Challenges for the Diagnostic Lab

Is phenotypic identification only to species complex acceptable?

Ana Alastruey-Izquierdo

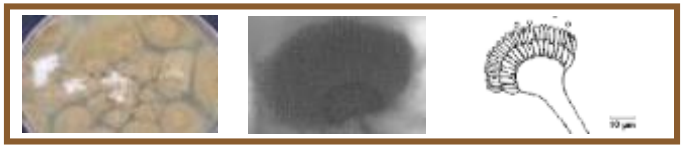
Mycology Reference Lab Spain

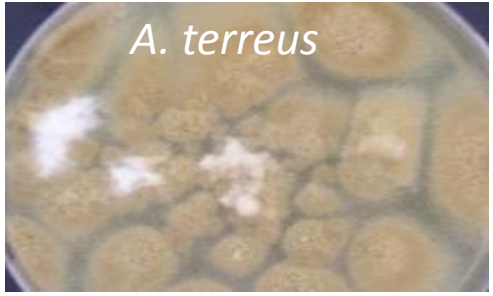
National Centre for Microbiology

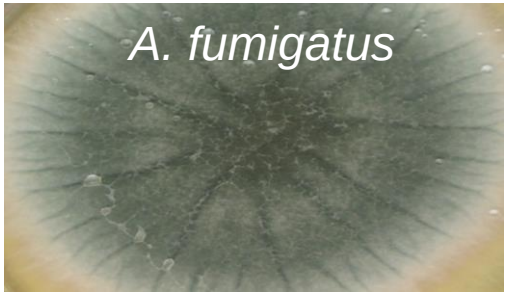
Instituto de Salud Carlos III

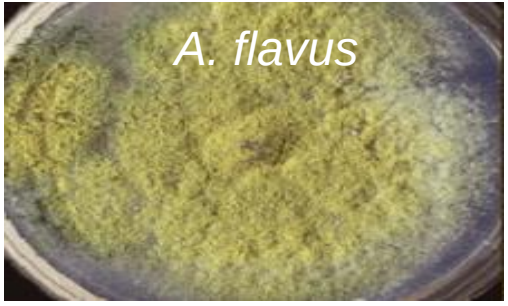
- **Is phenotypic identification only to species complex acceptable?**

Clinically relevant *Aspergillus*

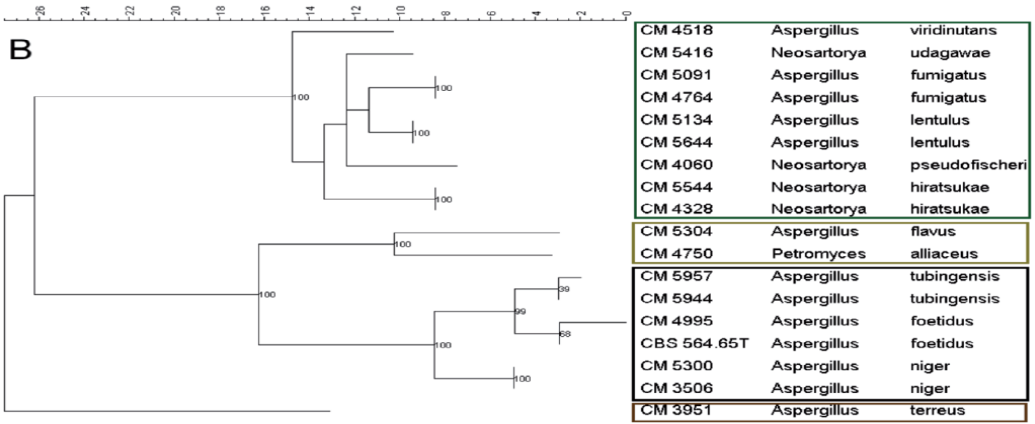


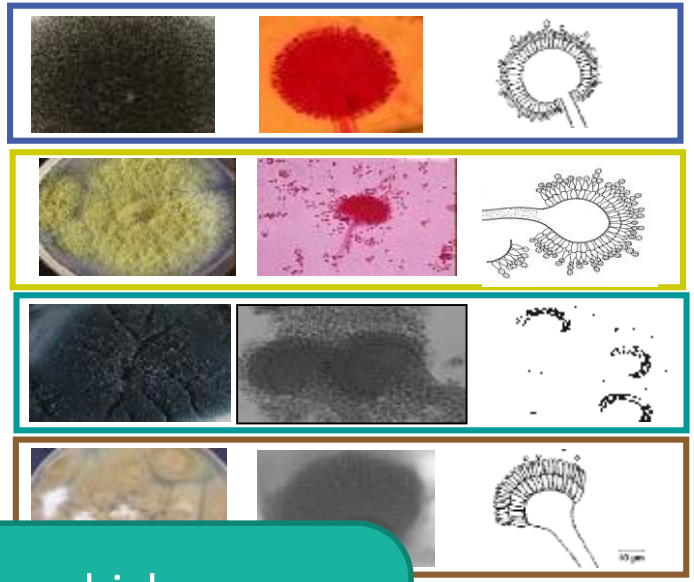






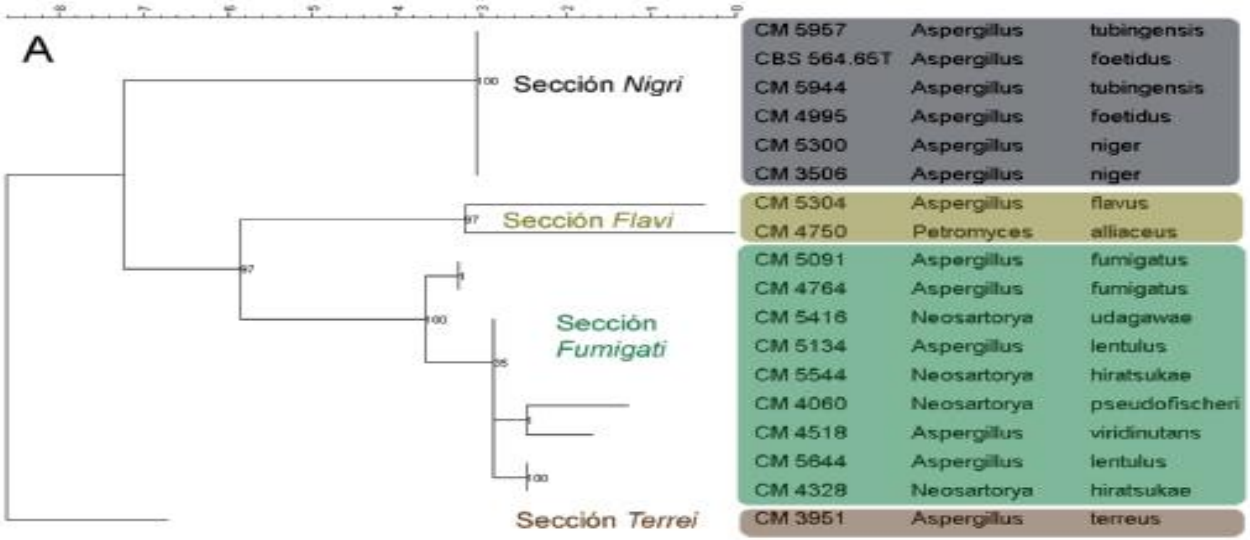
Species complex





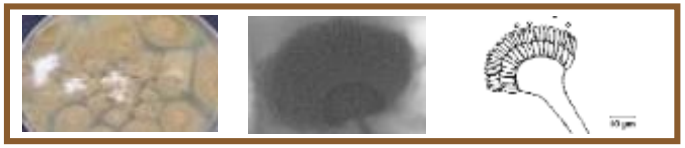
Cryptic species are defined as those which are morphologically indistinguishable, although their identifications can be confirmed using molecular or other techniques

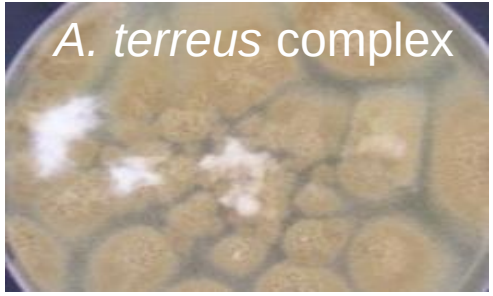
Species complex

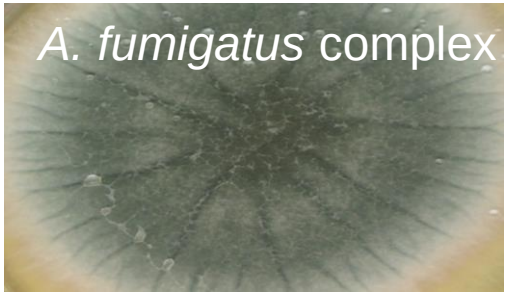


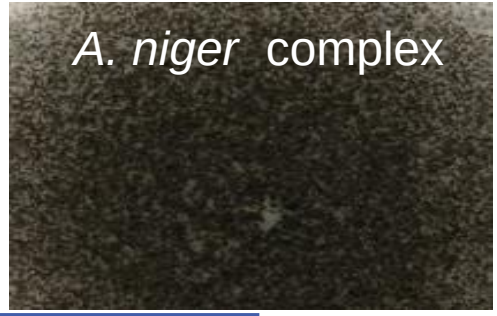
Aspergillus species complex

Clinically relevant *Aspergillus*

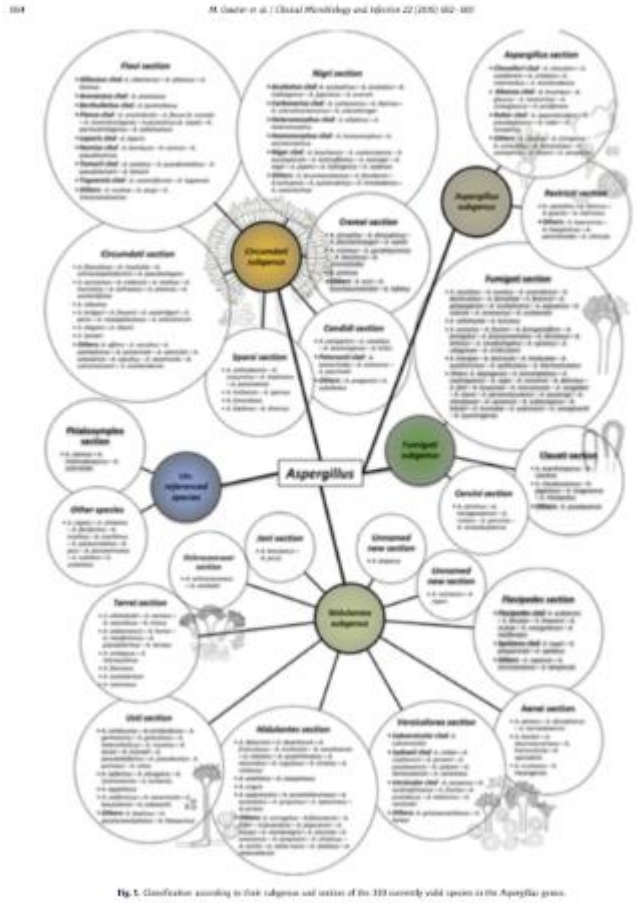






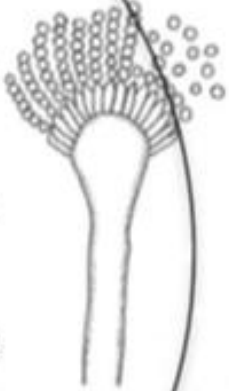


Species complex



Fumigati section

- *A. assulatus – A. auratus – A. australensis – A. denticulatus – A. fennelliae – A. ferenczii – A. galapagensis – A. multiplicatus – A. papuensis – A. solicola – A. stramenius – A. unilateralis*
- *A. nishimurae – A. turcosus*
- *A. aureolus – A. fischeri – A. fumigatiaffinis – A. fumigatus – A. fumisynnematus – A. laciniosus – A. lentulus – A. novofumigatus – A. spinosus – A. udagawae – A. viridinutans*
- *A. brevipes – A. duricaulis – A. hiratsukae – A. quadricinctus – A. spathulatus – A. thermomutatus*
- *Others: A. beijingensis – A. brevistipitatus – A. caatingaensis – A. cejpii – A. conversis – A. delicatus – A. felis – A. huiyaniae – A. marvanovae – A. neoglaber – A. otanii – A. pernambucoensis – A. qizutongii – A. shendaweii – A. siamensis – A. sublevisporus – A. takakii – A. tsunodae – A. waksmanii – A. wangduanlii – A. wyomingensis*



Gautier et al CMI 2016

Cryptic species

JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 2004, p. 925–928
0095-1137/04/$08.00+0 DOI: 10.1128/JCM.42.2.925–928.2004

Vol. 42, No.

Isolation of *Neosartorya pseudofischeri* from Blood: First Hint of Pulmonary Aspergillosis

H. Järv,[1]* J. Lehtmaa,[2] R. C. Summerbell,[3] E. S. Hoekstra,[3] R. A. Samson,[3] and P. Naaber[1]

Bathoorn et al. BMC Infectious Diseases 2013, 13:39
http://www.biomedcentral.com/1471-2334/13/39

BMC Infectious Diseases

CASE REPORT Open Access

Involvement of the opportunistic pathogen *Aspergillus tubingensis* in osteomyelitis of the maxillary bone: a case report

Erik Bathoorn[1,2*], Natalia Escobar Salazar[3], Shahrzad Sepehrkhouy[2], Martin Meijer[4], Hans de Cock[3] and Pieter-Jan Haas[1]

JOURNAL OF CLINICAL MICROBIOLOGY, June 2011, p. 2357–2360
0095-1137/11/$12.00 doi:10.1128/JCM.00134-11

Vol. 49, No. 6

Uncommon *Neosartorya udagawae* Fungus as a Causative Agent of Severe Corneal Infection

Brunella Posteraro,[1] Romano Mattei,[2] Fausto Trivella,[3] Andrea Maffei,[3] Antonio Torre,[3] Elena De Carolis,[1] Patrizia Posteraro,[4] Giovanni Fadda,[1] and Maurizio Sanguinetti[1]*

informa
Healthcare

nce-Based Methods

Mark D. Lindsley,[1] Naureen Iqbal,[1] James Ito,[2] Pappas,[3] and Mary E. Brandt[1]

Medical Mycology November 2010, 48, 990–999

Case Report

Aspergillus alliaceus and *Aspergillus flavus* co-infection in an acute myeloid leukemia patient

BETIL OZHAK-BAYSAN*, ANA ALASTRUEY-IZQUIERDO†, RABIN SABA‡, DILARA OGUNC*, GOZDE ONGUT*, AYSEN TIMURAGAOGLU§, GOKHAN ARSLAN¶, MANUEL CUENCA-ESTRELLA† & JUAN LUIS RODRIGUEZ-TUDELA†

Josep Guarro,* Esper G. Kallas,†‡ Patricio Godoy,† Anna Karenina, †‡ Josepa Gené,* Alberto Stchigel,* and Arnaldo Lopes Colombo†

We report the first case of infection by *Neosartorya hiratsukae*, an ascomycete in which the conidial state resembles *Aspergillus fumigatus*. The fungus caused a brain infection in a Brazilian woman, who died despite itraconazole treatment. Diagnosis was established by direct microscopic examination, computed tomographic scan, and magnetic resonance imaging of the brain, and repeated cultures from the lesions. The in vitro antifungal susceptibility of the isolate is provided.

and repetitively, with a loss of strength. Tendon reflexes were normal. The patient underwent surgical exploration, with drainage of the frontal and occipital lesions. Four samples of a yellowish, dense liquid were collected. Laboratory examination did not show neoplastic cells or neutrophils in the liquid. Direct microscopic examination showed septate hyphae in all the samples. Cultures were negative for aerobic and anaerobic bacteria and mycobacteria, and two samples were positive for a fungus, tentatively identified as *Aspergillus* sp. The patient was initially treated for 21 days with ceftriaxone, oxacillin, and metronidazole without major improvement. When the fungus was isolated, she was treated with amphotericin B and underwent postoperative magnetic resonance imaging (MRI) of

Chronic Invasive Aspergillosis caused by *Aspergillus viridinutans*

Donald C. Vinh,[1] Yvonne R. Shea,[1] Pamela A. Jones, Alexandra F. Freeman, Adrian Zelazny, and Steven M. Holland

Aspergillus viridinutans, a mold phenotypically resembling *A. fumigatus*, was identified by gene sequence analyses from 2 patients. Disease was distinct from typical aspergillosis, being chronic and spreading in a contiguous manner across anatomical planes. We emphasize the recognition of fumigati-mimetic molds as agents of chronic or refractory aspergillosis.

infiltrate was noted. Antifungal therapy was changed to posaconazole. Over the next 2 months, there was expansion of the right lung infiltrates and lymphadenopathy. Treatment was modified to posaconazole and caspofungin. Serial imaging over the next 3 weeks showed regression of the lung consolidations and mediastinal mass. Four months later, with ongoing resolution of the thoracic disease, the patient began receiving a maintenance dosage of posaconazole. As of 5 years later, he had experienced no recurrence.

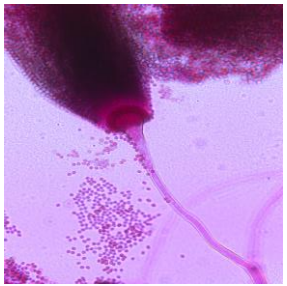
Patient 2 was an 8-year-old boy with hyperimmunoglobulin-E (Job) syndrome due to mutation in signal transducer and activator of transcription-3 in whom a right-sided pulmonary abscess developed and failed to improve after 1 month of antibacterial therapy. New left lung nodules were biopsied and specimens yielded a mold morphologically identified as *A. fumigatus*. During 3 months of treatment with voriconazole, the bilateral pulmonary lesions cavitated. Two months later, left lower lobe wedge resection yielded the same mold. Diaphragmatic injury required primary closure with sutures. One month later,

Annette Fothergill, [4] and Kieren A. Marr[1,5]*

Some things to consider

- Are they common?
- Are they more resistant?
- Do they translate into poorer outcomes?
- Is the susceptibility pattern predictable?

Cryptic species



11% cryptic species

14% cryptic species

Table 1. *Aspergillus* speci… …idemiological surveys from Spain and the U. S.[22]

Species	Section	Transnet N isolates	Transnet %	FILPOP N isolates	FILPOP %
A. fumigatus	Fumigati	139	63.8	156	56.1
A. lentulus	Fumigati	4	1.8	3	1.1
A. udagawae	Fumigati	3	1.4	0	0.0
N. pseudofischeri	Fumigati	1	0.5	1	0.4
A. viridinutans	Fumigati	0	0.0	1	0.4
A. fumigatiafinis	Fumigati	0	0.0	1	0.4
A. flavus	Flavi	29	13.3	27	9.7
A. alliaceus	Flavi	0			
A. terreus	Terrei	11			
A. carneus	Terrei	0			
A. tubingensis	Nigri	6			
A. niger	Nigri	13			
A. calidoustus	Usti	6			
A. insuetus	Usti	0	0.0	1	0.4
A. keveii	Usti	0	0.0	1	0.4
A. sydowii	Versicolores	2	0.9	1	0.4
A. versicolor	Versicolores	3	1.4	0	0.0
E. quadrilineata	Nidulantes	1	0.5	0	0.0
A. nidulans	Nidulantes	0	0.0	8	2.9
A. westerdijkiae	Circumdati	0	0.0	1	0.4
Total		218	100	278	100

Chowdhary et al. (2016)
16.6% cryptic species

Balajee et al, JCM 2009

Alastruey-Izquierdo et al. AAC 2013

Alustruey- Izquierdo et al. 2012, Ann N Y Acad Sci. 1273:18-24

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Cryptic species

	n	AMB	ICZ	VCZ	PCZ	CPF	MCF	ANF
A. lentulus	26	**3**	**2.3**	**3.4**	**0.23**	1.6	0.1	0.1
N. hiratsukae	9	1.7	0.9	1.1	0.16	0.11	0.03	0.03
N. pseudofischerii	6	0.25	**4**	**2.51**	**0.22**	0.86	0.03	0.03
A. fumigatiaffiinis	6	**4.8**	**5**	**3.1**	**0.4**	0.22	0,03	0,03
N. udagawae	5	**2**	0.6	**2.3**	**0.25**	0.3	0.03	0.03
A. viridinutans	3	0,7	**16**	**4**	**0,25**	5,66	0,06	0,09
A. tubingensis	22	0.11	0.42	0.76	0.09	0.3	0.05	0.03
A. calidoustus	19	0.9	**8.6**	**6.2**	**6.8**	0.5	0.04	0.04
A. insuetus	2	0.7	**11.3**	**8**	**2.8**	5.6	1.4	0.9
A. keveii	1	0,25	**16**	**16**	**16**	16	16	16
A. alliaceus	30	**19.25**	0.2	0.5	0.11	12.15	3.8	1.9

Some things to consider

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MICs distribution for AMB

Table II. Response to antifungal therapy in patients with IA caused by *Aspergillus terreus* and non-*A. terreus* between 1994 and 2004.

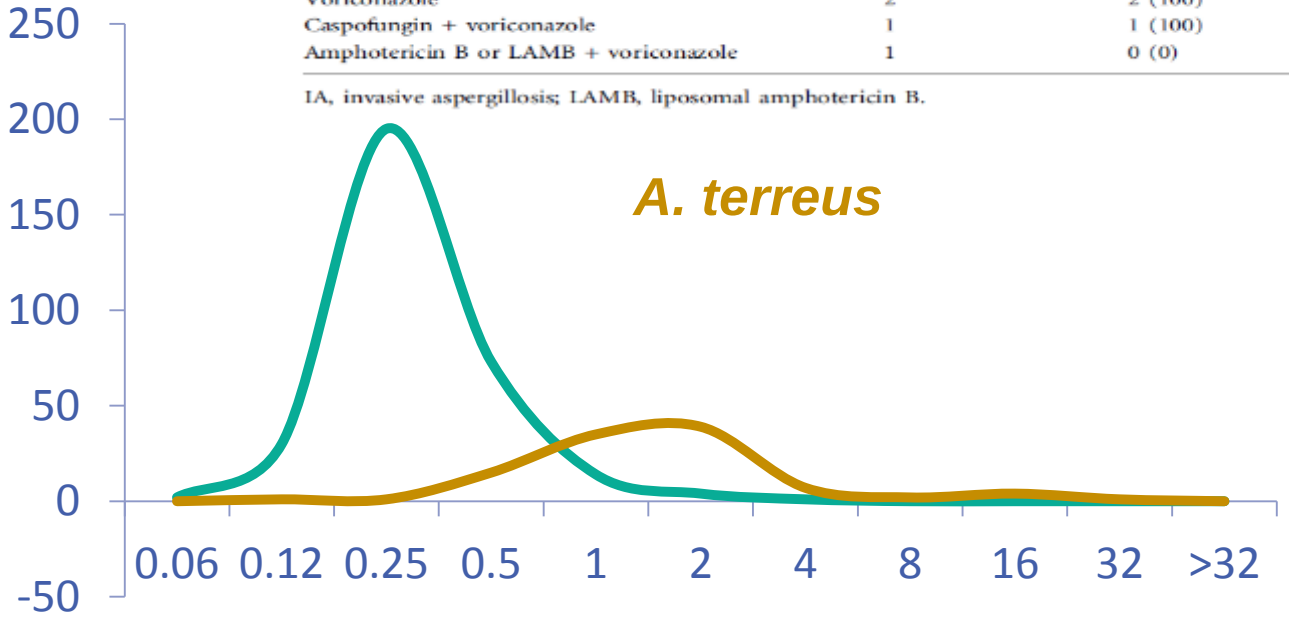
Treatment	*A. terreus*		Non-*A. terreus*	
	Patients (*n*)	R	Patients (*n*)	
Amphotericin B	13	1 (8)	14	5 (36)
LAMB	11	4 (36)	9	6 (67)
Itraconazole	4	2 (50)	2	1 (50)
Voriconazole	2	2 (100)	5	3 (60)
Caspofungin + voriconazole	1	1 (100)	3	3 (100)
Amphotericin B or LAMB + voriconazole	1	0 (0)	2	1 (50)

IA, invasive aspergillosis; LAMB, liposomal amphotericin B.

20%

47%

Lass-Flörl et al. *BJH* 2005



Data obtained from Mycology Reference Laboratory. Spain

Clinical significance

Alastruey-Izquierdo AAA 2018

Table 4. Characteristics of patients with azole-resistant invasive aspergillosis, the Netherlands, 2007–2009*

Patient age, y/ sex	Underlying disease	Disease	No. positive cultures†	Resistance mechanism	VCZ MIC, mg/L	Prior azole treatment (duration)‡	Treatment§	Outcome at 12 wk
66/M	Lung carcinoma	Proven pulmonary aspergillosis	1	TR/L98H	4	None	VCZ	Died
59/M	Hematologic malignancy, allo-SCT, GvHD	Proven pulmonary aspergillosis	4	TR/L98H	8	VCZ (>1 mo)	VCZ	Died
54/M	Acute myeloid leukemia relapse, all	Proven pulmonary	1	TR/L98H	8	ITZ (2–4 wk)	VCZ	Died
50/M	Non-Hodgkin allo-SCT, G caviti						VCZ	Died
36/F	Breast carcir metast						VCZ	Died
13/F	Non-Hodgkin						Z, CAS, AMB	Died
58/M	Liver transpla hepatic failure after methotrexate treatment for arteritis	CNS aspergillosis					B, VCZ	Died
60/M	Acute myeloid leukemia, allo-SCT, GvHD	Proven pulmonary and CNS aspergillosis	3	TR/L98H	4	FCZ (1–2 wk)	VCZ, CAS, AMB, POS	Survived

*VCZ, voriconazole; allo-SCT, allogeneic hematopoietic stem cell transplantation; GvHD, graft-versus-host disease; HSCT, hematopoietic stem cell transplantation; ITZ, itraconazole; CNS, central nervous system; CAS, caspofungin; AMB, amphotericin B; FCZ, fluconazole; POS, posaconazole.
† All cultures were *Aspergillus fumigatus*.
‡Azole treatment <12 wk before the first culturing of an azole-resistant isolate.
§Azole treatment after first culturing of resistant isolate.

	Aspergillosis	
	Susceptible strains	Resistant strains
Mortality	30-50%	88%

Van der Linden et al. Emerg Infect Dis 2011; 17:1846–1854.

A. lentulus

Alastruey-Izquierdo AAA 2018

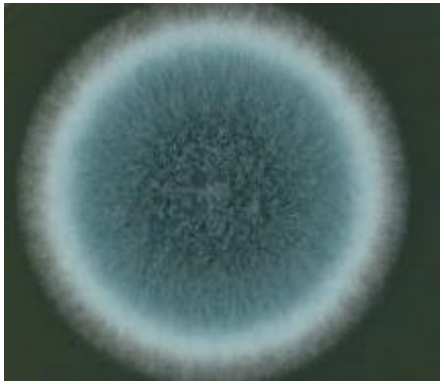
Summary on published clinical cases caused by *Aspergillus lentulus*

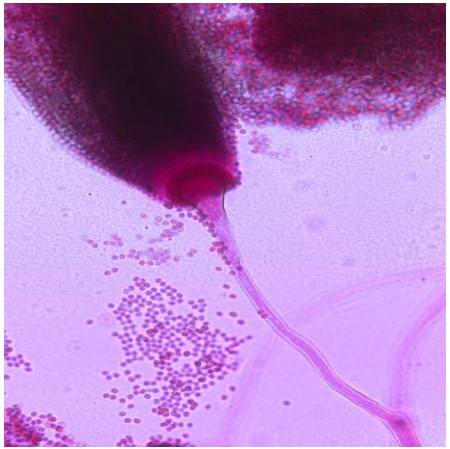
Year (Reference)	Number of patients	Underlying disease/ procedure	Source of isolate	Disease classification	Species identification	Susceptibility pattern	Treatment	Outcome
2004 (10)	4	Stem cell transplantation	Lung, mouth, kidney	Proven or probable IA	Genotypic	MIC Itra 0.5–2 mg/L, Vor 2–4 mg/L, AmB 1–4 mg/L; MEC Cas 4–>32 mg/L	NR	Died
2008 (11)	1	Chronic obstructive lung disease	Lung	Probable IA, Co-infection with *A. fumigatus*	Genotypic	MIC AmB 4 mg/L, Itra 3 mg/L, Vor 1.5 mg/L; MEC Cas >32 mg/L	Vor	Died
2009 (12)	1	Kidney transplantation	Lung	Probable IA, Co-infection with *A. fumigatus*	Genotypic	MIC Vor 2 mg/L, AmB 2 mg/L; MEC Cas >16 mg/L	L-AmB	Died
2009 (4)	4	Stem cell transplantation	Lung	Proven or probable IA	Genotypic	MIC AmB 0.5–2 mg/L, Itra 0.25–0.5 mg/L, Vor 1–4 mg/L, Pos 0.25 mg/L	NR	NR
2010 (13)	1	Cystic fibrosis	Lung	Colonization	Genotypic	MIC AmB 4 mg/L, Itra 2 mg/L, Vor 8 mg/L	NR	NR
2011 (14)	1	Cystic fibrosis	Lung	Colonization	Genotypic	MIC AmB 2 mg/L, Itra 2 mg/l, Vor 2 mg/L, Pos 0.5 mg/L	NR	NR
2012 (current report)	1	Heart transplantation	Lung	Proven IA	Genotypic	MIC AmB 2.0 mg/L, Itra 0.25 mg/L, Vor 1.0 mg/L, Pos 0.125 mg/L; MEC Cas 16 mg/L	Vor, Cas, AmB	Died

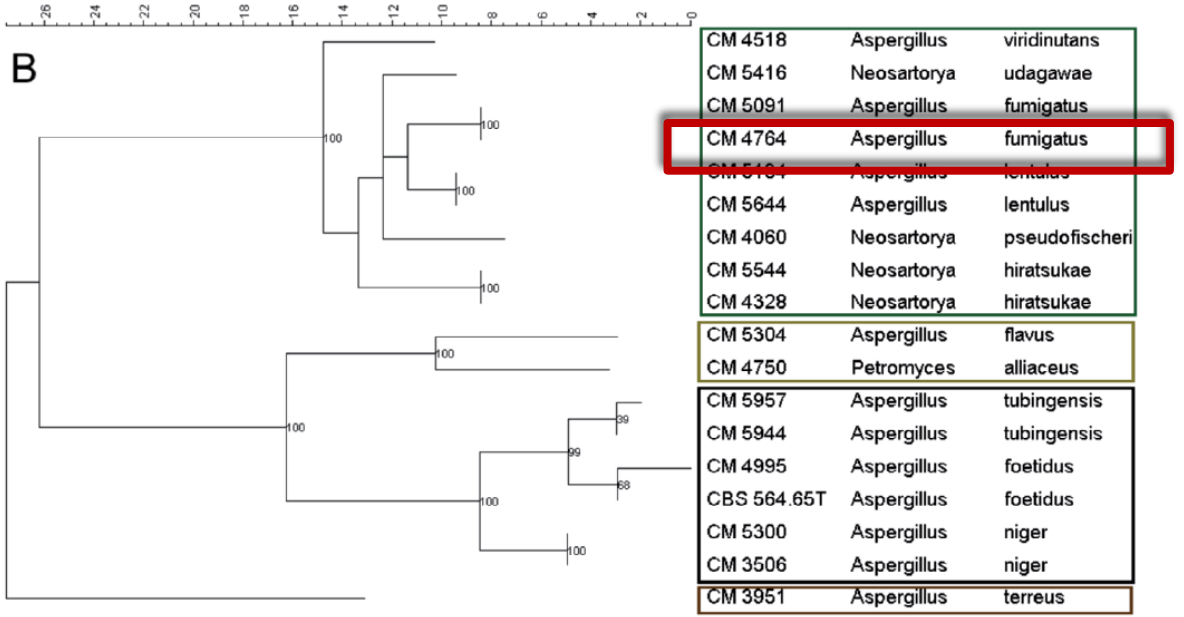
Zbinden et al, TID 2012

- **Is phenotypic identification only to species complex acceptable?**

A. fumigatus s.s.

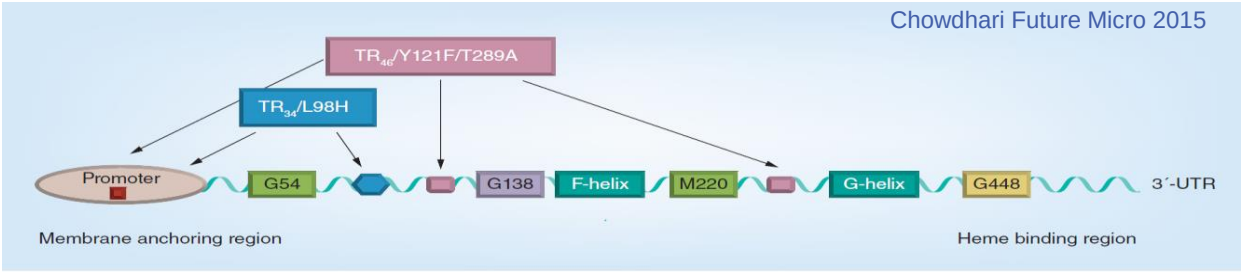


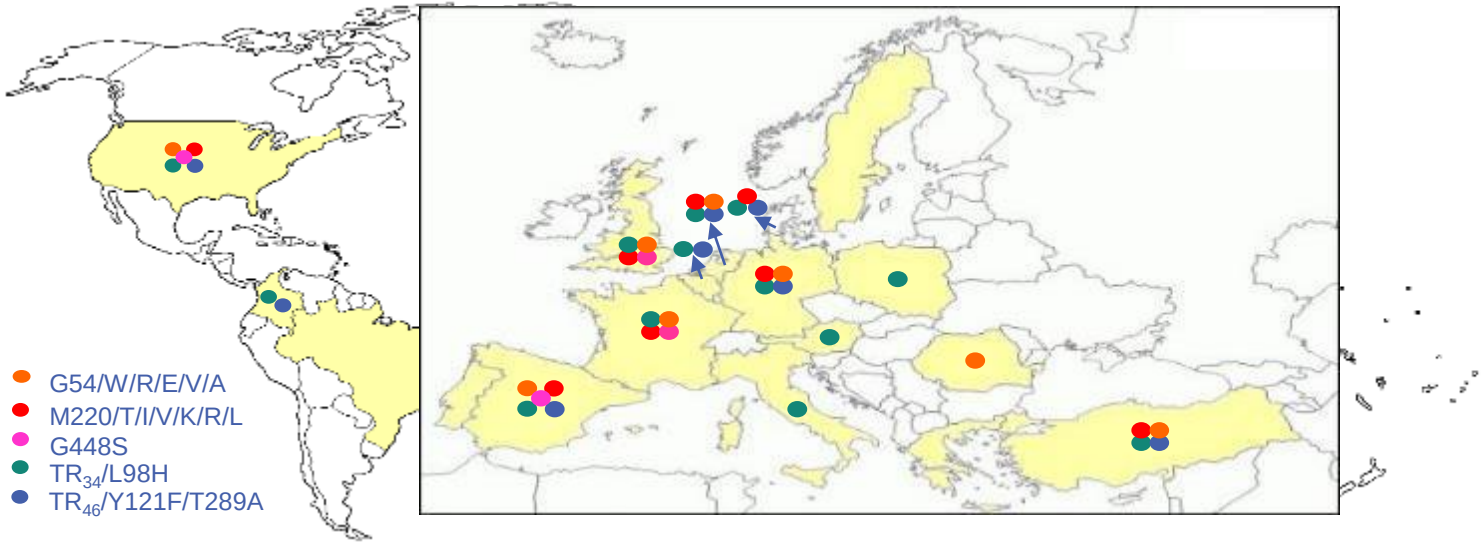




A. fumigatus s.s.

Chowdhari Future Micro 2015





Rivero-Menéndez Journal of Fungi 2016

A. fumigatus s.s.

Table 2. Azole resistance prevalence in *A. fumigatus* by continent and/or country. Only significant publications with more than 50 isolates tested are reported.

Continent/Country	% Resistance	Source of the Isolates	References
	Europe		
Belgium	5.7	C	[76]
France	0.85–10.6	C	[30,48,50]
Germany	1.1–12	C and E	[32,47,60]
Netherlands	2.1–20	C and E	[20,53,67,74]
Poland	2.25	C	[69]
Spain	1.8	C	[63]
Turkey	10.2	C	[71]
United Kingdom	6.6–28	C	[17,33]
	Other continents		
Asia *	1.9–11.1	C and E	[55,77,78,80–86,121]
Africa (Tanzania)	13.9	E	[90]
America (USA)	0.6–11.8	C	[58,122]
Oceania (Australia)	2.6	C	[59]
	International surveillance studies		
America-Asia-Australia-Europe	1.4–5.8	C and E	

C = clinical strains, E = environmental strains; * including China, India, Iran, J

Rivero-Menéndez Journal of Fungi 2016

Snelders et al., PLOS 2008

Local epidemiology

Some things to consider

- Are they common?
- Are they more resistant?
- Do they translate into poorer outcomes?
- Is the susceptibility pattern predictable?

Table 2 Susceptibility profile of cryptic *Aspergillus* species isolated in the Mycology Reference Laboratory of Spain

Species (no.)		MIC (mg/L)				MEC (mg/L)			
		AMB	ICZ	VCZ	PCZ	TRB	CPF	MCF	ANF
A. alliaceus (30)	GM	19.25	0.20	0.52	0.12	0.44	12.15	3.78	1.98
	Range	0.5–32.00	0.03–16.00	0.12–16.00	0.015–16.00	0.03–32.00	0.12–32.00	0.03–32.00	0.03–32.00
	MIC_{50}	32.00	0.12	0.50	0.06	0.25	32.00	32.00	32.00
	MIC_{90}	32.00	2.00	2.00	0.50	32.00	32.00	32.00	32.00
A. calidoustus (19)	GM	0.96	8.61	6.20	6.86	0.72	0.52	0.04	0.04
	Range	0.12–32.00	1.00–16.00	4.00–16.00	1.00–16.00	0.032–32.00	0.03–32.00	0.03–1.00	0.03–0.50
	MIC_{50}	1.00	16.00	8.00	16.00	0.50	1.00	0.03	0.03
	MIC_{90}	16.00	16.00	8.00	16.00	4.00	4.00	0.06	0.25
A. fumigatiaffinis (6)	GM	4.76	2.17	1.83	0.27	0.65	0.27	0.04	0.05
	Range	2.00–16.00	0.25–16.00	2.00–8.00	0.12–4.00	0.25–4.00	0.03–0.50	0.03–0.06	0.03–0.25
	MIC_{50}	16.00	16.00	4.00	0.50	1.00	0.50	0.03	0.03
	MIC_{90}	16.00	16.00	8.00	4.00	3.00	0.50	0.06	0.25
A. hiratsukae (5)	GM	1.74	0.87	1.15	0.16	2.30	0.29	0.06	0.12
	Range	0.50–32.00	0.12–16.00	0.25–16.00	0.03–6.00	0.12–32.00	0.03–4.00	0.03–0.50	0.03–2.00
	MIC_{50}	1.00	0.50	1.00	0.06	1.00	0.50	0.03	0.03
	MIC_{90}	32.00	16.00	16.00	16.00	32.00	4.00	0.50	2.00
A. lentulus (26)	GM	2.98	1.45	3.41	0.22	1.05	1.74	0.10	0.09
	Range	0.25–32.00	0.12–16.00	0.25–16.00	0.03–1.00	0.12–32.00	0.03–32.00	0.03–32.00	0.03–32.00
	MIC_{50}	4.00	0.50	4.00	0.25	0.75	2.00	0.03	0.03
	MIC_{90}	16.00	16.00	8.00	0.50	16.00	32.00	32.00	32.00
A. tubingensis (29)	GM	0.10	0.63	0.91	0.12	0.31	0.28	0.04	0.03
	Range	0.06–2.00	0.12–32.00	0.25–2.00	0.03–0.50	0.03–2.00	0.06–1.00	0.03–0.25	0.03–0.06
	MIC_{50}	0.12	0.50	1.00	0.12	0.50	0.50	0.03	0.03
	MIC_{90}	0.12	2.00	2.00	0.25	1.00	1.00	0.12	0.03
A. udagawae (5)	GM	2.00	0.57	2.30	0.22	0.66	0.33	0.04	0.03
	Range	0.50–4.00	0.25–1.00	2.00–4.00	0.12–0.25	0.25–2.00	0.25–2.00	0.03–0.12	0.03–0.06
	MIC_{50}	2.00	0.50	2.00	0.25	0.50	0.50	0.03	0.03
	MIC_{90}	4.00	1.00	4.00	0.25	2.00	2.00	0.12	0.05

struey-Izquierdo AAA 2018

Alastruey-Izquierdo et al. Mycopathologia 2014

Aspergillus terreus complex

Table 1
Distribution of amphotericin B MICs against *Aspergillus terreus* species complex isolates collected during the study period and tested according to EUCAST methodology

Aspergillus species	Amphotericin B MICs, mg/L								
	0.125	0.25	0.5	1	2	4	8	16	32
A. terreus sensu stricto	3	7	10	14	36	81	86	55	23
A. citrinoterreus					3	13	8	7	5
A. hortai					1	2	5	2	
A. alabamensis					2	3	1		
A. floccosus						1			
A. neoafricanus									1
Potential new species							1		

Risingler et al TerrNet CMI 2017

ies	PSC (mg/L) Range	PSC (mg/L) MIC_{50}	PSC (mg/L) MIC_{90}	VRC (mg/L) Range	VRC (mg/L) MIC_{50}	VRC (mg/L) MIC_{90}	ITC (mg/L) Range	ITC (mg/L) MIC_{50}	ITC (mg/L) MIC_{90}
reus sensu stricto (n=432)									
® (n=315)	<0.002-0.500	0.032	0.125	0.008-4.000	0.064	0.250	0.016-2.000	0.125	0.250
AST (n=117)	0.125-0.500	0.250	0.500	0.125-1.000	0.500	0.500	0.250-1.000	0.500	0.500
tic species section *Terrei*									
® (n=55)	<0.002.-0.190	0.032	0.064	0.012-4.000	0.064	0.500	0.003-0.380	0.064	0.250
AST (n=11)	0.125-0.250	NA	NA	0.125-2.000	NA	NA	0.125-0.250	NA	NA

Zoran et al TerrNet under revision

A. niger complex

TABLE 1. Source, molecular identification, MICs, and MECs for species of *Aspergillus* section *Nigri*[a]

Isolate	Source	Molecular identification (β-tubulin gene)	MIC (mg/liter)[b]						MEC (mg/liter)[c]	
			AMB	ITC	VCZ	RVC	POS	TRB	CAS	MICA
Isolates of *Aspergillus* section *Nigri* showing low ITC MICs										
CM-3236	Respiratory	*A. niger*	0.19	0.5	0.5	1.0	0.12	1.0	0.25	0.03
CM-3257	Respiratory	*A. niger*	0.25	1.0	1.0	1.0	0.25	1.0	0.25	0.03
CM-3506	Respiratory	*A. niger*	0.19	0.5	0.75	1.0	0.12	0.31	0.15	0.03
CM-3507	Respiratory	*A. tubingensis*	0.19	0.5	1.0	1.5	0.15	0.62	0.06	0.03
CM-3585	Environmental	*A. tubingensis*	0.19	0.5	1.0	1.67	0.12	0.42	0.37	0.03
CM-3586	Catheter	*A. niger*	0.25	0.5	1.0	2.0	0.12	0.12	1.0	0.03
CM-3636	Respiratory	*A. niger*	0.25	0.5	0.5	1.0	0.19	1.0	0.25	0.03
CM-3641	Respiratory	*A. niger*	0.25	0.5	1.0	1.0	0.125	0.25	0.5	0.03
CM-3672	Cutaneous	*A. niger*	0.12	0.5	1.0	1.5	0.19	0.07	0.15	0.03
CM-4004	Unknown									
CM-4213	Respiratory									
CM-4264	Blood culti									
CM-4296	Respirato									
CM-4316	Respirato									
CM-5094	Respirato									
CM-5095	Respirato									
GM for group										
Isolates of *Aspergillus* section *Nigri* showing much higher ITC MICs										
CM-3123	Respirato									
CM-3810	Respirato									
CM-4003	Unknown									
CM-4005	Unknown									
CM-4688	Respirato									
CM-5264	Respirato									
GM for group										
Isolates of *Aspergillus* section *Nigri* showing paradoxical effect against ITC										
CM-3125	Respiratory	*A. tubingensis*	0.12	0.5	1	1.67	0.12	0.5	0.05	0.03
CM-3177	Respiratory	*A. tubingensis*	0.16	1	2	3.33	0.25	0.67	0.05	0.03
CM-3551	Respiratory	*A. niger*	0.5	4.75	1	2	0.12	0.25	0.03	0.03
CM-3654	Blood culture	*A. tubingensis*	0.19	1	2	2.50	0.25	0.63	0.14	0.03
CM-4000	Unknown	*A. tubingensis*	0.16	1	2	2	0.25	0.33	0.10	0.03
CM-4001	Unknown	*A. tubingensis*	0.19	1	1.75	2.50	0.25	0.56	0.11	0.03
CM-4002	Unknown	*A. foetidus*	0.25	1	2	2.67	0.12	0.33	0.14	0.03
CM-4262	Ophthalmic	*A. niger*	0.25	1	2	2	0.25	0.29	0.13	0.03
CM-4352	Respiratory	*A. tubingensis*	0.28	1	0.88	2	0.25	0.31	0.15	0.03
CM-4897	Blood culture	*A. tubingensis*	0.16	1	2	2	0.25	0.42	0.10	0.03
CM-4899	Respiratory	*A. tubingensis*	0.16	1	2	2.67	0.25	0.33	0.10	0.03
CM-4995	Prosthesis	*A. foetidus*	0.21	1	2	2	0.16	0.33	0.14	0.03
GM for group			0.2	1.3	1.72	2.28	0.21	0.41	0.10	0.03

[a] GM, geometric means of MICs and MECs for the strains within each group.
[b] MIC geometric mean of amphotericin B (AMB), itraconazole (ITC), voriconazole (VCZ), ravuconazole (RVC), posaconazole (POS), and terbinafine (TRB).
[c] MEC geometric mean of caspofungin (CAS) and micafungin (MICA).

Alcazar-Fuoli et al AAC 2009

Is phenotypic identification only to species complex ENOUGH?

36% *A. awamori*
90% *A. tubingensis*
33% *A. niger*
100% *A. acidus*
67% unknown

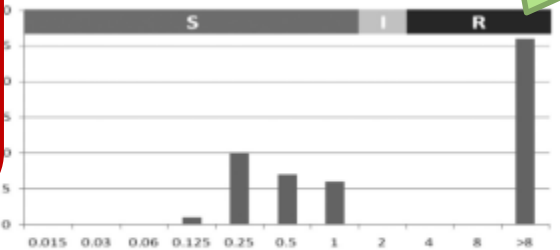
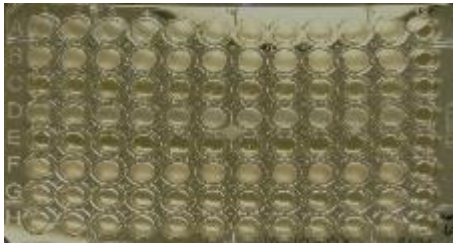


FIG. 1. Itraconazole MICs of *Aspergillus* section *Nigri* from the Mycology Reference Centre Manchester culture collection and proposed ECVs (S, susceptible; I, intermediate; R, resistant). The MIC is shown on the *x* axis, and the number of isolates is shown on the *y* axis.

Howard et al, AAC 2011

Antifungal Susceptibility



Conclussions

- ✓ Cryptic species are found in clinical samples
- ✓ Resistant to antifungals---> poorer outcomes
- ✓ Not all intrinsically resistant

- **Is phenotypic identification only to species complex acceptable?**

Thanks for your attention

Ana Alastruey-Izquierdo

Mycology Reference Lab Spain

Instituto de Salud Carlos III

anaalastruey@isciii.es