



# CANDIDIASIS

## FUNGAL INFECTION



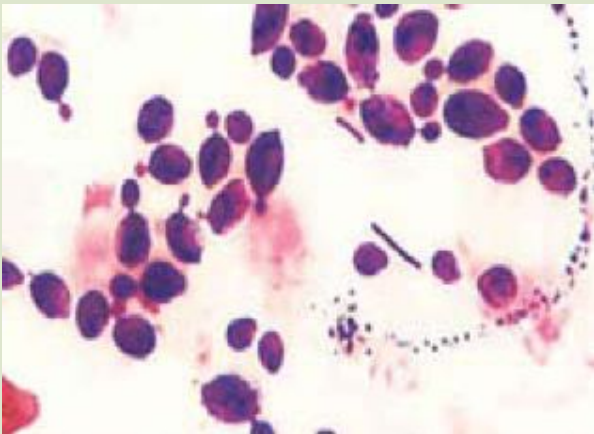
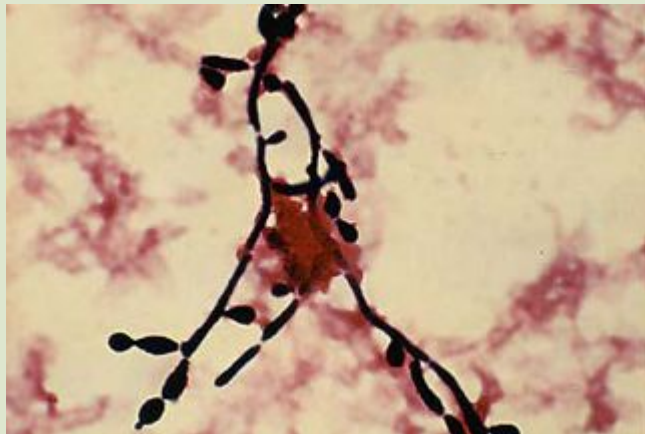
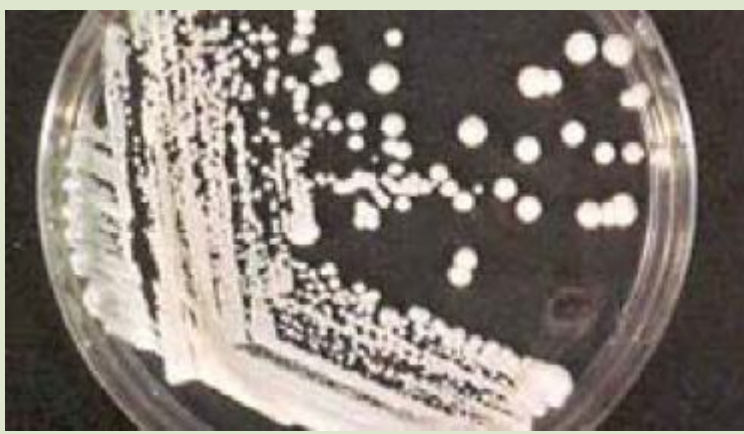
### Objectives

- 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 & treatment of these infections.



# Candida (the organism)

Candida is a **unicellular**, imperfect yeast fungus, reproduced by **budding**.  
(imperfect=unknown sexual state)

| Species   | Human Commensal  |
|---|--|
| <ul style="list-style-type: none"> <li>- There are many species of Candida (&gt;150)</li> <li>- <b>The common species are:</b> <ul style="list-style-type: none"> <li>- <b>Candida albicans</b>(most common)</li> <li>- C.parapsilosis</li> <li>- C.tropicalis</li> <li>- C.glabrata → Both Resistant</li> <li>- C.krusei → to fluconazole</li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>- Oral cavity</li> <li>- Skin</li> <li>- Gastrointestinal tract</li> <li>- Genitourinary tracts (urethra,vagina)</li> </ul>   |
| Microscopy  | Culture  |
| <ul style="list-style-type: none"> <li>- Budding yeast cells, and <b>Pseudohyphae</b>.</li> </ul> <div style="display: flex; justify-content: space-around;">   </div>                      | <ul style="list-style-type: none"> <li>- Creamy colony, <b>fast growing</b> on <b>Sabouraud Dextrose agar (SDA)</b>, Blood agar (48 hr)</li> </ul>  |

# Candidiasis (the disease)

- 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 bloodstream infection (BSI)**
- It is considered **opportunistic** fungal infection
  - Alteration in:
    - Immunity (HIV), normal physiology (pregnant) & normal flora (using antibiotics)
  - Damage in the barriers
  - Clinical spectrum of disease

## Transmission

| Endogenous (common)  | Exogenous (rare)  |
|--|---|
| <ul style="list-style-type: none"> <li>- Colonization precedes infection</li> <li>- Antibiotic suppression of normal flora, fungal overgrowth</li> </ul> | <p>Can happen in hospitalizations and usually transmitted by hand</p> |





# Clinical Features of Candida (superficial)

## Mucous Membrane Infections

### Oropharyngeal Candidiasis (oral thrush)

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

### Vaginitis (vulvovaginitis)

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

### Esophagitis

Inflammation that damages the esophagus with whitish discoloration on the mucous membrane of the esophagus



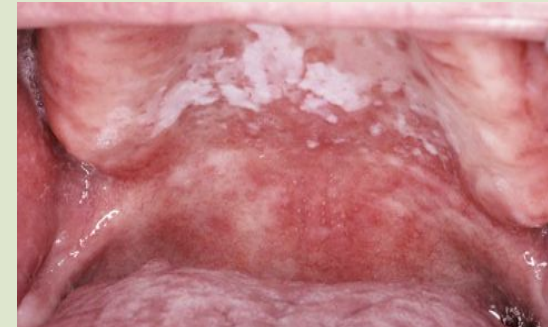
Oral thrush



pseudomembranous form



erythematous form  
مع الاسنان الاصطناعية (dentures)



Pseudomembranous-erythematous form.



Hyperplastic candidiasis, that was mistaken for leukoplakia  
Can be caused by EBV

## Cutaneous Infections

### Intertriginous\* Candidiasis

\*when two areas rub together  
Like axilla & between fingers

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

### Nail Infections

- Onychomycosis (nail it self). → dislodging & discoloration of the nail
- Paronychia (skin around nail bed)

### Chronic Mucocutaneous Candidiasis

- Children with T-cell abnormality
- Heterogeneous group of disorders characterized by recurrent, persistent superficial infections of the skin, mucous membranes & nails

## Diaper Rash



Intertriginous candidiasis



Diaper Rash



Onychomycosis



Paronychia



Chronic Mucocutaneous Candidiasis





# Clinical Features of Candida (systemic)

- ★ Urinary tract infection
- ★ Candidemia
- ★ Disseminated (systemic, invasive) infection
  - Endophthalmitis (eye) commonly in neonates
  - Liver, spleen, kidneys, skin, brain, lungs, & bone

## Pulmonary Candidiasis

### Primary Pneumonia (less common)

- Result of **aspiration**
- A patient might inhale food, stomach acid, or saliva into their lungs which contain the organism → causes aspiration pneumonia

### Secondary Pneumonia

- Seen with **hematogenous candidiasis** especially in immunocompromised patients
- Patient already has candidemia → goes to distal organs like the lungs

### Diagnosis

- Isolation of *Candida* from sputum, BAL (Bronchoalveolar lavage) is **not always significant** (because it is normal flora)
- To confirm the diagnosis:
  - Clinical features
  - Radiology
  - Other Lab investigations

## Candidemia

### Transmission

- Increased colonization (endogenous or exogenous factors)
- Damage in host barriers by **catheters**, trauma, surgery
- Immunosuppression
- **Central Venous Catheters (CVC)**

### Disseminated Candidiasis

- Involvement of any organ
  - Septic shock
  - Meningitis
  - Ocular involvement (retinitis)

### Clinical Manifestation






- Fever could be the only clinical manifestation



# Laboratory Diagnosis

Specimen (depend on site of infection)

- Examples: Swabs (skin rash), Urine(UTI), Blood (septicemia), Respiratory specimens, & CSF(meningitis).

| Method  | Description  |   |
|---|--|---|
| <b>Direct Microscopy</b><br>KOH for skin and nail samples   | <ul style="list-style-type: none"> <li>- What stain do we use? Gram stain, KOH, Giemsa, GMS, or PAS stained smears.</li> <li>- What do we see?                             <ul style="list-style-type: none"> <li>- Budding yeast cells and pseudohyphae will be seen in stained smear or KOH.</li> </ul> </li> </ul>  |   |
| <b>Culture</b>  | <ul style="list-style-type: none"> <li>- Media: SDA (Sabouraud Dextrose Agar) &amp; Blood agar at 37°C.</li> <li>- Creamy moist colonies in 24 - 48 hours.</li> <li>- We use the below agars for <b>Candida Albicans</b>:</li> </ul>   |   |
|   | <table border="1"> <tr> <td> <b>SDA</b> → creamy white yeast, may be dull, dry, irregular, heaped up, glabrous &amp; tough<br/>  </td> <td> <b>Chromagar</b> → producing <b>green</b> pigmented colonies on specially designed medium to speciate certain yeasts based on color they produce<br/>  </td> </tr> </table> | <b>SDA</b> → creamy white yeast, may be dull, dry, irregular, heaped up, glabrous & tough<br> |
| <b>SDA</b> → creamy white yeast, may be dull, dry, irregular, heaped up, glabrous & tough<br> | <b>Chromagar</b> → producing <b>green</b> pigmented colonies on specially designed medium to speciate certain yeasts based on color they produce<br>  |   |
| <b>Blood Culture</b><br>(2 sets of cultures b/f starting antibiotics is ideal)  | <ul style="list-style-type: none"> <li>- Used for the detection of circulation microorganism in septicemia</li> <li>- Description → different types of blood culture bottles and blood volume required:                             <ol style="list-style-type: none"> <li>1. Paediatric aerobic (0.5-4 ml of blood)</li> <li>2. Adult aerobic (5-10 ml of blood)</li> <li>3. Anaerobic (5-10 ml of blood)</li> </ol> </li> </ul>  |   |
| <b>Serology</b><br>(in invasive cases)  | <b>1. Test for Antigen</b> , e.g. Mannan antigen using ELISA (+ve in the early stages & can be used to monitor the therapy) <b>2. Test for Antibodies</b>  |   |
| <b>PCR</b>  | -  |   |

## Laboratory Identification of Yeast

Because *C. albicans* is the most common species to cause infection.

- The following three tests are used to identify **C. albican**: (all three should be positive)

| 1. Germ tube test   | 2. Chlamyospore production in corn meal agar   | 3. Resistance to 500 µg/ml Cycloheximide. |
|---|--|---|
| Formation of germ tube when cultured in serum at 37°C.<br> | Thickwall rounded spores<br> |   |

- If the tests were negative it could be any other yeast (they're used to differentiate bw the other types of candida)
  - Carbohydrate assimilations & fermentation. Commercial kits available for this like: API 20C, AP I32C.
  - Culture on Chromogenic Media (CHROMagar™ Candida) .





# Treatment

| Type of Candidiasis  | Treatment   |
|----------------------|---|
| <b>Oropharyngeal</b> | Topical Nystatin suspension, Clotrimazole troches, Miconazole, Fluconazole suspension.<br>(Or systemic treatment for AIDS pts)  |
| <b>Vaginitis</b>     | Miconazole, Clotrimazole, Fluconazole (topical azoles)  |
| <b>Systemic</b>      | Fluconazole, Voriconazole, Caspofungin, Amphotericin(used for zygomycosis)<br>Depending of the species and infection sites<br><b>Caspofungin is 1st choice when we don't know the species + less side effects</b> |
| <b>Candidemia</b>    | - Treat for 14 days after last negative culture and resolution of signs and symptoms<br>- Remove catheters, if possible   |

★ Antifungal **susceptibility testing** in **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



# Doctor's Notes

- Fungi can occur as:

## A. Mold (multicellular)

## B. Yeast (unicellular) C.dimorphic

### - Features:

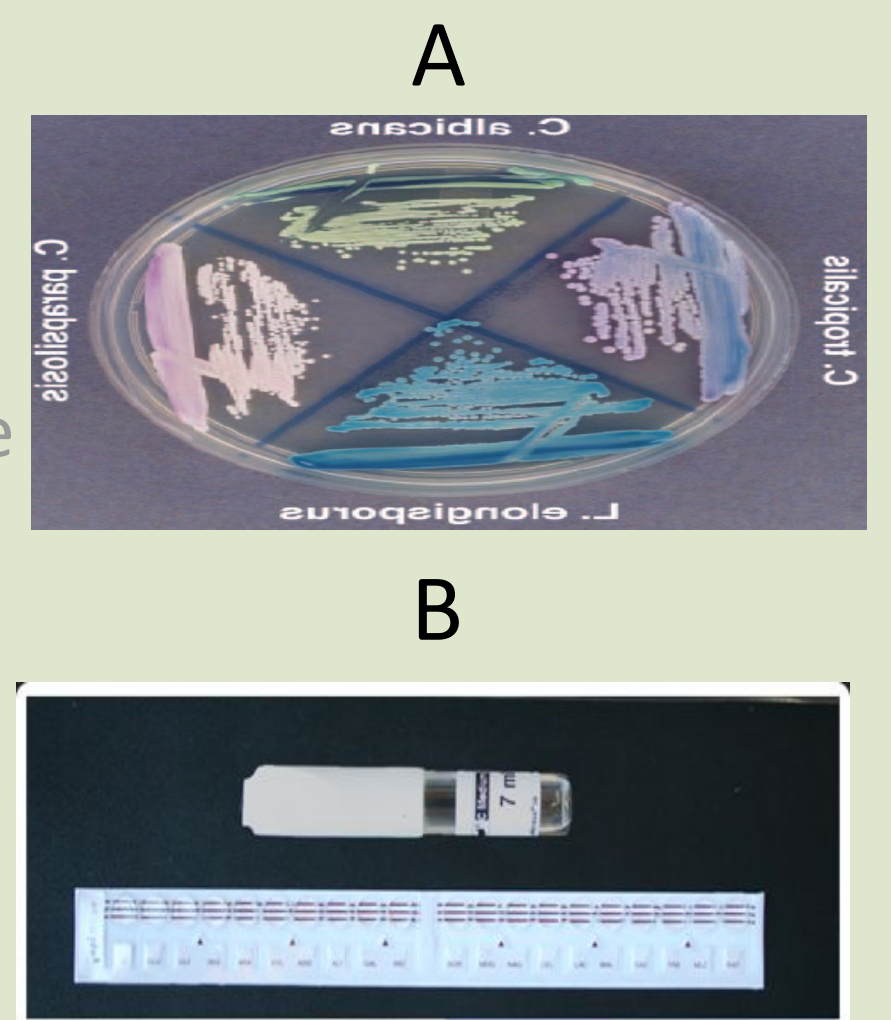
- Candida is an imperfect yeast which means that its sexual stage is unknown and its reproduced by budding; budding is when a small bud arises as an outgrowth of the parent's cell wall
  - The daughter cell might detach itself and become a new yeast cell or it could fail to detach and it will elongate itself and become pseudohyphae
- Candida is the normal flora located on the skin, oral cavity, GIT and genitourinary tract.
- Doesn't cause infection in normal healthy individuals but can causes opportunistic infections in immunocompromised e.g. (HIV, diabetes, steroid therapy, long use of antibiotics, immune defects, or chemotherapy)
- Any defect or breach on the skin or mucous membrane barrier might cause infection and let the organism reaches deep into the blood causing candidemia.
- Most common organism is candida albicans
- **Transmission:**
  - Mainly occur of an **endogenous** source(from own normal flora) & in immunocompromised patients
  - Can cause a **superficial** infection (skin and nails) & **deep** infection

### Mucocutaneous Infections :

- Oral thrush: easy to treat and sometimes the patient present with erythema only
- Vulvovaginites: most common and almost all women develop it during their life

**Candidemia** → candida in the blood (in patients receiving catheters)

- Most common feature of invasive candidiasis
- Most common cause is is C. albicans
- Can go to any organ e.g. (kidneys & brain) can cause brain abscess and if the patient is child examine the eye
- In cases of septic shock, the patient will be present w/ fever, leukocytosis, & leukopenia
- Remember! First thing you do is removal of central line then start an antifungal drugs
- The mortality reach 50% in ICU patient
- **Laboratory diagnosis:**
  - Why is laboratory identification very important? bc other organisms like C. glabrata and C. krusei might be the cause of infection and these organisms are resistant to fluconazole.
  - Most commonly used stan is KOH (Potassium Hydroxide) (best for skin and nail) and for other samples we use GMS → dissolve of the tissue to make the organism appear more clear on the slide.
  - **For C. albicans we use 3 test (3 criteria)**
    1. **Germ Tube:** put the sample in an incubator tube filled w/ serum → outgrowth (germ tube) → +ve
    2. **Chlamyospore**
    3. **Resistance to 500 µg/ml Cycloheximide.**
  - If -ve this means its another type of yeast .
  - A. Culture on chromogenic media: (chromagar is a differential test)
    - It will give us different colors for each specie. Then why do we use SDA? Its cheap and it is most likely will be positive for candida
  - B. Use carbohydrate assimilation and fermentation:
    - It is the ability of the yeast use carbohydrates as a sole source of carbon or energy. / Fermentation: under anaerobic conditions
    - Assimilation: under aerobic conditions



### - Treatment:

- **Caspofungin is the drug of choice in cases of systemic candidiasis**
- In candidemia we treat for 14 days and remove the catheter if we can, why? Bc we don't want the infection to reoccur.
- **C. glabrata might or might not be resistant to fluconazole.**
- **C. krusei is resistant to fluconazole**



# Doctor's Notes

## Details of Blood culture:

- Uses: septicemia
- Description:

We take 2 bottles 1 aerobic 1 anaerobic (5-10 ml each) and we put them in a machine and wait for 1-5 days (Usually two sets just in case one is contaminated = 4 bottles)

If there is no growth after 5 days it is negative, if there is a growth

we do the staining(gram stain for budding and pseudohyphae and culture (like in SDA agar)

You will see budding and SDA agar showed creamy moist colonies

Then we do:

1. Germ Tube: put the sample in an incubator tube filled w/ serum → outgrowth (germ tube) → +ve
2. Chlamydospore
3. Resistance to 500 µg/ml Cycloheximide.

We do carbohydrate assimilation and fermentation , culture on chromogenic media

to determine the exact species, so why we do not do it from the beginning ?? because the germ tube is fast, costless, and the most common is albicans.

Let's say it is c.krusei then we can't use fluconazole

Then we treat and take blood culture every 2 days , once the culture is negative

You treat for 14 days and then stop





# Summary

## Candidiasis

|  |  |   |  |  |   |             |
|--|--|---|--|--|---|-------------|
| <b>Pathogen</b>  | Candida is a unicellular yeast fungus  | <b>Common species</b>   | <i>Candida albicans</i> - <i>C.parapsilosis</i><br><i>C.tropicalis</i> - <i>C.glabrata</i> - <i>C.krusei</i> |  |   |             |
| <b>Morphology</b>  | Microscopy   | Budding yeast cells, <i>Pseudohyphae</i>  |  |  |   |             |
| <b>Affect</b>  | common invasive fungal infections in immunocompromised patients (opportunistic)  |   |  |  |   |             |
| <b>Risk factors</b>  | Alteration in Immunity, Normal physiology, Normal flora - Damage in the barriers (burn)  |   |  |  |   |             |
| <b>Transmission</b>  | Endogenous   | Colonization precedes infection - Antibiotic suppression of normal flora        |  |  |   |             |
|  | Exogenous  | rare  |  |  |   |             |
| <b>Mucocutaneous infections</b>  |  |   | <b>Cutaneous infections</b>  |  |   |             |
| Oropharyngeal Candidiasis (thrush)   | Vulvovaginitis   | Esophagitis   | Intertriginous candidiasis   | Nail infections  | <b>Chronic mucocutaneous candidiasis</b>                    | Diaper rash |
| <ul style="list-style-type: none"> <li>White patches on oral surfaces especially tongue.</li> <li>in neonates, infants, immunocompromised host</li> <li>Treatment: <b>Topical Nystatin suspension</b></li> </ul> | <ul style="list-style-type: none"> <li>Thick discharge, white patches on vaginal mucosa.</li> <li>in pregnancy, DM, contraceptives</li> </ul>  | AIDS  | <ul style="list-style-type: none"> <li>Infections of <b>skin folds</b> eg. Axilla.</li> </ul>                | <ul style="list-style-type: none"> <li>Paronychia (skin around nail bed)</li> <li>Onychomycosis (nails)</li> </ul> | children with <b>T-cell abnormality</b>                     |             |
| <b>Clinical</b>  | 1- Urinary tract infection -2- Disseminated infection: <b>Endophthalmitis</b> - Liver  |   |  |  |   |             |
|  | 3- Candidemia  | Caused by   | <b>Central venous catheters</b> - Immunosuppression - Damage in host barriers by catheters, trauma, surgery  |  |   |             |
|  |  | Lead to   | Septic shock - Meningitis - Ocular involvement (retinitis)   |  |   |             |
| <b>Diagnosis</b>   | 1-Specimen   | depend on site of infection   |  | 3-Serology   | <b>Mannan Ag using ELISA</b>                                |             |
|  | 2-Direct microscopy  | Gram stain, <b>KOH</b> , Giemsa, <b>GMS</b> , PAS stained smears                |  | 4-Culture  | <b>Sabouraud Dextrose agar</b><br>5- PCR<br>6-Blood culture |             |
| <b>Treatment</b>   | <b>Systemic treatment of Candidiasis: Caspofungin (best)</b>   | In candidemia: Treat for 14 days after last negative culture & Remove catheters |  |  |   |             |
| <b>IMPORTANT</b>   | <i>C. glabrata</i> can be less susceptible or resistant to fluconazole<br><i>C. krusei</i> is resistant to fluconazole   |   |  |  |   |             |
| <b>HOW TO to identify C. Albicans ?</b>  | 1-Germ tube test<br>2-Chlamyospore production in corn meal Agar<br>3- Resistance to Cycloheximide  |   |  |  |   |             |
|  | If negative, then it could be any other yeast,<br>1- use Carbohydrate assimilations and fermentation.<br>2- Culture on Chromogenic Media ( if <i>C. Albicans</i> green pigmented colonies) |   |  |  |   |             |





## MCOs:

1- Which of the following is more likely to develop Oropharyngeal Candidiasis ?

- A- A pregnant woman.
- B- An infant.
- C- woman using contraceptives.
- D- children with T-cell abnormality.

2- A kid came to the clinic, on examination you noticed erythematous lesion on his armpit and buttock. He most likely have?

- A- Chronic mucocutaneous candidiasis.
- B- Candidemia.
- C- Diaper rash.
- D- Intertriginous candidiasis.

3- C.Krusei is resistant to which of the following?

- A- Clotrimazole.
- B- Caspofungin.
- C- Fluconazole.
- D- Miconazole.

4- 27 year old female comes into the clinic. She has white patches on vaginal mucosa. You suspect Vulvovaginitis. What does the patient most likely have as a risk factor?

- A- Nothing, she's healthy.
- B- She has T-cell abnormality.
- C- She has SLE.
- D- she has diabetes.

5- The drug of choice in treatment of systemic candidiasis?

- A- Fluconazole.
- B- Voriconazole.
- C- Caspofungin.
- D- Amphotericin.

6- Which one of these agar is the best for growing the candida?

- A- Thayer-Martin agar.
- B- SDA.
- C- chocolate agar
- D- Macconkey agar

## SAQ:

3-C  
2-D  
1-B  
6-B  
5-C  
4-D

- A patient in the ICU is recovering from a major surgery has developed fever. You noticed that he has central venous catheter. Blood culture is positive and SDA agar shows Creamy moist colonies.

Microscopy shows Pseudohyphae.

1- What is the most likely pathogen?

Candida albicans.

2- How can you confirm your answer?

- 1-Germ tube test: formation of germ tube.
- 2-Chlamydospore production in corn meal Agar
- 3- Resistance to 500 µg/ml Cycloheximide

3- What is your diagnosis?

Candidemia

4- What further test would you order ?

PCR - serology - blood culture

5- Mention 3 complications?

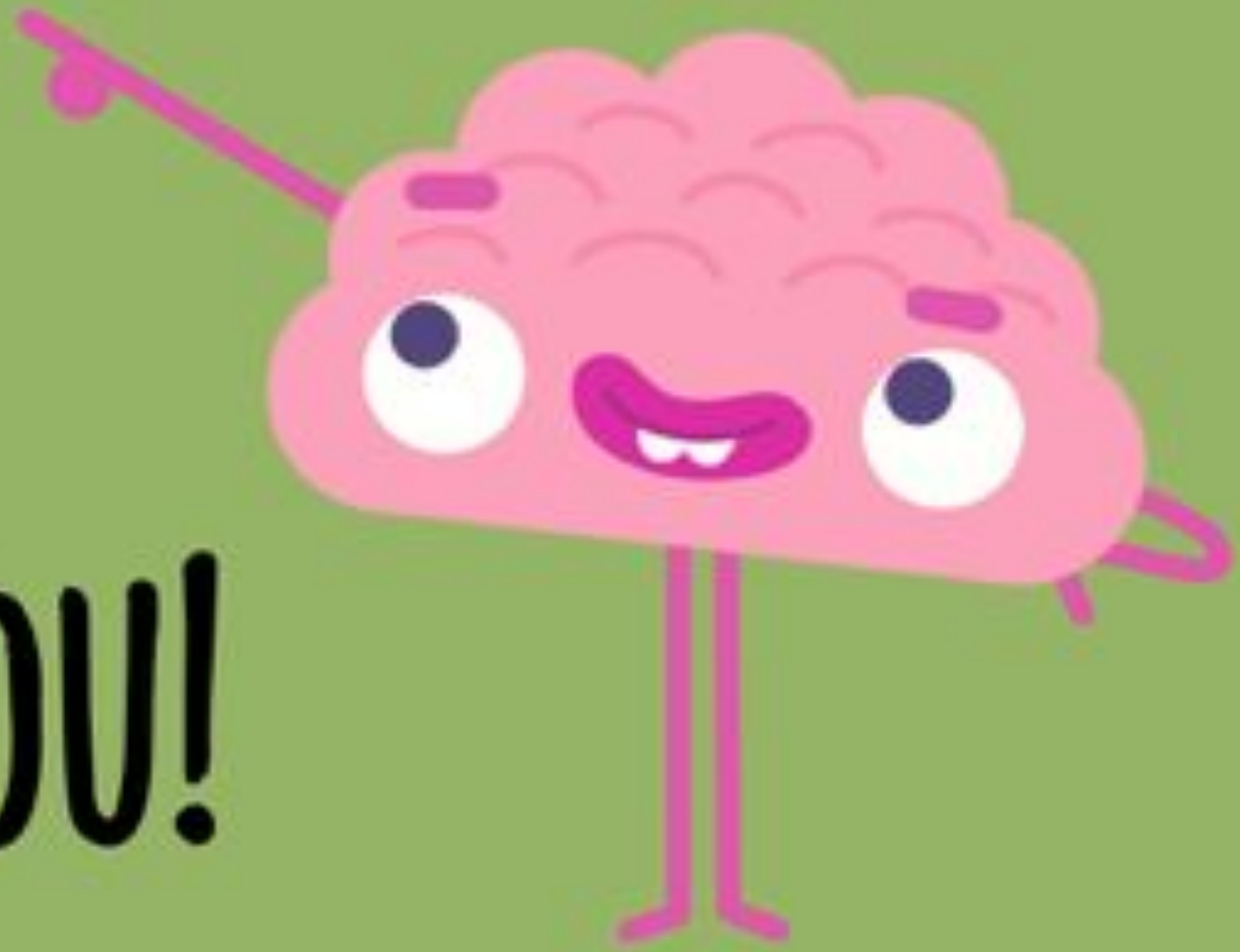
Septic shock – Meningitis - Ocular involvement (retinitis)

6- When do we perform antifungal susceptibility tests?

- For fungi isolated from sterile samples.
- If the patient is not responding to treatment.
- In case of recurrent infections.







THANK YOU!



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