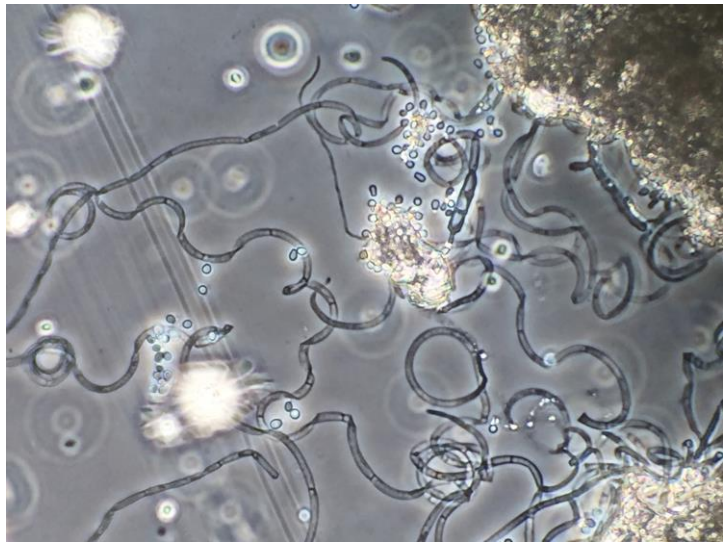

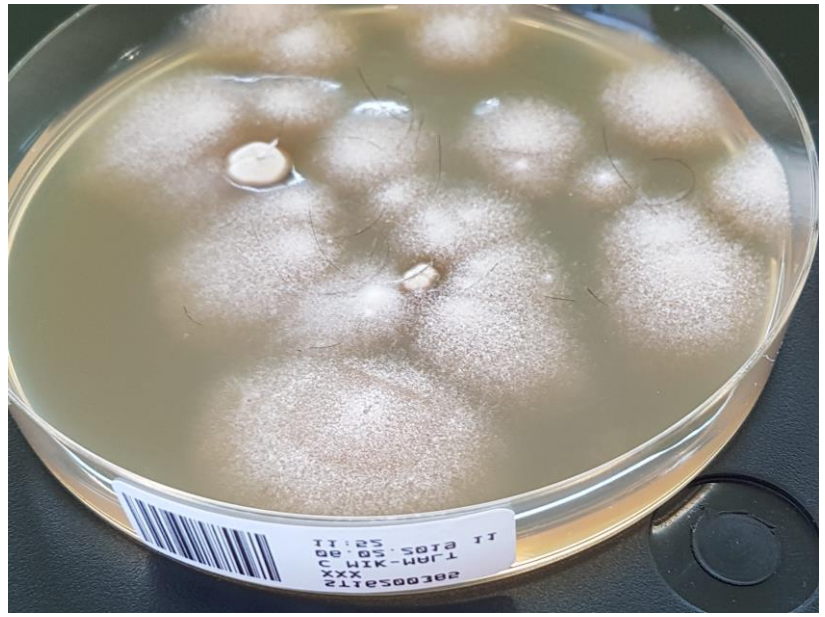

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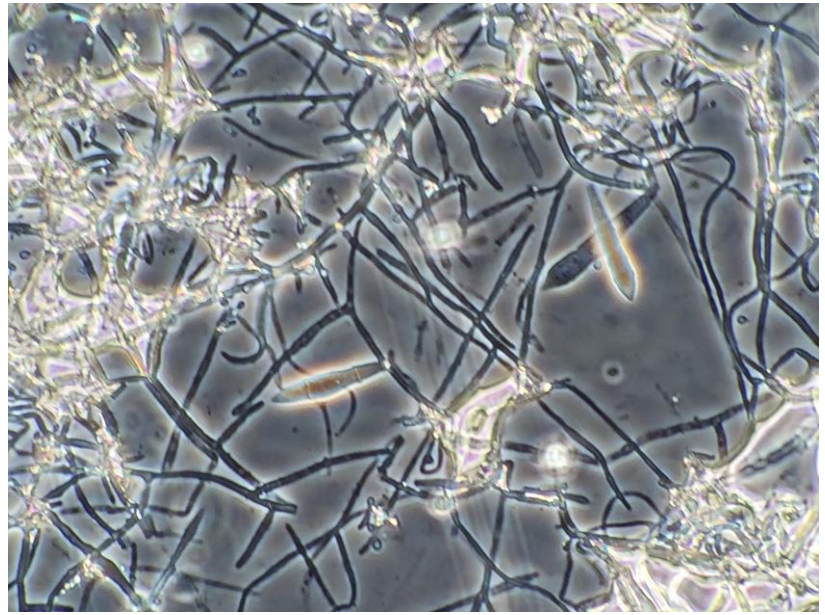


EUCAST AFST uudised

- **The subcommittee on antifungal susceptibility testing (the EUCAST AFST) has revised breakpoints and rationale documents as a consequece of the EUCAST change in the definition of the I-category and the introduction of ATU.**

- The following rationale documents and breakpoint table v 10.0 are under consultation 2019-09-25 - **2019-11-15**:
- Amphotericin B
- Anidulafungin
- Fluconazole
- Isavuconazole
- Itraconazole
- Micafungin
- Posaconazole
- Voriconazole
- AFST Breakpoint table v. 10 for consultation.

Please use the form for comments available from the link above and send to Jesus Guinea Ortega <jguineaortega[at]yahoo.es> no later than November 15, 2019.

Flukonasool

9. *Candida* clinical breakpoints

Non-species-related breakpoints

These have been determined mainly on the basis of PK/PD data and are independent of MIC distributions of specific species. EUCAST does not advocate terms such as SDD (susceptible dose-dependent) preferring to use "I" (Susceptible, increased exposure) to denote strains that are considered susceptible but require higher fluconazole exposure to be treated. The column of non-species related breakpoints is for use only for species not included in the table. They should not be used for species where susceptibility testing is not recommended (marked with - in the EUCAST breakpoint tables).

Non-species-related breakpoints are S ≤2 mg/L, R >4 mg/L.

Species-related breakpoints

Organism group	MIC breakpoints (mg/L) S ≤	MIC breakpoints (mg/L) R >	Notes
C. albicans	≤2	>4	
C. dubliniensis	≤2	>4	
C. tropicalis	≤2	>4	
C. parapsilosis	≤2	>4	
C. glabrata	≤0.001	>16	The entire wild-type population is classified as "I" (Susceptible, Increased exposure). Semi-automated machines and laboratory information systems prefer numerical values. 0.001 mg/L is an arbitrary value designed only to prevent the occasional organism to erroneously be reported as "S". A significant number of infections involve *C. glabrata*, for which fluconazole MICs are ≤16 mg/L in the absence of resistance mechanisms. As there are few agents suitable for the treatment of urinary tract infections and mucosal infections managed in the primary health care setting, fluconazole may be a suitable choice. In cases where fluconazole is the only available antifungal agent for treating *C. glabrata* infections the use of a higher dosage may be required.

Breakpoints for these *Candida* species were based on PK data, microbiological data, and patient outcomes.

Species without breakpoints

C. krusei is inherently resistant to fluconazole and regarded a poor target for the agent. Therefore, EUCAST-AFST has refrained from establishing *C. krusei* breakpoints for fluconazole and advises that an alternative agent should be used.
The MICs and ECOFF for *C. guilliermondii* are 5 two-fold dilution-steps higher than those for *C. albicans*. There are insufficient clinical data to indicate whether this species is a good target for fluconazole or not. Hence, EUCAST has refrained from setting breakpoint for this species.

Isavukonasool

9. Clinical breakpoints

PK/PD breakpoints	PK/PD breakpoints have been determined using PK/PD data and are independent of MIC distributions of specific species. They are for use only as a guide for organisms that do not have specific breakpoints. PK/PD breakpoints have been termed “non-species-related breakpoints” but this has led to confusion and it has become clear that PK/PD breakpoints for some agents may differ for different organisms.				
Species-related breakpoints	**Organism group**	**MIC breakpoints (mg/L)**			**Notes**
		S ≤	R >	ATU	
	Aspergillus flavus	1	2	2	MIC 2 mg/L = ATU for *A. flavus* and *A. fumigatus*.
	Aspergillus fumigatus	1	2	2	Recommendation: test voriconazole If voriconazole S, report as isavuconazole S and add the following comment: The MIC of 2 mg/L is one dilution above the S breakpoint due to overlapping wt and non-wt populations. If not S to voriconazole, report as isavuconazole R and refer to reference laboratory for CYP51A sequencing and confirmation of MICs.
	Aspergillus nidulans	0.25	0.25		
	Aspergillus niger	IE	IE		There is insufficient evidence that *A. niger* is a good target for therapy with the agent in question.
	Aspergillus terreus	1	1		

In version 2.0 of this rationale document, an ATU (Area of Technical Uncertainty) category has been introduced for isavuconazole against *A. fumigatus* and *A. flavus*, to avoid misclassifications of wt isolates as resistant due to the overlapping wt and non-wt distributions (MIC= 2 mg/L).

Dermatofüütide ravimtundlikkus & EUCAST AFST

- Indias ravimresistentse T. menatgrophytes/T. interdigitale epideemia, mis peagi võib osutuda globaalseks
- Seni puudub metoodika dermatofüütide ravimtundlikkuse määramiseks
- Metoodika osas võrdluskatsed „excellent centres“ vahel lõppenud, võib loota, et mikrolahjendusmeetod publitseeritakse peagi
- Resistentsed tüved on levinud Soomes, esimene tüvi ka Eestis
- Laboritel tuleb mõelda, kas ja kuidas korraldada dermatofüütide ravimtundlikkuse määramist lähitulevikus

macroconidia with granular ornamentation and lancet tips were seen in culture. *Trichophyton mentagrophytes* sub-type VIII was confirmed to be causative agent by multilocus sequencing.

Case 2

Patient is 35 years old, Indian male, lives in Finland but has travelled in India. *Trichophyton rubrum* infection was recorded in the groin area previously in 2018. On 25 February 2019 he came to doctor's visit in health care center in Jyväskylä, Finland, with very large dermatitis in the groins, thighs, buttocks and hand. He has used Pevisone cream. Three clinical samples were collected (Isolate B1 skin sample from thigh; Isolate B2 skin from left hand; Isolate B3 skin from buttock) for microscopy and culture. Atypical *T. mentagrophytes* isolate grew in culture in SYNLAB laboratory in Tallinn, Estonia. *Trichophyton mentagrophytes* sub-type VIII was confirmed by multilocus sequencing.

Case 3

Patient is 28 years old, male from Rauma, Satakunta County, western Finland. He had been in India in May 2018 and visited GP there with eczema. He used Itraconazole and Canesten (topical) for treatment of exzema. After 1 month he stopped the treatment. In Feb 2019 clinical signs reappeared and he made appointment to Rauma healthcare center. He had lesions on his hand (10 cm, overside), on the shoulder, upper back and lower stomach. He got Nizoral and Bemetson but he had no help of these two. Atypical *T. mentagrophytes* was isolated from skin sample (isolate C) on 18 of February 2019 in SYNLAB, Tallinn, Estonia and final identification was confirmed by multilocus sequencing.

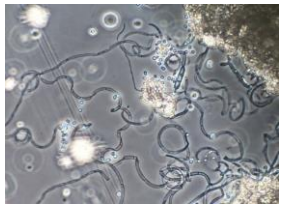


Photo 1. Round microconidia and spiral hyphae from isolate B2

Photo 2. Colony appearance of isolate C

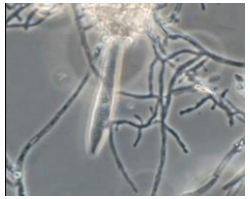


Photo 3. Lancet shape macroconidia from isolate D

microscopy was positive to fungal hyphae. Thin-walled macroconidia with slightly lancet tips were recorded in primary culture and final identification of *T. mentagrophytes* sub-type VIII was confirmed by multilocus sequencing.

Case 5

Patient is 26 years old, male from Turku, western Finland. Patient had *tinea cutis glabrae* with lesions in groin, belly and thigh area. He received fluconazole treatment in June 2019 and itraconazole treatment in July 2019. He has not travelled and has no pets at home, but he has had contact with a friend's dog. Sample was cultured 04 July 2019 in SYNLAB Tallinn, Estonia. Native microscopy was positive to fungal hyphae. Abundant macroconidia with lancet tips were seen in primary culture and final identification of *T. mentagrophytes* (sub-type VIII) was confirmed by multilocus sequencing.

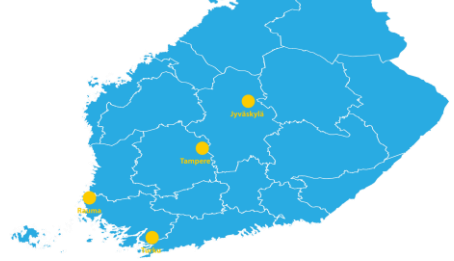


Fig 1. The distribution of *Trichophyton mentagrophytes* sub-type VIII with mutant squalene epoxidase gene (SQLE) in Finland

Case	Species	Isolate	SQLE mutation type	Substitution	Terbinafine MIC (mg/L)	Itraconazole MIC (mg/L)	Voriconazole MIC (mg/L)
1	*T. mentagrophytes*	Isolate A	Phe397Leu	TTC>CTC	4	0.0625	0.0312
2	*T. mentagrophytes*	Isolate B1	Phe397Leu	TTC>CTC	8	0.0625	0.0312
	T. mentagrophytes	Isolate B2	Phe397Leu	TTC>CTC	8	0.0625	0.0312
	T. mentagrophytes	Isolate B3	Phe397Leu	TTC>CTC	8	0.0625	0.0312
3	*T. mentagrophytes*	Isolate C	-	-	0.03	0.5	0.5
4	*T. mentagrophytes*	Isolate D	Phe397Leu	TTC>CTC	>8	0.125	0.0312
5	*T. mentagrophytes*	Isolate E	ND	ND	8	ND	ND

Table 1. Results of squalene epxidase (SQLE) gene analysis and susceptibility testing to terbinafine, itraconazole and voriconazole.

Methods

Primary fungal cultures were made on Sabouraud dextrose and 2% malt extract agar. Identification of fungal isolates was made by micromorphological appearance in SYNLAB laboratory in Estonia and by sequencing the ITS region of rDNA and TEF1-alpha gene in clinical microbiology laboratory in Mölbis, Germany.

The minimal inhibitory concentration (MIC) to terbinafine was determined by broth microdilution method (modified EUCAST) in clinical microbiology laboratory at Karolinska University Laboratory, Sweden. The sequencing of squalene epoxidase (SQLE) gene and MIC values for itraconazole and voriconazole by broth microdilution method were done in Lausanne University Hospital

Candida auris algoritm tuleb võtta aktiivselt kasutusse

Dewaele et al. Hospital Laboratory Survey for Identification of Candida auris in Belgium. J Fungi (Basel). 2019 Sep; 5(3): 84.

- Laboratories were asked to identify and report the isolate as they would in routine clinical practice, as if grown from a blood culture. Of 142 respondents, 82 (57.7%) obtained a correct identification of C. auris. Of 142 respondents, 27 (19.0%) identified the strain as Candida haemulonii. The remaining labs that did not obtain a correct identification (33/142, 23.2%), reported other yeast species (4/33) or failed to obtain a species identification (29/33).
- Awareness among Belgian microbiologists, therefore, remains inadequate more than two years after C. auris' emergence in European clinics.

API AUX 20C
VITEK 2-YST
BD Phoenix
MicroScan

ChromAgar
Candida

Candida spp, C. haemulonii, C. famata, C. lusitaniae, C. guilliermondii, C. parapsilosis, C. sake, Rhodotorula glutinis, Saccharomyces cerevisiae

Ebatüüpiline koloonia värv, mis ei võimalda liiki identifitseerida kui *C. albicans, C. glabrata, C. tropicalis* v *C. krusei* (kõikvõimalikud ebatüüpilised valged, roosad v kahvatud violetjates toonides kolooniad)

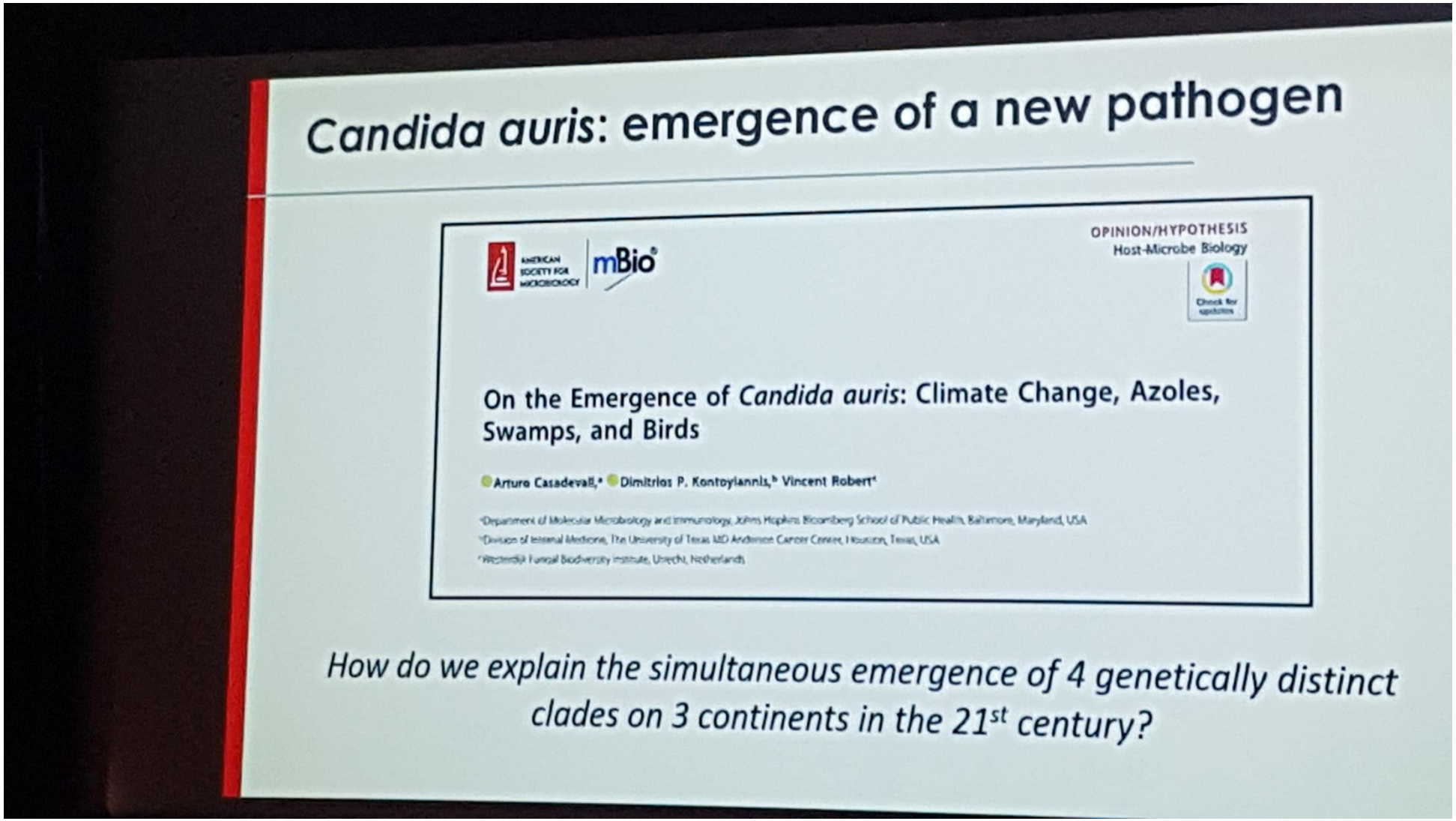
Temperatuuri
Test
42-45◦C 48 h

Kui pärmseen kasvab, siis püsib liigi *Candida auris* kahtlus, teostada ümberkülv Saboraud agarile, saata liigi lõplikuks samastamiseks MALDI TOF instrumendiga partnerlaborisse

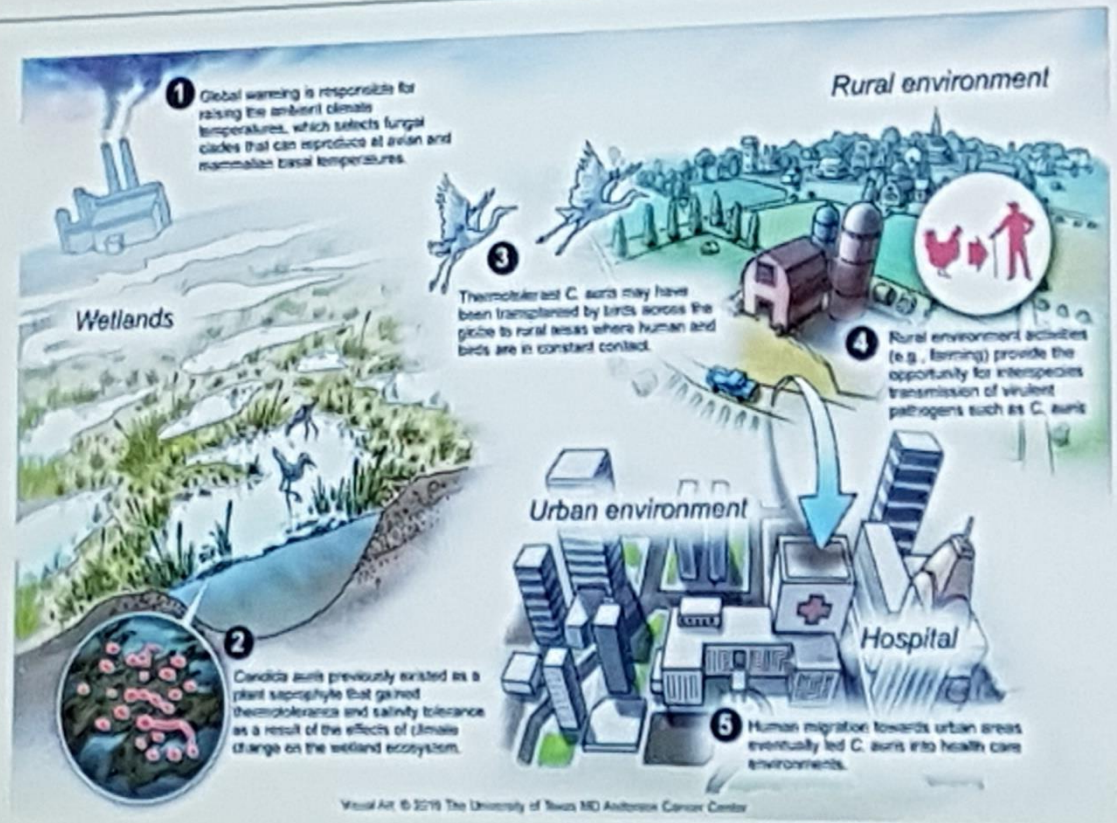
Identifitseerimine
MALDI TOF
instrumendiga

- Kontrolli, et MALDI TOF instrumendi andmebaasis sisaldub *Candida auris*!
- Kui pärmseen identifitseeritakse kui *Candida auris*, siis määra ravimtundlikkus 3 seenevastase ravimiklassi suhtes (asoolid, polüeenid, ehhinokandiinid)
- Kõikidest *C. auris* isolaatisest tuleb informeerida vastava haigla infektsioonikontrolli-teenistust

Arturo Casadevall, Dimitrios P. Kontoyiannis, Vincent Robert
doi: https://doi.org/10.1101/657635



Candida auris: emergence of a new pathogen



ELMÜ mikrobioloogia sektsioon on ECMM ametlik liige

- 11. oktoobril toimus ECMM council meeting

(konverentsi TIMM 2019 raames, Nizzas, Prantsusmaal)

- Sloveenia (26) ja Eesti (27) said ECMM liikmeks
- Meil on kohustus ja võimalus osaleda ECMM üldkoosolekutel
- Ettepanek, et dr Marika Jürna-Ellam hakkab Eestit ECMM esindama
- Võimalus osaleda töögruppides:

https://www.ecmm.info/working-groups/fungiscope/

SARAF Aspergillus fumigatus resistance global overview

Oleme ECMM liikmed

- 5th ECMM Educational Symposium “Rare Yeasts – A growing Threat”

11-12. juuni 2020 Rumeenias

https://www.ecmm.info/wp-content/uploads/5th_ECMM_Symposium_Iasi.pdf

Toimub järgmine ECMM liikmete üldkoosolek

- 10th TIMM in Aberdeen, UK 8-11. oktoober 2020