

Invasive fungal infections in paediatric patients

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The topic of this issue's theme is opportunistic invasive fungal infections (IFIs) in paediatrics. Is there a need to have a separate theme on paediatric IFIs in the Journal? The short answer is yes. Children are not little adults. There are distinct age-related differences in the epidemiology and pathophysiology of fungal infections, as well as in antifungal pharmacology in particular. Although the most frequent IFIs, such as candidiasis and aspergillosis, can occur at all ages, there are important differences in the frequencies of particular IFIs, and in the approaches by which they are diagnosed and treated. Indeed, there are important differences even between neonates and children in the pharmacokinetics of certain antifungal agents, as shown in recent years. Furthermore, there is a paucity of data on the optimal use of common antifungal agents, such as amphotericin B and fluconazole, in children and especially in neonates.

We have the honour and pleasure to host four excellent reviews in this issue of the Journal, covering the main areas of interest in IFIs of paediatric patients. The first review addresses the epidemiology of IFIs in neonates and children, which is, in some respects, very different from that in adults. Different underlying risk factors (i.e. prematurity, type of haematological malignancy, and congenital immunodeficiencies) and increasingly diverse spectra of causative species of fungi (i.e. more frequent *Candida parapsilosis* in neonates and more frequent *Candida glabrata* in adult haematological patients) with different pathogenicity and mortality have raised more questions about the management of IFIs in neonates and children. These questions have made even more challenging the state-of-the-art care of IFIs in young patients.

The second article is a comprehensive review of the non-culture diagnostic methods for IFIs and their current problems, particularly in neonates and children. Early recognition and rapid initiation of effective treatment is a prerequisite for successful management of children with IFIs. As culture methods are not helpful in many cases, immunodiagnostic and molecular methods have been developed.

The third review discusses the issue of IFIs in congenital immunodeficiencies, a particular paediatric group of diseases.

Both acquired and congenital immunodeficiencies may be associated with increased susceptibility to IFIs, depending on the type of immune deficit. Invasive aspergillosis is the most frequent cause of death in patients with chronic granulomatous disease. A number of diagnostic and therapeutic specifications differentiate the management of IFIs in these patients from that in haematological patients of similar age.

The last review is an excellent update on the pharmacokinetics, safety and dosing of antifungal agents in paediatric patients, as well as the clinical indications and therapies utilized to manage IFIs in neonates and children. Indeed, the sequence from neonate to adolescent and to adult involves many changes in the systematic antifungal therapy, such as dosing (frequently, larger doses are needed than in adults) and pharmaceutical formulations (oral solutions rather than capsules). However, the greatest problem in antifungal therapy in neonates and children is the lack of data on efficacy and safety in these ages. During the past decade, several new antifungal agents have been developed. Historically, the large trials have excluded young patients because of exactly these potential differences. These advances have also made the management of IFIs in neonates and children more challenging, requiring special knowledge and effort. Recently, Pediatric Investigation Plans for some older antifungals have been developed by the European Medicines Agency, and are expected to help paediatric antifungal research. Although not all of the newer agents are yet approved for children, the development of antifungal agents for paediatric use has moved forwards in a rapid manner. Although the availability of new therapeutic options is an important advance, antifungal therapy has become increasingly complex, and a thorough understanding of the available antifungal armamentarium is essential for optimal therapy of the individual patient.

These and several other issues are raised and discussed in the comprehensive reviews of this theme. We feel fortunate to be able to introduce these excellent articles, which we are sure will be beneficial to the readership of the Journal. Paediatric IFIs have started to attract considerable interest, from both the clinical and research points of view, because of their poor outcome and unfortunate sequelae for young

patients with a long life-expectancy. Multicentre and, indeed, multinational collaborative consortia, such as the International Pediatric Fungal Network (<http://pfn.pediatrics.duke.edu>) and the European Society of Paediatric Infectious Diseases Fungal Study Group, are expected to greatly help in conducting valuable epidemiological surveys as well as management studies in neonatal and paediatric patients in the near future. As the field of paediatric mycology advances, we believe that

the next special issue on paediatric IFIs will highlight new advances in the diagnosis and treatment of these devastating diseases.

Transparency Declaration

Both authors have no conflict of interest to declare.