REVIEW

EMERGING OPPORTUNISTIC YEAST INFECTIONS – LITERATURE REVIEW

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Abstract

The growing threat of fungal infections demands immediate attention from healthcare systems in all countries. With the advancement of modern medicine and a growing population of immunosuppressed and immunocompromised patients, as well as critically ill patients, increasingly frequent diagnoses of invasive yeast infections have become an important cause of morbidity and mortality. In the last decade, increased incidence of non-*albicans Candida species* infection compared to *C. albicans* has been registered worldwide. Several non-*albicans Candida species*, such as *C. glabrata* and *C. krusei,* may be resistant to azole antifungal therapy The emergence of multidrug-resistant *C. auris* is the latest threat in many countries, since this fungus can cause intrahospital infections. *Trichosporon* species are the second most common cause of invasive yeast infections in patients with haematological malignancies, and can be resistant to amphotericin and echinocandins. Despite diagnostic and therapeutic advances, cryptococcosis continues to be a disease with unacceptably high incidence and mortality, particularly in resource-limited settings. *Rhodotorula* species can be a significant cause of catheter-related fungaemia, sepsis, and invasive disease in severely immunosuppressed patients. Other uncommon yeasts that can cause invasive disease in severely immunosuppressed patients include *Magnusiomyces capitatus, Geotrichum candidum, Kodamaea ohmeri, Saccharomyces cerevisiae, Malassezia furfur and Sporobolomyces species*. Although rare yeasts are emerging as opportunistic human pathogens, diagnosis remains challenging and treatment suboptimal. Therefore, enhanced awareness of fungal infections is crucial among healthcare providers, and this requires great knowledge and understanding, and appropriate diagnostic testing, so every segment of the healthcare system can contribute to address the challenges posed by fungal infections.

ПРЕГЛЕД НА ЛИТЕРАТУРА

ПОНОВИ ОПОРТУНИСТИЧКИ ИНФЕКЦИИ СО КВАСНИЦИ - ПРЕГЛЕД НА ЛИТЕРАТУРАТА

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Извадок

Растечката закана од габични инфекции бара итна акција од здравствените системи на сите земји. Со напредокот на модерната медицина и растечката популација на имуносупримирани и имунокомпромитирани пациенти, како и критично болни пациенти, сè почестите инвазивни инфекции предизвикани од квасници стануваат важна причина за морбидитет и морталитет. Во последната деценија се регистрира зголемена инциденција на инфекции со non-*albicans Candida* видови во однос на *C. albicans*. Неколку non-*albicans* специеси, како *C. glabrata* и *C. krusei*, може да бидат отпорни на азолите. Појавата на мултирезистентната *C. auris* е најновата закана во многу земји, бидејќи оваа габичка може да предизвика интрахоспитални инфекции. *Trichosporon* species е втората најчеста причина за инвазивни габични инфекции кај пациенти со хематолошки малигни заболувања, а тие може да бидат отпорни на амфотерицин Б и ехинокандини. И покрај дијагностички и терапевтски напредок, криптококозата продолжува да биде болест со неприфатливо висока инциденција и смртност, особено во услови со ограничени ресурси. Видовите *Rhodotorula* може да бидат значајна причина за фунгемија поврзана со катетер, сепса и инвазивни болести кај сериозно имуносупримирани пациенти. Други невообичаени квасници кои можат да предизвикаат инвазивна фунгална инфекција кај сериозно имуносупримирани пациенти се: *Magnusiomyces capitatus, Geotrichum candidum, Kodamaea ohmeri, Saccharomyces cerevisiae, Malassezia furfur* и *Sporobolomyces species*. Иако ретките квасници се појавуваат како опортунистички човечки патогени, дијагнозата и понатаму е предизвик, а третманот е субоптимален. Затоа, зголемената свест за габичните инфекции е од клучно значење кај давателите на здравствени услуги, а тоа бара големо знаење и разбирање, како и соодветно дијагностичко тестирање, со цел секој сегмент од здравствениот систем да може да придонесе за справување со предизвиците што ги создаваат габичните инфекции.

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Печатарски права: ©2025 Гордана Мирчевска. Оваа статија е со отворен пристап дистрибуирана под условите на нелокализирана лиценца, која овозможува неограничена употреба, дистрибуција и репродукција на било кој медиум, доколку се цитираа оригиналниот(ите) автор(и) и изворот.

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Introduction

Fungi constitute an essential and diverse component of most of the Earth's ecosystems. They are eukaryotic organisms morphologically classified into yeast-like and filamentous forms. Currently, it is estimated that the number of fungal species on Earth ranges from 11.7 to 13.2 million, based on high-throughput sequencing. Nevertheless, only 150,000 fungal species have been described so far, establishing different types of relationships, such as symbiotic, commensal, opportunistic or pathogenic[1]. At least 300 fungal species are associated with human infections[2]. However, with the emergence of new pathogenic fungi, the number of fungi associated with human infections is constantly increasing. Also, sophisticated molecular investigational methods more easily identify fungi, which have led to the recognition of genetic and phenotypic diversity among different fungal pathogens. Recently, there has been a greater recognition of the importance of fungal co-infections with other microorganisms, especially respiratory pathogens, which often lead to poor patient outcome. Finally, decades of continuous use of antifungal and antibacterial agents in agriculture and medicine have changed the global microbiome, contributing to the emergence of drug-resistant fungal infections in plants, animals, and humans[3].

Fungal infections, considered rare in the past, are increasingly recognized as a major global health concern, and estimates suggest they cause over 1.6 million deaths annually[4]. Emerging evidence indicates that the incidence and geographic range of fungal infections are both expanding worldwide due to the global warming on the Earth, and the increase of international travel. Invasive fungal infections have become a major concern in modern medicine due to the increasing prevalence of immunocompromised conditions, such as HIV/AIDS, cancer, patients undergoing steroid treatment, chemotherapy resulting in severe neutropenia, hematopoietic stem cell and solid organ transplantation. Chronic lung diseases, tuberculosis and diabetes mellitus additionally increase the risk for development of invasive fungal infections. Critically ill patients in an intensive care unit (ICU), patients undergoing invasive medical procedures and receiving broad-spectrum antibiotics, are also high-risk patients. During the COVID-19 pandemic, the reported incidence of invasive fungal infections increased significantly among hospitalized patients, such as the outbreak of mucormycosis in COVID-19-infected Indian patients accounted for 71% of new mucormycosis cases globally[5]. Moreover, fungal pathogens may infect post-COVID-19 patients[6]. On October 25, 2022, the World Health Organization published the first-ever fungal priority pathogens list (WHO FPPL) of nineteen priority fungal pathogens that pose significant global threats. This was the first global effort to systematically prioritize fungal pathogens, to guide research, development, and public health actions of fungal infections. This list is divided into three groups: critical-priority, high-priority, and medium-priority. In the "critical-priority" group, *Candida albicans* and *Candida auris*, as well as *Aspergillus fumigatus* and *Cryptococcus neoformans* are included. These fungi were ranked as "critical" fungal pathogens based on

their antifungal resistance, mortality rates, lack of evidence-based diagnostic and treatment options, annual incidence, and complications and sequelae[7].

Fungal pathogens are becoming increasingly resistant to treatment with only four classes of systemically active antifungal drugs currently available, and few candidates in the clinical pipeline. Despite advancements in antifungal therapies, the mortality rates for invasive fungal infections remain unacceptably high, particularly for infections caused by multidrug-resistant fungal pathogens. Treatment is complicated by antifungal resistance to existing antifungal agents, drug toxicity, and the limited arsenal of effective antifungal agents. Also, fungal extracellular polymeric substances, which have the functions of adhesion, cell aggregation, and protection of antifungal agents contribute to treatment failure[8]. Accurate diagnosis of invasive fungal infection is still a clinical and diagnostic challenge due to nonspecific symptoms and sometimes due to lack of knowledge about the recurrence and emergence of new fungal pathogens. Limited availability of rapid and sensitive diagnostic tools also contributes to delayed or missed diagnoses of invasive fungal infections (IFI).

This review focuses on emerging yeast pathogens and is intended to raise awareness of the importance of early detection and treatment of fungal diseases in immunocompromised and critically ill patients in order to reduce the risk of mortality from IFI.

1. Candida species

Candida species is a member of the healthy microbiota, asymptomatically colonizing the gastrointestinal and reproductive tract, oral cavity, and the skin of most humans. In individuals with healthy immune system, *Candida species* is often harmless, and in balance with other members of the local microbiota. Alterations in the host microbiota (after broad spectrum antibiotic treatment), changes in the host immune response (stress, infection by microbes, or immunosuppressant therapy), or variations in the local environment (shifts in pH or nutritional content) can enable *C. albicans* to overgrow and cause infection. These infections range from superficial mucosal and dermal infections to hematogenously disseminated IFI, with mortality rates approaching 40%. *Candida* produces highly structured biofilms composed of multiple cell types. *Candida* is capable of causing infections in healthy people with implanted medical devices, and are usually the predominant fungal species isolated from medical device infections. Urinary and central venous catheters, pacemakers, mechanical heart valves, joint prostheses, contact lenses, and dentures are all very susceptible to *Candida* biofilms[9]. Once it forms on an implanted medical device, a *Candida* biofilm has the potential to seed disseminated bloodstream infections and to lead to invasive mycoses[10].

The main causative agent of candidiasis is C. albicans; however, in recent years, a tendency has been described to increase the incidence of mycoses caused by non-*albicans Candida* species in humans, such as *C. auris*, *C. glabrata*, *C. dubliniensis*, *C. tropicalis, C. blankii, C. lusitaniae, C. tropicalis, C. krusei*, and *C. parapsilosis*. However, five pathogens cause the most invasive infections: *C. albicans, C. gla-*

brata, C. tropicalis, C. parapsilosis and *C. krusei*[11].

The increasing prevalence of colonization and infection with non-albicans *Candida species* in recent years is thought to be driven largely by the increased use of prophylactic antifungals, such as fluconazole. Most of these species are inherently resistant or easily acquire resistance to commonly used antifungal drugs, usually due to the increased use and misuse of antifungal agents. Implementation of new diagnostic techniques document constant change in the epidemiology of *Candida* infections. The SENTRY Antifungal Surveillance Program, established back in 1997 in the USA, monitored the global epidemiology of invasive *Candida* infections with respect to species distribution and resistance to antifungals. This program has published its data after a 20-year surveillance period, which included over 20,000 clinical isolates collected through passive surveillance from 39 countries worldwide. According to this data, the total proportion of infections attributable to *C. albicans* has decreased from 57.4 to 46.4% over the 20-year surveillance period[12]. In 2017, the Centers for Disease Control and Prevention conducted active population-based surveillance for candidemia through the Emerging Infections Program in 45 counties in 9 states encompassing approximately 17 million persons. During this surveillance, 81 laboratories forwarded to CDC 1122 *Candida* species isolates. The most frequent *Candida* species isolated from culture was *C. albicans* (38%), followed by *C. glabrata* (30%), *C. parapsilosis* (14%), and *C. tropicalis* (7%). Six percent of all *Candida* isolates were resistant to fluconazole, with rates ranging from 0.5% in *C. albicans* to 7% in *C. glabrata* and 9% in *C. parapsilosis*. Two percent of Candida isolates were resistant to an echinocandin antifungal, of which most were *C. glabrata* (12). Recent epidemiological studies from Europe have reported an increased relative prevalence of non-*albicans Candida* species as well[13]. Prior to 1997, most data on *Candida* bloodstream infections were reported in studies carried out in the USA. Therefore, the ECMM initiated the first multicentre study aimed to present the epidemiological and mycological profile of candidemia across Western Europe[14]. The European Confederation of Medical Mycology (ECMM) conducted three pan-European multicentre studies between 1997 and 2022, to investigate epidemiology, resistance, and other aspects of invasive candidiasis[15,16,17].

There are differences in the epidemiology of *Candida* bloodstream infections among European countries, with a prevalence of *C. glabrata* and *C. parapsilosis* in Northern and Southern countries, respectively. An Italian 2-year observational survey on ICU was conducted to evaluate the species distribution and possible differences between bloodstream infections caused by *C. albicans* and non-*albicans Candida*. The results of this study confirmed 462 cases of candidemia. *C. albicans* was isolated with the highest frequency (49.4%); *C. parapsilosis* ranked on the second position (26.2%), followed by *C. glabrata* (10.4%), *C. tropicalis* (6.5%), *C. krusei* (2.8%), *C. guilliermondii* (1.5%), *C. lusitaniae* (1.3%), *C. lipolytica* (0.6%) and *C. famata, C. sake, C. utilis* (0.4%, each)[18]. Literature review of 24 articles demonstrated that *C. albicans* was the most common species in 21 countries, accounting for 51.3% to

76.3% of all *Candida* infections[19]. In four studies from southern European countries, the proportion of *C. albicans* was between 37.9% and 49%. In the remaining three studies, the proportion of *C. albicans* was extremely low. In two studies conducted in Turkey, *C. albicans* strains accounted for 18.6% and 22.9% of all *Candida* infections. In a survey from Greece, *C. albicans* and *C. parapsilosis* were almost equally distributed (33.3% and 36.4%, respectively). Regarding non-*albicans Candida* species, the three most prevalent species were *C. glabrata, C. parapsilosis* and *C. tropicalis. C. glabrata* was prevalent in studies from German-speaking countries, France, UK, and North Europe, reaching proportions of 13.2-31.2%. *C. parapsilosis* emerged as an important opportunistic fungal pathogen in the Mediterranean area: Turkey (77.1%), Italy (37%), Greece (36.4%) and Spain (28.8%). In contrast, C. parapsilosis was a less common cause of candidemia in recent surveys from France and Denmark (0% and 2.6%, respectively). *C. tropicalis* in these studies was less prevalent. It was the fourth most common species of Candida in German-speaking countries, France, Italy and Poland, and the second in Portugal and in Turkey, accounting for 21.2% and 12.7% of all *Candida* bloodstream infections, respectively. Data from a national, prospective multicentre study from Serbia, which analysed *Candida* BSI in ICUs demonstrated almost equal distributions of *C. albicans* (~56%) and non-albicans *Candida* (~44%). *C. albicans* and *C. parapsilosis* were prevalent (~90%), and the distribution of *C. parapsilosis* showed a significant variation relative to patients' age (P = .039). *C. albicans* and *C. parapsilosis* prevailed and were equally distributed in adult settings, while in paediatric/neonatal settings only *C. albicans* caused almost ¾ bloodstream infections[20].

With the emergence of the COVID-19 pandemic, these factors associated with the increased incidence of fungal infections have intensified, and non-albicans *Candida* species has been identified as emerging new infections[5].

The pathogenic potential of *Candida* species to cause invasive infections is facilitated by many virulence factors such as adherence to host tissues and medical devices, biofilm formation, and secretion of extracellular hydrolytic enzymes[8].

Candida auris and other multidrug-resistant fungi

The emergence of new fungal pathogens and the spread of multidrug-resistant strains represent a growing threat to global health due to their adaptability and ability to cause serious infections in vulnerable categories of patients.

Candida auris, a novel and major fungal pathogen in the *C. haemulonii* complex (Metchnikowiaceae), was first described in 2009 after its isolation from the external ear canal of a patient in Japan. This is an emerging pathogen that has already been isolated on five continents[21]. However, the earliest findings of multiple clades of *C. auris* were present as of 1996[22]. This fungal agent has appeared in different geographic locations simultaneously. Genomic analysis has been performed through single nucleotide polymorphism (SNP) analysis and whole genome sequencing, and results suggest that genetically distinct

clonal populations of *C. auris* emerged independently and simultaneously in different geographical areas[23]. Each clade presents unique and distinct microbiological and clinical characteristics. Clades I, III, and IV are mostly linked with IFI and nosocomial outbreaks. Warmer climates may have aided in the transmission of *C. auris*. It is hypothesized that halotolerance and thermotolerance of this fungus may have originated from a non-pathogenic strain found in high-salinity regions, and with subsequent evolutionary adaptation, this strain may have overcome the thermal barrier of mammals and become capable of causing infection.

C. auris has become a significant threat to global health. Its resistance to multiple antifungal classes, high mortality rates, ability to persist in the environment and increasing instances of outbreaks in healthcare settings constitute major concerns among healthcare practitioners across the globe. A feature that distinguishes *C. auris* from other fungal pathogens is its high capacity for skin colonization, where it persists for extended periods of time, leading to widespread outbreaks in healthcare facilities via patient-to-patient transmission. Infection and colonization have been detected mainly in critical care patients and affect both pediatric and adult populations.

Some of the most prevalent reported risk factors for *C. auris* colonization and infection include: prolonged exposure to broad-spectrum antimicrobial agents[24-26], presence of indwelling medical devices, diabetes mellitus, prolonged intensive care unit (ICU) hospitalization, haemodialysis, immunocompromised patients, admission to a hospital or long-term care (LTC) facility, and transfer from a healthcare facility with an ongoing *C. auris* outbreak[25-27].

Many studies have reported the isolation of *C. auris* from different countries, such as South Korea, India, Pakistan, Kuwait, Israel, Oman, South Africa, Colombia, Venezuela, the United States, Canada, and Europe, including the United Kingdom, Norway, Germany, and Spain[28].

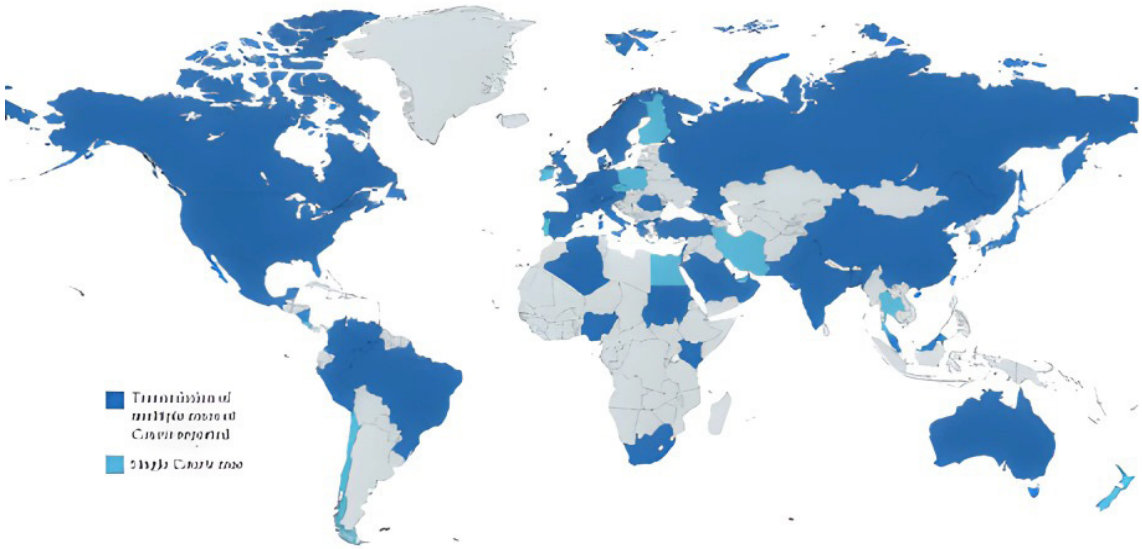


Figure 1. Global epidemiology of *Candida auris* until October 2023. The grey color represents countries with no *C. auris* cases published in the literature (Source: Silva I, Miranda IM, Costa-de-Oliveira S. Potential Environmental Reservoirs of *Candida auris*: A Systematic Review. J Fungi (Basel). 2024 May 8;10(5):336. doi: 10.3390/jof10050336. PMID: 38786691; PMCID: PMC11122228.)

Hospitalizations during the COVID-19 pandemic, frequent surgical procedures, subsequent use of catheters, misuse and overuse of antimicrobials and corticosteroids[29] and prolonged hospitalization, led to higher possibility of a fungal infection with multiresistant species[30].

There has been an increasing number of reports of *C. auris* in COVID-19 acute care units during the pandemic. Researchers suspect that these outbreaks may be related to changes in routine infection control practices due to health crisis, such as limited availability of gloves and poor cleaning and disinfection protocols[31].

2. Cryptococcus species

Cryptococcus is a budding, encapsulated, round to oval yeast found in soil, decaying wood and avian excreta. Historically, *Cryptococcus* was described as two species: *C. neoformans* (var. grubii and var. neoformans) and C. gattii. More recent phylogenetic analyses have distinguished seven clades representing species (VNI-III and VGI-IV), with varying virulence and regional distribution[32].

Members of the *C. neoformans* and *C. gattii* species complexes are the predominant causative agents of cryptococcosis, a life-threatening invasive fungal infection, that poses a significant global health challenge. *C. neoformans* is found worldwide, whereas *C. gattii* most often is found in Australia and similar subtropical regions and in the U.S. Pacific Northwest. *Cryptococcus* was included in the World Health Organization Fungal Priority Pathogens List, based on the results of systematic reviews, expert opinion, and data from the discrete choice experiments[7].

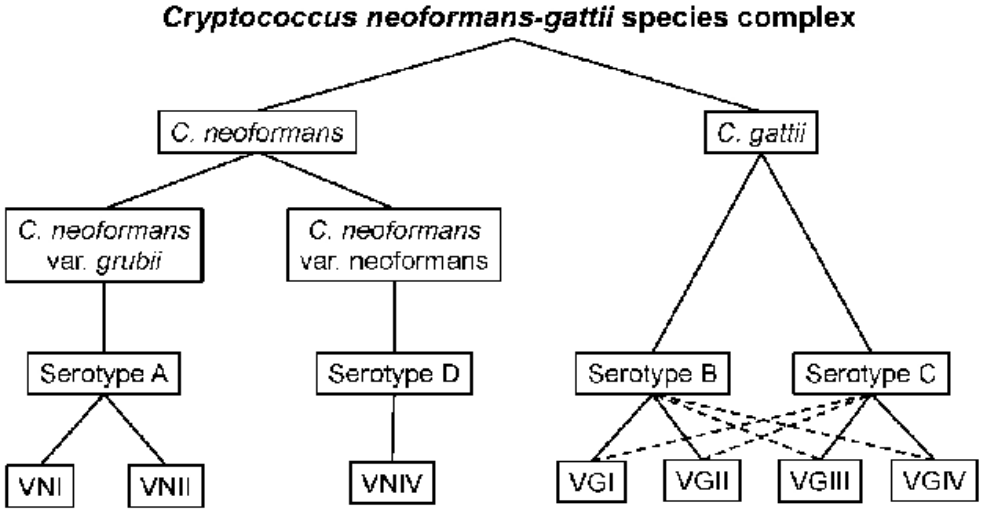


Figure 2. Schematic representation of the new taxonomic classification of the *Cryptococcus* species complexes (Source: Parums DV. Editorial: The World Health Organization (WHO) Fungal Priority Pathogens List in Response to Emerging Fungal Pathogens During the COVID-19 Pandemic. Med Sci Monit. 2022 Dec 1;28:e939088. doi: 10.12659/MSM.939088. PMID: 36453055; PMCID: PMC9724454)

C. neoformans and *C. gattii* species are acquired through the respiratory tract. *Cryptococcus* exists in the form of dehydrated spores. The ubiquitous spores are inhaled and then exposed to alveolar macrophages. This may lead to development of primary pulmonary cryptococcosis, which typically manifests as a self-limiting lower respiratory tract infection with

low-grade fevers and cough. In immunocompetent hosts, desiccated yeast cells can be cleared by the immune system or cause asymptomatic latent infection. It is estimated that up to 50% of primary infections are asymptomatic[33]. Depending on different host-related risk factors, some patients, like individuals living with HIV/AIDS, may progress rapidly to involvement of the central nervous system, causing cryptococcal meningitis, which is the most serious condition with a poor prognosis. *Although both C. neoformans and C. gattii species can cause a similarly broad range of cryptococcosis syndromes, C. neoformans has a predilection for CNS disease, and C. gattii is more often associated with pulmonary disease and large cryptococcomas.*

The most prominent features of cryptococcal pathogenesis are latency and dormancy. The pathogen may reside within phagocytes for years with incubation periods of 110 months for *C. neoformans* and 24 months for *C. gatti*. Reactivation of dormant cryptococci becomes a concern when the host's immune system becomes compromised, potentially leading to invasive disease. Most cases of invasive infection with this yeast probably arise from immunosuppression triggering conversion from latent to active infection, such as cytomegalovirus infection and tuberculosis.

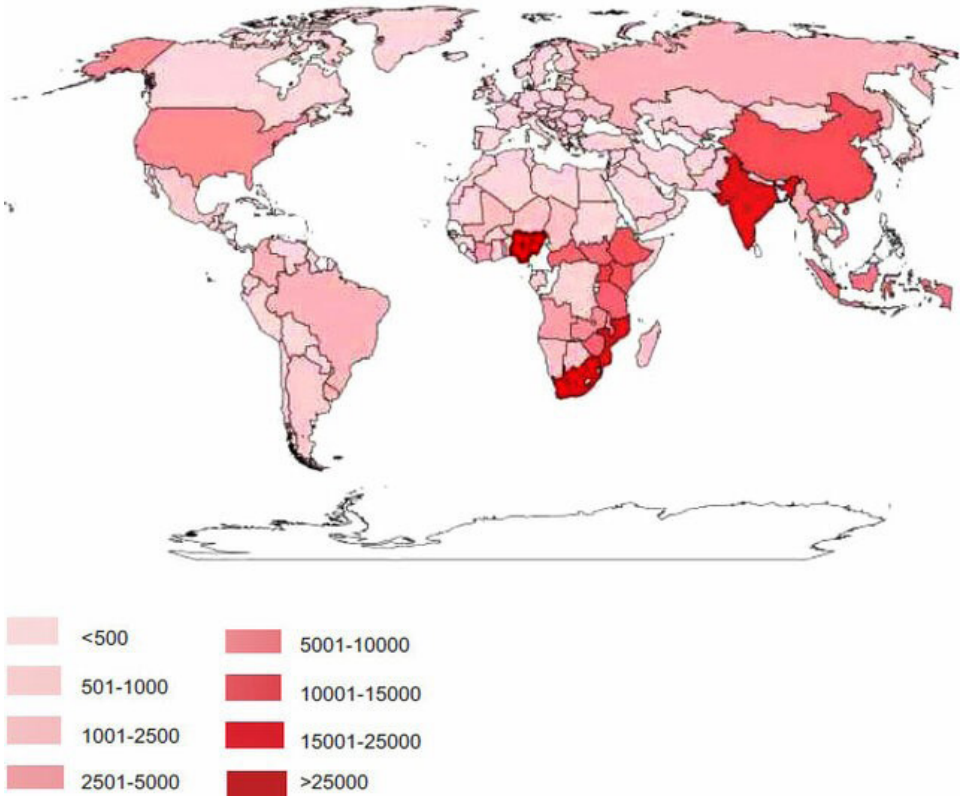


Figure 3. Global epidemiology of cryptococcal meningitis. Map depicting annual incidence of cryptococcal meningitis, per 100,000 people, as of 2023 (Source: Kebabonye K, Jongman M, Loeto D, Kasvosve I. Recent Advances in the Ecoepidemiology, Virulence and Diagnosis of Cryptococcus neoformans and Cryptococcus gattii Species Complexes, The Open Microbiology Journal, Volume 17, 2023, ISSN 1874-2858, https://doi.org/10.2174/18742858-v17-e230419-2022-28. (https://www.sciencedirect.com/science/article/pii/S1874285823000134)

Cryptococcal meningitis remains the most common cause of fungal meningitis worldwide with over 220.000 new cases and 180,000 deaths annually. The highest burden of disease is in low-income and middle-income countries, especially in sub-Saharan Africa, where HIV and AIDS are the dominant risk factor. Patients who survive cryptococcal meningitis may have long-term sequelae, such as focal neurologic deficits, blindness, deafness, cranial nerve palsies, and memory deficits[34]. Overall, the cases of cryptococcal meningitis have decreased since the advent of antiretroviral treatment for AIDS, especially in high-income countries. More recently, new, non-HIV immunocompromised risk groups, and putatively immunocompetent individuals have been increasingly reported in high-income settings and clinicians should consider this in all cases of lymphocytic meningitis. People with various types of immunodeficiency or underlying conditions and even unrecognized risk factors can also develop invasive disease. In large cohort studies of non-HIV cryptococcal meningitis, no underlying predisposing factors were found in 30% of US patients and 67% of Chinese patients[35]. Risk factors for non-HIV cryptococcal meningitis include chronic corticosteroids and treatment with biologic drugs[36], diabetes mellitus, transplantation of solid organs, malignancy and chemotherapy and liver cirrhosis. As corticosteroids potentiate fungal growth, it is important to specifically exclude cryptococcosis, if it is in the differential diagnosis before starting high-dose corticosteroid therapy. Solid organ transplant recipients account for 15%–20% of non-HIV cryptococcal meningitis cases, and this infection is the third most common fungal infection. Cryptococcal meningitis can also develop in non-transplant, non-HIV patients, in individuals with autoimmune and inflammatory conditions (systemic lupus erythematosus, rheumatoid arthritis and sarcoidosis). Despite only limited long-term follow-up data, clinical experience suggests that cryptococcal meningitis is a rare complication among patients on biologics, given their widespread use in patients with inflammatory gastrointestinal, dermatological and rheumatological conditions. Patients with cancer account for approximately 25% of non-HIV cryptococcal meningitis cohorts. Cryptococcosis manifestations vary with cancer type; pulmonary and skin involvement is more common in solid organ tumours and meningitis in haematological malignancy[37].

Treatment options for invasive cryptococcosis are limited, and development of novel anti-cryptococcal agents has been slow in recent decades. Short courses (≤7 days) of amphotericin-based therapy combined with flucytosine are currently the preferred options for induction therapy of cryptococcal meningitis. Cryptococci are intrinsically resistant to echinocandins. Optimal induction treatment is followed by a prolonged treatment with azoles[38].

3. Trichosporon species

In recent few decades, the world has also been witnessing an increasing incidence of infections caused by non-*Candida* yeast such as *Trichosporon* species. These infections are difficult to treat, due to an increased resistance to amphotericin and echinocandins, and have poor prognosis

with high mortality rates[39]. *Trichosporon* species is a ubiquitous yeast-like basidiomycete, which is found in water, soil, plants, mammals and birds. Geographical distribution of infections due to this yeast varies, but data collected from the ARTEMIS DISK Surveillance Study in the period between 1997-2005 showed that infections with *Trichosporon* were found with equal frequencies in both tropical and temperate areas, including South America, the Middle East, India, Southeast Asia, Africa, Europe, Japan, and parts of southeastern USA[40]. In humans, *Trichosporon* are occasionally found as part of gastrointestinal and oral microbiota and can also colonize the skin and mucosa of both respiratory and female genital tracts.

The pathogenic potential of *Trichosporon* has been first described by Beigel, back in 1865, explaining it as a cause of hair infection[41]. The classification of *Trichosporon* has changed over the years. Initially, all *Trichosporon* species were classified as *T. beigelii*, and it was thought that the strain mainly caused infection in superficial hair, but rarely disseminated systemic infections. However, research showed that *T. beigelii* has great morphologic, physiological and biochemical variation. In 1992, Gueho et al. revised the taxonomy of 20 species of *Trichosporon*, including six pathogens: *T. asahii, T. asteroides, T. cutaneum, T. inkin, T. mucoides and T. ovoides*[42]. Presently, 50 *Trichosporon* species are recognized, of which 16 are known to be pathogenic. *T. asahii* is the most important pathogen, with a reported mortality rate of 70% as a cause of invasive trichosporonosis. In certain conditions, they can become pathogenic causing wide spectrum of infections[39]. They are capable of causing superficial white piedra in immunocompetent children and young adults, particularly females. The main reported risk factors for transmission of superficial *Trichosporon* species are close contact, poor hygienic habits, long hair and humidity. Sexual transmission has been reported in cases of pubic white piedra. Epidemiology of invasive trichosporonosis is different. In patients with underlying history of hematological cancer, *Trichosporon species* is the second most common cause of disseminated yeast infections after *Candida*.

The mortality attributed to *Trichosporon species* in such patients, in spite of the antifungal therapy, is very high and ranges from 50-80%[43]. As per the European Organization for Research and Treatment of Cancer/Invasive Fungal Infection Cooperative Group (EORTC/IFICG) and the National Institute of Allergy and Infectious Disease Mycoses Study Group (NIAID/MSG), invasive trichosporonosis has been classified as proven or probable trichosporonosis, based on certain criteria[44]. Risk factors for invasive trichosporonosis include neutropenia, chemotherapy, diabetes, renal disease, HIV infection and immunosuppressive treatment, invasive medical devices, severe burns and cystic fibrosis[45]. Another group that has an increased risk of invasive trichosporonosis are premature neonates with low birth weight, patients on steroids or with intravascular catheters, patients undergoing heart valve surgery or liver transplant, and patients with kidney failure on dialysis[46]. *Trichosporon* species has many virulence factors that permit the establishment of the disease and its dissemination

within the human body. It has adherence abilities and capacity to form biofilms on implanted devices. It also produces and secretes enzymes for scavenging nutrients from the environment[47]. Most invasive *Trichosporon* species infections start with colonization and break in the integrity of the skin and mucous membranes, with subsequent seeding the bloodstream. This usually happens after an aggressive chemotherapy-induced epithelial damage or implantation of intravascular catheters. Antibiotics may also increase the risk of developing invasive *Trichosporon* infections. The guidelines developed by ESCMID/ECMM in 2014 recommend voriconazole for the treatment of trichosporosis[48].

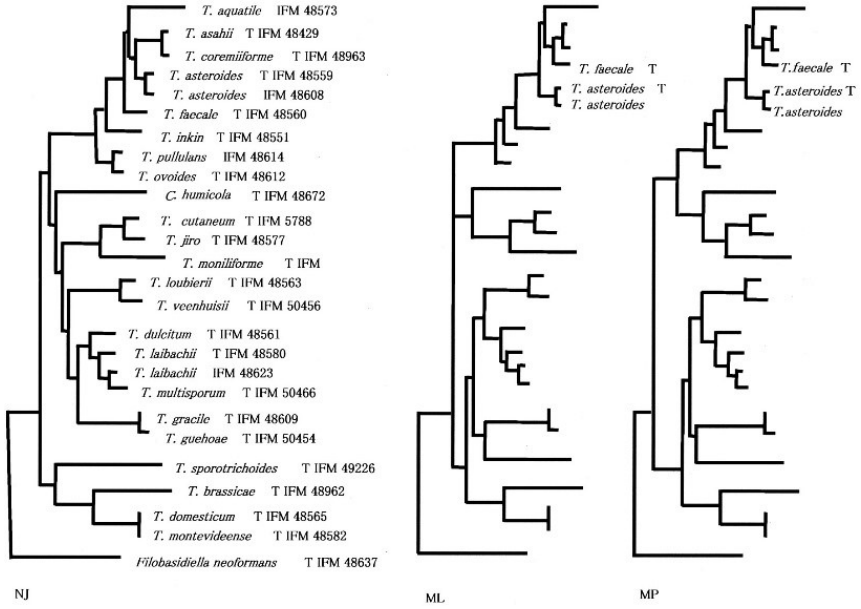


Figure 4. Phylogenetic trees based on nucleotide sequences of cyt b genes (Source: Biswas SK, Wang L, Yokoyama K, Nishimura K. Molecular phylogenetics of the genus trichosporon inferred from mitochondrial cytochrome B gene sequences. J Clin Microbiol. 2005;43(10):5171-8. doi: 10.1128/JCM.43.10.5171-5178.2005. PMID: 16207980; PMCID: PMC1248456.)

4. Magnusiomyces capitatus

Magnusiomyces capitatus (previously known as *Saprochaete capitate, Geotrichum capitatum, Trichosporon capitatum* or *Blastoschizomyces capitatus)* is an ascomycetous yeast, which is found in soil and animals. It is also found as part of the normal microbiota of human skin, respiratory and gastrointestinal tract in healthy people. *M. capitatus*, recently defined as an emerging pathogen, is mostly found in patients with hematological malignancies, particularly acute leukemia[49]. *It is* responsible for lethal fungaemia in patients with profound neutropenia in the haematology settings[50]. Systemic infections caused by *M. capitatus* have been mainly documented in the Mediterranean countries of Europe, including Italy[51], France[52], and Spain[53]. They have also been reported in other areas of Europe (Slovakia, Switzerland, and the Czech Republic)[54]. *M. capitatus* was also recently isolated from an alcoholic male patient in the United States[55]. *M. capitatus* has also been

responsible for prosthetic valve endocarditis[56]. Uncontrolled diabetes mellitus is also a high risk for invasive infection[57].

According to guidelines developed by the European Confederation for Medical Mycology and the European Society for Clinical Microbiology and Infectious Diseases, recommendations based on treatment response have been noted following amphotericin B formulation with or without flucytosine treatment and voriconazole[58]. The use of echinocandins might be associated with worse outcomes.

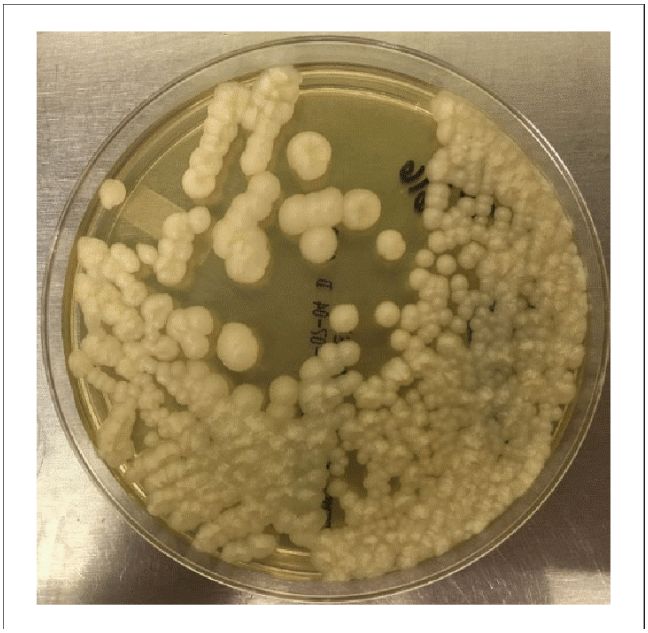


Figure 5. *Magnusiomyces capitatus*, peritoneal fluid, 5-day culture on Sabouraud Dextrose Agar (Source: D'Assumpcao C, Lee B, Heidari A. A Case of *Magnusiomyces capitatus* Peritonitis Without Underlying Malignancies. J Investig Med High Impact Case Rep. 2018;6:2324709618795268. doi: 10.1177/2324709618795268. PMID: 30151397; PMCID: PMC6104205.).

5. Geotrichum candidum

Geotrichum candidum (Galactomyces candidus) is a filamentous ascomycetous yeast that forms arthroconidia and is ubiquitous in soil, decaying organic matter and foods and is used in cheese manufacture[59].

Among 505 cases of rare invasive mycoses included in the recent FungiScope™ registry, 23 cases of invasive infections caused by these fungi have been reported from 10 countries over a 12-year period[57]. All cases of invasive infections were confirmed in adults and previous chemotherapy with subsequent neutropenia was the most common co-morbidity. Fungaemia was confirmed in 14 (61%) cases and deep organ involvement included lungs, liver, spleen, central nervous system and kidneys. The identified fungi were *S. capitata* (n=14), *S. clavata* (n=5), *G. candidum* (n=2) and *Geotrichum species* (n=2). Overall mortality in this study was 65% (n=15). Initial echinocandin treatment was associated with worse outcome at day 30 when compared to treatment with other antifungals (amphotericin B ± flucytosine, voriconazole, fluconazole and itraconazole) (P=.036). Echinocandins are not an option for these infections.



Figure 6. *Geotrichum candidum* culture (Source: Victoria, CC BY-SA 4.0, https://upload.wikimedia.org/wikipedia/commons/7/7d/Geotrichium_candidum.jpg)

6. Rhodotorula

Rhodotorula is a common environmental yeast found in air, soil, lakes, ocean water, milk, and fruit juice. *Rhodotorula* species have been isolated from skin, sputum and digestive tract samples including faeces, as part of the normal human microbiota. *Rhodotorula* produces pink to red colonies and blastoconidia that are unicellular lacking pseudohyphae and hyphae. The genus contains 46 species[60]. Three of these species have been described as rare human pathogens: *R. mucilaginosa, R. glutinis* and *R. minuta*. *R. mucilaginosa* account for the majority of infections (74–79%) followed by *R. glutinis* (7.7%)[61]. The most frequent risk factor is a CVC and underlying haematological disease[62].

Fungaemia, peritonitis, endocarditis or meningitis have also been reported in other patient groups (AIDS, extensive burns, continuous ambulatory peritoneal dialysis, cirrhosis, those who have undergone intra-abdominal surgery, intravenous drug abusers and critically ill ICU patients)[63]. *Rhodotorula* has a high affinity to adhere to plastic surfaces and can form biofilms. Hence, medical equipment can easily become colonized. *Rhodotorula* species are regarded as intrinsically resistant to azoles and echinocandins, but susceptible to amphotericin B and flucytosine[64].



Figure 7. *Rhodotorula* culture (Source: Hernández-Almanza A, Cesar Montanez J, et al. Rhodotorula glutinis as source of pigments and metabolites for food industry, Food Bioscience, Volume 5, 2014, Pages 64-72, ISSN 2212-4292, https://doi.org/10.1016/j.fbio.2013.11.007. (https://www.sciencedirect.com/science/article/pii/S2212429213000849)

7. Kodamaea ohmeri

Kodamaea (Pichia) ohmeri (previously known as *Pichia ohmeri or Yamadazyma ohmeri)* is a rarely occurring yeast that has recently been identified as a cause of fungaemia, endocarditis, cellulitis, funguria and peritonitis in neonates and children[65], and in both immunocompromised[66] and immunocompetent adult patients[67]. Most cases of invasive infections with this species have been treated with liposomal amphotericin B (or amphotericin B deoxycholate) showing good response[68].

As for treatment recommendation, amphotericin B appears to be an attractive first-line agent and echinocandins are possible promising alternatives.



Figure 8. *Kodamea (Pichia) ohmeri* culture (Al-Sweih N, Khan ZU, Ahmad S, Devarajan L, Khan S, Joseph L, Chandy R. *Kodamaea ohmeri* as an emerging pathogen: a case report and review of the literature. Med Mycol. 2011;49(7):766-70. doi: 10.3109/13693786.2011.572300. PMID: 21438792.)

8. Malassezia

Malassezia species are basidiomycetous yeasts, which are the most prevalent fungi colonizing human skin from birth and throughout life[69,70]. They are lipophilic, relying on exogenous (host) lipids for growth. It is difficult to detect them because they grow poorly in culture. *Malassezia* genus comprises 18 species with numerous functionally distinct strains based on morphology, physiological biochemistry and molecular biology[71]. Systemic infections due to lipid-dependent *M. furfur* mainly occur in premature neonates, infants on lipid-containing parenteral nutrition and children and adults with various forms of immunosuppression and underlying diseases[69]. In addition to fungemia, pneumonia, peritonitis, meningitis and disseminated infection caused by *M. furfur* have also been continuously reported worldwide in recent years[72,73].

Susceptibility testing of *Malassezia* has not been standardized because growth is not supported on the standard RPMI growth medium recommended for yeast testing by EUCAST. Most reports on treatment of these infections recommend fluconazole and amphotericin B, which are the preferred agents[74].

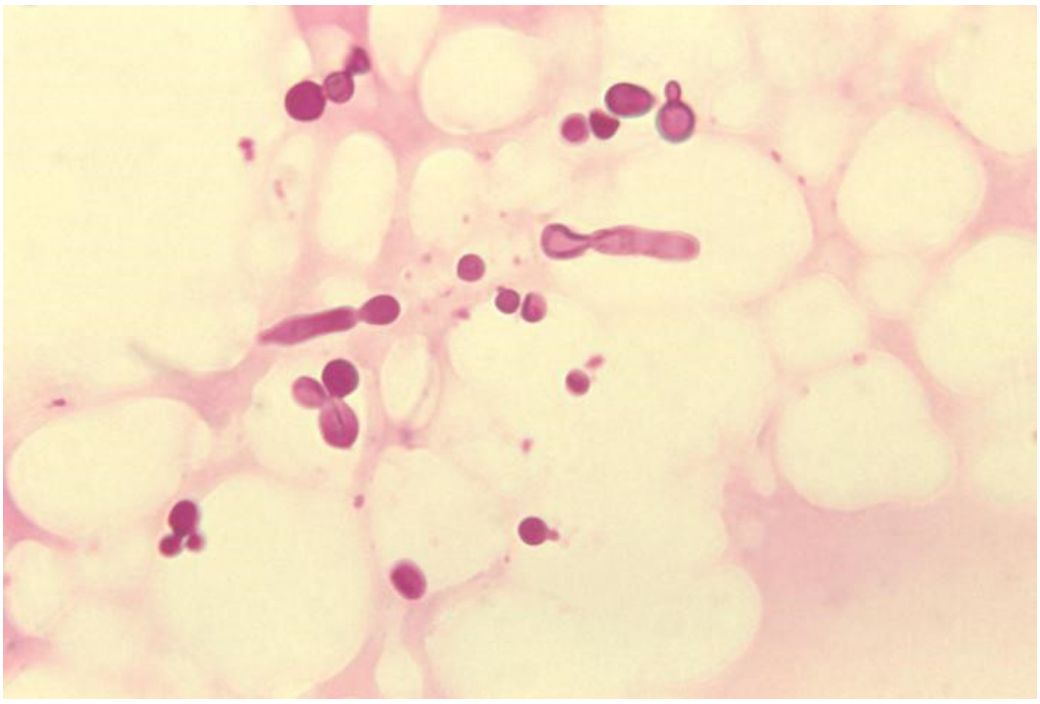


Figure 9. *Malassezia furfur* in skin scale from a patient with tinea versicolor (Source: CDS, Centers for Disease Control and Prevention, part of the United States Department of Health and Human Services. http://phil.cdc.gov/phil_images/20030610/22/PHIL_3938_lores)

9. Saccharomyces

Saccharomyces cerevisiae, also known as baker's or brewer's yeast, is a low pathogenic ascomycetous yeast. *S. cerevisiae* may be found as a harmless and transient digestive commensal and colonizer of mucosal surfaces of healthy people. Invasive infections caused by S. cerevisiae are increasingly reported in the general population, particularly in patients with risk factors and immunocompromised patients. In 1980, Mary L. Eschete and *et al*. reported the first case of fungemia caused by S. cerevisiae, showing its opportunistic characteristics[75]. Since then, cases of invasive infections have been reported all over the world, identifying *S. cerevisiae* as the 5th cause of fungemia[76]. Cases of fungaemia and disseminated infection have been described in vulnerable patients after treatment with *S. boulard*ii probiotic compound[77]. In a recent review of 92 cases of invasive *Saccharomyces* infections, *S. boulardii* accounted for half of these, was less often associated with an underlying immunocompromised condition and more often associated with a favourable outcome[78]. The use of probiotics in debilitated patients, ICU patients, neutropenic patients, preterm newborns or in patients with central lines should be carefully considered.

For the treatment of these invasive mycoses, most clinical experience exists with fluconazole and amphotericin B, for which favourable outcome was observed in 60% and 77.7% of cases, respectively[76]. Finally, amphotericin B with or without flucytosine has been used in severe or recurrent cases[79]. Also, it is strongly recommended that probiotics containing *S. boulardii* are discontinued and indwelling foreign bodies are removed, when possible, because this organism is capable of forming biofilms[76].

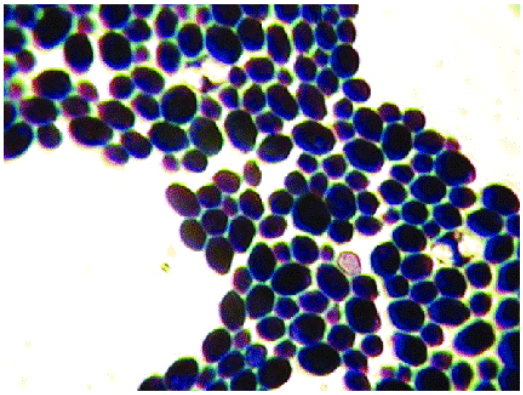


Figure 10. Morphology of *Saccharomyces cerevisiae* yeast culture („Biotechnologia Acta“ v. 6, no. 2, 2013 https://doi.org/10.15407/biotech6.02.097, P. 97-106, Bibliography 13, English. Universal Decimal classification: 634.8:632.93:661.74:663.2)

10. Sporobolomyces

Sporobolomyces species are usually red-to-orange pigmented basidiomycetous yeasts, that, along to regular budding cells, also form ballistoconidia[80]. These conidia are discharged into the air. Phylogenetically, they are closely related to *Rhodotorula* species. The 53 species occur widely in nature, especially in lake water, on tree leaves and in air, and with its natural habitat in humans, mammals, birds and plants. *Sporobolomyces* have been reported as the cause of sporadic invasive bloodstream infections, particularly in AIDS patients[81].

A single case of meningitis due to *Sporobolomyces* roseus was reported in an immunocompetent cocaine abuser[82]. This fungus was also described in a case of cerebral infection, fungemia, bone marrow involvement in AIDS patients, a prosthetic cranioplasty infection, encephalitis, and lymphadenitis[83]. Amphotericin B has been efficacious in fungaemic and meningitis cases. A single case of endogenous endophthalmitis due to *Sporobolomyces salmonicolor* was reported in a patient with a history of pelvic inflammatory disease 2 years earlier. The patient recovered following intravitreal amphotericin B (5 µg) and systemic voriconazole of 200 mg twice daily[84].



Figure 10. *Sporobolomyces roseus culture* (Source: Sharma V, Shankar J, Kotamarthi V. Endogeneous endophthalmitis caused by Sporobolomyces salmonicolor. Eye (Lond). 2006;20(8):945-6. doi: 10.1038/sj.eye.6702051.

Novel environmental fungi are increasingly being recognized as potential human pathogens, driven by ecological and climate changes, as well as human activities. The continued emergence of multidrug-resistant and environmentally adaptable fungal pathogens is expected to challenge public health systems in future, necessitating enhanced surveillance, innovative antimicrobial treatments and global collaboration to mitigate their impact on public human health.

References

1. Bahram M, Netherway T. Fungi as mediators linking organisms and ecosystems. FEMS Microbiol Rev 2022;46:fuab058. DOI: 10.1093/femsre/fuab058
2. Wickes BL, Wiederhold NP. Molecular diagnostics in medical mycology. Nat Commun 2018;9:5135. DOI: 10.1038/s41467-018-07553-8
3. Fisher MC, Hawkins NJ, Sanglard D, Gurr SJ. Worldwide emergence of resistance to antifungal drugs challenges human health and food security. Science 2018; 360:739-742. DOI: 10.1126/science.aap7999
4. Bongomin F, Gago S, Oladele RO, Denning DW. Global and multi-national prevalence of fungal diseases-estimate precision. J Fungi (Basel) 2017;3:57. DOI: 10.3390/jof3040057 PMID: 29371573 PMCID: PMC5753159
5. Hlaing KM, Monday LM, Nucci M, Nouér SA, Revankar SG. Invasive fungal infections associated with COVID-19. J Fungi (Basel) 2023;9:667. DOI: 10.3390/jof9060667 PMID: 37367582 PMCID: PMC10301787
6. Ulloque-Badaracco JR, Copaja-Corzo C, Hernandez-Bustamante EA, Cabrera-Guzmán JC, Huayta-Cortez MA, Carballo-Tello XL, et al. Fungal infections in patients after recovering from COVID-19: a systematic review. Ther Adv Infect Dis 2024;11:20499361241242963. DOI: 10.1177/20499361241242963 PMID: 38628602 PMCID: PMC11018917
7. Parums DV. Editorial: The World Health Organization (WHO) Fungal priority pathogens list in response to emerging fungal pathogens during the COVID-19 pandemic. Med Sci Monit 2022;28:e939088. DOI: 10.12659/MSM.939088 PMID: 36453151 PMCID: PMC9718879
8. Talapko J, Juzbašić M, Matijević T, Pustijanac E, Bekić S, Kotris I, et al. Candida albicans-the virulence factors and clinical manifestations of infection. J Fungi (Basel) 2021;7:79. DOI: 10.3390/jof7020079 PMID: 33578720 PMCID: PMC7917421
9. Nobile CJ, Johnson AD. Candida albicans biofilms and human disease. Annu Rev Microbiol 2015;69:71-92. DOI: 10.1146/annurev-micro-091014-104330 PMID: 26488273 PMCID: PMC4930275
10. Pappas PG, Lionakis MS, Arendrup MC, Ostrosky-Zeichner L, Kullberg BJ. Invasive candidiasis. Nat Rev Dis Primers 2018;4:18026. DOI: 10.1038/nrdp.2018.26 PMID: 29749387

11. Pfaller MA, Diekema DJ, Turnidge JD, Castanheira M, Jones RN. Twenty Years of the SENTRY Antifungal Surveillance Program: Results for Candida species from 1997-2016. Open Forum Infect Dis 2019;6:S79-S94. DOI: 10.1093/ofid/ofy358 PMID: 30895218 PMCID: PMC6419935

12. Tsay SV, Mu Y, Williams S, Epson E, Nadle J, Bamberg WM, et al. Burden of Candidemia in the United States, 2017. Clin Infect Dis 2020;71:e449-e453. DOI: 10.1093/cid/ciaa193 PMID: 32052053 PMCID: PMC7454394

13. Meneghello S, Bernabè G, Di Pietra G, Di Sopra S, Del Vecchio C, Cattelan AM, et al. Prevalence, species distribution and resistance of candidemia in pediatric and adult patients in a Northeast Italy University Hospital. J Fungi (Basel) 2024;10:707. DOI: 10.3390/jof10100707 PMID: 38921363 PMCID: PMC11207590

14. Tortorano AM, Peman J, Bernhardt H, Klingspor L, Kibbler CC, Faure O, et al. Epidemiology of candidaemia in Europe: results of 28-month European Confederation of Medical Mycology (ECMM) hospital-based surveillance study. Eur J Clin Microbiol Infect Dis 2004;23:317-22. DOI: 10.1007/s10096-004-1109-5 PMID: 15057529

15. Klingspor L, Tortorano AM, Peman J, Willinger B, Hamal P, Sendid B, et al. Invasive Candida infections in surgical patients in intensive care units: a prospective, multicentre survey initiated by the European Confederation of Medical Mycology (ECMM) (2006-2008). Clin Microbiol Infect 2015;21:87.e1-87.e10. DOI: 10.1016/j.cmi.2014.08.011 PMID: 25270048

16. Hoenigl M, Salmanton-García J, Walsh TJ, Nucci M, Neoh CF, Jenks JD, et al. Guideline adherence and survival of patients with candidaemia in Europe: results from the ECMM Candida III multinational European observational cohort study. Lancet Infect Dis 2023;23:751-761. DOI: 10.1016/S1473-3099(22)00872-6 PMID: 36738747

17. Wolfgruber S, Sedik S, Klingspor L, Tortorano A, Gow NAR, Lagrou K, et al. Insights from Three Pan-European Multicentre Studies on invasive Candida infections and outlook to ECMM Candida IV. Mycopathologia. 2024;189(4):70. doi: 10.1007/s11046-024-00871-0.

18. Montagna MT, Lovero G, Borghi E, Amato G, Andreoni S, Campion L, et al. Candidemia in intensive care unit: a nationwide prospective observational survey (GISIA-3 study) and review of the European literature from 2000 through 2013. Eur Rev Med Pharmacol Sci 2014;18:661-74. PMID: 24706310

19. Parambath S, et al. Candida albicans-A systematic review to inform the World Health Organization Fungal Priority Pathogens List. Med Mycol 2024;62:myae045. DOI: 10.1093/mmy/myae045 PMID: 38813851.

20. Arsić Arsenijević V, Otašević S, Janić D, Minić P, Matijašević J, Medić D, et al. Candida bloodstream infections in Serbia: First multicentre report of a national prospective observational survey in intensive care units. Myco-

ses. 2018;61(2):70-78. doi: 10.1111/myc.12700. Epub 2017 Sep 28. PMID: 28872706.

21. Satoh K, Makimura K, Hasumi Y, Nishiyama Y, Uchida K, Yamaguchi H. Candida auris sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. Microbiol Immunol 2009;53:41-44. DOI: 10.1111/j.1348-0421.2008.00083.x PMID: 19161556
22. Chowdhary A, Sharma C, Meis JF. Candida auris: A rapidly emerging cause of hospital-acquired multidrug-resistant fungal infections globally. PLoS Pathog 2017;13:e1006290. DOI: 10.1371/journal.ppat.1006290 PMID: 28542486 PMCID: PMC5436850
23. Du H, Bing J, Hu T, Ennis CL, Nobile CJ, Huang G. Candida auris: Epidemiology, biology, antifungal resistance, and virulence. PLoS Pathog 2020;16:e1008921. DOI: 10.1371/journal.ppat.1008921 PMID: 33091071 PMCID: PMC7580931
24. Caceres DH, Mohd Tap R, Alastruey-Izquierdo A, Hagen F. Detection and control of fungal outbreaks. Mycopathologia 2020;185:741-745. DOI: 10.1007/s11046-020-00479-0 PMID: 32737792 PMCID: PMC7393625
25. Cortegiani A, Misseri G, Fasciana T, Giammanco A, Giarratano A, Chowdhary A. Epidemiology, clinical characteristics, resistance, and treatment of infections by Candida auris. J Intensive Care 2018;6:69. DOI: 10.1186/s40560-018-0342-4 PMID: 30410743 PMCID: PMC6206787
26. de Cássia Orlandi Sardi J, Silva DR, Soares Mendes-Giannini MJ, Rosalen PL. Candida auris: Epidemiology, risk factors, virulence, resistance, and therapeutic options. Microb Pathog 2018;125:116-121. DOI: 10.1016/j.micpath.2018.09.014 PMID: 30223078
27. Sarma S, Upadhyay S. Current perspective on emergence, diagnosis and drug resistance in Candida auris. Infect Drug Resist 2017;10:155-165. DOI: 10.2147/IDR.S116229 PMID: 28652784 PMCID: PMC5478407
28. Jeffery-Smith A, Taori SK, Schelenz S, Jeffery K, Johnson EM, Borman A, et al. Candida auris: a review of the literature. Clin Microbiol Rev 2017;31:e00029-17. DOI: 10.1128/CMR.00029-17 PMID: 29142078 PMCID: PMC5740971
29. Mattingly AS, Rose L, Eddington HS, Trickey AW, Cullen MR, Morris AM, et al. Trends in US Surgical Procedures and Health Care System Response to Policies Curtailing Elective Surgical Operations During the COVID-19 Pandemic. JAMA Netw Open 2021;4:e2138038. DOI: 10.1001/jamanetworkopen.2021.38038 PMID: 34878550 PMCID: PMC8654261
30. Suleyman G, Alangaden GJ. Nosocomial fungal infections: epidemiology, infection control, and prevention. Infect Dis Clin North Am 2021;35:1027-1053. DOI: 10.1016/j.idc.2021.07.003 PMID: 34752221
31. Abalkhail A, Alslamah T. Institutional factors associated with

infection prevention and control practices globally during the infectious pandemics in resource-limited settings. Vaccines (Basel) 2022;10:1811. DOI: 10.3390/vaccines10111811 PMID: 36366344 PMCID: PMC9696233

32. Dao A, Kim HY, Garnham K, Kidd S, Sati H, Perfect J, et al. Cryptococcosis-a systematic review to inform the World Health Organization Fungal Priority Pathogens List. Med Mycol 2024;62:myae043. DOI: 10.1093/mmy/myae043 PMID: 38813850

33. Pappas PG. Cryptococcal infections in non-HIV-infected patients. Trans Am Clin Climatol Assoc 2013;124:61-79. PMID: 23874010 PMCID: PMC3715907

34. May R, Stone N, Wiesner D, et al. Cryptococcus: from environmental saprophyte to global pathogen. Nat Rev Microbiol 2016;14:106-117. DOI: 10.1038/nrmicro.2015.6 PMID: 26772911 PMCID: PMC4978612

35. Zhu LP, Wu JQ, Xu B, et al. Cryptococcal meningitis in non-HIV-infected patients in a Chinese tertiary care hospital, 1997-2007. Med Mycol 2010;48:570-9. DOI: 10.3109/13693780903437876 PMID: 20055735

36. Li X, Paccoud O, Chan KH, Yuen KY, Manchon R, Lanternier F, et al. Cryptococcosis associated with biologic therapy: A Narrative Review. Open Forum Infect Dis 2024;11:ofae316. DOI: 10.1093/ofid/ofae316 PMID: 38868304 PMCID: PMC11167057

37. Gangadharan SS, Raveendranath S. Cryptococcosis in oncology patients: a case series in a tertiary care cancer centre. Iran J Microbiol 2023;15:821-825. DOI: 10.18502/ijm.v15i6.14159 PMID: 38156302 PMCID: PMC10752525

38. Spadari CdC, Wirth F, Lopes LB, Ishida K. New approaches for cryptococcosis treatment. Microorganisms 2020;8:613. DOI:10.3390/microorganisms8040613 PMID: 32429590 PMCID: PMC7232474

39. Li H, Guo M, Wang C, Li Y, Fernandez AM, Ferraro TN, et al. Epidemiological study of Trichosporon asahii infections over the past 23 years. Epidemiol Infect 2020;148:e169. DOI: 10.1017/S0950268820001624 PMID: 32703332 PMCID: PMC7439294

40. Nguyen JK, Schlichte MJ, Schady D, Pourciau CY. Fatal disseminated Trichosporon asahii fungemia in a child with acute lymphoblastic leukemia and a morbilliform eruption. Pediatr Dermatol 2018;35:e86-e87. DOI: 10.1111/pde.13471 PMID: 29457264

41. Colombo AL, Padovan AC, Chaves GM. Current knowledge of Trichosporon spp. and Trichosporonosis. Clin Microbiol Rev 2011;24:682-700. DOI: 10.1128/CMR.00003-11 PMID: 21976604 PMCID: PMC3194828

42. Guého E, Improvisi L, de Hoog GS, Dupont B. Trichosporon on humans: a practical account. Mycoses 1994;37:3-10. DOI: 10.1111/j.1439-0507.1994.tb00277.x PMID: 7935588

43. Ruan SY, Chien JY, Hsueh PR. Invasive trichosporonosis caused by Trichosporon asahii and other unusual Trichosporon species at a medical center in Taiwan. Clin Infect Dis 2009;49:0-7. DOI:

10.1086/599614 PMID: 19489715

44. De Pauw B, Walsh TJ, Donnelly JP, et al. Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/ Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. Clin Infect Dis 2008;46:1813-1821. DOI: 10.1086/588660 PMID: 18462102

45. de Almeida Júnior JN, Hennequin C. Invasive Trichosporon infection: a systematic review on a re-emerging fungal pathogen. Front Microbiol 2016;7:1629. DOI: 10.3389/fmicb.2016.01629 PMID: 27803695 PMCID: PMC5067569

46. Kourti M, Roilides E. Invasive trichosporonosis in neonates and pediatric patients with malignancies or hematologic disorders. Pathogens 2022;11:242. DOI: 10.3390/pathogens11020242 PMID: 35215202 PMCID: PMC8878408

47. Castano G, Yarrarapu SNS, Mada PK. Trichosporonosis. StatPearls 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482477/ PMID: 29493986

48. Go SE, Lee KJ, Kim Y, Choi JK, Kim YJ, Lee DG. Catheter-related trichosporon asahii bloodstream infection in a neutropenic patient with myelodysplastic syndrome. Infect Chemother 2018;50:138-143. DOI: 10.3947/ic.2018.50.2.138 PMID: 29968983 PMCID: PMC6026363

49. Dolan AM, Hoban T, Brennan G, Flanagan PR, O'Rourke S, Teoh TK, et al. Magnusiomyces capitatus, an Unusual Cause of Invasive Fungal Infections in Neutropenic Patients: Case Reports and Outbreak Investigation. Mycopathologia 2025;190:8. DOI: 10.1007/s11046-024-00871-0

50. Ortiz-Álvarez J, Reséndiz-Sánchez J, Juárez-Montiel M, Hernández-García JA, Vázquez-Guerrero E, Hernández-Rodríguez C, et al. Invasive fungal infection caused by Magnusiomyces capitatus in an immunocompromised pediatric patient with acute lymphoblastic leukemia in Mexico City: A case report. J Fungi (Basel) 2022;8:851. DOI: 10.3390/jof8080851 PMID: 36012842 PMCID: PMC9409336

51. Bouza E, Muñoz P. Invasive infections caused by Blastoschizomyces capitatus and Scedosporium spp. Clin Microbiol Infect 2004;10(Suppl 1):76-85. DOI: 10.1111/j.1470-9465.2004.00862.x PMID: 14748806

52. Martino R, Salavert M, Parody R, Tomás JF, De La Cámara R, Vázquez L, et al. Blastoschizomyces capitatus infection in patients with leukemia: Report of 26 cases. Clin Infect Dis 2004;38:335-341. DOI: 10.1086/380643 PMID: 14727210

53. Girmenia C, Pagano L, Martino B, D'Antonio D, Fanci R, Specchia G, et al. Invasive infections caused by Trichosporon species and Geotrichum capitatum in patients with hematological malignancies: A retrospective multicenter study from Italy and review of the literature. J Clin Microbiol 2005;43:1818-1828. DOI: 10.1128/JCM.43.4.1818-1828.2005 PMID: 15814998 PMCID: PMC1081355

54. Buchta V, Bolehovská R, Hovorková E, Cornely OA, Seidel D, Žák P. Saprochaete clavata invasive infections- A new threat to hematological-oncological patients. Front Microbiol 2019;10:2196. DOI: 10.3389/fmicb.2019.02196 PMID: 31608031 PMCID: PMC6769163

55. D'Assumpcao C, Lee B, Heidari A. A Case of Magnusiomyces capitatus peritonitis without underlying malignancies. J Investig Med High Impact Case Rep 2018;6:2324709618795268. DOI: 10.1177/2324709618795268 PMID: 30186588 PMCID: PMC6123035

56. Meena S, Singh G, Dabas Y, Rajshekhar P, Xess I. Geotrichum candidum in infective endocarditis. J Glob Infect Dis 2017;9:127-128. DOI: 10.4103/jgid.jgid_29_17 PMID: 28855777 PMCID: PMC5563030

57. Duran Graeff L, Seidel D, Vehreschild MJ, Hamprecht A, Kindo A, Racil Z, et al. Invasive infections due to Saprochaete and Geotrichum species: report of 23 cases from the FungiScope Registry. Mycoses 2017;60:273-279. DOI: 10.1111/myc.12595 PMID: 28066941

58. Mawad TN, Alfaifi RA, Almazyed OM, Alhumaidi RA, Alsubaie AM. Fungemia due to Saprochaete capitata in a non-neutropenic critically ill patient. Cureus 2023;15:e51147. DOI: 10.7759/cureus.51147 PMID: 38196941 PMCID: PMC10776090

59. Pottier I, Gente S, Vernoux JP, Guéguen M. Safety assessment of dairy microorganisms: Geotrichum candidum. Int J Food Microbiol 2008;126:327-32. DOI: 10.1016/j.ijfoodmicro.2008.05.013 PMID: 18579247

60. Kurtzman C, Fell JW. The Yeasts - A Taxonomic Study. 4th Edition. Elsevier; 1998. ISBN: 9780080542690

61. Wirth F, Goldani LZ. Epidemiology of Rhodotorula: an emerging pathogen. Interdiscip Perspect Infect Dis 2012;2012:465717. DOI: 10.1155/2012/465717 PMID: 22536240 PMCID: PMC3321564

62. García-Suárez J, Gómez-Herruz P, Cuadros JA, Burgaleta C. Epidemiology and outcome of Rhodotorula infection in haematological patients. Mycoses 2011;54:318-24. DOI: 10.1111/j.1439-0507.2009.01807.x PMID: 19925568

63. Spiliopoulou A, Anastassiou ED, Christofidou M. Rhodotorula fungemia of an intensive care unit patient and review of published cases. Mycopathologia 2012;174:301-309. DOI: 10.1007/s11046-012-9553-8 PMID: 22623107

64. Jarros IC, Veiga FF, Corrêa JL, Barros ILE, Gadelha MC, Voidaleski MF, et al. Microbiological and virulence aspects of Rhodotorula mucilaginosa. EXCLI J 2020;19:687-704. DOI: 10.17179/excli2020-1198 PMID: 32665771 PMCID: PMC7349877

65. Zhou M, Li Y, Kudinha T, Xu Y, Liu Z. Kodamaea ohmeri as an Emerging Human Pathogen: A Review and Update. Front Microbiol 2021;12:736582. DOI: 10.3389/fmicb.2021.736582 PMID: 34566932 PMCID: PMC8456036

66. Santino I, Bono S, Borruso L, Bove M, Cialdi E, Martinelli D, et al. Kodamaea ohmeri isolate from two immunocompromised patients: first report in Italy. Mycoses 2013;56:179-81. DOI: 10.1111/j.1439-0507.2012.02232.x PMID: 22882303

67. Shaaban H, Choo HF, Boghossian J, Perez G. Kodamaea ohmeri fungemia in an immunocompetent patient treated with micafungin: case report and review of the literature. Mycopathologia 2010;170:223-8. DOI: 10.1007/s11046-010-9316-3 PMID: 20490634

68. Arendrup MC, Boekhout T, Akova M, Meis JF, Cornely OA, Lortholary O. ESCMID and ECMM joint clinical guidelines for the diagnosis and management of rare invasive yeast infections. Clin Microbiol Infect 2014;20(Suppl 3):76-98. DOI: 10.1111/1469-0691.12360 PMID: 24476100

69. Rhimi W, Theelen B, Boekhout T, Otranto D, Cafarchia C. Malassezia spp. Yeasts of emerging concern in fungemia. Front Cell Infect Microbiol 2020;10:370. DOI: 10.3389/fcimb.2020.00370 PMID: 32850475 PMCID: PMC7396662

70. Findley K, Oh J, Yang J, Conlan S, Deming C, Meyer JA, et al. Topographic diversity of fungal and bacterial communities in human skin. Nature 2013;498:367-70. DOI: 10.1038/nature12171 PMID: 23698366 PMCID: PMC3718715

71. Vijaya Chandra SH, Srinivas R, Dawson TL Jr, Common JE. Cutaneous Malassezia: commensal, pathogen, or protector? Front Cell Infect Microbiol 2021;10:614446. DOI: 10.3389/fcimb.2020.614446 PMID: 33585270 PMCID: PMC7873985

72. Baker RM, Stegink RJ, Manaloor JJ, Schmitt BH, Stevens JC, Christenson JC. Malassezia pneumonia: A rare complication of parenteral nutrition therapy. JPEN J Parenter Enteral Nutr 2016;40:1194-1196. DOI: 10.1177/0148607115588337 PMID: 26002912

73. Rosales CM, Jackson MA, Zwick D. Malassezia furfur meningitis associated with total parenteral nutrition subdural effusion. Pediatr Dev Pathol 2004;7:86-90. DOI: 10.1007/s10024-003-0101-x PMID: 15255036

74. Tragiannidis A, Bisping G, Koehler G, Groll AH. Minireview: Malassezia infections in immunocompromised patients. Mycoses 2010;53:187-95. DOI: 10.1111/j.1439-0507.2009.01814.x PMID: 19925569

75. Eschete ML, West BC. Saccharomyces cerevisiae septicemia. Arch Intern Med 1980;140:1539. PMID: 7425782

76. Fadhel M, Patel S, Liu E, Levitt M, Asif A. Saccharomyces cerevisiae fungemia in a critically ill patient with acute cholangitis and long term probiotic use. Med Mycol Case Rep 2018;23:23-25. DOI: 10.1016/j.mmcr.2018.11.003 PMID: 30505890 PMCID: PMC6251329

77. Stefanatou E, Kompoti M, Paridou A, Koutsodimitropoulos I, Giannopoulou P, Markou N, et al. Probiotic sepsis due to Saccharomyces fungaemia in a critically ill burn patient. My-

coses 2011;54:e643-6. DOI: 10.1111/j.1439-0507.2011.02020.x PMID: 21615541

78. Enache-Angoulvant A, Hennequin C. Invasive Saccharomyces infection: a comprehensive review. Clin Infect Dis 2005;41:1559-68. DOI: 10.1086/497632 PMID: 16267727

79. Hamoud S, Keidar Z, Hayek T. Recurrent Saccharomyces cerevisiae fungemia in an otherwise healthy patient. Isr Med Assoc J 2011;13:575-6. PMID: 21991721

80. Cobban A, Edgcomb VP, Burgaud G, Repeta D, Leadbetter ER. Revisiting the pink-red pigmented basidiomycete mirror yeast of the phyllosphere. Microbiologyopen 2016;5:846-855. DOI: 10.1002/mbo3.377 PMID: 27465122 PMCID: PMC5111565

81. Morris JT, Beckius M, McAllister CK. Sporobolomyces infection in an AIDS patient. J Infect Dis 1991;164:623-4. DOI: 10.1093/infdis/164.3.623 PMID: 1869844

82. McNicholas S, McDermott H, Power L, Johnson EM, Moroney J, Humphreys H, et al. Sporobolomyces roseus in the cerebrospinal fluid of an immunocompetent patient--to treat or not to treat? J Med Microbiol 2012;61:295-296. DOI: 10.1099/jmm.0.036715-0 PMID: 22034161

83. Rantala A, Niinikoski J, Lehtonen OP. Yeasts in blood cultures: impact of early therapy. Scand J Infect Dis 1989;21:557-61. DOI: 10.3109/00365548909037885 PMID: 2587957

84. Sharma V, Shankar J, Kotamarthi V. Endogeneous endophthalmitis caused by Sporobolomyces salmonicolor. Eye 2006;20:945-946. DOI: 10.1038/sj.eye.6702076 PMID: 16167077