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A Fungus Among Us

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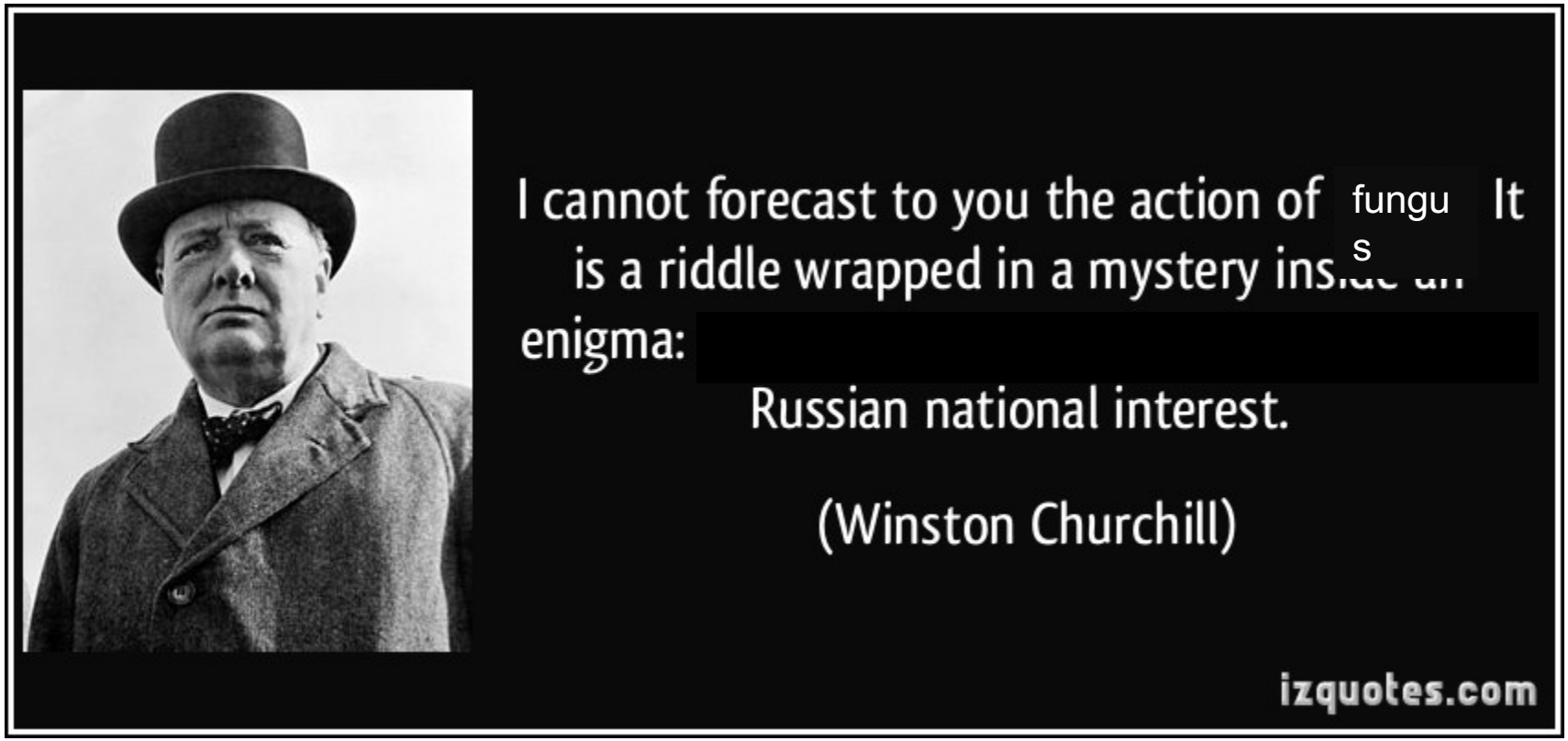
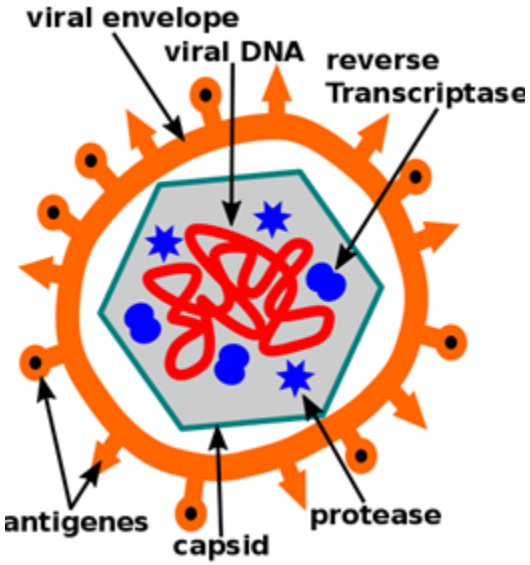
Plan

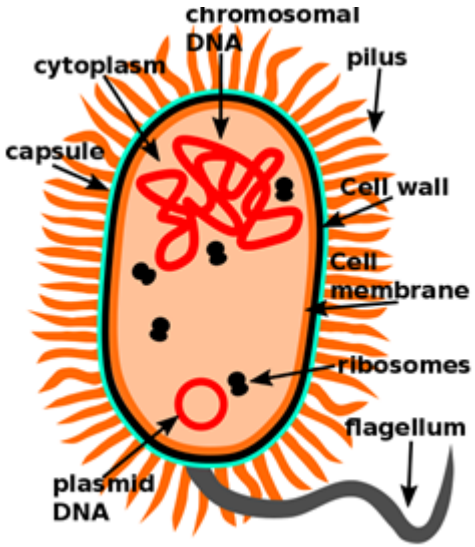
- What is a fungus?
- Which fungi do we really care about and why?
  - Target Candida
- Diagnosis
- Treatment
- Next week is stewardship in antifungals

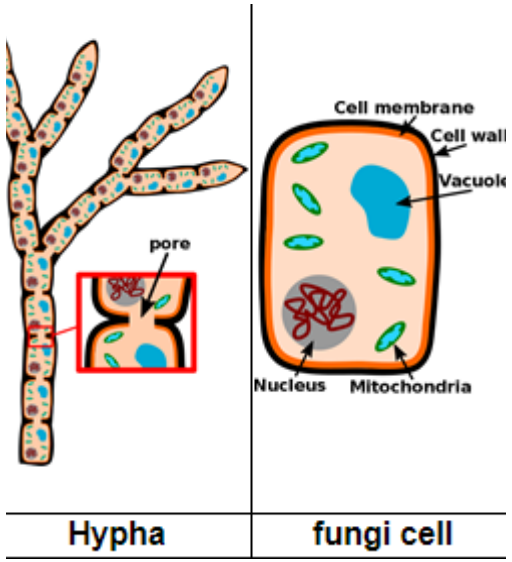
A Fungus Among Us

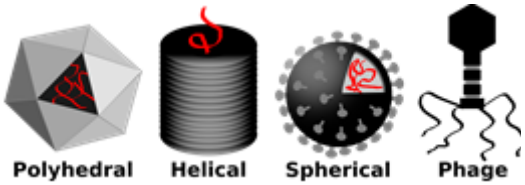


What is a Fungus?









http://www.scitk.org/subsides/Natural_Science/Biology/diff_bac_fung_vir/diff_bac_fung_vir.php

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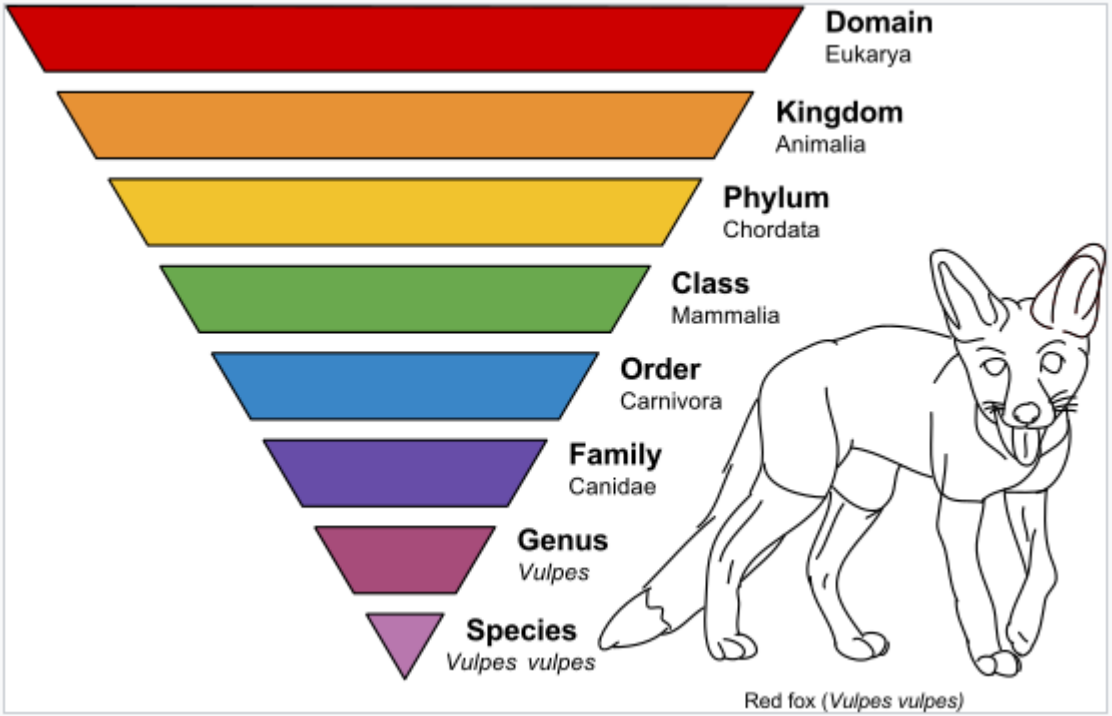
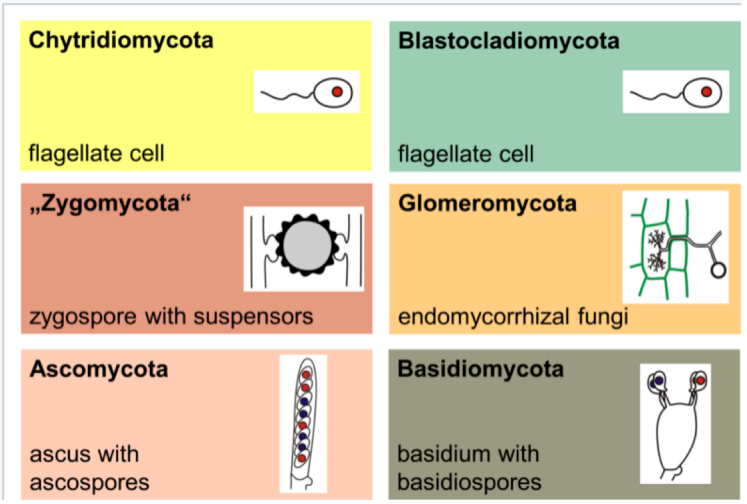
How science orders Fungi





https://en.wikipedia.org/wiki/Taxonomic_rank

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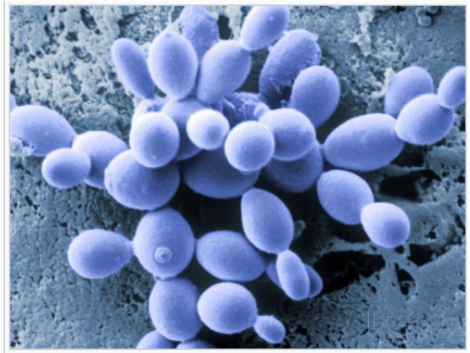
Basidiomycota

- Cryptococcus
- Mushrooms
- Many more



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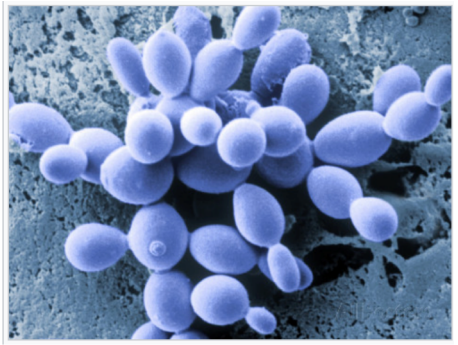
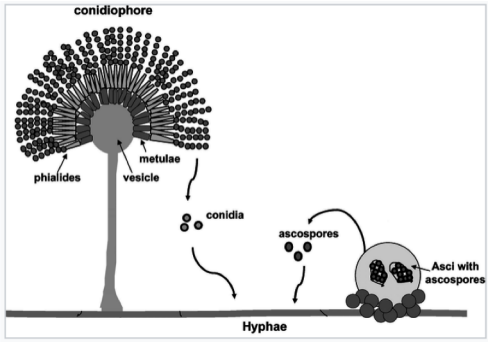
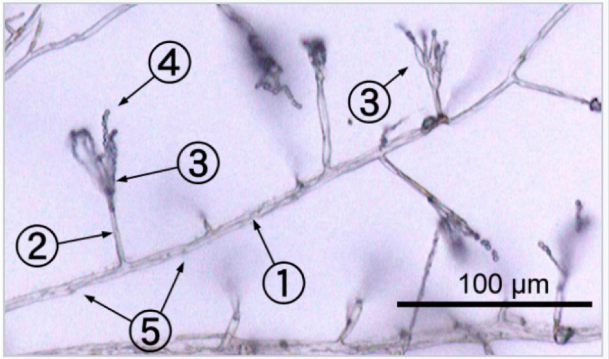
Ascomycota

- Candida
- Aspergillus
- Blastomyces
- Histoplasma
- Coccidioides
- Paracoccioides
- Penicillium
- Sporothrix
- Fusarium
- Scedosporium







An environmental isolate of *Penicillium*
1 hypha · 2 conidiophore · 3 phialide · 4 conidia · 5 septa

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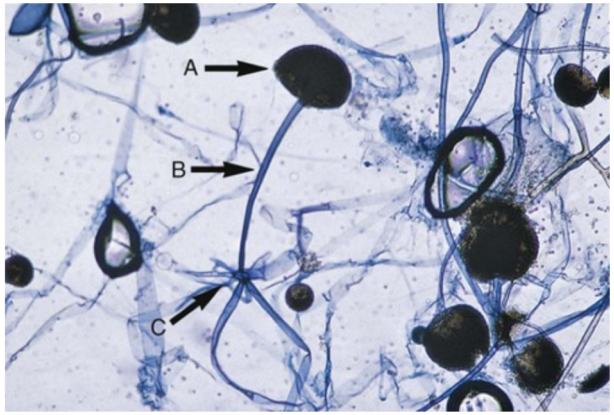
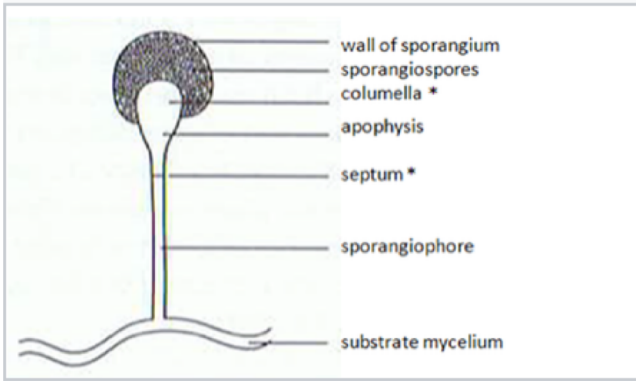
Zygomycota



- Mucor & Rhizopus
- Fast growing
- Sporangia



https://en.wikipedia.org/wiki/Zygomycota

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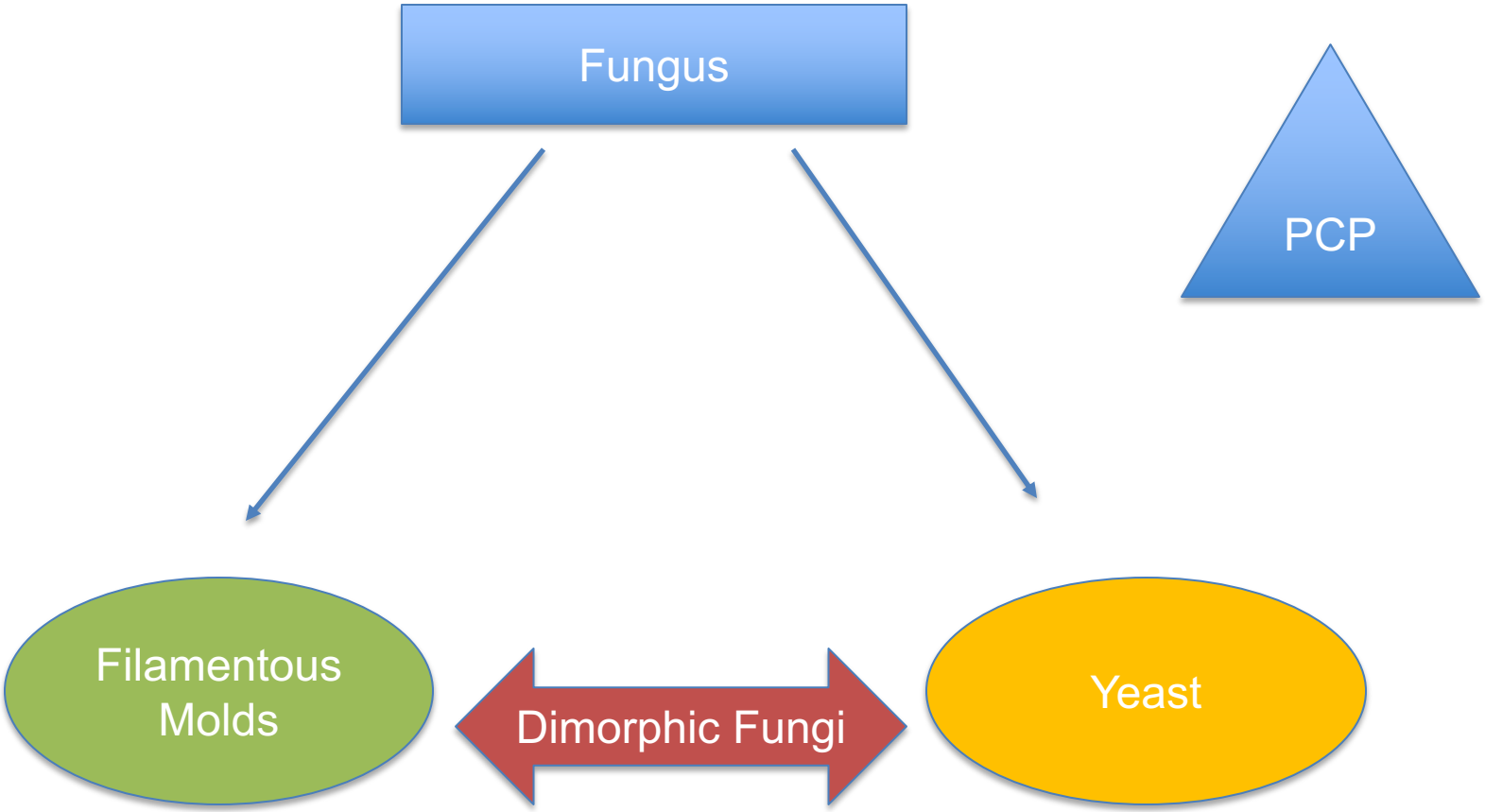
How we order Fungi



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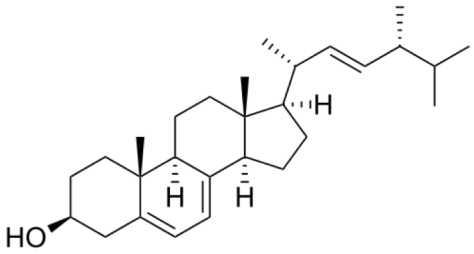
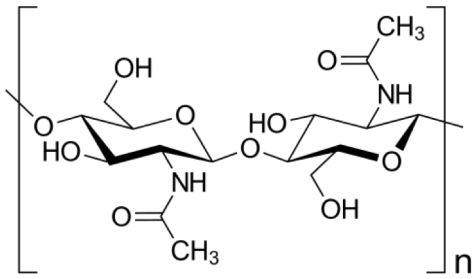
A Fun Guy

- Cell membrane:
  - Ergosterol (fungi version of cholesterol).
    - Amphotericin, echinocandins, azoles.



- Cell Wall: Surrounds the membrane. Contains Chitin.



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Treatment

Class	Mechanism
Polyenes Amphotericin B & Nystatin	Disrupt fungal membrane by binding to ergosterol
Azoles Vori, fluc, posa, isavu, keto	Inhibit synthesis of ergosterol
Nucleoside analogue 5-FU	Inhibit DNA and RNA synthesis
Allylamines Terbinafine	Inhibit ergosterol synthesis
Grisans Griseofulvin	Inhibit fungal mitosis
Candins Micafungin	Inhibit cell wall synthesis

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Amphotericin B

- Ampho B deoxycholate – data .
- Liposomal Ampho B – Tx .
- Nephrotoxicity
  - 50% of patients develop AKI on Ampho B.
  - Liposomal formulations much lower rates of AKI.

Pappas, et al. Clinical Practice Guidelines for the management of Candidiasis:2016 IDSA. CID. 2016:62.

Fluc, Itra, Posa, Isavu

- *C. Krusei* and C. *glabrata*??
- P450 inhibition - Interactions.
- Fluconazole:
  - 90% oral bioavailability and 70% penetrates the CSF. Concentrates in urine.
- Voriconazole
  - Better for C Krusei and glabrata.
  - Hepatic, CNS, and visual toxicity.
- Posa and isavu
  - Not used as primary tx for candidiasis.

Pappas, et al. Clinical Practice Guidelines for the management of Candidiasis:2016 IDSA. CID. 2016:62.

EchinoCANDIDAns

- Caspofungin, micafungin, anidulafungin.
- First line treatment for candidemia.
- Low MICs for most candida species.

Pappas, et al. Clinical Practice Guidelines for the management of Candidiasis:2016 IDSA. CID. 2016:62.

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Flucytosine

- No effect on C Krusei.
- High CNS penetration and eye penetration.
- CNS infections and endocarditis. Always used in conjunction with another antifungal.

Pappas, et al. Clinical Practice Guidelines for the management of Candidiasis:2016 IDSA. CID. 2016:62.

Candida **Sp**	Fluc	Itra	Vori	Posa	5-FU	Ampho	Candins
Albicans	S	S	S	S	S	S	S
Tropicalis	S	S	S	S	S	S	S
Parapsilosis	S	S	S	S	S	S	S or R?
Glabrata	S-DD to R	S-DD to R	S-DD to R	S-DD to R	S	S to I	S
Krusei	R	S-DD to R	S	S	I to R	S to I	S
Lusitaniae	S	S	S	S	S	S	S to R

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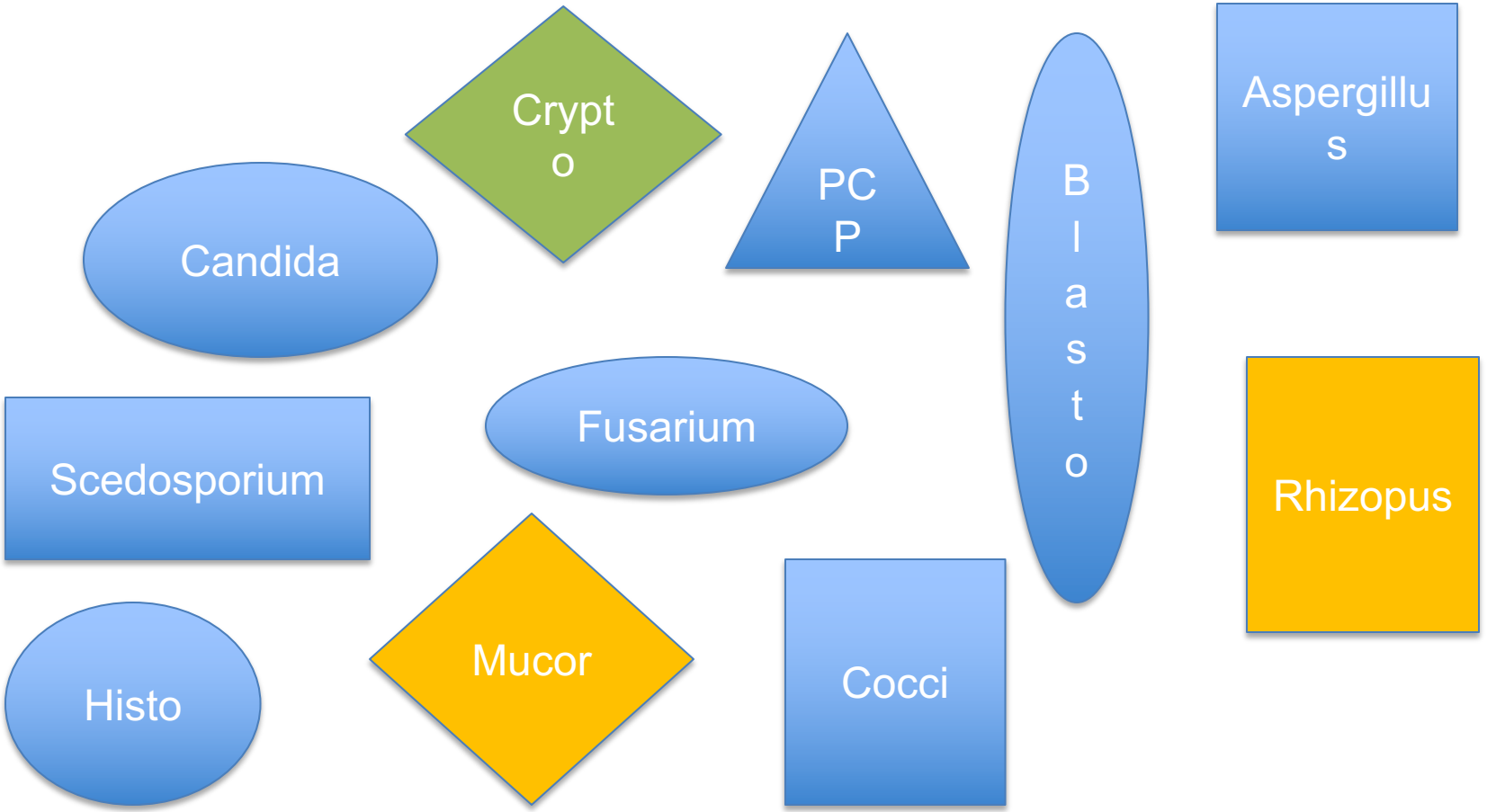
Favorite Fun Guy?



Candida : A Fun Guy

- Any organ system.
- >90% of invasive disease is due to *C. albicans, glabrata, krusei, parapsilolsis, tropicalis*.
- ~50% of invasive disease is due to non-albicans candida.
- 47% mortality with candidemia.

Pappas, et al. Clinical Practice Guidelines for the management of Candidiasis:2016 IDSA. CID. 2016:62.

Diagnosis

- Which of these tests is available at your facility?

A. Culture and stain

B. PCR

C. Ab testing

D. Beta-D-glucan testing (Fungitell)

Diagnosis

- Culture and Stain = Gold Standard
- Ag, Ab, and PCR still establishing a role.
- Beta-D-glucan, AKA fungitell:
- PCR Similar issues as fungitell.

Pappas, et al. Clinical Practice Guidelines for the management of Candidiasis:2016 IDSA. CID. 2016:62.

What do I do with those positive culture results?

When to Treat?

A. Candida in sputum cx.
B. Candida in urine cx of an asymptomatic non-neutropenic patient.
C. Candida from a wound culture
D. Candida from a ETT aspirate of an intubated patient.
E. Candida from the blood.
F. D and E
G. All of the above

Top three myths of fungal infections…

1. My patient has Candida pneumonia
2. My patients has Candida UTI
3. Fungi are simple.

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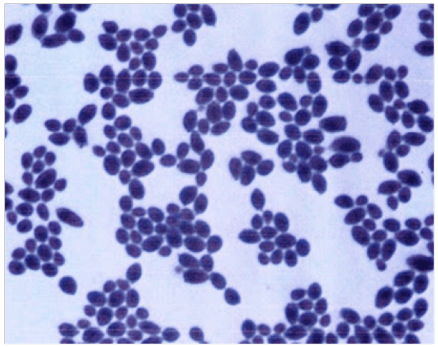
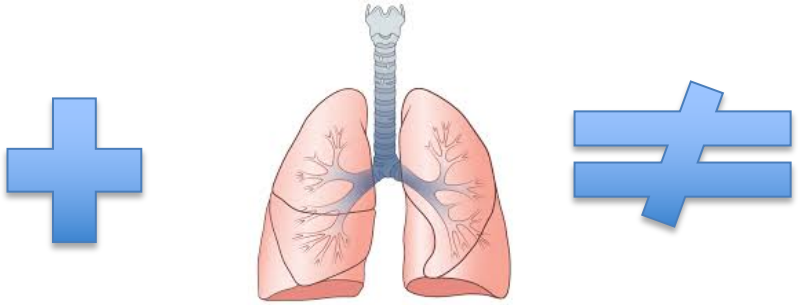
Candida Pneumonia ??





PNA

Colonizer 22% of healthcare workers & 55% of inpatients on abx will grow candida from their sputum. PPV with candida is 42% and on BAL its 29%.

Masur, H; et al. Pulmonary Disease Caused By Candida Species. The American Journal of Medicine. The American Journal of Medicine. 1977.
Andes; et al. Pulmonary Candidiasis in Patients with Cancer. CID. 2012:54.

Candida Pneumonia??

- 301 patients who died of pneumonia in ICU 77% had autopsy and 0% had histologically proven candida pneumonia. 44% had candida in sputum samples.
  - *Albicans* > *glabrata* > *Tropicalis* > *Parapsilosis* > *Krusei.*
- No correlation between amount of growth or number of sites colonized and propensity to develop invasive candidiasis.

Meersseman et al. Significance of the Isolation of Candida from airway samples in critically ill patients. Intensive Care Med. 2009. Vol 35.

Candida Pneumonia?

24% of ICU physicians would treat candidiasis in an intubated and immunocompetent patient.

Candida Pneumonia !!!

- True candida pneumonia is via candidemia with hematogenous spread.
  - Candida pneumonia without disseminated candida occurred in less than 1% of cases.
- Do not treat candida in sputum.
- Do treat disseminated candidemia presenting with hematogenous spread of candida to the lungs.

Haron et al. Primary Candida Pneumonia. Medicine. 1993. 72(3).

Candida Pneumonia

In an immunosuppressed patient with candidemia and Candida on a BAL which tx would you initiate?

A. Micafungin
B. Amphotericin B deoxycholate
C. Liposomal Ampho B
D. Isavuconazole
E. Fluconazole
F. Voriconazole

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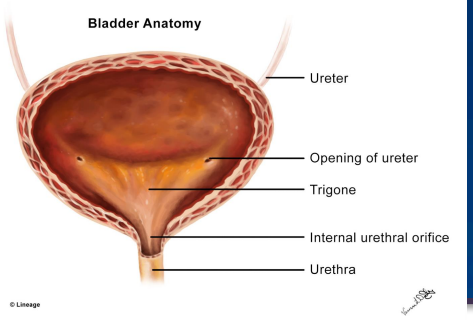
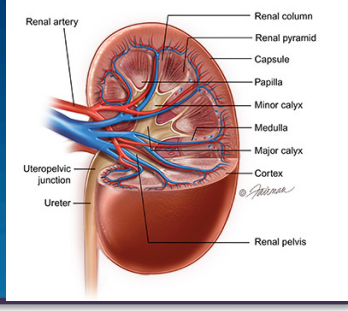
Candida UTI?



Candiduria



- Third most common nosocomial urine isolate in Europe.
  - After *E Coli* and *Enterococcus*.
- Candiduria ≠ Candidemia or cystitis
- When to tx asymptomatic candiduria?
  - Very low birth weight infants
  - Neutropenic patients
  - Impending urologic procedures.

Treat these patients with candiduria.

Bouza E; et al. A European Perspective on nosocomial UTI. Clinical Microbiol Infect. 2001

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Symptomatic Candiduria

- Hematogenous
  - Renal abscesses presenting with flank pain.
- Ascending
  - DM, female, foley catheter, and anatomic abnormalities.
  - Indolent. Often leads to pyelo or renal fungal ball before being discovered.
  - Change the foley, tx their diabetes, fix their GU reflux.

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Candiduria Treatment

- A gentleman is having lithotripsy for a persistent nephrolithiasis and has candida albicans growing from a recent urine cx. Which would you treat him with?

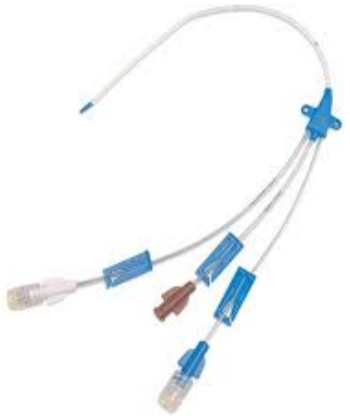
A. Micafungin
B. Amphotericin B
C. Liposomal Amphotericin B
D. Voriconazole
E. Fluconazole
F. Caspofungin

Candidemia

- 4th most common nosocomial cause of BSI.
- Rising prevalence of C. glabrata BSI.
- Neutropenic v non-neutropenic candidemia
- Prefer echinocandins but no head to head data to say it's outcomes are superior.
  - Safety profile and efficacy.

Non-Neutropenic Candidemia

- Think CVC!
  - 70% of non-neutropenic patients with candidemia have a CVC.
- DM, immunosuppression and TPN.
- Echinocandin, fluconazole, IV or PO, is acceptable alternative or step down.
- Get sensitivities.
- In 5-7 days de-escalate from echinocandin to fluconazole.
- Blood cx QD or QOD until cleared.
- Tx for 2 weeks.



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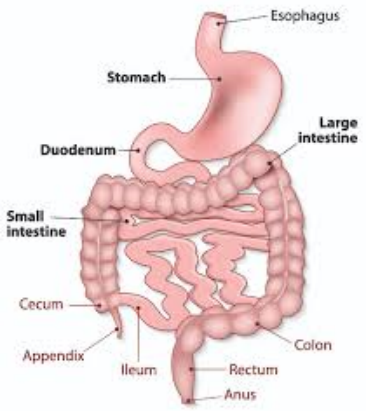
Neutropenic Candidemia

- Think gut source.
- Echinocandin still first line.
- CVC removal on case by case basis.
- Otherwise treat as for non-neutropenic candidemia



Candida Endocarditis

- Native valve endocarditis:
  - Liposomal Ampho B +/- 5-FU or high dose echinocandin (micafungin 150 mcg daily).
  - Stepdown to fluc 400 mg daily
  - Valve replacement!
  - If unable to undergo valve replacement then chronic suppressive fluc.
- Prosthetic Valve
  - Same recs.

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References

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