

Interactive Case Discussion SBIMC-BVIKM-BSHAM Symposium Antwerp - 29/03/2018



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Clinical case

81-year- old man

Institutionalized in a nursing home facility

Referred to the Emergency Room by GP

- Fever, chills
- Abdominal pain
- Weakness
- Hyperglycemia

Medical history :

- Advanced dementia of mixed origin (ethylism, vascular)
- Wernicke'encephalopathy
- Gastrostomy with enteral nutrition
- Type 2 Diabetes
- Chronic renal failure

Clinical case

T° 38,1°C HR 111 BPM BP 149/85 mmHg SpO2 93%

GCS 14/15

Confused, non collaborating, dehydrated

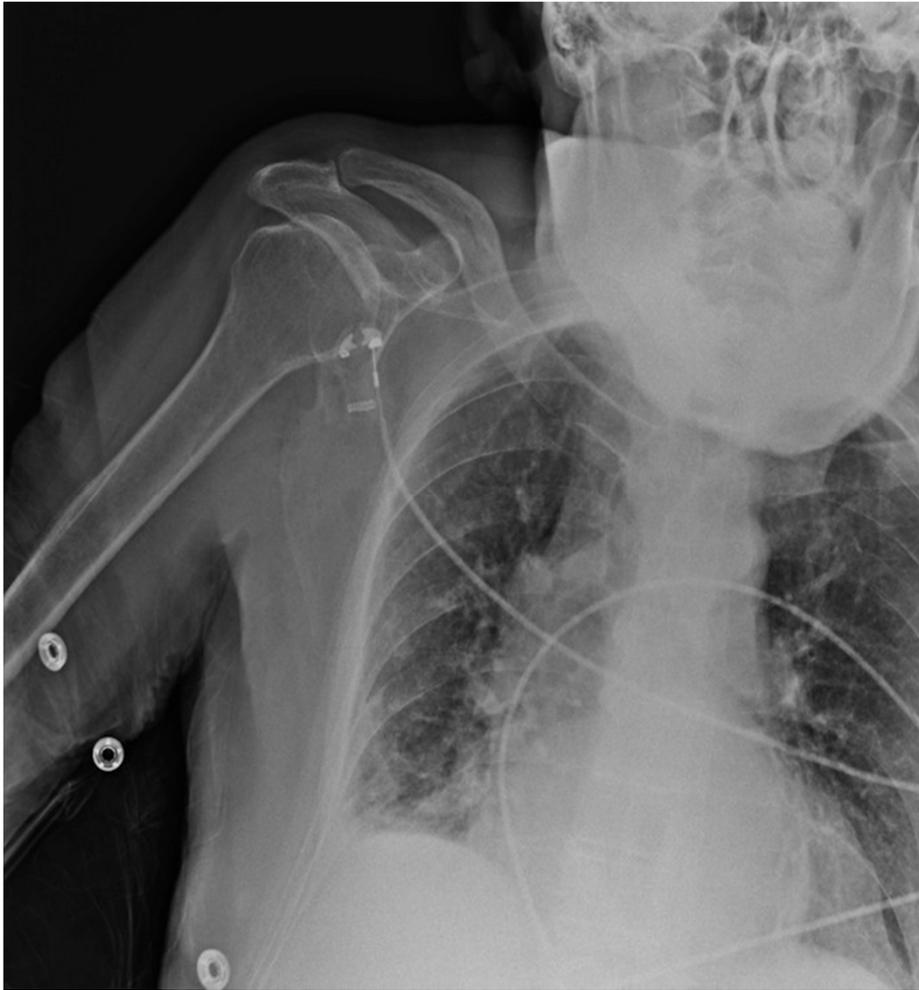
Lung hypoventilation & crackles

Abdomen sensitivity

Rectal exam : fecaloma

Lab : WBC 18,160 CRP 83 mg/L Creatinine 2,09 mg/dl

Glucose 550 mg/L



Presumed LRL pneumonia
R/ AmoxiClav 1g 3x/24h IV

Geriatric Ward

Day 2

Increase of CRP 336,7 mg/L

Abdominal pain

Day 3

Abdominal CT Scan

No acute process

Day 4

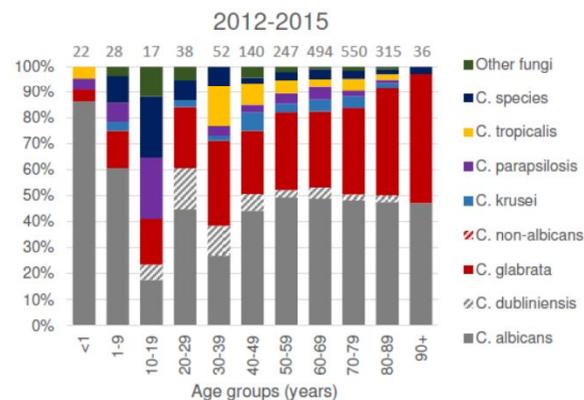
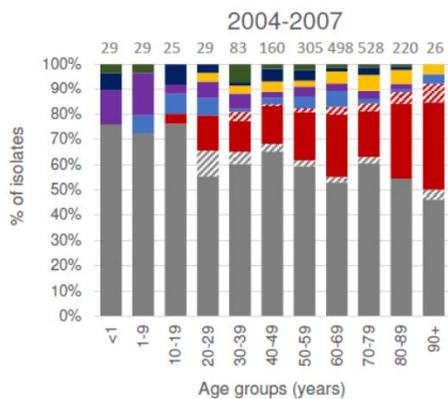
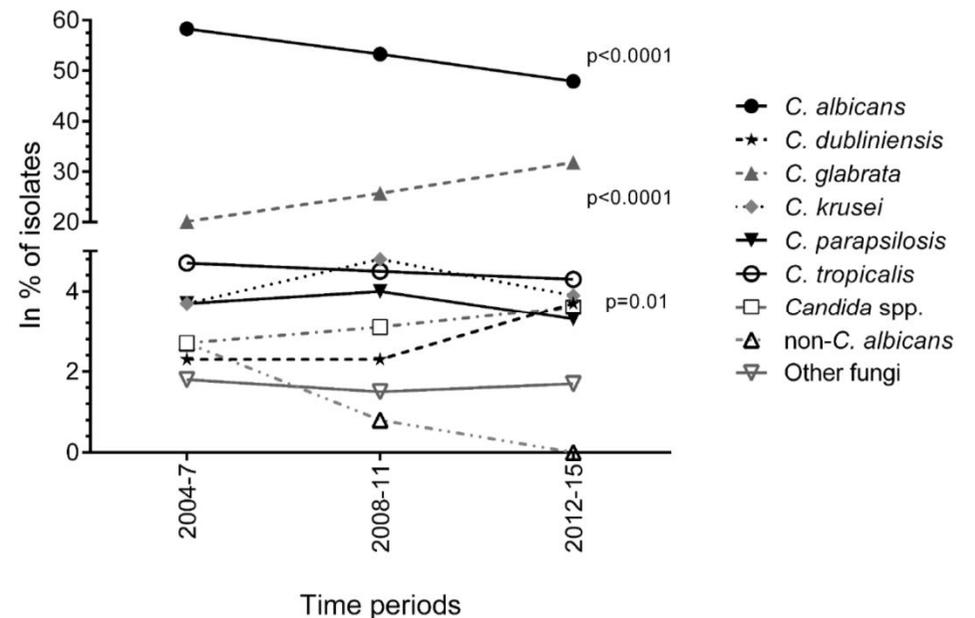
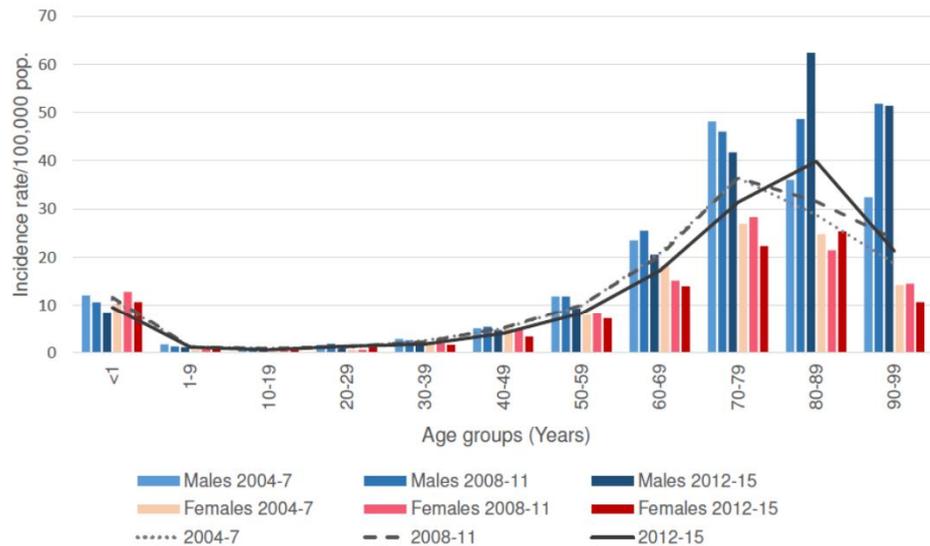
Admission blood cultures (2 sets)
positive for YEAST



Fungemia in an 81-year-old man with diabetes and renal insufficiency

1. *C. albicans* is the first cause of fungemia in the elderly, is generally fluconazole sensitive and the patient is not critically ill. I start Fluconazole therapy
2. *C. albicans* is the first cause of fungemia in the elderly but fluconazole resistance is worrying. I start an Echinocandin-based therapy
3. *C. glabrata* is the first cause of fungemia in this population. I start an Echinocandin based therapy
4. *Cryptococcus* is the first cause of fungemia in this population . I start liposomal amphotericin B & flucytosine

Danish National Fungemia Surveillance 2004-2015 : Epidemiological trends



Decrease in fluconazole susceptibility
68,5% (2004-2007) vs 60,6% (2012-2015)

Geriatric Ward

Day 5-Day 7

Apathic

Clinical status quo

CRP 159 – 199 – 167 mg/L

Day 7 (Day 7 AmoxiClav – D3 Fluconazole)

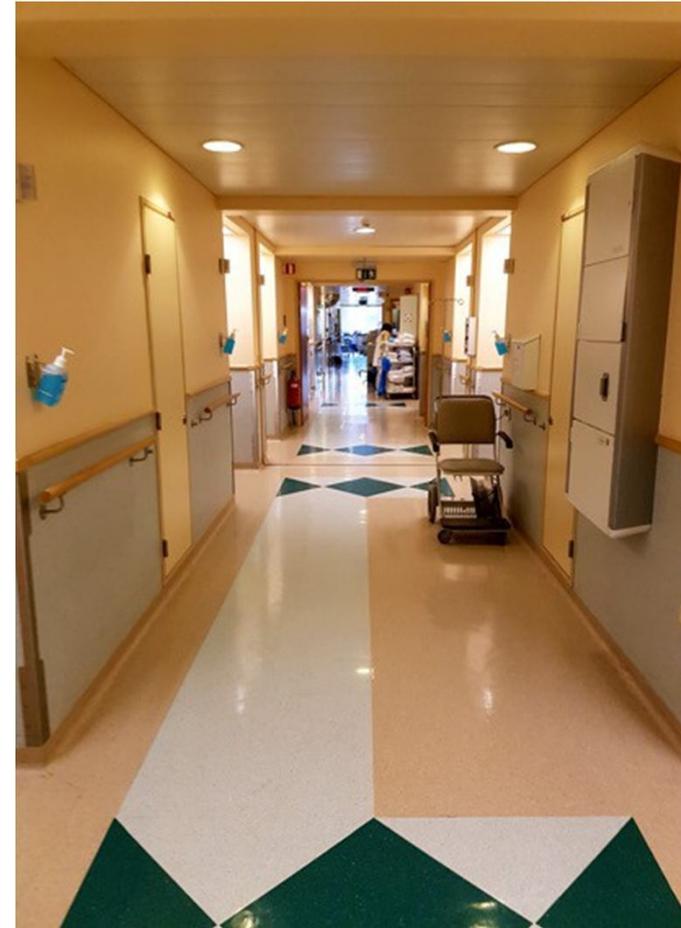
Yeast identification :

Saccharomyces cerevisiae

Call of the Nursing Home :

**Chronic administration of Enterol[®] through
gastrostomy**

Indication : « liquid stools ».....



Saccharomyces cerevisiae

« Baker's yeast » ; « Brewer's yeast »

Part of the human gut flora

Saccharomyces boulardii market as a probiotic since 1991 (Enterol or UltraLevure) for prevention of *C. diff* –associated diarrhea in adults

Large body of evidence :

- Fungemia following probiotic use
- Outbreaks in ICUs following aerosolized dissemination

Ho my god, it's alive !



Saccharomyces cerevisiae fungemia in a 81-year-old subject with renal insufficiency

According to published literature and/or guidelines, what treatment would you administer ?

1. Continue Fluconazole
2. Switch to Voriconazole
3. Switch to Amphotericin B+flucytosine
4. Switch to Echinocandin

Antifungal, reference(s)	MIC range, mg/L	MIC ₅₀ , mg/L	MIC ₉₀ , mg/L	No. of isolates
Amphotericin B				
[17]	0.12–2	1	1	74
[78, 79]	0.5–1	1	1	22
[80]	0.125–1	1	1	24
[81]	0.25–4	1	1	30
[81] ^a	0.25–1	0.5	1	30
[82]	0.25–0.5	0.25	0.25	11
[16]	0.25–4	0.5	1	160
[83] ^b	0.032–1	0.5	ND	104
5-Fluorocytosine				
[17]	0.25–32	0.25	0.25	74
[78, 79]	0.06–0.12	0.06	0.12	22
[80]	≤0.0313 to 0.25	0.0625	0.125	24
[81]	≤0.125 to 1	≤0.125	1	30
[81] ^a	≤0.125 to 0.5	≤0.125	≤0.125	30
Fluconazole				
[17]	0.12–16	2	8	74
[78, 79]	0.5–16	2	16	22
[80]	≤0.0313 to 4	0.5	2	24
[81]	0.5–16	2	4	30
[81] ^a	0.5–16	8	8	30
[82]	0.5–8	2	4	11
[16]	1–128	64	128	160
[83] ^b	2–64	32	ND	104

Ketoconazole				
[80]	≤0.0313 to 2	0.25	1	24
[81]	≤0.03 to 1	0.25	0.5	30
[81] ^a	0.03–1	0.5	1	30
Voriconazole				
[82]	≤0.008 to 8	0.032	0.125	11
[83] ^b	0.016–2	0.125	ND	104

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"We're not lost, Carrie.
We just don't know where we are."

ESCMID[†] and ECMM[‡] joint clinical guidelines for the diagnosis and management of rare invasive yeast infections

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Saccharomyces	Any	Amphotericin ^a	B-III	Most clinical experience; toxicity risk higher than for echinocandins	[178,182,183]
	Any	Echinocandins	C-III	Two successful cases in the literature (± neutropenic), no emergence of <i>S. cerevisiae</i> after intro of echinocandins as first line agents for candidaemia, two recent failure cases neutropenic (Arendrup MC unpublished data)	[27,182,183]
	Any	Amphotericin B ^a + Flucytosine ^b	B-III	Excellent <i>in vitro</i> susceptibility. May be used in severe cases or when penetration into an infected focus is challenging.	[70,170,181,184,185]
	Any	Fluconazole	D-III	Increased occurrence in patients exposed to fluconazole; high fluconazole MICs (similar to those for <i>C. glabrata</i>)	[26,178]
	Any	Discontinuation of probiotics	A-III	Probiotic containing <i>S. boulardii</i> has been documented to be the origin of systemic infections.	[175,176]

remains to be established. In addition to the systemic antifungal therapy, it is strongly recommended that probiotics containing *S. boulardii* are discontinued and indwelling foreign bodies are removed, when possible, because this organism, like many other yeasts, is capable of forming biofilms [176].

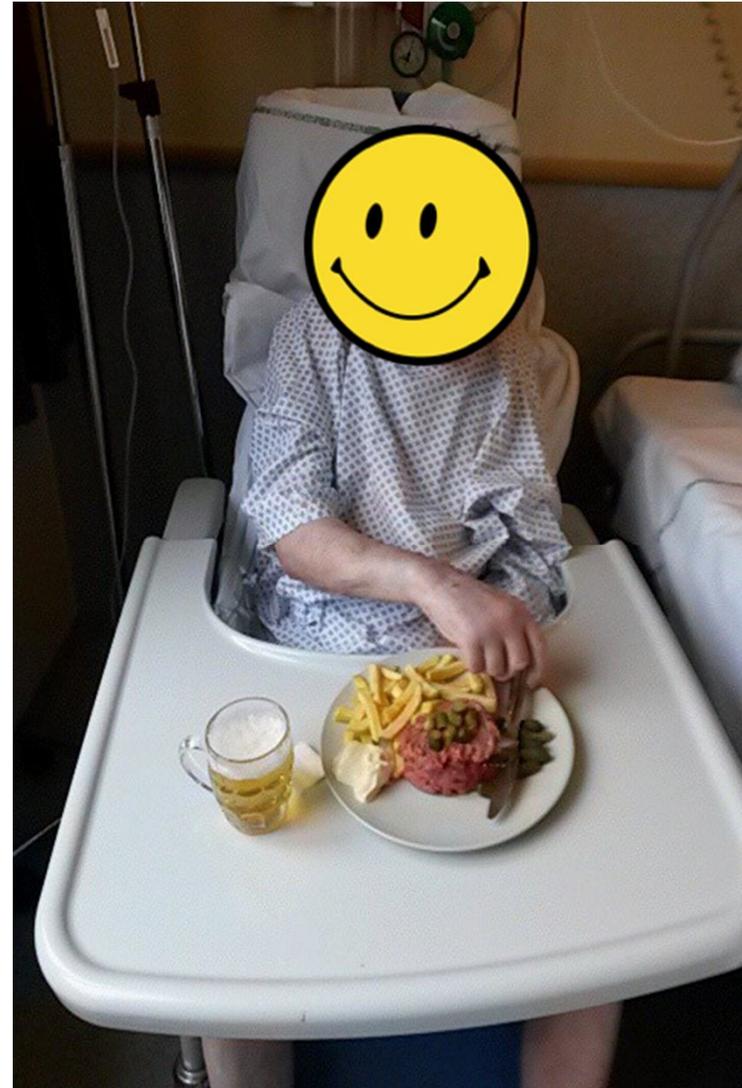
Geriatric Ward

Day 7 : Switch to Voriconazole

Cardiac US : no endocarditis

Removal of the gastrostomy feeding tube

Stop voriconazole after 2 sets of negative blood cultures (15 days)





***Saccharomyces cerevisiae* fungemia : risk factors, outcome and link with Entérol® administration**

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SBIMC-BVIKM-BSAHM Symposium – Antwerp – 29-03-2018



ULB

In the center of the city, in the center of life, with passion for care



Methods

Subject with documented *S. cerevisiae* fungemia in our institution between January 2005-June 2017

Risk factors, co morbidities, outcome, treatment and link with Enterol intake



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Results

Ten cases identified : Male (7/10)

Mean age : 60,4 years (21-88 years)

Co morbidities :

3/10 solid cancer, 1/10 HIV-infection

Enterol intake : 6/10

Overall mortality : 60%

Treatment

- FLC monotherapy (5/10)
- FLC + anidulafungin (1/10)
- VRC monotherapy (1/10)
- VRC followed by caspofungin (1/10)
- **2 deaths before treatment**

Enterol subgroup :

Prescription

- Nursing home (3/6)
- Hospital (2/6)
- Self-administration (1/6)

Foreign body

- Central veinous catheter (4/6)
- TPN (3/6)
- Enteral nutrition (2/6)

Enterol group mortality : 50%

Conclusions

S. Cerevisiae fungemia occurs in fragile patients and is associated with high mortality

High proportion is associated with Enterol intake

Enterol was removed from our institution pharmacy

Increased awareness of the risk of Enterol administration needed among MDs



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Nieuwe contra-indicatie voor *Saccharomyces boulardii* bij patiënten in kritieke toestand of immuungecompromitteerde patiënten.

Geachte zorgprofessional,

In overeenstemming met het Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten (FAGG) wil Biocodex Benelux u graag over het volgende informeren:

Samenvatting

- Er zijn zeldzame gevallen van fungemie gemeld bij patiënten die *Saccharomyces boulardii* kregen, met inbegrip van fatale gevallen bij patiënten in kritieke toestand.
- De Enterol producten zijn nu gecontra-indiceerd bij patiënten in kritieke toestand of immuungecompromitteerde patiënten. Deze producten waren al gecontra-indiceerd bij patiënten met een centraal veneuze katheter.
- Ook andere patiënten die zich in de dichte nabijheid bevinden van patiënten die met *S. boulardii* worden behandeld, lopen het risico om met die micro-organismen besmet te worden. Daarom is

**Flash VIG-news : SACCHAROMYCES BOULARDII
(en Belgique : ENTEROL®) : risque de fungémie et
contre-indication chez les patients gravement
malades ou immunodéprimés**

product gebruikt wordt in aanwezigheid van patiënten in kritieke toestand of immuungecompromitteerde patiënten of patiënten met een centraal veneuze katheter die behandeld worden met *S. boulardii*.

date:

19/01/2018

Les médicaments à base de *Saccharomyces boulardii* sont désormais contre-indiqués chez les patients gravement malades ou immunodéprimés en raison du risque de fungémie.

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Timely Use of Probiotics in Hospitalized Adults Prevents *Clostridium difficile* Infection: A Systematic Review With Meta-Regression Analysis

Nicole T. Shen,¹ Anna Maw,² Lyubov L. Tmanova,³ Alejandro Pino,⁴ Kayley Ancy,⁴ Carl V. Crawford,¹ Matthew S. Simon,^{5,6} and Arthur T. Evans⁵



No severe AEs reported in the probiotics group

Median age of subject included trials with *S. boulardii*-containing probiotics : **60 years**

In addition to the recent AFMPS/FAGG advice :

We believe that Enterol should not be administered in frail/elderly patients & subjects with enteral nutrition considering the higher risk of translocation

CORRESPONDENCE

Readers may submit letters to the editor concerning articles that have been published in this journal. Detailed guidelines regarding the content are included in the Instructions for Authors.

Risks of *Saccharomyces boulardii*-Containing Probiotics for the Prevention of *Clostridium difficile* Infection in the Elderly

Dauby *Gastroenterology* 2017