models with different antifungal drug classes have identified distinct pharmacodynamic characteristics. Results from these models have been useful for defining the relationship between antifungal exposures and efficacy. More recently clinical data has become available allowing similar investigation. These results of these studies have been similar to those from experimental models and have cemented the clinical significance of these pharmacodynamic concepts. The analyses have been shown to be helpful for the design of antifungal dosing intervals, choice of optimal dose levels, therapeutic drug monitoring, and the development of susceptibility breakpoints. Most of these preclinical and clinical studies have targeted therapeutic efficacy against Candida species. More recent studies have also considered other fungal pathogens and have begun to investigate the role of anifungal pharmacodynamics and drug resistance development. Although there remain many unanswered questions regarding antifungal pharmacodynamics, available data suggest usefulness in the application of pharmacodynamics to help guide antifungal therapy.

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12.003

New Generation Triazoles: What Do They Offer and When Do We Need Them?

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Voriconazole and posaconazole are the latest triazole drugs to be marketed. Voriconazole was developed from fluconazole by substituting a fluoropyrimidine ring for one of the azole groups to enhance the spectrum (to include Candida krusei, fluconazole-resistant C. glabrata, Aspergillus spp, some Fusarium strains, Scedosporium apiospermum and dimorphic fungi such as Histoplasma capsulatum) and adding the a-methyl group to provide fungicidal activity against Aspergillus spp. in particular. Posaconazole is structurally derived from itraconazole, with fluorine replacing chlorine substituents in the phenyl ring and hydroxylation of the triazolone side chain. These modifications enhance the potency and spectrum of antifungal activity to include the additional species covered by voriconazole with the exception of Fusarium and in addition, the zygomycetes.

Randomised controlled clinical trials (RCTs) have identified that voriconazole is the treatment of choice for invasive aspergillosis in the immunosuppressed. Efficacy has been demonstrated in candidiasis (including against small numbers of fluconazole-resistant Candida infections), in fusariosis, cryptococcosis and infections where cheaper agents such as fluconazole would be preferred. The major drawbacks to replacing fluconazole with voriconazole are its cost, adverse effects including a small incidence of photosensitivity, significant drug interactions, and pharmacokinetic issues, which may be resolved by therapeutic drug monitoring in some settings.

Posaconazole has been subject to RCTs of its use in prophylaxis against fungal infections in recipients of haematopoietic stem cell transplants where, despite some It has been used as salvage therapy in other settings. The main drawbacks to widespread use of posaconazole include cost, the lack of an intravenous formulation, reduced bioavailability in the absence of food and lack of RCTs of its therapeutic use.

Confirmation of improved clinical outcomes from the use of either agent in combination therapy is yet to be obtained.

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12.004

Understanding the Similarities and Differences of Existing and Emerging Echinocandins

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The echinocandins, comprising caspofungin, micafungin and anidulafungin, inhibit beta-(1,3)-glucan, Glucan is found in fungal cell walls but not mammalian cells. As large highly protein bound molecules, none are orally bioavailable or achieve levels in the CSF. The spectrum is consistent across all three agents with fungicidal activity against Candida, and fungistatic activity against Aspergillus. The echinocandins are not active against Cryptococcus,*Scedosporium prolificans* or Zygomycetes. All are fungicidal against *Candida species* although MIC_{90}s vary slightly between agents with the lowest MIC_{90}s seen with anidulafungin, then micafungin, and caspofungin. However, it is not clear if these differences are clinically relevant. All have higher MIC_{90}s for *C. parapsilosis*, *C. guilliermondii* and *C. lusitaniae* compared to other *Candida spp*. Although *C. parapsilosis* remains susceptible despite a higher MIC_{90}, resistance has emerged on treatment. All may rarely cause histamine release with pruritis, rash and swelling. The differences between the agents are shown in the table below:

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Emergence of EV71 in the Asia Pacific in the Last Decade

13.001

Epidemiology of EV71 Outbreaks in the Region in the Past Decade

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HFMD: Current Knowledge and Challenges for Malaysia and the Asia Pacific Region

Background: Hand, foot and mouth disease (HFMD), especially that caused by EV71 is an important re-emerging disease in the Asia Pacific region, with the potential to cause massive outbreaks that can last for many months, and with relatively high complications rates, and deaths.

Methods: A review of the first-hand experiences gained during the control of the four major HFMD outbreaks in