

Candidiasis



Microbiology's Team

Editing File
Summary



Color index

- Girls' slides
- Main content
- Important
- Boys' slides
- Extra
- Drs' notes

Objectives:

- Acquire the basic knowledge about candida as a pathogen
- Know the main infections caused by candida species
- Identify the clinical settings of such infections
- Know the laboratory diagnosis, and treatment of these infections

Candida

Introduction

- Candida is a unicellular **yeast** fungus.
- It is imperfect reproducing by budding.

Species

- There are many species of Candida (>150)
- The common species are:

Candida albicans (Most common), *C. parapsilosis*, *C. tropicalis*, *C. glabrata*, *C. krusei*

Human commensal



Oral cavity



Skin



Gastrointestinal tract

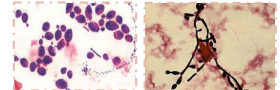


Genitourinary tracts

Morphology ⁽¹⁾

Microscopy

Budding yeast cells and **Pseudohyphae**.



Culture

Creamy colony, fast growing on Sabouraud Dextrose agar (SDA), Blood agar (48 hr)



Candidiasis (The disease)

Definition	<ul style="list-style-type: none"> ○ Any infection caused by any species of the yeast fungus Candida. ○ The most common invasive fungal infections in immunocompromised patients ○ 4th most common cause of nosocomial^[2] bloodstream infection 		
Mode of transmission	<p>1. Endogenous:</p> <ol style="list-style-type: none"> Colonization precedes infection Antibiotic suppression of normal flora, fungal overgrowth <p>2. Exogenous</p>		
Pathogenesis	<p>Opportunistic Fungal infections:</p> <ul style="list-style-type: none"> ○ Alteration in : Immunity , Normal physiology , Normal flora ○ Damage in the barriers ^[3] 		
Clinical spectrum of disease	Mucous membrane infections	Cutaneous infections	Other diseases
	<ul style="list-style-type: none"> ○ Thrush (oropharyngeal) ○ Esophagitis ○ Vaginitis 	<ul style="list-style-type: none"> ○ Paronychia (skin around nail bed) ○ Onychomycosis (nails) ○ Diaper rash ○ Chronic mucocutaneous candidiasis ○ children with T-cell abnormality 	<ul style="list-style-type: none"> ○ Urinary tract infection ○ Candidemia which may disseminate (systemic, invasive) to: Endophthalmitis (eye), Liver and spleen, Kidneys, Skin, Brain, Lungs and Bone

^[1] :Almost all candida have the same morphology, so you can't differentiate candida species by morphology.

^[2] : hospital acquired

^[3] : skin injury e.g. catheter line insertion site or sites of major surgeries

Mucocutaneous infections

Oropharyngeal Candidiasis

Oral thrush:

- White or grey Pseudomembranous patches on oral surfaces especially tongue with underlying erythema.
- Common in neonates ,infants , elderly, and In immunocompromised hosts ,e.g. AIDS.



Oral thrush

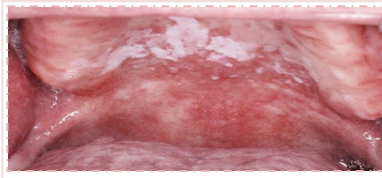
Forms of oral candidiasis

Erythematous Form



Sometimes we don't see white patches, we see something called erythematous candidiasis(redness and inflammation). It usually occurs in old people using dentures.

Pseudomembranous Forms



pseudomembranous-erythematous form.



pseudomembranous form.

Hyperplastic Form



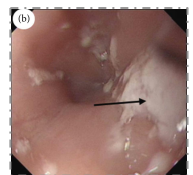
White patches but difficult to remove, that was mistaken for leukoplakia

Vulvovaginitis

- Common in pregnancy, diabetics, use of contraceptives.
- Thick discharge, itching irritation .
- Lesion appear as white patches on vaginal mucosa

Esophagitis

- The symptoms of esophageal thrush include: white lesions on the lining of your esophagus that may look like cottage cheese and may bleed if they're scraped, pain or discomfort when swallowing, dry mouth And difficulty swallowing.
- It is important to differentiate esophageal candidiasis from other forms of infectious esophagitis such as CMV, HSV, GERD and medication-induced esophagitis.



Pulmonary & Cutaneous candidiasis

Cutaneous infections

Intertriginous candidiasis

- Infections of skin folds eg. axilla, buttock, toe web, under breast.
- Erythematous lesion, dry or moist or whitish accompanied by itching and burning.



Nail infection

- Onychomycosis and paronychia



Diaper rash

- Candidal diaper dermatitis is the second most common type of diaper dermatitis
- commonly appears in the genitals and diaper area, particularly the deep folds, Erythema and/or erosions may be present



Chronic mucocutaneous candidiasis

- Persistent or recurrent candida infection due to inherited T-cell defects or IL-17 deficiency (more susceptible to candida infections)



Pulmonary Candidiasis

Pathogenesis	<ul style="list-style-type: none"> ○ Primary pneumonia is less common and could be a result of Aspiration ○ Secondary pneumonia commonly seen with hematogenous candidiasis <ul style="list-style-type: none"> ○ Immunocompromised patients
Diagnosis	<ul style="list-style-type: none"> ○ Isolation of Candida from sputum^[1], Bronchoalveolar lavage (BAL) is not always significant <ul style="list-style-type: none"> ○ Clinical features ○ Radiology ○ Other Lab investigations

^[1] : Isolation of candida from respiratory infections does not necessarily mean candida infection, because candida is usually found in the normal flora of the mouth..

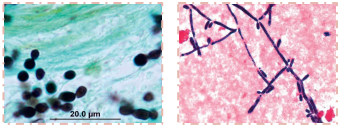

Candidemia & lab diagnosis

Candidemia

Pathogenesis	<ul style="list-style-type: none"> ○ Increased colonization (endogenous or exogenous factors) ○ Damage in host barriers by catheters, trauma, surgery ○ Immunosuppression ○ Central venous catheters (CVC) 																																																																																																										
Organ involvement	Disseminated candidiasis (involvement of any organ) <ul style="list-style-type: none"> ○ Septic shock ○ Meningitis ○ Ocular involvement (retinitis) 																																																																																																										
Clinical manifestation	Fever could be the only clinical manifestation																																																																																																										
Epidemiology	Candida is the fourth in causing nosocomial bloodstream infections (BSI) <table border="1" data-bbox="1098 808 1458 994"> <thead> <tr> <th rowspan="2">Rank</th> <th rowspan="2">Pathogen</th> <th rowspan="2">BSI per 1000 admissions</th> <th colspan="4">% BSI</th> <th colspan="3">% Crude Mortality</th> </tr> <tr> <th>Total (n=20,978)</th> <th>ICU (n=10,510)</th> <th>Non-ICU (n=10,468)</th> <th>Total</th> <th>ICU</th> <th>Non-ICU</th> </tr> </thead> <tbody> <tr> <td>1.</td> <td>CoNS</td> <td>15.8</td> <td>31.3</td> <td>35.9</td> <td>28.6</td> <td>20.7</td> <td>25.7</td> <td>13.8</td> </tr> <tr> <td>2.</td> <td>S aureus</td> <td>10.3</td> <td>20.2</td> <td>16.8</td> <td>23.7</td> <td>25.4</td> <td>24.4</td> <td>18.9</td> </tr> <tr> <td>3.</td> <td>Enterococcus spp.</td> <td>4.8</td> <td>9.4</td> <td>9.6</td> <td>9.0</td> <td>33.9</td> <td>40.0</td> <td>24.0</td> </tr> <tr> <td>4.</td> <td>Candida spp.</td> <td>4.6</td> <td>9.0</td> <td>10.1</td> <td>7.9</td> <td>29.2</td> <td>47.1</td> <td>29.0</td> </tr> <tr> <td>5.</td> <td>E coli</td> <td>2.8</td> <td>5.6</td> <td>3.7</td> <td>7.6</td> <td>22.4</td> <td>32.3</td> <td>16.9</td> </tr> <tr> <td>6.</td> <td>Klebsiella spp.</td> <td>2.4</td> <td>4.8</td> <td>4.0</td> <td>5.5</td> <td>27.6</td> <td>37.4</td> <td>20.3</td> </tr> <tr> <td>7.</td> <td>P.aeruginosa</td> <td>2.1</td> <td>4.3</td> <td>4.7</td> <td>3.8</td> <td>38.7</td> <td>47.9</td> <td>27.6</td> </tr> <tr> <td>8.</td> <td>Enterobacter spp.</td> <td>1.9</td> <td>3.9</td> <td>4.7</td> <td>3.1</td> <td>26.7</td> <td>32.5</td> <td>19.0</td> </tr> <tr> <td>9.</td> <td>Serratia spp.</td> <td>0.9</td> <td>1.7</td> <td>2.1</td> <td>1.3</td> <td>27.4</td> <td>33.9</td> <td>17.1</td> </tr> <tr> <td>10.</td> <td>A.baumannii</td> <td>0.6</td> <td>1.3</td> <td>1.6</td> <td>0.9</td> <td>34.0</td> <td>43.4</td> <td>16.3</td> </tr> </tbody> </table>	Rank	Pathogen	BSI per 1000 admissions	% BSI				% Crude Mortality			Total (n=20,978)	ICU (n=10,510)	Non-ICU (n=10,468)	Total	ICU	Non-ICU	1.	CoNS	15.8	31.3	35.9	28.6	20.7	25.7	13.8	2.	S aureus	10.3	20.2	16.8	23.7	25.4	24.4	18.9	3.	Enterococcus spp.	4.8	9.4	9.6	9.0	33.9	40.0	24.0	4.	Candida spp.	4.6	9.0	10.1	7.9	29.2	47.1	29.0	5.	E coli	2.8	5.6	3.7	7.6	22.4	32.3	16.9	6.	Klebsiella spp.	2.4	4.8	4.0	5.5	27.6	37.4	20.3	7.	P.aeruginosa	2.1	4.3	4.7	3.8	38.7	47.9	27.6	8.	Enterobacter spp.	1.9	3.9	4.7	3.1	26.7	32.5	19.0	9.	Serratia spp.	0.9	1.7	2.1	1.3	27.4	33.9	17.1	10.	A.baumannii	0.6	1.3	1.6	0.9	34.0	43.4	16.3
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Lab diagnosis

- **Specimen:** depend on site of infection. (Swabs, Urine, Blood, Respiratory specimens, CSF, Blood)

Direct Microscopy	Gram stain, KOH ^[1] , Giemsa, GMS ^[2] , or PAS ^[3] stained smears. Budding yeast cells (2 cells attached to each other) and pseudohyphae will be seen in stained smear or KOH. 
Media Culture	Media: SDA ^[4] & Blood agar at 37°C, Creamy moist colonies in 24-48 hours. C. albicans Morphology on Sabouraud Agar : Creamy white yeast, may be dull, dry irregular and heaped up, glabrous and tough 
Blood culture	USES: Detection of circulating microorganisms in blood DESCRIPTION: Different types of blood culture bottles and blood volumes required Two sets of cultures before starting antibiotics is ideal to exclude sample contamination
Serology	Patient serum Test for Antigen, e.g. Mannan antigen using ELISA Test for Antibodies e.g. Mannan antibodies
PCR	Detect the nucleic acid (DNA) of the fungi

[1] : KOH = potassium hydroxide stain

[2] : GMS = Grocott methenamine silver stain

[3] : PAS = Periodic acid-Schiff (PAS) stain

[4] : SDA = Sabouraud dextrose agar

lab diagnosis

Laboratory diagnosis of yeast Determining candida species

Because *C. albicans* is the most common species to cause infection
The following tests are used to identify *C. albicans*:

Germ tube test: ^[1]

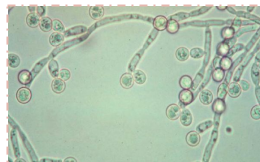
Formation of germ tube when cultured in serum at 37°C.

Differentiates *C. Albicans* **ONLY**



Corn meal Agar:

Chlamyospore production in corn meal Agar



Cycloheximide:

Resistance to 500 µg/ml Cycloheximide

If these 3 are positive this yeast is *C. albicans*,
If negative then it could be any other yeast, **we can differentiate all candida species by:**

Carbohydrate assimilations and fermentation:

Commercial kits available for this like: API 20C, API 32C

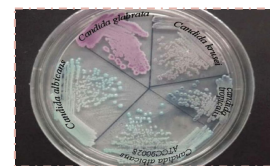


Culture on Chromogenic Media:

(CHROMagar™ Candida)

Chromagar: producing green pigmented colonies on specially designed medium to **speciate certain yeasts based on color they produce**

Main advantage is that it gives different colors for each species.



^[1]: We add the yeast to serum, and keep the sample in the incubator for 2hr and 30 min, only candida albicans will germinate and produce germ tubes.

Treatment

<p>Oropharyngeal</p>	<ul style="list-style-type: none"> ○ Topical Nystatin suspension ○ Clotrimazole troches ○ Miconazole ○ Fluconazole suspension
<p>Vaginitis Also can be topical</p>	<ul style="list-style-type: none"> ○ Miconazole ○ Clotrimazole ○ Fluconazole
<p>Systemic treatment of Candidiasis</p>	<ul style="list-style-type: none"> ○ Fluconazole ○ Caspofungin ○ Voriconazole ○ Amphotericin <p>In case of candidemia:</p> <ul style="list-style-type: none"> ○ Treat for 14 days after last negative culture and resolution of signs and symptoms ○ Remove source of infection e.g. catheters, if possible, or surgically remove abscess. ^[1]

- Antifungal susceptibility testing is not done routinely in the microbiology lab
It is done in the following cases:
 - For fungi isolated from sterile samples
 - If the patient is not responding to treatment
 - In case of recurrent infections
- ★ **Points to consider:**
 - *C. glabrata* can be less susceptible or resistant to fluconazole
 - *C. krusei* is resistant to fluconazole
 - So if candida species is not yet identified, **caspofungin** is the treatment to start with

^[1]: Meaning that you should remove source of infection if there is any & start the treatment, Then repeat cultures continuously until it comes negative, and then continue treatment for two more weeks.

- Candida can be stained with Gram stain (appears as Gram +ve), however; it is 5 to 6 times larger than bacteria.
- Budding in microscopy indicates yeast in general (not only candida). Sometimes, the bud grows to look like hyphae (but it is not a true one, so we call it pseudohyphae).
- Among all fungi, candida is the most common cause of infections in immunocompromised, and it is the one of the common causes of septicemia. Most common of candida species is Candida Albicans, and it accounts for almost 60% of all candida infections.
- Candida normally colonizes the skin, oral cavity, and GIT (it is normal constituent of the human flora). However; it can lead to a disease when there is:
 - Alteration of immunity (due to medications, diseases, and genetics factors)
 - Alteration of normal physiology (eg. pregnancy)
 - Alteration of normal flora (due to use of antibiotics)
 - Damage in barriers (skin injury e.g. catheter line insertion site or sites of major surgeries)
- 75% of females will have vulvovaginitis at least once in their life.
- In the erythematous appearance of oral candidiasis, there is no white patches (just inflammation/redness).
- Hyperplastic appearance of oral candidiasis can also be caused by a virus, so lab investigations must be done to identify the cause.
- Working in conditions where there is humidity, frequent water exposure, and lack of hygiene might lead to candida nail infection.
- **Chronic mucocutaneous candidiasis patients have defects in their immune system (mainly T lymphocytes and IL-17 deficiency) which makes them more susceptible and prone to candida infections.**
- Candida might disseminate to the lung causing pneumonia secondary to candidemia sometimes, but it rarely present as a primary lung disease.
- Isolation of candida from respiratory infections does not necessarily mean candida infection (as the sample might be contaminated with the oral flora constituents). Diagnosis is mainly dependent on the clinical history and radiology to some extent.
- **Candidemia is candida in the blood, and it can be caused by two routes:**
 - Insertion of catheter or IV lines colonized by candida in ICU patients (can lead to the formation of biofilm). Later on, the yeast will disseminate to the blood causing septicemia.
 - Entry to blood through damaged gut mucosa (due to surgery or malignancy).
- If septicemia was left untreated, it can lead to septic shock.
- When a patient comes with fever, bacterial infection is usually suspected first, and the patient will be given antibiotics empirically. (candidemia is usually investigated in those who do not respond to antibiotics).
- Mortality rate of candidemia is very high as it can reach to 50% in ICU patients and 30% in non-ICU patients.
- ★ **Laboratory investigations:**
 1. Microscopy of candida will show budding yeast cells and possibly pseudohyphae.
 2. Media culture (SDA / blood agar)
 3. Blood culture technique (when bloodstream infection is suspected):
 - 3.1. Withdraw 10 ml of blood from the patient and inject it in aerobic and anaerobic blood culture bottles (these bottles contain media to support growth).
 - 3.2. Put in in incubator and leave it for 5 days
 - 3.3. The system will automatically give alarm when there is growth in the bottles.
 4. Serology: Mannan antigens or Mannan antibodies.
 5. PCR
- **Germ tube test** is used to identify the candida albicans only (**+ve indicates candida albicans**), and it is the first test to be done because candida albicans is the most common type of candida species. If germ tube test came negative, **carbohydrate assimilation** should be done to differentiate between the species. **Chromagar** can be done too, and its main advantage is that it gives different colors for each species.
- In cases of oral candidiasis and Vaginitis, topical antifungals are generally used.
- Treatment of choice in case of systemic candidiasis (or its complications such as meningitis and abscess) is **Fluconazole** and **Caspofungin**. Source of infection has to be removed, and treatment should be **continued for 14 days after the last negative culture**.
- Caspofungin is the best treatment in cases of C. glabrata and C. krusei as they are **resistant** and less sensitive.

Quiz

MCQ

Q1: The candida infections that occur under the Breast or in the axilla classified as?

- A- Intertriginous candidiasis
- B- Mucocutaneous Candidiasis
- C- Chronic Mucocutaneous Candidiasis
- D- Hyperplastic oropharyngeal candidiasis

Q2: Which of the following is a specific diagnostic method for C. Albicans

- A- Chromagar
- B- Germ tube test
- C- Carbohydrate assimilations
- D- Serology by ELISA

Q3: Which of the following antifungal drugs can be used topically in case of oropharyngeal candidiasis?

- A- Caspofungin
- B- Amphotericin
- C- Voriconazole
- D- Nystatin

Q4: The best treatment in case of candidiasis caused by C. glabrata?

- A- Fluconazol
- B- Caspofungin
- C- Miconazole
- D- Voriconazole

Q5: Which to the following is true regarding the microscopic morphology of candida?

- A- Septate branching hyphae
- B- Broad non-septa team hyphae
- C- Budding yeast cells and Pseudohyphae
- D- Brown septa the hyphae

Q6: A 45 years old AIDS patient, his dentist noticed a White Pseudomembranous patches on oral surfaces especially tongue and palate with underlying erythema. what is the most likely diagnosis?

- A- Leukoplakia
- B- Esophagitis
- C- Oral thrush
- D- Mucocutaneous pemphigoid

Answers: Q1:A | Q2:B | Q3:D | Q4:B | Q5:C | Q6:C

SAQ

Case: A 37 years old patient had a complicated abdominal surgery and then admitted to the intensive care unit and he received some drugs through a central line, 10 days after the admission he developed fever, his doctors gave him broad spectrum antibiotics but there is no response.

Q1: What is the most likely diagnosis?

Candidemia

Q2: What are the risk factors in this patient?

- 1- Surgery
- 2- Central venous catheter

Q3: List three complications that could occur?

- 1- Septic shock
- 2- Meningitis
- 3- retinitis (in case of ocular involvement)

Q4: Enumerate the diagnostic methods that detect candida?

- 1-Direct microscopy using Gram stain, KOH, Giemsa, GMS, or PAS stained smears, Morphology: Budding yeast cells and pseudohyphae
- 2- Media Culture on SDA and blood agar, Morphology: Creamy moist colonies
- 3- Blood culture to Detection of circulating microorganisms in blood
- 4- Serology test for Mannan antigens by ELISA
- 5- PCR detect the nucleic acid of the fungi

Q5: Describe how to determine candida species?

We start with 3 tests that identify C. Albicans: 1-germ tube test 2- corn meal agar 3- cycloheximide. If these 3 are positive this yeast is C. albicans, If -ve we can differentiate between candida species by : 1- Carbohydrate assimilations and fermentation 2- Culture on Chromogenic Media

Q6: What is the treatment plan?

- 1- removing the source of infection (central line) if possible
- 2- starts caspofungin or fluconazole (if the species NOT C. glabrata nor C. krusei) continued for 14 days after the last negative culture

Members Board

○ Team Leaders



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