

# Candida

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*Candida* is a commensal of skin, oral and intestinal flora in humans, and disease generally results when immunity is lowered (e.g. antibiotics use, stress, diabetes) or completely compromised (e.g. HIV/AIDS). Infection can result in a spectrum of clinical presentations and some species are known to have a predilection for certain sites: *C. albicans* is the most common cause of oral and vulvovaginal candidiasis; *C. parapsilosis* is frequently reported in nail-related infections; and *C. parapsilosis* and *C. pelliculosa* are strongly associated with nosocomial infections. In recent years, the emergence of resistance has led to antifungal susceptibility testing and reporting in invasive specimens. *C. glabrata* and *C. krusei* are known for their resistance to fluconazole (the former acquired and the latter intrinsic).

## Clinical Presentation

**Table 3.2: Types of Candidiasis**

Invasive	Semi-invasive	Non-invasive
<ul style="list-style-type: none"> <li>• CNS candidiasis</li> <li>• Candida endophthalmitis</li> <li>• Candida endocarditis, pericarditis and endovascularitis</li> <li>• Intra-abdominal candidiasis</li> <li>• Candida pyelonephritis or urinary fungus ball</li> <li>• Candida osteomyelitis and arthritis</li> <li>• Candidemia</li> <li>• Chronic disseminated candidiasis</li> </ul>	<ul style="list-style-type: none"> <li>• Esophagitis</li> <li>• Chronic mucocutaneous candidiasis</li> </ul>	<ul style="list-style-type: none"> <li>• Oral thrush</li> <li>• Otitis externa</li> <li>• Cutaneous and onychomycosis</li> <li>• Chronic mucocutaneous candidiasis</li> <li>• Candiduria</li> <li>• Vulvovaginitis</li> </ul>

Oral thrush

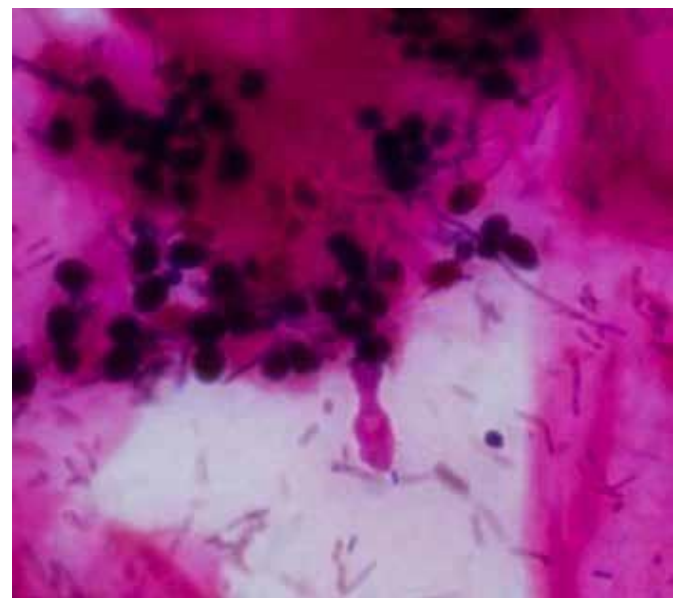
Fig. 3.1.1-1



One of the commonest presentations of candidiasis. White exudate on oral mucosa due to candida overgrowth and mucocutaneous inflammation. Oral thrush is associated with extremes of ages, antibiotic therapy, chronically ill patients and is generally considered an early manifestation of disturbance in innate immunity.

Genital thrush (vulvovaginitis), Gram stain of vaginal swab

Fig. 3.1.1-2



Stain reveals abundant unicellular (budding yeasts) and multicellular (pseudohyphae) forms on squamous cells. *Candida* typically stains Gram positive. Genital thrush is associated with diabetes, pregnancy and compromised host immune status (recurrence common if inadequately treated). (x100)

Onychomycosis

Fig. 3.1.1-3



Thickened and discoloured nail plate with subungual hyperkeratosis and onycholysis. White adherent plaque seen in intertriginous space of ring and little fingers.

Onychomycosis

Fig. 3.1.1-4



Discoloured and pitted nails with a crumbling nail plate. Nail folds are swollen and inflamed and show marked subungual hyperkeratosis.

Intertrigo

Fig. 3.1.1-5



Itchy and at times malodorous rash typically between fourth and fifth toes due to *Candida* or dermatophyte infection. Often a feature of tinea pedis (athlete's foot).

Chronic candidiasis

Fig. 3.1.1-6



Recurrent candidiasis. Despite repeated antifungal therapy, the patient's nails remained discoloured and pitted after 1 year. There is no evidence of invasive disease.

*Candida* esophagitis

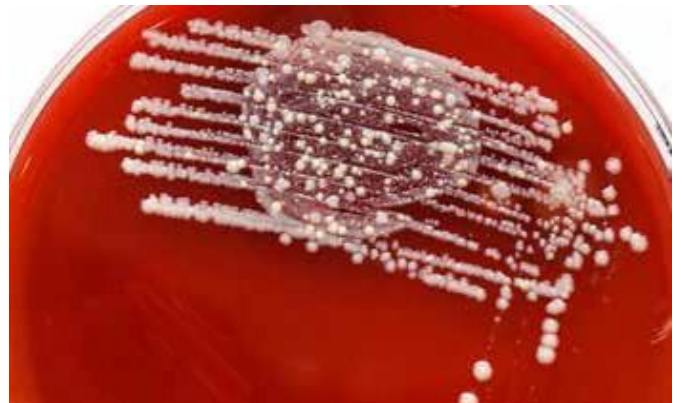
Fig. 3.1.1-7



Characterised by patches of pseudomembranous white slough along the esophageal mucosa that can be easily wiped. Frequently accompanied by

*Candida* otomycosis, culture on SBA

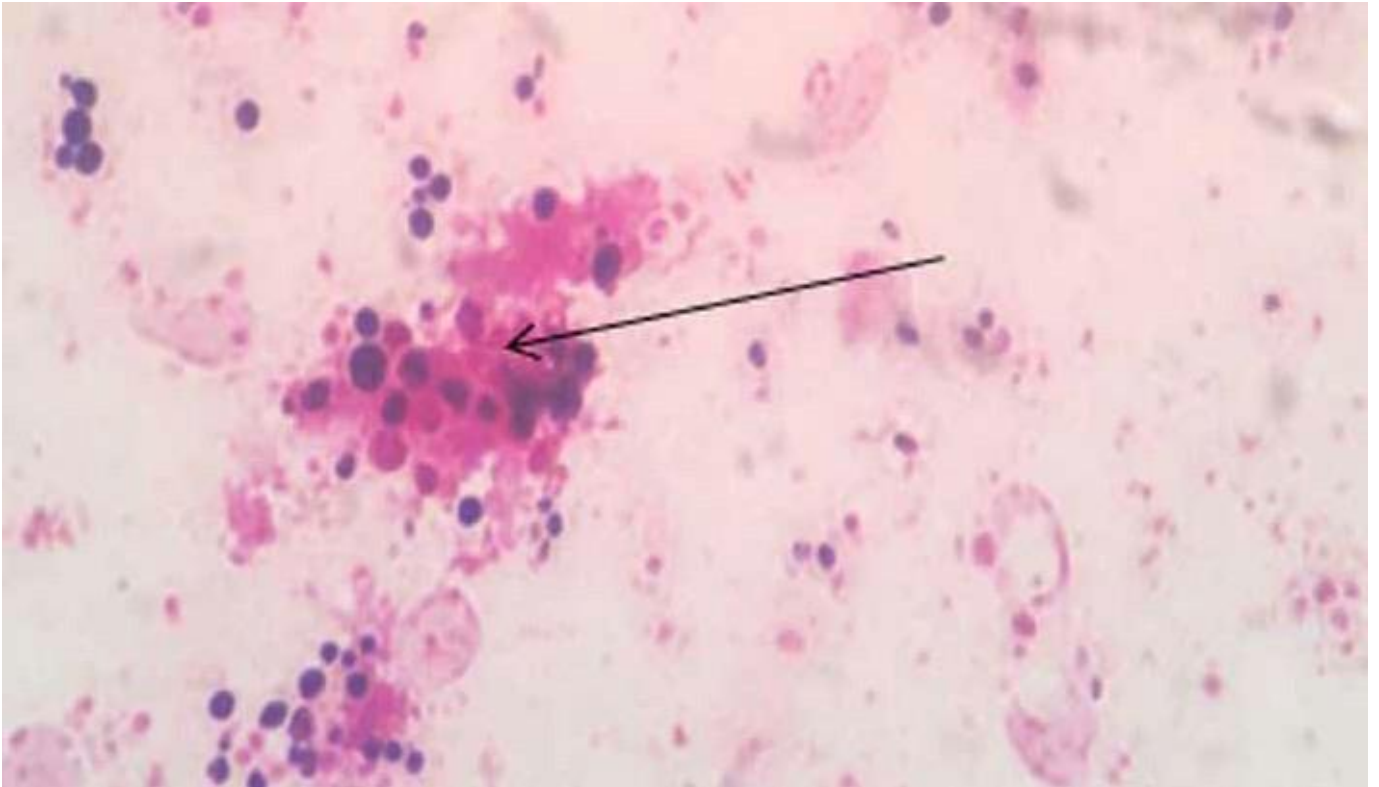
Fig. 3.1.1-8



oral thrush. *Candida* esophagitis is mostly seen in immunocompromised patients. Classic symptoms include dysphagia, odynophagia and weight loss due

to difficulty swallowing.

Culture of external auditory canal swab on blood agar showing white yeast colonies. However, interpret ear swab cultures cautiously as *Candida* is a known skin coloniser as well as an agent of otomycosis.



Pulmonary valve vegetation shows numerous budding yeast cells invading valve tissue. Yeast cells measure 6-8  $\mu\text{m}$  in diameter. (x100)

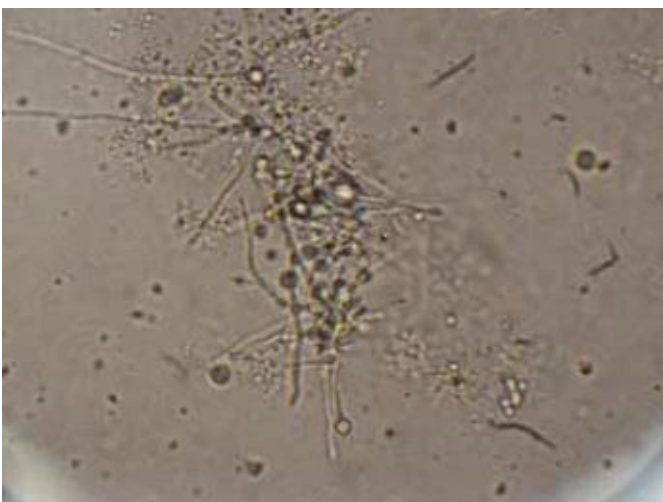
*Candida albicans*

*C. albicans* is a dimorphic fungus that is a skin and gut commensal. Infection results in oral and vaginovaginal candidiasis in immunocompetent hosts, and fatal disseminated infections in immunocompromised patients. *C. albicans* is the most common fungal species isolated from clinical specimens. More recently, it has emerged as a cause of hospital-acquired infections, especially with implantable medical devices where it covers the surface with a biofilm.

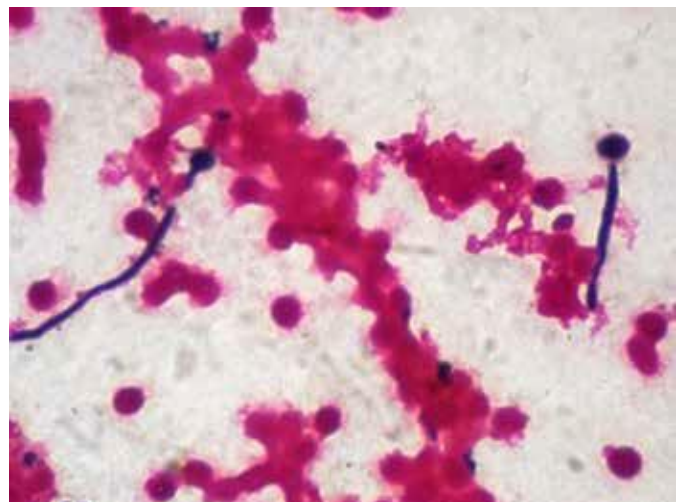
*C. albicans*, 10% KOH smear

Fig. 3.1.1-10

*C. albicans*, Gram stain from blood culture bottle Fig. 3.1.1-11



Oval to subspherical budding yeasts. Presence of abundant pseudohyphae in specimen suggests overgrowth and active infection. (x40)



Sometimes *C. albicans* can give the impression of spherical yeasts. The smear should be examined in several fields before deciding on the shape and morphology of the yeast cells. (x100)

*C. albicans*, culture on SDA

Fig. 3.1.1-12



Cream coloured colonies. Small colony variants in overnight cultures give the impression of mixed growth.

*C. albicans*, culture on chocolate agar

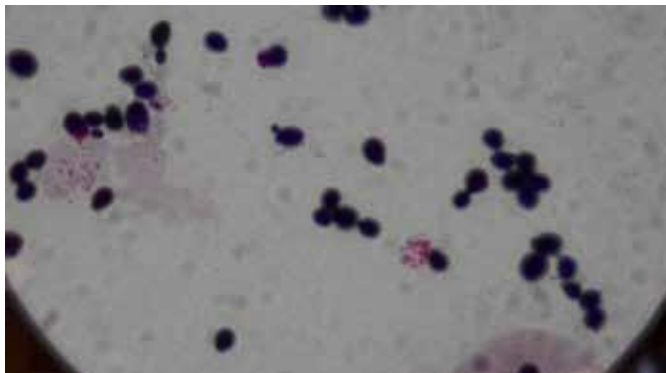
Fig. 3.1.1-13



Glistening creamy colonies sprouting mycelia or “fringes” – typical of *C. albicans*. These fringes may also rarely be seen in *C. tropicalis* colonies. Growth on chocolate agar shows even more prominent fringes or star-shaped colonies.

*C. albicans*, Gram stain

Fig. 3.1.1-14



Ovoid to subspherical budding yeast cells 6-8 µm in size. (x100)

Germ tube test

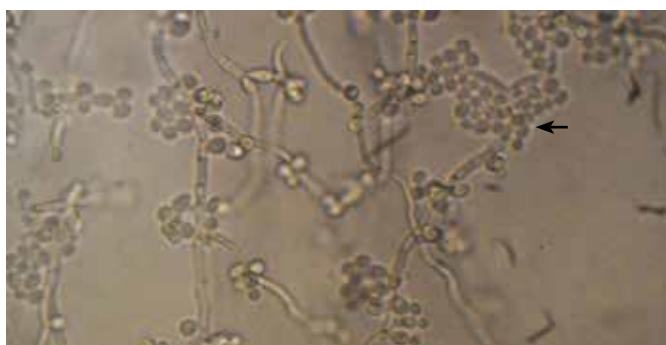
Fig. 3.1.1-15



Confirmatory test to differentiate *C. albicans* from other *Candida* species. *C. albicans* produces tubular outgrowths (germ tubes or true hyphae) as opposed to elongation of a budding yeast (pseudohyphae). It is also seen in *C. dubliniensis*. (x40)

*C. albicans*, microscopy of CMT agar

Fig. 3.1.1-16



On microscopy, pseudohyphae appear as long and slender tubules with clusters of round to oval blastoconidia (arrow). The presence of terminal double-walled round chlamydoconidia is diagnostic of

Susceptibility testing (disc diffusion, see chapter 4 for details)

Fig. 3.1.1-17



*C. albicans*. These chlamydoconidia may also be seen in *C. dubliniensis* but they are usually found in clusters and are more abundant as compared to *C. albicans*. (x40)

Most strains of *C. albicans* are susceptible to triazoles, echinocandins and amphotericin. However, due to emerging resistance, especially against triazoles and echinocandins, most labs perform antifungal susceptibilities. Clinical breakpoints for zone diameters (disc diffusion) and broth microdilution are now available in both EUCAST and CLSI References.

*Candida tropicalis*

*C. tropicalis* is part of skin and gut flora and frequently results in disseminated invasive infections in neutropenic and cancer patients.

*C. tropicalis*, culture on chocolate agar

Fig. 3.1.1-18

*C. tropicalis*, culture on SBA

Fig. 3.1.1-19



At 24-48 hours, small and large colony variants are seen. Smaller colonies are usually dome-shaped while the larger ones are dull white, dry and slightly elevated.

Similar to chocolate agar, culture in blood agar has both small and large colony variants which become less prominent after 72 hours (3 days). The colonies are initially non-haemolytic, dry and elevated but turn dome-shaped after the third day.

*C. tropicalis*, culture on SDA

Fig. 3.1.1-20

*C. tropicalis*, culture on BiGGY agar

Fig. 3.1.1-21



Day 4. Colonies do not glisten and are umbonated, with radial grooves around the edges only.

Colonies are dry, light to dark brown, with a silver metallic sheen, most prominent on the primary streak. They are also umbonated and have radial grooves around the edges.

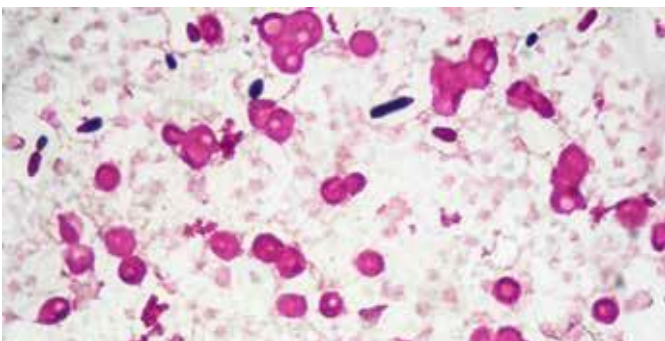
*C. tropicalis*, Gram stain from

positive blood culture bottle

Fig. 3.1.1-22

*C. tropicalis*, microscopy of CMT agar

Fig. 3.1.1-23



Yeast size is around 4-6  $\mu\text{m}$ , almost the same size as RBCs. Shape of cells is more oval than round. Pseudohyphae are frequently seen on smear made from clinical specimens. (x100)

Long slender pseudohyphae with elongated blastoconidia, arising successively from older blastoconidia. This gives the appearance of a rabbit head with long ears. (x40)

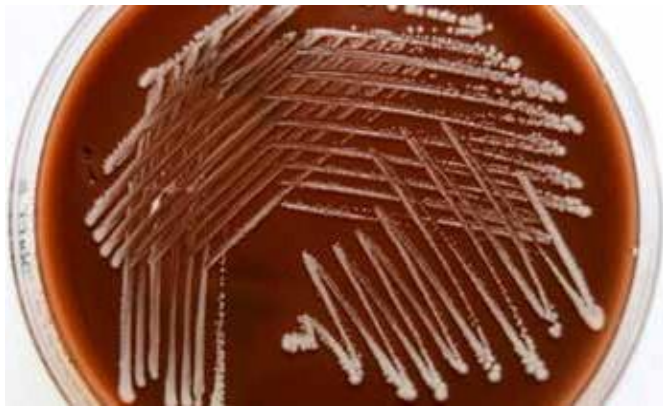


## *Candida parapsilosis*

*C. parapsilosis* is both a human commensal and an environmental pathogen, and is usually implicated in nail infections. It can result in a range of invasive diseases including endocarditis, endophthalmitis, meningitis and peritonitis.

*C. parapsilosis*, culture on chocolate agar

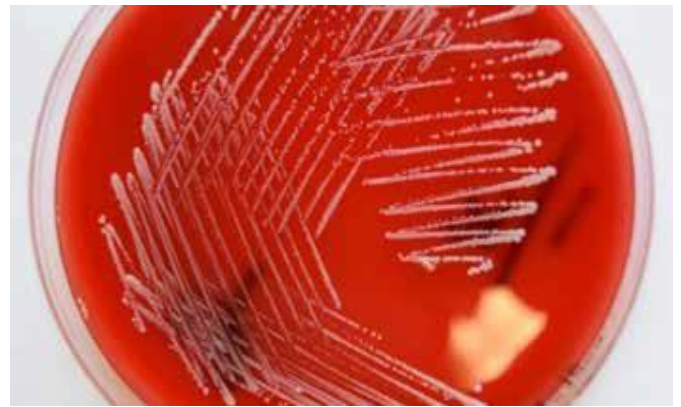
Fig. 3.1.1-24



Small cream-coloured dome-shaped glistening colonies appear after 48 hours of incubation.

*C. parapsilosis*, culture on SBA

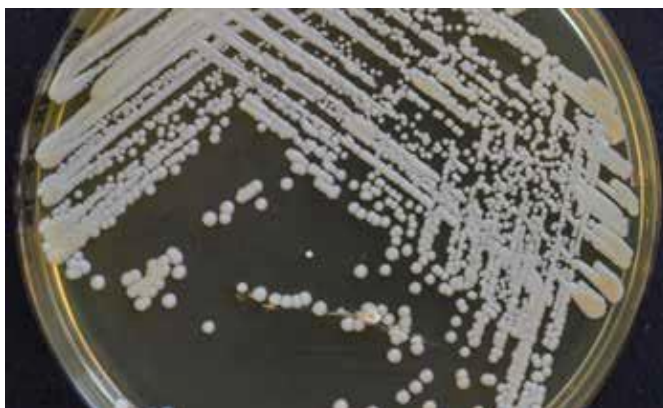
Fig. 3.1.1-25



Colonies are non-haemolytic dome-shaped glistening later curling up and becoming lacy. Prominent after 48 hours.

*C. parapsilosis*, culture on SDA

Fig. 3.1.1-26



Colonies are small and glistening at 48 hours but later wrinkle and appear lacy.

*C. parapsilosis*, culture on BiGGY agar

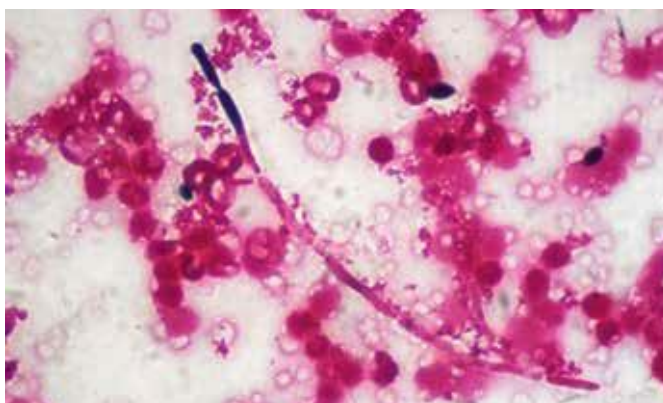
Fig. 3.1.1-27



Colonies are light brown with a purple or lilac tinge, sometimes bordering on grey. Later, colonies curl and become lacy.

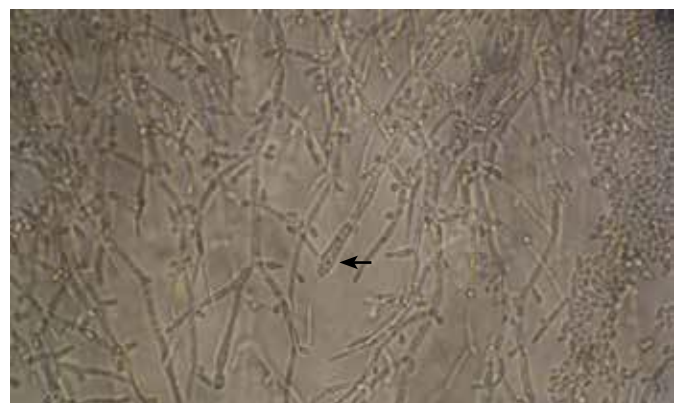
*C. parapsilosis*, Gram stain from blood culture

Fig. 3.1.1-28



*C. parapsilosis*, microscopy of CMT agar

Fig. 3.1.1-29



Yeasts are oval and 4-6  $\mu\text{m}$  in diameter, approximately the same size as red blood cells. Pseudohyphae are less common in clinical specimens. (x100)

Short slender delicate pseudohyphae with elongated blastoconidia, more tapered than *C. tropicalis*. Some swell up to form giant (balloon) cells (arrow). (x40)

## *Candida glabrata*

*C. glabrata* is both a commensal and environmental pathogen. It can cause mucosal surface infections (oropharyngeal, esophageal, and vaginal candidiasis) and is now increasingly isolated in disseminated fungemia.

*C. glabrata*, culture on chocolate agar

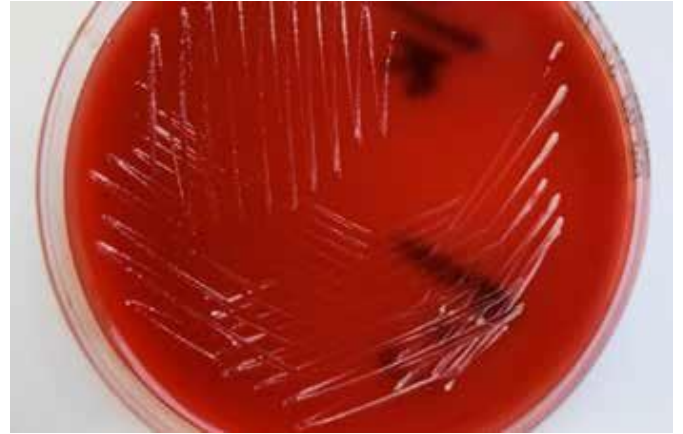
Fig. 3.1.1-30

*C. glabrata*, culture on SBA

Fig. 3.1.1-31



Tiny white glistening colonies appear at 48 hours. Texture is not creamy, more like bacteria.



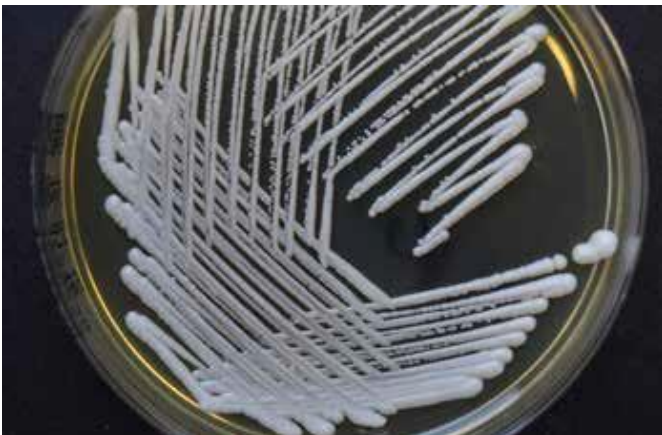
Similar to chocolate agar, tiny white non-haemolytic colonies.

*C. glabrata*, culture on SDA

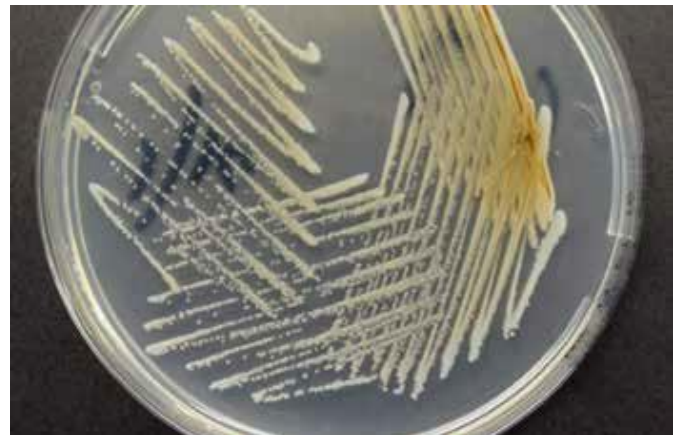
Fig. 3.1.1-32

*C. glabrata*, culture on BiGGY agar

Fig. 3.1.1-33



Colonies are small, glistening at 48 hours but older colonies wrinkle up and appear lacy.



Colonies appear off-white.

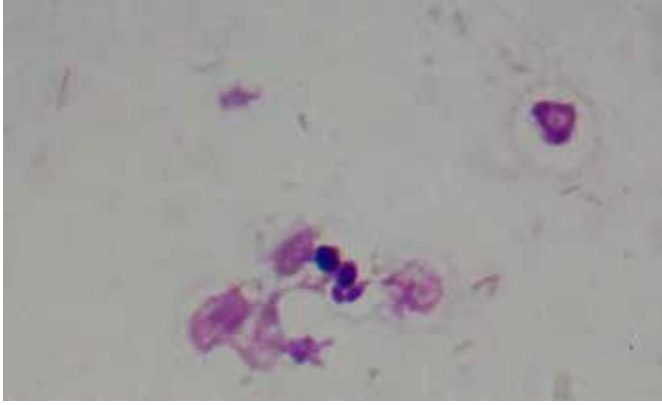
*C. glabrata*, Gram stain from positive

blood culture bottle

Fig. 3.1.1-34

*C. glabrata*, microscopy of CMT agar

Fig. 3.1.1-35



Yeasts are oval and smaller than red blood cells, approximately 2-4  $\mu\text{m}$  in diameter. Pseudohyphae are never seen. (x100)



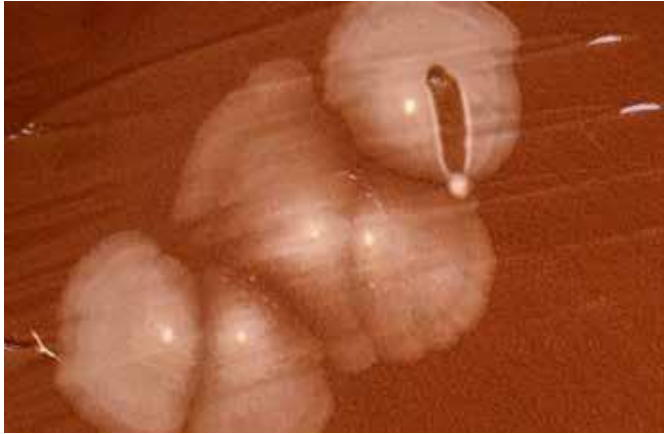
Yeast cells are small and oval. Pseudohyphae absent. (x10)

*Candida krusei*

*C. krusei* results in nosocomial disseminated infections in patients with haematological malignancies or in immunosuppressed states.

*C. krusei*, culture on chocolate agar

Fig. 3.1.1-36



Colonies are large flat, dry and grey. They resemble the large spreading colonies of *bacillus*.

*C. krusei*, culture on SBA

Fig. 3.1.1-37



Non-haemolytic flat, dry colonies, spreading over the agar surface.

*C. krusei*, culture on SDA

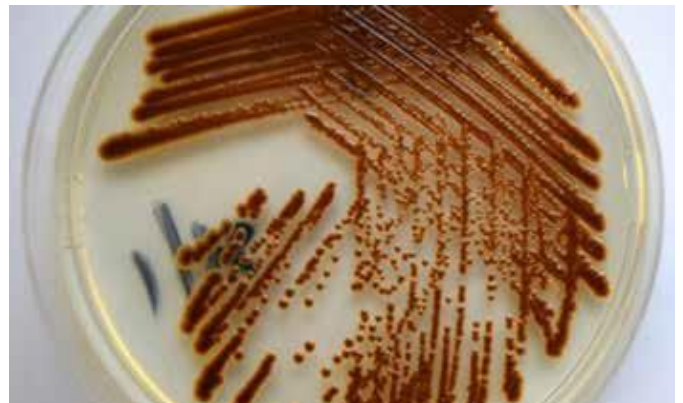
Fig. 3.1.1-38



Colonies are dry, almond-shaped and spreading across the plate.

*C. krusei*, culture on BiGGY agar

Fig. 3.1.1-39



Colonies are dark brown with a brown diffusible pigment and a silver metallic sheen.

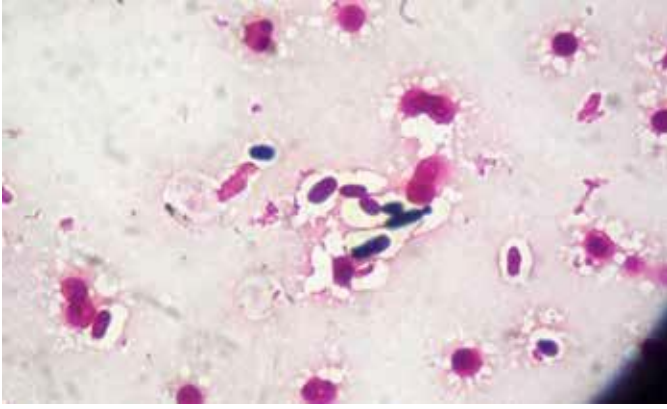
*C. krusei*, Gram stain on positive

blood culture sample

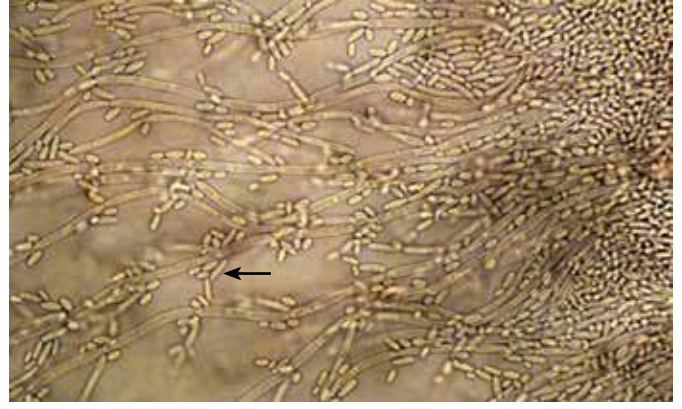
Fig. 3.1.1-40

*C. krusei*, microscopy of CMT agar

Fig. 3.1.1-41



Yeast form is 4-6  $\mu\text{m}$ , almost the same size as RBCs. Shape of cells is oval to elliptical. Pseudohyphae may be seen. (x100)



Long slender pseudohyphae with elongated blastoconidia, aligned both parallel and perpendicular to the axis of the pseudohyphae, giving a cross-matchstick arrangement (arrow). (x40)

*Candida lusitaniae*

*C. lusitaniae* is a gut commensal that is a very rare cause of invasive infections in patients with prolonged neutropenia, bone marrow transplantation or on high-dose cytoreductive chemotherapy.

*C. lusitaniae*, culture on chocolate agar

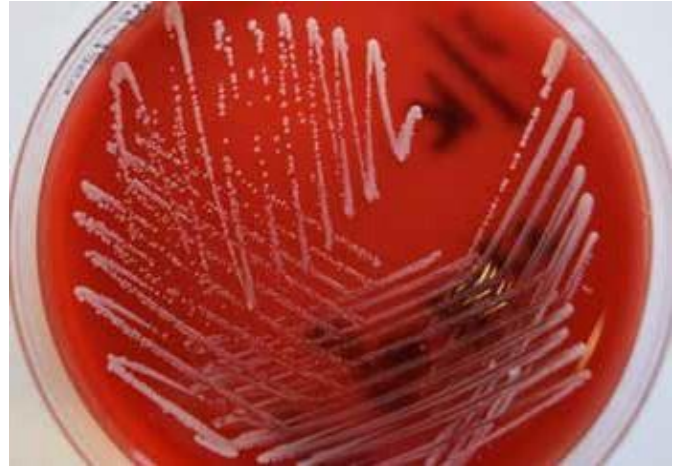
Fig. 3.1.1-42

*C. lusitaniae*, culture on SBA

Fig. 3.1.1-43



Small white glistening dome-shaped colonies.



Similar to chocolate agar, the colonies are white, small, glistening and dome-shaped. Like most yeasts, colonies are non-haemolytic.

*C. lusitaniae*, culture on SDA

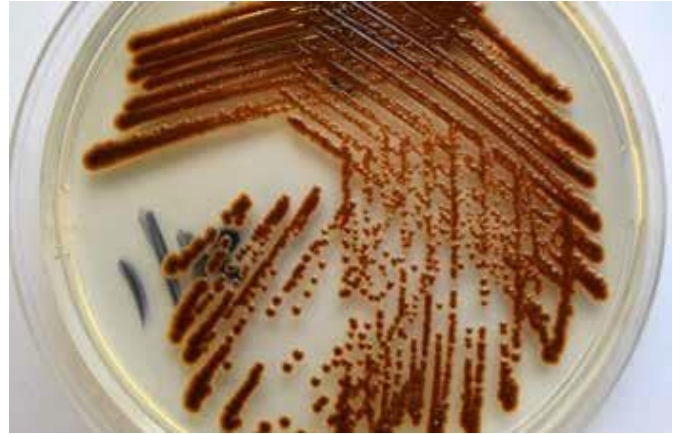
Fig. 3.1.1-44

*C. lusitaniae*, culture on SDA

Fig. 3.1.1-45



White glistening dome-shaped colonies.



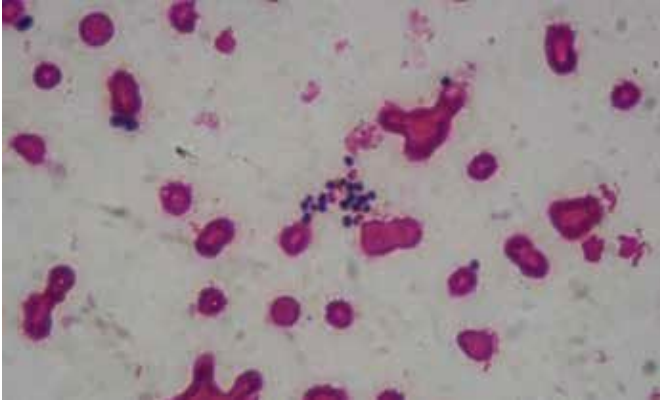
Uniformly coloured dark brown glistening colonies giving the impression of tempered chocolate.

*C. lusitaniae*, Gram stain

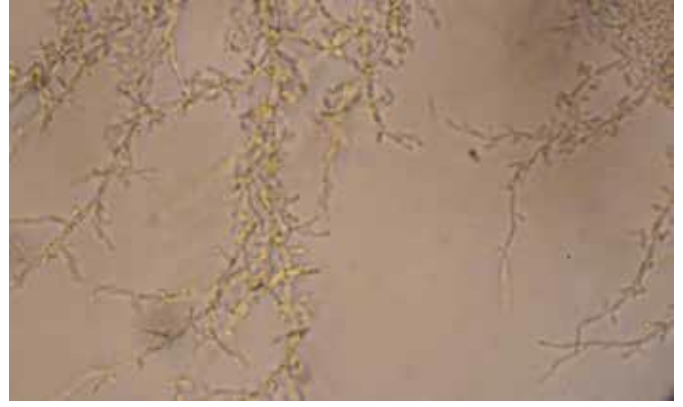
Fig. 3.1.1-46

*C. lusitaniae*, microscopy of CMT agar

Fig. 3.1.1-47



Small oval budding yeast cells, 2-4  $\mu\text{m}$  in size. Most do not form pseudohyphae in specimen. (x100)



Short curved, branched pseudohyphae, with elongated blastoconidia. (x40)



## *Candida guilliermondii*

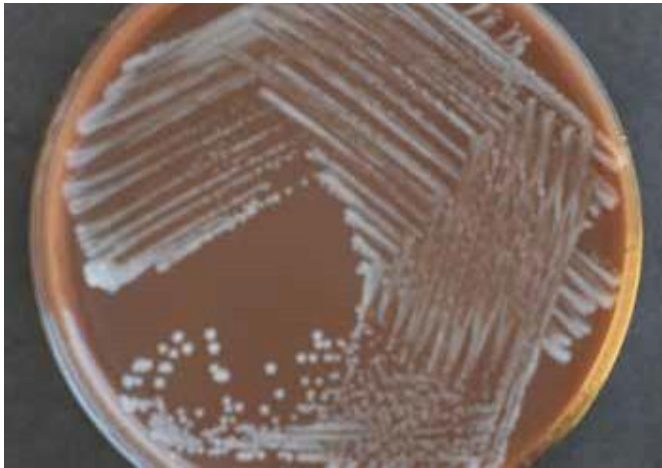
*C. guilliermondii* is an uncommon skin commensal as well as an environmental pathogen that is associated with onychomycosis and superficial cutaneous infections. Rarely seen as a cause of invasive fungal infection.

*C. guilliermondii*, culture on chocolate agar

Fig. 3.1.1-48

*C. guilliermondii*, culture on SBA

Fig. 3.1.1-49



Colony morphology is quite similar to *C. lusitanae*. Small white glistening dome-shaped colonies.



Growth similar to chocolate agar. Small white glistening dome-shaped non-haemolytic colonies.

*C. guilliermondii*, culture on SDA

Fig. 3.1.1-50

*C. guilliermondii*, culture on BIGGY agar

Fig. 3.1.1-51



Small white glistening dome-shaped colonies.



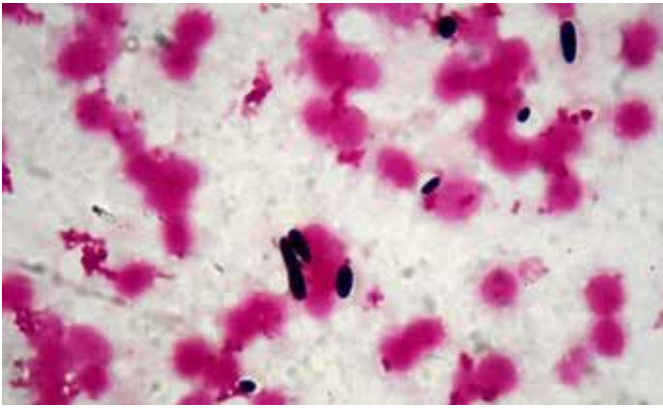
Uniformly coloured brown glistening colonies.

*C. guilliermondii*, Gram stain

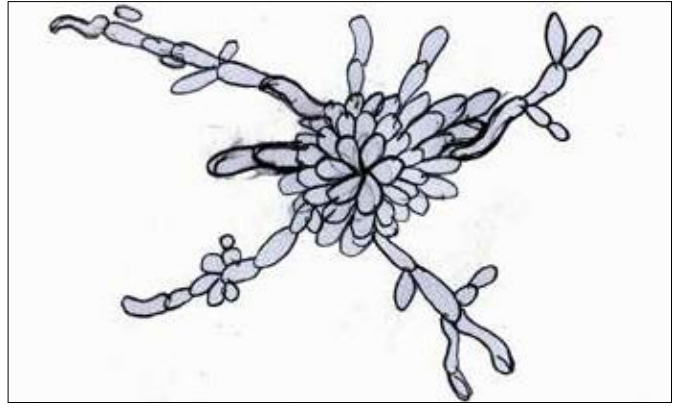
Fig. 3.1.1-52

*C. guilliermondii*, microscopy of CMT agar

Fig. 3.1.1-53



Small budding yeast cells oval to elliptical in shape. Pseudohyphae usually not seen in clinical specimens. (x100)



Small clusters of blastoconidia giving rise to short pseudohyphae. Yeast cells are oval to elliptical and 2-3  $\mu\text{m}$  in size. (x40)

*Candida auris*

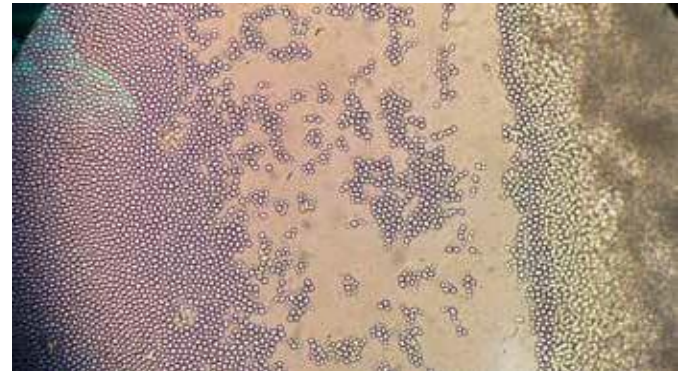
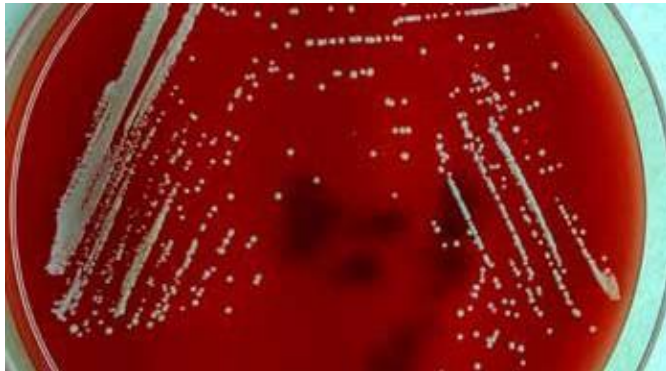
*C. auris* has recently emerged across the globe as a nosocomial pathogenic *Candida* species closely related to *Candida haemulonii*. It was first identified as a separate species in a report from South Korea in 2008, and there have been reports of outbreaks in Pakistan, Venezuela, South Africa and United Kingdom. The most alarming feature of this organism is the ability to develop multi-drug resistance, that is, resistance against two or more classes of antifungal agents, including amphotericin. Due to resistance to various group of antifungal drugs, morbidity and mortality is higher than other *Candida* infections.

*C. auris*, culture on SBA

Fig. 3.1.1-54

*C. auris*, microscopy of CMT agar

Fig. 3.1.1-55



Small white dome-shaped non-haemolytic colonies with a butyrous texture.

Microscopically, the cells are small to medium sized oval budding yeasts not forming any pseudohyphae. (x40)

*C. auris*, culture on BiGGY agar

Fig. 3.1.1-56

*C. auris*, culture on BiGGY agar

Fig. 3.1.1-57



Close-up view shows small to medium oval yeasts.

Light brown coloured colonies with a white margin.

Susceptibility testing

Fig. 3.1.1-58



Disc diffusion method. *C. auris* is considered inherently resistant to fluconazole (arrow) and is known to acquire resistance against several antifungal classes, including amphotericin and



