



UNIWERSYTET JAGIELLOŃSKI
COLLEGIUM MEDICUM

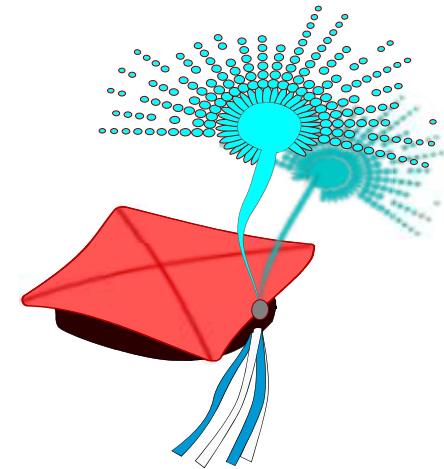
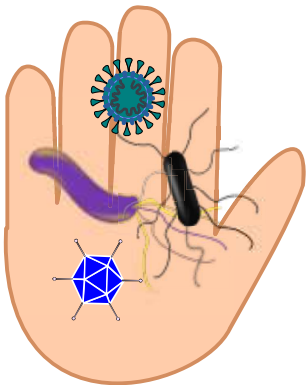
Grzyby w ataku niezbędna nowoczesna diagnostyka

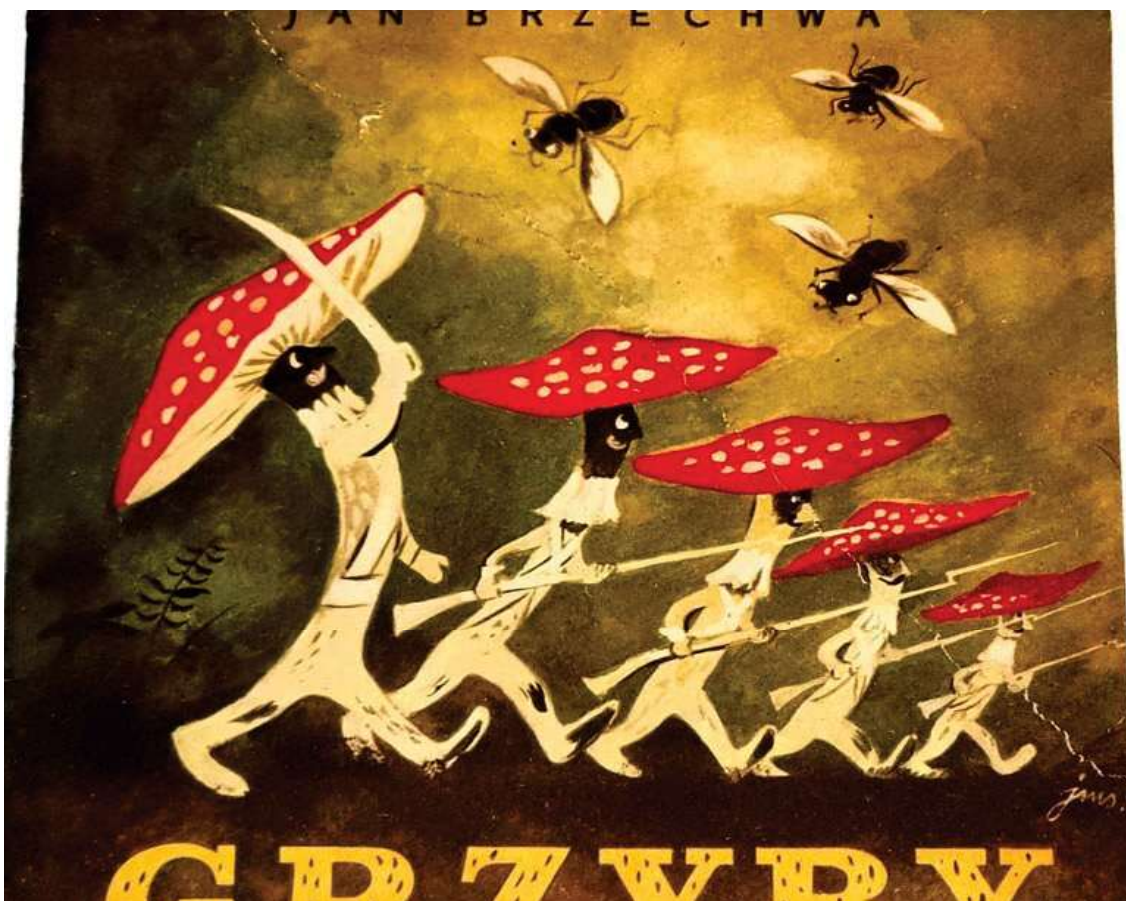
Postępy w Medycynie Zakazań 2024

sesja: Dylematy Diagnostyczne

Warszawa 7.12.2024

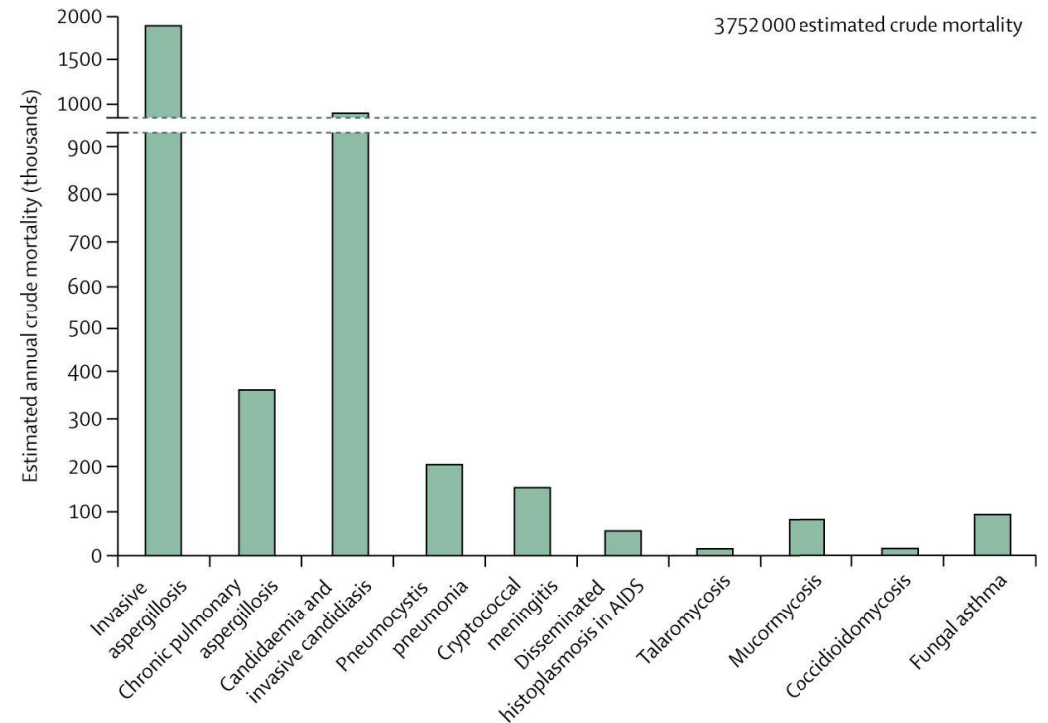
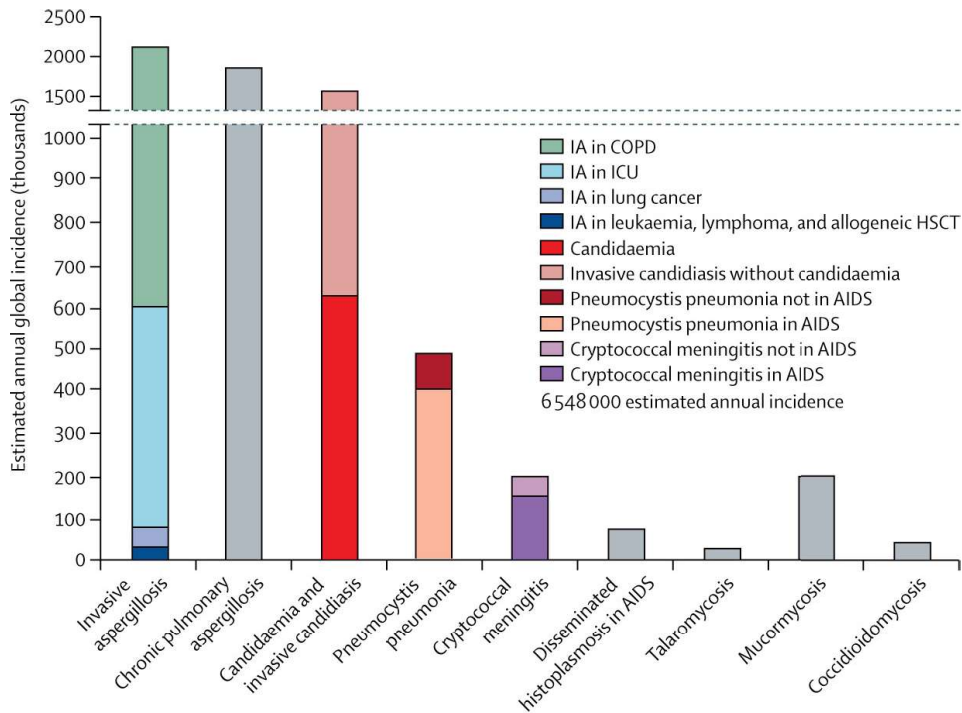
Zakład Kontroli Zakazań i Mykologii
Katedra Mikrobiologii





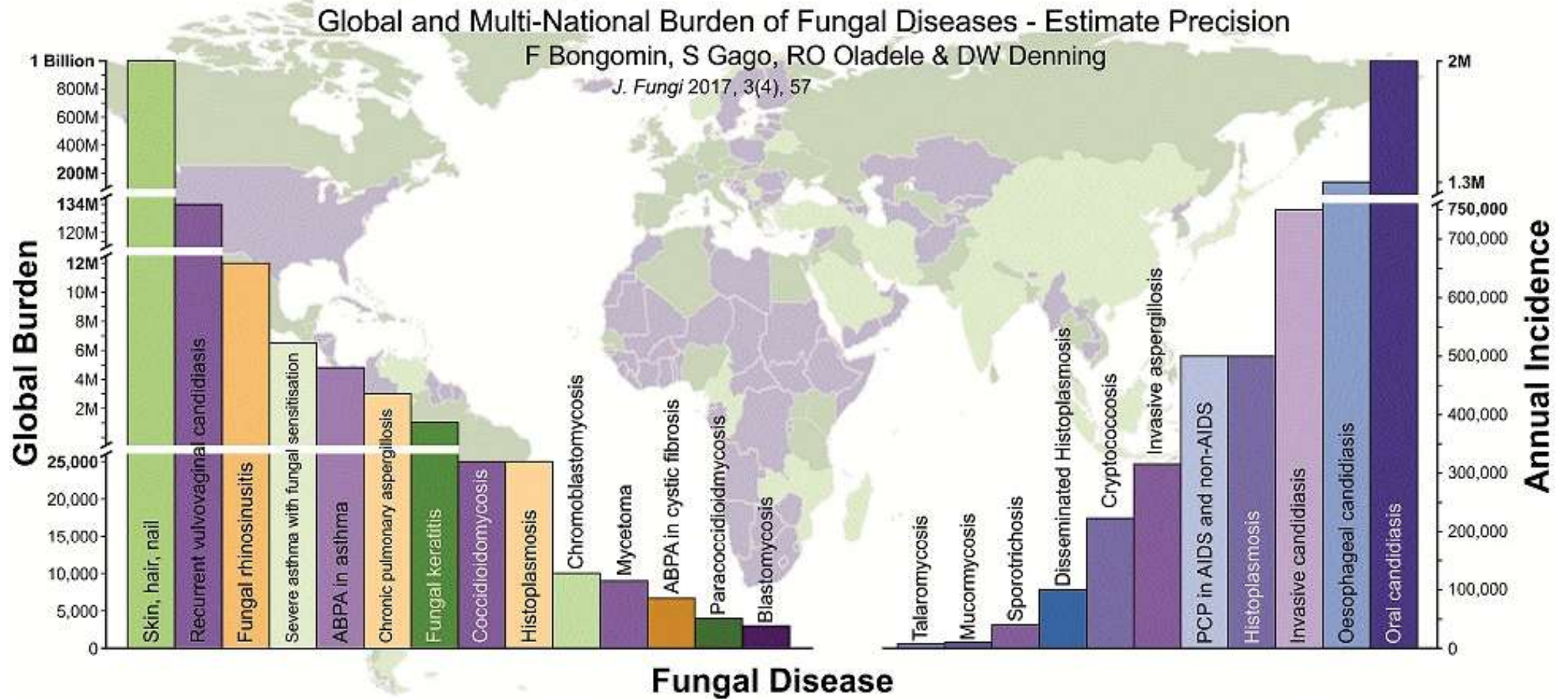
Grzyby w ataku

EPIDEMIOLOGIA (SZACOWANIE ZGRUBNE)

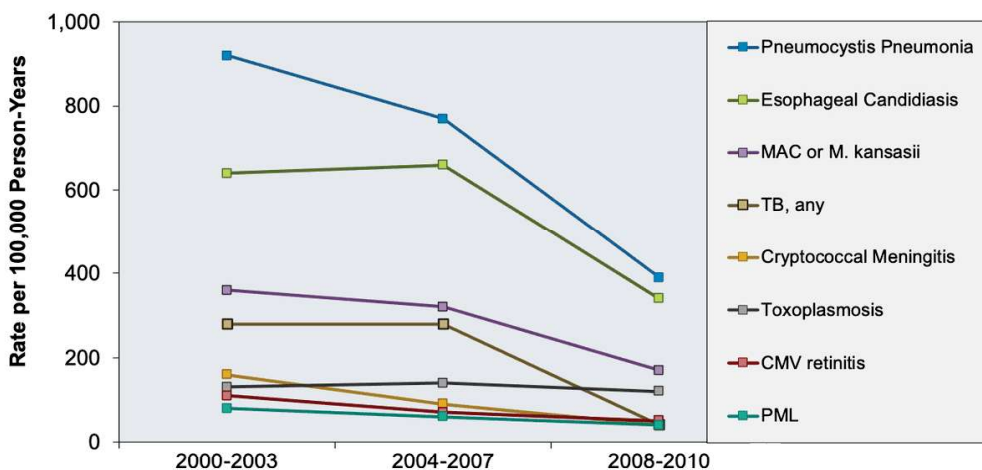
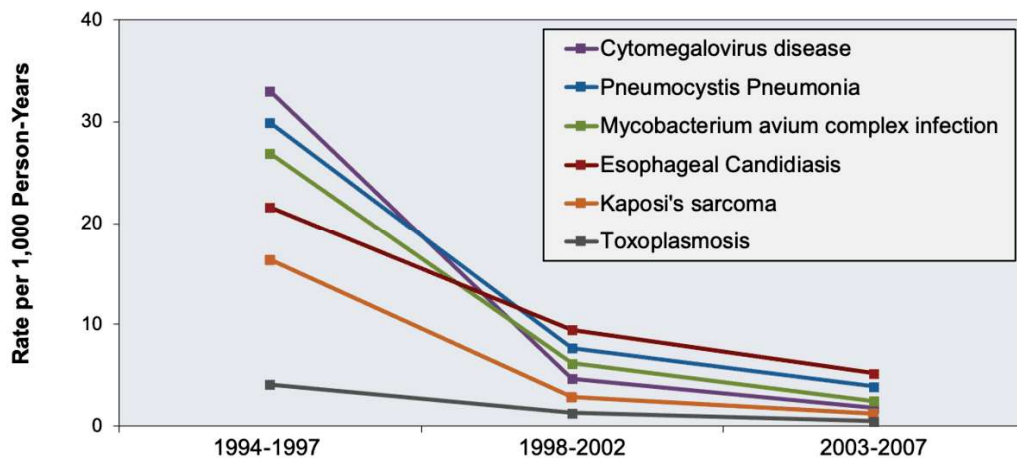


- każdego roku ponad **6,55 mln** ludzi zapada na zagrażające bezpośrednio życiu choroby grzybicze
- prowadzą one do ponad **3,75 mln** zgonów z czego ok. **2,55 mln** można bezpośrednio przypisać chorobie grzybiczej
- **2,1 mln IA; 1,8 CPA; 1,5 mln Candida BSI lub IC; 0,5 mln PcP; 194 tys. kryptokokowe ZOMR**

światowe obciążenie chorobami grzybiczymi



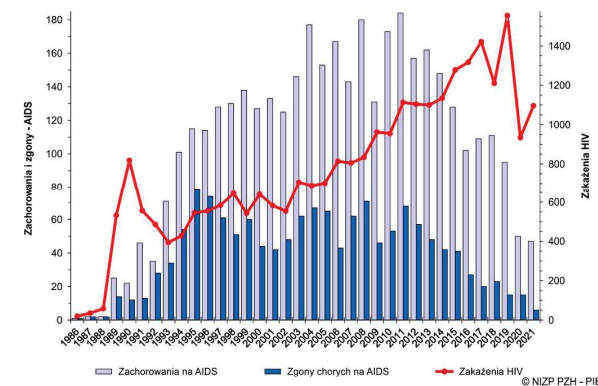
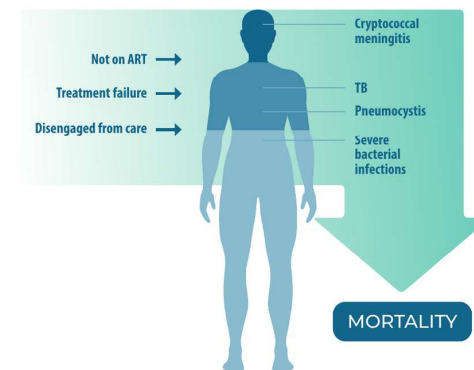
CHOROBY DEFINIUJĄCE AIDS U PACJENTÓW HIV+ (lata 80. - ~ 2000)



pneumocystoza
kandydoza przełyku

kryptokokowe ZOMR

ADVANCED HIV DISEASE



<https://www.hiv.uw.edu/go/co-occurring-conditions/opportunistic-infections-prevention/core-concept/all>

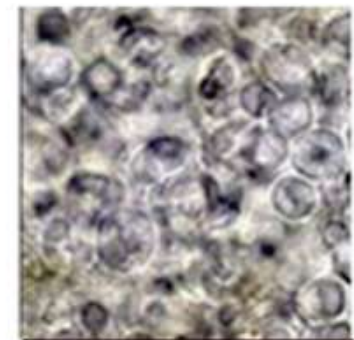
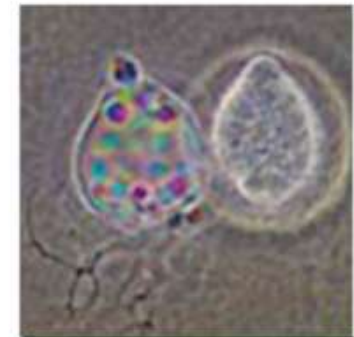
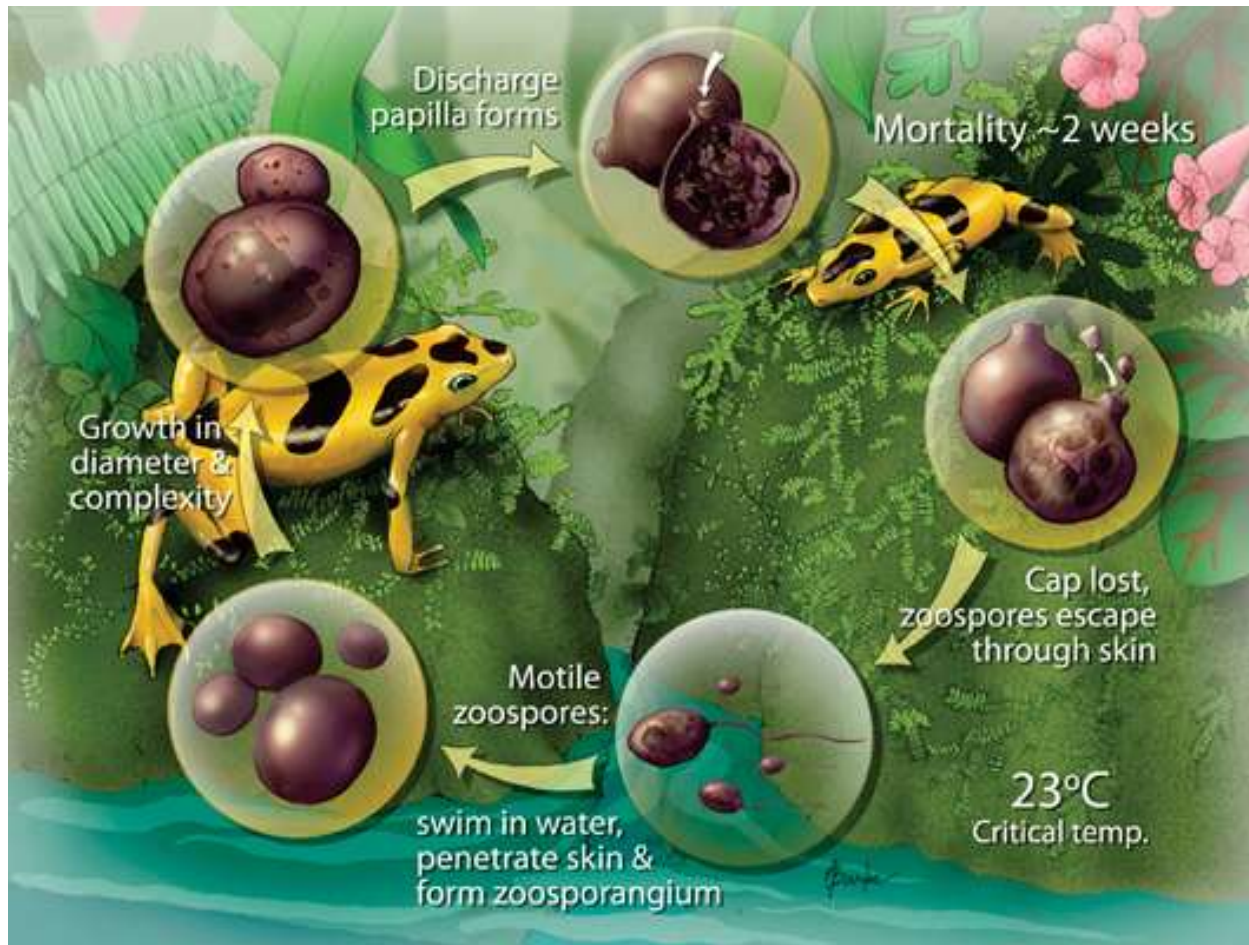
POMÓR PŁAZÓW (lata 90. - ~2010.)



<https://www.cabidigitallibrary.org/doi/10.1079/cabicompendium.109124>

Batrachochytrium dendrobatidis i *B. salamandrivorans*

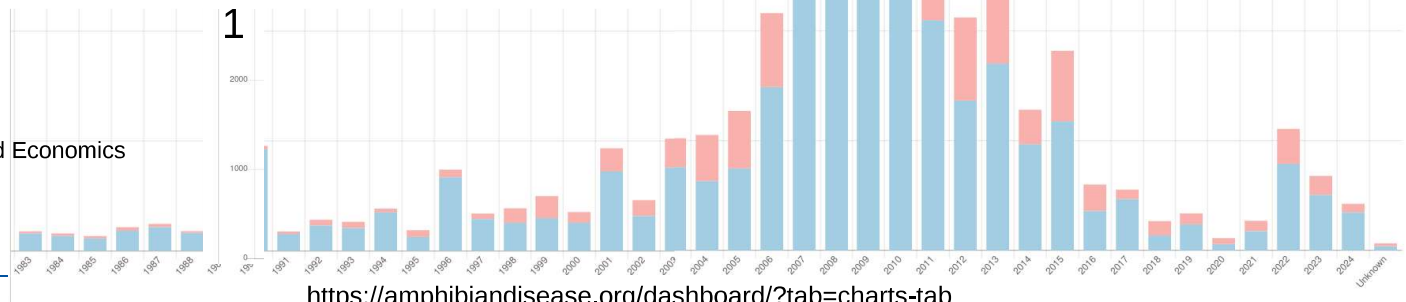
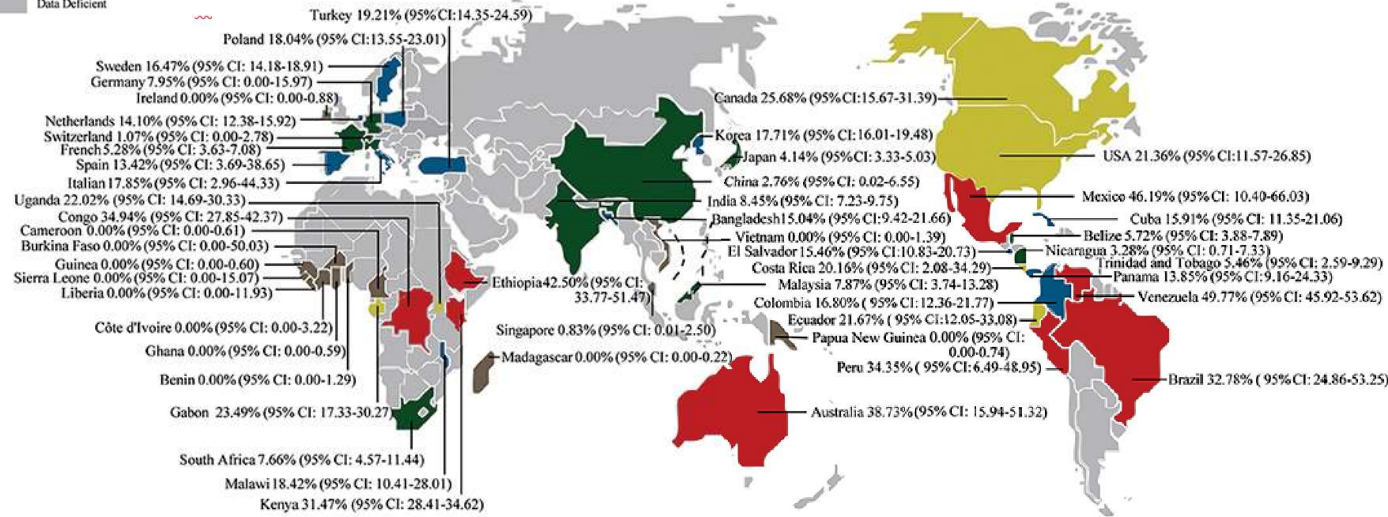
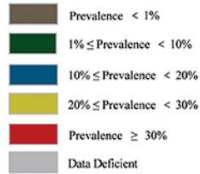
fot.: Joyce Longcore, from The University of Maine.



<https://www.broadinstitute.org/fungal-genome-initiative/batrachochytrium-genome-project>

Batrachochytrium dendrobatidis i B. salamandrivorans

Prevalence of Batrachochytrium in Amphibians From 2000 to 2024: Global Systematic Review and



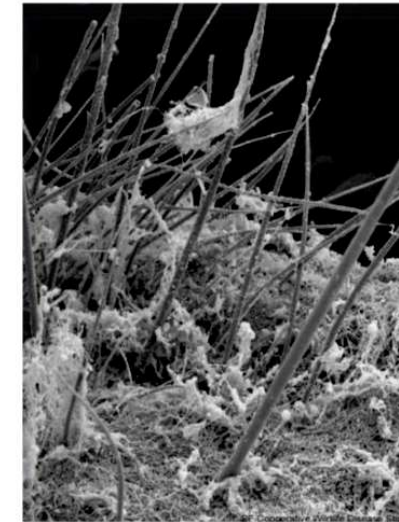
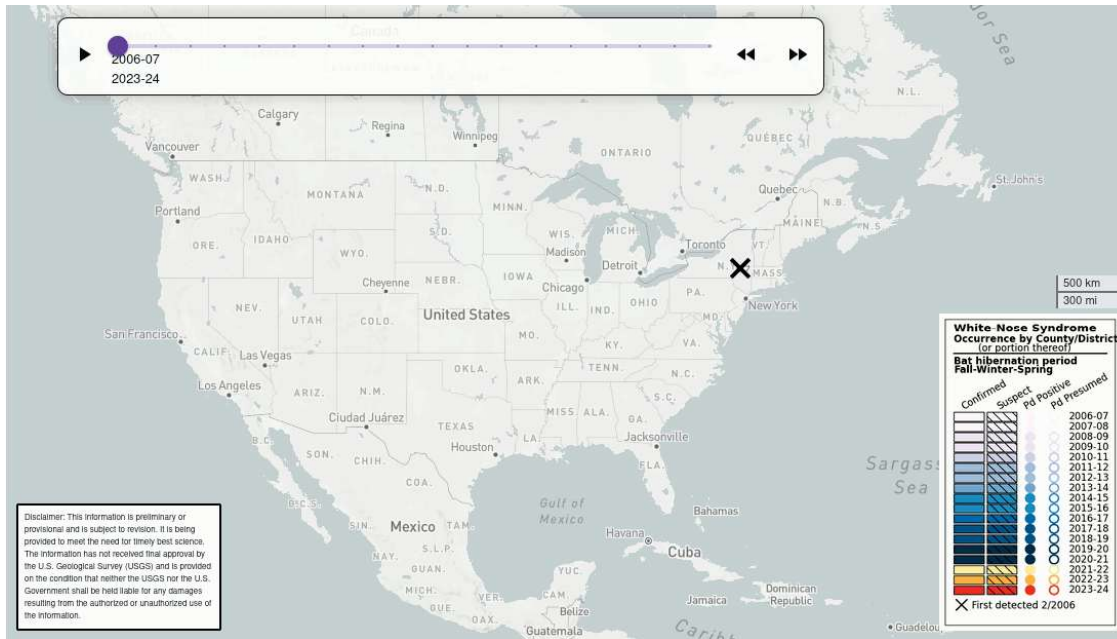
Front. Vet. Sci., 17 December 2021 Sec. Veterinary Epidemiology and Economics
 Volume 8 - 2021 | <https://doi.org/10.3389/fvets.2021.791237>

<https://amphibiandisease.org/dashboard/?tab=charts-tab>

SYNDROM BIAŁEGO NOSA (ok. 2010)

- choroba dotykająca hibernujące nietoperze
- grzyb wzrasta w chłodnych, ciemnych i wilgotnych miejscach
- atakując nietoperze wybudza je z hibernacji
 - mogą wylatywać w dzień w zimie
- pierwszy przypadek stwierdzony w 2007 roku w jaskiniach niedaleko Albany w stanie Nowy Jork
 - zdjęcie nietoperza z białym nosem wykonano rok wcześniej
- w niektórych miejscach śmiertelność sięgła 90-100% osobników
- różna podatność gatunkowa





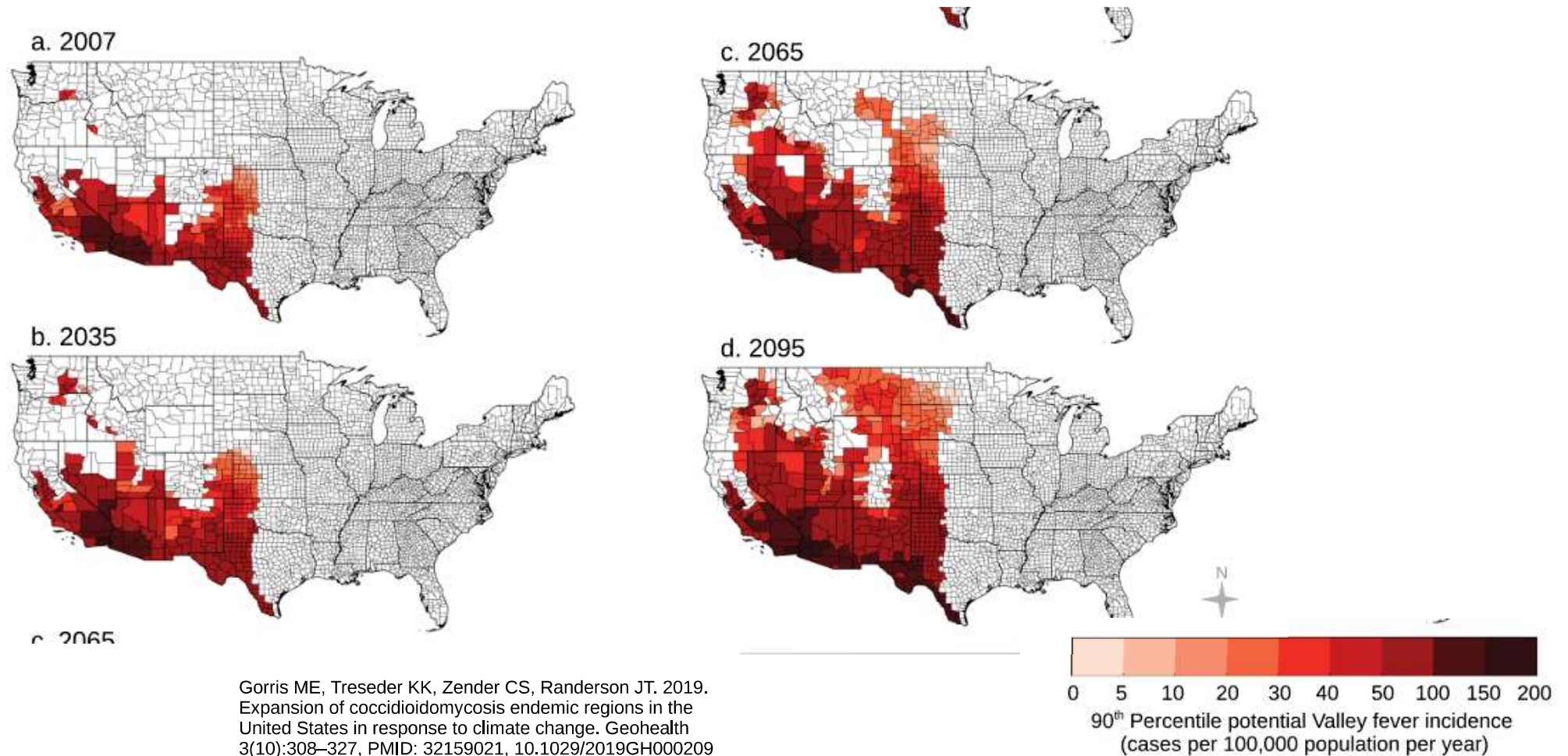
Electron microscopy image of Pd. Credit: K. Keel/Southeastern Cooperative Wildlife Disease Study



Differential interference contrast microscopy image of Pd spores. Credit: Barrie E. Overton/Lock Haven University

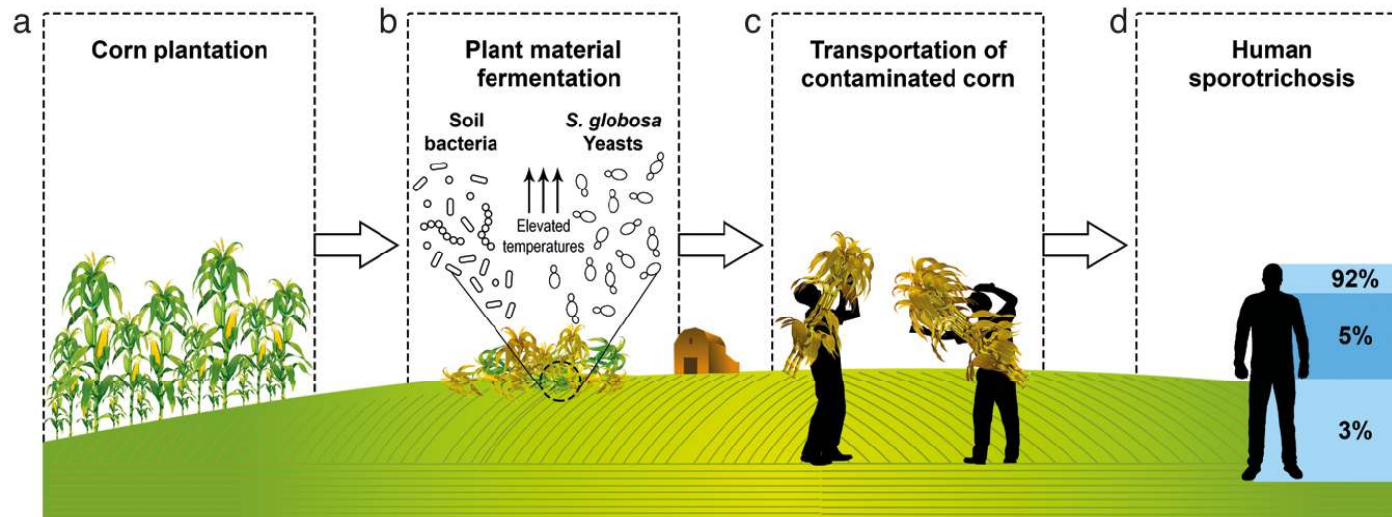
- opisany w 2008 roku
- początkowo *Geomyces destructans* reklasyfikowany w 2013
- prawdopodobnie wywodzi się z Europy
- przenoszony na futrze – zarażenia drogą kontaktową

GORĄCZKA DOLINNA - KOCYDIOIDOMYKOZA



Gorris ME, Treseder KK, Zender CS, Randerson JT. 2019. Expansion of coccidioidomycosis endemic regions in the United States in response to climate change. *Geohealth* 3(10):308–327, PMID: 32159021, 10.1029/2019GH000209

CHOROBA HODOWCÓW RÓŻ, CZY PLANTATORÓW KUKURYDZY



HIPOTEZA
ROZPRZESTRZENIANIA SIĘ
PATOGENU POCHODZENIA
ROŚLINNEGO PLANTACJI
KUKURYDZY CHINY

Persoonia 35, 2015: 1–20
www.ingentaconnect.com/content/nhn/pimj

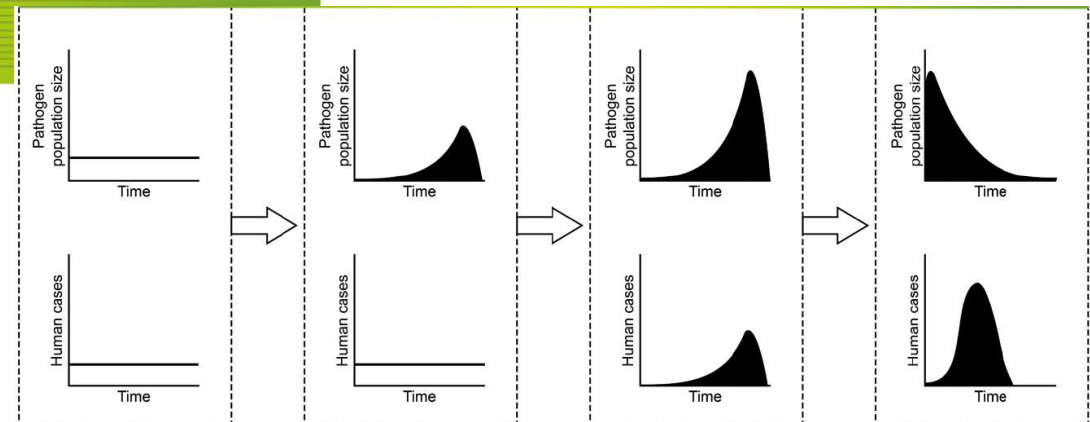
RESEARCH ARTICLE

<http://dx.doi.org/10.3767/003158515X687416>



Phylogeography and evolutionary patterns in *Sporothrix* spanning more than 14 000 human and animal case reports

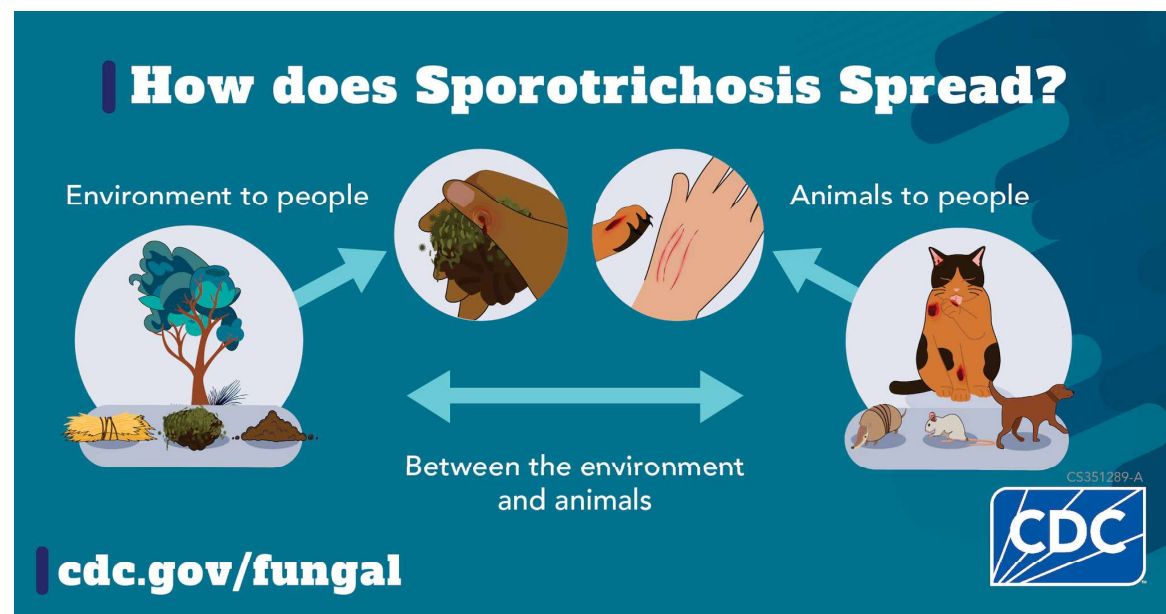
Y. Zhang^{1,2}, F. Hagen³, B. Stielow², A.M. Rodrigues⁴, K. Samerpitak^{2,5}, X. Zhou⁶, P. Feng⁷, L. Yang², M. Chen^{2,8}, S. Deng⁸, S. Li⁹, W. Liao⁸, R. Li¹⁰, F. Li¹¹, J.F. Meis^{3,12}, J. Guarro¹³, M. Teixeira¹⁴, H.S. Al-Zahrani¹⁵, Z. Pires de Camargo⁴, L. Zhang¹, G.S. de Hoog^{2,7,10,14,16}



ZOONOZA? – ZAKAŻENIA *SPOROTHRIX BRASILIENSIS*

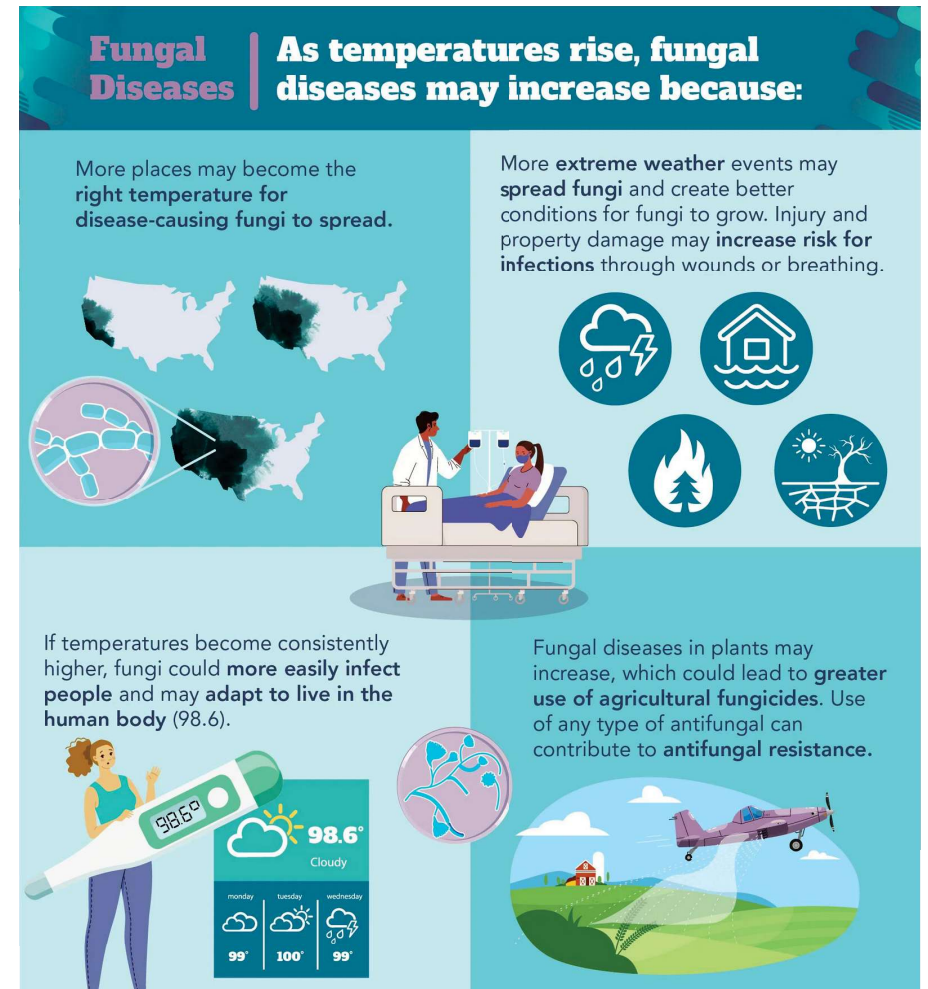
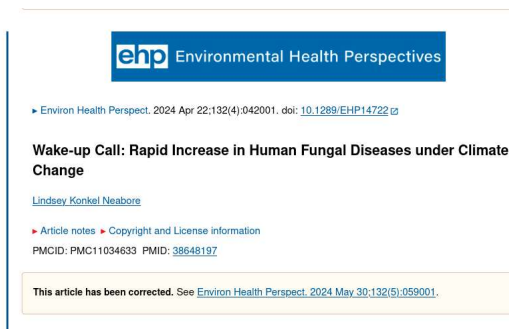
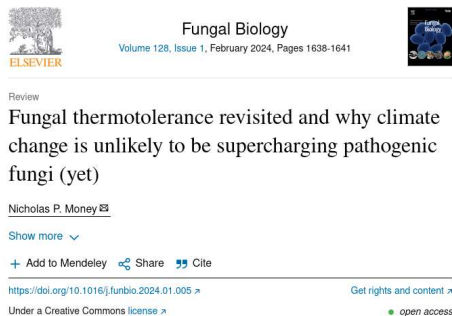


<https://www.healthline.com/health/sporotrichosis>

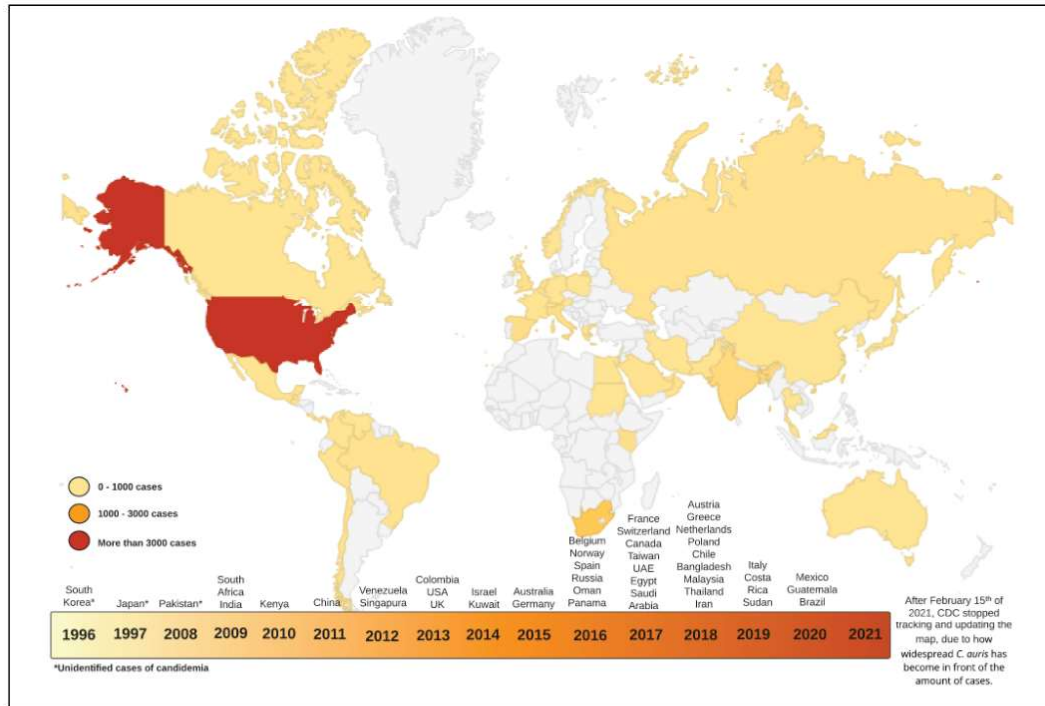


CZY ZMIANA KLIMATU MA WPŁYW NA WZROST LICZBY ZAKAŻEŃ GRZYBICZYCH

- **termotolerancja czynnikiem koniecznym do wywołania zakażenia**
 - ale wiele niepatogennych gatunków jest w stanie wzrastać w temperaturze ciała człowieka
 - czy zmiany klimatyczne odpowiadają za zwiększone ryzyko zakażeń grzybiczych
 - rozszerzenie się dotychczasowych endemicznych obszarów – wyjście grzybów poza te obszary

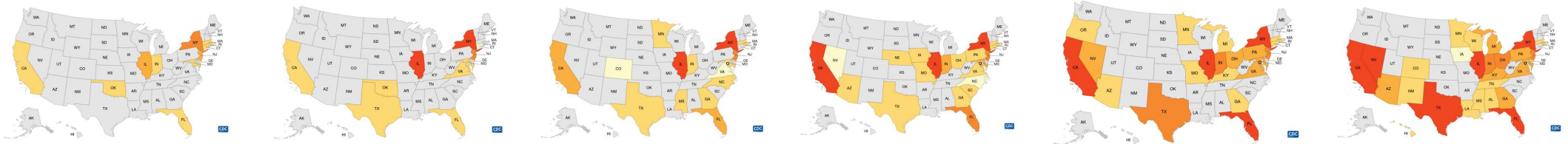


Candida auris – PRZEBUDZENIE? (lata 2010. - dziś)

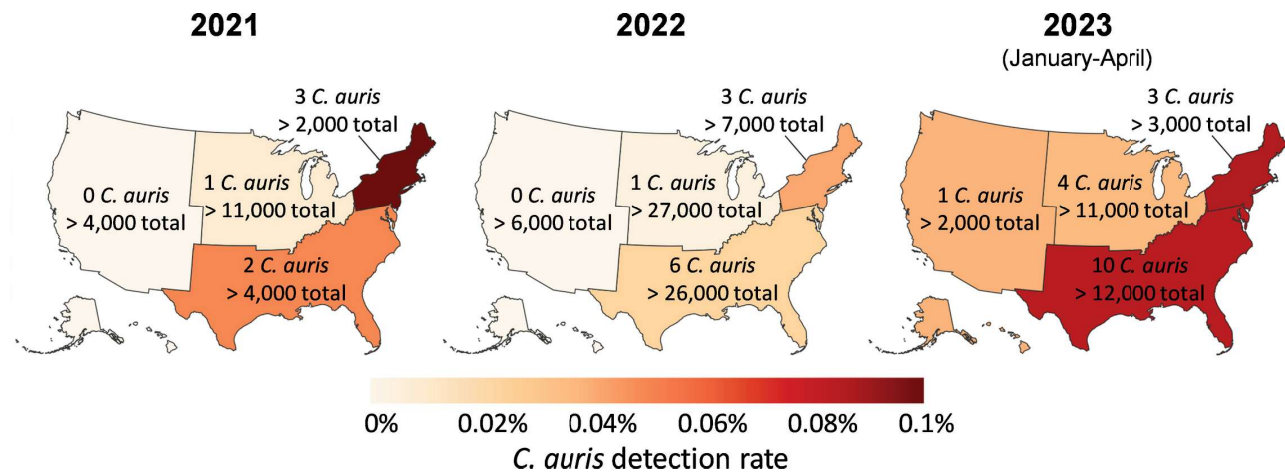
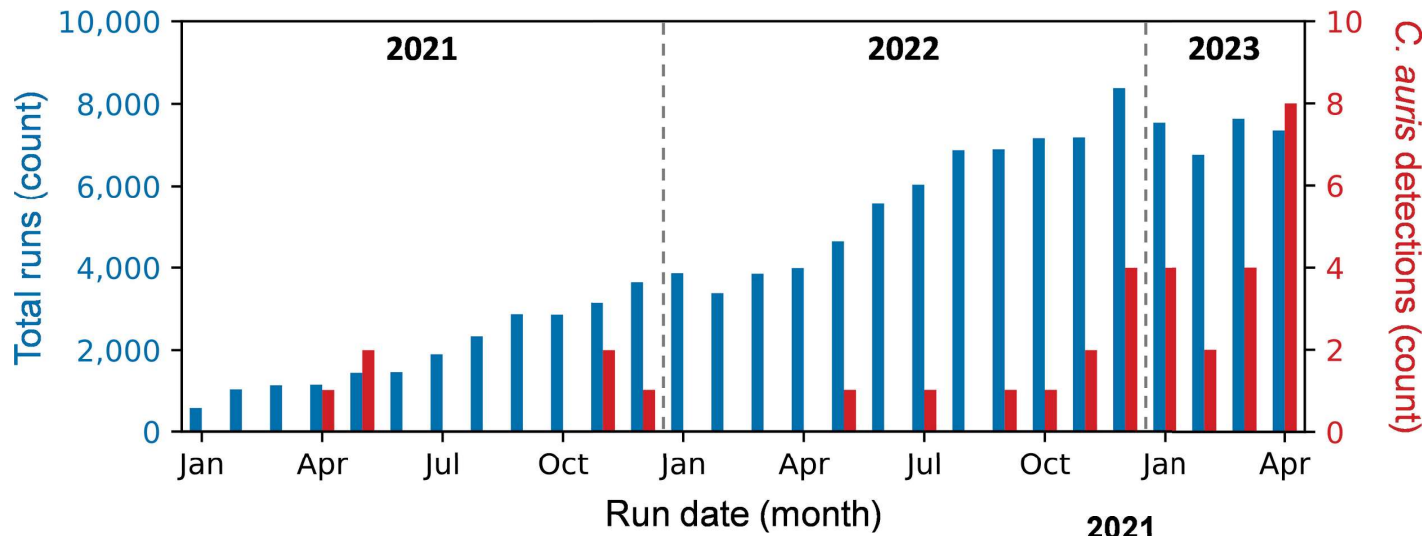


- powoduje ogniska epidemiczne
- trudny do usunięcia ze środowiska szpitalnego
- wielolekooporne szczepy
- w USA CDC zaleciło screening nosicielstwa

REV. BRAS. CIÊNC. BIOMED. VOLUME 3, E0682022, 1-12, 2022

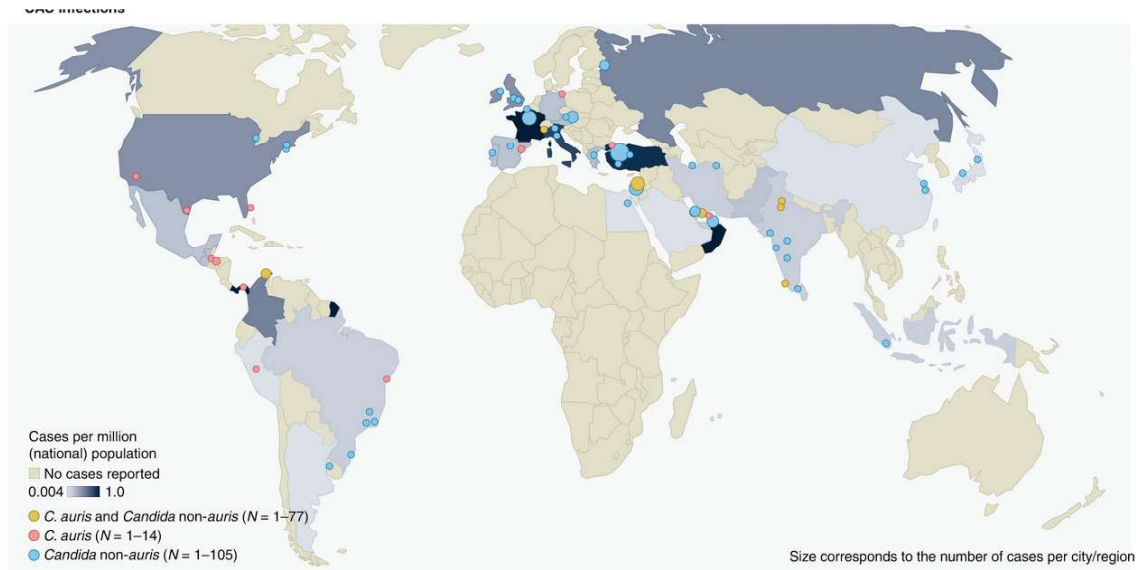


NARASTAJĄCY PROBLEM - ZERO TOLERANCJI?



Noble BA, Jurcic Smith KL, Jones JD, Galvin BW, Timbrook TT. 2023. Candida auris rates in blood culture on the rise: results of US surveillance. Microbiol Spectr 11:e02216-23. <https://doi.org/10.1128/spectrum.02216-23>

COVID19 - CAC



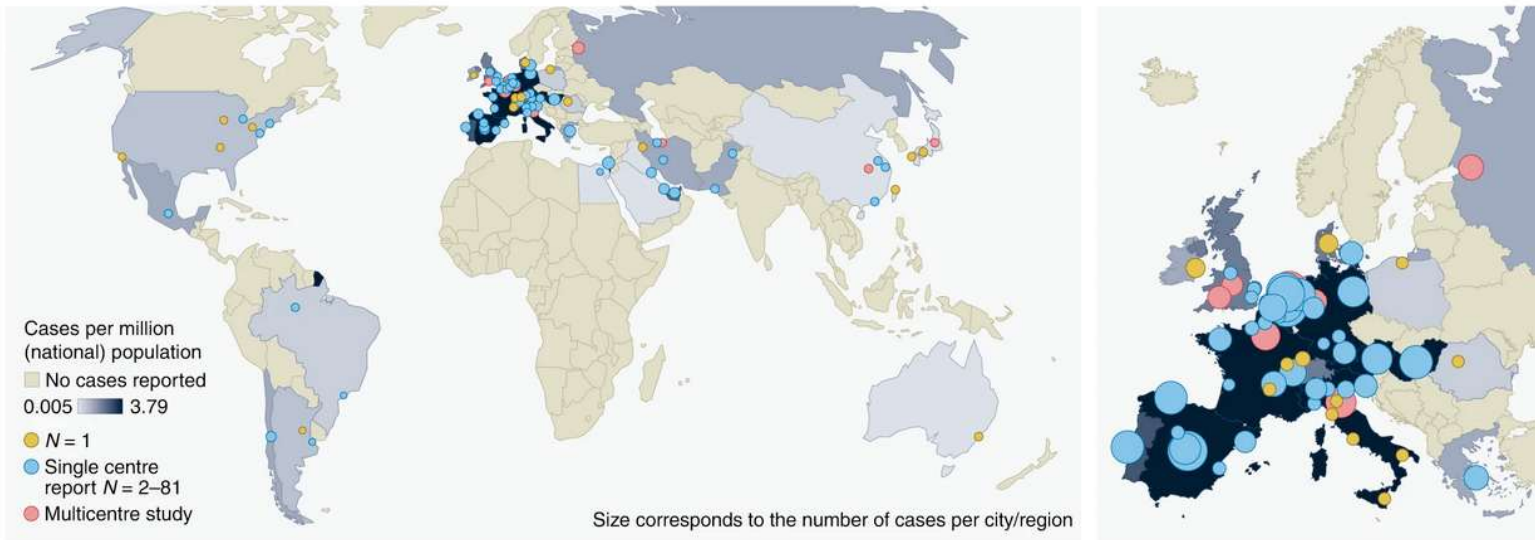
CAC



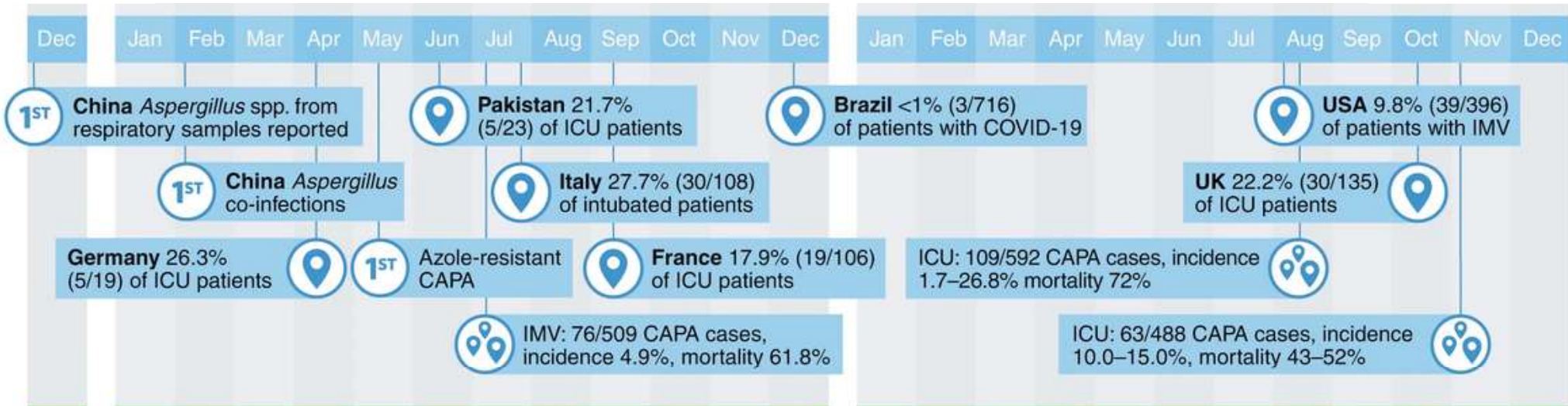
Hoenigl, M., Seidel, D., Sprute, R. et al. COVID-19-associated fungal infections. Nat Microbiol 7, 1127–1140 (2022). <https://doi.org/10.1038/s41564-022-01172-2>

COVID-19 - CA

a
CAPA

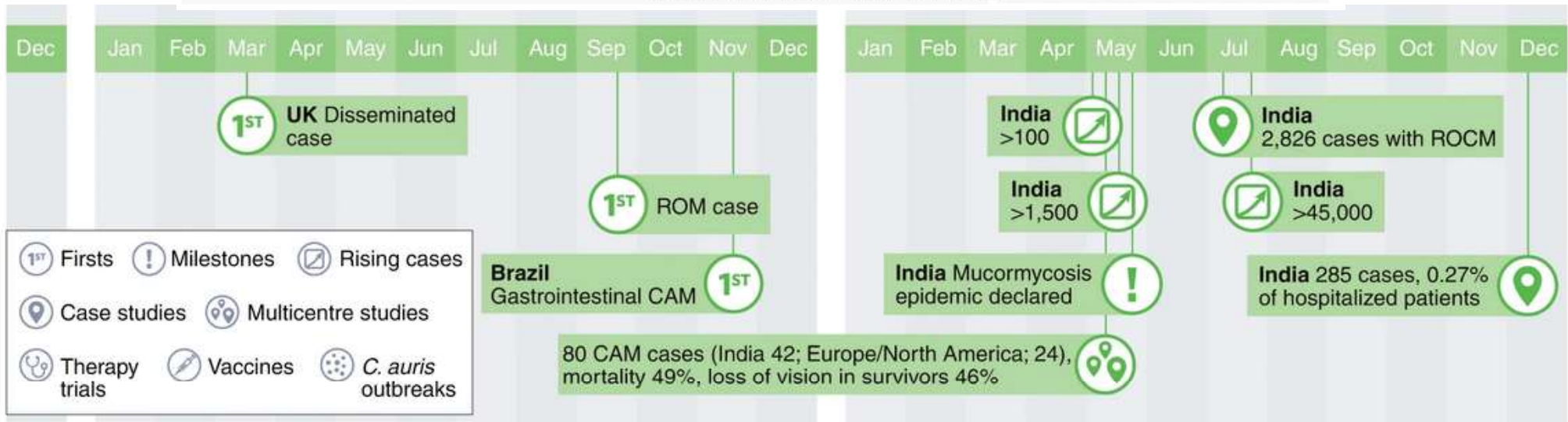
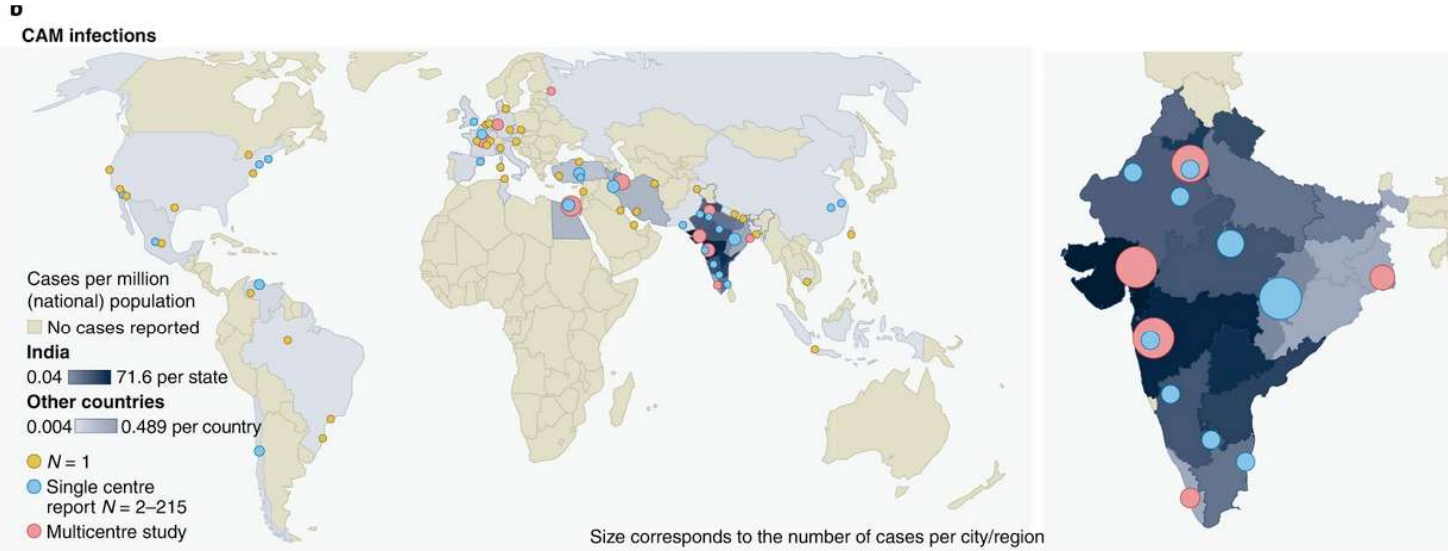


CAPA



Hoenigl, M., Seidel, D., Sprute, R. et al. COVID-19-associated fungal infections. Nat Microbiol 7, 1127–1140 (2022). <https://doi.org/10.1038/s41564-022-01172-2>

COVID19 - CAM



Hoeningl, M., Seidel, D., Sprute, R. et al. COVID-19-associated fungal infections. Nat Microbiol 7, 1127–1140 (2022). <https://doi.org/10.1038/s41564-022-01172-2>

ASPERGILOZA ZWIĄZANA Z GRYPĄ

Clinical Infectious Diseases

EDITORIAL COMMENTARY

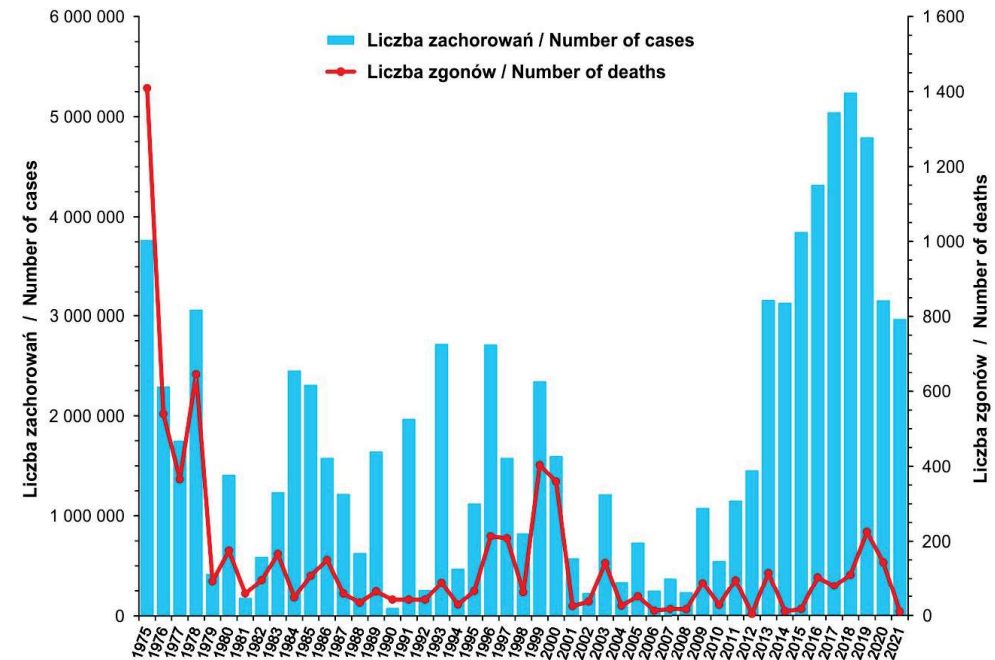
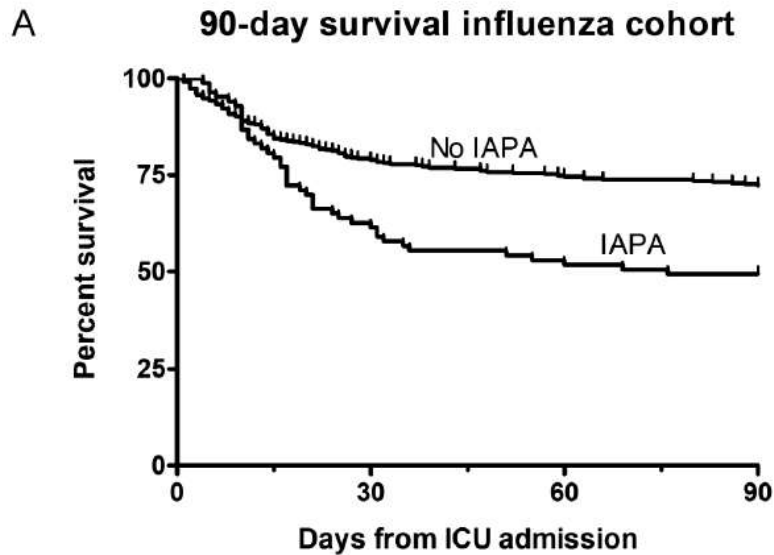


Influenza-Associated Pulmonary Aspergillosis: A Local or Global Lethal Combination?

Bart J. A. Rijnders,¹ Alexander F. A. D. Schauwvlieghe,^{1,2} and Joost Wauters³

¹Department of Internal Medicine, Section of Infectious Diseases, Erasmus MC, University Medical Center, Rotterdam, The Netherlands, ²Department of Hematology, Erasmus MC Cancer Center, Rotterdam, The Netherlands, and ³Medical Intensive Care Unit, University Hospitals Leuven, Leuven, Belgium

CID 2020:71 (1 October) • EDITORIAL COMMENTARY



<https://wwwold.pzh.gov.pl/oldpage/epimeld/grypa/index.htm>

Przegapiona epidemia...

- *Trichophyton benhamiae*
- wzrost liczby zakażeń
- patogenny szczep odmiany żółtej

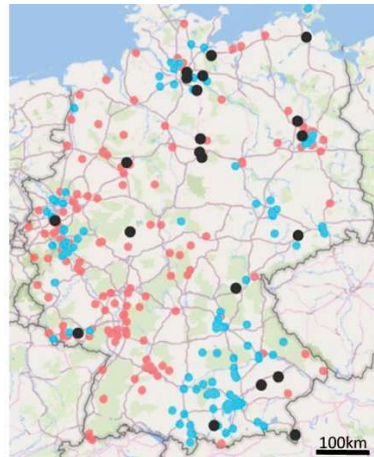
Open Access Article

German-Wide Analysis of the Prevalence and the Propagation Factors of the Zoonotic Dermatophyte *Trichophyton benhamiae*

by Max Berlin¹ ✉, Christiane Kupsch¹ ✉, Lea Ritter¹ ✉, Benjamin Stoelcker² ✉, Anton Heusinger³ ✉ and Yvonne Gräser^{1,*} ✉

Table 4. Detection of dermatophytes in guinea pig samples from SYNLAB VET and LABOKLIN, February–November 2019.

| Samples Analyzed | Number |
|-----------------------------------|--------|
| Total | 9636 |
| with suspected mycosis | 1035 |
| Tested positive for dermatophytes | 382 |
| <i>T. benhamiae</i> | 375 |
| <i>T. benhamiae</i> (yellow) | 357 |
| <i>T. benhamiae</i> (white) | 18 |
| <i>T. rubrum</i> | 3 |
| <i>Microsporum (M.) canis</i> | 1 |
| <i>T. mentagrophytes</i> | 1 |
| <i>T. spp.</i> | 1 |
| <i>T. interdigitale</i> | 1 |



J. Fungi 2020, 6(3), 161; <https://doi.org/10.3390/jof6030161>

2022 – PROBLEM ZOSTAJE NAGŁOŚNIONY

Critical Priority Group



Cryptococcus neoformans



Candida auris



Aspergillus fumigatus



Candida albicans

WHO fungal priority pathogens list to guide research, development and public health action

High Priority Group



Nakaseomyces glabrata
(*Candida glabrata*)



Histoplasma spp.



Eumycetoma causative agents



Mucorales



Fusarium spp.



Candida tropicalis



Candida parapsilosis

Medium Priority Group



Scedosporium spp.



Cryptococcus gattii



Lomentospora prolificans



Talaromyces marneffei



Coccidioides spp.



Pneumocystis jirovecii



Pichia kudriavzevii
(*Candida krusei*)



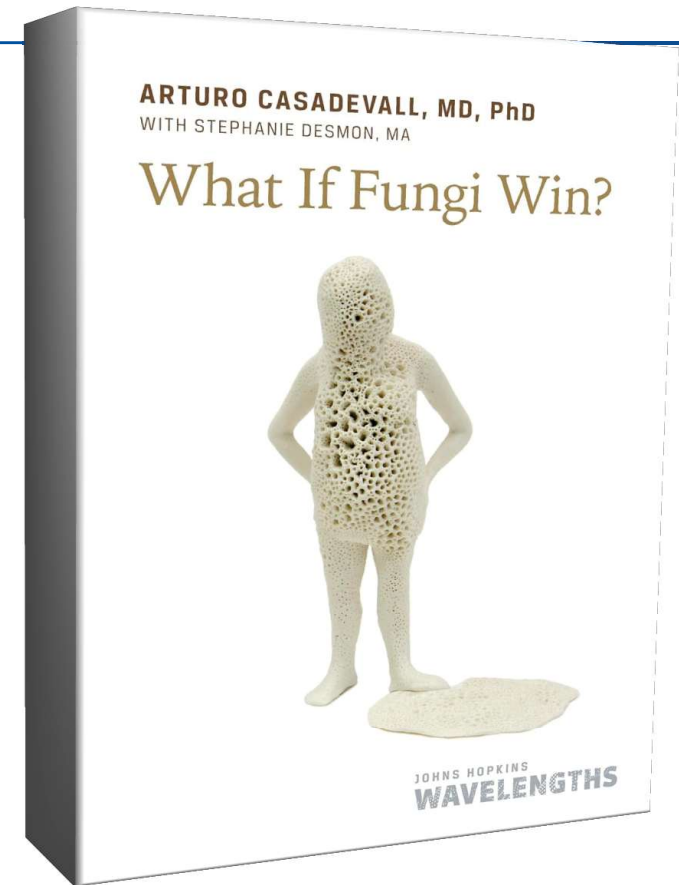
Paracoccidioides spp.

Czy grzyby są w ataku – a co jeśli wygrają?

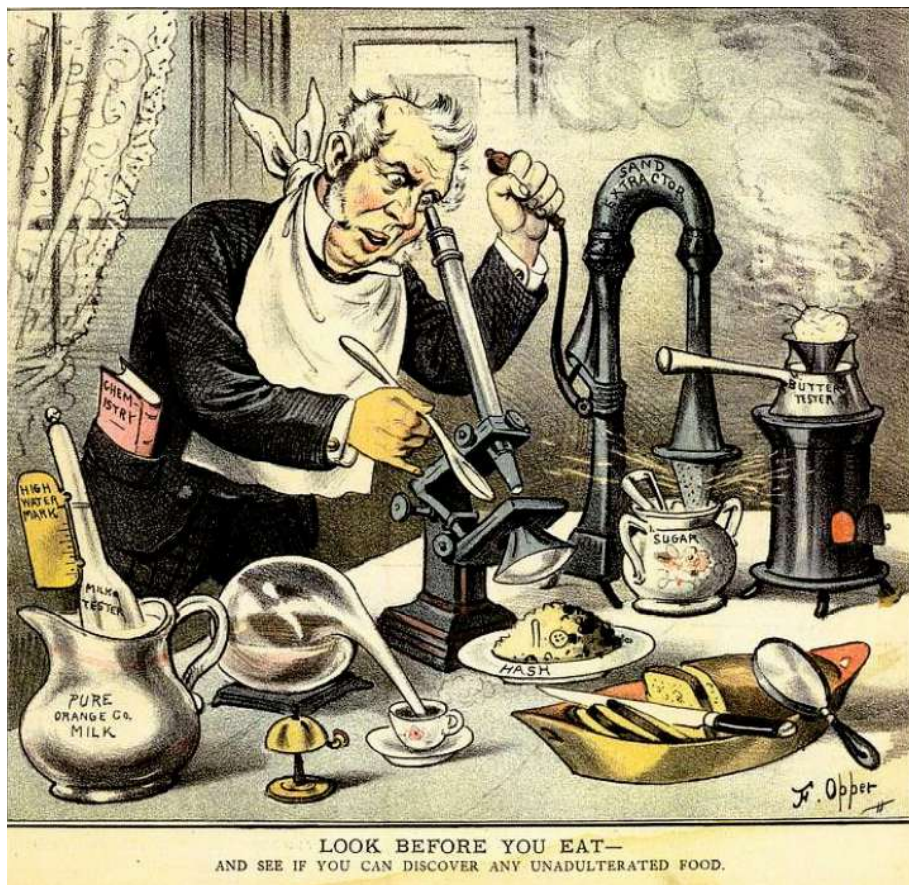
- **a co jeśli grzyby wygrają?**
- człowiek współdzieli z grzybami ok. 50% DNA

Arturo Casadevall profesor mikrobiologii molekularnej, immunologii i chorób zakaźnych w Johns Hopkins Bloomberg School of Public Health w Baltimore, Maryland, USA.

koncentruje się na mechanizmach obronnych gospodarza, sposobie wywoływania chorób przez grzyby oraz opracowywaniu terapii chorób zakaźnych opartych na przeciwciałach.



Johns Hopkins University Press – 14 maja 2024 r.
222 strony

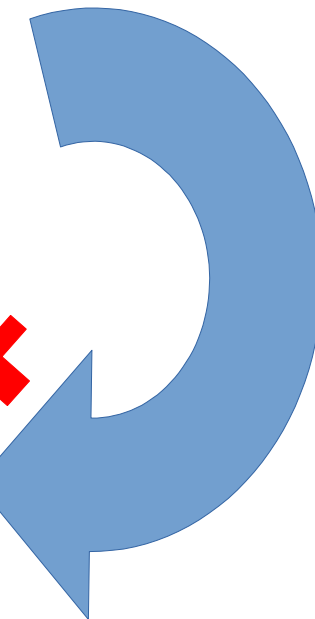


nowoczesna
diagnostyka

Frederick Opper

DIAGNOSTYKA GRZYBIC POWIERZCHNIOWYCH

| ZAKAŻENIA SKÓRY I JEJ PRZYDATKÓW | | ŁUPIEŻ PSTRY | | DROŹDZYCE BŁON ŚLIZOWYCH | |
|--|--|--|--|--|--|
| | | | | <p>zdjęcie: James Heilman, MD CC BY-SA 3.0</p> <p>wymaz z błon śluzowych</p> | |
| <p>do 4 tyg. 25°C</p> <p>SGA SGa z CHX</p> | | <p>do 7 dni 32°C</p> <p>SGA z oliwą z oliwek</p> | | <p>1-3 dni 32°C</p> <p>Gram</p> <p>SGA</p> | |
| <p>MIKROHODOWLA grzyby strzępkow...</p> | | <p>HODOWLA NA PODŁOŻU ZUBOŻONYM</p> | | <p>ureaza</p> <p>auksanogram</p> | |
| <p>TECHNIKI MOLEKULARNE</p> | | <p>PCR</p> <p>EUCAST</p> <p>LEKOWRAŻLIWOŚĆ</p> | | | |



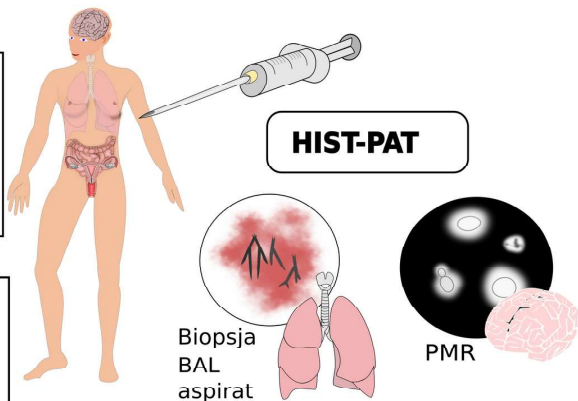
DIAGNOSTYKA GRZYBIC INWAZYJNYCH

PREDYSPOZYCJA

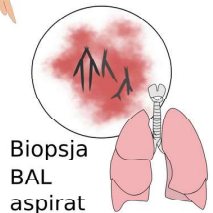
np.:
neutropenia
AIDS

OBJAWY

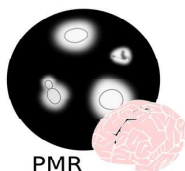
np.:
gorączka
zmiany w RTG, TK, NMR



HIST-PAT



Biopsja
BAL
aspirat

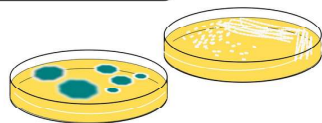


PMR

IMMUNO DIAGNOSTYKA

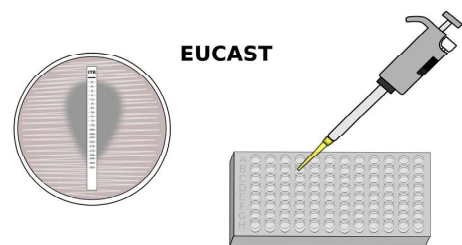
Galaktomannan
Ab anti-*Aspergillus*
Mannan
Ab anti-*Candida*
Ag kryptokokowy
Glukuronoksylomannan
 β -D-glukan

HODOWLA



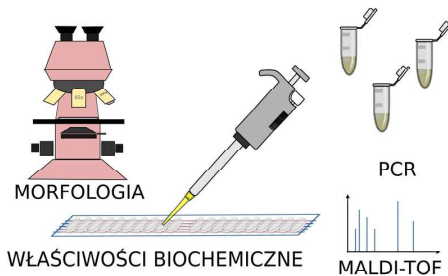
TECHNIKI MOLEKULARNE

LEKOWRWRAŻLIWOŚĆ



EUCAST

IDENTYFIKACJA

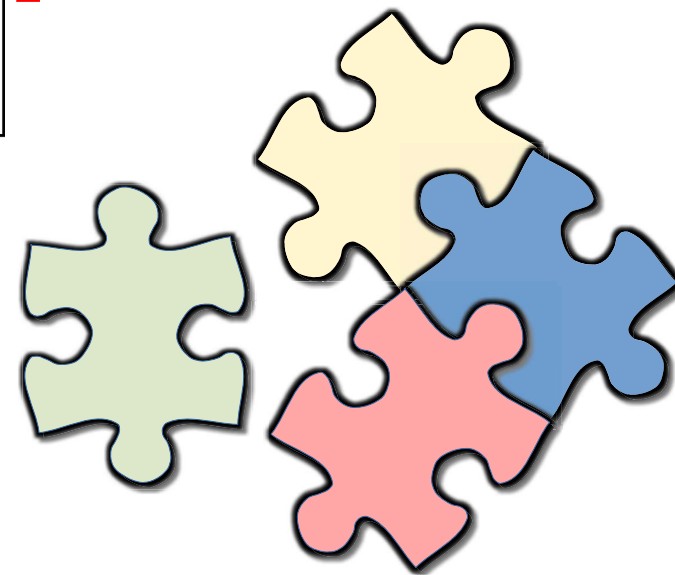


MORFOLOGIA

WŁAŚCIWOŚCI BIOCHEMICZNE

PCR

MALDI-TOF



NOWOCZESNA DIAGNOSTYKA OPARTA O NAJNOWSZE WYTYCZNE

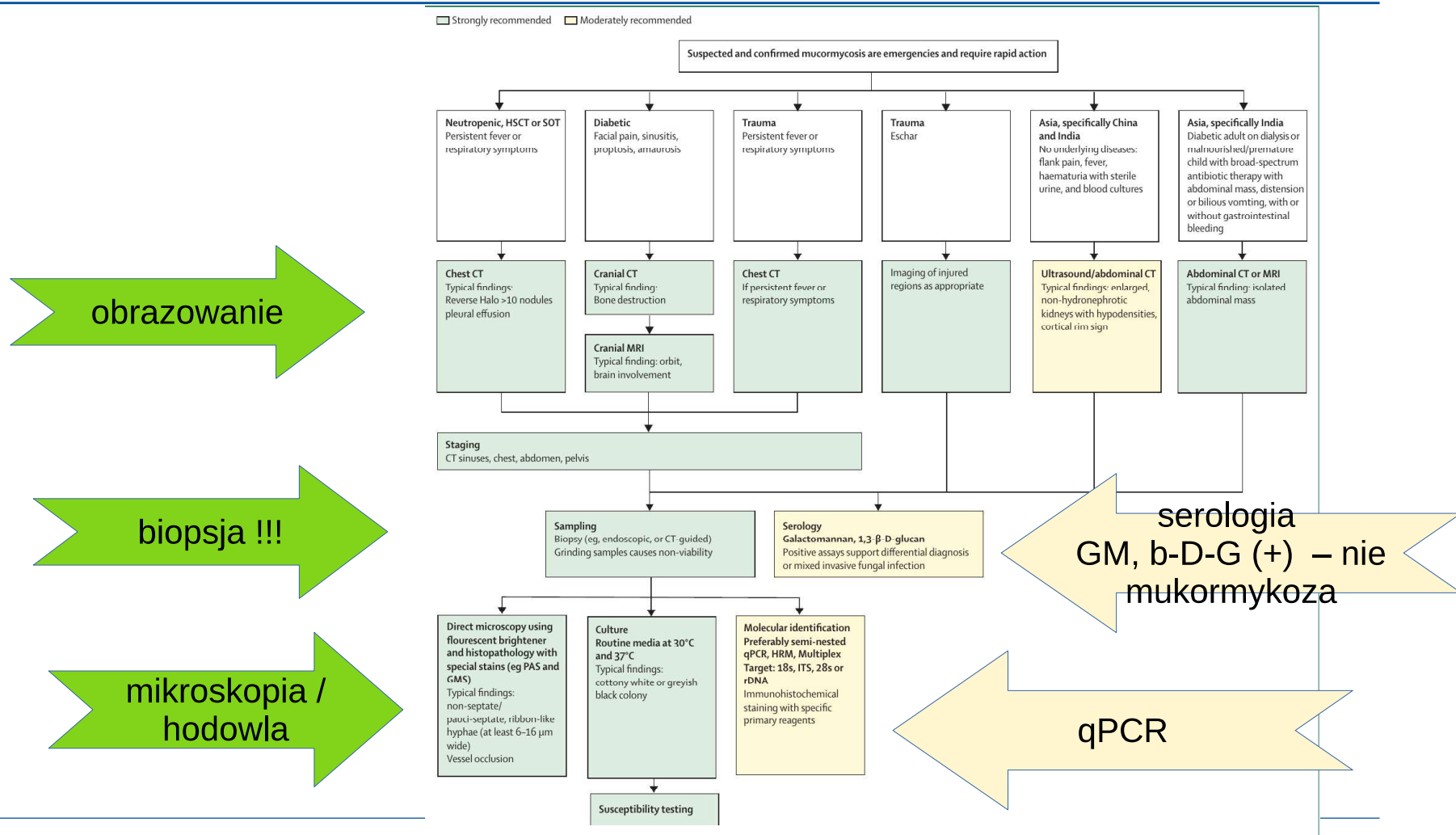
WYTYCZNE ECMM (ISHAM ASM)

- The Global guideline for the diagnosis and management of **aspergillosis 20??** ECMM ISHAM ASM
- The Global guideline for the diagnosis and management of **candidiasis 20??** ECMM ISHAM ASM
- The Global guideline for the diagnosis and management of **cryptococcosis 2024** ECMM ISHAM
- Global guideline for the diagnosis and management of **mucormycosis. 2019** ECMM MSGERC
- Global guideline for the diagnosis and management of **rare mould** infections **2021** ECMM ISHAM ASM
- Global guideline for the diagnosis and management of the **endemic mycoses 2021** ECMM ISHAM
- Global guideline for the diagnosis and management of **rare yeast** infections. **2021** ECMM ISHAM ASM
- Defining and managing **COVID-19-associated pulmonary aspergillosis. 2020:** ECMM/ISHAM consensus criteria for research and clinical guidance

• OCENA POSTĘPOWANIA

- EQUAL ASPERGILLUS SCORE
- EQUAL CANDIDA SCORE
- EQUAL MUCORMYCOSIS SCORE
- EQUAL CRYPTOCOCCOSIS SCORE
- EQUAL SCEDOSPORIOSIS/LOMENTOSPORIOSIS SCORE
- EQUAL TRICHOSPORONOSIS SCORE
- EQUAL CPA SCORE

PRZYKŁADOWE WYTYCZNE ECMM - MUKORMYKOZA



ŚCIAGAWKI

| PUNKTACJA ASPERGILLOZY (EQUAL Aspergillosis Score 2018) | | |
|---|---|----|
| ROZPOZNANIE | Neutropenia >10 dni lub allo-HCT → profilaktyka p/grzybom pleśniowym lub badanie GM 2-3x/tydzień | 3 |
| | Przetrwiała gorączka 72-96 godzin → KT płuc | 3 |
| | Jeśli nacieki płucne → wykonanie w BAL | |
| | - Galaktomannan | 1 |
| | - Mikroskopia bezpośrednia z fluoro-barwnikami: Calcofluor white, Uvitex 2B lub Blancophor | 1 |
| | - Posiew | 1 |
| | - PCR na grzyby (panfungal, Aspergillus, Mucorales) | 1 |
| | Jeśli hodowla w kierunku Aspergillus pozytywna: | |
| | - Identyfikacja gatunku | 1 |
| | - Mykogram (badanie wrażliwości) | 1 |
| W przypadkach opornych → badanie histologiczne | | |
| - Barwienie srebrem | 1 | |
| - PAS | 1 | |
| - Widoczne strzępki → diagnostyka molekularna | 1 | |
| TERAPIA I LINII | Terapia I linii: | |
| | - Izwukonazol lub worykonazol lub – po uprzedniej profilaktyce p/pleśniowej – liposomalna amfoterycyna B lub kaspofungina | 5 |
| | - Worykonazol bez TDM (wymagane stężenie przed kolejną dawką 1-5.5mg/L) | -1 |
| DALSZY OPIEKA | - KT w dniu 7 | 2 |
| | - KT w dniu 14 | 3 |
| | - KT w dniu 21 lub 28 | 2 |

| PUNKTACJA KANDYDEMII (EQUAL Candida Score 2018) ^{1,2} | | |
|--|--|---|
| ROZPOZNANIE | Początkowy posiew krwi (40mL) ^{3,4} | 3 |
| | Identyfikacja gatunku ^{3,4} | 3 |
| | Badanie lekowrażliwości ^{3,4} | 2 |
| | Echokardiografia ^{3,5} | 1 |
| | Oftalmoskopia ^{5,6} | 1 |
| Terapia | Echinokandyna ^{3,5} | 3 |
| | Zmiana na flukonazol w zależności od wyniku lekowrażliwości ^{3,5} | 2 |
| | Leczenie 14 dni po pierwszym ujemnym posiewie ^{3,5} | 2 |
| | Usunięcie cewnika centralnego ^{3,5,7} | 3 |
| | ≤ 24 godz od rozpoznania | 2 |
| 24-72 godz od rozpoznania | 2 | |
| DALSZY OPIEKA | Kontrolny posiew krwi (co najmniej jeden dziennie do negatywizacji) ^{3,5} | 2 |

* Pacjenci z cewnikiem centralnym otrzymują dodatkowe punkty w ocenie punktowej




UNIKLINIK
KÖLN





Maj 2019


| PUNKTACJA MUKORMYKOZY (EQUAL Mucormycosis Score) 2018 | | |
|---|---|---|
| ROZPOZNANIE | Neutropenia >10 dni lub allo-HCT → profilaktyka z lekiem aktywnym na grzyby pleśniowe | 3 |
| | Przetrwiała gorączka 72-96 godzin → KT płuc | 3 |
| | Odwrócony objaw halo | |
| | - KT/MRI: głowa, szyja, brzuch | 2 |
| | - Odwrócony objaw halo → BAL | |
| | - Mikroskopia bezpośrednia | 1 |
| | - Posiew | 1 |
| | - PCR na grzyby (panfungal, Aspergillus, Mucorales) | 1 |
| | Testy mikrobiologiczne negatywne → Biopsja | |
| | - Hodowla tkankowa | 2 |
| - Histopatologia | 2 | |
| - Badania molekularne na świeżym materiale klinicznym lub tkance z bloczka parafinowego | 1 | |
| Wzrost izolatu → identyfikacja gatunku i mykogram | 2 | |
| TERAPIA I LINII | Opracowanie chirurgiczne | 2 |
| | z mikroskopowo wolnym marginesem resekcji | 1 |
| | L-AmB ≥5 mg/kg/dobę LUB | 3 |
| | Izwukonazol z TDM LUB posakonazol z TDM | 2 |
| | Kontrola czynników ryzyka: neutropenia, hiperglikemia, kwasica metaboliczna, steroidy | 2 |
| DALSZY OPIEKA | KT w dniu 7 | 2 |
| | KT w dniu 14 | 2 |
| | KT co tydzień do momentu poprawy | 2 |

APLIKACJA CANDIDA EQUAL SCORE



Candida EQUAL Score now also as App



EQUAL Candida Score 2018: An ECMM Score Derived From Current Guidelines to Measure QUALity of Clinical Candidemia Management



Mellinghoff SC¹, Ruiz J, Köhler P¹, Cornely GA^{1,2}
¹Department of Internal Medicine, Excellence Center for Medical Mycology (ECMM), University of Cologne, Germany; ²CRCD Cluster of Excellence, University of Cologne, Germany
 DOI: 10.4269/mjeb.2018.1174

Background
 The EQUAL Candida Score weighs and aggregates factors recommended for the ideal management of candidemia and provides a tool for antifungal stewardship as well as for measuring guideline adherence. Current guidelines provided by the European Society for Clinical Microbiology and Infectious Diseases^{3,4} and by the Infectious Diseases Society of America⁵ were reviewed and the strongest recommendations for management quality selected as basis for this scoring tool.

Maximum Score

| Non-CVC carriers | | CVC carriers | |
|------------------|-----------|--------------|-----------|
| Diagnosis | 10 | 15 | 15 |
| Treatment | 7 | 10 | 10 |
| Follow-up | 6 | 9 | 9 |
| Total | 23 | 34 | 34 |

References
 1. Mellinghoff et al. *Mycoses* 2018; 2. Köhler et al. *Antonie van Leeuwenhoek* 2018; 3. Pappas et al. *Clin Infect Dis* 2016; 4. Cornely et al. *Clin Infect Dis* 2012; 5. Cornely et al. *Clin Microbiol Infect* 2015; 6. Muñoz et al. *Diagn Microbiol Infect Dis* 2017; 7. Andes et al. *Clin Infect Dis* 2012.

EQUAL scores quantify "adherence to guidelines".
 Studies show clearly:
Higher score points = higher chance of survival.

References: Hoenigl et. al. *Lancet Infectious Diseases* 2023;
 Mellinghoff et. al. *Mycoses* 2018



GLOBAL FUNGAL INFECTION REGISTRY









Questions?



OGÓLNY SCHEMAT DIAGNOSTYKI

TECHNIKI OBRAZOWANIA

H-CT / MRI / PET

lokalizacja ogniska infekcji

HODOWLA

podłoża chromogenne
(Candida), DTM

ID PATOGENU

TKANKA/HODOWLA:
qPCR

Właściwe
pobranie
właściwego
materiału

```
graph TD; A[Właściwe pobranie właściwego materiału] --> B[TECHNIKI OBRAZOWANIA]; A --> C[HODOWLA]; A --> D[MIKROSKOPIA BEZPOŚREDNIA]; A --> E[SEROLOGIA]; A --> F[ID PATOGENU];
```

panele biochemiczne
(VITEK2, API 20C AUX itp.
[BIOLOG – RUO])
MALDI-TOF
PCR

MIKROSKOPIA BEZPOŚREDNIA

histpat: H&E, Grocott;
CFW, KOH
FISH

SEROLOGIA

Galaktomannan
CrAg
Aspergillus Ab sIgG sIgM
1,3 β-D-glucan

DIAGNOSTYKA OBRAZOWA

TECHNIKI OBRAZOWANIA – RTG, TK, TECHNIKI WYSOKOROZDZIELCZE

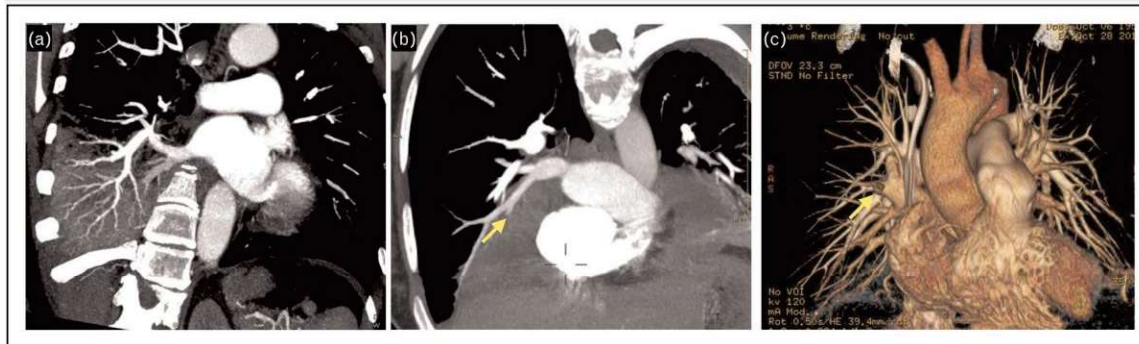
► [Curr Opin Infect Dis. 2023 Jun 9;36\(4\):250–256. doi: 10.1097/QCO.0000000000000937](#)

Radiology-based diagnosis of fungal pulmonary infections in high-risk hematology patients: are we making progress?

[Russell E Lewis](#)^a, [Marta Stanzani](#)^b, [Giovanni Morana](#)^c, [Claudia Sassi](#)^d

► [Author information](#) ► [Article notes](#) ► [Copyright and License information](#)

PMCID: PMC10351900 PMID: [37431554](#)



Computed tomography pulmonary angiography for detection of invasive fungal disease. (a) Negative vessel occlusion sign as patent contrast-enhanced vessels are visualized in the right lower lung consolidation of a neutropenic patient with *Pseudomonas aeruginosa* pneumonia; (b) positive vessel occlusion sign (arrow) in the right lung of a neutropenic patient with positive serum galactomannan (probable aspergillosis); (c) volumetric projection of the pulmonary vessel tree demonstrating obstructed vessel (arrow).

HR – CT tomografia komputerowa klatki piersiowej wysokiej rozdzielczości **standard w diagnostyce grzybiczego zapalenia płuc**, nawet jeśli wiele wyników TK sugerujących grzybice nie jest specyficznych

angiografia płucna TK

obiecująca strategia polepszenia swoistości obrazowania TK i możliwości wykluczenia IFD może być wykonana szybko nawet 5 min

MRI – alternatywa do powyższych, bez dodatkowego narażenia na promieniowanie i nefropatii związanej z podaniem kontrastu

FDG-PET/CT – wykrywanie rozsiewów pozapłucnych za pomocą znacznika fluorodeoksyglukozy - **niespecyficzna**

RADIOZNAKOWANIE (FLU, AMB, CSF, mAb)

The Journal of
Infectious Diseases

► J Infect Dis. 2023 Oct 3;228(Suppl 4):S259–S269. doi: [10.1093/infdis/jiad067](https://doi.org/10.1093/infdis/jiad067)

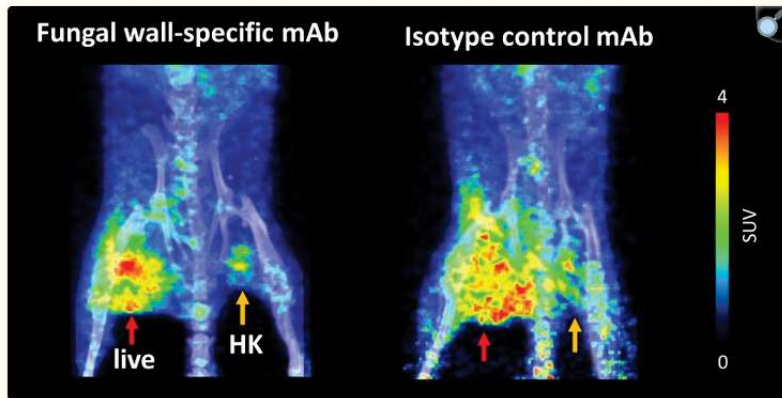
Radiotracer Development for Fungal-Specific Imaging: Past, Present, and Future

Jianhao Lai¹, Benjamin Wang², Milos Petrik^{3,4}, Nicolas Beziere^{5,6}, Dima A Hammoud^{7,8,2}

► Author information ► Article notes ► Copyright and License information

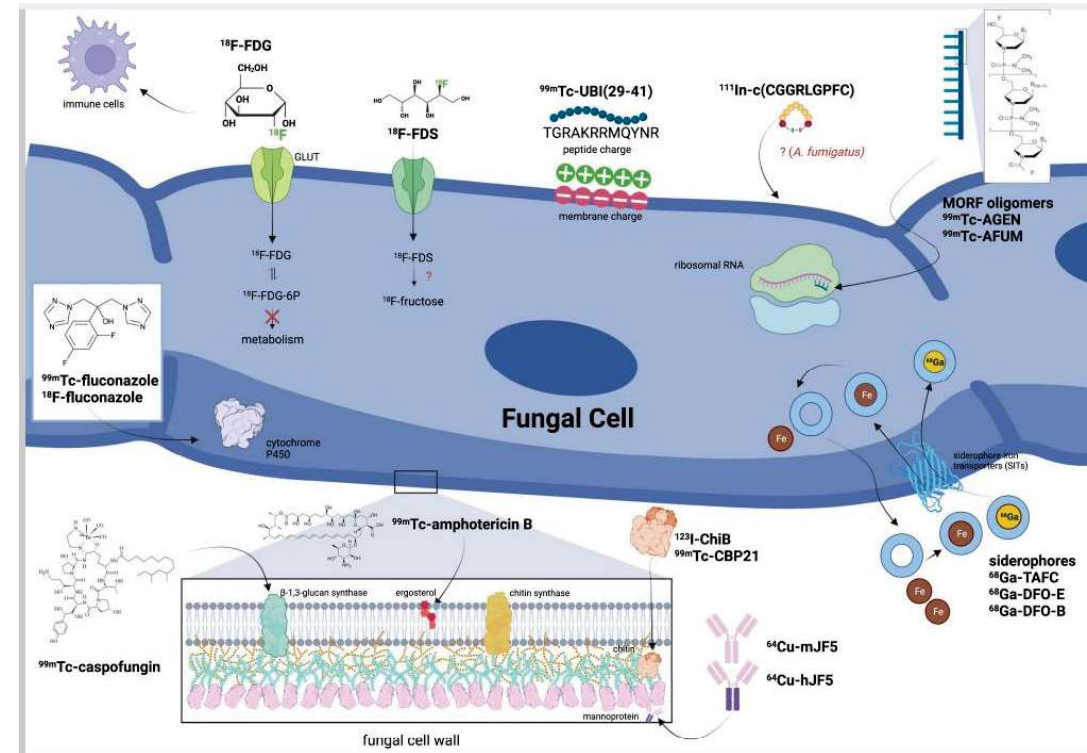
PMCID: PMC10547453 PMID: [37788500](https://pubmed.ncbi.nlm.nih.gov/37788500/)

J Infect Dis. 2023 Oct 3;228(Suppl 4):S259–S269. doi: [10.1093/infdis/jiad067](https://doi.org/10.1093/infdis/jiad067)



[Open in a new tab](#)

PET imaging with ⁸⁹Zr-labeled fungal cell wall-specific or isotype control antibodies in mouse models with *Aspergillus* myositis. PET imaging at 72 hours following injection shows high accumulation of both the specific and nonspecific antibodies in infected thighs and, to a lesser extent, in the thighs injected with HK *Aspergillus* spores. Abbreviations: HK, heat killed; mAb, monoclonal antibody; PET, positron-emission tomography; SUV, standardized uptake value.



raphical summary of various fungal imaging tracers and their targeting strategies. Abbreviations: 18F-FDG, 18F-fluorodeoxyglucose; GLUT, Glucose transporter; 18F-FDS, 18F-fluorodeoxysorbitol; 68Ga-DFO-E, 68Ga-desferrioxamine; 68Ga-TAFC, 68Ga-triacetylfusarinine; 99mTc-UBI(29–41), 99mTc-ubiquicidin(29–41); 123I-ChiB, 123I-chitinase B; AFUM, *A. fumigatus* species-specific MORF oligomer; AGEN, *Aspergillus* genus-specific MORF oligomer; MORF, morpholino.

POBRANIE PRÓBK

PRÓBKA KRWI – CZAS, !!! PODŁOŻE „DO GRZYBÓW”

Supplementary Table

Table S1. Simulated turnaround time for *Mycosis* and Aerobic blood cultures

| Incubation delay Hour | <i>Mycosis</i> BC TAT [h] (range ^b) | Aerobic BC TAT [h] (range ^b) | Difference TAT [h] (range ^b) | <i>P</i> value |
|-----------------------|---|--|--|----------------|
| 2 | 42.25 (36 – 48) | 59.25 (55 – 67) | 17.00 (7 – 24) | <.001 |
| 4 | 27.75 (28 – 28) | 46.58 (42 – 52) | 18.83 (14 – 24) | <.001 |
| 8 | 30.23 (30 – 32) | 41.92 (38 – 49) | 11.69 (6 – 19) | <.001 |
| 12 | 34.08 (34 – 35) | 51.00 (46 – 57) | 16.92 (11 – 23) | <.001 |
| 16 | 35.62 (34 – 40) | 39.08 (39 – 40) | 3.46 (0 – 5) | <.001 |

Note. Times are stated as means.

BC, blood culture; TAT, turnaround time.

^aRounded down to whole hours.

Färber, J., Kaasch, A.J. & Schalk, E. Shorter time-to-positivity and turnaround time with mycosis blood culture bottles when detecting *Candida albicans*. *Infection* 52, 701–703 (2024).
<https://doi.org/10.1007/s15010-024-02216-x>

Kiedy:

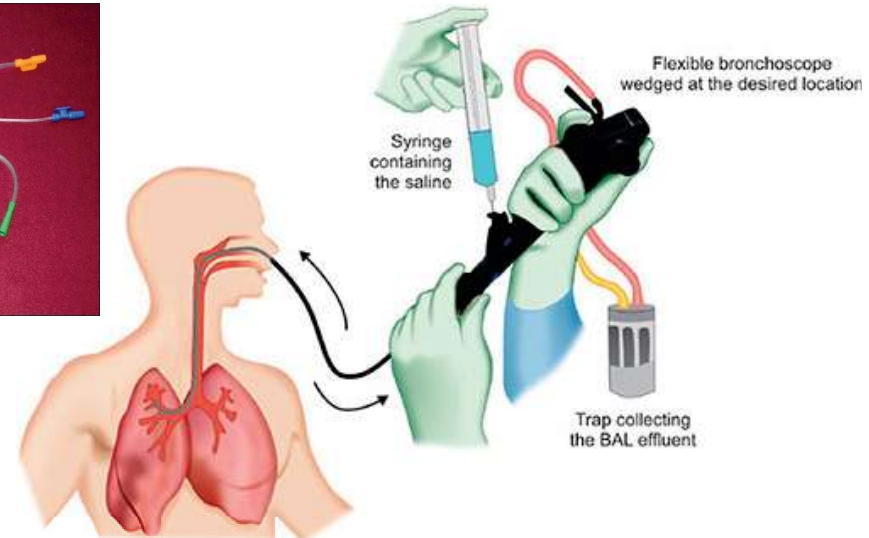
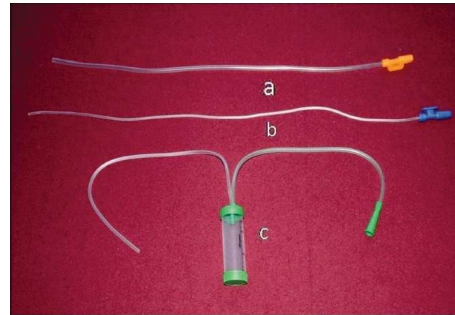
- wielokrotne ujemne posiewy
 - pacjent jest w immunosupresji
 - pacjent ma historię fungemii
 - pacjent ma żywienie pozajelitowe (TPN)
- Malassezia***

ICU 7% BSI Candida – każdy pacjent?

BAL, osocze, PMR – INNE MATERIAŁY STANDARYZACJA...

- Aparat do płukania niebronchoskopowego.
- Składa się z dwóch cewników ssących (a, b) i jednego próbnika śluzu (c).
- Cewniki ssące mają różne długości i średnice światła.
- Górny cewnik ssący (a) jest krótszy (około 47–48 cm) i ma szerszy prześwit (16 Fr).
- Drugi cewnik (b) jest dłuższy (50 cm) i ma węższy prześwit (8 Fr)

Indian J Crit Care Med. 2011 Jan-Mar; 15(1): 16–23.
doi: 10.4103/0972-5229.78218



10.5005/jp/books/13029_31

Diagnostic value of various sampling techniques

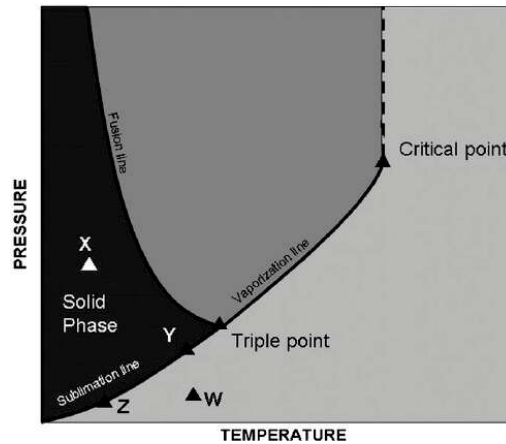
| Sampling techniques | Yield | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) |
|---------------------|-------|----------------------|----------------------|------------------|------------------|
| ETA | 52 | 55.6 (31.3–77.6) | 71.4 (30.3–94.9) | 83.3 (50.9–97.1) | 38.5 (15.1–67.7) |
| NPBAL | 68 | 83.3 (57.7–95.6) | 71.4 (24.1–94.0) | 88.2 (62.3–97.4) | 62.5 (21.5–88.2) |
| BAL | 64 | 77.8 (51.9–92.6) | 71.8 (24.1–94.0) | 87.3 (60.4–97.8) | 55.5 (17.4–82.6) |
| B Brush | 80 | 94.9 (70.6–99.7) | 57.1 (13.4–86.1) | 85 (61.1–96.0) | 80 (21.9–98.7) |

VAP – czy można interpolować do *Aspergillus*

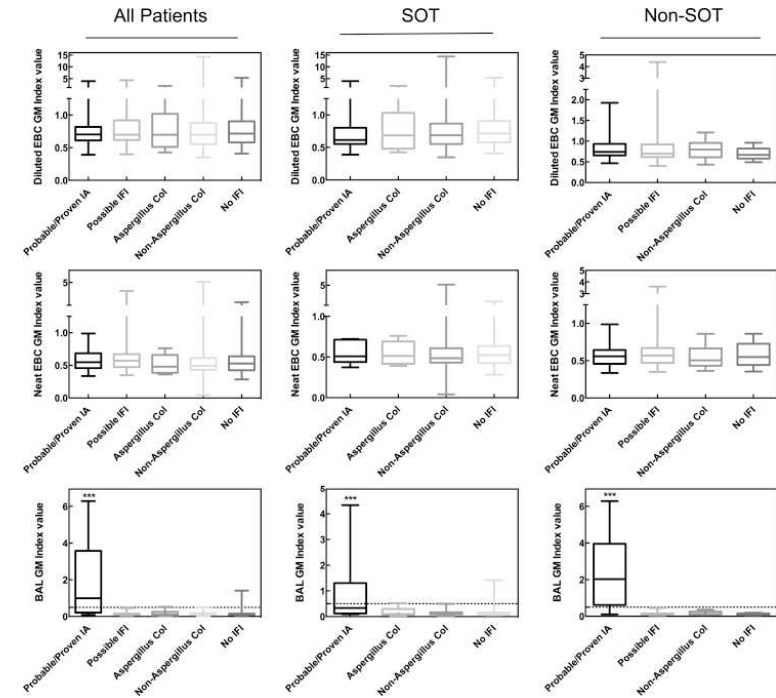
zakażenie grzybicze zlokalizowane

NPBAL – Non-bronchoscopic protected bronchoalveolar lavage; B brush – Bronchoscopic brush; ETA – Endotracheal aspirate; PPV – Positive predictive value; NPV – Negative predictive value

GM w KONDENSACIE WYDYCHANEGO POWIETRZA



. Breath Res. 2 (2008) 037004 (18pp)



Clinical Microbiology and Infection 24 (2018) 640e645

IMMUNODIAGNOSTYKA

- CPA
 - **immunodyfuzja (ID)** Aspergillus (Immy) / elektroforeza przeciwprądowa (CIE)
 - **EIA sIg Aspergillus** (ImmunoCAP™M-Immunolite™-Virion/Serion™-Dynamiker™-Gensis™-Bio-Rad™-Bordier Affinity™ *-Immy™)
 - **WB Aspergillus Ig** (LDBio)
- ABPA
 - EIA, CIE sIgE Aspergillus (antygeny: Asp f1, Asp f2)
- IA, IPA
 - **EIA GM**, EIA GP (- Bio-Rad GM-EIA™- Immy GM-EIA™- Euroimmun™GM-EIA)
 - GM w moczu / kreatynina
 - LFA (Immy) GM
- PcP
 - **test kolorymetryczny** (1→3)-β-D-Glucan -specific Limulus Amebocyte Lysate (LAL) reagent

-
- CPA
 - **immunodyfuzja (ID)** Aspergillus (Immy) / elektroforeza przeciwprądowa (CIE)
 - **EIA sIG Aspergillus** (ImmunoCAP™M-Immunolite™-Virion/Serion™-Dynamiker™-Gensis™-Bio-Rad™-Bordier Affinity™ *-Immy™)
 - **WB Aspergillus Ig** (LDBio)
 - ABPA
 - EIA, CIE sIgE Aspergillus (antygeny: Asp f1, Asp f2)
 - IA, IPA
 - **EIA GM**, EIA GP (- Bio-Rad GM-EIA™- Immy GM-EIA™- Euroimmun™GM-EIA)
 - GM w moczu / kreatynina
 - LFA (Immy) GM

BARDZIEJ SPECYFICZNE TESTY EIA – GM, LFA - GM

- opracowane w 2008 roku mysie monoklonalne przeciwciała IgG3
 - EB-A2 łączy się z galaktofuranozą
 - JF5
 - inne mAb
- większa specyficzność (mniej reakcji krzyżowych z antybiotykami lub produktami bakteryjnymi)

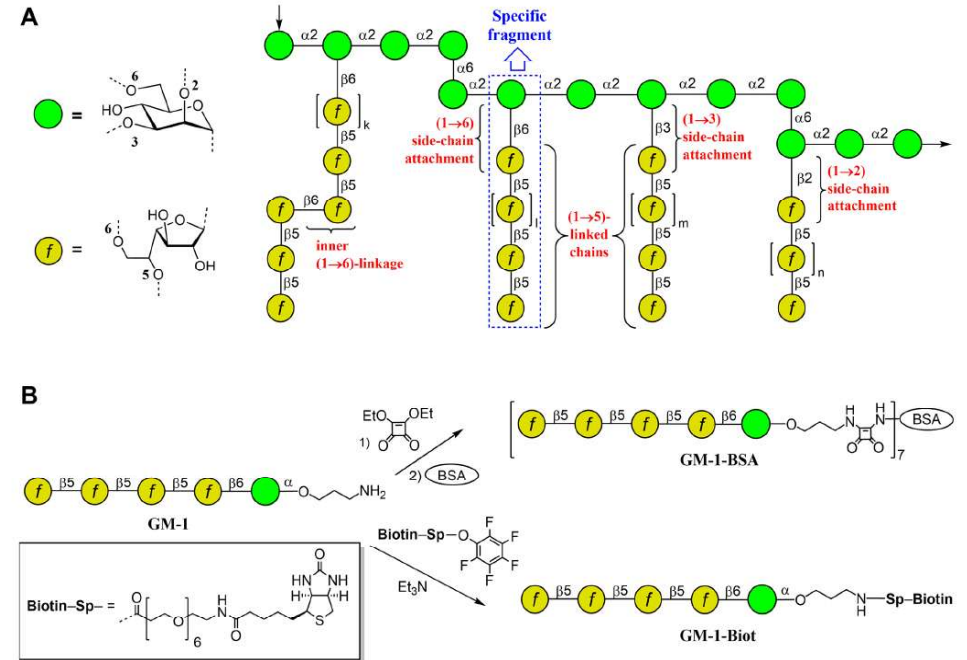


Fig 1. Structure of *Aspergillus fumigatus* galactomannan and its synthetic analogs. (A) Structural fragments of *A. fumigatus* galactomannan (summarized from refs. [6] and [8]). (B) Pentasaccharide GM-1 and its BSA (GM-1-BSA) and biotinylated (GM-1-Biot) conjugates used in mice immunization and mAb screening. The carbohydrate sequences are represented according to symbol carbohydrate nomenclature [26].

<https://doi.org/10.1371/journal.pone.0193938.g001>

Matveev AL, et. al. PLoS ONE 13(3): e0193938. <https://doi.org/10.1371/journal.pone.0193938>



Performance of the JF5-Based Galactomannoprotein EIA Compared to the Lateral Flow Device and the Galactomannan EIA in Serum and Bronchoalveolar Lavage Fluid

Rubina Aerts,^{1*} Toine Mercier,^{2*} Els Houben,^{3*} Alexander Schauwvlieghe,^{4*} Katrien Lagrou,^{5*} Johan Maertens^{6*}

Home > European Journal of Clinical Microbiology & Infectious Diseases > Article

Evaluation of the JF5-based *Aspergillus* galactomannoprotein lateral flow device for diagnosing invasive aspergillosis in cancer patients

Research | Published: 16 April 2024
Volume 43, pages 1221–1229, (2024) | [Cite this article](#)

Received: 20 September 2018
Revised: 20 December 2018
Accepted: 23 January 2019

Cite as: Vadim B. Krivlov, Arsenii S. Solov'ev, Dmitry A. Arzunov, Jean-Paul Latgé^{1,2,3,4,5,6*}, Nikolay E. Nifantiev.
Reinvestigation of carbohydrate specificity of EB-A2 monoclonal antibody used in the immune detection of *Aspergillus fumigatus* galactomannan.
Heliyon 5 (2019) e01173.
doi: 10.1016/j.heliyon.2019.011173



Reinvestigation of carbohydrate specificity of EB-A2 monoclonal antibody used in the immune detection of *Aspergillus fumigatus* galactomannan

Vadim B. Krivlov¹, Arsenii S. Solov'ev², Dmitry A. Arzunov³, Jean-Paul Latgé^{1,2,3,4,5,6*}, Nikolay E. Nifantiev^{1,2*}

SZYBKA IMMUNODIAGNOSTYKA

- test kanapkowy pozwalający na ocenę jakościową i ilościową GM w próbkach osocza i BAL
- czułość i swoistość porównywalna z oznaczaniem ELISA
- nie wymaga specjalistycznego sprzętu
- odczyt cyfrowy – ocena ilościowa – ODI_{525} (optic density index) ≥ 0.50 (+)

| SERUM | Visual | | Cube Reader | |
|---------|-----------|-----------|-------------|-----------|
| | # Correct | % Correct | # Correct | % Correct |
| Neg | 63 | 84% | 73 | 99% |
| Low Pos | 48 | 64% | 52 | 69% |
| Mod Pos | 74 | 96% | 74 | 100% |

| BAL | Visual | | Cube Reader | |
|---------|-----------|-----------|-------------|-----------|
| | # Correct | % Correct | # Correct | % Correct |
| Neg | 60 | 82% | 73 | 100% |
| Low Pos | 68 | 91% | 72 | 96% |
| Mod Pos | 75 | 100% | 74 | 99% |



Obtain 2 test tubes for each specimen: 1 screw cap, heat-resistant centrifuge tube for the dilution (tube A)
1 flat-bottom tube for running the test (tube B)



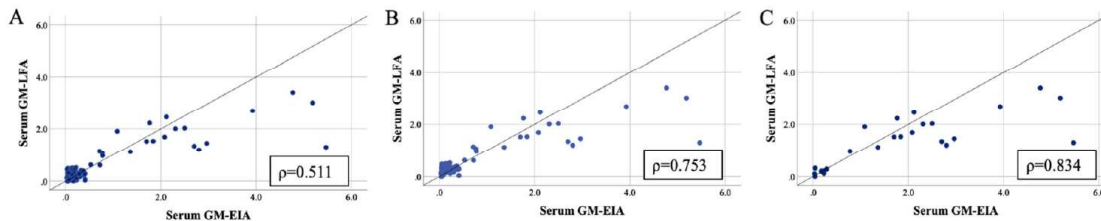
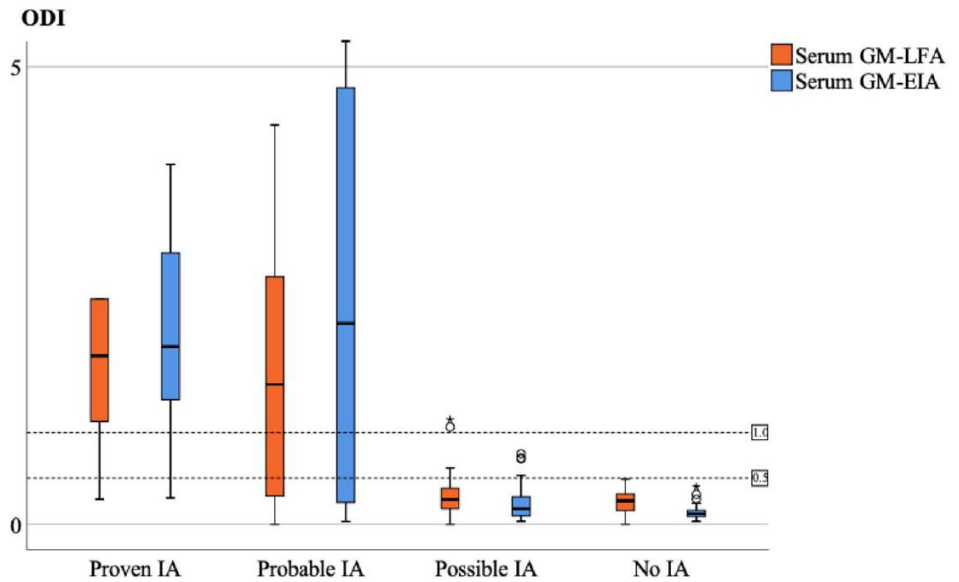
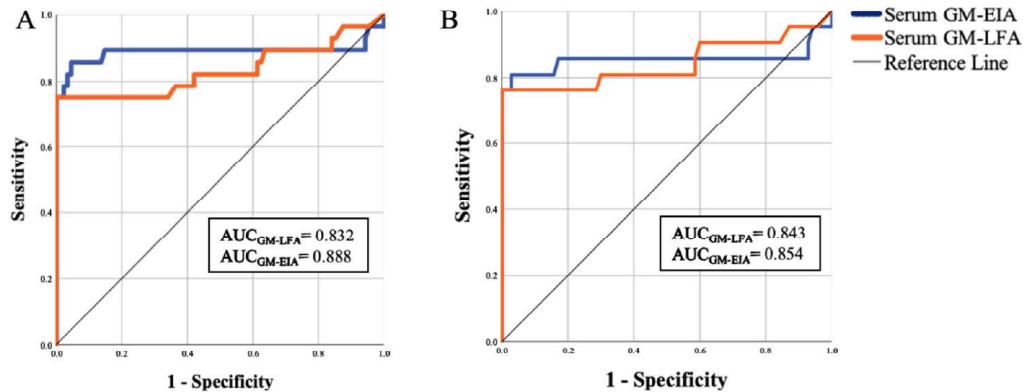
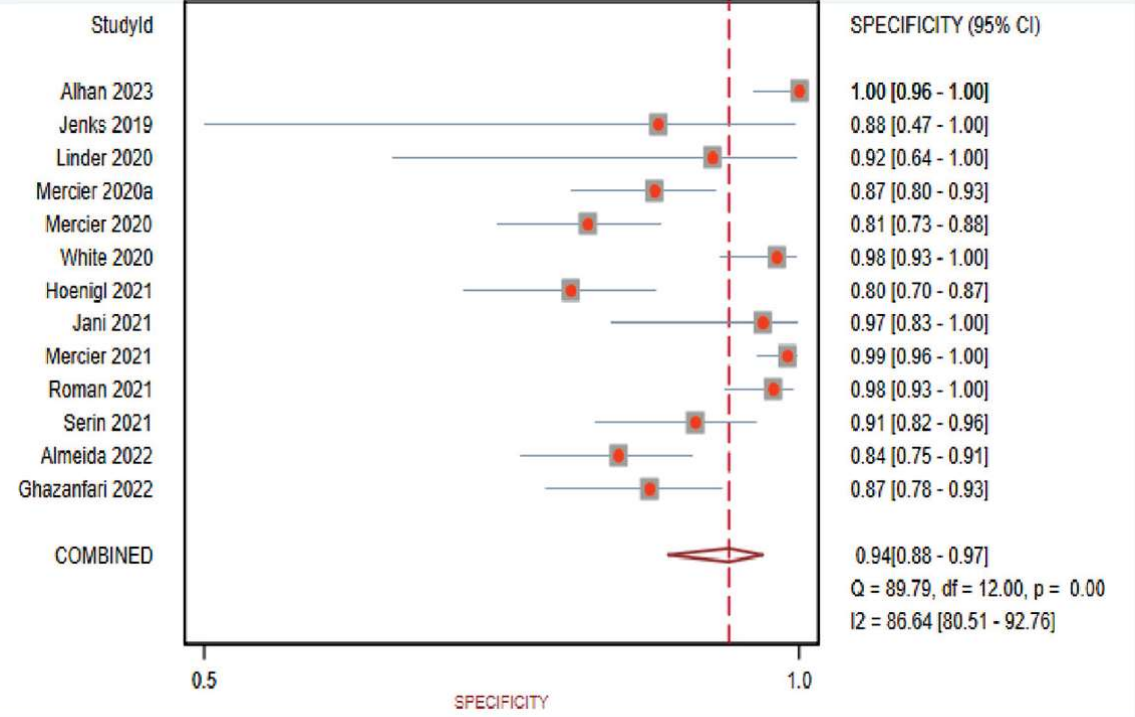
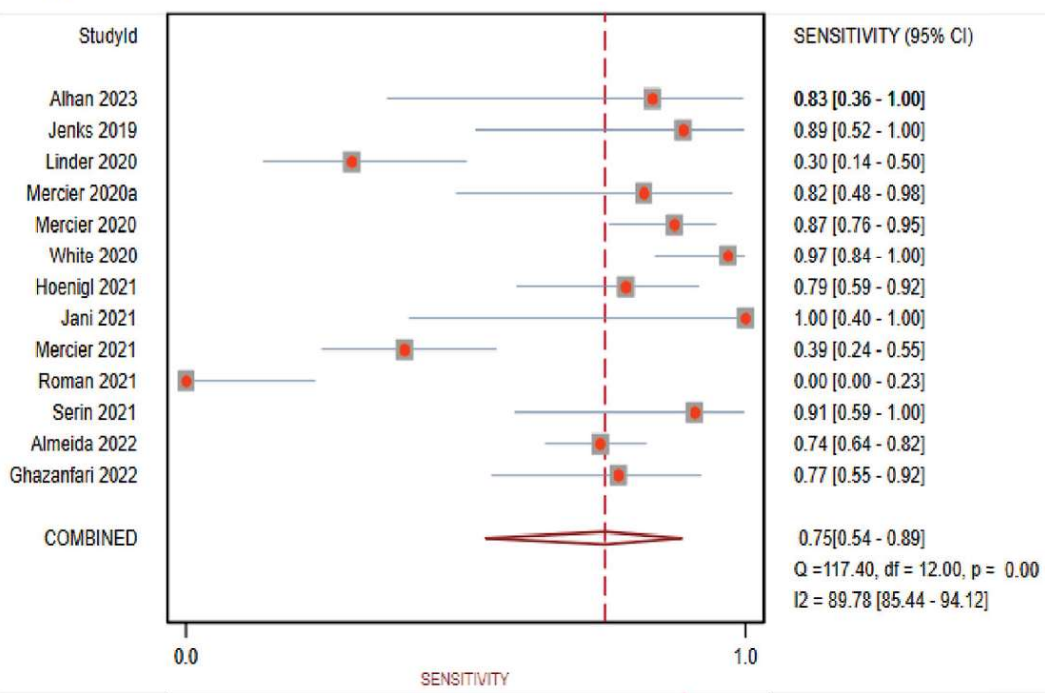


Fig. 2 Clustered box plot of serum GM-LFA and GM-EIA ODIs EIA: Enzyme immunoassay, GM: Galactomannan, IA: Invasive aspergillosis, LFA: Lateral flow assay, ODI: Optical density index

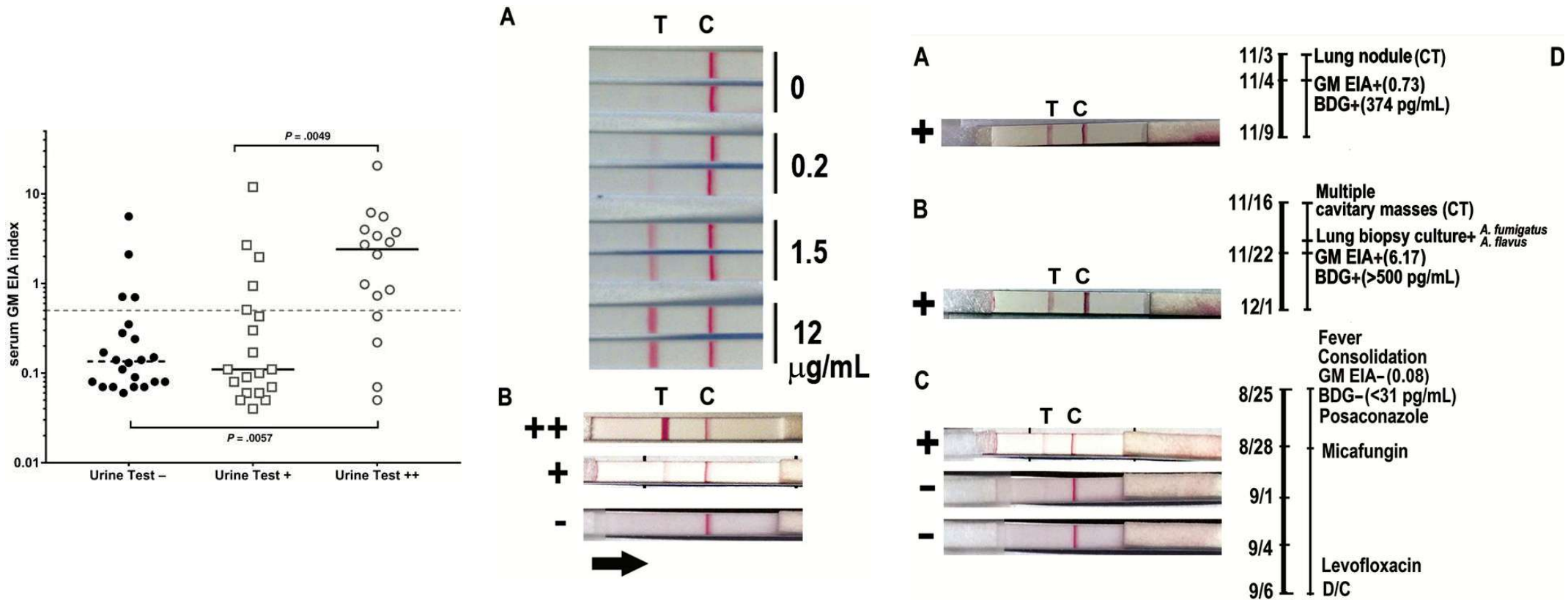
Alhan, O., Saba, R., Akalin, E.H. et al. Diagnostic Efficacy of Aspergillus Galactomannan Lateral Flow Assay in Patients with Hematological Malignancies: A Prospective Multicenter Study. *Mycopathologia* 188, 643–653 (2023). <https://doi.org/10.1007/s11046-023-00749-7>

(b) GM-LFA



X. Zhang et al. Heliyon 10 (2024) e34569
<https://doi.org/10.1016/j.heliyon.2024.e34569>

LATERAL FLOW URINE ASSAY (MAB476 P/GALAKTOFURANOZA)



Clinical Infectious Diseases, Volume 67, Issue 11, 1 December 2018, Pages 1705–1711, <https://doi.org/10.1093/cid/ciy326>

WYKRYWANIE METABOLITÓW



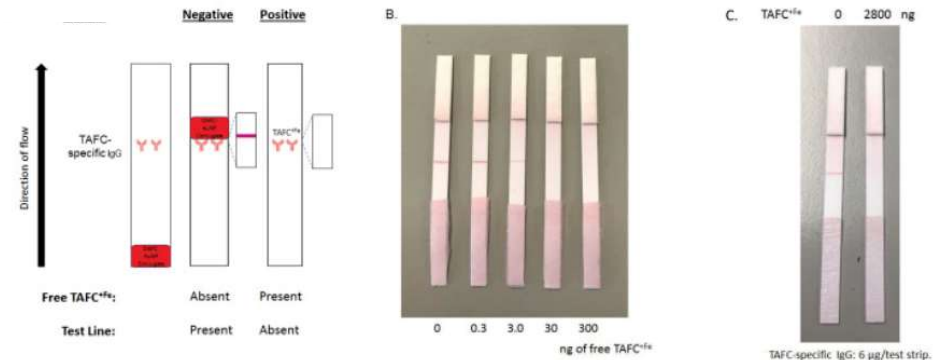
Analytical Biochemistry
Volume 632, 1 November 2021, 114384



- **syderofor T AFC** (triacetylfuzarynina C)
 - wykrywane za pomocą HPLC
 - immunologiczne
- **bmGT** (Bismethyltioglotoksyna)
 - ELISA/ LFA

Generation and characterisation of a semi-synthetic siderophore-immunogen conjugate and a derivative recombinant triacetylfusarinine C-specific monoclonal antibody with fungal diagnostic application

Nicola M. Moloney ^{a,1}, Annemarie Larkin ^{b,2}, Linan Xu ^a, David A. Fitzpatrick ^a, Holly L. Crean ^a, Kieran Walshe ^a, Hubertus Haas ^c, Clemens Decristoforo ^d, Sean Doyle ^{a,✉}



Appl Microbiol Biotechnol (2016) 100:2327–2334
DOI 10.1007/s00253-015-7209-6



APPLIED MICROBIAL AND CELL PHYSIOLOGY

Clinical validity of bis(methylthio)gliotoxin for the diagnosis of invasive aspergillosis

Matxalen Vidal-García ¹ · M. Pilar Domingo ² · Beatriz De Rueda ³ · Lourdes Roc ¹ · M. Pilar Delgado ³ · M. José Revillo ¹ · Julián Pardo ^{4,5,6,7} · Eva M. Gálvez ² · Antonio Rezusta ^{1,4,7}



Mycoses
Diagnosis, Therapy and Prophylaxis of Fungal Diseases

ORIGINAL ARTICLE

Gliotoxin and bis(methylthio)gliotoxin are not reliable as biomarkers of invasive aspergillosis

Toine Mercier ✉, Agustín Reséndiz Sharpe, Dieter Waumans, Koen Desmet, Katrien Lagrou, Johan Maertens

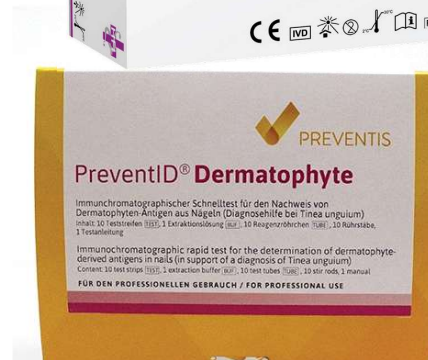
First published: 17 July 2019 | <https://doi.org/10.1111/myc.12967> | Citations: 6

POCT - ONYCHOMYKOZA



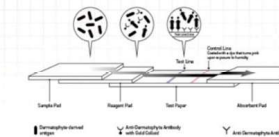
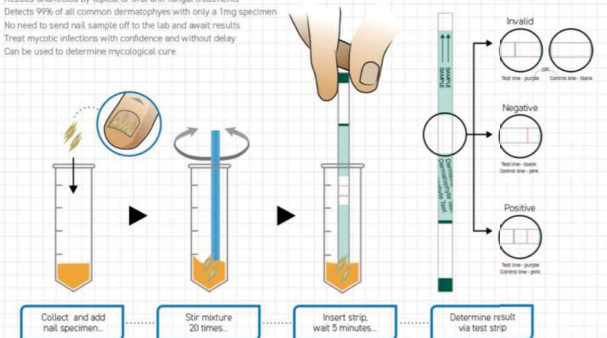
Table 1. Results of the Dermatophyte Test Strip and direct microscopy ($n = 222$)

| | Dermatophyte Test Strip | | Direct microscopy | |
|------------------------|-------------------------|-----------|-------------------|-----------|
| | <i>n</i> | Ratio (%) | <i>n</i> | Ratio (%) |
| Dermatophyte detection | | | | |
| Positive | 201 | 90.5 | 170 | 76.6 |
| Negative | 21 | 9.5 | 52 | 23.4 |



Diafactory Dermatophyte Test Strip

- Diagnosis in just 5 minutes
- 97% accurate
- Results unaffected by topical or oral anti-fungal treatments
- Detects 99% of all common dermatophytes with only a 1mg specimen
- No need to send nail sample off to the lab and await results
- Treat mycotic infections with confidence and without delay
- Can be used to determine mycological cure



The test strip contains anti-dermatophyte antibodies with gold colloid. In the presence of dermatophyte derived antigens, the antibodies with gold colloid bind to, and form an immune complex.

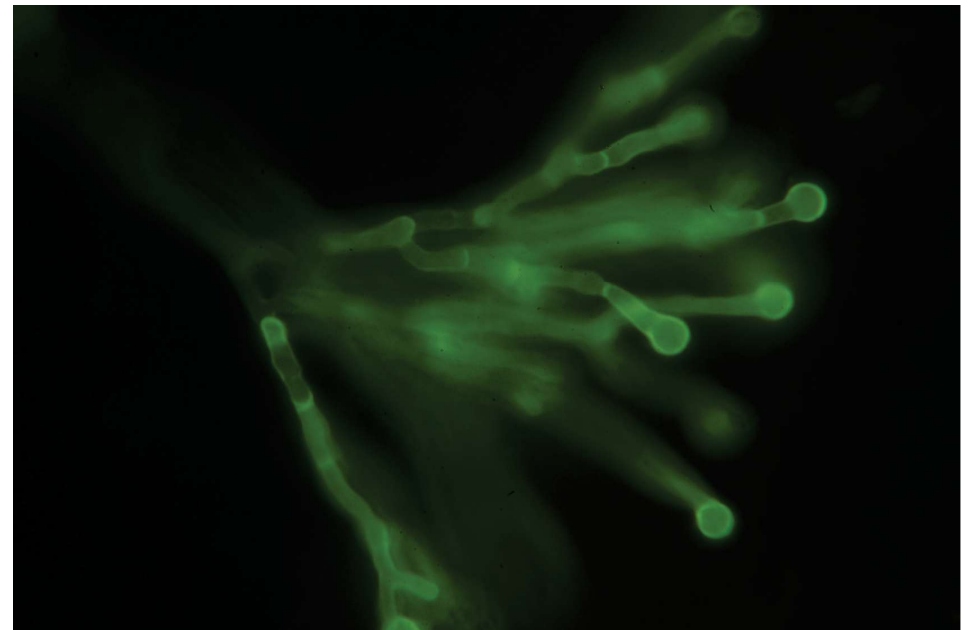
Comparison of Dermatophyte Test Strip with direct microscopy adjusted by PCR

| | | |
|----------------------|-----------------|-------------|
| Positive concordance | 97.5% (196/201) | (95.1–99.9) |
| Negative concordance | 71.4% (15/21) | (49.7–93.1) |
| Overall concordance | 95.0% (211/222) | (92.0–98.1) |
| Inconsistent | 5.0% (11/222) | (1.9–8.0) |

doi: 10.1111/1346-8138.13348

Journal of Dermatology 2016; : 1–7

MIKROSKOPIA



Histopathologic Diagnosis of Fungal Infections in the 21st Century

Jeannette Guarner^{1,*}, Mary E. Brandt²

¹Department of Pathology and Laboratory Medicine, Emory University, Atlanta, Georgia

²Mycotic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia

Guarner J, Brandt ME. 2011. Histopathologic Diagnosis of Fungal Infections in the 21st Century. Clin Microbiol Rev 24.: <https://doi.org/10.1128/cmr.00053-10>

Patologia: stan obciążenia krytycznego

Autor: Gazeta Lekarska www.gazetalekarska.pl Data publikacji: 5 listopada 2024

Patologia jest działem medycyny zajmującym się, jak sama nazwa wskazuje, opisywaniem chorób. Zdobyć umiejętności zobaczenia pod mikroskopem, opisanie i nazwanie wykładników morfologicznych chorób zajmuje co najmniej 5 lat. Pełną samodzielność diagnostyczną osiąga się zwykle po mniej więcej 10 latach – pisze dr Piotr Wiśniewski.

RynekZdrowia.pl » [Serwis Onkologia](http://SerwisOnkologia.pl) » Ten zawód wykonuje w Polsce 430 osób. "To wciąż za mało, ale sytuacja nie jest katastrofalna"

Ten zawód wykonuje w Polsce 430 osób. "To wciąż za mało, ale sytuacja nie jest katastrofalna"

Autor: oprac. MCD • Źródło: Rynek Zdrowia, Gazeta Lekarska • Opublikowano: 29 marca 2023 15:30

Jesienią przybyło dziewięciu nowych patomorfologów, a do tegorocznej sesji Państwowego Egzaminu Specjalizacyjnego przystąpiło 19 lekarzy. - W rzeczywistości wykonujących zawód jest ponad 430 osób. To wciąż za mało, ale sytuacja nie jest tak katastrofalna, jak przedstawiają ją krytycy - mówi w rozmowie z "Gazetą Lekarską" prof. Andrzej Marszałek, konsultant krajowy w dziedzinie patomorfologii.

ZALECANE BARWNIKI FLUORESCENCYJNE

Table 1. Results of direct examination of smears for the diagnosis of invasive fungal diseases.

| Invasive fungal diseases | Number of specimens | CFW | KOH | Gram staining |
|--------------------------|---------------------|------------|-----------|---------------|
| IPA | 26 | 17(65.38%) | 9(34.62%) | 1(3.85%) |
| Pulmonary cryptococcosis | 26 | 10(38.46%) | 1(3.85%) | 1(3.85%) |
| Talaromyces marneffeii | 2 | 2(100.00%) | 0 | 1(50.00%) |
| Schizophyllum commune | 2 | 2(100.00%) | 1(50.00%) | 1(50.00%) |
| Scedosporium apiospemum | 2 | 2(100.00%) | 0 | 0 |
| Mucor | 1 | 1(100.00%) | 0 | 0 |

Table 2. Comparison of the diagnostic efficiency of CW, KOH and Gram stain.

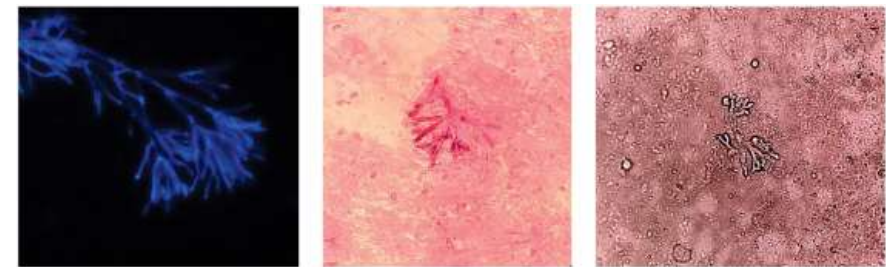
| Test method/P value | Sensitivity(%) | Specificity(%) | PPV(%) | NPV(%) | AUC |
|------------------------------|----------------|----------------|--------|--------|-------|
| CFW | 57.63 | 92.00 | 94.44 | 47.92 | 0.748 |
| KOH | 18.64 | 92.00 | 84.62 | 32.39 | 0.550 |
| Gram staining | 6.78 | 96.00 | 80.00 | 30.38 | 0.510 |
| P value CFW vs KOH | ≤ 0.001 | 1.000 | 0.604 | 0.088 | — |
| P value CFW vs gram staining | ≤ 0.001 | 1.000 | 0.806 | 0.047 | — |
| P value KOH vs gram staining | 0.065 | 1.000 | 1.000 | 0.791 | — |



Original Article

The value of calcofluor white in the diagnosis of invasive fungal diseases

Shuya Zhang ^a, Zhongbo Chen ^{a 1}, Zaichun Deng ^a, Panfeng Fu ^c, Yiming Yu ^a, Qidong Zhuang ^a, Xuechan Yu ^a, Hui Chen ^a, Anqi Li ^b, Lin Zheng ^b



(a)

(b)

(c)

Morphological characteristics of *Aspergillus* in the BALF sample, followed by staining. (a). CFW staining in the fluorescent separated hyphae. (b). Pink septate hyphae with a pink background in gram stain. (c). Septate hyaline hyphae in KOH.

CFW w PNEUMOCYSTOZIE

wirować BALF 10 min 1730 g
rozpuścić pelet w 10 ml 0,9% NaCl
odrzucić supernatant
powtórzyć procedurę
20 µl peletu nanieść na szkiełko
utrwać metanolem 10 min
dodać 0,2% CFW inkubować 10 min
mikroskopowanie św.wzbudzenia 510-560 nm
obiektyw 40x
zliczanie obiektyw 100 x

Table 2. Performance of the four laboratory methods in patients with validated diagnosis of *Pneumocystis jirovecii* pneumonia.

| | 0.2% calcofluor-blue brightener | MonoFluo™ <i>Pneumocystis jirovecii</i> IFA test kit® | MGG staining | In-house qPCR |
|---------------------------|---------------------------------|---|---------------|---------------|
| Sensitivity | 74.3% | 60.0% | 34.6% | 82.9% |
| 95% CI | [57.7–85.9] | [43.5–74.4] | [20.8–51.0] | [66.8–92.2] |
| Specificity | 99.6% | 99.3% | 100.0% | 99.4% |
| 95% CI | [98.2–100.0] | [97.9–99.9] | [98.9–100.0] | [97.0–99.4] |
| Predictive positive value | 92.9% | 87.5% | 100.0% | 82.9% |
| 95% CI | [83.3–100.0] | [74.3–100.0] | [100.0–100.0] | [70.4–95.3] |
| Predictive negative value | 98.0% | 96.9% | 95.1% | 98.7% |
| 95% CI | [96.7–99.3] | [95.4–98.5] | [93.1–97.1] | [97.6–99.7] |
| Positive likelihood ratio | 165.6 | 89.2 | +∞ | 61.6 |
| 95% CI | [41.0–669.4] | [28.0–284.5] | [+∞] | [27.4–138.3] |
| Negative likelihood ratio | 0.3 | 0.4 | 0.7 | 0.2 |
| 95% CI | [0.1–0.5] | [0.3–0.6] | [0.5–0.8] | [0.1–0.4] |

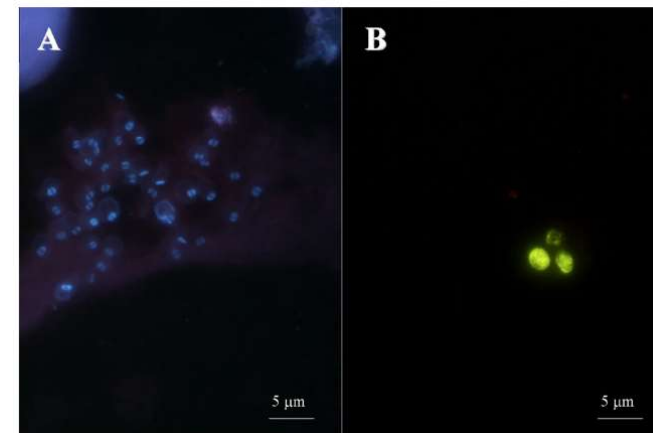
Abbreviations: IFA, immunofluorescence assay; MGG, May-Grünwald giemsa; qPCR, quantitative polymerase chain reaction; +∞, infinite; 95% CI, 95% confidence interval.

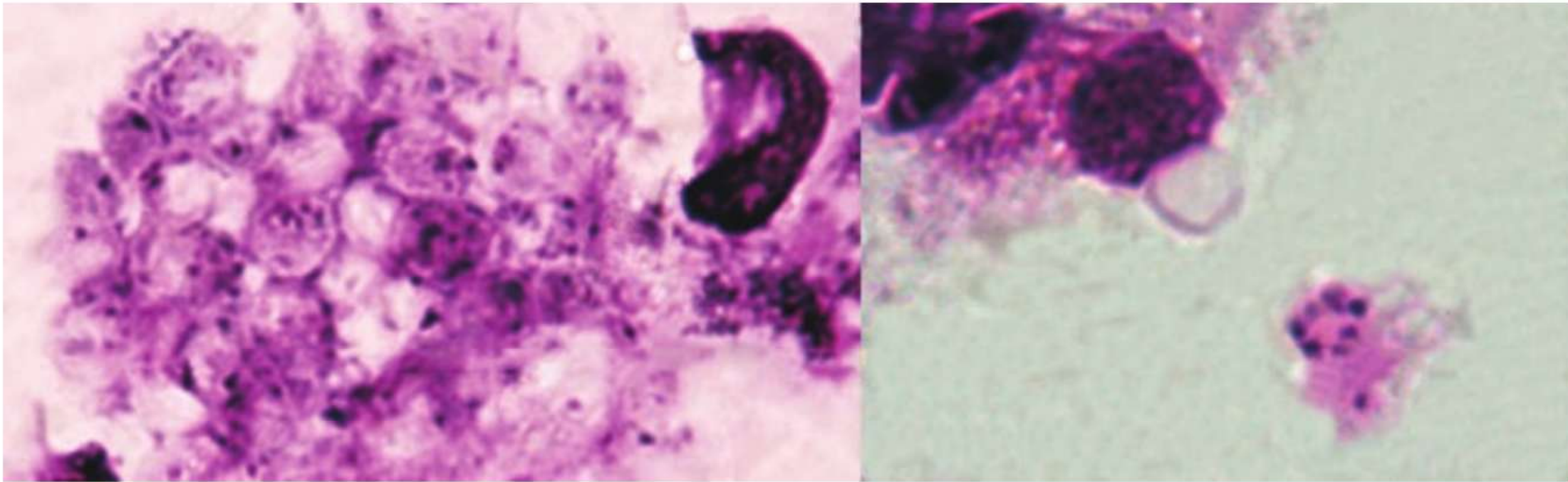


Original Article

Use of calcofluor-blue brightener for the diagnosis of *Pneumocystis jirovecii* pneumonia in bronchial-alveolar lavage fluids: A single-center prospective study

Guillaume Desoubeaux^{1,2,*}, Claire Franck-Martel¹, Agnès Caille^{3,4}, Nicolas Drillaud¹, Marie-Alix Lestrade Carlier de Kyvon^{1,2}, Éric Bailly¹ and Jacques Chandanier^{1,2}





fot. P. Krzyściak

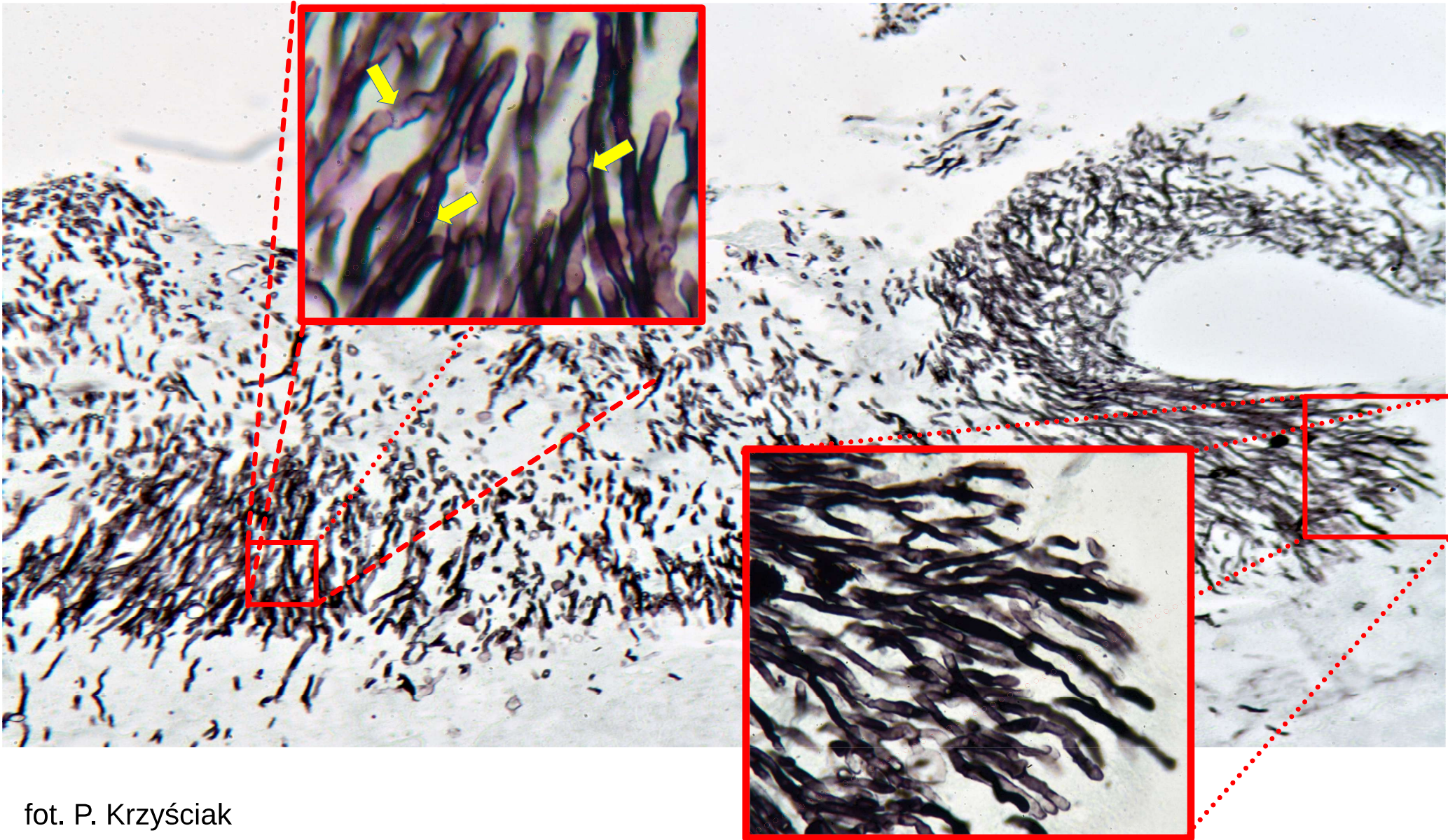
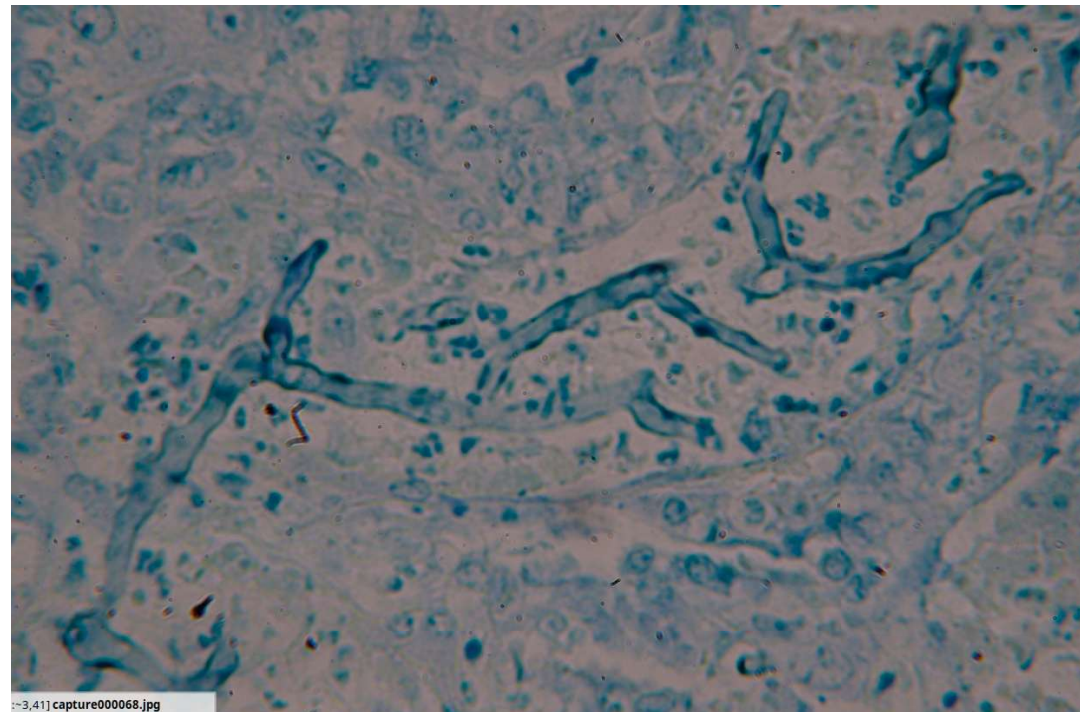
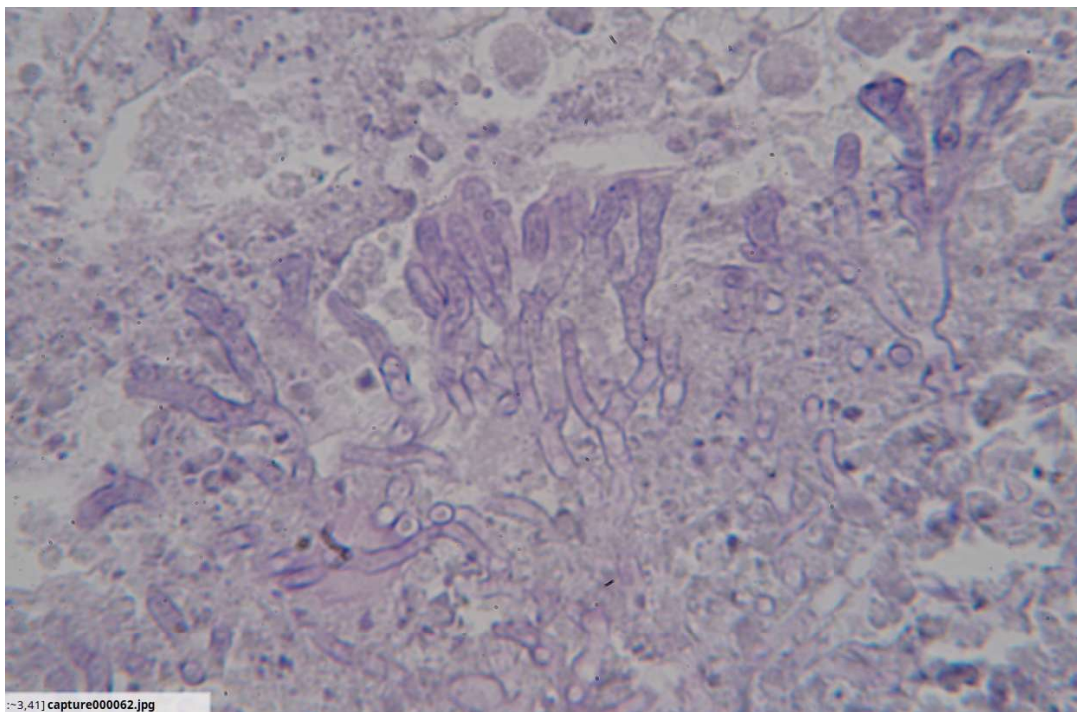


foto. P. Krzyściak

ASPERGILLUS vs MUCORMYCOTA



fot. P. Krzyściak

IDENTYFIKACJA PATOGENÓW

CZY HODOWLA ODEJDZIE DO LAMUSA?

- podłoże Sabourauda
- podłoża chromogenne dla grzybów
 - *Candida auris*
 - *Malassezia*
- dermatofity – DTM / Sab

| Identification Method | Organism <i>C. auris</i> can be misidentified as |
|--|---|
| Vitek 2 YST* | <i>Candida haemulonii</i> <i>Candida duobushaemulonii</i> |
| API 20C | <i>Rhodotorula glutinis</i> (characteristic red color not present) <i>Candida sake</i> |
| API ID 32C | <i>Candida intermedia</i> <i>Candida sake</i> <i>Saccharomyces kluyveri</i> |
| BD Phoenix yeast identification system | <i>Candida haemulonii</i> <i>Candida catenulata</i> |
| MicroScan | <i>Candida famata</i> <i>Candida guilliermondii</i> ** <i>Candida lusitaniae</i> ** <i>Candida parapsilosis</i> ** |
| RapID Yeast Plus | <i>Candida parapsilosis</i> ** |

<https://www.cdc.gov/candida-auris/hcp/laboratories/identification-of-c-auris.html>

NOWE NAZEWNICTWO – np. ZMIANY W RODZAJU *CANDIDA* – *PICHIOMYCETES*

- **PICHIACEAE**

- **Pichia**

- *P. kudriavzevii*, (*C. krusei*)
 - w *Index Fungorum*
 - Issathenkia orientalis*
 - *P. norvegensis*
 - *P. inkonsicua*
 - *P. kluyveri*

- **DEBARYOMYCETACEA**

- **CANDIDA**

- *C. albicans*, *C. africana*, *C. dubliniensis*
 - *C. orthopsilosis*, *C. parapsilosis*, *C. metapsilosis*
 - *Lodderomyces elongisporus*
 - *C. tropicalis*

- **DEBARYOMYCES**

- *D. hansenii* (*C. famata*)

- **DIUTINA**

- *D. rugosa*

- **MEYEROZYMA**

- *M. guilliermondii*

- **METSCHNIKOWIACEAE**

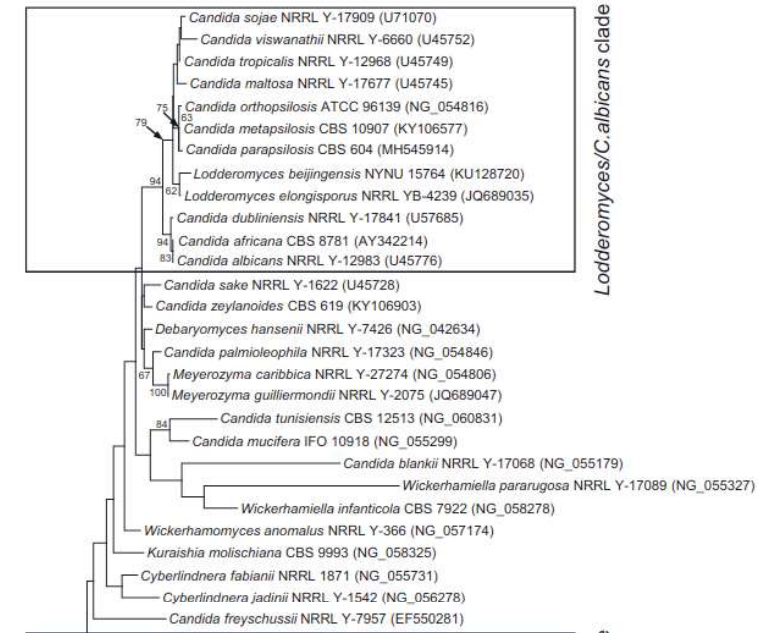
- **CANDIDOZYMA**

- *C. auris*
 - *C. pseudohaemulonii*

- **CLAVISPORA**

- *C. lusitaniae*

- **?? SUNGQUIELLA intermedia**



GATUNKI SIOSTRZANE, KRYPTOGATUNKI na przykładzie KRYPTOKOKÓW WŁAŚCIWYCH

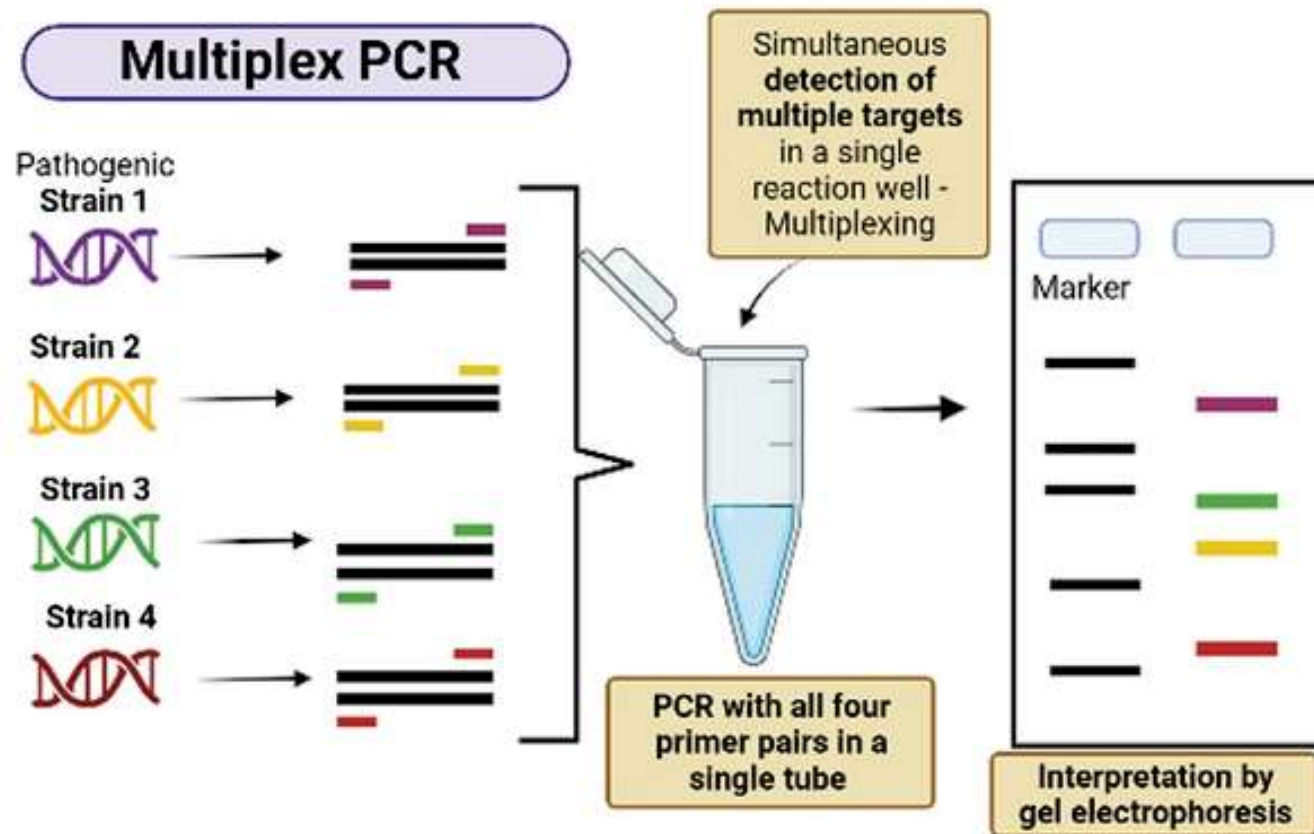
Table 2. Seven newly reclassified species of *Cryptococcus neoformans* and *Cryptococcus gattii*

| Current species name | Before 2015 |
|---|---|
| <i>Cryptococcus neoformans</i> | <i>Cryptococcus neoformans</i> var. <i>grubii</i> |
| <i>Cryptococcus deneoformans</i> | <i>Cryptococcus neoformans</i> var. <i>neoformans</i> |
| <i>Cryptococcus neoformans</i> × <i>Cryptococcus deneoformans</i> hybrid | <i>Cryptococcus neoformans</i> intervariety hybrid |
| <i>Cryptococcus gattii</i> | <i>Cryptococcus gattii</i> |
| <i>Cryptococcus bacillisporus</i> | |
| <i>Cryptococcus deuterogattii</i> | |
| <i>Cryptococcus tetragattii</i> | |
| <i>Cryptococcus decagattii</i> | |
| <i>Cryptococcus deneoformans</i> × <i>Cryptococcus gattii</i> hybrid | <i>Cryptococcus neoformans</i> var. <i>neoformans</i> × <i>Cryptococcus gattii</i> AFLP4/VGI hybrid |
| <i>Cryptococcus neoformans</i> × <i>Cryptococcus gattii</i> hybrid | <i>Cryptococcus neoformans</i> var. <i>grubii</i> × <i>Cryptococcus gattii</i> AFLP4/VGI hybrid |
| <i>Cryptococcus neoformans</i> × <i>Cryptococcus deuterogattii</i> hybrid | <i>Cryptococcus neoformans</i> var. <i>grubii</i> × <i>Cryptococcus gattii</i> AFLP6/VGII hybrid |

Med. Mycol. J. Vol. 63, 119-132, 2022

PCR z PRÓBKİ

METODY PCR - STANDARD



Journal of Biomedical Science volume 30, Article number: 42 (2023)

PCR

ASPERGILLUS

| | |
|---|---|
| Magicplex Sepsis Real eTime Test (Seegne) | - <i>Aspergillus fumigatus</i> |
| <i>A. fumigatus</i> Bio-Evolution (Bio-Evolution) | - <i>Aspergillus fumigatus</i> |
| MycAssay <i>Aspergillus</i> (Myconostica) | Eighteen <i>Aspergillus</i> species - <i>Aspergillus fumigatus</i> - <i>Aspergillus flavus</i> - <i>Aspergillus terreus</i> - <i>Aspergillus niger</i> |
| AsperGenius® (PathoNostics) | - <i>Aspergillus fumigatus</i> - <i>Aspergillus terreus</i> |
| <i>Aspergillus</i> spp. ELITe MGB® Kit (ELITechGroup) | - <i>Aspergillus niger</i> - <i>Aspergillus nidulans</i> - <i>Aspergillus terreus</i> - <i>Aspergillus flavus</i> - <i>Aspergillus versicolor</i> - <i>Aspergillus glaucus</i> |
| Mycoreal <i>Aspergillus</i> (Ingenetix) | - <i>Aspergillus fumigatus</i> - <i>Aspergillus flavus</i> - <i>Aspergillus nidulans</i> - <i>Aspergillus niger</i> - <i>Aspergillus terreus</i> |
| MycogenIE® <i>Aspergillus</i> Species | <i>Aspergillus</i> spp. including: <i>A. fumigatus</i> |

CANDIDA

| | |
|---|---|
| FungiPlex Candida (Bruker Daltonics) | <i>Candida albicans</i> - <i>Candida parapsilosis</i> - <i>Candida dubliniensis</i> - <i>Candida tropicalis</i> - <i>Candida glabrata</i> - <i>Candida krusei</i> |
| FilmArray Blood Culture Identification (BCID) Panel | <i>C. albicans</i> , <i>C. glabrata</i> , <i>C. krusei</i> , <i>C. parapsilosis</i> , <i>C. tropicalis</i> |
| CandID® and AurisID® (OlmDiagnostics) | CandID: - <i>Candida albicans</i> - <i>Candida dubliniensis</i> - <i>Candida glabrata</i> - <i>Candida krusei</i> - <i>Candida parapsilosis</i> - <i>Candida tropicalis</i> AurisID: - <i>Candida auris</i> |
| T2 Candida | <i>C. albicans</i> , <i>C. tropicalis</i> , <i>C. parapsilosis</i> , <i>C. krusei</i> , and <i>C. glabrata</i> |

Fang, W., Wu, J., Cheng, M. et al. Diagnosis of invasive fungal infections: challenges and recent developments. J Biomed Sci 30, 42 (2023). <https://doi.org/10.1186/s12929-023-00926-2>

PCR

CANDIDA I ASPERGILLUS FUMIGATUS

| | |
|---|--|
| Magicplex Sepsis Real eTime Test (Seegne) | <ul style="list-style-type: none">- <i>Aspergillus fumigatus</i>- <i>Candida albicans</i>- <i>Candida glabrata</i>- <i>Candida Krusei</i>- <i>Candida parapsilosis</i>- <i>Candida tropicalis</i> |
| SeptiFast LightCycler (Roche) | <ul style="list-style-type: none">- <i>Candida albicans</i>- <i>Candida tropicalis</i>- <i>Candida parapsilosis</i>- <i>Candida Krusei</i>- <i>Candida glabrata</i>- <i>Aspergillus fumigatus</i> |

PNEUMOCYSTIS

| | |
|---|-------------------------------|
| PneumoGenius (PathoNostics) | <i>Pneumocystis jirovecii</i> |
| AmpliSens <i>Pneumocystis jirovecii</i> (carinii)-FRT (AmpliSens) | <i>Pneumocystis jirovecii</i> |
| <i>Pneumocystis jirovecii</i> Bio-Evolution (Bio-Evolution) | <i>Pneumocystis jirovecii</i> |

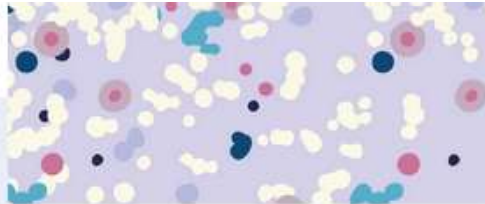
MUKORMYKOZA

| | |
|-----------------------------|--|
| MucorGenius® (PathoNostics) | <ul style="list-style-type: none">- <i>Rhizopus</i> spp.- <i>Mucor</i> spp.- <i>Lichtheimia</i> spp.- <i>Cunninghamella</i> spp.- <i>Rhizomucor</i> spp. |
|-----------------------------|--|

KRYPTOKOKOZA

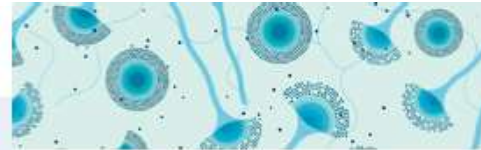
| | |
|---------------------------|--------------------------------|
| FungiXpert® PCR (Genobio) | <i>Cryptococcus neoformans</i> |
|---------------------------|--------------------------------|

Fang, W., Wu, J., Cheng, M. et al. Diagnosis of invasive fungal infections: challenges and recent developments. J Biomed Sci 30, 42 (2023). <https://doi.org/10.1186/s12929-023-00926-2>



CandidaGenius®

C. auris screening assay. A qualitative real-time PCR for the rapid screening of *Candida auris*



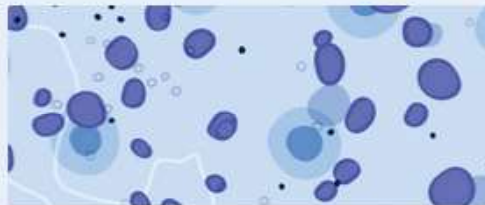
AsperGenius®

Detection and identification of *Aspergillus fumigatus*, *A. terreus*, *A. flavus*, *A. species* and azole resistance markers TR34 and TR46



DermaGenius®

Detection and identification of dermatophyte infections in nail, hair and skin samples and Terbinafine resistance in dermatophyte species



PneumoGenius®

Detection and quantification of *Pneumocystis jirovecii* and DHPS mutations

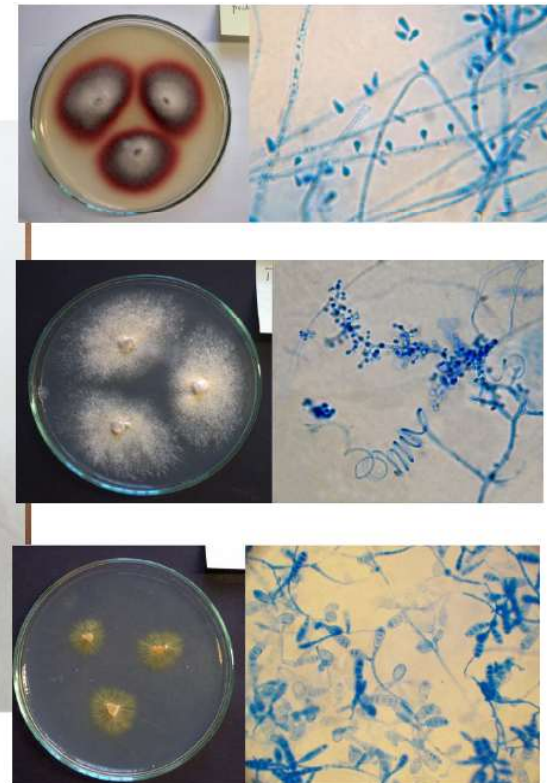


MucorGenius®

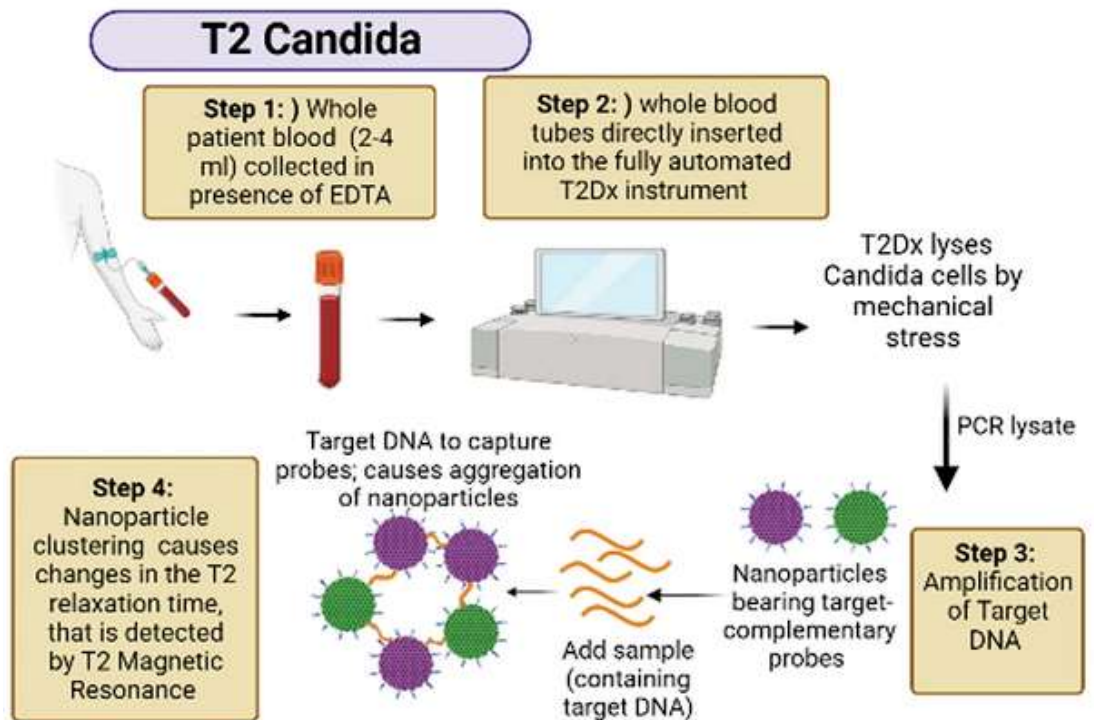
Detection of clinically relevant Mucorales species

DERMATOFITY –NOWY STANDARD Dx- MIKROSKOPIA + PCR?

- DermaGenius® 3.0 Nail Multiplex real-time PCR kit
- DermaGenius® 2.0/3.0 Complete Multiplex real-time PCR kit



T2 MR *Candida*

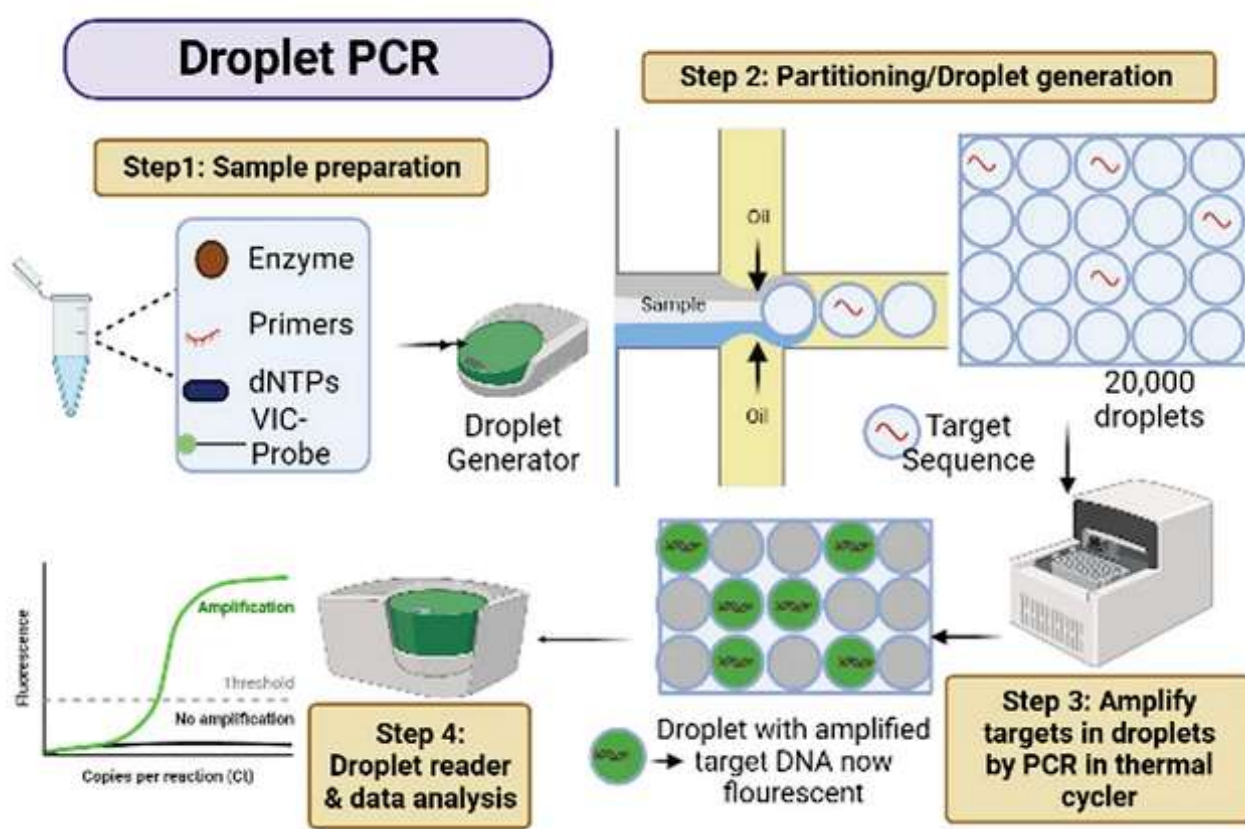


- Test T2Candida, zautomatyzowana jakościowa platforma instrumentów nanodiagnostycznych (T2Dx) (T2 Biosystems, Lexington, MA, USA)
- 5 najczęstszych patogenów we krwi pełnej bez konieczności hodowli
- amplifikacja ITS2,
- po amplifikacji produkt jest następnie wykrywany za pomocą indukowanej amplikonem aglomeracji cząstek supermagnetycznych i rezonansu magnetycznego T2 (T2MR)

<https://pmc.ncbi.nlm.nih.gov/articles/PMC7916227/>

Journal of Biomedical Science volume 30, Article number: 42 (2023)

NOWE METODY - ILOŚCIOWY PCR METODĄ EMULSYJNĄ



Fang, W., Wu, J., Cheng, M. et al. Diagnosis of invasive fungal infections: challenges and recent developments. J Biomed Sci 30, 42 (2023). <https://doi.org/10.1186/s12929-023-00926-2>



Pathology

Volume 55, Issue 5, August 2023, Pages 669-672






MICROBIOLOGY

Panfungal PCR on formalin-fixed, paraffin-embedded tissue: to proceed or not proceed?

Rebecca Sparks¹, Catriona L. Halliday¹  , Wendy Green¹, Sharon C-A. Chen^{1 2 3}

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<https://doi.org/10.1016/j.pathol.2023.03.011> 

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OZNACZANIE LEKOWRAŻLIWOŚCI

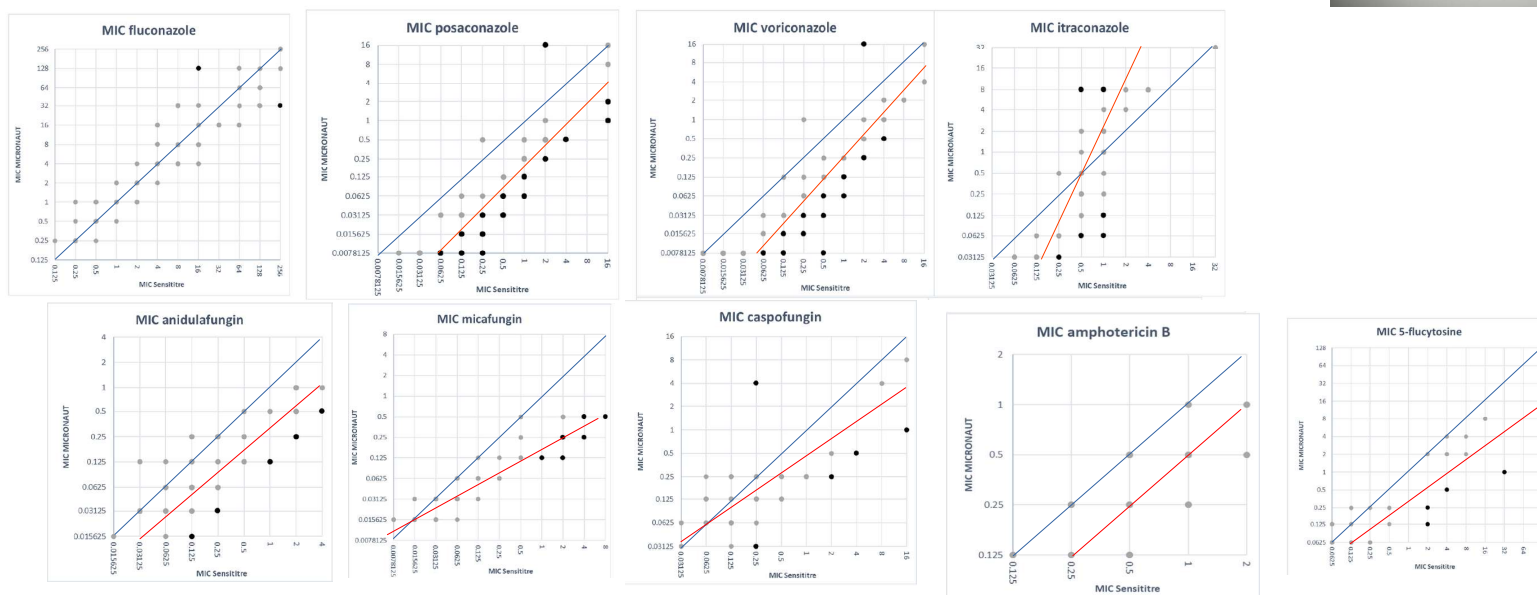
- ATBFungus 3 (bioMérieux)
- **Etest** (bioMérieux) - ?EUCAST
- ~~FUNGITEST (BioRad) – tylko graniczne MIC~~
- Integral System Yeasts Plus (Liofilchem)
- **MICRONAUT-AM** (Bruker)
- **Sensititre YeastOne** (Thermo Fisher Scientific)
 - Y010 (z ANF, MCF ; CE, CLSI poza USA)
- **Vitek 2** (bioMérieux)

METODY ROZCIĘNCZENIOWE – MIC RZECZYWISTY – ZGODNOŚĆ OZNACZEŃ

Article

Comparison of Two Commercial Colorimetric Broth Microdilution Tests for *Candida* Susceptibility Testing: Sensititre YeastOne versus MICRONAUT-AM

Sophie Philips ^{1,2,*}, Frederik Van Hoecke ¹, Emmanuel De Laere ¹, Steven Vervaeke ¹, Roos De Smedt ¹, Jerina Boelens ³, Deborah De Geyter ², Denis Piérard ² and Katrien Lagrou ⁴



Candida auris (n=31)

International Journal of Antimicrobial Agents 59 (2022) 106558

<https://doi.org/10.1016/j.ijantimicag.2022.106558>

CLSI
EUCAST
Etest
VITEK®2

| | 0.5 | 1 | 2 | 4 | 8 | >8 |
|------------|----------|------------------|----------|------------------|------------------|-----------------|
| AMB | 3 (9.7) | 28 (100) | 7 (100) | | | |
| | 5 (16.1) | 19 (77.4) | 3 (100) | | | |
| | 6 (19.4) | 22 (90.3) | | | | |
| | 3 (9.7) | 0 (9.7) | 2 (16.1) | 6 (35.5) | 13 (77.4) | 7 (100) |
| FLC | | | 2 (6.5) | 0 (6.5) | 29 (100) | |
| | | 3 (9.7) | 3 (19.4) | 1 (22.6) | 10 (54.8) | 14 (100) |
| | | | 2 (6.5) | 0 (6.5) | 1 (9.7) | 28 (100) |
| 1 (3.2) | 0 (3.2) | 3 (12.9) | 8 (38.7) | 10 (71.0) | 0 (71.0) | <u>9 (100)</u> |

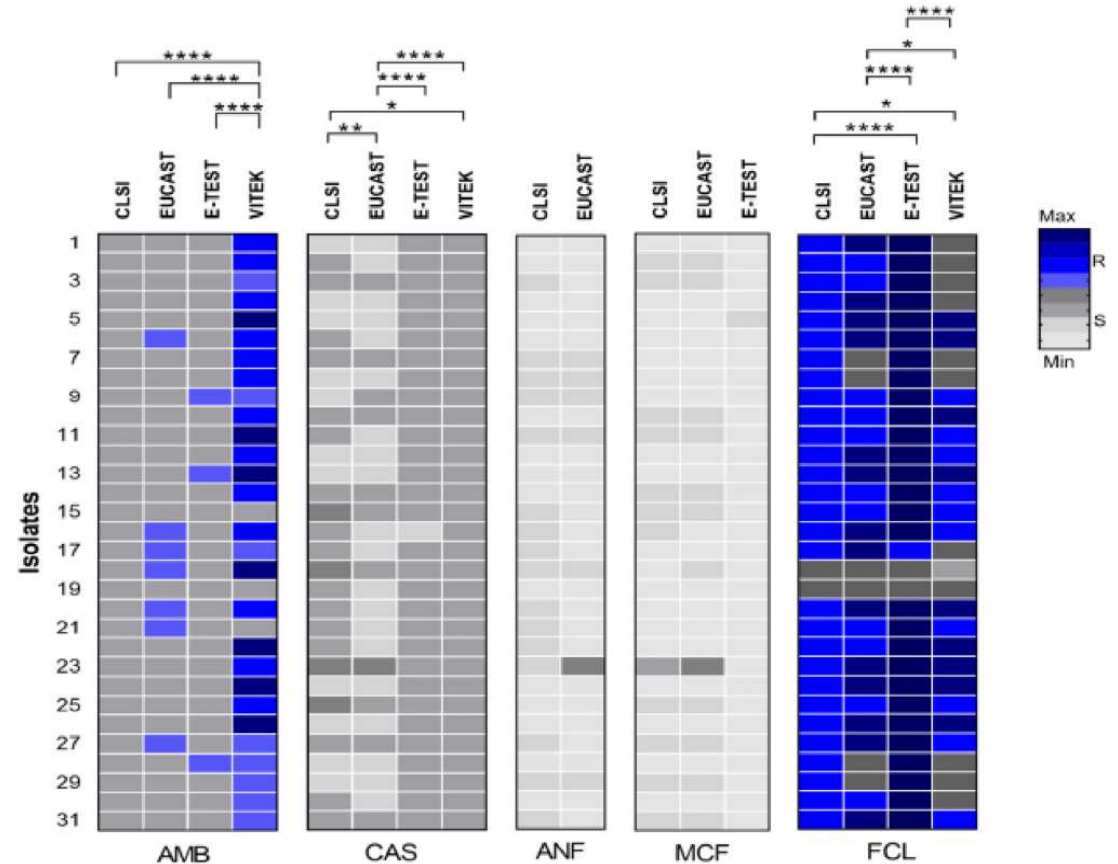


Fig. 1. In vitro antifungal susceptibilities of 31 clinical *Candida auris* isolates, with categorical classification following US Centers for Disease Control and Prevention (CDC) cut-off values. The grey and blue colours indicate susceptibility (S) and resistance (R) grades, respectively. A *P*-value of <0.05 was used to indicate statistical significance as follows. * *P* ≤ 0.05; ** *P* ≤ 0.01; *** *P* ≤ 0.001; **** *P* ≤ 0.0001. CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; AMB, amphotericin B; CSF, caspofungin; ANF, anidulafungin; MCF, micafungin; FLC, fluconazole.

UŻYTKOWNIKU WYBIERZ SOBIE INTERPRETACJĘ... ?!

| | Quality Control (MIC µg/mL) 48 hours incubation | | | CLSI INTERPRETATION MIC Criteria (µg/mL) | | | EUCAST INTERPRETATION MIC Criteria (µg/mL) | | Example of ANTIBIOGRAM 140 mm petri dish |
|--------------------------|---|--------------------------------|-----------------------------------|---|------|------|---|-------|--|
| | <i>C. parapsilosis</i> ATCC® 22019 | <i>C. krusei</i> ATCC® 6258 | <i>C. albicans</i> ATCC® 90028 | S | I | R | S | R | |
| | AND ANIDULAFUNGIN | 0.5-4 | 0.016-0.125 | 0.002-0.008 | | | | | |
| <i>C. albicans</i> | | | | ≤0.25 | 0.5 | ≥1 | ≤0.03 | >0.03 | |
| <i>C. glabrata</i> | | | | ≤0.12 | 0.25 | ≥0.5 | ≤0.06 | >0.06 | |
| <i>C. tropicalis</i> | | | | ≤0.25 | 0.5 | ≥1 | ≤0.06 | >0.06 | |
| <i>C. krusei</i> | | | | ≤0.25 | 0.5 | ≥1 | ≤0.06 | >0.06 | |
| <i>C. parapsilosis</i> | | | | ≤2 | 4 | ≥8 | ≤0.002 | ≥4 | |
| <i>C. guilliermondii</i> | | | | ≤2 | 4 | ≥8 | | | |
| FLU FLUCONAZOLE | 1-8 | 128-≥256 | 0.125-0.5 | | | | | | ✓ |
| <i>C. albicans</i> | | | | ≤2 | 4 | ≥8 | ≤2 | ≥4 | |
| <i>C. glabrata</i> | | | | ≤2 | 32 | ≥64 | ≤0.002 | ≥32 | |
| <i>C. parapsilosis</i> | | | | ≤2 | 4 | ≥8 | ≤2 | ≥4 | |
| <i>C. tropicalis</i> | | | | ≤2 | 4 | ≥8 | ≤2 | ≥4 | |



MIC Test Strip Technical Sheet Yeast - MTS24 - Rev.6 / 31.05.2021

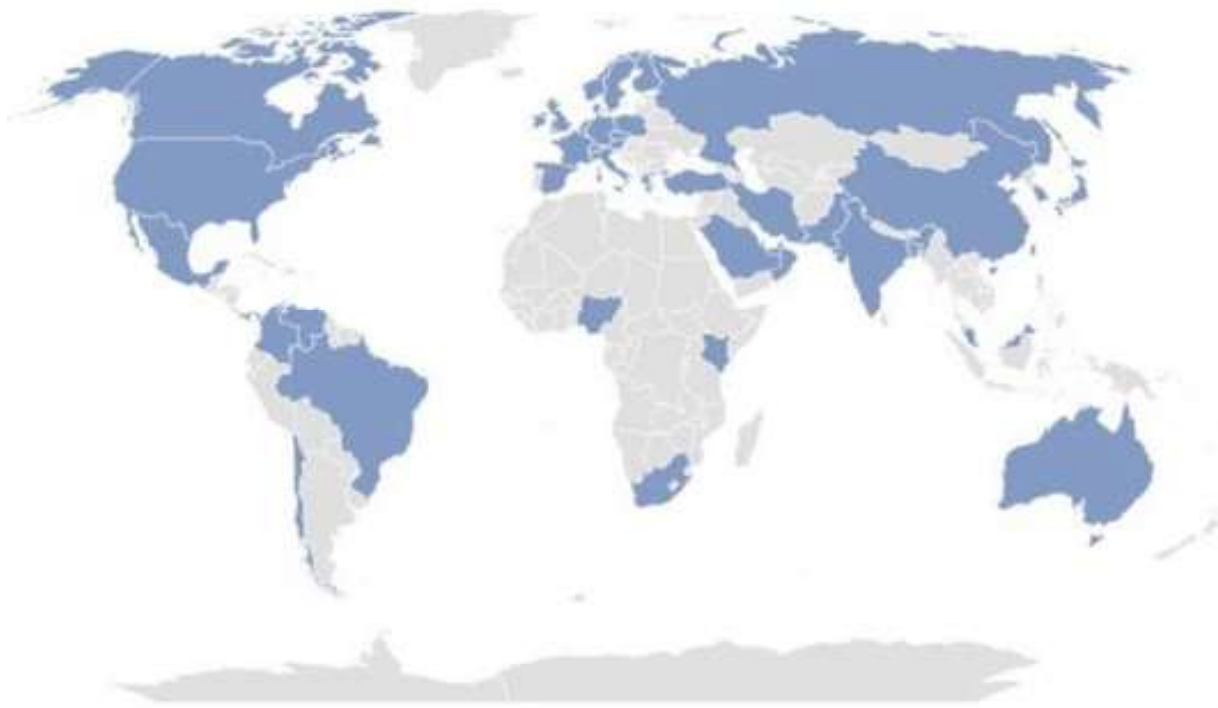
dopuszczalna wartość MIC AND dla szczepu odniesienia (C.p.) - 0,5 – 4 µg/ml]:

W, ŚW wg CLSI,
ŚW wg EUCAST

dopuszczalna wartość MIC FLC dla szczepu odniesienia (C.p.) - 1 – 8µg/ml:

W, ŚW wg CLSI
W, ŚW, O wg EUCAST

MDR DROŻDŻY - KRAJE RAPORTUJĄCE *CANDIDA AURIS*



Powered by King
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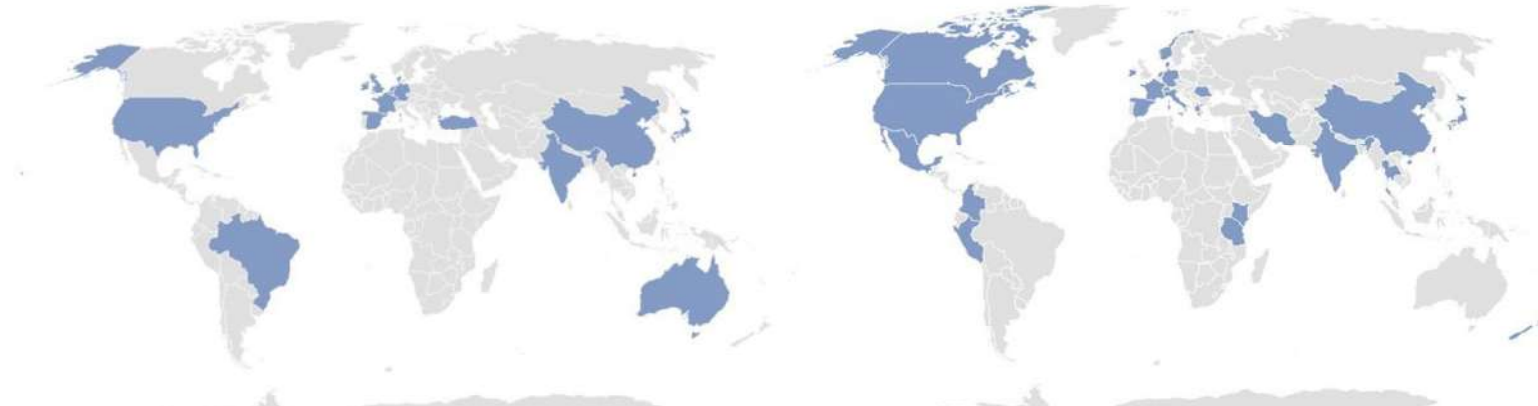


Nat Rev Microbiol. 2023 December ; 21(12): 818–832. doi:10.1038/s41579-023-00960-9.

TRIAZOLOPOROŚĆ U ASPERGILLUS FUMIGATUS

oporne szczepy od pacjentów

oporne szczepy ze środowiska



Nat Rev Microbiol. 2023 December ; 21(12): 818–832. doi:10.1038/s41579-023-00960-9.

TR34/L98H – oporność na ITR

TR46/Y121F/T289A – oporność na VOR

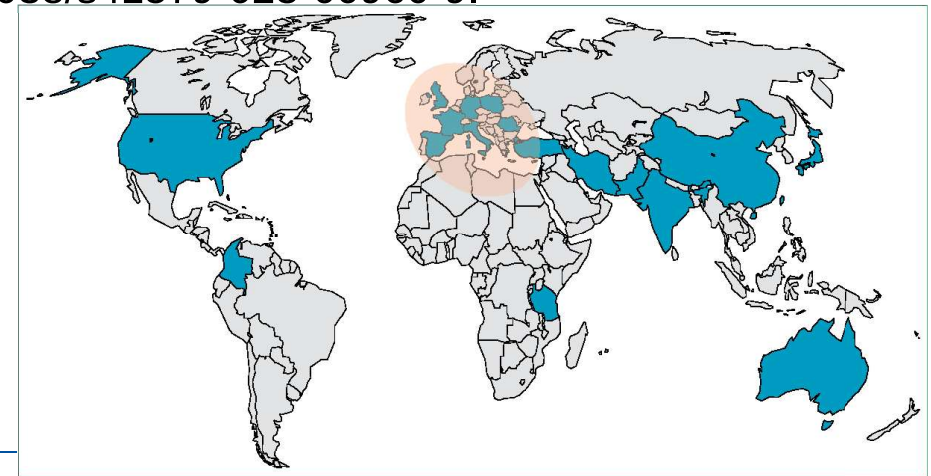


Figure 1: Countries reporting azole-resistant isolates of *Aspergillus fumigatus* with either TR₃₄/L98H or TR₄₆/Y121F/T289A modifications. Countries where mechanistic resistance is found are shown in blue. The region of highest burden of resistance is marked by the shaded oval (adapted from Verweij www.clinicaltrials.gov).

DERMATOFITY OPORNE NA TERBINAFINĘ

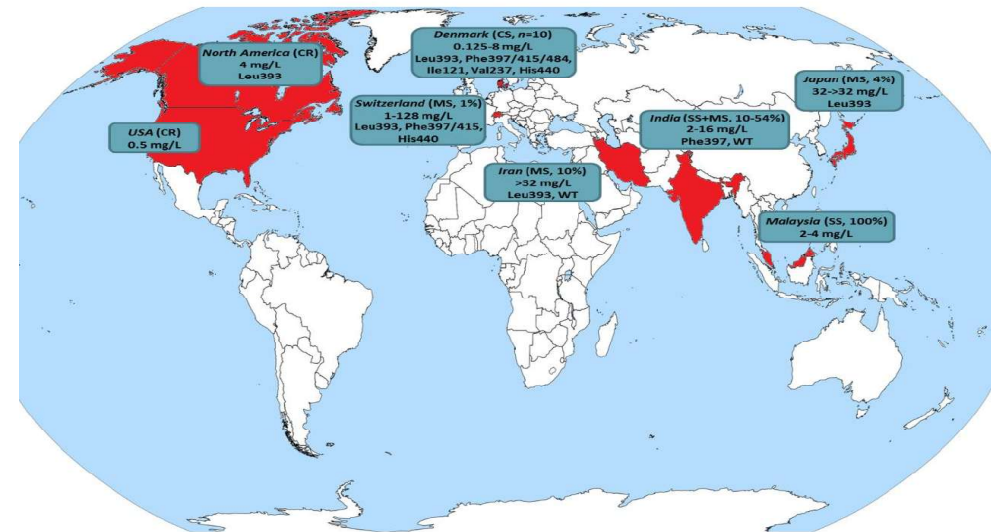
TRICHOPHYTON INDOTINEAE



Nat Rev Microbiol. 2023 December ; 21(12): 818–832. doi:10.1038/s41579-023-00960-9.

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TRICHOPHYTON RUBRUM



Siopi, M. et al. J. Fungi 2021, 7, x.
<https://doi.org/10.3390/xxxxx>

> JAMA Dermatol. 2024 Jul 1;160(7):699-700. doi: 10.1001/jamadermatol.2024.1125.

Resistant Trichophyton indotinea Dermatophytosis-An Emerging Pandemic, Now in the US

Toan S Bui ¹, Kenneth A Katz ²

Affiliations + expand

PMID: 38748418 DOI: 10.1001/jamadermatol.2024.1125

KONIECZNOŚĆ AFST PRZED LECZENIEM DERMATOFITÓZ??

Clinical Microbiology and Infection 27 (2021) 55–60



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journal homepage: www.clinicalmicrobiologyandinfection.com



Narrative review

How to: perform antifungal susceptibility testing of microconidia-forming dermatophytes following the new reference EUCAST method E.Def 11.0, exemplified by *Trichophyton*[☆]

Maiken C. Arendrup^{1,2,3,*}, Gunnar Kahlmeter⁴, Jesus Guinea^{5,6,7,†}, Joseph Meletiadis^{8,9,†}, the Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST)



European Committee on Antimicrobial Susceptibility Testing

Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.4, E.Def 9.4 and E.Def 11.0 procedures

Version 5.0, valid from 2024-12-02

This document should be cited as:
The European Committee on Antimicrobial Susceptibility Testing. Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and dermatophytes using the EUCAST E.Def 7.4, E.Def 9.4 and E.Def 11.0 procedures. Version 5.0, 2024. <http://www.euca.st.org>

Overview of antifungal ECOFFs and clinical breakpoints for yeasts, moulds and derma procedures

Version 5.0, valid from 2024-12-02

| Species | Drug | ECOFF (mg/L) WT ≤ | Clinical Breakpoints (mg/L) | | | | Re |
|-----------------------------------|----------------|-----------------------|-----------------------------|----|-----|-----|----|
| | | | S ≤ | I | R > | ATU | |
| <i>T. indotineae</i> ² | Amorolfin | (0,5) ¹ | ND | | ND | | |
| | Amphotericin B | ND | ND | | ND | | |
| | Anidulafungin | ND | ND | | ND | | |
| | Micafungin | ND | ND | | ND | | |
| | Fluconazole | ND | ND | | ND | | |
| | Isavuconazole | ND | ND | | ND | | |
| | Itraconazole | (0,25) ² | ND | | ND | | |
| | Posaconazole | ND | ND | | ND | | |
| | Terbinafine | (0,125) | ND | | ND | | |
| Voriconazole | (1) | ND | | ND | | | |
| <i>T. rubrum</i> | Amorolfin | (0,125) | ND | | ND | | |
| | Amphotericin B | ND | ND | | ND | | |
| | Anidulafungin | ND | ND | | ND | | |
| | Micafungin | ND | ND | | ND | | |
| | Fluconazole | ND | ND | | ND | | |
| | Isavuconazole | ND | ND | | ND | | |
| | Itraconazole | (0,25) ^{2,3} | ND | | ND | | |
| | Posaconazole | ND | ND | | ND | | |
| | Terbinafine | (0,03) | ND | | ND | | |
| Voriconazole | (0,125) | ND | | ND | | | |

Comments:

MOŻEMY WYKRYWAĆ GENY OPORNOŚCI - PCR

- AsperGenius® 2.0 Resistance TR Multiplex real-time PCR kit
 - Aspergillus fumigatus TR34
 - Aspergillus fumigatus TR46
 - Aspergillus fumigatus cyp51A (WT)
 - Internal Control (IC)
- DermaGenius® Resistance Multiplex real-time PCR kit



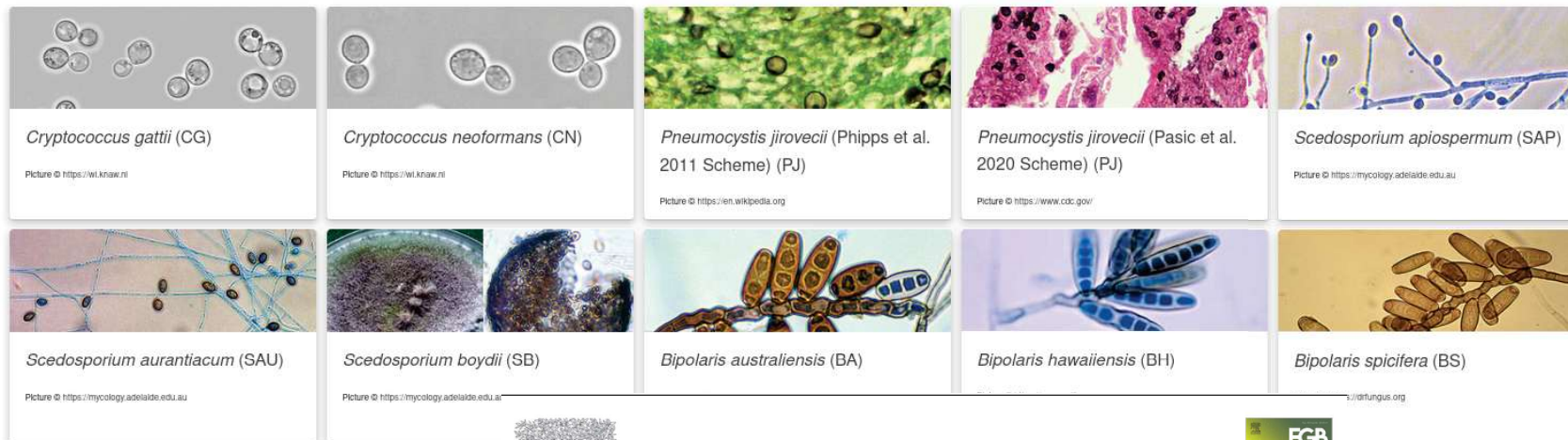
DOCHODZENIE EPIDEMIOLOGICZNE

szczepy grzybów też się typuje
– kandydoza nie jest z definicji zakażeniem endogennym

International Fungal Multi Locus Sequence Typing Database

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Fungal MLST website



Fungal Genetics and Biology

Volume 170, February 2024, 103845



Multi-locus sequencing typing reveals
geographically related intraspecies variability of
Sporothrix brasiliensis

Short Tandem Repeat Genotyping of Medically Important Fungi: A Comprehensive Review of a Powerful Tool with Extensive Future Potential

Review | [Open access](#) | Published: 03 August 2024

Volume 189, article number 72, (2024) [Cite this article](#)

> [Methods Mol Biol.](#) 2016:1356:199-214. doi: 10.1007/978-1-4939-3052-4_15.

Typing Candida Species Using Microsatellite Length Polymorphism and Multilocus Sequence Typing

[Dea Garcia-Hermoso](#)^{1 2}, [Marie Desnos-Ollivier](#)^{1 2}, [Stéphane Bretagne](#)^{3 4 5}

Affiliations [+](#) expand

PMID: 26510075 DOI: 10.1007/978-1-4939-3052-4_15

ROZWIĄZANIA SYSTEMOWE

ROZWIĄZANIA SYSTEMOWE

- **TOWARZYSTWO MYKOLOGII MEDYCZNEJ**
 - sekcja mykologii PTMyk, **PTD**, PTM
 - edukacja
 - współtworzenie wytycznych
- **REFERENCYJNE LABORATORIUM MYKOLOGICZNE**
 - edukacja
 - gromadzenie danych
 - tworzenie wytycznych
- **AFST EUCAST NETWORK LABORATORY**
 - gromadzenie danych
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Polish Delegate of ECMM
Anita Hryniewicz-Gwóźdź
Contact: anita.hryniewicz-gwozdz@am.wroc.pl



MYŚL O GRZYBICACH: diagnostyka – badania i rozwój – ratowania życia

Think Fungus

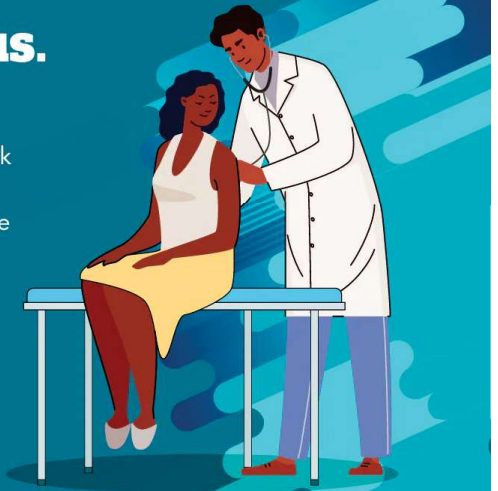
Diagnostic tests keep antifungals working their best.



cdc.gov/fungal

Think Fungus. Save Lives.

Some fungal infections can look like other illnesses. Early diagnosis and appropriate treatment are essential.



cdc.gov/fungal

Research and development

Learning more about the impact of fungal diseases inspires **research and development.**





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