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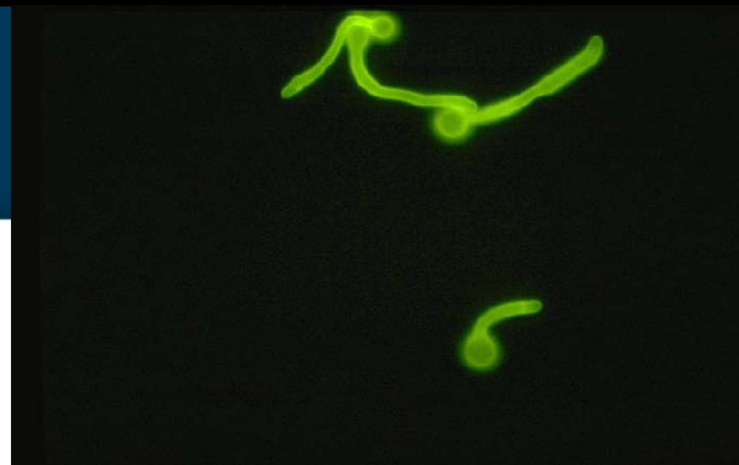
Which antifungal treatment in real life?

You decide !! I am listening or I 'll try to.

- 85 year old man
- In May and July 2011 two abdominal interventions for rectum cancer with temporary ileostomy
- Prolonged ICU stay
- Slow response due to postoperative paralytic ileus
- Central venous catheter and total parenteral nutrition
- Meropenem during +/- one month
- Blood cultures positive for yeasts and pseudomycelium in four sets on 8 September (separate venipuncture sites)
- Catheter removed and tip positive for the same yeast. Urine positive for the same agent

- **Which yeasts are the possible agents of this fungaemia?**
- **Which yeasts are not “in the running” if this proves to be a single agent?**
- **And now: which antifungal agent to start with in this azole naive patient ?**
  - Fluconazole ?
  - Echinocandin ?
  - Voriconazole ?
  - Posaconazole ?
  - Amphoterin B or a lipid formulation ?



- Possible agents: *Candida albicans*, *Candida parapsilosis*
- If this is not a mixed infection: *Candida glabrata* is excluded, as well as *Saccharomyces cerevisiae* (role of Enterol® in Belgium)
- 2010: 14 cases of candidaemia (11 *Candida albicans*, 3 *Candida glabrata*). *Candida* sp.: 10th place on the ranking score of our septicemia agents
- Fluconazole is started on 9 September

- Is this a high risk patient for invasive candidiasis?
- Do we have to ask for other investigations and why?

“the Candida score”: **A bedside scoring system (“Candida score”) for early antifungal treatment in nonneutropenic critically ill patients with *Candida* colonization. León C et al. Crit Care Med 2006 34 (3): 730-737.**

Table 4. Calculation of the Candida score: Variables selected in the logistic regression model

Variable	Coefficient (β)	Standard Error	Wald χ^2	p Value
Multifocal *Candida* species colonization	1.112	.379	8.625	.003
Surgery on ICU admission	.997	.319	9.761	.002
Severe sepsis	2.038	.314	42.014	.000
Total parenteral nutrition	.908	.389	5.451	.020
Constant	−4.916	.485	102.732	.000

ICU, intensive care unit.

Candida score = .908 × (total parenteral nutrition) + .997 × (surgery) + 1.112 (multifocal *Candida* species colonization) + 2.038 (severe sepsis). Candida score (rounded) = 1 × (total parenteral nutrition) + 1 × (surgery) + 1 (multifocal *Candida* species colonization) + 2 × (severe sepsis). All variables coded as follows: absent, 0; present, 1.

The list of risk factors used in our institution:

Risicofactoren voor invasieve candidose en candidemie op intensieve zorgen:

- **Breedspectrumantibiotca (langdurig)**
- **Chirurgie (vooral abdominale waarbij de darmwand ingesneden wordt)**
- **Diabetes**
- Nierinsufficiëntie
- **Hemodialyse**
- **Totale parenterale voeding**
- Immuunsuppressieve therapie (vooral corticoïden)
- Maligniteit en chemotherapie
- Transplantatie
- **Zeer ernstige algemene toestand of sepsis (**gaan dan ook meestal dood **met** een *Candida*probleem en niet **door** een invasieve candidose**)**
- Langdurige hospitalisatie
- ***Candida* kolonisatie op verschillende plaatsen**
- Centraal veneuze katheter?

- **The patient doesn’t respond well**
- **On 11 September again positive blood cultures (two sets): persistant candidaemia under fluconazole**
- **What is going wrong?**
  - Resistance ?
  - Endocarditis ?
  - Metastatic infection (bone, CNS, ….)
  - Other suggestions ?

Deep venous thrombosis

Medical Mycology Month 2011, **Early Online**, 1–6

healthcare

Case Report

Candidal thrombophlebitis of central veins: case report and review

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- Role of ophthalmoscopy?
- What if the blood cultures had been obtained via the central catheter instead of a peripheral site?
- What if the patient had received an azole before his candidaemia episode?
- Does severity (stable vs. unstable patient) of illness would influence your antifungal choice?
- If you want to use an echinocandin, which one do you prefer (caspofungin, anidulafungin or micafungin)?

- Dou you want all isolates from a candidaemia episode to be tested for susceptibility?
- And what if a *Candida glabrata* appears to be susceptible to fluconazole in one of these susceptibility assays?
- Was this patient a candidate for antifungal prophylaxis? Or for empiric antifungal therapy?

The patient died although deep venous thrombosis had been looking for, but at the wrong place (lower limbs) and treatment was switched to an echinocandin.

The most difficult question now: did this patient died from invasive candidiasis or with invasive candidiasis (attributable versus crude mortality)?

- 39 year old man. Admission on 7June 2010
- Medical history: none, except for chronic sinsusitis
- Medication: none declared on admission but afterwards history of chronic use of a corticosteroid containing nasal spray, declared “innocent” by his otorhinolaryngologist
- Progressive headache and recently diplopia
- CT scan on 8 June.

aspergillosis

A115

R 125

L 125

P135

- "mass with floating calcifications in the paranasal sinuses (sphenoidal sinus and ethmoidal cells) …extending into the sella turcica, into the hypophysial fossa and into the middle cranial fossa."
- Tumor or fungal infection?
- Neurosurgical intervention: fungus ball with destruction of the bone. Surgical removal and rinsing.
- Direct examination: mycelium ++++. Culture (difficult): *Aspergillus fumigatus* one CFU.

- **Treatment was required after surgery (extended infection with bone loss)**
- **Amphotericin B desoxycholate removed from the Belgian market**
- **Small reserve of Ampho B in the pharmacy to start with**
- **No reimbursement possible for this “immunocompetent” patient if treated with other antifungals with anti-*Aspergillus* activity**

- The Belgian solution: contacting the advisory doctor of the insurance company and voriconazole treatment allowed
- The patient is now in good health but developed diabetes insipidus wich is under control
- If further investigations are undertaken “from above” in this case, the prescribing MD remains responsible for any “inappropriate” use of an antifungal agent
- Otolaryngologists still think corticosteroid nasal sprays are innocent