Mycology in motion

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Emerging risk factors

Emerging resistance

New diagnostic tests

CHALLENGING CONTEXT

Evolving risk factors for invasive mould infections

Risk factors for invasive aspergillosis

Haematological malignancy
Neutropenia
Allogeneic haematopoietic stem-cell transplantation
Solid organ (lung) transplantation

Invasive aspergillosis in the ICU:
Prolonged treatment with corticosteroids before admission to the ICU
Chronic obstructive pulmonary disease
Liver cirrhosis

Critically ill with viral pneumonitis
Influenza
COVID-19

Meersseman W, et al. Clin Infect Dis. 2007;45:205–16; Wauters J, et al. Intensive Care Med. 2012;38:1761–8; Dewi IMW, et al. Curr Opin Microbiol. 2021;62:21–7.

Management of haematological patients at high risk of IA

Profound and prolonged neutropenia or active graft-versus-host disease

Primary prophylaxis

No screening with biomarkers

Start antifungal

Diagnostic work-up

Empiric treatment

No screening with biomarkers

Persistent fever or new fever after resolution

Trigger to start antifungal

Diagnostic work-up

Pre-emptive strategy

Screening with biomarker(s)

Positive biomarker

New pulmonary infiltrate (X-ray/CT)

Trigger to start antifungal

Diagnostic work-up

Management of ICU patients at high risk of IA

Patients with severe influenza or COVID-19

Primary prophylaxis

Not standard of care

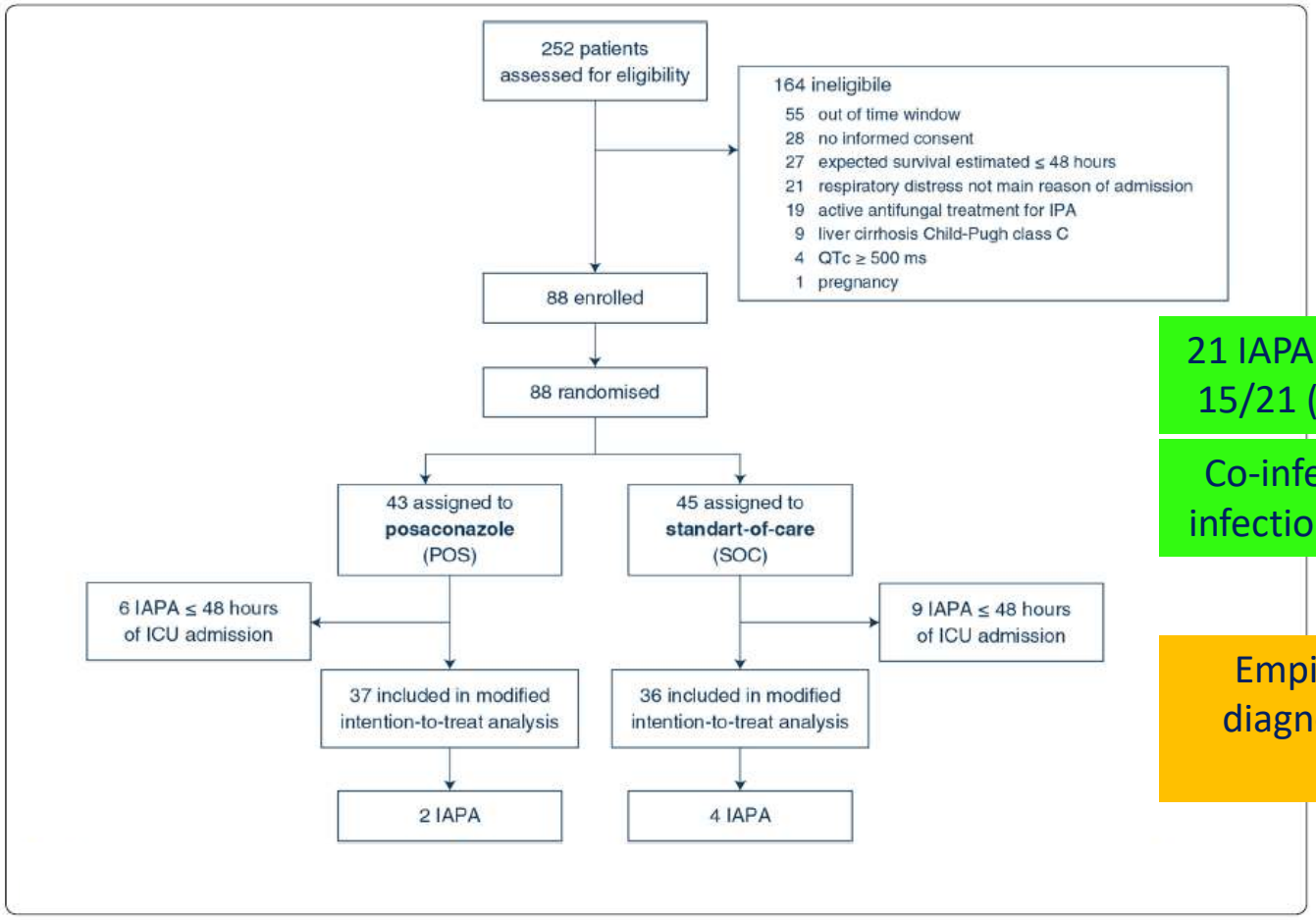
Empiric treatment

Not standard of care

Pre-emptive strategy

Not standard of care

The majority of invasive aspergillosis is diagnosed within 48h of ICU admission in influenza patients



Early IAPA

Late IAPA

21 IAPA cases (21/88 patients, 24%)
15/21 (71%) diagnosed within 48h

Co-infection instead of secondary infection in majority of the patients

Empirical antifungal therapy + diagnostic mycological work-up within 24–48h?

Vanderbeke L, et al. Intensive Care Med. 2021;47:674–86.

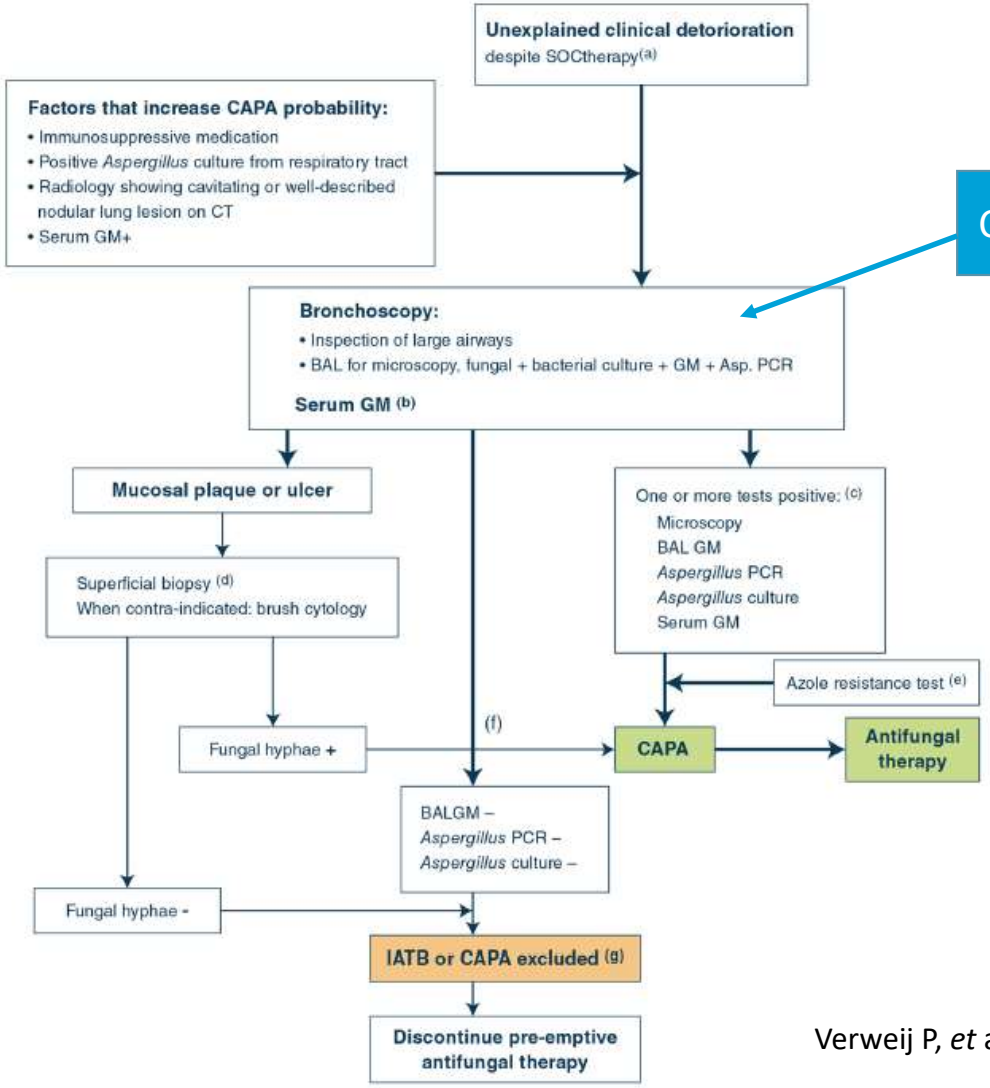
Duizenden Belgen kregen behalve COVID-19 ook een gevaarlijke schimmelinfectie... de helft overleefde het niet

Peter Brems

za 26 jun 07:00

Proposed clinical guidance for the management of CAPA

Consider empirical antifungal treatment
if visible plaques in trachea/bronchi or while awaiting results of diagnostic BAL tests in patients with rapidly deteriorating clinical condition



Cornerstone of CAPA diagnosis

Verweij P, *et* al. Intensive Care Med. 2021;47:819–34

Diagnosis and management of CAPA in ICU patients

Strong recommendations in mechanically ventilated, critically ill COVID-19 patients:

- To perform a CAPA diagnostic work-up in case of:
  - Unexplained respiratory deterioration OR
  - A positive *Aspergillus* culture from the respiratory tract
- Not to screen for serum GM or BDG
- Detection of *Aspergillus* in sputum and tracheal aspirates is insufficient evidence to support CAPA diagnosis but warrants bronchoscopy and BAL
- Maximum efforts are recommended to perform a bronchoscopy for inspection of the airways and BAL

Verweij P, et al. Intensive Care Med. 2021;47(8):819–34.

Aspergillus tracheobronchitis

Invasive Pulmonary Aspergillosis

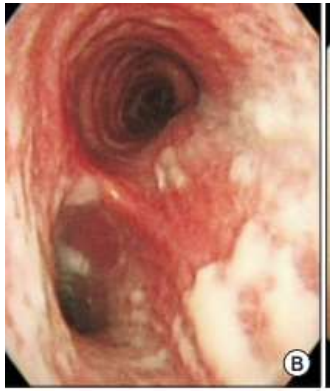
Alveolar disease **AND/OR** Airway disease (= tracheobronchitis)

- Up to **56**% if severe **influenza**, **early** after ICU admission, high mortality
- Up to **20**% if severe **COVID-19**, later after ICU admission

- Also in lung transplant recipients

Invasion of large airway, pseudomembrane formation and focal ulceration
(especially anastomotic infection in lung Tx)

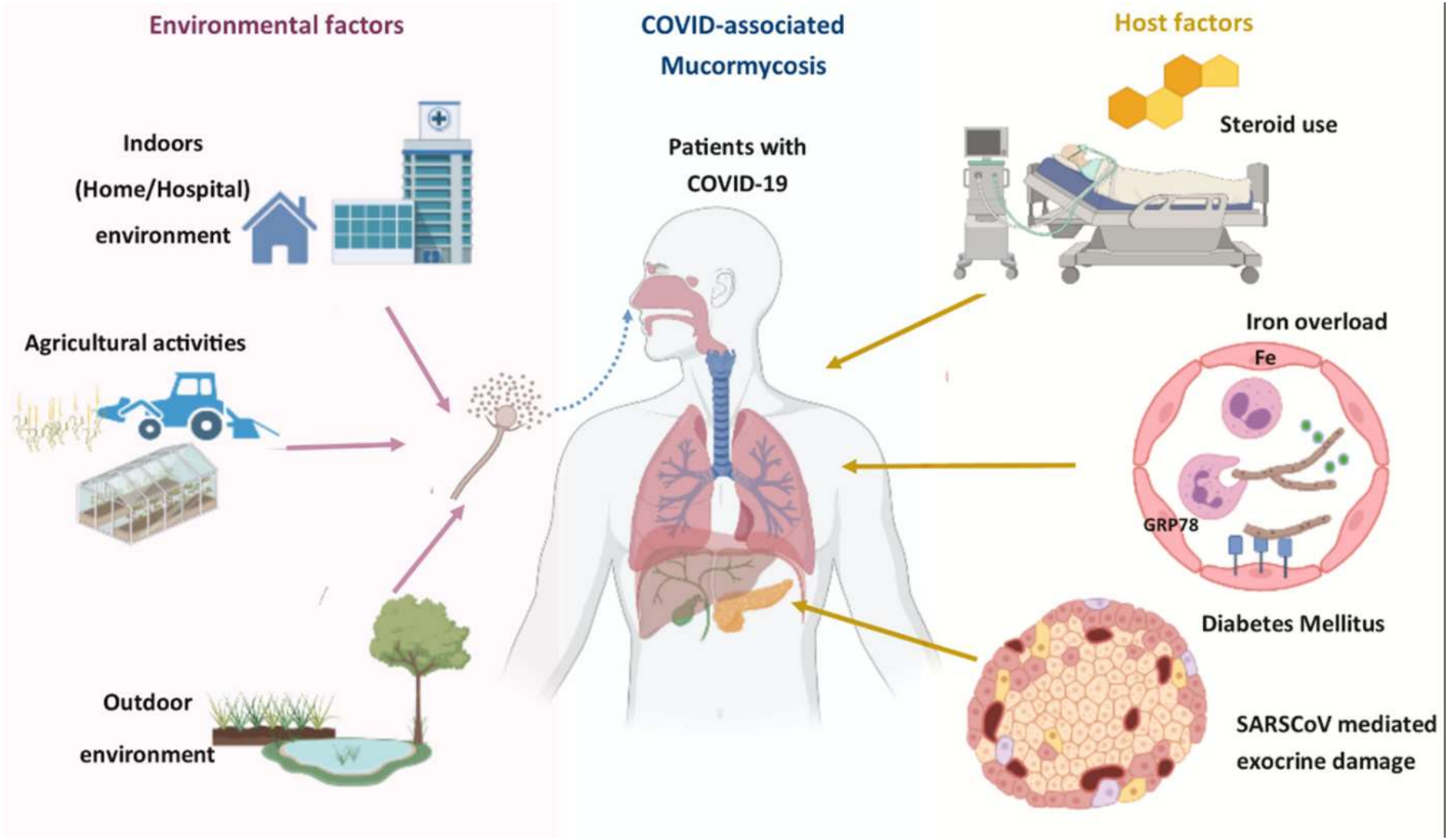
Diagnosis by bronchoscopic examination + demonstration of *Aspergillus* in biopsy specimen



BH Cho et al. Tuberc Respir Dis 2014, 77: 223-226 (picture)
F. Van de Veerdonk et al. Lancet Respir Med 2021, 9

Dodental door zwarte schimmel in India loopt op naar 4.252, uitbraak geassocieerd met Covid-19

Koen Marée 21 juli 2021 Leestijd 1 minuut



Shivaprakash M Rudramurthy et al. Mycoses 2021

Management of ICU patients at high risk of IA

Patients with severe influenza or COVID-19

Primary prophylaxis

Not standard of care

Studies ongoing but majority of influenza associated aspergillosis already diagnosed upon admission

Infection probably later in COVID-19 patients

Empiric treatment

Not standard of care

To be evaluated in patients with severe influenza while waiting results of diagnostic work-up?

Pre-emptive strategy

Not standard of care

Screening of blood for GM and BDG is not advised

Screening of tracheal aspirates for *Aspergillus* in COVID-19 patients?

Bartoletti M, et al. CID 2021;73:e3606-3614
Verweij P, *et* al. Intensive Care Med. 2021;47:819–34
Vanderbeke L, et al. Intensive Care Med. 2021;47:674–86.
Van Grootveld et al. Mycoses 2021, 64: 641-650

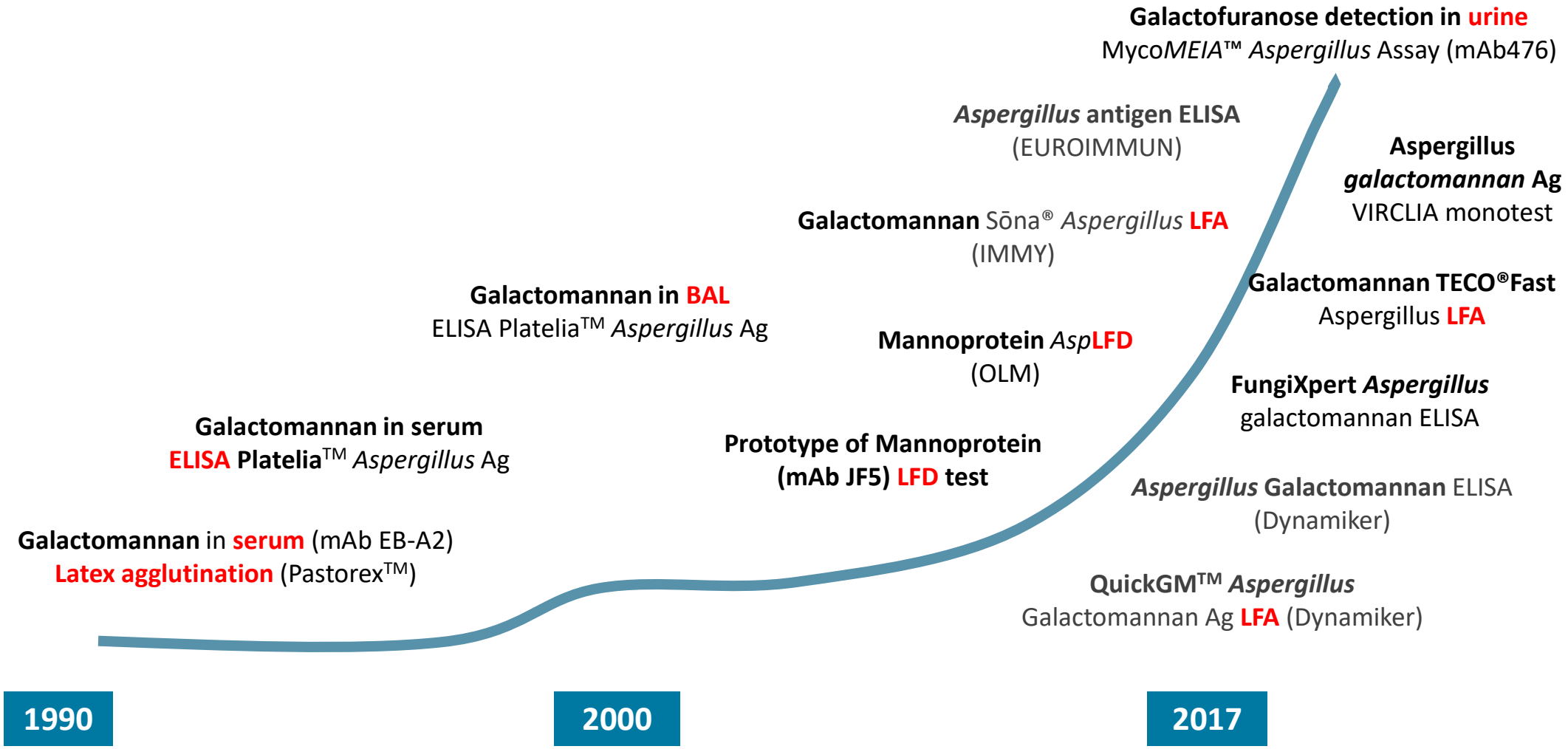
Emerging risk factors

Emerging resistance

New diagnostic tests

CHALLENGING CONTEXT

Expansion of antigen detection assays for invasive aspergillosis



Aspergillosis antigen detection assays

Choices are expanding rapidly, based on detection of

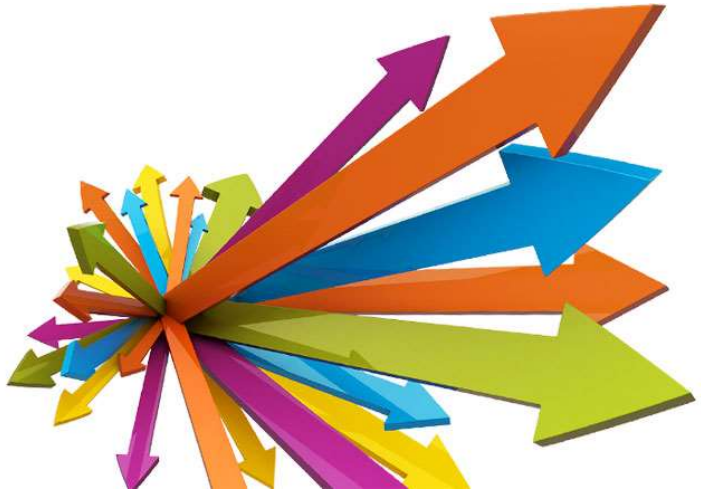
- Galactomannan
- Mannoprotein

Lateral flow assays/devices:

- Initial naming LFD for OLM test, LFA for IMMY test
- But now also other assays available

Other single test format assays

Validation data of most assays still limited



UZ LEUVEN

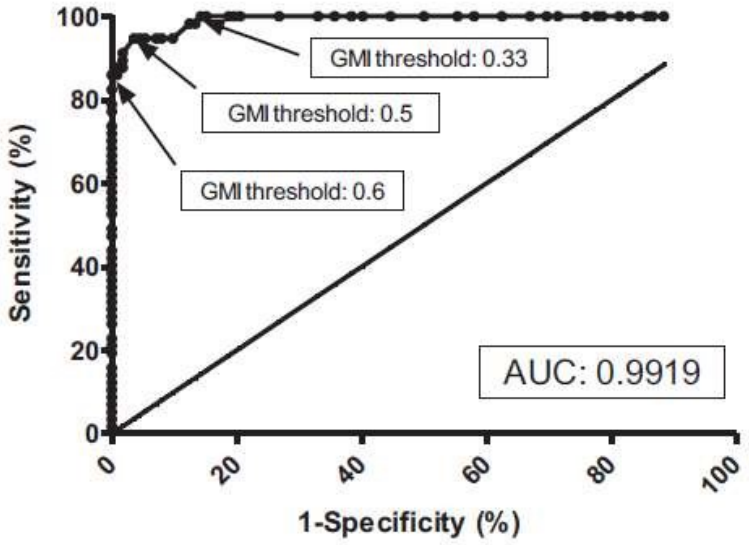
Evaluation of lateral flow device tests

Haematology/cancer patients

Evaluation Sōna® *Aspergillus* galactomannan LFA in patients at risk for IFD

- Retrospective
- Single centre
- Case/control

- 134 patients/179 **serum**
- 82% patients with haematological malignancy
- 27 proven/probable IA
- 2020 EORTC/MSGERC criteria



Performance parameters	Galactomannan index positivity threshold: 0.33	0.5	0.61
Sensitivity (95% CI)	100% (89.3–100)	96.9% (94.3–99.5)	90.6% (75.8–96.8)
Specificity (95% CI)	87.0% (79.0–92.2)	98.0% (93.0–99.5)	100% (96.3–100)
PPV (95% CI)	71.1% (56.6–82.3)	93.9% (80.4–98.3)	100% (88.3–100)
NPV (95% CI)	100% (95.8–100)	99.0% (94.5–99.8)	97.1% (91.8–99.0)
LR +tive	7.69	48.44	>906*
LR –tive	<0.0001*	0.03	0.09
DOR	>76,900*	1,519	>10,067*
Youden's statistic	0.87	0.95	0.91

- The LFA outperformed the GM-EIA
- Median GMI was significantly greater with LFA compared to GM-EIA
- The LFA is a rapid alternative to the well-established GM-EIA when used with a cube reader

PL White et al. 2020, 58

UZ LEUVEN

Evaluation of lateral flow device tests

COVID-19 associated pulmonary aspergillosis (CAPA)

Evaluation of Sōna® *Aspergillus* Galactomannan LFA for diagnosis of CAPA

- Retrospective
- Multicentre
- Case/control
- ECMM/ISHAM criteria (exclusion Aspergillus LFA)
- 196 respiratory samples/148 serum

	0.5 ODI cutoff		1.0 ODI cutoff	
	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Respiratory samples				
Tracheal aspirate (TA) (N_{CAPA}=16; $N_{ØCAPA}$=18)	100% (79–100)	44% (22–69)	81% (54–96)	67% (41–87)
Nondirected bronchial lavage (NBL) (N_{CAPA}=20; $N_{ØCAPA}$=52)	90% (68–99)	83% (70–92)	80% (56–94)	88% (77–96)
Bronchoalveolar lavage fluid (BALF) (N_{CAPA}=29; $N_{ØCAPA}$=61)	72% (53–87)	79% (66–88)	52% (33–71)	98% (91–100)
BALF and NBL combined[b] (N_{CAPA}=49; $N_{ØCAPA}$=113)	80% (66–90)	81% (72–87)	63% (48–77)	94% (88–97)
All combined[b] (N_{CAPA}=58; $N_{ØCAPA}$=127)	83% (71–91)	76% (67–83)	66% (52–78)	90% (83–94)
Serum samples (N_{CAPA}=46; $N_{ØCAPA}$=102)	20% (9–34)	93% (86–97)	9% (2–21)	99% (95–100)

- Aspergillus GM LFA shows good performance especially on respiratory samples with the 1.0 ODI cutoff
- Can be implemented as screening test on tracheal aspirates, triggering BAL analysis if positive
- Isolated ODI slightly above the 0.5 ODI should lead to further mycological investigations

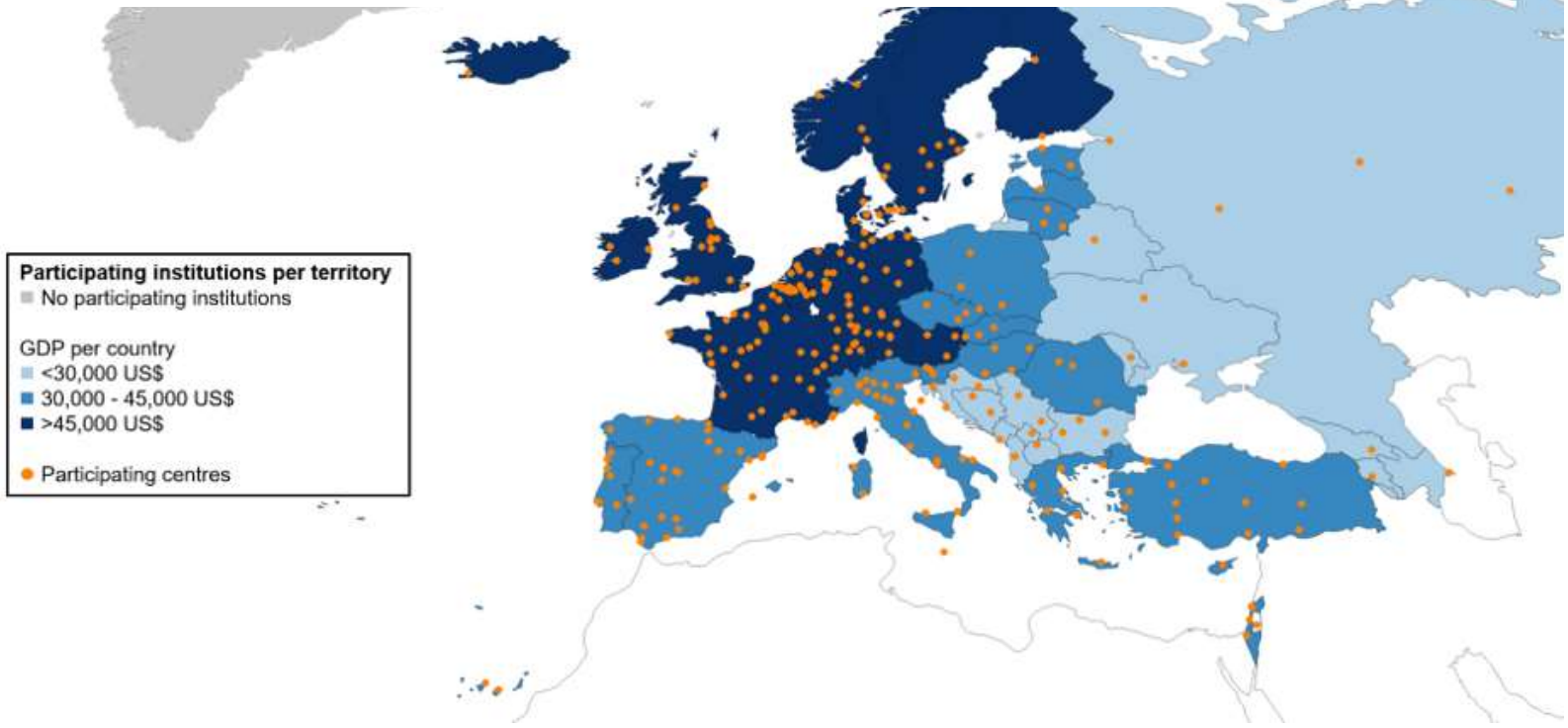
B. Autier et al. JCM 2022

Current state of laboratory mycology in Europe

ECMM survey

Participants of 388 institutions in 45 countries

Online electronic case report November 2021-January 2022



Jon Salmanton-Garcia et al. The Lancet Microbe 2022

Current state of laboratory mycology in Europe

Type of institution	n	%
Public hospital	140	36.1%
University hospital	247	67.7%
Aspergillus antigen detection		
Aspergillus LF (mannoprotein)		
Onsite	53	13.7
Outsourced	41	10.6
Aspergillus LF (galactomannan)		
Onsite	80	20.6
Outsourced	49	12.6
Galactomannan ELISA		
Onsite	258	66.5
Outsourced	82	21.1

Jon Salmanton-Garcia et al. The Lancet Microbe 2022

Galactomannan ODI values of different assays/sample types may not be the same

TECO®*Fast* Aspergillus IVD CE

Galactomannan Ag Lateral Flow Assay

- Same assay as Dynamiker QuickGM™ Lateral Flow Assay
- Different standard curve for serum and BAL samples with the aim to use 1 threshold (but different thresholds in definitions)
- Poor performance in evaluation performed at UZ Leuven but procedure meanwhile adapted

Conclusions

- Several lateral flow device tests for the diagnosis of invasive aspergillosis are currently available
- Check validation data for the specific test you consider implementing both for serum/BAL and different patient populations
- Validation data are still limited
- Most data available for IMMY galactomannan lateral flow assay which reveal that the performance of the IMMY test is at least as good as the Platelia galactomannan test and thus may replace this test
- Performance evaluation for diagnosis of CAPA is difficult due to incorporation bias (presence of the evaluated laboratory test in the reference mycological criteria) which may lead to an overestimation of the diagnostic accuracy
- Lateral flow device tests are most useful when a rapid response is important and the number of samples is low

General reflections on *Aspergillus* PCR

Low fungal load regularly encountered when testing blood samples, become negative promptly after starting treatment

In BALf fungal often higher than in blood in patients with invasive aspergillosis (however often still a low load)

Clinical significance of weak positive PCR tests: due to testing specimens not directly associated with the infected site or contaminants?

Optimal use of *Aspergillus* PCR is in combination with an antigen detection test:

- Both test are negative, sensitivity is sufficient to exclude invasive aspergillosis
- Both assays are positive: high specificity, strongly supports the diagnosis of invasive aspergillosis
- Discordant results are frequently encountered in clinical practice and remain difficult to interpret

Lewis PL et al. CID 2021, 72: S95S101

Diagnosis of mucormycosis: detection of DNA in serum

- Inclusion
  - Patients with suspicion of invasive mould disease (host factor, suggestive imaging and clinical symptoms) were **prospectively** recruited in 9 university hospitals in France (=cohort 1, n= 232)
  - Additional patients diagnosed with probable/proven mucormycosis (same centers, same period) (=cohort 2, n=13): to study mucorales DNA kinetics
- Screening twice weekly with mucorales PCR on serum samples
- Recommendations were given for extraction and qPCR but participants were free to use kits and reagents available in their lab
  - PCR targeting the Mucorales genera *Lichtheimia*, *Rhizomucor*, *Mucor/Rhizopus*

L. Millon et al. CID 2022

Diagnosis of mucormycosis: detection of DNA in serum

Cohort 1

- 27 (12%) proven/probable mucormycosis including 9 (1/3!) mixed *Aspergillus*-mucorales infection
  - 23/27 at least 1 positive mucorales qPCR
    (4 negative patients had suboptimal sampling, median of 2 samples/patient)
  - Recommendation to perform serum mucorales PCR in patients already diagnosed with IPA, especially if voriconazole therapy is not rapidly effective
- 67 (29% proven/probable aspergillosis)
- 6 (2.6%) other moulds

L. Millon et al. CID 2022

Diagnosis of mucormycosis: detection of DNA in serum

Cohort 1

- 18 patients (8%): mucorales PCR was the only positive mycological test
  - Meaning not entirely clear, treatment with L-AMB started in 16/18 patients
  - Significantly higher number patients with a haematological malignancy in this group

Good performance of qPCR detection of circulating DNA in serum:

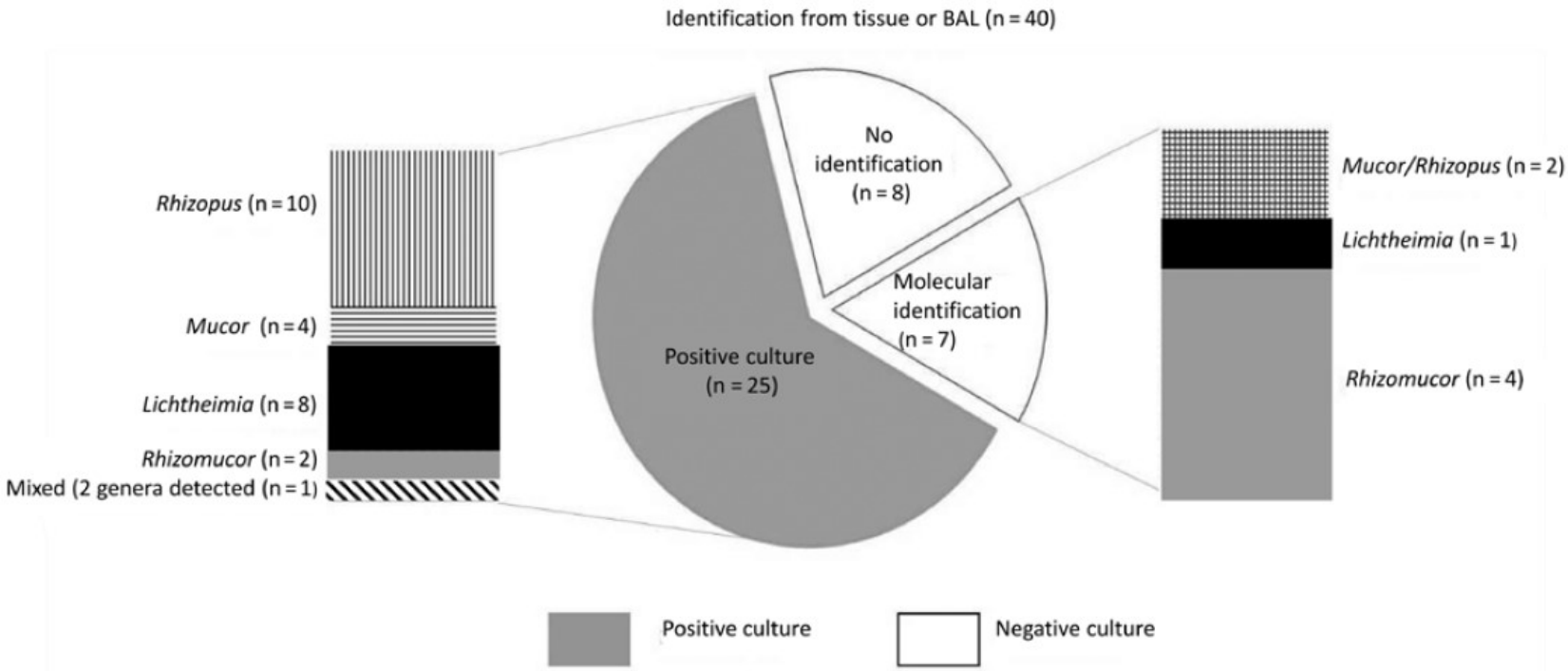
85% sensitivity; 90% specificity

Early marker: positive 4 days before mycological or histopathological examination

100% mortality rate if qPCR remains positive despite appropriate antifungal treatment

L. Millon et al. CID 2022

Diagnosis of mucormycosis: detection of DNA in serum



Positive cultures from tissue samples may be more difficult to obtain in case *Rhizomucor* infection

L. Millon et al. CID 2022

Panfungal PCR + sequencing now included in EORTC/MSGERC definitions

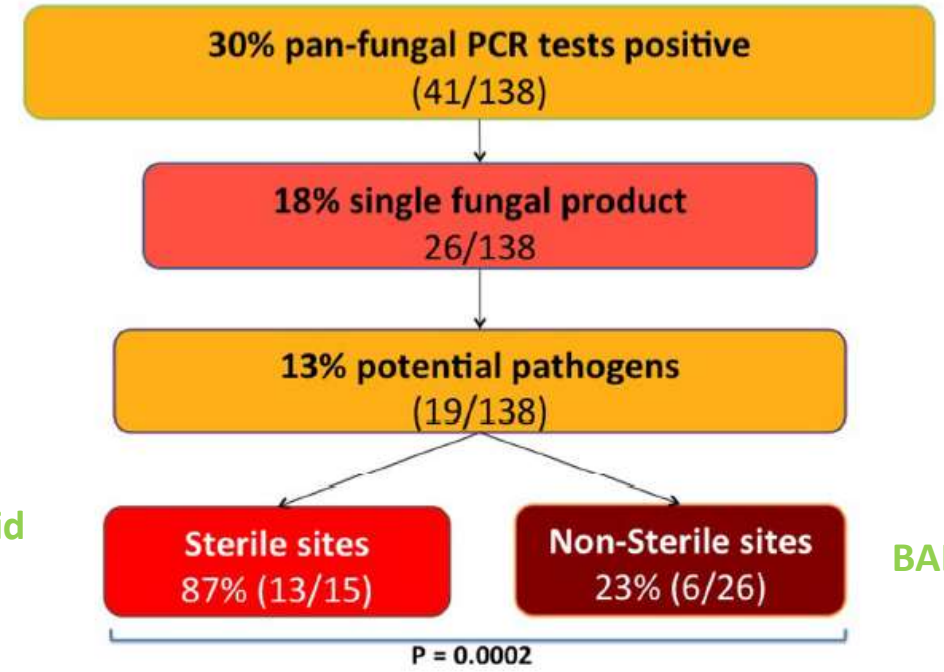
Revision and Update of the Consensus Definitions of Invasive Fungal Disease From the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium

- We recommend amplification of fungal DNA by PCR combined with DNA sequencing, but **only** when fungal elements are seen by histopathology.
- PCR would **add value** by allowing **identification** of the fungus to genus and possibly species levels.
- Because the technique used should be rigorously quality controlled, only **laboratories** with a **proven record** in performing DNA extraction from formalin-fixed tissue should undertake this.
- The identity of the fungus should be consistent with the histopathologic findings.

JP Donnelly et al. CID 2020;71:1367–76

Clinical utility of panfungal PCR for the diagnosis of invasive fungal disease

- ITS-1 panfungal PCR (lab-developed)
- Tertiary referral transplant centre, Alfred Health Melbourne (Australia)
- Retrospective review 2009-2014



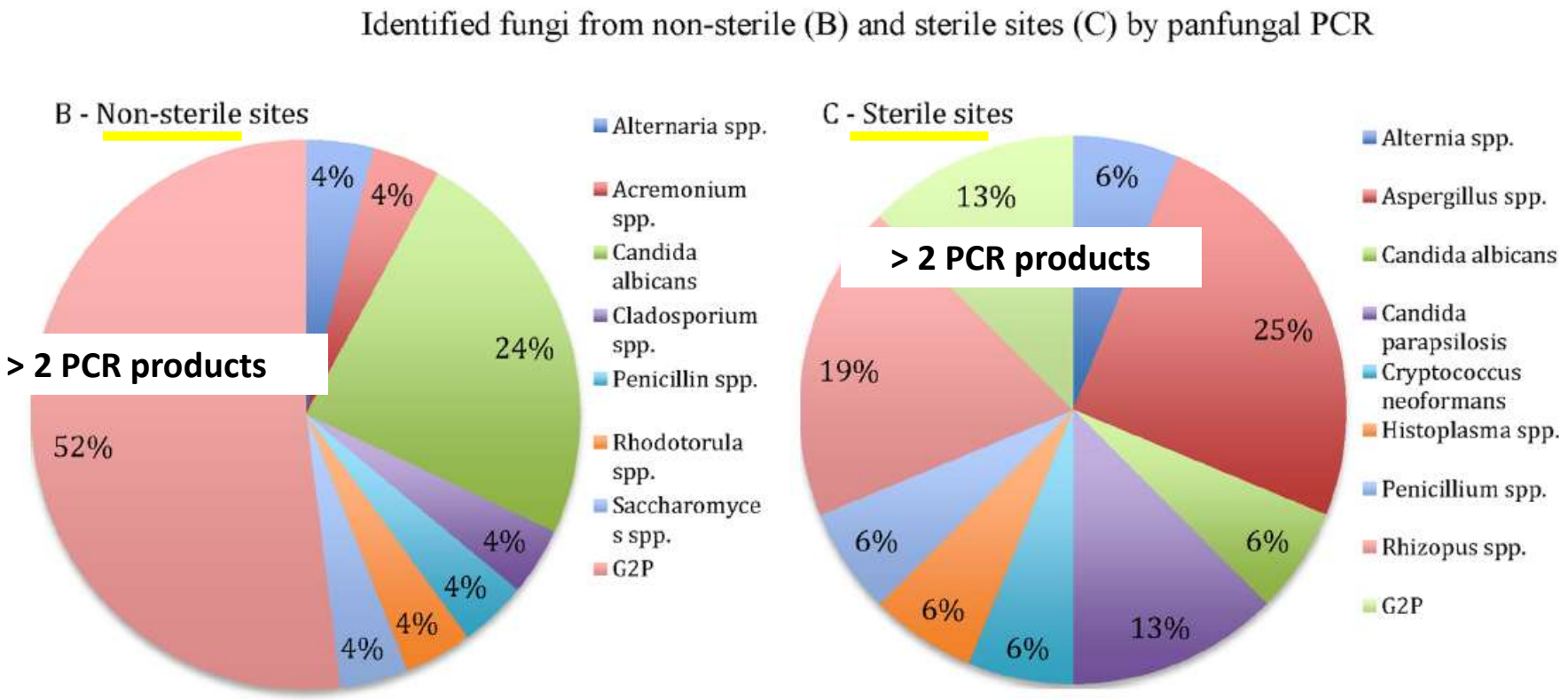
Pleural fluid
Tissue
CSF

BAL fluid

- **Histopathology neg**: potential pathogen identified in only 12% (11/94 specimens)
- **Culture neg/histopathology pos**: diagnosis of IFD at species level in 35% (6/20)

JA Trubiano et al. Med Mycol 2016, 54, 138-146

Clinical utility of panfungal PCR for the diagnosis of invasive fungal disease



JA Trubiano et al. Med Mycol 2016, 54, 138-146

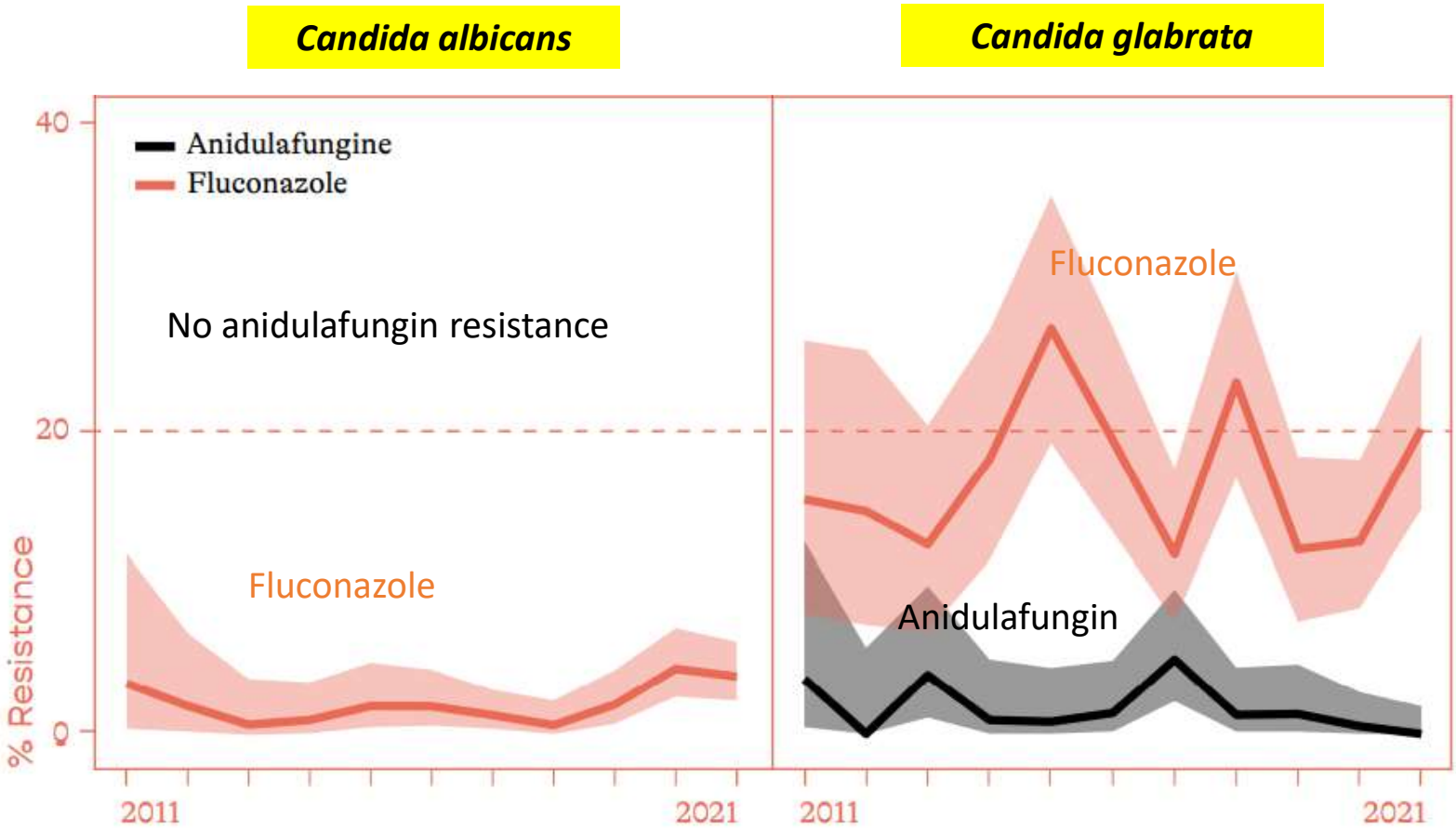
Emerging risk factors

Emerging resistance

New diagnostic tests

CHALLENGING CONTEXT

BELMAP



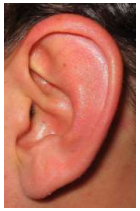
Data NRC Mycosis (UZ Leuven)

https://www.health.belgium.be/sites/default/files/belmap2022_report.pdf


CANDIDA AURIS

JAPAN

***Candida auris* sp. nov.,** a novel ascomycetous yeast isolated from the external ear canal of an in patient in a Japanese hospital.
Satoh K et al. Microbiol Immunol. 2009;53(1):41-4.



KOREA

JOURNAL OF CLINICAL MICROBIOLOGY, Sept. 2011, p. 3139–3142 Vol. 49, No. 9
0095-1137/11/$12.00 doi:10.1128/JCM.00319-11

First Three Reported Cases of Nosocomial Fungemia Caused by *Candida auris*▽

Wee Gyo Lee,[1] Jong Hee Shin,[2]* Young Uh,[3] Min Gu Kang,[1] Soo Hyun Kim,[2] Kyung Hwa Park,[4] and Hee-Chang Jang[4]

Simultaneous Emergence of Multidrug-Resistant *Candida auris* on 3 Continents Confirmed by Whole-Genome Sequencing and Epidemiological Analyses

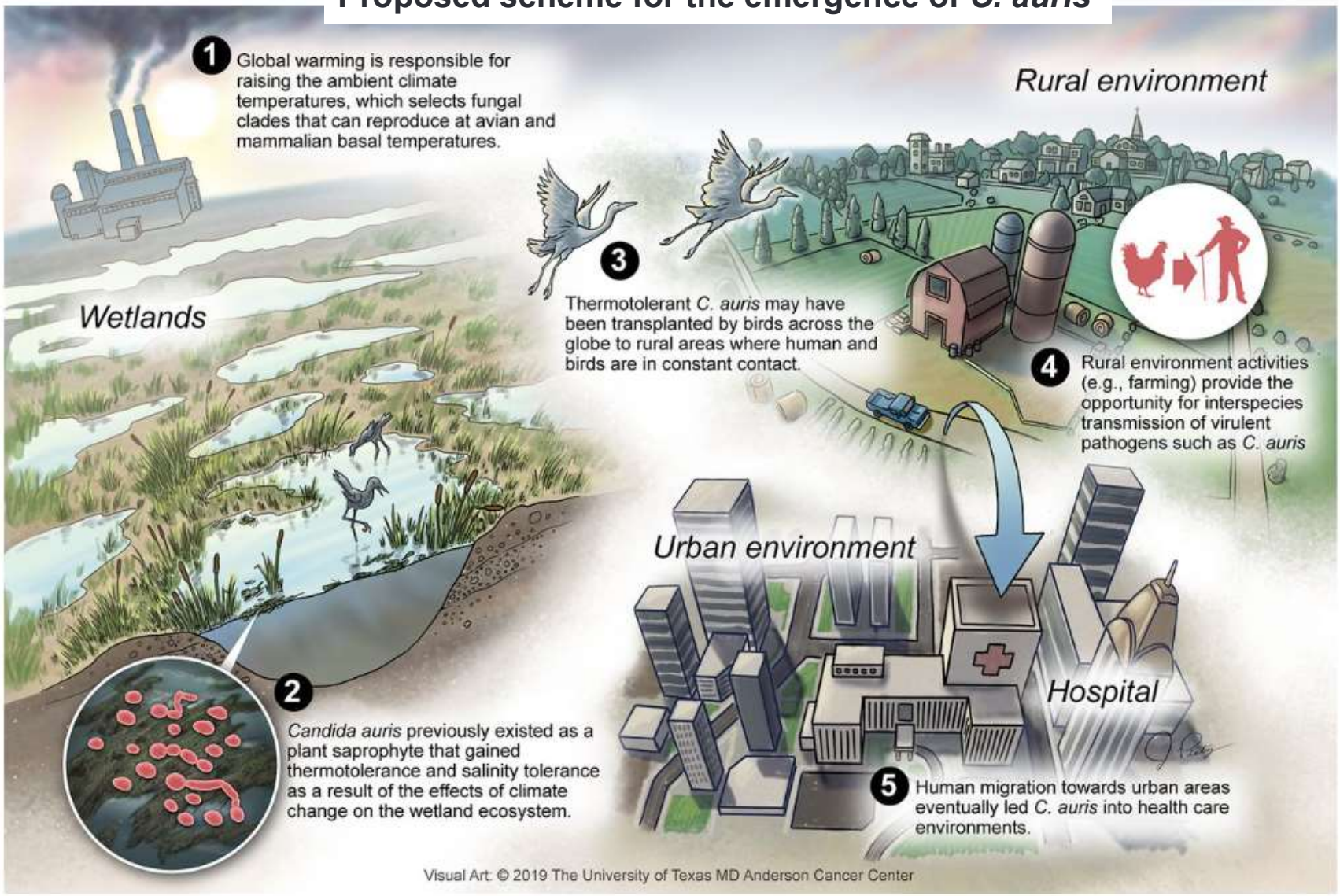
Shawn R. Lockhart,[1] Kizee A. Etienne,[1] Snigdha Vallabhaneni,[1] Joveria Farooqi,[4] Anuradha Chowdhary,[6] Nelesh P. Govender,[7] Arnaldo Lopes Colombo,[8] Belinda Calvo,[9] Christina A. Cuomo,[2] Christopher A. Desjardins,[2] Elizabeth L. Berkow,[1] Mariana Castanheira,[3] Rindidzani E. Magobo,[7] Kauser Jabeen,[4] Rana J. Asghar,[5] Jacques F. Meis,[10,11] Brendan Jackson,[1] Tom Chiller,[1] and Anastasia P. Litvintseva[1]

- Strains from 54 patients with *C. auris* infection from Pakistan, India, South Africa, and Venezuela during 2012–2015 and the type specimen from Japan.
- Antifungal susceptibility testing and whole-genome sequencing (WGS).

- Huge genetic differences among geographic clades
- Very high clonality within the geographic clades
- **Recent independent emergence in different places**

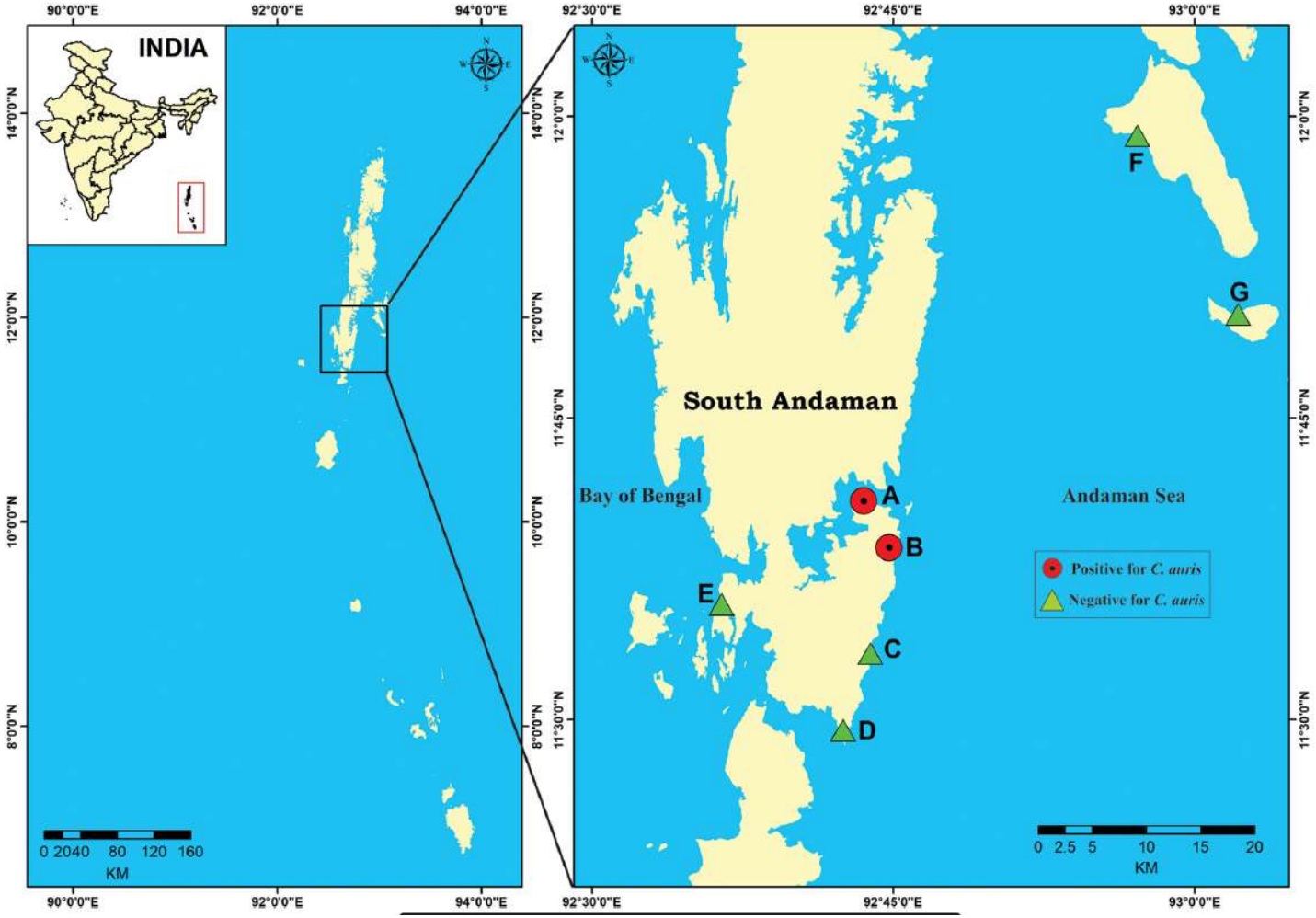
Clinical Infectious Diseases® 2017;64(2):134–40

Proposed scheme for the emergence of *C. auris*

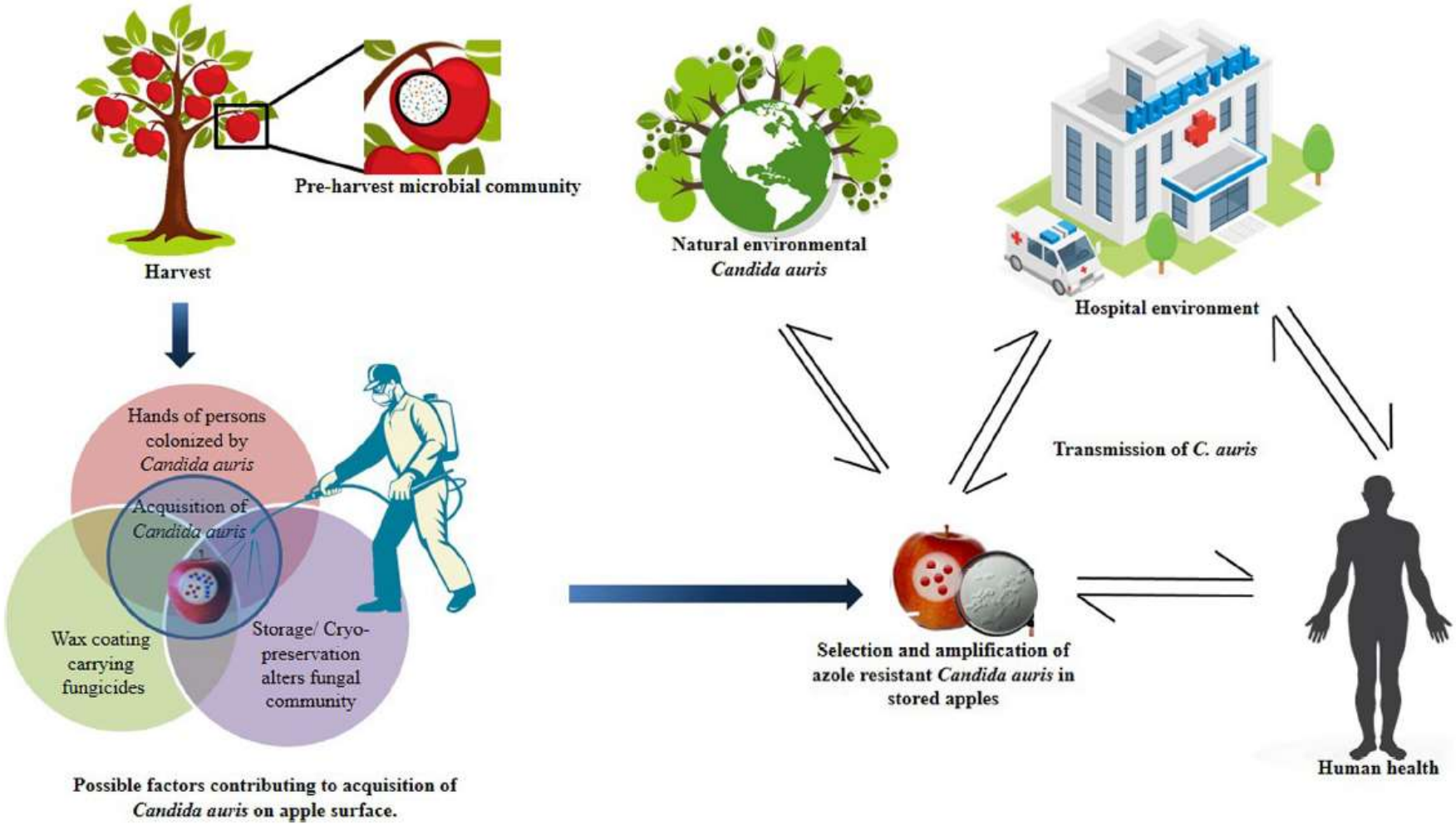


A. Casadevall et al. mBio 2019

Environmental Isolation of *Candida auris* from the Coastal Wetlands of Andaman Islands, India



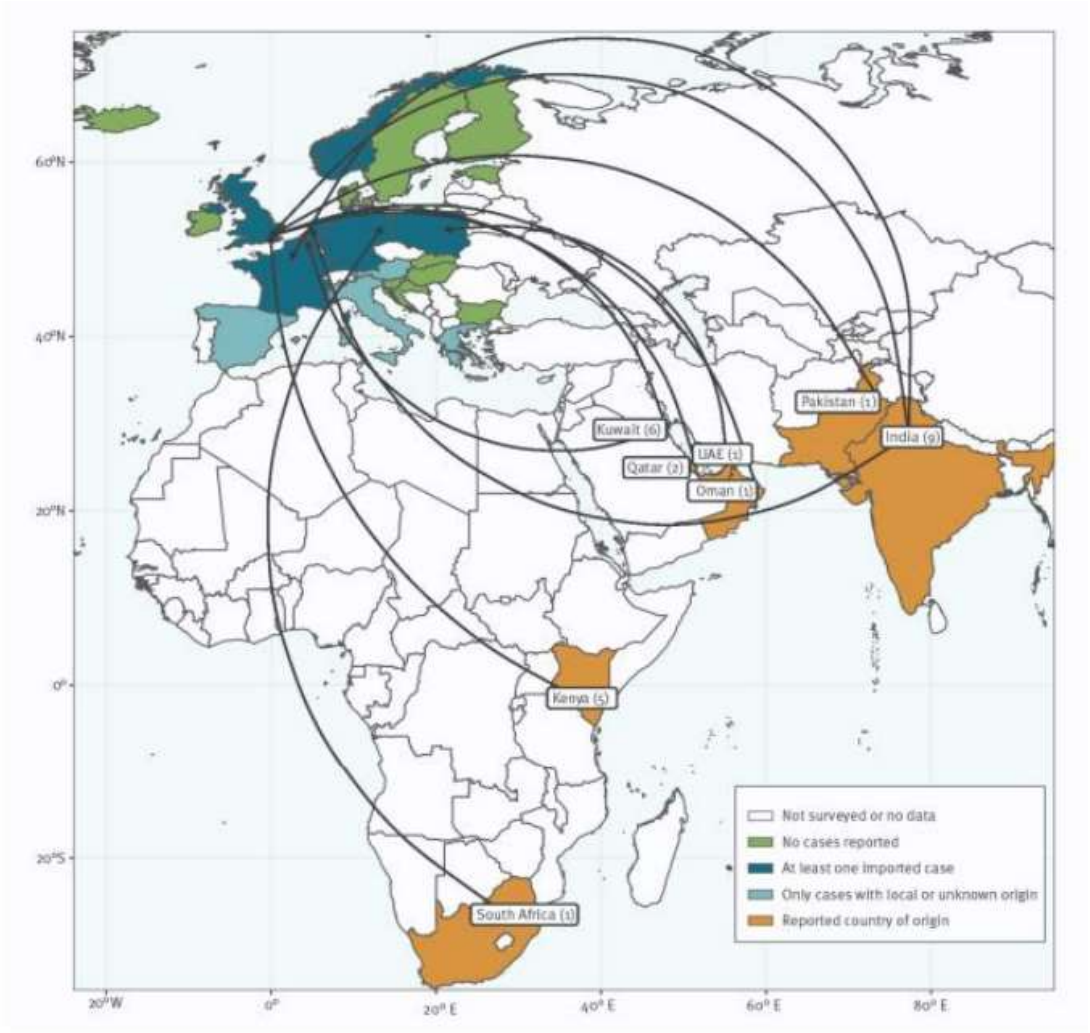
P. Arora et al. mBio 2021



Schematic representation of stored apples as a possible reservoir of selection and transmission of azole-resistant *C. auris*.

A. Yadav et al. mBio 2022

Reported origin of *C. auris* Europe, Jan 2013- May 2019 (n=26)



Survey 2019

Most cases of *C. auris* in Europe were part of previous outbreaks in two countries (Spain and the UK), sporadic cases with a reported origin outside of the EU/EEA were reported from an increasing number of countries

India (9)
Pakistan (1)

Kuwait (6)
UAE (1)
Qatar (2)
Oman (1)

Kenya (5)
South Africa (1)

https://www.ecdc.europa.eu/sites/default/files/documents/RRA-candida-auris-Feb2022.pdf

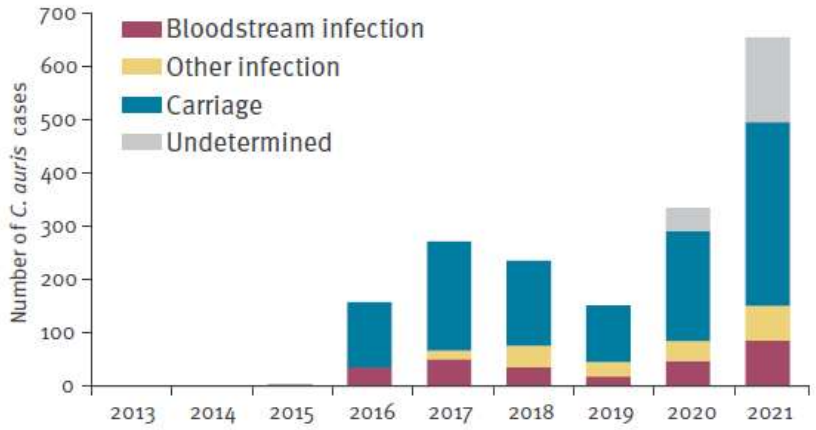
RAPID COMMUNICATION

Increasing number of cases and outbreaks caused by *Candida auris* in the EU/EEA, 2020 to 2021

Anke Kohlenberg[1] , Dominique L Monnet[1] , Diamantis Plachouras[1] , *Candida auris* survey collaborative group[2]
1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
2. The members of the *Candida auris* survey collaborative group are listed under Collaborators and at the end of the article

Correspondence: Anke Kohlenberg (anke.kohlenberg@ecdc.europa.eu)

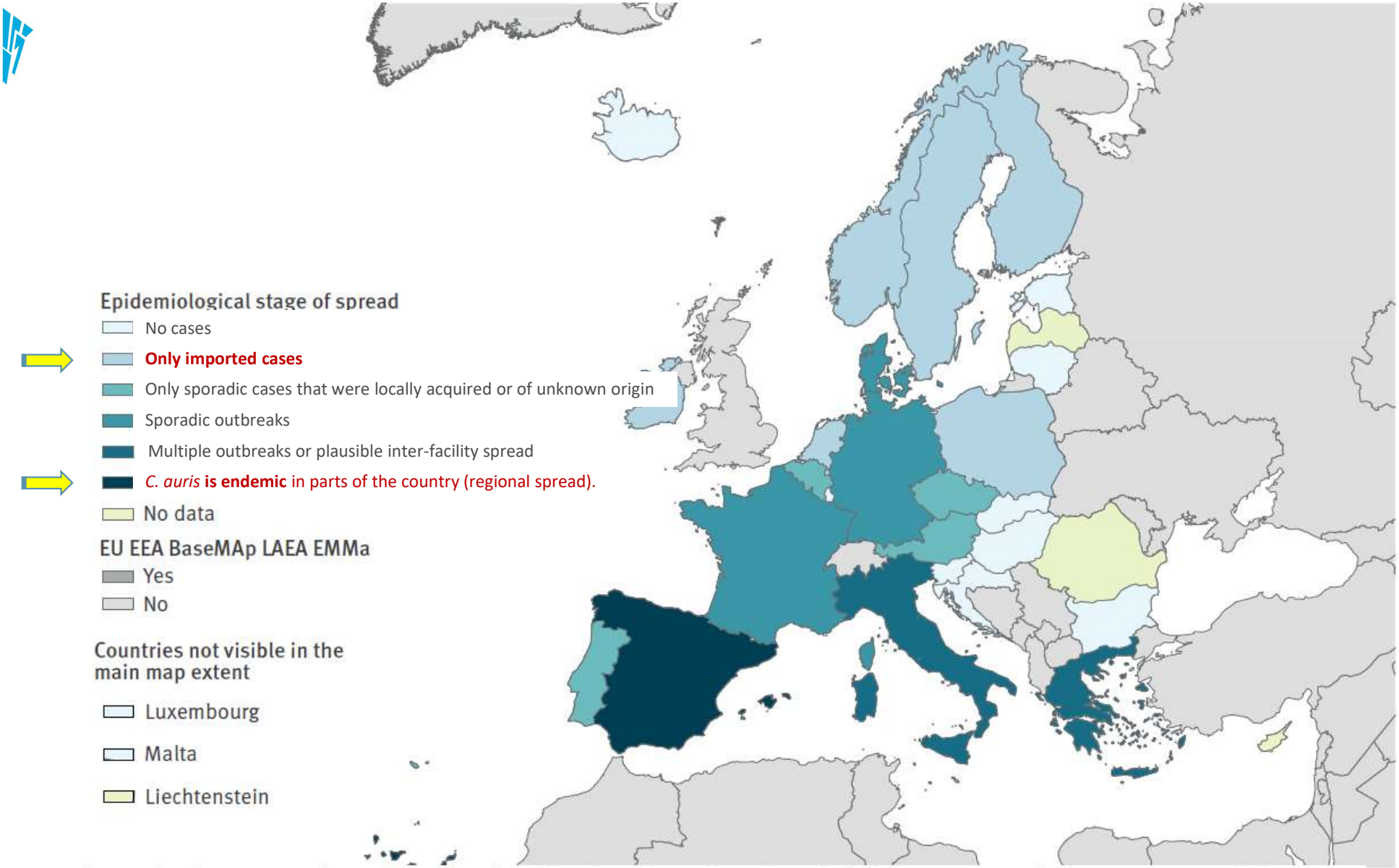
Reported cases of *Candida auris* infection or carriage, EU/EEA, 2013–2021 (n = 1,812)[a]



EEA: European Economic Area; EU: European Union.

Five countries experienced outbreaks while one country reported regional endemicity

Eurosurveillance 17 Nov 2022



Administrative boundaries: © EuroGeographics © UN–FAO © Turkstat.The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. Map produced on: 26 Oct 2022

Belgian *C. auris* cases

1 Kuwait

infection

1 Kuwait

colonisation

1 S Africa

colonisation

1 India

colonisation

1 Belgium

infection

1 Kuwait

infection

1 Belgium

colonisation

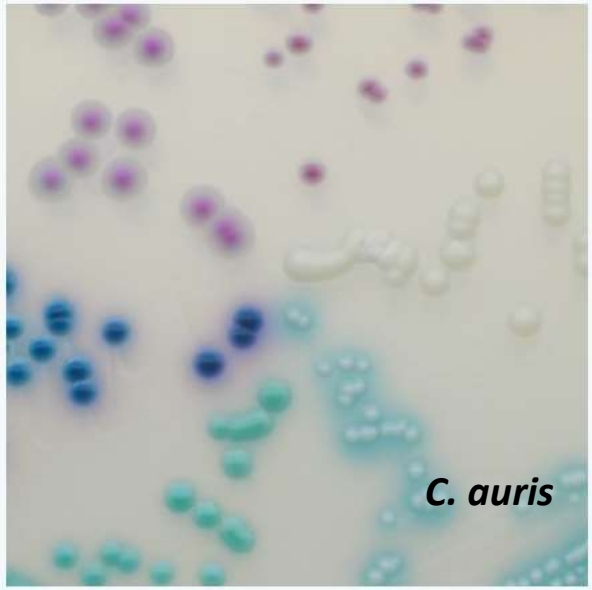
1 Albania

infection

2016	2017	2018	2019	2020	2021	2022

Nu ook CHROMagar voor detectie *Candida auris*

CHROMagar™ Candida Plus



CHROMagar™ Candida Plus

For detection and differentiation of major clinical *Candida* species, including *C. auris*

Order References

Please use these references when contacting your local distributor:

5000 mL Pack CA242

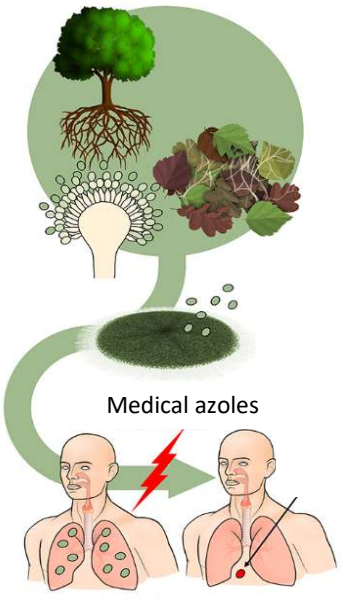
25 L Pack CA243-25

10 kg Pack CA243-10kg

CE IVD

Triazole resistance development in *Aspergillus fumigatus*

Patient route

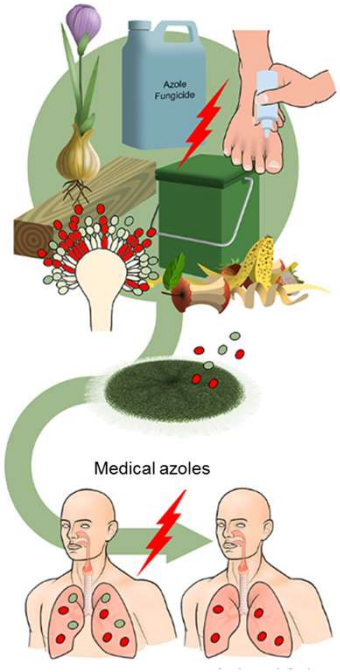


Long-term triazole treatment for aspergilloma or cavitary lung disease

Variety of resistance mechanisms

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

Environmental route



TR_{34}/L98H
TR_{46}/Y121F/T289A

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

‘Hotspots’ for triazole resistance selection in *A. fumigatus*

Specific conditions and sites are thought to exist in the environment that facilitate the emergence, amplification and spread of triazole-resistance mutations in *A. fumigatus* (‘hotspots’).

Hotspot characteristics according to experts:

✓ Ability *of A. fumigatus* to grow and complete its life-cycle (to achieve genetic diversity)

✓ Presence of azole residues with activity against *A. fumigatus*

Flower bulb compost heap

***A. fumigatus* +++**
Azole fungicides +++
Azole R: 6.2 – 24.5%

https://www.tweedekamer.nl/kamerstukken/brieven_regering/detail?id=2017Z16992&did=2017D35356

‘Hotspots’ for triazole resistance selection in *A. fumigatus*

Professional storage of processed wood

***A. fumigatus* +++**
Azole fungicides +
Azole R: 5.8– 20%

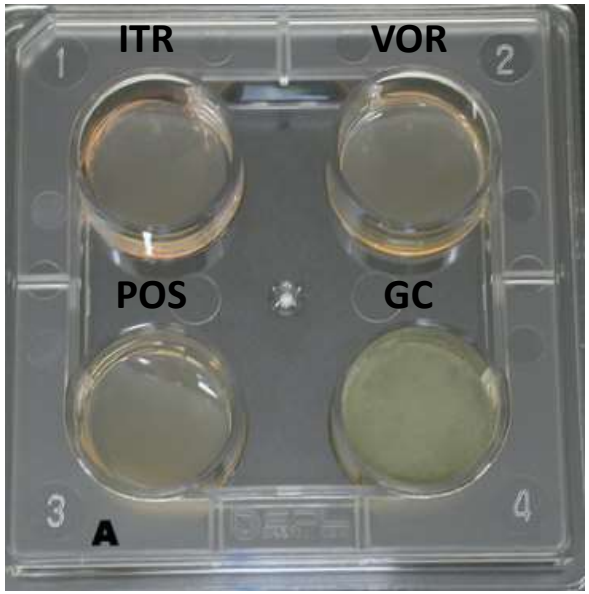
Professional green composting

***A. fumigatus* +++ (timing dependent)**
Azole fungicides +
Azole R: 8.5 – 30%

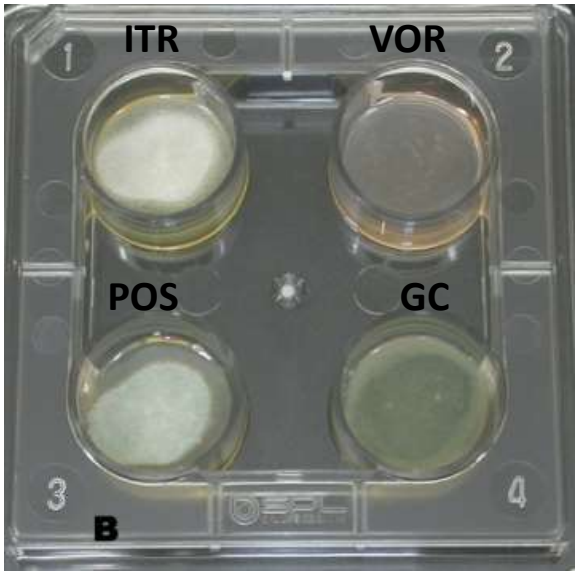
https://www.tweedekamer.nl/kamerstukken/brieven_regering/detail?id=2017Z16992&did=2017D35356

Triazole resistance detection in *Aspergillus fumigatus*

Screening method



Susceptible



Resistant

ITR: itraconazole
VOR: voriconazole
POS: posaconazole
GC: growth control

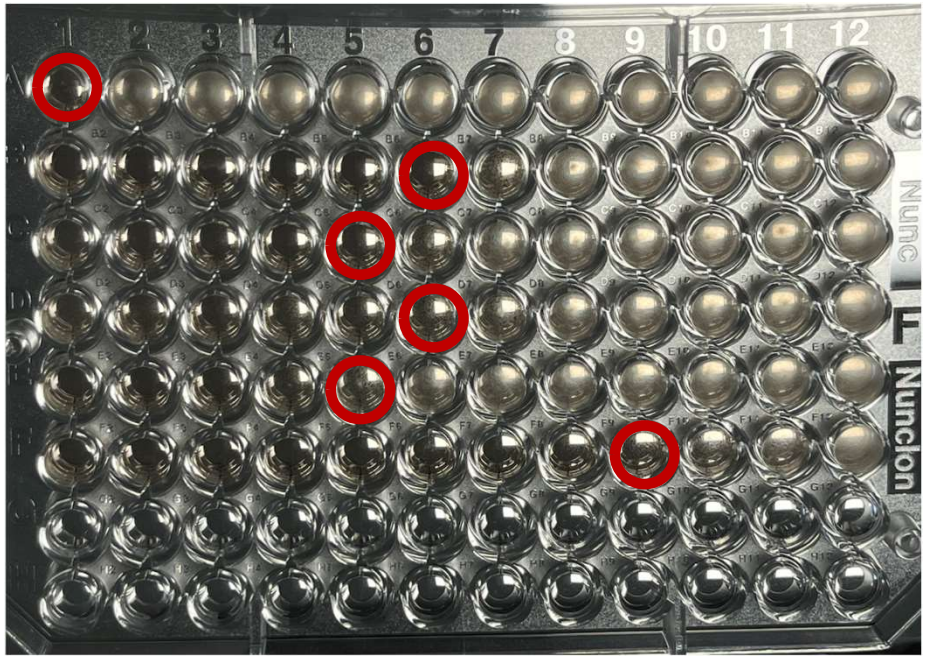
Always perform susceptibility testing if antifungal therapy is intended
Both azole-susceptible and azole-resistant phenotypes can be simultaneously present in culture, test multiple colonies!

Triazole resistance detection in *Aspergillus*

Confirmation methods

MIC determination

AMB
VOR
POS
ITR
ISA
OLO



Molecular methods

Detection of specific mutations
Resistance multiplex
– L98H
– Tandem repeat 34
– T289A
– Y121F

Sequencing *Cyp51A* gene

National surveillance study azole resistance in *Aspergillus* diseases (2011-2012)

- 1 year prospective surveillance study
- 18 hospitals

220 isolates from 182 patients

triazole resistance %

Disease (number of patients)

- Invasive aspergillosis (122) — **4.6%**
- ABPA (39)
- Chronic pulmonary aspergillosis (10)
- Aspergillus bronchitis (7)
- Aspergilloma (5)

— **7.0%**

— **5.5%**

- 6 TR34/L98H
- 1 TR46/Y121F/T289A
- 2 non-Cyp51A

National surveillance study azole resistance in *Aspergillus* diseases

Surveillance 2011-2012: triazole resistance detected in 2/58 deceased patients

➡ Clinical impact of *A. fumigatus* resistance seems to be limited

New (after 10 years) prospective surveillance currently ongoing (2022-2023)

- All Belgian hospitals were invited to participate
- Focused on invasive aspergillosis

Data *A. fumigatus* isolates send to NRC for mycosis (2017-2021)

A. fumigatus		2017		2018		2019		2020		2021		Overall	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Number of isolates screened		**537**	**100**	**532**	**100**	**520**	**100**	**607**	**100**	**674**	**100**	**2870**	**100**
Growth on VIP Check		33	6.1	38	7.1	44	8.5	44	7.2	34	5	193	6.7
Susceptibility testing													
	Resistant	**26**	**4.8**	**31**	**5.8**	**28**	**5.4**	**42**	**6.9**	**30**	**4.5**	**157**	**5.5**
	Susceptible	4	0.7	7	1.3	16	2.1	2	0.3	2	0.3	31	1.1
Resistance mechanisms													
No *cyp51A* mutation		8	30.8	3	9.7	2	7.1	3	7.1	1	3.3	17	10.8
Cyp51A gene mutation	**TR_{34}/L98H**	14	**53.8**	23	**74.2**	20	**71.4**	27	**64.3**	25	**83.3**	109	**69.4**
	TR_{46}/Y121F/T298A	2	**7.7**	3	**9.7**	3	**10.7**	4	**9.5**	**1**	**3.3**	13	**8.3**
	TR_{46}/Y121F/T289A/ S363P/I364V/G448S	0	0	0	0	0	0	2	**4.8**	**1**	**3.3**	3	**1.9**
	Y121F, T289A, S363P, I364V, G448S	0	0	0	0	0	0	0	0	1	0	1	0.6
	G54W	0	0	1	3.2	0	0	0	0	0	0	1	0.6
	G54E/G513A	1	3.8	0	0	0	0	0	0	0	0	1	0.6
	Other	1	3.8	1	3.2	1	3.6	0	0	0	0	3	1.9

Data Belgian National Reference Centre for Mycosis UZ Leuven

Data UZ Leuven *A. fumigatus* isolates (2017-2021)

Hospitalisation beds: 1900 total, 94 ICU, 45 hematology

	2016		2017		2018		2019		2020	
	No.	%	No.	%	No.	%	No.	%	No.	%
Patients										
Total	**337**	**100**	**386**	**100**	**301**	**100**	**294**	**100**	**282**	**100**
Resistant	**28**	**8.3**	**26**	**6.7**	**21**	**7.0**	**21**	**7.1**	**21**	**7.4**
Isolates										
Total	**495**	**100**	**534**	**100**	**503**	**100**	**485**	**100**	**478**	**100**
Resistant	**30**	**6.0**	**28**	**5.2**	**25**	**5.0**	**21**	**4.3**	**30**	**6.3**

- Susceptible cases: 1-24 isolates received per year
- Resistant cases: 1-4 isolates received per year, 40% also had cultures with susceptible *A. fumigatus* isolates

A. Resendiz-Sharpe et al. Journal of Infection and Chemotherapy, 2021, 27: 1774-1778

When to perform antifungal susceptibility testing?

All isolates from patients invasive infections

- *Candida*:
  - Isolates from normal sterile sites
  - Higher change of resistance in patients exposed to antifungal agents before
- *Aspergillus*:
  - All invasive infections
  - Resistance mainly develops in the environment and thus also occurs in azole naïve patients
- Rare moulds, rare yeasts

Difficult to treat mucosal infections, e.g. recurrent vulvovaginal candidiasis

National Reference Center: what do we do?

Candida species

Sensititre Yeast One

\+ CLSI breakpoints

All other fungi

Candida auris

EUCAST reference method

\+ EUCAST breakpoints

unexpected results/difficult to read

25 October 2022

The WHO fungal priority pathogens list (WHO FPPL) is the first global effort to systematically prioritize fungal pathogens, considering their unmet research and development (R&D) needs and perceived public health importance.

Critical group


Cryptococcus neoformans


Candida auris


Aspergillus fumigatus


Candida albicans

High group


Nakaseomyces glabrata (Candida glabrata)


Histoplasma spp.


Eumycetoma causative agents


Mucorales


Fusarium spp.


Candida tropicalis


Candida parapsilosis

Medium group


Scedosporium spp.


Lomentospora prolificans


Coccidioides spp.


Pichia kudriavzeveii (Candida krusei)


Cryptococcus gattii


Talaromyces marneffei


Pneumocystis jirovecii


Paracoccidioides spp.

Proposed priority areas for action