

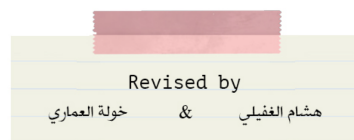
Microbiology

435's Teamwork

Endocrine Block

Kindly check our [Editing File](#) before studying the document

Important **Males note** **Females note** **Team's note** **Organism**



Team Leader:

Sara Alenezy

Team Members:

Areeb Alogaiel

Afnan Almaleki

Samar Alotaiby

Lina Alshehri

Nojood Alhaidri

Ola Alnuhayer

Kayan Kaaki

Noura Altawil

Noura Alkharraz

Maryam Saidan

Resources:

2016-2017 Dr. Albarrag's Lecture

2016-2017 Dr. Maha Almuhaizae's Lecture

434's Teamwork

Sherris Medical Microbiology

Lippincott's Microbiology

Candidiasis

Learning Objectives:

By the end of this lecture, you should know the...

1. Definition
2. Main infections
3. Clinical presentation
4. Diagnostic approaches
5. Management and Prevention

Of Candida as a pathogen, and Candidiasis as an infection.

Opportunistic Fungal Infections:

- ❖ An opportunistic fungal infection is an infection caused by fungi that take advantage of an **opportunity not normally available**, such as a host with a **weakened immune system** (Diabetic patient, HIV patient, Cancer patient treated with chemotherapy... etc), an **altered microbiota** (such as a disrupted gut flora due to broad-spectrum antibiotics), or others.
- ❖ Cause an alteration in the immune system, normal physiological barriers¹, and normal flora.
- ❖ Clinically significant as a cause of morbidity and mortality.

Transmission of Opportunistic Infections	
Endogenous (most common)	Exogenous
<ul style="list-style-type: none">❖ Colonization precedes infection.❖ Antibiotics suppress normal flora and cause fungal overgrowth.	Can happen during hospitalization and will be transmitted by the hand.

Introduction:

Candida is a **unicellular, imperfect (unknown sexual state) yeast fungus reproduced by budding**. Although many species of Candida are harmless, it is the most common cause of fungal infections worldwide, and there are >150 Species of it. It is human commensal and can be found in the oral cavity, skin, gastrointestinal tract and genitourinary tract.

The most common pathogenic species of Candida² are:

- 1- *Candida Albicans* (Most common)
- 2- *Candida Parapsilosis*
- 3- *Candida Tropicalis*
- 4- *Candida Glabrata*
- 5- *Candida Krusei*

Note that *C. Krusei* and *C. Glabrata* are resistant to the antifungal Fluconazole.

¹ Physical barriers that can be damaged during catheterization or trauma.

² Candida most likely comes from normal flora **rarely** from an exogenous source.

Candidiasis:

Any infection caused by any species of the yeast fungus *Candida*.³

- ❖ The most common⁴ invasive fungal infections in immunocompromised patients.
- ❖ 4th most common cause of nosocomial (hospital related) bloodstream infection⁵.
- ❖ It is considered to be an opportunistic infection.⁶

Clinical Features			
1. Mucocutaneous Infections (mucus membranes)			
Oropharyngeal Candidiasis (oral thrush) ⁷	Esophagitis	Vulvovaginitis	
<ul style="list-style-type: none"> ❖ White or gray or red (erythematous) pseudomembranous patches on oral surfaces especially tongue. ❖ Very common in neonates (less than 4 weeks of age), infants and elderly. ❖ Occurs in an immunocompromised host, e.g. AIDS patient.⁸ 	<p>Inflammation that damages the esophagus with whitish discoloration on the mucous membrane of the esophagus.</p>	<ul style="list-style-type: none"> ❖ Inflammation of the vagina that result in thick discharge, itching and pain. ❖ Common in pregnancy, diabetics and contraceptive drugs users. ❖ 75% of females will have this in their life it's very common and very easy to treat. 	
2. Cutaneous Infections (skin)			
Chronic Mucocutaneous Candidiasis ⁹	Diaper Rash	Nail Infection (Most common)	Intertriginous Candidiasis
<p>Children with T-cell abnormality (Autoimmune)</p>	<p>In the buttocks of children.</p>	<p>Such as onychomycosis (Nail) and paronychia (skin around nail bed).</p>	<ul style="list-style-type: none"> ❖ Infections of skin fold e.g. axilla, buttock, toe web, under breast... etc. ❖ Erythematous lesion, dry or moist or whitish accompanied by itching and burning.

Forms of Oral Thrush	
Pseudomembranous-Erythematous	Pseudomembranous
Erythematous ¹⁰	Painful depapillation of the dorsal tongue
Painful hyperplastic candida of the lateral tongue ¹¹	

³ The infection could be in the oral cavity, brain, or blood.

⁴ Most common fungal infections is always candida, what comes in second is the Aspergillus.

⁵ Causes Candidemia and spread hematogenously to other organs. It has a high rate of morbidity and mortality since it affects immunocompromised patients in the first place.

⁶ If the immune system is compromised in a pt. Candida will most likely be found. I.e. HIV, Cancer, immunosuppressive drugs, **Congenital defect in T cells**, **Chronic mucocutaneous candidiasis** it is difficult to treat. Any alterations in the physiology i.e. stress, pregnancy, LH.

⁷ Can go down and cause esophagitis. Mainly in HIV patients.

⁸ One of the contributors to discovering AIDs was the oral candidiasis. If you see a healthy adult (in his 30s) with oral thrush this raises a flag, because normally it is very rare for a healthy adult to present with oral thrush. Therefore if it is seen, you have to question his immunity. If he's an in pt. On immunosuppressive drugs then they may be the cause if he's not on any medication then you suspect AIDs.

⁹ Chronic, resistant non-invasive in the skin, nails and mucous membranes and may present with a resistant oral thrush or vaginitis. Mostly occurs in infants or children of 10 to 12 years old with autoimmune or endocrine disorders. Rarely seen in elderly with mostly thymoma (tumor of the thymus gland), or Myasthenia Gravis or Aplastic anemia.

¹⁰ Seen in old people who wear dentures.

¹¹ Seen in HIV pts, and other viruses such EBV. you can't remove the white patches as easily as the oral thrush. If you remove this the pt will bleed.

Chronic Mucocutaneous Candidiasis

1. Pulmonary Candidiasis (Rare)

- ❖ Primary pneumonia is less common and could be a result of aspiration, **mostly in comatose patients**.
- ❖ Secondary pneumonia commonly seen with hematogenous candidiasis.
- ❖ Usually, the fungal infections associated with immunocompromised patients.
- ❖ Isolation of *Candida* from sputum with bronchoalveolar lavage is not always significant because it could be NORMAL FLORA.
- ❖ **To confirm infection, you have to overlap the following:**
 - Clinical features.
 - Radiology.
 - Other Lab investigations.

2. Candidemia (Candida in the blood)

- ❖ *Candida* is the fourth in causing nosocomial bloodstream infections (BSI).
- ❖ Increased colonization due to endogenous or exogenous factors.
- ❖ Damage in host barriers by **catheters**, trauma or surgery.
- ❖ Fever could be the only clinical manifestation.
- ❖ Immunosuppression and central venous catheters (CVC).

3. Disseminated Candidiasis (Candida at any organ)

Septic Shock	Meningitis	Retinitis (Common in neonates)
Medical condition that occurs when sepsis, body-wide inflammatory response to infection, leads to dangerously low blood pressure.	-	-

Laboratory Diagnosis: Specimen collection depends on the site of infection

Swabs if oral, Urine if UTI¹², Blood if Candidemia, Respiratory specimens if RTI, CSF if Meningitis.

Direct Microscopy	<p>WE MUST ALWAYS START WITH MICROSCOPY. You CANNOT diagnose candida from the smear, all you can say is that it is a yeast. So you only report that they are budding yeast cell. In order for you to confirm that it is a candida then we must do a culture. Depending on the labs's protocol and on the specimen received. KOH mostly in skin and hair, GMS & Giemsa for biopsies for example. The most important thing is that we have to use two or more.</p> <ul style="list-style-type: none"> ❖ Look for Budding yeast cells and pseudohyphae using gram stain or KOH¹³. ❖ Silver stain, Giemsa, Gram stain, KOH, GMS¹⁴, or PAS¹⁵ stained smears.
Culture	<ul style="list-style-type: none"> ❖ SDA media (Sabouraud agar) is used for <i>C. Albicans</i>, and it appears as Creamy white yeast. May be dull, dry, irregular and heaped up, or glabrous and tough. ❖ Blood agar is used at 37°C.
Blood Culture	Used if septicemia is suspected.
Serology Serum	Test for antigens and antibodies e.g. mannan antigen ¹⁶ using ELISA.
PCR	-

¹² You need to look for signs and symptoms of UTI and you also need to grow at least 10,000 colonies from the urine to make sure it's an infection, so a very high count of candida means it's an infection. But if it's low then it does not necessarily mean it's a candida infection.

¹³ Known as a potassium hydroxide examination, used to diagnose fungal infections of the skin.

¹⁴ Gomori Methenamine-Silver (GMS) stain.

¹⁵ Periodic acid-Schiff (PAS).

¹⁶ **Present on the cell wall, it is very specific. It's only positive for candida infection.** Mannan antigen (Mn) and anti-mannan antibodies (A-Mn) are present in patients with invasive candidiasis.

Confirming Candidiasis:

We need to confirm because the sensitivity to antifungal treatment differs between different species of *Candida*. Because *C. Albicans* is the most common *Candida* species to cause infection, the following tests are used to identify *C. Albicans*:

1. Formation of germ tube when cultured in serum at 37°C.^{17 18 19}
2. Chlamydospore production in corn meal agar.^{20 21}
3. Resistance to 500 µg/ml Cycloheximide.²²

If these 3 tests are positive → this yeast is *C. Albicans*.

If negative → it could be any other yeast. Use Carbohydrate assimilation²³ and fermentation²⁴ and culture on Chromogenic media for Chromagar²⁵ *Candida*.

Treatment	
Type of Candidiasis	Drugs that can be used
Oropharyngeal ²⁶	Topical Nystatin, Clotrimazole, Miconazole or Fluconazole.
Mucocutaneous	Mix both topical and systemic drugs.
Vaginitis	Miconazole, Clotrimazole or Fluconazole.
Systemic ²⁷	Fluconazole, Voriconazole, Caspofungin ²⁸ or Amphotericin B.
Candidemia (Prolonged)	Treat for 14 days after the last negative culture and resolution of signs and symptoms and remove catheters, if possible.
Points to consider	
<ul style="list-style-type: none"> ❖ Antifungal susceptibility testing is not done routinely in the microbiology lab.²⁹ ❖ It is done in the following cases: <ul style="list-style-type: none"> - For fungi isolated from sterile samples (like CSF or blood). - If the patient is not responding to treatment. - In case of recurrent infections. ❖ <i>C. Glabrata</i> can be less susceptible or resistant to Fluconazole. ❖ <i>C. Krusei</i> is resistant to Fluconazole. 	

¹⁷ If the germ tube test was (+ve) and the chlamydospore is (-ve) then you can say that it's *albicans* but if the result was the opposite germ tube was (-ve) and chlamydospore (+ve) then something went wrong and you must repeat the test.

¹⁸ Small tub projections without constrictions.

¹⁹ Germ tube test is **very important**, this is how you know it's a *Candida*. So you will take your colony and add it to your serum sample. You will then incubate it for 2 hrs, then examine it using the microscope. If you see the germ tube then it's positive for *Candida albicans*. THIS IS THE FIRST TEST TO DO IN THE LAB. all the yeast grown in microbiology you have to do the germ tube test.

²⁰ Rounded, thick walled spores after 48 hours. So the test is positive for *albicans* if you see the spores

²¹ A culture medium that is low in nutrients, widely used for producing the distinctive chlamydospores of *Candida albicans*.

²² Anti-fungal. It is resistant to it so if it grows then it is positive for *Candida*.

²³ Identify what other species it is based on which type grew out of the sugars. By using this method you can identify all types of yeast.

²⁴ It is the ability of the yeast to use carbohydrates as a sole source of carbon or energy.

Fermentation: under anaerobic conditions / Assimilation: under aerobic conditions.

²⁵ In this media, each species of *Candida* will have a specific color.

²⁶ They rarely need systemic drugs it's mostly topical, unless it's an HIV pt. In this case they may need systemic drugs for their oral thrush.

²⁷ IV, tablets or suspension it all depends on the species and sensitivity to the antifungal agent, as well as the site of the disease.

²⁸ If a pt comes to you and you know that he has a yeast infection but you don't know what it is exactly then you give them Caspofungin, Amphotericin B because they are good for the yeast and they also have less side effects.

²⁹ It is only done if the source of the *Candida* was from a sterile body site such as: blood, CSF, or tissue or if it was a very invasive or serious disease. And if it was not responding to drugs so, we have to think about the resistance.

Integrated MCQs and SAQs

Q1: Which one of those candida is resistant to fluconazole?

- 1- c. kruzi
- 2- c. albican
- 3- c. tropicalis
- 4- c. glabrata

A: 1

Q2: Most common mode transmission of candida?

- 1- exogenous
- 2- endogenous
- 3- hematogenous
- 4- i.v fluid

A :2

Q3: How to differentiate between candida albicans and other yeast?

- 1- germ-tube test
- 2- carbohydrate assimilation
- 3- carbohydrate fermentation
- 4- blood agar

A : 1

Q4: 1 month old infant presented to the ER with white plaques on the tongue, soft palate in his mouth , what is the most causative agent?

- 1- yeast
- 2- viral infection
- 3- hypersensitivity
- 4- discoloration

A: 1

Q5: The antifungal susceptibility test is only done if?

- 1- the patient is not responding to treatment
- 2- if the sample was taken from the mouth
- 3- if the patient was immunocompromised
- 4- if the disease reoccurred

A: 1, 4

Q6: Which one of these agar is the best for growing the candida?

- 1- SDA
- 2- Mcconkey agar
- 3- chocolate agar
- 4- horse blood agar

A: 1

Q7: How long does it take for candida to grow in the lab?

- 1- 24 hrs
- 2- 3 days
- 3- 48 hrs
- 4- one week

A: 3

Q8: What do we mean by (imperfect reproducing) regarding the candida species?

Are fungi which do not fit into any classifications of fungi that are based on morphological characteristics of sexual structures because their sexual form of reproduction has never been observed.

Q9: a 72-year old saudi man previously diagnosed with AIDS was admitted to the ED for a 3 days of non-stopping fever and he noticed some whitish patches in his mouth as well as some abnormalities in his nail and the skin around the nail. After some lab work , the attending physician diagnosed the patient with infection caused by a type of yeast.

What is the type of yeast ? and how to describe its morphology?

Candida, unicellular, budding yeast cell, pseudohyphae.

What is the most probable subtype of this type of yeast, hence the nationality of the patient?

C. albicans

Enumerate some lab work , that the attending physician asked for?

- 1 - direct microscopy
- 2 - culture
- 3 - blood culture
- 4 - serology
- 5 - PCR

What do we call the abnormalities on the nail and the skin around the nail?

On the nail: onychomycosis

Around the nail (on skin): paronychia

What is the most important precipitating agent that made the patient susceptible to such infection?

He is an immunocompromised patient (AIDS) .

How to treat this disease?

We have to use topical for the mouth and systemic antifungal agent for the nails and skin and the probable invasion to some interior organs or to blood

Topical: Topical Nystatin suspension or Clotrimazole troches or Miconazole, or Fluconazole suspension

Systemic: Fluconazole or Voriconazole or Caspofungin or Amphotericin .

Q10: A 40 year old immunocompromised woman was admitted to king Khalid hospital with fever and malaise , the doctor finally after 47 hrs of lab work and some other investigations diagnosed her with a yeast infection in the lungs.

What do we call this disease?

Pulmonary candidiasis.

How many types of this disease are there, and the route of transmission?

2 types: primary and secondary .

primary by: aspiration

secondary by: hematogenous spread

Which one is more frequent?

The secondary in immunocompromised patients .