

Infections fongiques émergentes, la réanimation est-elle concernée?

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Liens d'intérêts

- Aucun pour cette présentation
- Rémunération :
 - MSD, PFIZER, GILEAD, BIOMERIEUX, BD, ADVANZ-Pharma
- Invitation congrès : MSD, PFIZER, ADVANZ-Pharma
- Participation à Board: Pfizer

Comment envisager les émergences ?

- Emergence d'espèces résistantes aux anti fongiques
 - Naturellement résistantes
 - *Candida krusei* ; *Candida auris*
 - Ayant acquis des mécanismes de résistances
- Augmentation des infections et épidémies à champignons rares
 - Infections à mucormycoses
 - Infections à autres champignons filamenteux
- Complications liées aux infections virales

Quelles seraient les hypothèses ?

- 2 phénomènes complémentaires
 - Augmentation et survie des patients immunodéprimés
 - Augmentation de l'exposition au réservoir
 - Transplantation d'organe
 - Immunodépression
 - Augmentation de la consommation des antifongiques
 - Monde humain
 - Environnement

Infections fongiques et émergence :

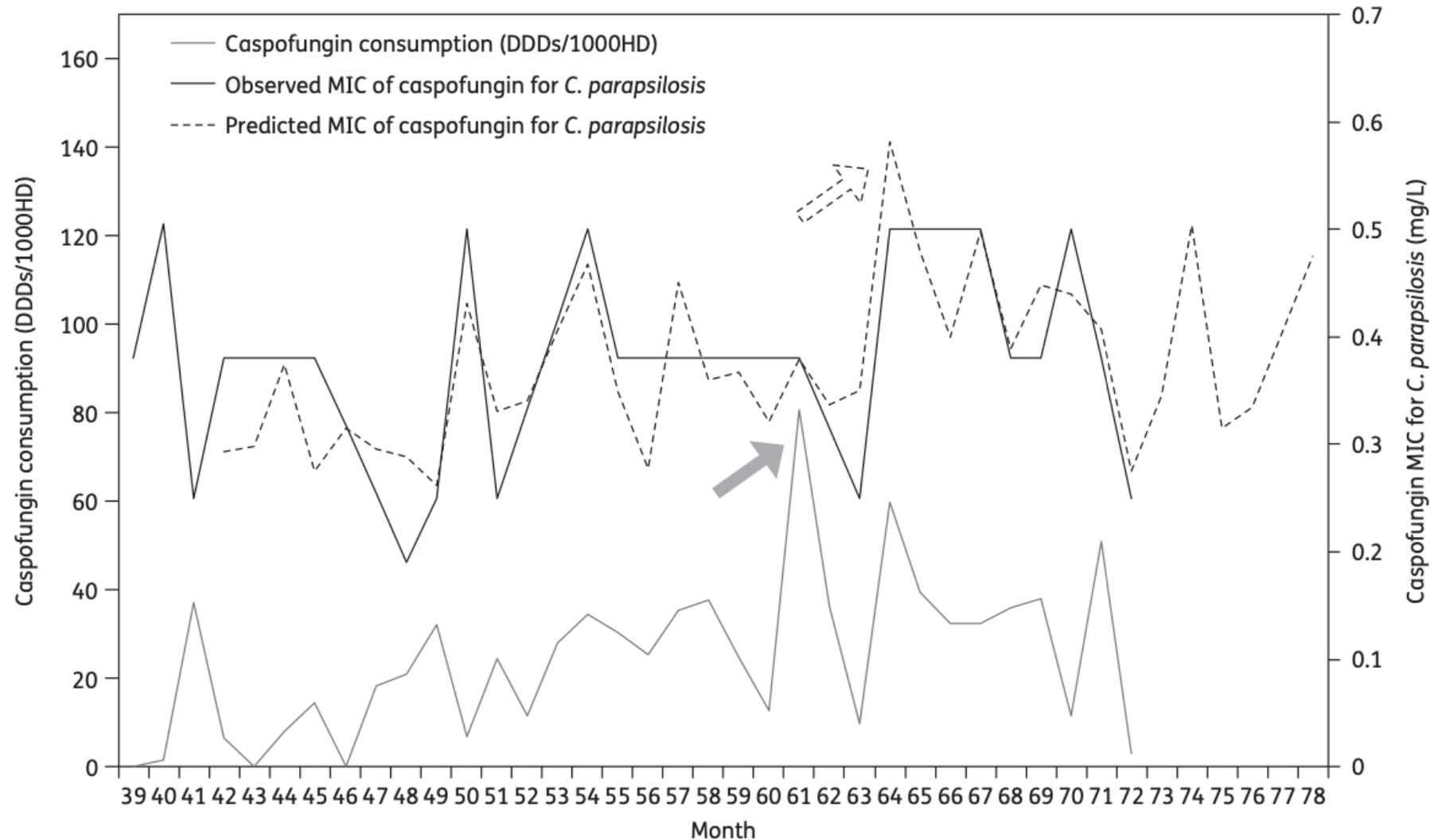
Poids de la prescription des anti fongiques

Table 1. Overall antifungal drug use in mean defined daily doses per 1000 hospital days: DDDs/1000HD (standard deviation) from 2004 to 2009

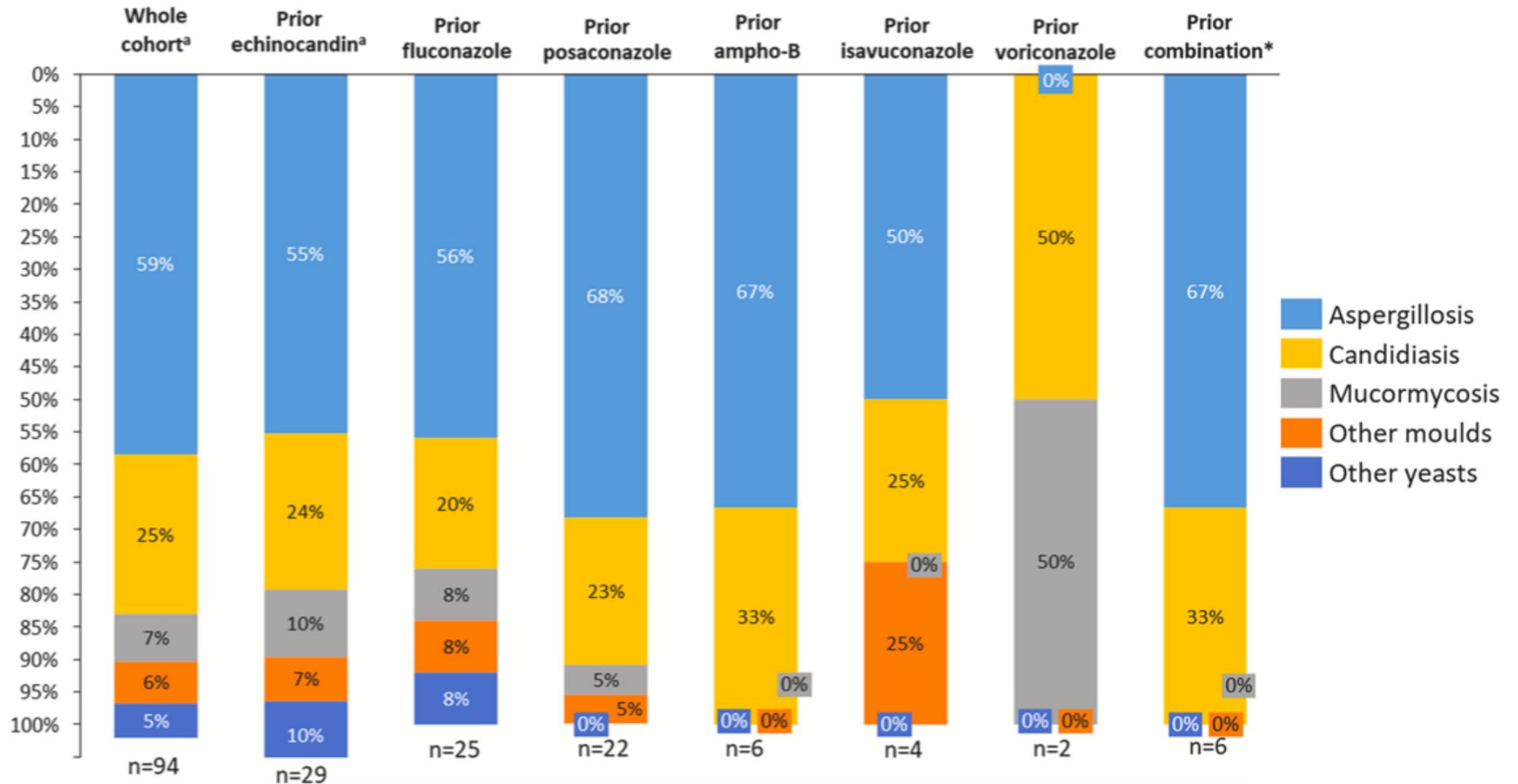
Drug	Drug use [DDDs/1000HD (SD)]						P value ^a
	2004	2005	2006	2007	2008	2009	
Amphotericin B ^b	45.9 (47.1)	35.2 (26.3)	23.8 (22.4)	30.4 (28.4)	53.4 (50.5)	45.3 (33.0)	0.5
Fluconazole	34.0 (23.5)	33.5 (30.2)	25.5 (14.7)	24.2 (18.1)	13.1 (11.9)	17.9 (15.9)	<0.0001
Caspofungin	17.9 (19.3)	35.7 (35.7)	46.7 (31.4)	22.9 (25.7)	56.2 (25.5)	69.9 (40.1)	<0.0001
Voriconazole	14.8 (34.8)	20.9 (17.9)	26.2 (37.7)	14.1 (22.5)	10.2 (19.6)	37.5 (21.2)	0.22

Organism	2004	2005	2006	2007	2008	2009	Total	P value ^a
<i>C. albicans</i>	100 (57.5)	147 (54.0)	144 (50.9)	136 (49.5)	126 (50.2)	141 (55.1)	794 (52.5)	0.57
<i>C. glabrata</i>	26 (14.9)	57 (20.9)	56 (19.8)	42 (15.3)	35 (13.9)	35 (13.7)	251 (16.6)	0.16
<i>C. parapsilosis</i>	10 (5.7)	10 (3.7)	16 (5.6)	24 (8.7)	22 (8.8)	32 (12.5)	114 (7.5)	0.0005
<i>C. tropicalis</i>	13 (7.8)	16 (5.9)	23 (8.1)	22 (8)	15 (6.0)	22 (8.6)	111 (7.3)	0.41
<i>C. kefyr</i>	10 (5.7)	14 (5.1)	15 (5.3)	14 (5.1)	20 (8.0)	9 (3.5)	82 (5.4)	0.16
<i>C. krusei</i>	6 (3.4)	13 (4.8)	14 (4.9)	13 (4.7)	19 (7.7)	5 (1.9)	70 (4.6)	0.98
Other <i>Candida</i> spp.	9 (5)	15 (5.6)	15 (5.4)	24 (8.7)	14 (5.4)	12 (4.7)	89 (6.1)	
All <i>Candida</i> spp.	174 (100)	272 (100)	283 (100)	275 (100)	251 (100)	256 (100)	1511 (100)	

Infections fongiques et émergence : Poids de la prescription des anti fongiques



Antifongiques et Résistances



Puerta-Alcalde P, Monzó-Gallo P, Aguilar-Guisado M, Ramos JC, Laporte-Amargós J, Machado M, Martin-Davila P, Franch-Sarto M, Sánchez-Romero I, Badiola J, Gómez L, Ruiz-Camps I, Yáñez L, Vázquez L, Chumbita M, Marco F, Soriano A, González P, Fernández-Cruz A, Batlle M, Fortún J, Guinea J, Gudiol C, García J, Ruiz Pérez de Pipaón M, Alastruey-Izquierdo A, Garcia-Vidal C. Breakthrough invasive fungal infection among patients with haematologic malignancies: A national, prospective, and multicentre study. *J Infect.* 2023 Jul;87(1):46-53.

Aspergillus et résistance

2288 souches environnementales

20% *Aspergillus*

1,3% Azoles-R

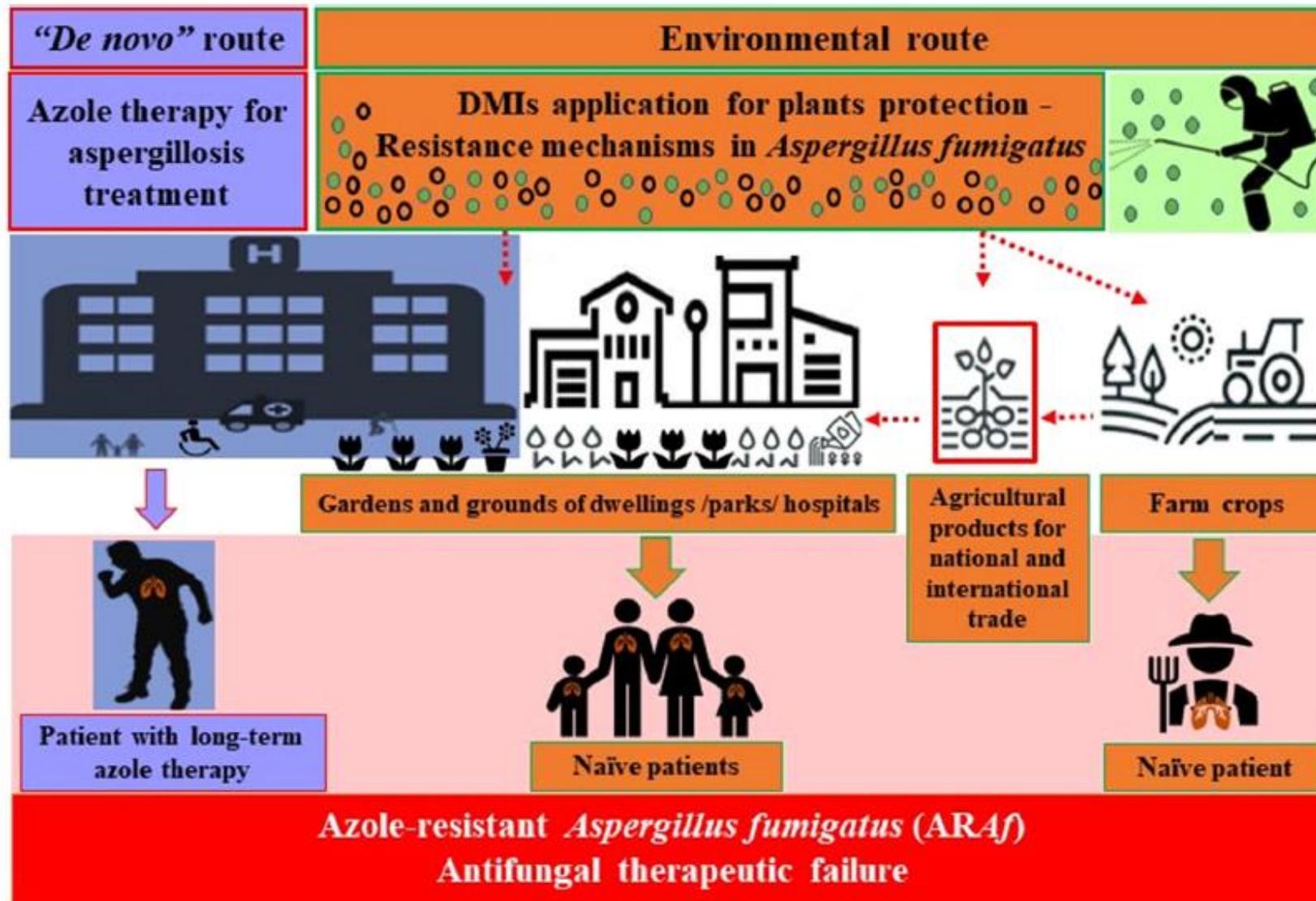
392 souches cliniques

3,3% Azoles-R

Table 1. MICs determined using the EUCAST microdilution method (E.DEF 9.3) and mutations in the *cyp51A* gene using the agar screening method

Isolate	City code	Sample type	Age (years)	MIC (mg/L) - EUCAST E.DEF 9.3			<i>cyp51A</i> mutation
				itraconazole	voriconazole	posaconazole	
ÇK1	34	hospital environment	-	4	4	2	none
CRK1	34	hospital environment	-	4	4	2	none
CRK2	34	hospital environment	-	4	4	2	none
011KS06SN-B1	06	agricultural soil	-	>8	4	0.5	none
011KS06SN-B2	06	agricultural soil	-	>8	4	0.5	none
267MT22MR/B	22	agricultural soil	-	4	4	2	none
60986	16	sputum	45	>8	>8	2	TR34/L98H
61568	16	sputum	63	>8	>8	2	TR34/L98H
62946	16	bronchoalveolar lavage fluid	81	>8	>8	2	TR34/L98H
63413	16	sputum	74	>8	>8	2	TR34/L98H
63653	16	tracheal aspirate	67	>8	>8	2	TR34/L98H
64955	16	bronchoalveolar lavage fluid	80	>8	>8	2	TR34/L98H
2455	06	pleural fluid		>8	>8	2	TR34/L98H
457	06	pus		>8	>8	2	TR34/L98H
MY	27	bronchoalveolar lavage fluid		2	2	0.5	TR34/L98H
RT1	34	sputum	75	4	4	0.5	none
RT2	34	sputum	75	4	4	0.5	none
11b	07	sputum	18	4	4	2	none
13b	07	sputum	54	>8	4	2	none

Aspergillus et Résistance



Des agents pathogènes de l'environnement !!!

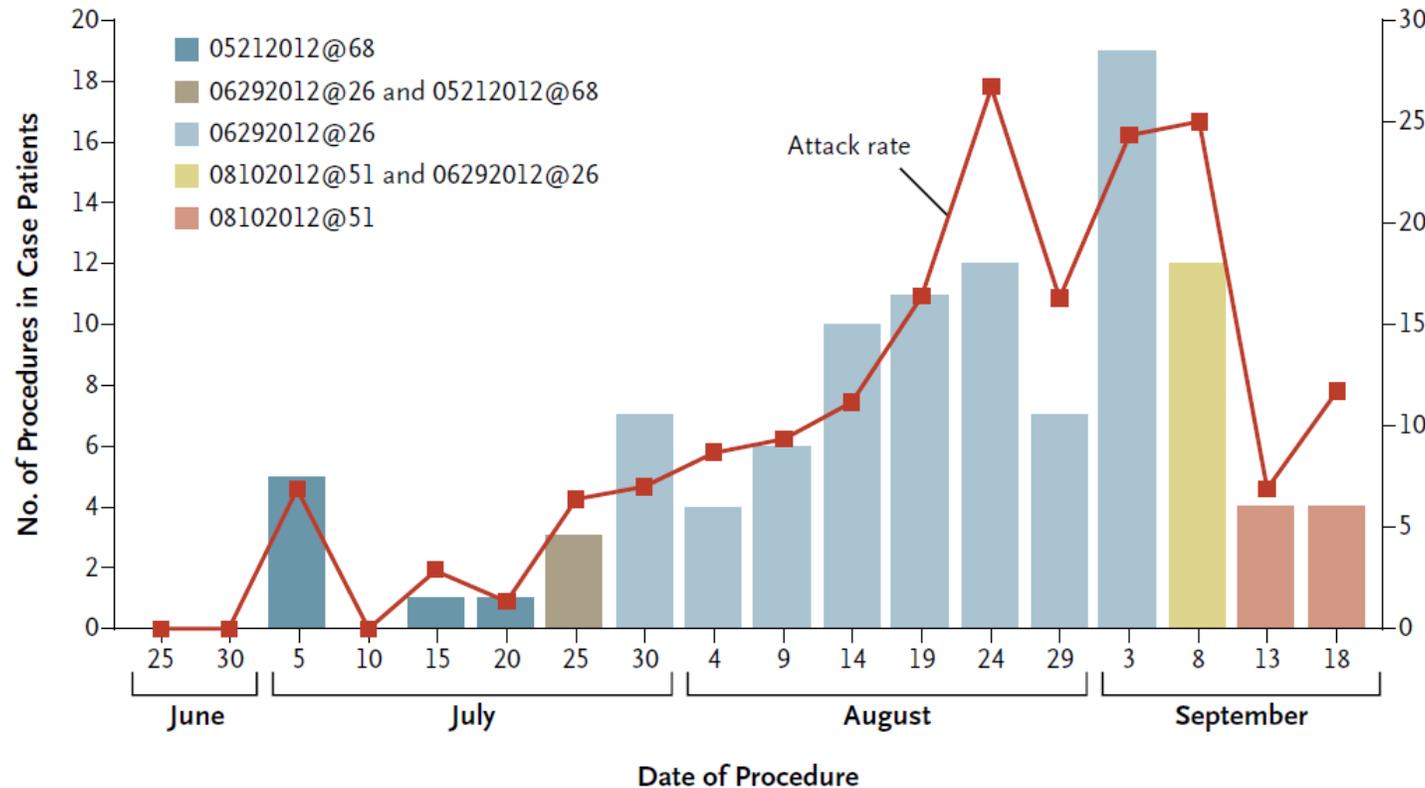
Table 1. Published Outbreaks of Healthcare-Associated Mucormycosis

Reference	No. of Cases	Origin of Contamination	Microorganism	Location
[103]	17	Elastoplast	<i>Rhizopus microsporus</i> (8 of 17)	Skin
[104]	5	Elastoplast	<i>Lichtheimia corymbifera</i>	Skin
[72]	5	Wooden tongue depressors	<i>R. microsporus</i>	Digestive tract
[105]	4	Wooden tongue depressors	<i>R. microsporus</i>	Skin
[79]	2	Building construction	<i>Mucor indicus</i> (1 of 2)	Lungs
[78]	3	Building construction	<i>Cunninghamella bertholletiae</i>	Lungs
[96]	2	Ostomy bags	<i>Rhizopus</i> species	Skin
[60]	2	Water circuitry damage	<i>Rhizomucor pusillus</i> (1 of 2)	Rhinocerebral dissemination

Table 3. Various Food Items Contaminated With Mucorales

Foodstuffs Known to Contain Mucorales [2]	Foodstuffs Containing Mucorales Found in Hematological Unit [147]
Barley	
Sorghum	
Wheat	
Corn	
Oat	
Rice	Regular tea
Onions	Biscuits
Cotton	Freeze-dried soup
Groundnuts	Pepper
Sweet potatoes	
Pecans	
Brazil nuts	
Oranges	
Honey	
Tomatoes	

Infections fongiques et contamination de flacons de methylprednisolone



A total of 22 patients had laboratory confirmation of *Exserohilum rostratum* infection (21 patients) or *Aspergillus fumigatus* infection (1 patient)

Figure 1. Number of Epidural and Paraspinal Glucocorticoid Injections and Attack Rate.

Shown are the number of epidural and paraspinal glucocorticoid injection procedures performed in case patients, as well as the attack rates among persons who received methylprednisolone acetate from the implicated lots during these procedures. Data are shown according to 5-day time periods.

Comment cela se traduit-il en pratique ?

- Nombreuses descriptions d'épidémies
- Agents pathogènes retrouvés dans l'environnement
- Populations/réservoirs multiples et hétérogènes

Médiastinites fongiques

Case Report

10 cas décrits

Aspergillus mediastinitis after cardiac surgery

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Dominique Vodovar^{a,b}, Issam Ben Ayed^{a,b}, Lauria
Marie-Line Hillion^{a,c}, Françoise Botterel^{a,d}, Gilles

European Journal of Cardio-Thoracic Surgery 61 (2022) 523–530
doi:10.1093/ejcts/ezab437 Advance Access publication 18 October 2021

40 cas décrits

Cite this article as: Moyon Q, Lebreton G, Huang F, Demondion P, Desnos C, Chommeloux J *et al.* Characteristics and outcomes of patients with postoperative *Candida* versus bacterial mediastinitis: a case-matched comparative study. *Eur J Cardiothorac Surg* 2022;61:523–30.

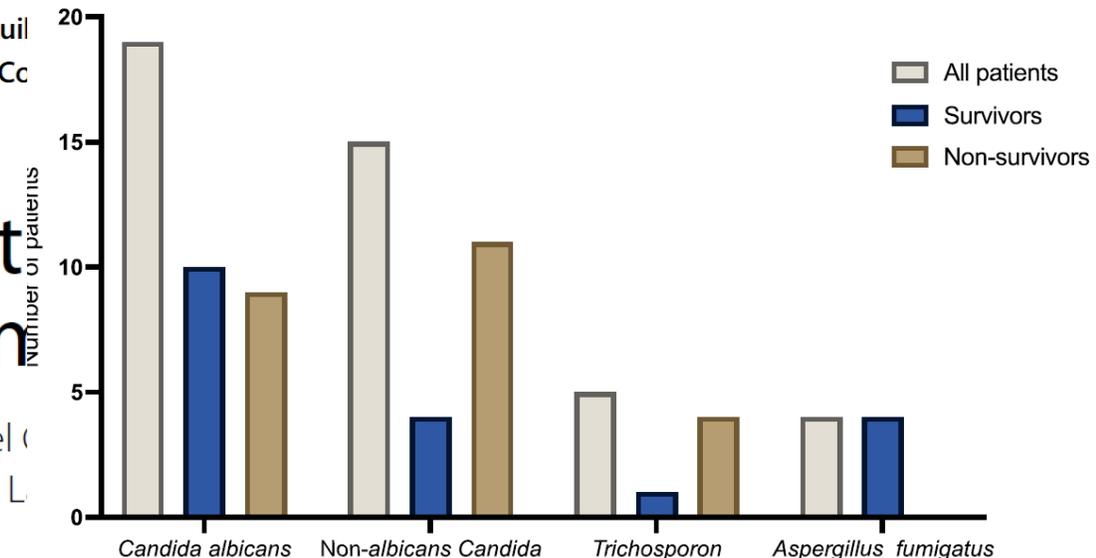
Characteristics and outcomes of patients with postoperative *Candida* versus bacterial mediastinitis: a case-matched comparative study

Quentin Moyon^{a,b}, Guillaume Lebreton^{c,d}, Florent Huang^a, Pierre Demondion^{c,d}, Cvrille Desnos^a,
Juliette Chommeloux^a, Guil
Pascal Leprince^{c,d}, Alain Cc

0,5 cas/1000

Post-cardiac surgery fungal mediastinitis clinical features, pathogens and outcom

Geoffroy Hariri^{1,2†}, Mathieu Genoud^{3†}, Vincent Bruckert^{1,4}, Samuel Chosidow⁵, Emmanuel C
Antoine Kimmoun⁷, Nicolas Nessler^{8,9}, Emmanuel Besnier^{10,11}, Fabrice Daviaud¹², David L
Julien Imbault^{14,15}, David Grimaldi¹⁶, Adrien Bouglé^{1†} and Nicolas Mongardon^{5,17,18†*}



Autres épidémies décrites

Table 1: Healthcare-associated outbreaks due to four new or uncommon fungal pathogens

Species	Year	Country	N° of cases	Infection sites	At risk population	Source	Main preventive measures
<i>Candida auris</i>	Since 2011	Four continents	> 500	IFI and colonization	Risk of invasive candidiasis	Human and environmental surfaces	Improve hand hygiene Contact isolation Improve environmental disinfection
<i>Saprochaete clavata</i> (formerly <i>Geotrichum clavatum</i>)	Sept 2011-Oct 2012	France	30	Blood and colonization	Hematological malignancies	Unknown	Define and identify at risk population
	Oct-Dec 2014	Italy	3	Spleen, liver, lung	Hematological malignancies	Unknown	Search for a common source
<i>Sarocladium kiliense</i> (formerly <i>Acremonium kiliense</i>)	June 2013-Jan 2014	Chile (8 hospitals in Santiago)	67	Blood	Chemotherapy	Antinausea ondansetron (company A)	Recall of all ondansetron lots of the company A
	Nov 2013	Colombia	16	Blood	Chemotherapy	Ondansetron (company A)	
	March-May 2011	Greece	3	Blood	Stem cell transplantation	CVC	
<i>Exserohilum rostratum</i>	Sept 2012-Oct 2013	USA (20 states)	751	Paraspinal/spinal Meninges Peripheral joint	Epidural/paraspinal injection of MPA	MPA (compounded drug)	Recall of the 3 contaminated lots

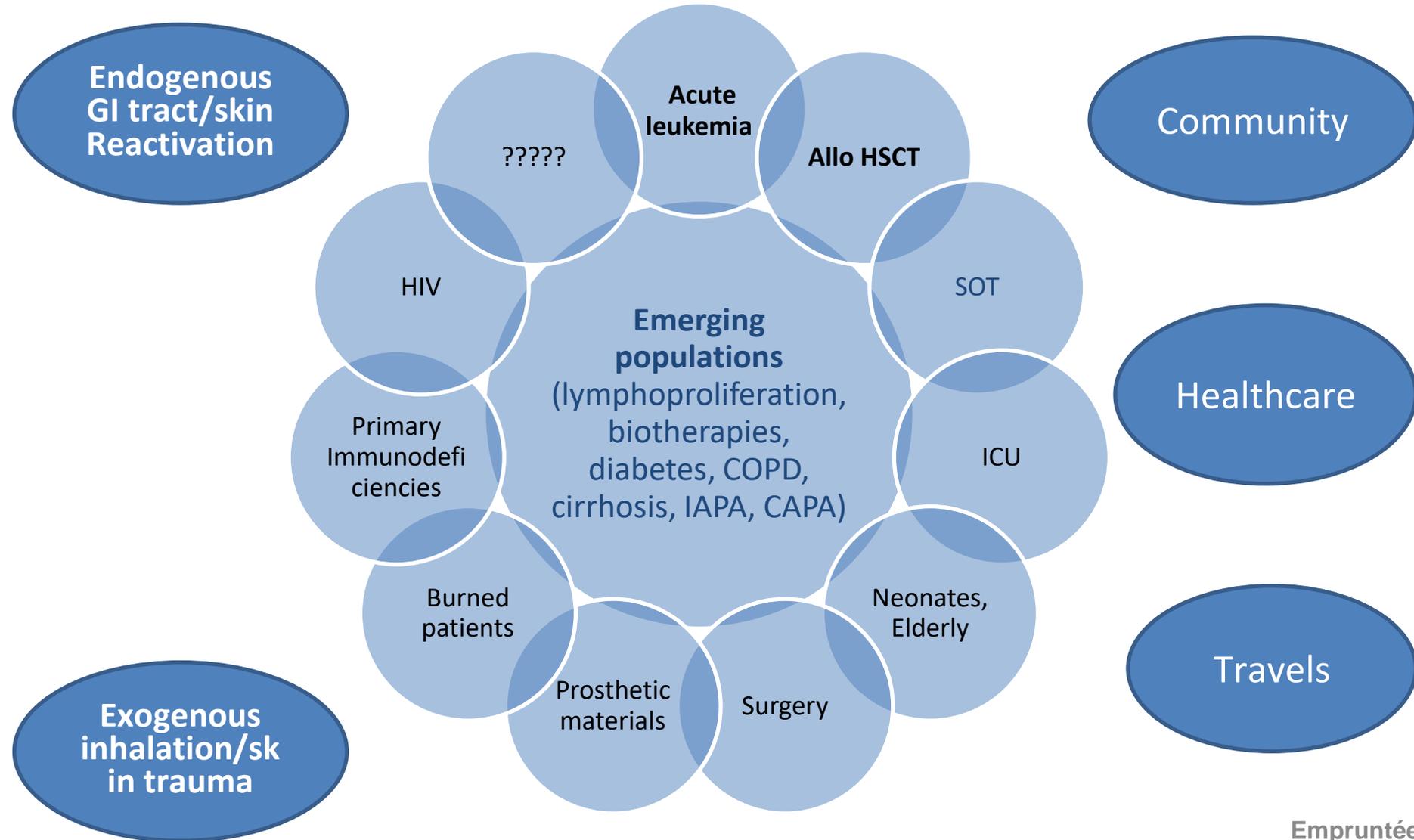
CVC, central venous catheter; IFI, invasive fungal infection; MPA, mycophenolic acid.

Sarocladium and *Acremonium* infections: New faces of an old opportunistic fungus

TABLE 1 Summary of the reported data on human *Acremonium/Sarocladium* infections

Total number of clinical cases	309	Immunocompromised patients	125
Fungaemia	106	Patients with underlying conditions	113
Ocular infections	104	Organ solid transplant	7
Respiratory infections	18	Solid tumour	24
Cutaneous and subcutaneous infections	14	Haematological malignancies	44
Mycetoma	15	Trauma	10
Onychomycoses	13	Diabetes	5
Disseminated infections	10	Others	23
Joint and bone infections	7		
Peritonitis	7		
Endocarditis	6		
Central nervous system infections	6		
Gastrointestinal infections	3		

Quelles sont les populations à risque ?



C'était mieux avant ?

Les risques sont-ils aujourd'hui plus fréquents ?

- Evolution de la médecine
- Généralisation/démocratisation
- Amélioration et survie

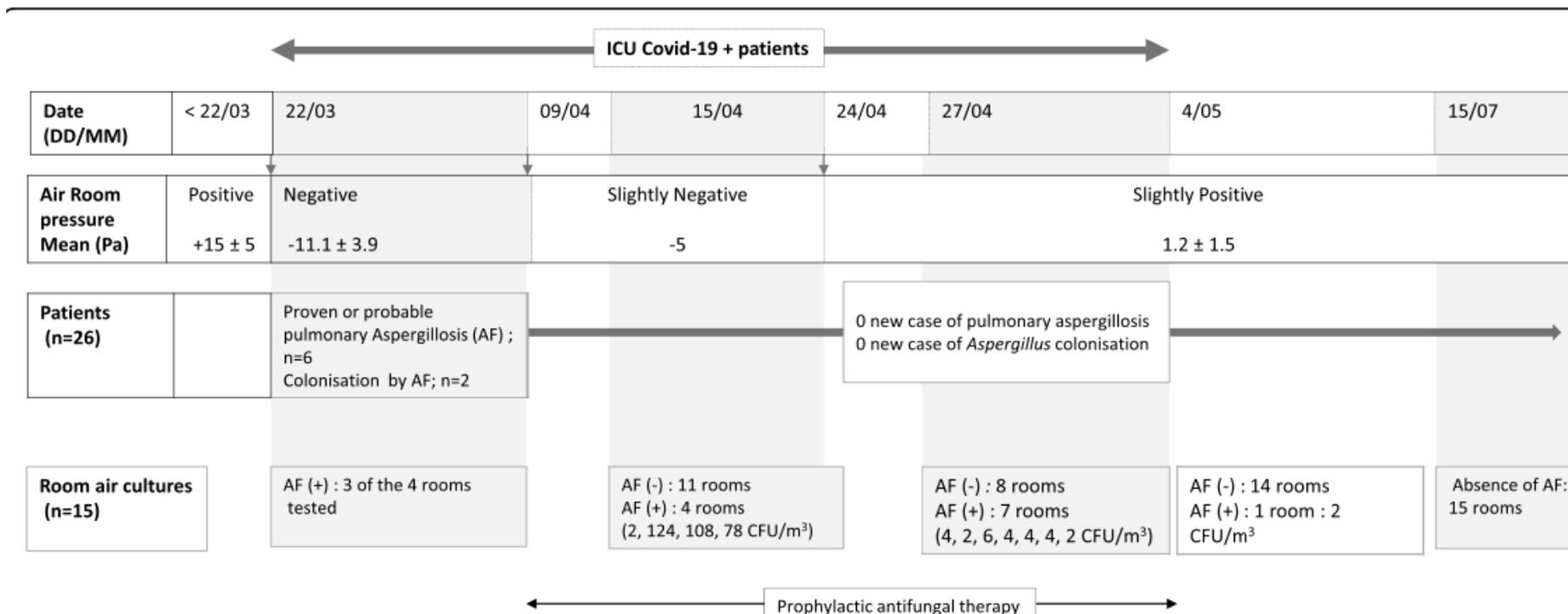
Risk factor	Mechanism increasing risk of IFI
Acute leukaemia ^{18,22,34,81,101,102}	Increased proliferation of leukaemic cells leads to decreased production of normal neutrophils ¹⁸
Neutropenia ^{19,20,22,34,36,92,101,102}	Decreased production of normal neutrophils ¹⁸
Immunosuppression including glucocorticoids ^{20,22,89,102}	Impaired innate and/or adaptive immune response ¹⁰⁵ ; Glucocorticoid-associated dysregulation of immunity ¹⁰⁶
Mucositis ^{35,36,81,102} fungal translocation ^{109,110,146}	Impaired mucosal barrier with translocation of pathogens, primarily <i>Candida</i> , to the blood ^{107,109,110,146}
Central venous catheters ^{34,81,102}	Port of entry and nidus of infection for fungal pathogens, primarily <i>Candida</i> ¹²²
Broad-spectrum antibiotic use ^{20,22,35,81,101}	Alters gut flora and increases colonisation from <i>Candida</i> spp., increasing risk for IC; selective pressures and increase in <i>Candida</i> spp. resistance; alterations in host immune response to <i>Candida</i> spp. ¹²³
Genetic factors ^{27-29,126,127}	Impaired adaptive and/or innate immune function ^{27-29,126,127}

Profils des patients de réanimation

	2022	2021	2020	2018
<500 PNN	2,6%	1,5%	1,5%	1,9%
Immunodépression autre	14,1%	12,3%	13,2%	12,9%
ATB à l'admission	57,3%	57,1%	57,8%	55%
ECMO	2,8%	2,2%	2,4%	1,5%
Champignons	4,9%	4,6%	4,3%	5%
<i>Candida</i> sp	3,7%	3,5%	3,8%	4,8%
<i>Aspergillus</i> sp	1%	1,1%	0,4%	0,1%
Levures	0%	0,1%	0%	0,1%
Autres filaments	0,1%	0%	0%	0%

Les risques que nous générons ?

- La charge fongique dépend de plusieurs facteurs
 - La charge extérieure (travaux, période de l'année, conditions météorologiques)
 - Les conditions de travail et d'activité
 - Le type de traitement d'air



Ce que nous avons appris de la littérature

Table II Number of patients with different underlying diseases and associated mortality

Underlying disease	No. of patients	Mortality (%)
Haematologic malignancy	299	57.6
Solid organ transplantation		55.9
Renal transplantation	36	
Liver transplantation	8	
Other immunocompromised patients		52.3
High-dose steroid therapy	15	
Neonates	5	
Other malignancy	4	
Chronic lung disease	2	
ICU patients ('high risk')	2	
No exact classification possible	49	
Patients without severe immunodeficiency		39.4
Thoracic surgery	25	
Cataract surgery	5	
ICU patients ('low risk')	5	
Other surgical patients	3	
Total	458	55.0

ICU, intensive care unit.

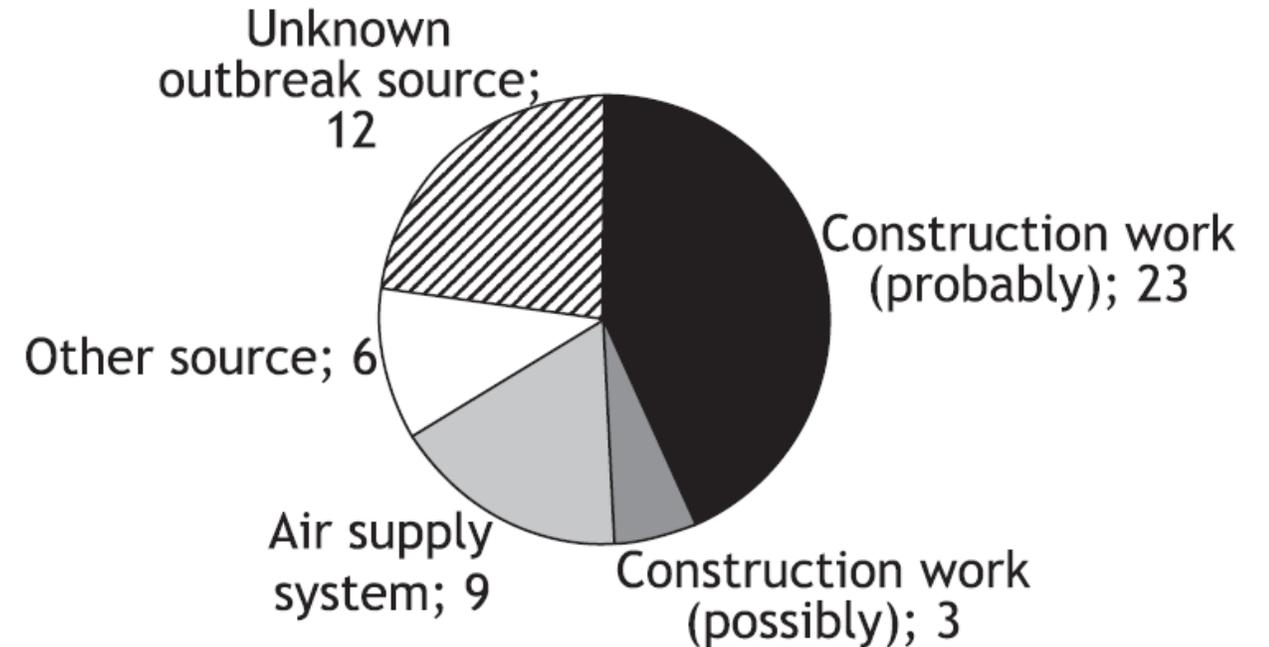


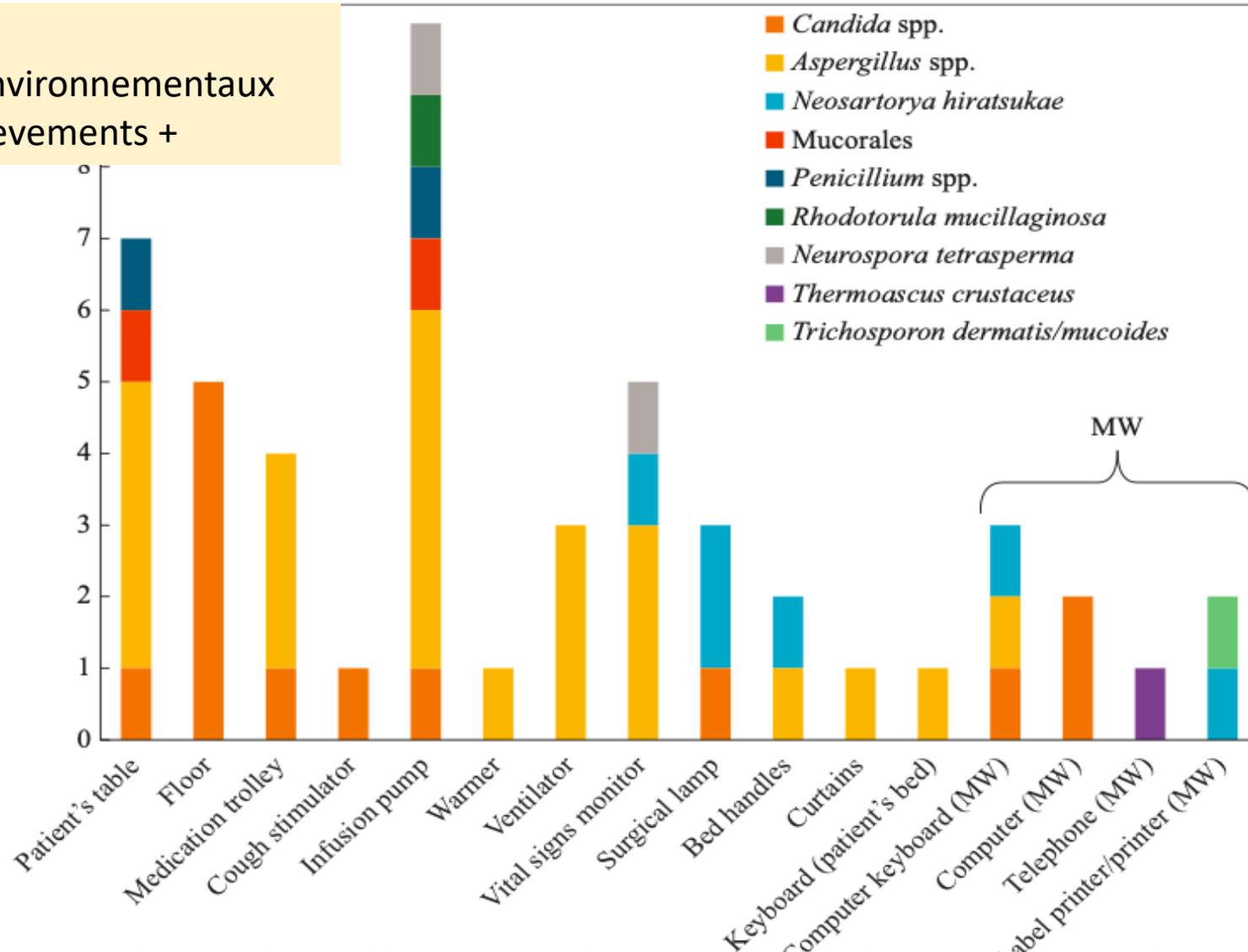
Figure 1 Distribution of sources of nosocomial aspergillus outbreaks.

Réservoir « méconnu » en réanimation ?

12 Réanimations

401 prélèvements environnementaux

4% - 24% (12%) prélèvements +

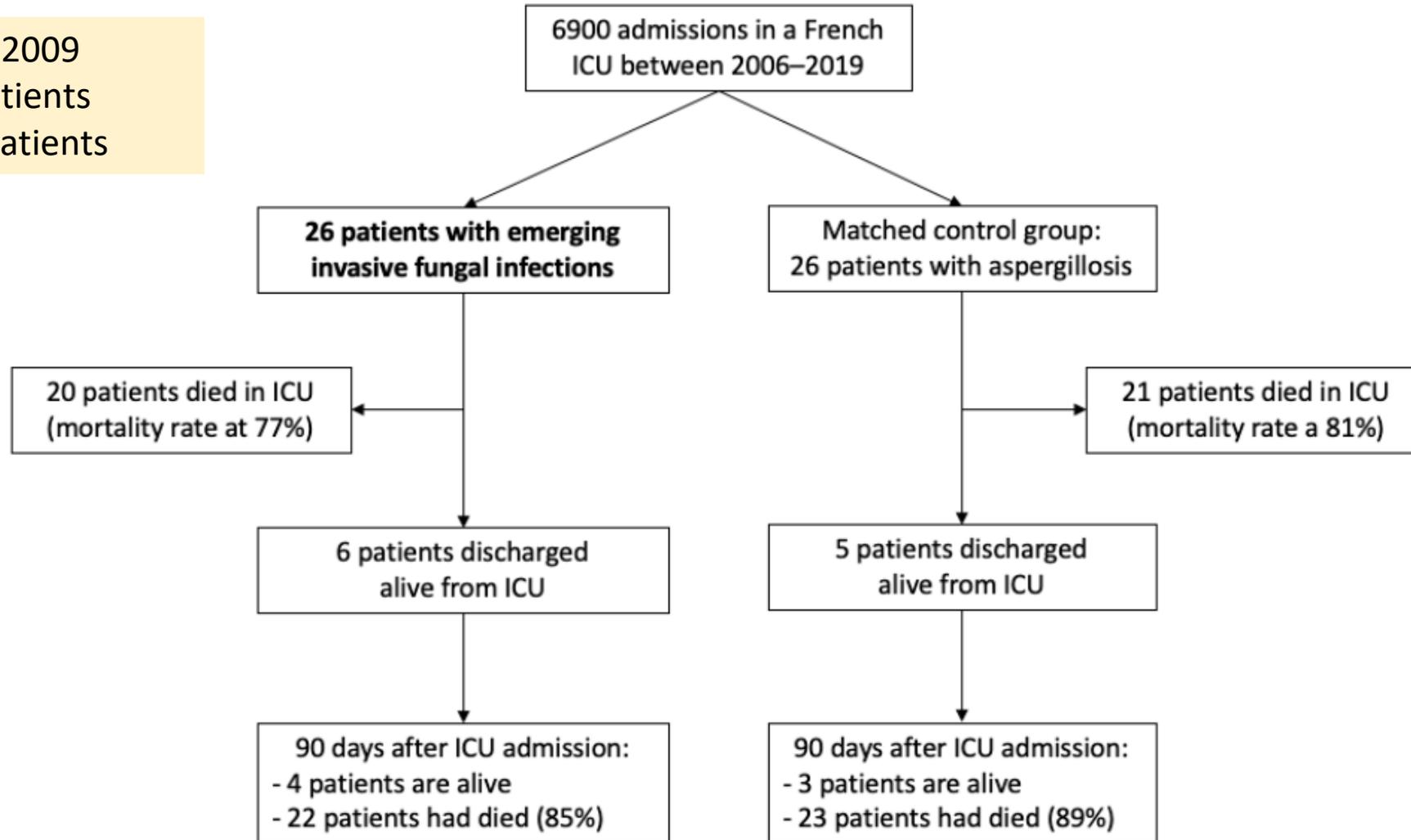


Et maintenant en réanimation ?

- Le risque a-t-il déjà été décrit ?
- Existe-t-il des pathologies émergentes ?
- Quelles espèces ? Et pour qui ?

Les infections fongiques sont-elles fréquentes ?

2006 – 2009
6900 patients
4/1000 patients



Les infections fongiques sont-elles fréquentes ?

2006 – 2009
6900 patients
4/1000 patients

Table 2. Details on molds isolated and antifungal treatments.

	Total (n = 26)	Survivor (n = 6)	Deceased (n = 20)	p-Value
Mucormycosis, n (%)	13 (50%)	3 (50%)	10 (50%)	>0.99
<i>Rhizopus</i> sp., n (%)	9 (35%)	1 (17%)	8 (40%)	0.31
<i>Lichtheimia corymbifera</i> , n (%)	2 (8%)	2 (33%)	0 (0%)	>0.99
<i>Rhizomucor pusillus</i> , n (%)	1 (4%)	0 (0%)	1 (5%)	0.99
<i>Mucor circinelloides</i> , n (%)	1 (4%)	0 (0%)	1 (5%)	0.99
Other EIFIs, n (%)	13 (50%)	3 (50%)	10 (50%)	>0.99
<i>Saprochaete clavata</i> , n (%)	1 (4%)	1 (17%)	1 (5%)	0.59
<i>Saprochaete capitata</i> , n (%)	4 (19%)	0 (0%)	4 (20%)	0.99
<i>Trichosporon asahii</i> , n (%)	1 (4%)	0 (0%)	1 (5%)	0.99
<i>Fusarium</i> sp., n (%)	2 (8%)	0 (0%)	2 (10%)	>0.99
<i>Scedosporium apiospermum</i> , n (%)	2 (8%)	0 (0%)	2 (10%)	>0.99
<i>Chaetomium cymbiformis</i> , n (%)	1 (4%)	1 (17%)	0 (0%)	0.99
<i>Saccharomyces cerevisiae</i> , n (%)	1 (4%)	1 (17%)	0 (0%)	0.99
Antifungal therapy	24 (92%)	6 (100%)	18 (90%)	>0.99
Adequate	20 (77%)	5 (83%)	15 (75%)	0.67
Amphotericin B, n (%)	18 (69%)	3 (50%)	15 (75%)	0.26
Echinocandin, n (%)	6 (23%)	1 (17%)	5 (25%)	0.67
Fluconazole, n (%)	1 (4%)	1 (17%)	0 (0%)	0.99
Voriconazole, n (%)	2 (8%)	0 (0%)	2 (10%)	>0.99
Isavuconazole, n (%)	2 (8%)	2 (33%)	0 (0%)	>0.99
Flucytosine, n (%)	1 (4%)	1 (17%)	0 (0%)	0.99
Association, n (%)	5 (19%)	2 (33%)	4 (20%)	0.37

Infections fongiques et ECMO

Table 2 Prevalence and outcome of colonization and fungal infections

Fungus/diagnosis	Total	Prevalence	Survival	Survivors	Nonsurvivors
Diagnosis of blastomycosis	17	0.1%	53%	9	8
Diagnosis of other fungal infection	33	0.2%	42%	14	19
Total	2129	11%	50%	1059	1070

Table 3 Risk factors for <i>Aspergillus</i> colonization or infection			
Variable	OR	95% CI	p Value
Male sex	1.55	1.16–2.08	0.003
Weight/10 kg	0.87	0.82–0.93	< 0.001
Hematological malignancy	2.18	0.99–4.78	0.052
Aspiration pneumonitis	0.33	0.12–0.93	0.036
ARDS	0.75	0.50–1.12	0.154
Acute respiratory failure NOS	0.58	0.42–0.79	0.001

Table 4 Risk factors for <i>Candida</i> bloodstream infection			
Variable	OR	95% CI	p Value
Age/10 years	1.13	1.03–1.25	0.011
Weight/10 kg	1.05	1.00–1.10	0.061
Sepsis	1.60	1.15–2.23	0.005
Renal replacement therapy	1.55	1.12–2.13	0.007
Nonviral pneumonia	0.70	0.48–1.03	0.068
Intra-aortic balloon pump	1.46	0.94–2.26	0.091
Cardiopulmonary bypass	0.56	0.28–1.15	0.112

Candida haemulonii complex, an emerging threat from tropical regions?

Ugo Françoise^{1a}, Marie Desnos-Ollivier², Yohann Le Govic^{1ab}, Karine Sitbon², Ruddy Valentino³, Sandrine Peugny⁴, Taieb Chouaki⁵, Edith Mazars⁶, André Paugam⁷, Muriel Nicolas⁸, Nicole Desbois-Nogard^{1c}, Olivier Lortholary^{2,9,10*}, French Mycoses Study Group¹

Critically ill patients with severe infections related to *Geotrichum* species: A French retrospective multicentre study

Sandrine Valade¹ | Muriel Picard² | Djamel Mokart³ | Laure Calvet⁴ |

Genomic Analyses of a Fungemia Outbreak Caused by *Lodderomyces elongisporus* in a Neonatal Intensive Care Unit in Delhi, India

Anamika Yadav^{a,b}, Peeyush Jain^c, Kusum Jain^{a,b}, Yue Wang^d, Aditi Singh^c, Ashutosh Singh^{a,e}, Jianping Xu^d, Anuradha Chowdhary^{a,e}

Systematic Review

Trichoderma spp.-Related Pneumonia: A Case Report in Heart–Lung Transplantation Recipient and a Systematic Literature Review

Carlo Burzio¹, Eleonora Balzani^{2,*}, Giorgia Montrucchio^{1,2}, Anna Chiara Trompeo¹, Silvia Corcione^{3,4} and Luca Brazzi^{1,2}

Narrative review

Intensive care management of influenza-associated pulmonary aspergillosis

P. Koehler^{1,2,*}, M. Bassetti³, M. Kochanek¹, A. Shimabukuro-Vornhagen¹, O.A. Cornely^{1,2,4,5}

Take home message

- La population à risque est en constante augmentation (IMND)
- Nos pratiques (en réanimation) exposent nos patients à de nouveaux multiples risques
- Le réservoir des agents pathogènes est environnemental....sa maîtrise en milieu hospitalier est donc possible
- 2 types d'émergences : au sein des espèces usuelles et apparition de nouvelles