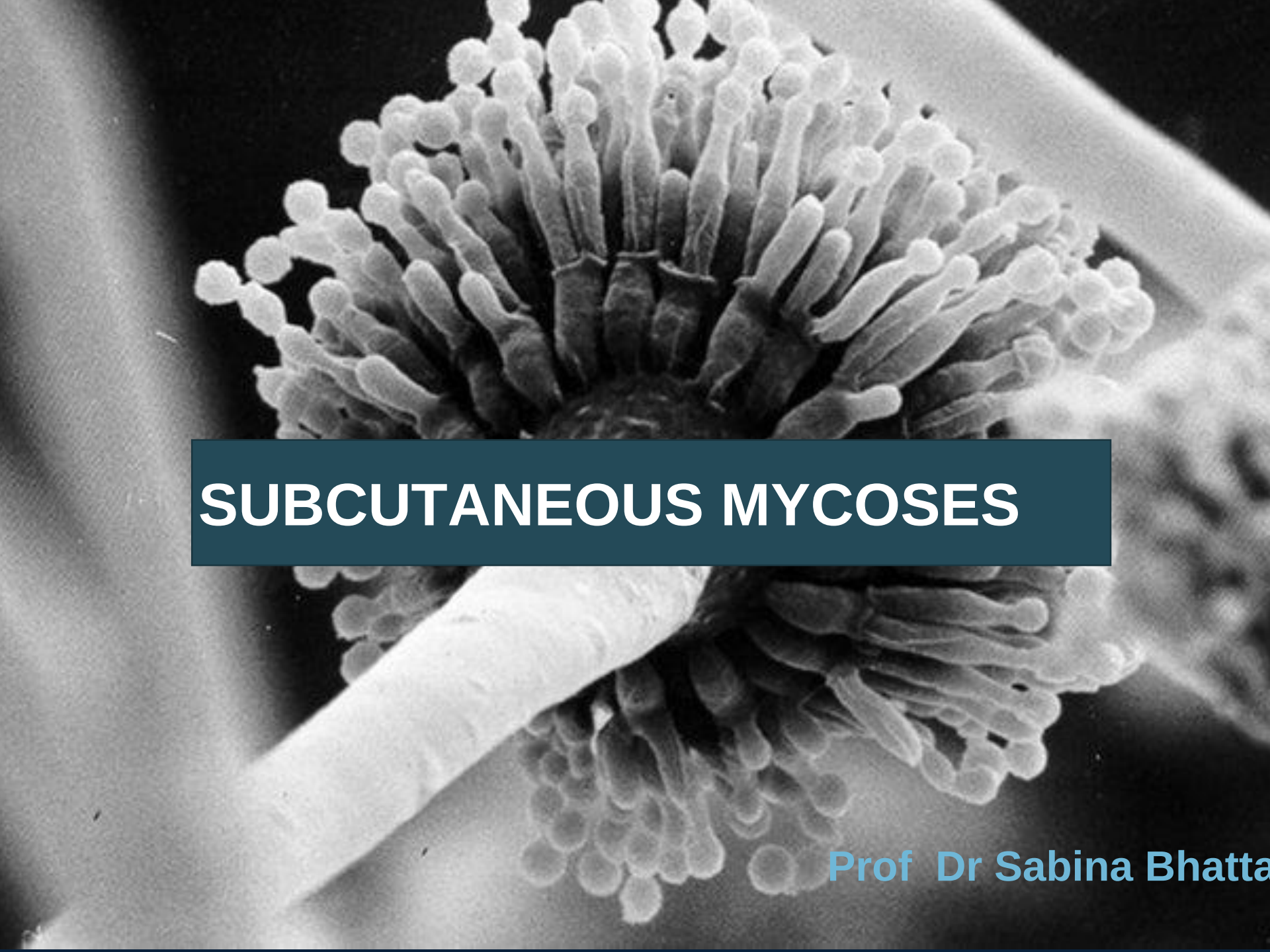
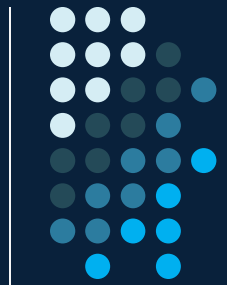


SUBCUTANEOUS MYCOSES

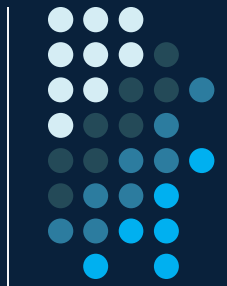
Prof Dr Sabina Bhatta

TOPICS TO DISCUSS



- Sporotrichosis
- Mycetoma
- Chromoblastomycosis
- Phaeohyphomycosis
- Lobomycosis
- Rhinosporidiosis
- Subcutaneous zygomycosis

INTRODUCTION



- Subcutaneous mycoses (mycoses of implantation) - sporadically occurring infections caused by fungi present in natural environment - which are directly inoculated into dermis or subcutaneous tissue through penetrating injury
- Mainly seen in tropics
- Many have long incubation periods

CLASSIFICATION

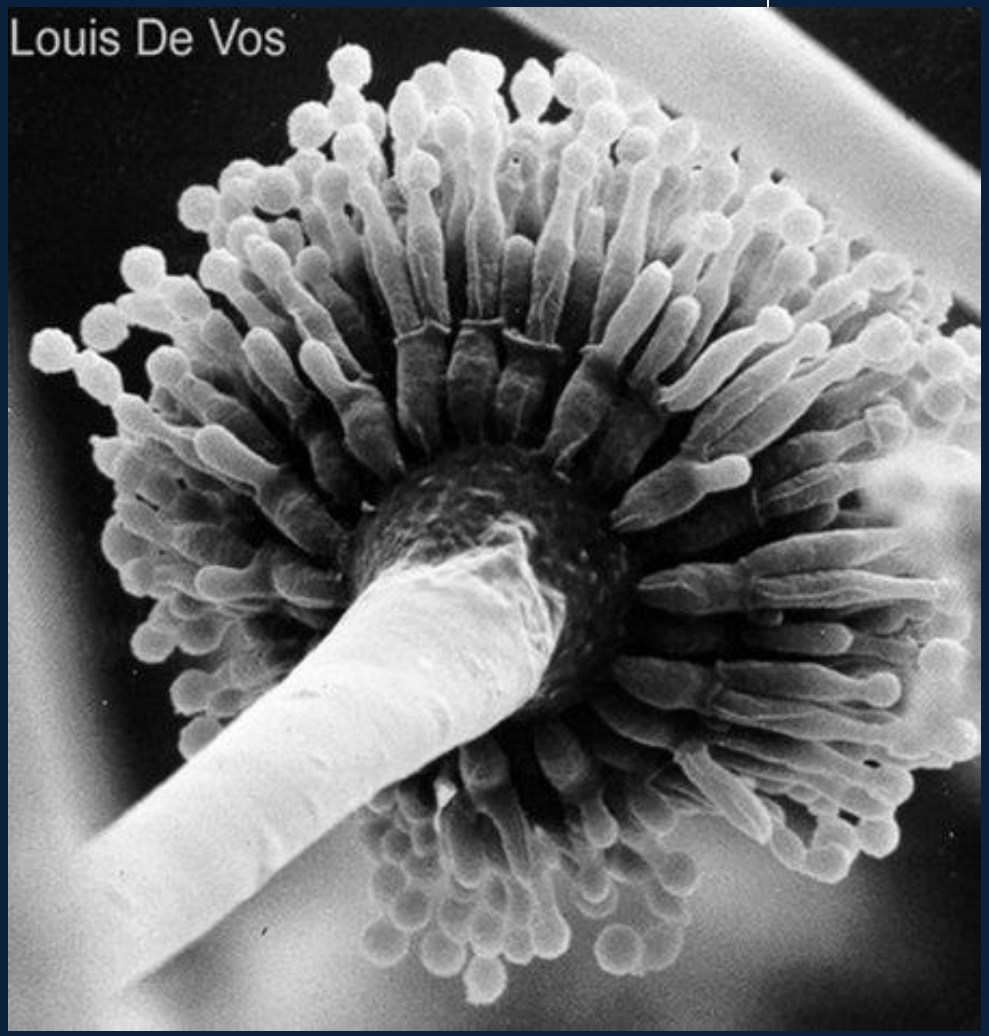
- Sporotrichosis
- Mycetoma
- Chromoblastomycosis

COMMON

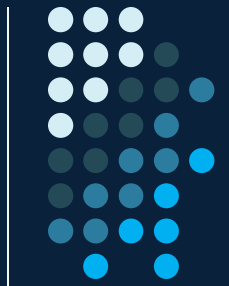
- Pheohyphomycosis
- Rhinosporidiosis
- Lobomycosis
- Subcutaneous Zygomycosis

RARER

SPOROTRICHOSIS



DEFINITION & ETIOLOGY



- Subacute or chronic infection caused by *Sporothrix schenckii*
- Dimorphic fungus
- Exhibits mycelial forms at 25°C and a yeast form at 37°C
- Both cutaneous and systemic forms
- In temperate and tropical climate

- *Sporothrix* species typically exist as saprophytic mould on vegetative matter
- Cutaneous infection often results from a puncture wound involving thorns, splinter, plant matter or insect bite
- Can also be transmitted via cat bites, scratches or nasal secretions

Other species of pathogenic Sporothrix -

- S. braziliensis
- S. mexicana
- S. globosa
- S. lurei

EPIDEMIOLOGY

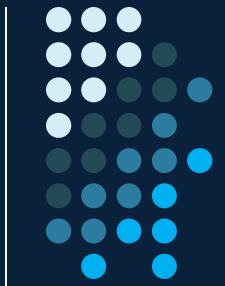
- Sporotrichosis is mainly seen in the tropics and subtropics
- More in autumn and first half of winter
- Grows on decaying matter - timber in mines
- Occupation - miners, forestry workers, florists, gardeners
- Age - any age
- Sex - males more exposed

PATHOGENESIS

- Not much known
- Pathogen host interaction due to 70-kd **(Gp70)** glycoprotein from the cell wall of *S. schenckii*
- Involved in fungal **adherence** to the dermal extracellular matrix

- Cutaneous sporotrichosis - fungus introduced into skin or mucous membrane by trauma
- Not contagious , transmission from cats seen
- Systemic sporotrichosis - rare, portal of entry is lungs
- Incubation period - 8 to 30 days

CLINICAL FEATURES



- History of a recent prick injury at the site of infection

- Usually clinical disease apparent within 3 weeks of injury ; may take as long as 6 months

- Common - indurated and ulcerating nodules

- Clinical variants -

1. Cutaneous form
2. Systemic form

TYPES of cutaneous form -

2. Lymphocutanoeus (Lymphangitic) sporotrichosis
3. Fixed cutaneous sporotrichosis
4. Mycetoma or cellulitis like

TYPES of systemic form -

- Pulmonary sporotrichosis
- Disseminated sporotrichosis

Lymphocutaneous

- Most common presentation (upto 80%) - localised lymphatic variety
- Follows implantation of spores in wound and results from lymphangitic spread of infection
- Common on exposed skin - upper extremity

- A subcutaneous nodule or pustule develops at the site of inoculation
- Ulcerate as the result of central abscess formation
- Satellite lesions form along the associated lymphatic chain
- Chain of lymphatic nodules (lymphadenopathy) develop

- New nodules appear at intervals of few days to 3 weeks
- They soften and ulcerate
- Connected by tender lymphatic cords
- Thin purulent discharge from earliest lesion
- Primary lesion heals spontaneously - leaves LN enlarged
- Heals with scarring after weeks or months

Lymphocutaneous sporotrichosis

Lymphocutaneous sporotrichosis

Fixed cutaneous

- Pathogen is limited to point of inoculation
- Less common - in endemic areas
- Scaly, acneiform, verrucous or ulcerative nodule that remains localized
- Infiltrated plaques or red scaly patches, occasionally small satellite lesions appear nearby
- High degree of immunity of patient
- Sites - upper extremities and face

- Mucous membrane can be involved
- Pain is important
- Occasionally remit spontaneously

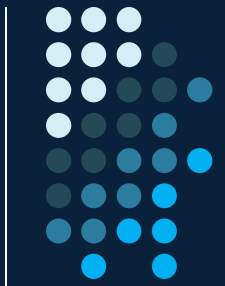
Pulmonary sporotrichosis

- Due to inhalation of conidia
- Chronic cavitary fibronodular disease
- Middle aged men
- Risk factor - alcoholism and COPD
- Acute pneumonitis, bronchitis, fever, cough and malaise
- Leads to dissemination

Extracutaneous

- Very rare
- Seen in immunosuppressed patients (HIV, alcoholics)
- Common site : joints (knee, ankles, wrists)
- Due to direct, deep implantation, direct contiguous spread or hematogenous spread

DIFFERENTIAL DIAGNOSIS

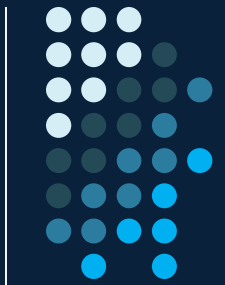


- Lupus vulgaris
- Atypical mycobacterial infection (*M.marinum, M.kansasii, M. chelonei*)
- Foreign body granuloma
- Nocardia infections
- Chromoblastomycosis
- Leishmaniasis

COURSE

- May resolve spontaneously
- Chronic cases - may last for 5 years

INVESTIGATIONS

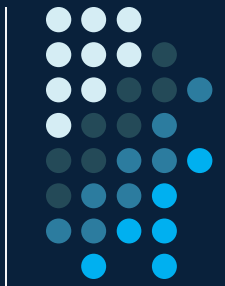


- FUNGAL CULTURE
- MICROSCOPY
- PHYSIOLOGICAL TEST
- HISTOPATHOLOGY
- PAS STAIN
- SPOROTRICHIN TEST

FUNGAL CULTURE

- Gold standard
- Sabouraud dextrose agar at 25°C

FUNGAL CULTURE

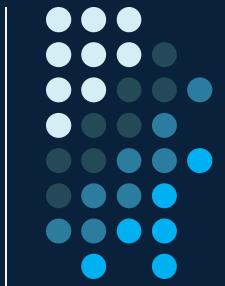


- Colony - leathery, lobated, smooth or verrucous, moist, cream-colored colony, maturing to a black leathery colony
- Yeast growth at 37°C must be demonstrated to confirm

MICROSCOPY

- 2 micrometer hyphae - small, oval conidia`along sides of hyphae
- Flower like arrangement of conidia at the tip of hyphae

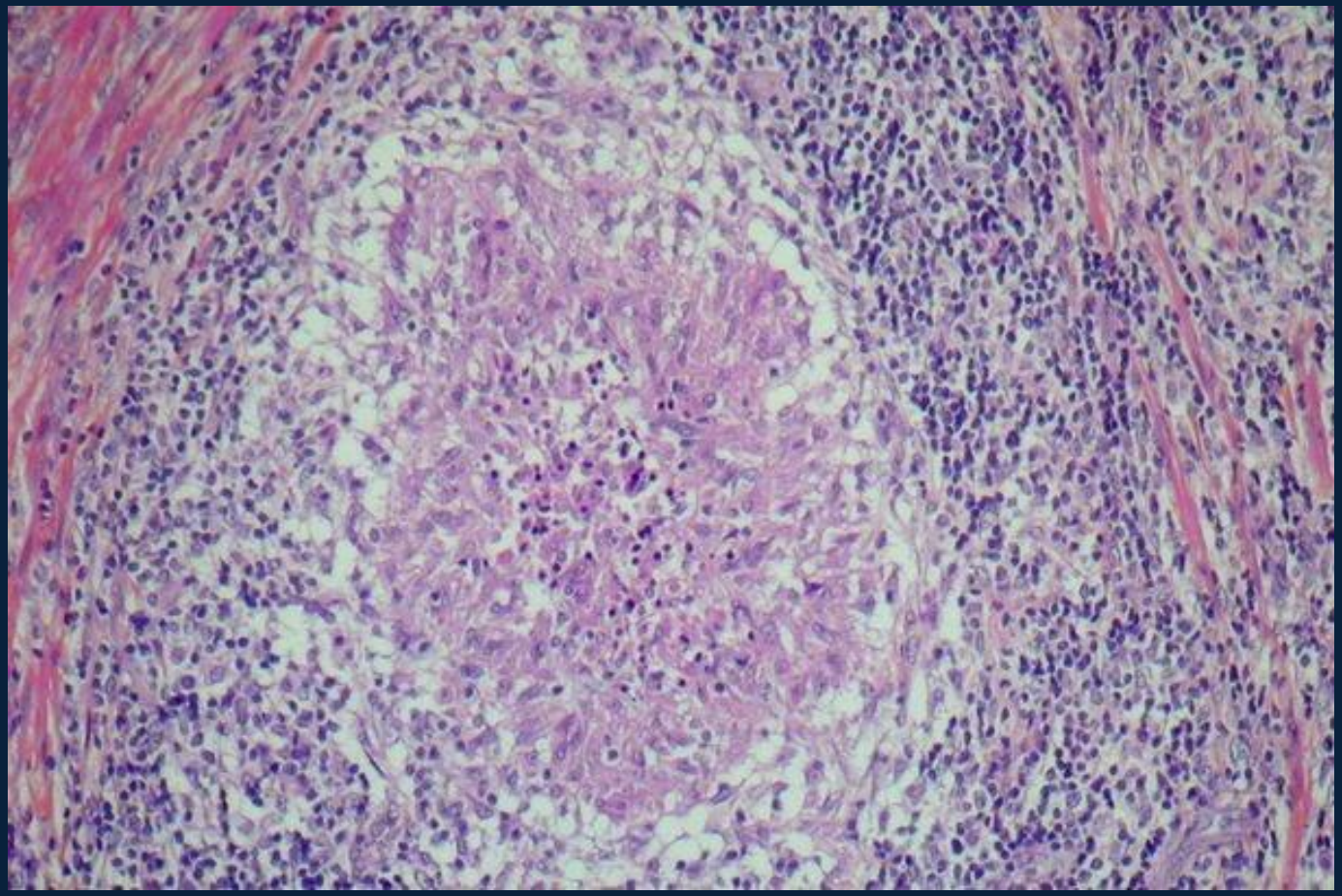
PHYSIOLOGICAL TESTS



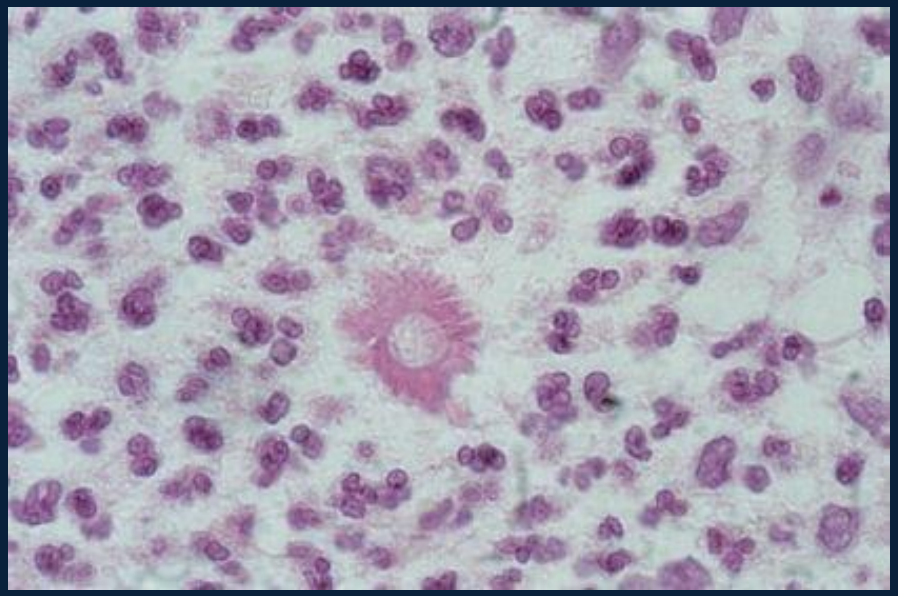
- Conversion of thermally dimorphic fungus to the yeast phase
- Brain–heart infusion agar supplemented with sheep’s blood and incubated at 37°C
- Yeasts - typically oval or cigar-shaped

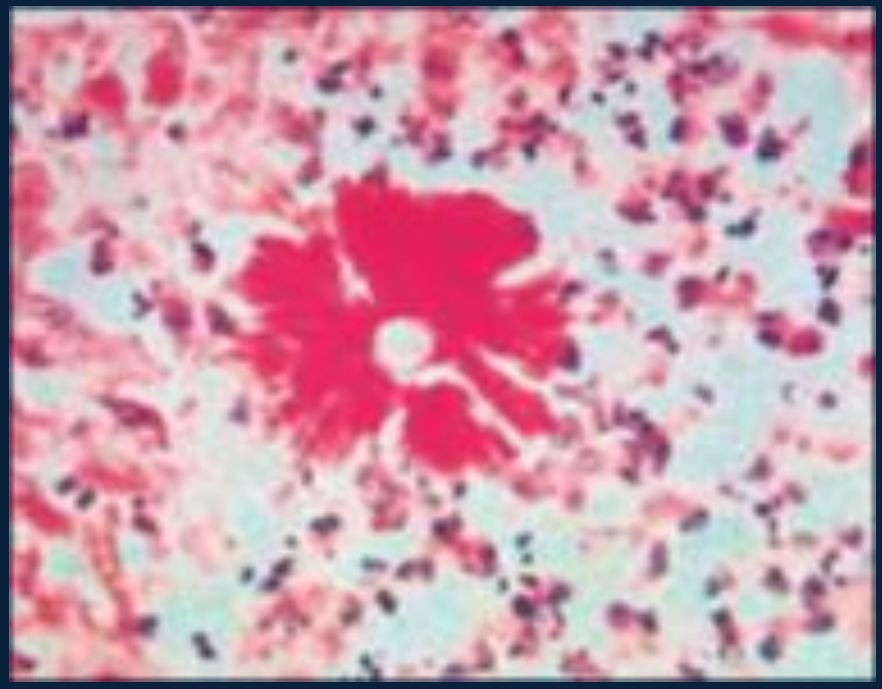
HISTOPATHOLOGY

- Epidermal hyperplasia
- Hyperkeratosis
- Intraepidermal abscesses
- Mixed granulomas with asteroid bodies



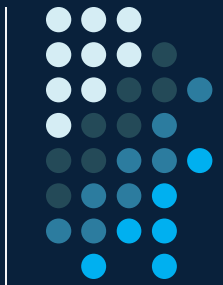
“Suppurative” zone
“Tuberculoid” zone
“Round cell”





Asteroid bodies

HISTOPATHOLOGY



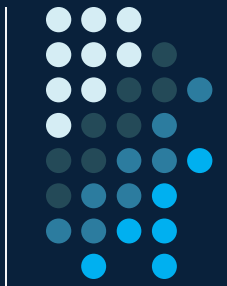
- The sporothrix **asteroid body** is - extracellular and consists of a central cigar shaped or oval basophilic yeast with thick radiating eosinophillic spicules - known as ‘Splendore - Hoeppli phenomenon’

- Specific for sporotrichosis

PAS STAIN

- Rarely, PAS stain reveals round to oval, cigar-shaped spores within the granuloma

SPOROTRICHIN TEST



- An **intradermal skin test** using sporotrichin as an antigen
- Detects a delayed-type hypersensitivity reaction - can be a useful tool
- Found to be positive in > 90% of proven cases of sporotrichosis, but may indicate **previous infection**

TREATMENT

- Systemic antifungal agents : mainstay of treatment

- Thermal adjuvant therapy to systemic antifungals may be beneficial, as *S.schenckii* does not survive above 39°C

Infectious Disease Society of America Guidelines for the Management of Sporotrichosis - 2007

TREATMENT

- Itraconazole - 1st line
- Terbinafine - 1st line
- Potassium iodide - 2nd line
- Amphotericin B
- Fluconazole

ITRACONAZOLE

- Drug of choice for cutaneous disease

Infectious Disease Society of America Guidelines for the Management of Sporotrichosis - 2007

Adult doses

SPOROTRICHOSIS	ITRACONAZOLE
Lymphocutaneous/Cutaneous sporotrichosis	200 mg/d until clinical recovery (at least 3 months) if no response - upto 500 mg BD or add potassium iodide
Osteoarticular sporotrichosis	200 mg BD for at least 12 mths
Pulmonary sporotrichosis (less severe cases)	200 mg BD for at least 12 mths
Meningeal and disseminated sporotrichosis (*after response to amphotericin B)*	200 mg BD for at least 12 mths

Infectious Disease Society of America Guidelines for the Management of Sporotrichosis - 2007

Pediatric doses

- Disseminated sporotrichosis (after amphotericin B response):-

- 6 to 10 mg/kg (not > 400 mg/d)

TERBINAFINE

- 1st line
- 250 - 500 mg/ day until clinical recovery (at least 3 months)

POTASSIUM IODIDE

- Made by adding potassium iodide (KI) to hot purified water, using sodium thiosulfate as a preservative
- SSKI contains approximately 1000mg/ml i.e 50mg of iodide per drop
- Mixed with juice for intake

Infectious Disease Society of America Guidelines for the Management of Sporotrichosis

KI

- It is unclear whether KI works by a fungicidal mechanism or by enhancing the body's immunologic and nonimmunologic defense mechanisms

KI

- Treatment usually initiated with 5 drops tid and is increased as tolerated to 40–50 drops tid
-
- Treatment should be continued for at least 4 weeks after apparent clinical ‘cure’
- For children, start with 1 drop tid, increasing as tolerated, not to exceed 1 drop/kg or 40-50 drops tid, which ever is lowest

Infectious Disease Society of America Guidelines for the Management of Sporotrichosis

AMPHOTERICIN B

- Drug of choice for **systemic disease**
- Amphotericin B lipid formulation: 3-5 mg/kg/d
- Amphotericin B deoxycholate: 0.7-1 mg/kg/d

Infectious Disease Society of America Guidelines for the Management of Sporotrichosis

AMPHOTERICIN B

- Switch to itraconazole after response
- **Pediatric doses:** Amphotericin B deoxycholate: 0.7 mg/kg/d

Infectious Disease Society of America Guidelines for the Management of Sporotrichosis

FLUCONAZOLE

- Modestly effective and thus reserved for itraconazole-intolerant patients

- Doses for lymphocutaneous or cutaneous disease intolerant of itraconazole: 400-800 mg/d

Infectious Disease Society of America Guidelines for the Management of Sporotrichosis

MYCETOMA

INTRODUCTION

Synonyms

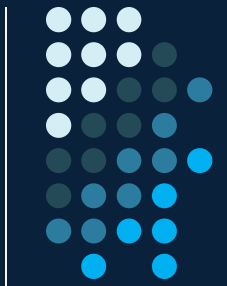
- Maduromycosis
- Madura foot

- Chronic subcutaneous localized infection characterized by the triad of -
  - Swelling
  - Discharging sinuses
  - Discharge of granules (sclerotia)

INTRODUCTION

- Granules - aggregates of causative organisms found within abscesses
- Granules drain via sinuses onto skin surface - involve adjacent bone (osteomyelitis)

INTRODUCTION



- First described by Gill of Madura in South India in 1842 - hence the name 'madura foot'

- Dr. Henry Vandyke, Grant Medical College, Mumbai - coined ' mycetoma' - fungal tumor

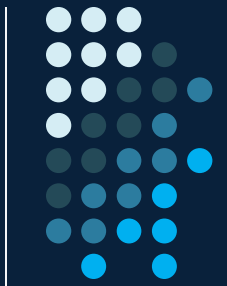
- Divided into two separate categories, based on etiology, by Pinoy in 1913-

1. Actinomycetoma due to bacteria
2. Eumycetoma due to true fungi

EPIDEMIOLOGY

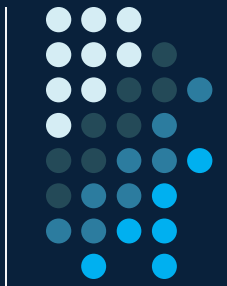
- Endemic in tropical and subtropical area
- Common - in agricultural workers (barefoot)
- Most common cause of mycetoma worldwide is eumycetes
- Actinomycotic mycetoma more common in South East Asia

EPIDEMIOLOGY



- Age incidence : 20-40 years
- Male : Female - 4-5:1
- One study suggests that progesterone levels in females may inhibit growth of certain causative species

EPIDEMIOLOGY

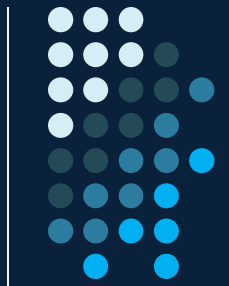


Incidence and Incubation period

- Unknown due to -
- slow, chronic nature of disease
- late presentation by majority of individuals

- Varies between 1 -2 years

Environmental factors



- Found in soil, plant material
- Thorns - Acacia bushes

ETIOLOGY

EUMYCETOMA

- Dark Grains

  Madurella mycetomatis
  Madurella grisea
  Leptosphaeria senegalensis
  Curvularia (Cochliobolus) lunata

- Pale Grains

  Scedosporium apiospermum
  Neotestudina rosatii
  Acremonium (Sarocladium) spp
  Fusarium spp

ACTINOMYCETOMA

- Actinomadura species

  Actinomadura madurae
  Actinomadura pelletieri

- Streptomyces species

  Streptomyces somaliensis

- Nocardia species

  Nocardia brasiliensis
  Nocardia otitidis- caviarum
  Nocardia asteroides

PATHOPHYSIOLOGY

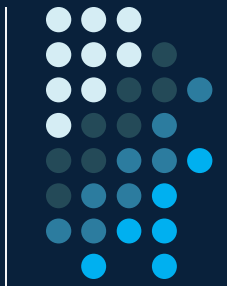
- Ability to form cell clusters or grains - critical for survival
- Actinomycetes - protective matrix present
- Fungi - cell wall thickening due to intrahyphal growth and linkage of adjacent cell wall
- In M. mycetomatis - Deposition of melanin in cell wall and as surrounding matrix
- Melanin - binds to antifungals and inhibits action

CLINICAL FEATURES

Depends upon

- Duration of the disease
- Type of causative organism
- Site of the infection
- Possibly - immune response of the host

CLINICAL FEATURES



- Clinical features of both fungal and actinomycete mycetomas are very similar
- Site - most common on the foot, lower leg, or hand
- Head or back involvement may occur

CLINICAL FEATURES

Earliest stage of infection

- A firm, painless nodule that spreads slowly with the development of papules and draining sinus tracts over the surface
- Sinuses may open for months or may close or reopen; or replaced by new sinuses

CLINICAL FEATURES

- Usually painless
- Mycetoma lesion has been suggested to produce substances that have an anaesthetic effect

In final stages of the disease,

- Pain might be due to invasion of the bone or to secondary bacterial infections

CLINICAL FEATURES

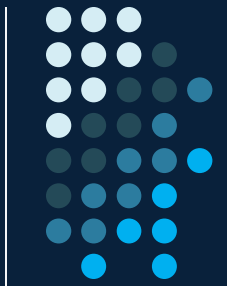
- With progression new nodules are formed around the original abscesses, which may heal
- These structures develop slowly below the thickened scar tissue

CLINICAL FEATURES

- Skin attaches to underlying granulomata - which expand stretching the overlying skin - resulting in a smooth and shiny appearance

- Portions of sclerotia breaks from parent structure - transported deeper to muscle tissue - between muscular layers following fascial planes

CLINICAL FEATURES



- Whole area becomes hard and swollen
- Extension to underlying bones and joints gives rise to periostitis, osteomyelitis and arthritis
- Gross deformity
- Lymphadenopathy is rare

Mycetoma

Mycetoma

Clinical differences between actinomycotic and eumycotic mycetoma

	Actinomycetes	Eumycetes
Causitive organisms	Bacteria	Fungus
Clinical lesions	Diffuse with no clear margin	Well encapsulated with well defined margins
Sinuses	Many	Few
Colour of grains	Various but not black	Various usually white or black
Gram's stain	Gram-negative centers with Gram-positive, fine, radiating fringes ≈1μm in diameter	Gram-negative septate hyphae embedded in intercellular cement with filaments wider than 1μm
Course of infection	Inflammatory with rapid progression	Slowly progressive
Bony involvement	Rapid	After a long period of time

DIAGNOSIS

- Clinical diagnosis
- Direct microscopy
- Gram stain
- KOH mount
- Fungal culture
- Histopathology

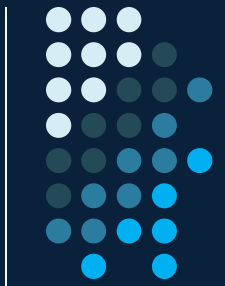
Clinical diagnosis

- Triad of -

1. subcutaneous swelling
2. nodules
3. discharging sinuses

- should raise the suspicion of mycetoma

Direct microscopy



- Pus, serosanguinous scrapings of biopsy material examined for presence of granules
- Grains collected by saline dressings applied over the swelling for 24 hrs
- Mycetoma grains may be key to establishing diagnosis

- Direct microscopy of grains : show whether grain is composed of small actinomycete or broader fungal filaments

- Black grains - fungi
- Red grains - actinomycetes

Gram stain and KOH mount

- Actinomycotic granules - composed of gram positive filamentous mycelium of bacterial width

- Eumycetic granules - consist of broad septate hyphae

- Nocardia spp. are weakly acid fast (1% sulphuric acid is used to decolourise)

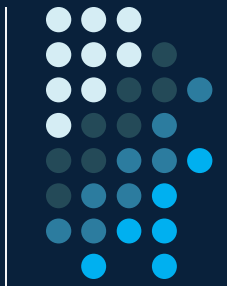
- Crushed grains stained with lactophenol blue allows differentiation between -
- thin filaments of actinomycetoma
- thicker filament of eumycetoma

FUNGAL CULTURE

- Madurella mycetomaitis - initially pale and leathery colonies - - become brown or grey after few days

- Scedosprorium apiogpermum - rapid growth of grey or brown surfaced colonies

HISTOPATHOLOGY

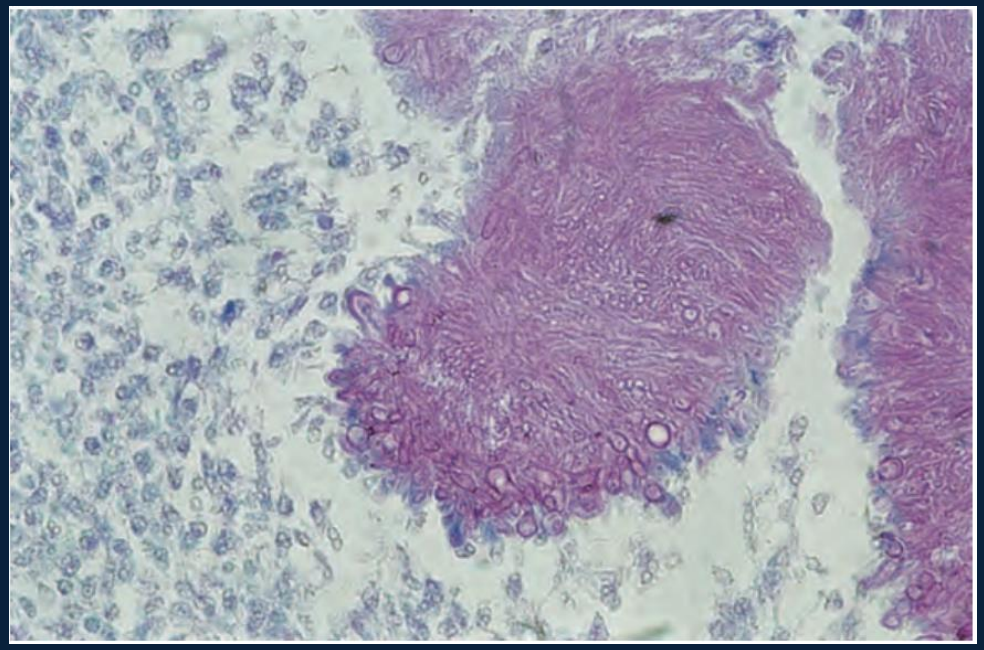


- Skin biopsy should be deep and taken from small abscess or an unruptured sinus
- Multiple biopsies (at least 3) should be taken because all parts of swelling do not contain grains uniformly

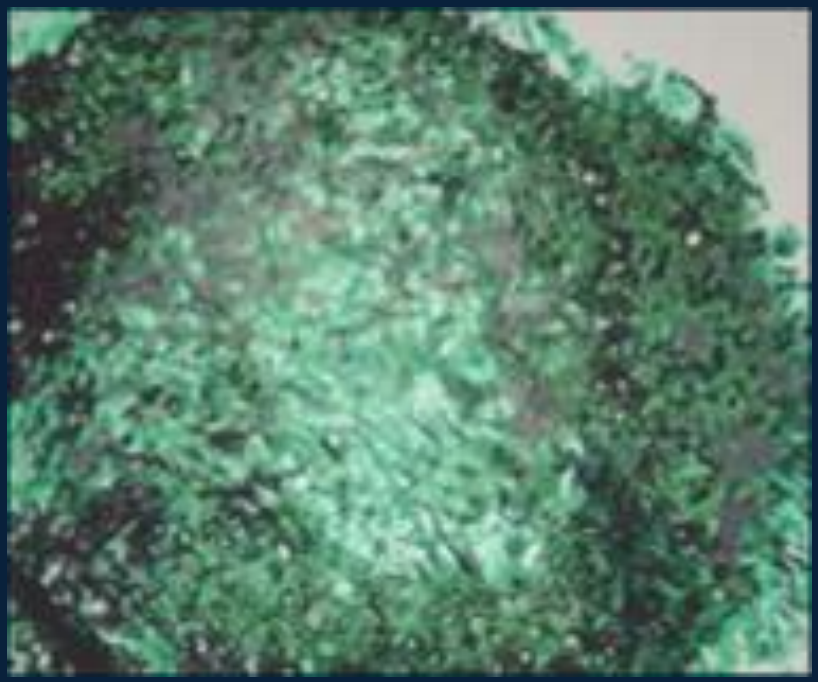
- Chronic inflammatory reaction with neutrophil abscesses and scattered giant cells and fibrosis
- Grains (50 to 250 μm) are found in the centre of the inflammation
- Granulation tissue nonspecific in appearance

- Diagnosis established only by finding sulphur granules
- Granules of both mycetoma stain with PAS and methamine silver
- Granules of eumycetoma - composed of septate hyphae 4-5μm
- Granules of actinomycetoma - consist of fine branching filaments of 1μm thickness

Distinct hyphal filaments, stained pink with periodic acid–Schiff (PAS), are clearly visible in a pale-grained eumycetoma

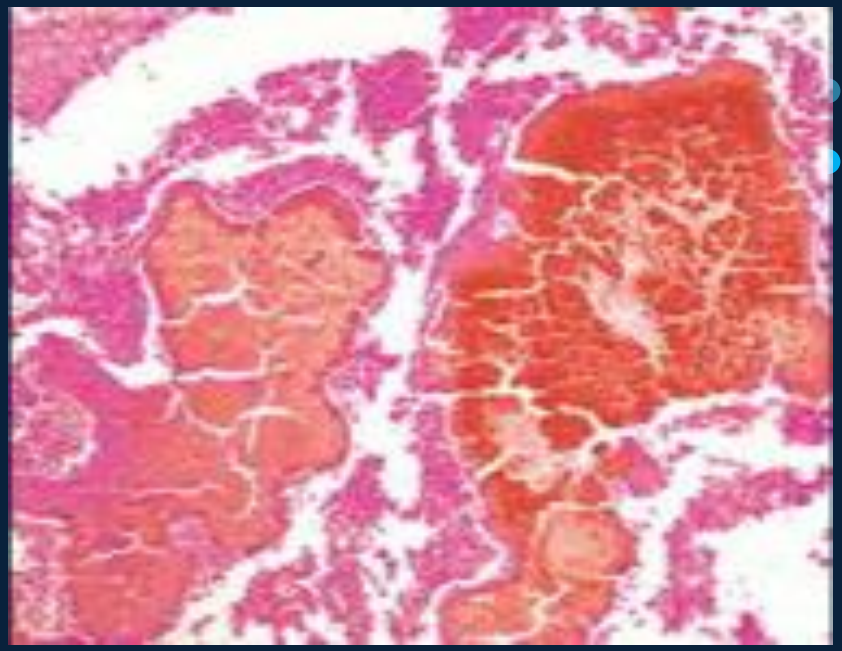


EUMYCETOMA

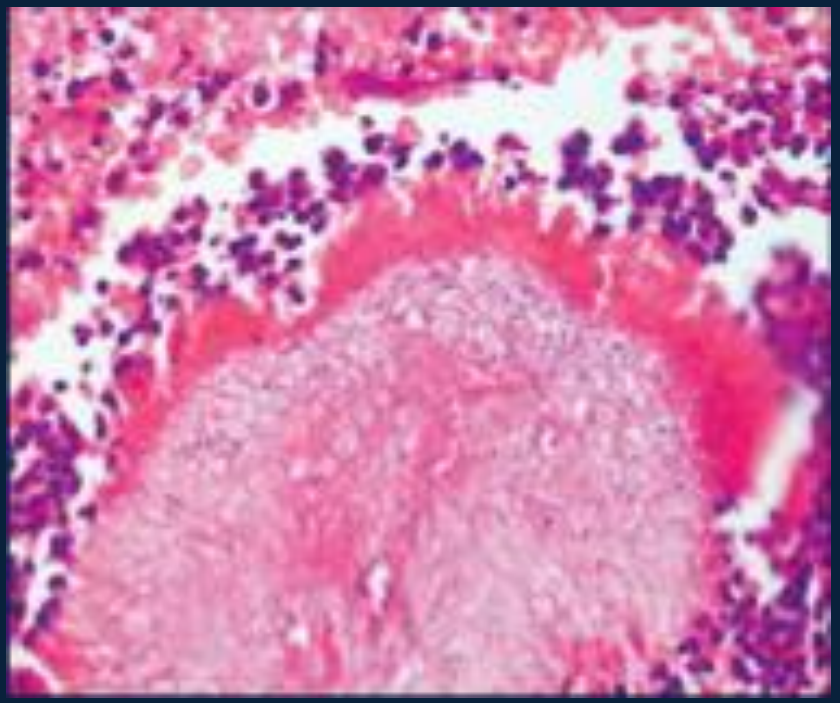


Grain made up of numerous stained fungal hyphae and larger thick walled chlamydospores - GMS stain

Grain of Madurella - Brown grain is surrounded by a thin layer of Splendore - Hoeppli material and collection of neutrophils

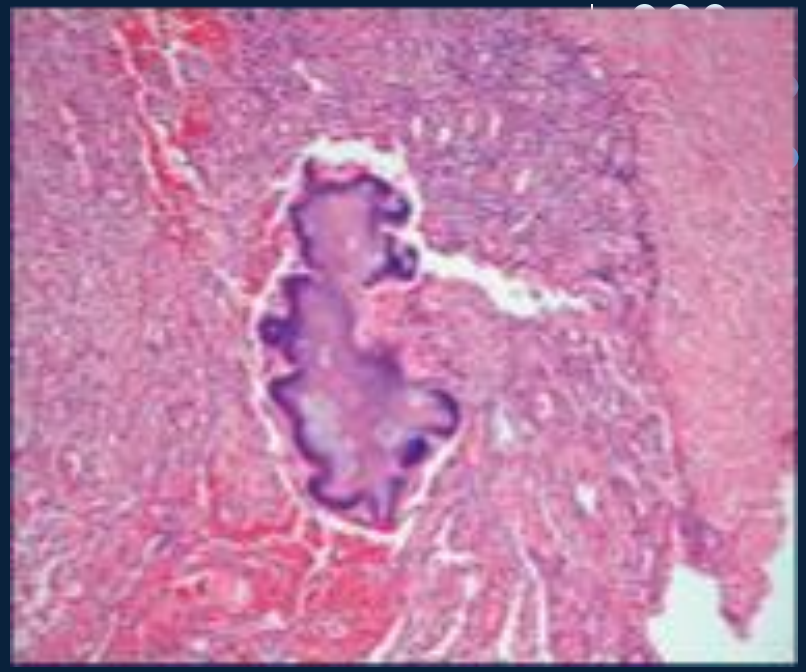


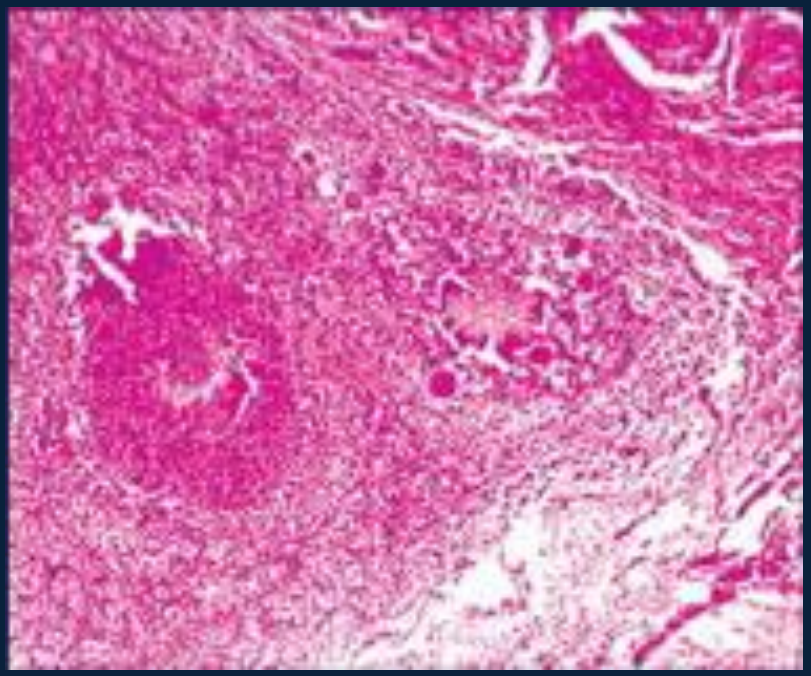
EUMYCETOMA



Grain consisting of multiple, thick walled chlamydospores and hyphae. Prominent Splendore - Hoeppli reaction

Grain surrounded by homogenous eosinophilic material (Splendore Hoeppli reaction)





ACTINOMYCETOMA

Small eosinophilic grains at the centre of suppurative granulomatous inflammation

DIFFERENTIAL DIAGNOSIS

- Early - fibroma, lipoma, sebaceous cyst, dermoid cyst, foreign body granuloma, chronic abscess
- Developing stage - Neoplasms, Kaposi’s sarcoma, syphilis, yaws, leprosy, TB, leishmaniasis
- Late stage - actinomycosis, botryomycosis, osteomyelitis

COMPLICATION

- Bone destruction - leading to deformity
- Osteomyelitis
- If on scalp - skull penetration
- If on chest wall - lung invasion

COURSE

- Does not spontaneously resolve
- Slow progression

MANAGEMENT

- Localized lesions - excised without residual disability
- First line - Dapsone + streptomycin / rifampicin OR co trimoxazole + streptomycin or rifampicin
- Second line - Radical surgery (amputation)

TREATMENT

Actinomycetoma

- Usually responsive to antibiotic treatment
- Cure rates vary widely (60% to 90%)
- Mean duration of treatment being >1 year
- Recurrence rates - increase if treatment course not completed

TREATMENT

Medical Treatment of Actinomycetoma -

- Sulfonamide
- Trimethoprim sulfamethoxazole
- Isoniazide
- Tetracyclines
- Oxytetracycline
- Minocycline
- Streptomycin
- Rifampin
- Amikacin
- DDS: diamino-diphenyl-sulfone(Dapsone)
- Imipenem

Table 3 Various regimens used for actinomycetoma

Regimen	Intensive phase	Maintenance phase
Welsh regimen[3] (1987)	Amikacin 15 mg/kg/d IM 12 hourly in two divided doses + Tab sulfamethoxazole (35 mg/kg/d) and trimethoprim (7 mg/kg/d) equally divided in three doses for 21 days constituting one cycle. One to three such cycles are given at the interval of 15 days during which tablet sulfamethoxazole-trimethoprim is given in same dose	Tab sulfamethoxazole-trimethoprim in same dose 2 weeks after last cycle.
Ramam regimen[4] (2000)	Crystalline penicillin 10 lakh units IV 6 hourly + Gentamicin 80 mg IV 12 hourly+ Tab cotrimoxazole(80/400) two tablets twice daily (Duration – 5 to 7 weeks)	Tab cotrimoxazole(80/400) two tablets twice daily + Tab amoxicillin 500 mg thrice daily for 2–5 months after disease becomes inactive
Modified two step Ramam regimen[5] (2007)	Step1- Gentamicin 80 mg IV 12 hourly + Tab cotrimoxazole(80/400 mg) two tablets twice daily (Duration – 4 weeks)	Step-2- Cap doxycycline 100 mg twice daily + Tab cotrimoxazole (80/400 mg) two tablets twice daily (Duration-till 5–6 months after complete healing of all sinuses)
Modified Welsh regimen (Damle *et al.* 2008)[10]	Amikacin 15 mg/kg/d in two divided doses + Tab sulfamethoxazole-trimethoprim 35 + 7 mg/kg/d + Cap rifampicin 10 mg/kg/d for 21 days constituting one cycle. One to three such cycles were given at interval of 15 days during which tab sulfamethoxazole-trimethoprimin and cap rifampicin in same doses were given.	Tab sulfamethoxazole-trimethoprim 35 mg/kg/d + Cap rifampicin 10 mg/kg/d after last cycle for 3 months

TREATMENT

Eumycetoma

- Usually require both medical and surgical intervention
- Medical management - to reduce size of lesion and prevent recurrence
- Medical management of eumycetes discontinued - with clinical, serologic, radiologic, and ultrasonic cure

TREATMENT

Drugs used for Eumycetomas -

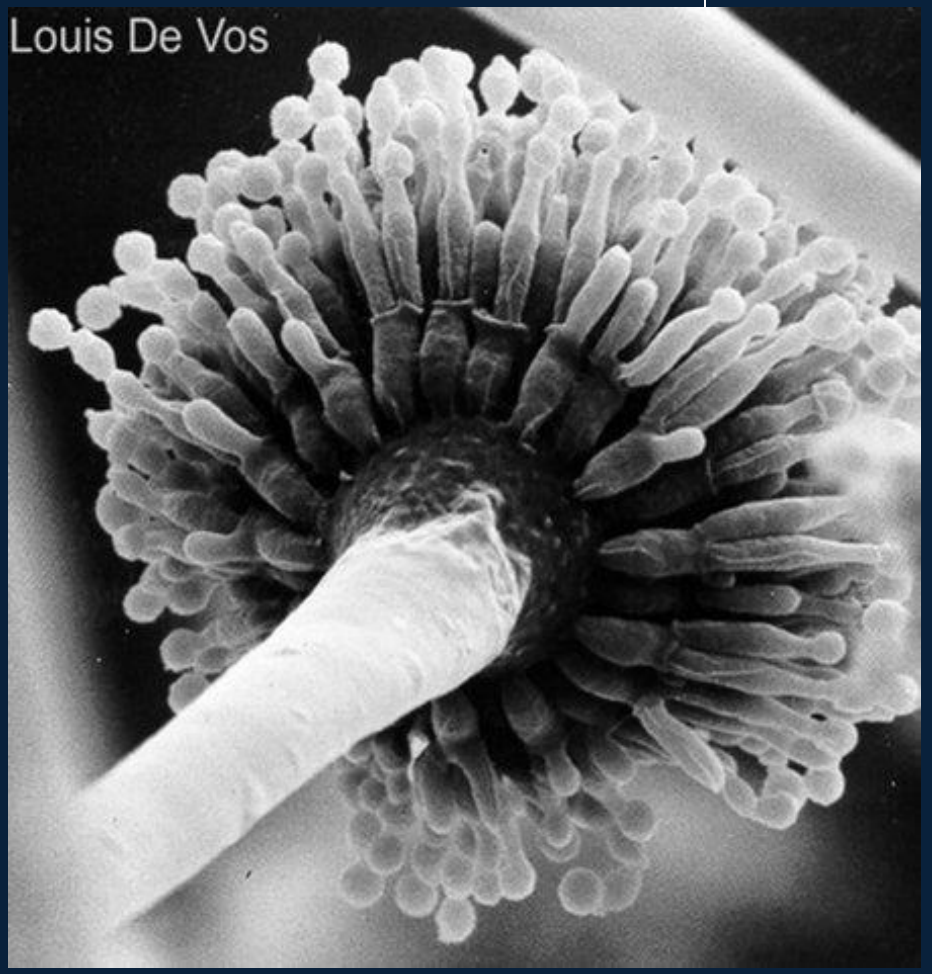
- Ketoconazole: 200-400mg/ d
- Itraconazole: 300-400mg/d
- Terbinafine: 500mg BD
- Voriconazole: 400-600mg/d
- Posaconazole: 800mg/d

TREATMENT

Causes of resistance to antifungals :-

- Cell wall modification: thickening, duplication, proliferation of polysaccharide cytoskeleton of cell wall
- Deposition of immunoglobulin (IgM) around grain
- Production of extracellular matrix – cement composed of phenols and melanin
- Pigment production – melanin
- Extracellular toxins
- Immunomodulation

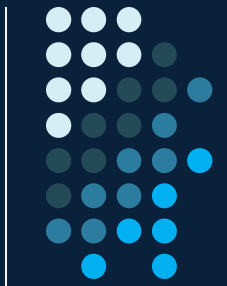
CHROMOBLASTOMYCOSIS



Synonyms

- Chromomycosis
- Verrucous dermatitis

DEFINITION



- A chronic fungal infection of skin and subcutaneous tissues caused by brown black pigmented fungi (dematiaceous fungi)
- Produce thick walled single- or multicelled clusters (sclerotic or muriform bodies) in tissue
- Characterized by production of slow growing exophytic lesions - on feet and legs

ETIOLOGY

- Different pigmented fungi, the most common being :
  - *Phialophora verrucosa*
  - *Fonsecaea pedrosoi*
  - *Fonsecaea compactum*
  - *Wangiella dermatitidis*
  - *Cladophialophora carrionii*

- Rare causes include *Rhinocladiella aquaspersa*

- Usually found in tropics and areas of rainfall
- Causal fungi - isolated from wood and soil
- Infection - trauma - puncture from splinter of wood
- Found in rural communities of tropical countries
- Adult male agricultural workers are most often affected

CLINICAL FEATURES

- Lesions - usually found on exposed sites (feet, legs, arms, face and neck)
- A warty papule slowly enlarges to form a hypertrophic plaque
- In some - plaque is flat and expands slowly with central scarring
- Sometimes, cauliflower like
- Early lesion may occasionally be an ulcer
- Secondary ulceration may occur

Chromoblastomycosis

It may present as -

- localized (m/c)
- multiple - satellite lesions seen
- sporotrichoid - lymphatic spread

- After months or years - large hyperkeratotic masses are formed, and these may be as large as 3 cm thick
- Lesion is usually painless unless presence of secondary infection - itching and pain
- Satellite lesions - produced by scratching
- Lymphatic spread to adjacent areas
- Haematogenous spread - rare (brain abscesses)

- Secondary infection - after several years - lymphatic stasis - elephantiasis
- Some forms of infection - psoriasiform lesions
- Squamous carcinomas may develop in chronic lesions

LAB DIAGNOSIS

- Superficial skin scrapings from the surface of lesions - pigmented hyphae
- Histopathology
- Fungal culture

Histopathology

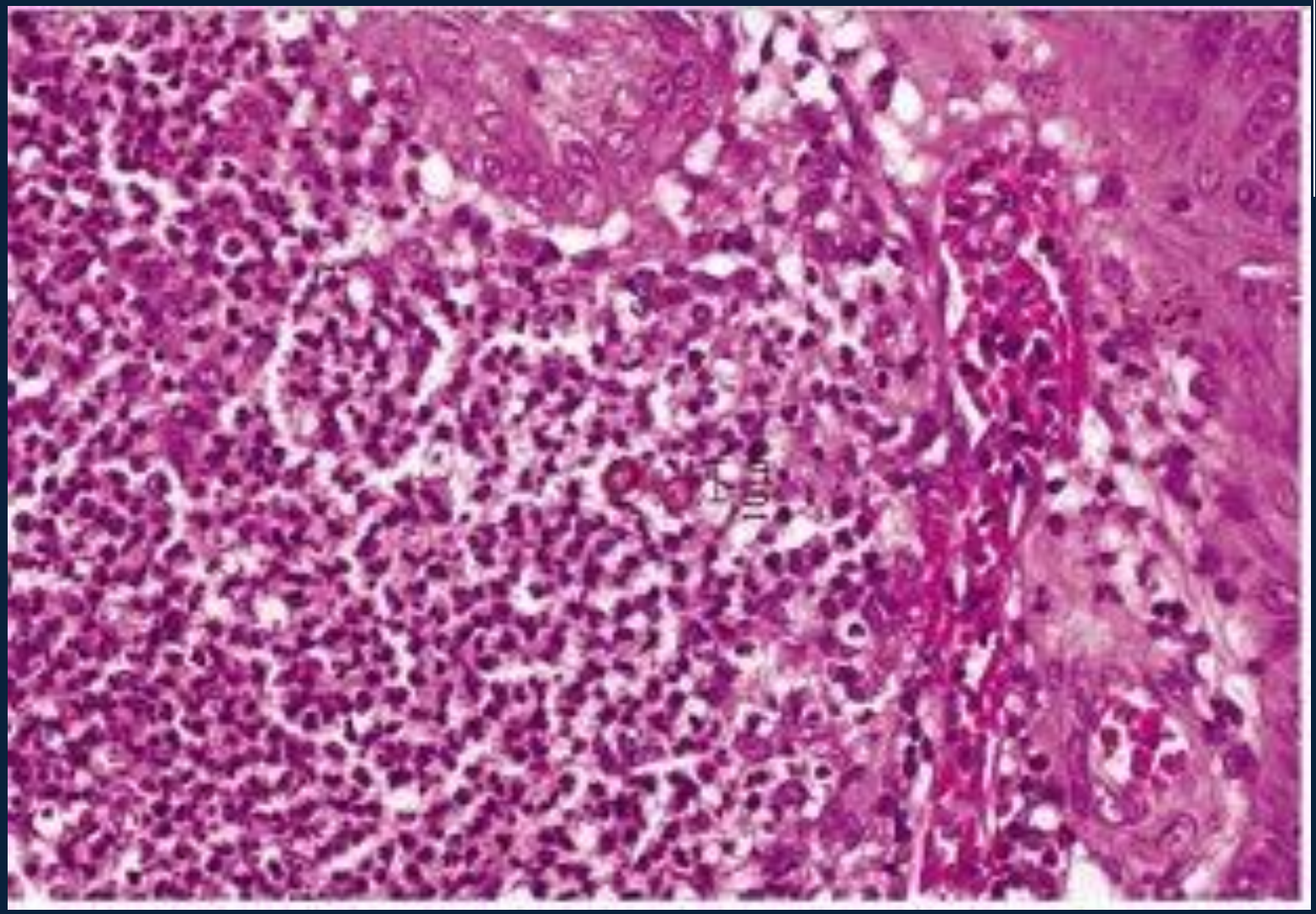
- Suppurative granulomas - epithelioid cells, lymphocytes, histiocytes and Langhans giant cells
- Eosinophils, neutrophils and plasma cells
- Epidermis - acanthosis, elongation of rete ridges, hyperkeratosis, parakeratosis

- Biopsy sections - deeply pigmented, thick-walled muriform or sclerotic cells in abscesses, giant cells or epidermis

- Fungi found in epidermis - k/a transepithelial elimination

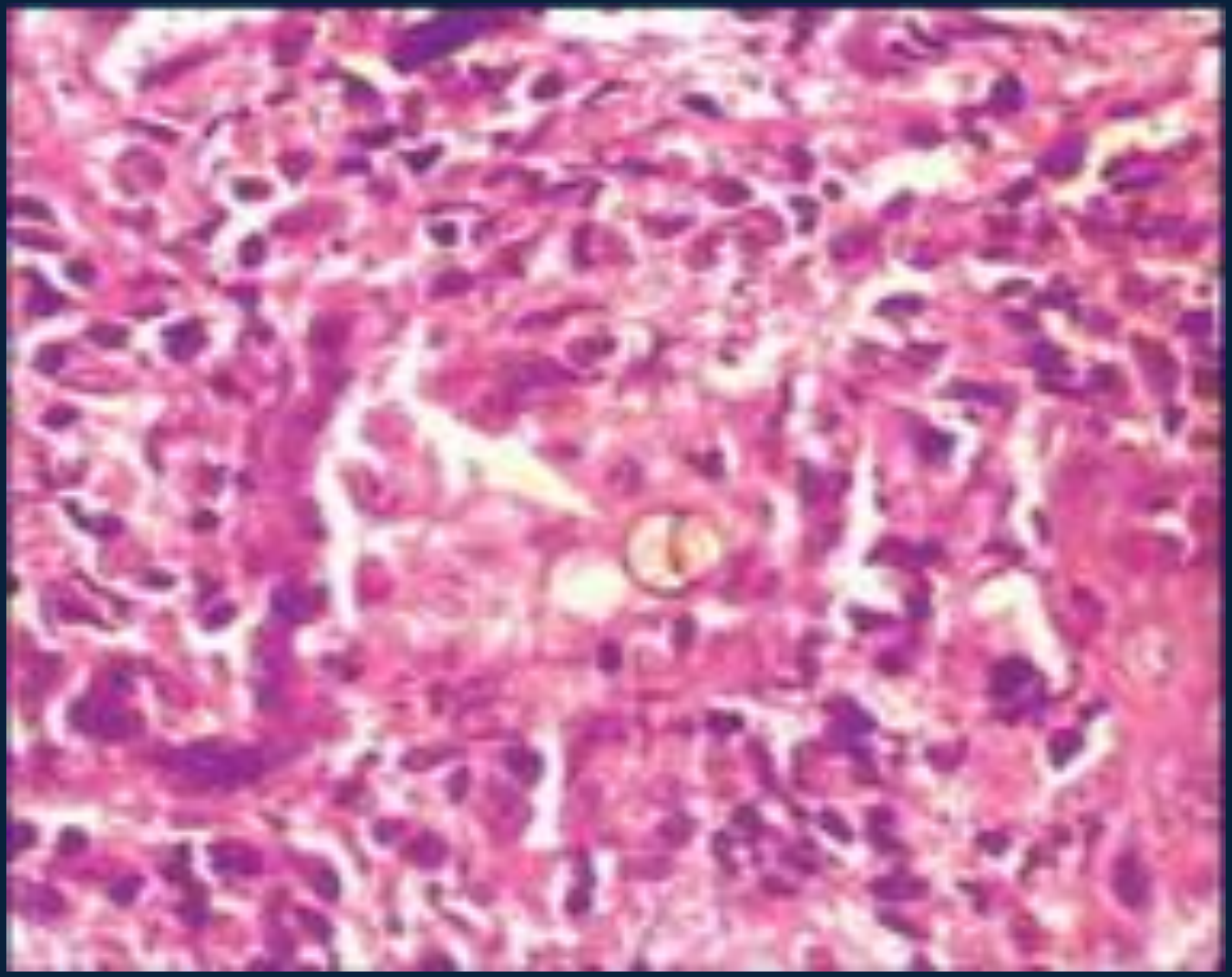
- Sclerotic bodies / muriform cells - pigmented fungal structures known as ‘medlar bodies, copper pennies or fumagoid bodies’

- Dematiceous ells dividing in more than one plane, results in splitting of cells, forming single, two celled or multiple celled clusters



Pigmented spores (adjacent to scale marker) resembling "copper pennies" are surrounded by a neutrophilic infiltrate (H&E stain)

Chromoblastomycosis: tissue section. The natural brown pigment of the fungal muriform cells is clearly visible. The cells divide by fission and may form septa in more than one plane of division



Septate, thick walled yellow brown sclerotic body within a granuloma

Fungal culture

- Colonies of all species - dark grey–green to black and velvety or downy, with a black reverse

- Three forms of conidial production:

1. acropetal budding
2. production of phialides
3. sympodial conidiation

Phialophora verrucosa:

- Microscopy: flask-shaped phialides with a pronounced dark collarette at the apex
- Laterally or terminally
- Hyaline thin-walled elliptical conidia - at the tip of the phialide in basipetal succession and collect as balls
- On nutritionally weak media - few sympodial or acropetal conidiogenous cells

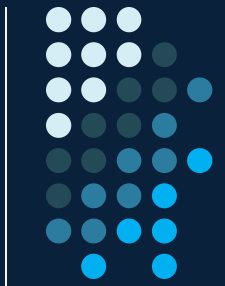
Cladophialophora carrionii

- Microscopy: acropetal budding is dominant, producing long chains of pale, oval or lemon-shaped conidia
- The chains branch at frequent intervals
- On starvation media, such as half-strength cornmeal agar - bulbous phialides may be produced by the conversion of some of the cells within the branched chains

Fonsecaea pedrosoi

- Microscopy: the dominant form of conidiation is sympodial with the conidia confined to the upper part of the cell
- The brown single-celled conidia are produced on short denticles and may in turn produce secondary conidia in a similar manner
- Conidia produced by acropetal budding are also present in the majority of isolates, and some isolates will produce scanty phialides

DIFFERENTIAL DIAGNOSIS



- Cutaneous tuberculosis (TBVC)
- Lupus vulgaris
- Blastomycosis
- Sporotrichosis
- Leishmaniasis
- Syphilis
- Yaws
- Leprosy

COMPLICATION

- Secondary infection
- Lymphatic stasis - elephantiasis
- SCC - in chronic cases

- Has chronic course but not fatal

TREATMENT

- Itraconazole (100-200 mg daily)
- Terbinafine (250 mg daily)
- Flucytosine used on its own or combined with amphotericin B may also be effective

- Cryotherapy or the local application of heat

- Surgery - only indicated in very small lesions, and even in these should be combined with chemotherapy

PHAEOHYPHOMYCOSIS

Synonym

- Phaeomycotic subcutaneous cyst

DEFINITION

- **A rare, and generally localized,** subcutaneous or intramuscular infection, usually a cyst or abscess caused by a range of brown-pigmented (dematiaceous) fungi

- Systemic forms also exist

ETIOLOGY

- Exophiala jeanselmei
- Exophiala dermatitidis
- Cladophialophora bantiana
- Phialophora spp.
- Bipolaris spp.
- Exserohilum spp.
- Alternaria spp.

CLINICAL FEATURES

- Implantation from an exogenous source, and occasionally fragments of plant
- Initially a firm, sometimes tender nodule, which later may develop into a large cyst up to several centimetres in diameter
- Overlying epidermis - not conspicuously thickened

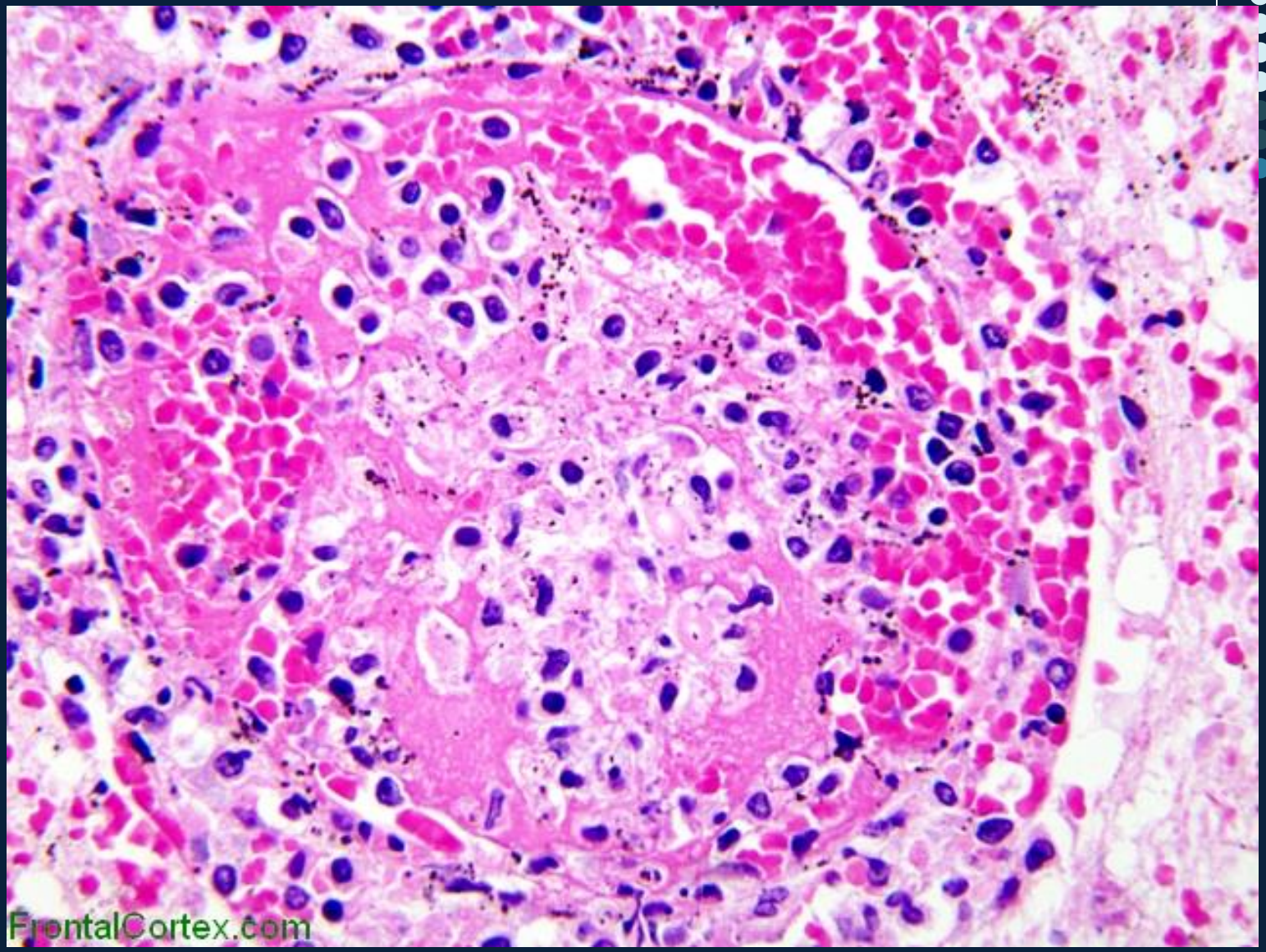
- Site - trunk pr limbs
- No tendency towards lymphatic spread
- Dissemination - uncommon
- Some patients are immunocompromised, usually through steroid therapy
- D\D: Baker’s cyst, large pilar cyst

HISTOPATHOLOGY

- The cyst wall consists of palisades of macrophages and other inflammatory cells surrounded by a fibrous capsule, and the fungal hyphae are found in the macrophage zone

- Haematoxylin and eosin sections - fungi - the brown colour

- Masson Fontana stain for melanin must be used - hyphae appear unpigmented
- Beaded or distorted hyphae - sections through these structures may give the appearance of yeast-like structures
- Specific fungal stains such - Grocott or PAS will mask the natural colour of the hyphae



Cyst with inflammatory cells and brown coloured fungi

FUNGAL CULTURE

- Fungus culture : different species may be involved, together with the failure of some primary isolates to sporulate

Exophiala jeanselmei -

- ***Colony: this fungus belongs to the group*** sometimes termed ‘black yeasts’
- The colony is initially glabrous or moist, and black in colour
- As the culture matures, it becomes more filamentous and eventually is covered with a grey velvety mycelium

- Microscopy: initially, the culture is made up of single cells, which are annellides reproducing by budding

- When the filamentous stage has developed, the septate brown hyphae bear slender annellides producing elliptical conidia, which collect in a mass at the tip of the conidiogenous cell or slide down to form a row along the side of the annellide

- Physiological tests: will not grow at 40°C

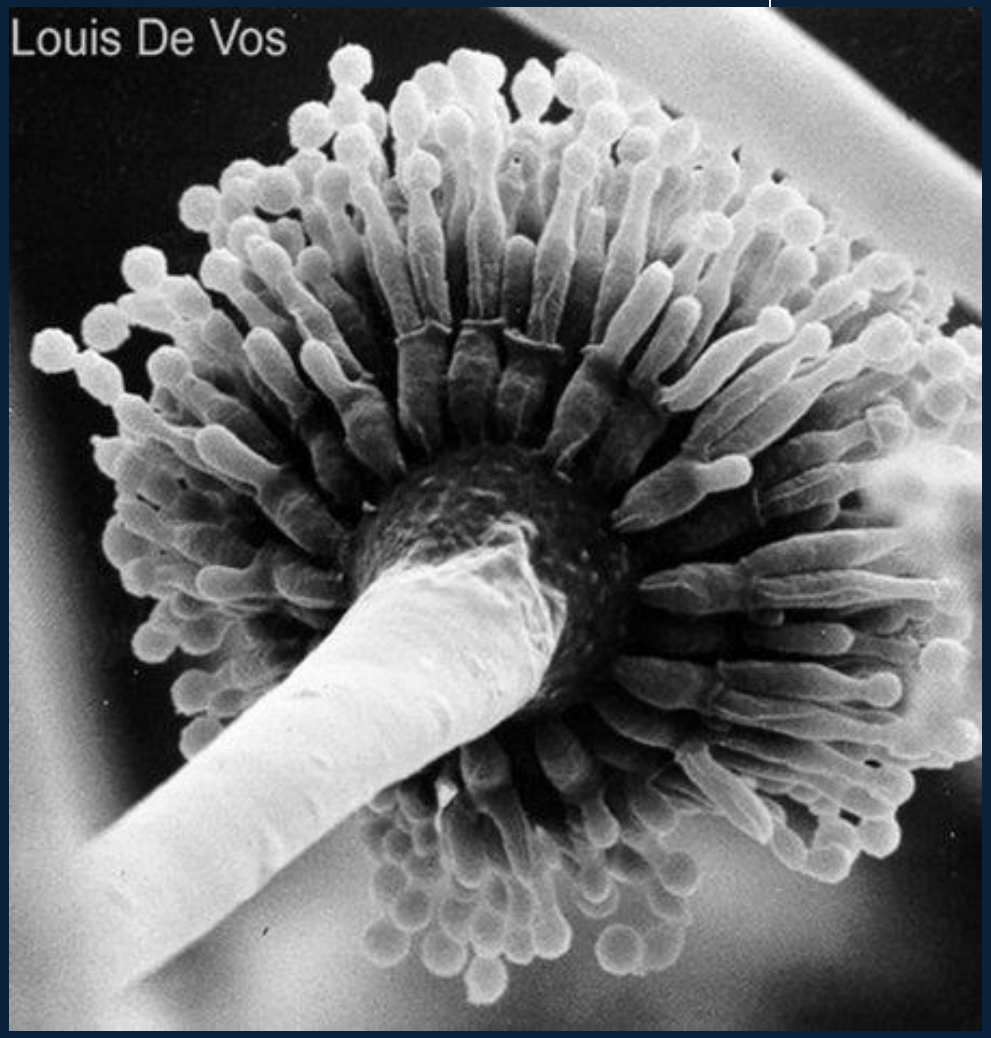
Bipolaris species

- The colonies grow rapidly
- Initially downy and pale grey, the colour darkens to olive grey or black on both surface and reverse
- Microscopy: the conidiogenous cells are geniculate, producing the brown multicellular phragmoconidia in a sympodial sequence
- The hilum at the base of the conidium is only slightly protuberant

TREATMENT

- Excision
- Relapse, particularly in immunocompromised patients
- Itraconazole is often given after surgery

LOBOMYCOSIS



Synonyms

- Keloidal blastomycosis
- Lobo’s disease

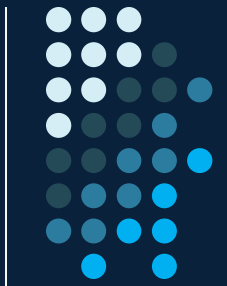
DEFINITION

- This rare disease is characterized by keloidal skin lesions that remain fairly well localized and apparently do not affect the general health of the patient
- Caused by *Lacazia loboi* associated with water and gain entry through a wound
- Also found in dolphins

PATHOGENESIS

- IP - months to years
- Local spread - auto inoculation
- Distant spread - lymphohematological dissemination
- Melanin containing birefringent cell wall resists digestion by macrophages - thus chronic

CLINICAL FEATURES



- Lesions may be found anywhere on the body, but are usually on exposed parts: legs, arms and face
- Associated with injuries to the skin, and spread from one site to another - by autoinoculation following injury
- No marked lymphangitis and no visceral dissemination

- Variable sized nodules and plaques, hyper or hypopigmented
- Ulcers, sclerodermoid, keloidal, verrucous, keratotic and vegetating plaques
- Old chronic lesions - as elevated crusted fungoid plaques
- Squamous cell carcinoma - develop in chronic lesions

multiple elevated keloidal plaques

LAB DIAGNOSIS

- Not isolated in culture
- Recognition of the characteristic cells of *Lacazia loboi in tissue*
- *Performed* with KOH mounts of epidermal crusts or sections, which need not be specially stained

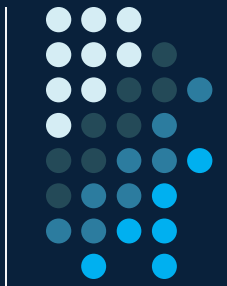
Histopathology

- Fungi, lymphocytes, macrophages and giant cells are abundant
- Fungus cells are usually round or lemon-shaped, sometimes joined one to the other with a narrow tubular neck in chains of 3 to 8
- Grenz zone sometimes
- Transpepidermal elimination
- Asteroid bodies
- Necrosis and suppuration absent

Differential diagnosis

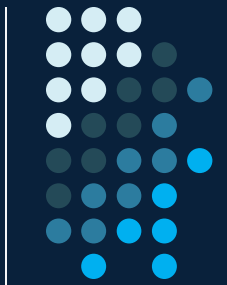
- Chromoblastomycosis
- Leprosy
- Leishmaniasis
- Keloid
- SCC/BCC

Course



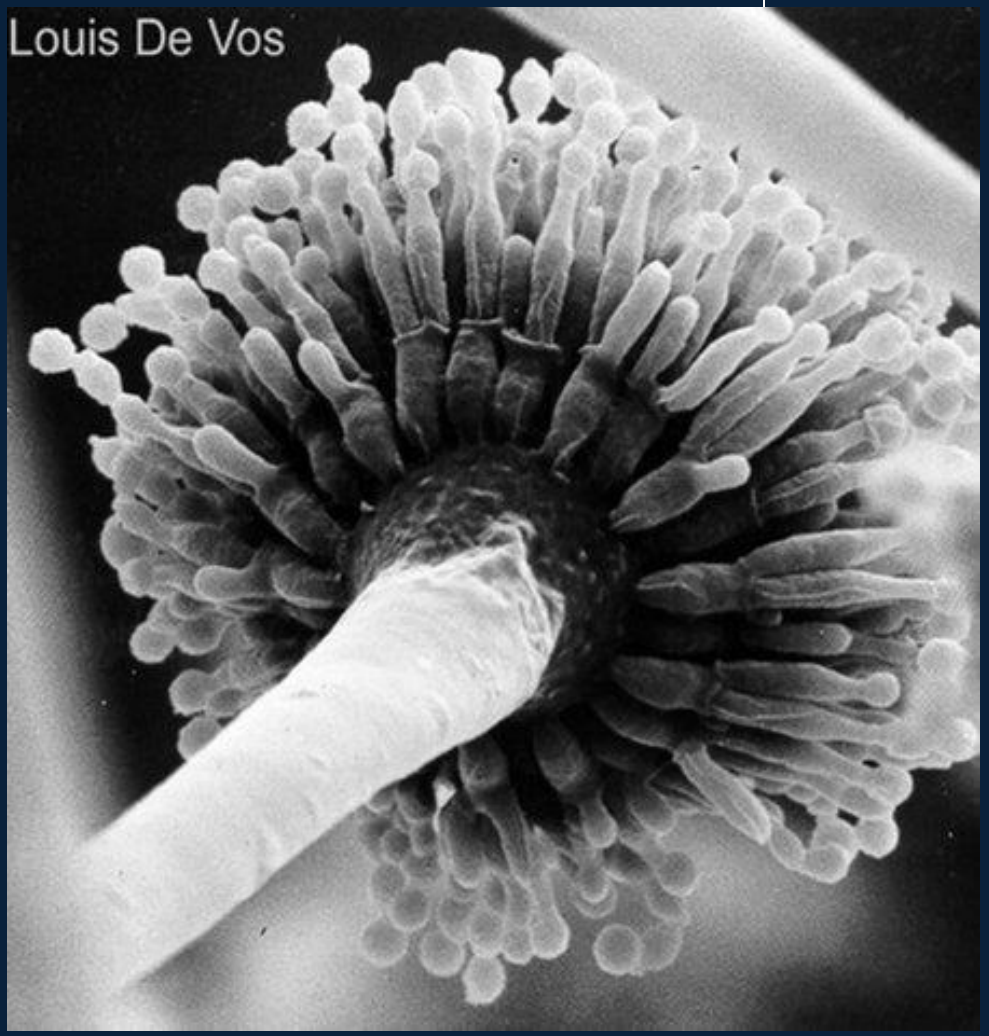
localized or slowly expands over years

TREATMENT



- No effective medical therapy
- Possible lesions are excised surgically/ cauterized, cryotherapy
- Clofazimine - 300mg/day - maintain for 100mg/d for 2 years
- Itraconazole/ Posaconazole

RHINOSPORIDIOSIS



DEFINITION AND ETIOLOGY

- A chronic granulomatous mycosis caused by *Rhinosporidium seeberi,* inducing polyps of the mucous membrane
- The organism has never been cultured, and it is now thought to be an aquatic protist and a member of the Mesomycetozoea
- Seen most often in Southern India and Sri Lanka
- Affects adult male workers

CLINICAL FEATURES

- Mucosal - friable, vascular, sessile/pedunculated polyps
- Cutaneous - friable, wart like, tumorous growths with crenated surface (dermospridiosis)
- Disseminated - lungs, liver, spleen and brain

- Vascular polyps, which may be pedunculated, occur on any mucosal surface
- Common sites: mucous membrane of the nose, the nasopharynx or the soft palate
- The conjunctiva or the lacrimal sac, the larynx, penis, vagina & rectum may be involved

- Lobulated or cauliflower like surface
- Examination of surface - small white spots, which represent mature sporangia of the fungus
- Disease may last for many years

Rhinosporodiosis

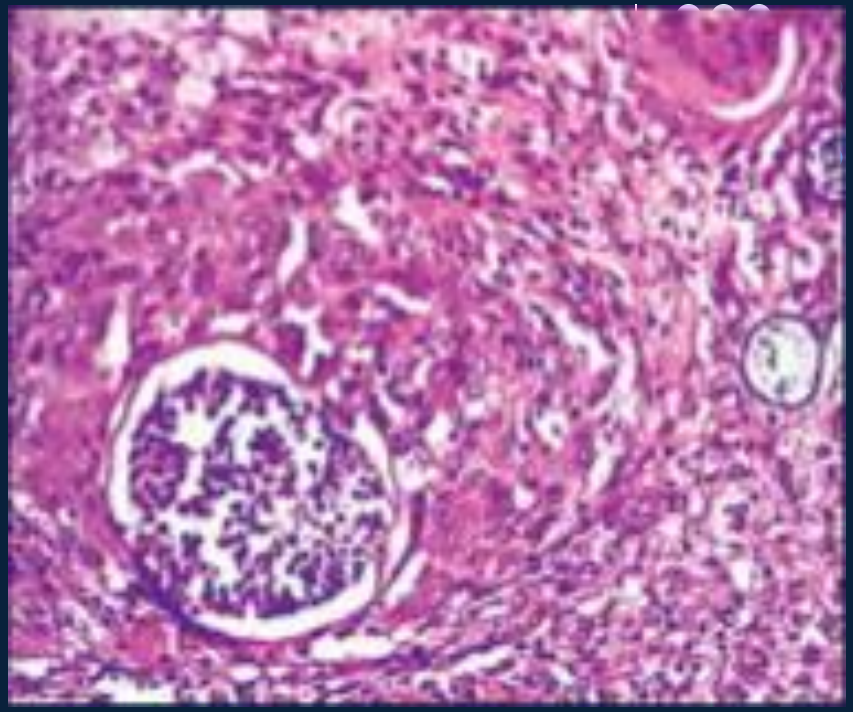
DIAGNOSIS

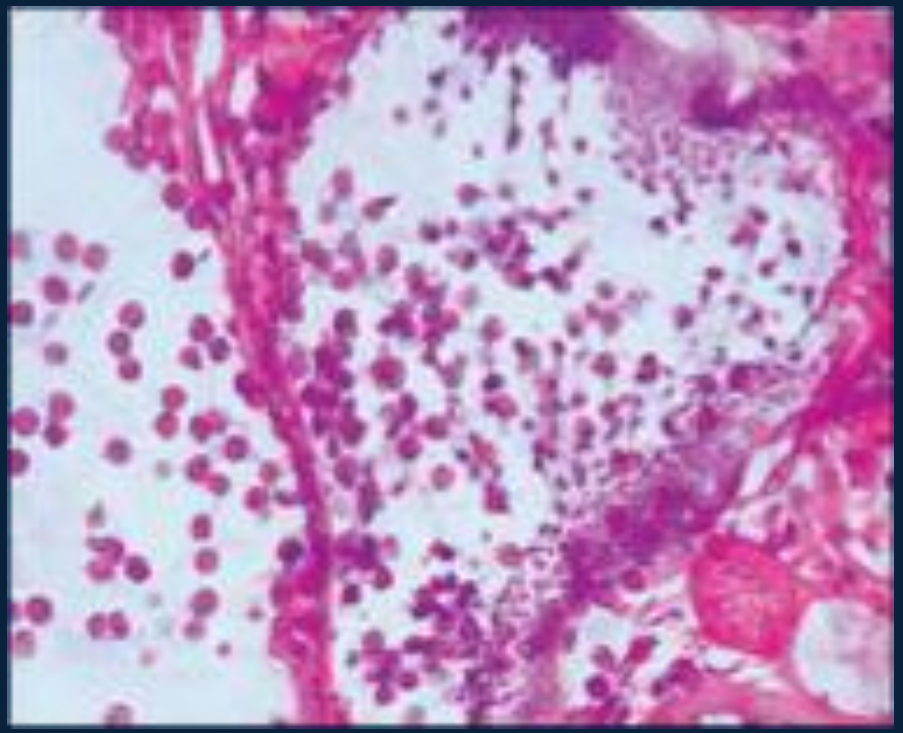
- The causative organisms cannot be cultured
- The diagnosis depends on histopathology—recognition of the sporangia seen on the surface of the polyp or in tissue sections
- Microscopy - single, thick walled, spherical, packed with numerous rounded endospores, 6-7 micrometer

HISTOPATHOLOGY

- Superficially like that of a nasal polyp but with conspicuous, sharply defined, globular cysts up to 0.5 mm in diameter
- Occasionally, microabscesses may be found

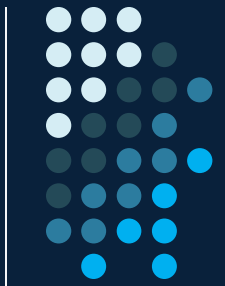
Sporangia of R. seeberi with numerous endospores. Intact mature sporangium of R. seeberi has a thick chitinous wall and variably shaped spores, some of which show eosinophilic globules





Ruptured sporangium dischaging multiple spores

DIFFERENTIAL DIAGNOSIS

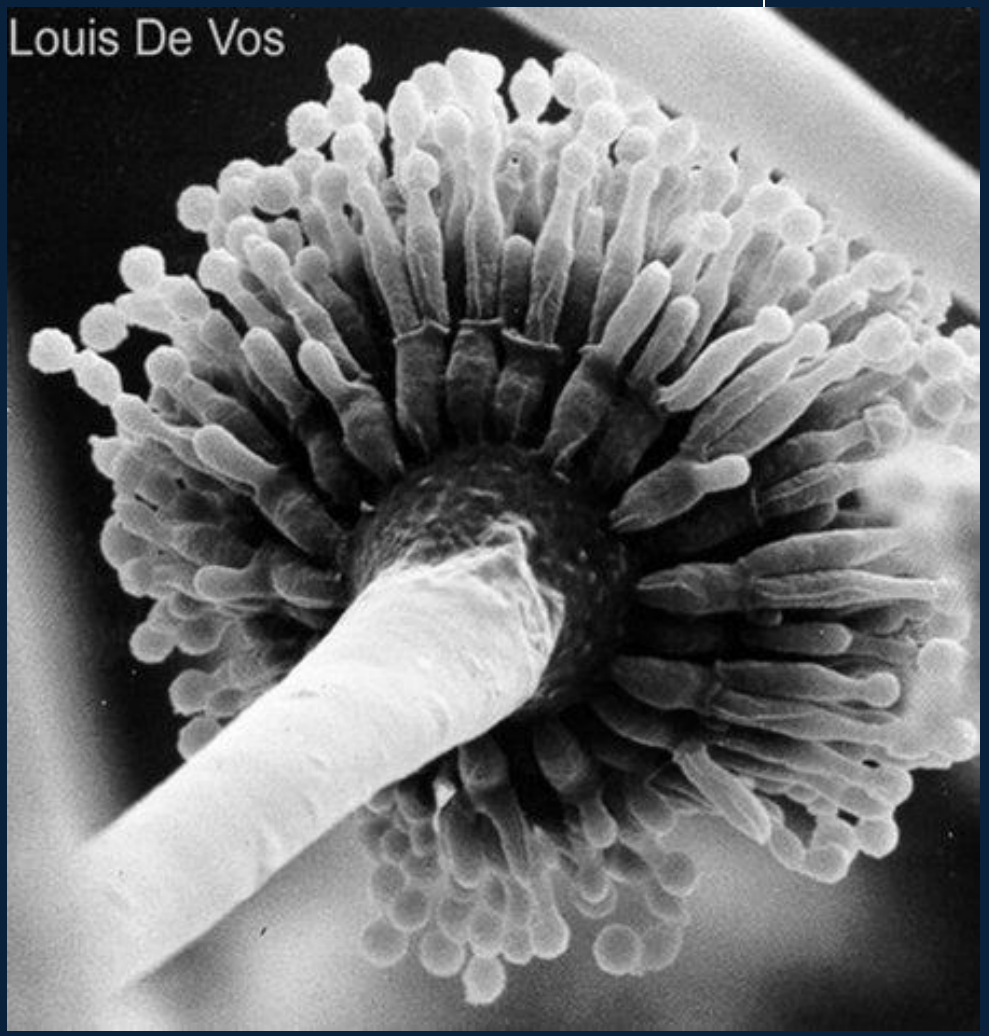


- nasal polyp
- mucocele
- hemagiomas
- pyogenic granuloma
- warts
- condylomas
- haemorrhoids

TREATMENT

- Surgical excision with cautery of floor

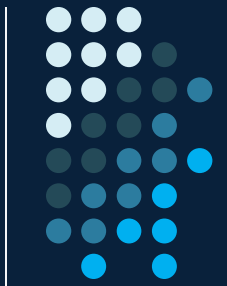
SUBCUTANEOUS ZYGOMYCOSIS



Synonyms

- Basidiobolomycosis
- Subcutaneous phycomycosis
- Conidiobolomycosis
- Rhinoentomophthoromycosis

DEFINITION



- A localized subcutaneous and predominantly tropical mycosis characterized by chronic, woody swelling of subcutaneous tissue

- Caused by order ‘ Entomophthorales’

ETIOLOGY

- *Basidiobolus ranarum*
- *Conidiobolus coronatus*

- Found in decaying vegetation and GI of frogs

CLINICAL FEATURES

Basidiobolus infections -

- *the lesion usually involves the limbs* or limb-girdle areas and the infection is most often seen in children

Conidiobolus infections
(rhinoentomophthoromycosis) -

- similar but affect the face, apparently spreading from the region of the inferior turbinates to involve the central facial tissues. It is mainly seen in young adults
- Both subcutaneous infections are very disfiguring

- Slowly spreading, painless, subcutaneous swelling
- May be single, or there may be multiple satellite lesions
- The disc shaped masses have a uniform hard consistency, and they do not pit
- The smooth rounded edge, which may be lobulated, can be raised up by inserting the fingers underneath it
- Pain and tenderness may be absent or, less often, pronounced

- The overlying skin may be tense, oedematous, desquamating, hyperpigmented or normal

- Ulceration does not occur, and the regional lymph glands are not often enlarged

Subcutaneous zygomycosis

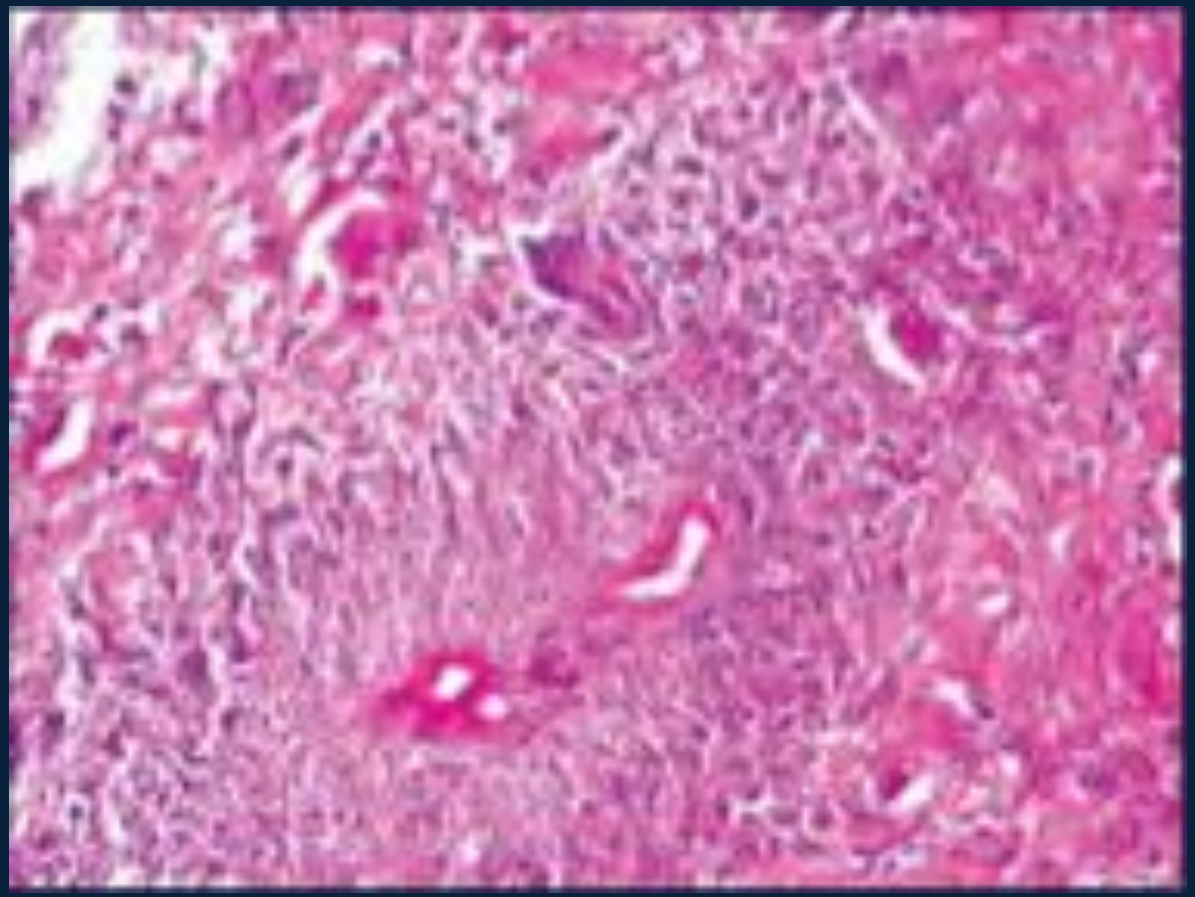
DIAGNOSIS

- Histologically by biopsy
- Culture

Histopathology

- Eosinophilic granuloma lying deep in the subcutaneous tissue and largely replacing fat

- Wide, sparsely septate hyphae, branching at right angles, are scattered throughout the granuloma and there is often dense fibrosis



Unstained, broad hyphae surrounded by an eosinophilic sleeve and a granulomatous infiltrate

Fungal culture

Basidiobolus ranarum -

- *Colony: on cycloheximide-free media at* 30°C, *as waxy cream or yellow colonies* with many radial folds
- Microscopy: the hyphae are broad, 8–20 µm in diameter and have few septa
- After 10–14 days, sexual zygospores with a prominent beak may be produced

- In addition, unicellular sporangia—sporangiola—are formed, which are forcibly ejected into the air from the tip of the sporangiophore

Subcutaneous *Basidiobolus* infection tissue section. Wide, aseptate hyphae stained bl

Conidiobolus coronatus

- *Colony: waxy white to* grey, becoming more powdery and beige as a short aerial mycelium develops
- Microscopy: wide, sparsely septate hyphae are present
- Sporangiola are forcibly discharged, and impact on the sides and lid of the Petri dish
- Some sporangiola may form small protuberances or villi all over their surfaces

DIFFERENTIAL DIAGNOSIS

- Subcutaneous malignant lymphoma (grows more rapidly)

TREATMENT

- Itraconazole is useful
- Oral treatment with potassium iodide given in similar doses to those used in sporotrichosis
- Some evidence that co-trimoxazole can be used in addition in conidiobolomycosis

Buruli Ulcer

- **Mycobacterium ulcerans infection**
- **Affects the skin and sometimes bone and can lead to permanent disfigurement and long-term disability**
- Exact mode of transmission of *M. ulcerans* is still unknown

- Painless swelling (nodule), a large painless area of induration (plaque) or a diffuse painless swelling of the legs, arms or face (oedema)

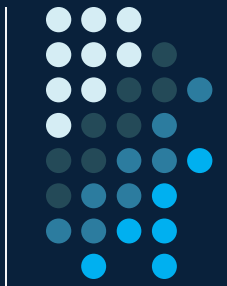
- Nodule, plaque or oedema will ulcerate within 4 weeks

- Lesions frequently occur in the limbs: 35% on the upper limbs, 55% on the lower limbs, and 10% on the other parts of the body

Clinical Classification

- Category I, single small lesion (32%) less than 5 cm on diameter;
- Category II, non-ulcerative and ulcerative plaque and oedematous forms between 5-15 cm (35%);
- Category III lesions more than 15 cm in diameter including, disseminated and mixed forms such as, osteomyelitis and joint involvement (33%).

Diagnosis



- IS2404 polymerase chain reaction (PCR)
- Direct microscopy,
- Histopathology
- Culture. The bacterium grows best at temperatures between 29–33 °C (*Mycobacterium tuberculosis* grows at 37 °C) and needs a low (2.5%) oxygen concentration.

Treatment

- Combination of rifampicin (10 mg/kg once daily) and clarithromycin (7.5 mg/kg twice daily)

- Combination of rifampicin (10 mg/kg once daily) and moxifloxacin (400 mg once daily)

Other neglected Skin diseases

THANK YOU…