

Gemelli



Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore

Fungal Infections non-*Aspergillus* and non-*Candida*

Livio Pagano

UOC di Ematologia Geriatrica ed Emopatie Rare

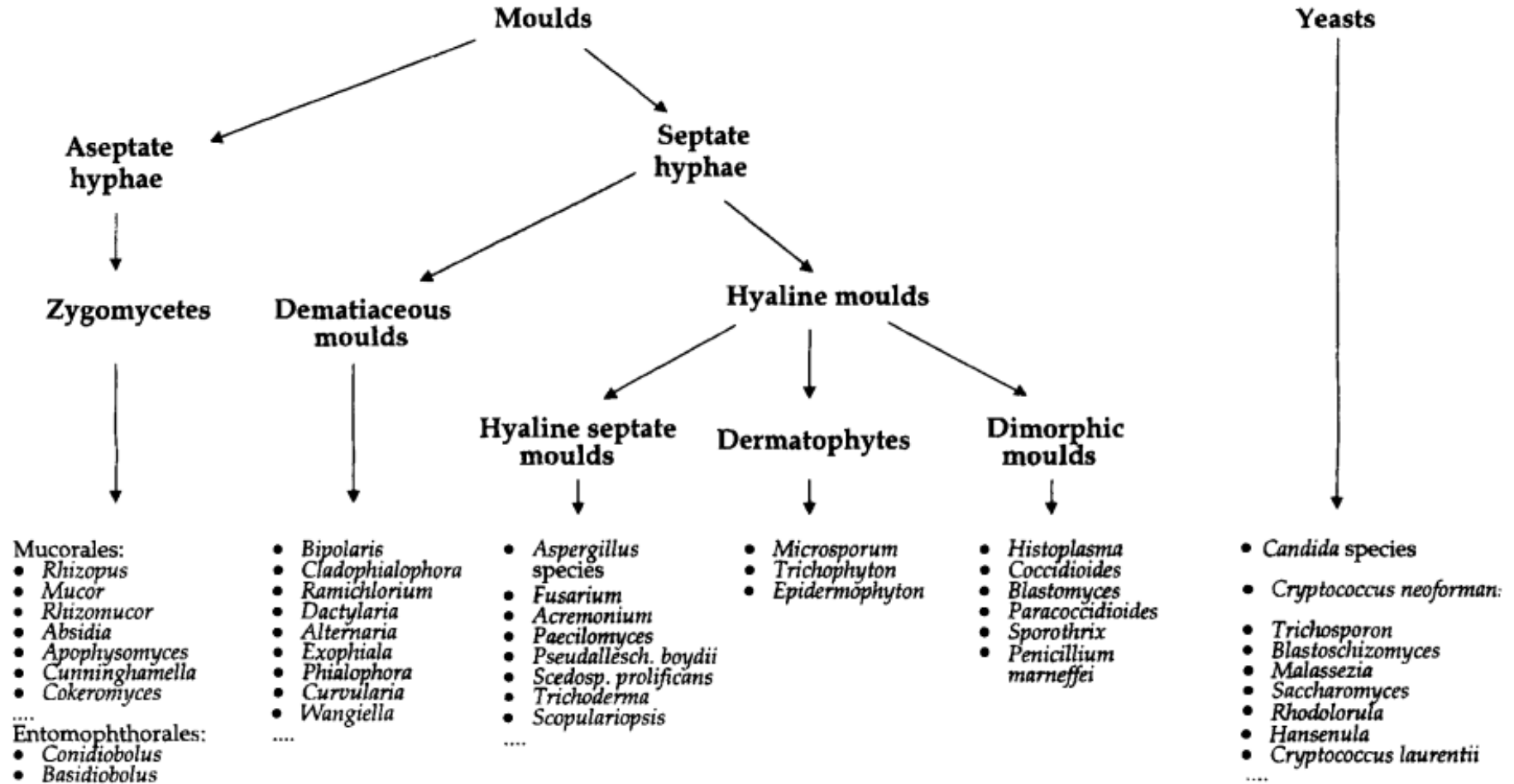
Roma



EUROPEAN
HEMATOLOGY
ASSOCIATION



Opportunistic Fungi



Epidemiology

- On the increase
 - Ever expanding populations at risk
 - New immunotherapeutic treatments
 - Prolonged immunosuppression and unexpected/understudied off-target effects
 - Selection pressure due to the increasing use of broad spectrum antifungal agents as prophylaxis.
- Mortality is high
 - Late recognition
 - Difficulty in diagnosis
 - Limited currently available therapeutic options

Epidemiology and Diagnosis of Mucormycosis: An Update

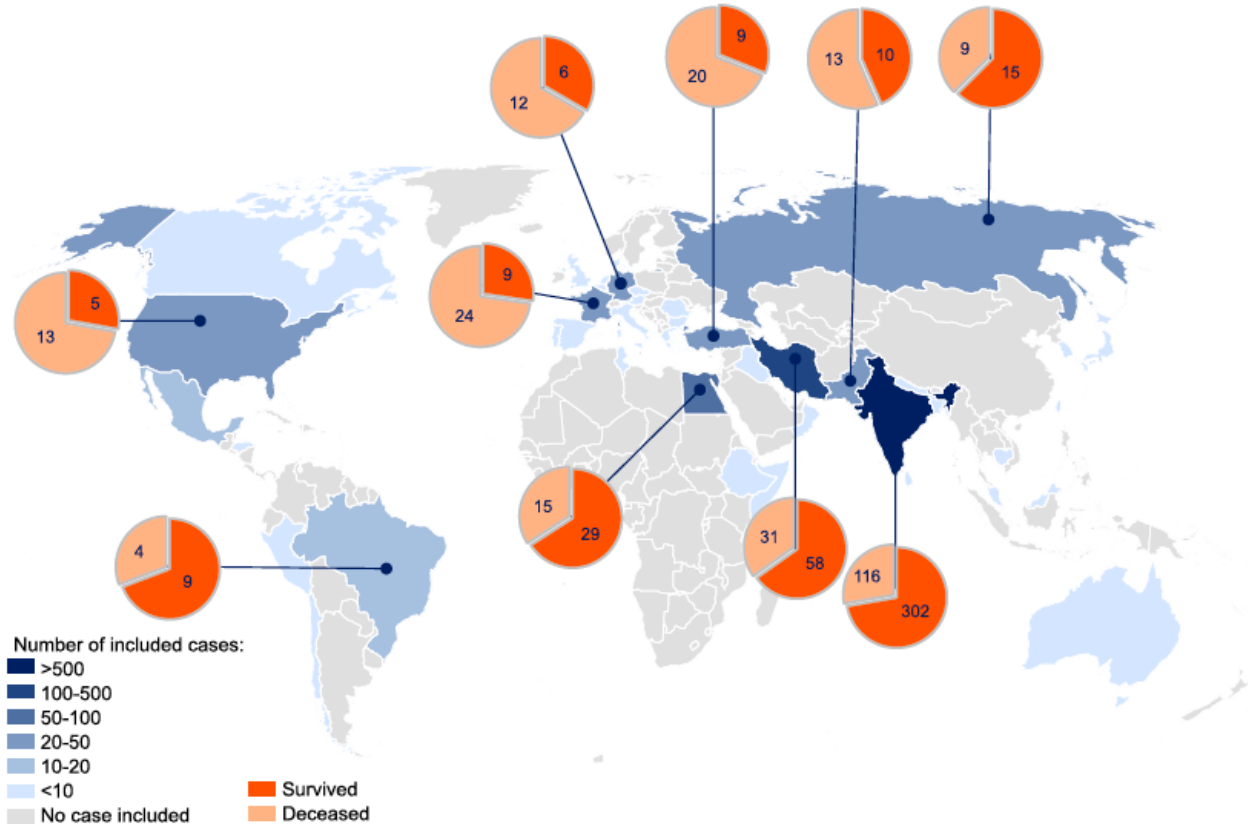
Skiada et al. J Fungi 2020

Reference	Characteristics of Studies					Risk Factors/Underlying Diseases (%)							
	Countries of Origin of Cases	Prospective Study	Multicenter Study	Time Period	Total no. of pts	DM	HM	HSCT	SOM/SOT	AI/CO	Trauma [#]	HIV	None
Roden et al. 2005 [8]	Global	No	Yes	1940–2003	929	36	15.8	5	1/7	1	8 [#]	2	19
Jeong et al. 2019 [9]	Global	No	Yes	2000–2017	851	40	32		1/14	3/33	20		18
Skiada et al. 2011 [14]	Europe	Yes	Yes	2005–2007	230	17	44		5/4	44	17	2	8
Lanternier et al. 2012 [10]	France	No	Yes	2005–2007	101	23	50	12	2/3	13	18	1	1
Pagano et al. 2009 [27]	Italy	Yes	Yes	2004–2007	60	18	62	3	8/	3/50	2	17	3
Kontoyiannis et al. 2016 [18]	USA	No	Yes	2005–2014	555	52	40	11	6/15	NA	4	2	NA
Nucci et al. 2019 [28]	South America	No	Yes	1960–2018	143	42	11	2	/13	NA	20	2	7.7
Corzo-Leon et al. 2017 [12]	Mexico	No	Yes	1982–2016	418	72	17		1/	1	2.3	0.7	4
Chakrabarti et al. 2006 [5]	India	No	No	2000–2004	178	73.6	1.1		/0.6	1.7	7.3	0.6	11.8
Chakrabarti et al. 2009 [20]	India	Yes	No	2006–2007	75	44	9		/5	29	11	1	3
Prakash et al. 2019 [29]	India	Yes	Yes	2013–2015	303	56.8	6		/6	9.9	10	-	10.5
Patel et al. 2020 [11]	India	Yes	Yes	2016–2017	465	74	8	1	1.5/6.5	/3.7	6.9	-	11.8
Dolatabadi et al. 2018 [30]	Iran	No	Yes	2008–2014	208	75	3	2	3/3	NA	4	-	2
Vaezi et al. 2016 [31]	Iran	No	Yes	1990–2015	98	48	6	1	/23	NA	1	-	10
El Zein et al. 2018 [32]	Lebanon	No	No	2008–2018	20	35	65		/5	70	-	-	-
Kennedy et al. 2016 [33]	Australia	No	Yes	2004–2012	74	27	48.6	18	3/11	12/ 53	23		11
Stemler et al. 2020 [34]	Middle East and North Africa	No	Yes	1968–2019	310	49.7	16.5		2/17	21.6	12	0.3	5.8

[#] Penetrating trauma and surgery. SOM = Solid organ malignancy, SOT = Solid organ transplantation, AI = Autoimmune disease, CO = corticosteroids.

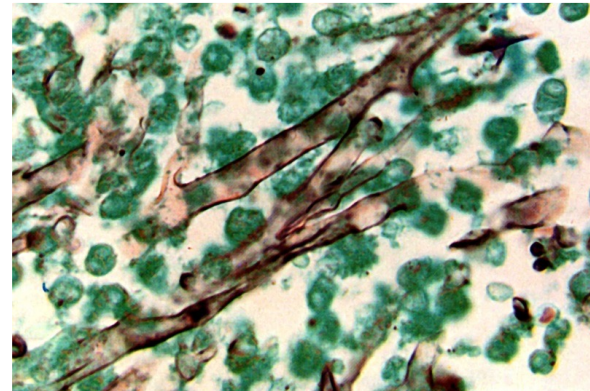
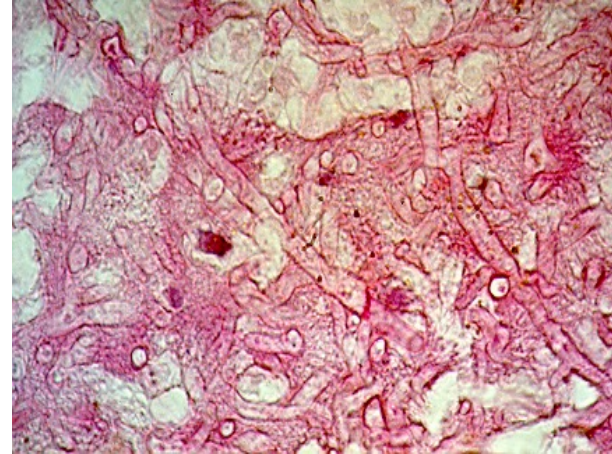
COVID-19–associated mucormycosis: a systematic review and meta-analysis of 958 cases

Comorbidities	% of patients with the comorbidity
Diabetes mellitus	77.9 (738/948)
Post–COVID-19	5.7 (51/889)
Poorly controlled/uncontrolled	84.2 (341/405)
DKA	9.5 (61/643)
Hypertension	26.4 (231/876)
Malignancy	4.1 (36/878)
Hypothyroidism	3.0 (26/875)
Pulmonary disease	5.0 (44/877)
Renal disease	11.2 (97/870)
Cardiovascular disease	10.7 (94/876)
Neutropenia	1.5 (13/869)
Transplant history	4.6 (40/871)
SOT	4.0 (35/871)
HSCT	0.6 (5/871)
Obesity (BMI > 30.0)	3.7 (32/877)



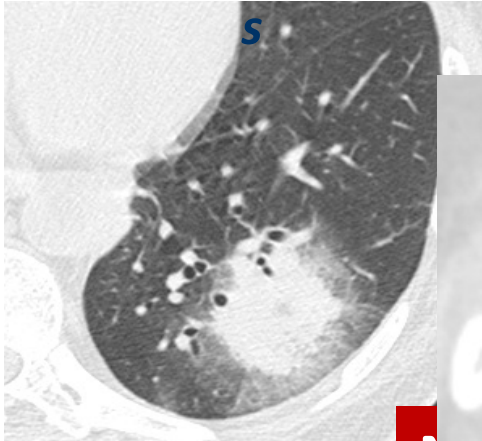
Laboratory diagnostics

- ❖ Colonization by Zygomycetes seems definitely rare (it's easier to isolate a *Rhizopus* as a contaminating agent than a *Mucor*)
- ❖ Culture studies show a low sensitivity (more than 75% of cases with histologically diagnosed zygomycetes pneumonia don't develop fungi at cultures)
- ❖ Reduced growth in culture
- ❖ Galctomannan and beta-glucan negative !

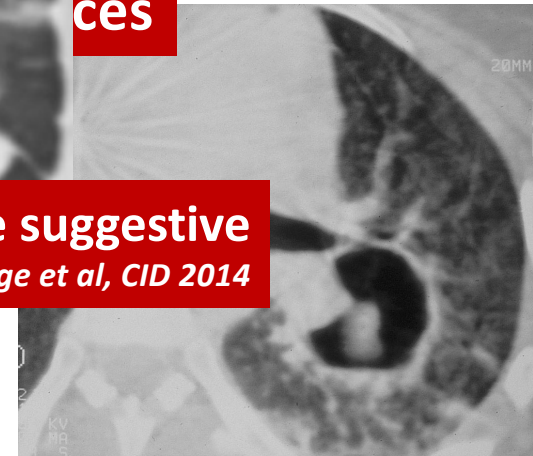


Radiological Pictures

Mucormycete



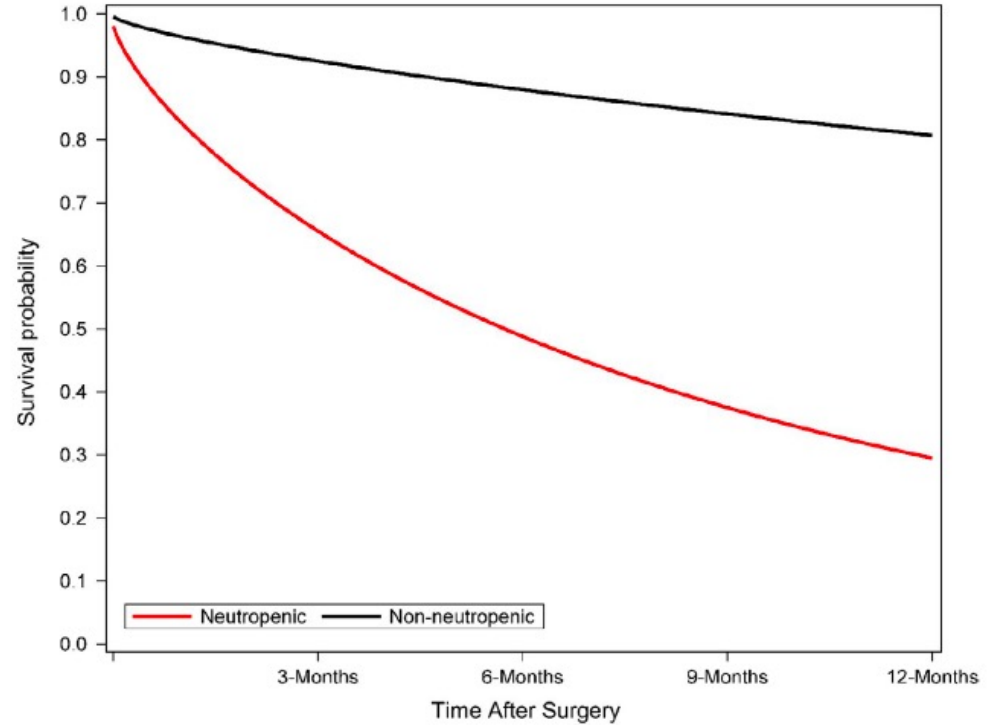
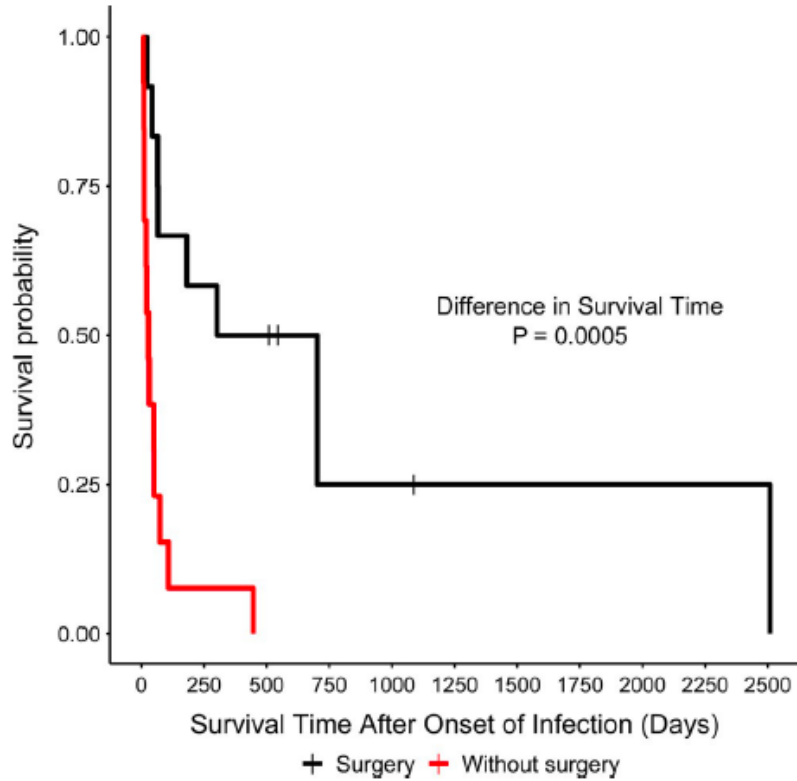
Aspergillus



But “reversed halo sign” may be suggestive

Legouge et al, CID 2014

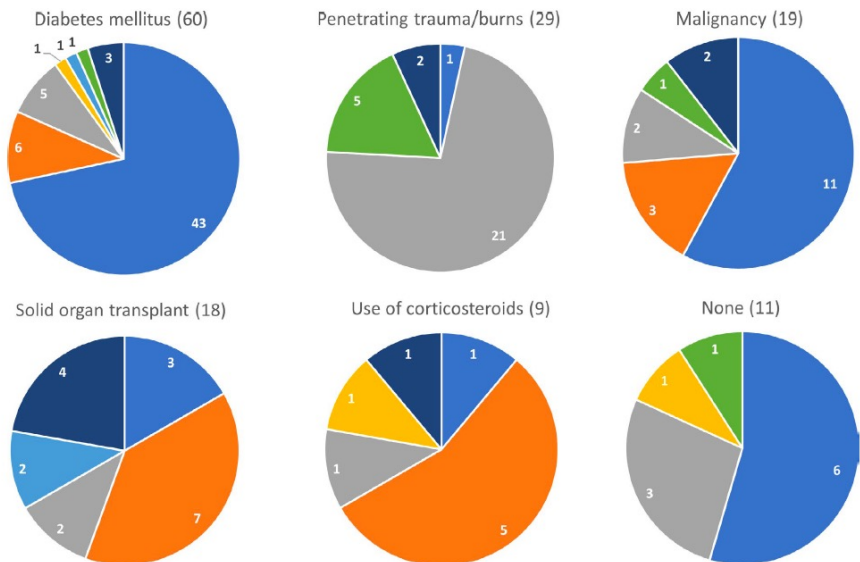
Cut it out! Thoracic surgeon's approach to pulmonary mucormycosis and the role of surgical resection in survival



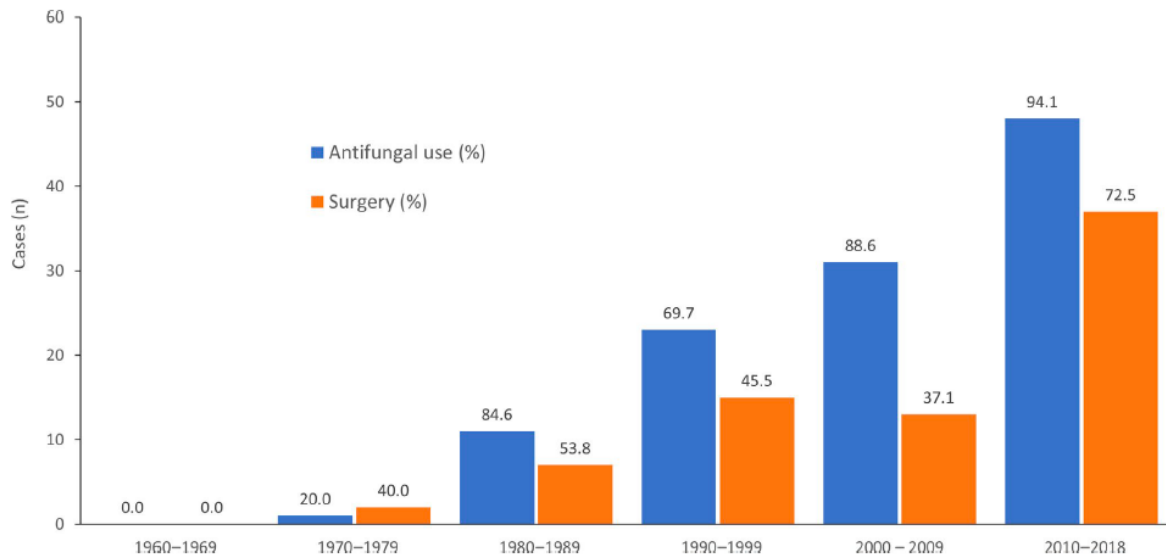
- 12 patients treated with surgery
- 13 with only antifungal

Mucormycosis in South America: A review of 143 reported cases

Nucci et al, Mycoses 2019



- Rhino-sino-orbito-cerebral
- Skin and soft tissues
- Liver or kidneys
- Disseminated infection
- Pulmonary
- Gastrointestinal or peritoneum
- Other



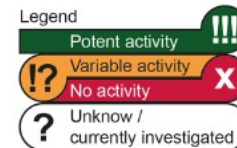
	Brazil		Other South American countries		Total	
	Incidence (N = 59) n (%)	Mortality n (%) ^a	Incidence (N = 84) n (%)	Mortality n (%) ^a	Incidence (N = 143) n (%)	Mortality n (%) ^a
Treatment (overall)						
Antifungal only	28 (47.5)	16 (57.1)	15 (17.9)	9 (60.0)	43 (30.1)	25 (58.1)
Antifungal + surgery	21 (35.6)	5 (23.8)	50 (59.5)	12 (24.0)	71 (49.7)	17 (23.9)
No antifungal treatment	10 (16.9)	10 ^b (100.0)	19 (22.6)	17 ^c (89.5)	29 (20.3)	27 (93.1)


Combined surgery and antifungals improves the prognosis of IM

Global Guideline for the Diagnosis and Management of Mucormycosis: An initiative of the ECMM in cooperation with ESCMID/EFISG

Population	Intention	Intervention	SoR	QoE
Any	To increase survival rates	Surgical debridement	A	IIu
Any	To cure and to increase survival rates	Surgery in addition to antifungal treatment	A	IIu
Any	To cure and to increase survival rates	Amphotericin B, liposomal 5-10 mg/kg	A	IIu
Any	To cure	Isavuconazole PO/IV 3x200 mg d1-2, 1x200 mg/d from d3	B	IIh
Any	To cure	Posaconazole DR tablet or IV 2x300 mg d1, 1x300 mg from d2	B	IItu
Any	To cure	Posaconazole oral suspension 4x200 mg/d or 2x400 mg/d	C	IIu
Any	To cure	Amphotericin B, deoxycholate, any dose	D	I
Any	To cure	AmB formulation + caspofungin	C	III
Any	To cure	LAMB + caspofungin	C	IIh
Any	To cure	LAmB + MICA or ANID	C	III
Any	To cure	LAmB + POS DR tablet or iv	C	IIu
Hema malignancy	To cure	LAMB + posaconazole	C	IIu
Hema malignancy	To cure	AmB formulations + caspofungin	C	IIu
Hema malignancy	To cure	L-AMB + caspofungin	C	IIu
Hema malignancy	To cure	L-AMB + caspofungin + posaconazole	C	IIu

The Antifungal Pipeline: Fosmanogepix, Ibrexafungerp, Olorofim, Opelconazole, and Rezafungin



Antifungal agents	Fosmanogepix	Ibrexafungerp	Olorofim	Opelconazole	Rezafungin
Pathogens					
 <i>Cunninghamella</i>	Variable activity	No activity	No activity		
<i>Lichtheimia</i>	Variable activity	No activity	No activity		
<i>Mucor</i>	Variable activity	No activity	No activity		
<i>Rhizopus</i>	Variable activity	No activity	No activity	Potent activity	

Ibrexafungerp and olorofim have no activity against Mucorales, while opelconazole seems effective

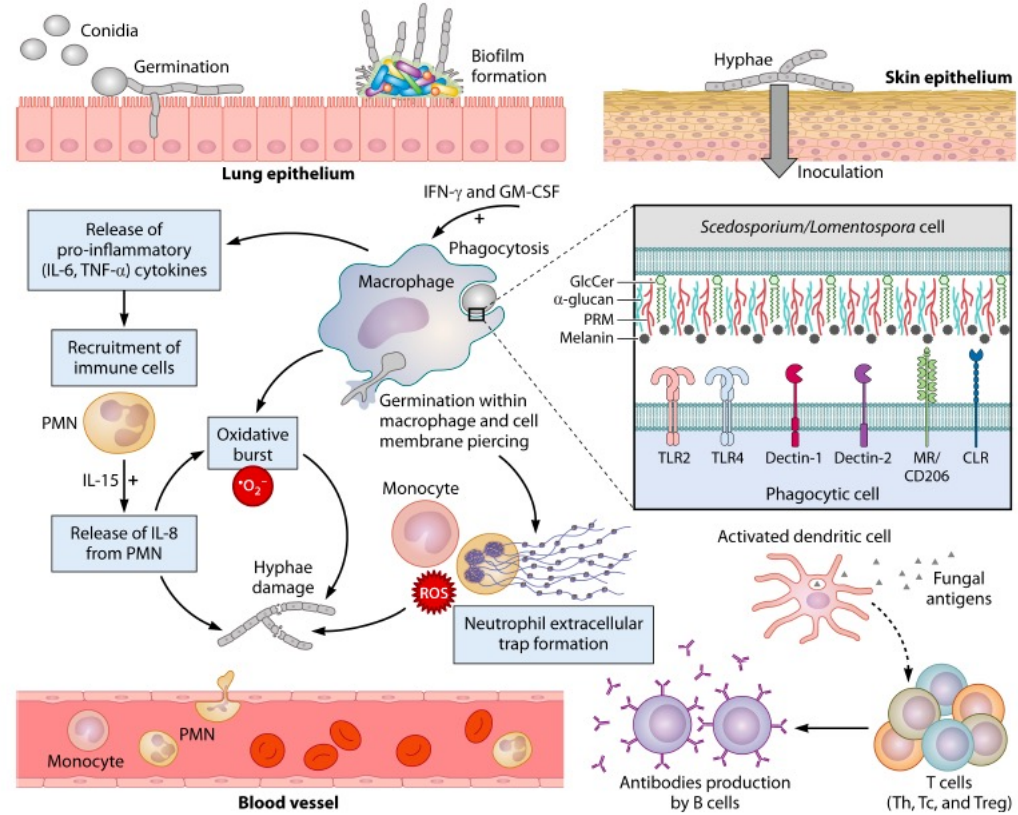
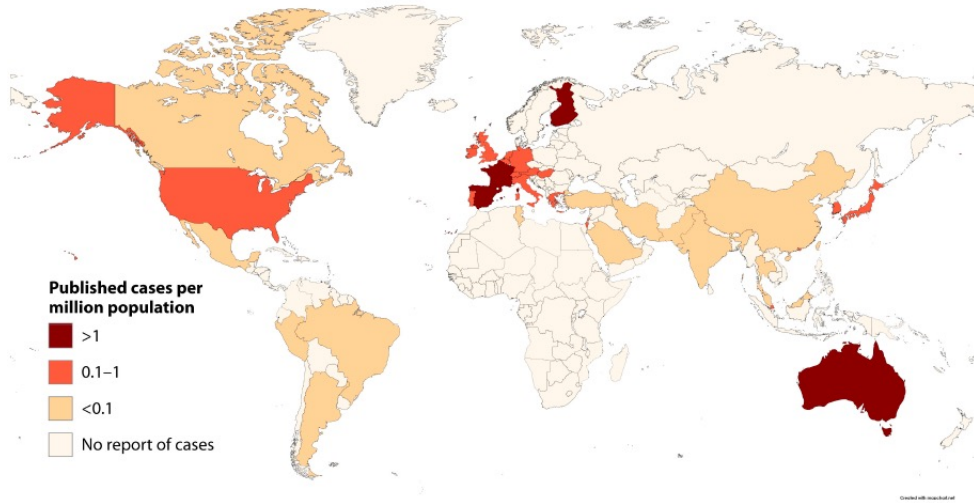
Scedosporium spp.

- Ubiquitous saprophytic hyaline moulds
- Found mostly in temperate climates
- Regional/geographical variation in incidence
- Most common
 - *S. apiospermum* species complex (SC)
 - *S. apiospermum* and *S. boydii*
 - *S. aurantiacum*

Risk factors

- Hematological malignancy
- HSCT
- T-cell immunodeficiency

Scedosporiosis and lomentosporiosis: modern perspectives on these difficult-to-treat rare mold infections



Scedosporiosis and lomentosporiosis: modern perspectives on these difficult-to-treat rare mold infections

Species	<i>Scedosporium apiospermum</i>	<i>Scedosporium boydii</i>
Disseminated IFDs	26%	35%
Fungemia	0%–4%	40%
Frequent localization in disseminated IFDs	Skin 67% Lung 58% CNS 33%	CNS 71% Lung 57% Skin 29%
Frequent location in localized IFDs	Osteoarticular/skin 46% Lung 20%	Lung 62% Osteoarticular/skin 31%

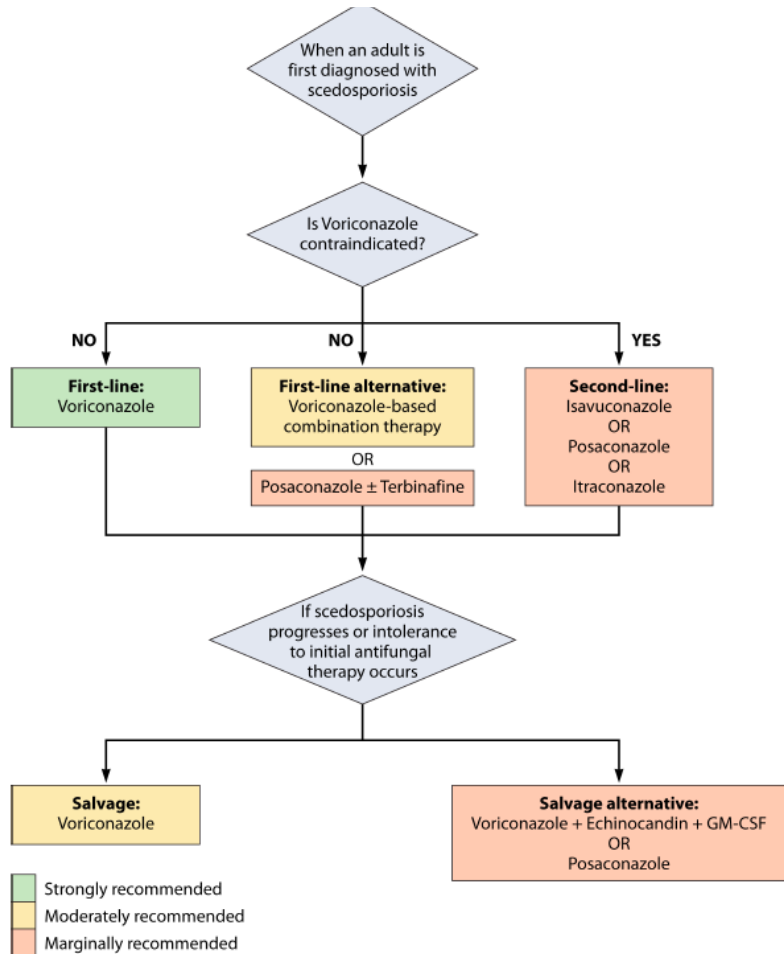
Imaging

- Imaging
 - Determine the degree of dissemination
 - Modality is determined by site of infection
 - CT scan for chest vs. MRI for brain
 - **Identify sites for biopsy**
 - CT scan chest
 - **No specific lesions** that would differentiate it from other rare moulds
 - **Determine response to treatment**
 - Should be used in combination with microbiology results

Diagnosis

- Dissemination
 - Blood cultures
 - Skin
- Obtain specimens
- Microscopy
- Culture
 - Species identification
 - Susceptibility testing
- Histology
- MALDI-TOF MS
 - Genus level only
- Molecular-based
 - Not species specific
 - Not standardised
 - Panfungal on tissue samples
 - ITS/ β -tubulin sequencing on cultures

Scedosporiosis and lomentosporiosis: modern perspectives on these difficult-to-treat rare mold infections



Olorofim for treatment of mould IFD in patients with limited or no treatment options: Results from a Phase 2b open-label study (NCT03583164, Study 32)

Johan Maertens, GR Thompson, Andrej Spec, Fariba Donovan, Stephen Walsh, Lesley Fitton, Aaron Dane, Daniela Zinzi, John H. Rex, Sharon Chen. AAAM2024

	DRC-adjudicated response rate ¹ n (%)		ACM n(%)	
	Day 42	Day 84	Day 42	Day 84
Overall (n = 202)	58 (28.7)	55 (27.2)	23 (11.4)	32 (15.8)
Aspergillus spp. (n = 101)	35 (34.7)	34 (33.7)	18 (17.8)	26 (25.7)
Lomentospora prolificans (n = 26)	11 (42.3)	11 (42.3)	3 (11.5)	3 (11.5)
Scedosporium spp. (n = 22)	8 (36.4)	5 (22.7)	2 (9.1)	2 (9.1)
Scopulariopsis spp. (n = 6)	5 (83.3)	5 (83.3)	0	0
Other Olorofim-susceptible fungi (n = 8)	1 (12.5)	2 (25.0)	0	1 (12.5)
Coccidioides spp. (n = 41)	0	0	0	0

Lomentospora prolificans

- Dematiaceous hyphomycete
- **Now phylogenetically distinct from *Scedosporium* spp.**
- Found in the soil in hot and dry climates
 - Australia, Spain and USA

Risk factors

- Hematological malignancy
- HSCT
 - **Fungaemia and disseminated infection**
- Solid organ transplant
 - Less likely than HSCT
 - 17% vs. 39%; $p=0.045$
- **Breakthrough infections on voriconazole**

Diagnosis

- Dissemination
 - Blood cultures
 - Skin
- Obtain specimens
- Microscopy
- Culture
 - Differentiate from *Scedosporium* spp. using cycloheximide
- Histology
 - Pigmented hyphae
- MALDI-TOF MS
- Molecular-based
 - Not standardised
 - Examined in the CF population mainly
 - Several methods
 - Broad-based assay with subsequent sequencing, hybridisation or microarray

Clinical characteristics and outcomes of invasive *Lomentospora prolificans* infections: Analysis of patients in the FungiScope[®] registry

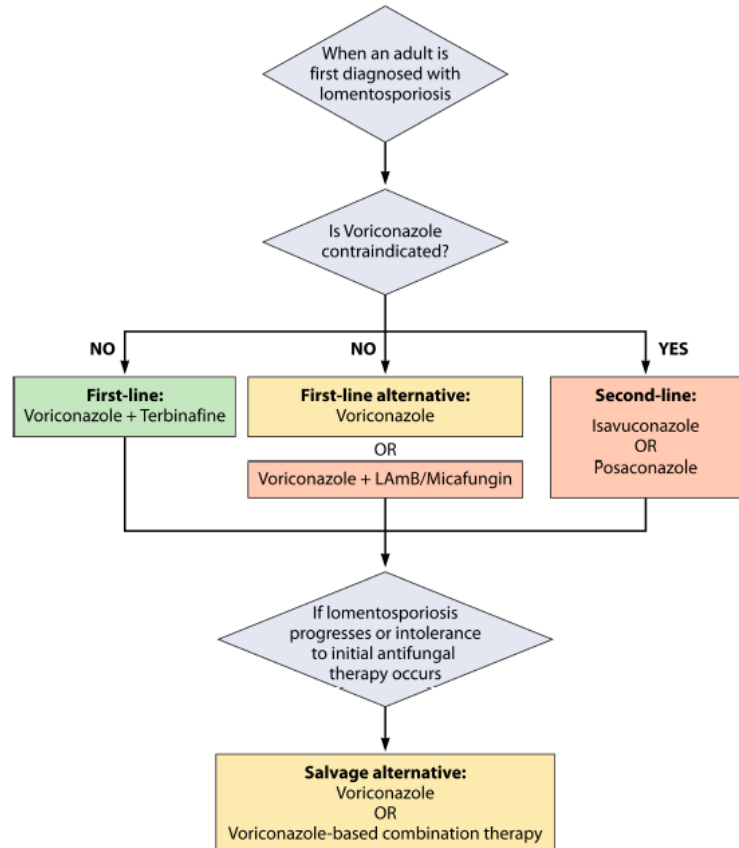
Jenks et al, mycoses 2020

Female sex	16 (39%)
Age (median, interquartile range)	65 (48-69)
Country case occurred	
Australia	17 (41%)
United States	11 (27%)
Germany	8 (20%)
Other ^a	5 (12%)
Underlying diseases/main risk factors	
Haematological/oncological malignancies	27 (66%)
Trauma/surgery	6 (15%)
Solid organ transplantation	3 (7%)
Other ^b	5 (12%)
Intensive care unit	6 (15%)
Site(s) of infection	
Disseminated infection	25 (61%)
Growth in blood culture	19 (46%)
Lung	18 (44%)
Eye	9 (22%)
Skin/deep soft tissue	5 (12%)
Bone	4 (10%)
Brain/central nervous system	5 (12%)

Breakthrough infection	24 (59%)
Antifungal treatment ^c	
Voriconazole ± other antifungals	31/40 (78%)
Terbinafine ± other antifungals	19/40 (48%)
LAmB ± other antifungals	15/40 (38%)
Antifungal combination therapy (vs monotherapy)	24/40 (60%)
Combination voriconazole + terbinafine ± other antifungals	16/40 (40%)
Surgery	7 (18%)
Outcomes ^d	
Progression, deterioration, or failure of antifungal treatment	23/40 (58%)
28-d overall mortality	21 (51%)
Death attributable to <i>Lomentospora prolificans</i> infection	21 (51%)

41 patients from 8 Countries mainly Australia and USA (California)

Scedosporiosis and lomentosporiosis: modern perspectives on these difficult-to-treat rare mold infections



- Strongly recommended
- Moderately recommended
- Marginally recommended

Neoh et al, Clin Micr Rev 2024

Olorofim for treatment of mould IFD in patients with limited or no treatment options:

Results from a Phase 2b open-label study (NCT03583164, Study 32)

Johan Maertens, GR Thompson, Andrej Spec, Fariba Donovan, Stephen Walsh, Lesley Fitton, Aaron Dane, Daniela Zinzi, John H. Rex, Sharon Chen. AAAM2024

	DRC-adjudicated response rate ¹ n (%)		ACM n(%)	
	Day 42	Day 84	Day 42	Day 84
Overall (n = 202)	58 (28.7)	55 (27.2)	23 (11.4)	32 (15.8)
Aspergillus spp. (n = 101)	35 (34.7)	34 (33.7)	18 (17.8)	26 (25.7)
Lomentospora prolificans (n = 26)	11 (42.3)	11 (42.3)	3 (11.5)	3 (11.5)
Scedosporium spp. (n = 22)	8 (36.4)	5 (22.7)	2 (9.1)	2 (9.1)
Scopulariopsis spp. (n = 6)	5 (83.3)	5 (83.3)	0	0
Other Olorofim-susceptible fungi (n = 8)	1 (12.5)	2 (25.0)	0	1 (12.5)
Coccidioides spp. (n = 41)	0	0	0	0

Global guideline for the diagnosis and management of rare mould infections: an initiative of the European Confederation of Medical Mycology in cooperation with the International Society for Human and Animal Mycology and the American Society for Microbiology



Hoeningl et al, Lancet Infect Dis 2021

Strongly recommended
Moderately recommended
Marginally recommended
Recommended against

	First-line	First-line alternative	Second-line	Treatments to avoid	Salvage treatments
Lomentosporosis	Voriconazole plus terbinafine	Voriconazole	Isavuconazole, or posaconazole	L-AmB	Voriconazole

The Antifungal Pipeline: Fosmanogepix, Ibrexafungerp, Olorofim, Opelconazole, and Rezafungin



Pathogen	Fosmanogepix	Ibrexafungerp	Olorofim	Opelconazole	Rezafungin
<i>Scedosporium spp.</i>	Potent activity	Variable activity	Potent activity	Potent activity	Potent activity
<i>Lomentospora prolificans</i>	Potent activity	Variable activity	Potent activity	Potent activity	Potent activity

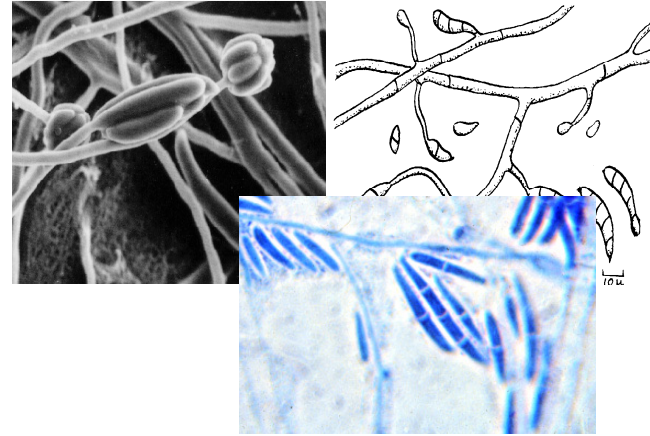
Legend

- !!! Potent activity
- !? Variable activity
- X No activity
- ? Unknown / currently investigated

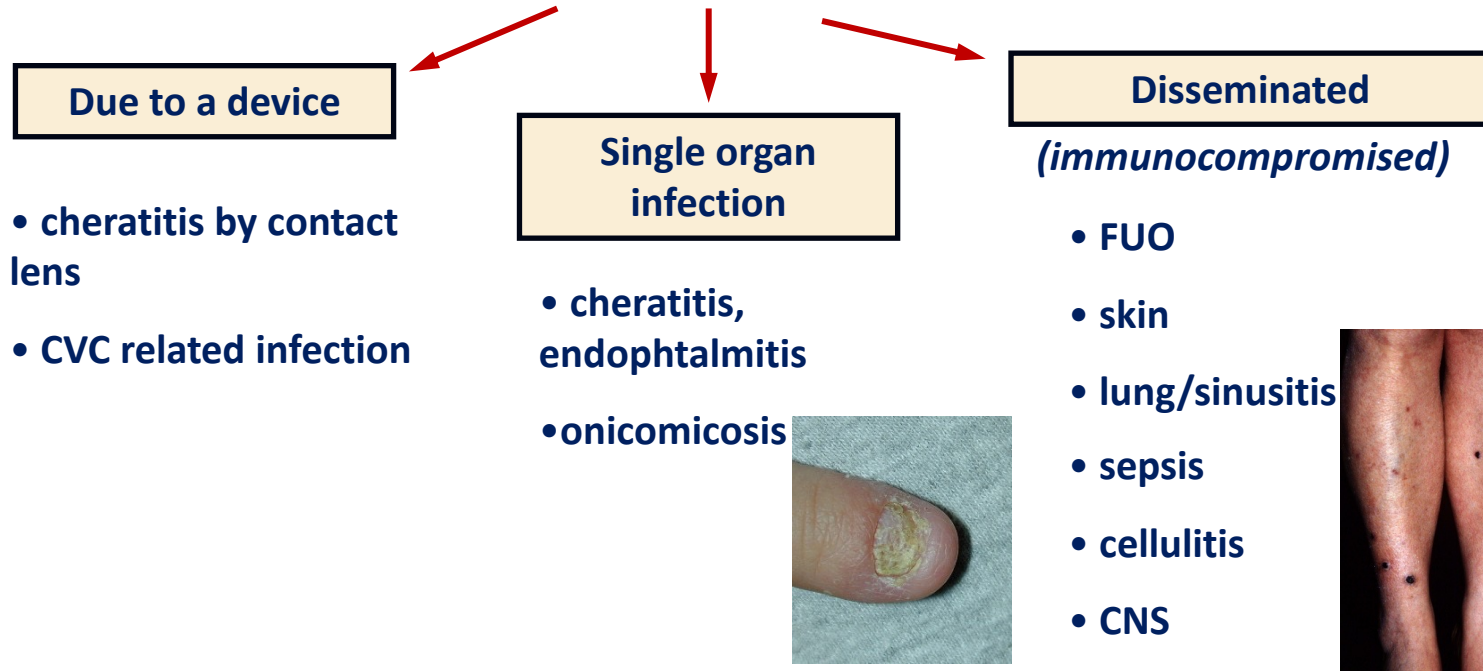
Hoeningl et al, Drugs 2021

Fusarium spp.

- Plant pathogen, soil saprophyte
- Inalation, ingestion, direct inoculation
- Includes *F.solani* (50% isolates), *F.moniliforme*, *F.oxysporum*



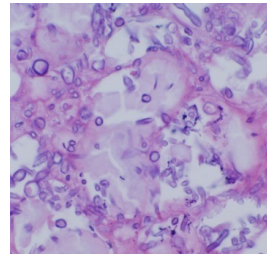
A wide spectrum of clinical manifestations



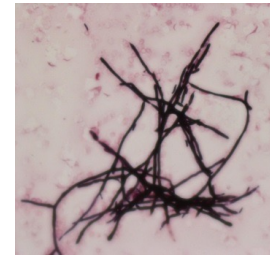
Diagnosis

- Because of their ubiquitous nature, however, isolation of *Fusarium* species in culture may be due environmental contamination.
- Therefore, the microbiologist and clinician must work together to interpret the results.
- Clues for clinically significant results are:
 - ☑ Fungi seen on direct stain of tissue.
 - ☑ Site of isolation and the host.
 - ☑ Same fungus from multiple specimens.
 - ☑ Multiple colonies from same specimen.

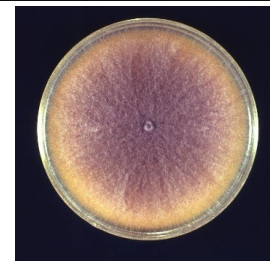
In Tissue



From Blood



Multiple Specimens



Diagnosis

- Histology
 - Stain with PAS or GMS
- MALDI-TOF MS
 - Research tool only
- Molecular-based
 - Several methods
 - Multi-locus sequence typing
 - Real-time PCR
- Galactomannan
 - Cross-reacts with *Fusarium*
 - Sensitivity and specificity
 - 83% and 67%
 - In 73% of cases positive before clinical signs
 - Prognostication ✓
- β -D-glucan
 - Sensitivity of 90% and specificity of 60%
 - 2 sequential tests with threshold >80 pg/mL ✓

Invasive Fusariosis in Patients with Hematologic Diseases

Country	Setting	Number of Patients (Denominator)	Number of Cases	Incidence
Italy [30]	Adult patients with hematologic diseases	351 episodes of infection by molds	6	1.7%
Italy [1]	Adult patients with hematologic malignancies	11,802 patients at risk	15	0.1%
Italy [31]	Adult patients undergoing HCT	3228 patients at risk	3	0.1%; 0.2% in allogeneic and no case in autologous HCT
USA [12]	Adult patients undergoing HCT	1607 patients at risk	12	0.7%; 1.2% in allogeneic and 0.2% in autologous HCT
USA [32]	Cancer patients	Not reported	44	0.04 cases per 1000 patients-day in 1998 and 0.012 cases per 1000 patients-day in 2007–2008
Spain [28]	Hospitalized patients	Not reported	58	0.55 cases per 100,000 admissions
USA and Brazil [29]	HCT recipients (adults and children)	Not reported	61	Cases per 1000 HCT: 5.97 overall; 6.18 in Brazil, 5.89 in the USA; 4.21–5.0 in MRD, 2.28 in HLA-compatible MUD, 20.19 in MMRD, 1.4–2.0 in autologous
Brazil [33]	Adults and children with AML/MDS or HCT	937	23	1-year cumulative incidence: 5.2% in allogeneic HCT, 3.8% in AML/MDS, 0.6% in autologous HCT
Brazil [34]	Adults and children with AML/MDS, ALL or HCT	192	3	1.6% overall; 4.3% in AML/MDS, 2.0% in autologous HCT
Brazil [35]	Adult patients with hematologic diseases	980	17	1.7% overall; 3.1% in allogeneic HCT; 3.1% in acute leukemia

HCT = hematopoietic cell transplantation; MRD = matched-related donor; MUD = matched-unrelated donor; MMRD = mismatched-related donor; AML = acute myeloid leukemia; MDS = myelodysplasia; ALL = acute lymphoid leukemia.

Invasive Fusariosis in Patients with Hematologic Diseases

	Fusariosis	Aspergillosis
Most common setting	Acute leukemia, induction remission and allogeneic HCT ¹	Acute leukemia, induction remission and allogeneic HCT
Mode of acquisition	Airways and skin at sites of breakdown	Airways
Hospital reservoirs	Air and water	Air and water
Clinical manifestations [44]		
Fever	Yes, 96%	Yes, 64%
Pneumonia	Yes, 50%	Yes, 89%
Nodules with halo sign	Yes, 23%	Yes, 62%
Centrilobular micronodules	Yes, 54%	Yes, 44%
Tree-in-bud infiltrates	Yes, 8%	Yes, 12%
Sinusitis	Yes, 38%	Yes, 64%
Skin lesions	Yes, 73%	No
Positive blood cultures	Frequent	Rare
Positive serum galactomannan [44]	Yes, 73%	Yes, 89%
Positive 1,3-beta-D-glucan	Yes	Yes

¹ HCT = hematopoietic cell transplantation.

Global guideline for the diagnosis and management of rare mould infections: an initiative of the European Confederation of Medical Mycology in cooperation with the International Society for Human and Animal Mycology and the American Society for Microbiology



Hoeningl et al, Lancet Infect Dis 2021

Strongly recommended
 Moderately recommended
 Marginally recommended
 Recommended against

	First-line	First-line alternative	Second-line	Treatments to avoid	Salvage treatments
Fusariosis	Voriconazole, or voriconazole plus L-AmB, or voriconazole plus ABLC	L-AmB, or ABLC	Isavuconazole, or posaconazole	D-AmB	Posaconazole

The Antifungal Pipeline: Fosmanogepix, Ibrexafungerp, Olorofim, Opelconazole, and Rezafungin



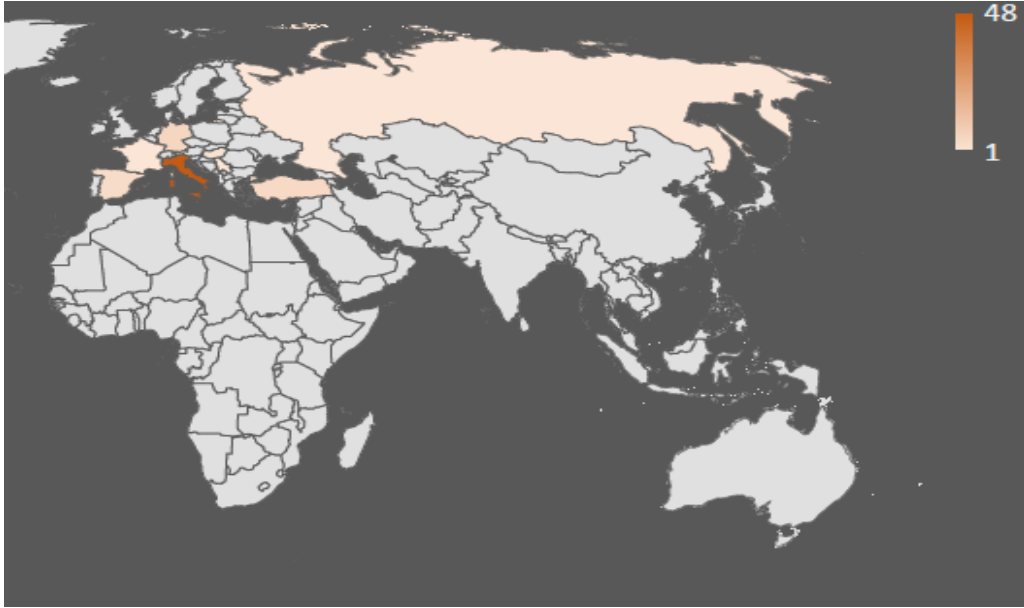
Fusarium spp.

Legend

- !!! Potent activity
- !? Variable activity
- X No activity
- ? Unknow / currently investigated

Hoeningl et al, Drugs 2021

Clinical features and prognostic factors of *Magnusiomyces* (*Saprochaete*) infections in haematology. A multicentre study of SEIFEM/Fungiscope



2010-2020
90 pts
75/90 blood infection

Patients Characteristic	N (%)	<i>S. capitata</i> N(%)	<i>S. clavata</i> N(%)	P value
Total patients	90	60(71%)	30(21%)	
Gender,				0.45
Male	44 (49%)	31(70%)	13(30%)	
Female	46 (51%)	29(63%)	17(27%)	
Age, years				.012
≥60 years	35(39%)	29(83%)	6(17%)	
<60 years	55(61%)	31(56%)	24(44%)	
Comorbidity				.71
Yes	35(39%)	24(68%)	11(31%)	
No	54(61%)	35(65%)	19(35%)	
Underlying HM				0.18
AML	50(65%)	34(51%)	16(33%)	
ALL	19(21%)	9(47%)	10(53%)	
NHL	13(16%)	9(69%)	4(31%)	
HL	2(2%)	2(100%)	0(0%)	
Others	6(6%)	6(75%)	0(0%)	
CVC				.58
Yes	71(79%)	46(65%)	25(35%)	
No	19(21%)	14(74%)	5(26%)	

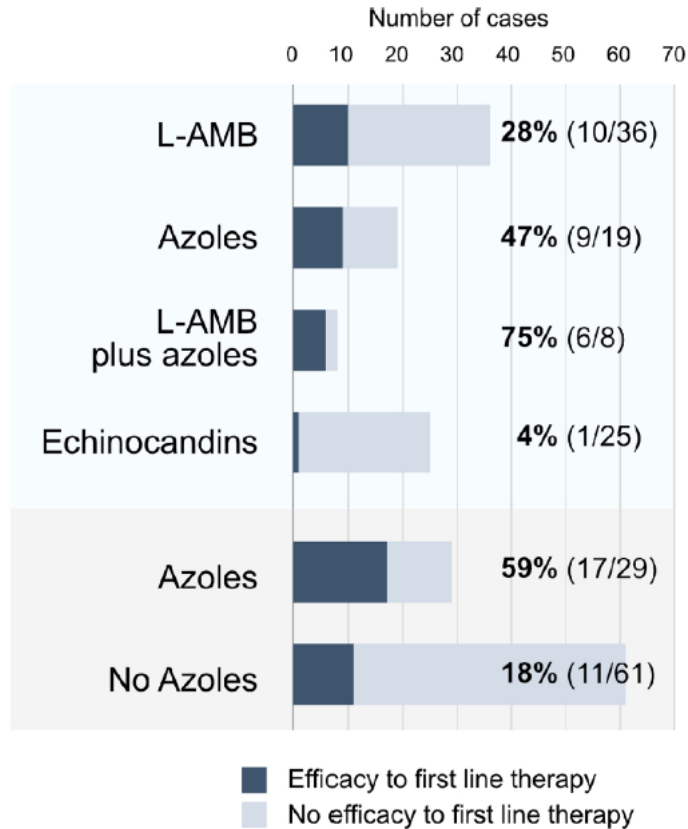


FIGURE 1 Response to first-line antifungal therapy by different antifungal agents used. AT, antifungal therapy; L-AMB, liposomal amphotericin B.

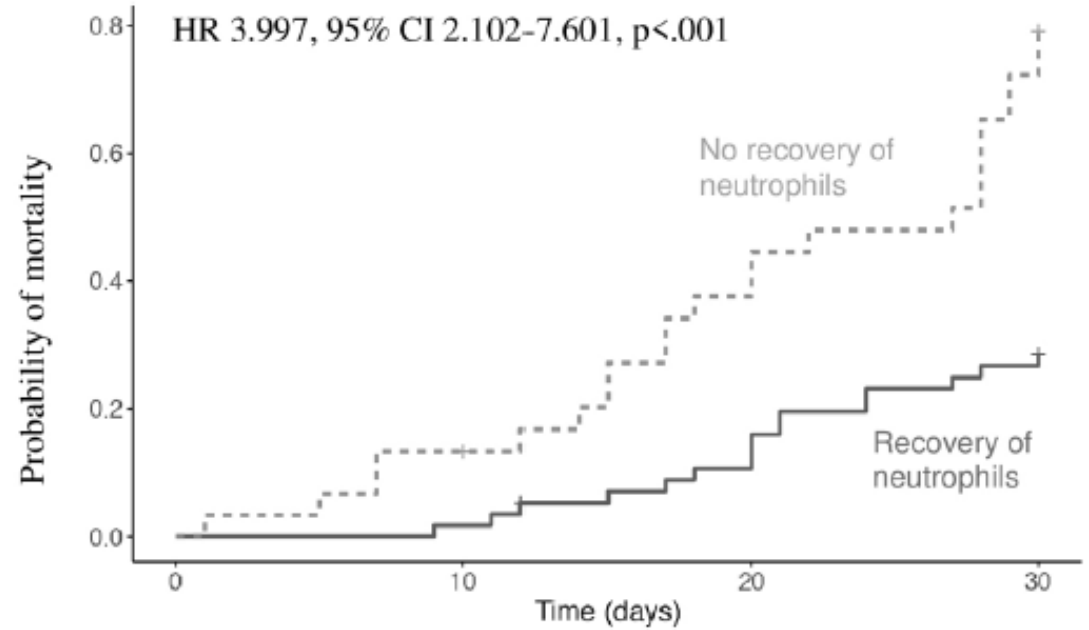
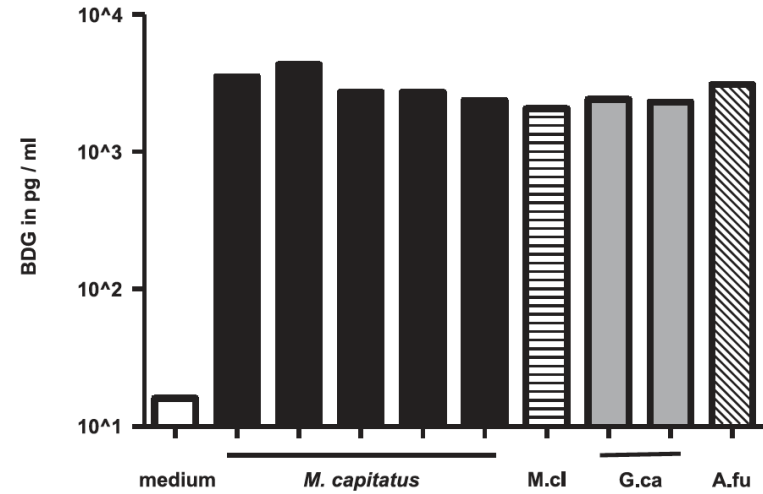
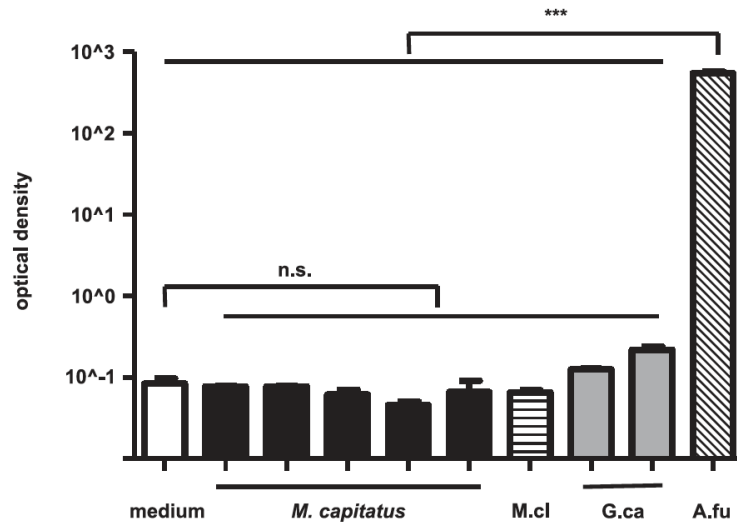


FIGURE 2 Overall Mortality (OM) based on neutrophil recovery. Kaplan-Meier plot comparing OM of patients with recovery of neutrophils (continuous dark gray line) versus OM of patients without recovery of neutrophils (dotted gray line)

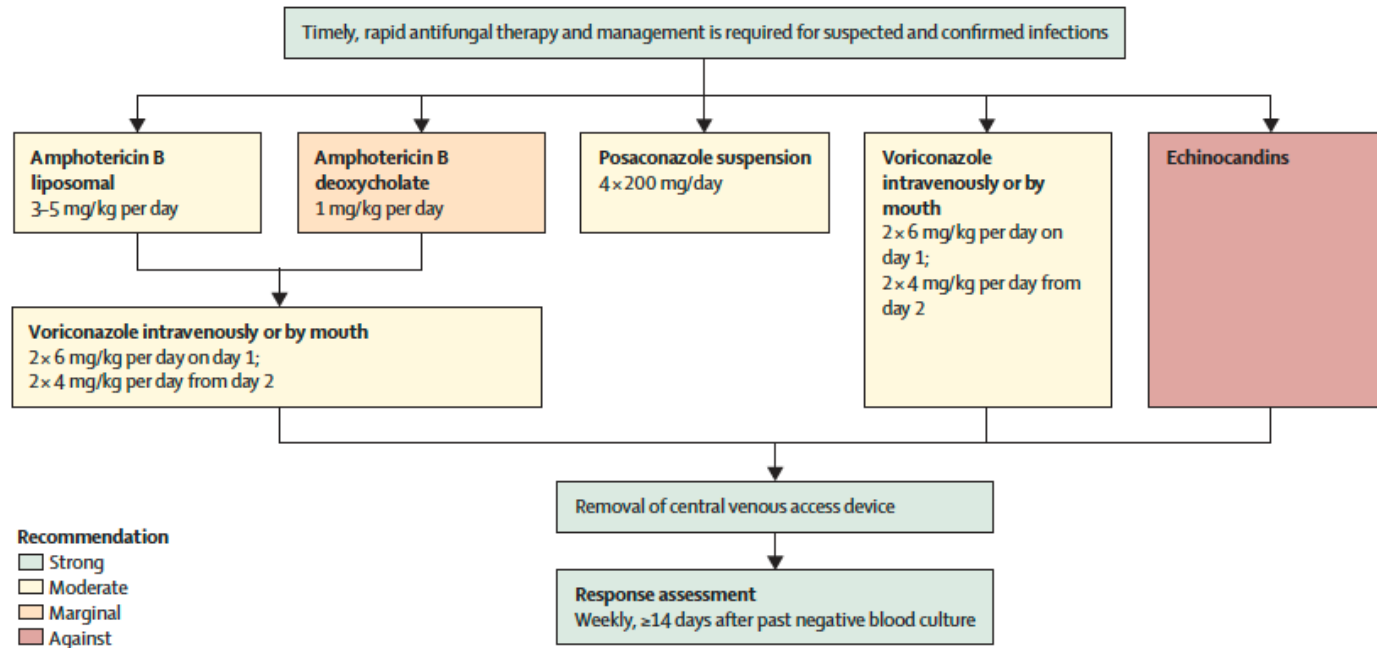
β -1,3-D-Glucan and Galactomannan as Biomarkers for the Detection of Invasive *Geotrichum* and *Magnusiomyces* Infections: a Retrospective Evaluation



While BDG sensitivity was 65%, none of the sera was GM positive. This finding was supported by in vitro experiments analyzing fungal culture supernatants: *M. capitatus* secretes significant amounts of BDG but not GM. Specificity was 96% for BDG and 100% for GM. BDG sensitivity is comparable to that of candidemia

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

Suspected and confirmed infections due to *Saprochaete* or *Magnusiomyces* spp are emergencies and require rapid action



Invasive infections due to *Saprochaete* and *Geotrichum* species:
Report of 23 cases from the FungiScope Registry

Host factor	n=23 (100%) ^a	Favourable response n (%)	Mortality n (%)
Chemotherapy	16 (70%)	6 (38%)	11 (69%)
Haematopoietic stem cell transplantation	8 (35%)	3 (38%)	5 (62%)
Diabetes mellitus	6 (26%)	3 (50%)	4 (67%)
Intensive care unit	5 (22%)	1 (20%)	4 (80%)
Chronic pulmonary diseases	3 (13%)	2 (67%)	1 (33%)
Chronic granulomatous disease	1 (4%)	1 (100%)	0 (0%)
Chronic renal disease	1 (4%)	1 (100%)	0 (0%)
Chronic alcohol abuse	1 (4%)	0 (0%)	1 (100%)
High-dose steroids	1 (4%)	0 (0%)	1 (100%)
Solid organ transplantation	1 (4%)	0 (0%)	1 (100%)
Trauma	1 (4%)	0 (0%)	1 (100%)

Duran Graeff et al, Mycoses 2014

Geotrichum capitatum
Trichosporon capitatum
Blastoschizomyces capitatus
Saprochaete capitata

Invasive Infections Caused by *Trichosporon* Species and *Geotrichum capitatum* in Patients with Hematological Malignancies: a Retrospective Multicenter Study from Italy and Review of the Literature

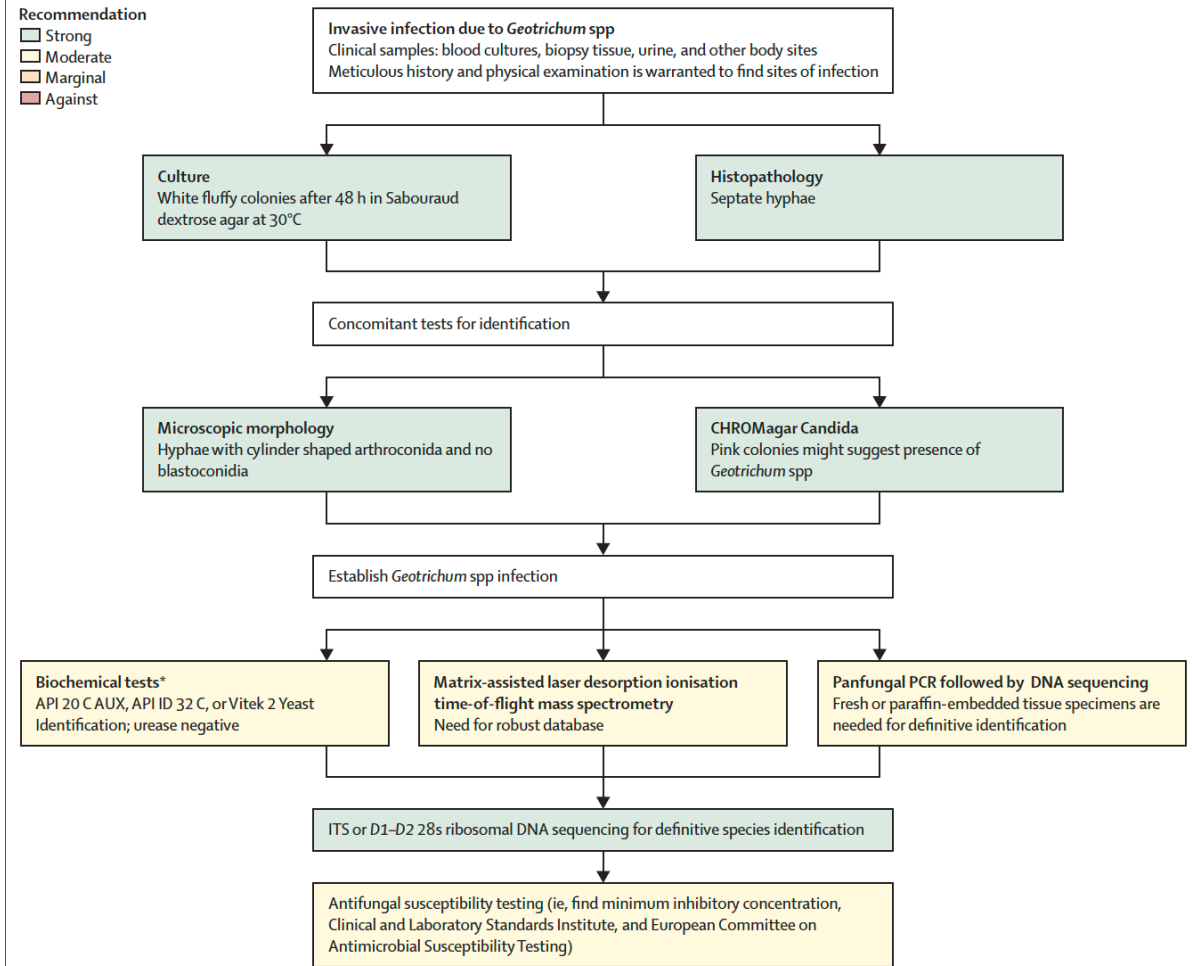
TABLE 2. Characteristics of the 396 cases of invasive *Trichosporon* spp. and *G. capitatum* infections in immunocompromised patients reported in the literature^a

Characteristic	<i>Trichosporon</i> spp. infection ^b (n = 287)	<i>G. capitatum</i> infection (n = 99)	<i>T. pullulans</i> infection (n = 8)	<i>T. loubieri</i> infection (n = 2)
Sex (male/female) [no. of evaluable cases]	138/65 [203]	56/28 [84]	6/1 [7]	1/1 [2]
Mean age (range) [no. of evaluable cases]	40 (1–78) [205]	44 (1–76) [80]	57 (47–65) [7]	50 (45–56) [2]
Underlying disease or condition, no. of evaluable cases	266	96	8	2
Hematological disease, no. of cases (%)	167 (62.8)	88 (91.7)	6 (75)	1 (50)
Solid tumor, no. of cases (%)	18 (6.8)	3 (3.1)	1 (12.5)	
Organ transplant, no. of cases (%)	10 (3.8)	0	1 (12.5)	
Prosthetic cardiac valve, no. of cases (%)	10 (3.8)	2 (2.1)		
Peritoneal dialysis, no. of cases (%)	22 (8.3)	0		
HIV infection, no. of cases (%)	4 (1.5)	0		
Newborn, no. of cases (%)	15 (5.6)	1 (1.0)		
Burn, no. of cases (%)	5 (1.9)	0		
Other diseases or conditions, no. of cases (%)	15 (5.6)	2 (2.1)		1 (50)

Girmenia et al, JCM 2005

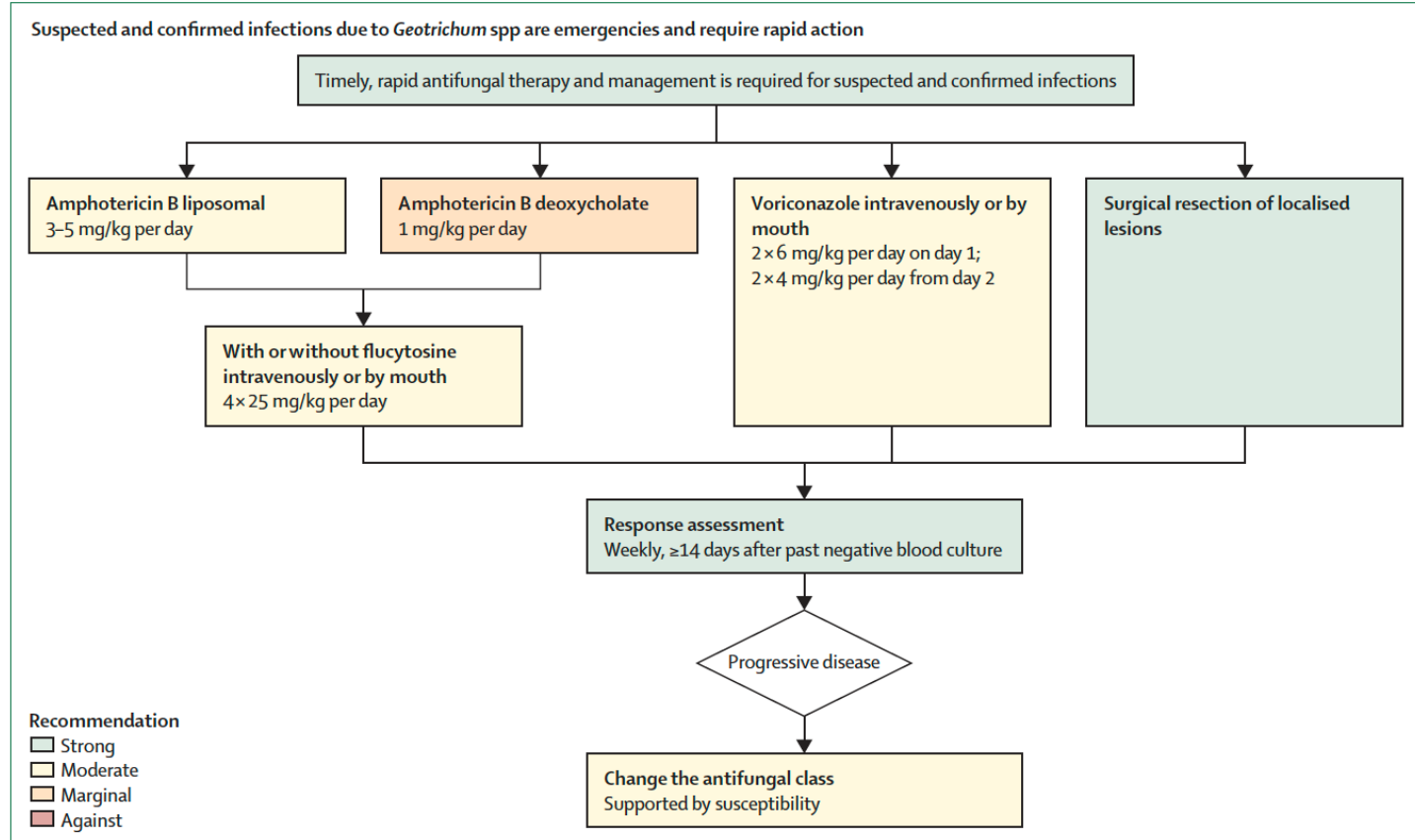
Global guideline for the diagnosis and management of rare yeast infections: an initiative of the ECMM in cooperation with ISHAM and ASM

Geotrichum spp.



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

Geotrichum spp.



Key points

- A high level of suspicion is required
- Knowledge of the risk factors
- Prompt investigation with multiple tools
- Species identification critical to guide antifungal therapy
- Molecular tools are increasingly available and used for diagnosis
- Antifungal treatment is evolving
- Further research is required in the area of diagnostics and the development of further novel antifungal agents