Commentary

The fight against mycoses in Africa: are we making progress?

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The burden of mycoses has been a neglected problem, especially in Africa, but hopes are rising as it is now getting the attention it deserves, although with serious setbacks. Globally, fungal pathogens account for an estimated 1.2 billion infections, with a significant number being superficial and amenable to antifungal treatment [1]. However, an important minority of infections—which are invasive and deep-seated to systemic/chronic—are difficult to prevent, diagnose and treat. This has led to an estimated 1.5–2 million deaths annually, surpassing deaths due to malaria and tuberculosis [2], with approximately 500,000 and 450,000 being related to AIDS and chronic pulmonary aspergillosis, respectively. Africa accounts for an estimated 67% of the more than 37 million people living with HIV infection, and about 50% of deaths may be due to mycosis-derived complications.

In Africa today, efforts are being made to understand the extent to which mycoses have ravaged our society through the leading international fungal education (LIFE) [2] and the global action fund for fungal infection (GAFFI) [1], but the actual incidence and prevalence remain unknown. Available data indicate that about 54.8 million people suffer from mycoses annually, with approximately 3 million mycoses being invasive and life-threatening (Table 1) [3–8]. These data are either estimated or extrapolated from neighbouring countries due to lack of manpower and lack of or poorly established diagnostic facilities. Lack of access to healthcare facilities and expensive hospital bills have been identified as challenges partly responsible for the high prevalence of self-medication. In Nigeria, for example, only an estimated two out of ten people in rural communities or five out of ten in urban communities visit the hospital when ill, while some rural communities have no access to a healthcare facility; thus, the current estimated burden of mycoses may be considerably lower.

The impact of mycoses in Africa calls for research to facilitate the development of better prophylactics, diagnostics and therapeutics, and the establishment of a network to foster cooperation. Most governments in Africa (with the exception of South Africa) have no programme for mycoses and thus conduct no mycological surveillance. Funding for medical mycology compared to other infectious diseases is underrepresented, although this may be due to a scarcity of specialists. However, almost no government of an African country has research funds dedicated to surveillance, diagnosis, public health response, epidemiology investigation and control of mycoses, although there are life sciences research grants in most African countries, such as the tertiary education trust fund (TETFund) research grant in Nigeria. There is also no active medical mycology networking platform in Africa (except for the medical mycology society of Nigeria and Ghana medical mycology group) at least in the past decade where researchers and specialists can share knowledge and ideas, present setbacks, and have productive discussions on the best practices and plan a way forward [3]. Consequently, gaps in our knowledge remain unaddressed, and the efforts of individual countries have been relatively ineffective.

The limited availability of manpower in medical mycology affects every aspect of the efforts to improve healthcare services to combat mycoses the world over. However, lack of/limited diagnostics may be partly due to the unavailability of diagnostic facilities in resource-poor areas and partly due to lack of well-trained medical mycologists to conduct the tests. There is also the problem of lack of standardization and validation of tests, resulting in

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uncertainty about the tests' performance. In developed countries, most of the clinical decisions are based on the results of diagnostic tests which will inform the choice of treatment. Mycoses are complex and require infrastructure, facilities, and specialist skills for their rapid and accurate diagnosis. In Africa, the range of laboratory services available in most countries have not exceeded microscopy and classical culture on non-selective media [5], as non-culture-based techniques (except for cryptococcal antigen/antibody testing) and drug sensitivity testing are not common. The sensitivity of culture and microscopy is limited, and both procedures are almost out of use in developed countries. One consequence of the limitation in diagnostics is the misdiagnosis of chronic pulmonary aspergillosis for tuberculosis, leading to pointless presumptive therapy [5]. Similarly, the misdiagnosis of tuberculous meningitis for cryptococcal meningitis, or vice versa (both conditions being strongly associated with HIV-infected people), due to lack of confirmatory tests, results in delayed or inadequate treatment associated with increased fatality [10].

The burden of mycoses in the world, and robust and accurate diagnostics are lacking. The disease is endemic in Senegal, Uganda, and Sudan. Sudan remains the country with the highest number of cases of mycostoma in the world, and robust and accurate diagnostics are unavailable. However, an integrated management approach has been proposed for mycostoma in Sudan [11], but the establishment of healthcare facilities with trained mycologists remains a priority. GAFFI partner with some African governments to establish forums aimed at providing manpower to expand coverage and improve the quality of diagnostic services and quality assurance; however, the FIP was short-lived due to lack of funds. Currently, there is a global initiative by CDC/CHAI/Unitaid towards ending cryptococcal meningitis deaths by 2030, and most African countries are benefitting from this. The programme provides increased support for cryptococcal antigen screening and treatment. In 2018, GAFFI led training in Uganda aimed at ensuring universal access to diagnostics for serious mycoses by 2025. The training aimed to recommend the inclusion of essential in vitro diagnostics for HIV/AIDS-associated serious mycoses and other opportunistic infections into the WHO essential in vitro diagnostics list [12]. WHO's third essential diagnostics list, launched in January 2021, included antigen and antibody tests for Aspergillus and a PCR test for Pneumocystis. Although these efforts are encouraging, most African countries still lack access to modern facilities and diagnostics such as quick and simple lateral flow assay (LFA) and ELISA assay for cryptococcosis, histoplasmosis and aspergillosis, and a PCR test for Pneumocystis. There is the problem of funding on the side of African governments to make these tests available to patients, but even where they are available, they are expensive and require expertise to use; thus, diagnosis of mycoses remains a major setback to achieving accurate epidemiology data in Africa.

There are no immunotherapies or vaccines for mycoses, and available antifungal agents to treat mycoses are also limited. Unfortunately, most invasive mycoses are diagnosed too late and provide little chance for treatment success. Matters are worse in Africa, as most first-line drugs for most mycoses are either too expensive or unavailable. For example, the echinocandins are the first-line therapy for invasive candidiasis or azole-resistant Candida species such as Candida auris, but are mostly unavailable or expensive. However, they have recently become available in a few African countries: Algeria and South Africa (caspofungin), Tunisia, Ghana, Egypt (anidulafungin) and South Africa, Namibia, Botswana, Zambia, South Sudan, Uganda, Kenya (micafungin). Terbinafine is not available in sub-Saharan Africa, while natamycin is available only in Egypt, Uganda, Namibia, and South Africa. The available drugs in most African countries include amphotericin B, fluconazole, griseofulvin, miconazole, nystatin,itraconazole, ketoconazole and topical azoles. Itraconazole is unavailable in Congo, Morocco, Niger, Ethiopia, Eritrea, Gambia, Senegal and Burundi and some other countries. Most developed countries and developing countries (including Nigeria) have recommended against the use of ketoconazole for most indications, citing severe liver damage and potential drug—drug interactions, but this has not been the case in most other African countries. In the treatment of cryptococcal meningitis the fungus responds poorly to fluconazole, with more than 60% fatality at 10 weeks in sub-Saharan Africa even

Table 1

<table>
<thead>
<tr>
<th>Country</th>
<th>Total burden of mycoses</th>
<th>Fungal keratitis</th>
<th>Tinea capitis</th>
<th>Oral candidosis</th>
<th>Oesophageal candidosis</th>
<th>Recurrent vulvovaginal candidosis</th>
<th>Total serious mycoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Algeria</td>
<td>568 942</td>
<td>4265</td>
<td>721 000</td>
<td>178 400</td>
<td>7460</td>
<td>4860</td>
<td>7488 188</td>
</tr>
<tr>
<td>BFaso</td>
<td>1 360 280</td>
<td>1 132 781</td>
<td>24 300</td>
<td>43 300</td>
<td>316 555</td>
<td>179 002</td>
<td>56 000</td>
</tr>
<tr>
<td>Cameroon</td>
<td>1 126 332</td>
<td>721 000</td>
<td></td>
<td>4860</td>
<td></td>
<td>316 555</td>
<td>45 477</td>
</tr>
<tr>
<td>Congo</td>
<td>293 918</td>
<td>700</td>
<td>178 400</td>
<td>4860</td>
<td>85 440</td>
<td>412 936</td>
<td>16 521*</td>
</tr>
<tr>
<td>C‘droit</td>
<td>1 744 277</td>
<td>3350</td>
<td>1 295 786</td>
<td>17 280</td>
<td>421 936</td>
<td>1 307 766</td>
<td>327 420</td>
</tr>
<tr>
<td>Egypt</td>
<td>1 649 686</td>
<td>11 550</td>
<td>7 051 736</td>
<td>166 050</td>
<td>57 344</td>
<td>1 426 988</td>
<td>118 319</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>8 820 437</td>
<td>810</td>
<td>598 840</td>
<td>18 292</td>
<td>442 621</td>
<td>1 426 988</td>
<td>30 000</td>
</tr>
<tr>
<td>Ghana</td>
<td>1 030 563</td>
<td>318 673</td>
<td>114 000</td>
<td>594 660</td>
<td></td>
<td>1 426 988</td>
<td>459 187</td>
</tr>
<tr>
<td>Kenya</td>
<td>1 186 523</td>
<td>1 712 676</td>
<td>306 000</td>
<td>594 660</td>
<td>1 426 988</td>
<td>1 426 988</td>
<td>459 187</td>
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<tr>
<td>Madagascar</td>
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<td>843 875</td>
<td>415</td>
<td>265 248</td>
<td></td>
<td>1 426 988</td>
<td>7069*</td>
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<tr>
<td>Malawi</td>
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<td>1836</td>
<td>670 900</td>
<td>216 000</td>
<td>326 960</td>
<td>1 426 988</td>
<td>49 837</td>
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<tr>
<td>Mozambique</td>
<td>1 836 374</td>
<td>1 181 688</td>
<td>184 307</td>
<td>75 718</td>
<td>348 179</td>
<td>1 426 988</td>
<td>46 484</td>
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<tr>
<td>Namibia</td>
<td>60 456</td>
<td>6660</td>
<td>7 961</td>
<td>37 290</td>
<td></td>
<td>1 426 988</td>
<td>65 455</td>
</tr>
<tr>
<td>Nigeria</td>
<td>17 983 371</td>
<td>15 581 400</td>
<td>253 062</td>
<td>1 512 520</td>
<td>492 340</td>
<td>1 426 988</td>
<td>459 187</td>
</tr>
<tr>
<td>Senegal</td>
<td>1 743 507</td>
<td>1 523 700</td>
<td>1946</td>
<td>191 228</td>
<td></td>
<td>1 426 988</td>
<td>26 633</td>
</tr>
<tr>
<td>S/Loutroum</td>
<td>376 643</td>
<td>1017</td>
<td>266 645</td>
<td>5786</td>
<td>4221</td>
<td>85 440</td>
<td>7834*</td>
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<tr>
<td>S/Africa</td>
<td>4 047 138</td>
<td>1 003 490</td>
<td>1 150 560</td>
<td>623 598</td>
<td>1 002 499</td>
<td>266 991</td>
<td>266 991</td>
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<tr>
<td>Tanzania</td>
<td>1 422 204</td>
<td>420 000</td>
<td>81 051</td>
<td>88 509</td>
<td>759 500</td>
<td>73 144</td>
<td>73 144</td>
</tr>
<tr>
<td>Uganda</td>
<td>2 500 000</td>
<td>1 300 000</td>
<td>30 959</td>
<td>12 062</td>
<td>375 540</td>
<td>781 439</td>
<td>30 000</td>
</tr>
<tr>
<td>Ziambwwe</td>
<td>2 122 715</td>
<td>1 806 700</td>
<td>77 143</td>
<td>203 585</td>
<td></td>
<td>1 426 988</td>
<td>24 945*</td>
</tr>
<tr>
<td>Total</td>
<td>54 480 354</td>
<td>54 281 544</td>
<td>7 961 451</td>
<td>1 426 988</td>
<td>1 426 988</td>
<td>1 426 988</td>
<td>2 881 141</td>
</tr>
</tbody>
</table>

* Estimated from systemic, invasive, deep-seated, and potentially fatal infections.
in combination with flucytosine. Flucytosine in combination with amphotericin B is better in managing cryptococcal meningitis, but flucytosine is available only in Ghana and Tanzania, plus it requires experience to administer. However, a new low-cost cryptococcal meningitis treatment has been proposed [13]. Lack of limited access to more effective antifungal agents, as well as their unaffordability, has a huge negative and mostly fatal outcome on those with serious and life-threatening mycoses. Thus, effective implementation of WHO diagnostics and therapeutics guidelines, including GAFFI recommendations, will be a great step towards combating the mycoses nightmare in Africa.

The appropriate responses to mycoses in Africa are yet to be instituted, despite millions contracting life-threatening invasive mycoses annually. For example, there is only one mycology reference laboratory (South Africa) and one mycetoma research centre (Sudan) in the whole of Africa. Most countries have no mycology training centres and manpower is significantly suboptimal and will require a great investment to bring critical mass to the sector. To invest in and build manpower, which would be one of the major steps in tackling the problem of mycoses, will involve integrated development strategies (Fig. 1). This will allow institutions/governments for strategy development, prioritization of actions and development of local skills leading to employment.

Manpower building will help to establish a coordinated national effort towards training and research programmes that will bring together diverse expertise within and outside Africa to understand and treat mycoses and to train a new generation of mycologists. Manpower availability will promote excellence in research and new multidisciplinary scientific initiatives in medical mycology. It will also increase our understanding of mycoses and translate basic research findings to the patient’s bedside, and finally will promote the understanding of the public and make them aware of the health implications of this often underappreciated and misrepresented area of science. The growth of manpower and increasing public awareness of medical mycology in this important sector is critical. The medical mycology society of Nigeria has drawn a roadmap to combat mycoses.

Finally, even as we struggle with these setbacks, new problems—such as antifungal drug resistance in Aspergillus and Candida species, and emerging multidrug-resistant Candida auris—are quickly becoming major health threats. These threats enforce the urgent need for high-quality research in medical mycology, with dedicated grant funding to encourage manpower development and research collaboration to provide better health management in our home continent while countering these global threats. In all, however, it appears that we have not made significant progress.

**Transparency declaration**

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**References**