

How Common are Fungal Diseases?

Oral, oesophageal and vulvovaginal candidiasis (thrush)

- Oral thrush occurs in ~2.0 million people worldwide based on ~90% of HIV/AIDS patients¹ not taking but needing anti-retroviral therapy, estimated by the WHO in 2016². The number affected is probably falling as anti-retroviral therapy usage grows.
- Oral thrush also occurs in normal babies, people taking inhaled steroids for asthma, following radiotherapy to the head and neck for cancer, in denture wearers and in some leukaemia and transplant patients.
- Candida infection of the oesophagus (gullet) affects an estimated ~1.3 million people as ~20% of HIV/AIDS patients³ are not on anti-retroviral therapy, and ~0.5% if on antiretroviral therapy⁴ develop it.
- Repeated attacks of vulvovaginal candidiasis affect at least 135 million women annually as 5–10% have at least 4 attacks annually^{5,6,7,8}. The impact of on quality of life is substantial⁹. About 70% of all premenopausal women develop thrush at some point in their lives¹⁰.

Invasive and life-threatening fungal infection

Candida infection

- Candidaemia occurs at a population rate of 2-26/100,000^{11,12,13}, so using 5.9 cases/100,000, ~400,000 cases are predicted worldwide, with a mortality of 30-55%¹⁴. The numbers rose in the US by 52% between 2000 and 2005¹⁵. Blood culture is only about 40% sensitive for detecting invasive candidiasis (including intra-abdominal candidiasis/Candida peritonitis)^{16,17} so it is likely that nearly a 1 million people have invasive candidiasis each year. Rates in India and Brazil are much higher, so the overall estimate could be greater.
- Candida peritonitis affects both those undergoing long term peritoneal dialysis for renal failure (CAPD) and post-surgical patients, usually in intensive care. In a large multicentre study in 101 French intensive care units (ICU), hospital-acquired Candida peritonitis was documented in 73 patients over 8 months, compared with 123 patients with candidaemia without Candida peritonitis; 26 patients had both¹⁸. Assuming this is generalisable to other populations, this suggests a ratio of 1 patient with hospital-acquired (almost all post-operative) Candida peritonitis for every 2 patients with candidaemia, in ICU. As between 30 and 50% of candidaemia cases occur in ICU, and there are about 400,000 episodes of candidaemia globally, this suggests about 60,000 - 100,000 cases of Candida peritonitis each year. The mortality of Candida peritonitis was 38%. In those with end stage renal disease worldwide (~1.7M) CAPD is used in about 50%. Patients get 1 infection per 18 months on average and ~0.05 episodes per patient year are attributable to Candida spp., equivalent to ~42,500 cases annually.

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- Around 150,000 of the 7.5 million patients admitted to intensive care (ICU) in Europe, USA and Japan each year grow *Candida* in their urine (a rate of 2.7% of ICU admissions¹⁹) and is a common finding in hospitalised patients²⁰ and those with catheters (~16%)²¹ especially those in ICU.

Invasive aspergillosis

- Over 10 million patients in Europe, USA and Japan are at risk of invasive aspergillosis (IA) each year because of corticosteroid or other therapies. Over 50% of patients with IA die, even with treatment.
- Over 300,000 patients develop IA annually. Key groups include ~10% of acute leukaemia (300,000 new cases annually)²² (30,000 IA cases) and stem cell and other transplants (>75,000 annually in the USA, Europe and Japan) (7,500 IA cases) and 1.3-3.9% of COPD patients admitted to hospital^{23,24} (7% of the global number of moderate and severe COPD = 65M (WHO)) (60,000-180,000 confirmed IA cases). There are 11.9M COPD admissions in China each year and a mean rate in OECD countries of 198/100,000 (range 364 (Ireland) to 71 (Portugal)²⁵. IA also complicates lung cancer, at a rate of 2.63%²⁶. Worldwide there are 1,242,000 lung cancer cases annually²⁷, consistent with an additional 32,600 IA cases. A recent large survey of IA in liver failure in China documented a 5% rate, with a 95% mortality²⁸. All these patient groups above probably account for 80% of IA patients, with those admitted to intense care (ICU), with lymphoma or chronic leukaemia and various immunological disorders and treatments accounting for the remainder. Under diagnosis is a major problem in this disease.

Cryptococcal meningitis

- The incidence of cryptococcal meningitis in AIDS has probably been falling as antiretroviral therapy is extended. An initial estimate of a million cases each year, resulting in ~ 600,000 deaths, of which ~ 70% are in sub-Saharan Africa,²⁹ has been replaced with lower estimates. A recent one is 223,100 cases in AIDS³⁰. Deaths are high, because of a lack of diagnostic capability and optimal treatment and thought to be about 181,100, 15% of all AIDS deaths³⁰. In addition, cases occur in other immunocompromised groups and in normal people. In Thailand the records are good, and an estimated 108 'normal' and 251 immunocompromised people develop cryptococcal meningitis each year³¹.

Pneumocystis pneumonia

- About 2.2 million HIV/AIDS infected patients² who should be receiving anti-retroviral therapy are at risk of *Pneumocystis pneumonia* (PCP), as well as many other immunocompromised patients, unless taking oral antifungal prophylaxis with cotrimoxazole.
- The rate of PCP as an AIDS indicator disease is very variable. In African children, using reasonably sensitive diagnostic methods

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prevalence rates were 10% (South Africa, 2000), 49% (South Africa, 2002), 31% (Botswana, 2003) and 5% (Malawi, 2011). In adults from Africa, rates were 9% (Malawi, 2001), 33% (Tunisia, 2002), 37% (Kenya, 2003), 11% (Malawi, 2007), 30% (Ethiopia, 2008), 4% (Uganda, 2010), 5% (Namibia, 2012), 10% (Tanzania, 2012) and 11% (Uganda, 2012). Patient inclusion varied in these studies [<http://www.gaffi.org/media/fact-sheets/>]. Pneumocystis pneumonia has a 10-30% mortality in the USA and UK^{32,33}.

- Precise estimates of annual incidence are difficult because of diagnostic deficiencies but case numbers certainly exceed 400,000 globally per year^{28,34}.
- Given the number of other patients at risk for Pneumocystis pneumonia and rising rates in the UK³⁵ and elsewhere in non-AIDS patients, a rough estimate of 100,000 additional cases per year is estimated³⁶.

Histoplasmosis

- In AIDS, disseminated histoplasmosis is a devastating infection and difficult to diagnose rapidly enough to save the patients, even with either rapid antigen or PCR testing. As the rates are highly variable from one locality to another, a global burden estimate is missing. An approximation of ~100,000 is likely³⁷, with Central and parts of South America most affected, and some cases in Africa and SE Asia.
- Up to 50 million people are thought to have been infected with histoplasmosis, with ~500,000 new infections each year, most asymptomatic and based on skin testing³⁸. About 25,000 cases of symptomatic histoplasmosis are estimated in the USA annually¹⁴.

Mucormycosis

- Three population analyses of mucormycosis have been conducted in the USA, France and India. A population estimate from the USA of 2 cases of mucormycosis per million³⁹ and from France of 0.6 per million⁴⁰. The high rate of diabetes in India is probably accountable for a much higher rate of mucormycosis there, as well as unique presentations such as renal mucormycosis; the projected annual incidence is as high as 13 per 100,000⁴¹. No global estimate is available.

Coccidioidomycosis

- About 25,000 cases of coccidioidomycosis occur in the US each year¹⁴, but this is thought to a significant underestimate with probably 7 times as many cases (i.e. 140,000-150,000) cases annually. Many more cases occur in Central and South America, but there are no good estimates.

Allergic fungal disease

Allergic bronchopulmonary aspergillosis (ABPA)

- Approximately 4.8 million people develop ABPA among the 193 million adults with active asthma worldwide⁴².

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- Individual country estimates of asthma for 70 countries are now available⁴³, superceding older estimates⁴¹.
- ~ 15% of adults with cystic fibrosis develop ABPA with ~6,675 affected, although many teenagers and some younger children are also affected⁴⁴.

Severe Asthma with Fungal Sensitisation (SAFS)

- SAFS is predicted to affect ~6.5 million (range 3.25-13 million) adults worldwide depending on the frequency of severe asthma (5-20% of all asthmatics) ^{14,45}. There is some duplication between ABPA and SAFS (collectively termed 'fungal asthma') because all ABPA patients are sensitized to fungi, and some have severe asthma.

Allergic fungal rhinosinusitis

- Allergic fungal sinusitis and rhinitis affects ~12 million people at any time. Allergic sinusitis and rhinitis affects ~15% of the world's population or around 900 million people⁴⁶ and ~1.3% is predominantly fungal allergy (assuming a 50% endoscopic examination rate)⁴⁷. Two country rates have been ascertained – Israel and India. In Israel, nearly 0.5% of the population (40,000) is thought to be affected⁴⁸. In India, a community survey of allergic fungal rhinosinusitis (FRS) in rural India found a population prevalence of 0.11% of chronic FRS with allergic FRS in 41 (56.1%), chronic granulomatous FRS in 13 (17.8%), eosinophilic FRS in 11 (15.0%), fungal ball in 7 (9.5%) and chronic invasive FRS in one (1.3%)⁴⁹.

Chronic fungal disease

- Prevalence of chronic pulmonary aspergillosis following tuberculosis is estimated at about 1.2 million cases⁵⁰. Rates are particularly high in smear negative (ie clinically diagnosed) non-HIV patients (22%), but HIV positive patients may also be affected⁵¹. Chronic pulmonary aspergillosis complicates many respiratory disorders including tuberculosis, ABPA, sarcoidosis and COPD^{22,52,53}, and so the total burden of this debilitating disorder is ~3 million³⁴.
- There are no global estimates for the Neglected Fungal Diseases mycetoma and chromoblastomycosis. A 2013 survey reported a total of 8,763 cases of mycetoma⁵⁴. The prevalence of chromoblastomycosis varies from 14/100,000 in Madagascar (3,500) to 3/100,000 (6,200) in Brazil and fewer elsewhere⁵⁵. Sporotrichosis is probably more common but very variable in frequency with hyper-endemic areas in Mexico and Peru with rates as high as 25/1,000⁵⁶. There are fewer data on other similar conditions such as cutaneous phaeohyphomycosis.

Fungal eye infections

- Estimates of the annual incidence of fungal keratitis vary from 1 million to 6 million in SE Asia annually. Rates vary from as low as 6.3/100,000 in Hong Kong⁵⁷ to as high as 799/100,000 in Kathmandu⁵⁸.



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Rates in Nepal have fallen in recent years to 73/100,000 (20,000 affected)⁵⁹. Rates of keratitis in S. America and Africa are not known. Among causes of avoidable blindness, corneal opacities (caused by fungi or bacteria) accounts for 10% of the 284 million people visually impaired worldwide⁶⁰.

Cutaneous fungal infections

- Fungal infection of the skin, hair or nails affects ~1 billion people⁶¹ and in the US alone accounted for 4M outpatient medical visits⁶².
- Fungal nail infection (onychomycosis) is common in the general adult population, probably 5-25% rate with an increasing incidence in elderly people^{63,64}.
- Athlete's foot (tinea pedis) is more common than onychomycosis and is more common in younger people and sportsmen.
- Hair infection (tinea capitis) is most common among children, often resulting in bald patches with psychosocial consequences. In a recent US survey, tinea capitis was found in 6.6% with ranges from 0% to 19.4%⁶⁵, is more common in deprived areas and black children (with rates up to 41%)^{66,67,68,69}, suggesting a global prevalence of 200 million cases.

The Fungal Infection Trust
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