

# Mortality rate of cryptococcus neoformans



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Compare the mortality rate of C. neoformans in Australia and sub-Saharan Africa.

Do they differ? Provide an explanation for any discrepancy observed.

Mortality due to cryptococcosis in Australia and sub-Saharan Africa

One of the most severe complications of C. neoformans infection is cryptococcal meningitis. It accounts for 720, 000 estimated cases and 504, 000 deaths yearly in sub-Saharan Africa, 100 cases and 9 deaths in the Oceania region (mainly Australia). From these statistics, we can observe a stark difference in mortality rate; 70% and 9% (1). Cryptococcal meningitis is also an AIDS-defining illness in which AIDS patients are greatly susceptible due to immunosuppression. Various socio-economic elements also play a part in the great variation in mortality between the two regions. Such possible factors include availability/costs of drugs and healthcare facilities and nutritional status (2)(3).

Drugs used for cryptococcosis

Amphotericin B (AmB) is a recommended mainstay drug used to treat cryptococcosis and fluconazole and flucytosine are recommended to be used in conjunction with AmB in Australia. The main reason for this is AmB is fungicidal due to the affinity for it to bind to ergosterol of the fungal cell membrane, causing leakage of ions and nutrients from the fungal cell and leading to cell death (4). Fluconazole has more fungistatic properties as it inhibits ergosterol synthesis and resistance to flucytosine develops easily. Although fluconazole has a slow therapeutic onset, it has good absorption

and CNS penetration to suppress CNS infections but fluconazole monotherapy is unreliable as there are incidences of treated patients with acute meningitis and at least one of them with relapse each month in sub-Saharan Africa (5). AmB is nephrotoxic and lipid formulations of AmB have been created to alleviate this adverse side effect. One of such formulations is AmBisome.

#### Availability, costs and side effects of drugs

AmB and AmBisome are costly and not readily available to sub-Saharan Africa. The cost of AmBisome has recently been reduced from 96 GBP to US\$20 to allow distribution to the developing world (6). In the 1990s, the estimated treatment costs for a 60kg patient would be US\$1431 for a short course of Amb and US\$7840 for a long course of fluconazole. In recent years, the same treatment would cost US\$2438 for Amb and US\$1267 for fluconazole (7). Given the average daily income of less than US\$1.50 daily for the sub-Saharan Africans, these costs are just too exorbitant as compared to the Australians, who averaged as low as A\$130 daily (8)(9). Thus, the unavailability of AmB and fluconazole to the sub-Saharan Africans contributed significantly to the mortality rate. Fortunately at the start of 2000, Pfizer Pharmaceuticals initiated the Diflucan Partnership Programme to distribute fluconazole to developing countries free of charge (10). This partnership could have led to the suppression of mortality rate in the presence of an increasing HIV incidence in sub-Saharan Africa (11). Additional costs are incurred when the side effects of the drugs manifest in the patients. Common symptoms such as fever, chills, nausea and diarrhoea may seem minor to Australians as healthcare facilities are present almost

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everywhere and drugs can be bought off-the-shelves at an affordable price. However, to the sub-Saharan Africans, present treatments already cost them a bomb, not to mention extra costs in buying medicine to alleviate the side effects. Ultimately, they will get progressively weaker and some of them do not pull through (12).

#### Healthcare facilities and palliative care

Such facilities in sub-Saharan Africa are uncommon and adequately equipped clinics are much rarer. It is especially important to monitor patients with cryptococcal meningitis due to increased intracranial pressure which can lead to death if neglected (13). Sub-Saharan Africans who are susceptible to recurrent infections are also not always present at clinics due to distance, work or even simply too weak to travel (8). Amphotericin B causes nephrotoxicity which cannot be overlooked and renal signs need to be monitored closely (14). Given the efficient healthcare facilities in Australia, these clinical abnormalities can be rectified swiftly to prevent mortality. Furthermore, the total government expenditure on healthcare for Australia and Africa are 20% and 10% respectively (15)(16). This reflected the different standard of treatment the sub-Saharan Africans will encounter.

#### Nutritional status

The antifungal drugs exhibit certain side effects that vary between individuals. These variations are partly determined by the nutritional constitution of the body and predisposed diseases in the individual. Sub-Saharan Africa has been plagued by a variety of debilitating diseases such as hookworm/schistosome infections, malaria, HIV, tuberculosis etc. and when

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these diseases are coupled with cryptococcosis, it is almost impossible for anyone to survive to his potential in addition to the insufficient healthcare facilities in sub-Saharan African (8).

### Conclusion

The high incidence of mortality in sub-Saharan Africa is contributed by not only the unavailability and high costs of suitable drugs but also the absence of adequate healthcare facilities and high incidence of AIDS patients. The low incidence of mortality in Australia is due to the wide availability and affordability of suitable drugs and an adequate and efficient healthcare system in place.