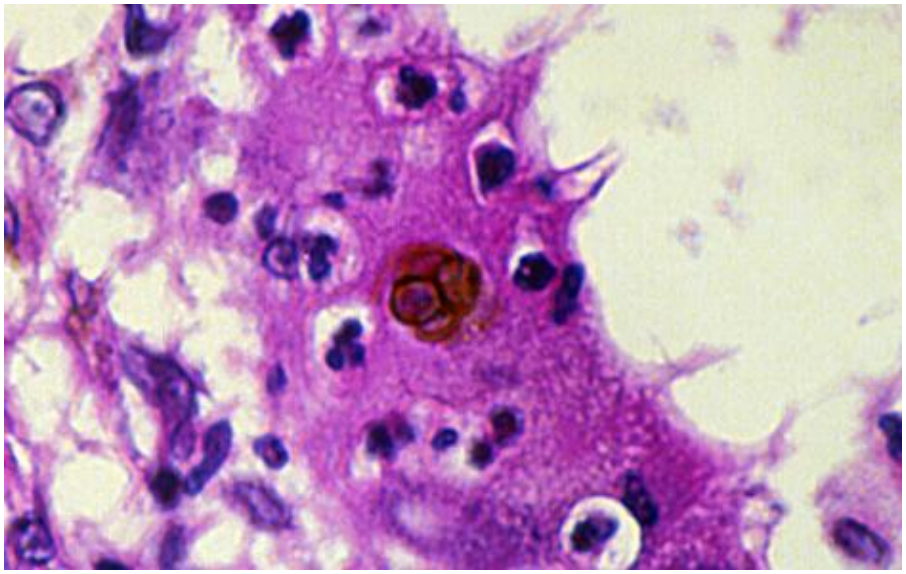
3. Culture:

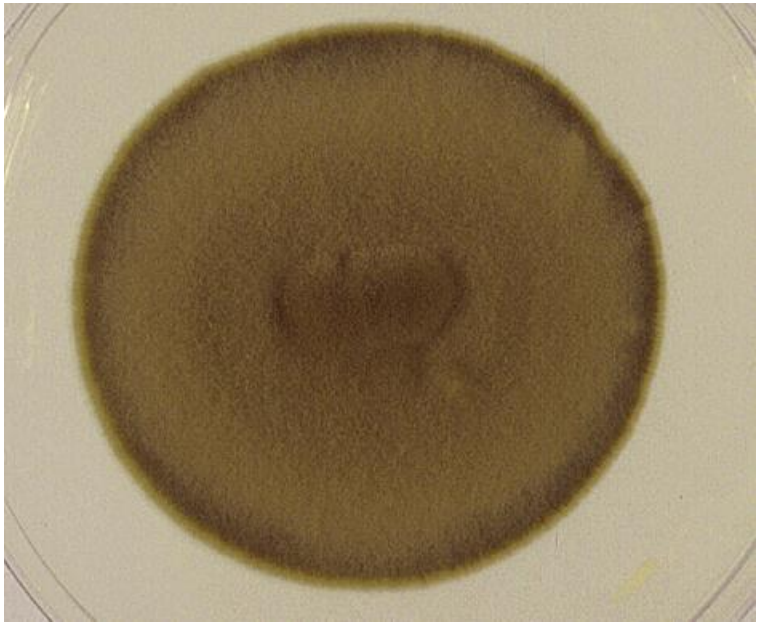
Clinical specimens should be inoculated onto primary isolation media, like Sabouraud's dextrose agar.

Culture characteristics and microscopic morphology are important, especially conidial morphology, the arrangement of conidia on the conidiogenous cell and the morphology of the conidiogenous cell.

- **4. Serology:**
  There are currently no commercially available serological procedures for the diagnosis of chromoblastomycosis.
- **6. Causative agents:**
  Cladophialophora carrionii, Fonsecaea species complex, *Phialophora verrucosa*







Lab diagnosis:

- KOH preparations reveal sclerotic cells.
- Culture to identify the organism involved.
- On histology pigmented yeasts resembling "copper pennies".

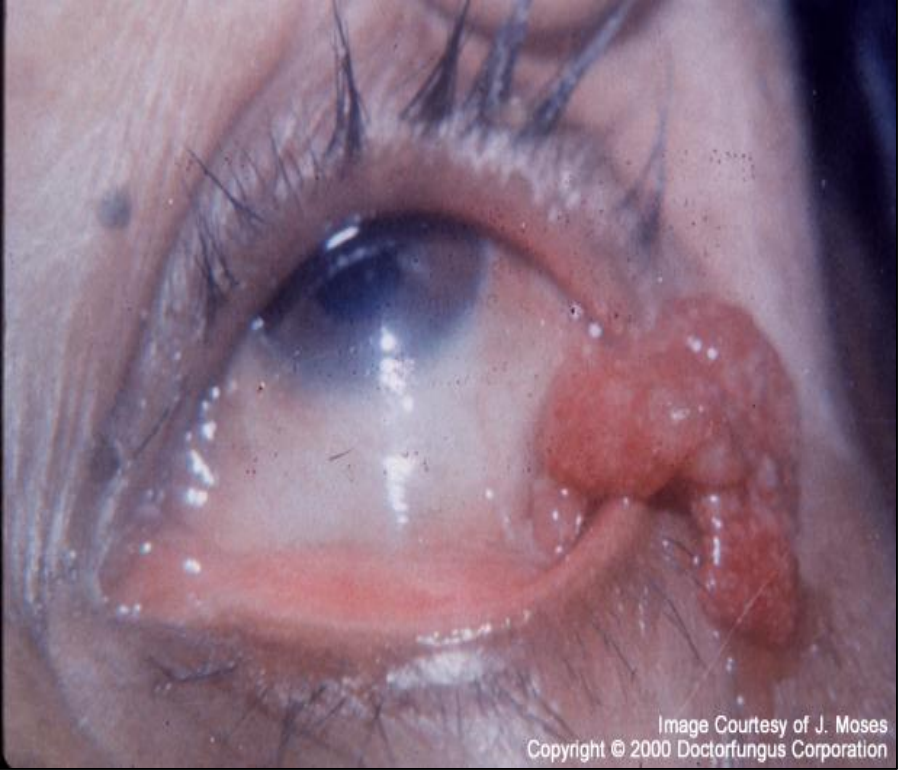
Treatment:

- Agents of choice include: Itraconazole, Terbinafine ,Flucytosine
- Cryosurgery with liquid nitrogen to excise tumorous- cauliflower-like lesions
- Antibiotics may be used to treat bacterial super-infections.

4. RHINOSPORIDIOSIS

- *Rhinosporidium seeberi* is the causative agent of rhinosporidiosis, a chronic subcutaneous mycosis.
- Fish and aquatic insects are the natural reservoirs of *R. seeberi*…patient history of exposure to contaminated water /Seen in communities near swamps
- The infection is characterized by formation of polypoid masses at nasal mucosa, conjunctiva, genitalia, and rectum.
- Floor of the nose and inferior turbinate are the most common sites

- Laryngeal rhinosporidiosis may be due to inoculation from the nose during endotracheal intubation.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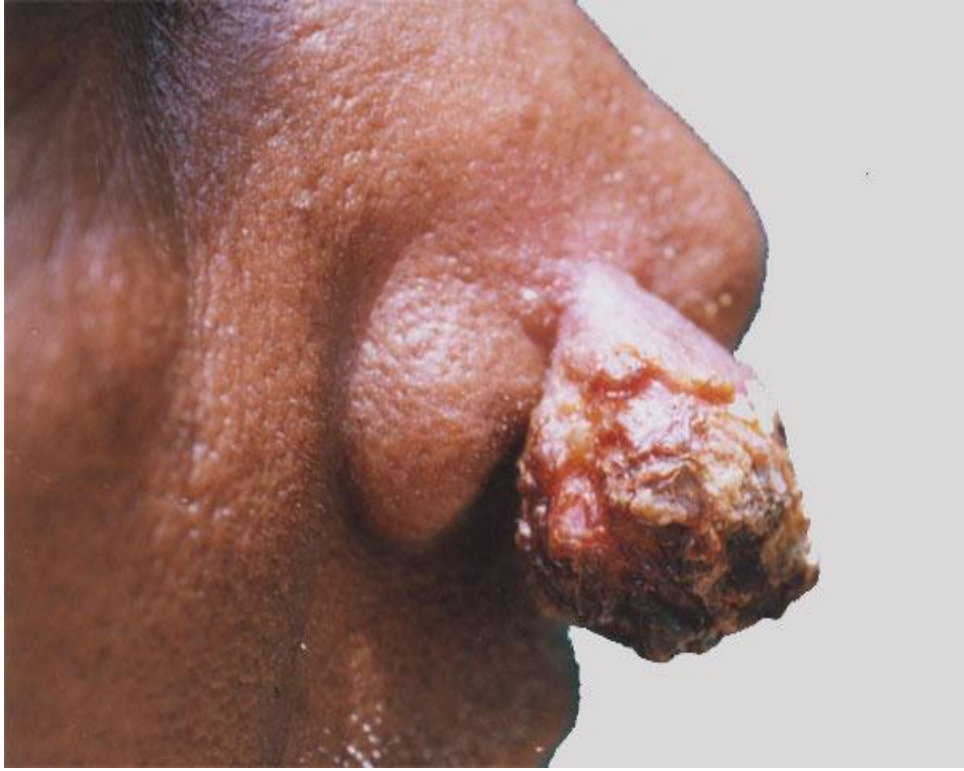
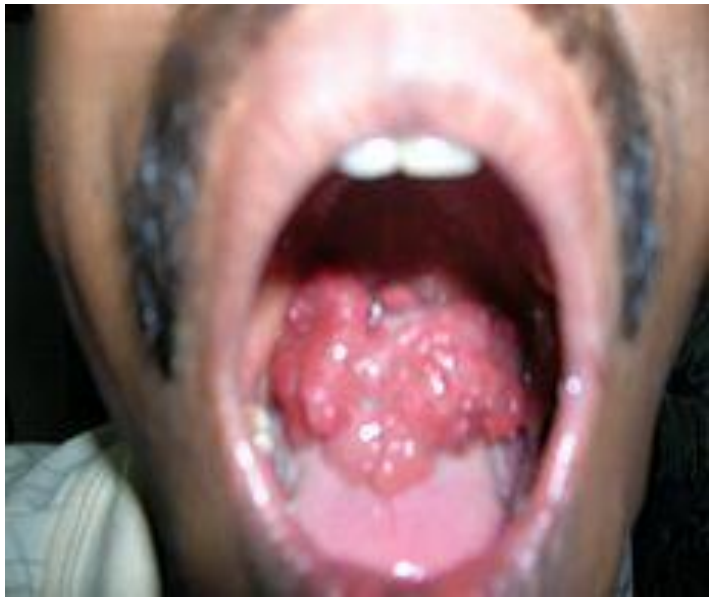
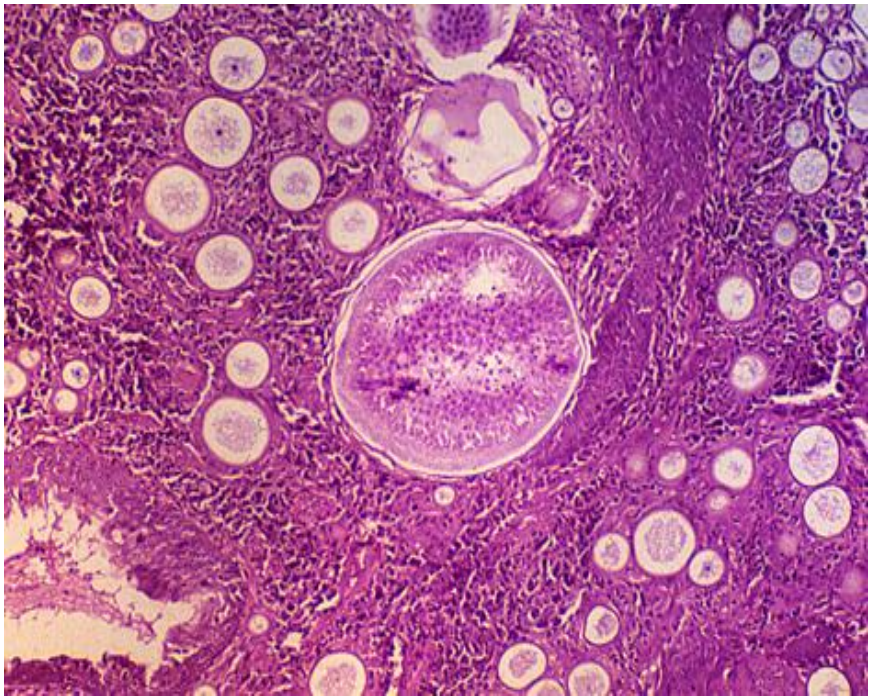
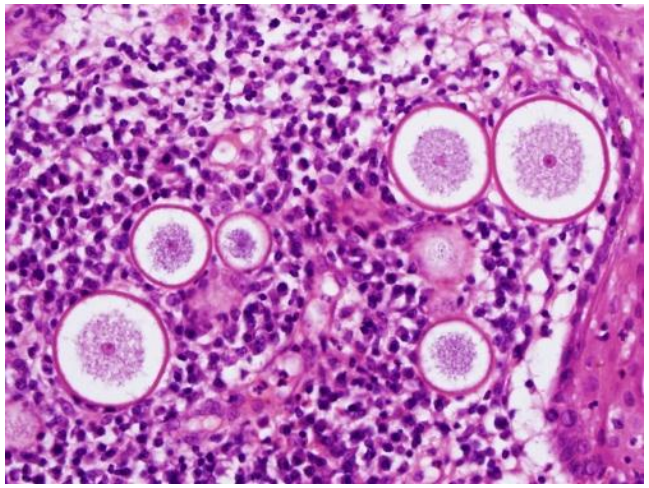




Microscopically, *R. seeberi* produces spherules in infected tissue and these spherules are filled with endospores.
This microorganism cannot be cultured *in vitro* on artificial media.





5. SPOROTRICHOSIS

- Sporotrichosis is primarily a chronic mycotic infection of the cutaneous or subcutaneous tissues and adjacent lymphatics characterized by nodular lesions which may suppurate and ulcerate.
- Infections are caused by the traumatic implantation of the fungus into the skin, or very rarely, by inhalation into the lungs

Clinical manifestations:

1. Fixed cutaneous sporotrichosis:

- Primary lesions develop at the site of implantation of the fungus, usually at more exposed sites mainly the limbs, hands and fingers.
- Lesions often start out as a painless nodule which soon become palpable and ulcerate often discharging a serous or purulent fluid.
- Importantly, lesions remain localized around the initial site of implantation and do not spread along the lymphatic channels.
- Isolates from these lesions usually grow well at 35^{o}C but not at 37^{o}C

2. Lymphocutaneous sporotrichosis:

- Primary lesions develop at the site of implantation of the fungus
- secondary lesions then appear along the lymphatic channels which follow the same course as the primary lesion ie they start out as painless nodules which soon become palpable and ulcerate.
- Isolates from these lesions usually grow well at both 35^{o}C and 37^{o}C.

3. Pulmonary sporotrichosis:

- This is a rare entity usually caused by the inhalation of conidia but cases of haematogenous dissemination have been reported.
- Symptoms are nonspecific and include cough, sputum production, fever, weight loss..
- Haemoptysis may occur and it can be massive and fatal.

4. Osteoarticular sporotrichosis:

- Most patients also have cutaneous lesions and present with stiffness and pain in a large joint, usually the knee, elbow, ankle or wrist.

- Other rare forms of sporotrichoisis include endophthalmitis, chorioretinitis and meningitis

Laboratory diagnosis:

1. Clinical material:

A tissue biopsy is the best specimen.

2. Direct Microscopy:

Tissue sections should be stained using PAS digest, Grocott's methenamine silver (GMS) or Gram stain.

Interpretation:

Look for small narrow base budding yeast cells (2-5um). **Note** they are often present in very low numbers and may be difficult to find. PAS and GMS stains are essential.

3. Culture:

Clinical specimens should be inoculated onto primary isolation media, like Sabouraud's dextrose agar and Brain heart infusion agar supplemented with 5% sheep blood.

- **Interpretation:** A positive culture from a biopsy should be considered significant.

4. Serology:

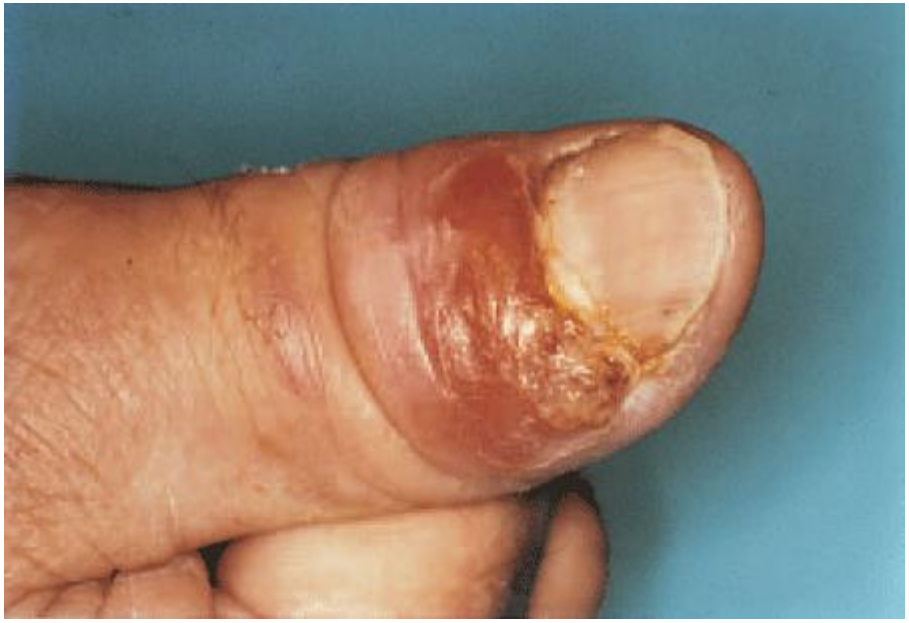
Serological tests are of limited value in the diagnosis of Sporotrichosis.

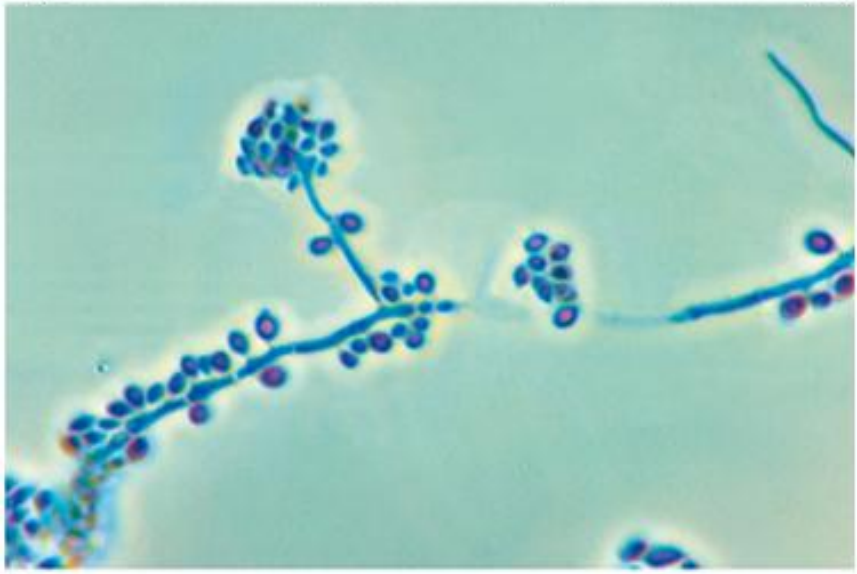
Identification:

Fungi characterized by thermal dimorphism and clusters of ovoid conidia produced on short conidiophores.

6. Causative agents:

Sporothrix schenckii complex.





(a)

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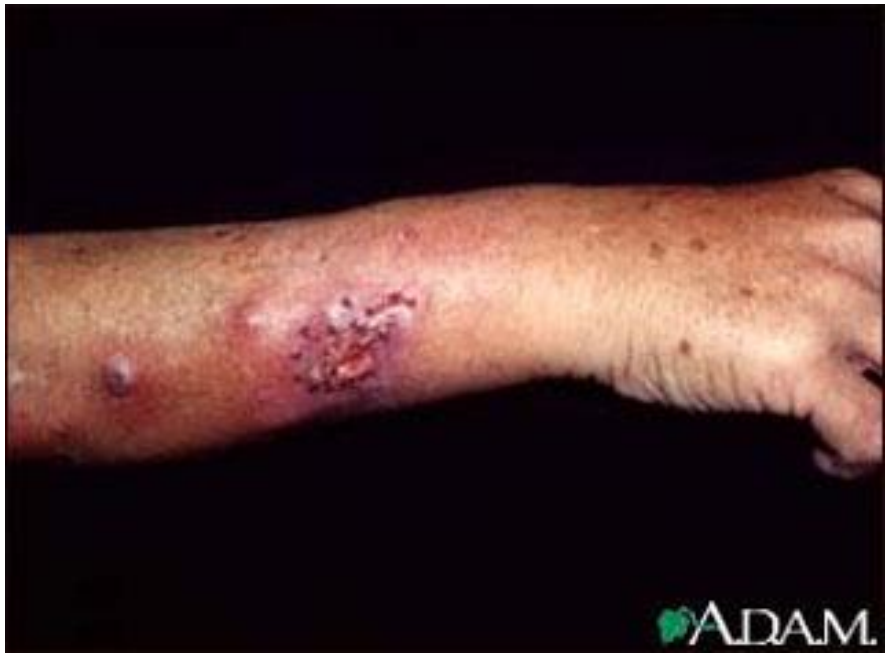

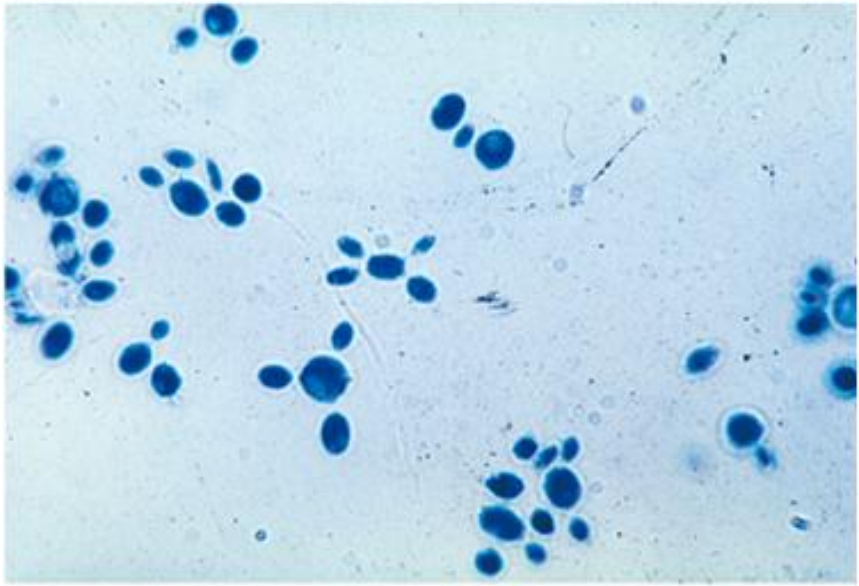

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6. LOBOMYCOSIS

(Jorge) Lobo's disease, Lacaziosis

-caused by *Lacazia loboi*(formerly named *Loboa loboi*), discovered by Brazilian dermatologist Jorge Lobo

-restricted to the Amazon valley

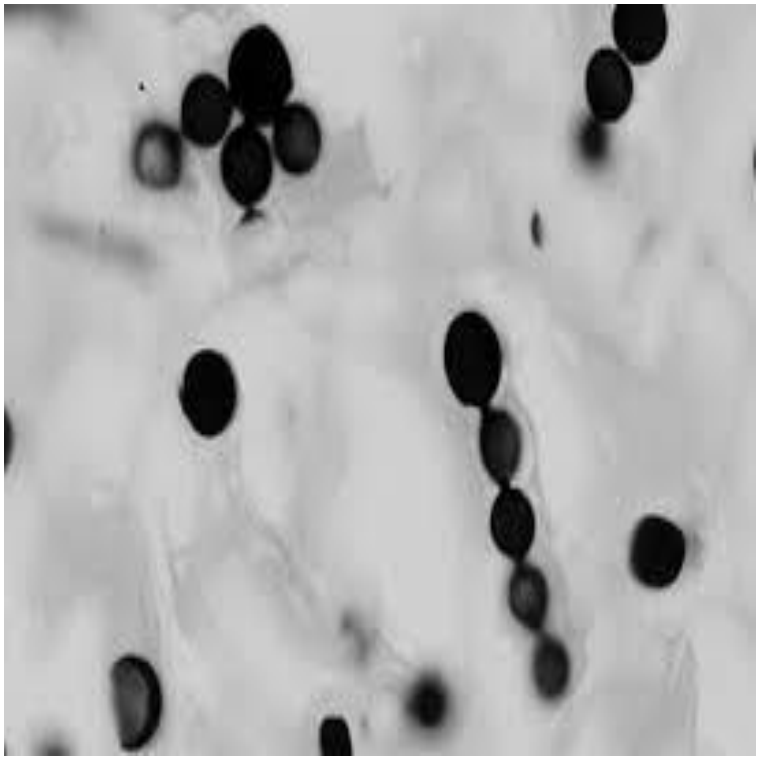
- This disease is usually found in humans and bottle-nosed dolphins

- Human-to-human transmission does not occur, infection is only acquired from the environment

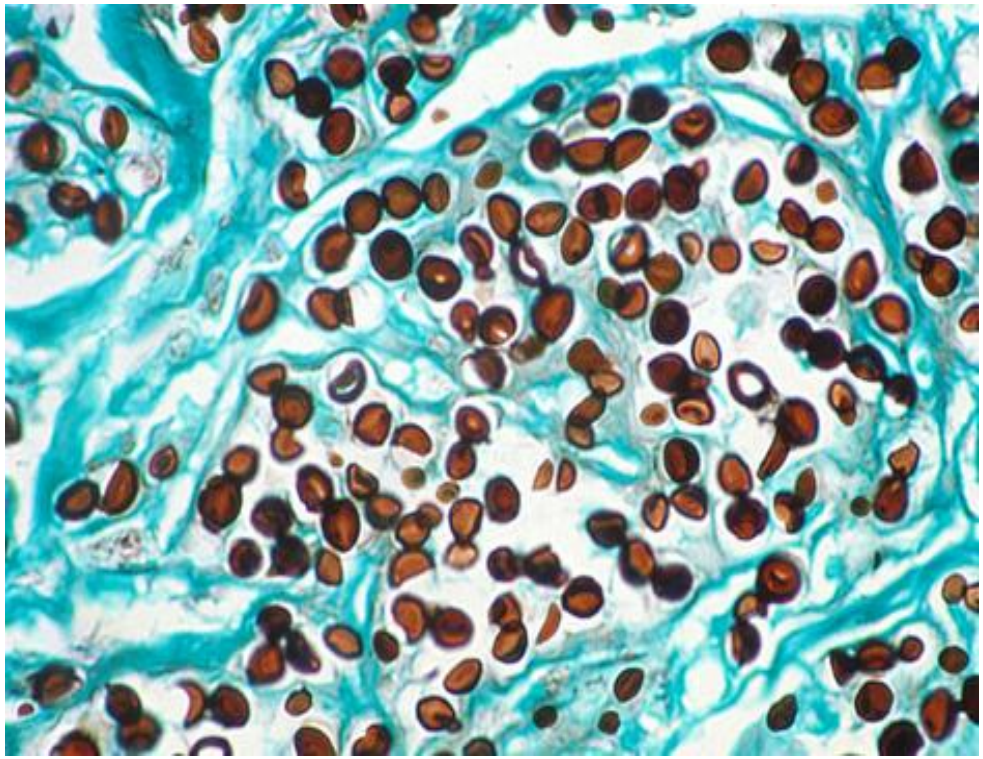
-is a chronic, localized infection characterised by the presence of keloidal, nodular lesions or sometimes by crusty plaques and tumours. There is no systemic spread.

-The lesions contain masses of spheroidal, yeast-like cells

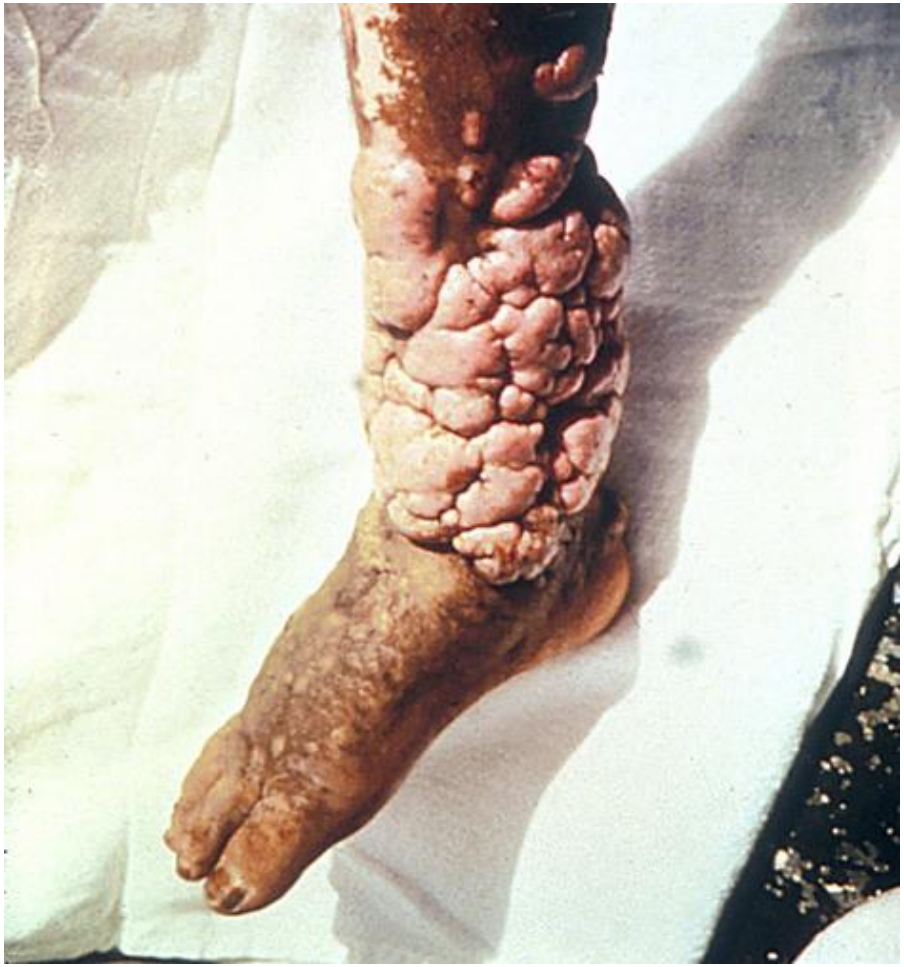
-a skin biopsy microscopy will reveal long chains of spherical cells interconnected by tubules.



chains of spherical cells interconnected by tubules.



Spheroidal yeast-like cells

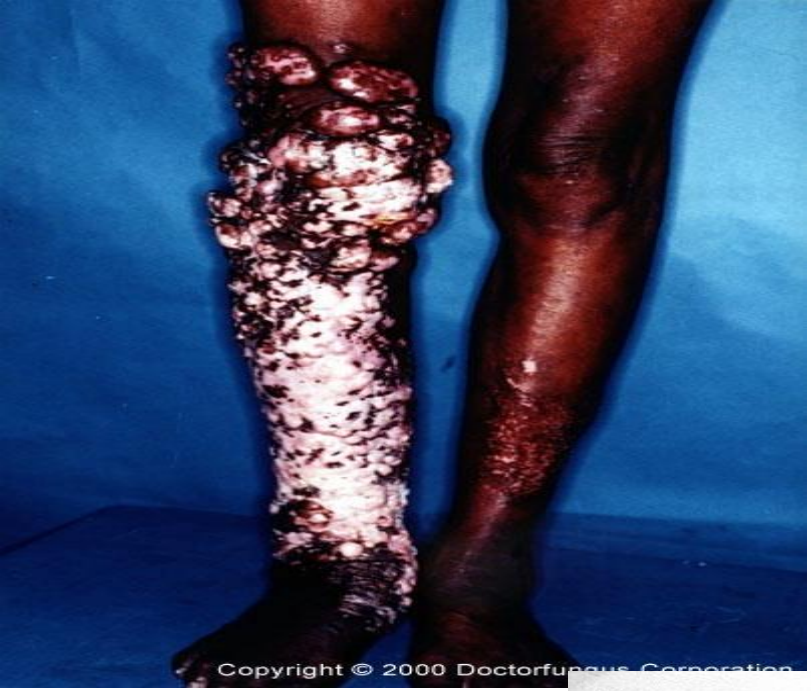


keloidal nodular lesions

Treatment:

-Surgical excision or cryosurgery

-Itraconazole has been used to prevent recurrence after surgery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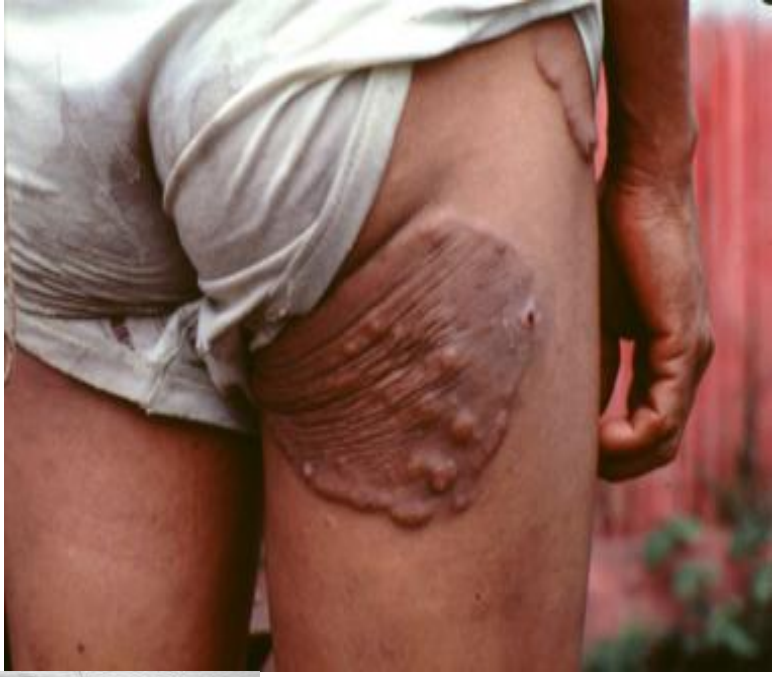

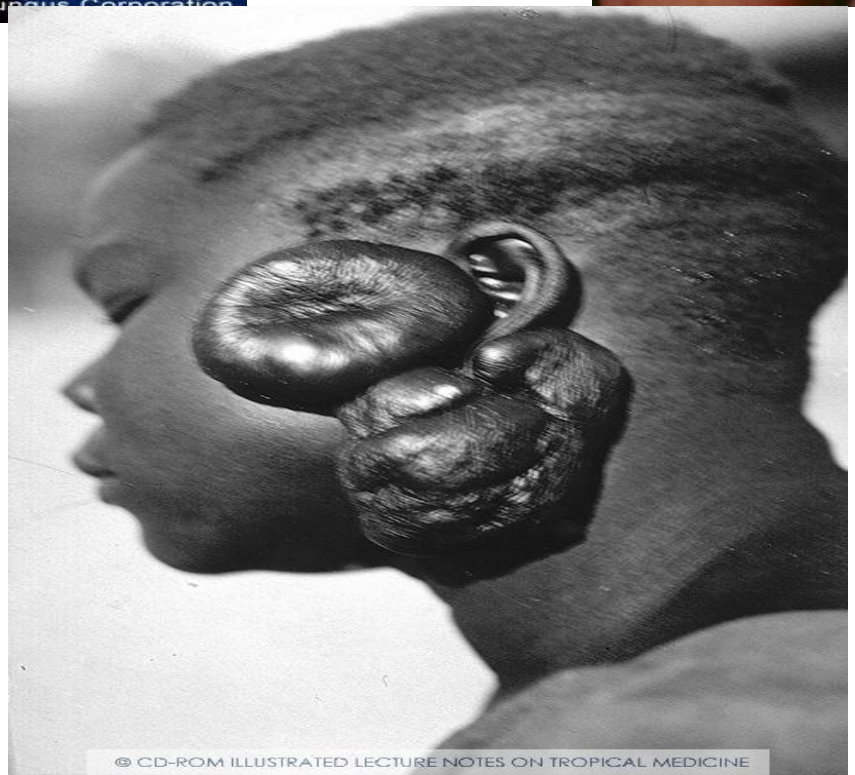
© CD-ROM ILLUSTRATED LECTURE NOTES ON TROPICAL MEDICINE

Management of subcut. infxns

1. Antifungal agents – amphotericin B, flucytosine, itraconazole..other azoles.
2. Antibacterial agents in actinomycetoma and in 2° bacterial infection – sulphonamides, rifampicin, streptomycin, amikacin, etc
3. Surgery for some lesions e.g. for mycetoma..amputation, excision of polyps..rhinosporidiosis,