



Report on activities for 2018

95/95
BY 2025

April 2019

Summary

GAFFI continues to make progress in its mission to reduce illness and death associated with fungal diseases worldwide. GAFFI appointed Professor Patrick Francioli to its Board as part of an internal re-organisation that saw Professor Denning step down from Board Chairman to Chief Executive of GAFFI and Professor Nigel Lightfoot take over as Chairman. Its achievements in 2018, its fifth year of operation, include:

- **Defining Essential Diagnostics for the new WHO Model List of in vitro Diagnostics:** GAFFI hosted a meeting in Kampala 2018 with >90 participants to discuss and agree key diagnostic tests for fungal diseases and advanced AIDS. Microscopy, fungal culture, blood culture, histopathology and cryptococcal antigen were accepted on the WHO's initial list, with other tests to follow.
- **Diagnosing lethal AIDS infections in Guatemala:** GAFFI's demonstration project in Guatemala "Minimising HIV deaths through rapid diagnosis and better care in Guatemala" has its second full year of data. A single GAFFI-supported laboratory enabled diagnostic tests for the commonest fungal infections and TB in 2,563 HIV patients in 2018 with 17% having a life-threatening infection (62% fungal). These are similar figures to those obtained in 2017 with a little increase in the number of patients analyzed. This year, for the first time in Guatemala, *Pneumocystis jirovecii* pneumonia can be diagnosed by means of PCR technique. The program has an annual cost of <\$100 per patient in diagnostic testing.
- **Fungal Infections Program – Kenya (FIP-Kenya):** A second national demonstration project is to be launched in Kenya in 2019. FIP-Kenya is a unique initiative that will improve clinical outcomes by strengthening public health capabilities and promoting research on the understanding, prevention, diagnosis and treatment of fungal infections. GAFFI appointed Ms Emma Orefuwa as Chief Executive Kenya to drive this transformational project forward.
- **Burden of Fungal Diseases:** The program of mapping how many fungal diseases there are in each country has now reached 92 countries. In 2018, burden papers were published for a further 15 countries and have recently been added to this list: Colombia, Uruguay, Argentina, Burkina Faso, Cameroon, Mozambique, Malawi, Iran, Jordan, Romania, Italy, Serbia, Norway, Turkey, Kazakhstan and Malaysia. Histoplasmosis in AIDS, and at least as many deaths, was found to be at least as common as TB in the Americas, published in Lancet infectious Diseases. The first estimation of the global burden of recurrent vulvovaginal candidiasis was published (138 million) was published in Lancet Infectious Diseases, with individual country estimates.
- **Fungal keratitis:** GAFFI has submitted a request to the WHO for fungal keratitis to be adopted as a Neglected Tropic Disease (NTD). Over 1,100,000 are thought to be affected although the disease is barely recognized in Africa. This initiative still requires individual country (member state) support to proceed.
- **GAFFI's Ambassadors' activities:** Multiple educational programs and awareness have been delivered in Madagascar, Mozambique, Nigeria, Argentina, Mexico, Chile, Iran, Kuwait, Russia, Sri Lanka, Indonesia, Serbia, Hungary, France, Portugal and the UK. Major non-culture diagnostic improvements are required in laboratories in Indonesia, Philippines and Thailand, as identified in a 7 country survey in Asia.
- **Health professional education:** GAFFI's educational partner LIFE-Worldwide has produced multiple online videos and podcasts on key fungal disease topics <http://life-worldwide.org/life-education-slide-sets-video-presentations-and-reading-materials>. These include some diagnostic procedures which will be expanded over the coming months. The online microscopy and histology course in English, Spanish, French and Portuguese at www.microfungi.net has been accredited by the Royal College of Pathologists for CPD/CME credits.

GAFFI's Goals

GAFFI has 4 primary long term goals, supported by advocacy:

Goal 1 - Increase awareness of the impact of fungal disease

Goal 2 - Improve access to diagnostics for fungal disease

Goal 3 - Improve access to appropriate and affordable antifungal therapeutics with a focus on generic agents

Goal 4 - Improve education of health professionals about fungal disease.

GAFFI 10 year Roadmap '[95-95 by 2025](#)' focused and fleshed out these objectives as follows:

- Ensure that 95% of people with serious fungal disease are diagnosed and 95% treated by 2025 (95-95)
- Support the goal of reducing AIDS deaths to under 500,000 by 2020, with a determined focus on the commonest lethal fungal infections cryptococcal meningitis, *Pneumocystis* pneumonia, disseminated histoplasmosis and chronic pulmonary aspergillosis after tuberculosis

To accomplish these goals, it is necessary in each country to:

- Ensure that affordable diagnostic tests for all common and uncommon fungal infections are made available, focused on rapid, non-culture testing
- Develop and maintain at least one laboratory led by an expert in fungal disease diagnostics with a comprehensive diagnostic portfolio and critical mass of healthcare professionals per country
- Develop a network of expert clinicians and 'train the trainer' programs, supported by clinical guidelines
- Ensure distribution of antifungal agents on the WHO Essential Medicine List to reach all those who need them
- Establish ongoing surveillance of fungal infections of high burden to inform clinical practice, training and research needs
- Develop local experts in public health mycology

GAFFI's organisation

GAFFI appointed Professor Patrick Francioli to its Board as part of an internal re-organisation that saw Professor David Denning step down from Board Chairman to Chief Executive of GAFFI and Professor Nigel Lightfoot take over as Chairman. GAFFI and GAFFI UK now have identical Board membership to facilitate achieving GAFFI's aims.



Ms Emma Orefuwa was appointed Chief Executive Kenya. Communications responsibility was transferred from Dr Jennifer Bartholomew to Dr Katherine Dobb.

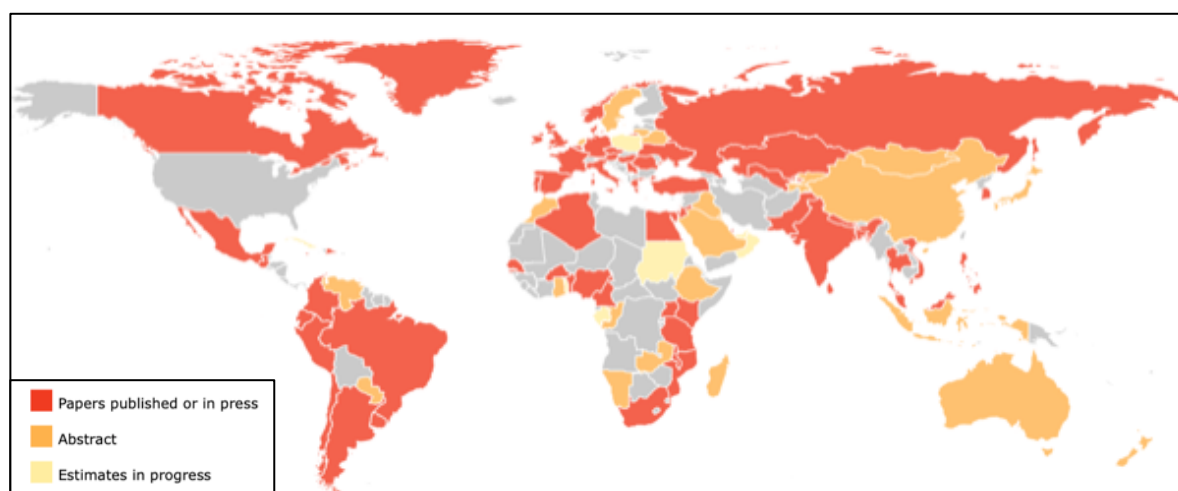
Goal 1 - Increase awareness of the impact of fungal disease

A major GAFFI goal is increase awareness of fungal disease globally, especially among global health agencies and country medical opinion leaders and decision-makers. GAFFI has approached this by estimating the burden of fungal diseases country by country, identifying and highlighting diagnostic and therapeutic gaps and supporting epidemiological studies to better define fungal disease locally.

1.1 Burden of fungal disease

By the end of 2018, burden of fungal disease estimates were published for 58 countries [www.gaffi.org/media/academic-papers/] and presented for another 18 countries. Published papers are now available or in press for Algeria, Argentina, Austria, Bangladesh, Belgium, Brazil, Burkina Faso, Cameroon, Canada, Chile, Colombia, Czech Republic, Denmark, Dominican Republic, Ecuador, Egypt, France, Germany, Greece, Guatemala, Hungary, India (partial), Iran, Ireland, Israel, Italy, Jamaica, Jordan, Kazakhstan, Kenya, Malawi, Malaysia, Mexico, Mozambique, Nepal, Nigeria, Norway, Pakistan, Peru, Philippines, Portugal, Qatar, Romania, Russia, Senegal, Serbia, South Korea, Spain, Sri Lanka, Tanzania, Thailand, Trinidad and Tobago, Turkey, Uganda, UK, Ukraine, Uruguay, Uzbekistan and Vietnam.

Summary abstracts and posters were presented in 2018 summarising the burden of serious fungal diseases for Benin, Sweden, South Africa, Ethiopia, Ghana and Taiwan www.gaffi.org/gaffi-annual-report-released-alongside-burden-of-fungal-diseases-estimates-for-benin-and-sweden/ and www.gaffi.org/burden-of-serious-fungal-diseases-in-ghana-south-africa-ethiopia-and-taiwan-presented-in-dubai-at-gccmid/.



Collaborators have also re-estimated the burden of cryptococcal disease in AIDS by country (Radha Rajasingham et al), histoplasmosis in Africa (Rita Oladele et al, published in 2018), histoplasmosis in AIDS in the Americas (Antoine Adenis et al, submitted for publication) and the prevalence of chronic pulmonary aspergillosis after tuberculosis in Nigeria (Rita Oladele).

1.2 Deaths from histoplasmosis in AIDS probably exceed TB in Latin America

GAFFI collaborators in Cayenne, French Guyana have re-estimated symptomatic HIV-associated histoplasmosis in Latin America – 6,710 to 15,657 cases. Hotspot areas for histoplasmosis prevalence (>30%) and incidence (>1.5 cases per 100 people living with HIV) were Central America, the northernmost part of South America, and Argentina. Different scenarios, indicate a wide range of deaths related to histoplasmosis 671 to 9,394, compared with 5,062 deaths related to tuberculosis reported in Latin America. These data

1.3 Global burden of recurrent vulvovaginal candidiasis

GAFFI's Chief Executive and colleagues have estimated the global prevalence and lifetime incidence of recurrent vulvovaginal candidiasis (rVVC) for the first time, with individual country estimates. RVVC is a debilitating, long-term condition that can severely affect the quality of life of affected women. Worldwide, rVVC affects about 138 million women annually (range 103–172 million), with a global annual prevalence of 3,871 per 100,000 women. It can persist for 1-2 years or many years. Overall, an estimated 372 million women are affected by rVVC over their lifetime. The 25–34 year age group has the highest prevalence (9%). In high-income countries, the economic burden from lost productivity is estimated to be US\$14.39 billion annually.

1.4 Report to SE Asian Regional WHO office (SEARO) on fungal diseases in the region

A commissioned report summarises the current status of several potentially fatal fungal diseases in the SEARO countries, as well as some that are serious and disabling, but not usually fatal. The WHO South East Asia Region includes the countries Bangladesh, Bhutan, Democratic People's Republic of Korea (North Korea), India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand and Timor-Leste. Diagnostic capability varies hugely across SEAR and no country is fully equipped with Mycology Reference Laboratories serving the whole population. The incidence, prevalence and mortality from the commonest life- and sight-threatening infections was estimated (Table 1). Antifungal resistance is an emerging challenge: terbinafine resistance in dermatophyte infections of the skin (best documented in India), triazole resistance in *Aspergillus fumigatus* rendering all oral antifungals useless, and multi-drug resistance in *Candida glabrata* and *Candida auris*.

SE Asia Region	Measure	Number
Cryptococcal meningitis in AIDS	Incidence	30,000
Cryptococcal meningitis in AIDS	Deaths	27,000
<i>Pneumocystis pneumonia</i> in AIDS	Incidence	80,000
<i>Pneumocystis pneumonia</i> in AIDS	Deaths	67,000
Invasive aspergillosis	Incidence	196,000
Invasive aspergillosis	Deaths	176,000
Invasive candidiasis and candaemia	Incidence	745,000
Invasive candidiasis and candaemia	Deaths	>370,000
Chronic pulmonary aspergillosis	Prevalence	670,000
Chronic pulmonary aspergillosis	Deaths	100,000
Mucormycosis	incidence	200,000
Fungal asthma	Prevalence	2,785,000
Fungal keratitis	Incidence	768,000

Goal 2 - Improve access to diagnostics for fungal disease

Both improved diagnostic tests for low and middle income countries and improved access to diagnostics are critically important GAFFI goals. Fungal disease is often clinically silent and/or mimics other infections and specific diagnostic tests are required for diagnosis. Many hospitals and countries have little or no diagnostic capability. Complex test formats, expense, inadequate laboratory infrastructure and a lack of training are all barriers to diagnostic testing. Accurate assessment of the burden of disease requires accurate diagnosis.

2.1 Essential Diagnostics for fungal diseases and advanced HIV infection

GAFFI organized an international meeting to make recommendations to the WHO about which tests should be listed in the new Model List of Essential *in vitro* Diagnostic tests for LMICs. The meeting was timed to precede and help inform the WHO's Strategic Advisory Group of Experts on In Vitro Diagnostic (SAGE-IVD) meeting. An initial selection was made to focus on key non-culture diagnostics, i.e. TB urinary antigen (LAM), cryptococcal antigen, *Histoplasma* antigen, *Aspergillus* IgG, *Pneumocystis* PCR and *Toxoplasma* IgG/IgM and one on antifungal therapeutic monitoring. Summary arguments were also presented for culture based diagnostics and direct microscopy. Experts in HIV, Microbiology, Mycology, Parasitology, Public Health and laboratory sciences were invited from



LMICs, global organisations, research institutes, academic institutions and diagnostic and antifungal marketing companies globally. Open invitations were made available on social media (LinkedIn, Twitter etc.). Diagnostic companies with studies in progress were invited to submit any data for consideration at the meeting to ensure the most up to date information was available to the participants.

Ninety-five participants comprising experienced clinicians, senior laboratory staff and public health practitioners contributed to the meeting.

Participants were drawn from 27 countries, mainly LMICs, including Brazil, Cameroon, Egypt, Ethiopia, France, French Guiana, India, Ireland, Japan, Kenya, Malawi, Mozambique, Nigeria, Pakistan, Portugal, Senegal, Slovenia, South Africa, South Sudan, Spain, Swaziland, Tanzania, Uganda, UK, Ukraine, USA and Zambia. Contributors were from the WHO, UNITAID, MSF, African Society for Laboratory Medicine, Clinton Health Access Initiative, Medical Access, WHO Collaborating Centers for Reference and Research on Fungi of Medical Importance/ Antimicrobial Resistance (India/ South Africa/ USA), ministries of health, national reference laboratories including the US Centres for Disease Control and Prevention, research institutes and



both diagnostic and pharmaceutical companies with an interest in AIDS and/or fungal diseases, as well as GAFFI itself.

2.1.2 Recommendations

Basic mycology and microbiology procedures were recommended including direct microscopy, culture including blood culture and histology. In addition, the following specific non-culture-based tests were recommended for inclusion the WHO EDL listing:



Very strong recommendations for inclusion onto the EDL included the:

- Cryptococcal antigen lateral flow assay to screen for and diagnose cryptococcal meningitis on whole blood, serum and cerebrospinal fluid (accepted)
- *Mycobacterium tuberculosis* antigen (lipoarabinomannan) in urine to diagnose disseminated TB in AIDS in those with C4 counts under 100 cells per μL . (accepted)
- *Histoplasma* antigen in serum or urine to diagnose disseminated histoplasmosis in AIDS in countries where the disease is common (applied for – see below).

Strong recommendations for EDL inclusion were for:

- *Aspergillus* IgG detection to diagnose chronic pulmonary aspergillosis which is often misdiagnosed as TB
- Cryptococcal antigen quantification (and as an alternative to a lateral flow assay) to determine the likelihood of meningitis based on antigen amount in serum (titre of $\geq 1:160$)
- *Pneumocystis* PCR (strong recommendation for middle income countries and reference laboratories in low income countries).
- Therapeutic monitoring of itraconazole and voriconazole using bioassay to ensure enough antifungal is present for efficacy and not in excess causing toxicity. Low levels increase the risk of acquired resistance.



These tests will be the subject of future applications to the WHO for inclusion onto the EDL.

Strong/Moderate recommendation for EDL inclusion:

Included *Toxoplasma* IgG serology (moderate recommendation to allow discontinuation of toxic empirical therapy of brain disease, but a strong recommendation in middle income countries with a high sero-prevalence).

Not recommended for EDL inclusion

Beta-1, 3-D-glucan (not recommended because of test complexity, likelihood of false positives from blood tubes and a lack of data in HIV associated infection) and galactomannan (not recommended as value outside neutropenic leukaemia patients (serum) and bronchoscopy samples not clear).



2.1.3 Tests not considered

Several diagnostic tests were not considered at the workshop for multiple reasons as shown in this table:

Test	Purpose	Reason for exclusion
<i>Coccidioides</i> antibody	To diagnose coccidioidomycosis	Geographically limited, some high performance tests not commercially available. Other means of making most diagnoses.
<i>Paracoccidioides</i> antibody	To diagnose paracoccidioidomycosis	Very geographically limited, no tests commercially available. Other means of making most diagnoses
<i>Talaromyces marneffe</i> PCR	To diagnose <i>T. marneffe</i> infection, usually in AIDS	Very geographically limited, no tests commercially available.
MALDI-TOF MS identification of fungi	Rapid identification of yeasts and moulds	Complex equipment and incomplete identification database currently.
Sequence-based identification of fungi	Definitive identification of yeasts and moulds, including cryptic species	Complex process for most laboratories and transport to a sequencing center expensive in many locations; interpretation requires a high level of skill.
Antifungal susceptibility testing	To detect antifungal resistance in fungi	Skill required is not widespread, pure antifungal compound and other key equipment required.
<i>Candida albicans</i> germ tube antibody	To diagnose or rule out invasive candidiasis caused by <i>C. albicans</i>	Increasing trend in non- <i>albicans Candida</i> species which are multi-antifungal resistant

Abbreviations: MALDI-ToF, Matrix assisted laser desorption ionization-time of flight mass spectrometry; PCR, polymerase chain reaction.

2.2 Histoplasma antigen

Disseminated histoplasmosis is a lethal disease in AIDS and some other immunocompromised patients (link: www.gaffi.org/media/fact-sheets/). Two significant papers were published this year – one documenting a similar number or more cases compared with TB in AIDS in Latin America (Adenis, 2018). It is best diagnosed with a urinary antigen test (or a blood PCR). The immense diagnostic value of the urinary antigen was described at GAFFI's Essential Diagnostic meeting in Kampala in April 2018 (link: www.gaffi.org/global-fungal-infection-forum-3-in-kampala/).

GAFFI has applied for histoplasma antigen to be included on the WHO's list of Essential in vitro Diagnostic tests, in areas of the world where histoplasmosis occurs. There are currently 2 tests commercially available, both in ELISA format. One has a sensitivity of 81% and a specificity of 99% and a diagnostic accuracy of 96% (Link: [immy](http://immy.com/)). The other has a sensitivity of 95% (100% against culture positives) and a specificity of 70% with a diagnostic accuracy of 86%. (Link: <http://optimumidx.com/>)

2.3 Demonstration project in Guatemala (Contribution of Professor Juan Luis Rodriguez Tudela)

The third year of GAFFI's demonstration project in Guatemala is complete: '**Minimising HIV deaths through rapid fungal diagnosis and better care in Guatemala.**' This project in collaboration with

the Asociación de Salud Integral (ASI) (Medical Director Dr Eduardo Arathoon, and Dr Blanca Samoya GAFFI Ambassadors for Guatemala) with external input from GAFFI Senior Advisor Prof Juan Luis Rodriguez Tudela and GAFFI Ambassador for Spain Dr Ana Alastruey-Izquierdo. GAFFI is indebted to the JYLAG Foundation for financial support.

In 2017, in Guatemala 46,000 (40,000 – 52,000) people were infected with HIV and there were an estimated 2,000 (1,500 – 2,500) AIDS-related deaths. Of those who know their HIV status (31,000), only 18,000 are on anti-retroviral therapy, the lowest in Latin America. Only 13,000 have their HIV disease under control with suppressed viral loads. About 50% of the diagnosed patients are in advanced HIV stage which results in long periods of hospitalization and often death.



2.3.1 Training activities

1. The Third Annual National Workshop reporting the results of the project was held in March 2018 in Guatemala City; Title: "Manejo y Tratamiento de las Infecciones Fúngicas en VIH, Compartiendo los primeros logros ". During this annual meeting, talks were provided by different experts such as Juan Luis Rodríguez Tudela (GAFFI), Ana Alastruey Izquierdo (Instituto de Salud Carlos III), Pilar Ramón-Pardo (PAHO), Dalia Mei Ling Lau (ASI), Eduardo Arathoon (CFLAG), Diego Caceres (CDC), Anneliese Moller (ASI), Blanca Samayoa (ASI), and Juan Carlos Pérez (CFLAG). This meeting was attended by 100 participants.



2. Three other workshops (September 21th, 28 and October 5th) were focussed on handling and transport of clinical samples to the Diagnostic Reference Laboratory & reinforcement of LFA CrAg procedures. The workshop was attended by 32 microbiologists and technicians from 13 HIV units.

3. One meeting at Hospital Nacional de Escuintla with oral presentations based on clinical cases. The meeting was coordinated by an expert from the Clínica Familiar Luis Angel Garcia. There were 40 participants from HIV unit, hospital directorate, internal medicine, laboratory personnel and students.

4. Three online conferences about diagnosis, management and treatment of *Pneumocystis jirovecii* pneumonia, were delivered on the ZOOM platform. These activities involved all HIV units. The first conference was on June 4th from Guatemala to Hospital Infantil Elisa Martinez in Izabal, the second one on June 27th to HIV Unit from Hospital Nacional de Retalhuleu, the last one on September 5th, to all HIV Units.



2.3.2 New diagnostic Portfolio at Reference Laboratory and technology transfer to HIV units

In late 2017, the diagnosis of *Pneumocystis jirovecii* pneumonia had been set up at the reference laboratory by means of a commercial PCR real time kit, FTD *Pneumocystis jirovecii*. For the first-time, patients in Guatemala have access to the diagnosis of this infection. Now this test is available to all 13 HIV Units in the Fungired program.

Internal standardization of *Aspergillus* IgG antibodies was started in late 2017. They have used the kit from Bordier based on its superior performance.

2.3.3 Website improvements

The website (www.fungired.gt) has been improved in 2018 and comprises: i) General information; ii) Education and Training and; iii) Laboratory System.

General information

The first layer called “General information” describes the FUNGIred™ network, the participants, HIV care units and the Diagnostic Reference Laboratory (DRL), as well as the clinical advisor for fungal infections. This section also provides information about its activity, workshops, results of the project and links to others web sites with related information.

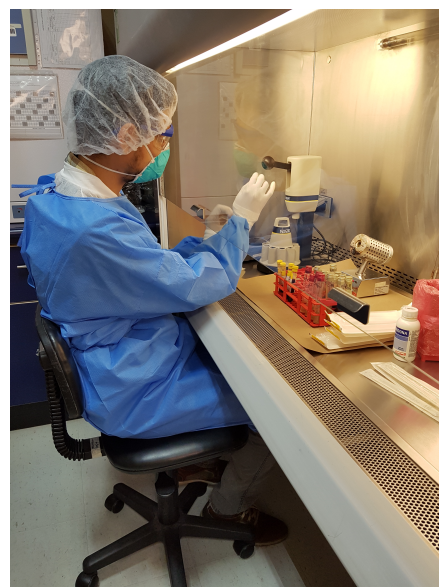


Educational and Training

The second layer, called “Education and training”, links to an e-Learning course entitled “Opportunistic Infections Care in HIV patients”. In 2019, the second e-learning course will be available for the medical personnel of the HIV Units. An online learning course in microscopy and histopathology of fungal infections is also linked in here (www.microfungi.net).

Laboratory System

The third layer comprises the “Laboratory system” that has been developed on a web environment, which allows remote access from computers, tablets or smartphones. Through this system, HIV units request on line individual diagnostic tests for opportunistic infections for their patients. The system allows a permanent communication between HIV units and ASI DRL enabling quicker diagnosis and treatment of patients with a fungal infection than previously. This system also allows entering of clinical data for each patient, including clinical signs and symptoms, results of local laboratory tests and radiological and clinical images as well as treatment given and follow up. This information can be exported to an Excel sheet for later analysis. Each HIV care unit has access to their cases.



Global results can be found at www.fungired.gt as well as local information about the number of cases by region, HIV unit and opportunistic infection. This information is publicly accessible and updated monthly.

2.3.4 Cohort results

Patients with advanced HIV infection and AIDS are screening for disseminated histoplasmosis, cryptococcal meningitis and tuberculosis. Additional testing is done for clinical suspicion, including PCR for *Pneumocystis*.

Samples from 2,563 patients were sent to the DRL by the network in 2018; 437 patients had an opportunistic infection; 246 of which were fungal. Histoplasmosis was diagnosed in 33.4% patients

with an opportunistic infection, 16.0% had cryptococcosis and *Pneumocystis jirovecii* pneumonia was diagnosed in 6.9% compared to 37.8% with tuberculosis and other mycobacterial infections. Amongst these infections, 26.2% had two or more coinfections. Table 1 shows all the results. In addition, the network ruled out these infections in 2,126 HIV cases, allowing an earlier start of antiretroviral therapy and therefore the chance of a better outcome.

Table 1. Opportunistic Infections preliminary results until December 31th 2018


2018 cases	Total	%
Fungal infections	246	56%
Histoplasmosis	146	33%
Cryptococcosis	70	16%
Pneumonia <i>P. jirovecii</i>	30	7%
Mycobacterial infections	164	38%
Tuberculosis	139	32%
Non-tuberculous mycobacteria Infections	25	6%
Coinfections	27	6%
Cryptococcosis+Histoplasmosis	7	2%
Histoplasmosis+PJP	2	0%
TB+NTMI	1	0%
TB+Histoplasmosis	5	1%
TB+PJP	4	1%
PJP+NTMI	3	1%
Histoplasmosis+PJP	1	0%
Histoplasmosis+NTM	2	0%
Cryptococcosis+Histoplasmosis+TB	1	0%
PJP+Cryptococcosis+TB	1	0%
Positive cases	437	17%
Negative cases	2126	83%
Total of cases	2563	

PJP: *Pneumocystis jirovecii* pneumonia, TB: tuberculosis, NTMI: Non-tuberculous mycobacteria infection


2.3.5 Next steps

- Document the successes of the project in publications
- Facilitate country and government ownership of the project
- Work with the government to ensure antifungal drug access and no cost to patients or affordable prices, including flucytosine.
- Assess the value of additional tests in the diagnostic portfolio, including *Aspergillus* IgG, and probably *Toxoplasma* serology and TB antigen (LAM) testing.

2.4 Survey of Mycology Laboratory Practices in Asia



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Advance Access Publication Date: 20 September 2017
Original Article



Several GAFFI Ambassadors delivered an online survey of mycology laboratories in seven Asian countries to assess the status, competence, and fungal diagnostic services available. In total, 241 laboratories responded, including 71 in China, 104 in India, 11 in Indonesia, 26 in the Philippines, four in Singapore, 18 in Taiwan, and seven in Thailand. Overall, 129/241 (53.5%) laboratories

operate a separate designated mycology laboratory, 75/241 (31.1%) conduct regular formal staff training, 103/241 (42.7%) are accredited, and 88/157 (56.1%) participate in external quality assurance scheme (EQAS) programs. Microscopy and culture methods are available in nearly all laboratories, although few perform DNA sequencing (37/219; 16.9%) or currently use MALDI-TOF. (27/219; 12.3%) for isolate identification. Antifungal susceptibility testing is performed in 142/241 (58.9%) laboratories, mainly for yeasts. The most commonly performed non-culture diagnostic is cryptococcal antigen testing (66 laboratories), followed by galactomannan testing (55), polymerase chain reaction (PCR) diagnosis (37), and beta-D-glucan testing (24). Therapeutic drug monitoring is conducted in 21 laboratories. There is almost no access to advanced diagnostic tests, like galactomannan, β -D-glucan, and PCR, in the surveyed laboratories in Indonesia, the Philippines, and Thailand. These results highlight the need for development of quality laboratories, accreditation and training of manpower in existing laboratories, and access to advanced non-culture-based diagnostic tests to facilitate the diagnosis of fungal infections in Asia.

2.5 Kenya – the FIP-Kenya program

GAFFI has been working in partnership with the governments of Kenya and Japan to provide much greater capacity for fungal disease diagnosis in Kenya. The Fungal Infections Program (FIP-Kenya) development program aims to provide 13 of the major urban centers with excellent radiology, histopathology and fungal disease diagnostics and support leading clinical personnel through training, in combination with networking, quality assurance and surveillance programs. GAFFI appointed Emma Orefuwa to oversee FIP-Kenya implementation with the Ministry of Health and individual counties. GAFFI's partners in the program include the Fungal Infection Trust (Educational materials), Amref (Education of clinicians and radiographers), the National Public Health laboratory in Nairobi (laboratory training, reference laboratory support and IT networking for laboratories) and the Kenya Medical Research Institute (KEMRI) (research and fungal registry).



Goal 3 - Improve access to appropriate and affordable antifungal therapeutics with a focus on generic agents

Access to affordable antifungal agents remains a critical goal for GAFFI, with some progress made in 2018.

3.1 Engagement with manufacturers of antifungals.

3.1.1 Flucytosine for cryptococcal meningitis

Advocacy from numerous organisations including GAFFI resulted in approval of flucytosine being approved as a WHO as prequalified medicine (PQ) by Mylan Pharmaceuticals. WHO PQ would allow rapid approvals in Armenia, Botswana, Burkina Faso, Burundi, Caribbean Community (CARICOM), Cameroon, Côte d'Ivoire, Democratic Republic of the Congo, Eritrea, Ethiopia, Georgia, Ghana, Kenya, Kyrgyzstan, Lao People's Democratic Republic, Madagascar, Malawi, Mali, Mozambique, Namibia, Nigeria, Philippines, Senegal, Sierra Leone, South Africa, Tanzania, Thailand, Uganda, Ukraine, Zambia, Zanzibar and Zimbabwe. GAFFI expects registrations to occur in some or all of these countries in 2019.

3.1.2 Improved pricing of liposomal amphotericin B for cryptococcal meningitis

After pressure from multiple agencies including GAFFI, Gilead agreed to supply liposomal amphotericin B (Ambisome) at USD\$16.25 per 50mg vial, a significant price reduction. The liposomal formulation of amphotericin B is less toxic than conventional amphotericin B and penetrates into the brain better. The price differential between the 2 formulations is still considerable as a 3x higher dose of Ambisome is required, so typically 150mg/day compared with 50mg/day. Logistical issues are formidable as Ambisome is not yet registered for use in many of the most needy countries (see <https://antifungals-availability.org/maps/map/liposomal-amphotericin-b-ambisome>), so import requires individual country and shipment arrangements.

3.2 Global mapping of current availability and price of antifungal drugs

GAFFI has replaced its mapping software to show availability and price of amphotericin B, liposomal amphotericin B, fluconazole, flucytosine, itraconazole, voriconazole and topical natamycin (<http://antifungals-availability.org/>). Software has also been built to allow our Ambassadors to update the information directly and to display the date of the information.

Enormous gaps in coverage still exist, notably with liposomal amphotericin B, flucytosine, voriconazole in Africa and topical natamycin.

Goal 4 - Improve education of health professionals about fungal disease

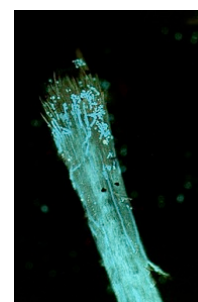
Health professionals need to have fungal disease at the front of their mind when dealing with patients with complex health problems. Laboratory training is critical for building diagnostic capability. Antifungal prescribing can be complex and pharmacists need to be aware of drug interactions and dose adjustments. GAFFI, in concert with many others, is committed to improving health professional competence related to fungal diseases. In addition to its 'Fact sheets': <http://www.gaffi.org/media/fact-sheets/> GAFFI also has a twitter account with >1,400 followers.

4.1 GAFFI Ambassadors

GAFFI's Ambassadors network expanded in 2018 to include Argentina, (Fernando Riera), Burkina Faso (Sanata Bamba), Colombia (Jorge Cortes and Carlos Alvarez-Moreno), Jordan (Jamal Wadi), Kuwait (Wadha Alfouzan), Malawi (Khumbo Kalua), Norway (Ingild Norday), Paraguay (Gloria Aguilar-Barreto), Turkey (Süleyha Hilmioğlu Polat and Macit Ilkit), Uruguay (Marina Macedo) and second Ambassadors for Uganda (Felix Bongomin) and Mexico (Alexandro Bonifaz). All GAFFI's Ambassadors visible here: <https://www.gaffi.org/who/our-ambassadors/> GAFFI is extremely grateful to its Ambassador group for their sterling efforts related to raising awareness of fungal diseases, direct advocacy and educational initiatives.

4.2 Online lectures on fungal diseases

GAFFI's educational partner LIFE-Worldwide has produced multiple online videos and podcasts on key fungal disease topics <http://life-worldwide.org/life-education-slide-sets-video-presentations-and-reading-materials>. These include many diagnostic procedures but principally video lectures with accompany powerpoint presentations on over 35 fungal diseases topics, including antifungal chemotherapy. More intend to be added over the coming months.



4.3 Online course on fungal microscopy and histology

Launched in 2016, the online free course www.microfungi.net is translated into 4 languages (Spanish, French and Portuguese as well as English) and accredited by the UK Royal College of pathologists. Laboratory technicians and doctors can earn continuing professional education points (CPD and CME) while learning a critical skill. Over 800 students have enrolled from across the world and completion rates are likely to rise as certification has been granted by the RCPATH

4.4 GAFFI's Ambassadors awareness and educational initiatives

4.4.1 Madagascar (Professor Lala Soavina Ramarozatovo)

In Madagascar since 2012, there has been an ongoing mycological, epidemiological and clinical pilot study on deep mycoses such as chromomycosis, sporotrichosis and mycetoma. This study is still in progress and as Madagascar is large and an island, we have carried out field missions in 2018. We will publish this year our preliminary results and have as project to develop a deep mycosis department within our Ministry of Health.

4.4.2 Mozambique (Professor Jahit Sacarlal)

From 2 to 6 October 2018, the Microbiology Department at Faculty of Medicine, Eduardo Mondlane University, organized the 1st Mycology Course with clinical and laboratory component to Dermatologists from the main referral hospital in Mozambique (Maputo Central Hospital), as well as to laboratory technicians from the Faculty of Medicine and researchers. The International facilitator was the Prof. Dr. Victor Silva V. from Escuela de Tecnología Médica, Universidade Mayor do Chile (see picture). This course was organized by GAFFI Ambassador of Mozambique and funded by World Bank through the Institutional Development Fund of Mozambique.



Research in Department of Pneumology with aim of estimate frequency of three main invasive fungal infections (*Pneumocystis jirovecii*, aspergillosis and histoplasmosis) in adults HIV with severe pneumonia is still ongoing. Lab work will finish in 2019. Another main work is the fungal disease surveillance at Maputo Central Hospital which was started in the last quarter of 2018. We expect in 3 years period to have more information regarding fungal disease incidence in Mozambique.

GAFFI Ambassador in Mozambique, Prof. Jahit Sacarlal, published in the Journal Fungi the first estimation of the burden of serious fungal diseases in Mozambique (see reference section) and worked with Ministry of Health to produce the first clinical guidelines for Advanced HIV Disease, which is responsible for ~60,000 deaths annually.

4.4.3 Nigeria (Dr Rita Oladele)

1. Between May 2018 and December 2018, across 13 states of the federation, 761 health care workers were trained on diagnosis and management of cryptococcal meningitis. Emphasis was placed on screening and pre-emptive therapy. The impact of the training was assessed and the findings will be presented at AIDS Mycoses meeting in South African (July 2019). Aid tools were developed for clinicians and patients.





Nigeria (MMSN) were nominated and won places to attend the one week lecture and practical course in medical mycology that was organized by the AFGrica Unit (University of Aberdeen/ University of Cape Town), Institut Pasteur, Paris and the AMBITION-cm Trial Consortium. They will be holding a step down training 8th and 9th April 2019.

2. A multicenter (14 sites) cryptococcal antigen screening survey has just been completed and the data generated will be used to determine the cost effectiveness of screening and pre-emptive therapy in the Nigerian setting.
3. A study on the standardization of *Aspergillus* IgG for Nigerians was conducted and the findings were presented as a poster in Fungal update conference in London (March 2019). It won second best abstract presentation.
4. Four members of Medical Mycology Society of



4.4.4 Argentina (Dr Fernando Riviera)

In May 2019, we are formalising a new study group with clinical and diagnostic professionals. This group will amplify GAFFI's activities.

4.4.5 Mexico (Dr Dora Corza-Leon and Professor Alexandro Bonifaz)

We published two papers in collaboration with several Mexican hospitals. One of the published papers reported costs of antifungal treatment and we estimated the burden of IFIs (candidiasis, aspergillosis, endemic infections) in Mexico based on the incidences reported by four Mexican hospitals. The second paper reports the incidence of invasive fungal infections in HIV individuals from an indigenous origin in a Southwest Mexican State. Fungal infections were the main cause of in-hospital stay in that HIV population and histoplasmosis the most frequent of these infections.

From May 2019, we'll start training activities for clinical microbiologists, to improve their skills in fungal identification. We'll use the tools in life-worldwide.org, including the microscopy and histology E-course.

4.4.6 Chile (Dr Eduardo Alvarez-Duarte)

The problem of fungal diseases has been discussed in several meetings and conferences:

- January 2018, in the IV International Course of Taxonomy on Opportunistic Filamentous Fungi, Chile.
- September 2018, Medical Mycology Update, Hospital Guillermo Grant Benavente, Concepción, Chile.
- October 2018, Medical Mycology Update, Universidad Santo Tomás, Osorno, Chile.



Also Dr. Eduardo Alvarez-Duarte also notes that their lab have detected 23 cases of histoplasmosis since 2017. Due this new scenario, serological and molecular tests were implemented. Today, our

lab is now able to detect histoplasmosis by molecular tests in 24-36 hours. Moreover, *Candida auris* and azole-resistant *Aspergillus fumigatus* has been detected in Chile. These results will be published soon.



Additionally, Dr. Eduardo Alvarez-Duarte, Professor in the mycology unit of Microbiology and Mycology Department, Universidad de Chile has launched a new practical atlas of medical mycology called “Reconociendo los hongos: Micología Médica”.

4.4.7 Iran (Professor Mohammad Hedayati)

The 5th conference of Iranian Society of Medical Mycology was held in November 4-6th 2018 in Tehran (<http://www.ismm.ir/content/news/174>). The Iranian GAFFI ambassador, Professor Mohammad Hedayati introduced GAFFI and its aims and activities for all participants focusing especially on improvement in the knowledge of health care workers on fungal diseases and development of educational and research activities in medical mycology field.

4.4.8 Kuwait (Dr Wadha AM Alfouzan)

Kuwait was hit by *Candida auris* and has had to adapt its laboratory methods to address the problem. An educational program in mycology is being conducted in Kuwait in March 2019.

4.4.9 Russia (Professor Nick Klimko)

Six educational courses on clinical mycology were held in Russia which included GAFFI’s activities and aims.

4.4.10 Sri Lanka (Dr Primali Jayasekera)

GAFFI’s Ambassador in Sri Lanka Dr Jayasekera (Consultant Medical Mycologist, Head / Department of Mycology, Medical Research Institute, Colombo, Sri Lanka) delivered a guest lecture on “Management of invasive fungal infections in patients with haematological malignancies” in “Haemato-oncology” symposium. At the Annual Scientific Sessions of the Sri Lanka College of Oncologists 2018.



She also delivered two guest lectures on ‘Fun in managing fungi’ organized by Ratnapura Clinical Society at Provincial General Hospital Ratnapura and on ‘Fascinating fungi’ organized by Horana Clinical Society at Base Hospital Horana.

Other mycological research in the country was well received:

1. Non *Candida* non Cryptococcal invasive blood stream infections in cancer patients. Thabrew H, Sigera LSM, Jayawardena MN, Jayasekera PI. Poster presentation at the Annual Academic Sessions of Sri Lanka College of Oncologists – 2018. This paper won the award for the best poster presentation.
2. *Candida* blood stream infections in Sri Lanka: a retrospective evaluation by the National Mycology Reference Laboratory. Jayawardena M.N., Sigera L.S.M., Thabrew H., Kudavidanage S., Malkanthi M.A., Perera P.D., Jayasekera P.I. Oral presentation at the Annual Scientific Sessions of the Ratnapura Clinical Society 2018. This paper won the best scientific paper award for the best oral presentation.

3. First case of dermatophytosis caused by *Microsporium persicolor* in Sri Lanka. L.S.M. Sigera, U.L.F. Shabry, M.A. Malkanthi, P.I. Jayasekera. Poster presentation at the Annual Scientific Sessions of the Ratnapura Clinical Society 2018. This paper won the commended scientific paper award (poster) second place.
4. Invasive infections due to filamentous fungi – a review of epidemiology and antifungal therapy in a tertiary care hospital in Sri Lanka. S. Vathshalan, D. Perera, P. Jayasekera, C. Patabendige. Poster presentation at the 17th Asia –Pacific Congress of Clinical Microbiology and Infection cum 8th International Infection Control Conference, Hong Kong 2018.

4.4.11 Indonesia (Professor Retno Wahyuningsih)

Various activities to disseminate knowledge about fungal diseases have been carried out. The dissemination was done by presentation both at Indonesia and abroad. In addition to presentations, surveys and research have been conducted on various fungal diseases in Indonesia. The activities of Retno Wahyuningsih as Indonesia GAFFI ambassador are as follows:

1. As an AFWG member, a task force group from ISAHM, she has participated in several workshops and symposia held by AFWG in 2018. The scientific activity was called Medical Mycology Training Network (MMTN) conference held in Taipei, Taiwan, November 15-18, 2018.
The title of her presentations were as follows:
 - a. Identification of Zygomycetes (workshop)
 - b. Slide culture for mould identification (workshop)
 - c. Black Mycelial fungal infection (symposium)
 - d. Chronic pulmonary aspergillosis (symposium)
2. A lecture entitled **Understanding patho-mechanism of invasive fungal infection** for doctors who joined the The Indonesia Society for the Study of Tropical Diseases. It was held in Bandung, October 14th, 2018
3. In collaboration with US-NIH a workshop was conducted to discuss on the opportunistic infection in AIDS with doctors from many parts of Indonesia, who taking care of AIDS patients. The INA-Respond HIV Training was held in Jakarta on December 5 – 7. Her presentation was entitled **Systemic Fungal Infection in AIDS**.
4. Disseminating knowledge about superficial fungal diseases and how to diagnose for hospital laboratory technicians. A workshop held in August 26th, 2018, in Jakarta.
5. Presentation entitled **Important role of diagnostic approach to support optimum patient outcome** at the meeting of Indonesian Society of Intensive Care Medicine, held in Jakarta August 12th 2018
6. Presentation on the relationship of pulmonary fungal infections and respiratory failure for the members of The Society of Respiratory Care Indonesia (Respina), July 21st, in Jakarta. The title of the presentation is, **Respiratory failure: the role of fungal infection**.
7. In the year 2017 -2018 a survey on the mycology laboratory in seven Asia countries was held, including Indonesia. There is almost no access to advanced diagnostic tests, like galactomannan, β -D-glucan, and PCR, in the surveyed laboratories in Indonesia.
8. Participated in the national formulary committee organized by the Ministry of Health of the Republic of Indonesia to determine the availability of antifungal drugs in Indonesia.

4.4.12 Portugal (Dr Raquel Sabino)

In Portugal several efforts to increase the awareness of fungal diseases were undertaken:

- Organization of the 2nd Meeting of the National Network of Laboratory Surveillance of Invasive and Subcutaneous Fungal Infections, 21 November 2018; Lisbon

- Participation in a course organized by the Institute of Tropical Medicine in cooperation with the Health Ministry of Mozambique with the following oral communication: “Deep and Invasive fungal infections”, 18 July 2018.
- Participation in a workshop on Invasive fungal infections with the following oral communication: “Surveillance and epidemiology of *Aspergillus* – the perspective of a reference laboratory”., Hotel Sana, Lisboa., 6 April 2018
- Participation in the meeting 8th Advances Against Aspergillosis with the following oral communication: “Risks for *Aspergillus*-Related Diseases: Occupational exposure and diseases”, 3 fevereiro 2018;, Lisboa, 1-3 Fevereiro 2018.
- Online News:

www.insa.min-saude.pt/instituto-ricardo-jorge-apresenta-resultados-nacionais-do-programa-de-vigilancia-de-resistencias-em-aspergillus/

www.insa.min-saude.pt/ii-reuniao-da-rede-nacional-para-vigilancia-laboratorial-das-infecoes-fungicas-invasivas-e-subcutaneas/

www.facebook.com/institutoricardojorge/posts/2349204415109099?

4.4.13 Hungary (Dr Janos Sinko)

A new educational program in infectology for medical students at Semmelweis Medical University Budapest was started, as well as a residency training both including basic concepts of invasive mycoses. Important discussion points of antifungal prophylaxis in high risk pediatric patient groups were raised at the 13th Regional Central-Eastern/South-Eastern European Pediatric Oncohematology Meeting. There are ongoing negotiations with the National Health Insurance Fund on more effective techniques in financing antifungal therapy and prophylaxis.

4.4.14 Serbia (Professor Valentina Arsic Arsenijevic)

Traditional national educational meeting Diagnosis and therapy of fungal diseases 6th (DTFD-6) was organized by Serbian Society of Medical Mycology - SSMM (www.mikologija.org.rs) in Belgrade on May 30, 2018, and June 20, 2018 (A-1-1110/18) and promoted GAFFI's goals as well as been an important educational meeting. (<http://mikologija.org.rs/2014/wp-content/uploads/2018/06/Pozivnica-Holiday-Inn-20.06.2018.pdf>);

In 2018 SSMM celebrated 10 years of existence and has announced a prize for the best published work in mycology for a young scientist, as well as a prize "Professor Sima Milosevic" for the significant contribution and development of medical mycology in Republic of Serbia.



First Balkan Conference on Medical Mycology and Mycotoxicology - young mycologists from Serbia - representatives of SSMM.

A new regional Balkan mycology platform has been initiated by Serbian Society of Medical Mycology (during TIMM 2017, Belgrade, Serbia) and established thanks to Prof Dr Mihai Maresh (Romanian Society of Medical Mycology and Mycotoxicology). First Balkan Conference on Medical Mycology and Mycotoxicology took place in Timișoara - Romania in September 2018, and attracted more than 220 participants, as well as experts in medical mycology (<http://balkanfungus.eu/>).

Liposomal amphotericin B was approved for use in Serbia for the first time in 2018.

Future actions:

- strengthening quality of fungal diseases surveillance data by improving reporting from hospitals and laboratories to National Reference Medical Mycology Laboratory;
- Concluding the "National guidelines for diagnosis and treatment of invasive fungal diseases";

4.4.15 France (Prof Jean-Pierre Gangneux)

France's GAFFI activities have focused principally in supporting and providing educational opportunities to several Maghreb countries.

4.4.16 UK (Professor David Denning)

Public Health England now publish an annual report on microbial resistance in the UK.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/759975/ESPAUR_2018_report.pdf Significant findings were a rate of azole resistance in *Aspergillus fumigatus* of 6% in South Wales, azole resistance of 5% in *Aspergillus terreus* (which is also amphotericin B resistant), and fewer *Candida auris* infection than in 2017. In 2017 they had highlighted limited laboratory capacity in medical mycology.

Future actions:

The ESPAUR subgroup on antifungal consumption and resistance surveillance will work co-operatively to wind down the subgroup without jeopardising stakeholder relationships. Antifungal surveillance will continue encompassing activities including:

- exploring options for presenting antifungal resistance and/or prescribing data on PHE's Fingertips web portal, including for example, antifungal stewardship indicators and routine surveillance data quality indicators such as species level identification and reporting of antifungal susceptibility test results for *Candida* isolates from blood
- strengthening quality of antifungal surveillance data by improving species-level reporting from NHS laboratories to SGSS
- continuing to scope harmonisation of breakpoints and access to diagnostic testing in collaboration with relevant networks given that reporting of AMR data for *Candida* and *Aspergillus* will be considered by WHO GLASS in the next the evaluation phase

In view of concerns about possible increases in fungal keratitis, a UK-wide one year surveillance study under the auspices of the British Ophthalmic Surveillance Unit (BOSU) at the Royal College of Ophthalmologists, with support from Public Health England, has received approval and will begin in Q2 2019 (The UK Fungal Keratitis in Incidence Study). BOSU studies involve all consultant ophthalmologists in the UK, who are expected to report the presentation of specific conditions on a monthly basis, leading to raised awareness and nationally representative incidence data.

Advocacy supporting the above 4 goals

Advocacy is a key continuing mission for GAFFI. Advocacy has and remains focused on the WHO and its regional offices, but is broadening to include country ministries of health and related institutions.

5.1 Neglected Tropical [Fungal] Diseases

GAFFI has proposed that sporotrichosis and paracoccidioidomycosis are added as NTDS, as fitting the WHO criteria, as the 'other deep mycoses'. www.gaffi.org/where/neglected-fungal-diseases/

A short paper summarizing the arguments for paracoccidioidomycosis being adopted as an NTD has been accepted for publication in the journal PLoS NTD. The GAFFI webpage has been updated to include fact sheets on mycetoma, sporotrichosis and paracoccidioidomycosis to accompany those on chromoblastomycosis and fungal keratitis: <https://www.gaffi.org/media/fact-sheets/>



5.2 ISHAM consensus meeting with WHO

56 attendees discussed the Fungal NTDs, diagnostics and future developments on June 30th, at the ISHAM congress in Amsterdam. After introductions and status summaries of mycetoma, chromoblastomycosis and sporotrichosis, Professor Roderick Hay presented the results of a survey on diagnostic approaches for these 3 fungal NTDs. There was wide agreement on the gold standards for laboratory investigations including imaging techniques for the Fungal NTDs and the potential way forward for providing better training for clinical, settings where there was limited access to laboratory facilities through strengthening skills in direct microscopy. Sporotrichosis remains a problem but a way forward would be to capture the key clinical elements of lymphatic spread or granuloma or plaque formation spread as entry points to further investigation.



There was widespread agreement to group fungal NTDs under a common grouping which would have significant benefits in terms of training and diagnostic capability, research, epidemiology and public health strategies – it would also foster alliances with other NTD groupings.

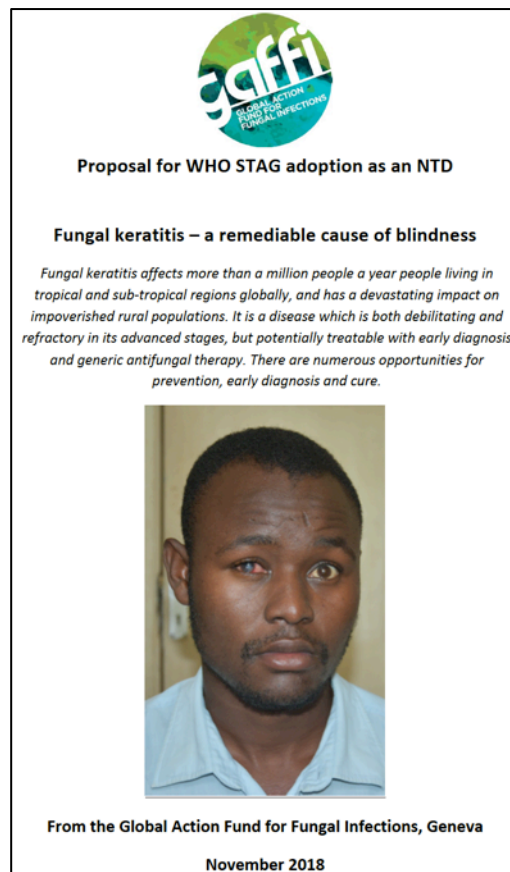
Resolutions - summary

- A. To develop a common strategy for the fungal NTDs and that as a consequence sporotrichosis would be brought into this grouping (Action: All)
- B. To produce a draft consensus paper on the investigation and diagnosis of fungal NTDs – mycetoma, chromoblastomycosis and sporotrichosis (Action: RJH)

5.3 Fungal keratitis as an NTD

GAFFI has applied to the WHO for Fungal Keratitis to be accepted as an NTD. A number of feasible initiatives, if widely implemented, could have a very substantial impact on reducing the global fungal keratitis disease burden, thought to exceed 1.2 million cases annually:

1. Encourage the generation of local epidemiological studies to accurately estimate incidence, DALYs and QALYs, morbidity and mortality rates of fungal keratitis, so that the true burden of fungal keratitis can be quantified,
2. Develop a point of care antigen test as a tool for rapid, primary diagnosis, that is suitable for low resource settings, that accurately differentiates bacterial infection from fungal infection,
3. Provide training in conventional microbiological diagnostic procedures including sampling, microscopy (see www.microfungi.net), culture techniques and fungal species identification,
4. Optimise use of antifungal therapy in resource limited settings through promoting a global approach to the prevention, diagnosis and management of microbial keratitis:
 - a. Enhance laboratory diagnostic capability through the provision of resources and training (direct microscopy and culture) thereby improving diagnostic accuracy and appropriate prescribing of antimicrobial chemotherapy
 - b. Investigate the value of introducing combination treatment with antibiotic and antifungal eye drops versus early diagnosis of the cause and targeted therapy,
 - c. Ensure that antifungal treatments, especially natamycin eye drops, are readily accessible, especially in deprived, rural settings by implementing sustainable drug donation programmes. Natamycin 5% eye drops are registered and available in a few countries but its global availability at an affordable cost is necessary. The incentives to manufacture and distribute antifungal eye drops is low compared with other products. Sustainable drug donation programmes are required to provide effective treatment for the many people affected by this condition, especially in small countries.
 - d. Develop prophylactic, pre-emptive management guidelines for ocular injuries,
 - e. Revise the SEARO 2004 guidelines on microbial keratitis,
 - f. Support research into the development of new, more effective antifungal agents and the improvement and adaptation of current medications so that they are more practical.
5. Engage local communities in education and awareness of the symptoms of microbial eye infection, encourage self-referral and provide local community health workers with effective training in detecting corneal abrasion and prophylactic topical antimicrobial medication.



6. Advocate for the introduction of protective glasses for agricultural workers and encourage employers to adopt safer farming practices.

This initiative on fungal keratitis is formally supported by the governments of India, Bangladesh, Myanmar, Malawi and Togo.

5.4 Chronic pulmonary aspergillosis

In August 2018, GAFFI consensus paper on chronic pulmonary aspergillosis diagnosis in LMICs was published in Emerging Infectious Diseases. In September, the topic was aired in front of 1000 participants at the European Respiratory Society meeting in Paris in a 2 hour session wholly devoted to this topic. The awareness of this severe and ultimately fatal chronic lung fungal disease is much more widespread as a result.



2019 plans and aspirations

The clinical outcomes of GAFFI's project in Guatemala are currently being analysed and we anticipate that these data will demonstrate the importance of a) rapid diagnosis, b) screening HIV patients for life-threatening infections rather than relying on clinical impression and individual requests, c) the value of a partially disbursed and partially centralized diagnostic service utilising a well run reference laboratory and d) the importance of linked training between clinicians and diagnostic providers.

GAFFI is planning regional meetings to address integration of fungal disease diagnosis and management into national health systems. The first of these meetings will be for Latin America and be held in Lima, Peru in September 2019.

GAFFI will apply for *Aspergillus* antigen, *Aspergillus* antibody and therapeutic drug monitoring of the essential medicines itraconazole and voriconazole to be included in the WHO Essential Diagnostics list.

GAFFI has applied for fungal keratitis to be accepted as a NTD and if approved, plans made with the WHO and global ophthalmology community to implement improvements in care, partly through access to natamycin eye drops. The arguments have been made to extend Neglected [Fungal] Tropical Diseases to include sporotrichosis and paracoccidioidomycosis, and further efforts are necessary to achieve this.

A second national demonstration project is to be launched in Kenya in 2019. FIP-Kenya is a unique initiative that will improve clinical outcomes by strengthening public health capabilities and promoting research on the understanding, prevention, diagnosis and treatment of fungal infections. Ms Emma Orefuwa as Chief Executive Kenya will drive this transformational project forward.

GAFFI will submit an application to be accepted as a Non-State Actor by the WHO by being in 'Official Relations' with the WHO.

Further advocacy and action is necessary to ensure that antifungals (especially flucytosine, topical natamycin and voriconazole) are available to everyone is necessary and will be addressed, with partners. Access to antifungals by country will be updated in 2019.

Glossary of terms, organisations and abbreviations:

AMR – Antimicrobial Resistance

CDC – US Centers for Disease Control and Prevention

EDL – Essential Diagnostics List

FIP-Kenya – Fungal Infections Program Kenya

JICA – Japan International Co-operation Agency

LIFE – Leading International Fungal Education

MALDI-TOF – Matrix-assisted laser desorption/ionization time-of-flight mass spectroscopy

MSF – Medicines Sans Frontières

PAHO – Pan-American Health Organization

PCR – Polymerase chain reaction

UNITAID – Agency hosted by WHO in Geneva.

WHO – World Health Organisation

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www.gaffi.org/global-fungal-infection-forum-3-in-kampala/

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From <https://www.gaffi.org/media/news/>

Histoplasmosis in Africa is under-recognised and under-reported

Posted January 23, 2018

Global health improvement targets announced on World Aspergillosis Day

Posted February 11, 2018.

Guatemala programme doubles the diagnosis of fatal fungal infections in AIDS

Posted March 12, 2018.

Flucytosine takes centre stage for cryptococcal meningitis in AIDS

Posted March 15, 2018.

Addressing the importance of building diagnostic capacity in East African Hospitals

Posted March 27, 2018.

Consensus on 'Essential Diagnostics for Advanced AIDS and fungal diseases?'

Posted April 11, 2018.

GAFFI annual report released alongside burden of fungal diseases estimates for Benin and Sweden

Posted April 23, 2018.

WHO releases its first Essential Diagnostic List

Posted May 17, 2018.

Two point-of-care tests for invasive aspergillosis launched

Posted June 21, 2018.

Burden of fungal disease for 13 countries published in Journal of Fungi

Posted June 28, 2018.

Doctors and scientists meeting in Uganda sets new standards for essential diagnostics in AIDS

Posted July 10, 2018.

GAFFI establishes new executive structure to strengthen strategy implementation

Posted July 17, 2018.

[**New figures show 138 million women suffer from recurrent thrush**](#)

Posted August 2, 2018.

[**Is it TB or a fungal lung infection? New life saving guidelines released today**](#)

Posted August 7, 2018.

[**Histoplasmosis competes with TB as top killer of Latin American AIDS patients**](#)

Posted August 30, 2018.

[**Article published in Le Monde highlights threats from fungal infections of humans, crops and wildlife**](#)

Posted September 20, 2018.

[**Donald Mackay Medal \(RSTMH\) awarded to Professor Ahmed Hassan Fahal of the Mycetoma Research Centre in Khartoum**](#)

Posted September 21, 2018.

[**Gilead reduces price of AmBisome \(liposomal amphotericin B\) for cryptococcal meningitis in HIV/AIDS**](#)

Posted September 28, 2018.

[**Director-General of WHO calls for more mycetoma research during visit to Mycetoma Research Centre in Khartoum \(Sudan\)**](#)

Posted October 18, 2018.

[**Burden of serious fungal diseases in Ghana, South Africa, Ethiopia and Taiwan presented in Dubai at GCCMID**](#)

Posted November 14, 2018.