



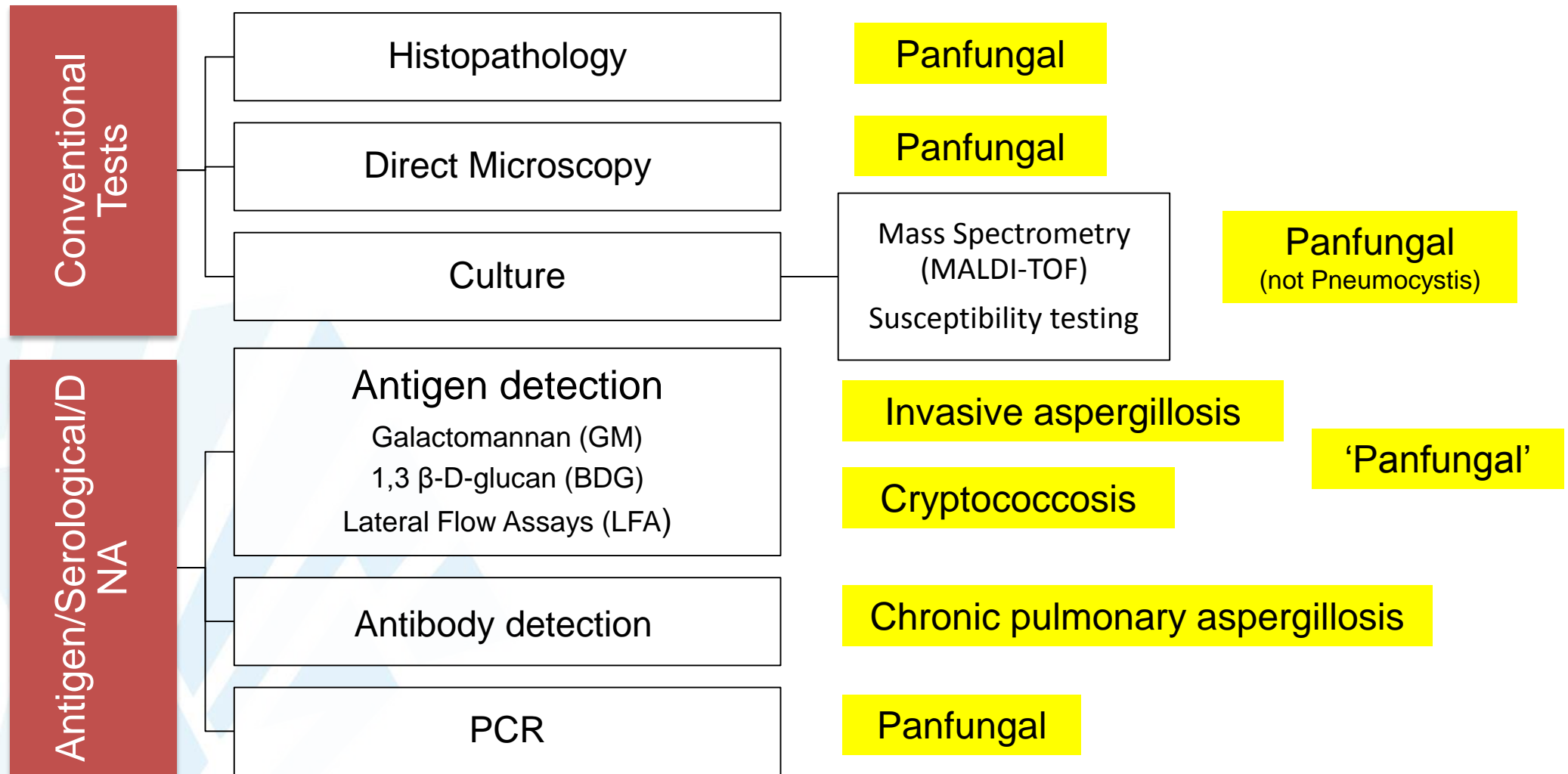
# MYCOLOGY

**Katrien Lagrou, PharmD, PhD**

**University Hospitals Leuven and KU Leuven, BELGIUM**



# Which tests can the lab offer to you for the diagnosis of fungal infection?





# Casus: V, 80j

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- Mei 2015: diagnose MDS-RAEB
- Jan 2016: evolutie naar AML (supportief beleid)
- 24 jan 2017:
  - opname op de dienst hematologie omwille van blijvende malaise met hoest en groene sputa ondanks twee antibioticakuren peroraal
  - RX thorax: verdichting rechteronderkwab, klinisch crepitaties rechts basaal overeenkomend met verdichting op RX thorax
  - Opstarten van meronem. Hieronder oplopend CRP en persisterende koorts ondanks negatieve influenza PCR (hMPV positief, andere parameters van respiratoir panel negatief) en negatieve hemoculturen.
  - HRCT: uitgebreide consolidaties met omgevende matglashalo, compatibel met angio-invasieve aspergillose dd. atypisch infectie.

**30-01-2017 08:00 - bloed**

Hemoglobine	7.8	g/dL	12.0 - 16.0
Hematocriet	0.269		0.370 - 0.470
RBC telling	2.84	10**12/L	3.90 - 5.60
MCV	94.7	fL	76.0 - 96.0
MCH	27.5	pg	27.0 - 32.0
MCHC	29.0	g/dL	30.0 - 35.0
RDW (maat voor anisocytose)	18.7	%	11.7 - 14.5
Reticulocyten telling	67	10**9/L	20 - 100
Immature reticulocyten fractie	29.6	%	5.0 - 21.0
Reticulocyten hemoglobinisatie (Ret-He)	24.9	pg	30.3 - 35.7
Erytroblasten telling	0.33	10**9/L	0.00 - 0.07
Erytroblasten telling	1.20	/ 100 WBC	0.00 - 0.70
WBC telling	28.25	10**9/L	4.00 - 10.00

**WBC differentiatie microscopie**

Aantal gedifferentieerde WBC

119

Blasten %

67

%

 $\leq 0$ 

Blasten aantal

19.0

 $10^{**9}/L$ 

Myelocyten %

21

%

 $\leq 0$ 

Myelocyten aantal

5.9

 $10^{**9}/L$ 

Metamyelocyten %

4

%

 $\leq 0$ 

Metamyelocyten aantal

1.2

 $10^{**9}/L$ 

Neutrofielen %

5

%

38 - 77

Neutrofielen aantal

1.4

 $10^{**9}/L$ 

2.5 - 7.8

Eosinofielen %

0

%

 $\leq 6$ 

Eosinofielen aantal

0.0

 $10^{**9}/L$ 
 $\leq 0.4$ 

Basofielen %

0

%

 $\leq 1$ 

Basofielen aantal

0.0

 $10^{**9}/L$ 
 $\leq 0.1$ 

Lymfocyten %

2

%

20 - 50

Lymfocyten aantal

0.5

 $10^{**9}/L$ 

1.2 - 3.6

Monocyten %

1

%

2 - 10

Monocyten aantal

0.2

 $10^{**9}/L$ 

0.2 - 0.8

Bloedplaatjes telling

327

 $10^{**9}/L$ 

150 - 450

## ▢ **Bacteriologie Culturen**

### **Respiratoir specimen**

30-01-2017 13:27 - bronchuslavage/BAL

Macroscopisch uitzicht	muceus bloederig
Gramkleuring	mondepitheelcellen zeldzaam
Gisten/Schimmelcultuur	
positief	
Cultuur	
mondfloora zeldzaam	
Aspergillus fumigatus complex zeldzaam	
Screening azole resistentie	negatief

## **Bacteriologie Serologie**

30-01-2017 13:27 - bronchoalveolaire lavage

Aspergillus Ag detectie	positief
<i>Het resultaat is hoger dan het meetbereik. De index is waarschijnlijk groter dan de gerapporteerde waarde.</i>	
index	5.4

31-01-2017 08:00 - bloed

Aspergillus Ag detectie	negatief
index	0.0



# INVASIVE FUNGAL DISEASE: EORTC/MSG CRITERIA

**PROVEN**

Sterile material microscopy and/or culture positive

**PROBABLE**

Host  
factors

+

Clinical  
features

+

Mycology

**POSSIBLE**

Host  
factors

+

Clinical  
features

### Host factors

Neutropenia  
aHSCT  
Corticosteroids  
T cell immunosuppressants

### Clinical features

CT/MRI signs  
Clinical criteria

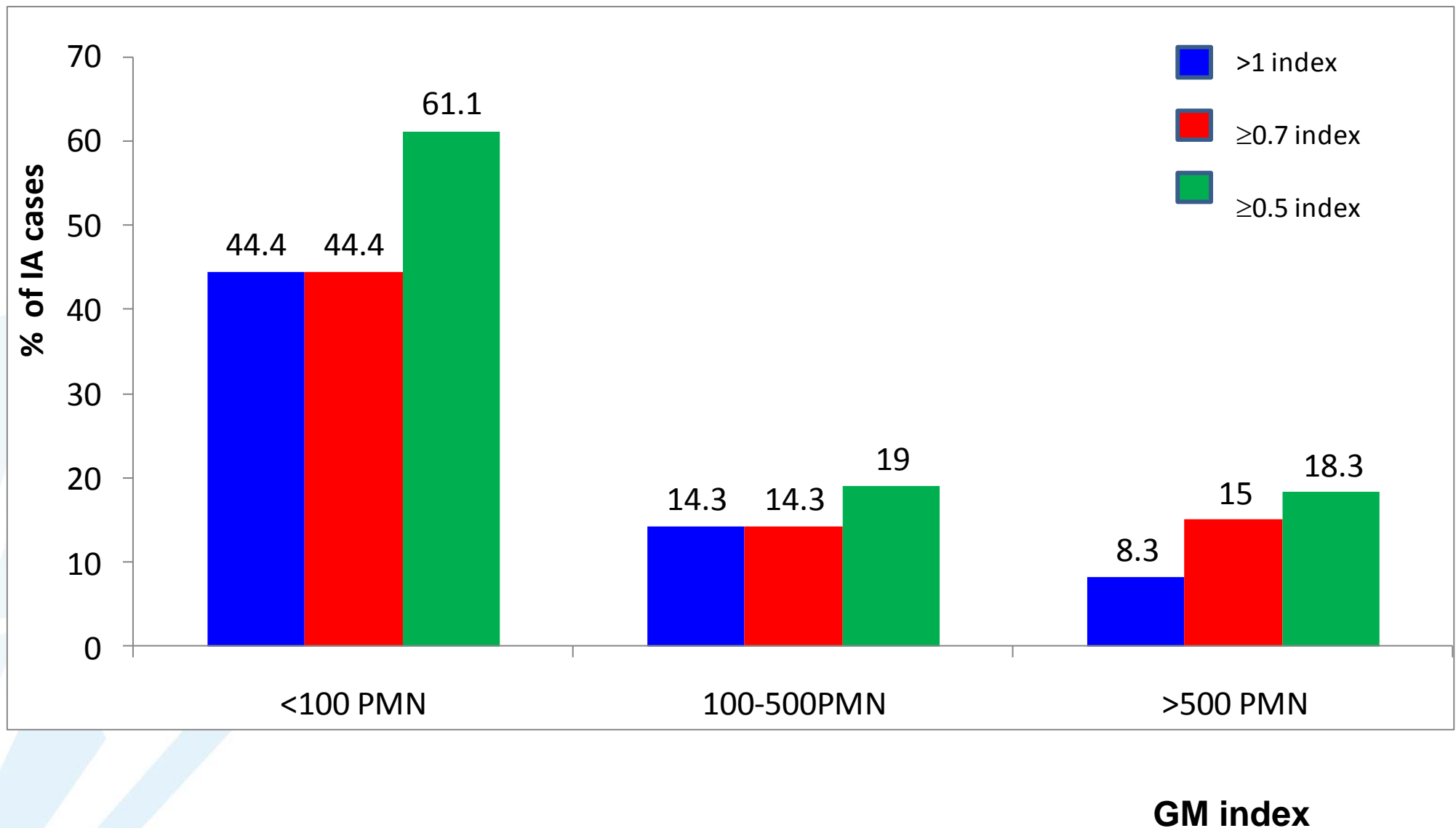
### Mycology

Microscopy  
Culture  
Antigen (galactomannan,  $\beta$ -D-glucan)



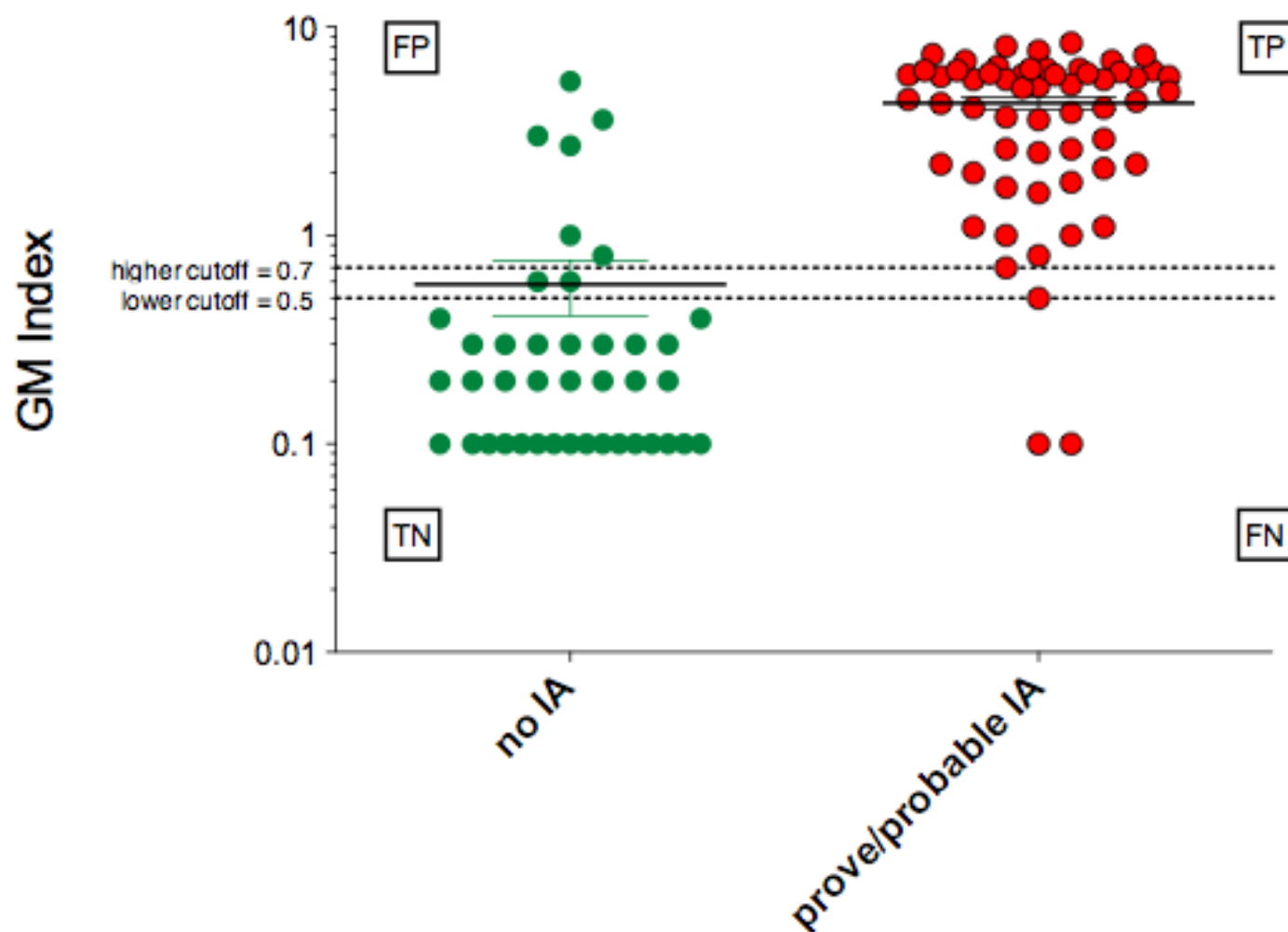


# Serum galactomannan assay: good sensitivity in neutropenic patients only!





# Clear influence of neutropenia on serum GM but not on BAL GM value



Jan 2005 – Sept 2008  
58 proven/probable IA  
41 controls

	Neutropenic	non-Neutropenic	P-value
BAL, 1.0	100%	94.7%	0.99
Serum, 0.5	90%	36.8%	0.008

**PROPHYLAXIS**

**PRE-EMPTIVE  
THERAPY**

**DIAGNOSTICS**

**EMPIRICAL THERAPY**

**TARGETED THERAPY**



# Antifungal agents

## TARGET

DNA/RNA synthesis

5-FC

## CELL WALL

## CELL MEMBRANE

Nystatin  
Amphotericin B

Miconazole  
Ketoconazole

Fluconazole  
Itraconazole

Voriconazole

Terbinafine

L-AmB, ABLC  
ABCD

Posaconazole  
Isavuconazole

Caspofungin

Anidulafungin

Micafungin

1950

1960

1970

1980

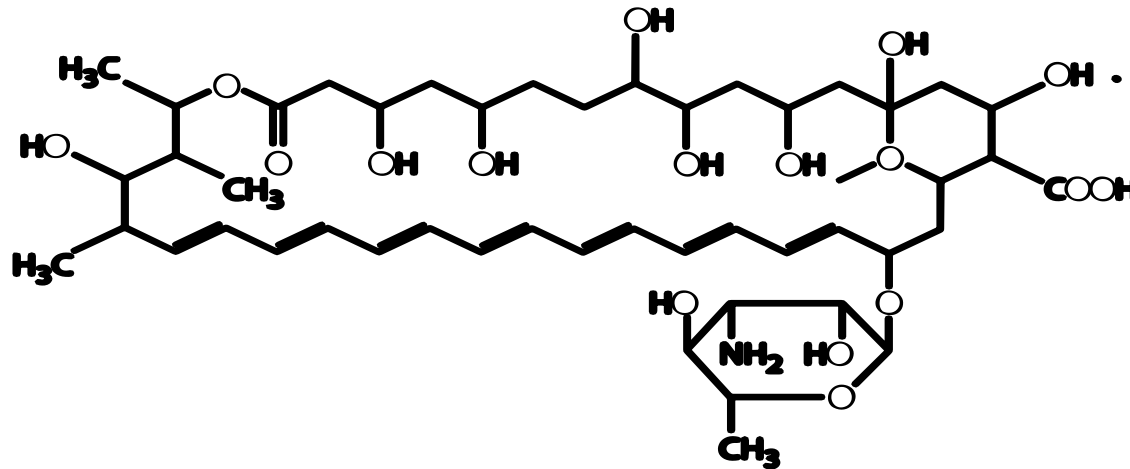
1990

2000

2010



# Amphotericin B



- Classic amphotericin B deoxycholate formulation is a colloidal suspension of amphotericin B. A bile salt, deoxycholate, is used as the solubilizing agent.
- Many side effects: infusion related, nephrotoxicity, ...
- Not available anymore in Belgium
- Very broad spectrum, active against most fungi except *Aspergillus terreus*, *Scedosporium*, *Trichosporon* and *Candida lusitanae* (intrinsic resistance)
- Acquired resistance is rare
- Fungicidal

Binds to sterols  
(preferentially ergosterol)



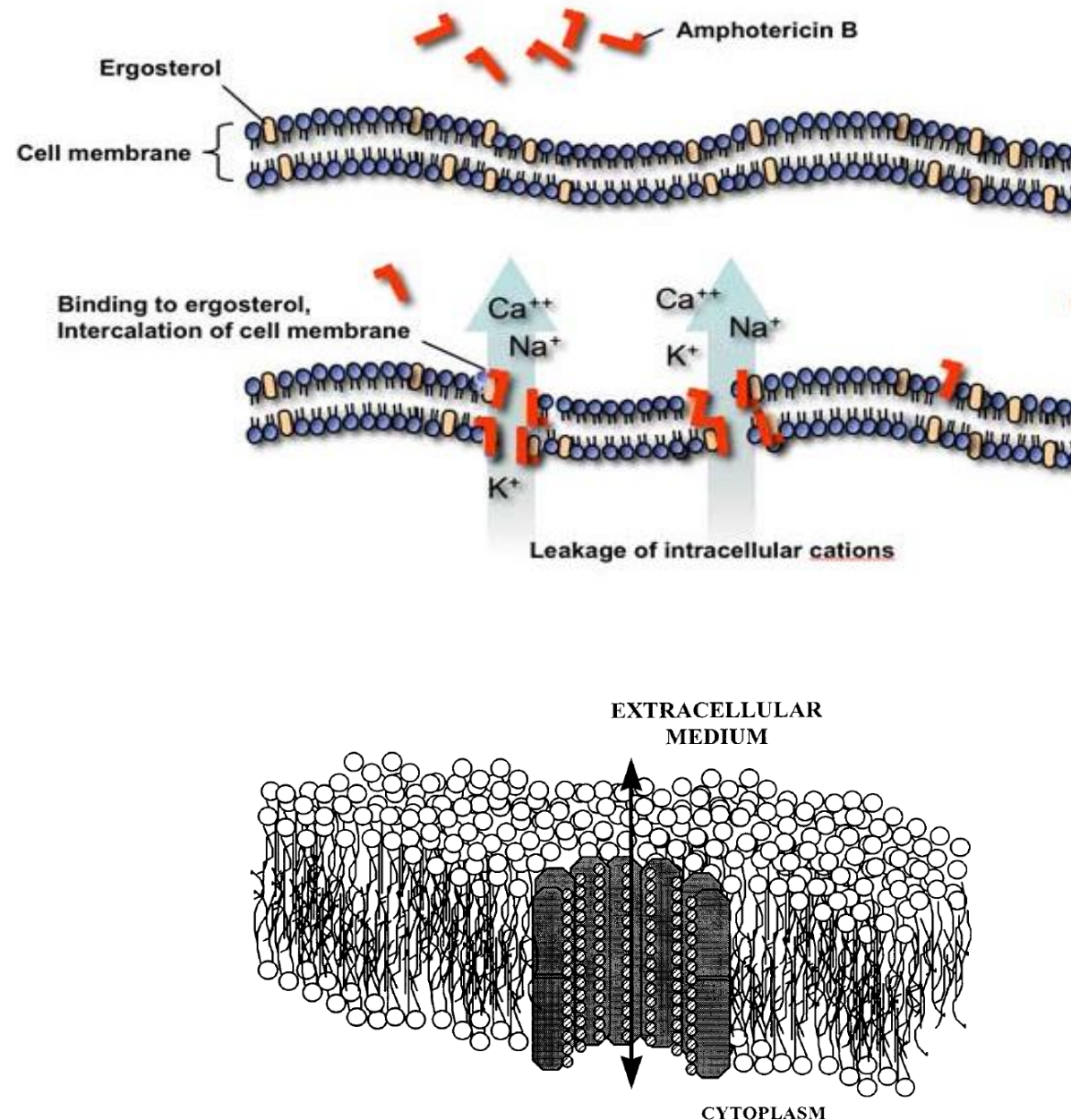
Disruption osmotic integrity  
of fungal membrane



Leakage of intracellular  
components



Fungal death





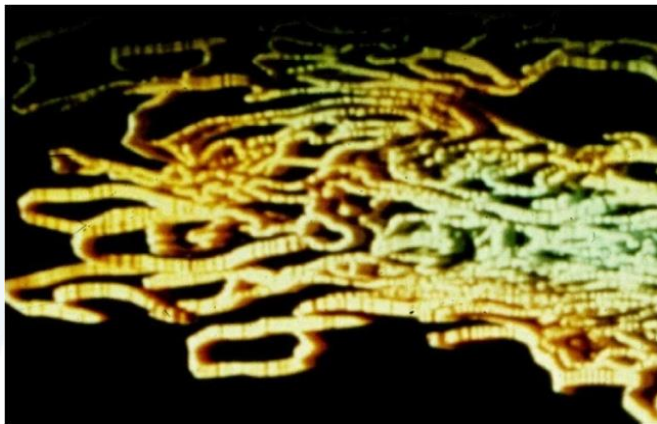
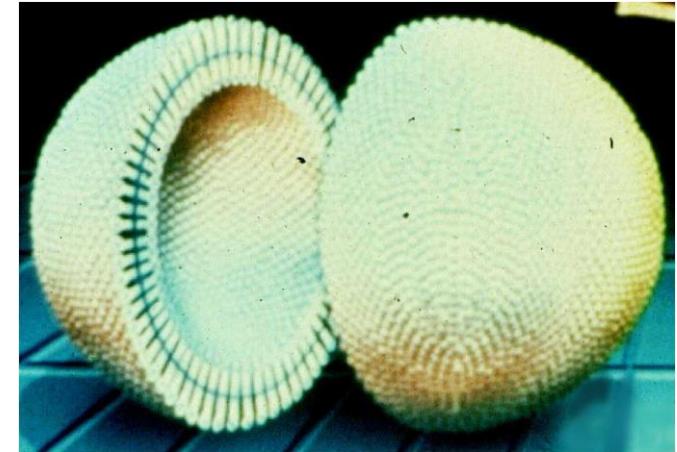


# Lipid formulations of amphotericin B

## liposomal amphotericin B (0.08 $\mu\text{m}$ )

(L-Amb, Ambisome<sup>®</sup>): 3 mg/kg IV

higher dose for the treatment of mucormycosis  
(5-10 mg/kg IV)



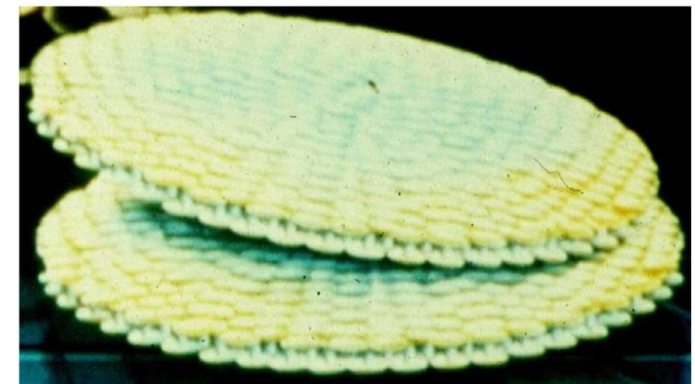
## amphotericin B lipid complex (1.6-11 $\mu\text{m}$ )

phospholipid ribbons

(ABLC, Abelcet<sup>®</sup>): 5 mg/kg IV

## amphotericin B colloidal dispersion (0.12-0.14 $\mu\text{m}$ )

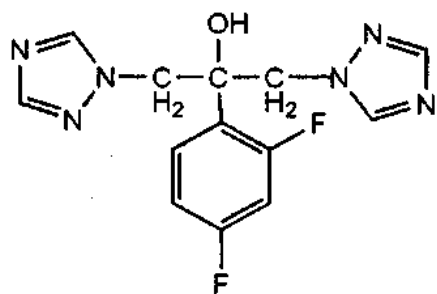
cholesteryl sulfate complex  
not available in Belgium



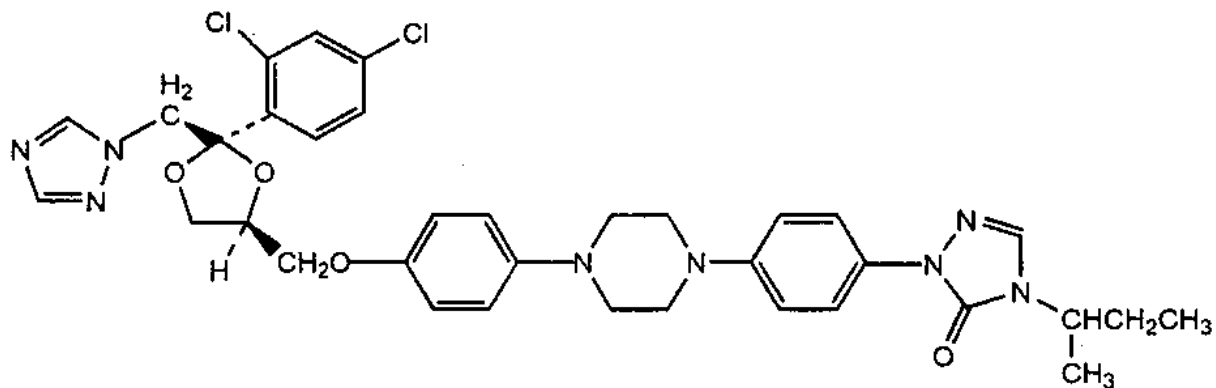




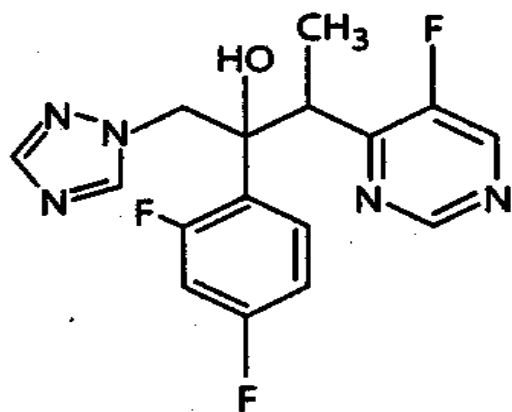
# TRIAZOLES



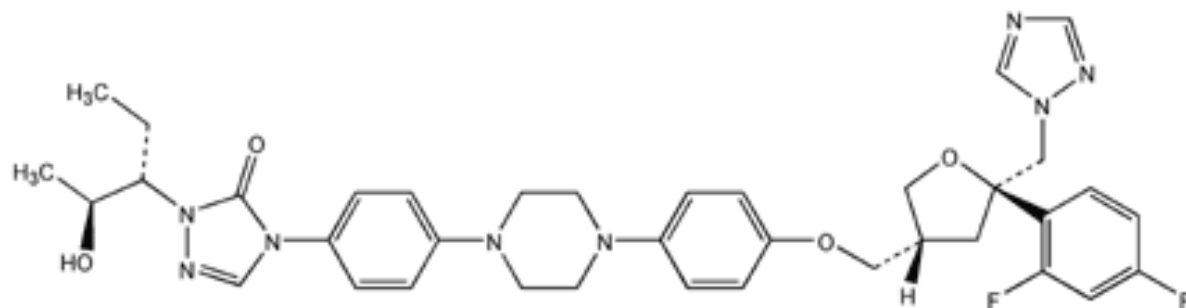
**FLUCONAZOLE**



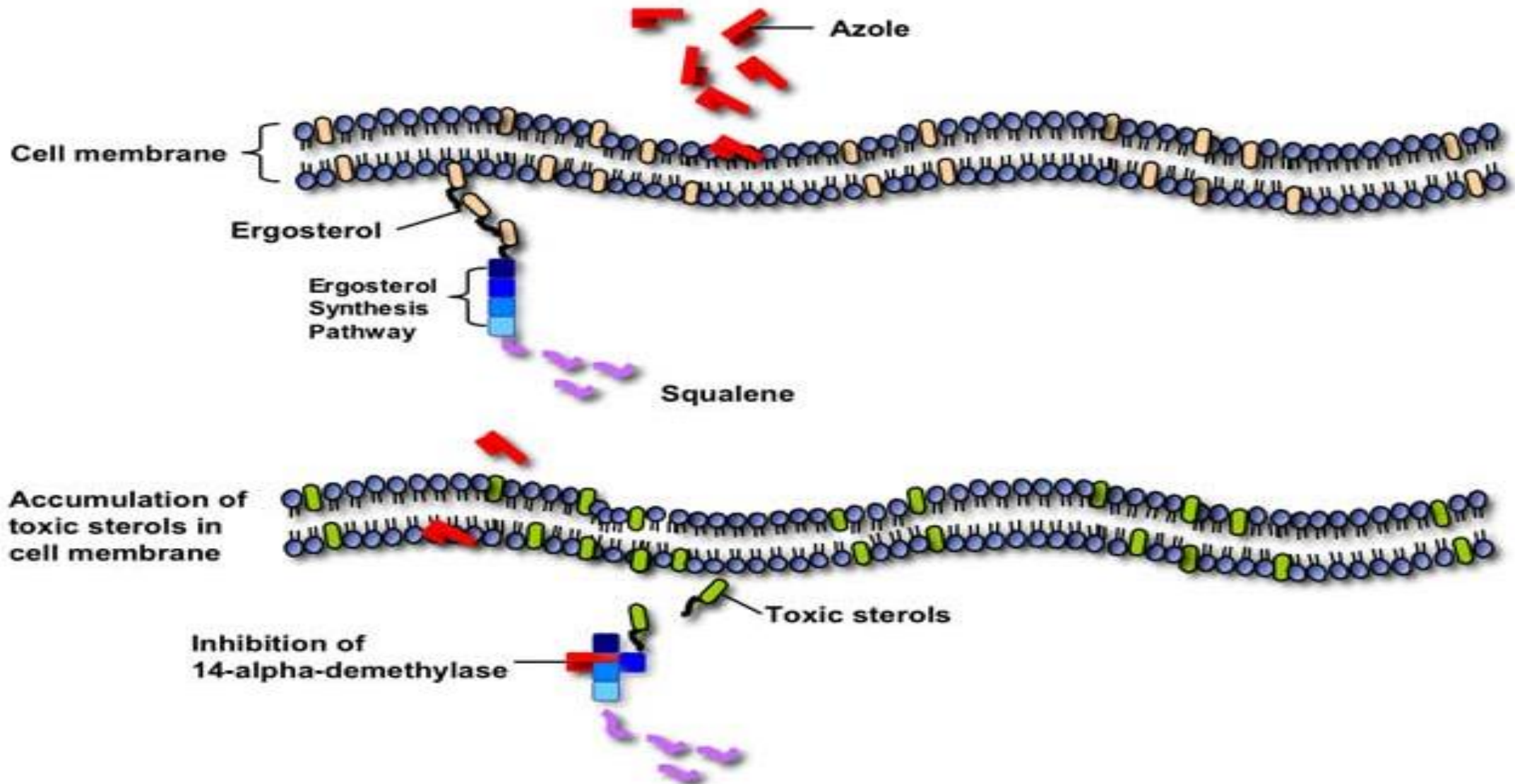
**ITRACONAZOLE**



**VORICONAZOLE**



**POSACONAZOLE**



Organism	AmB <sup>a</sup>	Flu	Itr	Vor	Pos
<i>Aspergillus</i> species	+	—	+	+	+
<i>A. flavus</i>	±	—	+	+	+
<i>A. fumigatus</i>	+	—	+	+	+
<i>A. niger</i>	+	—	±	+	+
<i>A. terreus</i>	—	—	+	+	+
<i>Candida</i> species	+	+	+	+	+
<i>C. albicans</i>	+	+	+	+	+
<i>C. glabrata</i>	+	±	±	+	+
<i>C. krusei</i>	+	—	±	+	+
<i>C. lusitaniae</i>	—	+	+	+	+
<i>C. parapsilosis</i>	+	+	+	+	+
<i>C. tropicalis</i>	+	+	+	+	+
<i>Cryptococcus neoformans</i>	+	+	+	+	+
<i>Coccidioides</i> species	+	+	+	+	+
<i>Blastomyces</i>	+	+	+	+	+
<i>Histoplasma</i> species	+	+	+	+	+
<i>Fusarium</i> species	±	—	—	+	+
<i>Scedosporium apiospermum</i>	±	—	±	+	+
<i>Scedosporium prolificans</i>	—	—	—	±	±
Zygomycetes	±	—	—	—	+

Active (cidal)  
against  
*Aspergillus* spp.

Newer triazoles  
better activity (static)  
against *Candida*  
spp.

No activity against  
*Mucorales* except  
*posaconazole*

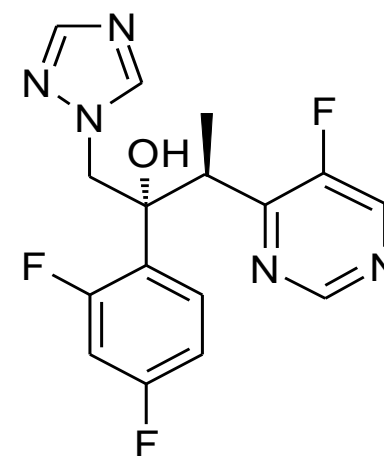
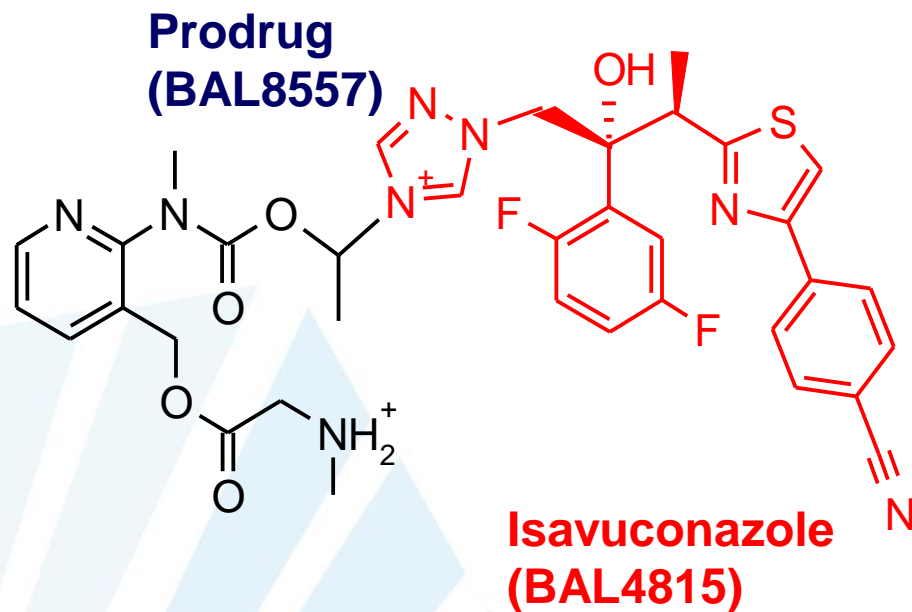


# Activity of azoles

- Binding affinity of each drug defined by:
  - differences in the conformation of the 14 $\alpha$ -demethylase binding pocket
  - azole structure
- Resistance in ***Candida***: mutations in *ERG11* and/or overexpression of efflux pumps
  - ***C. krusei***: impaired binding of fluconazole to 14 $\alpha$ -demethylase of *C. krusei*, newer triazoles retain activity
  - ***C. glabrata***: often due to expression of multidrug efflux pumps, cross resistance may occur
- Resistance in ***Aspergillus***: mutations in the *Cyp51A* gene (+ promotor region), overexpression of efflux pumps described



# Isavuconazole



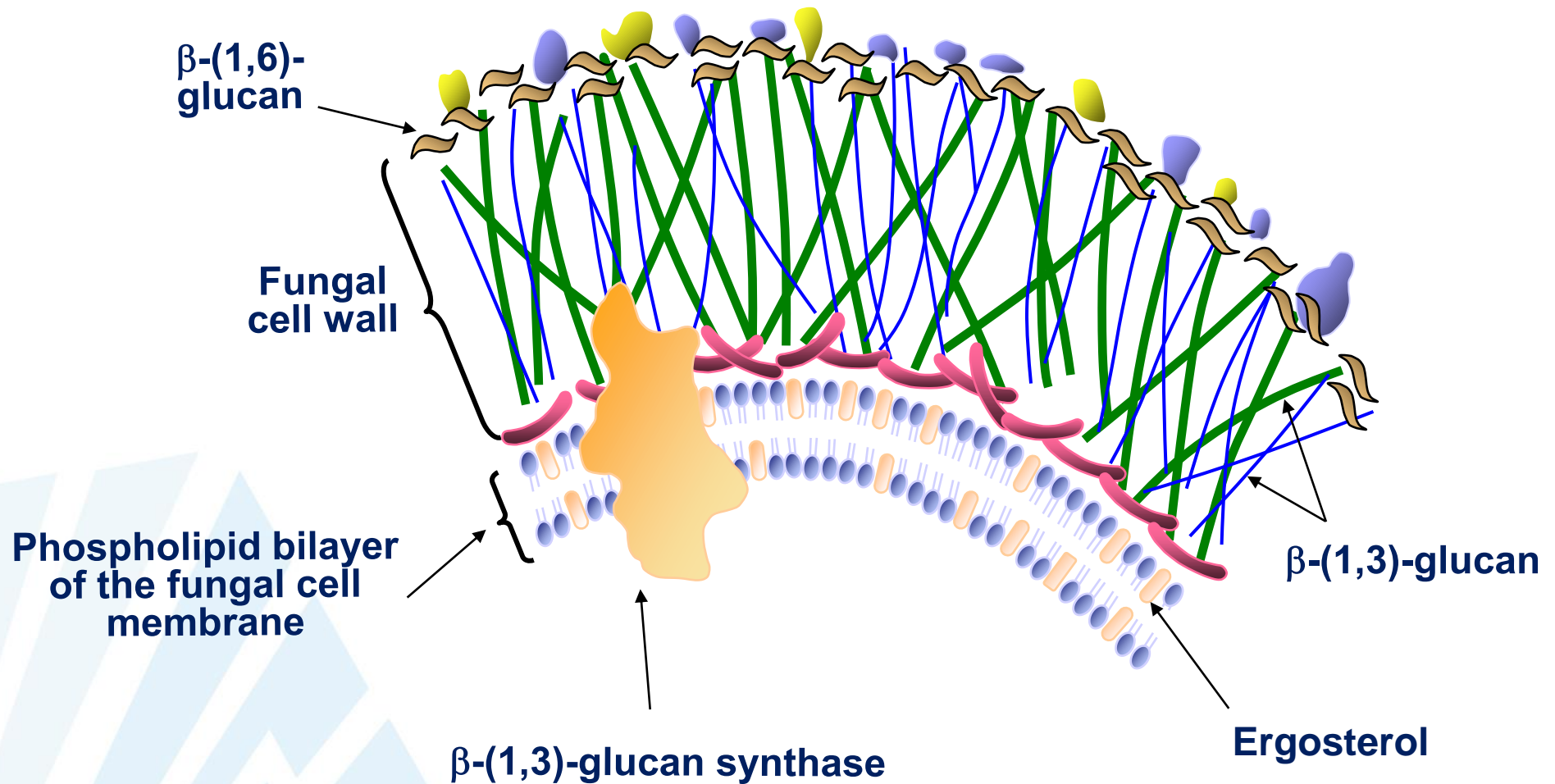
High water solubility of prodrug isavuconazonium sulfate

	AMB	CAN	FLC	ITC	VRC	POS	ISA
<b>Candida albicans</b>							
<b>Candida tropicalis</b>							
<b>Candida parapsilosis</b>							
<b>Candida krusei</b>							
<b>Candida glabrata</b>							
<b>Aspergillus fumigatus</b>							
<b>Aspergillus terreus</b>							
<b>Cryptococcus neoformans</b>							
<b>Trichosporon spp.</b>							
<b>Mucormycetes</b>							
<b>Fusarium solani</b>							
<b>Scedosporium apiospermum</b>							
<b>(Chromoblastomycosis)</b>							
<b>(Phaeohyphomycosis)</b>							
<b>Paracoccidioides brasiliensis</b>							
<b>Histoplasma capsulatum</b>							
<b>Blastomyces dermatitidis</b>							
<b>Coccidioides immitis</b>							

	<b>Active</b>
	<b>Some resist.</b>
	<b>Not active</b>



# Echinocandin drugs



**Development of echinocandin resistance during therapy is a relatively rare clinical phenomenon.**

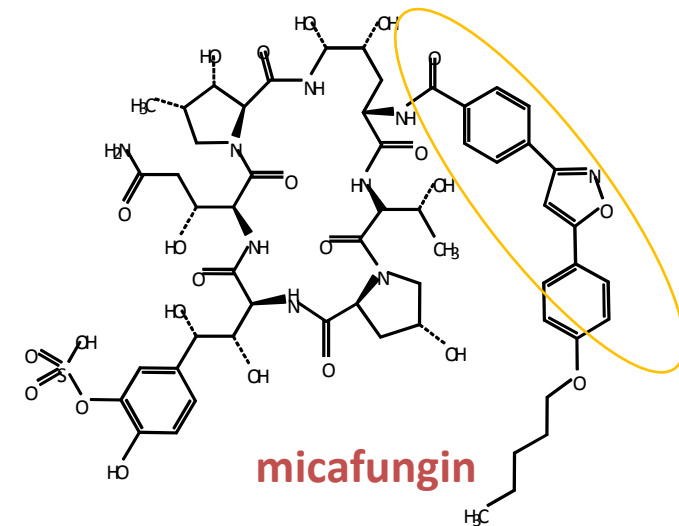
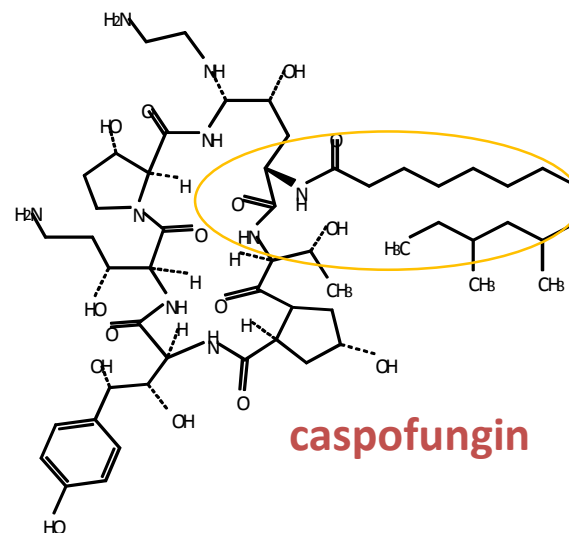
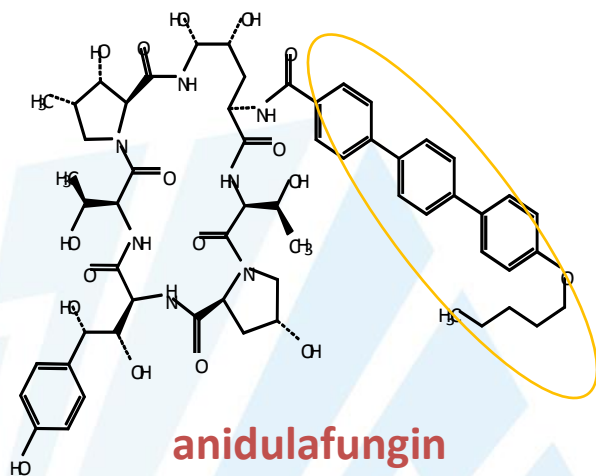
Mutations in 'hot spot' regions of the FKS1 and FKS2 catalytic subunits of the glucan synthase are associated with reduced inhibitory activity.





# ECHINOCANDINS

PK is specific for each echinocandin



Side chain determines:

- Activity: interaction with the cell wall
- Pharmacokinetics: more lipophilic → higher distribution volume



Organism	Antifungal agent		
	Anidulafungin	Caspofungin	Micafungin
<i>Aspergillus</i> species	+	+	+
<i>A. flavus</i>	+	+	+
<i>A. fumigatus</i>	+	+	+
<i>A. niger</i>	+	+	+
<i>A. terreus</i>	+	+	+
<i>Candida</i> species	+	+	+
<i>C. albicans</i>	+	+	+
<i>C. glabrata</i>	+	+	+
<i>C. krusei</i>	+	+	+
<i>C. lusitaniae</i>	+	+	+
<i>C. parapsilosis</i>	±	±	±
<i>C. tropicalis</i>	+	+	+
<i>Cryptococcus neoformans</i>	—	—	—
<i>Coccidioides</i> species	± <sup>b</sup>	± <sup>b</sup>	± <sup>b</sup>
<i>Blastomyces</i>	± <sup>b</sup>	± <sup>b</sup>	± <sup>b</sup>
<i>Histoplasma</i> species	± <sup>b</sup>	± <sup>b</sup>	± <sup>b</sup>
<i>Fusarium</i> species	—	—	—
<i>Scedosporium apiospermum</i>	—	—	—
<i>Scedosporium prolificans</i>	—	—	—
<i>Zygomycetes</i>	—	—	—

Active (static)  
against  
*Aspergillus spp.*

Active (cidal)  
against  
*Candida spp.*



**Fusarium species**

**Scedosporium apiospermum**

**Scedosporium prolificans**

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# Resistance to echinocandins/ amphotericin B

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- Echinocandins:

Little known about echinocandin resistance in *Aspergillus*, susceptibility testing is not routinely performed, technical difficulties, mechanisms not well understood

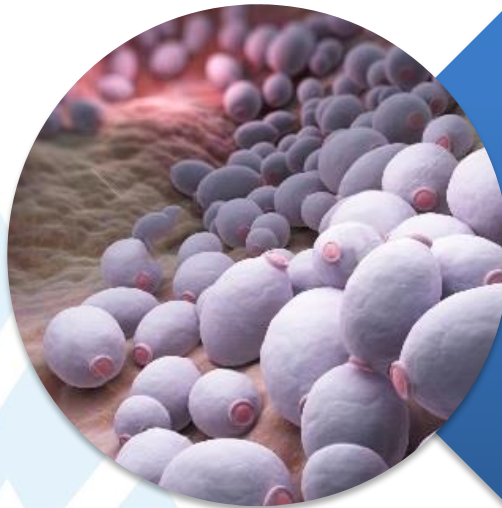
- Polyenes:

- Primary and secondary polyene resistance reported but generally considered a rare phenomenon
- No clear in vitro/in vivo correlation
- *Aspergillus terreus*: less ergosterol in membrane

Is emergence of (multi)drug resistance in *Candida* and *Aspergillus* a matter of concern?

Is susceptibility testing of *Candida* and *Aspergillus* important to guide therapy?



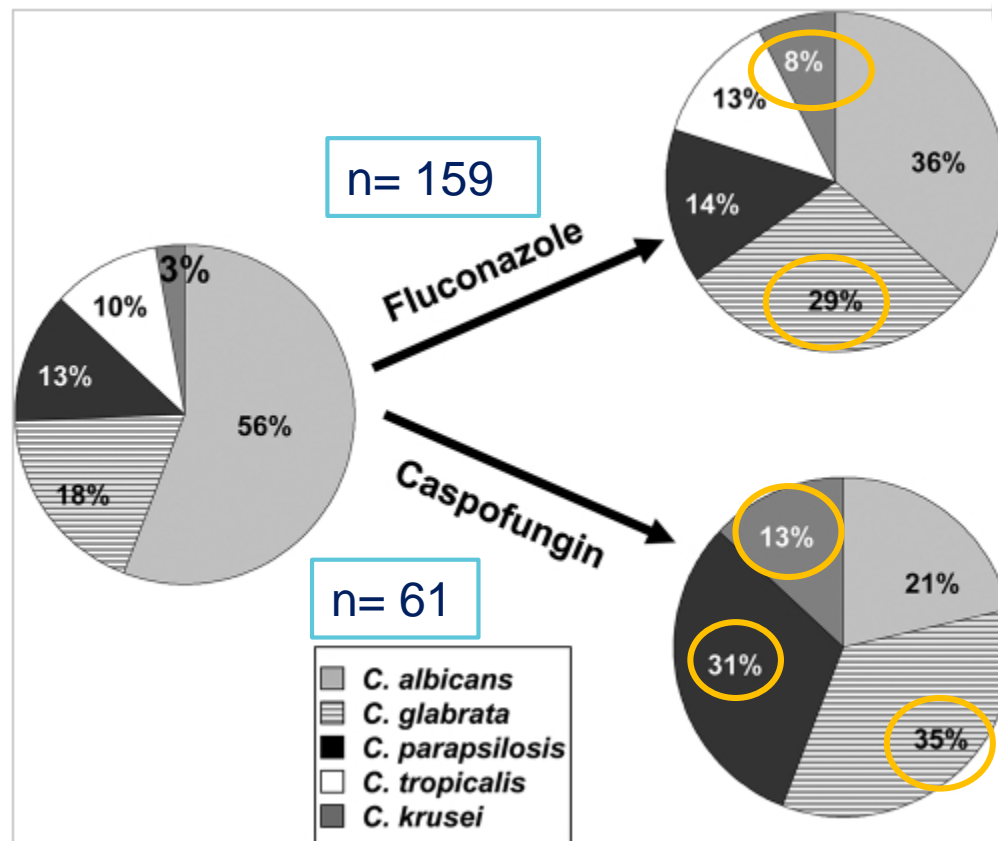


# Candida



# Recent exposure to caspofungin or fluconazole influences the epidemiology of candidemia

- Prospective multicenter surveillance, Paris
- 2618 isolates from 2441 patients (2002-2009)



MICs were significantly higher in the cases of pre-exposure to fluconazole and caspofungin, respectively.





# Drug resistant *Candida glabrata* in cancer patients

- Retrospective study
- MD Anderson Cancer Center Houston (Texas)
- March 2005-Sept 2013

**146 *C. glabrata* candidemia episodes (144 patients)**

**30 (20.5%) fluconazole R**

**15 (10.3%) caspofungin R**

30%

66.6%

**10 (6.8%) multidrug R**

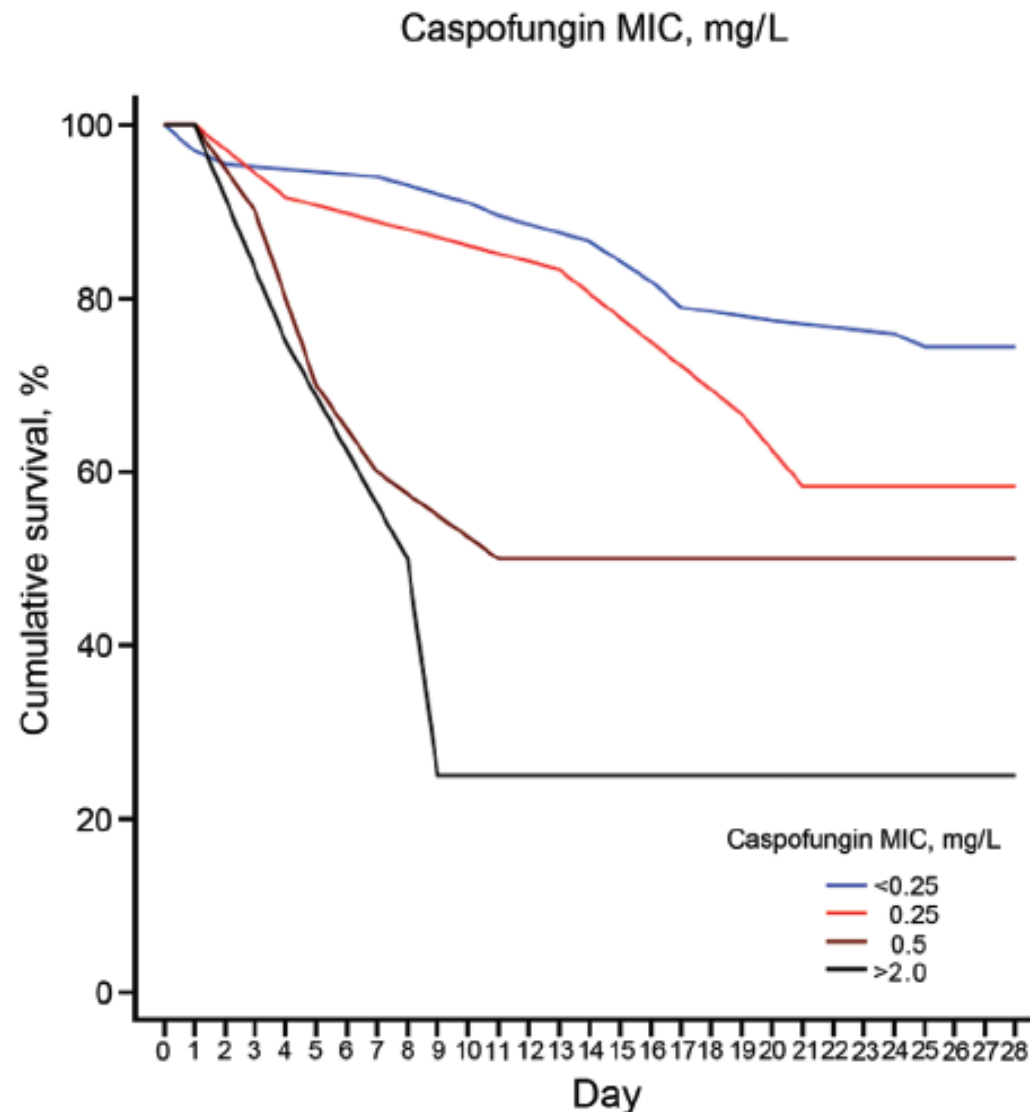
9 fluco/caspo  
1 caspo/amphoB

**Independently associated with:**

- Echinocandin preexposure
- Total parenteral nutrition



# Drug resistant *Candida glabrata* in cancer patients



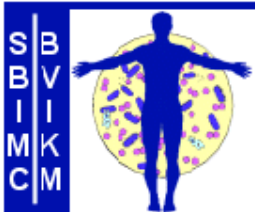
Strong correlation of all-cause mortality rates with in vitro caspofungin MICs but not with other factors classically associated with poor outcomes

2012 intermediate susceptibility

2012 breakpoint for R

2008 breakpoint for R





Société belge d'infectiologie et de microbiologie clinique

Belgische vereniging voor infectiologie en klinische microbiologie

# BELGIAN DATA

Eur J Clin Microbiol Infect Dis  
DOI 10.1007/s10096-016-2841-3



ORIGINAL ARTICLE

## Epidemiology and reporting of candidaemia in Belgium: a multi-centre study

C. Trouvé<sup>1</sup> • S. Blot<sup>2,3</sup> • M.-P. Hayette<sup>4</sup> • S. Jonckheere<sup>5</sup> • S. Patteet<sup>1,9</sup> •  
H. Rodriguez-Villalobos<sup>6</sup> • F. Symoens<sup>7</sup> • E. Van Wijngaerden<sup>8</sup> • K. Lagrou<sup>1,9</sup>



# Objectives TANSIR study

Time to cANdida

Species

Identification and

Reporting

- **Gather epidemiological data on candidemia in Belgium**
  - Incidence
  - Species distribution
  - Antifungal profiles
- **Assess clinical reporting times in “real life” setting**
  - Blood sampling => positive blood culture
  - Positive blood culture => ID communication to clinician
  - Positive blood culture => AB communication to clinician



# Species distribution per ward

Top 5 ward species distribution of the 325 patients which had an episode of candidemia during the study period

Ward	No. of isolates (%)					Overall
	<i>C. albicans</i>	<i>C. glabrata</i>	<i>C. parapsilosis</i>	<i>C. tropicalis</i>	Other species	
ICU	70 (71.4)	18 (18.4)	5 (5.1)	3 (3.1)	2 (2.0)	98 (100)
Internal medicine	49 (52.7)	30 (32.3)	11 (11.8)	1 (1.1)	2 (2.1)	93 (100)
Surgery	20 (43.5)	19 (41.3)	4 (8.7)	2 (4.3)	1 (2.2)	46 (100)
Haematology-Oncology	18 (51.4)	5 (14.3)	2 (5.7)	5 (14.3)	5 (14.3)	35 (100)
Pediatrics	9 (50.0)	1 (5.6)	4 (22.2)	1 (5.6)	3 (16.6)	18 (100)

→ Different species distribution according to ward ( $P < 0.001$ )

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H. Rodriguez-Villalobos<sup>6</sup> · F. Symoens<sup>7</sup> · E. Van Wijngaerden<sup>8</sup> · K. Lagrou<sup>1,9</sup>

	FLC		VRC		POS		AND		MCF		AMB	
	% S	% R	% S	% R	% S	% R	% S	% R	% S	% R	% S	% R
<i>C. albicans</i>	92.7	3.9	96.1	3.9	96.6	3.4	100	0	100	0	100	0
<i>C. glabrata</i>	0	11.3	/*	/*	/*	/*	99.0	1.0	99.0	1.0	100	0
<i>C. parapsilosis</i>	94.4	5.6	94.4	5.6	97.2	2.8	0**	0**	0**	0**	100	0
<i>C. tropicalis</i>	75.0	20.0	80.0	20.0	80.0	20.0	100	0	/*	/*	100	0
Total	65.5	7.6	/*	/*	/*	/*	99.7	0.3	99.7	0.3	100	0

FLC: fluconazole; VRC: voriconazole; POS: posaconazole; AND: anidulafungin; MCF: micafungin; AMB: amphotericin B

\*No EUCAST breakpoints available

\*\*All strains were classified as intermediate susceptible

**Drug resistance**  
The Observer

## Millions at risk as deadly fungal infections acquire drug resistance

Researchers believe widespread use of fungicides on crops is reducing effectiveness of frontline medicines

Robin McKie Science Editor

Saturday 27 August 2016 21.00 BST



◀ Shares

3,528



Save for later



📷 *Aspergillus fumigatus*, one of the most common aspergillus species to cause disease in individuals with an immunodeficiency. Photograph: Alamy



Scientists have warned that potentially deadly fungal infections are acquiring resistance to many of the medicines currently used to combat them. **More than a million people die of fungal infections every year**, including about 7,000 in the UK, and deaths are likely to increase as resistance continues to rise. **Researchers say the widespread use of fungicides on crops is one of the main causes of the rise in fungal resistance**, which mirrors the rise of resistance to antibiotics used to treat bacterial infections in humans.

“There are close parallels between bacterial and fungal resistance, though the problems we face with the latter are particularly worrying,” said Prof Adilia Warris, a co-director of the **newly opened Centre for Medical Mycology at Aberdeen University**.

**“There are more than 20 different classes of antibacterial agents. By contrast, there are only four classes of anti-fungal agents. Our armory for dealing with deadly fungi is much smaller than the one we have for dealing with bacteria.**

Doctors have recently uncovered another worrying development: outbreaks of fungal infections – mainly cryptococcus – that have appeared in previously healthy people. In one outbreak, in the northwest US, dozens of people died.

In the wake of these developments, it was decided by Britain’s Medical Research Council to open its Aberdeen mycology centre earlier this year.

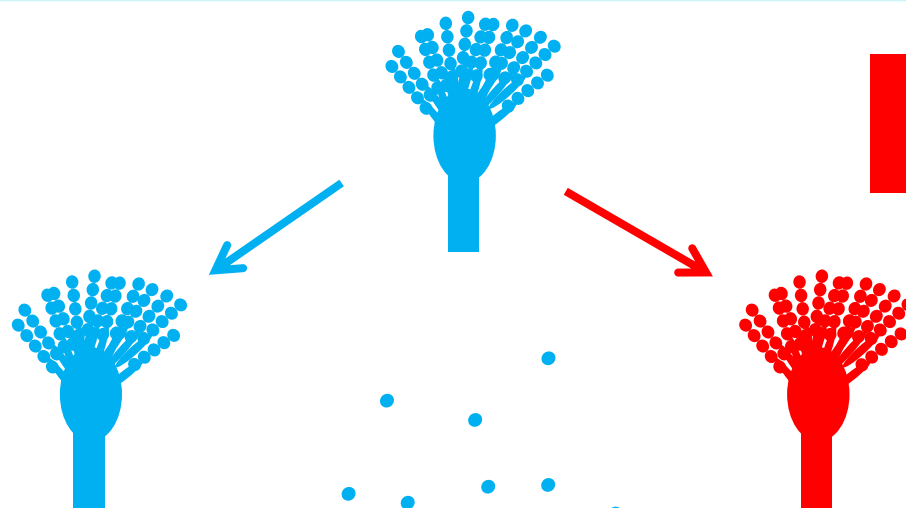
It will employ experts in the field to gain new understanding of how fungi move into the human body and survive there. It will also work on the development of new drugs and tests for pinpointing specific fungi that are infecting patients.

**“Fungal infections are going to be an increasing problem in coming years and we need to develop the best defences,” said Brown.**



# Routes of resistance development in *A. fumigatus*

## ENVIRONMENT

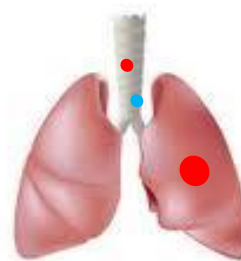
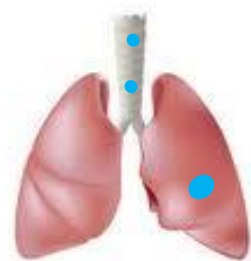


Triazole fungicides in agriculture

TR<sub>34</sub>/L98H  
TR<sub>46</sub>/Y121F/T289A

- Patients with IA and chronic Aspergillus diseases
- Low genetic diversity between azole-resistant isolates from unrelated patients
- No apparent fitness cost

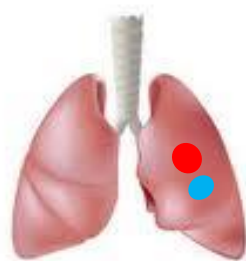
## PATIENT



Long-term triazole treatment for aspergilloma or cavitary lung disease

Variety of resistance mechanisms

- High genetic diversity between azole-resistant isolates from unrelated patients
- Lack of sporulation and reduced growth rate may occur





# Global presence of azole resistance in *A. fumigatus*



Countries that reported the TR<sub>34</sub>/L98H and TR<sub>46</sub>/Y121F/T289A resistance mechanism in clinical or environmental *A. fumigatus*





# High prevalence of azole resistance in patients on the hematology ward in Utrecht

Patient characteristics

Year	No. of patients	Age (years), median (range)	Male, %	Hospital ward	No. of patients (percentage of voriconazole-resistant isolates)	Resistance to voriconazole <sup>a</sup>		Resistance to itraconazole <sup>a</sup>		Resistance to posaconazole <sup>a</sup>	
						phenotype	no. of patient isolates (%)	phenotype	no. of patient isolates (%)	phenotype	no. of patient isolates (%)
2011	30	58.5 (10–80)	70.0	Haematology ICU	20 (50.0) 10 (0.0)	susceptible intermediate resistant	20/30 (66.7) 0 10/30 (33.3)	susceptible intermediate resistant	19/30 (63.3) 0 11/30 (36.7)	susceptible intermediate resistant	18/30 (60.0) 2/30 (6.7) 10/30 (33.3)
2012	42	63.5 (1–82)	42.9	Haematology ICU	19 (5.3) 23 (8.7)	susceptible intermediate resistant	34/42 (81.0) 5/42 (11.9) 3/42 (7.1)	susceptible intermediate resistant	36/42 (85.7) 0 6/42 (14.3)	susceptible intermediate resistant	34/42 (81.0) 3/42 (7.1) 5/42 (11.9)
2013	33	58 (9–78)	57.6	Haematology ICU	22 (18.2) 11 (0.0)	susceptible intermediate resistant	27/33 (81.8) 2/33 (6.1) 4/33 (12.1)	susceptible intermediate resistant	29/33 (87.9) 0 4/33 (12.1)	susceptible intermediate resistant	24/33 (72.7) 5/33 (15.2) 4/33 (12.1)
Total	105	60 (1–82)	55.2	Haematology ICU	61 (24.6) 44 (4.5)	susceptible intermediate resistant	81/105 (77.1) 7/105 (6.7) 17/105 (16.2)	susceptible intermediate resistant	84/105 (80.0) 0 21/105 (20.0)	susceptible intermediate resistant	76/105 (72.4) 10/105 (9.5) 19/105 (18.1)

<sup>a</sup>Voriconazole: resistant MIC >2 mg/L and susceptible MIC ≤1 mg/L; itraconazole: resistant MIC >2 mg/L and susceptible MIC ≤1 mg/L; posaconazole: resistant MIC >0.25 mg/L and susceptible MIC ≤0.12 mg/L.<sup>8,9</sup> Values between resistant and susceptible were considered intermediate.<sup>8,9</sup>

- 105 positive cultures collected; proven IA (5), probable IA (48) and no infection (52)
- 21/105 (20%) isolates were resistant to at least one azole
- 16/105 (15.2) isolates showed pan-azole resistance
- 16/17 (94.1%) of voriconazole resistant isolates exhibit *cyp51A* gene mutation



# **BELGIAN DATA**



# Belgium nationwide surveillance

	# Isolates	# Patients	Rate of azole-resistance	Prevalence of azole-resistance	Mechanism of resistance (number of patients)
<b>Invasive aspergillosis</b>					
<i>A. fumigatus</i>	115	108	5/115 (4·4%)	5/108 (4·6%) <sup>4</sup>	4 TR <sub>34</sub> /L98H, 1 non-Cyp51A
<i>A. niger</i>	9	9	8/9 (89%)	8/9 (89%)	8 intrinsic (8 <i>A. tubingensis</i> )
Other species	10	10	0/10	0/10	
<b>ABPA and bronchitis</b>					
<i>A. fumigatus</i>	62	44	6/62 (9·7%)	4/44 (9·1%)	2 TR <sub>34</sub> /L98H, 1 TR <sub>46</sub> /Y121F/T289A, 1 non-Cyp51A mediated
<i>A. niger</i>	1	1	1/1	1/1	1 intrinsic (1 <i>A. tubingensis</i> )
Other	3	2	0/3	0/2	/
<b>Chronic aspergillosis<sup>1</sup></b>					
<i>A. fumigatus</i>	15	13	0/15 (0%)	0/13 (0%)	/
<i>A. niger</i>	0	0	/	/	/
Other	5	3	0/5	0/3	/
<b>Total</b>					
<i>A. fumigatus</i>	192	164	11/192 (5·7%)	9/164 (5·5%)	6 TR <sub>34</sub> /L98H, 1 TR <sub>46</sub> /Y121F/T289A, 2 non-Cyp51A mediated
<i>A. niger</i>	10	10	9/10 (90%)	9/10 (90%)	9 intrinsic (9 <i>A. tubingensis</i> )
Other	18	15	0/18 (0%)	0/15 (0%)	/

Drug Resistance Updates 21–22 (2015) 30–40



Contents lists available at ScienceDirect

## Drug Resistance Updates

journal homepage: [www.elsevier.com/locate/drug](http://www.elsevier.com/locate/drug)



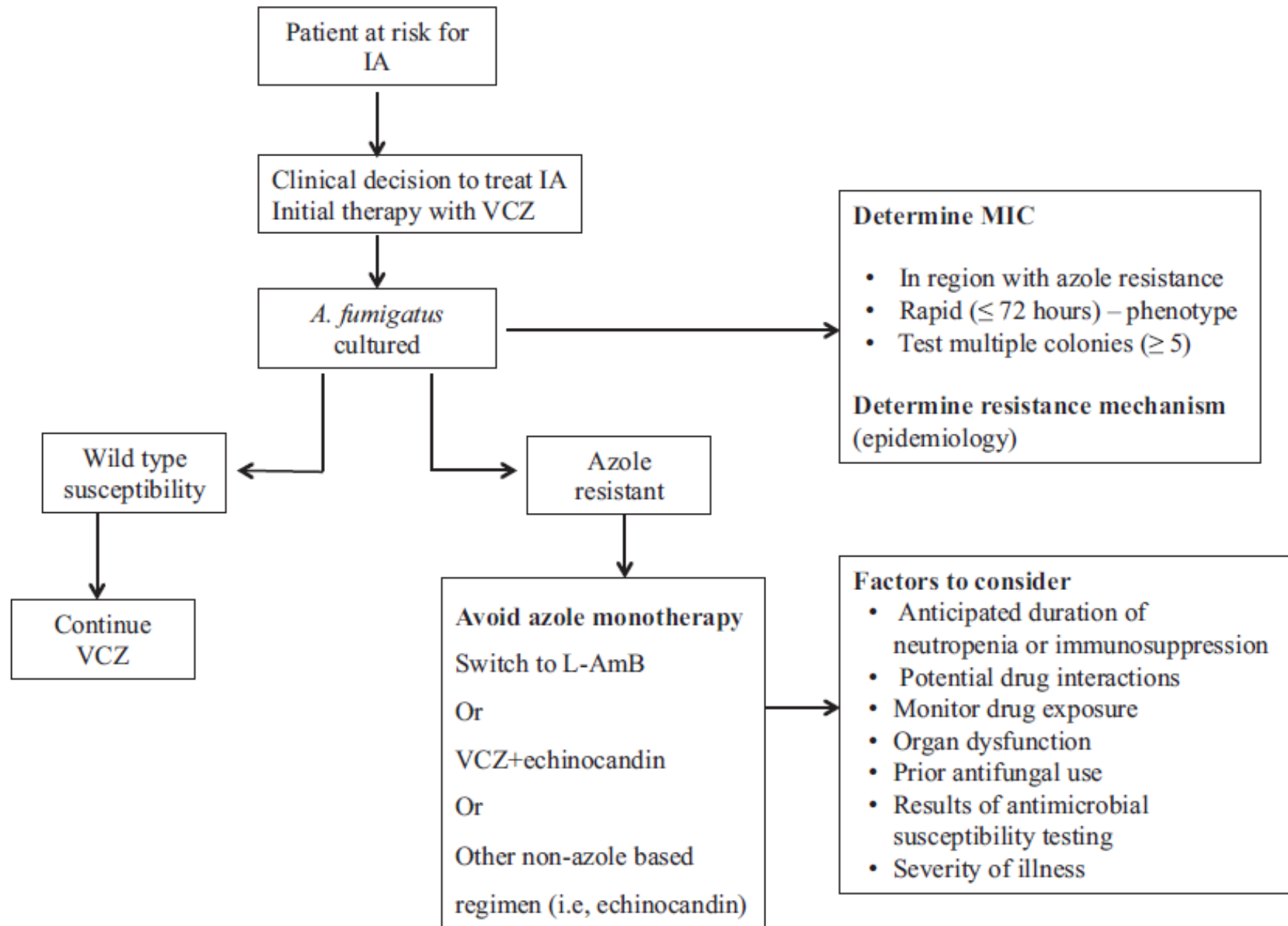
### International expert opinion on the management of infection caused by azole-resistant *Aspergillus fumigatus*



Paul E. Verweij<sup>a,\*</sup>, Michelle Ananda-Rajah<sup>b</sup>, David Andes<sup>c</sup>, Maiken C. Arendrup<sup>d</sup>, Roger J. Brüggemann<sup>e</sup>, Anuradha Chowdhary<sup>f</sup>, Oliver A. Cornely<sup>g</sup>, David W. Denning<sup>h</sup>, Andreas H. Groll<sup>i</sup>, Koichi Izumikawa<sup>j</sup>, Bart Jan Kullberg<sup>k</sup>, Katrien Lagrou<sup>l</sup>, Johan Maertens<sup>m</sup>, Jacques F. Meis<sup>a,n</sup>, Pippa Newton<sup>h</sup>, Iain Page<sup>h</sup>, Seyedmojtaba Seyedmousavi<sup>a</sup>, Donald C. Sheppard<sup>o</sup>, Claudio Viscoli<sup>p</sup>, Adilia Warris<sup>q</sup>, J. Peter Donnelly<sup>r</sup>

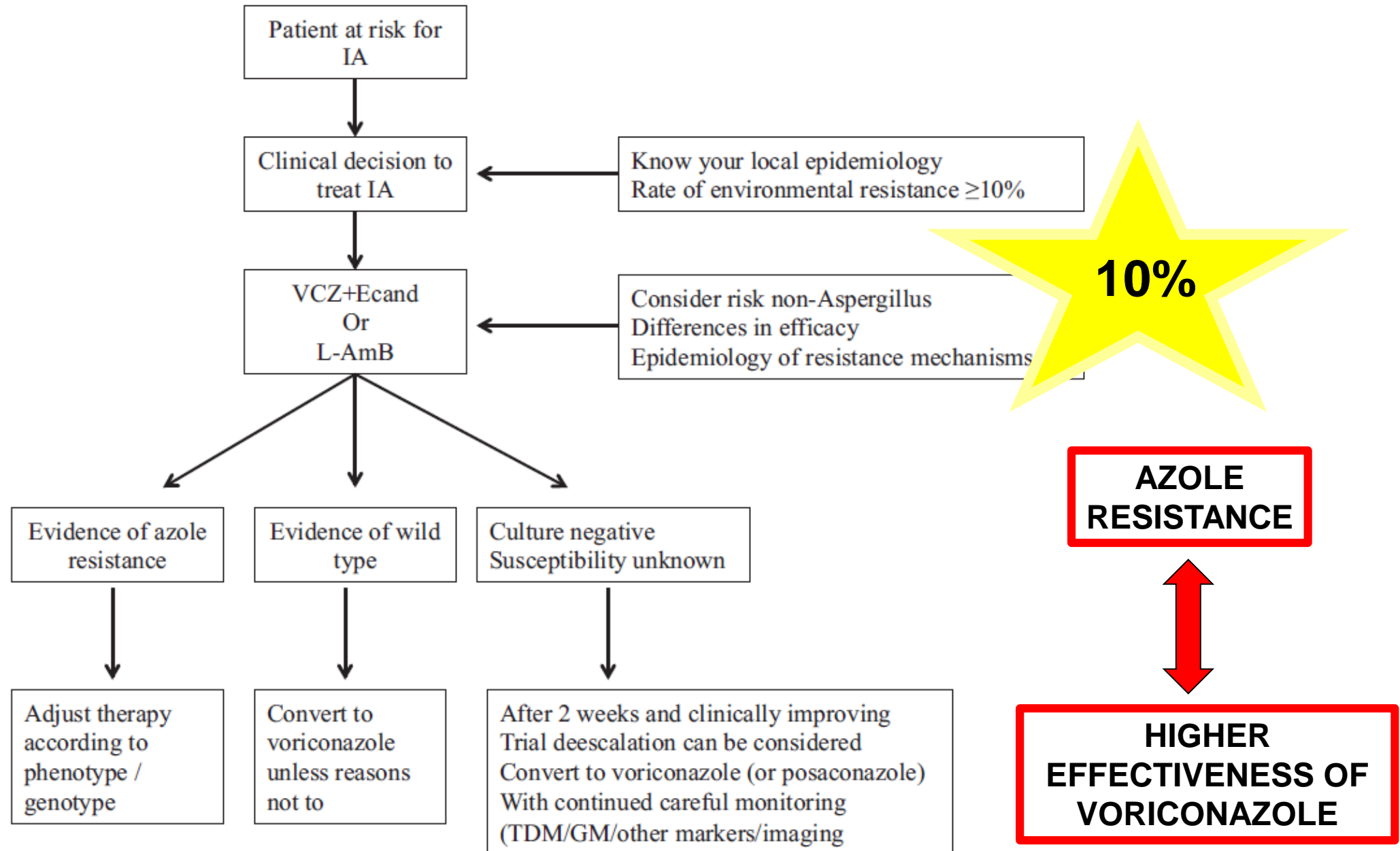


# Management of patients with IA in regions with no/minimal azole resistance in the environment





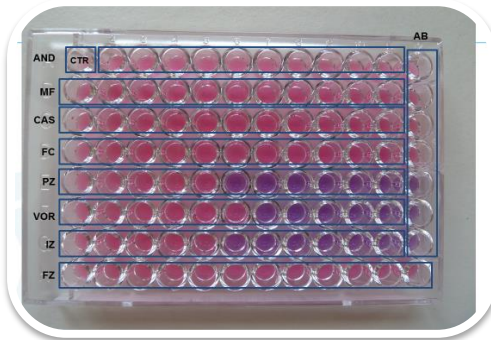
# Management of patients with IA in regions with $\geq 10\%$ environment resistance







# Triazole resistance detection in *Aspergillus*



## MIC determination

- CLSI/EUCAST
- Commercial systems



## Triazole resistance screening agar (VIPcheck™)

Sensitivity 97%  
Specificity 98%



## Molecular methods

- In house
- AsperGenius® assay

Resistance multiplex

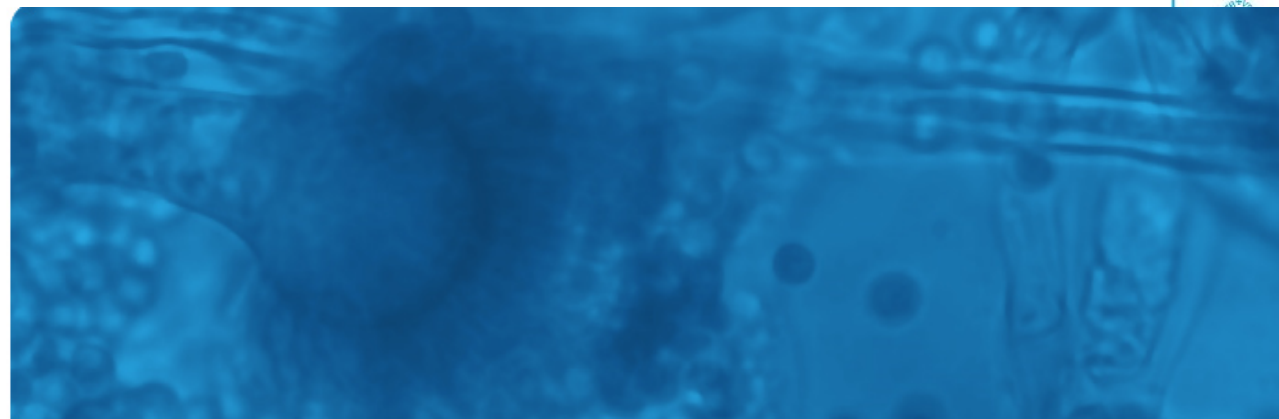
- L98H
- Tandem repeat 34
- T289A
- Y121F

- Always perform susceptibility testing if antifungal therapy is intended – contact the lab!
- Both azole-susceptible and azole-resistant phenotypes can be simultaneously present in culture, test multiple colonies!





# Belgian Society Human Animal Mycology



The society

Mycology courses

National meetings

International meetings

Members

Composition

Membership

International study

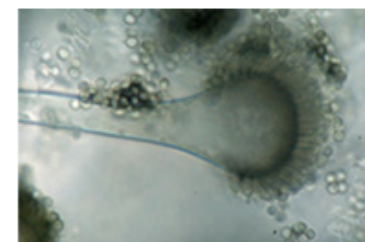
Links

Contact us

## Belgian Society of Human and Animal Mycology

The **Belgian Society for Human and Animal Mycology (BSHAM)** was created in 1964 by Raymond Vanbreuseghem, physician, Professor of Parasitology at the Free University of Brussels, and Professor of Medical Mycology at the Institute of Tropical Medicine in Antwerp.

It is an VZW/ASBL concerned with pathologies induced by fungi and yeasts such as fungal allergies, mycotoxicoses, mycetism and mycoses.



BSHAM is a bilingual society with about 85 members presently.

It is directed by a Board meeting 2 or 3 times per year, most of the information being given by e-mail. A plenary administrative meeting (general meeting) is organised once a year. The annual scientific meeting takes place successively in Brussels, Flanders and Wallonia.

All BSHAM members are automatically members of the European Confederation of Medical Mycology. Many of them are also member of the **International Society for Human and Animal Mycology (ISHAM)**.

Account: IBAN BE 35 0011 2595 0637- BIC GEBABEBB

<http://www.medmycol.be/>