New Era of Antifungal Agents
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Fungal infections particularly nosocomial ones have increased greatly in recent years, mainly due to the rising number of immunocompromised patients and cause wide-ranging morbidity and mortality. However, the current antifungal therapy in total is limited, and the development of unique drugs has been slow. Yet only a few drug classes are available to treat fungal infections, and this problem is compounded by the emergence of antifungal resistance. Current drug therapy is often toxic, long-term, and expensive and has limited effectiveness. Natural products such as plants have been the most productive source for new drug development and could produce a variety of medicinal components that can inhibit fungal growth. Nano particles (NPs) have also been considered as novel antifungal agents with high surface area and high reactivity. It is hoped that the new agents e.g. natural & nano products will usher in a new era of antifungal therapy.

Brain Infection Due to Black Yeast like Fungi; How Come We Are Alive?
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Cerebral phaeohyphomycosis is the collective name for a group of cerebral fungal infections that are characterized by black necrotic tissue or black CSF. If untreated, the infection leads to death within weeks, months, or, occasionally, years. This infection is caused by a variety of fungi and has primarily been reported in immunocompromised patients. Although rare, Rhinocladiella, mackenziei and Cladophialophora bantiana are extremely lethal neurotropic filamentous fungi related to the black yeasts. Despite therapy, the mortality rates reach up to 75%. The infection also occurs in patients with decreased immunity due to organ transplants, long-term corticosteroid administration, or in interaction of clinical mycology and host physiology along with living environment, the target and concept of mycosis is also changing and new terminology and disease classifications are emerging. Until 1970 there were less species noted as pathogens of cerebral fungal infections that are characterized by black necrotic tissue or black CSF. If untreated, the infection leads to death within weeks, months, or, occasionally, years. This infection is caused by a variety of fungi and has primarily been reported in immunocompromised patients. Although rare, Rhinocladiella, mackenziei and Cladophialophora bantiana are extremely lethal neurotropic filamentous fungi related to the black yeasts. Despite therapy, the mortality rates reach up to 75%. The infection also occurs in patients with decreased immunity due to organ transplants, long-term corticosteroid administration, or in interaction of clinical mycology and host physiology along with living environment, the target and concept of mycosis is also changing and new terminology and disease classifications are emerging. Until 1970 there were less species noted as pathogens of cerebral fungal infections that are characterized by black necrotic tissue or black CSF. If untreated, the infection leads to death within weeks, months, or, occasionally, years. This infection is caused by a variety of fungi and has primarily been reported in immunocompromised patients. Although rare, Rhinocladiella, mackenziei and Cladophialophora bantiana are extremely lethal neurotropic filamentous fungi related to the black yeasts. Despite therapy, the mortality rates reach up to 75%. The infection also occurs in patients with decreased immunity due to organ transplants, long-term corticosteroid administration, or in interaction of clinical mycology and host physiology along with living environment, the target and concept of mycosis is also changing and new terminology and disease classifications are emerging. Until 1970 there were less species noted as pathogens of cerebral fungal infections that are characterized by black necrotic tissue or black CSF. If untreated, the infection leads to death within weeks, months, or, occasionally, years. This infection is caused by a variety of fungi and has primarily been reported in immunocompromised patients. Although rare, Rhinocladiella, mackenziei and Cladophialophora bantiana are extremely lethal neurotropic filamentous fungi related to the black yeasts. Despite therapy, the mortality rates reach up to 75%. The infection also occurs in patients with decreased immunity due to organ transplants, long-term corticosteroid administration, or in interaction of clinical mycology and host physiology along with living environment, the target and concept of mycosis is also changing and new terminology and disease classifications are emerging.
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Diagnosis of non-invasive pulmonary aspergillosis is not easy; however, in addition to pulmonary cavitations on chest X-ray, even the presence of fungus ball and hyphae and also mass in a pulmonary cavity, with a positive culture (preferably positive direct examination), the presence of *Aspergillus* IgG antibodies must be definitively demonstrated for the diagnosis of aspergillosis or CPA. Often the diagnosis of CPA is difficult because of its overlapping clinical and radiological characteristics with tuberculosis; hence, it is important to use microbiological and serological testing for the early diagnose CPA. *Aspergillus* PCR and/or antigen in sputum or bronchoscopy may be helpful. There is not a population study for the evaluation of CPA incidence in exposed hosts; therefore, the determination of real incidence of aspergillosa and CPA after tuberculosis has remained a dilemma because most of the existing reports are case reports or case series on previous diagnosed CPA patients.

In this review, we presented our new findings on the prevalence of CPA in patients with tuberculosis from Iran, the global epidemiology of CPA, different laboratory diagnostic methods, and a discussion on the question “are we encountering a berg phenomenon in CPA in patients with underlying pulmonary conditions.

**Diagnostic Challenges in Opportunistic Invasive Fungal Infections, New Approaches for Detection, Identification and Typing**

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The most critical point among challenges with opportunistic invasive fungi mainly *Aspergillus* spp. and *Candida* spp., is the reliable diagnosis of the infections. Early diagnosis and species identification are critically important for successful treatment, while strain typing is necessary for tracing infection sources and ways of transmission of infection in outbreaks as well as for pathogenesis investigations. Conventional diagnostic methods, such as direct microscopy, histopathology and culture, which are still the gold standards, are deficient in both sensitivity and rapidity. Novel diagnostic approaches include serological and molecular methods especially the detection of fungal cell wall components or metabolites and the detection of fungal DNA mainly PCR-based methods, in clinical specimens. Galactomannan antigen test for aspergillosis and the universal β-glucan test, as well as other antigen and antibody tests, for *Cryptococcus* spp. and *Pneumocystis* spp, have already been established and implemented in routine clinical laboratories. Detection of fungal DNA is being developed, but has not had a significant impact on clinical laboratories yet, largely because these methods have not been standardized and validated. Sequencing of suitable gene targets, FISH, NASBA, MALDI-TOF MS and NMR spectroscopy are examples of recently developed tools for species identification. Strain typing is an essential need because it helps strain identification, determining the epidemiological relationships between isolates in outbreaks, patients’ monitoring and treatment follow-up, environmental monitoring, local and global epidemiology and database construction. Several sequence and non-sequence-based methods have been evaluated; namely, MLEE, PFGE, RAPD-PCR, STR, MLST, SSDP, MSP, RFLP, AFLP, PCR–SSCP, microsatellites, Rep-PCR, VNTR, and Whole genome sequencing.

In this presentation, various diagnostic approaches for detecting opportunistic invasive fungal infections and associated challenges were described.

**Application of Chromatography in Antifungal Drug Discovery from Medicinal Plants**

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Plants are promising sources of bioactive compounds for the development of new antifungal drugs. Although probable synergistic effect of natural compounds or combination dosage form. Combination of myrrh and rose oil is a famous poultice applicable for such skin lesions. Aforementioned symptoms are seen if infected by dermatophyte fungi like *Trichophyton rubrum*, *T. mentagrophytes*, *Microsporum canis*, *M. gypseum*, and *T. verrucosum*. The antifungal effects of myrrh oil against dermatophyte hyphae have been established in current studies because of its active ingredients. Some natural and herbal products have shown evidence of antifungal activities and could be used in modern mycology as inexpensive favorable substitutes for antifungal agents. *Mycorrhiza molmol* is a good example derived from TPM textbooks and could be applied as a poultice for curing cutaneous fungal infections caused by dermatophytes. New clinical studies to assess this claim are highly suggested.

**Role of Fungi in Diabetic Foot Ulcer- a Superficial Colonizer or True Pathogen**

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Foot ulcer is the most common problem in patients with diabetes and the leading cause of hospitalization which may proceed with limb amputation. The pathophysiology of foot ulcer in these patients is complex and it is mainly due to neuropathy, peripheral vascular disease, slower wound healing and immunopathology. Secondly, it is a sentinel disease and an indicator of infection involving pathogens. The most common pathogens responsible for acute Diabetic Foot Infection (DFI) are aerobic bacteria. The diverse causative pathogens with vast virulence factors, and polymicrobial nature of DFI have further complicated antibiotic treatment. Opportunistic and/or fungal infection is still a challenging issue and should be considered in chronic foot ulcer with delayed healing in diabetic patients. One of the most controversial issues
confronting the DFI is lack of widely agreed guidelines for its
diagnosis, treatment, and management.
This review was aimed to address the role of fungi in chronic
diabetic foot ulcer—true as pathogen or a superficial colonizer,
to discuss the current diagnostic methods and report a rare case
with calcaneal osteomyelitis caused by *Aspergillus ochraceus* in a
patient with diabetic foot osteomyelitis.