

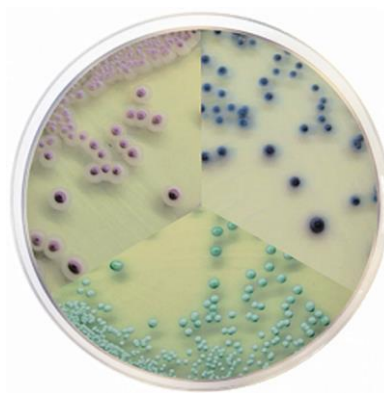
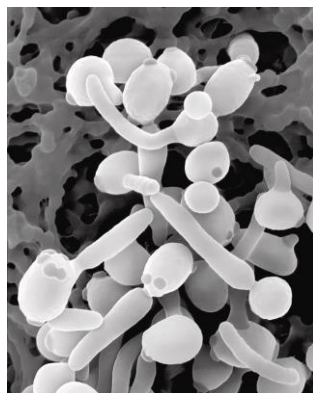
# Candidoses invasives

# Pneumocystose

B. Henry

Maladies Infectieuses Bicêtre

12 Mars 2025



Candidoses invasives/candidémies

# Candidoses invasives

- Fréquence du problème
- Epidémiologie microbienne
- Facteurs de risque
- Comment faire le diagnostic?
- Quel est le bilan d'extension?
- Que faire des cathéters centraux?
- Comment traiter?
  
- Quelques formes cliniques spécifiques

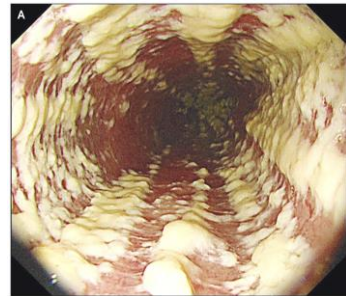
# Les infections à *Candida*

« Superficielles »

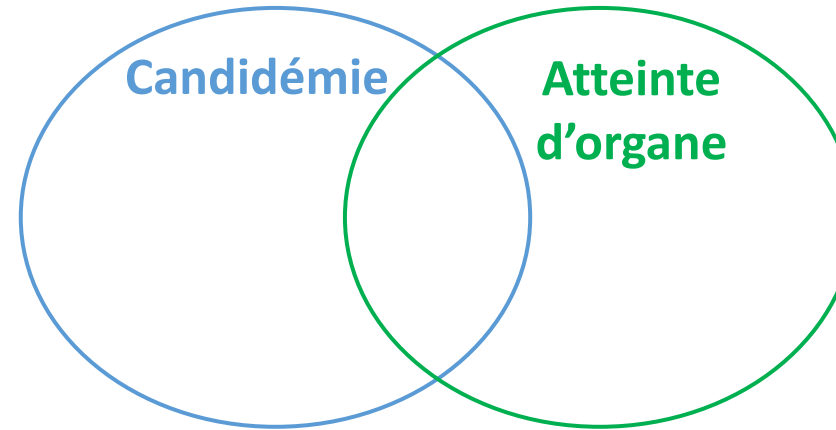
Cutanées



Muqueuses



« Profondes »



Hépatosplénique  
UTI  
Ophtalmo  
Os  
SNC  
Cœur  
Abdomen  
Médiastin  
...

Attention à la colonisation des muqueuses (20-50%)

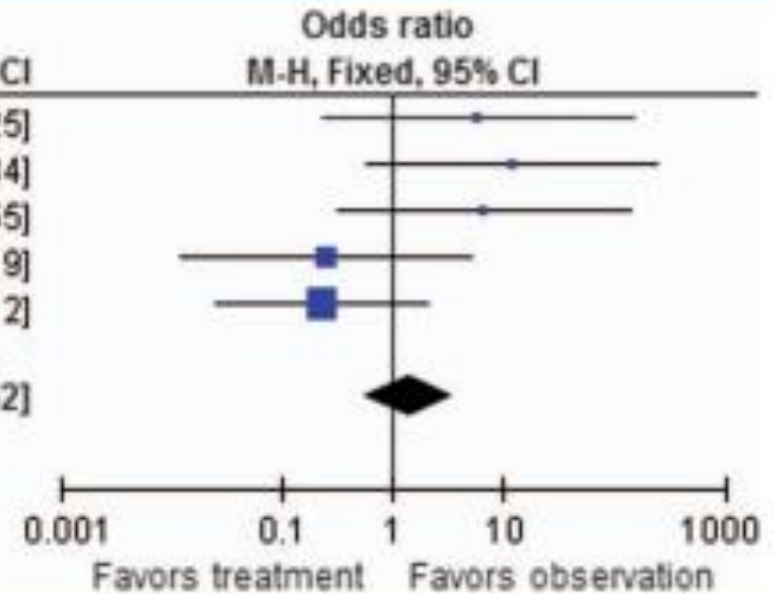
# Candidémie: définitions

- Une seule hémoculture (périph/CVC) suffit
- *Candida* n'est pas 1 contaminant!
- En cas d'extrémité de CVC isolément positive en culture ?

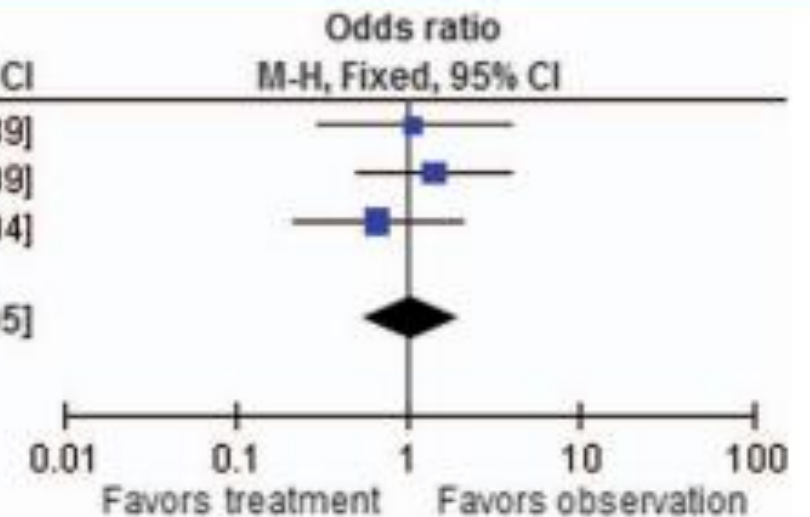
Signification clinique débattue Khatib R *et al.* JCM 1995

# Positivité isolée de l'extrémité d'un CVC

Study or Subgroup	Treated		Untreated		Weight	Odds ratio M-H, Fixed, 95% CI
	Events	Total	Events	Total		
Perez-Parra et al., 2009 (22)	1	20	0	38	4.3%	5.92 [0.23, 152.25]
Leenders et al., 2011 (24)	3	27	0	41	4.6%	11.86 [0.59, 239.34]
Lopez-Medarno et al., 2012 (26)	3	22	0	18	6.1%	6.64 [0.32, 137.55]
Park et al., 2010 (23)	0	13	3	26	30.3%	0.25 [0.01, 5.19]
Khatib et al., 1995 (25)	1	26	5	34	54.7%	0.23 [0.03, 2.12]
<b>Total (95% CI)</b>		<b>108</b>		<b>157</b>	<b>100.0%</b>	<b>1.41 [0.56, 3.52]</b>
Total events	8		8			
Heterogeneity: $\text{Chi}^2 = 7.49$ , $\text{df} = 4$ ( $P = 0.11$ ); $I^2 = 47\%$						
Test for overall effect: $Z = 0.73$ ( $P = 0.47$ )						



Study or Subgroup	Treated		Untreated		Weight	Odds ratio M-H, Fixed, 95% CI
	Events	Total	Events	Total		
Lopez-Medarno et al., 2012 (26)	9	22	7	18	24.9%	1.09 [0.30, 3.89]
Khatib et al., 1995 (25)	13	26	14	34	33.3%	1.43 [0.51, 3.99]
Perez-Parra et al., 2009 (22)	7	20	17	38	41.8%	0.67 [0.22, 2.04]
<b>Total (95% CI)</b>		<b>68</b>		<b>90</b>	<b>100.0%</b>	<b>1.02 [0.54, 1.95]</b>
Total events	29		38			
Heterogeneity: $\text{Chi}^2 = 0.98$ , $\text{df} = 2$ ( $P = 0.61$ ); $I^2 = 0\%$						
Test for overall effect: $Z = 0.07$ ( $P = 0.94$ )						



O1054 **Impact of antifungal treatment on mortality in patients with positive catheter tip cultured for Candida with or without concurrent candidaemia**

Yvonne Schmiedel\*<sup>1</sup>, Stefan Zimmerli<sup>3</sup>, Frederic Lamothe<sup>2</sup>, Veronique Erard<sup>2</sup>, Oscar Marchetti<sup>2</sup>

<sup>1</sup>Inselhospital, Universitätsspital Bern, Infektiologie, Bern, Switzerland, <sup>2</sup>CHUV, ID, Lausanne, Switzerland, <sup>3</sup>Inselhospital, Universitätsspital Bern, ID, Bern, Switzerland

**Materials/methods:** In this retrospective cohort study nested within an ongoing candida surveillance study of the FUNGINOS (fungal infections network of Switzerland) group, we analyzed clinical characteristics and outcomes of patients with a positive catheter tip culture for Candida. The primary outcome was to assess mortality 1) in catheter tip positives without candidemia comparing those who did and did not receive antifungal treatment; 2) in patients with or without concurrent candidemia irrespective of treatment. Mortality was assessed based on univariate analysis as well as logistic regression using known risk factors for candidemia.

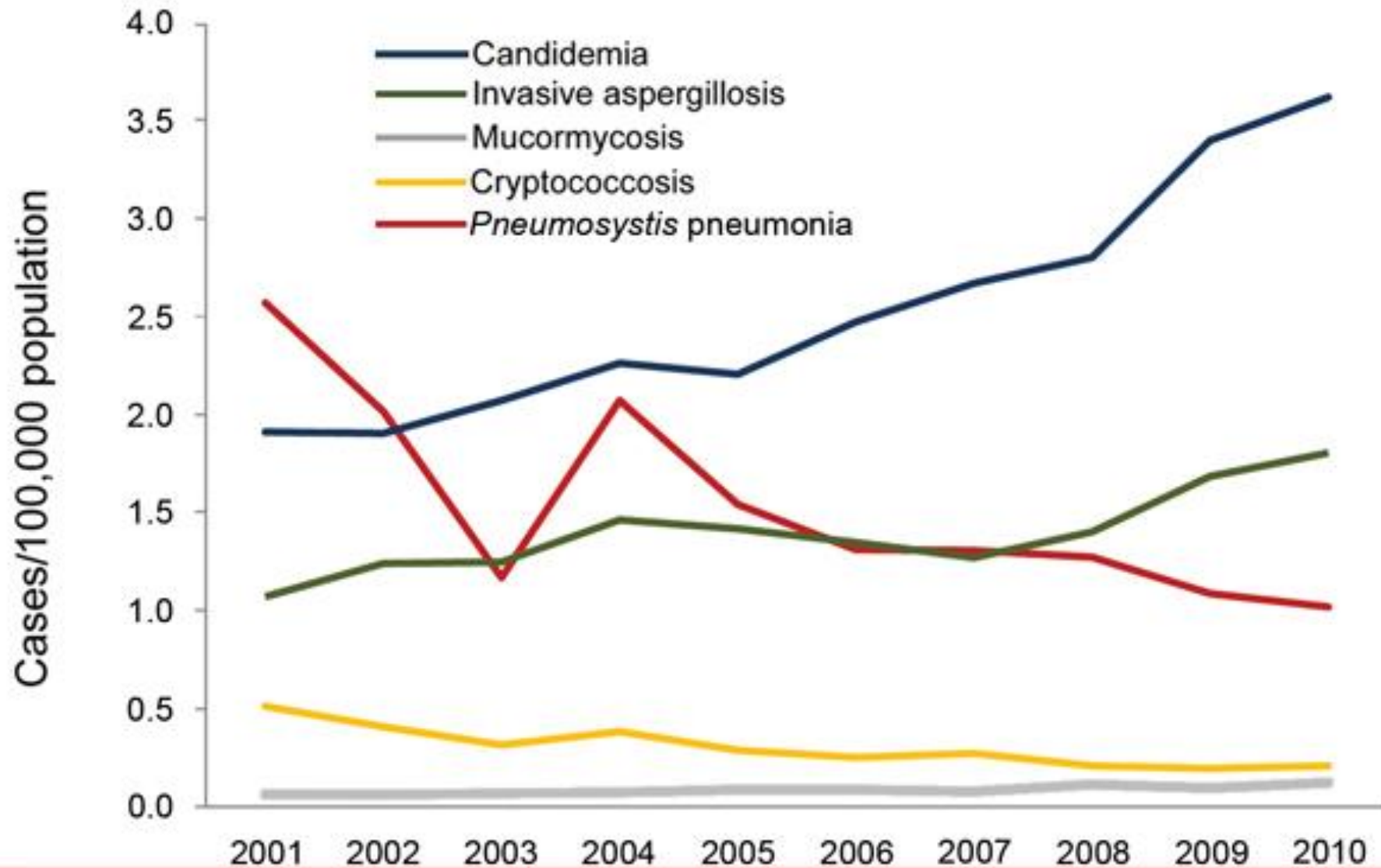
**Results:** Among a total of 212 patients with a positive catheter tip culture for Candida, 84 had candidemia and 75/128 blood culture negative patients received antifungal treatment. Neither antifungal treatment nor positive blood cultures were individual risk factors for death. In the multivariate analysis, in both groups 1) no treatment vs. treatment and 2) non-candidemia vs. candidemia mortality was associated with older age, ICU admission or prolonged stay in ICU, liver cirrhosis, hemodialysis or septic shock, respectively. Close to 80% of catheters were removed within three days of blood culture positivity. Although not associated with mortality, catheter tips with >1000 candida colonies/ml were positively associated with candidemia.

**Conclusions:** Antifungal treatment in patients with positive catheter tip cultures for Candida without concurrent Candidemia has no effect on mortality.

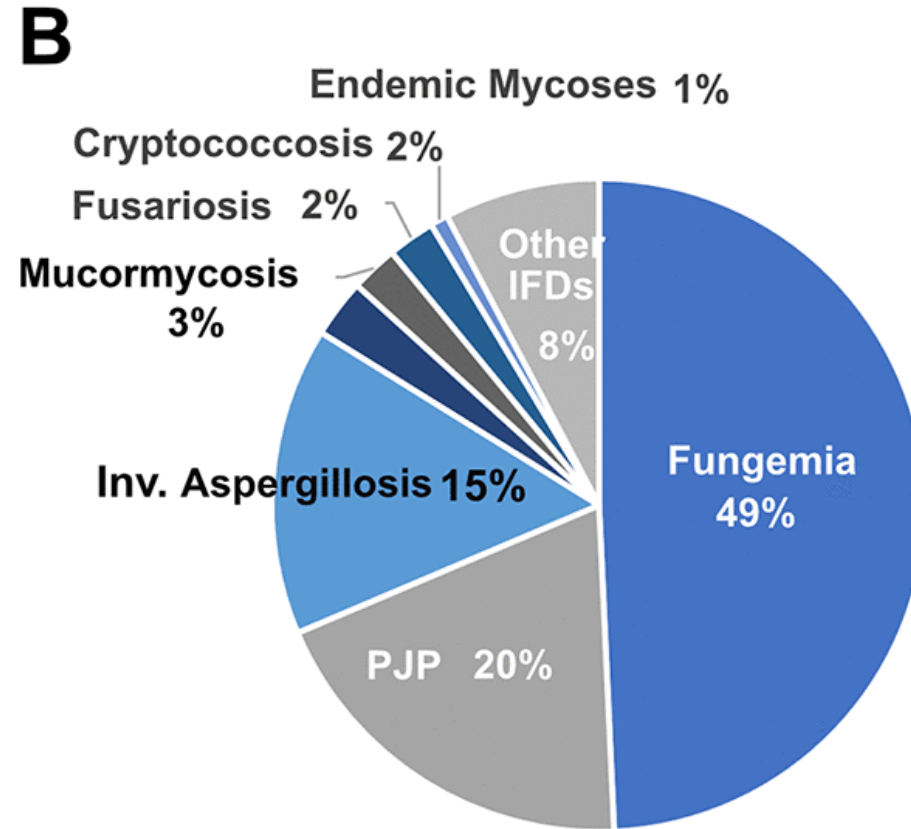
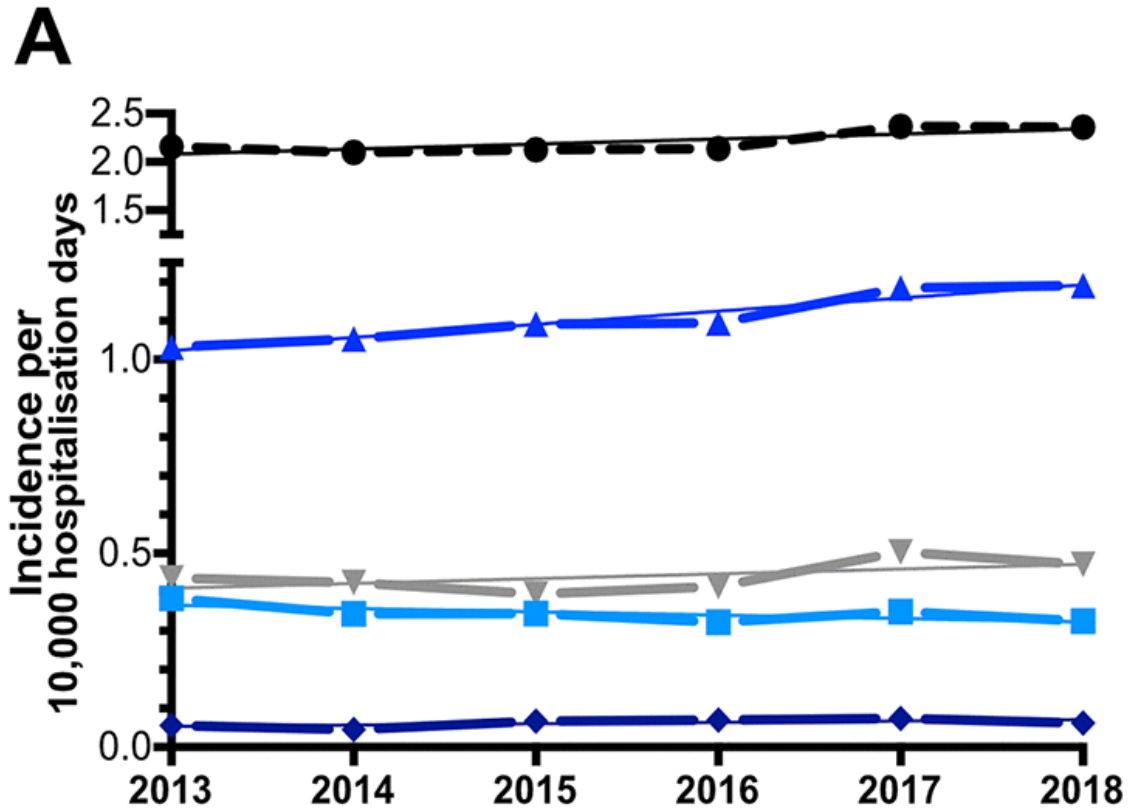
# Epidémiologie

- Varie selon pays, type d'établissement, âge...
- Tendance à l'augmentation globale
- Incidence: en moyenne 3 - 5/100 000 en population générale
- Rôle de la pré-exposition aux ATF dans l'épidémiologie microbienne
- Epidémies parfois (*C. auris*...)

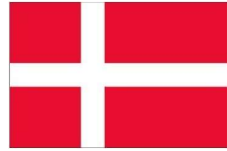
# Candidémie: augmentation globale



# Candidémie: augmentation



# Candidemia: not only ICU & Haematology

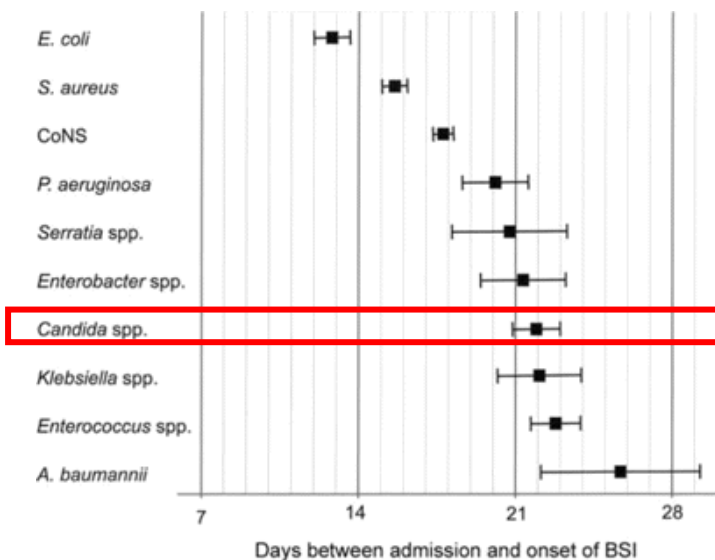


- Nationwide
- Jan 2010-Dec 2011
- 912 cases
- National incidence rate for 1<sup>st</sup> episode:  
8.8/100 000

	Patients	
	No	%
<b>Total</b>	<b>912</b>	<b>100.0</b>
<b>Intensive care unit</b>	<b>394</b>	<b>43.2</b>
<b>Departments of medicine</b>	<b>306</b>	<b>33.6</b>
General Medicine	176	19.3
Gastroenterology	40	4.4
Haematology	36	3.9
Cardiology	18	2.0
Nephrology	14	1.5
Oncology	12	1.2
Infectious Diseases	9	1.0
Neurology	1	0.1
<b>Departments of Surgery</b>	<b>166</b>	<b>18.2</b>
General Surgery	153	16.8
Urology	13	1.4
<b>Paediatrics</b>	<b>30</b>	<b>3.3</b>
<b>Emergency department</b>	<b>16</b>	<b>1.8</b>

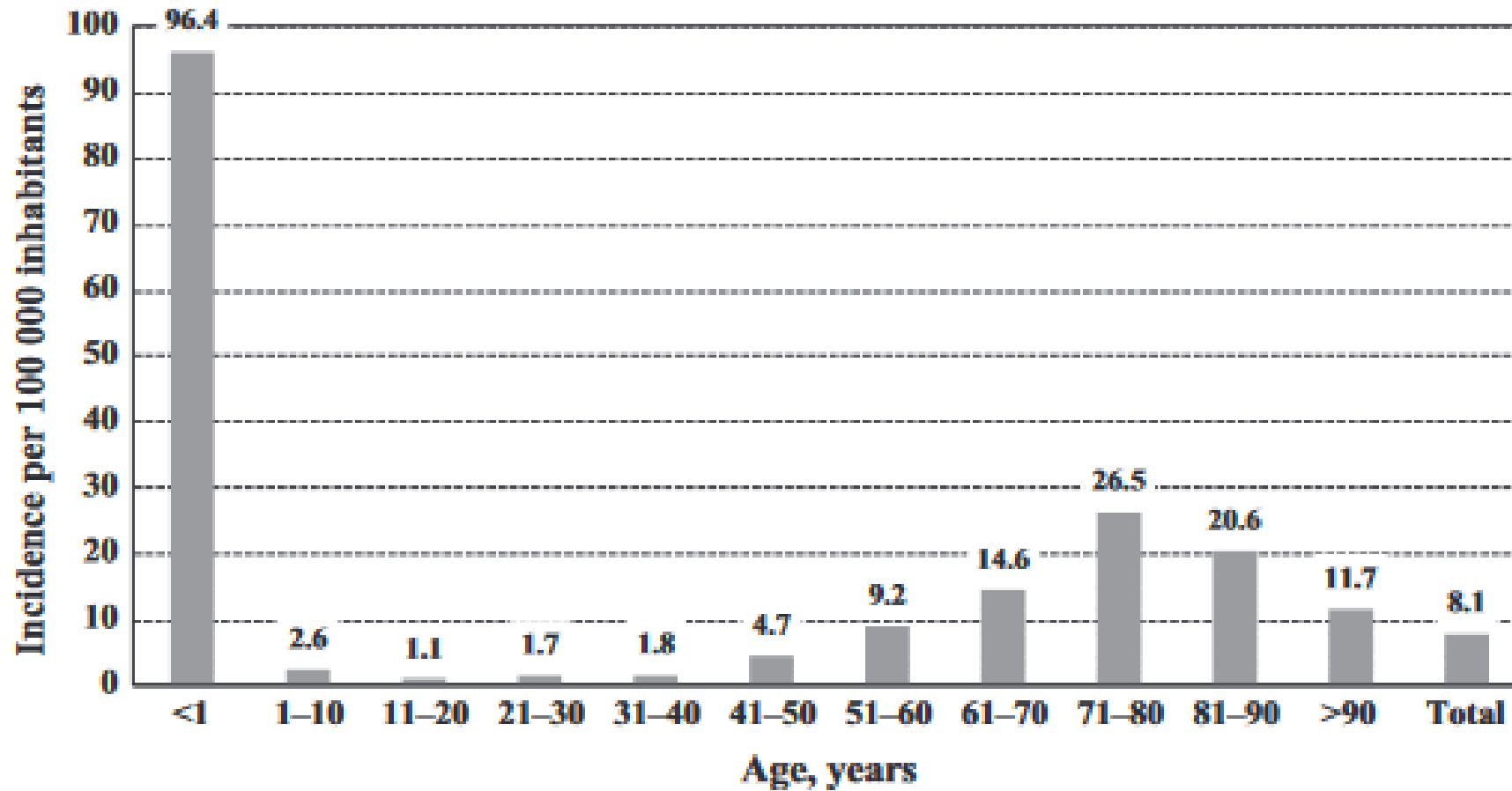
# Candida au sein des “septicémies” nosocomiales

- 49 centres, USA
- 1995-2002
- 24 179 cas de BSI nosocomiales



Pathogen	BSIs per 10,000 admissions	Percentage of BSIs (rank)			Crude mortality, %		
		Total (n = 20,978)	ICU (n = 10,515)	Non-ICU ward (n = 10,442)	Total	ICU	Non-ICU ward
CoNS	15.8	31.3 (1)	35.9 (1) <sup>a</sup>	26.6 (1)	20.7	25.7	13.8
<i>Staphylococcus aureus</i> <sup>b</sup>	10.3	20.2 (2)	16.8 (2) <sup>a</sup>	23.7 (2)	25.4	34.4	18.9
<i>Enterococcus</i> species <sup>c</sup>	4.8	9.4 (3)	9.8 (4)	9.0 (3)	33.9	43.0	24.0
<i>Candida</i> species <sup>c</sup>	4.6	9.0 (4)	10.1 (3)	7.9 (4)	39.2	47.1	29.0
<i>E. scherichia coli</i>	2.8	5.6 (5)	3.7 (8) <sup>d</sup>	7.6 (5)	22.4	33.9	16.9
<i>Klebsiella</i> species	2.4	4.8 (6)	4.0 (7) <sup>a</sup>	5.5 (6)	27.6	37.4	20.3
<i>Pseudomonas aeruginosa</i>	2.1	4.3 (7)	4.7 (5)	3.8 (7)	38.7	47.9	27.6
<i>Enterobacter</i> species	1.9	3.9 (8)	4.7 (6) <sup>a</sup>	3.1 (8)	26.7	32.5	18.0
<i>Serratia</i> species <sup>b</sup>	0.9	1.7 (9)	2.1 (9) <sup>a</sup>	1.3 (10)	27.4	33.9	17.1
<i>Acinetobacter baumannii</i>	0.6	1.3 (10)	1.6 (10) <sup>a</sup>	0.9 (11)	34.0	43.4	16.3

# Candidémie: role de l'âge



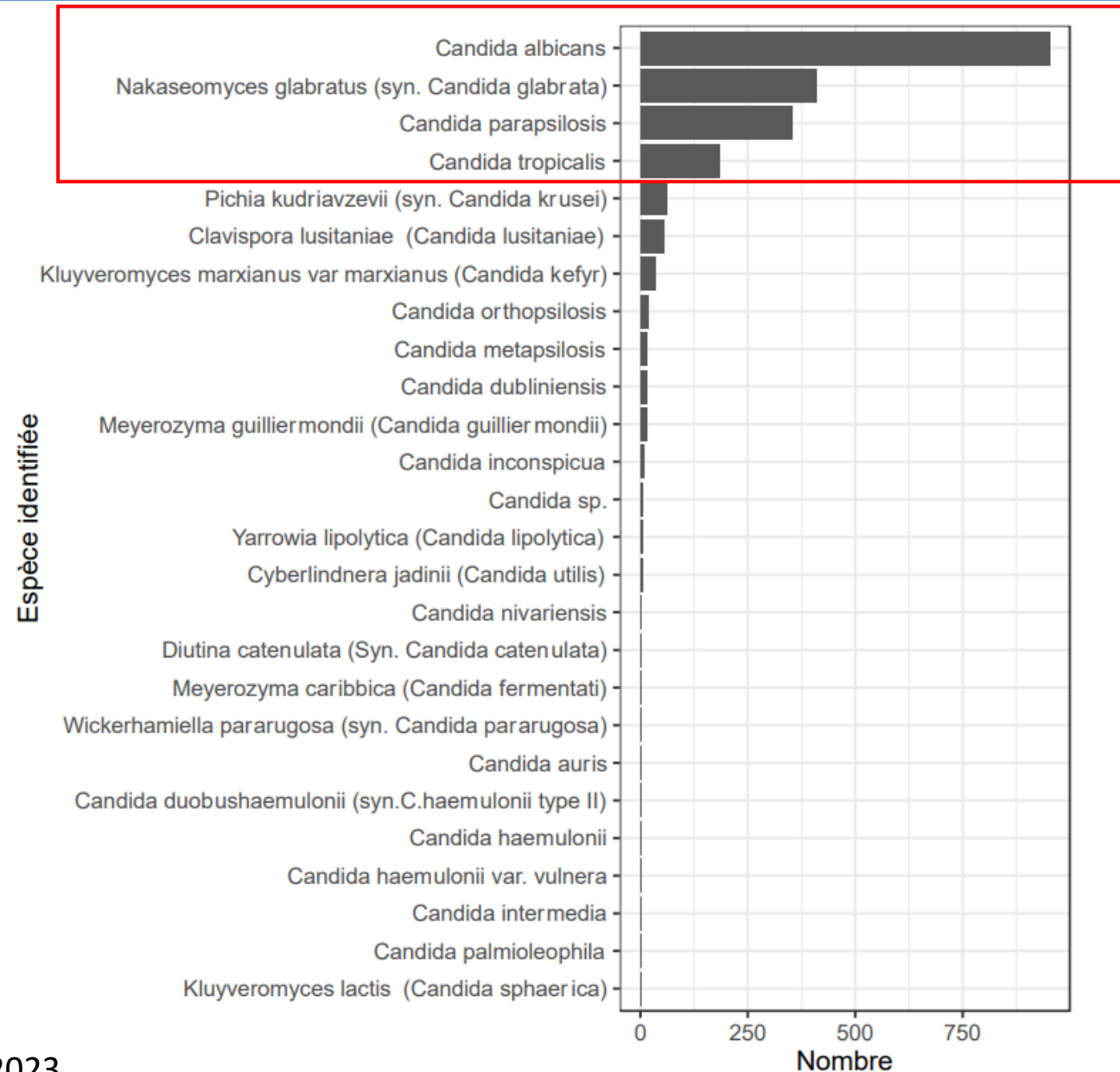
# Candida in fungemia of cancer patients

13 European cancer hospitals  
2005-2009  
145 030 admissions

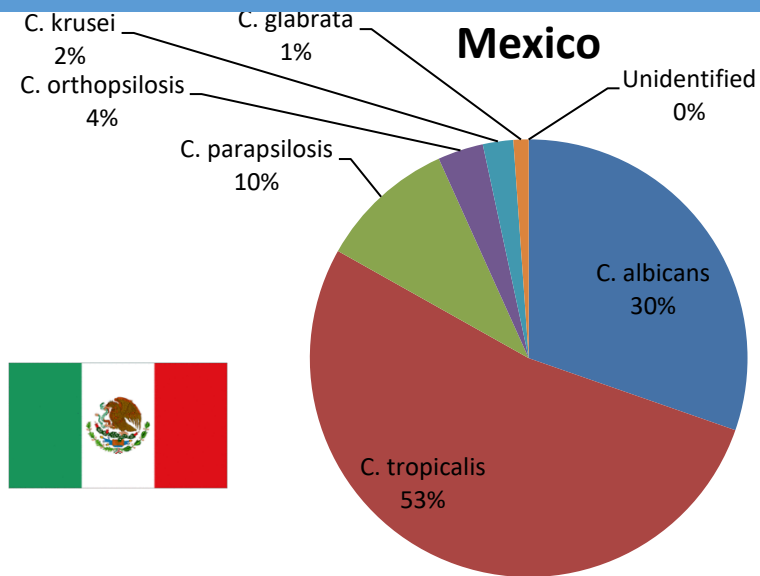
Patient Group	Incidence [% (95% CI)]	Patients With Fungemia per Observed Group; N/N
Overall	<b>0.23% (.21–.26)</b>	<b>333/145 030</b>
Solid tumor without HSCT	<b>0.15% (.13–.18)</b>	<b>174/114 811</b>
Solid tumor with HSCT	<b>1.55% (.19–5.49)</b>	<b>2/129</b>
Hematological malignancies without HSCT	<b>0.42% (.35–.50)</b>	<b>114/27 195</b>
Hematological malignancies with HSCT	<b>1.46% (1.06–1.97)</b>	<b>42/2871</b>

Pathogen Isolated by Treating Center	Total n = 297 (%)	Solid Tumor <sup>b</sup> n = 165 (%)	Hematological Malignancy <sup>b</sup> n = 140 (%)	Allogeneic HSCT n = 28 (%)	Autologous HSCT n = 22 (%)	No Transplant n = 247 (%)
Single pathogen	<b>288 (97.0%)</b>	<b>159 (97%)</b>	<b>137 (98%)</b>	<b>27 (96.4%)</b>	<b>22 (100%)</b>	<b>239 (96.8%)</b>
<i>Candida albicans</i>	120 (40.4%)	<b>92 (56%)</b>	31 (22%)	2 (7.1%)	7 (31.8%)	111 (44.9%)
Non-albicans candida	138 (46.5%)	59 (36%)	<b>82 (59%)</b>	<b>21 (75.0%)</b>	12 (54.6%)	105 (42.5%)
<i>C. glabrata</i>	29 (9.8%)	25 (15.2%)	6 (4.3%)	1 (3.6%)	1 (4.5%)	27 (10.9%)
<i>C. tropicalis</i>	39 (13.1%)	11 (6.7%)	30 (21.4%)	2 (7.1%)	4 (18.2%)	33 (13.3%)
<i>C. parapsilosis</i>	28 (9.4%)	16 (9.7%)	11 (7.9%)	5 (17.9%)	2 (9.1%)	21 (8.5%)
<i>C. krusei</i>	25 (8.4%)	5 (3.0%)	20 (14.3%)	6 (21.4%)	4 (18.2%)	15 (6.1%)
<i>C. kefyr</i>	7 (2.4%)	1 (<1%)	6 (4.3%)	2 (7.1%)	1 (4.5%)	4 (1.6%)
<i>C. norvegensis</i>	3 (1.0%)	...	3 (2.1%)	1 (3.6%)	...	2 (0.8%)
<i>C. dubliniensis</i>	2 (<1%)	...	2 (1.4%)	1 (3.6%)	...	1 (0.4%)
<i>C. guilliermondii</i>	2 (<1%)	1 (<1%)	1 (<1%)	1 (3.6%)	...	1 (0.4%)
<i>C. rugosa</i>	1 (<1%)	...	1 (<1%)	...	...	1 (0.4%)
Other Candida <sup>c</sup>	2 (<1%)	...	2 (1.4%)	2 (7.1%)	...	...

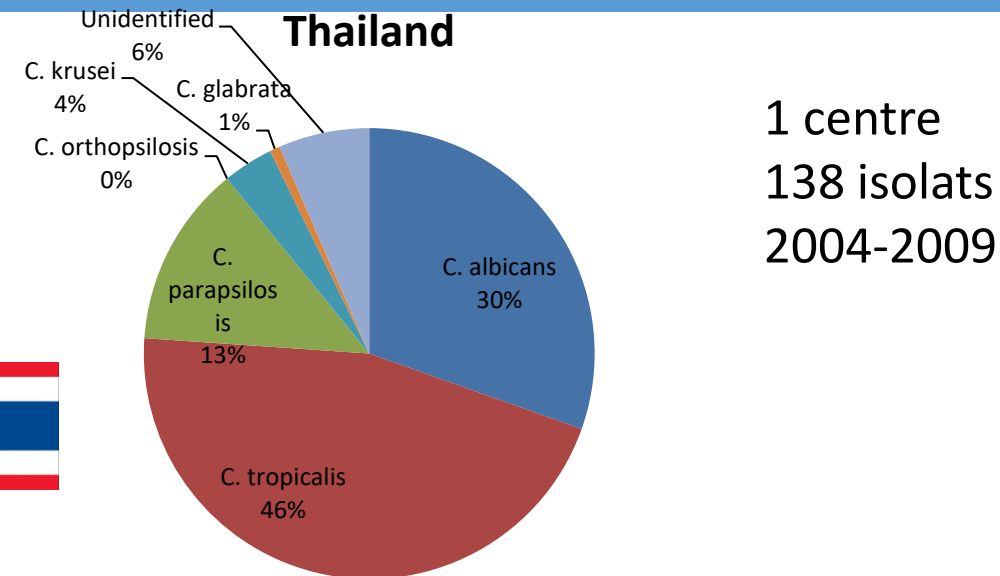
# Les fongémies en France en 2023



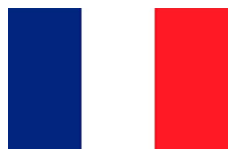
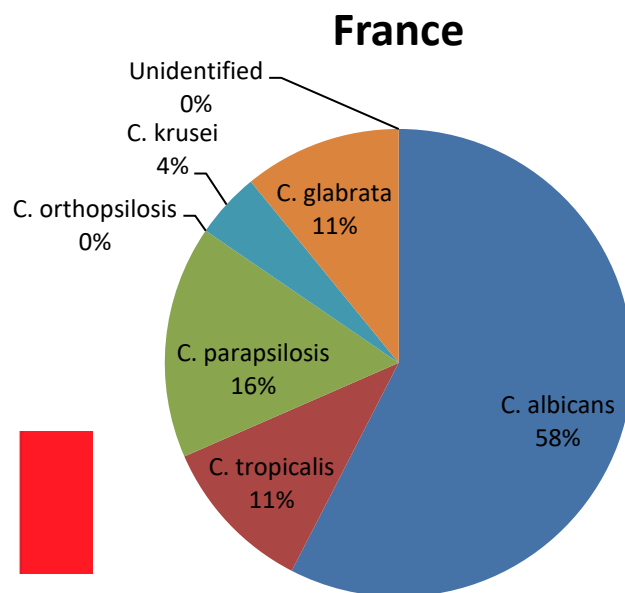
# Candidémies: épidémiologie selon le pays



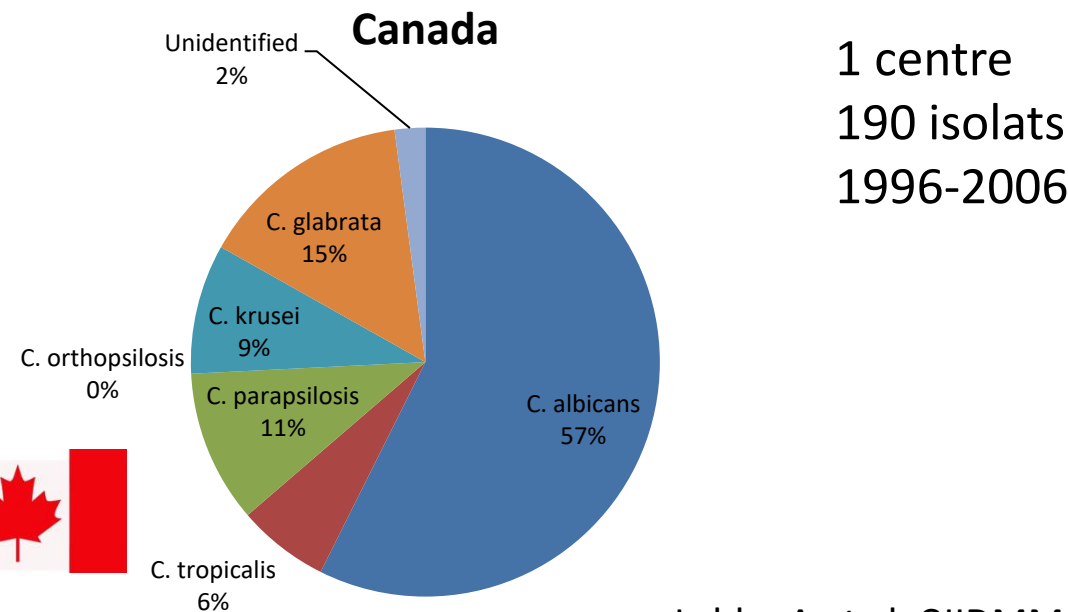
1 centre  
89 isolats  
2006-2015



1 centre  
138 isolats  
2004-2009

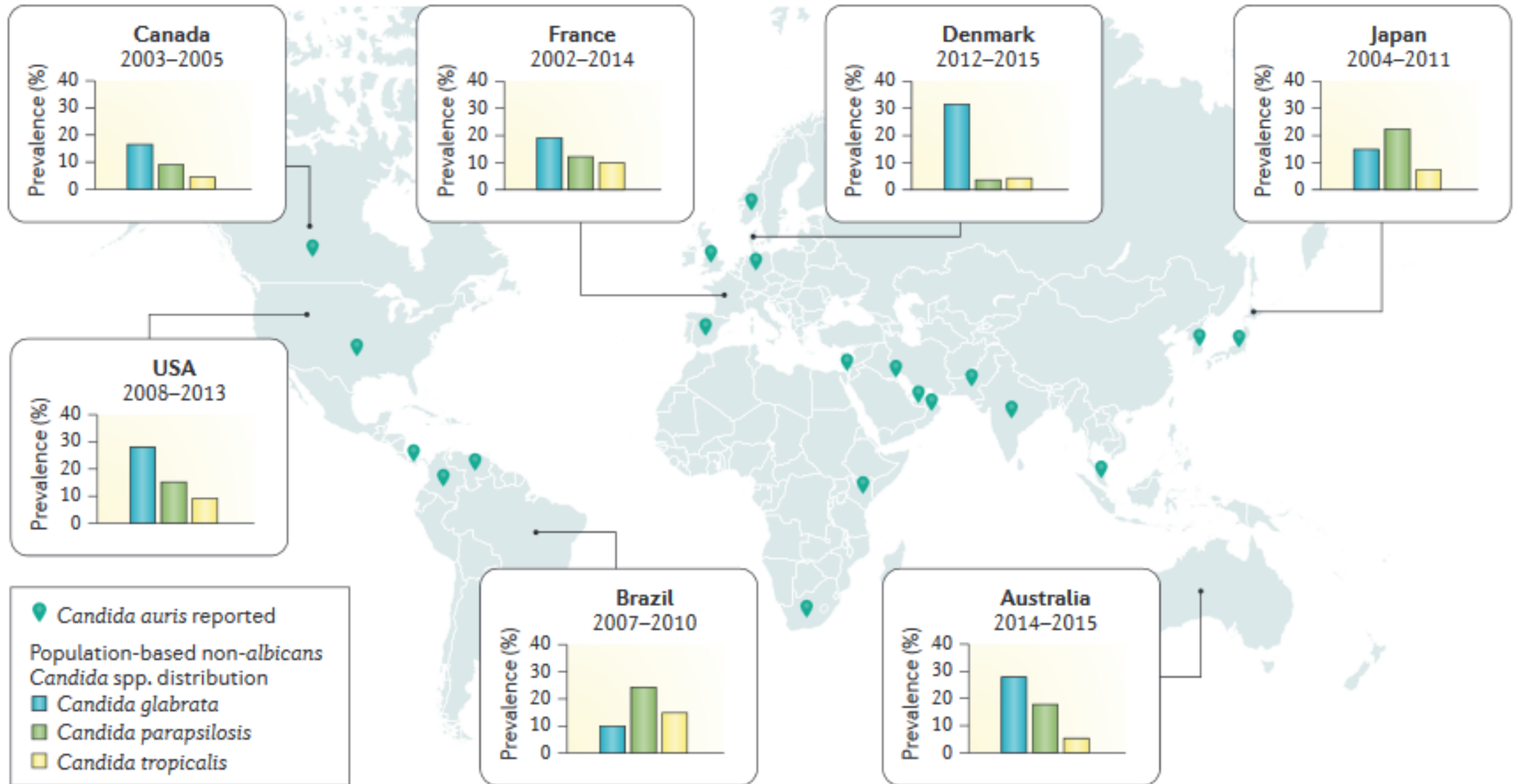


1 centre  
191 isolats  
2004-2010



1 centre  
190 isolats  
1996-2006

# Candidémies: épidémiologie selon le pays



# Impact de la pré-exposition aux antifongiques

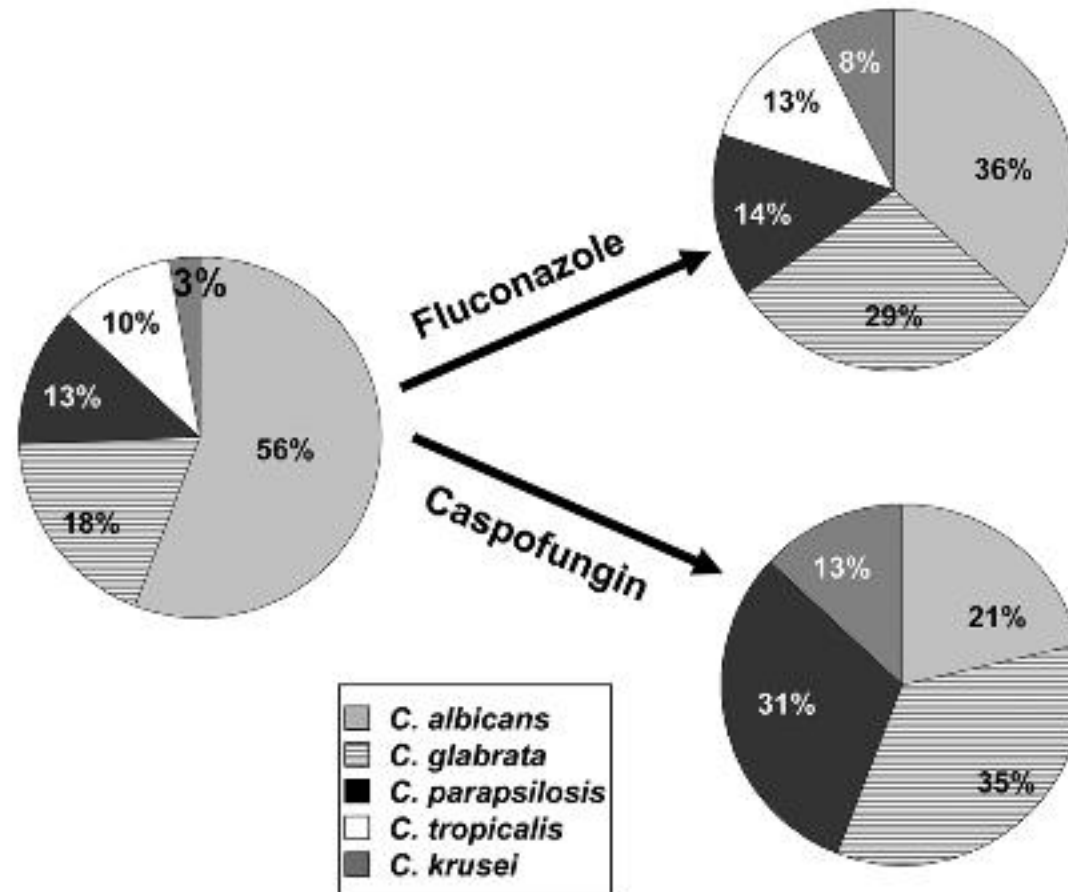
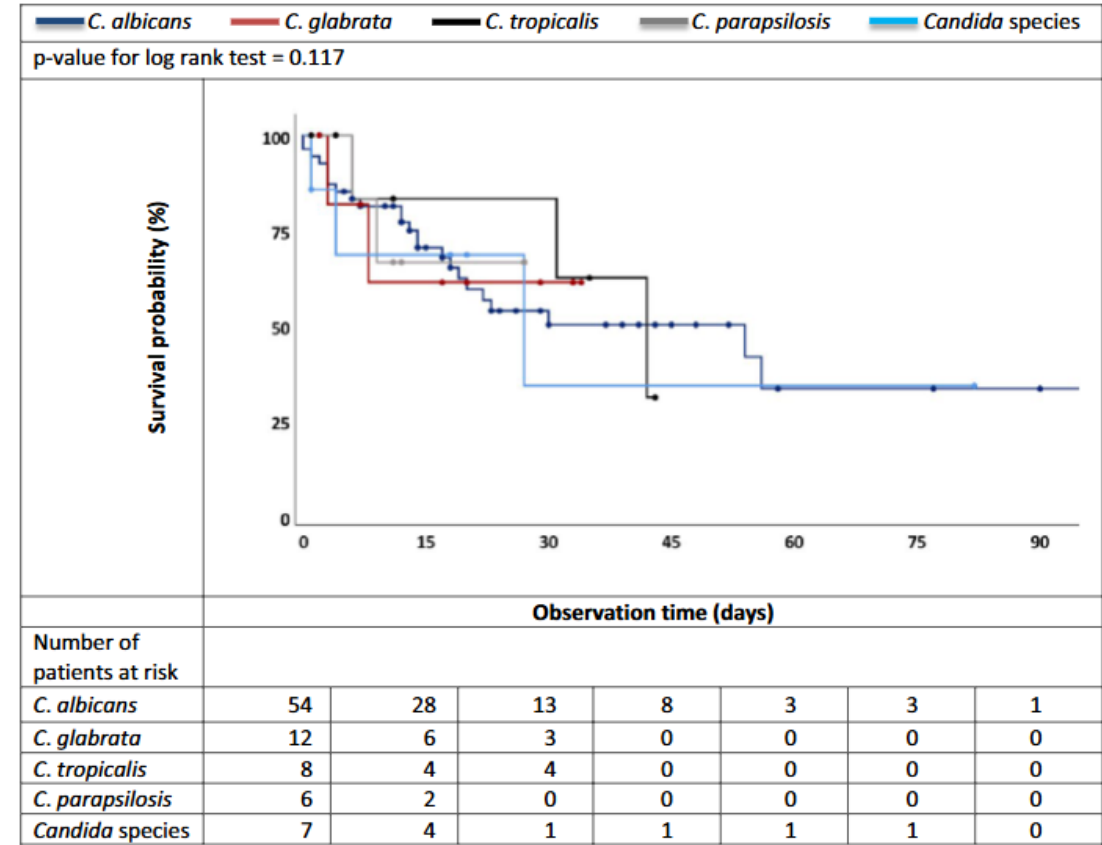
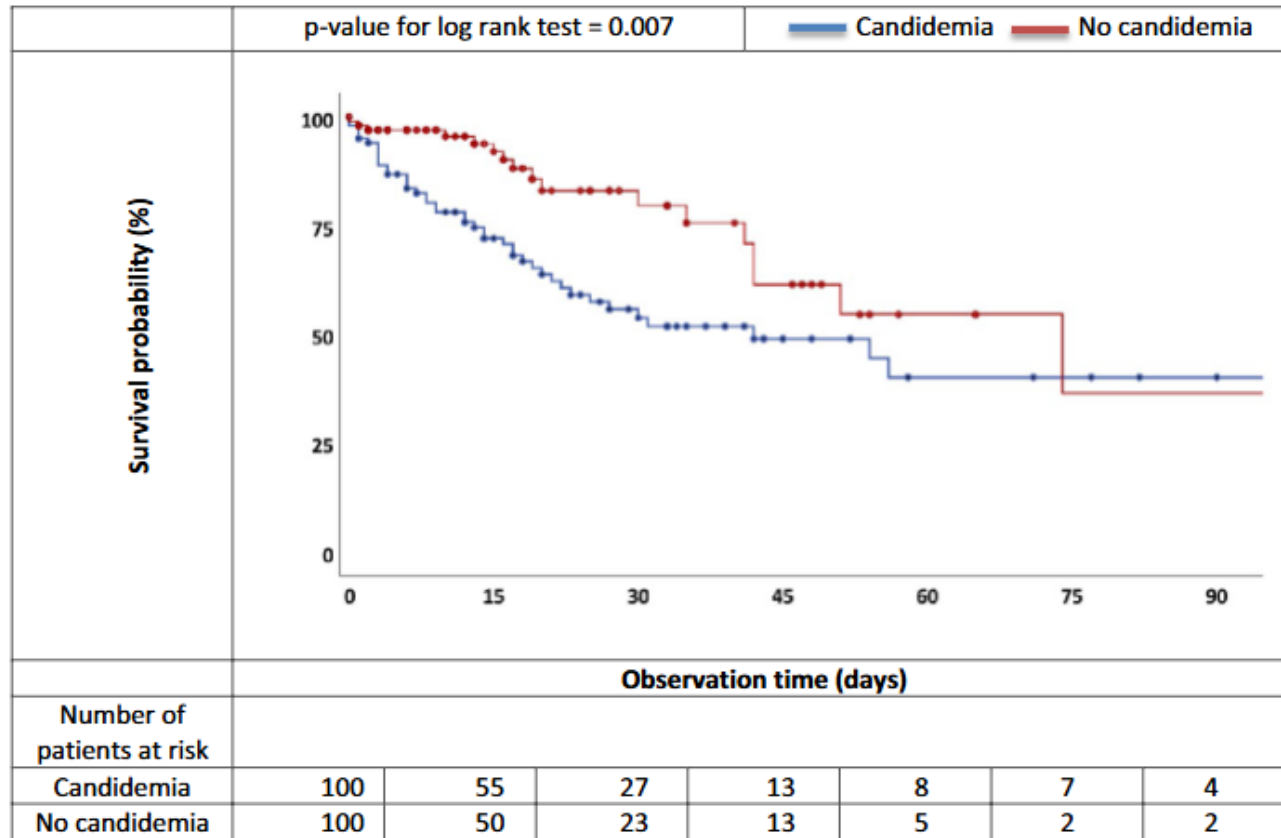


FIG. 2. Proportion of the five major *Candida* species responsible for fungemia in patients with ( $n = 159$ ) or without ( $n = 2,289$ ) prior exposure to fluconazole ( $P = 0.001$ ) or with ( $n = 61$ ) or without ( $n = 2,387$ ) prior exposure to caspofungin ( $P < 0.001$ ) (incident episodes and recurrences are included).

# Candidémie: mortalité

Sans traitement: 60% environ Fraser V *et al.* CID 1992

Traînée:



# Candidémie: mortalité attribuable

Variable	Pediatric patients			Adult patients		
	With candidemia ( <i>n</i> = 1118)	Without candidemia ( <i>n</i> = 2062)	Attributable increase (95% CI)	With candidemia ( <i>n</i> = 8949)	Without candidemia ( <i>n</i> = 17,267)	Attributable increase (95% CI)
Mortality, %	15.8	5.9	10.0 (6.2–13.8)	30.6	16.1	14.5 (12.1–16.9)
Length of stay, mean no. of days per patient	44.8	23.7	21.1 (14.4–27.8)	18.6	8.5	10.1 (8.9–11.3)
Total charges, mean US\$ per patient	183,645	91,379	92,266 (65,058–119,474)	66,154	26,823	39,331 (33,60–45,602)

# Candidémie: facteurs de risque

## Immunodépression

Néoplasie  
Neutropénie  
SOT/HSCT  
Maladie rénale chronique (+/- dialyse)  
Diabète  
Âges extrêmes  
*Rare: DIP (Th17, CARD9...)*

## Corps étrangers

CVC (*C. parapsilosis*) a fortiori si NPT  
Drains

## Brèche muqueuse

Chimiothérapie  
Brûlures  
Chirurgie (abdominale)  
Pancréatite aiguë nécrosante

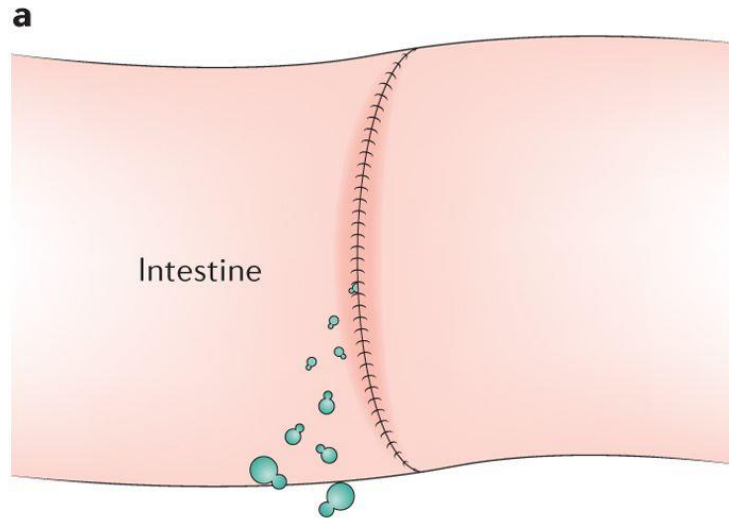
## Atteinte du microbiote

ATB large spectre

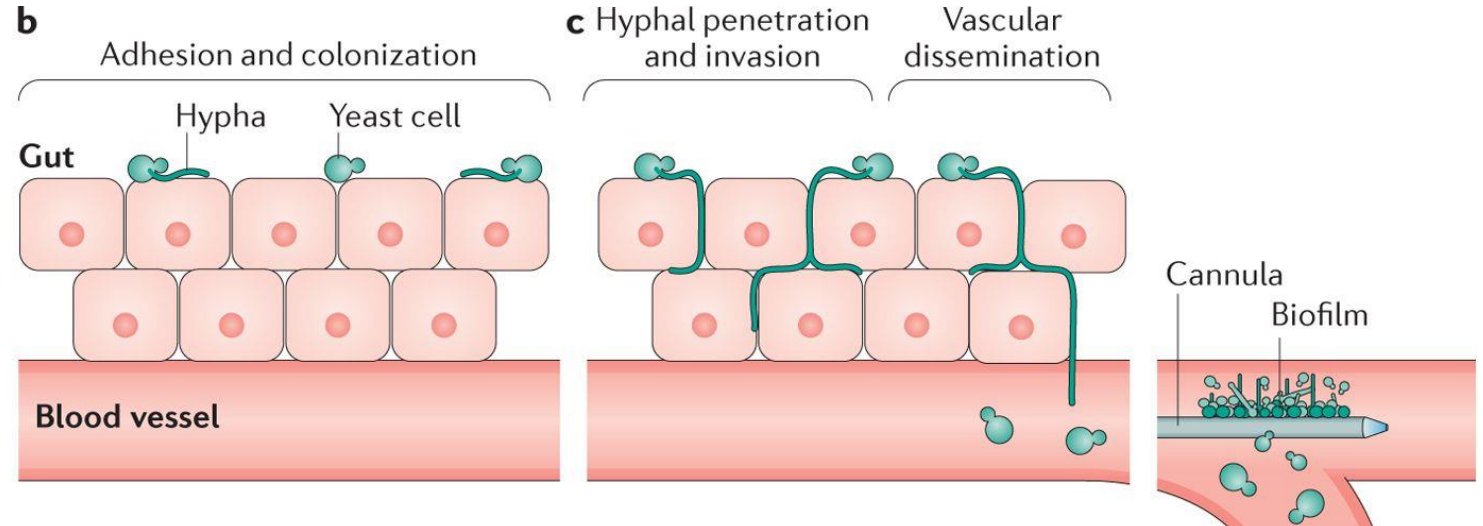
- Majoritairement associé aux soins
- Populations typiques: réa, onco-hématologie

# Physiopathologie

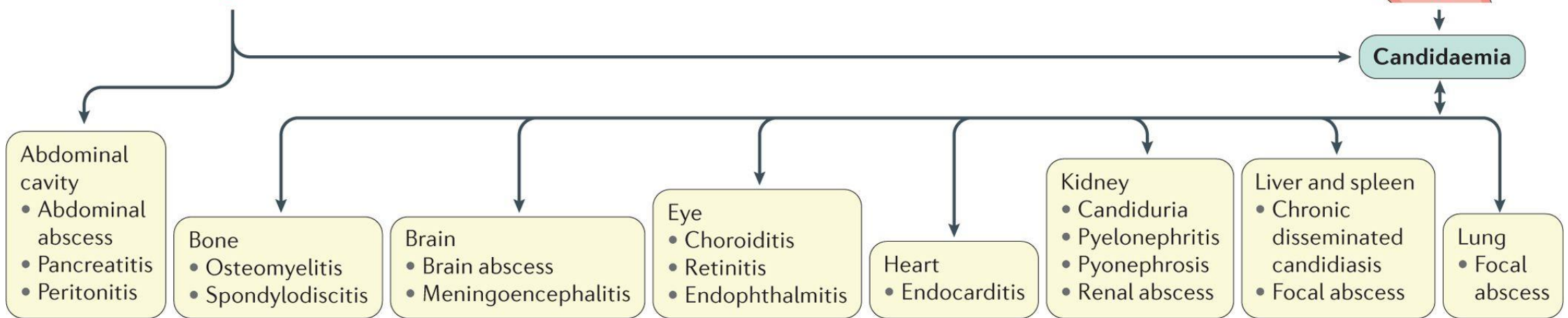
## Mucosal breach and translocation



## Intravascular catheter



## Other source of infection



# Diagnostic des candidémies

## Clinique

Fièvre isolée

Sepsis/choc septique

Rare: atteinte d'organe (peau...)

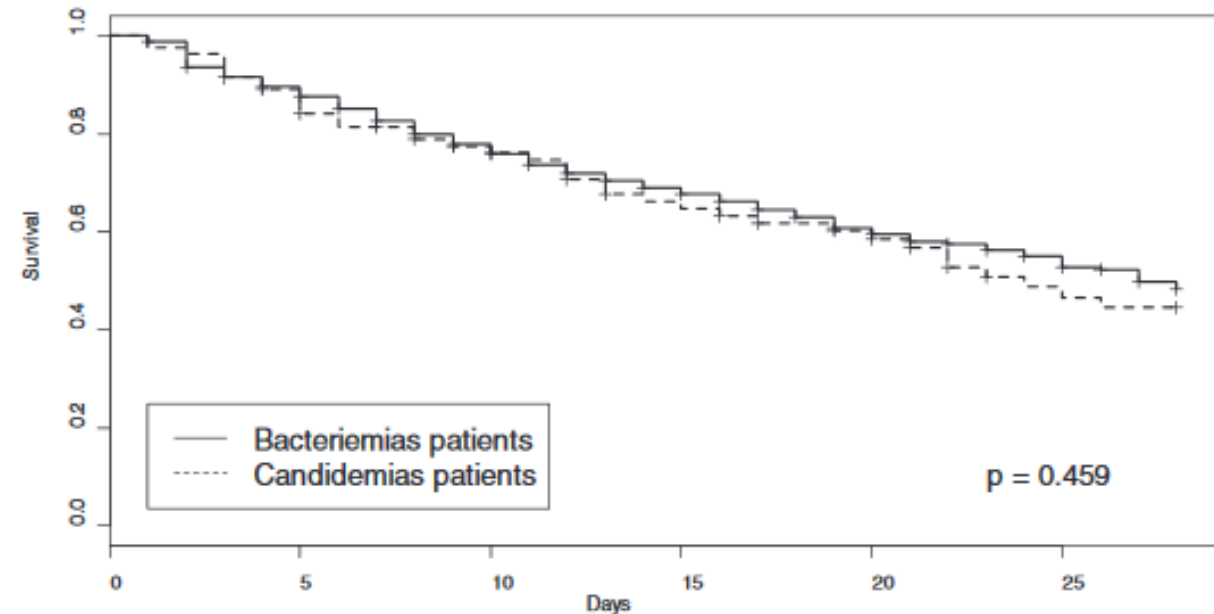
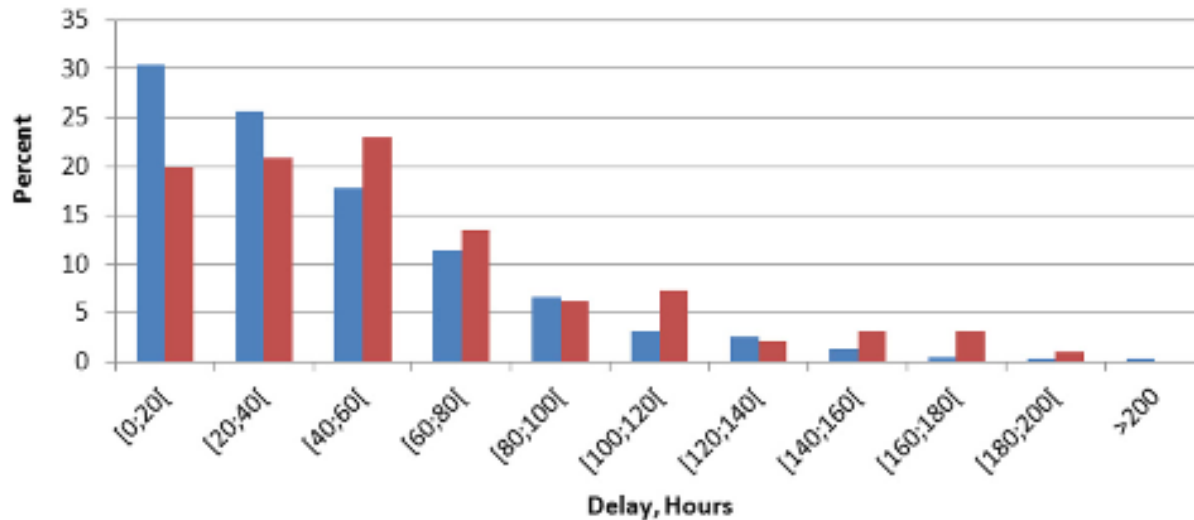
Multicentrique européen, réanimations

1096 bactériémies nosocomiales vs 96 fongémies nosocomiales

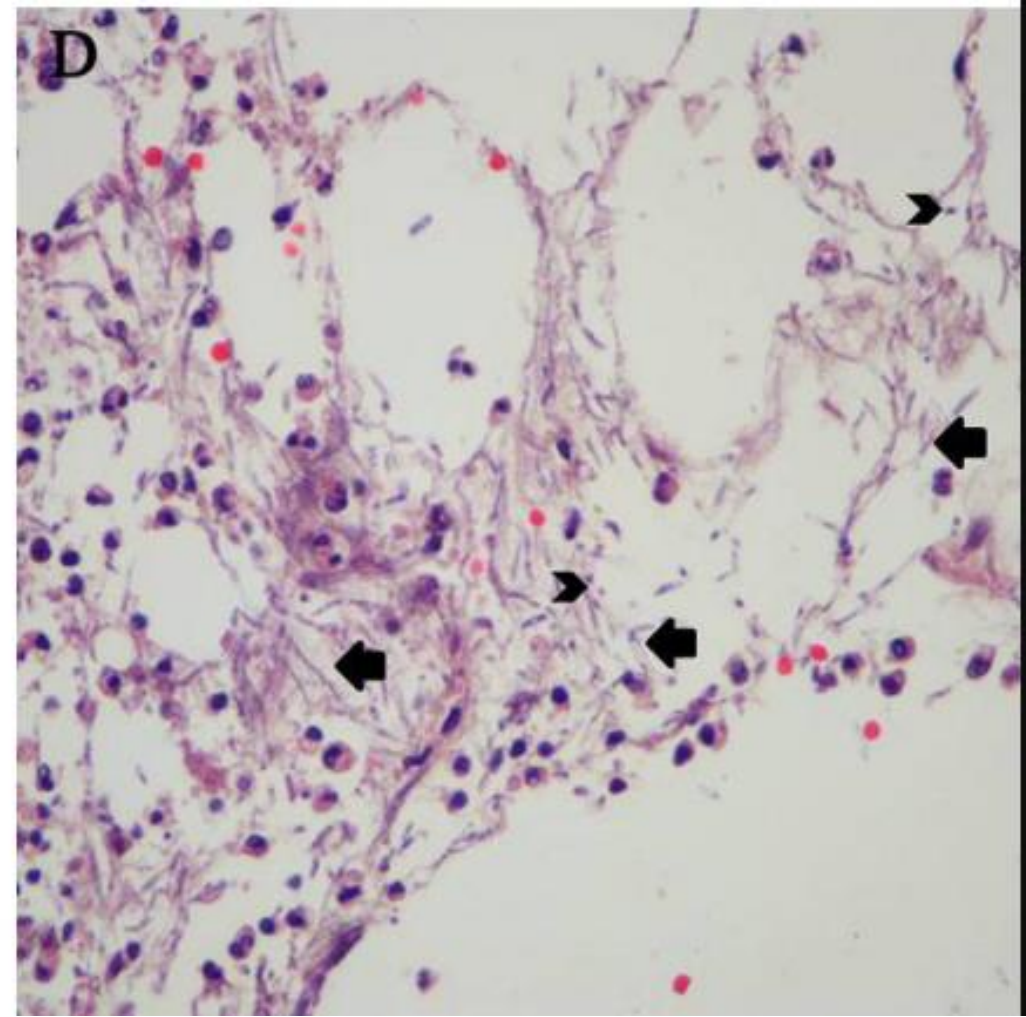
**At baseline:** choc septique et I rénale plus fréquents

Présentations cliniques comparables

Ttt adapté plus tardif si fongémie ( $p < 0.0001$ )



# Candidémies: atteinte cutanée



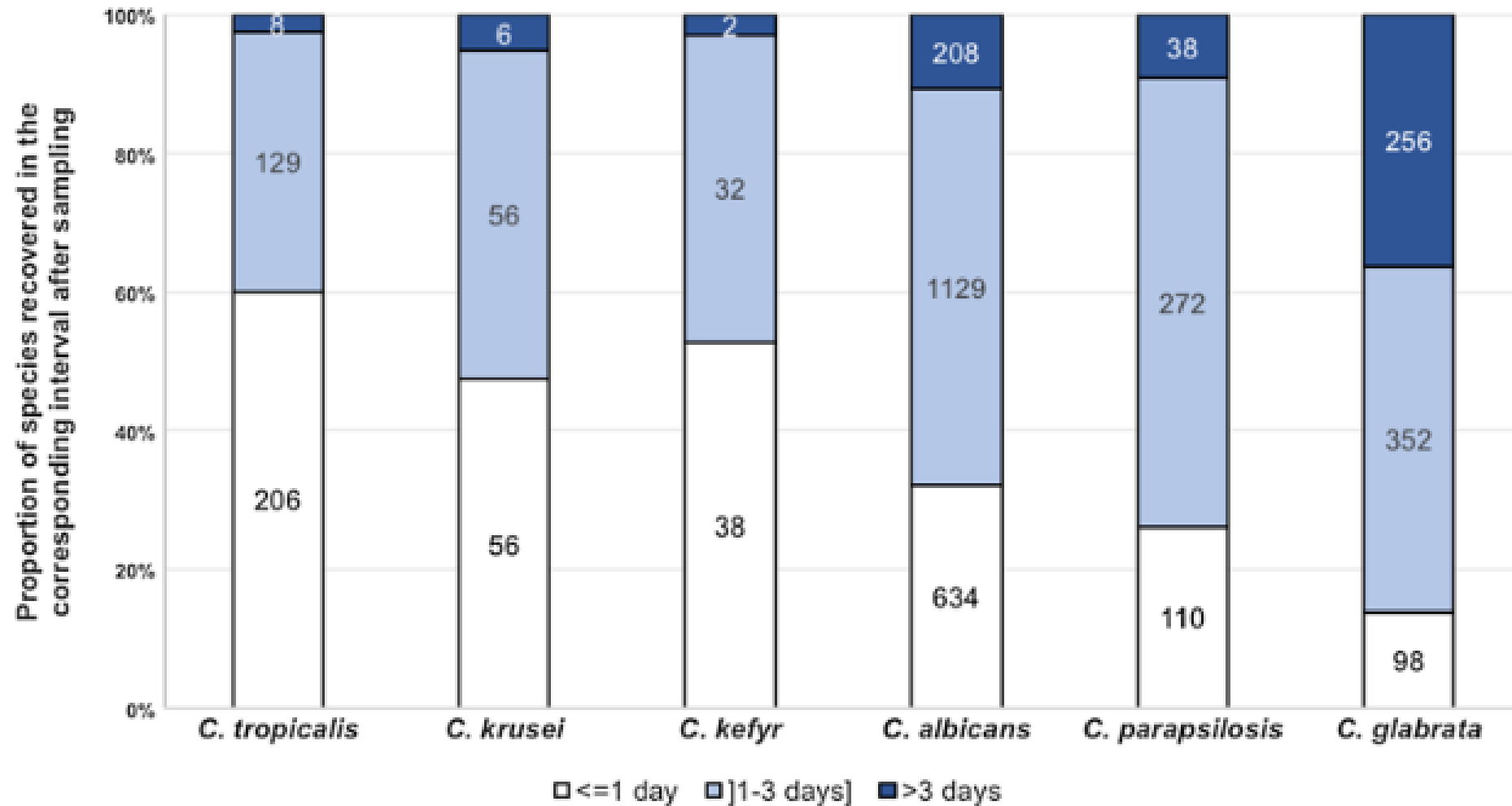
# Techniques diagnostiques des candidémies

Diagnostic test	Specimen(s)	Advantages	Disadvantages
Fungal culture	Blood	<ul style="list-style-type: none"><li>• Enables species identification and subsequent susceptibility testing</li></ul>	<ul style="list-style-type: none"><li>• Slow (median detection time 2–3 days)</li><li>• Sensitivity suboptimal, particularly if high volume (<math>\geq 60</math> ml) and a fungal blood culture bottle are not employed</li></ul>
	Tissue and sterile body fluids	<ul style="list-style-type: none"><li>• Enables species identification and subsequent susceptibility testing</li></ul>	<ul style="list-style-type: none"><li>• Selective media, proper spreading of the sample and 3 days of incubation required for optimal performance</li></ul>
Microscopy	Cerebrospinal fluid, tissue and sterile body fluids	<ul style="list-style-type: none"><li>• Highly sensitive, particularly if using fluorescent brightener staining</li></ul>	<ul style="list-style-type: none"><li>• No species identification</li><li>• Lower sensitivity in absence of fluorescent brightener staining</li></ul>

# Les hémocultures manquent de sensibilité

Reference	Year	No. of Patients	Underlying Disease	Sensitivity
Louria (from [13])	1962	19	Hematologic malignancies, solid tumors, medical and surgical conditions	42%
Bodey (from [13])	1966	61	Acute leukemia	25%
Taschdjian (from [13])	1969	17	Malignancies and other medical conditions	47%
Hart (from [13])	1969	16	Hematologic malignancies, solid tumors, transplant, medical and surgical conditions	44%
Bernhardt (from [13])	1972	14	Transplant and surgical conditions	36%
Gaines (from [13])	1973	26	Hematologic malignancies, solid tumors, medical and surgical conditions	54%
Myerowitz (from [13])	1977	39	Hematologic malignancies, solid tumors, medical and surgical conditions	44%
Ness [9]	1989	7	Hematologic malignancies and bone marrow transplant recipients	71%
Singer [37]	1977	16	Hematologic malignancies	31%
Berenguer [13]	1993	37	Mostly hematologic malignancies and solid tumors	43%
Van Burik [38]	1998	62	Bone marrow transplant recipients	52%
Kami [39]	2002	91	Hematologic malignancies	21%
Thorn [40]	2010	10	Hematologic malignancies, gastrointestinal disease, transplant, prematurity	50%

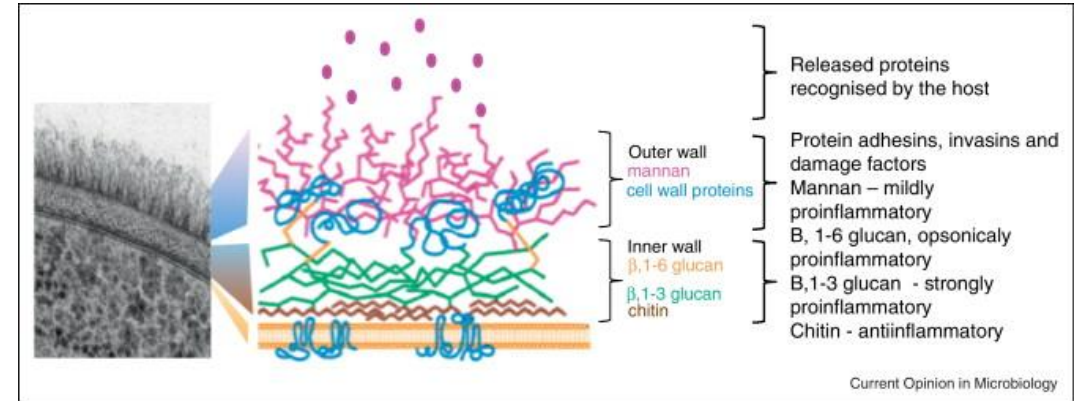
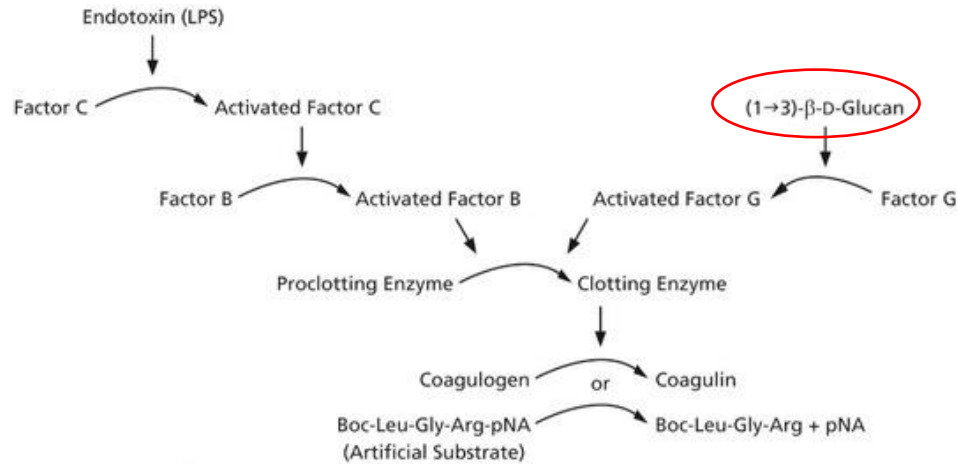
# Délai de pousse des hémocultures



# Susceptibility testing

Will add figures from the paper

# Beta D glucane



Nombreuses espèces fongiques

Seuil 60 à 80 pg/ml

Détectable dans le LCR

Nombreux faux positifs: Ig IV

albumine

colonisation fongique muqueuse

atteinte muqueuse digestive

compresses chirurgicales

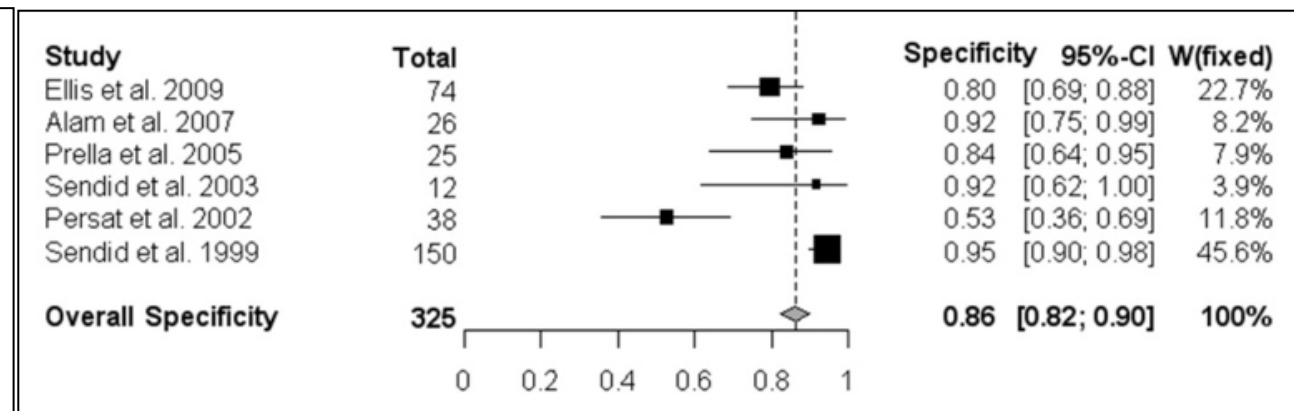
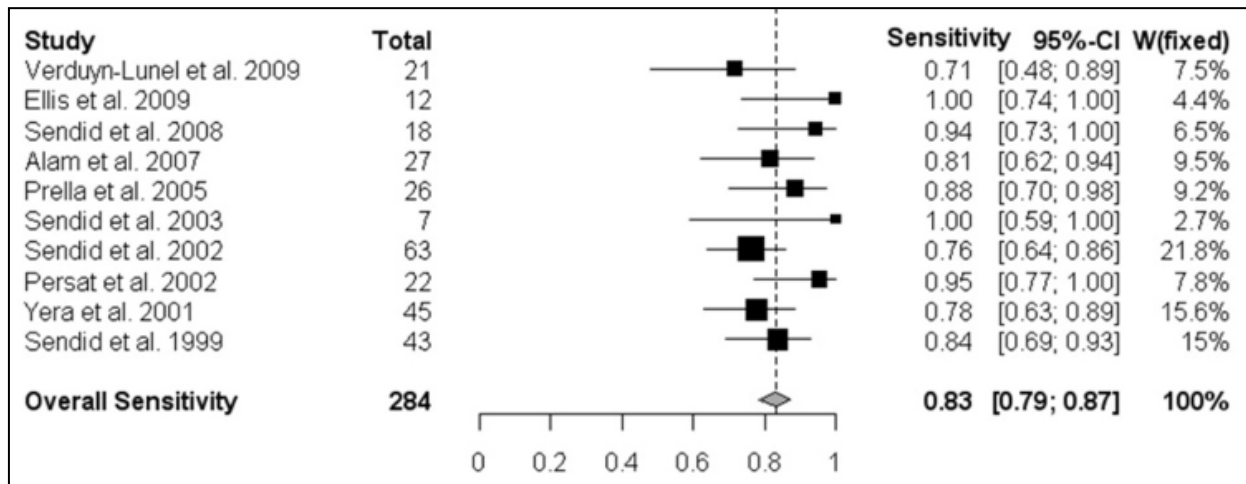
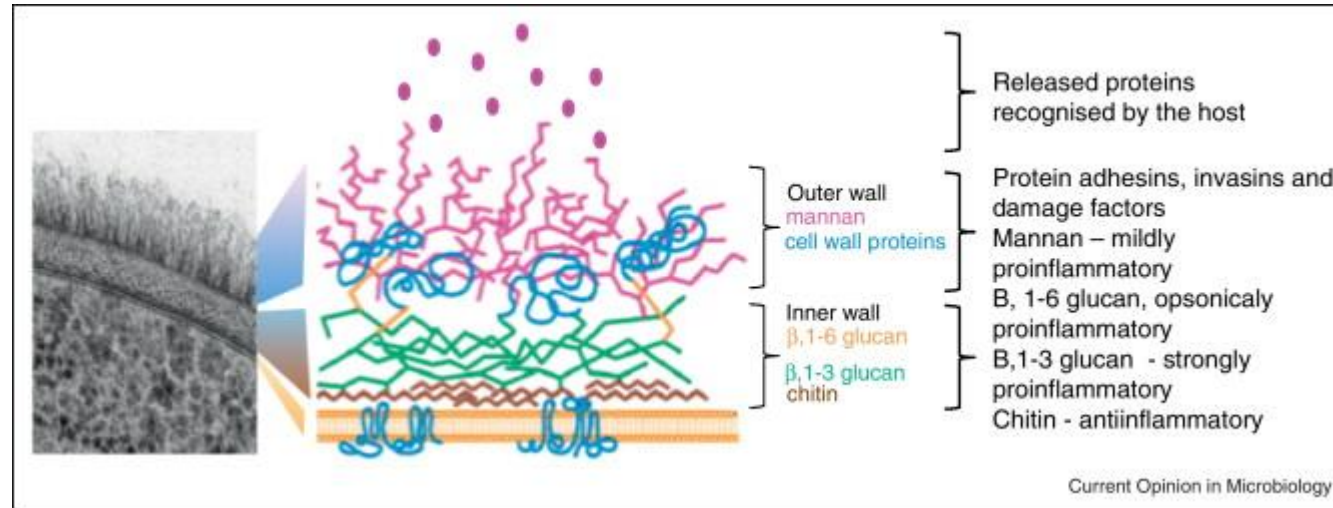
Bonne VPN, peu spécifique

# Beta D Glucane et CI

Study	Cutoff(pg/mL)	Systemic <i>Candida</i> infections, proportion (%)	Invasive aspergillosis, proportion (%)
Hachem et al 2009 [27]	80 (2 consecutive values)	13/21 (62)	14/21 (67)
Koo et al 2009 [28]	80	26/41 (63)	24/32 (75)
→ Obayashi et al 2008 [19]	30	3/3 (100)	28/28 (100)
Persat et al 2008 [31]	80	22/26 (85)	48/70 (69)
Senn et al 2008 [32]	7 (2 consecutive values)	10/17 (59)	9/15 (60)
→ Akamatsu et al 2007 [33]	40	7/14 (50)	5/5 (100)
Ostrosky-Zeichner et al 2005 [36]	80	83/107 (78)	8/10 (80)
Odabashi et al 2004 [20]	80	9/11 (82)	4/4 (100)
Mori et al 1997 [43]	1000	11/12 (92)	4/4 (100)
Mitsutake et al 1996 [44]	60	27/32 (84)	5/5 (100)
Miyazaki et al 1995 [45]	10	11/11 (100)	3/3 (100)
Total from all studies <sup>a</sup>	...	222/295 (75)	152/197 (77)

# Mannane/Anti Mannane et candidémie/CI

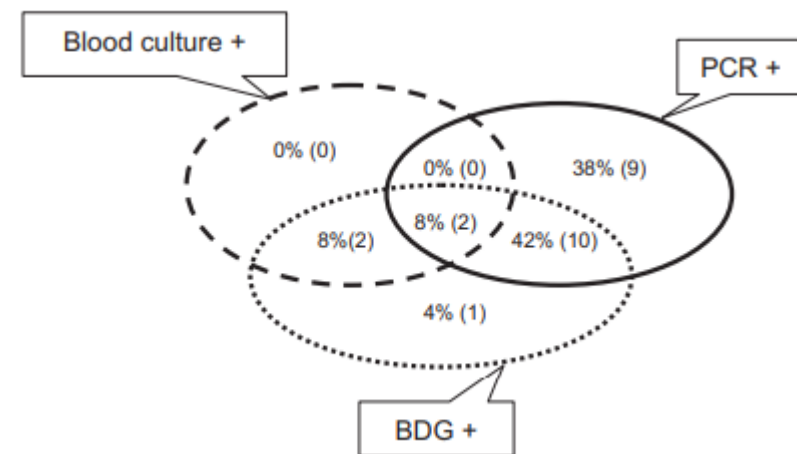
**Populations:**  
réanimations  
hématologie  
Pas SOT



# PCR *Candida* dans le sang

Assay	Invasive Candidiasis (n = 55)	Candidemia <sup>a</sup> (n = 22)	Deep-Seated Candidiasis <sup>a,b</sup> (n = 38)	Intra-abdominal Candidiasis (n = 34)
<b>PCR<sup>c</sup></b>				
Sensitivity	80% (44/55)	59% (13/22)	89% (34/38)	88% (30/34)
Specificity	70% (51/73)			
<b>BDG (positive <math>\geq 80</math> pmol/mL)</b>				
Sensitivity	56% (31/55)	68% (15/22)	53% (20/38)	56% (19/34)
Specificity	73% (53/73)			
<b>BDG (positive <math>\geq 60</math> pmol/mL)</b>				
Sensitivity	69% (38/55)	81% (18/22)	66% (25/38)	65% (22/34)
Specificity	63% (46/73)			
<b>P value<sup>d</sup></b>				
PCR vs BDG (positive $\geq 80$ pmol/mL)	.03	.77	.004	.0015
PCR vs BDG (positive $\geq 60$ pmol/mL)	.31	.23	.04	.06

Performances assez proches de celles du  $\beta$  D glucane  
Non standardisé



# Procédures diagnostiques

	ED & Cultures		Beta D glucane	Mannane/anti mannane	PCR <i>Candida</i>
	<i>Plasma</i>	<i>Tissu</i>			
Candidémie	Oui		Recommandé (moderately?)	Recommandé	Non recommandé
Candidose invasive	Oui	Oui	Recommandé (moderately?)	Non recommandé	Non recommandé
CHS	Oui	Oui	Recommandé (moderately?)	Recommandé	Non recommandé

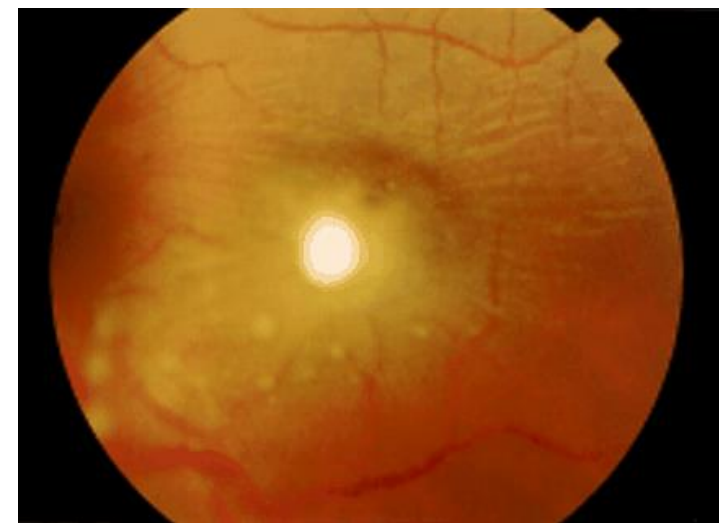
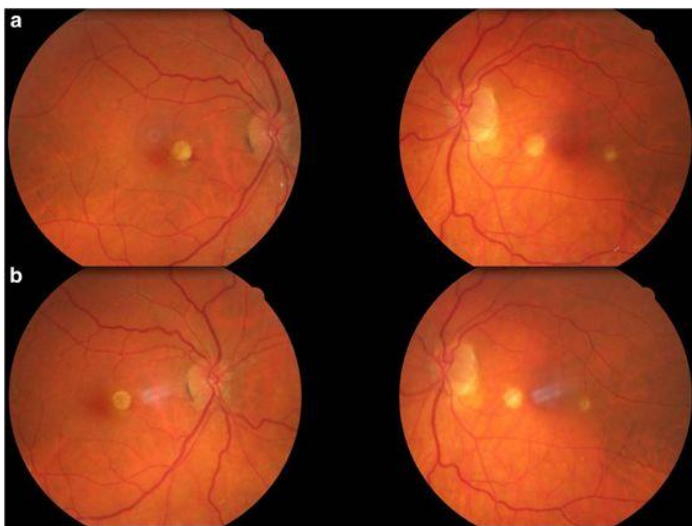
# Candidémie: bilan d'extension

- Clinique: peau, souffle cardiaque, arthrite/rachis
- Biopsie si lésion cutanée
- FO
- Imagerie profonde?



# Atteinte ophtalmologique

- 1 à 26% des candidémies (?)
- FO pour toute candidémie
- Neutropéniques: après résolution de la neutropénie
- *C. albicans* > non-*albicans*?
- FDR: - dialyse
  - autres localisations



# Atteinte ophtalmologique

	N	Period	Proportion of eye involvement	Chorioretinitis	Endophtalmitis
Horcajada <i>et al.</i> 2007	?	1993-2004	?	76%	24%
Karmisholt <i>et al.</i> 2008	86	1995-2004	12%	90%	10%
Krishna <i>et al.</i> 2000	31	1996-1997	26%	100%	0%
Oude Lashof <i>et al.</i> 2011	370	1998-2003	16%	90%	10%
Shah <i>et al.</i> 2008	38	2006	7.9%	100%	0%
Blennow <i>et al.</i> 2013	60	2000-2009	20%	100%	0%
Nagao <i>et al.</i> 2012	204	2005-2011	26.5%	81%	19%
Munoz <i>et al.</i> 2017		2010-2011	7.7%	85%	15%
Kato <i>et al.</i> 2018	174	2011-2016	20.1%	88.6%	11.4%
Lehman <i>et al.</i> 2024	148		6%	100%	0%
Shah <i>et al.</i> 2025	285	2017-2024	3.5%	90%	10%

Les échinocandines ne semblent pas protectrices Munoz P *et al.* DMID 2017

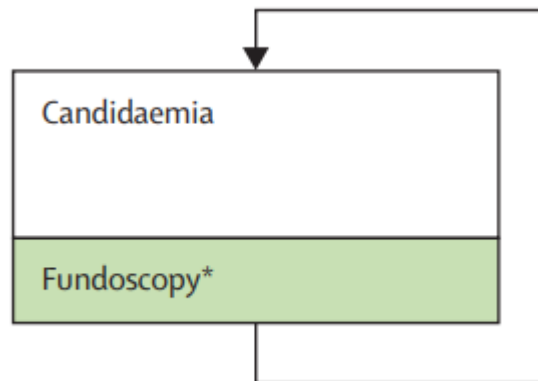


ORIGINAL ARTICLE · [Volume 129, Issue 1, P73-76, January 2022](#)

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## American Academy of Ophthalmology Recommendations on Screening for Endogenous *Candida* Endophthalmitis

[Mark P. Breazzano, MD<sup>1</sup>](#) · [John B. Bond, III, MD<sup>2</sup>](#) · [Srilaxmi Bearely, MD, MHS<sup>3</sup>](#) · [Donna H. Kim, MD<sup>4</sup>](#) · [Sean P. Donahue, MD, PhD<sup>2</sup>](#) · [Flora Lum, MD<sup>5</sup>](#)   · [Timothy W. Olsen, MD<sup>6</sup>](#) for the [American Academy of Ophthalmology](#) [Show less](#)



Si: symptômes visuels  
candidémie persistante  
immunodépression  
impossibilité de communiquer

Global guideline for the diagnosis and management of candidiasis: an initiative of the ECMM in cooperation with ISHAM and ASM

# Atteinte endocarditique

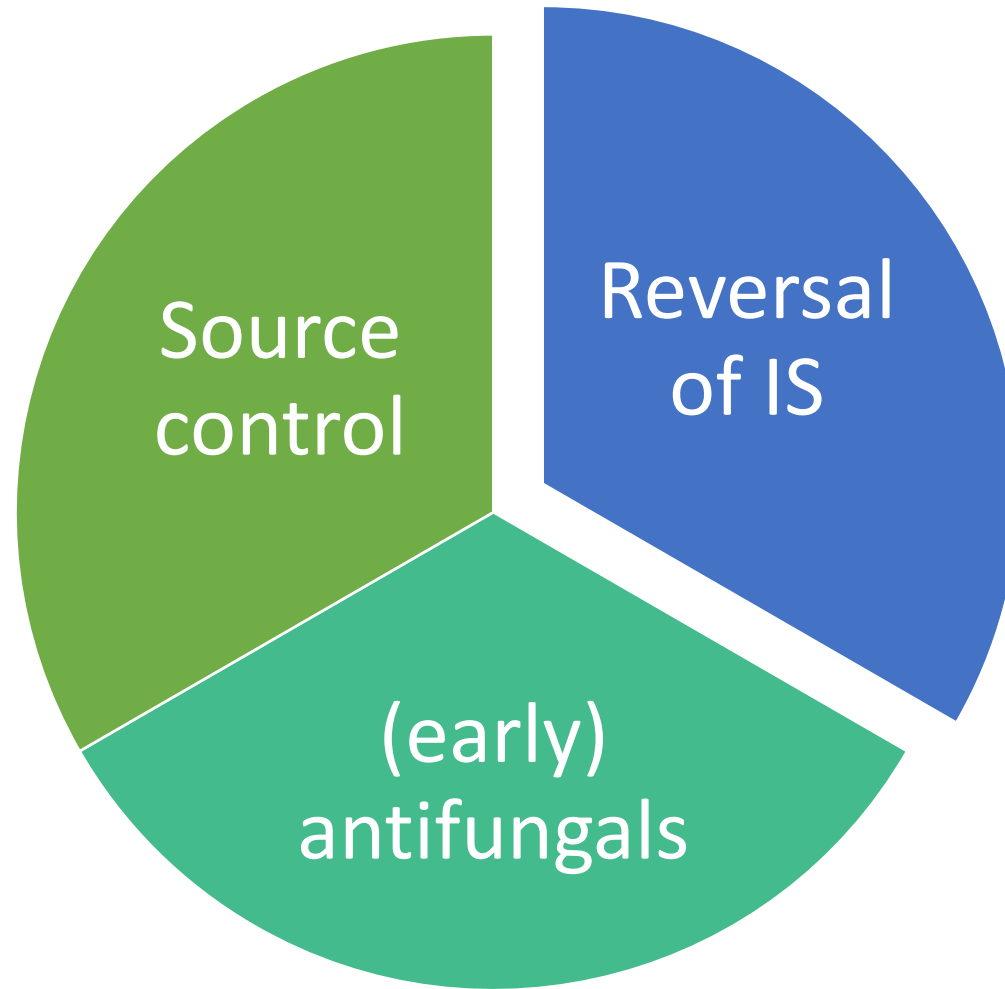
- Environ 5% des candidémies
- **ESCMID**: échocardiographie systématique
- **IDSA**: échocardiographie si FDR:
  - Hémocultures restant positives
  - IVDU
  - Prothèse valvulaire
  - Signes cliniques d'EI

**The search for endocarditis in patients with candidemia:  
a systematic recommendation for echocardiography?  
A prospective cohort**

A. Fernández-Cruz<sup>1,6</sup> · M. Cruz Menárguez<sup>1</sup> · P. Muñoz<sup>1,3,4,5</sup> · M. Pedromingo<sup>1</sup> ·  
T. Peláez<sup>1,3,4,5</sup> · J. Solís<sup>2</sup> · M. Rodríguez-Crèixems<sup>1,3,4,5</sup> · E. Bouza<sup>1,3,4,5,7</sup> · on behalf of the  
GAME Study Group (Grupo de Apoyo al Manejo de la Endocarditis)

- Cohorte prospective, monocentrique, 2007-2012
- 187 patients
- *C. albicans* 48.7%
- Endocardite 4.2% de la pop (5.9% des échographies faites)
- 11 cas; ETT positive chez 5  
ETO positive chez 10
- Si EI: score de Charlson plus élevé  
mortalité ↑  
plus souvent sur prothèse

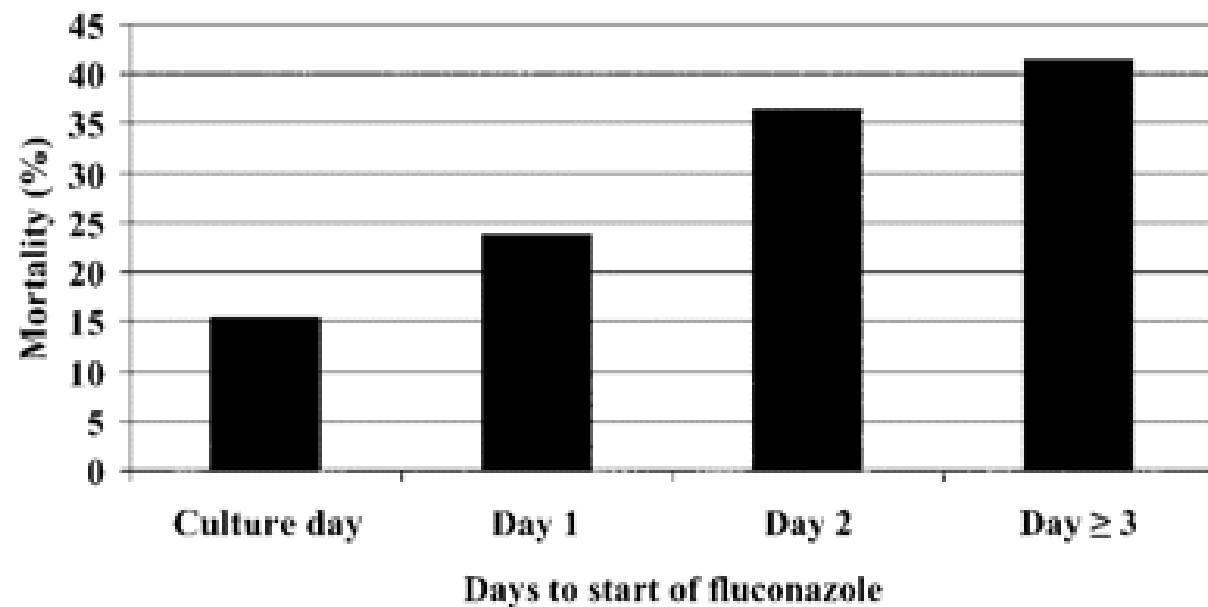
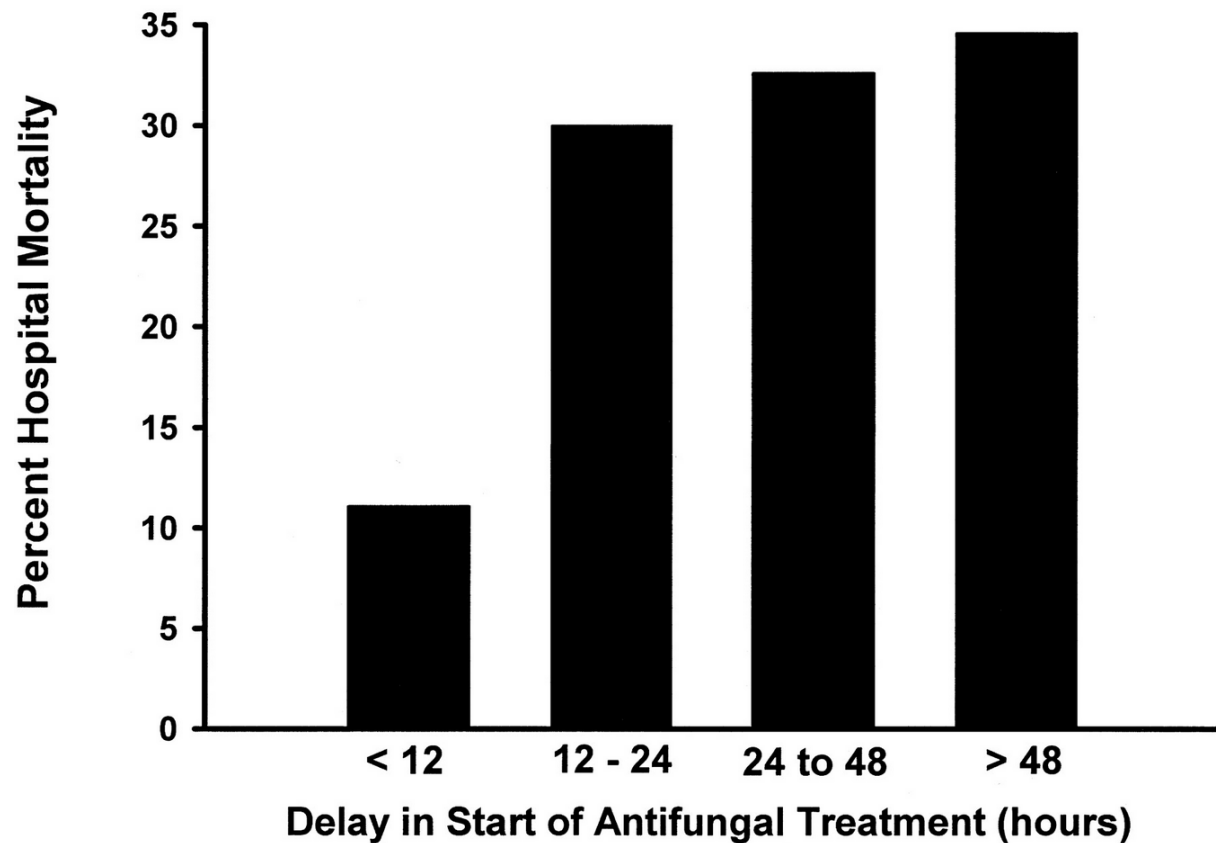
# Traitement



# Activité des antifongiques contre *Candida*

	Polyenes	FCZ	VCZ	PCZ	IVCZ	Candins	5 FC
<i>C. albicans</i>	S	S	S	S	S	S	S
<i>C. tropicalis</i>	S	S	S	S	S	S	S
<i>C. glabrata</i>	S	SDD	S/SDD	S/SDD	S/SDD	S	R
<i>C. krusei</i>	S	R	S	S	S	S	S
<i>C. parapsilosis</i>	S	S	S	S	S	SDD	S
<i>C. lusitaniae</i>	R	S	S	S	S	S	S
<i>C. auris</i>	S	S	S	S	S	S	

# Traiter le plus tôt possible!





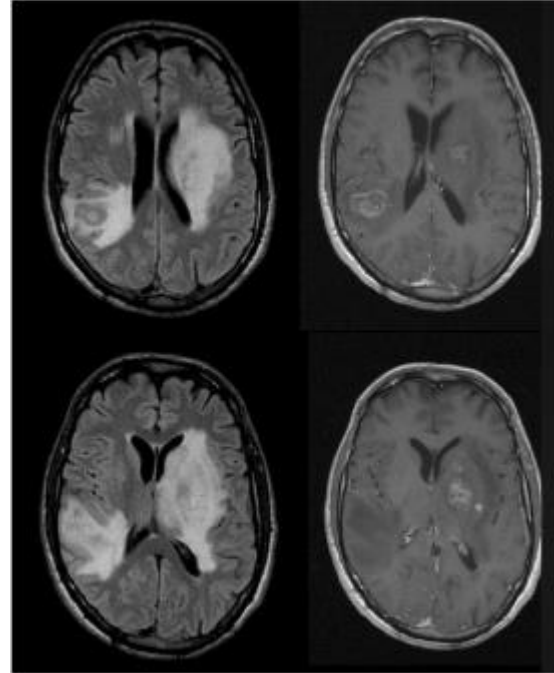
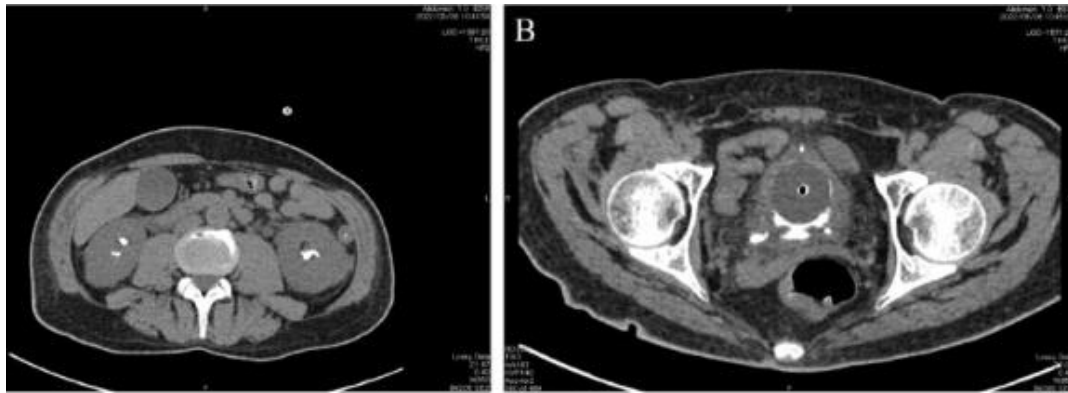
# Echinocandines: choix de première intention

Organisms <sup>a</sup>	Factor	Mortality			Success			
		P	OR	95% CI	Factor	P	OR	95% CI
All organisms (n = 978)	Age	.02	1.01	1.00–1.02	APACHE II	.0001	0.94	.93–.96
	APACHE II score	.0001	1.11	1.08–1.14	Echinocandin	.01	2.33	1.27–4.35
	Immunosuppressive therapy	.001	1.69	1.18–2.44	CVC removed	.001	1.69	1.23–2.33
	<i>Candida tropicalis</i>	.01	1.64	1.11–2.39	Study	NS		
	Echinocandin	.02	0.65	.45–.94				
	CVC removed	.0001	0.50	.35–.72				
	Study	NS						
<i>Candida albicans</i> (n = 408)	APACHE II score	.0001	1.09	1.05–1.13	APACHE II score	.005	0.92	.92–.99
	Immunosuppressive therapy	.002	2.22	1.30–3.70	Echinocandin	.005	3.70	1.49–9.09
	Surgery	.05	0.58	.34–.98	Study	NS		
	Malignancy	.03	1.89	1.05–3.45				
	Echinocandin	.03	0.55	.32–.95				
	CVC removed	.01	0.52	.31–.90				
	Study	NS						

# Intérêt des échinocandines?

- **Spectre large anti *Candida***
- **Résistance reste rare**
- **Tolérance satisfaisante**
- **Interactions rares**
- **Actives sur le biofilm**
- **Fungicides**

# Situations où les échinocandines ne sont pas idéales



Neves *et al.* BMC Res Notes 2014

Alrabadi A *et al.* Clin Med Insights Case Rep 2023

Dodds Ashley *et al.* CID 2006

# Cas particuliers

- ***C. parapsilosis***

- CMI des échinocandines plus élevées
- Candidémies plus souvent persistantes
- Pronostic semblant similaire: pas de challenge des échinocandines Fernandez Ruiz CID 2014

- ***C. glabrata***

- Désescalade à HD FCZ ou VCZ

- ***C. krusei***

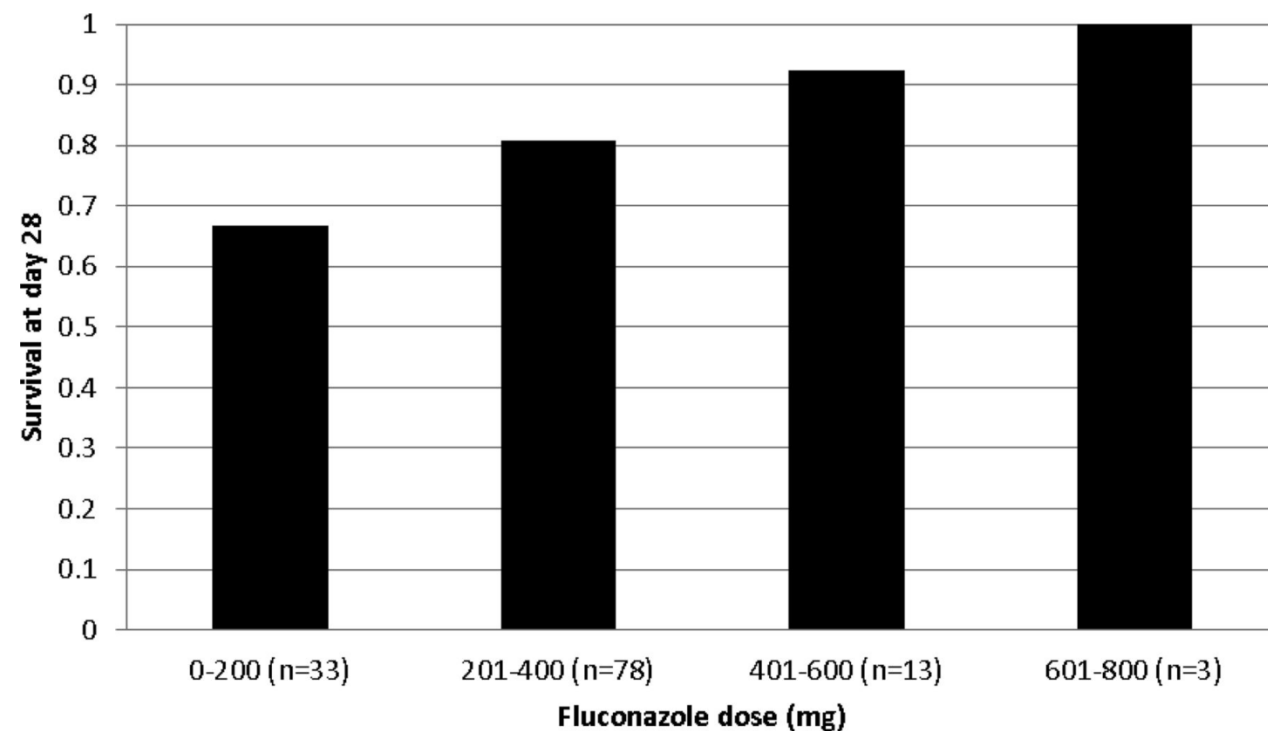
- VCZ

# Candida glabrata & fluconazole

127 *C. glabrata* fungemia receiving FCZ, 4 centers, 2002-2011

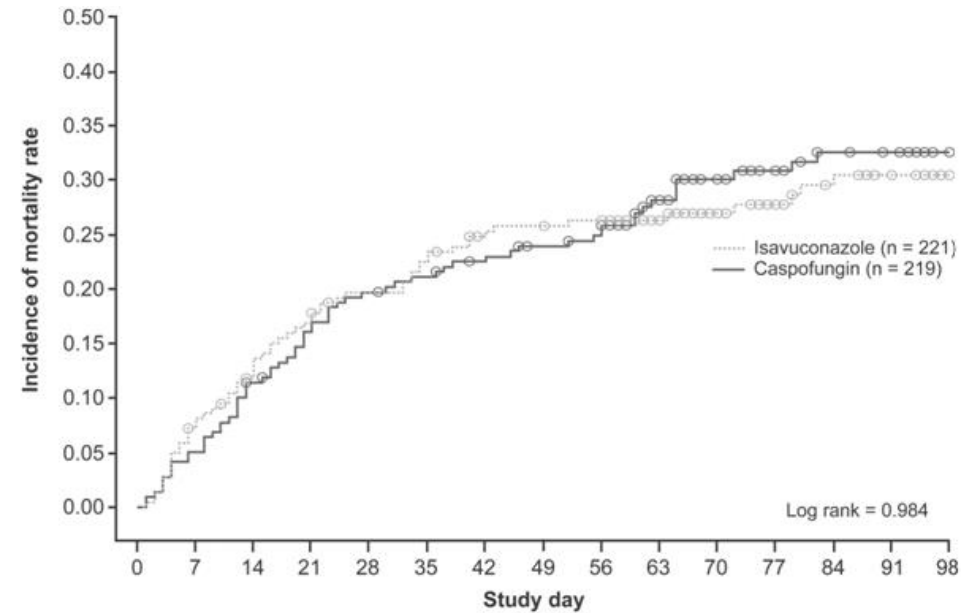
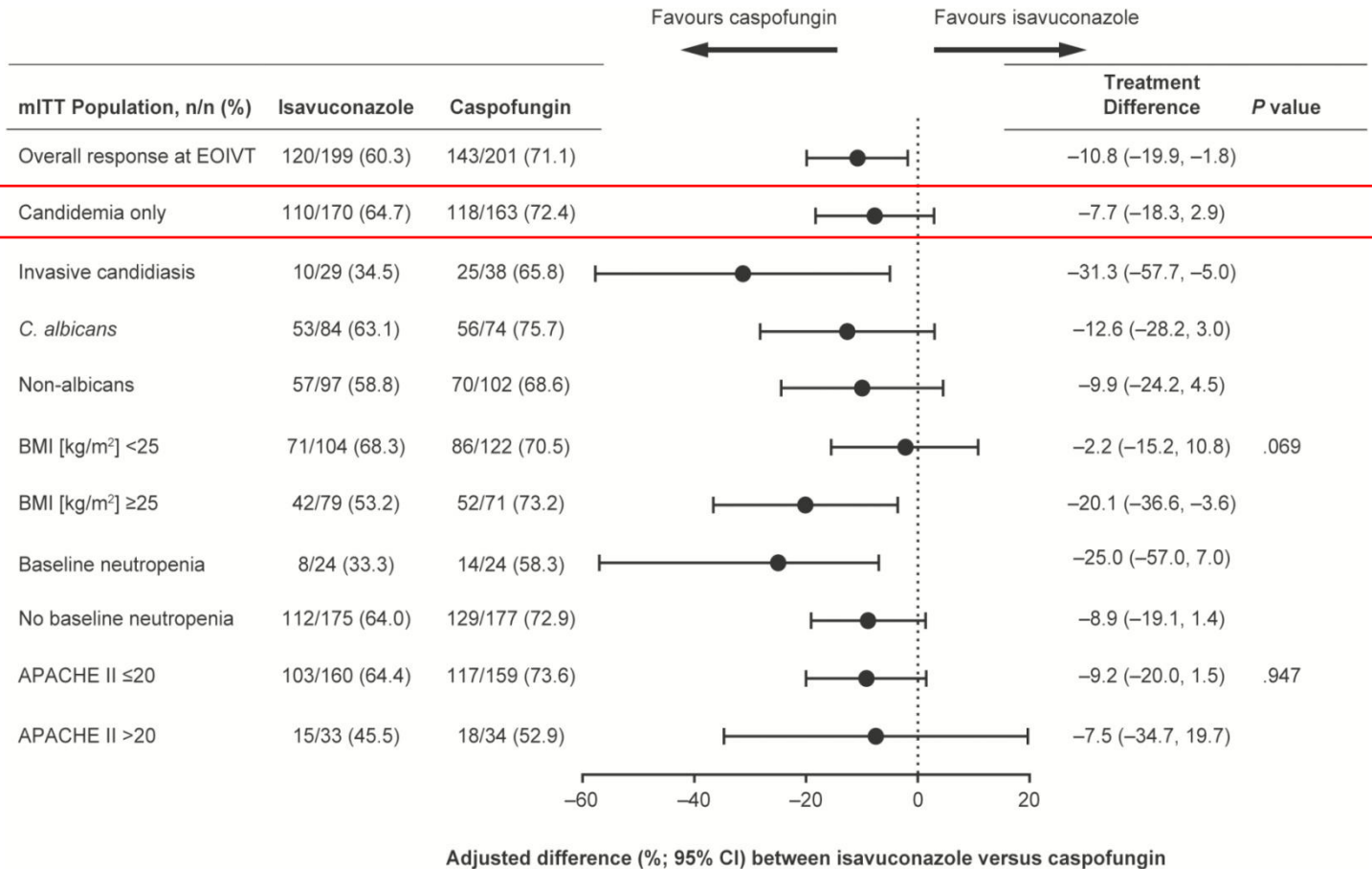
Endpoint: 28 days mortality

Variable	Survived (n = 100)	Died (n = 27)	P
Time to initiation of therapy (mean ± standard deviation) (h)	51.7 ± 52	37.4 ± 39.9	0.188
Average dose (median [IQR]) (mg)	400 (240–400)	240 (200–400)	0.009
Average AUC (median [IQR]) (mg · h/liter)	345.5 (221–519)	381 (231–478)	0.66
MIC (median [IQR]) (µg/ml)	16 (4–32)	16 (8–32)	0.11
MIC category (no. [%])			
≤8 µg/ml	46 (47.4)	10 (40)	0.51
16–32 µg/ml	40 (41.2)	9 (36)	0.63
≥64 µg/ml	11 (11.3)	6 (24)	0.114
Average AUC/MIC ratio (median [IQR])	27.7 (10.7–83.5)	28.6 (9.5–48.8)	0.22
Average AUC of >400 mg · h/liter (no. [%])	40 (40)	12 (44.4)	0.67
Average AUC/MIC ratio of >12.5 (no. [%])	70 (72.2)	16 (64)	0.43
Average AUC/MIC ratio of >25 (no. [%])	52 (53.6)	14 (56)	0.83
Average AUC/MIC ratio of >50 (no. [%])	36 (37.1)	6 (24)	0.22
Average dose of ≥400 mg (no. [%])	64 (64)	9 (33.3)	0.004
First-day AUC (median [IQR]) (mg · h/liter)	358 (218–555)	374 (229–448)	0.90
First-day dose (median [IQR]) (mg)	400 (200–400)	200 (200–400)	0.002
First-day AUC/MIC ratio (median [IQR])	25.7 (10.8–87.2)	28.6 (8.5–48.9)	0.22



# “Nouveaux” triazolés

- **Posaconazole:** pas d’essai
- **Isavuconazole:** un RCT



	0	7	14	21	28	35	42	49	56	63	70	77	84	91	98
Isavuconazole	221	204	191	180	172	166	157	155	153	113	94	84	77	72	58
Caspofungin	219	208	193	182	174	170	165	160	157	114	102	88	78	73	65

# Rezafungine

	Rezafungin group (n=100)	Caspofungin group (n=99)
Age	59.5 (15.8)	62.0 (14.6)
<65 years	60 (60%)	58 (59%)
≥65 years	40 (40%)	41 (41%)
Sex		
Male	67 (67%)	56 (57%)
Female	33 (33%)	43 (43%)
Race		
Asian	27 (27%)	31 (31%)
Black or African American	5 (5%)	4 (4%)
White	61 (61%)	60 (61%)
Other or not reported	7 (7%)	4 (4%)
Diagnosis		
Candidaemia only	70 (70%)	68 (69%)
Invasive candidiasis*	30 (30%)	31 (31%)
Mean modified APACHE II score†	12.5 (8.0)	13.1 (7.1)
≥20	15 (15%)	18 (18%)
<20	84 (84%)	81 (83%)
Body-mass index mean, kg/m <sup>2</sup>	25.4 (7.0)	24.5 (6.5)
Absolute neutrophil count, <500 cells per μL†	9 (9%)	6 (6%)

	Rezafungin group (n=93)	Caspofungin group (n=94)	Treatment difference (95% CI)
<b>All-cause mortality at day 30 (US FDA primary outcome)</b>			
Died	22 (24%)	20 (21%)	2.4 (-9.7 to 14.4)*
Known to have died	19 (20%)	17 (18%)	..
Unknown survival	3 (3%)	3 (3%)	..
<b>All-cause mortality at day 30 by diagnosis</b>			
Candidaemia only	18/64 (28%)	17/67 (25%)	2.8 (-12.5 to 18.0)*
Invasive candidiasis	4/29 (14%)	3/27 (11%)	2.7 (-16.7 to 21.7)*
<b>Global response at day 14 as assessed by DRC (EMA primary outcome)</b>			
Cure	55 (59%)	57 (61%)	-1.1 (-14.9 to 12.7)†
Failure	28 (30%)	29 (31%)	..
Indeterminate	10 (11%)	8 (9%)	..
<b>Global response at day 14 as assessed by DRC by diagnosis</b>			
<b>Candidaemia only</b>			
Cure	39/64 (61%)	43/67 (64%)	-3.2 (-19.6 to 13.3)*
Failure	21/64 (33%)	19/67 (28%)	..
Indeterminate	4/64 (6%)	5/67 (7%)	..
<b>Invasive candidiasis</b>			
Cure	16/29 (55%)	14/27 (52%)	3.3 (-22.4 to 28.6)*
Failure	7/29 (24%)	10/27 (37%)	..
Indeterminate	6/29 (21%)	3/27 (11%)	..

# Que disent les recommandations?



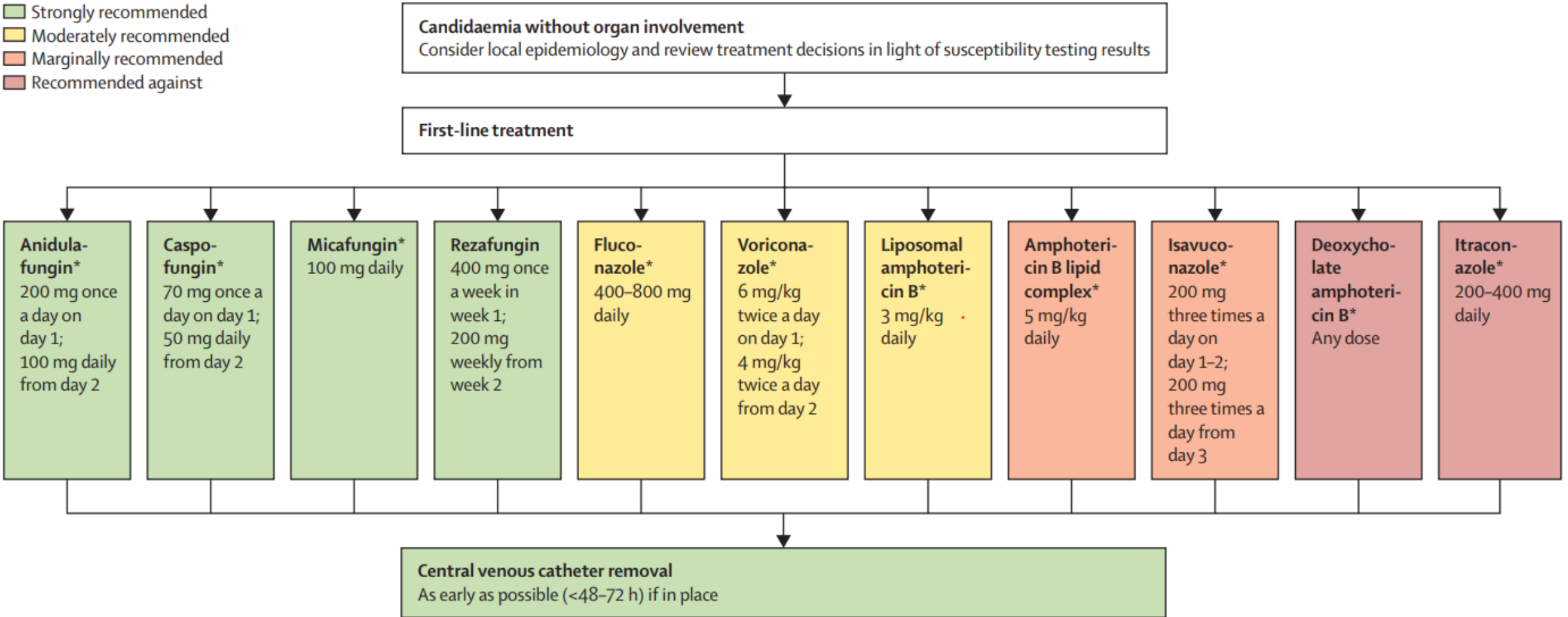
	ESCMID non neutropénique	ESCMID neutropénique	IDSA non neutropénique	IDSA neutropénique
Fluco		CII	Strong, high*	
Caspofungin	AI	AII	Strong; high	Strong, moderate
Anidulafungin	AI		Strong; high	Strong, moderate
Micafungin	AI		Strong; high	Strong, moderate
VCZ	CI	CII		
AmBL	BI		Strong, high	Strong, moderate
AmBLC	CII	CII		
AmBd	DI	DII		



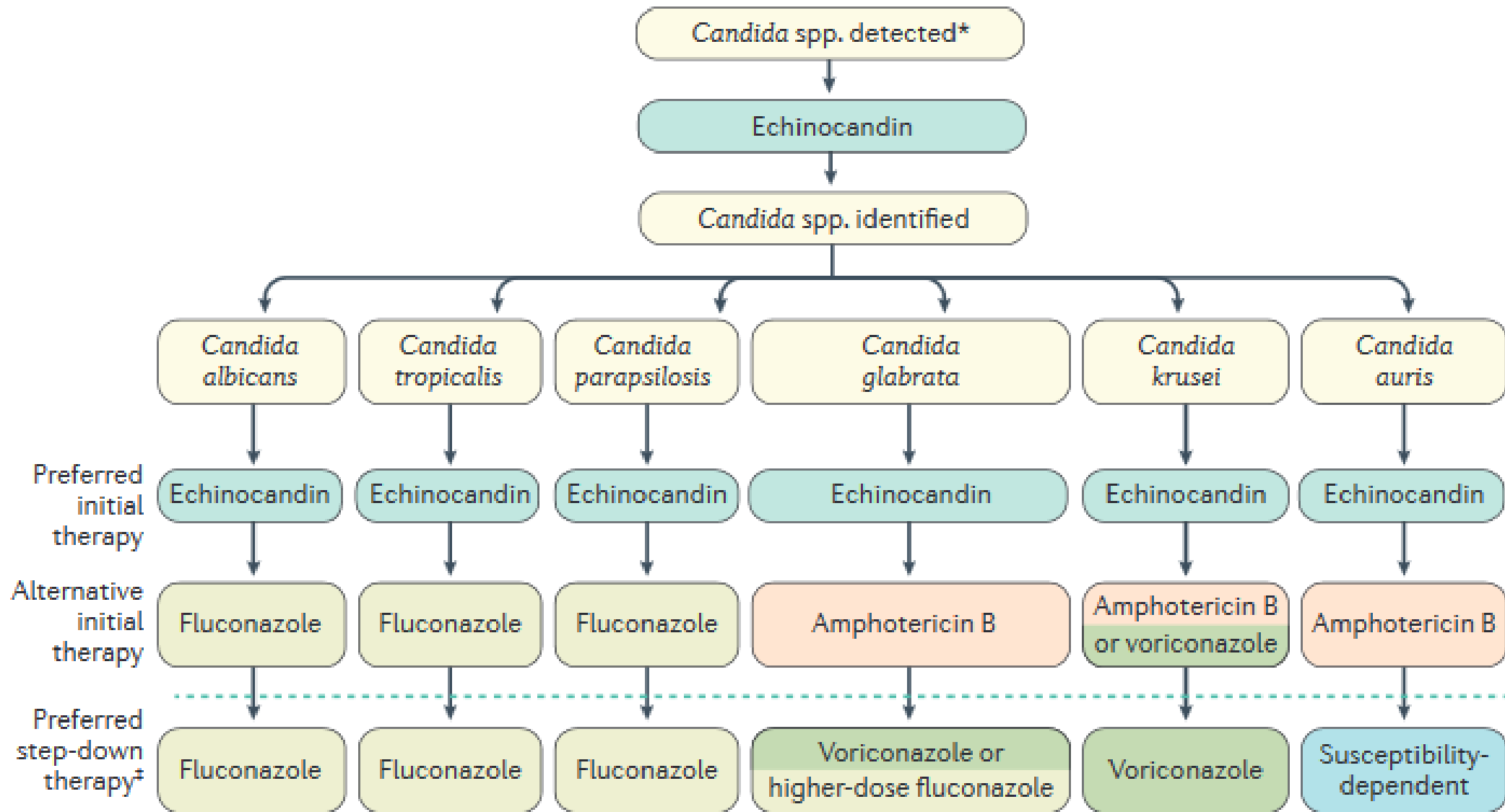
\*: no neutropenia, no critical illness, no previous exposure to candins

# Que disent les recommandations?

- Strongly recommended
- Moderately recommended
- Marginally recommended
- Recommended against



# Traitement: en résumé



# Durée de traitement

- Nombre d'essais contrôlés évaluant la durée: **zero**
- J 0 = première hémoculture négative
- 14 jours
- Relais oral: J 10, patient stable (ESCMID)
- Relais oral: J 5-7, patient stable (IDSA/ECMM-ISHAM-ASM)



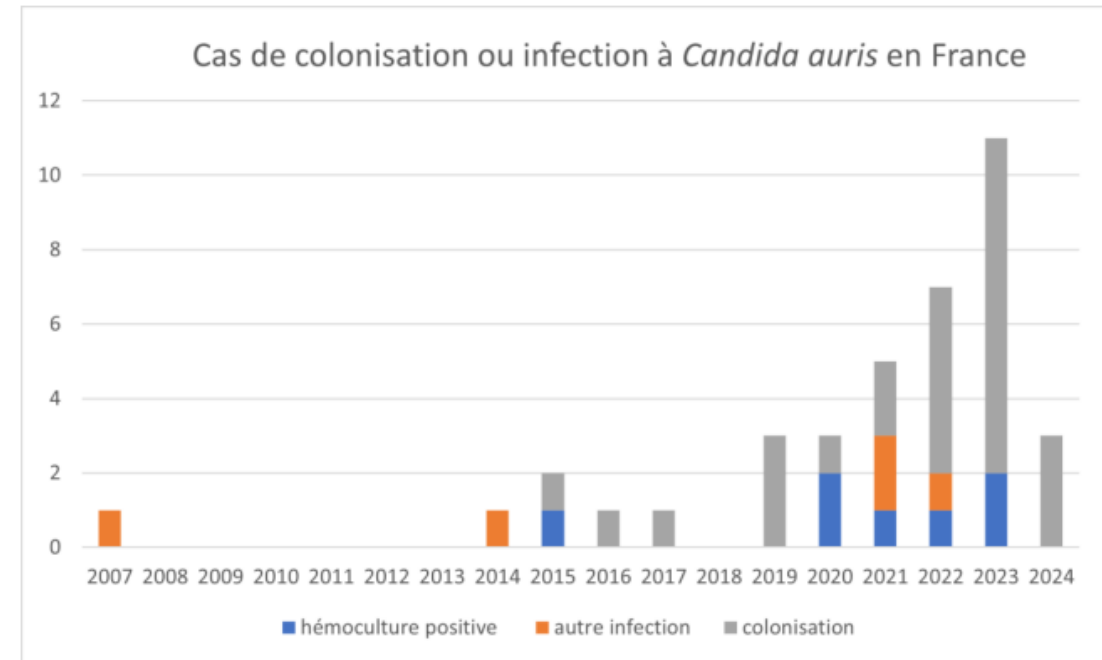
The screenshot shows the header of the ESCMID website. On the left, the logo for 'CMI CLINICAL MICROBIOLOGY AND INFECTION' is displayed. To its right is the ESCMID logo, which consists of a stylized network of nodes and lines. Below the logos is a navigation menu with the following items: 'Articles', 'Publish', 'Collections', 'About', and 'Contact'. The main content area features a 'COMMENTARY' section for 'Volume 31, Issue 2, P147-151, February 2025'. A blue button with a download icon and the text 'Download Full Issue' is positioned to the right of the volume information. The title of the article is 'Which trial do we need? Shorter antifungal treatment for candidemia – challenging the 14-day dogma'. Below the title, the authors are listed: Nico Bekaun<sup>1),2)</sup>, Oliver A. Cornely<sup>1),2),3),4)</sup>, Tim Friede<sup>5)</sup>, Jürgen Prattes<sup>6)</sup>, Rosanne Sprute<sup>1),2),3)</sup>, Martin Hellmich<sup>7)</sup>, Philipp Koehler<sup>1),2),8)</sup>, Jon Salmanton-García<sup>1),2),3)</sup>, Jannik Stemler<sup>1),2),3)</sup>, and Ilana Reinhold<sup>1),2)</sup>. A 'Show less' link is located at the end of the author list.

# Que faire des cathéters centraux?

- Bénéfice en survie?
- Le maintien est associé à la persistance de la candidémie
- Retirer les CVC dès que possible
- Activité anti-biofilm: échinocandines ou AmBL > azoles

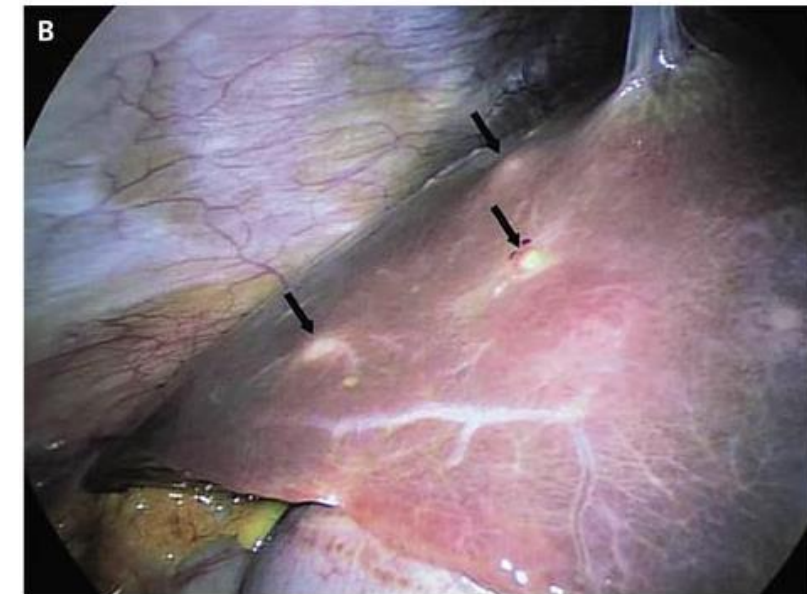
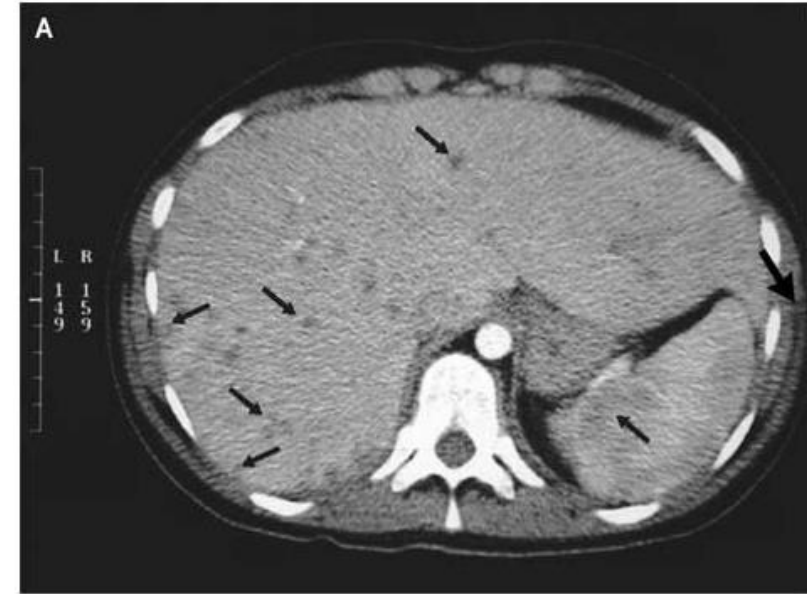
# The threat of *Candida (Candidozyma) auris*

- Description initiale: 2009 Satoh K *et al.* Microbiol Immunol 2009
- Première infection: Corée du Sud, 1996?
- Identification difficile
- Très résistant: FCZ 80%, souvent MDR
- Potentiel épidémique, colonisant de la peau
- Mortalité élevée
- Health care associated in most cases
- Echinocandines en 1ère intention



# La candidose hépatosplénique

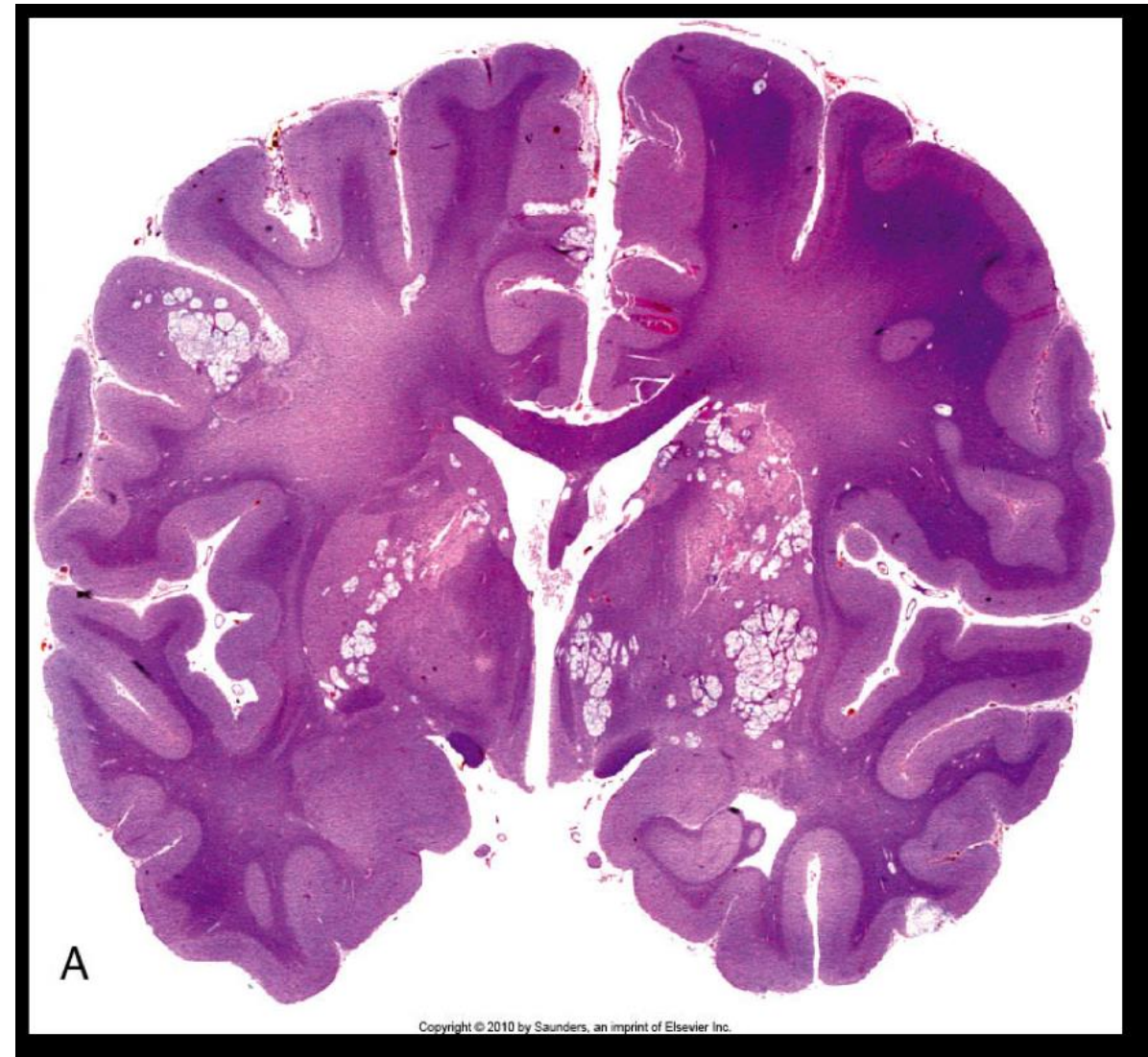
- **Terrain:** neutropénie prolongée
- **Clinique:** fièvre en sortie de neutropénie  
HMG/SMG
- PAL élevées
- **Imagerie:** IRM > TDM > échographie
- **Microbiologie:** hémoc rarement positives

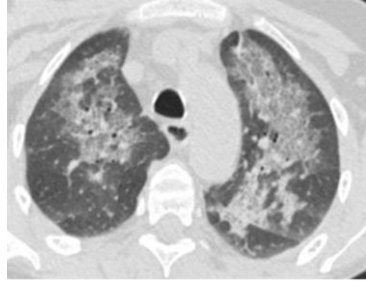
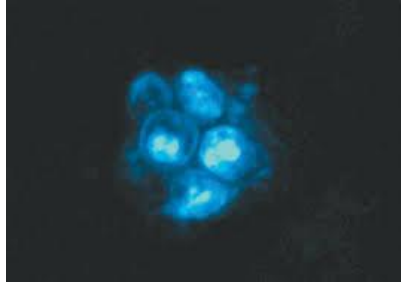


# La candidose hépatosplénique: un IRIS?

Characteristic	Value
Antifungal therapy before commencement of CST, no. of patients	
Deoxycholate amphotericin B	1
Liposomal amphotericin B	7
Amphotericin B lipid complex	1
Caspofungin	2
Voriconazole	1
Interval between CDC diagnosis and commencement of CST, median days (range)	40 (1–120)
Antifungal therapy received after commencement of CST, no. of patients	
Fluconazole	8
Amphotericin B lipid complex	1
Voriconazole	1
Time to fever and abdominal pain resolution after commencement of CST, median days (range)	4.5 (1–30)
Initial CST regimen, median mg/kg of prednisone equivalent per day (range)	0.66 (0.4–2)
Duration of CST, median days (range)	109 (49–240)
Time to normalization of C-reactive or fibrinogen level after commencement of CST, median days (range)	14.4 (2–30)
Time to normal abdominal ultrasound or CT findings after commencement of CST, median days (range)	107 (30–210)
Time between commencement of CST for CDC and commencement of chemotherapy, median days (range)	33 (2–60)
Status	
Alive	
No. of patients	4
Time after CDC diagnosis, median years (range)	6.5 (4–9)
Death due to leukemia relapse, no. of patients	6

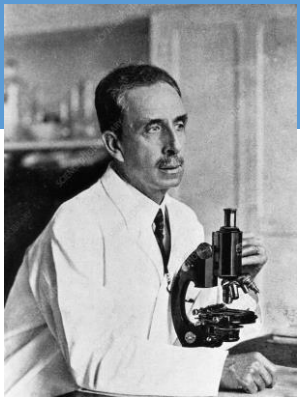
# Beware of the Friday evening “yeast” blood culture



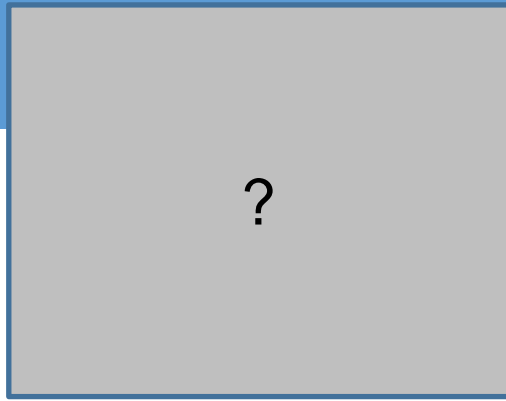


# Pneumocystose

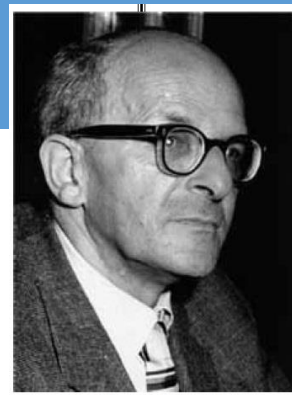
# Historique



1909



1912: Delanoë & Delanoë

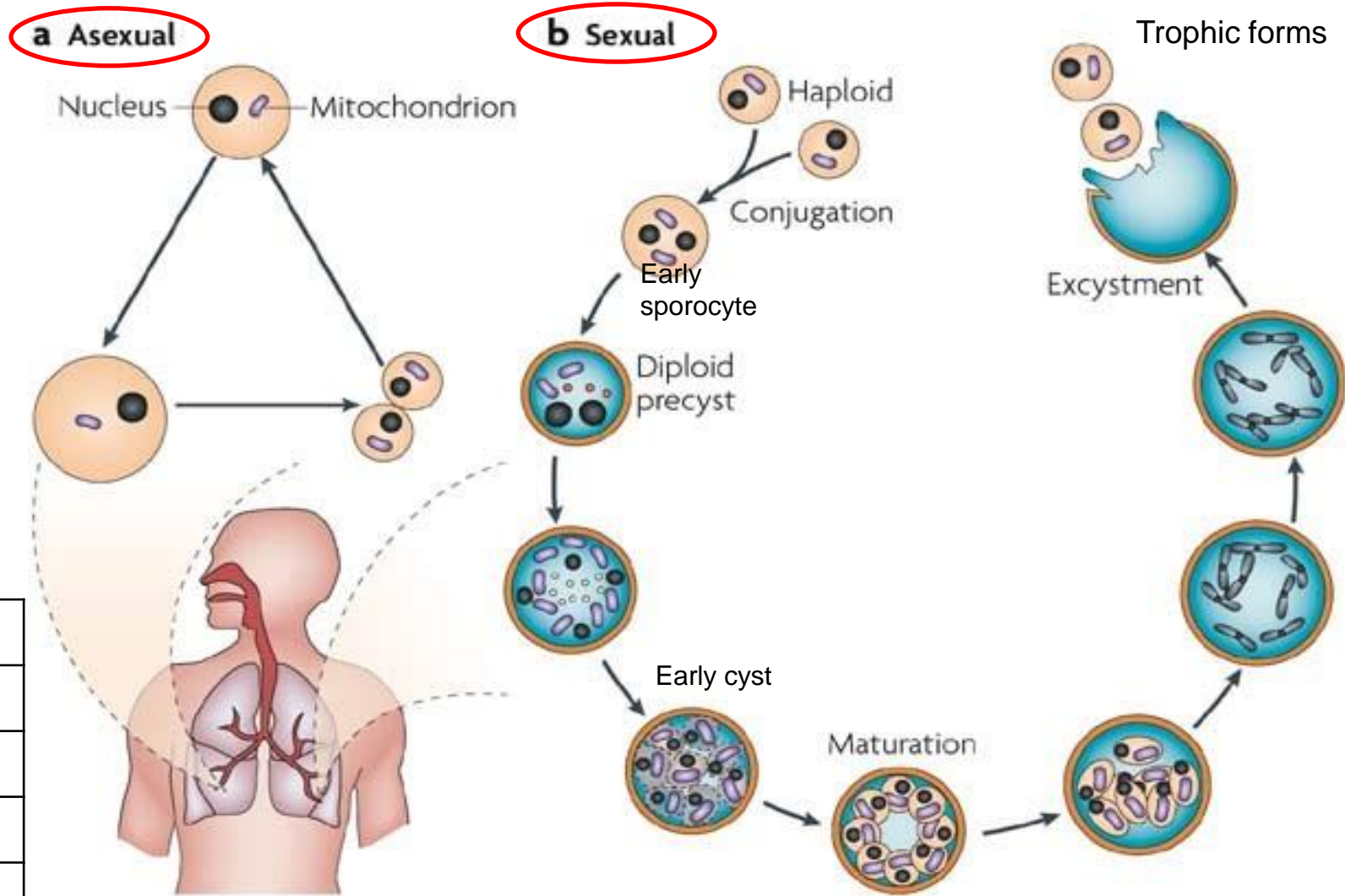
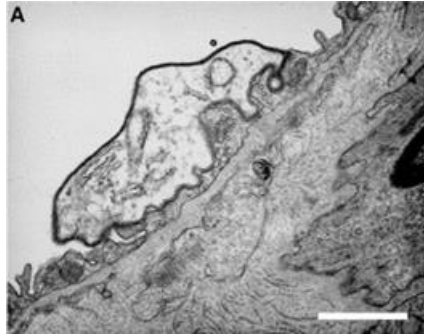
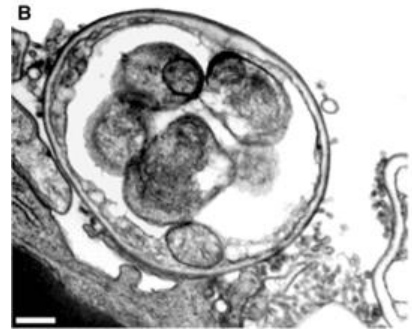


Otto Jirovec (1907-1972)

- Initialement décrit comme protozoaire
- Années 1930-1940 « pneumonie interstitielle plasmocytaire » des prématurés & enfants dénutris
- 1981: augmentation des requêtes de pentamidine au CDC
- Reclassé en champignon en 1988 (ARNr), *Ascomycota*



# *Pneumocystis*: cycle de vie

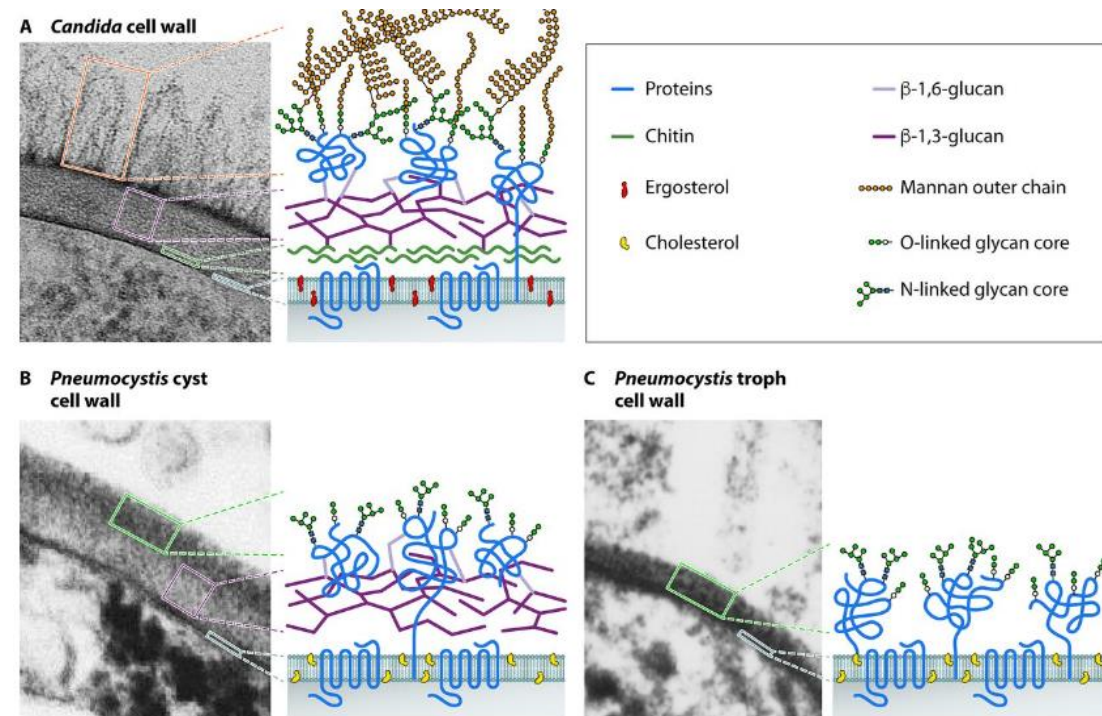


Asques/Kystes	Trophozoïtes
Transmissible/Infectante	Réplivative
Colorée GMS	Non colorée GMS
Paroi épaisse β D glucane	Pas de vraie paroi
Immunogène	Peu immunogène

Nature Reviews | Microbiology

# Un champignon pas comme les autres

- Ubiquitaire
- Tous mammifères mais spécificité d'hôte totale
- Pas d'ergostérol mais du cholestérol: R azoles et AmB
- Génome petit, très compact, 29% GC
- Perte de nombreuses voies métaboliques
- Paroi particulière:
- **Incultivable**



# Une physiopathologie encore mal comprise

Uniquement dans les espaces alvéolaires des mammifères

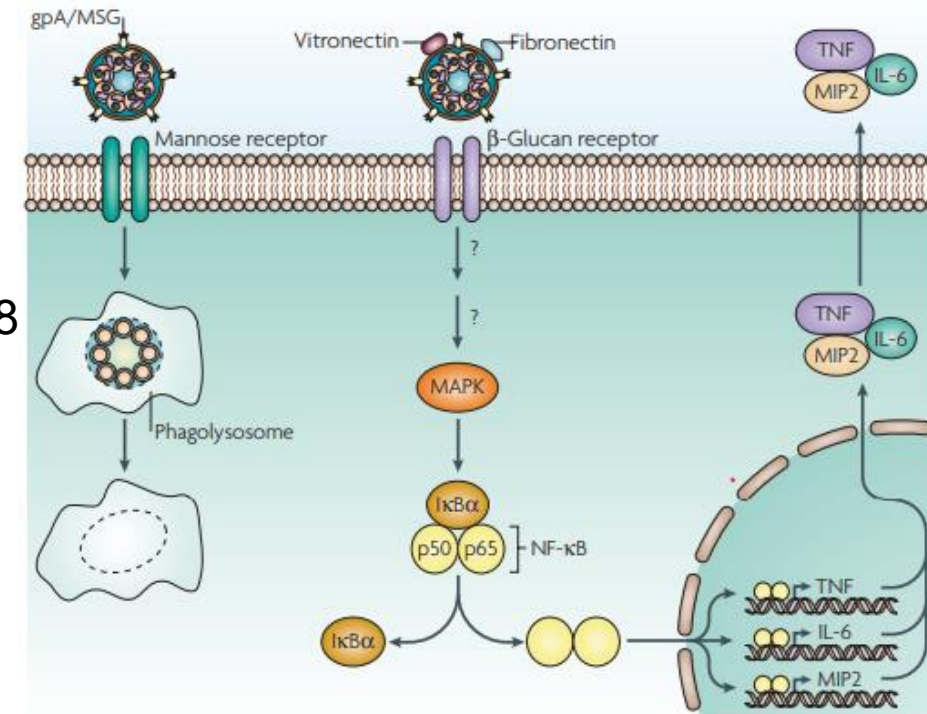
Contact dans les premières années de vie Pifer L *et al.* Pediatrics 1978

Inhalation de spores vers les alvéoles

Attachement aux pneumocytes I (fibro/vitronectine ↔ intégrines)

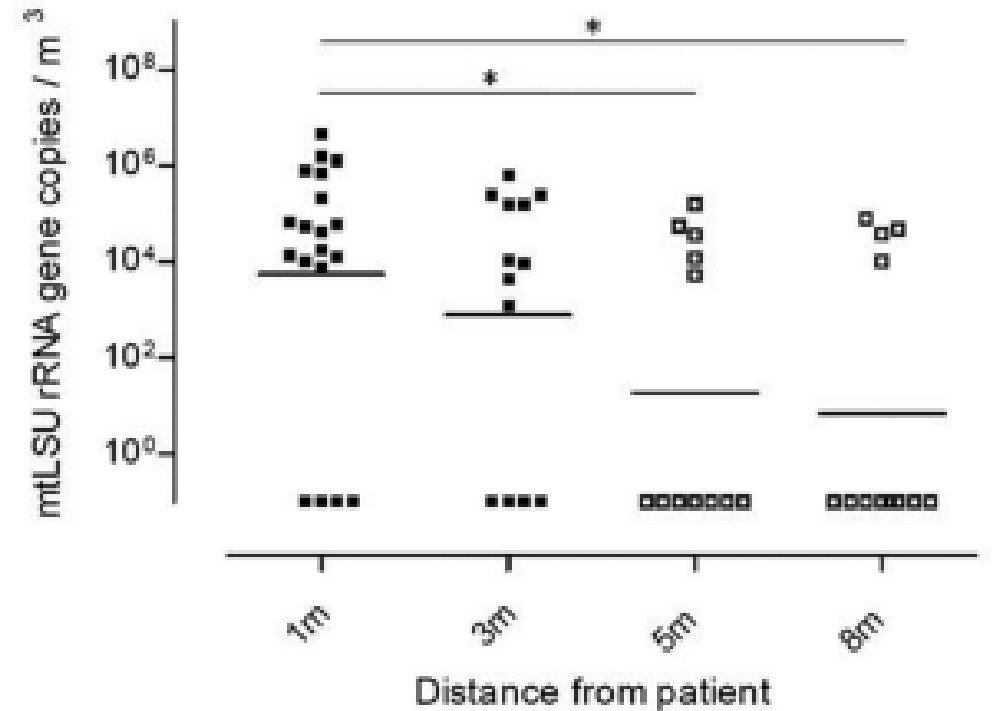
Activation de nombreuses voies de signalisation chez le champignon  
chez l'hôte

Maladie surtout due à l'inflammation, médiée notamment par CD8/PNN/IL8

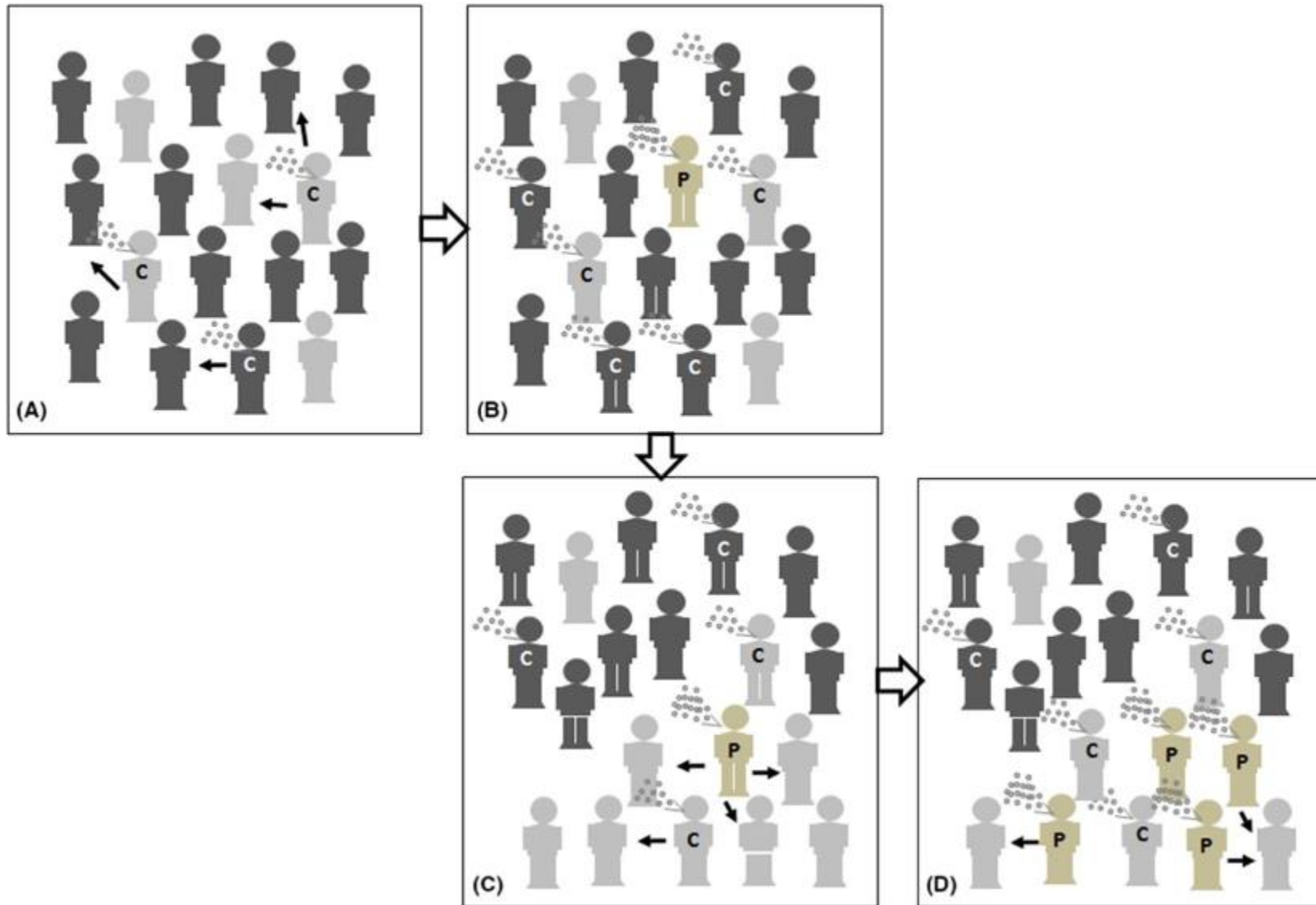


# Transmission aérienne

Category	Conditioned environment				No. with <i>P. carinii</i> /no. tested
	Water	Food	Infected tissue	Air	
Experiment 1					
A	Sterile	Sterile	No	Sterile	0/10
B*	Sterile	Sterile	No	Sterile	0/7
Experiment 2					
A (Baltimore)	Sterile	Sterile	No	Sterile	0/10
	Unsterile	Unsterile	No	Unsterile	10/10
B (Memphis)	Sterile	Sterile	No	Sterile	0/10
	Unsterile	Unsterile	No	Unsterile	8/10
Experiment 3					
A	Sterile	Sterile	No	Unsterile	7/8
B	Sterile	Unsterile	No	Sterile	0/8
C	Unsterile	Sterile	No	Sterile	0/8
Experiment 4					
A*	Sterile	Sterile	Yes + drug <sup>†</sup>	Sterile	0/10
B*	Sterile	Sterile	Yes + drug <sup>†</sup>	Sterile	0/10



# Transmission aérienne & épidémies



# La colonisation est-elle fréquente?

Author	Year	Country	Patients	N	Sample	Technique	Colonization
Vargas	2003	Chile	Immunocompetent (pregnant or not)	33+28	NP aspirate	PCR	15% & 0%
Garcia	2020	Peru	Immunocompetent women	92	NP aspirate & oral washes	PCR	5,43%
Mekinian	2011	France	Systemic autoimmun dis	67	Induced sputum	PCR	16%
Maskell	2003	USA	Immunosuppressed adults	93	BAL	PCR	18%
Vidal	2006	Spain	CF	88	BAL	PCR	22,8%
Amato	2000	Portugal	Chronic lung dis	43	BAL	PCR	24,4%
Calderon	2007	Spain	COPD	51	Sputum	PCR	55%
Le Gal	2010	France	CF	76	Sputum	PCR	1,3%
Nevez	2006	France	COPD & Healthy	50+30	Sputum	PCR	16% & 0%
Huang	2003	USA	HIV infected	32	Induced sputum/BAL	PCR	69%
Fritzsche	2012	Germany	Autoimmun dis & healthy	102+117	Induced sputum	PCR	29% & 3%
			Heart-lung Tx		BAL		88%

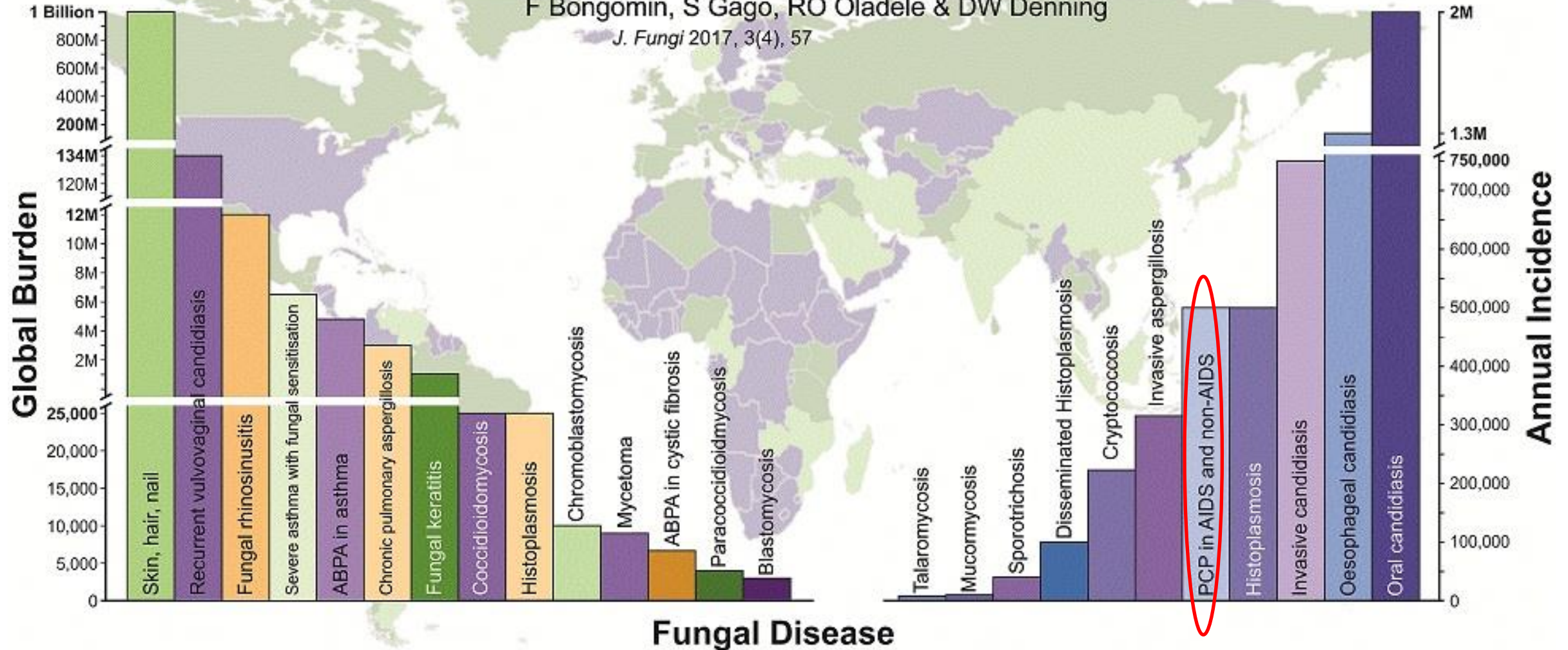
Rare si immunocompétent; non négligeable si immunodépression « locale » ou cellulaire

# Amplitude du problème dans le monde

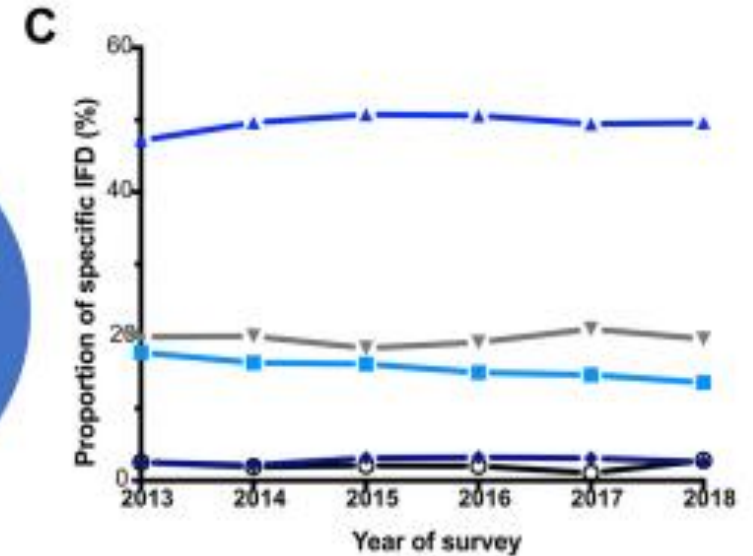
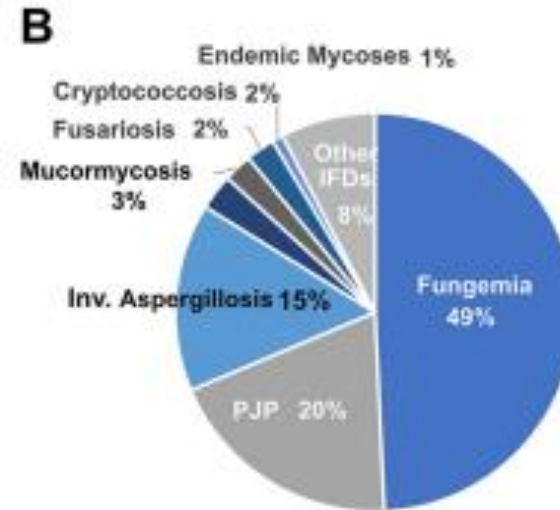
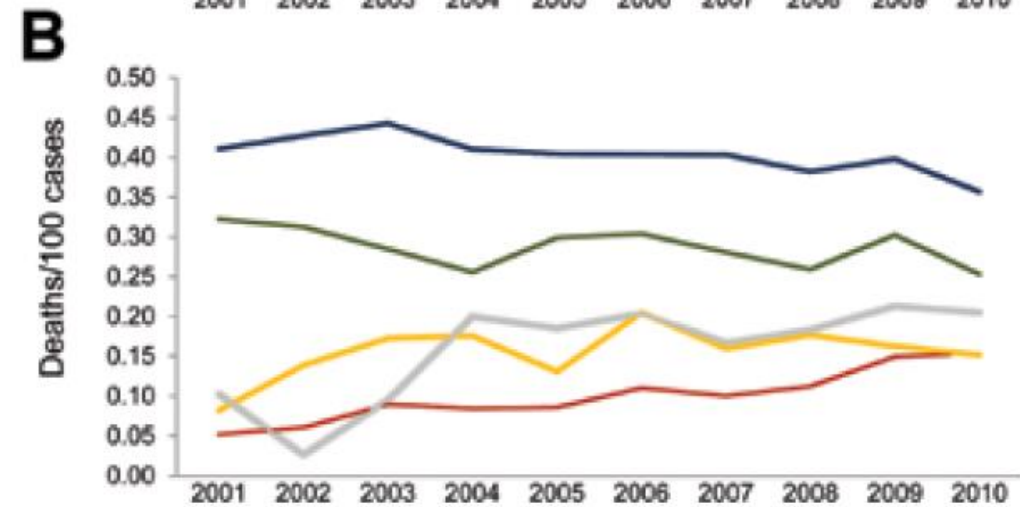
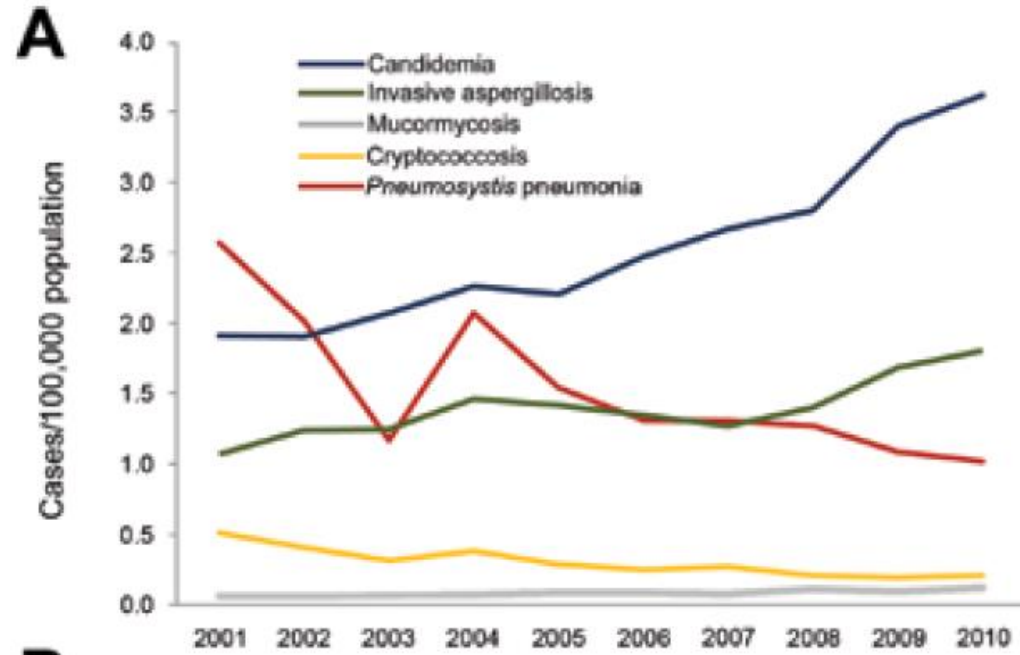
Global and Multi-National Burden of Fungal Diseases - Estimate Precision

F Bongomin, S Gago, RO Oladele & DW Denning

*J. Fungi* 2017, 3(4), 57



# Amplitude du problème en France



# Pneumocystose: populations à risque

## Estimation du risque sans prophylaxie:

LAL enfant: 20%

LNH enfant: 20%

LNH adultes: 20-30%

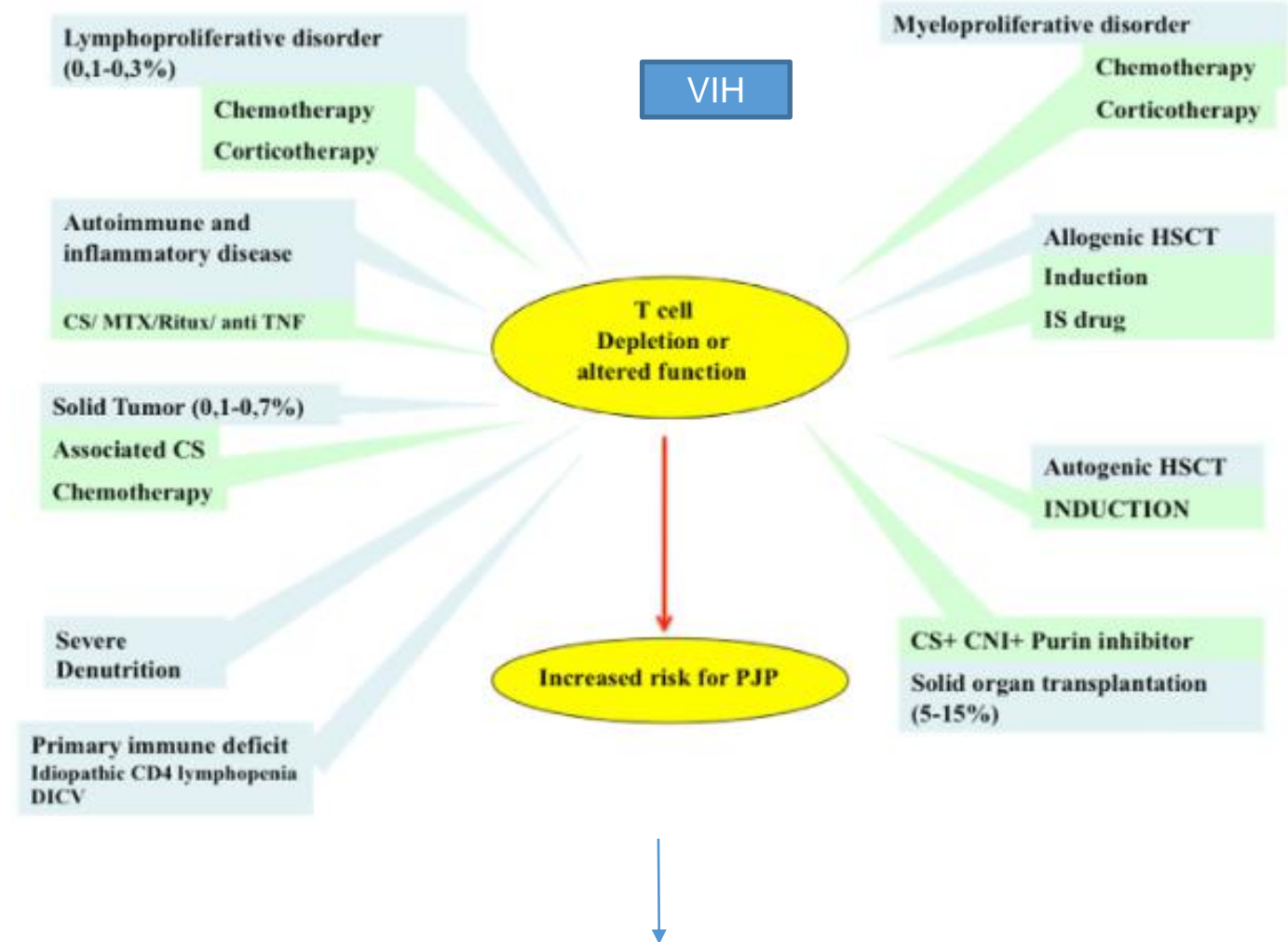
AlloHSCT: 5-15%

SOT: 5-15% (rénal << poumon), Htx: 2-10%

Kidney Tx: 0.6 to 14%

Tumeurs solides: rare, 1% (CS)

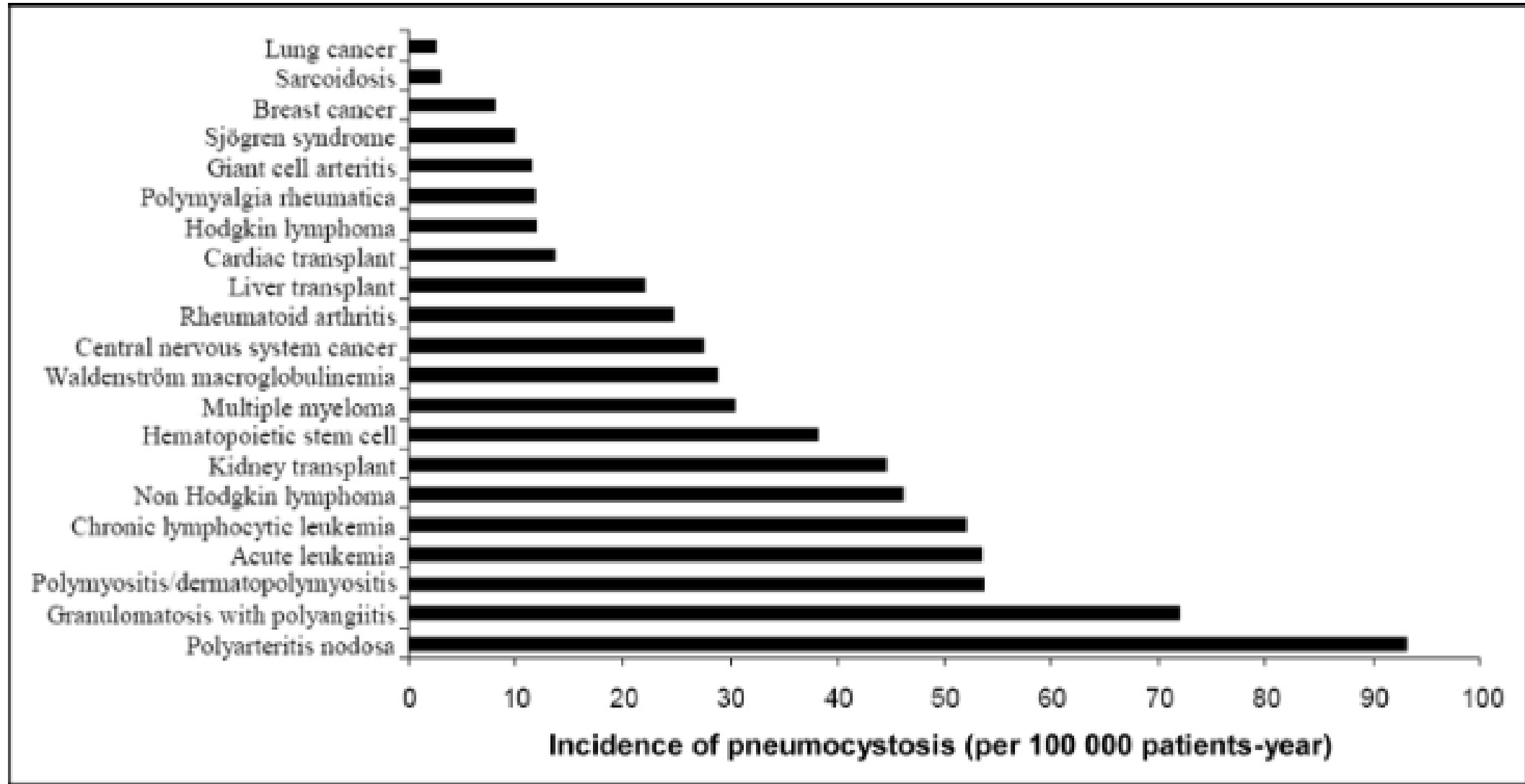
Pathologies systémiques: 1-2%



Immunocompétent: **non**

# Pathologies à risque

CHU Rennes, 1990-2010, VIH neg, n=154



# Pourquoi les corticoïdes?

# Pneumocystose et pathologies systémiques

- **Horton/PPR**: risque semblant faible (0 à 0,07/1000 PA) Anumolu N *et al.* Semin Arthritis Rheum 2023 & Krijthe Clin Exp Rheumatol 2021

- **Lupus**: risque peu clair; environ 5%?

- **Vascularites à ANCA**: risque substantiel notamment GPA (89/10000 hospit-années) Ward *et al.* ARD 2016

FDR: lymphocytose pré ttt et à M3 post induction Godeau B *et al.* ARD 1995.

Par extension, également au cours des autres VAA

- **DM/PM**: risque non négligeable, surtout si atteinte pulmonaire (20 à 27/10000 hospit-années)

- **Sclérodermie**: 8/10000 hospit-années; plus important si atteinte pulmonaire?

Pas de consensus sur le seuil de lymphocytes/CD4

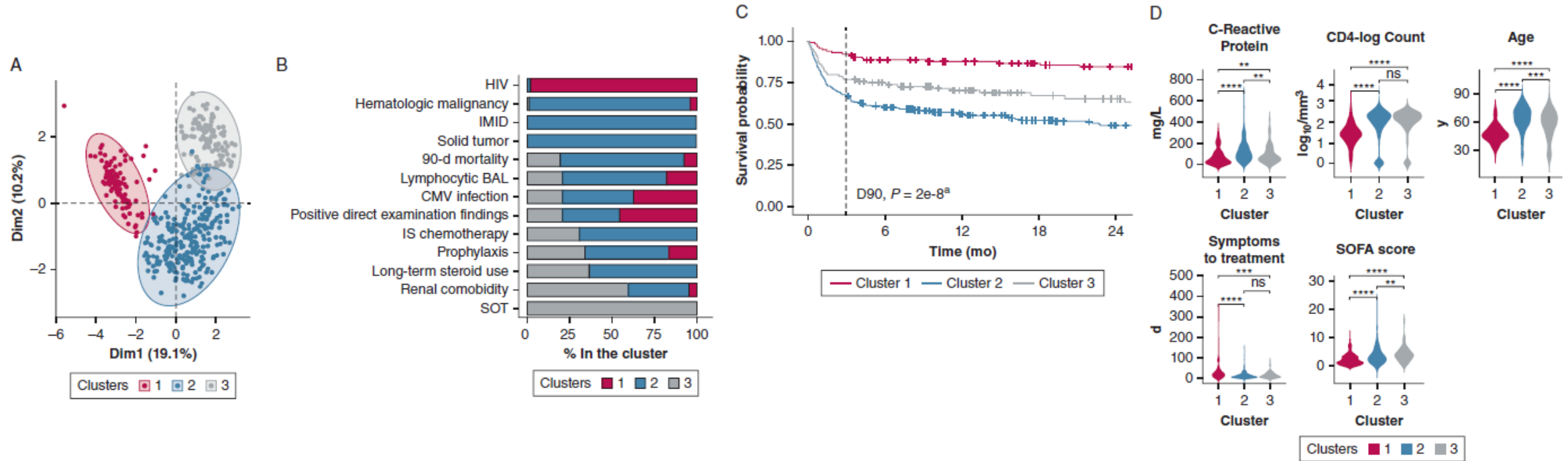
**Incidence et mortalité de la pneumocystose au cours des maladies systémiques**

	Incidence	Mortalité
Maladie de Wegener	8 à 12 % [5,6]	
Périarterite noueuse	6,5 % [4,5]	Mortalité globale : 40 %
Dermatopolymyosite	2,7 % [8]	
Lupus érythémateux disséminé	2 % [9,10]	Si les patients sont intubés : 60 %
Polyarthrite rhumatoïde	0,2 % [5]	

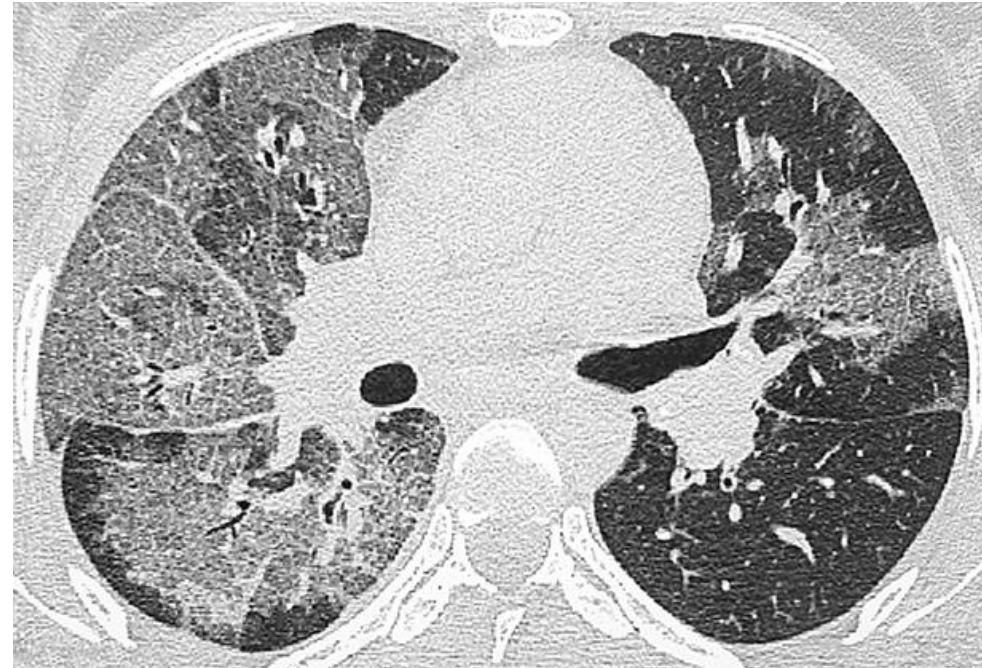
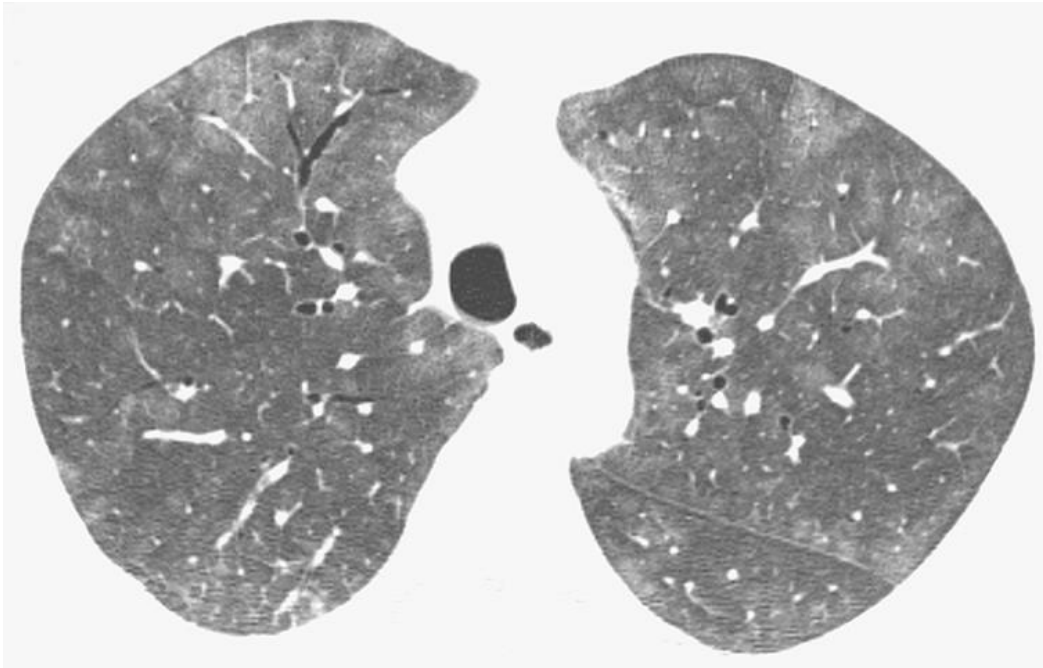
# VIH + vs VIH -

	<b>VIH+</b>	<b>VIH-</b>
<i>Début</i>	progressif	Rapide
<i>Charge fongique</i>	élevée	faible
<i>Seuil CD4</i>	< 200	mal défini
<i>LDH</i>	Élevé	Peu élevé
<i>Cellularité LBA</i>	Peu inflammatoire	Inflammatoire (PNN)
<i>Admission en USI</i>	Rare	Fréquente
<i>Mortalité</i>	faible	élevée

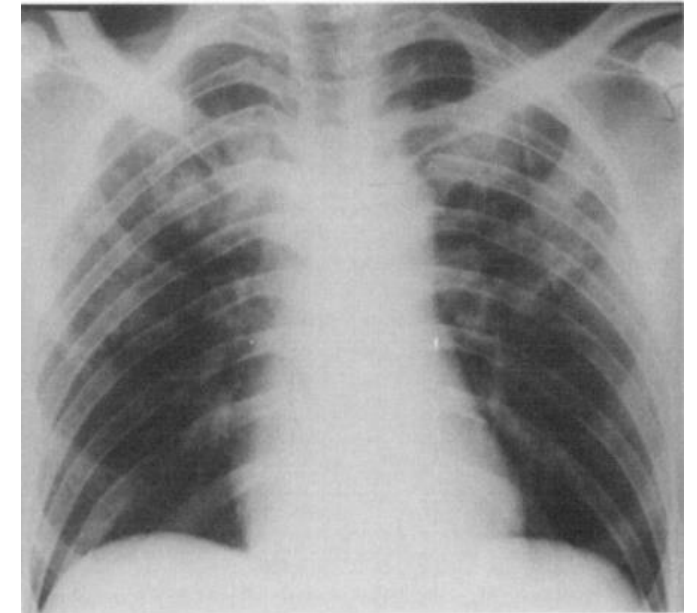
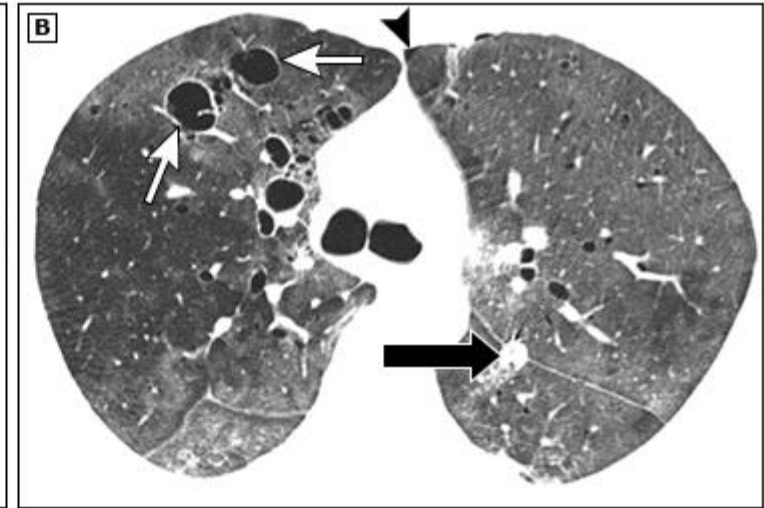
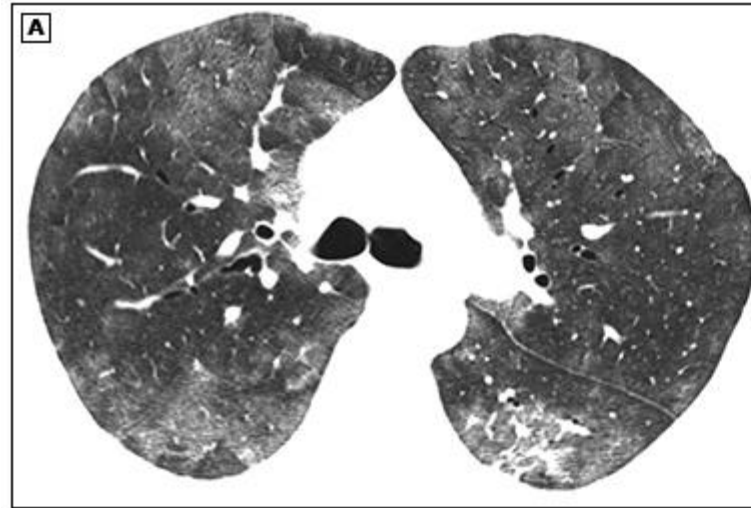
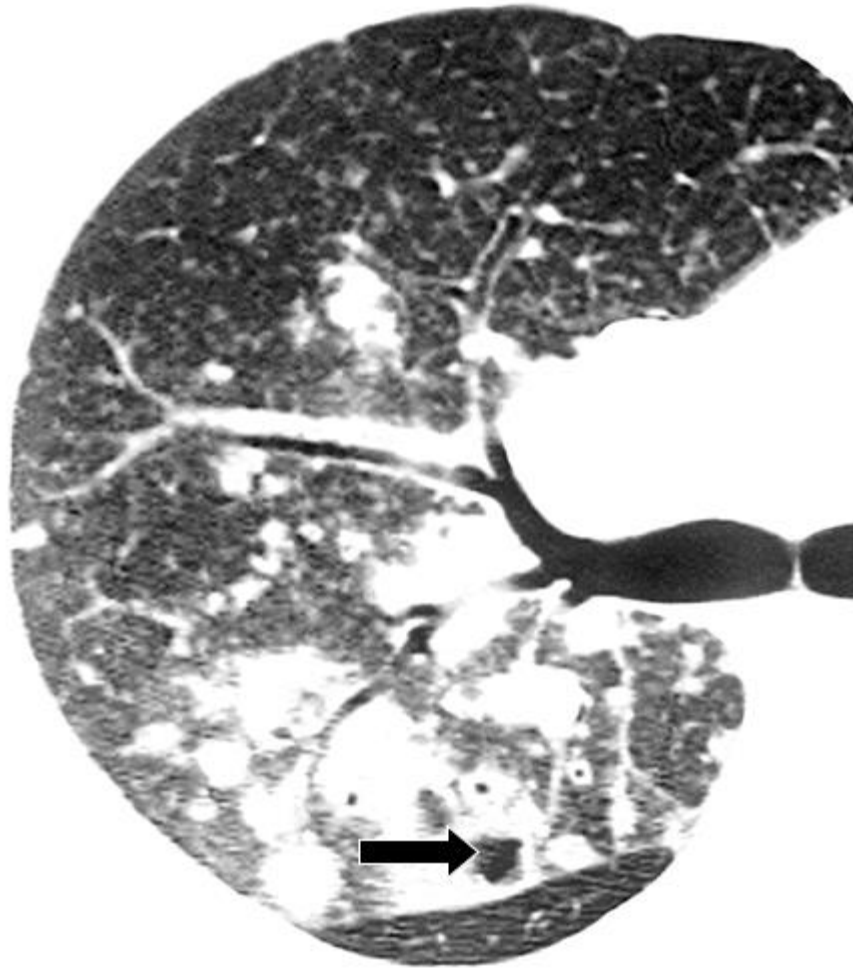
# VIH + vs VIH -



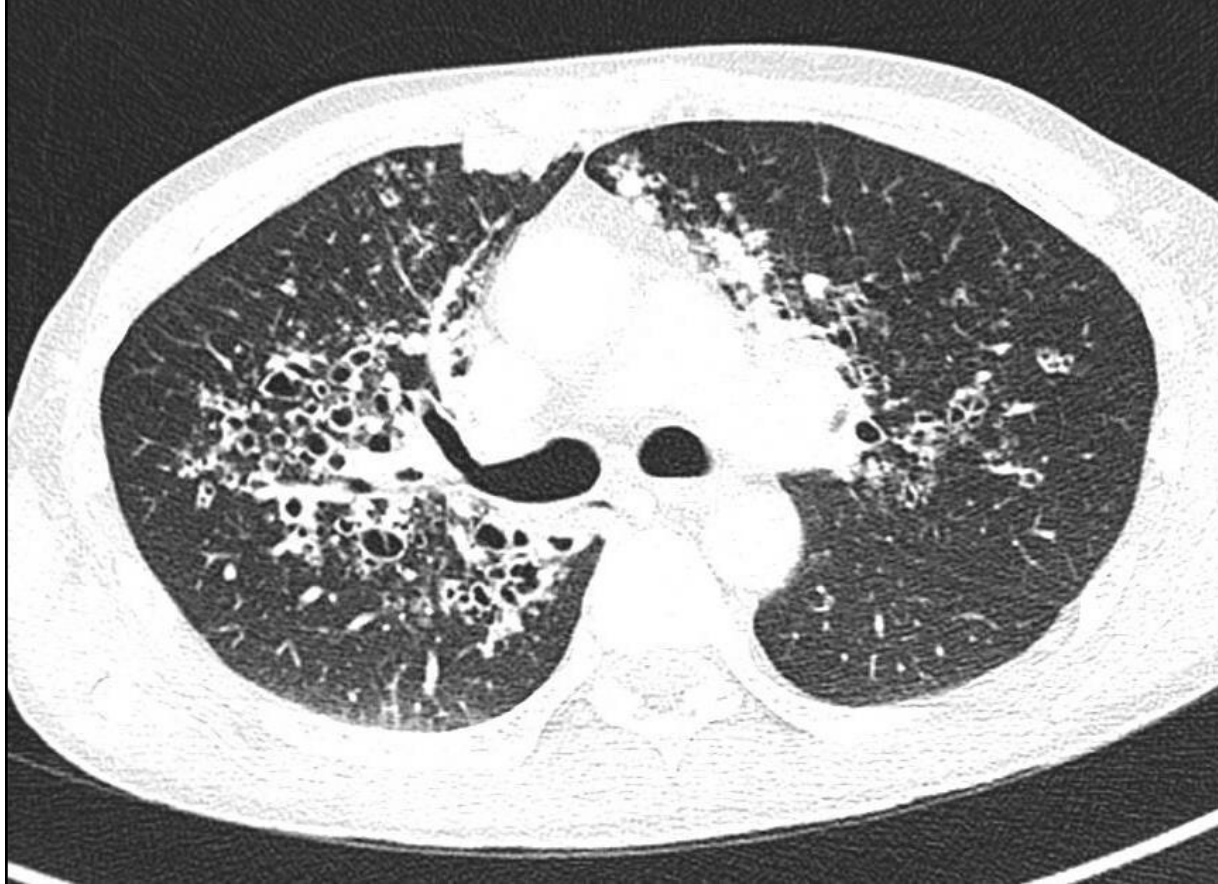
# Imagerie: les classiques



# Imagerie: les moins classiques



# Imagerie: les moins classiques



# Formes extrapulmonaires

Extrêmement rares

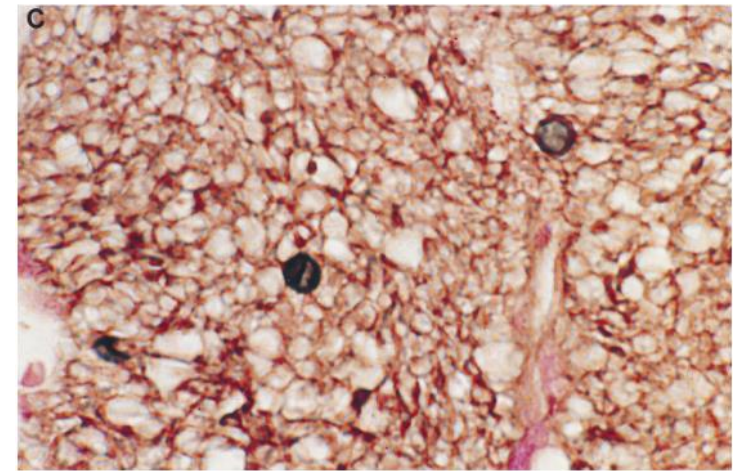
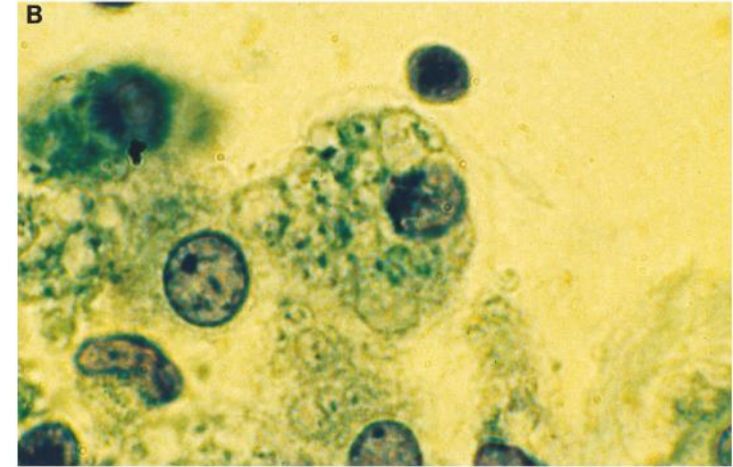
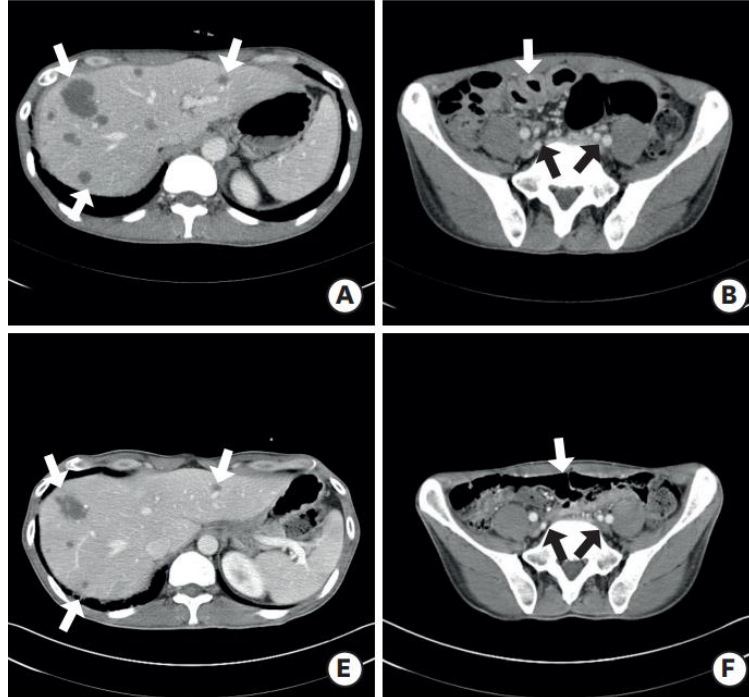
Surtout décrites chez VIH+

Pas nécessairement d'atteinte pulmonaire concomitante

Souvent cliniquement silencieuse

Sites très variés: hépatosplénique, surrénales, oreille, œil, ADP...

Diagnostic: anapath, confirmation PCR



# Diagnostic

## Visualisation directe

Colorations: MGG, methenamine, Calcofluor...

Immunofluorescence

## PCR

Nombreuses cibles & protocoles:  
mtSSU...

LAMP

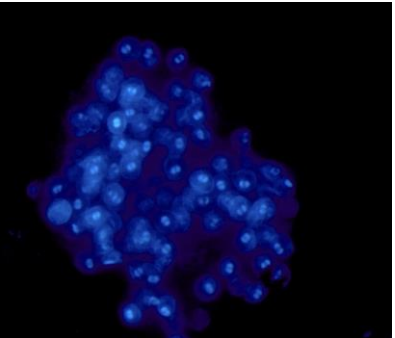
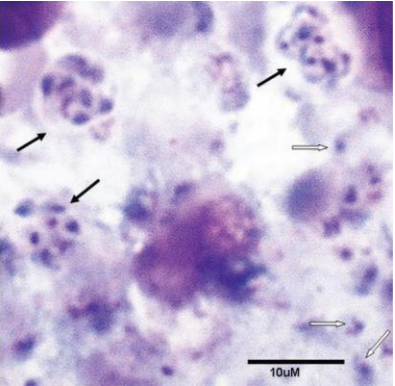
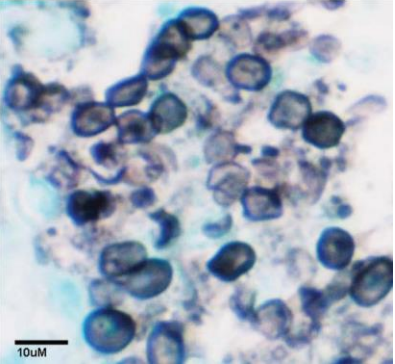
## Diagnostic indirect

Beta D Glucane

Sérologie: pas en  
pratique

# Diagnostic

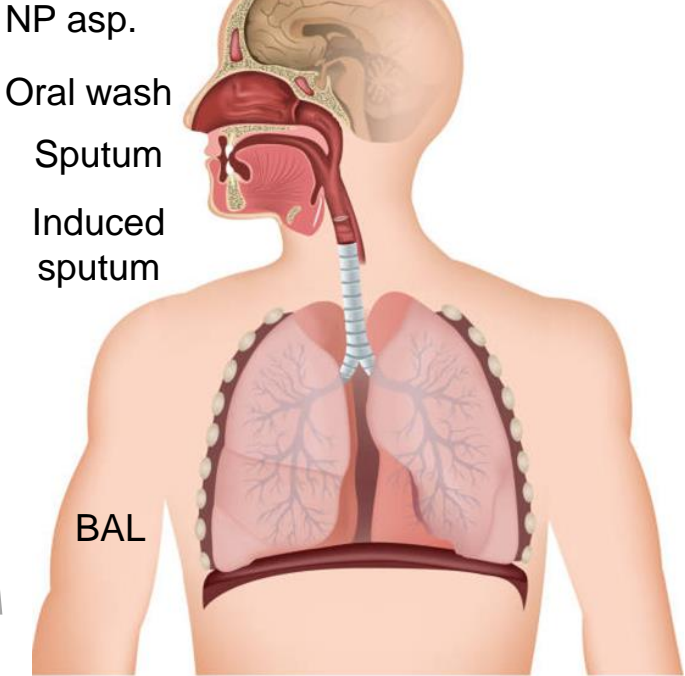
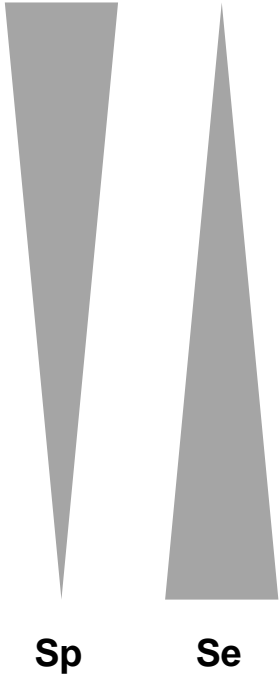
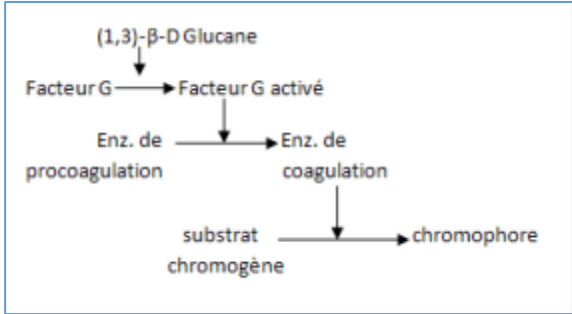
## Visualisation directe



## PCR



## Diagnostic indirect

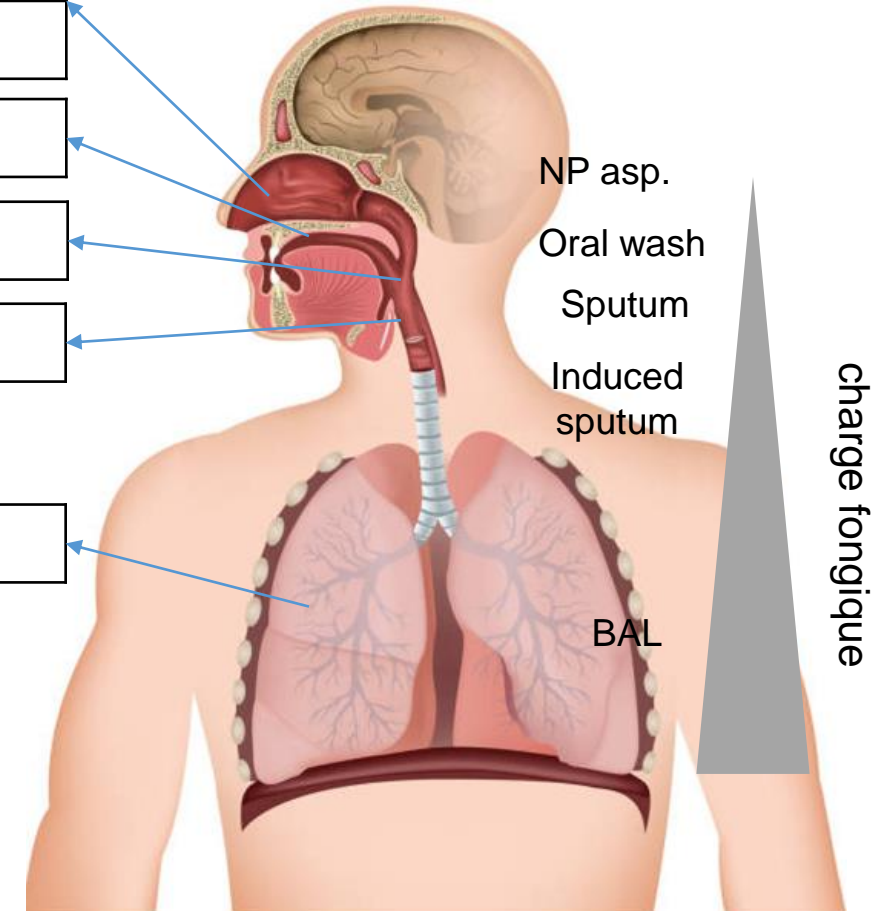


# Diagnostic

## Visualisation directe

## PCR

Sensibilité	Spécificité	Sensibilité	Spécificité
NA	NA	89%	98%
NA	NA	77%	94%
87-92% stain	92%	100% (n=1)	93%
50% stain-74% IF	99%	99%	96%
89-100%	97-100%	98%	91%

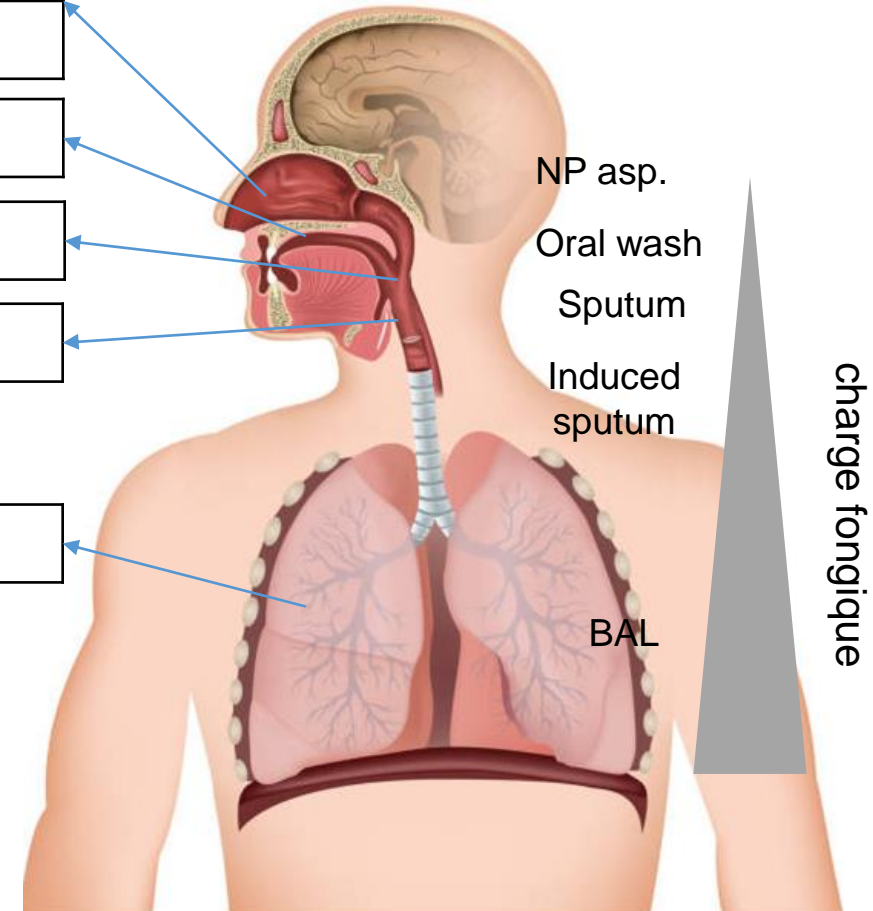


# Diagnostic chez VIH+

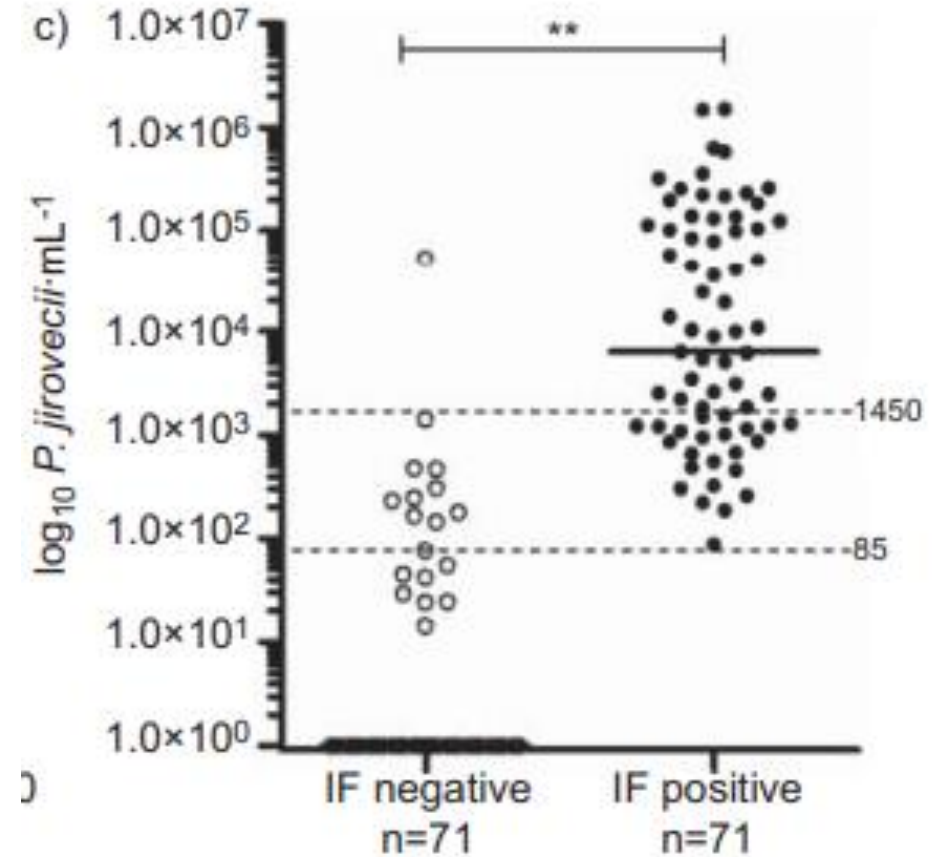
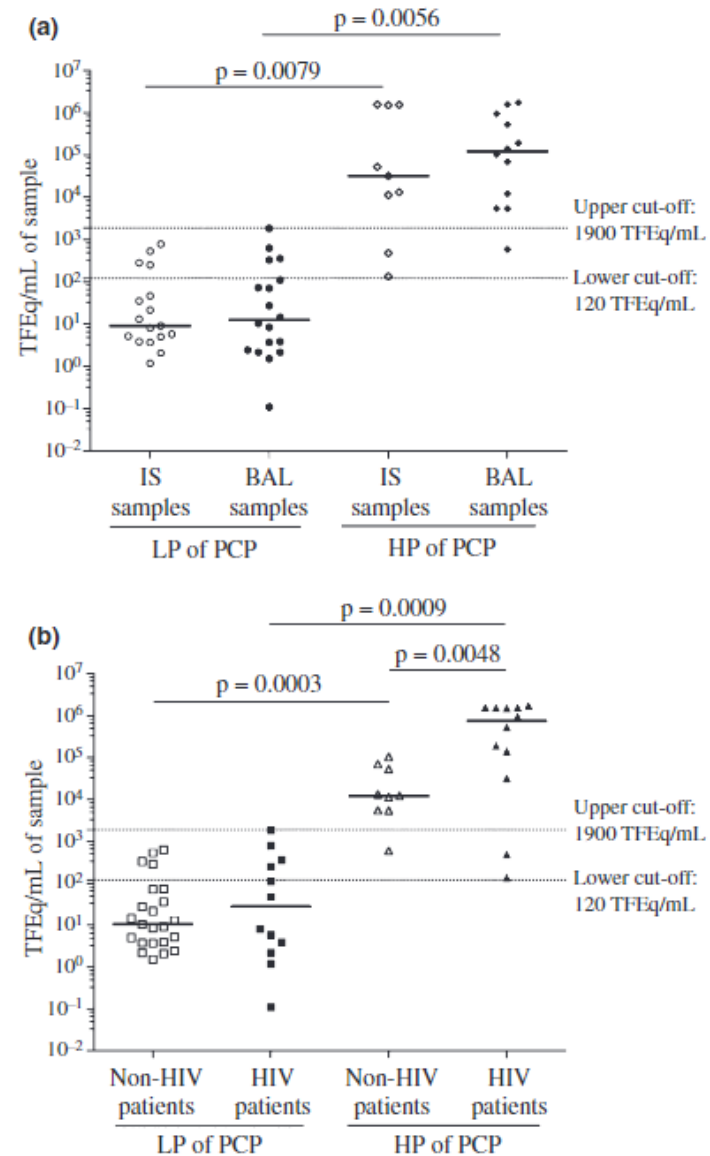
## Visualisation directe

## PCR

Sensibilité	Spécificité	Sensibilité	Spécificité
95%	100%	95%	
		74%	95%
43% stain-67% IF	96% stain-97% IF	99%	98%



# Diagnostic: PCR

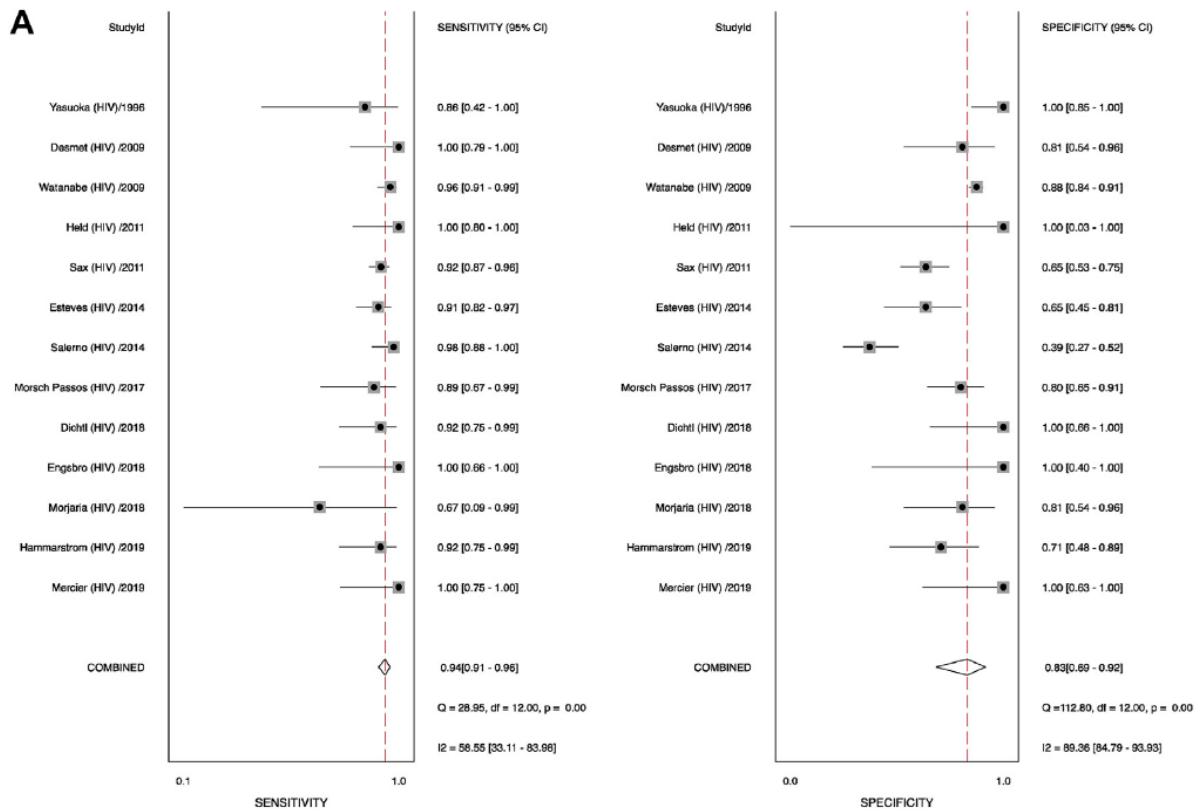


# Diagnostic: beta D glucane

**VIH+**

**VIH neg**

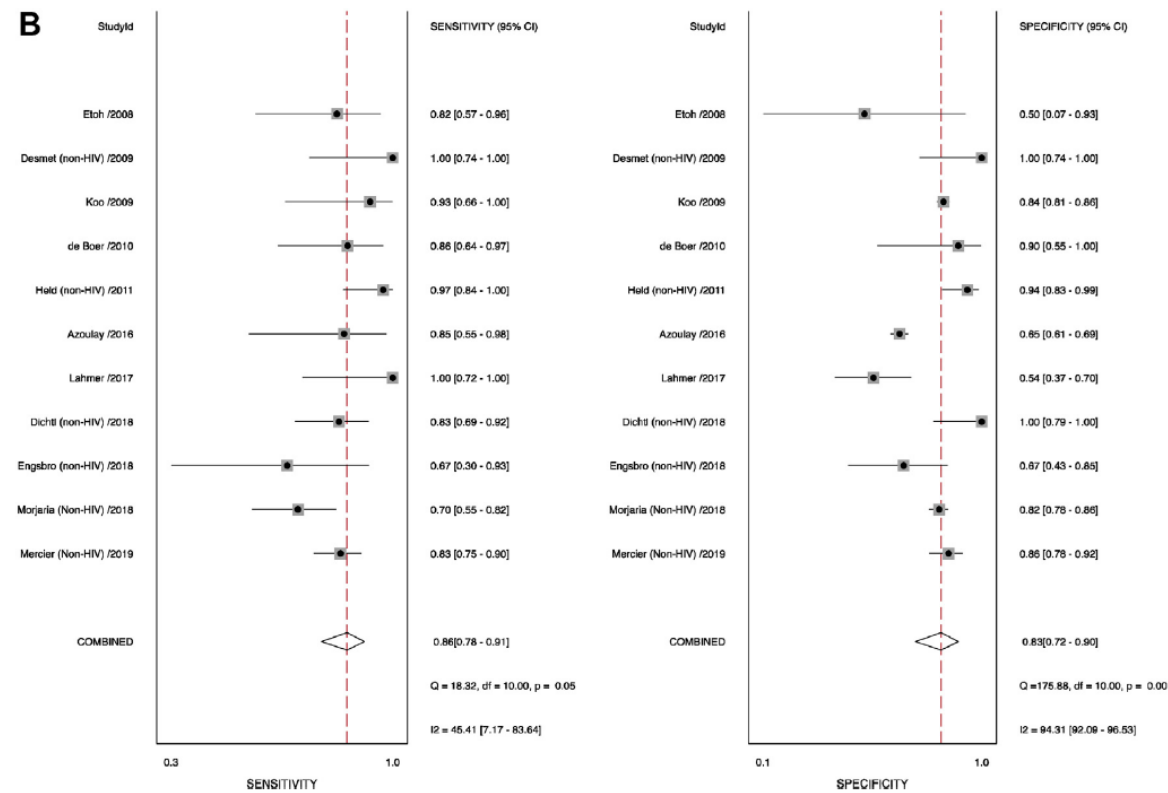
**A**



**Se 94%**

**Sp 83%**

**B**



**Se 86%**

**Sp 83%**

# Coinfections

328 patients with PcP after BAL examination

74 HIV-positive patients

254 HIV-negative patients

VIH +: 30%, VIH nég: 54%

<b>Viral</b>	125 (38.1)
Herpesviridae	94 <sup>a</sup> (28.7)
Cytomegalovirus	79 (24.1)
Herpes simplex virus type 1	25 (7.6)
Varicella zoster virus	1 (0.3)
Picornaviridae	22 <sup>b</sup> (6.7)
Rhinovirus	21 (6.4)
Enterovirus	2 (0.6)
Coronaviridae	
Coronavirus	8 (2.4)
Orthomyxoviridae	
Influenza virus	6 (1.8)
Paramyxoviridae	7 (2.1)
Parainfluenza virus	5 (1.5)
Respiratory syncytial virus	2 (0.6)
Adenoviridae	
Adenovirus	2 (0.6)
Pneumoviridae	
Metapneumovirus	1 (0.3)

<b>Bacterial</b>	76 (23.2)
Gram-negative bacteria	49 (14.9)
Nonfermenting	25 <sup>c</sup> (7.6)
<i>Pseudomonas</i> spp.	20 (6.1)
<i>Stenotrophomonas</i> spp.	5 (1.5)
<i>Achromobacter</i> spp.	1 (0.3)
Enterobacteriaceae	12 (3.7)
<i>Klebsiella</i> spp.	4 <sup>d</sup> (1.2)
<i>Escherichia coli</i>	3 (0.9)
<i>Serratia marcescens</i>	2 (0.6)
<i>Enterobacter aerogenes</i>	1 (0.3)
Untypable	2 (0.6)
Others	
<i>Haemophilus</i> spp.	7 (2.1)
<i>Moraxella catarrhalis</i>	3 (0.9)
<i>Bordetella bronchiseptica</i>	1 (0.3)
<i>Neisseria macacae</i>	1 (0.3)
Gram-positive bacteria	39 (11.9)
<i>Staphylococcus aureus</i>	20 <sup>e</sup> (6.1)
<i>Streptococcus</i> spp. (excl. pneumococcus)	15 (4.6)
<i>Enterococcus faecium</i>	2 (0.6)
<i>Streptococcus pneumoniae</i>	1 (0.3)
<i>Corynebacterium urealyticum</i>	1 (0.3)

<b>Mycobacteria</b>	6 (1.8)
<i>M. avium</i> complex	3 (0.9)
<i>M. genavense</i>	1 (0.3)
<i>M. kansasii</i>	1 (0.3)
<i>M. tuberculosis</i>	1 (0.3)
<b>Parasitic/fungal</b>	36 (11)
<i>Aspergillus</i> spp.	30 <sup>f</sup> (9.8)
<i>Cryptococcus neoformans</i>	4 (1.2)
<i>Toxoplasma gondii</i>	2 (0.6)

Co-existent opportunistic disease (% , 95 % CI)

- Overall	29.3 [25.4–33.6] (26 studies, <i>n</i> = 474)
- Tuberculosis	14.8 [11.8–18.5] (25 studies, <i>n</i> = 431)
- Bacterial pneumonia	8.7 [0.6–11.8] (22 studies, <i>n</i> = 445)
- Pulmonary cryptococcosis	1.4 [0.4–3.6] (17 studies, <i>n</i> = 283)
- Pulmonary Kaposi sarcoma	4.1 [2.4–6.6] (21 studies, <i>n</i> = 410)
- Pulmonary CMV	3.9 [1.4–8.2] (11 studies, <i>n</i> = 155)
- Pulmonary MAC	0.8 [0.1–2.8] (19 studies, <i>n</i> = 254)

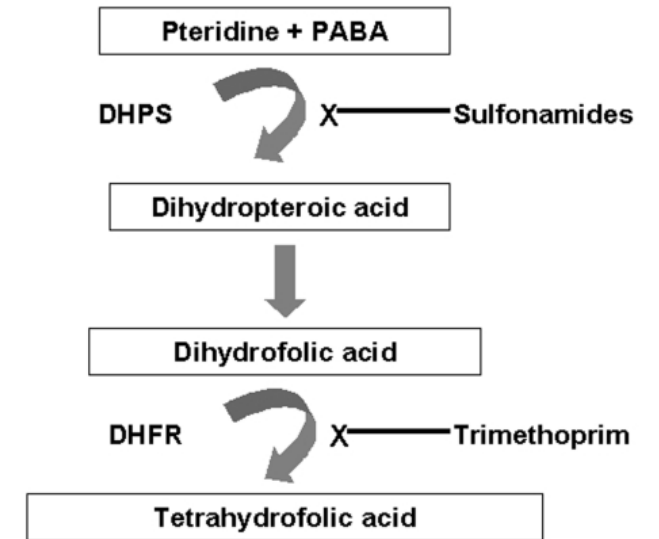
Case fatality rate (% , 95 % CI) 18.8 % [11.0–26.5] (12 studies, *n* = 334)

# Résistance au cotrimoxazole?

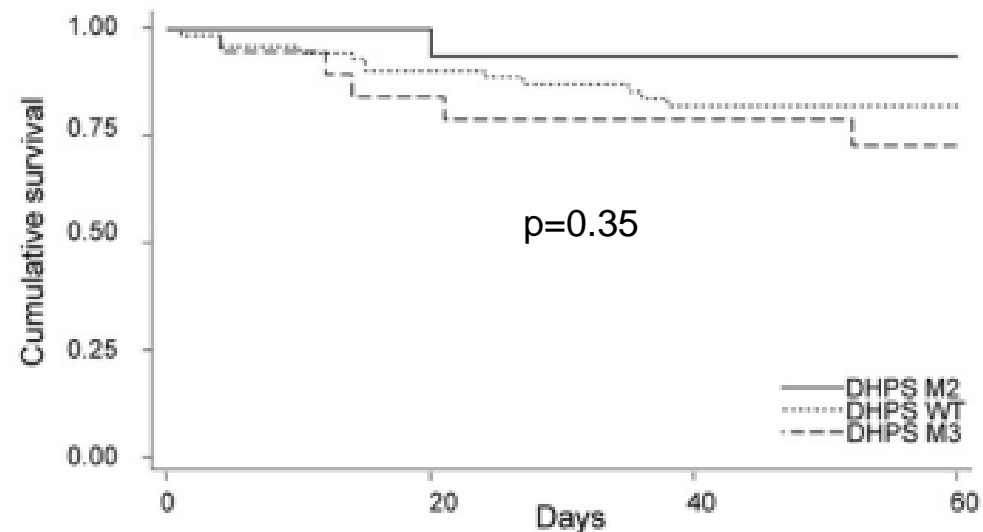
**Mécanismes:** mutations de DHFR ou DHPS (site actif)

Corrélié au degré d'exposition aux sulfamides

**Impact clinique** mal établi



Exposure	Relative risk	P
Sulfa or sulfone prophylaxis	2.5	.001
Duration of sulfa or sulfone prophylaxis		
Each month of prophylaxis	1.06	.010
>12 Months of prophylaxis	1.16	.003
Choice of sulfa or sulfone agent (dapsones vs. TMP/SMX)	0.98	.150
Dose of sulfa or sulfone agent	1.02	.191
Sex	0.95	.23
Race	1.11	.13
CD4 count <sup>a</sup>	1.01	.71
HIV viral load <sup>b</sup>	1.07	.62
Prior episode of PCP	0.99	.21
Outcome		
Sulfa or sulfone treatment failure	2.1	.01
Nonsulfa or nonsulfone treatment failure	1.003	.11
Survival	0.98	.23



# Critères diagnostiques EORTC 2019 pour les VIH-

Description	
Host factors	<ul style="list-style-type: none"><li>• Use of therapeutic doses of <math>\geq 0.3</math> mg/kg prednisone equivalent for <math>\geq 2</math> weeks in the past 60 days</li><li>• Low CD4+ lymphocyte counts (observed or expected; <math>&lt; 200</math> cells/mm<sup>3</sup>) induced by a medical condition, anticancer, anti-inflammatory, and immunosuppressive treatment, including but not limited to:<ul style="list-style-type: none"><li>- Primary immunodeficiencies with numeric/functional T-cell deficiency</li><li>- Acute leukemia, non-Hodgkin's lymphoma, solid tumors, allogeneic HSCT</li><li>- Solid-organ transplantation</li><li>- Autoimmune- and hyperinflammatory disorders, including treatment with agents that lead to functional T-cell deficiencies</li></ul></li></ul>
Clinical criteria	<ul style="list-style-type: none"><li>• Fever</li><li>• Respiratory symptoms including cough, dyspnea, or hypoxemia</li><li>• Bilateral or diffuse GGO on X-ray with interstitial infiltrates as the predominant feature; alveolar, alveolar-interstitial, and unilateral infiltrates are less frequent</li><li>• Extensive, mostly diffuse GGO on CT scans, which typically has an upper lobe and perihilar predominance, sometimes with peripheral sparing or a mosaic pattern; consolidations, small nodules, and unilateral infiltrates are less frequent</li></ul>
Microbiologic criteria	<ul style="list-style-type: none"><li>• Visualization of <i>P. jirovecii</i> by microscopy using conventional staining methods (Gomori methenamine silver, Toluidine Blue O, Giemsa, Calcofluor White) or immunofluorescence staining in tissue, BAL fluid, induced sputum, expectorated sputum, or oral wash</li><li>• Amplification of <i>P. jirovecii</i> DNA by quantitative real-time PCR in BAL fluid, induced sputum, or oral wash</li><li>• Detection of <math>\beta</math>-D-glucan in serum if another invasive fungal infection and a false-positive result can be ruled out</li></ul>

Proven PCP	<ul style="list-style-type: none"><li>• Clinical and radiologic criteria, plus:<ul style="list-style-type: none"><li>- Demonstration of <i>P. jirovecii</i> by microscopy using conventional or immunofluorescence staining in tissue or</li><li>- Demonstration of <i>P. jirovecii</i> by microscopy using conventional or immunofluorescence staining in respiratory specimens</li></ul></li></ul>
Probable PCP	<ul style="list-style-type: none"><li>• Appropriate host factors and clinical and radiologic criteria, plus:<ul style="list-style-type: none"><li>- Amplification of <i>P. jirovecii</i> DNA by quantitative real-time PCR in respiratory specimen or</li><li>- Detection of <math>\beta</math>-D-glucan in serum (alternative method; another IFD and a false-positive result should be ruled out)</li></ul></li></ul>

# Traitement: recommandations

## ECIL guidelines for treatment of *Pneumocystis jirovecii* pneumonia in non-HIV-infected haematology patients

Georg Maschmeyer<sup>1</sup>, Jannik Helweg-Larsen<sup>2</sup>, Livio Pagano<sup>3</sup>, Christine Robin<sup>4,5</sup>, Catherine Cordonnier<sup>4,5\*</sup> and Peter Schellongowski<sup>6,7</sup> on behalf of the 6th European Conference on Infections in Leukemia (ECIL-6†), a joint venture of The European Group for Blood and Marrow Transplantation (EBMT), The European Organization for Research and Treatment of Cancer (EORTC), the International Immunocompromised Host Society (ICHS) and The European LeukemiaNet (ELN)



SPECIAL ISSUE-TRANSPLANT INFECTIOUS DISEASES

*Pneumocystis jirovecii* in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice

Jay A. Fishman✉, Hayley Gans, on behalf of the AST Infectious Diseases Community of Practice

**Essais contrôlés publiés (traitement):**  
16 essais  
Seulement 2 chez VIH neg (1978 et 1984)

# Quel traitement antifongique?

1<sup>ère</sup> intention: **cotrimoxazole** 4 amp/8h IV, éventuellement oral si non grave

## Seconde intention

Primaquine 30 mg/j  
+ Clinda 600 mg/8h

Pentamidine IV  
4 mg/kg/j

Atovaquone po  
750 mg/12h

Cotrimoxazole  
+ caspofungine  
70/50 mg/j

Dapsone  
+ caspofungine  
70/50 mg/j

Primaquine: hémolyse si  
déficit G6PD

Clinda: *C. difficile*,  
hépatites

Pancréatites  
Tr hydroélectrolytiques  
Hypoglycémie  
IRA

Inconfort digestif  
(A prendre avec un repas)  
Toxidermie

Cytopénies  
Cytolyse  
IRA  
Hyperkaliémie  
Toxidermie

Hémolyse (G6PD)  
Méthémoglobinémie

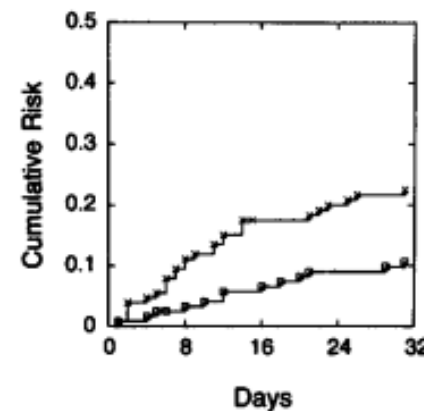
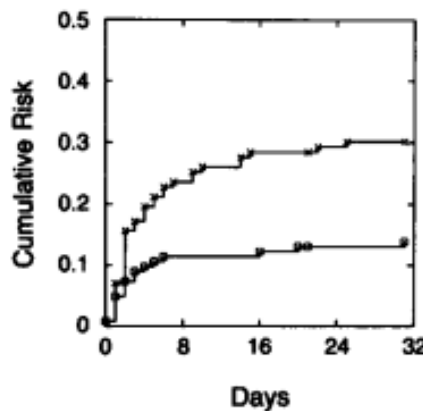
(Dapsone + TMP)

# Corticothérapie adjuvante: chez VIH+

9 essais contrôlés

Si PaO<sub>2</sub> < 70 mmHg en AA

END POINT	CORTICOSTEROID (N = 12)	PLACEBO (N = 11)	P VALUE*
	no. (%)		
Survival to discharge	9 (75)	2 (18)	<0.008
Respiratory failure	3 (25)	9 (82)	<0.008
Completion of antibiotic therapy	10 (83)	4 (36)	<0.024



N=333

**Annals of Internal Medicine** Search Journal

LATEST ISSUES IN THE CLINIC JOURNAL CLUB MULTIMEDIA CME/MOC AUTHORS/SUBMIT

Articles | 1 July 1990

**Corticosteroids Prevent Early Deterioration in Patients with Moderately Severe *Pneumocystis carinii* Pneumonia and the Acquired Immunodeficiency Syndrome (AIDS)**

Julio S.G. Montaner, MD, Lindsay M. Lawson, MD, Nirvair Levitt, MD, Allan Belzberg, MD, Martin T. Schechter, MD, PhD, John Ruedy, MD [View fewer authors](#)

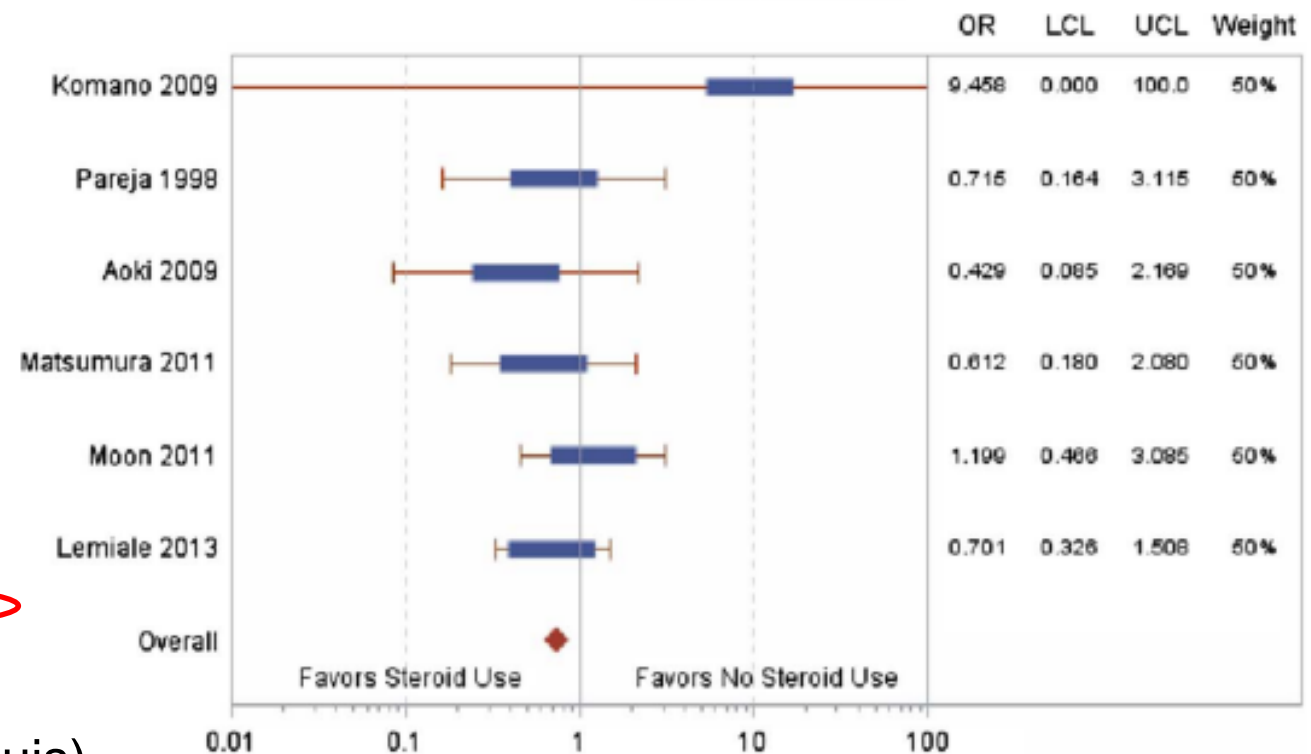
# Corticothérapie adjuvante: chez VIH neg

## A Systematic Review and Meta-Analysis of the Data Behind Current Recommendations for Corticosteroids in Non-HIV-Related PCP: Knowing When You Are on Shaky Foundations

Patil Injean, BA,<sup>1</sup> Samantha J. Eells, MPH,<sup>2,3</sup> Hoover Wu, BA,<sup>4</sup> Imani McElroy, BA,<sup>4</sup> Aric L. Gregson, MD,<sup>4</sup> and James A. McKinnell, MD<sup>3,4,5</sup>

Variables	OR [CI95%]	p
Age (> or < 65 years)	2.37 [1.35–4.18]	0.003
Gender (female)	0.92 [0.52–1.64]	0.77
Underlying conditions		
Solid tumor and IS* treatment	1	
Solid organ transplantation	0.18 [0.07–0.44]	0.0002
Hematological malignancy or chronic lymphoid leukemia	0.56 [0.29–1.08]	0.083
Allogeneic stem cell transplantation	2.45 [0.77–7.83]	0.13
Prophylaxis		
None	1	
Continuous	0.25 [0.09–0.70]	0.009
Duration of respiratory symptoms		
<7 days	1	
7–21 days	0.58 [0.27–1.25]	0.17
>21 days	0.74 [0.26–2.13]	0.58
T>38°C	1.47 [0.59–3.64]	0.40
Cough	0.54 [0.27–1.09]	0.083
Dyspnea	1.32 [0.59–2.93]	0.49
SaO2 at diagnosis	0.96 [0.93–1.00]	0.029
Oxygen flow at diagnostic	1.15 [1.08–1.22]	<0.0001
Shock at admission	4.95 [2.03–12.1]	0.0005
Hospital acquired or coinfection	1.72 [0.95–3.13]	0.075
Adjuvant Steroid therapy	1.58 [0.86–2.93]	0.14

Impact of Adjunct Corticosteroids on Survival of NH-PCP by Study  
Odds Ratio and 95% CL



PHRC national en cours: **PIC** (V. Lemiale, St Louis)

# Corticoïdes adjuvants et SOT


## American Journal of TRANSPLANTATION

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ORIGINAL ARTICLE · Volume 24, Issue 4, P653-668, April 2024

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### Adjunctive glucocorticoid therapy for *Pneumocystis jirovecii* pneumonia in solid organ transplant recipients: A multicenter cohort, 2015-2020

[Seyed M. Hosseini-Moghaddam](#)<sup>1</sup> · [Sagar Kothari](#)<sup>1</sup> · [Atul Humar](#)<sup>1</sup> · ... · [Kathleen Doss](#)<sup>27</sup> · [Robert M. Rakita](#)<sup>27</sup> · [Jay A. Fishman](#)<sup>18</sup> 

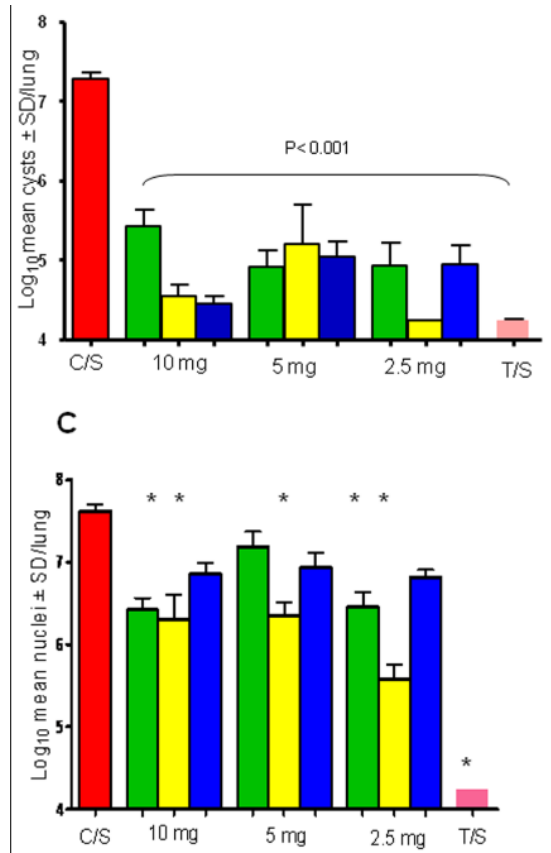
[35.1%];  $P = .78$ ). We did not observe significant associations between AGT and ICU admission or death in SOTRs with PJP. Our findings should prompt a reevaluation of routine AGT administration in posttransplant PJP treatment and highlight the need for interventional studies.

# Echinocandines

Actives sur kystes seulement

Environ 50 case reports/séries: rarement en monothérapie, efficacité 60 à 100%

PHRC National: CaspoNEB: caspo inhalée + ttt conventionnel (G. Desoubeaux, Tours)



# Prophylaxie

**VIH:** tant que CD4 < 200 ou < 100 et CV < 20 (rapport Morlat, EACS)

**SOT:** poumon & grêle à vie, autres 6 à 12 mois Fishman J *et al.* Clin Transplant 2019

## Hématologie:

Adults		
Indication for prophylaxis	disease/condition	duration of prophylaxis
Main (A)	ALL allogeneic HSCT  alemtuzumab fludarabine/cyclophosphamide/ rituximab steroids (>20 mg/day prednisone for 4 weeks)	from induction to end of maintenance from engraftment to ≥6 months and as long as immunosuppression is ongoing >6 months after completion of treatment ≥6 months after completion of treatment
Optional (B)	Lymphoma treated with R-CHOP14 or escalated BEACOPP nucleoside analogues (fludarabine, cladribine, mycophenolate mofetil) radiotherapy for brain tumours/ metastasis + high-dose steroids	

**NB:** CAR-T cells: de la lymphodéplétion à 12 M post ttt

Franciane P *et al.* Bull Cancer 2021

Lewalle P *et al.* Bull Cancer 2021

Maertens J *et al.* JAC 2016

# Prophylaxie

## Pathologies autoimmunes:

**Vascularites à ANCA:** oui, au moins 6 mois après induction (EULAR, ACR, French Vasculitis Study Group)

Attention MTX et Bactrim

**MICI:** rare, probablement pas

**Lupus, DM/PM, Sclérodemie: ?**

Disease	Prophylaxis?	To whom?	Conditional factors <sup>b</sup>	NNT [5••]
GPA	Yes	All patients undergoing induction therapy		32
SLE	Conditional <sup>a</sup>	High dose GC	Lymphopenia Low CD4+ count Immunosuppressive regimen	110
PM/DM	Conditional <sup>a</sup>	High-dose GC	Lymphopenia Low CD4+ count More severe disease	73
PAN, AAV	Conditional <sup>a</sup>	During induction therapy and/or high dose GC	Lymphopenia Low CD4+ count	110
RA	No	–	–	1099
GCA	No	–	–	–
Scleroderma	No	–	–	110

Wolfe R *et al.* Curr Rheumatol Rep 2017

Yates *et al.* ARD 2016

Terrier B *et al.* Presse Med 2020

# Prophylaxie: options

	drug grading	dose
First-line choice		
trimethoprim/sulfamethoxazole; all other alternatives are inferior ( <b>A-II</b> )	<b>A-II</b>	one single-strength (80/400 mg) tablet/day or one double-strength tablet (160/800 mg)/day or thrice a week: <b>B-II</b>
Second-line choice <sup>a</sup>		
dapsone	<b>A-II</b>	50 mg × 2/day: <b>B-II</b>
atovaquone	<b>B-II</b>	1500 mg/day: <b>B-II</b>
pentamidine aerosols	<b>A-II</b>	300 mg once/month: <b>B-II</b>
pentamidine intravenously	no data	—

Characteristic	Pentamidine, 300 mg	Dapsone, 100 mg	Atovaquone, 1500 mg
Route of administration	inhalation (intravenous)	oral	oral solution with fatty meal
Frequency of administration	monthly	daily	daily
During neutropenia/pre-engraftment	yes	yes	yes
Special equipment or trained personnel needed	yes	no	no
Anti- <i>Toxoplasma</i> activity <sup>a</sup>	no	yes, if combined with pyrimethamine	uncertain <sup>b</sup>
Antibacterial activity	no	no	no
Use in glucose-6-phosphate dehydrogenase deficiency	yes	no	yes
Particular toxicity	respiratory	haemolytic anaemia, methaemoglobinaemia	gastrointestinal
Cost	low	low	high

# Conclusions

Transmission inter humaine

Diagnostic: le plus dur est de ne pas oublier d'y penser!

PCR dans le LBA: excellente VPN

Interpréter soigneusement une PCR positive

Connaître les limites du BetaD glucane

Corticoïdes adjuvants: données en attente pour les VIH négatifs

La prophylaxie bien prise rend le diagnostic improbable

Merci!

# Score prédictif en réanimation

Variables	Odds Ratio (95% CI)	P Value	Score Points
Age		<0.0001	
<50 yr	—		0
50–70 yr	0.51 (0.33–0.79)		–1.5
>70 yr	0.32 (0.17–0.61)		–2.5
Lymphoproliferative disease	2.79 (1.86–4.19)	<0.0001	+2
No prophylaxis	1.50 (0.95–2.37)	0.08	+1
Days between respiratory symptom onset and ICU admission		<0.0001	
<3 d	—		0
3–5 d	4.35 (2.53–7.49)		+3
>5 d	4.98 (3.12–7.92)		+3
Shock at ICU admission	0.47 (0.29–0.75)	<0.0001	–1.5
Chest X-ray: not alveolar	3.31 (1.55–7.06)	<0.0001	+2.5
Pleural effusion	0.38 (0.14–1.01)	0.05	–2