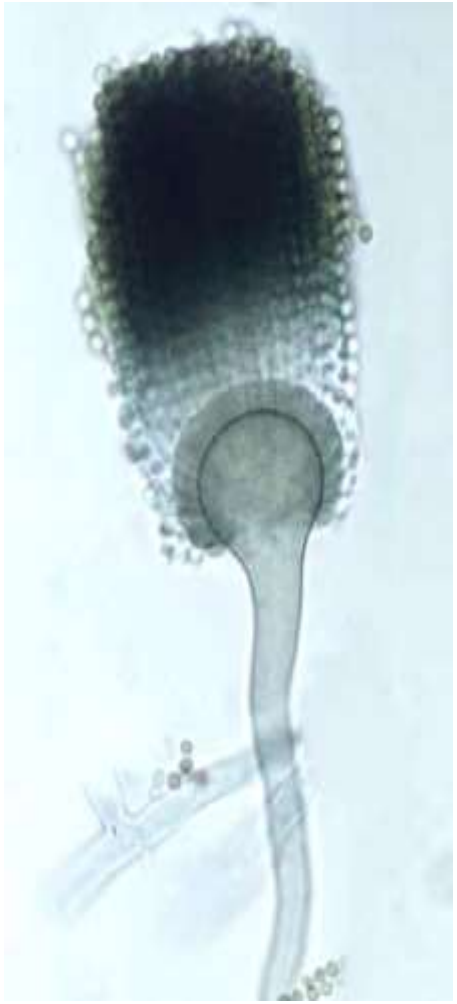
Epidemiology of infections by cryptic species of *Aspergillus*

Jan W.M. van der Linden, M.D.
Departments of Paediatrics and Medical Microbiology
Radboud University Medical Centre Nijmegen, the Netherlands

Radboudumc

Aspergillus



1729: Pier Antonio Micheli, priest and biologist: holy water sprinkler or ‘aspergillum’

Different *Aspergillus* spp.

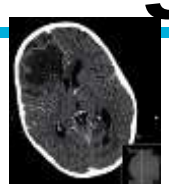
~180 spp., 38 pathogenic spp.

The genus *Aspergillus* is classified into eight subgenera, and each subgenus is subdivided into several sections that include many related species by molecular analyses.

Aspergillus spp. are present in

- Soil
- Air: we inhale 100-200 conidia a day
- Water
- Food (carrots, peppermint tee)
- Compost
- Wall paper paste
- Pillows, matrasses
- Ventilation/airco-systems

Aspergillus – the multi-artist



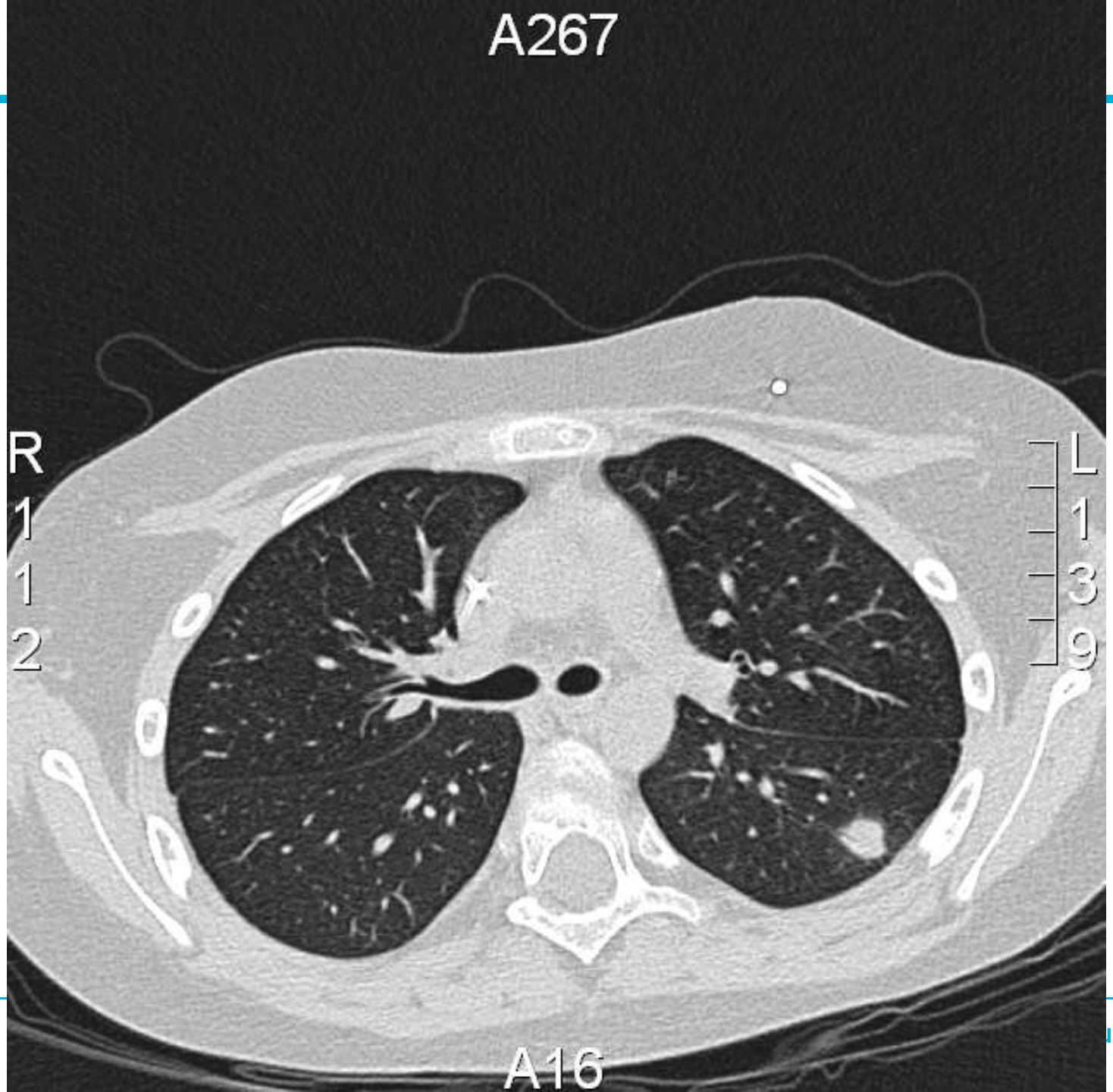
Invasive aspergillosis

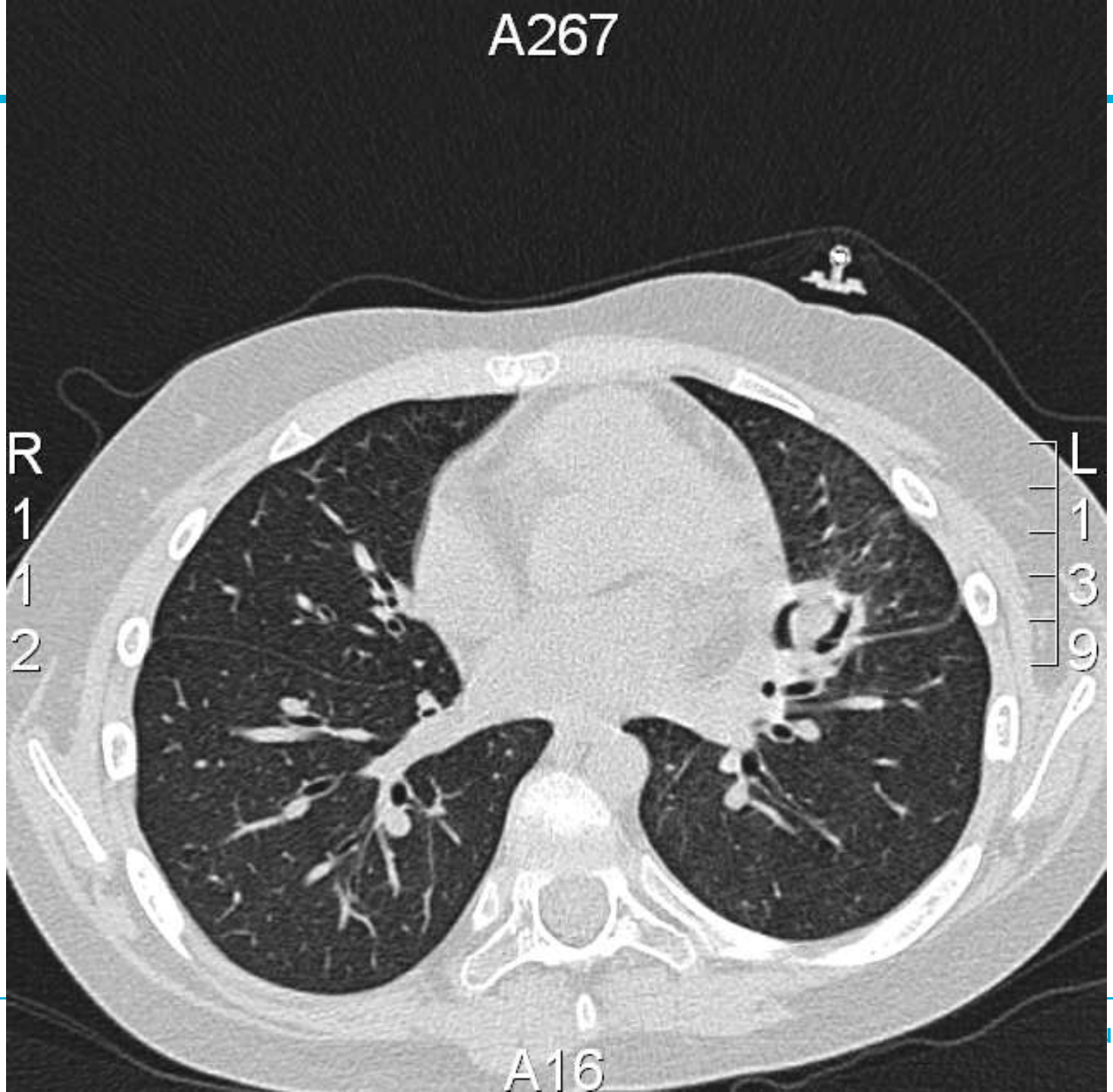
Allergic aspergillosis

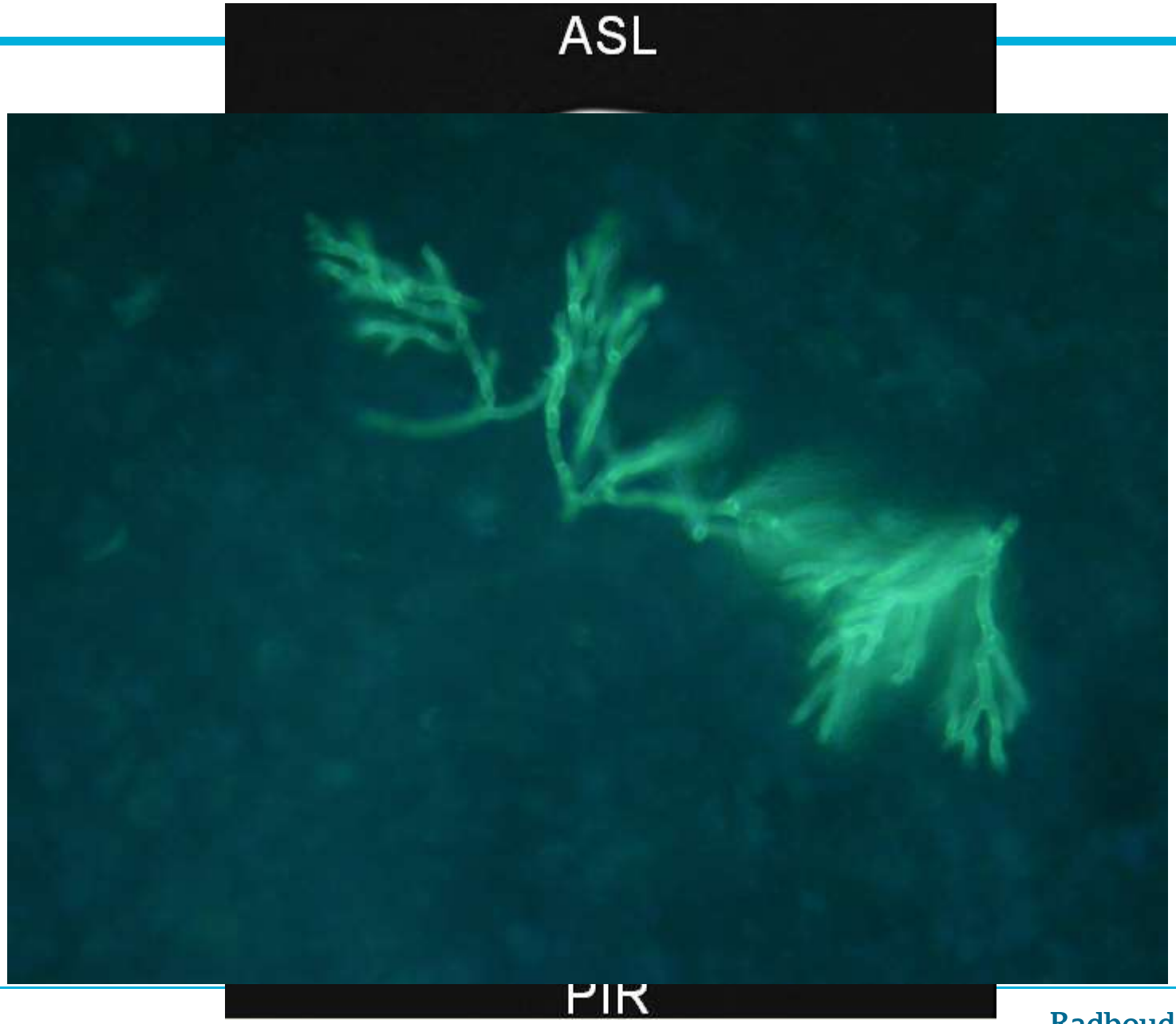
No. infections

Aspergilloma

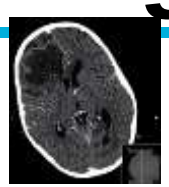
Immunodef./dysf. Immunocompetent ‘Hyper-immunity’


A267
R
1
1
2
L
1
3
9
A16


A267
R
1
1
2
L
1
3
9
A16


ASL
PIR

Aspergillus – the multi-artist



Invasive aspergillosis

Allergic aspergillosis

No. infections

Aspergilloma

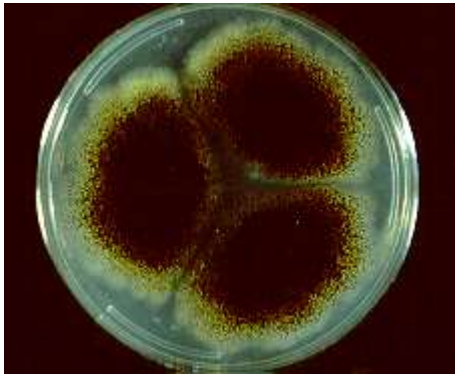
Immunodef./dysf. Immunocompetent ‘Hyper-immunity’

Aspergillus niger complex spp.

- Food spoilage fungi.
- Biotechnology: production of enzymes and citric acid.
- In patients mostly otomycosis, rarely disseminated.

Fungal otitis externa: 45% A. niger.

Ozcan KM, Ozcan M, Karaarslan A, Karaarslan F. Otomycosis in Turkey: predisposing factors, aetiology and therapy. J Laryngol Otol 2003; 117(1):39-42.



Schuster E, Dunn-Coleman N, Frisvad JC, Van Dijck PW. On the safety of *Aspergillus niger*--a review. Appl Microbiol Biotechnol 2002; 59(4-5):426-435.

Aspergillus flavus complex spp.

Epidemiology of cryptic species

- Clinical relevance??
- Prevalence and incidence??

- Variability across institutions:
  - Varying methods in detection/diagnosis
  - Different patient populations: different underlying diseases and co-morbidity
  - Different practices: transplantation practices, surgical techniques, antifungal prophylaxis

TRANSNET

MAJOR ARTICLE

Prospective Surveillance for Invasive Fungal Infections in Hematopoietic Stem Cell Transplant Recipients, 2001–2006: Overview of the Transplant-Associated Infection Surveillance Network (TRANSNET) Database

Dimitrios P. Kontoyiannis, Kieren A. Marr, Benjamin J. Park, Barbara D. Alexander, Elias J. Anaissie, Thomas J. Walsh, James Ito, David R. Andes, John W. Baddley, Janice M. Brown, Lisa M. Brumble, Alison G. Freifeld, Susan Hadley, Loreen A. Herwaldt, Carol A. Kauffman, Katherine Knapp, G. Marshall Lyon, Vicki A. Morrison, Genovefa Papanicolaou, Thomas F. Patterson, Trish M. Perl, Mindy G. Schuster, Randall Walker, Kathleen A. Wannemuehler, John R. Wingard, Tom M. Chiller, and Peter G. Pappas[a]

Clin Inf Dis 2010:50; 1091-1100

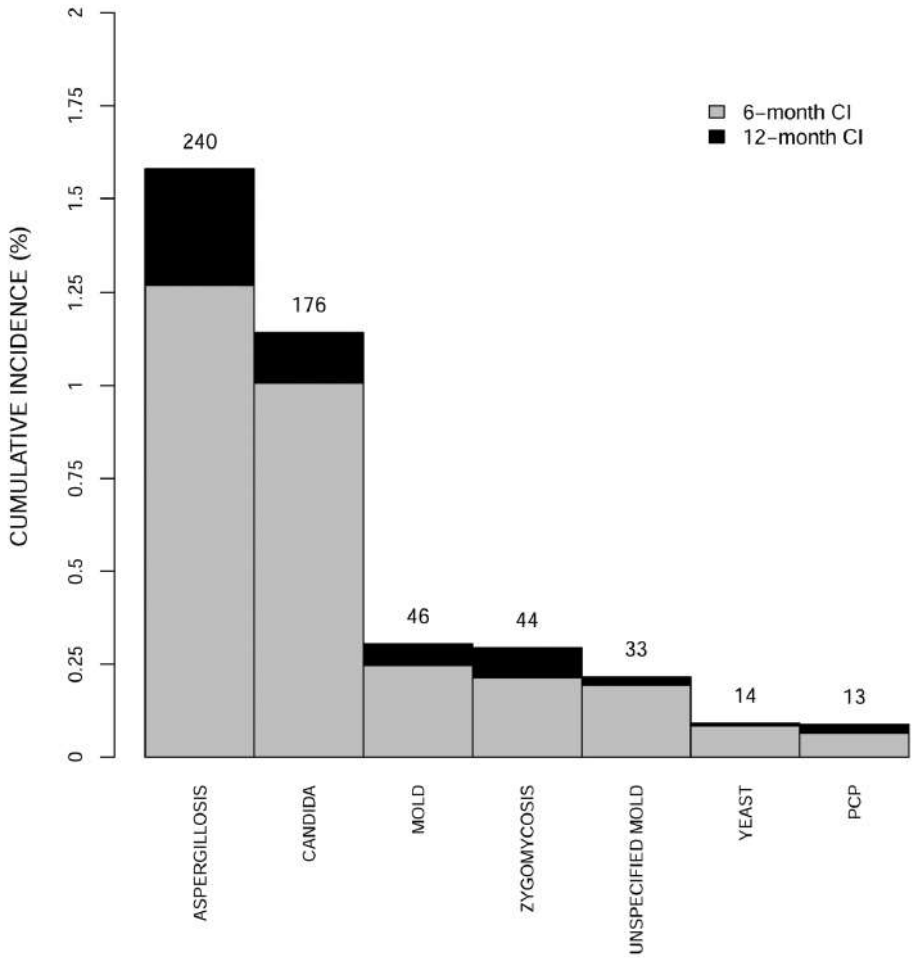
Radboudumc

Transplant Associated Infections Surveillance Network

- 23 US transplant centres
- 2001-2006

- 983 IFI in 875 HSCT-recipients
- IFI (56% proven, 44% probable):
  - Invasive aspergillosis 43% (44% *Aspergillus fumigatus*)
  - Invasive candidiasis 28%
  - Zygomycosis 8%

Non-*Aspergillus* mold infections were uncommon



TRANSNET

MAJOR ARTICLE

Invasive Fungal Infections among Organ Transplant Recipients: Results of the Transplant-Associated Infection Surveillance Network (TRANSNET)

Peter G. Pappas, Barbara D. Alexander, David R. Andes, Susan Hadley, Carol A. Kauffman, Alison Freifeld, Elias J. Anaissie, Lisa M. Brumble, Loreen Herwaldt, James Ito, Dimitrios P. Kontoyiannis, G. Marshall Lyon, Kieren A. Marr, Vicki A. Morrison, Benjamin J. Park, Thomas F. Patterson, Trish M. Perl, Robert A. Oster, Mindy G. Schuster, Randall Walker, Thomas J. Walsh, Kathleen A. Wannemuehler, and Tom M. Chiller[a]

Clin Inf Dis 2010:50; 1100-11

Transplant Associated Infections Surveillance Network

- 15 US transplant centres
- 2001-2006

- 1208 IFI in 1063 transplant-recipients
- IFI (42% proven, 58% probable):
  - Invasive aspergillosis 19% (78% IPA)
  - Invasive candidiasis 53%
  - Zygomycosis 2%

Invasive aspergillosis	227 (18.8)
Aspergillus fumigatus	136/227 (59.9)
Aspergillus terreus	10/227 (4.4)
Aspergillus niger	13/227 (5.7)
Aspergillus flavus	16/227 (7.1)
Multiple *Aspergillus* species	28/227 (12.3)
Other *Aspergillus* species	8/227 (3.5)
Unspecified *Aspergillus* species	16/227 (7.1)

Molecular Identification of *Aspergillus* Species Collected for the Transplant-Associated Infection Surveillance Network[▽]

S. Arunmozhi Balajee,[1]* Rui Kano,[1] John W. Baddley,[2,11] Stephen A. Moser,[3] Kieren A. Marr,[4,5] Barbara D. Alexander,[6] David Andes,[7] Dimitrios P. Kontoyiannis,[8] Giancarlo Perrone,[9] Stephen Peterson,[10] Mary E. Brandt,[1] Peter G. Pappas,[2] and Tom Chiller[1]

Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia[1]; Department of Medicine[2] and Department of Pathology,[3] University of Alabama at Birmingham, and Department of Medicine, Birmingham Veterans Affairs Medical Center,[11] Birmingham, Alabama; Fred Hutchinson Cancer Research Center, Seattle, Washington[4]; Johns Hopkins University, Baltimore, Maryland[5]; Duke University, Durham, North Carolina[6]; University of Wisconsin, Madison, Wisconsin[7]; M. D. Anderson Cancer Center, Houston, Texas[8]; Institute of Sciences of Food Production, National Research Council, Bari, Italy[9]; and National Center for Agricultural Utilization Research, U.S. Department of Agriculture, Peoria, Illinois[10]

218 isolates: 10% cryptic species!

J Clin Microbiol 2009; 47: 3138-41.

Aspergillus species identification

Table 2 Distribution of *Aspergillus* species according to sequence-based identification in the transplant associated infection surveillance network [17,18].

Species complex	Frequency (%)	Sequence-based identification	Frequency (%)
A. fumigatus	147/218 (67.4)	*A. fumigatus*	139/147 (93.9)
		A. lentulus	4/147 (2.7)
		A. udagawae	3/147 (2.0)
		N. pseudofischeri	1/147 (0.8)
A. flavus	29/218 (13.2)	*A. flavus*	29/29 (100)
A. niger	19/218 (8.7)	*A. niger*	13/19 (68)
		A. tubingensis	6/19 (32)
A. terreus	11/218 (7.4)	*A. terreus*	11/11 (100)
A. ustus	6/218 (2.7)	*A. calidoustus*	6/6 (100)
A. versicolor	5/218 (2.3)	*A. versicolor*	3/5 (60)
		A. sydowii	2/5 (40)
A. nidulans	1/218 (0.5)	*A. tetrazonus*	1/1 (100)

J Clin Microbiol 2009; 47: 3138-41.

IA and susceptibility

TABLE 1. Isolate identity, type of IA, and antifungal susceptibilities of rare aspergilli recovered in this study

Strain no.	Transplant type	Site of isolation[a]	Molecular identity	Center	MIC µg/ml			
					AMB	ITZ	VRZ	POS
IFI03-0026	Heart	Hip (biopsy specimen)	*A. calidoustus*	A	0.5	>8	4	>8
IFI01-0058	Kidney/pancreas	Lung	*A. calidoustus*	A	1	>8	8	>8
IFI03-0056	HSCT[b]	Lung	*A. sydowii*	B	1	0.5	2	0.5
IFI03-0059	HSCT	Lung	*A. calidoustus*	B	0.5	>8	4	>8
IFI02-0227	HSCT	Lung	*A. tubingenesis*	C	0.25	1	1	0.06
IFI05-0038	HSCT	Lung	*A. tubingenesis*	D	0.125	1	1	0.25
IFI05-0048	HSCT	Lung	*A. sydowii*	E	1	0.25	1	0.25
IFI04-0143[c]	HSCT	Lung (BAL fluid)	*A. calidoustus*	E	1	>8	8	>8
IFI04-0137	HSCT	Lung	*A. udagawae*	E	1	0.25	2	0.25
IFI04-0142[c]	HSCT	Skin	*A. calidoustus*	E	1	>8	4	>8
IFI06-0001	HSCT	Lung	*A. lentulus*	E	2	0.5	4	0.25
IFI05-0046	HSCT	Lung	*A. lentulus*	E	2	0.5	2	0.25
IFI06-0011	HSCT	Lung (sputum)	*A. lentulus*	E	0.5	0.25	1	0.25
IFI06-0014	HSCT	Lung	*A. lentulus*	E	2	0.5	4	0.25
IFI02-0149	HSCT	Skin	*N. pseudofischeri*	F	0.125	0.25	2	0.5
IFI04-0005	HSCT	Lung	*A. tubingenesis*	G	0.125	1	1	0.5
IFI03-0138	Heart	Lung	*A. udagawae*	G	2	0.25	0.5	0.125
IFI06-0129	HSCT	Lung (sputum)	*A. tubingenesis*	H	0.125	0.5	0.5	0.25
IFI06-0126	HSCT	Blood	*E. quadrilineata*	H	0.5	0.25	0.5	0.25
IFI02-0093	HSCT	Skin lesion	*A. tubingenesis*	I	0.125	0.25	0.5	0.06
IFI02-0091	Liver	Lung (sputum)	*A. udagawae*	I	2	2	2	0.25
IFI03-0055	Lung	Lung	*A. calidoustus*	J	1	>8	4	>8
IFI04-0017	HSCT	Lung	*A. tubingenesis*	K	0.125	0.5	1	0.25

[a] The site of isolation from the lung includes cultures of biopsy specimens or bronchoalveolar lavage (BAL) fluid, unless otherwise indicated.
[b] HSCT, hematopoietic stem cell transplant.
[c] Previously identified as *A. calidoustus* (17).

Susceptibility

- 274 *Aspergillus* isolates
- A. calidoustus: triazoles not effective
- One resistant *A. fumigatus* isolate (MIC >4)
- Higher VOR MIC: increased mortality at 6 wks? (p = 0.065)

Baddley et al. J Clin Microbiology 2009:47(10); 3271-5

TABLE 1. In vitro susceptibilities of 274 *Aspergillus* isolates causing IA in transplant recipients

Species (no. of isolates)[a]	Antifungal agent	MIC (μg/ml)	
		Range	50%/90%
Aspergillus fumigatus[b] (181)	AMB	0.125–2	0.5/1
	ITR	0.125–4	0.25/0.5
	VOR	0.125–8	0.5/0.5
	POS	0.03–1	0.06/0.125
	RAV	0.25–1	0.5/1
Aspergillus niger (28)	AMB	0.125–0.25	0.125/0.25
	ITR	0.25–1	0.5/1
	VOR	0.5–1	1/1
	POS	0.06–0.5	0.25/0.25
Aspergillus flavus (27)	AMB	0.5–1	1/1
	ITR	0.06–0.25	0.125/0.25
	VOR	0.125–1	0.5/0.5
	POS	0.06–0.125	0.06/0.125
	RAV	0.25–0.5	0.5/0.5
Aspergillus terreus (22)	AMB	0.25–4	2/2
	ITR	0.03–0.25	0.125/0.25
	VOR	0.25–0.5	0.5/0.5
	POS	0.03–0.06	0.06/0.06
	RAV	0.5	0.5/0.5
Aspergillus versicolor (7)	AMB	0.125–1	0.5/1
	ITR	0.125–16	0.25/16
	VOR	0.25–2	1/2
	POS	0.06–16	0.25/16
	RAV	0.25–4	1/4
Aspergillus calidoustus (5)	AMB	0.5–1	1/1
	ITR	16	16/16
	VOR	4–8	4/8
	POS	16	16/16
	RAV	4	4/4
Other *Aspergillus* spp. (4)[c]	AMB	0.5–4	0.5/4
	ITR	0.06–0.25	0.125/0.25
	VOR	0.5–1	0.5/1
	POS	0.06–0.25	0.06/0.25

[a] POS was tested for 181 *A. fumigatus*, 27 *A. niger*, 13 *A. flavus*, 23 *A. terreus*, seven *A. versicolor*, six *A. ustus*, and 10 other *Aspergillus* species isolates. RAV was tested for 181 *A. fumigatus*, zero *A. niger*, 13 *A. flavus*, seven *A. terreus*, four *A. versicolor*, three *A. ustus*, and zero other *Aspergillus* species isolates.

[b] Includes three *A. lentulus*, two *Neosartorya udagawae*, and one *Neosartorya fischeri* isolates.

[c] Includes two *Aspergillus* species isolates and two *Aspergillus nidulans* isolates.

Medical Mycology Month 2010, **Early Online**, 1–8

informa
healthcare

Review Article

Aspergillus species intrinsically resistant to antifungal agents

JAN W. M. VAN DER LINDEN*†‡, ADILIA WARRIS†‡ & PAUL E. VERWEIJ*‡

*Departments of *Medical Microbiology, †Pediatrics, and ‡Nijmegen Institute for Infection, Inflammation and Immunity (N4i), Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands*

Table 1 Characteristics and intrinsic resistance profiles of *Aspergillus* species.

Species	Characteristics	Resistance profile	Comments	References
A. lentulus	Newly recognized to cause IA	Reduced susceptibility to amphotericin B, azoles and variable susceptibility to caspofungin	Sibling species of *A. fumigatus*	9,17,20,22–24
A. udagawae	Uncommon cause of IA	Reduced susceptibility to amphotericin B and voriconazole	Sibling species of *A. fumigatus*	9,17–19,25
N. pseudofisheri	Uncommon cause of IA	Variable susceptibility to amphotericin B and reduced susceptibility to azoles	Sibling species of *A. fumigatus*	10,17,20
A. fumigatiaffinis	No cases of IA reported	Reduced susceptibility to amphotericin B and azoles	Sibling species of *A. fumigatus*	20
A. viridinutans	Newly recognized to cause IA in patients with primary immunodeficiencies	Reduced susceptibility to amphotericin B and azoles	Sibling species of *A. fumigatus*	20,21
A. flavus	Common in dry climates	Reduced susceptibility to amphotericin B		17,18,26–31
A. nidulans	Primarily causes IA in patients with CGD	Reduced susceptibility to amphotericin B		16,17,32–34
A. tetrazonus (E. quadrilineata)	Newly recognized to cause IA in CGD	Susceptible to amphotericin B but reduced susceptibility to caspofungin	Sibling species of *A. nidulans*	17,34
A. terreus	Propensity to disseminate with positive blood cultures	Reduced susceptibility to amphotericin B		18,41–46
A. alabamensis	No cases of IA reported	Reduced susceptibility to amphotericin B	Sibling species of *A. terreus*	55
A. niger	Uncommon cause of IA; Common cause of otomycosis	Variable susceptibility patterns with reduced activity of azoles		27,52–54,56
A. tubingensis	Newly recognized to cause keratitis and IA	Variable susceptibility patterns with reduced activity of azoles	Sibling species of *A. niger*	17,53,57
A. calidoustus	Uncommon cause of IA; Propensity to disseminate	Resistant to the triazoles and variable susceptibility to caspofungin	Previously reported as *A. ustus*	17,35–40
A. versicolor	Uncommon cause of IA; Common cause of onychomycosis	Reduced susceptibility to amphotericin B and variable susceptibility to azoles		18,56,58
A. sydowii	Newly recognized to cause onychomycosis and peritonitis in patients undergoing dialysis; Uncommon cause of IA.	Reduced susceptibility to amphotericin B and variable susceptibility to azoles	Sibling species of *A. versicolor*	17,54,59,60
A. persii	Newly recognized to cause onychomycosis	Reduced susceptibility to amphotericin B and caspofungin	Recently recognized as being a new species in section *Circumdati*	61

Population-Based Survey of Filamentous Fungi and Antifungal Resistance in Spain (FILPOP Study)

A. Alastruey-Izquierdo,[a] E. Mellado,[a] T. Peláez,[b] J. Pemán,[c] S. Zapico,[d] M. Alvarez,[e] J. L. Rodríguez-Tudela,[a] M. Cuenca-Estrella,[a] FILPOP Study Group

National Center for Microbiology, Madrid, Spain[a]; Hospital General Universitario Gregorio Marañón, Madrid, Spain[b]; Hospital Universitario La Fe, Valencia, Spain[c]; Hospital Universitario Donostia, Guipuzcoa, Spain[d]; Hospital Universitario Central de Asturias, Oviedo, Spain[e]

Antimicr Agents Chem, 2013;57(7): 3380-7

FILPOP

- 23 Spanish hospitals
- October 2010 and May 2011
- 325 strains

TABLE 2 Species isolated and number of strains by study period (October versus May)

Species	No. (%) of strains		
	October 2010	May 2011	Total
Aspergillus fumigatus	98 (47.6)	58 (50.0)	156 (48.5)
Aspergillus flavus	18 (8.74)	9 (7.76)	27 (8.39)
Aspergillus terreus	18 (8.74)	8 (6.90)	26 (8.07)
Aspergillus tubingensis	21 (10.2)	1 (0.86)	22 (6.83)
Aspergillus niger	17 (8.25)	4 (3.45)	21 (6.52)
Aspergillus nidulans	5 (2.43)	3 (2.59)	8 (2.48)
Rhizopus arrhizus	6 (2.91)	1 (0.86)	7 (2.17)
Scedosporium boydii	1 (0.49)	5 (4.31)	6 (1.86)
Aspergillus species[a]	9 (4.37)	9 (7.76)	17 (5.28)
Scedosporium species[b]	4 (1.94)	5 (4.31)	9 (2.80)
Penicillium species[c]	1 (0.49)	5 (4.31)	6 (1.86)
Fusarium species[d]	1 (0.49)	3 (2.59)	4 (1.24)
Mucorales species[e]	4 (1.94)	1 (0.86)	5 (1.55)
Other[f]	3 (1.46)	4 (3.45)	7 (2.17)
Total	206 (100.00)	116 (100.00)	322 (100.00)

[a] The *Aspergillus* species isolated included *A. alliaceus*, *A. calidoustus*, *A. carneus*, *A. fumigatiaffinis*, *A. insuetus*, *A. keveii*, *A. lentulus*, *A. sygowii*, *A. viridinutans*, *A. weterdijkiae*, and *N. pseudofischeri*.

278 *Aspergillus* isolates, 40 (14.5%) were classified as cryptic species

- *Aspergillus section Fumigati* i(162 strains): 6 (3.7%) non-*A. fumigatus sensu stricto:*
  - *3 Aspergillus lentulus*
  - 1 *Aspergillus viridinutans*
  - 1 *Aspergillus fumigatiaffinis*
  - 1 *Neosartorya pseudofischeri*
- *Aspergillus* section *Flavi* (30 strains):
  - 27 *A. flavus*
  - 3 *A. alliaceus*
- *Aspergillus section Nigri* (43 strains):
  - 22 *A. tubingensis*
  - 21 *A. niger*
- *Aspergillus section Terrei* (27 strains):
  - 26 *A. terreus*
  - 1 *Aspergillus carneus*
- *Aspergillus section Nidulantes* included 8 *A. nidulans* strains.
- Other *Aspergillus* sections: *Usti* (4 *A. calidoustus*, 1 *A. insuetus*, 1 *A. keveii*), *Versicolores* (1 *A. sydowii*) and *Circumdati* (1 *A. westerdijkiae*)

Clinical relevance

TABLE 1 The genera most commonly isolated in the FILPOP study, the numbers and percentages of isolates, and their clinical relevance according to researchers' reports

Genus or order	No. (%) of strains clinically relevant	No. (%) of colonizers	Total no. % of isolates in FILPOP study
Aspergillus	117 (86.6)	161 (86.1)	278 (86.3)
Scedosporium	5 (3.7)	10 (5.3)	15 (4.7)
Mucorales	8 (6.0)	4 (2.2)	12 (3.7)
Penicillium	2 (1.5)	5 (2.6)	7 (2.2)
Fusarium	1 (0.7)	3 (1.6)	4 (1.2)
Other[a]	2 (1.5)	4 (2.2)	6 (1.9)
Total	135 (100.0)	187 (100.0)	322[b] (100.0)

[a] The other species (one each) belonged to the genera *Arthrinium*, *Psathyrella*, *Cladosporium*, *Purpureocillium*, *Phialemonium*, and *Scopulariopsis*.

[b] Three isolates could not be analyzed at the reference center because of absence of growth or contamination when received.

Resistance

IN VITRO

16 (40%) were resistant:

- *A. lentulus*: ITZ
- *A. calidoustus*: VCZ, POS
- *A. alliaceus*: AMB

TABLE 4 *Aspergillus* species strains resistant to amphotericin B, itraconazole, voriconazole, and posaconazole *in vitro*

Species (no. of isolates)	No. (%)[a] with: AMB MIC > 2 mg/liter	ITC MIC > 2 mg/liter	VRC MIC > 2 mg/liter	PSC MIC > 0.25 mg/liter
A. fumigatus (156)	0	0	0	1 (0.6)
A. flavus (27)	4 (14.8)	0	0	0
A. terreus (26)	7 (27)	0	0	0
A. tubingensis (22)	0	1 (4.5)	0	0
A. niger (21)	0	0	0	0
A. nidulans (8)	1 (12.5)	0	0	0
A. calidoustus (4)	0	2 (50)	4 (100)	4 (100)
A. alliaceus (3)	3 (100)	0	0	0
A. lentulus (3)	1 (33.7)	3 (100)	0	0
A. sydowii (1)	0	0	0	1 (100)
A. carneus (1)	0	0	0	0
N. pseudofischeri (1)	0	0	0	0
A. viridinutans (1)	0	0	0	0
A. fumigatiaffinis (1)	1 (100)	1 (100)	0	0
A. insuetus (1)	1 (100)	1 (100)	1 (100)	1 (100)
A. westerdijkiae (1)	1 (100)	0	0	0
A. keveii (1)	0	1 (100)	1 (100)	1 (100)
Total (277)	19 (6.8)	10 (3.6)	6 (2.2)	8 (2.9)

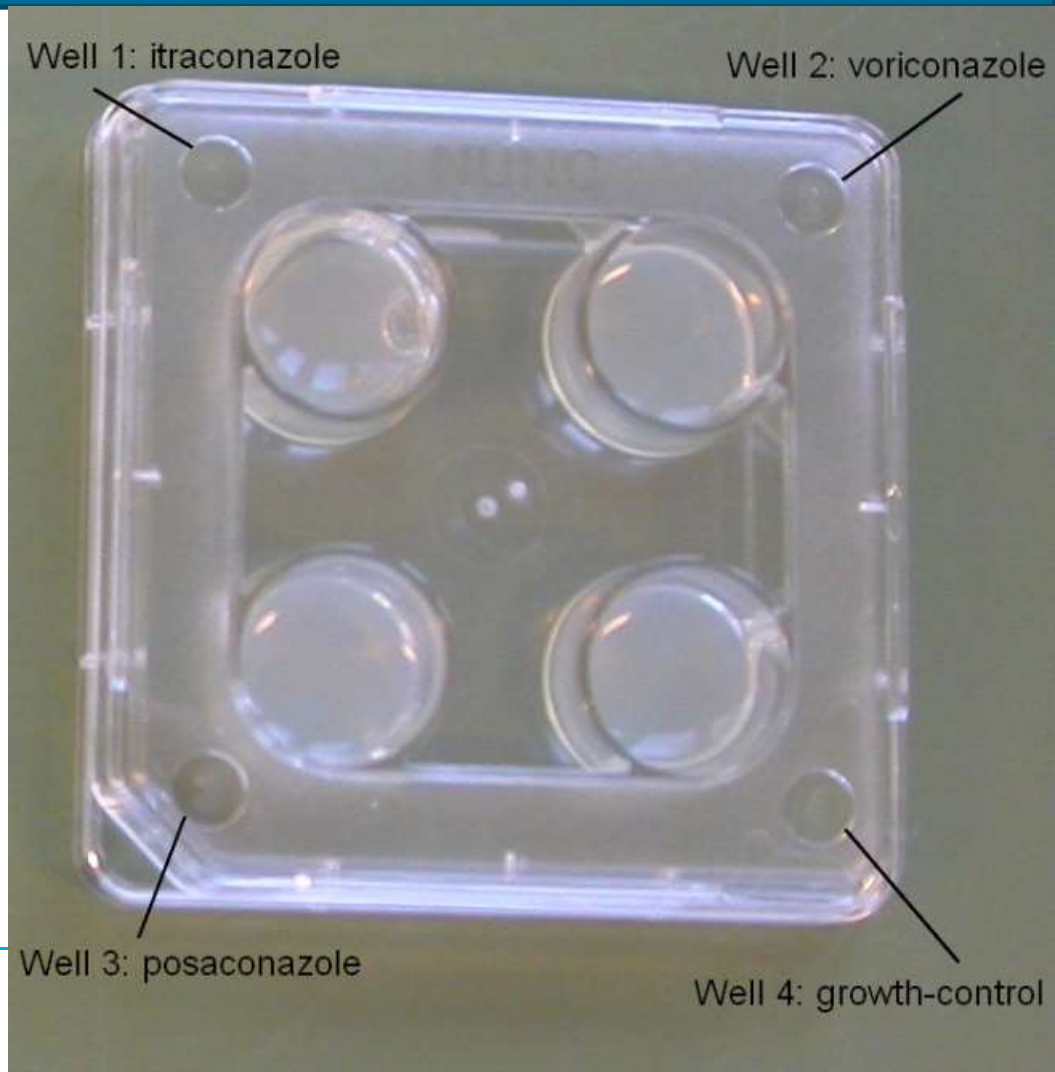
[a] AMB, amphotericin B; ITC, itraconazole; VRC, voriconazole; PSC, posaconazole.

Screening for resistance:

Contains:

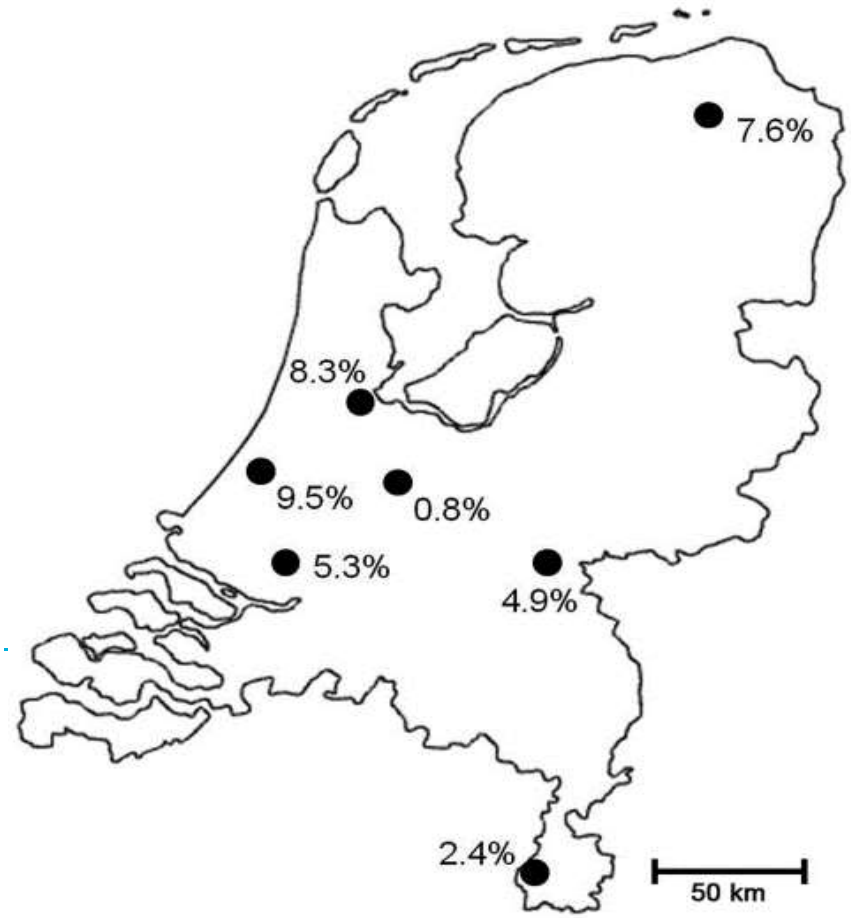
- Itraconazole 4 mg/L
- Voriconazole 1 mg/L
- Posaconazole 0.5 mg/L

Sensitivitity: 94%
Specificitity: 99%



Clinical Implications of Azole Resistance in *Aspergillus fumigatus*, the Netherlands, 2007–2009

Jan W.M. van der Linden, Eveline Snelders, Greetje A. Kampinga, Bart J.A. Rijnders, Eva Mattsson, Yvette J. Debets-Ossenkopp, Ed J. Kuijper, Frank H. Van Tiel, Willem J.G. Melchers, and Paul E. Verweij

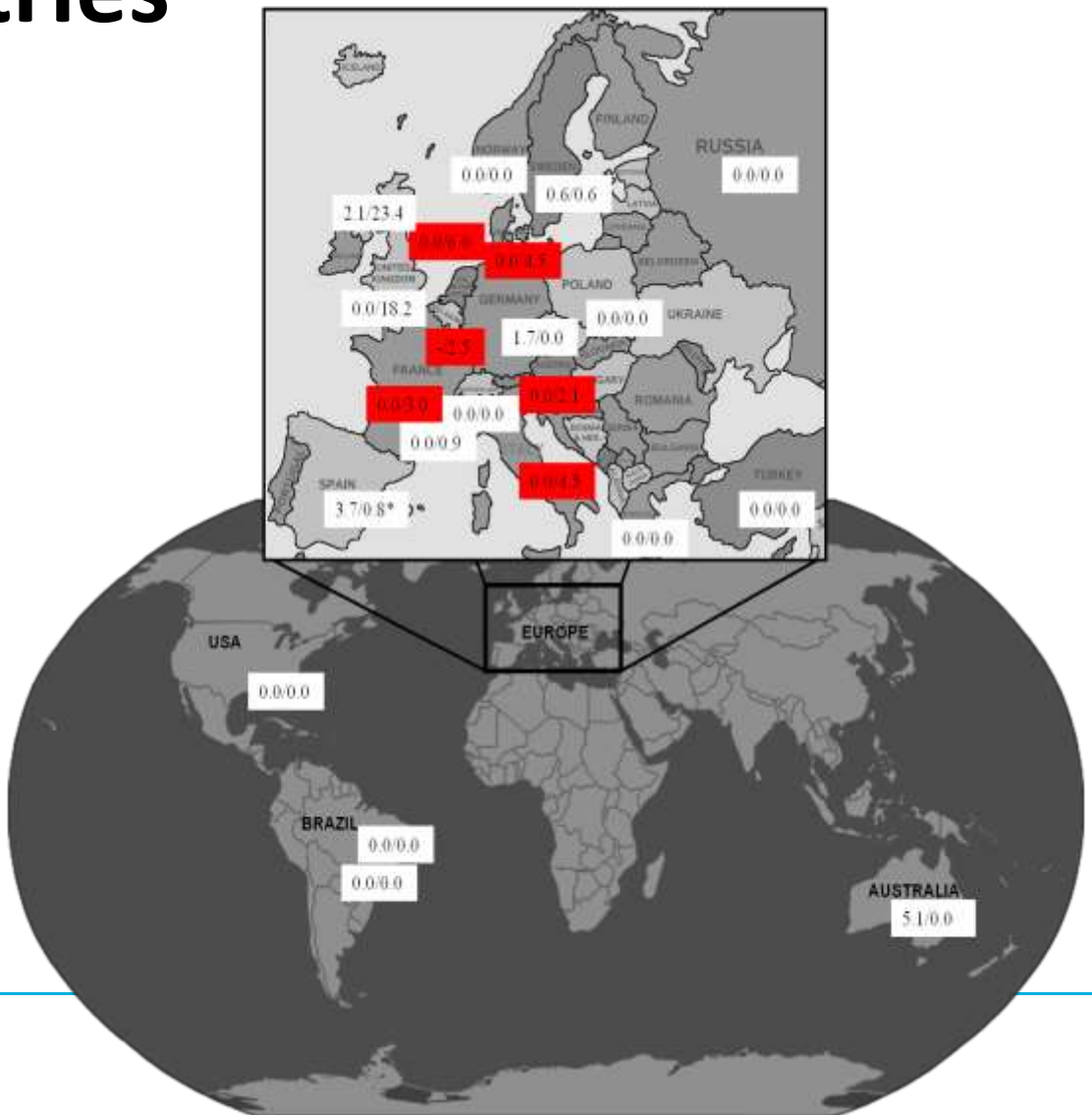


Emerg Infect Dis. 2011 Oct;17(10):1846-54.

Radboudumc

SCARE-study

22 participating centers from 19 countries



Genotypic analysis

Sequencing of the *β*-tubulin-gene classified 47 azole-resistant isolates (78.3%) as *A. fumigatus*. The other 13 azole-resistant isolates were classified as *A. lentulus* (n=7), *Neosartorya pseudofisheri* (n=4) and *N. udagawae* (n=2). In the control-group all 60 isolates were classified as *A. fumigatus*.

Phenotypic analysis

***A. fumigatus*: (47 isolates)**

ITZ-resistant (>2 mg/L)	89%
VCZ-resistant (>2 mg/L)	72%
POS-resistant (>0.5 mg/L)	54%

Sibbling species: (13 isolates)

ITZ-resistant (>2 mg/L)	39%
VCZ-resistant (>1 mg/L)	100%
POS-resistant (>0.5 mg/L)	23%

Take home massages

- Aspergillus ‘the multi-artist’.
- Aspergillus diseases by cryptic species occur in HSCT and SOT recipients.
- Prospective studies show an incidence of 1-2%, of which 10% is cryptic.
- Cryptic species may be less susceptible to azoles and clinically relevant.