



Report on activities for 2019

95/95
BY 2025

May 2020

Summary

There is palpable progress in GAFFI's mission to reduce illness and death associated with fungal diseases worldwide and support greater awareness. Its achievements in 2019, its sixth year of operation, include:

- GAFFI organized and lead the world's first conference on **fungal diseases and health systems** in Lima, Peru in September 2019 with PAHO and CDC. This meeting, in Spanish, was attended by 18 Latin American and Caribbean countries and developed a 7-point plan to adopt the latest diagnostics for fungal diseases and integrate these within HIV/AIDS, TB and hospital programs. The meeting also addressed antifungal drug resistance (AMR) and the new GLASS program on collecting data on resistance in *Candida* spp.
- **Burden of Serious Fungal Diseases:** The program of mapping how many fungal diseases there are in each country has now reached 98 countries. New maps of histoplasmosis hot spots for SE Asia were published. The first estimation of the burden of fungal keratitis was presented – an annual incidence of 1.05-1.40 million eyes affected.
- Application to the WHO to include ***Histoplasma* antigen as Essential** on the Model List of in vitro Diagnostics: GAFFI's application for *Histoplasma* antigen to be included the WHO Essential Diagnostic list was accepted and further applications for *Aspergillus* antigen, *Aspergillus* antibody and *Pneumocystis* PCR submitted.
- **Diagnostic Laboratory Hub in Guatemala:** In 2017-18, there was a 22% incidence of life-threatening infection among 4,666 people with HIV, rising to 33.1% in those with low (< 200 CD4/mm³) counts. Advanced HIV disease is the norm (52%) in newly presenting people with HIV and in these, histoplasmosis is found in 7.9% followed by tuberculosis (7.1%). Patients are screened for disseminated histoplasmosis, cryptococcal meningitis, tuberculosis and non-tuberculosis mycobacteria. Additional testing is done for clinical suspicion, including PCR for *Pneumocystis* pneumonia.
- **State Diagnostic Mycology Laboratories in India:** The Indian Council of Medical Research (ICMR) has initiated mycology reference laboratories at 40 different locations of the country over the next 5 years, with 4 established in Bhopal, New Delhi, Jodhpur and Puducherry.
- **Fungal NTDs:** GAFFI made the case of paracoccidioidomycosis in S. America and sporotrichosis to be accepted as NTDs and this has been taken up by PAHO. GAFFI initiated a survey of experts on the optimal diagnostic approach to the skin NTDs, mycetoma, chromoblastomycosis and sporotrichosis, which is now published. The case for fungal keratitis to be adopted as a Neglected Tropic Disease (NTD) by WHO was made again, and the first estimate of annual incidence (over 1,000,000 eyes) presented at ECCMID in April.
- **GAFFI's Ambassadors' activities:** Multiple educational programs and awareness have been delivered in Mexico, Indonesia, India, Serbia, Hungary, France, Norway, Portugal, Nigeria, Cameroon, Ghana and South Africa.
- **Health professional education:** GAFFI's educational partner LIFE-Worldwide has expanded its offerings of multiple online videos and podcasts on key fungal disease [topics](#). Many diagnostic procedures are now demonstrated by video for the first time.

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 fewer than 500,000 by 2020, with a determined focus on the commonest lethal fungal infections.

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. The WHO endorsed [Essential Diagnostic tests](#) (2019) for fungal diseases
- Integrate fungal diseases diagnostics into the health system of each country including at least one laboratory led by an expert in fungal disease and a 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's Board is chaired by Professor Nigel Lightfoot (UK) and supported by Victor Rydgren (Vice-Chair) (Norway), Yasu Mori (Japan), Professor Michel Glauser (Switzerland), Professor Patrick Francioli (Switzerland) and Oddi Aasheim (UK). Professor David Denning is Chief Executive, Ms Emma Orefuwa Chief Executive Kenya and Timothy Moss Head of Administration. GAFFI and GAFFI UK have identical Board membership to facilitate achieving GAFFI's aims.



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 in part 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

In 2019, burden papers were published for a further 8 countries including Ghana, South Africa, Namibia, Ethiopia, Kyrgyzstan, Tajikistan, Taiwan and Sweden. Fungal disease estimates are now published for 65 countries as shown [here](#):

Abstracts and posters of country serious fungal disease burdens were presented in 2019 at several [ECCMID](#) and [TIMM](#) congresses for Paraguay, Sudan, Morocco, Cote d'Ivoire and Azerbaijan. The Health Systems meeting in Lima (Section 5) generated the first burden estimates for Bolivia, Panama, Nicaragua, Honduras, Costa Rica and Cuba, [here](#).

1.2 DALYs estimated for invasive aspergillosis

In Iran, where there is great interest and focus on fungal disease, the societal impact of invasive aspergillosis was assessed using disability-adjusted life years (DALYs) (Tavakoli, 2019). The DALYs of invasive aspergillosis was estimated at 164.13 per 100,000 population, of which years of life lost (YLLs) constitute the majority of IA burden. The age groups most affected were 30-49 years. An increasing burden of IA in Iran, despite the extensive use of prophylaxis, is challenging the public health. This is the first DALY estimate for this disease, and one of very few for fungal diseases generally.

1.3 Global burden of fungal keratitis

A poster at ECCMID in Amsterdam, April 2019, reported a systematic review of the literature. A minimum global annual incidence estimate of 1,052,794 cases (range 736,970-1,368,660) was found, with the highest rates in Asia and Africa. The outcomes were generally poor, with 8-11% of patients having to have the eye removed, an annual loss of an estimated 94,753 to 115,810 eyes.



Goal 2 - Improve access to diagnostics for fungal disease

In the last 10 years, there has been a true revolution in fungal diagnostics shifting from 'classical' culture and microscopy to PCR, antigen and antibody detection. Improved access to sensitive and rapid diagnostics is a critically important GAFFI goal, especially in low- and middle-income countries and as fungal diseases are often clinically silent in their early stages and can mimic other infections, 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.

2.1 Integration of fungal diseases into health systems in Latin America

In Lima, Peru in September 2019, the Global Action Fund for Fungal Infections (GAFFI) convened 60 delegates from 18 Latin American and Caribbean countries to discuss how fungal disease diagnosis and antifungal therapy could be better integrated into healthcare systems across the continent (GFIF4, 2019). The growing problem of antifungal resistance was one of the meeting's focal points, emphasised by the global emergence of *Candida auris*. See section 5.1.



2.2 Essential Diagnostics for fungal diseases and advanced HIV infection

GAFFI's application for *Histoplasma* antigen to be included on the WHO Model List for in vitro Diagnostics was approved. 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](#)). 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/>). In late 2019, the lateral flow assay for *Histoplasma* antigen was launched with excellent performance on stored and culture proven cases (sensitivity of 96% and specificity 90%, when the LFA was read manually). This application followed GAFFI's successful meeting on Essential Diagnostics in Kampala in April 2018 and publication of a summary of that meeting in 2019.



In 2019, GAFFI has applied for *Aspergillus* antigen, *Aspergillus* IgG antibody and *Pneumocystis* PCR to be adopted onto the Essential Diagnostic list. The outcome will be known in mid 2020. Discussions with the EDL team in Geneva about therapeutic drug monitoring of the essential medicines itraconazole and voriconazole lead to a conclusion that these would not be supported currently as 'diagnostics'.

The first case of chronic pulmonary aspergillosis diagnosed with *Aspergillus* antibody LFA in Kagando, Uganda

There is a need to standardise (possibly via commercialization) of the antibody tests for paracoccidiodomycosis, chronic and subacute histoplasmosis and sporotrichosis.

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 Samayoa 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.

The first publication of this project is already available: Samayoa B et al. The Diagnostic Laboratory Hub: A New Health Care System Reveals the Incidence and Mortality of Tuberculosis, Histoplasmosis, and Cryptococcosis of PWH in Guatemala (see publication list).

2.3.5 Next steps

- Document the successes and challenges of the project in publications. A fellowship awarded to the Guatemala team is being trained at the Medical Mycology Reference Laboratory in Spain and her PhD thesis includes the complex data analysis of the project.
- Analyse in 2020, by means of a survey, the performance of the project in order to design which interventions are needed to implement a program to decrease the mortality of patients living with HIV and OIs
- 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 and liposomal amphotericin B
- Assess the value of additional tests in the diagnostic portfolio, including *Aspergillus* IgG, and probably *Toxoplasma* serology and TB antigen (LAM) testing.

2.4 Guidelines for disseminated histoplasmosis in HIV/AIDS – the Manaus declaration

In Latin America, probably more people die of histoplasmosis complicating AIDS than tuberculosis. In March 2019, in Manaus, Brazil, the [2nd meeting on Histoplasmosis in the Americas and Caribbean](#) was held with representation from most Latin American countries as well as Jamaica, Cuba, Dominican Republic and Trinidad and Tobago. The focus of the meeting was a discussion on how best to utilize the new knowledge about the value of new rapid testing for histoplasmosis. A Manaus Declaration was issued for all advanced HIV patients in the Americas and Caribbean:

1. Timely access to antigen or PCR diagnostic tests (ie with 48 hours in a working week).
2. Access to amphotericin B, liposomal amphotericin B and itraconazole in the public sector by 2025.



2.5 Diagnosis of fungal NTDs

Following meeting of >50 delegates to ISHAM congress in Amsterdam, 2018 (see GAFFI 2018 Annual Report), 23 experienced mycologists and clinicians participated in a survey to describe current practice in the diagnosis of mycetoma, chromoblastomycosis and sporotrichosis (Hay et al, 2019). Questions were in three categories: 1) for well-equipped diagnostic or clinical settings in each respondent's country, 2) confirmatory tests that could be used in peripheral clinics or laboratories with little expertise in mycological techniques and 3) the best methods of obtaining diagnostic specimens. The responses are summarized here:

Table 1. Optimal diagnostic methods in a well provided laboratory—positive responses.

Disease	Clinical Features	Direct Microscopy	Culture	Serology	Molecular Diagnosis	Histopathology	Other
Mycetoma	92%	88%	96%	8%	71%	88%	imaging, dermoscopy
Chromoblastomycosis	88%	92%	96%	8%	50%	92%	dermoscopy
Sporotrichosis	83%	25% ¹	96%	4%	50%	67%	intra-dermal test

and

Table 2. Diagnostic methods of use in peripheral clinics and laboratories (positive results).

Disease	Clinical Features	Direct Microscopy	Culture	Serology	Molecular Diagnosis	Histopathology	Other
Mycetoma	96%	88%	33%	-	13%	43%	imaging
Chromoblastomycosis	96%	92%	33%	8%	4%	54%	
Sporotrichosis	88%	42%	50%	4%	45	21%	

The survey identified that the diagnosis of sporotrichosis is the most problematic with most tests having poor sensitivity except fungal culture. A clear need to improve mycological diagnostic capacity is required, including more robust evaluations of antibody detection and skin testing, as well as developing innovative diagnostic solutions.

2.6 Mycology Diagnostic Reference centres in India

The Indian Council of Medical Research (ICMR), New Delhi has taken up a major initiative to set up mycology reference laboratories at 40 different locations of the country over five years period; one laboratory each in small provinces, and more than one in large provinces. The reference laboratories will provide advanced diagnostics in each catchment area and establish

a strong platform for training and research on fungal infections. This initiative was actively promoted by GAFFI's Senior Advisor Dr Swarup Sarkar and Prof. Arunaloke Chakrabarti (GAFFI Senior Advisor and Head of the National Mycology Reference Laboratory) is mentor to the program.

The reference laboratories will also form a mycology network for surveillance of mapping of fungal disease of the country, organize CMEs to create awareness and training of doctors and laboratory. In this year, four centres have been identified at All India Institute of Medical Science, Jodhpur; Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry; All India Institute of Medical Science, Bhopal; and Lady Hardinge Medical College, New Delhi, complementing the National Mycology Reference Laboratory and WHO Collaborating Centre at PGIMR, Chandigarh.



Funds have been sanctioned for the purchase of equipment, consumables and recruitment of dedicated staff in mycology. It has been decided to incorporate non-culture based diagnostics in this year at those centres. Manpower will be trained in Chandigarh. They will also participate in the external quality assurance program run by the National Reference Laboratory

2.7 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 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. Emma Orefuwa (GAFFI) is in close collaboration with the Ministry of Health to enable the program to start, probably in 2021 (delayed because of COVID-19).

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 Global mapping of current availability and price of antifungal drugs

GAFFI has substantially updated its antifungal [maps](#), notably with voriconazole and numerous other country data. This is ongoing. Enormous gaps in coverage still exist, notably with liposomal amphotericin B, flucytosine, voriconazole in Africa and topical natamycin.

3.2 Echinocandin antifungals (caspofungin, micafungin and anidulafungin)

The recurrent outbreaks and endemic foci of *Candida auris* have prompted GAFFI to reconsider applying to the WHO for the intravenous echinocandins as 'Essential Medicines'. Countries with known ongoing problems (i.e. endemicity) with *Candida auris* have included Kuwait, India, Kenya and South Africa. The WHO application will be submitted in 2020 and accompanied by global maps of availability.



3.1.2 Improved pricing of liposomal amphotericin B for cryptococcal meningitis

In 2017, 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. Logistical and access issues continue (see [antifungal availability maps](#)), and there is only limited success of this program so far.

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’](#): GAFFI also has a [twitter](#) account with >1,600 followers.

4.1 GAFFI Ambassadors

GAFFI’s Ambassadors network expanded in 2019 to include Wadha A m Alfouzan (Kuwait), Gloria Aguilar Barreto (Paraguay), Bright Ocansey (Ghana), Christophe Hennequin (France), Tafese Tufa (Ethiopia), Cara Mia Dunaiski (Namibia), Luis Ostrovsky- Zeichner (USA), Aiah Khateb (Saudi Arabia). GAFFI’s Ambassador group from Latin America played an important part in the Lima Health Systems meeting and follow up. All GAFFI’s [Ambassadors](#) are listed here: Their country reports for 2019 are found in the last section of this report.

GAFFI is extremely grateful to its Ambassadors for their continuing efforts related to raising the awareness of fungal diseases, direct advocacy, educational initiatives and providing information about their country.



Here Dr Samuel Fayemiwo (GAFFI Ambassador, Nigeria, second from right) hosts a dinner in Manchester with (from left) Dr Haruna Muda (Manchester Metropolitan University), Emma Orefuwa (GAFFI), Prof Isaac Adewole (Minister for Health, Nigeria), Dr Kelechi Njoku (University of Manchester), and Dr Akan Inyene Otu (Manchester).

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](#). 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 Royal College of Pathologists in the UK.

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 Health Systems and Fungal Diseases – Latin America

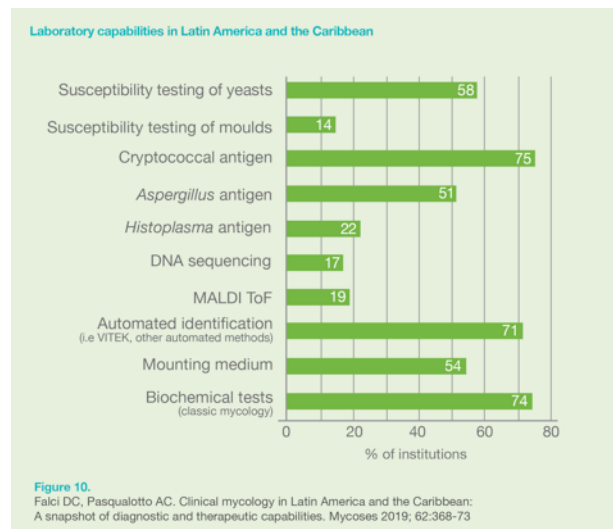
In Lima, Peru in September 2019, GAFFI convened 60 delegates from 18 Latin American and Caribbean countries to discuss how fungal disease diagnosis and antifungal therapy could be better integrated into healthcare systems across the continent. The stimulus for the GFIF4 meeting was a paper published in *Lancet Infectious Diseases* by Cole et al (2017) “Improvement of fungal disease identification and management: combined health systems and public health approaches.” This paper noted that a) “Fungal disease diagnosis requires a high level of clinical suspicion and specialised laboratory testing, in addition to culture, histopathology, and imaging expertise” and b) “Health systems linking diagnostic facilities with therapeutic expertise are typically fragmented, with major elements missing in thousands of secondary care and hospital settings.” There was also a significant focus on capturing susceptibility data of *Candida* spp. from the continent, via the WHO GLASS program. The meeting was held in Spanish with simultaneous translation into English. The program and estimate of the burden of fungal disease in Latin America is [here](#). The full report is due to be issued in June 2020.

5.1.1 Healthcare systems, workforce and burden of fungal diseases

The meeting heard about the burden of fungal diseases, the complexity of many of the patients’ health problems, challenges in interpretation of radiology and the current status of healthcare systems in many countries. In particular, health expenditure, healthcare access and quality of care were shown to be highly variable across the continent. A major threat to healthcare was the shortage of healthcare workers: 30% of countries did not have enough healthcare workers to cover basic health needs. Health workforce per 10,000 population (2017-2018) for all the Americas was 89.3, distributed as North America 170.8 and Latin America and the Caribbean 42.6.

5.1.2 Fungal disease diagnostics

The meeting also addressed diagnostics for fungal diseases. Many non-culture tests are unavailable across the region. The Region is participating in the early implementation of the Global WHO initiative to strengthen laboratory mycology capacity, data management, and AMR *Candida* surveillance. The National Reference Laboratory in Clinical Mycology at the Instituto Carlos G. Malbrán, Buenos Aires, Argentina is an example of a well-established laboratory in the region, and the Diagnostic Laboratory Hub at the



ASI in Guatemala another innovative example of a progressive approach to diagnostics.

The meeting made multiple recommendations with respect to adoption of rapid non-culture diagnostics and defined 3 priorities regarding diagnostics:

Key priority 1:

All WHO recommended Essential Diagnostics for fungal diseases should be implemented for routine use in public hospitals (provincial-state equivalent and above) and AIDS focused clinics. This will strengthen diagnostic capability throughout the Region.

Key priority 2:

These developments should be accompanied by engagement with external proficiency quality assurance programs. Development of National Diagnostic Mycology laboratories and networks would support critical mass in this discipline.

Key priority 3:

Applications should be made to the WHO to include *Pneumocystis* PCR as an Essential Diagnostic.

5.1.3 Essential antifungal medicines

Both conventional amphotericin B (approved 1957) and fluconazole (approved 1990) are available in all countries but liposomal amphotericin B (approved 1995) is not approved or available in several countries. Itraconazole (approved 1991) is mostly available across the region but voriconazole (approved 2002) is not available in several countries. Flucytosine (approved 1974) , is only available in Colombia, Cuba and Surinam. Topical natamycin is only available in Argentina, Colombia, Cuba and Mexico. The problem of *Candida auris* and a general increase in azole resistance prompted many discussions on how best to address resistance with current antifungals.

The meeting was introduced to the PAHO Strategic fund which is able to 1) negotiate competitive prices, which is particularly helpful to smaller countries, 2) provide technical support for planning, procurement and distribution, and 3) provide a line of credit a line of credit for governments. All the Essential systemic antifungals are available through the Fund apart from topical natamycin.

With respect to antifungal therapy, the meeting agreed that:

Key priority 4:

Applications should be made to the WHO to include echinocandins as Essential Medicines.

5.1.4 Addressing public health, antifungal resistance and stewardship

Several presentations addressed the role of diagnostics for antifungal (and anti-bacterial) stewardship and laboratory capability in detecting antifungal resistance. In Latin America, limited resources have been allocated for addressing antifungal drug resistance, and few countries perform any surveillance. Little information exists about the population prevalence or clinical incidence of antifungal resistance in many parts of Latin America.

The meeting made multiple recommendations for laboratories and well as defining 2 priorities:

Key priority 5:

Strengthening of public health for fungal diseases including a) development of specific surveillance programs to track fungal infections of public health importance, including *Candida auris*, the NTD sporotrichosis and serious endemic fungal infections and b) active epidemiology research programs, using point of care and non-culture diagnostics.

Key priority 6:

National antifungal resistance surveillance programs should be developed in public hospitals (provincial/state equivalent and above), with national reporting.

5.1.5 Education

Ongoing training is essential to provide quality care to patients with fungal diseases. Fungal diseases present to numerous different medical specialties including primary care, dermatology, respiratory medicine, HIV/AIDS and infectious diseases, intensive care, gynaecology, haematology,

ophthalmology, otolaryngology, paediatrics and pharmacy. There are courses for fungal diseases in several countries of Latin America including Argentina, Brazil, Chile, Colombia, Costa Rica, Ecuador, Peru, Uruguay and Venezuela (listed in the report). The meeting endorsed a common medical curriculum for fungal diseases as well as identifying 2 priorities:

Key priority 7:

Substantial educational efforts of healthcare

professionals, notably in the use of non-culture diagnostics, antifungal usage and stewardship programs, WHO Guidelines for Advanced HIV disease, cryptococcal meningitis and other international clinical and laboratory practice guidelines.

Key priority 8:

Assessment and then implementation of artificial intelligence systems to counteract the shortfall in healthcare professionals, notably in radiology, histopathology, dermatology and ophthalmology.

5.1.6 Fungal diseases, health systems and Sustainable Development Goals

The meeting fulfilled its direct objective of addressing how to reduce premature death and improve the health of people in Latin America, which is (SDG3). In addition, several other SDGs are addressable by implementing improvements for fungal disease diagnosis and care. These include SDGs 1, 4, 8, 9, 12, 16 and 17.

5.3 Fungal keratitis may be included as a priority disease by the WHO

GAFFI applied to the WHO for Fungal Keratitis to be accepted as an NTD, but this has not been accepted because of the number of unfulfilled tasks for many other NTDs. GAFFI's focus will therefore shift to the Blindness prevention program at WHO. In October 2019, launched its first [World Report](#) on vision.



5.4 Fungal Disease Awareness Week

The National Institute for Communicable Diseases in Johannesburg, South Africa hosted several activities for Fungal Disease Awareness Week in 2019. This included an educational fungal fact walk across the NICD campus with interactive games (PCP game pictured below).



5.5 GAFFI West and North African meeting at TIMM

At the TIMM meeting in Nice, Jean Pierre Gangneux and Christophe Hennequin hosted a dinner of GAFFI Ambassadors and fungal experts from North and West Africa.



5.6 GAFFI presents to the Global Health committee at the Bundestag, Germany

As part of the One Health concept, GAFFI's Chief Executive Professor David Denning and Senior Medical Adviser Professor Juan Luis Rodriguez Tudela spoke at the hour long meeting in the Bundestag presenting the case for more investment into fungal diseases by Germany and EU. Separate meetings with Federal Ministry of Health and Federal Ministry of Education and Research officials responsible for Global Health to exchange ideas about how Germany could best contribute to improving health in Africa and Eastern Europe related to fungal diseases.



2020 plans and aspirations

The Diagnostic Laboratory Hub in Guatemala is preparing several publications, including the diagnostic outcomes over 2017 and 2018 and any trends. An economic evaluation of the program is also underway.

GAFFI has applied to the WHO for *Aspergillus* antigen, *Aspergillus* antibody and *Pneumocystis* PCR to be Essential Diagnostics.

A second national demonstration project was to be launched in Kenya in 2020, but is delayed because of the COVID-19 crisis. 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.

Further advocacy and action are necessary to ensure that antifungals (especially flucytosine, topical natamycin and voriconazole) are available to everyone is necessary and will be addressed, with partners. The antifungals country database will be continually updated in 2020.

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

SDG – Sustainable Development Goals

UNITAID – Agency hosted by WHO in Geneva.

WHO – World Health Organisation

Publications

Burden of disease papers:

1. Hedayati MT, Armaki MT, Jamshid, Charati Y, Hedayati N, Seyedmousavi S, Denning DW. Burden of fungal infections in Iran. **J Infect Dis Dev Ctries** 2018; 12:910-18.
2. Hilmioğlu-Polat S, Seyedmousavi S, Ilkit M, Hedayati MT, Inci R, Tumbay E, Denning DW. Estimated burden of serious human fungal diseases in Turkey. **Mycoses** 2019;62:22-31.
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4. Turdumambetova GN, Osmanov A, Denning DW. The burden of serious fungal infections in Kyrgyzstan. **J Fungi (Basel)** 2019;5:66.
5. Bobokhojaev OI, Osmanov A, Aliev SP, Radjabzoda AS, Avgonov ZT, Manonov ST, Denning DW. The burden of serious fungal infections in Tajikistan. **J Fungi (Basel)** 2019;5:68.
6. Dunaiski CM, Denning DW. Estimated burden of fungal infections in Namibia. **J Fungi (Basel)** 2019; 5:75.
7. Huang YS, Denning DW, Shih S-M, Hsiung CA, Wu U-I, Sun H-S, Chen P-Y, Chen Y-C, Chang SC. Fungal diseases in Taiwan – National Insurance Data and Estimation. **J Fungi (Basel)** 2019;5: 78.
8. Özenci V, Klingspor L, Ullberg M, Chryssanthou E, Denning DW, Kondori N. Estimated burden of fungal infections in Sweden. **Mycoses** 2019;62:1043-1048.
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12. van Schalkwyk E, Mpembe RS, Thomas J, Shuping L, Ismail H, Lowman W, Karstaedt AS, Chibabhai V, Wadula J, Avenant T, Messina A, Govind CN, Moodley K, Dawood H, Ramjathan P, Govender NP; GERMS-SA. Epidemiologic Shift in Candidemia Driven by *Candida auris*, South Africa, 2016-2017. **Emerg Infect Dis** 2019;25(9):1698-1707.
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Key papers, reviews and position papers

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Press releases and GAFFI news items in 2019:

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

February 1st

[**New crop fungicides could increase antifungal resistance WHO requested to act**](#)

February 11th

[**GHANA'S CPA AWARENESS SEMINAR ON WORLD ASPERGILLOSIS DAY**](#)

March 19th

[**1 in 15 TB sufferers go on to develop chronic pulmonary aspergillosis, treatment could save 1000s of lives**](#)

March 26th

[**The Manaus Declaration on Histoplasmosis in the Americas and Caribbean 100 by 2025**](#)

April 9th

[**GAFFI issues its 5th annual report highlighting its extensive advocacy work**](#)

April 16th

[**ECCMID 2019 presentations: burden of fungal disease estimates for Namibia, Paraguay and Kyrgyzstan; and fungal keratitis leads to over 600,000 blind eyes annually**](#)

May 20th

[**Paracoccidioidomycosis in South America should be a Neglected Fungal Tropical Disease**](#)

June 5th

[**Dr Swarup Sarkar joins GAFFI as a Senior Advisor**](#)

July 5th

[**LDBio rapid Aspergillus IgG test is sensitive and specific for chronic pulmonary aspergillosis**](#)

July 11th

[**Following GAFFI submission WHO endorses Histoplasma antigen as an Essential Diagnostic**](#)

August 6th

[**Hyper-endemic areas for histoplasmosis revealed in new SE Asian maps**](#)

September 6th

[**GAFFI calls together experts in Lima to formulate new thinking on fungal disease management in Latin America**](#)

September 20th

[**THE GLOBAL ACTION FUND FOR FUNGAL INFECTIONS \(GAFFI\) WILL #FIGHTFUNGUS WITH GLOBAL AWARENESS CAMPAIGN**](#)

October 1st

[**Medical experts stress the need for new ways of diagnosing neglected tropical fungal skin disease**](#)

October 14th

[**Fungal infection burden in Morocco, Sudan, Cote d'Ivoire, Tajikistan and Azerbaijan presented at TIMM**](#)

December 12th

[**GAFFI presents the case for investment into fungal diseases to Bundestag, Berlin.**](#)

GAFFI's Ambassadors awareness and educational initiatives:

Latin America

The GAFFI Ambassadors from Latin America made major contributions to the Lima Health Systems meeting, described above (Section 5.1). Argentina (Dr Fernando Riviera), Brazil (Dr Flavio Quieros Telles), Chile (Dr Eduardo Alvarez-Duarte), Colombia (Dr Jorge Professor Jorge Alberto Cortés and Professor Carlos Arturo Alvarez-Moreno), Ecuador (Dr Jeannete Zurita), Guatemala (Dr Eduardo Arathoon and Dr Blanca Samayoa), Mexico (Dr Dora Corzo-Leon and Professor Alexandro Bonifaz), Paraguay (Dr Gloria Celeste Aguilar Barreto), Peru (Dr Beatriz Bustamante), Uruguay (Dr Marina Macedo).

Mexico (Dr Dora Corzo-Leon and Professor Alexandro Bonifaz)

An online course was developed by two Mexican infectious diseases specialists (Dora Corzo-Leon and Norma Rivera). The course aimed to improve diagnosis of SFIs and was delivered from April-June 2019. The course was carried out 100% in Spanish and consisted of 9 online interactive sessions every week. The topics were: biosecurity, staining techniques, cytology, histology, fungal culture techniques and diagnostics without culture. Several online resources were used, including <http://www.life-worldwide.org> and <http://www.microfungi.net>. A total of 137 people registered for the course. Registrants were from four different countries, Mexico (126, 92%), Ecuador (9, 6.6%), Australia (1, 0.7%) and Bolivia (1, 0.7%). Mexican participants connected from 15 of the 32 regions (47%) in Mexico. Most participants were physicians (76%), 54 were ID specialists and 19 were ID residents. Sixty participants (60/137, 44%) completed the course. Preliminary results of this course were presented at FIS 2019 (abstract published at access microbiology <https://doi.org/10.1099/acmi.fis2019.po0195>) at Edinburgh and final results will be presented in Mycology 2020 at London.

India (Professor Arunaloke Chakrabarti_

Training in diagnostic mycology

The National Mycology Reference Center conducted regular training of faculty/scientists and technical staff twice annually for the last 12 years. The topics covered in the course include; processing of clinical specimen for culture and direct microscopy, phenotypic identification of yeast and moulds, serological techniques for the diagnosis of fungal infections, therapeutic drug monitoring (TDM) of antifungals, DNA and MALDI -TOF based molecular techniques for the diagnosis of fungal infections, identification of fungal agents and typing of fungi, antifungal susceptibility testing; preservation of fungi, tissue reactions & histopathology of fungal infections. Nearly 350 participants have been trained from this center over these years.

Other than National Reference Centre at Chandigarh, Vallabhai Patel Chest Institute at Delhi, St Johns Medical College and Research Institute at Bengaluru and Ram Chandra Medical College at Chennai have conducted training programs for participants of India.

Training on clinical mycology

With the aim of creating awareness on the clinical mycology, 'Fungal Infections Study Forum' (FISF) in India conducts educational and training activities for clinicians. Six training courses over the last 2 years have been run at different cities in India. This course is supported by an educational fund from Gilead. The training objectives of the course are: To enumerate common invasive fungal diseases in India and describe their epidemiology; To provide triggers for suspicion of invasive fungal infection using clinical parameters and radiological findings; Ensure appropriate laboratory tests are ordered and interpret laboratory reports; Optimise the management of invasive fungal infections and; To clarify when and when not to use antifungals. Each course is attended by 60-80 clinicians. In 2020, the plan is to conduct 10 more courses at different cities in India. FISF has also developed e-training course with 16 modules covering the taxonomy of fungi, epidemiology, diagnosis, management of

invasive and allergic fungal diseases. This e-course has been running successfully for the last three years with the education grant from Pfizer, India.



Clinical training course at Pune, India

In addition, a short-term training program for 1-3 months is also available for the people of southeast member countries under SEARO. The center also conducted training in Myanmar, Thailand and Nepal in last two years.



Training course at Yangon, Myanmar

Indonesia (Professor Retno Wahyuningsih)

Throughout 2019 various activities involving the dissemination of knowledge about fungal diseases have been carried out. These activities include presentations; workshops and research on fungal diseases in Indonesia. The activities of Retno Wahyuningsih (RW) as Indonesia GAFFI ambassador are as follows

1. In June 2019 a kick off meeting and workshop to initiate a study on histoplasmosis epidemiology in Indonesia was held. The study is a collaboration with Prof. D. Denning from Manchester University, UK and Prof. Conchita Toriello from Universidad Nacional Autónoma de México, Mexico City (UNAM). We are implementing histoplasmin skin testing among patients with chronic lung diseases. The study was conducted in hospitals in Jakarta, Sukabumi, Bandung, Semarang, Malang, Surabaya, Bali, Manado, and Medan, The study will be continued until September 2020.

2. At the Asia Pacific Society of Medical Mycology conference, RW gave a lecture entitled Mucormycosis: diagnosis and management. The conference was held in Guangzhou, China in November 22-24, 2019.

3. As an Asia Fungal Working Group (AFWG) member, an ISHAM task force, she has participated in several workshops and symposia held by AFWG in 2019. The scientific activity was called Medical Mycology Training Network (MMTN). The training sessions were held July 20-21 in Penang, Malaysia and in December 6-8 2018 in Hanoi, Vietnam. Her presentations were:

- a. Chronic pulmonary aspergillosis (CPA) – Penang
- b. Identification of Mucoromycotina (Zygomycetes) - Penang
- c. Direct examination for the diagnosis of fungal infection - Hanoi
- d. Slide culture for mold identification - Hanoi
- e. Identification of Zygomycetes - Hanoi

4. A lecture entitled “Diagnosis Driven Approaches of Invasive Fungal Infection (IfIs): What Test Should We Do” was presented before doctors in internal Medicine at 16 November 2019 in Jakarta.

5. 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.

6. Our study on the *Candida krusei* in Jakarta, Indonesia found out something different. Some strains were susceptible to fluconazole in vitro and in vivo. *C. krusei* has been known as a species that is resistant to fluconazole.

Iran (Professor Mohammad Hedayati)

Mohammad lead the world’s first estimate of the impact of invasive aspergillosis on years of life lost (YLLs) and disability adjusted life years (DALYs) (Tavakoli, 2019).

France (Prof Jean-Pierre Gangneux and Christophe Hennequin)

At the TIMM meeting in Nice, Jean Pierre and Christophe hosted a dinner of GAFFI ambassadors and other experts from Burkina Faso

Portugal (Dr Raquel Sabino)

During 2019, 8 physicians (pathologists and infectious diseases clinicians) performed their training in the Reference Mycology laboratory at the National health Institute Dr. Ricardo Jorge. These training periods included raising the awareness to the majority of fungal infections, etiological agents, epidemiology of those infections and available diagnostic methods. GAFFI leaflets were delivered to all.

A radio interview to Raquel Sabino was given to a national channel, focusing fungal infections: <https://www.rtp.pt/play/p2063/e432194/ponto-de-partida>

Serbia (Professor Valentina Arsic Arsenijevic) and Romania (Professor Mihai Mares)

Regional cooperation has been stepped up in several ways including the Balkan Fungus meetings as well as collaborative training and studies in the field.

<https://balkanfungus2020.com/>



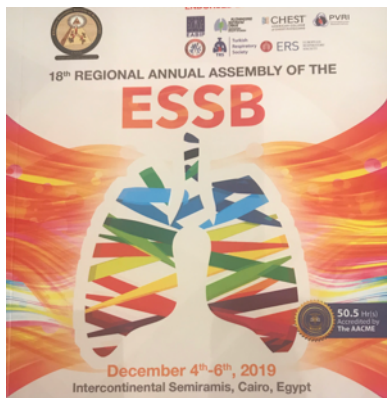
Hungary (Dr Janos Sinko)

In Hungary, extensive training and awareness activities were undertaken:

1. Courses and case discussions for medical students and residents at Szeged University and at Semmelweis University Budapest Faculty of Medicine. (In Hungarian and in English)
2. Postgraduate course on invasive fungal infections for intensive care specialists at Semmelweis University Budapest.
3. Presentation and discussion on the management of nosocomial candida infections at Jahn Ferenc Hospital, Budapest.
4. Round table discussion on mould infections in oncohematology at the University of Pecs, Hungary.
5. Update on antifungal management at the 47th Congress of the Hungarian Society of Infectology and Clinical Microbiology, 2019.
6. Choice of antifungal compounds in invasive mould diseases, special focus on isavuconazole at the 47th Congress of the Hungarian Society of Infectology and Clinical Microbiology, 2019.
7. Presentation and discussion on invasive mould infections in the ICU at Pfizer Infectology Day standalone meeting, with an online version recorded.

Egypt (Dr Sherif Zaki)

The Egyptian Association of Medical Mycologists (EAMM) was decreed at 10th of April 2019 by Sherif Zaki to unify all the efforts for verifying (GAFFI) Goals in Egypt. Until now 40 medical mycologists registered for membership from Egypt, Libya, and Iraq.



The occasion of the Egyptian Scientific Society of Bronchology (ESSB) annual meeting in Cairo in December 2019, provided an opportunity for Sherif and David Denning (GAFFI) to meet up with the leadership of the WHO Regional Office (EMRO) and with the a representative of the Ministry of health, responsible for chest diseases and TB. Discussions centered around improved diagnostic access for Aspergillus in the region and in Egypt as well as setting up a national network of mycology labs.



Cameroon (Dr Christine Mandengue)

A one-day Sensitisation Meeting on Histoplasmosis in HIV and Mycetoma was held in at the *Université des Montagnes* in Bangangté, a rural savanna zone in the west region of Cameroon on October 1st 2019.

There are 2 hospitals in Bangangté and the *Université des Montagne's* teaching hospital is being constructed as well as 6 rural health centers. There are 2 AIDS-care units in Bangangté with a recruitment of ~ 50 new HIV-infected cases monthly; but histoplasmosis is unknown in these units.

Despite farming being the predominant activity in this rural savanna area, no clinical cases of mycetoma are known. Cases diagnosed as melanoma and Kaposi's sarcoma of the foot could be misdiagnosis of mycetoma.

110 participants attended comprising 74 medicine and biology students, 16 health-care professionals (practitioners, dentist, nurses, laboratory technicians), and 19 other lecturers and non-health care professionals. The key speakers were a dermatologist, histopathologist, molecular biologist, and a lab technician masters student from the *Université des Montagnes* and a guest medical mycology from the University of Douala. Sticky auto posters on histoplasmosis and mycetoma, algorithm of suspicion of the diseases and certificate of participation were given to all at the end of the event.

The aspirations after the meeting are to identify potential patients for diagnosis (urine; surgical biopsies) (histoplasma antigen kits are awaited). Concerning mycetoma, Prof Fahal from the Mycetoma Research Centre in Khartoum has offered to process for diagnosis all specimens sent. Finally with our results, we will make the case for itraconazole to be available via engagement of the Ministry of Health, and work with the WHO office in Cameroon on mycetoma.

South Africa (Dr Nelesh Govender)

Several papers were published in 2019 documenting the burden of fungal diseases in South Africa.

The Federation for Infectious Diseases Societies of Southern Africa (FIDSSA) (www.fidssa.co.za) launched a Mycoses Interest Group at its national biennial conference in Johannesburg, 7-9 November 2019. Approximately 40 FIDSSA members have signed up to this small working group.

A situation update on *Candida auris* in South Africa was discussed at the Ministerial Advisory Committee for Antimicrobial Resistance and concrete actions proposed for 2020. SA will participate in WHO GLASS for *Candida* bloodstream infections.

The SA National Department of Health constituted a task team for advanced HIV disease which will address access to essential medicines, healthcare worker training and patient education for important mycoses in this population.

SA continued its flucytosine access programme for cryptococcal meningitis at pilot hospitals across the country in 2019 – at these sites, eligible patients are treated with amphotericin B and



flucytosine for 1 week. At non-access sites, combination amphotericin B and fluconazole continues to be offered as the standard of care for induction phase treatment.

The Southern African HIV Clinicians Society updated its influential guidance document on diagnosis, prevention and management of cryptococcal disease among people living with HIV. This guideline was published in December 2019. The guideline writing committee is pictured here.

Republic of Congo (Amona Modeste Fructueux)

Following the preliminary estimate of serious fungal infection report in 2016, a re-estimate is submitted for publication.

Nigeria (Dr Rita Oladele and Dr Samuel Fayemiwo)



The Medical Mycology Society of Nigeria organised the 2nd National Conference of Medical Mycology in Lagos, 10-12th, April 2019. The theme of the conference was “Managing serious mycoses: circumventing challenges in a resource limited country”. It was attended by over 80 people including GAFFI Ambassadors from France (Jean Pierre Gangneux), Cameroon (Christine Mandengue) (who presented on histoplasmosis) and Ghana (Bright Ocansey). The Independent newspaper in Nigeria featured long article: “Scientists urge FG to establish Mycology Laboratories.”

<https://nnn.com.ng/society-urges-fg-to-provide-reference-laboratory-to-tackle-fungi-infections/>

In collaboration with the CDC and GAFFI, the Medical Mycology Society of Nigeria (MMSN) organised the Fungal Disease Awareness week between September 21-25, 2019 across Nigeria to highlight the critical need for increased recognition and awareness of fungal diseases. The Fungal Disease Awareness Week 2019 tagged: “Think Fungus.” was focused on the “Increased awareness about fungal diseases as one of the most important ways to improve early recognition and reduce delays in diagnosis and treatment. The press conferences were attended by prominent Physicians in different centers like Lagos, Ibadan, Awka, Benin, Calabar, and others across the country.”



Ghana (Bright Ocansey)

An NGO, Fungal Infections Kare Initiative (FIKI) Ghana was set up to mirror GAFFI activities in Ghana based on the four goals mentioned above.

The 1st Fungal Disease Awareness Seminar was held on the 1st February, 2019 at the Korle-Bu Teaching Hospital (KBTH), Accra, Greater Accra region in commemoration of the World Aspergillosis Day. It was organized by FIKI Ghana in collaboration with Chest Diseases Clinic, KBTH and Medical Journalists Association of Ghana. The theme of the seminar was “Considering CPA for improved TB management”. Speakers were Dr Rita Oladele (Nigeria GAFFI ambassador) presented on “CPA: A cause of smear negative TB and/or TB treatment failure” and Prof David Denning (GAFFI Chief Executive) via a pre-recorded video presented on “CPA: Clinical spectrum, Diagnosis and Treatment”. The seminar was chaired by Dr Jane Afriyie-Mensah (Head, Chest Diseases Clinic)



There were 82 attendees from four regions. Attendees comprised of clinicians, microbiologists, medical laboratory scientists, nurses, lecturers, pharmacists, allied healthcare practitioners, health sciences students and non-health care professionals. Education materials from LIFE and FIT, UK were distributed to attendees.

Throughout the year educational materials were distributed to healthcare professionals in various medical facilities in Ghana.

Financial support was obtained from FIT, UK to undertake gap analysis surveys in Ghana, which is ongoing.

During the CDC's FDAW2019, flyers were created and shared on social media platforms. However, a planned presentation on 25th Sept on the “Burden on SFI in Ghana” at the Ketu South Municipal Hospital, Aflao, Volta region was called off but educational materials were distributed to healthcare professionals.

Kenya (John Guto)

The UK East African Health Alliance had its annual meeting in London April 2019 and has agreed to set up a UK Kenya Health Alliance, to mirror the UK Uganda Health Alliance.



in

Uganda (Dr Felix Bongomin and Dr David Meya)

In addition to 2 publications supporting GAFFI's mission (Essential Diagnostics – report of the Kampala meeting and histoplasmosis review, Felix Bongomin has supported the testing of possible cases of chronic pulmonary aspergillosis with the lateral flow assay for Aspergillus antibody. Here he met with Dr Oliver Penney who is volunteering in Kagando and provided some tests for him.

Dr David Meya and colleagues published the first review on fungal asthma in Africa. A prospective multi-country assessment of fungal sensitisation and asthma severity was presented in Nairobi at the 5th Kenya International Lung Health Conference

