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ArunalokeChakrabartiis serves as Professor and Head of Department of Medical Microbiology at PGIMER, Chandigarh and Chief of National Mycology Reference Laboratory & WHO Collaborating Center. He is currently the President-elect of International Society for Human & Animal Mycology (ISHAM), Chair of Asian Fungal Working Group, Chair of Fungal Infection Study Forum, Coordinator of ISHAM working groups on Fungal sinusitis and ABPA in asthmatics. He is Editor/Associate Editor/Deputy Editor of five journals –Medical Mycology, Journal of Medical Microbiology, Mycoses, Current Fungal Infection Report and Medical Mycology Case Report. He has published 245 papers in the field of Medical Mycology & has written chapters in 13 books. He has recently edited the book 'Fungal Infections in Asia-The Eastern Frontier of Mycology'. His major contribution is in the field of epidemiology of fungal sinusitis, mucormycosis, and hospital acquired fungal infections.

Invasive aspergillosis in Intensive Care Units (ICUs)

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Aspergillus spp. are important causes of morbidity and mortality in hospitalized patients. The spectrum of Aspergillus infection vary from invasive aspergillosis, chronic aspergillosis to allergic diseases including allergic broncho-pulmonary aspergillosis (ABPA). Invasive aspergillosis is the most devastating from Aspergillus infection. The classical risk factors for invasive aspergillosis include patients with hematological malignancies undergoing chemotherapy, transplant recipients, autoimmune diseases etc. In recent years, invasive aspergillosis in critically ill patients in ICU without neutropenia is an emerging problem affecting 0.3 to 6.9 % patients. The new risk factors for those patients include chronic obstructive pulmonary disease (COPD), long term use of systemic and inhaled corticosteroids, cirrhosis, renal failure, severe sepsis, long stay in ICU etc. Construction or renovation work near ICU has also been implicated in outbreak of invasive pulmonary aspergillosis. The mortality in this group is high (reaching 90%), as the disease in one of the most frequently undiagnosed infections in critically ill patients. The clinical presentation of invasive aspergillosis in ICUs is non-specific, and diagnostic criteria are poorly defined. Unlike neutropenic host, colonization of respiratory tract with Aspergillus spp. does not correlate well with invasive aspergillosis. EORTC-MSG proposed scheme for diagnosis of invasive fungal infection does not fit in those patients, as host criteria are different and classical radiological findings are missing. A group of ICU experts proposed a clinical algorithmic to discriminateAspergillus colonization from putative pulmonary aspergillosis. In the laboratory, though galactomannan test is not well validated for diagnosis of invasive aspergillosis in critically ill patients, recent studies on detection of galactomannan in broncho-alveolar lavage fluid has yielded promising results. Aspergillus PCR may also help in early diagnosis in near future. To treat these patients voriconazole is recommended as the drug of choice, and amphotericin B, echinocandins are other alternatives. However, the treatment of invasive aspergillosis remains difficult, as data concerning the safety and efficacy of these antifungal agents in ICU setting and early diagnosis of invasive aspergillosis are still lacking. Recent emergence of azole resistance in Aspergillus fumigatus is another challenge.

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Bernhard Hube

Bernhard Hube studied microbiology at the University of Göttingen, Germany, where he also did his PhD. He performed his postdoctoral research in Aberdeen, Scotland, where upon he moved back to Germany, first to Hamburg as a senior postdoc and assistant professor and then to the Robert Koch Institute in Berlin as an independent group leader and the Head of the division of Mycology. Since 2007, he has been Professor at the Friedrich Schiller University of Jena and Head of Department of Microbial Pathogenicity Mechanisms at the Hans Knöll Institute of the Leibniz Association in Jena. His main research interest is the molecular and infection biology focusing on the pathogenicity mechanisms of Candida species. He has authored >170 papers on host/pathogen interactions, functional genomics, and others. He is an Editorial board member of several journals, co-organizer of the FEBS advanced practical course "State-of-the-art infection models for human pathogenic fungi", former Vice President of the International Society for Human and Animal Mycology (ISHAM) and former Co-Chair of the ISHAM 2012 conference in Berlin. He has been the recipient of awards, including the Seeliger Award (2003), a Fellowship of the American Academy of Microbiology (2008), an Honorary Membership of the German-speaking Mycology Society (2013) and the Main Award of the German Society for Hygiene and Microbiology (2014).

From Commensalism to Pathogenicity: Stages of Candida albicans Infections

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The dimorphic fungus Candida albicans can be both, a normally harmless commensal of mucosal surfaces in most healthy individuals, but also an aggressive human pathogen in susceptible hosts.

In the commensal phase, fungal cellsare associated with host mucosal surfaces and co-exist with the microbiota. These conditions change during the transition to a pathogenic life style. This transition includes direct attachment to, invasion into, and damage of epithelial cells.

Adhesion to host epithelial cells is a dynamic event and is mostly mediated by surface proteins, the adhesins. Fungal−host surface contact during the adhesion process can induce the production of hyphae and expression of hyphae-specific genes, which, in turn, drive further adhesion. Hyphae are not only more adhesive, but also more invasive than yeast cells. In fact, the yeast-to-hyphal transition of C. albicans is important for a variety of essential pathogenic processes, including, but not limited to, adhesion to epithelial cells, as well as invasion via two different routes: induced endocytosis or active penetration. Induced endocytosis by C. albicans is entirely host-driven, while active penetration is a fungal-driven process. Active penetration is the major contributor to pathogen entry, and involves direct hyphae-mediated penetration of the epithelial cell. Induced endocytosis is also a hyphae-mediated process, mostly triggered by the hyphae-associated invasin Als3. Although induced endocytosis is an overall minor contributor to pathogen entry in vitro, it is possibly important at early stages of infection. Interestingly, initial invasion is not associated with significant damage. Most of the tissue damage associated with C. albicans infections is due to deep and destructive inter-epithelial invasion via elongated hyphae, along with the release of destructive factors.

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Updates on Mucorals and Mucormycosis

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Mucormycosis is an emerging infection due to several species belonging to Mucorales. Indeed, Mucorales represent a large group of fungi including very diverse species that can be found all over the world. Among the several hundreds of known species of Mucorales, more than 20 different species belonging to more than 10 genera can be responsible for infections in humans. It is clear that they are very diverse in terms of genetics and biology, geographical distribution and epidemiology, antifungal susceptibility, predisposing factors of the patients, and clinical presentation of the diseases they are causing. This diversity could have a direct impact on the performance of diagnostic tools and may have, in the future, when more active drugs are available, an impact on the therapeutic strategies.

Recently, the taxonomy of Mucorales has been largely revised and molecular studies have shown the great diversity among the genera and even among species belonging to a given genus. One the practical consequences of these large genetic variations are that a single DNA target (ITS region) can be easily used for a precise molecular identification of almost all the pathogenic species.

Although Mucorales seems to be worldwide distributed, the frequency of the species is related to the geographical area. For example, species belonging to Saksenaea or Apophysomyces are more often recovered in tropical countries and Lichtheimia species seems more frequent in Europe than in North America.They are also difference between species for their antifungal susceptibility. Some species such as Cunningha mella spp. are less susceptible to amphotericin B than others and variable susceptibilities to posaconazole have also been reported among Mucorales. The clinical impact of these differences are nevertheless currently largely unknown.The underlying conditions of the patients with Mucormycosis and the clinical presentation of the disease is also dependent on the species. Some species such as Saksenaea and Apophysomyces are mainly responsible of post-traumatic cutaneaous/subcutaneous infections in immunocompetent patients. In contrast, Rhizopus species are more often responsible for rhino-cerebral infections in diabetic patients.

Major advances have also been made for diagnosis of Mucormycosis. In particular, recent studies showed that PCR in tissues and in serum may be of value for an accurate and early diagnosis.

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Jacques F. Meis is a consultant of Medical Microbiology and Infectious Diseases at Canisius Wilhelmina Hospital and an honorary consultant at Radboud University Medical Center in Nijmegen, The Netherlands. Dr Meis received his bachelor's, master's, and doctorate degrees from the University of Nijmegen, Faculty of Science, and his medical degree from the University of Nijmegen Medical School in Nijmegen, The Netherlands. He completed his fellowship in the Department of Medical Microbiology at the University Hospital Nijmegen, The Netherlands, where he worked as an associate professsor until 2000.

Among his clinical and laboratory interests are treatment of fungal infections in intensive care and other compromised patients, in vitro activities of antifungals against filamentous fungi and molecular typing of fungi. More than 450 articles on these issues and many other topics have been published by him in several medical journals. Dr.Meis is the previous president of the Dutch Society for Medical Mycology and European Confederation of Medical Mycology and elected as the fellow of the Infectious Diseases Society of America, the Royal College of Pathologists and the American Academy of Microbiology. At present, he serves as the vice-president of ISHAM.

Emergence of global azole resistant Aspergillus fumigatus

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Aspergillus fumigatus, a ubiquitously distributed opportunistic pathogen, is a global leading cause of aspergillosis. Azole antifungals play an important role in the management of aspergillosis. However, over a decade azole resistance in A. fumigatus isolates have been increasingly reported especially in Western Europe and is potentially challenging the effective management of aspergillosis. The high mortality rates observed in patients with invasive aspergillosis caused by azole resistant A. fumigatus isolates pose serious challenges to the clinical microbiologist for timely identification of resistant isolates and appropriate therapeutic interventions. The 'TR34/L98H' mutation in the cyp51A gene of Aspergillus fumigatus is responsible for most multi-azole resistance seen in many European countries, the Middle East, including Iran,, Asia and the USA. Azole-resistant isolates carrying this mutation have been reported from both patients and the environment. In addition, a new resistance mechanism, TR46/Y121F/T289A, in A. fumigatus conferring high voriconazole and variable itraconazole MICs was lately described in the Netherlands, Denmark, Belgium, Germany, France, Spain, Tanzania, China, USA, Colombia and India. Azole resistant A. fumigatus has now been reported from 6 of the seven continents and will become a future reality for many centers. Considering that azole antifungals are mainstay of therapy, especially for chronic invasive and allergic aspergillosis, emergence of resistance especially in resource limited countries will have profound impact on healthcare. This presentation highlights the emergence in development of azole resistance in A. fumigatus and the possible relation with environmental fungicide use.

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Candida Vaginitis: an Update

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Vulvovaginal candidiasis (VVC), a common problem among women, affects an estimated ~75% of women during their lifetime, with ~45-50% having recurrent episodes, and 5-8% of women having recurrent VVC (RVVC), defined as four or more episodes each year. The recommended diagnostic work-up for VVC consists of at least vaginal pH measurement and microscopy using potassium hydroxide (KOH) or Gram staining; fungal culture is highly encouraged, particularly in RVVC cases. In most cases, history and physical examination alone will fail to provide sufficient information to arrive at a definite diagnosis. Candida albicans remains the most common pathogen in acute and recurrent VVC cases worldwide; although C. glabrata is the second most common pathogen, its prevalence differs globally. The optimal management of VVC, particularly RVVC, requires species-specific recognition of the pathogen. Therefore, establishing a proper diagnosis will lay the foundation for an effective therapeutic plan. Notably, in some developed countries and many developing countries, topical imidazoles have available over-the-counter (OTC) and without prescription, since the 1990s. The misuse of OTC antifungal drugs can lead to delay to accurate diagnosis and, therefore, to higher health costs. Here, I review the current knowledge about the available diagnostic methods and tests that accurately diagnose VVC, and highlight the therapeutic management.

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