

Bringing fungal infections in from the cold

A new roadmap attempts to raise the profile of fungal infections, highlighting the benefits of tackling these infections on other infectious disease targets. Onisillos Sekkides reports.

There are many infectious diseases clamouring for attention, with varying levels of success. However, fungal infections seem to be an entire category that is almost ignored by default. To raise the profile of these infections and to show how tackling them might benefit other ambitious goals to address infections such as HIV and tuberculosis, the Global Action Fund for Fungal Infections (GAFFI) have launched their roadmap 95-95 by 2025.

In keeping with many other global infectious disease targets, this title highlights the ultimate aim of the roadmap, in this case to “ensure that 95% of people with serious fungal disease are diagnosed and 95% treated by 2025”. At its launch, the president of GAFFI, David Denning, said “we propose a systematic approach to greatly reducing deaths and disease from fungal disease, using tried and tested rapid diagnosis and antifungal therapy”.

Most striking is the lack of availability of diagnostics and drugs, although in many cases, this is not because we are waiting for new developments. For example, amphotericin B, an antifungal available since 1959, is still not available in 76 countries. Also, advances in the diagnoses of

fungal pneumonia and meningitis made in the past 15 years are still not available in most countries. Then there is a problem that is becoming increasingly familiar in the infectious diseases field: other drugs are “excessively expensive”.

“This problem is almost entirely neglected at present, with neither diagnosis nor testing available in most resource poor settings.”

Beyond their direct effects, fungal infections also have a strong bearing on many other diseases. Fungal infections are very common in people with AIDS, and they probably contribute to more than 500 000 deaths in this population each year. Therefore, concrete measures to deal with fungal infections will substantially reduce the number of deaths attributable to AIDS. As outlined by Peter Godfrey-Faussett of the London School of Hygiene and Tropical Medicine, “unless we can treat opportunistic infections in AIDS, we can’t reach the Three Zeros target, particularly Zero Deaths”.

But the synergy between treating fungal diseases and tackling HIV/AIDS does not stop there. Many people with advanced HIV infection still die of fungal diseases soon after starting antiretroviral drugs, drawing attention to the need to treat fungal infections rather than expecting that the treatment of HIV will address the patients’ vulnerability.

Despite the substantial effects of fungal infections on people with HIV/AIDS, the effects of fungi on the general hospitalised population in low-income and middle-income countries are probably even more sobering. The mortality from fungal

infections in hospitalised patients is generally unknown in these countries, but it can be inferred that deaths due to these infections approach 100% because many such countries lack diagnostic tools and antifungal drugs to treat these diseases.

Outside the hospital setting, fungal infections complicate other diseases. 10–20% of people treated for pulmonary tuberculosis develop antibodies to aspergillus, suggesting that they also acquired an infection with this fungus. Many of these patients then go on to develop chronic pulmonary aspergillosis, a slowly progressive lung infection that, if untreated, can be fatal. The solution then seems simple: treat those with the infection. But this is where the neglect of fungal infections becomes particularly evident, since in Africa and many other regions, chronic pulmonary aspergillosis does go untreated because the key diagnostic, the aspergillus antibody test, is not available.

“Ending the fungal infection crisis means that patients with debilitating and life-threatening fungal infections will be diagnosed and treated in a timely manner, so that they can resume a normal life, maintain their family structure, and contribute to society”, said David Perlin of the New Jersey Medical School.

Modelling estimates suggest that 375 000 tuberculosis patients go on to develop chronic pulmonary aspergillosis each year, with an annual 15% mortality. Complicating this picture are suggestions that many cases of so-called smear-negative tuberculosis are not actually tuberculosis. The report quotes unpublished findings from Kampala, Uganda, that suggest roughly a quarter of people infected with HIV

For the GAFFI roadmap see <http://www.gaffi.org/roadmap/>



had detectable aspergillus antibodies. Other medical assessments also supported the likelihood that these people had chronic pulmonary aspergillosis. In view of the normal scarcity of appropriate diagnostics, it is reasonable to conclude that these patients would otherwise have been diagnosed with tuberculosis.

Should tuberculosis treatment then fail in these patients, a natural conclusion would be that they have multidrug-resistant tuberculosis and they would be moved to treatment with second-line drugs. The report adds that, of the roughly 4 million people with multidrug-resistant tuberculosis, some probably have chronic pulmonary aspergillosis or some other fungal infection. "Chronic pulmonary aspergillosis is a serious public health issue in countries with a high prevalence of tuberculosis and AIDS", said Iain Page of the University of Manchester. "This problem is almost entirely neglected at present,

with neither diagnosis nor testing available in most resource poor settings."

Naturally, fungal infections that can cause death attract the greatest attention. However, fungi are also important causes of blindness in many countries. In temperate climates most causes of infectious keratitis are bacteria or viruses, but in tropical and semitropical regions about half of the cases are attributable to fungal infection. Early antifungal treatment saves the sight of those infected, but late diagnosis and treatment can lead to severe consequences, including eye loss. This infection can have substantial effects beyond the individual, as the most affected are male agricultural workers who are then left unable to support their families.

Much of the roadmap highlights the diagnostic and treatment gaps that need to be addressed. Given almost all fungal infections are caused by about 30 species, the task at hand is great but

not insurmountable. And the needs are clearly itemised in the roadmap. Maybe the most urgent clinical need emphasised is the need for new drugs, since without treatment new diagnostics test will be of little benefit.

The roadmap concludes with a 10-year plan broken down into short, medium, and long term goals stating that "if the recommendations in this report are implemented diligently" they are confident they will achieve their overarching aim.

Mike Turner of the Wellcome Trust emphasised the value of this roadmap, stating "there are several very serious diseases caused by fungal infection, many of which are extremely difficult for doctors to treat". He added, "GAFFI are bringing a new energy to raising the profile of fungal infections and highlighting the need for a renewed international effort to care for people who suffer from them".

Onisillos Sekkides

Infectious disease surveillance update

Chagas outbreak in Venezuela

12 people from the same family in a municipality of Merida State, Venezuela, have fallen ill with the parasitic infection Chagas disease. The illness is transmitted via the faeces of the blood-sucking triatomine bug infected with the *Trypanosoma cruzi* parasite. The faeces can also contaminate food sources and the disease can spread through the oral route; this is the suspected cause of this outbreak. Of those who fell ill, three have died. Chagas disease is mainly found in endemic areas of 21 Latin American countries. The Health Corporation in Merida State is investigating the outbreak to establish the cause and control measures required.

Ebola virus disease in Liberia

On June 29, 2015, routine surveillance in Liberia detected a case of Ebola virus disease. This is more than 7 weeks

after Liberia was declared free of Ebola virus transmission. The case was a 17-year-old man who had died on June 28, 2015, from a febrile illness, which was managed as malaria but later confirmed positive for Ebola virus disease. The young man received a safe burial in Nedowein, Margibi, the same day he died. The source of infection continues to be under investigation because the case reportedly had no recent history of travel or contact with visitors from affected areas. An incident management team so far has identified close to 200 contacts, from these three people have also been confirmed as positive for the disease and another case also met the probable case definition.

Moses Massaquoi, the case management team leader for Liberia's Ebola task force, stated that the three men with confirmed or probable infection had shared a meal of dog meat. He added that an investigation is

underway to discover whether domestic animals might be carrying the virus

Update: MERS in South Korea

Between May 20 and July 5, 2015, 186 laboratory-confirmed cases of MERS-CoV were reported in South Korea (33 died, 116 recovered, and 37 are being treated at present). 12 of those on treatment are reported to be in a critical state. The case fatality rate in this country is 17.8%, whereas in Saudi Arabia it is 44%. The 186th confirmed case was a fourth-generation infection, the spouse of a third-generation case. As of July 3, 2 067 contacts are being monitored. MERS-CoV was first discovered in Saudi Arabia in 2012, since then WHO has been notified of 1363 laboratory confirmed cases including at least 487 deaths.

Ruth Zwizwai

For more on **Chagas in Venezuela** see <http://www.promedmail.org/direct.php?id=3475040>

For more on the **Ebola outbreak data** see <http://apps.who.int/gho/data/view Ebola-sitrep Ebola-summary-20150703?lang=en>

For more on the **new cases of Ebola in Liberia** see <http://www.promedmail.org/direct.php?id=3487558>

For more on **MERS in South Korea** see <http://www.promedmail.org/direct.php?id=3486383>

For more on **MERS public health response in South Korea** see <http://www.who.int/csr/don/03-july-2015-mers-korea/en/>