

Global burden of human fungal diseases and their underlying diseases

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Global Action Fund for Fungal Infections (GAFFI)

in association with

Leading Fungal Education International (LIFE)



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Fungal infections

- Mucosal i.e. oral or vulvovaginal thrush
- Cutaneous i.e. athlete's foot, ringworm and onychomycosis
- Chronic fungal infections such as chronic pulmonary aspergillosis
- Allergic i.e. allergic fungal sinusitis and allergic bronchopulmonary aspergillosis (ABPA)
- Invasive and life-threatening i.e. candidaemia, invasive aspergillosis and cryptococcal meningitis

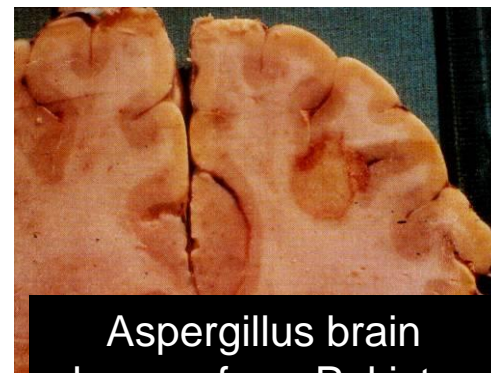
Some fungal infections



Disseminated *Penicillium marneffeii* infection in AIDS from Thailand



Coccidioidomycosis from Mexico



Aspergillus brain abscess from Pakistan



Chromoblastomycosis from PNG



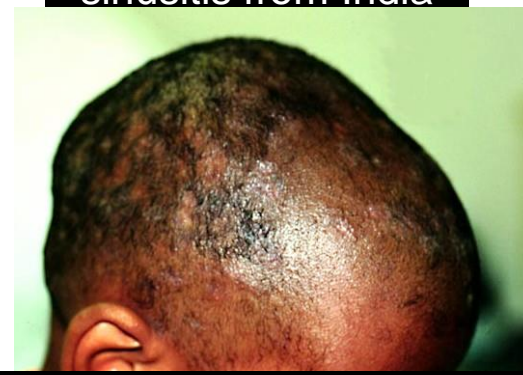
Oral candidiasis in AIDS from France



Allergic fungal sinusitis from India



Disseminated candidiasis in premature infant from USA



Tinea capitis from Uganda



Estimating fungal disease incidence and prevalence

- Almost no regular or national surveillance
- No obligatory reporting
- Diagnostic test performance often poor
- Clinician suspicion poor outside specialised units
- Some fungal diseases only recently recognised

Int. J. Social Research Methodology
Vol. 8, No. 1, February 2005, pp. 19–32

Scoping Studies: Towards a Methodological Framework

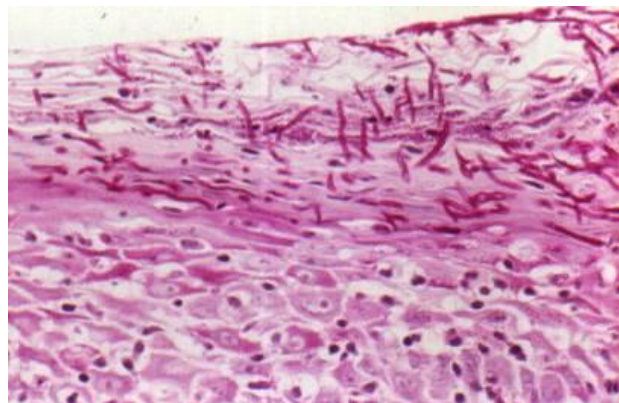
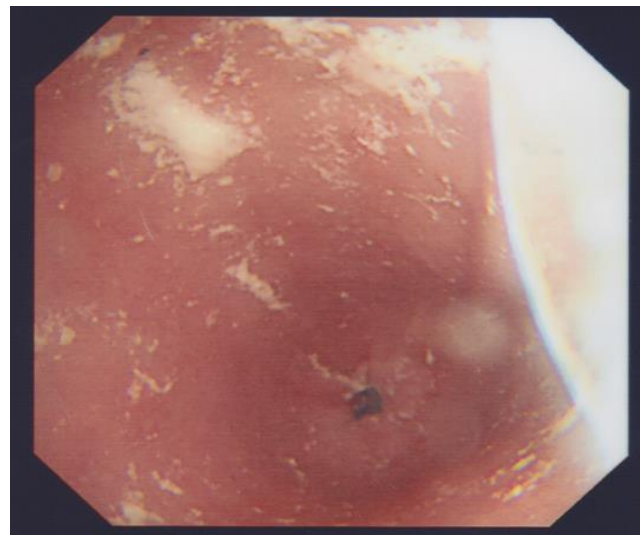
Hilary Arksey & J. Malley

Not listed in Pubmed

Received 10 September 2002; accepted 11 March 2003

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Oral, vaginal and oesophageal candidiasis



- ~10 million people with oral thrush in AIDS**
- ~ 2 million people with oesophageal thrush in AIDS**
- ~137 million women with 4+ attacks/year of Candida vaginitis – non-AIDS**

Fluconazole responsive (usually)



Vulvovaginal candidiasis (VVC)

- 55% of women have VVC by mid 20's
- 6-9% of women have VVC ≥ 4 times per year,
- Global estimate of the problem of recurrent VVC is ~137 million women annually (range 103 - 172M) aged 15-54 years.
- Duration of recurrent VVC is highly variable, 1-2 years commonly, sometimes >8 years.



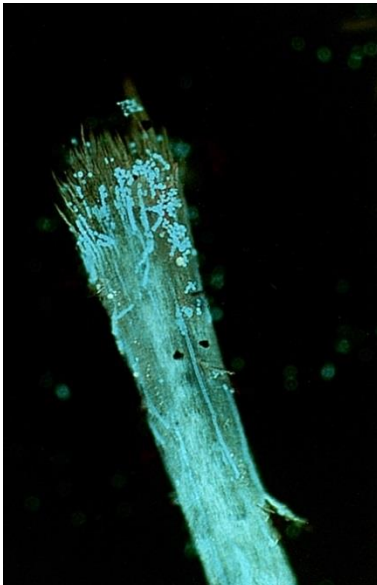
Vulvovaginal candidiasis (VVC)

- ~492 million develop recurrent VVC over their lifetime
- Hormone replacement therapy increases risk in post-menopausal women.

Unpublished and Fischer & Bradford, J Low Genit Tract Dis 2011;15:263



Fungal hair infection – tinea capitis



~25% of children in schools all over Africa.

Common in other communities

~200 million children affected

May be disfiguring, certainly affects children's self esteem

Griseofulvin or fluconazole Rx

Transmissible



Cutaneous fungal infections



Ringworm, tinea versicolor, tinea pedis (athlete's foot). onychomycosis

Very common

Terbinafine, itraconazole, fluconazole and griseofulvin all effective

Transmissible



Cutaneous fungal infections

4th most prevalent chronic disease problem after dental caries, tension headache and migraine.

985 million people affected, 14.3% of the global population

	Deaths	Years life lost	Years lost due to disability	Disability adjusted life years
HIV/AIDS*	1,465,369	77,204,868	4,342,499	81,547,368
Tuberculosis*	1,195,990	42,622,051	6,774,195	49,396,246
Asthma	345,736	8,624,215	13,834,882	22,459,097
Fungal skin diseases	<1,000	<200,000	2,302,796	2,302,796

* Including fungal complications

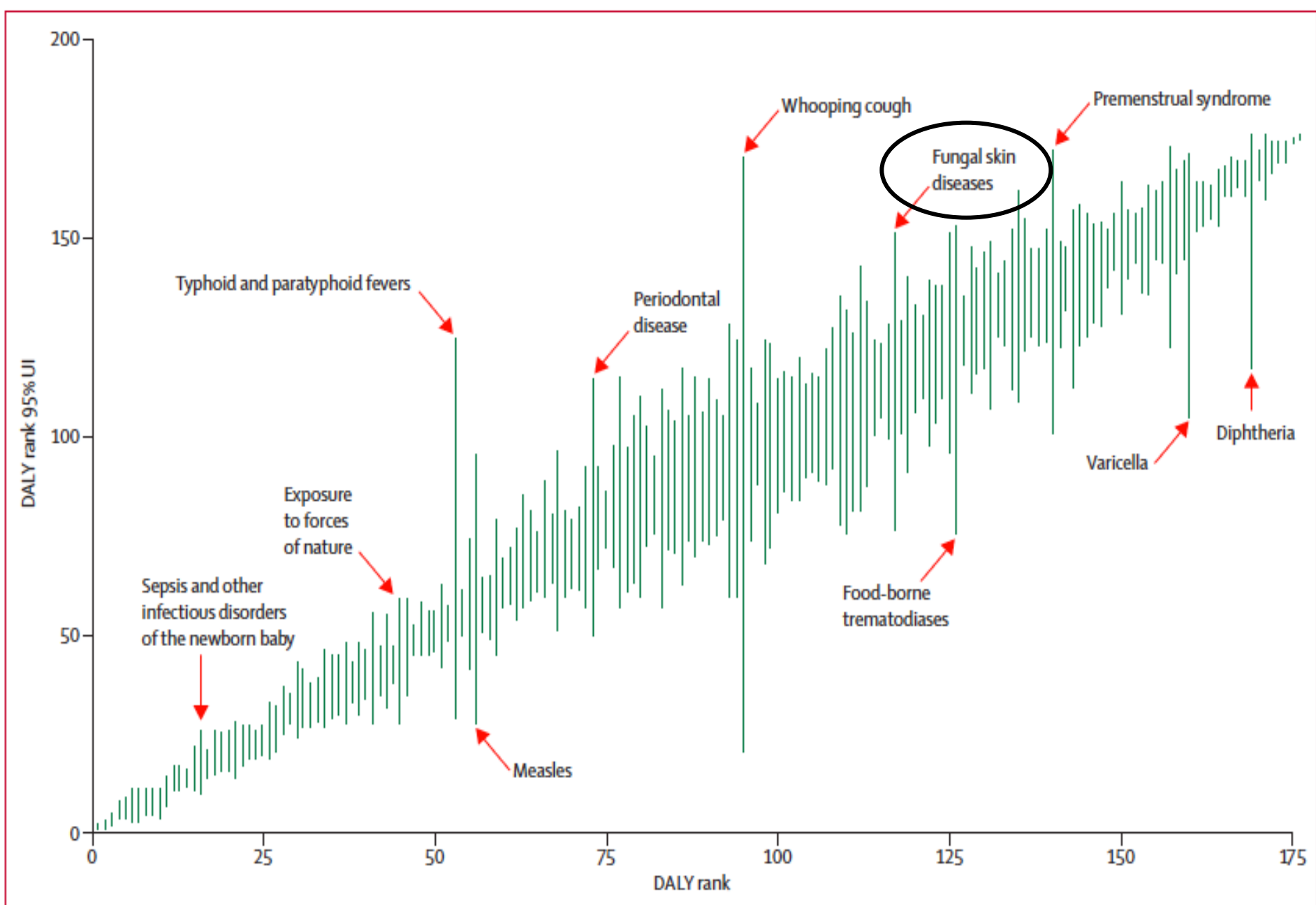
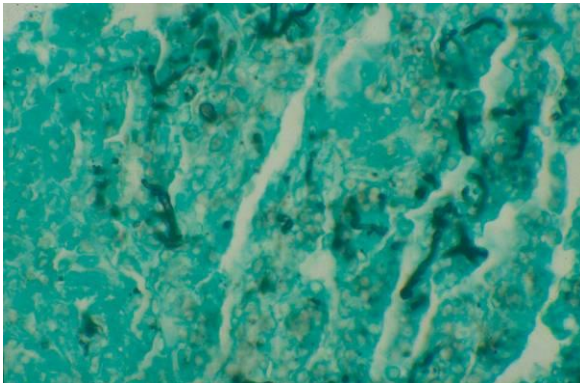
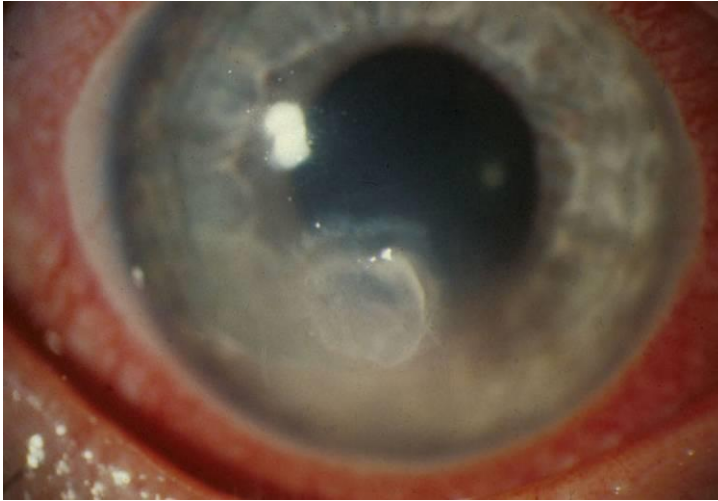


Figure 3: Global disability-adjusted life years (DALY) rank with 95% UI by cause in 2010

Fungal keratitis



**Implantation disease, often injury related,
sometimes contact lens**

**10-50% of keratitis = fungal
>300 fungal species implicated
Aspergillus and *Fusarium* predominate**

**Diagnosis requires
microscopy/histopathology + culture**

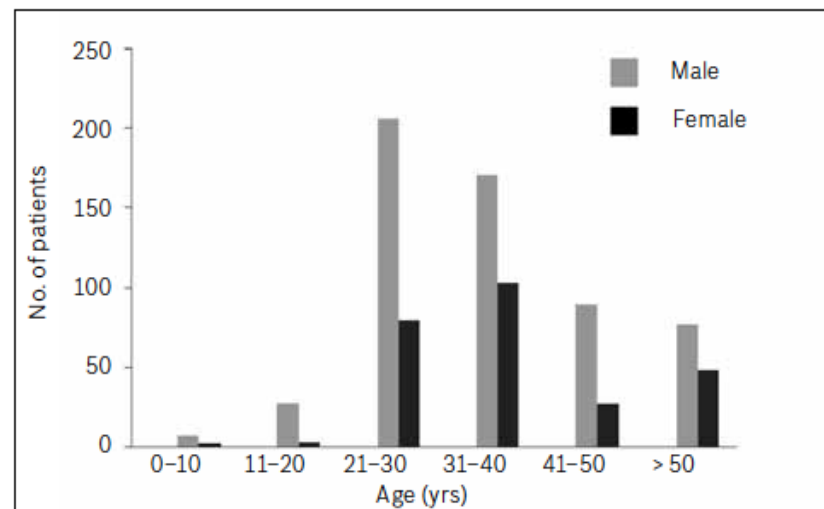


Fungal keratitis

- 1-12 million affected worldwide,
- Usually farmers and labourers
- 4% children



USA	11 /100,000
Denmark	0.06 /100,000
UK	0.034 /100,000
Hong Kong	6.3 /100,000
India	13 /100,000
Bhutan	339 /100,000
Myanmar	710 /100,000
Nepal	799 /100,000



Deorukhkar S, Singapore Med J 2012;53:264



Aspergillus otitis externa

- Acute otitis affects 1 in 250 people annually
- Chronic otitis affects 3-5% of the population (200-350 million)
- ~10% are fungal in origin, usually *A. niger*

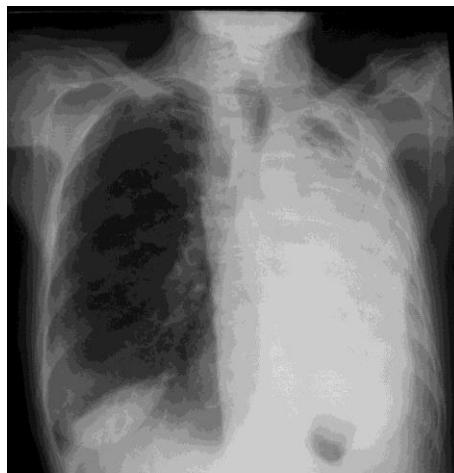




Chronic pulmonary aspergillosis after TB



July 2001, untreated



April 2003, untreated



Fungal ball removed from lung

Mimics TB

No diagnostic capability throughout Africa

1.2 million affected worldwide

Global burden of chronic pulmonary aspergillosis as a sequel to pulmonary tuberculosis

David W Denning,^a Alex Pleuvry^b & Donald C Cole^c

1,170,000 patients (5 year period prevalence)

375,000 annual incident cases

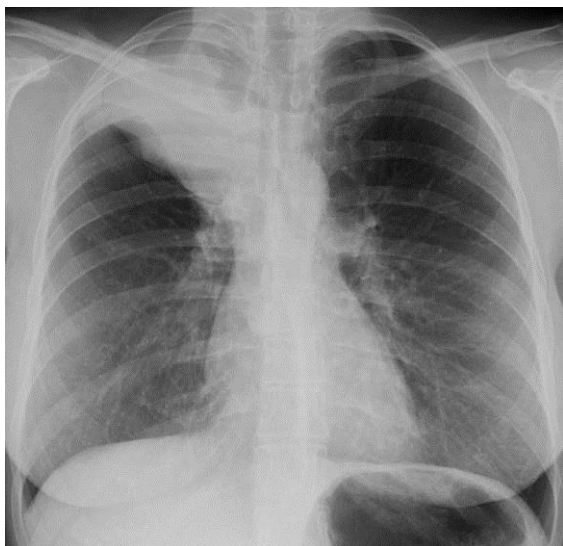
~15% annual mortality

Underlying diseases in patients with CPA (%)

	<u>Smith</u>	<u>Others</u>
Classical tuberculosis	17	31-81
Atypical tuberculosis	16	?
ABPA	14	12
COPD/emphysema	33	42-56
Pneumothorax	17	12-17
Lung cancer survivor	10	?
Pneumonia	22	9-12
Sarcoidosis (stage II/III)	7	12-17
Thoracic surgery	14	8-11
Rheumatoid arthritis	4	2
Asthma / SAFS	12	6-12
Ankylosing spondylitis	4	2-11
None	1	15



'Fungal asthma' – ABPA and SAFS



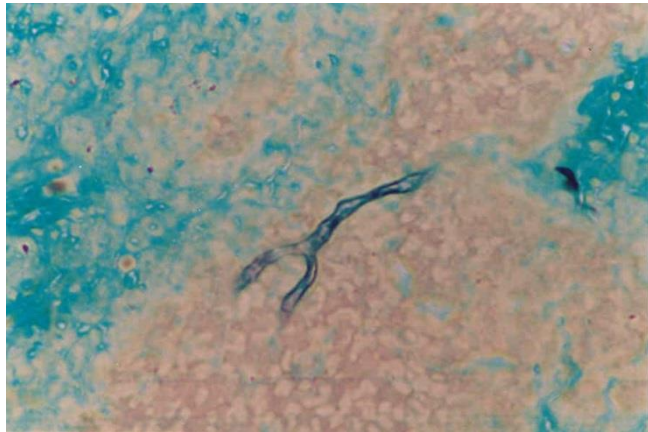
Asthma – 200 million adults

Allergic bronchopulmonary aspergillosis (ABPA) - ~2.5% asthmatics, ~5 million

**Severe asthma with fungal sensitisation (SAFS) - ~50% of severe asthmatics
~3.5 – 15 million**

Responsive to itraconazole

Allergic fungal sinusitis



Chronic rhinitis ~900 million adults

6.8% have fungal rhinosinusitis

~25 million with fungal rhinosinusitis

Responsive to polyp removal, nasal steroids, saline douches and antibiotics

Antifungals have a minor role



Invasive fungal infections

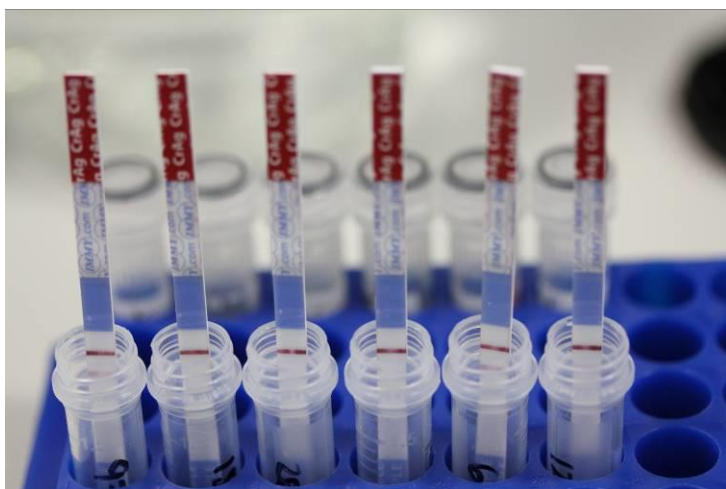
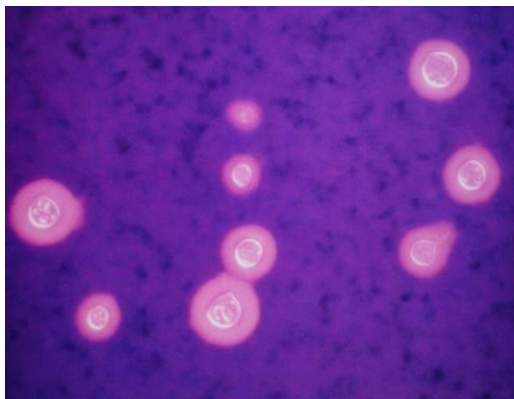
Disease Most common species	Location	Estimated Life- Threatening Infections / Year	Mortality Rates (% in infected populations)
Opportunistic Systemic Mycoses			
Invasive aspergillosis <i>Aspergillus</i> spp.	worldwide	>200,000	30 - 95%
Invasive candidiasis <i>Candida</i> spp.	worldwide	>400,000	46 - 75%

Rate varies by country from 3.0 to 26 /100,000

Brown et al, Sci Transl Med 2012;4:165rv13



Cryptococcal meningitis in AIDS



1,000,000 episodes; 600,000 deaths
Excellent diagnostic test
Can identify disease before symptoms
Takes 10 mins
Costs \$2
Highly cost effective



Invasive fungal infections

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Invasive aspergillosis <i>Aspergillus</i> spp.	worldwide	>200,000	30 - 95%
Invasive candidiasis <i>Candida</i> spp.	worldwide	>400,000	46 - 75%
Cryptococcosis <i>Cryptococcus neoformans</i>	worldwide	>1,000,000	20 - 70%
Mucormycosis <i>Rhizopus oryzae</i>	worldwide	>10,000	30 - 90%
Pneumocystis <i>Pneumocystis jirovecii</i>	worldwide	>400,000	20 - 80%

170,000 in India alone

Aspergillosis burden in Europe

Type of aspergillosis	Predominant risk groups	Risk population size (000's)	Aspergillosis rate	Annual aspergillosis burden (000's)
ABPA	Asthma	35,474	2.5%	887 (248 - 1,242)
	Cystic fibrosis	2,061,300		4.3
SAFS	Severe asthma	3,547	33%	1,170 (886 - 1,774)
Chronic pulmonary aspergillosis	COPD, TB, sarcoidosis, ABPA, Pneumothorax	>13,600	1-10%	240
Invasive aspergillosis	Myeloid leukaemia, Other haematological	44	7%	3.1
	HSCT	11.4		3.1
	COPD hospital admissions	3,600	63,250	
	Solid organ transplantation	30	0.75%	0.25
	Medical ICU	1,100 (all ICU)	2%	22
Total aspergillosis annual burden	All	-	-	2,364.55



Deaths from fungal infection

Fungal Infection	TB (2012)	Malaria (2013)
1,350,000	1,420,000	627,000



Conclusions

Burden of fungal disease is much much greater than generally appreciated

Their impact on quality of life is not well studied.

Estimations based on local epidemiological data and modelling a good start, but high quality epidemiological data are required.

Improved diagnosis is the key to better data and clinical outcomes

Chronic fungal infections (NCDs) need more attention generally