

0605-1 *Candida albicans*

HISTORY This sample was sent as a blood culture isolate.

CMPT QA: Pure growth of 4+ *Candida albicans*, viable for 33 days.

Reference Laboratory: Growth of *Candida albicans* confirmed.

All laboratories correctly identified *Candida albicans*. Media and methods reported are shown in Tables 1 and 2. One laboratory also reported using the phenol oxidase and urease tests to rule out *Cryptococcus*.

Table 1. 0605-1 Media used by laboratories to isolate *C. albicans*.

| Media | No. of labs |
|---|-------------|
| Sabouraud (used with 1 or more media listed below) | 4 |
| BHI w/ sheep blood; w/ chloramphenicol, gentamicin;w/ cycloheximide | 6 |
| Inhibitory mould agar (IMA) w/ chloramphenicol, 30°C/25°C/(37°C [1]) | 5 |
| Sabhi, Littman – this combo used by 1 lab (& SAB) | 1 |
| Mycosel, Candiselect 4, potato dextrose agar (PDA) – this combo used by 1 lab | 1 |

Table 2. 0605-1 Methods reported by laboratories to identify *C. albicans*.

| Methods | No. of labs |
|--------------------------|-------------|
| Germ tube (positive) | 4 |
| Cornmeal agar | 2 |
| CHROMagar <i>Candida</i> | 3 |
| Vitek 2 | 1 |
| Auxacolor | 1 |
| API 20C AUX | 1 |

IDENTIFICATION¹ There are more than 100 species of *Candida* (yeast) in nature, but only a few species are recognized causes of disease in humans. *Candida albicans* is the most common medically significant *Candida* species identified. *Candida stellatoidea*, once accepted to be a separate *Candida* species, is now classified as a subspecies of *Candida albicans* which differs from *Candida albicans* by not assimilating sucrose and not being resistant to cycloheximide^{2,3,4}.

Isolation from Blood Maximum blood volumes should be collected². In automated blood culture systems a 5-day duration of incubation is the current standard for the most common *Candida* species. Data is not available for the

detection times necessary for *C. glabrata* and *Cryptococcus neoformans* (p. 187 ref. 2.). BACTEC Myco/F-Lytic® medium is not more sensitive, than conventional blood culture media, but it may reduce time to detection.

Colony morphology^{2,3} On solid media (e.g., Sabouraud) *Candida albicans* rapidly matures in 1 to 3 days as white or cream, smooth and glistening or occasionally dull and rough colonies, but these features are not really helpful in distinguishing it from other *Candida* spp. When grown on enriched agar (blood and chocolate) small extensions ('feet') may be seen around the border of the colony. Presumptive identification of *C. albicans* may be made by observing growth on commercially available chromogenic media, which is especially useful for detecting mixed yeast infections in blood².

Microscopic morphology A Gram stain of a colony grown on routine primary media (e.g., Sabouraud, BAP, chocolate) reveals round to oval budding yeast-like cells or blastoconidia, measuring 3.5-7 by 4-8 µm that retain crystal violet. On cornmeal-Tween 80 agar incubated at 25°C for 72 hours, pseudohyphae (some true hyphae may be present) with clusters of round blastoconidia at the septa may be easily found. *Candida albicans*, together with *Candida dubliniensis*, are the two *Candida* spp. that produce large thick-walled asexual spores called chlamydoconidia* (chlamydospores). In *C. albicans* these terminal vesicles are usually single, while isolates of *C. dubliniensis* will produce them in pairs, triplets, and clusters². They are most likely seen near the edge of the coverslip, but are inhibited if the medium is incubated at 30-37°C. Pseudohyphae without chlamydoconidia indicate another *Candida* spp.

Tests^{2,3} The serum **germ tube test** is a rapid "presumptive test" for *C. albicans*. A light inoculum of cultured yeast is incubated in bovine serum for 2-3 hours at 37°C. The test is positive if there are short hyphae without a constriction where the hypha joins the parent cell. Not all *C. albicans* isolates are germ tube positive and false-positive results are a possibility, especially with *C. tropicalis*. Carbohydrate assimilation tests are commercially available. Rapid identification tests based on preformed enzymes are particularly good for confirmation of a germ-tube positive organism as *C. albicans*, but *C. dubliniensis* is positive too. However, unlike *C. albicans*, *C. dubliniensis* either will not grow or grows very poorly at 42-45°C and has unusual carbohydrate assimilation patterns⁵.

All *Candida* isolated from invasive sites need to be biochemically confirmed (speciated) either in-house or by a reference laboratory.

CLINICAL SIGNIFICANCE Isolation of yeast from a blood culture is clinically relevant and, as mentioned above, all yeast should be identified to the species level¹. Currently, *Candida* species are the fourth most

commonly isolated organism from blood cultures, but this number may under-represent true cases of candidemia since retrospective studies have shown that blood cultures are positive in less than 50% of patients with autopsy-proven invasive candidiasis. The most basic form of invasive candidiasis is candidemia. Actually, it is likely thought that all other forms of invasive candidiasis follow an episode of candidemia⁴.

Prognosis depends on several factors, such as the site of infection, the degree and type of immunosuppression, and the rapidity of diagnosis and treatment. Management of serious and life-threatening invasive candidiasis remains severely hampered by delays in diagnosis and the lack of reliable diagnostic methods that allow detection of both fungemia and tissue invasion by *Candida* species. The longer the delay to initiate antifungal therapy, the higher the morbidity and mortality associated with candidemia and disseminated candidiasis.

TREATMENT Susceptibility testing should be performed either in-house or by forwarding the isolate to a reference laboratory¹.

A critical component in the management of candidemia and disseminated candidiasis is the removal of the focus of infection, e.g., Foley catheters. Treatment includes amphotericin B, but this *may* change with the advent of newer azoles such as voriconazole. Dosing of fluconazole is highly controversial and even *C. albicans* may be resistant.

Increasingly, laboratories are performing antifungal susceptibilities.

REFERENCES

1. CMPT critique 0509-1 Blood culture: *Candida glabrata*. September 2005.
2. Hazen KC, Howell SA. 2003. p. 1693-1711. *Candida*, *Cryptococcus*, and other yeasts of medical importance. In PR Murray et al. (ed.) *Manual of Clinical Microbiology*. Ch. 114. 8th ed. ASM Press. Washington, DC. 2003.
3. Larone DH. 2002. *Medically Important Fungi*. 4th ed. ASM Press. Washington, DC.
4. <http://www.doctorfungus.org/mycoses/human/CANDIDA/Candidemia.htm>
5. http://www.mycology.adelaide.edu.au/Fungal_Descriptions/Yeasts/Candida/index.html

NOTE^{3,4,5}

***Chlamydoconidium (pl. chlamydoconidia):** A rounded, enlarged conidium that usually has a thickened cell wall and contains stored food functioning as a survival propagule. It is larger in diameter than the hypha and may be located at the end or along the hypha either singly or in pairs. It does not readily separate from the hypha.

Chlamyospore: A resting conidium, formed as the enlargement of a hyphal cell; the term is technically incorrect, although commonly used (the 'correct' term is actually a chlamydoconidium).