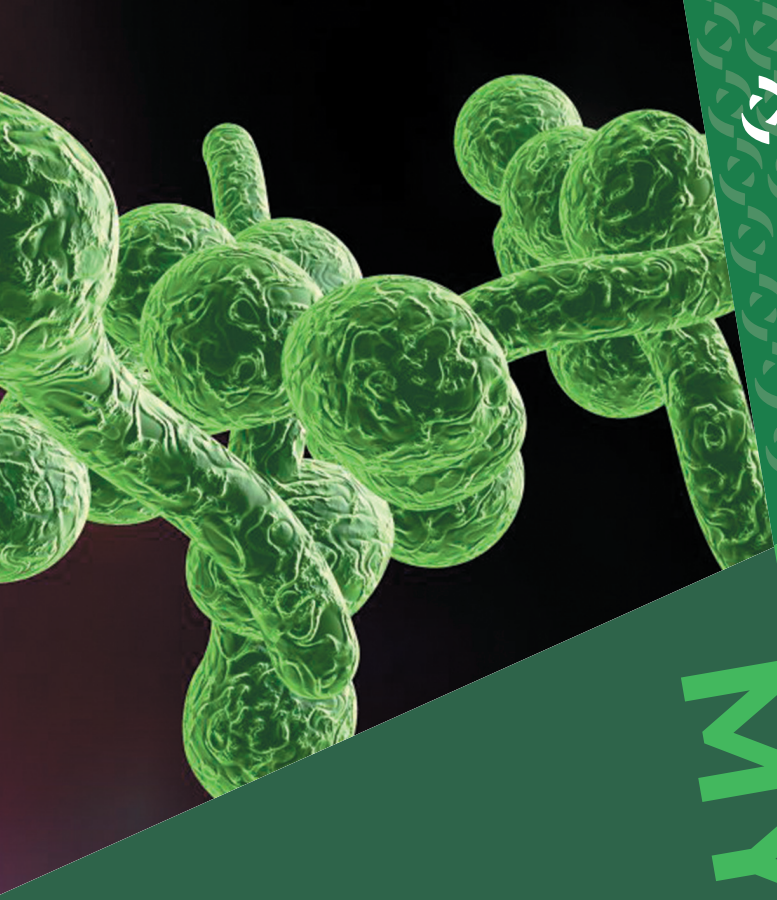


DNA-TECHNOLOGY

MYCOSES

MYCOSOSCREEN

REAL-TIME PCR KIT FOR DETECTION AND TYPING OF PATHOGENS CAUSING MYCOSES FROM GENERA CANDIDA, MALASSEZIA, SACCHAROMYCES AND DEBARYOMYCES

CLINICAL SIGNIFICANCE

Infections caused by yeast-like fungi (mycoses) have a wide range of clinical manifestations from local skin lesions, mucous membranes of the urogenital, respiratory and gastrointestinal tracts to fungemia and multiple organ damage with a severe disease and possible death.

Fungal diseases are widespread and are especially dangerous for premature infants, immunocompromised patients and hematological cancer patients [1–3]. The use of cytostatics, corticosteroids, broad-spectrum antibiotics, invasive diagnostic and therapeutic procedures leads to the increase of mycoses incidences.

Mycoses are divided into superficial (non-invasive) and invasive infection by their clinical manifestation [4–7].

Clinical manifestations of superficial mycoses depend on the localization of the fungal infection. Superficial mycoses manifest lesions of cutaneous structures and the mucous membranes of the oral cavity, oropharynx, esophagus, vagina and intestines.

Invasive mycoses are a severe form of fungal infection that requires long-term systemic treatment. The pathogens penetrate into the blood and lymph flow [8–9], causing candidemia [10], spread throughout the body, affecting the organs.

The main risk factors of invasive mycoses' development include [11–18]:

- the presence of superficial (non-invasive) mycoses;
- premature birth;
- the central venous catheter (CVC);
- tracheal intubation;
- drainages, catheters;
- therapy with broad-spectrum antimicrobials, especially third-generation cephalosporins and carbapenems;
- total parenteral nutrition (TPN);
- surgical interventions on the abdominal organs, peritoneal dialysis;
- perforation of the gastrointestinal tract;
- pancreatitis;
- necrotizing enterocolitis (NEC);
- therapy with antacids and H2-blockers.

The list of potential causative agents of mycoses includes about 400 species of fungi. The most common pathological processes being caused by yeast-like fungi of the genera *Candida, Saccharomyces, Debaryomyces* and *Malassezia*.

FUNGI OF THE GENUS *CANDIDA*

The genus *Candida* includes more than 100 species, about 20 species are pathogenic for humans: *C. albicans, C. tropicalis, C. krusei, C. kefyr, C. glabrata, C. guilliermondii, C. parapsilosis, C. famata, C. auris, C. lusitaniae*.

The generic affiliation and list of several species were changed based on the new knowledges about its genome taking into account their morphological and biochemical features (Table 1).

Changes in the list of some yeast-like fungi

Original title	New title
Candida guilliermondii	*Meyerozyma guilliermondii*
Candida krusei	*Pichia kudriavzevii*
Candida famata	*Debaryomyces hansenii*
Candida kefyr	*Kluyveromyces marxianus*

Candida non-albicans species cause candidiasis more often in recent years (Table 2). One of the reason of it is the irrational use of azole antimycotics in prophylactic and therapeutic purposes [19].

Candida auris was discovered in 2009, it may cause invasive mycoses with a high mortality rate (up to 60%). *C. auris* is antifungal multidrug resistant and some its strains may be resistant to all three major antifungal drugs' classes: azoles, polyenes, and echinocandins. It is also resistant to environmental factors, including disinfectants widely used in medical centers. At the same time, *C. auris* can colonize wide range of surfaces and form stable biofilms, what makes it a significant threat for the spread of nosocomial candidiasis and invasive candidal infection [20–24]. Clinical diagnosis of this type of candidiasis is difficult due to the lack of specific symptoms, and its identification is possible only by physicochemical (for example, MALDI-TOF) or molecular genetics (PCR) methods.

Species of *Candida* non-albicans and associated pathological conditions

Species	Association with pathology
C. glabrata	• Highly active in biofilm formation. • The causative agent of vulvovaginal candidiasis, especially in patients with diabetes mellitus; patients taking maintenance doses of azoles; and patients who regular douche. • The most common causative agent of urinary tract infections, endocarditis and meningitis among other fungi of the genus *Candida*. • The predominant species of *Candida* non-albicans isolated from patients with candidemia. Risk factors of candidemia are similar to those of other species, but mortality from *C. glabrata*-associated infection is higher than with other *Candida* species. It is predominantly the causative agent of candidemia in patients undergoing abdominal surgery (the risk is higher in patients older than 60 years) and HIV-infected [19, 25–26].
C. tropicalis	• Has a high activity in biofilm formation. • The causative agent of catheter-associated candidemia and candidal osteomyelitis. • Associated with the development of chronic candidiasis of the oral mucosa and gastrointestinal tract with necrotic changes (the highest risk in immunocompromised individuals, especially oncohematological patients). • May cause candidemia in newborns in the ICU. • The causative agent of invasive candidiasis in patients with neutropenia (acute leukemia, bone marrow transplantation) [27–28].
C. krusei (Pichia kudriavzevii)	• Associated with candidemia with a high mortality rate in surgical and neutropenic patients. • The causative agent of multiresistant invasive candidiasis [29–31].
C. dubliniensis	• The causative agent of oropharyngeal candidiasis in HIV-infected and patients with cystic fibrosis (especially with steroid drugs therapy, cystic fibrosis-associated diabetes mellitus and prolonged antibiotic therapy). • May be the causative agent of vulvovaginal candidiasis in non-immunosuppressed patients. • Associated with the development of eye infections (dacryocystitis and endophthalmitis). • Rarely associated with invasive candidiasis in adults [32–34].
C. guilliermondii (Meyerozyma guilliermondii)	• The causative agent of onychomycosis. • The causative agent of invasive candidiasis in patients with oncopathologies (oncohematological diseases, solid tumors and neutropenia), patients after cardiovascular or intra-abdominal operations. • May cause catheter-associated candidemia. • May be the causative agent of candidal osteomyelitis [27, 35].

Species	Association with pathology
C. parapsilosis	• A common cause of candidemia in ICU neonates and children. • Associated with the development of candidemia in ICU patients after neurosurgical operations, patients with multiple injuries and infants. • The causative agent of catheter-associated candidemia and candidemia in patients on parenteral nutrition [19, 25–26, 36].
C. famata (Debaryomyces hansenii)	• Associated with chronic adenoiditis and endophthalmitis. • The causative agent of candidal meningitis. • One of the causative agents of catheter-associated fungemia and invasive candidiasis in immunocompromised patients. • The causative agent of disseminated candidiasis (respiratory distress syndrome, pneumonia, sepsis or candiduria) in preterm infants [37-40].
C. kefyr (Kluyveromyces marxianus)	• May be the causative agent of vulvovaginal candidiasis. • Associated with chronic tonsillitis, chronic pharyngitis and other mycotic lesions of the upper respiratory tract. • Associated with the development of candidemia in patients with neoplastic myeloproliferative and lymphoproliferative diseases [41-44].
C. auris	• The causative agent of catheter-associated infection and invasive candidiasis. • Associated with urinary tract infections, otitis media, surgical wound infections, skin abscesses (associated with catheter insertion), myocarditis, meningitis, bone tissue infections and wound infections [20, 45–47].
C. lusitaniae	• The causative agent of invasive candidiasis, mainly in the exogenous route of infection. • The causative agent of vulvovaginal and oropharyngeal candidiasis. • Etiological factor of late neonatal infections and chronic candidiasis in patients with cystic fibrosis. • Associated with the development of candidemia in patients with hemoblastoses [42, 44, 48].

The treatment of candidiasis is based on four main groups of antimycotics: echinocandins, azoles, polyenes and fluorinated pyrimidines [35, 38]. Different types of fungi have different sensitivity to antimycotics.

Laboratory diagnostics of candidiasis is currently based on the following methods:

- light microscopy of native specimen or microscopy of Gram-stained smears (detection of yeast budding cells, pseudomycelium);
- microbiological methods are used for pathogen determination (*C. albicans* or non-albicans) [49]: blood culture for the diagnosis of systemic infections and classical culture method with further species identification by biochemical parameters or MALDI-TOF-MS analysis.
- serological methods include detection of 1,3-β-D-glucan of the fungal cell wall, detection of circulating antigens of *Candida spp.* (mannan) and antibodies to *Candida spp.* (antimannan) in blood serum
- molecular biological methods are designed to detect specific DNA and/or RNA fragments of *Candida spp.* and species identification of the pathogen.

FUNGI OF THE GENUS *SACCHAROMYCES*

Fungi of the genus *Saccharomyces* are opportunistic microorganisms that normally present on the mucous membrane of the oral cavity and vagina, in feces and sputum.

Saccharomyces cerevisiae is one of the most common species which can cause the infectious pathology. Some patients are at higher risk, including patients with low reactivity of the immune system; premature babies; patients taking probiotics; food industry workers directly contacting with brewer or baking yeasts.

S. cerevisiae can cause superficial and invasive mycoses: vulvovaginitis, osteomyelitis, allergic bronchopulmonary mycosis (most often observed in patients with cystic fibrosis and bronchial asthma), acute pyelonephritis and fungemia especially in people with oncopathology, endoprosthesis and other surgical interventions [50 –53].

Diagnostics of diseases associated with *S. cerevisiae* includes serological methods recommended by the European Society of Clinical Microbiology and Infectious Diseases: determination of b-1-3-D-glucan (BDG) in blood culture or cultivation on agar, however, diagnostic efficiency of these assays has not been proven [54]. Molecular genetics methods may be promising for the identification of causative agents of mycoses and species differentiation.

FUNGI OF THE GENUS *MALASSEZIA*

Fungi of the *Malassezia* genus are components of the normal microflora of human skin, but can also cause superficial skin infection or invasive lesions under certain conditions [55].

The etiological role of *Malassezia spp.* has been proven in tinea versicolor , seborrheic dermatitis, atopic dermatitis, folliculitis, psoriasis and other skin diseases. Also, *Malassezia* fungi can cause fungemia and invasive lesions of the lungs and heart [2]. There were isolated cases of thrombophlebitis, sinusitis, otitis, meningitis, septic arthritis, soft tissue abscesses associated with *Malassezia spp.* [2, 13].

Significant factors in the pathogenicity of *Malassezia spp.* are their lipophilicity and the ability to form a biofilm [57–58]. These peculiarity plays a significant role in the development of antimycotics resistance. *Malassezia spp.* are classified as difficult-to-culture microorganisms, what greatly complicates their study and diagnostics [14].

Appropriate treatment depends on the pathogen species and its amount. At the same time, early therapy can significantly increase the efficiency of treatment.

Real-time PCR method quickly determines causative agent`s species with high accuracy.

The MycosoScreen kit is designed for detection and typing of pathogens causing mycoses from genera *Candida, Malassezia, Saccharomyces* and *Debaryomyces* in DNA material obtained from human biological samples, catheter and endotracheal tube washings, and fungal cultures with an aid of Polymerase Chain Reaction (PCR) method.

INDICATIONS FOR THE USE:

- a suspicion for candidiasis, candidemia, candiduria and *Candida* carrier state
- monitoring of the dynamic of colonization normally non-sterile loci, lesions and catheters with fungi
- infectious control in patients including risk groups
- identification of fungal species in fungal cultures

BIOMATERIAL:

1. human biological material:
   - blood
   - phlegm
   - urine
   - smears/scrapes from respiratory tract, gastrointestinal and urogenital tracts
   - faeces
   - bioptates
2. catheter and endotracheal tube washings
3. fungal cultures

ADVANTAGES OF PCR DIAGNOSTICS IN COMPARISON WITH STANDARD METHODS OF DIAGNOSIS OF MYCOSES

- Possibility of **species identification** of microorganisms
- Identification of **difficult-to-culture** microorganisms
- **High speed** of assay
- **Direct method:** has high sensitivity and accurate determination of the causative agent
- Possibility to study a **wide range of biomaterials**

SPECIAL FEATURES OF THE KIT

- **Detection of 14 microorganisms**, including *Candida auris*
- **The possibility of assessment the efficiency of treatment in dynamics** (the result of the assay is expressed as a decimal logarithm of the number of copies of DNA target in 1 mL of sample
- **Multiplex format** – several DNA targets are detected simultaneously in one tube
- **Sample intake control (SIC)** in case of using human biomaterial
- **Internal control** – assessment of PCR quality
- **Automatic generation of the results form** when using the recommended Real-time PCR instruments of the DT series and RealTime_PCR software
- **Availability of preset templates with test parameters, which automatically set the necessary settings** and calculate the results

KIT SPECIFICATIONS

Composition of the kit:

- Paraffin sealed PCR-mixes
- Taq-polymerase solution
- Mineral oil
- Positive control
- Strip's caps

The kit is designed for 24 tests, including positive and negative controls.

Hands-on time
(without sample preparation): from 1.5 hour.

DETECTION CHANNELS OF AMPLIFICATION PRODUCTS:

strip tube №	Detection channel			
	Fam	Hex	Rox	Cy 5
1	*Meyerozyma guilliermondii (C.guilliermondi)*	IC	–	–
2	*Candida albicans*	IC	–	*Pichia kudriavzevii (C.krusei)*
3	*Saccharomyces cerevisiae*	IC	Marker	*Candida auris*
4	*Candida tropicalis*	IC	–	*Clavispora lusitaniae (Candida lusitaniae)*
5	*Debaryomyces hansenii (C.famata)*	IC	–	*Candida dubliniensis*
6	*Candida glabrata*	IC	–	*Candida parapsilosis*
7	*Malassezia spp.*	IC	–	*Malassezia furfur*
8	*Kluyveromyces marxianus (C.kefyr)*	SIC	–	–

Analytical sensitivity:	5 copies of DNA per amplification tube.

RECOMMENDED MATERIALS AND EQUIPMENT

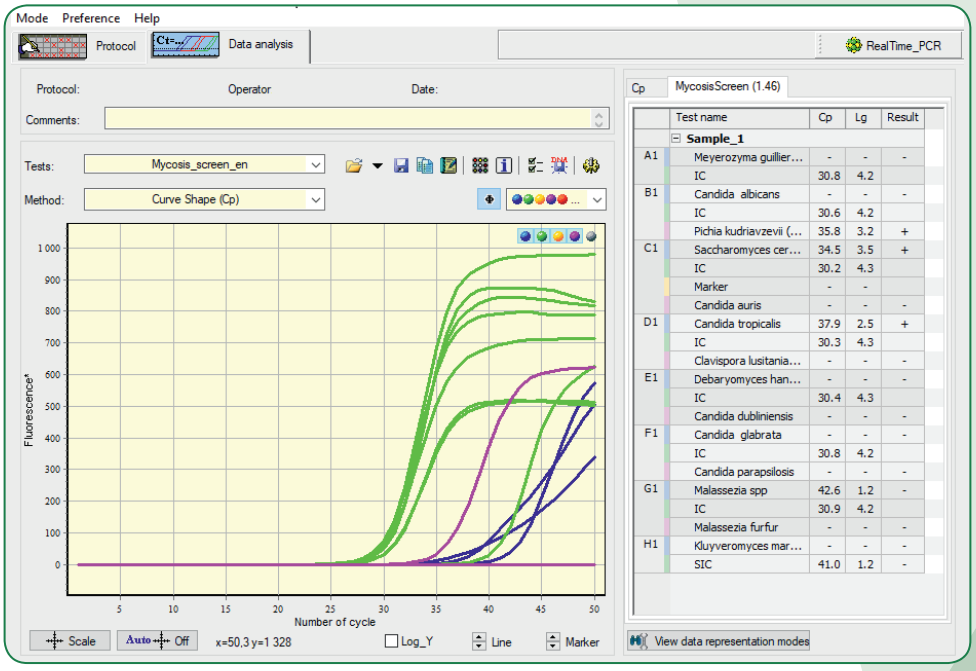
DNA extraction kits	Real-time PCR instruments
▪ PREP-NA DNA/RNA Extraction Kit ▪ PREP-NA PLUS DNA/RNA Extraction Kit ▪ PREP-GS DNA Extraction Kit ▪ PREP-GS PLUS DNA Extraction Kit	▪ DTprime ▪ DTlite

produced by DNA-Technology

SOFTWARE

- RealTime_PCR Software;

Registration and interpretation of the reaction results are carried out automatically using the Real-Time PCR software for Real time PCR instruments of the «DT» series manufactured by «DNA-Technology».



	Test name	Cp	Lg	Result
	Sample_1			
A1	Meyerozyma guillier…	-	-	-
	IC	30.8	4.2	
B1	Candida albicans	-	-	-
	IC	30.6	4.2	
	Pichia kudriavzevii (…	35.8	3.2	+
C1	Saccharomyces cer…	34.5	3.5	+
	IC	30.2	4.3	
	Marker	-	-	
	Candida auris	-	-	-
D1	Candida tropicalis	37.9	2.5	+
	IC	30.3	4.3	
	Clavispora lusitania…	-	-	-
E1	Debaryomyces han…	-	-	-
	IC	30.4	4.3	
	Candida dubliniensis	-	-	-
F1	Candida glabrata	-	-	-
	IC	30.8	4.2	
	Candida parapsilosis	-	-	-
G1	Malassezia spp	42.6	1.2	-
	IC	30.9	4.2	
	Malassezia furfur	-	-	-
H1	Kluyveromyces mar…	-	-	-
	SIC	41.0	1.2	-

An example of the result of a PCR-assay using the «DT» series real-time PCR instrument and related software: analysis of optical measurements.

AN EXAMPLE OF THE RESULTS FORM

MycosoScreen

Data:
Tube number:
Patient:
Sex:
Age:
Physician:
Comment:

Sample ID:

logotype

information about laboratory

№	Test name	Result
1	*Meyerozyma guilliermondii (C. guilliermondii)*	not detected
2	*Candida albicans*	not detected
3	*Pichia kudriavzevii (C. krusel)*	DETECTED **(5,6 Lg)**
4	*Saccharomyces cerevisiae*	not detected
5	*Candida auris*	not detected
6	*Candida tropicalis*	not detected
7	*Clavispora lusitaniae (C. lusitaniae)*	not detected
8	*Debaryomyces hansenii (C. famata)*	not detected
9	*Candida dubliniensis*	not detected
10	*Candida glabrata*	not detected
11	*Candida parapsilosis*	not detected
12	*Malassezia spp.*	not detected
13	*Malassezia furfur*	not detected
14	*Kluyveromyces marxianus (C. kefyr)*	not detected
15	SIC	not detected

Study was carried out by:

Data:
Signatyre:

Results Form of MycosoScreen PCR analysis was obtained using a real-time PCR instrument of the «DT» series and related software.

TRANSPORT AND STORAGE CONDITIONS

The kit must be stored at temperatures from 2 °C to 8 °C during the storage period.

Transportation is allowed in thermoboxes with ice packs by all types of roofed transport at temperatures from 2 to 25 °C but no more than 5 days.

REFERENCES

1. Ostreikov I.F., Melnikova N.I., Babaev B.D., Shtatnov M.K. Fungal infection in children with surgical pathology in the ICU. Anesthesiology and Resuscitation. —2017. — V. 62. — No. 4. — P. 310-315.

2. Bell S.G. Micafungin. Neonatal network // J. National Nurs. — 2011. — V. 30 (5). — P. 329-333.

3. Meersseman W., Lagrou K., Maertens J., Wilmer A., Hermans G., Vanderschueren S., et al. Galactomannan in bronchoalveolar lavage fluid: a tool for diagnosing aspergillosis in Intensive Care Unit patients // Am. J. Respir. Crit. Care Med. — 2008. — V. 177. — P. 27–34.

4. Berezhnova I.A. Infectious Diseases: Textbook. // M.: RIOR. — 2007. — P. 319.

5. Bogdanova T.V., Elinov N.P. Physiological characteristics of yeast organisms — Malassezia species (Malassez, 1874) Bailon, 1889 (review) // Problems of Medical Mycology. — 2011. — V. 13. — No. 1. — P. 3–13.

6. Rodchenko Yu.V., Priputnevich T.V., Zubkov V.V. Malassezia furfur in neonatal intensive care units (literature review) // Problems of Medical Mycology. — 2019. — T. 21. — No. 3. — P. 9–12.

7. Sakharuk N.A. Candidiasis: etiology, clinic, diagnosis, treatment: [monograph] / N.A. Sakharuk, V.V. Kozlovskaya; Ministry of Health of the Republic of Belarus, Vitebsk State Medical University. — Vitebsk: [VSMU], 2010. — 191 P.

8. Magill S.S. et al. Changes in prevalence of health care–associated infections in U.S. hospitals // N Engl J Med. — 2018. — Vol. 379. — P. 1732–1744.

9. Wisplinghoff H. et. al. Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study external icon // Clin Infect Dis. — 2004. — V. 39 (3). — P. 309–317.

10. Kullberg B.J. et al. Invasive candidiasis // N Engl J Med — 2015. — Vol. 373. — P. 1445–1456.

11. Antonov A.G. Clinical guidelines for the prevention and treatment of fungal infections in newborns in the intensive care unit / Antonov A.G., Nikitina I.V., Mitrokhin S.D. // Neonatology: news, opinions, training. — 2013. — No. 2. — P. 80–88.

12. Nikitina I.V., Ionov O.V., Prikhodko N.A., Priputnevich T.V., Antonov A.G., Lyubasovskaya L.A., Kirtbaya A.R., Balashova E.N., Zubkov V .V., Degtyarev D.N. Invasive mycoses in neonatology: prevention, diagnosis and therapy. // Obstetrics and gynecology. - 2015. - No. 4. - P. 84–90.

13. Prikhodko N.A., Priputnevich T.V., Nikitina I.V., Ionov O.V., Lyubasovskaya L.A., Antonov A.G., Degtyarev D.N. The use of the drug micafungin in the treatment of invasive candidiasis in premature infants in the neonatal intensive care unit. // Neonatology. — 2015. — No. 4. — P. 84–90.

14. Austin N. Prophylactic systemic antifungal agents to prevent mortality and morbidity in very low birth weight infants / N. Austin, W. Guire // Cochrane Database Syst. Rev. — 2013. — CD003850.

15. Barton M. Invasive candidiasis in low birth weight preterm infants: risk factors, clinical course and outcome in a prospective multicenter study of cases and their matched controls / M. Barton // BMC Infect. Dis. — 2014. — № 14. — P. 327.

16. Greenberg R.G., Benjamin D.K., Gantz M.G., Cotton C.M., Stoll B.J., Walsh M.C. et al. Empiric Antifungal Therapy and Outcomes in Extremely Low Birth Weight Infants with Invasive Candidiasis. // J Pediatr. — 2012. — V. 161. — P. 264–269.

17. Hope W.W. ESCMID guideline for the diagnosis and management of Candida diseases 2012: prevention and management of invasive infections in neonates and children caused by Candida spp / W.W. Hope [et al.] // Clin. Microbiol. Infect. — 2012. — V. 18 (7). — P. 38–52.

18. Hospenthal D.R. Diagnosis and treatment of human mycoses / D.R. Hospenthal, M.G. Rinaldi. — 2013. — P. 16–18.

19. Klingspor L. et al. Invasive Candida infections in surgical patients in intensive care units: a prospective, multicentre survey initiated by the European Confederation of Medical Mycology (ECMM) (2006–2008) // Clin Microbiol Infect. — 2015. — Vol. 21. — Issue 1. — P. 1–87.

20. Cortegiani A., et al. Epidemiology, clinical characteristics, resistance, and treatment of infections by Candida auris. // J Intensive Care. — 2018. — Vol. 6. — No. 69. — P. 13.

21. Jeffery-Smith A., et al. Candida auris: a Review of the Literature // Clin Microbiol Rev. — 2017. — Vol. 31. — Issue 1. — e00029–17.

22. Leon C. et al. Contribution of Candida biomarkers and DNA detection for the diagnosis of invasive candidiasis in ICU patients with severe abdominal conditions // Crit Care. — 2016. — Vol. 20. — P. 149–163.

23. Lone S. A., Ahmad A. Candida auris — the growing menace to global health // Mycoses. — 2019. — Vol. 62. — Issue 8. — P. 620–637.

24. Welsh R.M., et al. Survival, persistence, and isolation of the emerging multidrug–resistant pathogenic yeast Candida auris on aplastic healthcare surface // J Clin Microbiol. — 2017. — Vol. 55. — Issue 10. — P. 2996–3005.

25. Deorukhkar S. C. Non–albicans Candida Infection: An Emerging Threat // Interdisciplinary Perspectives on Infectious Diseases. — 2014. — Vol. 2014. — Article ID 615958.

26. Spampinato C. and Leonardi D. Candida Infections, Causes, Targets, and Resistance Mechanisms: Traditional and Alternative Antifungal Agents // BioMed Research International. — 2013. — Vol. 2013. — Article ID 204237.

27. Gamaletsou M. N. et al. Candida Osteomyelitis: Analysis of 207 Pediatric and Adult Cases (1970–2011 // Clinical Infectious Diseases. — 2012. — Vol. 55. — Issue 10. — P. 1338–1351.

28. Kothavade R.J. et al. Candida tropicalis: its prevalence, pathogenicity and increasing resistance to fluconazole // J Med Microbiol. — 2010. — Vol. 59 (Pt 8). — P. 873–880.

29. Abbas J. et al. Candida krusei Fungemia An Escalating Serious Infection in Immunocompromised Patients // Arch Intern Med. — 2000. — Vol. 160. — Issue 17. — P. 2659–2664.

30. Forastiero A. et al. Rapid Development of Candida krusei Echinocandin Resistance during Caspofungin Therapy // Antimicrob Agents Chemother. — 2015. — Vol. 59. — No 11. — P. 6975–6982.

31. Gong J. et al. Genetic Differentiation, Diversity, and Drug Susceptibility of Candida krusei // Front. Microbiol. — 2018. — Vol. 9. — Article 2717.

32. Espinosa–Heidmann D.G. Candida dubliniensis endophthalmitis: first case in North Americ // International Ophthalmology. — 2012. — Vol. 32. — Issue 1. — P. 41–45.

33. Wahab A.A. et. al. High prevalence of Candida dubliniensis in lower respiratory tract secretions from cystic fibrosis patients may be related to increased adherence properties / International Journal of Infectious Diseases. — 2014. — Vol. 24. — P. 14–19.

34. Wahab A.A. et. al. Persistence of Candida dubliniensis and lung function in patients with cystic fibrosis // BMC Res Notes. — 2017. — Vol. 10. — Issue. 1. — P. 326–331.

35. Pfaller M. A. et al. Candida guilliermondii, an opportunistic fungal pathogen with decreased susceptibility to fluconazole: geographic and temporal trends from the ARTEMIS DISK antifungal surveillance program // J Clin Microbiol. — 2006. — Vol. 44. — Issue 10. — P. 3551–3556.

36. Pfaller M. A. et al. Epidemiology and outcomes of invasive candidiasis due to non–albicans species of Candida in 2,496 patients: data from the Prospective Antifungal Therapy (PATH) registry 2004–2008 // PLoS One. — 2014. — Vol. 9. — Issue 7. — e101510.

37. Antonov A.G. et al. Treatment of fungal infection in very premature babies // Ros. Vestn. Perinatol. Pediat. — 2012. — No. 5. — P. 13–17.

38. Machulin A.I. Diagnosis and treatment of chronic adenoiditis of fungal etiology in children: dissertation ... candidate of medical sciences: 14.01.03 / Machulin Alexey Ivanovich; [Place of protection: State Health Institution “Moscow Scientific and Practical Center of Otorhinolaryngology”]. — Moscow, 2013. — 108 P.: ill.

39. Beyda N.D. et al. Treatment of Candida famata bloodstream infections: case series and review of the literature // Journal of Antimicrobial Chemotherapy. — 2013. — Vol. 68. — Issue 2. — P. 438–443.

40. Prinsloo B. et al. Candida famata central nervous system infection // S Afr Med J. — 2003. —Vol. 93. — Issue 8. — P. 601–602.

41. Baymuratova M.A. Dominant role of candida-infections in various inflammatory infectious processes of the human body // Vestnik AGIUV. — 2012. — No. 4. — P. 30–32.

42. Blokhina E.V. Candidemia in hemoblastoses: dissertation ... candidate of medical sciences: 14.01.21 / Blokhina Elena Valerievna; [Place of defence: Federal State Budgetary Institution "Hematological Research Center" of the Ministry of Health of Russia]. — Moscow, 2015. — 130 P..

43. Popova A.L. et al. Modern aspects of treatment and prevention of vulvovaginal candidiasis (literature review) // Vyatskiy Medical Bulletin. — 2013. — No. 4. — P. 31–36.

44. Papon N. et al. Emerging and Emerged Pathogenic Candida Species: Beyond the Candida albicans Paradigm // PLoS Pathog. — 2013. — Vol. 9. — No 9. — e1003550

45. Rhodes J., Fisher M. C. Global epidemiology of emerging Candida auris // Current Opinion in Microbiology. —2019. — Vol. 52. — P. 84–89.

46. Rossato L. and Colombo A. L. Candida auris: What Have We Learned About Its Mechanisms of Pathogenicity? //Front Microbiol. — 2018. — Vol. 9. — Article 3081.

47. Snyder G.M., Wright S.B. The Epidemiology and Prevention of Candida auris // Curr Infect Dis Rep. —2019. — Vol. 21. — No. 6. — P. 19.

48. Chumicheva I.V. Oropharyngeal candidiasis in children: dissertation ... candidate of medical sciences: 14.00.04 / Chumicheva I.V.; [Place of defence: State institution "Scientific and clinical center of otorhinolaryngology"]. — Moscow, 2004. — 161 P.: ill.

49. Cuenca-Estrella M. et al. ESCMID guidelines for the diagnosis and management of Candida diseases 2012: diagnostic procedures // Clinical Microbiol Infect. — 2012. — Vol. 18. — Suppl. 7. — P. 9–18.

50. Papaemmanouil V. et al. Prevalence and susceptibility of Saccharomyces cerevisiae causing vaginitis in Greek women // Anaerobe. — 2011. — Vol. 17. — Issue 6. — P. 298–299.

51. Piseth S. et al. Saccharomyces cerevisiae osteomyelitis in an immunocompetent baker // IDCases. — 2016. — Vol. 5. — P. 1–3.

52. Popiel K. Y. Invasive Saccharomyces cerevisiae in a liver transplant patient: case report and review of infection in transplant recipients // Transpl Infect Dis. — 2015. — Vol. 17. — Issue 3. — P. 435–441.

53. Rana S. Spectrum of Misdiagnosis of Allergic Bronchopulmonary Mycosis: Case Reports // J Assoc Chest Physicians. — 2018. — Vol. 6. — P. 21–25.

54. Arendrup M.C. et al. ESCMID and ECMM joint clinical guidelines for the diagnosis and management of rare invasive yeast infections // Clinical Microbiology and Infection. — 2013. — Vol. 20. — Suppl. 3. — P. 76–98.

55. Bachurskaya N.S. et al. Modern problems of the biology of fungi of the genus Malassezia // Vestnik OSU. —2007. — No. 12. — P. 8–17.

56. Gaitanis G. et al. The Malassezia Genus in Skin and Systemic Diseases // Clinical Microbiology Reviews. — 2012. — Vol. 25. — No 1. — P. 106–141.

57. Blumberg, H.M., Jarvis, W.R., Soucie, J.M. et al. Risk factors for candidal bloodstream infections in surgical intensive care unit patients: the NEMIS prospective multicenter study. The National Epidemiology of Mycosis Survey // Clin Infect Dis. — 2001. — Vol. 33. — P. 177–86.

58. Brand A. Hyphal Growth in Human Fungal Pathogens and Its Role in Virulence // International Journal of Microbiology. — 2012. — Vol. 2012. — Article ID 517529.

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DNA-Technology LLC
125 Zh, Varshavskoye Highway, bld. 6, Moscow, Russia
Phone/Fax: +7 (495) 640-17-71
www.dna-technology.com, info@dna-technology.com

CUSTOMER SUPPORT:
Phone/Fax: +7 (495) 640-17-71
hotline@dna-technology.ru