



Swiss TPH



# Overview on Mycetoma & other deep mycoses

**Andreas Neumayr**

# Neglected tropical diseases (NTDs)

WHO Recognized NTDs	Common features of these diseases
<ul style="list-style-type: none"> <li>• Buruli ulcer</li> <li>• Chagas disease</li> <li>• Dengue and chikungunya</li> <li>• Dracunculiasis (guinea-worm disease)</li> <li>• Echinococcosis</li> <li>• Foodborne trematodiasis</li> <li>• Human African trypanosomiasis</li> <li>• Leishmaniasis</li> <li>• Leprosy (Hansen's disease)</li> <li>• Lymphatic filariasis</li> <li>• Mycetoma</li> <li>• Onchocerciasis (river blindness)</li> <li>• Rabies</li> <li>• Schistosomiasis</li> <li>• Soil-transmitted helminthiasis</li> <li>• Taeniasis/cysticercosis</li> <li>• Trachoma and vaws</li> <li>• Chromoblastomycosis and other deep mycoses</li> <li>• Scabies (and other ectoparasites)</li> <li>• Snakebite envenoming</li> </ul>	<ul style="list-style-type: none"> <li>• Being a proxy for poverty and disadvantage</li> <li>• Affecting populations with low visibility and little political voice</li> <li>• Having a relatively stable endemic foci</li> <li>• Often overlapping geographically</li> <li>• Causing stigma and discrimination, especially for girls and women</li> <li>• Having an important impact on morbidity and mortality</li> <li>• Being relatively neglected by research</li> <li>• Can be controlled, prevented, and possibly eliminated using simple, effective, and feasible solutions</li> </ul>

# Mycetoma, Chromoblastomycosis & other deep mycoses

...the most neglected among the NTDs...

Graphic source: WHO - A road map for neglected tropical diseases 2021–2030

## Current situation

Scientific understanding

Diagnostics

Effective interventions

Operational guidance

Governance

Monitoring & surveillance

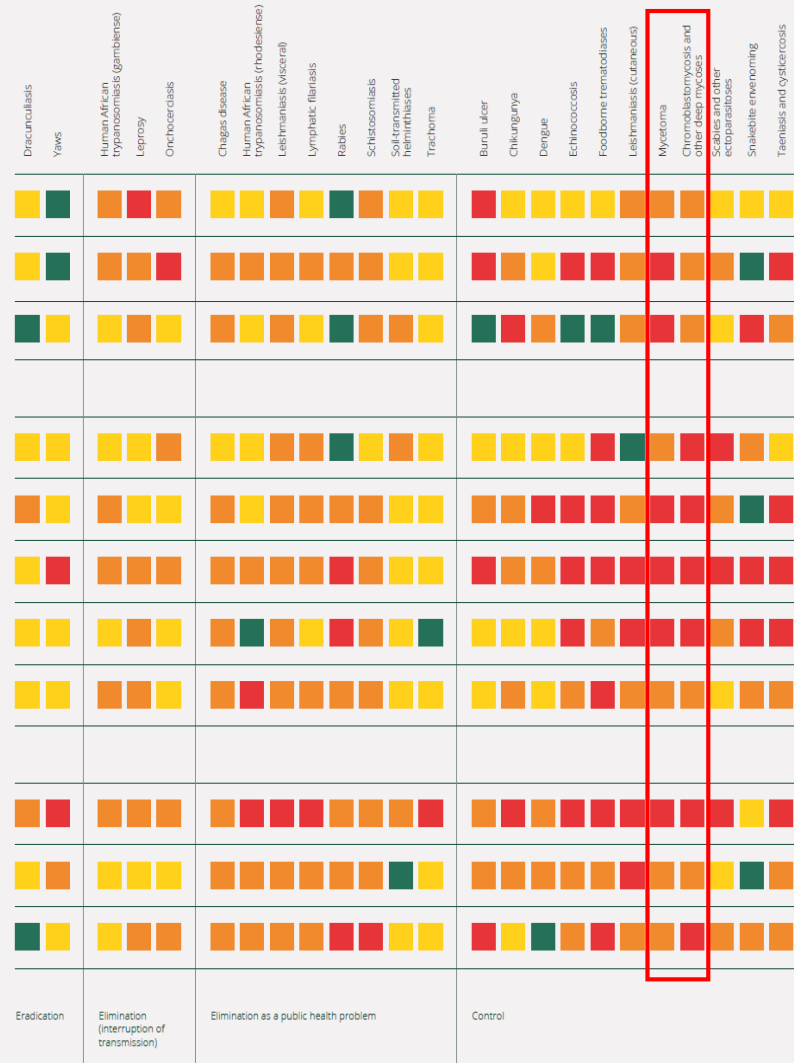
Access & logistics

Health care infrastructure

Advocacy & funding

Collaboration

Capacity building



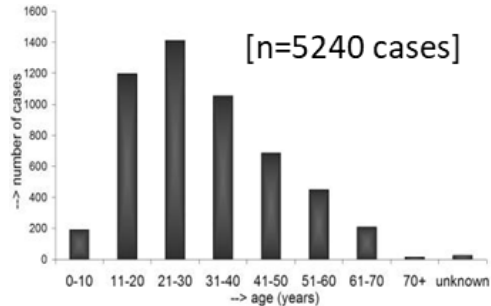
# Mycetoma (*Maduramycosis, Madura foot*)



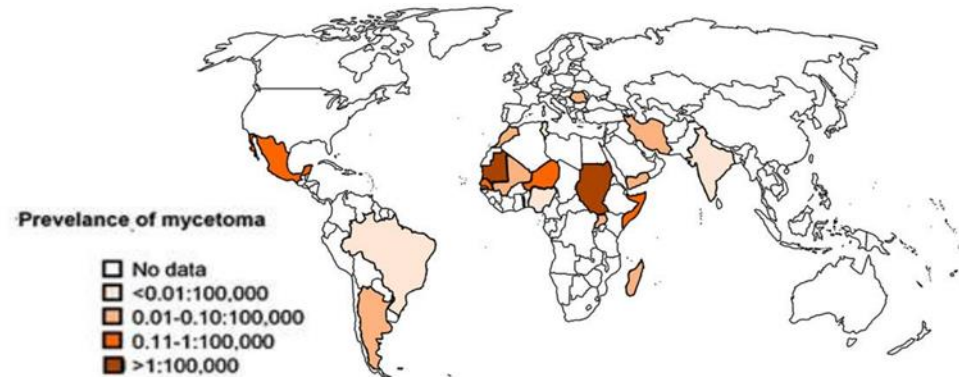
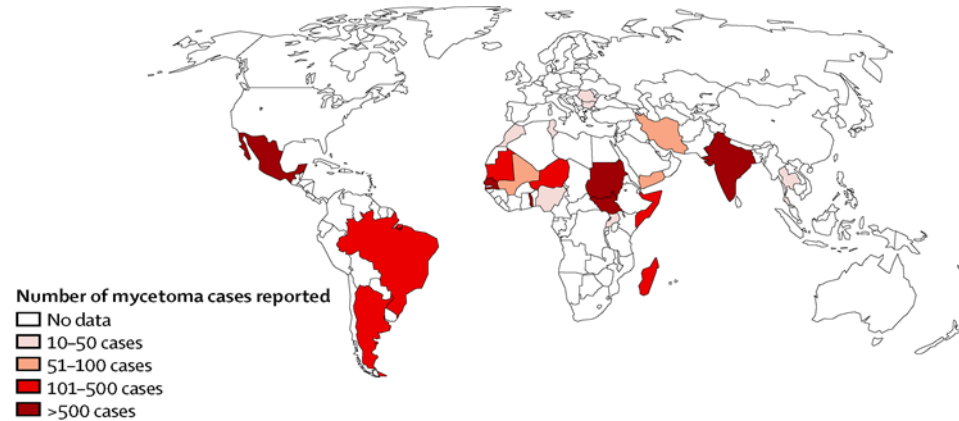
# Mycetoma – Epidemiology

- relatively rare occurrence overall
- primarily affects poor populations in rural regions of Africa, Latin America, and Asia near the equator ("mycetoma belt"), characterized by a hot, dry climate with a short, heavy rainy season
- regional prevalence rates vary widely. In Sudan, the prevalence rate is as high as 14.5/1'000

- age distribution:



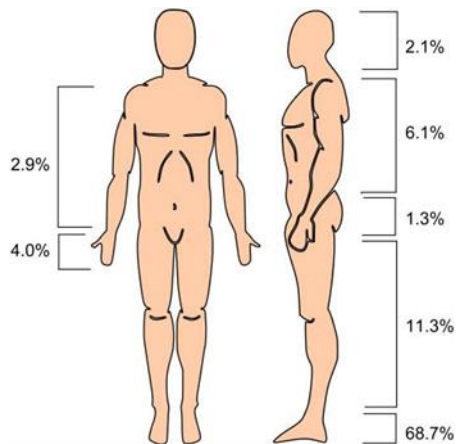
- gender ratio: ♂ / ♀ = 1.6–6.6 / 1





# Mycetoma – Route of infection

- the infection occurs through injuries / breaks in the skin
  - primarily feet/legs affected
  - in Mexico, the 2<sup>nd</sup> most frequent location is the back (carrying of wood/logs on the back)



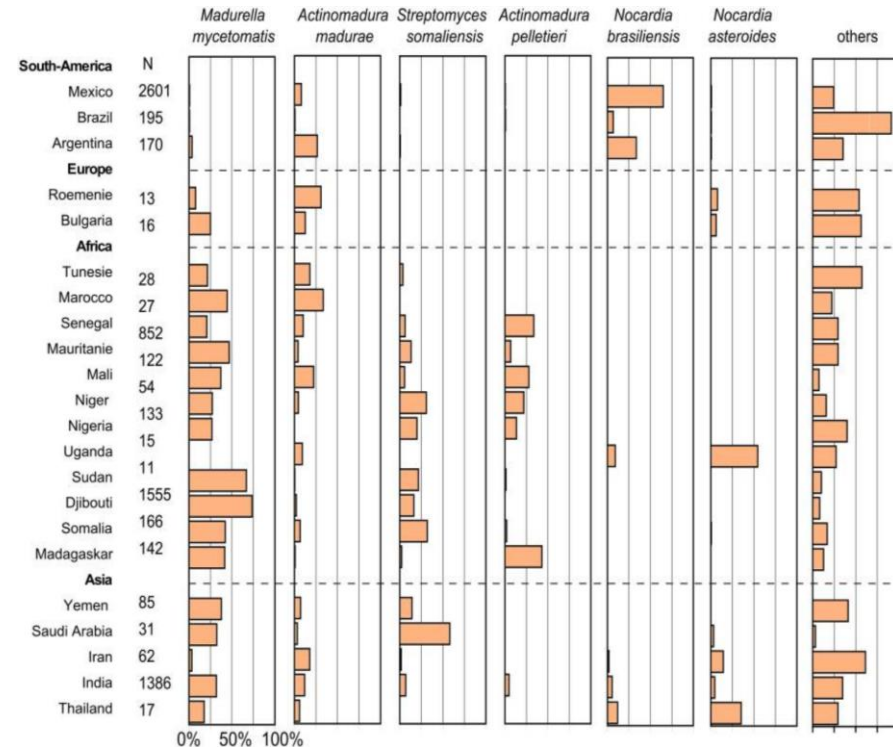
[reported location of mycetoma in 4581 cases; multiple lesions in 1% of the cases]

- occupational exposure may explain the disease's high prevalence in young male farmers and herdsman



# Mycetoma – Pathogens

- Mycetoma can be caused by
  - fungi (**Eumycetoma**) or
  - bacteria (**Actinomycetoma**)
- the primary niche of these pathogens is **soil**
- to date, >70 different pathogens have been reported to cause Mycetoma
- approximately 40% of mycetoma cases worldwide are fungal with regional differences:
  - Sudan: mostly **Eumycetomas** (70% *Madurella mycetomatis*)
  - Mexico: mostly **Actinomycetomas** (97%: *Nocardia brasiliensis* and *Actinomyces madurae*)

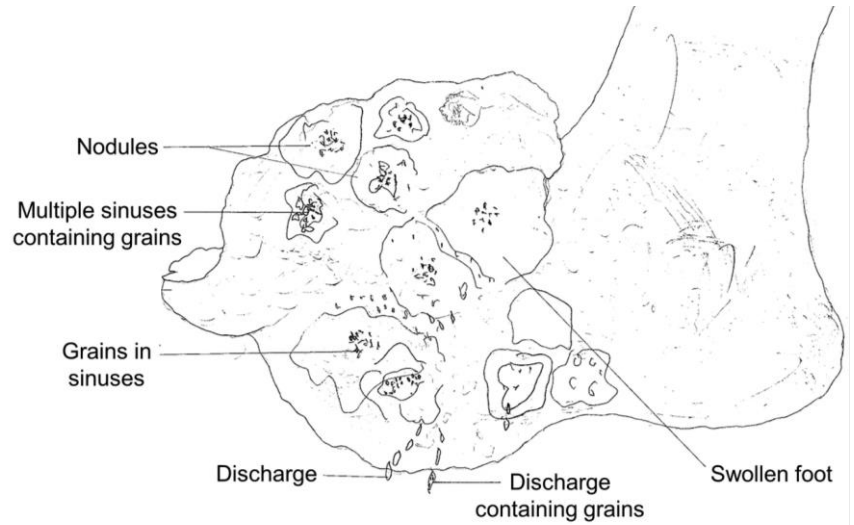
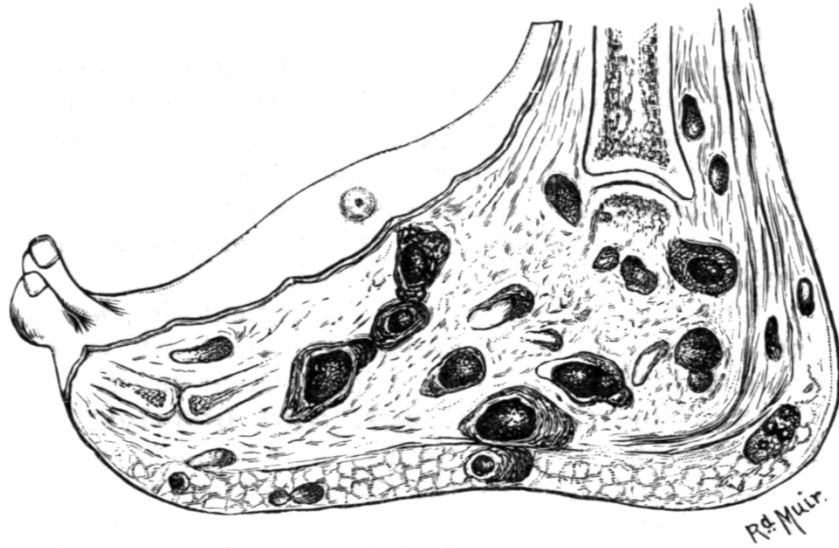


# Mycetoma – Clinical picture

- presentation of slow evolving, firm, usually painless subcutaneous masses
  - infection of the subcutaneous tissue that gradually spreads to deep structures including the bones
  - typically associated with the formation of
    - small abscesses
    - fistulating sinus tracts
    - discharge of grains
- = Mycetoma is a «syndrome» defined by these signs which may be caused by various pathogens







*Madurella mycetomatis* grains:

- black
- Ø 0.5–1(–5) mm







## Common causative agents of eumycetoma grouped by grains

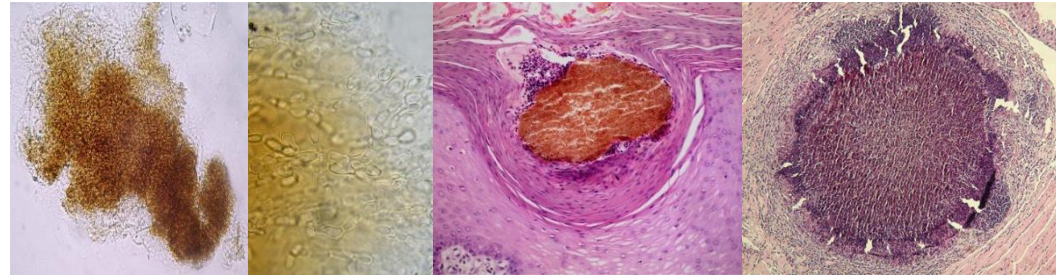
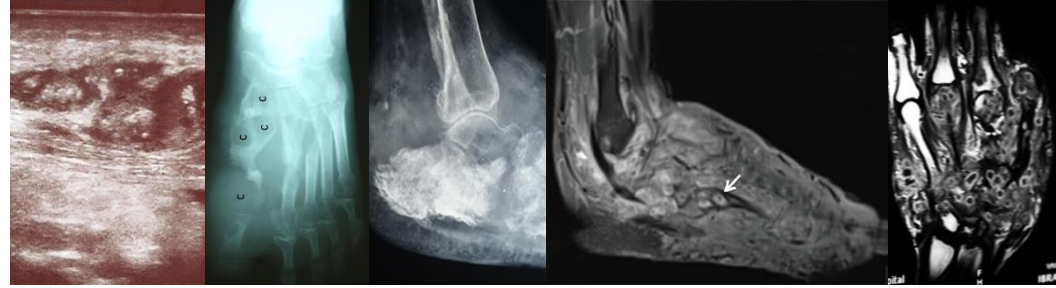
Color of grains	Agents
Black	<i>Madurella</i> spp. <i>Leptosphaeria</i> spp. <i>Curvularia</i> spp. <i>Exophiala</i> spp. <i>Pyrenochaeta</i> spp.
White	<i>Pseudallescheria boydii</i> <i>Acremonium</i> spp. <i>Fusarium</i> spp.

## Common causative agents of actinomycetoma grouped by grains

Color of grains	Agents
White	<i>N asteroides</i> , <i>N brasiliensis</i> , <i>N transvalensis</i> complex
White to yellow or pink	<i>Actinomadura madurae</i>
Red	<i>Actinomadura pelleteri</i>
Yellow to brown	<i>S somaliensis</i>

# Mycetoma – Diagnostics

- Imaging:
  - sonography
  - X-ray, CT
  - MRI
- Fine-needle aspiration
  - cytology
  - culture
- Biopsie
  - histopathology
  - culture

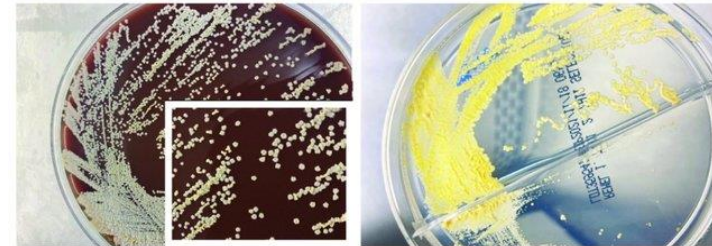
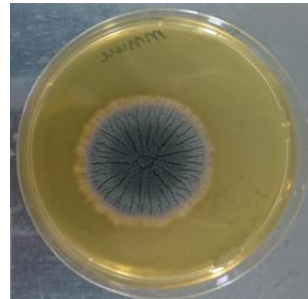


Direct microscopy *M. mycetomatis* grain/hyphae (KOH)

Black grain of *M. mycetomatis* in tissue biopsy (HE)

***Madurella mycetomatis***

***Nocardia brasiliensis***



Left: chocolate agar; right: Middlebrook 7H11/7H11 selective agar.





Name: Wesam A. Ali Date: 2 / 10 / 2022

Age: 35 yr Sex: M  F

Anatomical Site of the lesion: Buttocks

The lesion containing:

- No pocket
- Single pocket
- Multiple pockets
- Connected: aggregated  Separated
- Pocket wall: Thick  Thin
- Pocket size: x x cm
- Pocket containing:
  - Fluid
  - Echogenic grains
  - Foreign body
- Echogenicity: Sharp  Fine
- Surrounding: Halo  No halo
- Acoustic enhancement: Absent  Present
- Pocket site: Superficial  Deep to tendons & other structures
- Bone: Intact  Eroded  Cavities present
- Vascularity :.....

Diagnosis:

Findings are compatible with:

- Actinomycetoma
- Eumycetoma
- No evidence of mycetoma

# Mycetoma – Treatment

- antimicrobial therapy for months–years
  - antifungal (**eumycetoma**) or
  - antibacterial (**actinomycetoma**)
- ± surgery



## Eumycetoma:

Antifungal therapy without surgery is not curative!

Small lesions (<5 cm) without bone involvement	Wide local excision	Itraconazole 400 mg daily for three months	Follow up for recurrence	
Moderate lesions (5–10 cm) with bone involvement	Itraconazole 400 mg daily for six months	Wide local excision at six months	Itraconazole 400 mg daily for another six months	Follow up for recurrence
Massive lesions (>10 cm) with bone involvement and secondary bacterial infection	Itraconazole 400 mg daily for six months with repetitive lesion surgical debridement	Wide local excision at six months	Itraconazole 400 mg daily for another six months	Amputation for <ul style="list-style-type: none"> <li>Multiple surgical recurrences</li> <li>No response to medical treatment</li> <li>Life saving</li> </ul>

## Actinomycetoma:

- In most cases prolonged antibiotic therapy alone is curative:
- continuous cycles of TMP/SMX (5 weeks po) + Amikacin (for 1st 3 weeks of each cycle iv) or
  - continuous TMP/SMX + Amoxicillin/clavulanic acid

# Mycetoma – Outcome

**Eumycetoma:** cure in only 25–35% of the cases

**Actinomycetoma:** cure in >90% of the cases

- Associated issues:
- due to limited access to health care, patients often come late with advanced disease being more difficult to treat
  - amputation as last option -> problem of providing prosthesis, loss of limb function affects the ability to work
  - limited availability and affordability of antifungal / antibacterial drugs in endemic areas
  - the potential side effects of antifungal / antibacterial drugs demand regular laboratory monitoring
  - long-term compliance regarding drug intake and follow-up

# Mycetoma – Differential diagnoses

Besides eumycetoma, there are other fungal infections that can cause "subcutaneous / implantation mycosis". These infections are also caused by environmental fungi, have the same mode of infection by inoculation trauma, but differ in epidemiology and clinical presentation:

Subcutaneous / implantation mycoses	Causative pathogen(s)
<b>Eumycetoma</b> <b>("Maduramycosis", "Madura foot")</b>	<i>Madurella mycetomatis</i> , <i>M. grisea</i> , <i>Scedosporium boydii</i> , <i>Leptosphaeria senegalensis</i> & others
Chromoblastomycosis	<i>Fonsecaea</i> spp., <i>Cladophialophora</i> , <i>Exophiala</i> , <i>Phialophora</i> , <i>Rhinocladiella</i> spp.
Sporotrichosis	<i>Sporotrix schenckii</i> , <i>S. brasiliensis</i> , <i>S. globosa</i>
Lobomycosis (Lacaziosis)	<i>Lacazia loboi</i>
Phaeohyphomycosis	A broad range of "dark cell-walled"/"dematiaceous" fungi (mycetoma and chromoblastomycosis are specific forms of phaeohypohomycosis)





Besides actinomycetoma, there are also other bacterial (and parasitic) infections that can cause similar clinical presentations:

	Causative Pathogen(s)
<b>Actinomycetoma</b>	chronic bacterial infection due to <i>Actinomyces</i> spp., <i>Nocardia</i> spp.
<b>Botryomycosis</b>	chronic bacterial infection due to <ul style="list-style-type: none"> <li>• <i>Staphylococcus aureus</i> (40%)</li> <li>• <i>Pseudomonas aeruginosa</i> (20%)</li> <li>• others: coagulase-neg. <i>Staphylococci</i>, <i>Streptococci</i>, <i>E. coli</i>, <i>Proteus</i>...</li> </ul>
Mycobacterial infections <ul style="list-style-type: none"> <li>– cutaneous tuberculosis</li> <li>– leprosy</li> <li>– environmental mycobacteria</li> </ul>	<i>M. tuberculosis</i> <i>M. leprae</i> MOTT
Yaws	<i>Treponema pallidum pertenue</i>
Cutaneous Leishmaniasis	<i>Leishmania</i> spp.



# Non-infectious differential diagnoses

Kaposi sarcoma



Podoconiosis







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WHO Collaborating Center on Mycetoma

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<https://www.mycetoma.edu.sd>