Microbe of the month

Breaking The Chain of Infection

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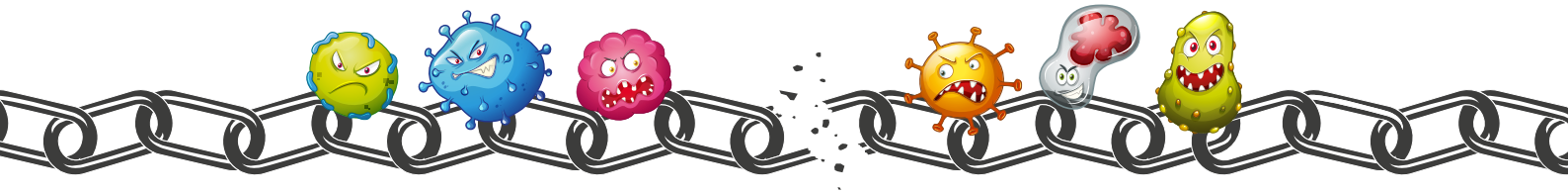
AUGUST 2019
Newsletter

Compiled by Helen Loudon, Independent IPC Practitioner



Featured this month:

Back to Basics

All about FUNGI

Hello reader! Since the beginning of the year, Microbe of the Month has focused on important microbiological aspects of bacteria; however, it would be a grave omission not to also address the many and potentially-deadly infections currently posed by **fungi** in the healthcare setting.

SOME BASIC MYCOLOGY

Fungi are a diverse group of microorganisms with over 80 000 identifiable species!
Medically-important fungi capable of causing invasive fungal infection can be broadly split into three categories:

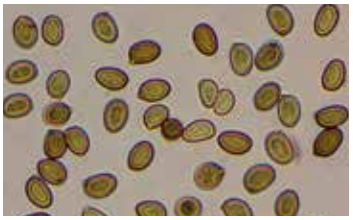
- **Yeasts** (e.g., *Candida* spp. and *Cryptococcus spp.*)
- **Moulds** (e.g., *Aspergillus* spp. and the *zygomycetes*)
- **Dimorphic fungi (**e.g., *Histoplasma* spp.)

Note: The *dermatophytes* (e.g., *Microsporum spp.*), whilst capable of causing superficial infections of the skin, hair and nails, rarely cause invasive infections.

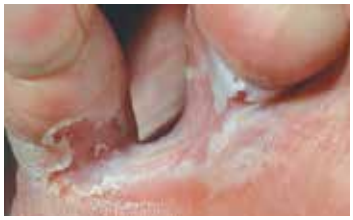
Pathogenesis: Most fungi grow best at about 25ºC, which is close to room temperature. However, pathogenic (disease-causing) fungi thrive at body temperature (37ºC), and under acidic conditions at a pH of 5-6.

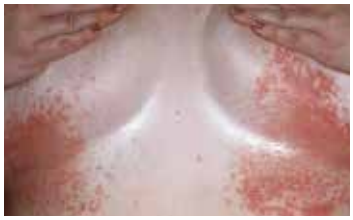
Moulds typically grow as long 'budding' filaments called *'hyphae'*; whereas yeasts are single cells which may reproduce by 'budding' as well as fusion with other yeast cells. Although usually aerobic, facultative yeasts can multiply in anaerobic conditions, especially in the presence of high concentrations of sugar (hence the diabetic predisposition to fungal infections).

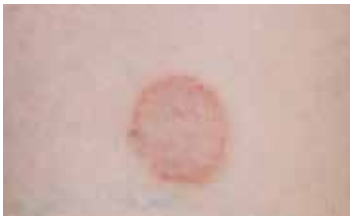
Clinical significance?
Both yeasts and moulds form thousands of spores in the reproductive process, each of which is capable of germinating into new yeast cells and fungal hyphae.



Fungal spores







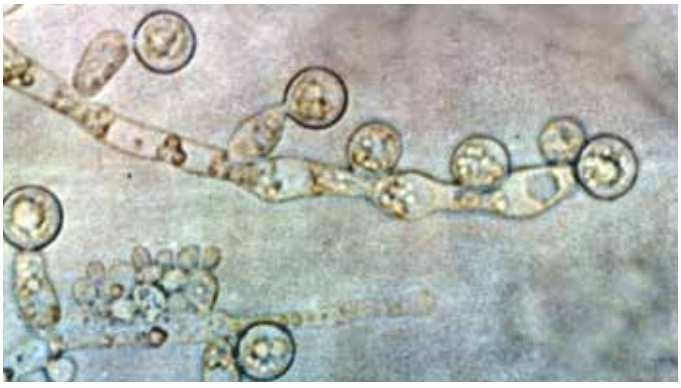
Common superficial fungal infections of the skin

TYPES OF FUNGAL INFECTIONS WHICH MAY CAUSE INVASIVE DISEASE INCLUDE:

- ***Candida albicans*** is the most commonly isolated strain of Candida, mainly because it forms part of the normal commensal flora in body sites such as the skin, mouth, gut and vagina without causing any problems, and was historically considered to be non-pathogenic.

  However, with the increasing use of invasive devices, the overuse and abuse of antibiotics, and ever-increasing patient populations with Diabetes mellitus or other underlying immune-compromising conditions, *Candida species* have become a formidable healthcare-associated pathogen.

  Therefore, invasive candidiasis is the most common fungal disease among hospitalised patients in the developed world, either seen as deep-seated tissue candidiasis (i.e., *Candida spp*. in a sterile site) or ***candidaemia*** (*Candida spp*. in the bloodstream).



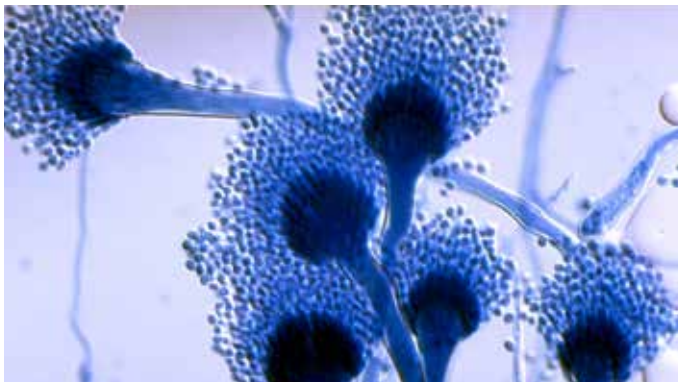
Candida albicans depicting branching hyphae and budding

Clinical relevance?

- *The most common fungal pathogens are Candida albicans, C. glabrata, C. parapsilosis, C. tropicalis, and C. krusei;* however, species distribution varies by patient risk, population and geographic region.
- Most infections arise from the endogenous flora of patients with underlying risk factors (commonly HIV/AIDS) following disruption of the skin and mucosal barriers by invasive devices or following surgical procedures. Less commonly, *Candida* can be transmitted via healthcare workers' hands or contaminated medical devices.
- Invasive candidiasis is a poor prognostic indicator and associated with high mortality rates.
- *Candida auris* has emerged globally as a deadly pathogen since 2009 and is of great concern because it is highly drug-resistant, causes invasive infections associated with high mortality, and spreads easily between patients in healthcare settings.

- **Aspergillosis** is an infection caused by ***Aspergillus***, a common mould which is present in both indoor and outdoor environments. Most people breathe in *Aspergillus* spores every day without getting sick. Invasive *aspergillosis* is a serious and invasive infection (usually pneumonia) which tends to affect the immuno-compromised.

  Risk factors include haematological malignancy, solid organ transplant recipients, haematopoietic stem cell transplant (HSCT) recipients, solid tumours, HIV/AIDS, and inherited immunodeficiency disorders (e.g., Rheumatoid arthritis, Lupus erythematosus, idiopathic thrombocytopaenia).

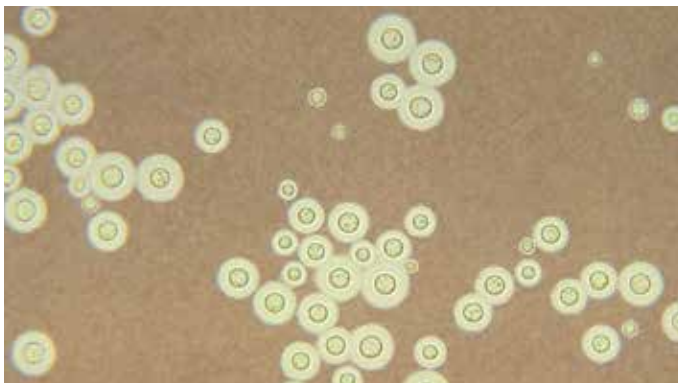


Aspergillus flavus and budding spores

- ***Cryptococcus neoformans*** is a fungus that lives in the environment throughout the world. The fungus is typically found in soil, on decaying wood, in tree hollows, or in bird droppings.

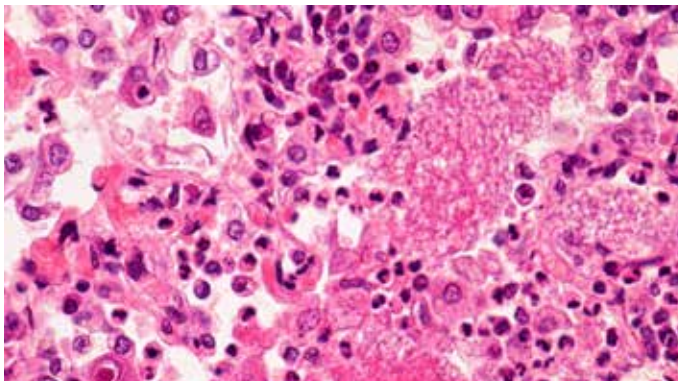
  People can become infected with *C. neoformans* after breathing in the microscopic fungus; however, *C. neoformans* infections are rare in people who are otherwise healthy. Most cases occur in people who have weakened immune systems, particularly those with advanced HIV/AIDS.

  C. neoformans usually infects the lungs or the central nervous system (the brain and spinal cord), but it can also affect other organ systems. The symptoms of the infection depend on the parts of the body that are affected - *C. neoformans* infections are **not** contagious.



Cryptococcus neoformans

- ***Pneumocystis jirovecii*** (also known as pneumocystis pneumonia or 'PCP') is a serious infection caused by the fungus *Pneumocystis jirovecii*. PCP pneumonia is extremely rare in healthy people. This fungus may colonise the lungs without causing symptoms - up to 20% of adults might carry *Pneumocystis jirovecii* at any given time – and the immune system removes the fungus after several months. Most individuals who develop PCP pneumonia have an underlying immune condition such as HIV/AIDS or take medication which affects the immune system's ability to fight off infection. Fortunately, with the availability of antiretroviral therapy, people living with HIV are less likely to succumb to PCP - however, PCP remains a substantial public health problem in developing countries and low resource settings.



Pneumocystis jirovecii in lung tissue

SIGNS AND SYMPTOMS

Initially, signs and symptoms are often non-specific and include fever and chills that do not respond to antibacterial treatment. Symptoms of invasive fungal disease will depend on the organ system affected. Candidemia is the most common form of invasive candidiasis; other forms include endocarditis, peritonitis, meningitis, osteomyelitis, arthritis, and endophthalmitis.

INVASIVE CANDIDIASIS

Invasive candidiasis is an infection caused by a species of yeast called Candida. Unlike Candida infections in the mouth and throat (also called "thrush") or vaginal "yeast infections" - which are localised to one part of the body - invasive candidiasis is a serious infection that can affect the blood, heart, brain, eyes, bones, or other parts of the body.

WHO IS AT RISK?

- Critically ill patients with invasive devices, e.g., central venous catheters, urinary catheters
- Long term ICU patients and pre-term babies
- Patients receiving total parenteral nutrition (TPN)
- Those with weakened immune systems (e.g., organ transplantation, corticosteroid therapy, HIV/AIDS)
- Diabetics
- Patients with leukaemia and malignant tumours, especially if they have a low neutrophil count (neutropenia) following cytotoxic chemotherapy
- People who have received multiple courses of broad-spectrum antibiotics
- People with kidney failure or who are on haemodialysis
- Patients who have undergone major gastrointestinal surgery, with subsequent anastomotic leakage or repeated laparotomies.

DIAGNOSIS [1,2,4,5]

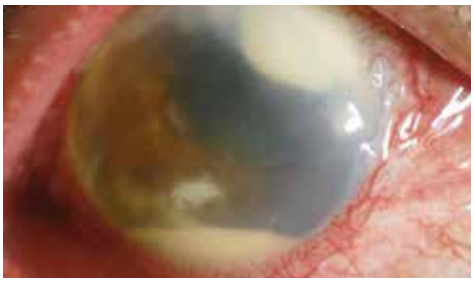
Clinical diagnosis of invasive fungal infection is complicated by a lack of specific clinical signs and symptoms. Access to timely diagnostics is essential, because identification of the fungal species causing the infection is critically important to guide appropriate antifungal treatment.
Specimens collected depend upon the suspected location(s) of the infection. They may include the collection of blood, sputum, urine, cerebrospinal fluid (CSF) or tissue biopsy.
Invasive candidiasis is primarily diagnosed with blood culture – multiple blood cultures taken on successive days, especially after the removal or in the absence of central lines, are compelling evidence for invasive disease.
Unfortunately, microbiological confirmation may also be 'hit and miss', because blood cultures can be negative in up to 50% of cases or may only become positive late in the infection (positive urine cultures which yield >10^4 cfu/ml - in the absence of an indwelling urinary catheter - should also raise suspicion of infection).
In general, tests may include microscopic examination and Gram staining, culture and sensitivity, antibody-antigen assays and molecular testing (PCR) – the latter may be more accurate for detecting the specific genetic profile of the fungus causing the infection.

Yeasts can survive and multiply inside macrophages and neutrophils! Removal of intravenous catheters is recommended, especially for neutropenic patients.

TREATMENT [1,2,5]

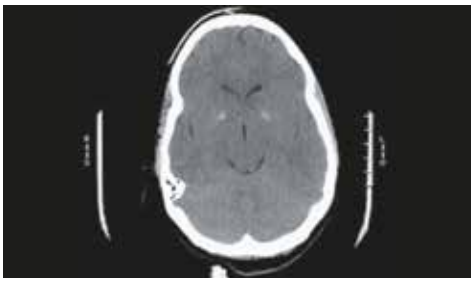
The specific type and dose of antifungal medication used to treat invasive candidiasis usually depends on the patient's age, immune status, and location and severity of the infection. For most adult patients with laboratory confirmed candidemia, an echinocandin is recommended as initial therapy, with de-escalation to fluconazole once the infecting species and antifungal susceptibility are known and blood cultures have cleared.

Fluconazole is an acceptable alternative to an echinocandin as initial therapy in selected patients who are not critically ill and who are considered unlikely to have a fluconazole-resistant *Candida* infection (amphotericin B or voriconazole may also be appropriate in certain situations, depending on recommendations from the medical microbiologist). In general, treatment should continue for two weeks after clearance of *Candida* from the bloodstream and resolution of symptoms.



Bacterial and fungal endophthalmitis following cataract surgery

'Cotton wool' spots typical of fungal retinopathy in HIV/AIDS



Cryptococcal meningitis - AIDS

ANTIFUNGAL RESISTANCE

Fluconazole resistance has been recognized for several years, especially in *C. glabrata* (dose dependent) and *C. krusei* (which is intrinsically resistant to fluconazole). Azole resistance has also been seen in *C. parapsilosis* and *C. auris*. Predictors associated with fluconazole-resistant *Candida* spp. include neutropenia, chronic renal disease, and previous fluconazole exposure. Resistance can emerge rapidly while the patient is on therapy.

Azole resistance has also been demonstrated in *Aspergillus fumigatus*. Fungal **biofilm-associated infections** are recognised as an escalating clinical problem and are frequently refractory to conventional therapy because of resistance. As with bacterial infections, *in-vitro and in-vivo* biofilm models have demonstrated less susceptibility to antimicrobial therapy than planktonic (free-floating) fungal cells. Not surprisingly, Echinocandin resistance is also being increasingly recognized.

Echinocandins cannot be used for CNS, urine and eye infections caused by Candida species.

The medical microbiologist should be consulted for advice.

INFECTION PREVENTION AND CONTROL MEASURES

The main mode of transmission is via dissemination of fungal spores by air currents and dust. Investigations into outbreaks suggest that these pathogens are able to survive for long periods in the hospital environment (e.g., floors, trolleys, windowsills, medical equipment, cell phones and computer keypads), colonise healthcare workers, and cause persistent colonisation of previously-infected patients, despite exposure to antifungal therapy.

Standard precautions are a legal requirement (The Occupational Health and Safety Act 85 of 1993) *to be practiced by ALL healthcare workers, for EVERY patient and in ALL situations. They are based on the principle that all blood, body fluids, secretions, excretions (except sweat), non-intact skin, and mucous membranes may contain transmissible infectious agents.*

In addition to standard precautions, **CONTACT precautions** are an important fundamental component of the infection prevention and control measures necessary to prevent cross infection and control the incidence of healthcare-associated infections (HAIs).

- Wash hands promptly after contact with infective material, and upon glove removal.
- Apply alcohol-based hand rub frequently during tasks when hands are not visibly soiled, before and after touching a patient, his environment or possessions.
- Wear gloves when in contact with blood, body fluids, secretions, mucous membranes and contaminated items such as drainage tubes.
- Use strict aseptic precautions during the preparation of medication for injection and during the manipulation IV lines.
- Avoid the use of invasive devices where possible, and practice strict aseptic technique for their insertion and after-care. Remove vascular catheters as soon as possible.
- Bathe critically-ill patients with chlorhexidine gluconate antiseptic liquid soap daily.
- Ensure that single-use items are discarded appropriately, and that patient care equipment is cleaned and disinfected prior to re-use on another patient.
- Frequently touched surfaces (cot sides, lockers, monitors and light switches, etc.) should be cleaned and disinfected twice daily with a *sodium hypochlorite-based* agent.
- Handle used linen and waste with care and ensure appropriate disposal at the point of use.

Broad-spectrum antibiotic therapy disrupts the composition and function of the normal protective gut flora (referred to as ***dysbiosis***), resulting in overgrowth of Candida species and the development of 2° disease

BE ANTIBIOTICS AWARE
SMART USE, BEST CARE

Always liaise with your Infection Control Specialist and Medical Microbiologist if you require guidance on a laboratory culture report or are unsure of the clinical precautions to be taken!

Lessons learned for infection prevention and control

- ***Candida auris***, ***Candida glabrata*** and ***Candida parapsilosis*** are emerging fungi which present a serious global health threat.
- These fungi are ***multidrug-resistant***; i.e., they are resistant to the few antifungal drugs currently available to treat infections caused by Candida species. (e.g., Amphoteracin B, fluconazole, itraconazole, voriconazole or even caspofungin, which is from a new class of antifungals called the *echinocandins*).
- Fungal diagnostics may be unavailable in some hospitals, or the turnaround time may be so long as to render them ineffective, leading to empirical treatment of infections.
- Laboratory identification and differentiation may also be difficult, as there are fewer diagnostic and monitoring tests available for fungal infections than for bacterial infections, and personnel are generally less confident in interpreting the results. This may lead to inappropriate clinical management and high mortality rates.
- Patients requiring antifungal therapy are often on complex medication regimens and therefore toxicity and drug-to-drug interactions may be more prevalent than when treating bacterial infections.
- Hand hygiene before and after every episode of patient contact, and standard infection control precautions augmented with strict contact precautions, must be implemented by ***everyone*** involved in the patient's care.
- *Long, gel-coated and/or artificial nails are a known risk for the transmission of fungal spores.*
- ***Practice antimicrobial stewardship!***
- Order recommended cultures before antibiotic therapy is commenced and start drugs promptly (i.e., 'hang time' should be within one hour of prescribing).
- Verify that positive cultures represent true infection and not just colonisation (in which case, no antibiotic therapy is required).
- Use a designated prescription and administration chart for all antimicrobial agents, ensuring that the indication, dose and expected duration are specified in the patient record.
- Reassess antimicrobial therapy after 48 hours and liaise with the medical microbiologist where possible to exclude possible drug resistance.

Your input is important to us

Your feedback helps us make this newsletter a valuable resource for healthcare practitioners.
Please send all queries, comments or requests for future topics to

askcutimed@essity.com

and we will do our best to address them in the next issue!

1. British Society for Antimicrobial Therapy in collaboration with ESGAP/ESCMID (2018). ANTIMICROBIAL STEWARDSHIP: From Principles to Practice e-Book. **2.** Centers for Disease Control and Prevention (CDC). A-Z Diseases and Conditions. Available from https://www.cdc.gov/diseasesconditions/az/p.html **3.** Centers for Disease Control (CDC) 2013 Report. Antibiotic Resistant Threats in the USA. **4.** Ellepola, A.N., Morrison, C.J. (2005). Laboratory diagnosis of invasive candidiasis. Journal of microbiology (Seoul, Korea). 43 Spec No. 65-84. **5.** Pappas, P., Kaufmann, C.A., Andes, D.R. (2016). Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America.

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* P. J. Stanirowski, et al. Dialkylcarbamoyl chloride-impregnated dressing for the prevention of surgical site infection in women undergoing cesarean section: a pilot study. Arch Med Sci 2016; 12, 2

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