Subcutaneous Mycoses

- **Acquired**: traumatic implantation of organism
- **Involving**: the dermis, subcutaneous tissues and adjacent bone
- **Organisms**: the pathogen usually a soil or plant saprophyte
- **Patients**: rural population of the tropical and subtropical
- **Dissemination**: blood or lymphatic is uncommon
subcutaneous fungal infections

1. Mycetoma
2. Sporotrichosis
3. Chromoblastomycosis
4. Lobomycosis
5. Rhinosporidiosis
6. .....
Mycetoma & madura foot & maduromycoses

- Skin, the underlying subcutaneous tissue
- **Symptoms**: from 1 month to 25 years
- **Multiple** etiologic microorganisms
- Immunocompetent
- The male-to-female ratio **3:1 and 5:1**
- No consistent differential **sex** distribution
- Feet, barefoot hands, and the back, neck....
Clinical manifestations

- Tumor(swell)
- Sinuses
- Grains

**Fig. 2** Eumycetoma due to *Madurella mycetomatis* showing multiple sinus tracts
Mycetoma show three clinical characteristics:

- Tumor
- Sinuses
- Grains
Eumycetoma:

Eumycetoma: **Africa** (Sudan, Somalia, Senegal, Nigeria, Chad and Niger), in **India** and **America** (Mexico, Venezuela, Brazil)

- Clinical course?
- Small, firm, painless subcutaneous nodule
- **Lymphatic spread?**
- Spread to adjacent tissues
- Pain, fever? When?
- Slower and less destructive course
- **Bone involvement (70%)**
Actinomycetoma:

- More common in Latin America
- Clinical course?
- Lymphatic spread?
- Progression: rapid
- Involvement of bone: earlier and more extensive
<table>
<thead>
<tr>
<th>Species</th>
<th>Geographical distribution</th>
<th>Colour of grain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eumycetomas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leptosphaeria senegalensis</td>
<td>West Africa</td>
<td>Black</td>
</tr>
<tr>
<td>Madurella grisea</td>
<td>Africa, Central and South America</td>
<td>Black</td>
</tr>
<tr>
<td>Madurella mycetomatis</td>
<td>Worldwide</td>
<td>Black</td>
</tr>
<tr>
<td>Neotestudina rosatii</td>
<td>Africa</td>
<td>White</td>
</tr>
<tr>
<td>Pyrenochaeta romeroi</td>
<td>Africa and South America</td>
<td>Black</td>
</tr>
<tr>
<td>Scedosporium apiospermum</td>
<td>North America</td>
<td>White</td>
</tr>
<tr>
<td>Acremonium species</td>
<td>Africa and Middle East</td>
<td>White</td>
</tr>
<tr>
<td>Aspergillus nidulans</td>
<td>Africa and Middle East</td>
<td>White</td>
</tr>
<tr>
<td>Actinomyetomas</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actinomadura madurae</td>
<td>Worldwide</td>
<td>White/yellow</td>
</tr>
<tr>
<td>Actinomadura pelletieri</td>
<td>Africa</td>
<td>Red</td>
</tr>
<tr>
<td>Nocardia asteroides</td>
<td>Worldwide</td>
<td>White/yellow</td>
</tr>
<tr>
<td>Nocardia brasiliensis</td>
<td>Central America</td>
<td>White/yellow</td>
</tr>
<tr>
<td>Streptomyces somaliensis</td>
<td>North Africa and Middle East</td>
<td>Yellow/brown</td>
</tr>
</tbody>
</table>
(Eumycetoma): caused by septated pigmented or hyaline filamentous fungi

- Madurella mycetomatis (black grain)
- Pseudallescheria boydii (white grain)
- Leptosphaeria senegalensis (black grain)
- Madurella grisea (black grain)
- Curvularia (black grain)
- Acremonium (white grain)
- Aspergillus (white grain)

95% of eumycetoma cases
- **Bone involvement**: occurs in up to 76% of cases

- **Radiological examination**
  - Bone destruction with formation of cavities

  - **Actinomycetoma**: small and abundant
  - **Eumycetoma**: large and less numerous

- **Magnetic resonance imaging (MRI)**
Tumorous swelling on the heel

Soft tissue swelling and osteolytic changes of the heel
DIFFERENTIAL DIAGNOSIS:

- Actinomycetoma
- Botryomycosis
- Elephantiasis
- ....
Mycetoma in Iran: Causative Agents and Geographic Distribution

- 35 cases from 1994 to 2009
- Actinomycetoma and eumycetoma was 19:16
- The male to female ratio was 22:13
- Ages ranged from 14–80 years old
- The duration of the disease: two months to 38 years
- Most common site of infection is foot
- Housewife and farmer: greater occupation risk
### Distribution of causative agents of mycetoma in Iranian patients

<table>
<thead>
<tr>
<th>Mycetoma</th>
<th>Organism</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actinomycetoma</td>
<td><em>Actinomadura madurea</em></td>
<td>11</td>
</tr>
<tr>
<td></td>
<td><em>Actinomyces israelii</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Nocardia asteroides</em></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td><em>Nocardia. caviae</em></td>
<td>1</td>
</tr>
<tr>
<td>Eumycetoma</td>
<td><em>Aspergillus fumigatus</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus flavus</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus terreus</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Petriellidium boydii</em></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td><em>(Pseudallescheria boydii)</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Fusarium solani</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td><em>Paecilomyces lilacinus</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td><em>Acremonium sp.</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td><em>Fonseca pedrosoi</em></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><em>Candida albicans</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td><em>Candida tropicalis</em></td>
<td>1</td>
</tr>
</tbody>
</table>
Diagnosis

- **Macroscopic examination:**
  - Sterile needle, puncturing, squeezing the sinus
  - The grains: rinsed in 70% alcohol and sterile saline
  - Failing this?
  - 10-20% KOH
  - Histopathology (H&E), (PAS)

- This direct examination for?
- Differentiate the grains of eumycetomas from the grains of actinomycetomas

- Hyphae ( >15 µm in diameter) Filaments (2-5 µm in diameter)
Direct examination showing broad hyphae and swollen cells
Granulomatous inflammatory reaction

Bacterial granule
Fungal granule
Diagnosis

- **Culture**
  - Grains:
    - Washed?
    - Crushed
  - Sabouraud dextrose agar media & Brain Heart Infusion or Blood Agar

- Sabouraud’s agar **without** antibiotics but with cycloheximide (actidione) for isolation of?
- Sabouraud’s agar **with** antibiotics but without cycloheximide for?
Madurella mycetomatis
SERODIAGNOSIS

- There is no reliable serologic test available for diagnosis
- Enzyme linked immunosorbent assay (ELISA)

Helpful for?
**Treatment**

**Eumycetoma:** Medical and Surgical treatment

- Itraconazole (200–400 mg/day) and terbinafine (500–1000 mg/day) 18–24 months or longer, preferably at the higher dosage if tolerated
- Voriconazole (400-600 mg once daily) and posaconazole (400 mg twice daily)
- Fluconazole: ineffective

**Actinomycetoma:**

Combination treatment

- Sulphamethoxazole and dapsone
- Trimethoprim and sulphamethoxazole from 6 months to several years
- Aminoglycoside (streptomycin, gentamicin) plus trimethoprim-sulphamethoxazole
Sporotrichosis

- *Sporothrix schenckii*

- Thermally dimorphous fungi

- Minor **trauma**: introduce the organism

- Lesion: 1-4 weeks after inoculation

- Predominance of **males**

- **Farmers**, gardeners, miners, etc.
Clinical findings

- Lymphocutaneous sporotrichosis (70% of cases)
- Fixed cutaneous sporotrichosis (25% of cases)
- Mucocutaneous sporotrichosis (Lymphatic spread)
- Extracutaneous sporotrichosis (lungs, joints, bones, meninges)
**Lymphocutaneous sporotrichosis**

- Erythematous **papule and nodules** along the lymphatic system
- **Ulcerative** lesion
- Painless, fever, malaise, weight loss, and chills are usually **absent**
- **Cutaneous sporotrichoid leishmaniasis**
lymphocutaneous sporotrichosis
Hyperpigmented lymphocutaneous sporotrichosis
- **Fixed cutaneous sporotrichosis**

  - The face, neck, trunk
  - **Plaque-like** or verrucous; *ulceration* is uncommon
  - Without pain
  - **Disseminated** disease is very low
  - Resistant to **local** treatment
  - Less **thermo tolerant** than more invasive strains
Plaque-like lesion due to *S. schenckii* on the anterior chest wall
**Mucocutaneous sporotrichosis**

- *Rare form*
- The mouth, Throat, Nose
- Hematogenous spread
- Unlike *cutaneous* form has pain
- Not chronic

- Similar to *Aphthous ulcers* and Secondary *cutaneous leishmaniasis*
Extracutaneous sporotrichosis

- Diabetics, alcoholics, drug abusers and AIDS patients

- Arthritis & Osteomyelitis
- Endophthalmitis
- Meningitis (AIDS)

Pulmonary sporotrichosis

- Chronic obstructive pulmonary disease and alcoholism
- Symptoms are non-specific
- Cavitary lung lesions
- Similar to tuberculosis
Diagnostic approach

- **Direct microscopy and staining**
  - Purulent cutaneous lesions
  - Purulent sputum
  - Synovial fluid
  - (PAS or GMS) to detect round, oval or cigar-shaped cells

- **Diagnosis is made by isolating Sporothrix schenckii from culture media**
  - Sabouraud dextrose agar with antibiotics and brain-heart infusion agar
Periodic Acid-Schiff (PAS): yeast cells
Macromorphology: Sabouraud dextrose agar
Micromorphology
Serologic assays

- **A skin test** (sporotrichin test)
  - Detect exposure to *S. schencki*
  - Cutaneous sporotrichosis

- **Serological tests**
  - Immunodiffusion and agglutination tests
Therapy

- **Potassium iodide**
  - Adverse effects: anorexia, nausea, a metallic taste, swelling of the salivary glands.

- **Hyperthermia?**

- **Antifungal agents:**
  - Itraconazole & Terbinafine (lymphocutaneous disease)
  - **Amphotericin B (disseminated or life-threatening sporotrichosis)**
  - **Surgery?**
<table>
<thead>
<tr>
<th>Year</th>
<th>Sex</th>
<th>Age</th>
<th>Site of Infection</th>
<th>Type of Infection</th>
<th>Occupation</th>
<th>DE</th>
<th>HP</th>
<th>C</th>
<th>TD</th>
<th>SL</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1983</td>
<td>F</td>
<td>36</td>
<td>Right arm</td>
<td>Fixed cutaneous</td>
<td>Housewife</td>
<td>N</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>Yes</td>
<td>KI</td>
<td>Recovered</td>
</tr>
<tr>
<td>1983</td>
<td>F</td>
<td>60</td>
<td>Left lower leg</td>
<td>Fixed cutaneous</td>
<td>Housewife</td>
<td>N</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>Yes</td>
<td>KI</td>
<td>Recovered</td>
</tr>
<tr>
<td>1987</td>
<td>F</td>
<td>50</td>
<td>Right forearm</td>
<td>Fixed cutaneous</td>
<td>Waiter</td>
<td>P</td>
<td>NP</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>Yes</td>
<td>KI</td>
<td>Recovered</td>
</tr>
<tr>
<td>1988</td>
<td>M</td>
<td>55</td>
<td>Left index finger and lymph nodes</td>
<td>Lymphocutaneous</td>
<td>Farmer</td>
<td>N</td>
<td>N</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>Yes</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>1997</td>
<td>F</td>
<td>36</td>
<td>Right knee</td>
<td>Arthritis</td>
<td>Housewife</td>
<td>P</td>
<td>NP</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>No</td>
<td>KTZ</td>
<td>Recovered</td>
</tr>
<tr>
<td>2000</td>
<td>F</td>
<td>56</td>
<td>Right forearm</td>
<td>Lymphocutaneous</td>
<td>Housewife</td>
<td>N</td>
<td>N</td>
<td>P</td>
<td>P</td>
<td>P</td>
<td>Yes</td>
<td>Flu</td>
<td>Unchanged</td>
</tr>
<tr>
<td>1994</td>
<td>Male horse</td>
<td>4</td>
<td>Left gaskin</td>
<td>Fixed cutaneous</td>
<td>-</td>
<td>P</td>
<td>NP</td>
<td>P</td>
<td>NP</td>
<td>No</td>
<td>KI</td>
<td>Unchanged</td>
<td>[26]</td>
</tr>
</tbody>
</table>

DE: direct examination, HP: histopathology, C: culture, TD: thermal dimorphism, SL: suspected of leishmaniasis, N: negative, P: positive, NP: not performed, NR: not reported, KTZ: ketoconazole, Flu: fluconazole
Chromoblastomycosis (Chromomycosis)

- **Clinical manifestations**
  - unilateral
  - Particularly the **feet** (about 50% of cases)
  - Nodule and papule with an irregular friable surface
  - Multiple large hyperkeratotic verrucous lesions
  - Pedunculated
  - **Pruritus** is frequent

- **Bacterial super-infection**: lymphadenopathy and lymphoedema (elephantiasis)
Nodular, cauliflower-like lesions of chromoblastomycosis  Plaque lesion of chromoblastomycosis
Common etiologic agents include

- Fonsecea pedrosoi
- Phialophora verrucosa
- Cladosporium carrionii
- Cladophialophora
- Exophiala jeanselmei
Differential diagnosis

- Blastomycosis
- Sporotrichosis
- verrucose variants of leishmaniasis and tuberculosis
-...

...
DIAGNOSIS AND PATHOLOGIC FINDINGS

- **Microscopic examination:** sclerotic bodies
  - Dark brown in color
  - Thick walls
  - Septate
  - Single, in pairs, or in clusters

- **Culture:**
  - Sabouraud’s dextrose agar with chloramphenicol and cycloheximide
  - At 25°C to 30°C
  - Kept for 1-2 weeks but cultures should be retained for 4 weeks
Sclerotic bodies
**TREATMENT**

**Without treatment:** permanent scarring and disfigurement

**Surgical excision:** for small lesions, in conjunction with antifungal treatment

Small lesions: Cryotherapy, Thermotherapy (42-45°C for 2-6 months)

**The most effective drugs:**
- Itraconazole (200-400 mg/day) and terbinafine (500-1000 mg/day)
- 6-12 months

**Flucytosine**
Thank You!