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World Health Organization Fungal Priority Pathogens List

In 2022, the World Health Organization (WHO) published its first ever fungal priority pathogens list in response to the increase of invasive fungal disease globally (WHO, 2022). This was the first report to categorise fungal pathogens in order to focus and prioritize an international and concentrated public health response to fungal infections and antifungal resistance. With over 300 million severe cases and 1.5 million deaths annually, invasive fungal diseases are a source of global morbidity and mortality and are a significant burden on finite medical resources (Zhang et al, 2023).

Most pathogenic fungi are opportunistic and cause disease in those who are immunocompromised. This includes people with an underlying condition such as HIV infection, those undergoing chemotherapy for the treatment of cancers or long-term immune suppressive drug therapy following transplantation surgery. Concurrently, there is a rise in the incidence of invasive fungal diseases due to the limited systemic antifungal therapies available. There are only four classes of systemic antifungal medicines (polyenes, azoles, echinocandins and pyrimidines) commonly used in clinical practice. In addition, there are very few new antifungal therapies in development with the increasing emergence of drug resistance to existing therapies.

Antifungal therapies.

The polyenes are the oldest family of antifungal drugs and were introduced in the late 1950s. Amphotericin B belongs to the class of polyene macrolides and is the most widely used antifungal drug in the treatment of serious systemic fungal infections (Cavassin et al. 20210).

Second generation azoles are the largest family of antifungal drugs and act by interfering with fungal cell wall biosynthesis. Azoles inhibit fungal growth by altering the function and structure of the fungal cell membrane while remaining inactive against the host cells (Pristov & Ghannoum, 2019). Fluconazole is effective against fungal meningitis due to its ability to penetrate the cerebrospinal fluid. Itraconazole can be used as prophylaxis of deep fungal infections for those undergoing bone-marrow transplantation who are expected to become neutropenic (BNF, 2024). Echinocandins are broad spectrum antifungals with a fungicidal activity of interfering with glucan synthesis resulting in impaired cell wall formation and cell lysis. Micafungin has antifungal properties in relation to treatment and prophylaxis of *Candida* infections (Drug Bank, 2024).

Calculation skills

Question 1

Adult, weighing 65kg with aspergillosis is prescribed IV Amphotericin B by intravenous infusion. BNF recommends 3 mg/kg once daily with a maximum dose of 5 mg/kg per day. What minimum and maximum daily dose could be prescribed?

Question 2

Adult, weight 43kg with systemic fungal infection is prescribed IV Amphotericin B by intravenous infusion. BNF recommends Day 1 dose of 250 micrograms/kg daily to be increased as tolerated to 1.5 mg/kg on alternate days.
What is the dose to be prescribed for Day 1. What is the maximum alternate day dose?

Question 3

5-year-old child, weighing 24 kg with oropharyngeal candidiasis is prescribed Fluconazole by intravenous infusion. BNF recommends 3–6 mg/kg, dose to be given on first day, then 3 mg/kg daily (max. per dose 100 mg) for 7–14 days.

What is the minimum or maximum dosage that can be prescribed on the first day? What is the maintenance dose up to day 7 or 14?

Question 4

15-day old neonate, weighing 5.6kg with invasive candidiasis is prescribe Micafungin. BNF recommends 2 mg/kg once daily for at least 14 days; increased if necessary to 4 mg/kg once daily.

What is the minimum and maximum dosage that could be prescribed?

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ANSWERS

Question 1: Amphotericin B

Minimum dose 3mg x 65kg = 195mg
Maximum dose 5mg x 65kg = 325mg

Question 2: Amphotericin B

Day 1 dose: 250micrograms x 43kg = 10.75mg
Alternate maximum dose: 1.5mg x 43kg = 64.5mg

Question 3: Fluconazole

Day 1 minimum 3mg x 24kg = 72mg
Day 1 maximum 4mg x 24kg = 96mg. Prescribing 5mg/kg of 6mg/kg would exceed maximum dose.
Day 2–14. 3mg x 24kg = 72mg per dose daily.

Question 4: Micafungin

Minimum 2mg x 5.6 kg = 11.2mg
Maximum 4mg x 5.6kg = 22.4mg