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FUNGAL DISEASE: THE 'TROJAN HORSE' THAT THREATENS THE WORLD AS DEATH TOLL RISES TO 150 PEOPLE EVERY HOUR

There's a call for policy makers and health agencies to wake up to the plight of more than 300 million people worldwide who suffer and die every year from fungal disease.

It comes from GAFFI (Global Action Fund for Fungal Infections); an international organisation set up last year to highlight what doctors believe is a worldwide catastrophe that is growing year on year, yet could be halted with local access to diagnostics, antifungal medicines and better medical training.

Fungal infections kill at least 1,350,000 patients with or following AIDS, cancer, TB and asthma, as well as causing untold misery and blindness to tens of millions more worldwide. Yet, like a Trojan horse its symptoms are mostly hidden, and occur as a consequence of other health problems.

In Tanzania, fungal infections affect 3% of the population every year. Life-threatening infections among people living with HIV accounts for over 73% of the total national burden. Cryptococcal infection is the leading cause of death due to fungal infections in the country. Unfortunately, easy and simple CRAG LFA diagnostic tests for cryptococcal meningitis is not widely available in the

country and neither is Amphotericin B, the optimal first line recommended anti-fungal therapy. <https://vimeo.com/107046272>

Hollywood star and actor, Rupert Everett, who is best known for co-starring with Julia Roberts in the hit romantic comedy *By Your Side*, has pledged to help GAFFI raise awareness among health professionals and the public. He says: "I understand from the experts that this is complicated and not straightforward. Only when it is too late is the diagnosis possible on clinical grounds, but even then many conditions overlap. The tragedy is that many of the best drugs have been available in some countries for 40-50 years, yet not where they are now most needed."

GAFFI's founding President is Dr David Denning, Professor of Infectious Disease in Global Health at the University of Manchester. They explain: "Fungal disease is the Trojan horse – the silent, unappreciated global catastrophe on a scale no one has grasped until recently. For example, after TB as many as 20 per cent of patients develop lung fungal infection, which slowly progresses to death over five years, unless arrested with treatment, an estimated burden of 1.2 million people worldwide. Severe asthma with fungal allergy could account for half of the 350,000 deaths from asthma each year, yet it is treatable with antifungal drugs. Blindness caused by fungal infection of the eye affects over 1 million adults and children globally yet the tools are not available for rapid diagnosis and treatment for millions of people."

The Ifakara Health Institute in collaboration with GAFFI, SWISS TPH and the Ministry of Health Tanzania has made an effort to estimate the burden of serious fungal infections in Tanzania. Diana Faini the lead researcher in this project mentions: "It is highly intolerable that people living with AIDS succumb to treatable fungal infection such as cryptococcal meningitis especially in an era that simple, easy, fast diagnostic tests that can even be used in remote settings are available. It is sad to see 70% of patients with cryptococcal meningitis in the country die because of unavailability of first line recommended antifungal regime. Gladly, GAFFI has pioneered the lead to address these gaps in diagnostics and management of fungal infections globally."

In the last 12 months GAFFI has identified and estimated the burden of fungal disease in almost 40 countries including Tanzania, successfully lobbied the World Health Organisation to include two life-saving drugs on the Essential Medicines List and convinced the World Medical Association to address governments across the world to improve diagnostics and treatments of fungal disease.

For more information, or for images of the maps that show the gaps in access to antifungal treatments in most countries, please contact Susan Osborne, Director of Communications at The Goodwork Organisation, on 07836 229208. www.gaffi.org

The video embed code for the short (2.06") is:

<https://vimeo.com/107046272>

There is a longer version (3'52") here: <https://vimeo.com/107802357>

Please note the film is downloadable at broadcast quality and may be used without any restrictions.

GAFFI successes in the past 12 months are listed here:

1. Ifakara Health Institute is supporting the following GAFFI activities: (i) estimating burden of fungal infections in Tanzania; (ii) Leading research projects and clinical trials on maximizing detection and improving treatment outcomes of cryptococcal meningitis.
2. GAFFI has estimated the global burden of serious fungal infections for 59% of the world's population including Argentina, Australia, Austria, Belgium, Brazil, China, Czech Republic, Denmark, Dominican Republic, France, Germany, Hungary, Guatemala, India, Iran, Iraq, Ireland, Israel, Jamaica, Kenya, Mexico, Mongolia, Netherlands, New Zealand, Nigeria, Russia, Saudi Arabia, Senegal, Singapore, South Korea, Spain, Sri Lanka, Tanzania, Trinidad and Tobago, Uganda, the UK, Ukraine, Uruguay, Vietnam and Zambia.
3. Successfully lobbied the WHO to place amphotericin B and flucytosine on the Essential Medicines List to treat cryptococcal meningitis and other life-threatening fungal infections, in a coalition with other agencies including US Centers for Disease Control, attendees from LIFE, WHO, Medicines Sans Frontieres (MSF), Clinton Health Access and numerous universities and public health institutions.
4. GAFFI has successfully lobbied the World Medical Association to adopt a statement addressed to governments on the need for improved access to diagnostics and treatments for fungal diseases, including the development of training for personnel in laboratories and for physicians. They also encouraged members to undertake and support epidemiological studies. [WMA statement].
5. Advocacy has been initiated by GAFFI with the World Health Organization, UNAIDS, the Global Fund to fight AIDS, Tuberculosis and Malaria, MSF, and others. In particular, a combined burden and costing model for the diagnoses and management of cryptococcal meningitis is shortly to be handed to WHO, UNAIDS and Global Fund to facilitate countries accessing diagnostic testing and treatment for this lethal infection.
6. GAFFI has developed a national 'Fungal Diseases' development plan for Kenya and another for China and one related to fungal diseases in AIDS for Guatemala.

7. Prospective epidemiology studies of chronic pulmonary aspergillosis after TB, in HIV positive and negative patients, and smear negative TB ongoing northern Uganda (Gulu and Kampala), with GAFFI support.
8. Supported the nascent cryptococcal disease access programme (CryptoMAG), a collaboration between the WHO (HIV Treatment and Care), CDC (Mycotic Diseases Branch), MSF (Access Campaign) Clinton Health Access Initiative and Management Sciences for Health (Technical Strategy and Quality Center for Pharmaceutical Management).
9. Work has started at The University of Manchester on the fungal keratitis 'eye drops' to immediately visualise hyphae or yeasts cells in the eye.
10. Development work on a simple and inexpensive method for DNA extraction from sputum for Pneumocystis diagnosis is nearing completion.

Diana Faini MD, Medical and Research officer at the Ifakara Health Institute in association with the University of Minnesota.

Trained at the Muhimbili University of Health and Allied Sciences (MUHAS), Diana Faini currently works for the Ifakara Health Institute researching on HIV and associated fungal opportunistic infection with a special focus on cryptococcal meningitis. She is the site clinician for a NIH funded phase III, randomised, double blinded placebo control clinical trial for Adjunctive Sertraline for the Treatment of HIV-Associated Cryptococcal Meningitis (ASTRO-CM) in association with the University of Minnesota and The Infectious Disease Institute-Uganda. She has recently completed a project on estimation of the burden of serious fungal Infections in collaboration with the Swiss Tropical and Public Health Institute (Swiss TPH). The results of this study were presented at the 54th ICAAC Sept 2014 in Washington DC. The manuscript is being reviewed to be published by the end of 2014. Her forthcoming project on health care service delivery model to maximize detection and Improve treatment outcomes of cryptococcal meningitis in a rural African district is submitted for funding at the Meningitis Research Foundation (MRF) and expected to start early 2015.

Emilio Letang, MD, MPH, PhD, Head of the Chronic Diseases Clinic of Ifakara, Swiss Tropical and Public Health Institute, Ifakara Health Institute

Emilio Letang is an infectious diseases specialist with expertise in HIV/AIDS in Africa and opportunistic infections. He trained as a MD in the Universitat Autònoma de Barcelona, got a MSc in Tropical Medicine and International Health and a MSc in AIDS at the University of Barcelona, and got his MSc in public health in developing countries by the London School of Hygiene and Tropical Medicine, University of London. In 2011 he completed his PhD by the University of Barcelona on Kaposi sarcoma-associated immune reconstitution inflammatory syndrome in Africa. He is currently leading the Chronic Diseases

Clinic of Ifakara (CDCI), a platform developed in collaboration with the Saint Francis Referral Hospital of Ifakara, the Ifakara Health Institute, the Swiss Tropical and Public Health Institute, and the Government of Tanzania. The CDCI aims to be a centre of excellence in HIV/AIDS care, training and research. Research at the CDCI is focused on the main relevant problems leading morbidity and mortality associated with HIV in Tanzania, including cryptococcal meningitis. Dr Letang and colleagues performed the first assessment of the burden of cryptococcal antigenemia and its impact in mortality in Tanzania. The results of this study were presented at the Conference on Retrovirus and Opportunistic Infections (CROI) in March 2014 and are about to be submitted for publication.

**Professor David Denning FRCP FRCPATHFMedSci
Director, National Aspergillosis Centre, University Hospital of South
Manchester (Wythenshawe), Manchester, UK**

David Denning is an infectious diseases clinician with expertise in fungal diseases. He is Director of the National Aspergillosis Centre, Manchester, UK which sees over 300 new patients annually with aspergillosis. He leads a multi-disciplinary research and clinical group, spanning fundamental genomics to randomised and phase 4 clinical trials in fungal diseases (infection and allergy). Major past contributions include describing azole resistance and mechanisms in *Aspergillus*, leading the effort to sequence the *A. fumigatus* genome (3 papers published in Nature), leading the phase 2 study and then RCT demonstrating the superiority of voriconazole over amphotericin B for invasive aspergillosis and describing and demonstrating antifungal efficacy in severe asthma with fungal sensitisation (SAFS). His current interests are chronic and allergic pulmonary fungal disease, the global burden of fungal infection and azole resistance in *Aspergillus*. He has published more than 450 papers, books and book chapters, including an undergraduate textbook of Medicine. He is heavily involved in postgraduate teaching, both clinical scientists and physicians. He was instrumental in the establishment of the Mycology Reference Centre in Manchester (2009), which grew out of the Fungal Testing Laboratory he founded in 1991. His work has been cited over 37,500 times (Google scholar H-index 93).