

## GAFFI POLICY BRIEF

### Neglected Fungal Tropical Diseases – truly neglected and not so tropical

#### Overview

Fungi are everywhere; in the air, on surfaces, on fruit and vegetables and in soil. Following a random minor injury penetrating the skin or eye, some can cause disease. Unlike most other serious fungal diseases, most of those affected by skin and eye fungal infections have normal immune function and are unlucky casualties.

#### Additional Background

Several fungal diseases are classified as Neglected Tropical Diseases (NTDs) by various agencies and journals, alongside many parasitological conditions, leprosy and snake bite. GAFFI's focus is on fungal NTDs included on the World Health Organization's NTD listing<sup>1</sup> together with fungal keratitis.

Fungal NTDs are infrequently fatal, but chronic disability and morbidity is common and profound. Some examples of extensive disease (left to right) of chromoblastomycosis (China), fungal keratitis (India) and mycetoma (Sudan) are shown here.



Condition (see fact sheets for detail) <sup>2</sup>	Number of fungal species implicated	Approximate fungal burden	Geographical zone range
Mycetoma	Over 20; 5 common	25,000 -50,000	Tropical and subtropical
Chromoblastomycosis	3 common	25,000 -50,000	Tropical and subtropical, with some temperate
Sporotrichosis	5; 3 most common	Over 30,000	Global with recent focus in South America. Spread partly by feral cats.
Paracoccidioidomycosis	2	3,000 – 10,000	South and Central America
Fungal keratitis	Over 100; 3 are the most common	1.1 to 1.4 million	Global, most common in tropical and subtropical regions

<sup>1</sup> WHO. Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021–2030 <https://www.who.int/publications/i/item/9789240010352>

<sup>2</sup> <https://gaffi.org/where/neglected-fungal-diseases/>

## Current gaps in diagnosis and therapy

Current tools for diagnosis fungal NTDs include

- direct microscopy on samples from skin and eye
- histopathology
- fungal culture with identification systems and access to affordable antifungal therapy

Diagnosis needs trained people at the bedside and in well equipped laboratories; these capabilities are often missing or distant from patients in many global communities and countries.

Community awareness and new diagnostics techniques are needed to allow earlier diagnosis than shown in the pictures. Treatment outcome is worse with extensive disease.

Few diagnostic or management guidelines for clinicians and laboratories are published for these diseases.

## GAFFI recommends:

1. Laboratory diagnosis is improved:
  - WHO Essential Diagnostics (direct microscopy for fungi, histopathology and fungal culture with identification) be implemented in general and specialist hospitals in all countries, with a rapid turnaround for eye samples in particular.
  - Isolation of fungal species in culture can be to genus and species level identification, if necessary by referral of cultures to Mycology Reference Laboratories.
  - If histopathology is not available and the diagnosis is still uncertain, formalin fixed or paraffin embedded samples or high quality images of stained sections of tissue should be transferred to those with the skills to interpret abnormalities.
2. Training in clinical diagnostic procedures with regular of simple equipment required:
  - Where corneal scraping is not already a routine procedure, training should be provided to enable this for ophthalmologists and eye clinic staff, along with sample handling (direct microscopy and culture).
  - Where skin biopsy is not already a routine procedure, training should be provided for dermatologists and physicians in primary and secondary care.
3. Improvements in treatment:
  - For fungal keratitis, topical natamycin<sup>3</sup> should be made available for all those with fungal keratitis and failing that other topical antifungals. Detailed clinical appraisal is required, and sometimes surgical intervention during therapy.
  - For chromoblastomycosis, sporotrichosis and paracoccidioidomycosis, oral treatment with itraconazole for several months is necessary and should preferably be provided as part of each country's Universal Health Coverage.
  - For mycetoma, appropriate surgery, high dose prolonged antibiotics (actinomycetoma) or itraconazole (or alternative azole such as voriconazole) (eumycetoma) should be used, as guided by the pathogen.
  - Itraconazole or voriconazole use to be closely monitored for adverse events.

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<sup>3</sup> Map of current country availability of topical natamycin:  
<https://antifungalsavailability.org/maps/map/natamycin>

4. As sporotrichosis caused by *S. brasiliensis* is acquired from cats, monitoring the spread of infections in affected regions and adjacent countries.

#### **How much will these recommendations cost?**

1. If the global prevalence of the fungal skin NTDs is 100,000 and diagnosis costs \$25 per patient, the global diagnostic cost would be under \$10 million, given similar diseases can mimic these infections.
2. Treatment with itraconazole for 6 months for 75,000 people would cost ~\$54 million at \$4 daily.
3. Monitoring costs are similar to those for TB therapy.
4. The investigation of all corneal ulcers (assumed to be ~4.5 million annually) would be ~\$115 million. A course of natamycin eye drops varies in price, from \$10 upwards.

#### **What will the benefits of change bring?**

Improved quality of life, reduction in disability and social stigma and improved economic activity are the major benefits realizable with better care for patients with fungal NTDs.

The NTD portfolio<sup>4</sup> includes diseases which have a profound impact on affected populations. They are both a symptom of poverty and a powerful contributor to the 'poverty trap'. About 800 million people still live in extreme poverty (<\$1.90 per day) (a 50% reduction on 20 years ago). Poor health contributes to self-perpetuating poverty along with conflict, limited earning potential and low educational attainment. Most NTDs affect rural populations or populations living in areas of urban deprivation – people with little political voice and little power to influence government health policies.

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<sup>4</sup> [www.who.int/teams/control-of-neglected-tropical-diseases](http://www.who.int/teams/control-of-neglected-tropical-diseases)