Medical Mycology I.

7. 5. 2026
2. LF UK

1. Fungi – characteristics important in medical mycology
2. Fungal taxonomy and medical mycology
3. Pathogenicity factors in fungi
4. Classification of fungal diseases
5. Antifungals
6. Dermatophytes

Fungi

Regnum, eucaryotic

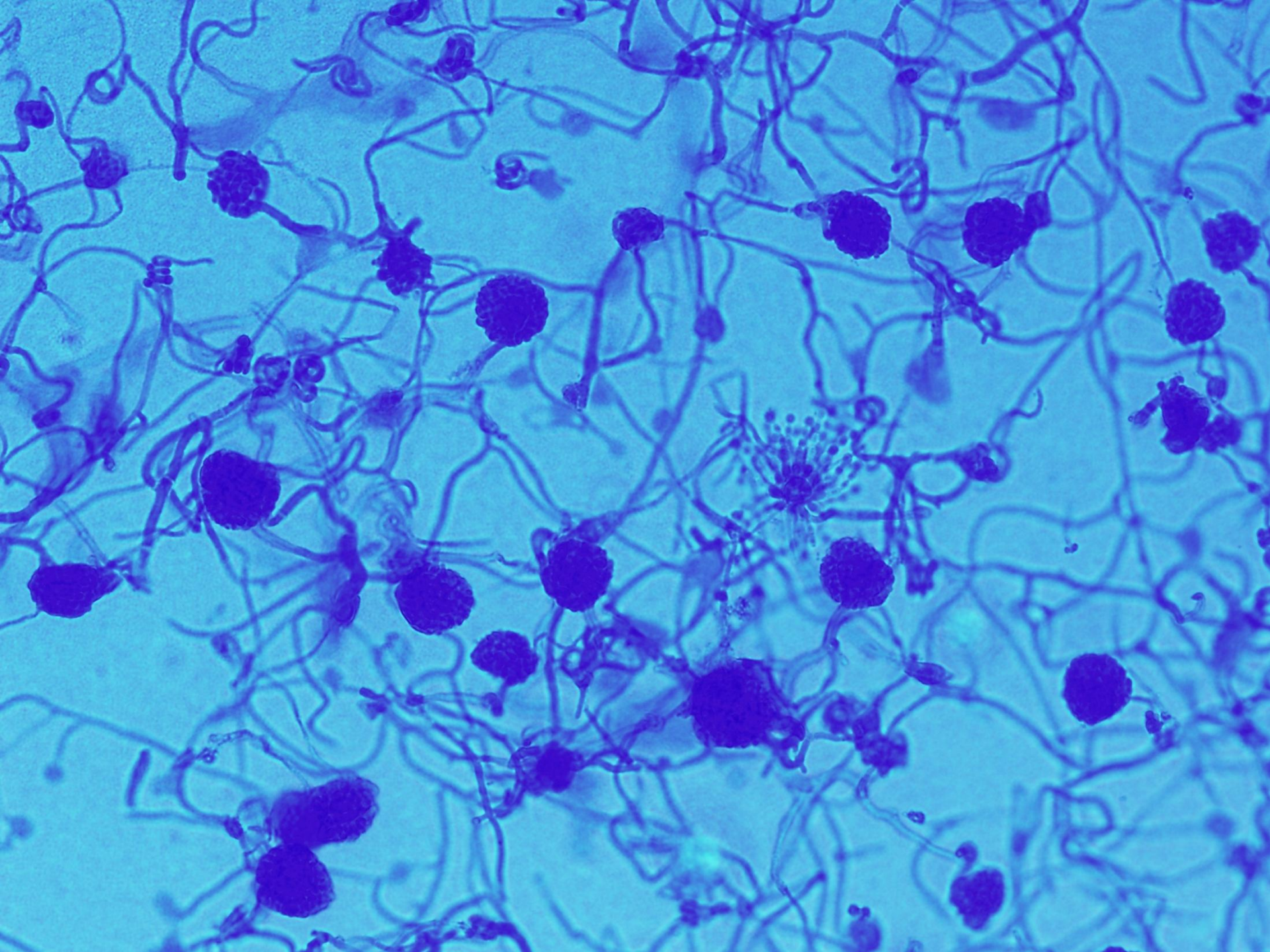
Heterotrophic metabolism – saprophytes, parasites

Unicellular: yeast, multicellular: Hyphae ➡ thallus

Cell wall – **chitin**, polysaccharides (**beta-D-glucan, galactomannan, mannan**)
Cell membrane - **ergosterole**

Replication – sexual, parasexual, asexual

Sexual (**teleomorph**) and asexual (**anamorph**) forms described in some species – differences in morphology, ecology, virulence



Fungi as human pathogens

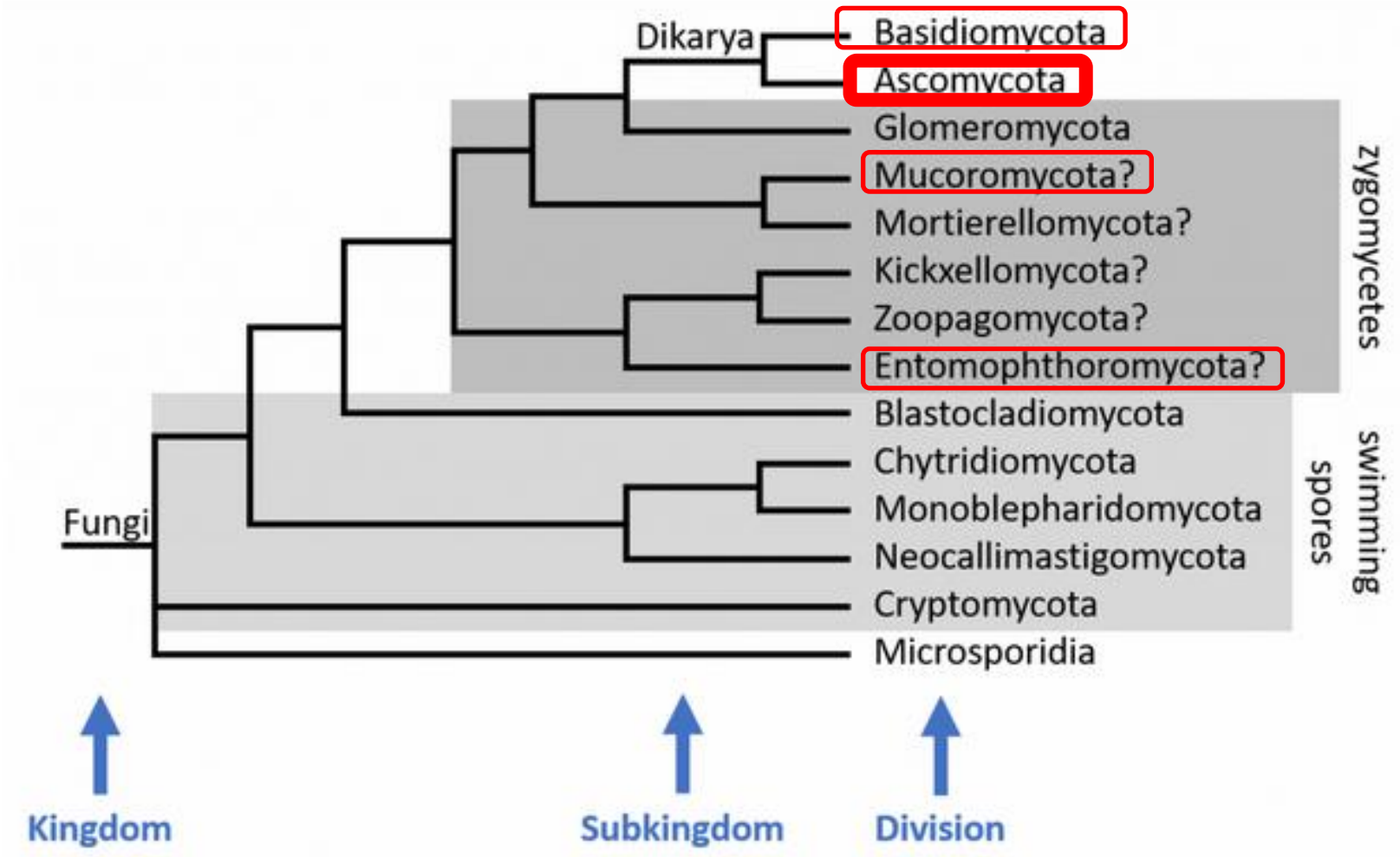
6,28 million species worldwide estimated, 10 000 species in Czechia (Institute of Microbiology, Czech Academy of Science – estimation 2021)

Proven human pathogens
300 – 500 species, most other species have the potential

Low number of species highly adapted to human organism prevail among fungal pathogens

Asexual forms (anamorphs) more frequently pathogenic

Fungal taxonomy and medical mycology



https://www.fungusfactfriday.com/011-fungi/

Fungal names in medicine

Classification of fungi based on phenotypic characteristics

↓

Different forms – different taxon names

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Genome sequencing, finding the same genome in different forms

↓

Connecting different forms under one taxon name – the name of sexual form (teleomorph) is further valid

↓

„New“ names of well known pathogens (previously known under anamorph name)
How to deal with this?

de Hoog S et al. A conceptual framework for nomenclatural stability and validity of medically important fungi: a proposed global consensus guideline for fungal name changes supported by ABP, ASM, CLSI, ECMM, ESCMID-EFISG, EUCAST-AFST, FDLC, IDSA, ISHAM, MMSA, and MSERGC, J Clin Microbiol 2023 10.1128/jcm.00873-23

WHO Fungal Priority Pathogens list (2022)

Critical group	High group	Medium group
Cryptococcus neoformans	*Nakaseomyces glabrata (Candida glabrata)*	*Scedosporium* spp.
Candida auris	*Histoplasma* spp.	*Lomentospora prolificans*
Aspergillus fumigatus	Eumycetoma causative agents	*Coccidioides* spp.
Candida albicans	Mucorales	*Pichia kudriavzeveii (Candida krusei)*
	Fusarium spp.	*Cryptococcus gattii*
	Candida tropicalis	*Talaromyces marneffei*
	Candida parapsilosis	*Pneumocystis jirovecii*
		Paracoccidioides spp.

https://iris.who.int/bitstream/handle/10665/363682/9789240060241-eng.pdf?sequence=1

Pathogenicity factors in fungi

Thermotolerance – growth and multiplication in human body temperature

Dimorphism

- Ability to change between yeast (invasive) and filamentous form under different conditions
- Primary (endemic) fungal pathogens

How does environment influence pathogenicity in fungi?

Climate change
•Enhanced thermotolerance, new pathogens - ***Candida auris***
•Change in occurence of known pathogens – *Coccidioides*, USA

Weather variability, disasters – adaptation to stress
•Enhanced virulence, easier spread
•Opportunistic infections after major trauma

Antifungal resistance of environmental origin
•Azoles – fungicides in agriculture – azole resistant ***Aspergillus fumigatus***

Environment-associated changes in human
UV radiation – immune response – skin, T lymphocytes, cytokines, complement
Infection treatment and prevention – lower average temperature in human population

Antifungals

Antifungal effect **in vivo** in human (eukaryotic!) organism

Low number of targeted structures

Toxicity, interactions, increasing resistance

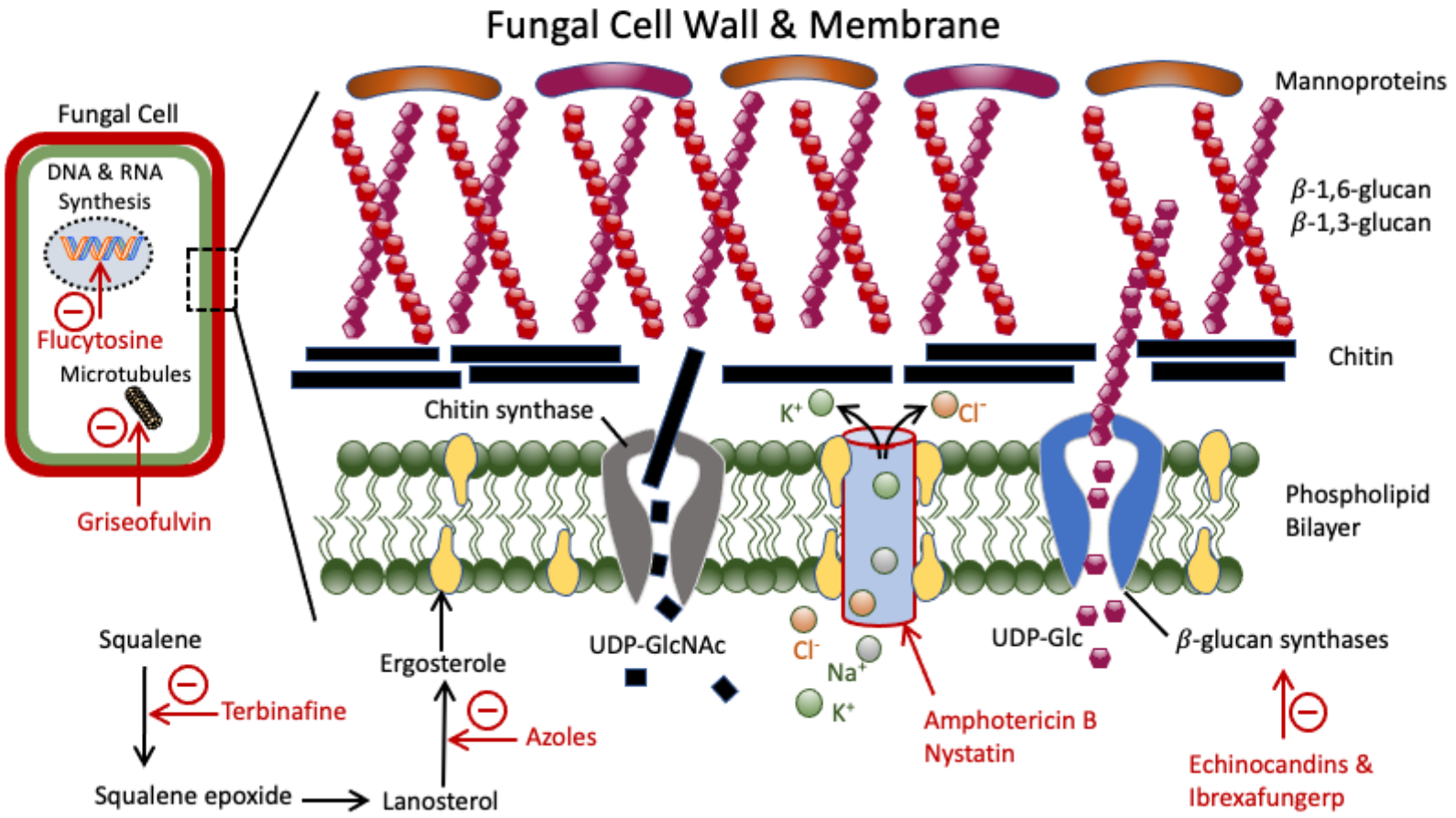
Fungicidal/fungistatic effect – different in different fungal species

Targeted structures/processes	
Cell wall	echinocandins, ibrexafungerp
Cytoplasmatic membrane	polyenes, azoles, terbinafin
Mikrotubules	griseofulvin
Nucleic acid synthesis	5 – fluorocytosin

Antifungals – mechanism of action

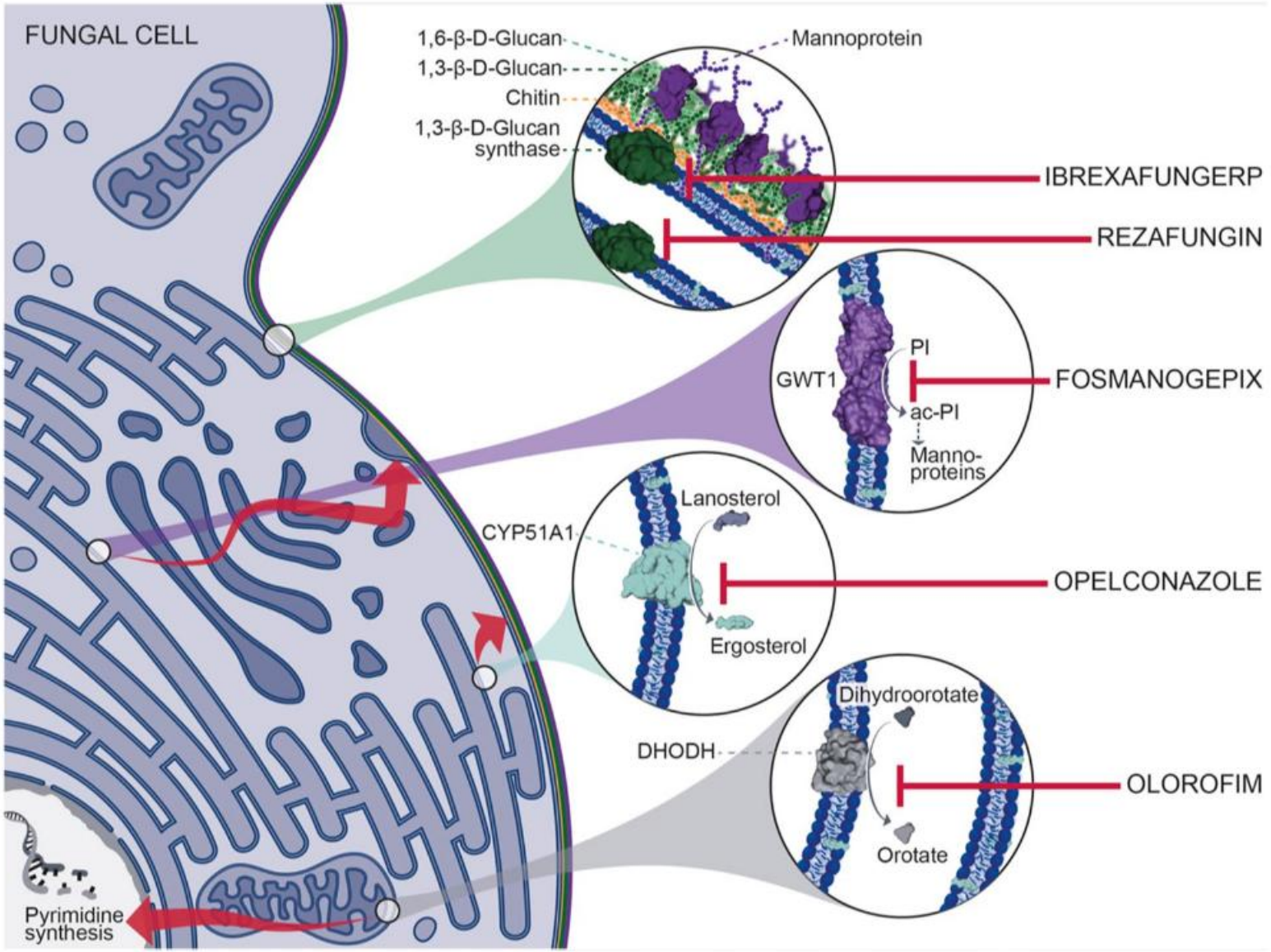
Antifungal Molecular Targets

Antifungal Sites of Action



https://tmedweb.tulane.edu/pharmwiki/doku.php/all_antifungals

New antifungals – mechanism of action



Hoenigl M et al. Drugs (2021) 81:1703–1729

Echinocandins

Caspofungin, micafungin, anidulafungin, rezafungin

Inhibit beta-D-glucan (cell wal polysaccharide) synthesis
Enzyme **beta-D-glucan-synthase**

- Fungicidal effect – *Candida*
- Fungistatic effect – aspergilli
- No effect – Mucorales, cryptococci

Acquired resistance

- ***Candida* sp.** - mutation in FKS gene coding catalytic subunit of β-1,3-d-glucan synthase
- Long-term echinocandidn exposition (prophylaxis, treatment)

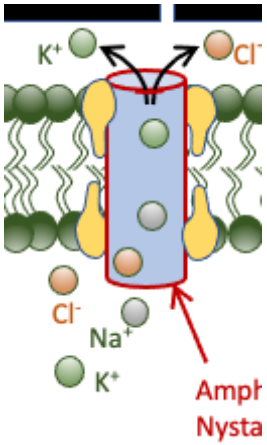
- Minimal adverse effects

Healey KR, Perlin DS. Fungal resistance to echinocandins and the MDR phenomenon in Candida glabrata. J Fungi. 2018;4(3):105.
https://tmedweb.tulane.edu/pharmwiki/doku.php/all_antifungals
Cornely O et al. Lancet Infect Dis 2025;25: e280–93

Polyenes

Amphotericin B (systemic)
- Amphotericin B deoxycholate (D-AMB)
- Amphotericin B lipid complex (ABLC)
- Amphotericin B liposomal (L-AMB)

Nystatin – topical



Mechanism of action

Binds directly to ergosterole in cell membrane, pore forming, cell death

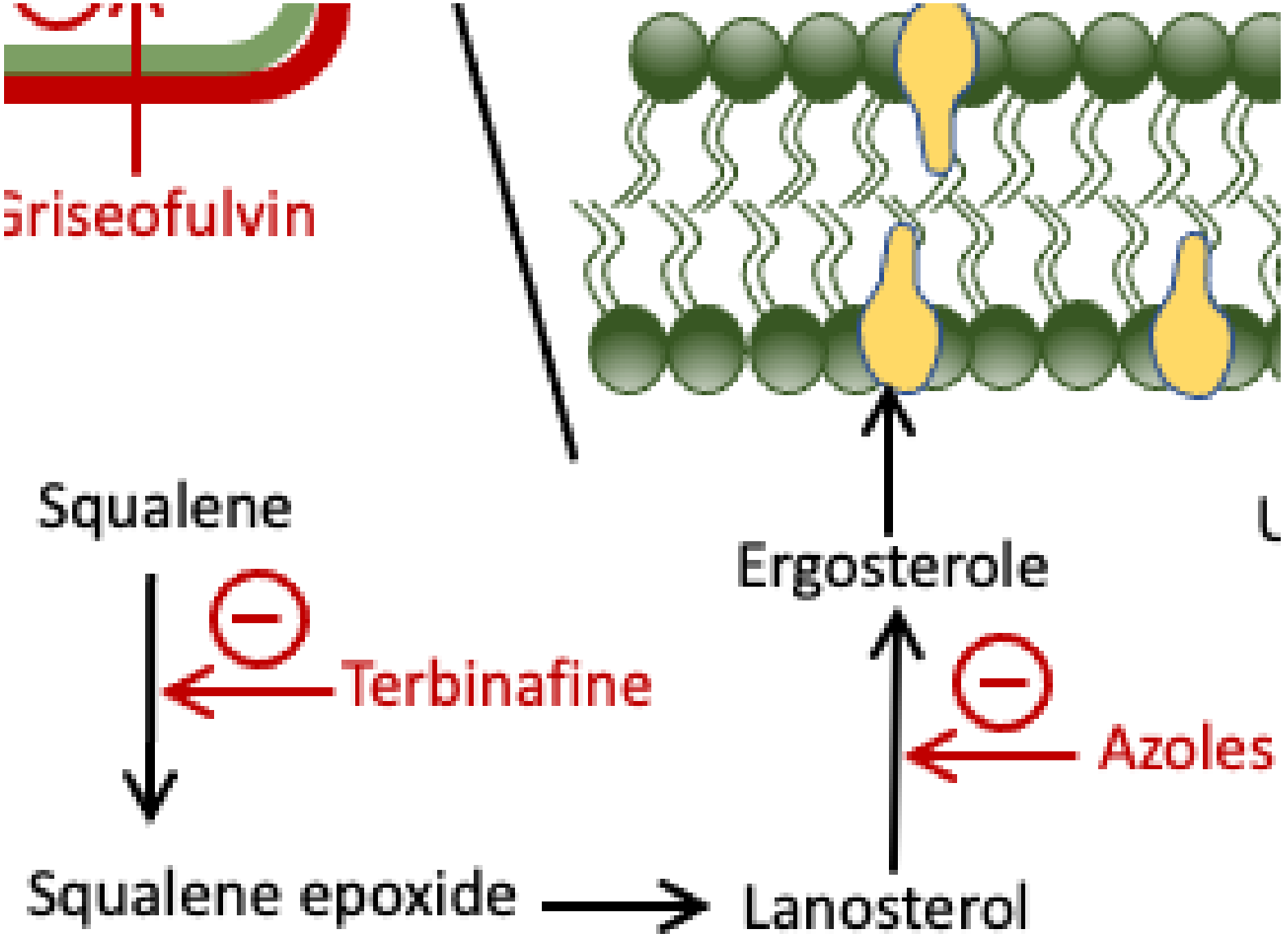
Indications
- **Mucormycosis**
- **Disseminated cryptococcosis** (+5-FC)
- **Azole resistant aspergillosis**

Resistance – primary in some molds, acquired rare (*C. auris*)

Adverse effects – similarity of ergosterole and cholesterole molecules
- Infusion administration acute reaction – fever, chills, seizure, vomiting, hypotension
- Renal tubular acidosis, hypocalemia, hypomagnesemia

https://tmedweb.tulane.edu/pharmwiki/doku.php/all_antifungals
Lancet Infect Dis. 2019 December ; 19(12): e405–e421. doi:10.1016/S1473-3099(19)30312-3
Chang CC et al. Lancet Infect Dis February 9, 2024, https://doi.org/10.1016/S1473-3099(23)00731-4

Ergosterole synthesis inhibitors



https://tmedweb.tulane.edu/pharmwiki/doku.php/all_antifungals

Azoles

Imidazoles – topical

Triazoesy – systemic treatment

- **Fluconazole**
- **Itraconazole**
- **Voriconazole**
- **Posaconazole**
- **Isavuconazole**

Mechanism of action

- Ergosterole synthesis inhibition
- Enzyme **lanosterole-14α-demethylase** (gene ERG11 – *Candida, Cryptococcus*, gene CYP51A – *Aspergillus*)

Azoles

Fluconazole

Indications
Disseminated cryptococcal infection – consolidation, maintenance
Invasive candidiasis
•targeted therapy, susceptible strains
•UTI, ocular, intracranial candidiasis
Mucosal/mucocutaneous candidiasis, esophagitis - systemic therapy

No effect in moulds

Adverse effects – rare severe hepatotoxicity cases

TDM available, not essential in most situations

Resistance
•Primary - *Candida krusei* and related species (*Pichia*)
•Acquired – *Candida parapsilosis* (significant epidemiological threat!)*, C. tropicalis*

https://tmedweb.tulane.edu/pharmwiki/doku.php/all_antifungals
Arastehfar A et al. Antibiotics 2020, 9, 877
Cornely O et al. Lancet Infect Dis 2025;25: e280–93
Chang CC et al. Lancet Infect Dis February 9, 2024, https://doi.org/10.1016/S1473-3099(23)00731-4

Azoles

Voriconazole

1st choice – invasive aspergillosis
No effect in Mucorales

Adverse effects
- Reversible vision impairment
- Hepatotoxicity
- Fotosensibility
- Severe cutaneous hypersensitivity
- Dysrrhythmia, QTc interval elongation
- Neuropsychiatric AE

TDM obligatory

Acquired resistance
- *Candida sp*. frequently associated with fluconazole
- *Aspergillus fumigatus* – ARAF, environmental CYP51A mutations

https://tmedweb.tulane.edu/pharmwiki/doku.php/all_antifungals
Zhang J et al. Journal of Fungi 2021, 7, 599
Jeanvoine A et al. Médecine et maladies infectieuses 50 (2020) 389–395
Ullmann AJ et al. Clinical Microbiology and Infection 24 (2018) e1ee38

Azoles

Posaconazole

Alternative in aspergillosis and mucormycosis
Prophylaxis of mould infections in the immunocompromised

Isavuconazole

Alternative in aspergillosis and mucormycosis

Itraconazole

- Dermatophytosis
- Chronic pulmonary aspergillosis
- Endemic mycoses
- Mucosal and mucocutaneous candidiasis

Prophylaxis of mould infections in the immunocompromised

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Cornely O et al. Lancet Infect Dis. 2019 December ; 19(12): e405–e421. doi:10.1016/S1473-3099(19)30312-3
Ullmann AJ et al. Clinical Microbiology and Infection 24 (2018) e1ee38

Allylamines

Mechanism of action

Ergosterole synthesis inhibition - enzyme squalenepoxidase

Terbinafine

Dermatophytosis

Terbinafine resistance

- **Point mutations in squalenepoxidase gene**
- ***Trichophyton indotineae*** (*T. mentagrophytes/interdigitale* complex)
- ***Trichophyton rubrum***

5-fluorocytosin (flucytosin, 5-FC)

Mechanism of action

- Intracellular conversion to 5-fluorouracil – fungal cells, not human
- DNA and RNA synthesis inhibition

Disseminated cryptococcal infection

- Initial treatment (+L-AMB)
- Rapid resistance development – no monotherapy

Adverse effects

- Haematopoiesis impairment
- Hepatotoxicity

https://tmedweb.tulane.edu/pharmwiki/doku.php/all_antifungals

Chang CC et al. Lancet Infect Dis February 9, 2024, https://doi.org/10.1016/S1473-3099(23)00731-4

Antifungals - resistance

Resistance – **stable** genetic changes

Primary – all strains belonging to certain taxon

- Aspergilli – fluconazole
- Mucorales – voriconazole, echinocandins
- *Candida krusei* – fluconazole
- Cryptococci - echinocandins

Acquired – only some strains, adaptation to external conditions

- *Aspergillus fumigatus* – voriconazole, posaconazole, itraconazole, isavuconazole
- *Candida parapsilosis* – fluconazole
- *Candida* sp. – echinocandins
- *Candida auris* – azoles, amphotericin B, echinocandins

Tolerance – **unstable** genomic, epigenomic or physiological changes

Hoenigl M et al. Drugs (2021) 81:1703–1729

Fungi with acquired antifungal resistance of critical epidemiological significance

Candida auris

- Environmental origin, **thermotolerant**
- 5 different clades, **simultaneous global spread**
- Long-term survival – skin, surfaces
- Most strains resistant to fluconazole, acquired resistance – echinocandins, AmB

Fluconazole resistant *Candida parapsilosis*

- Human cutaneous microbiota
- Epidemics in healthcare settings, highly tolerant to environmental effects

Azole resistant *Aspergillus fumigatus* (ARAF)

Environmental mutations in CYP51A prevail
Fungicides, agriculture

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Zhang J et al. Journal of Fungi 2021, 7, 599
Jeanvoine A et al. Médecine et maladies infectieuses 50 (2020) 389–395

Human fungal diseases

Superficial fungal infections

Cutaneous and localized subcutaneous fungal infections

- **Dermatophytoses**
- Onychomycosis
- Chromoblastomycosis, mycetoma

Endemic mycoses

Opportunistic mycoses

- **Candidiasis**
- **Cryptococcosis**
- **Aspergillosis**
- **Mucormycosis**
- **Pneumocystis jirovecii pneumonia**

Primary human fungal pathogens

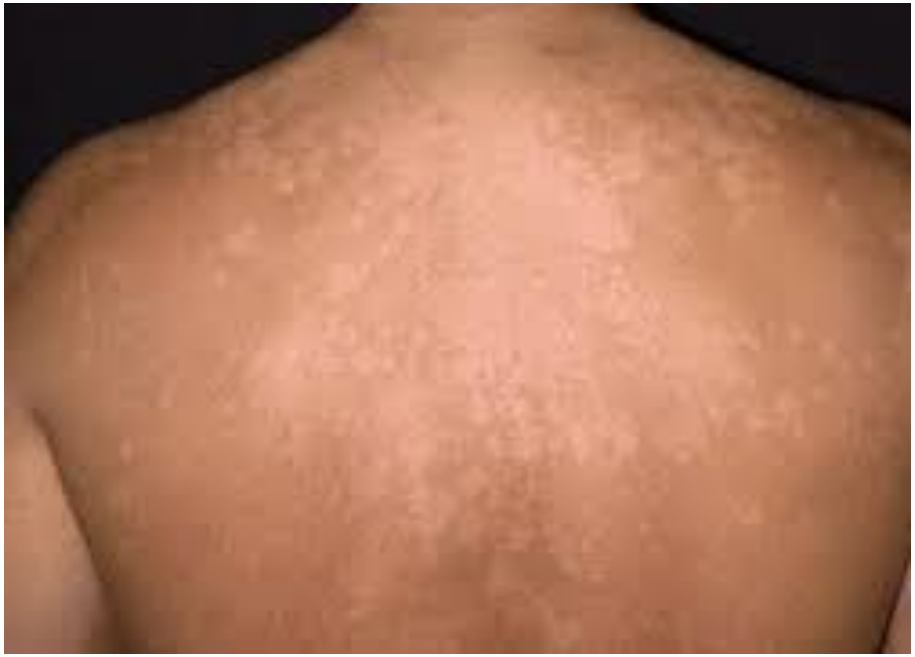
- *Blastomyces dermatitidis*
- *Coccidioides immitis, Coccidioides posadasii*
- *Histoplasma capsulatum*
- *Paracoccidioides brasiliensis*
- *Talaromyces marneffei*
- *Cryptococcus gattii*

- **Endemic systemic fungal infections**
- Americas, Asia, Africa - endemic
- Europe – imported cases

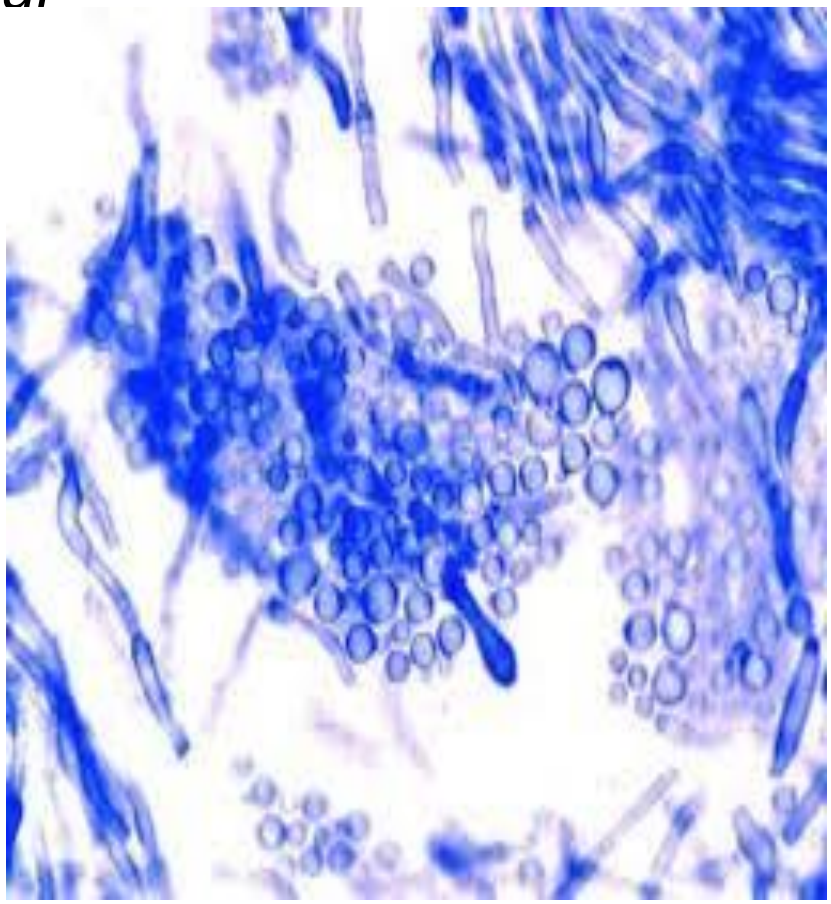
Superficial fungal infections

Superficial layers of skin and adnexa, minimal clinical significance

Pityriasis versicolor, *Malassezia furfur*



Merckmanuals.com



Link.springer.com

Cutaneous fungal infections

Dermatophytosis – caused by dermatophytes
Dermatomycosis – other fungal species (yeasts and environmental moulds)

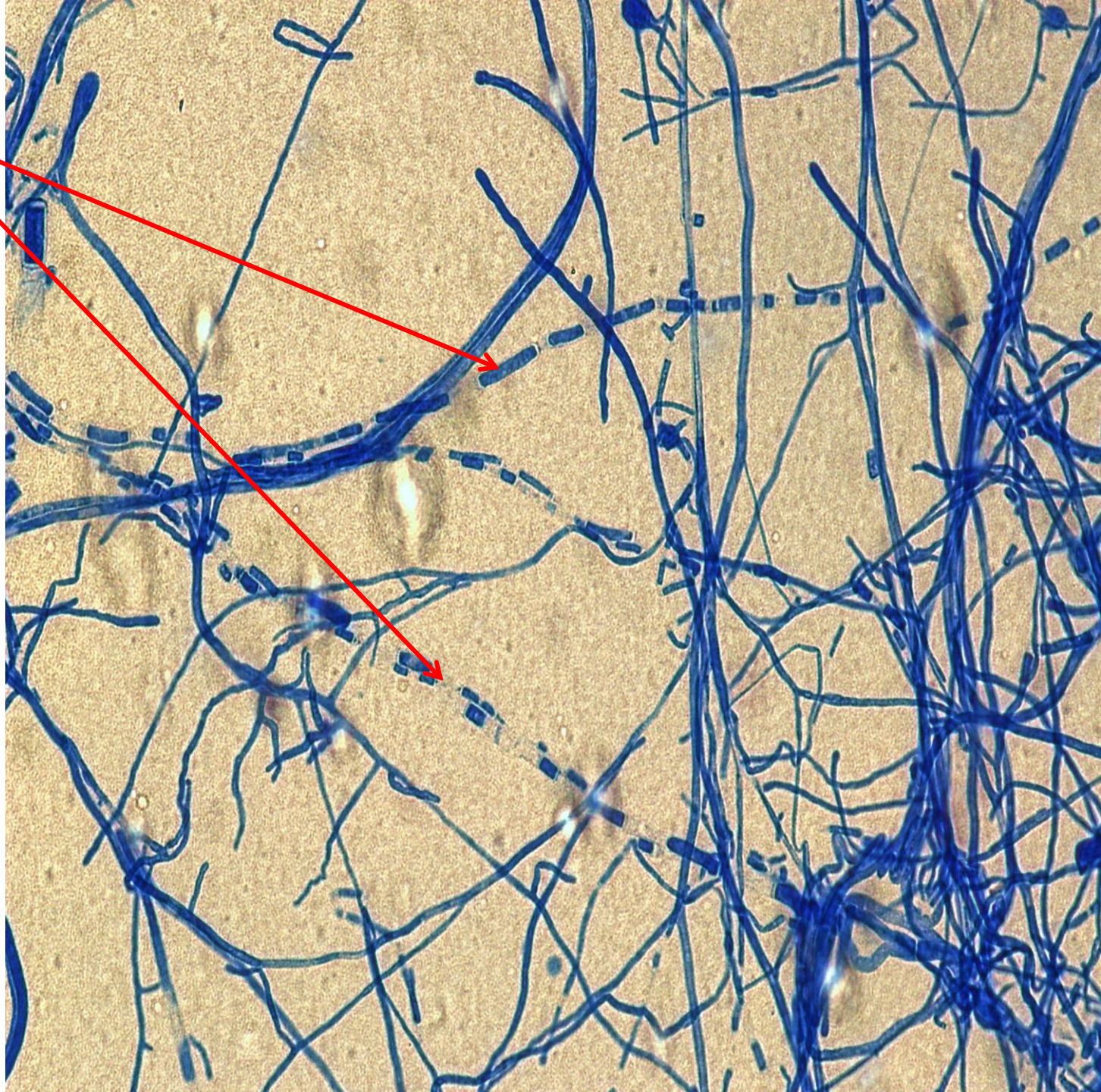
Dermatophytes
Keratinophilic, keratinolytic fungi

Temperature optimum 28 – 30 °C

Invade stratum corneum and keratinized layers of hair and nails
Name of disease - tinea + anatomic localisation

Infectious particles (propagules) – **arthroconidia – particles formed by breaking of the hyphae**
Transmitted by desquamated epidermal cells
Fomites, contaminated surfaces

Arthroconidia



Dermatophytes – ecology, epidemiology

Antropophilic – Adapted to human organism and interhuman transmission

- Chronic disease course
- Mild inflammatory reaction
- Difficult and long-lasting treatment

Trichophyton rubrum, *Trichophyton mentagrophytes/interdigitale* complex, *Trichophyton tonsurans*

Zoophilic – low adaptation to human and interhuman transmission – animal resource

- Acute disease course
- Severe inflammatory reaction
- Rapid response to therapy

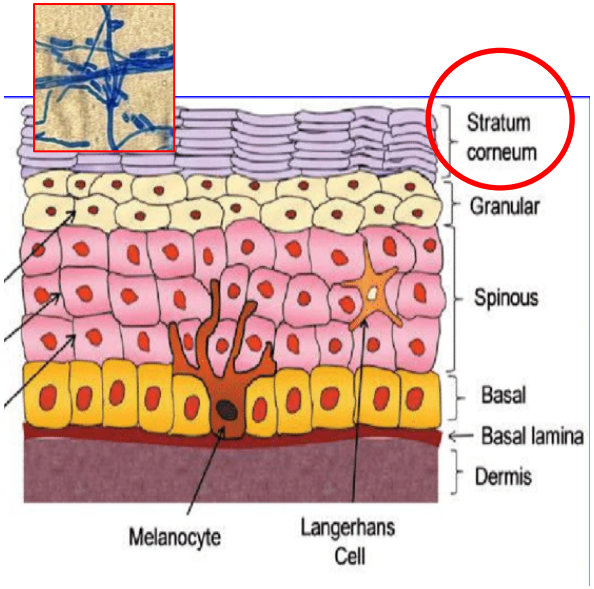
***Trichophyton mentagrophytes* complex**, *Trichophyton benhamiae*, *Microsporum* sp.

▪Geophilic – low adaptation to human and interhuman transmission, environmental source (soil)

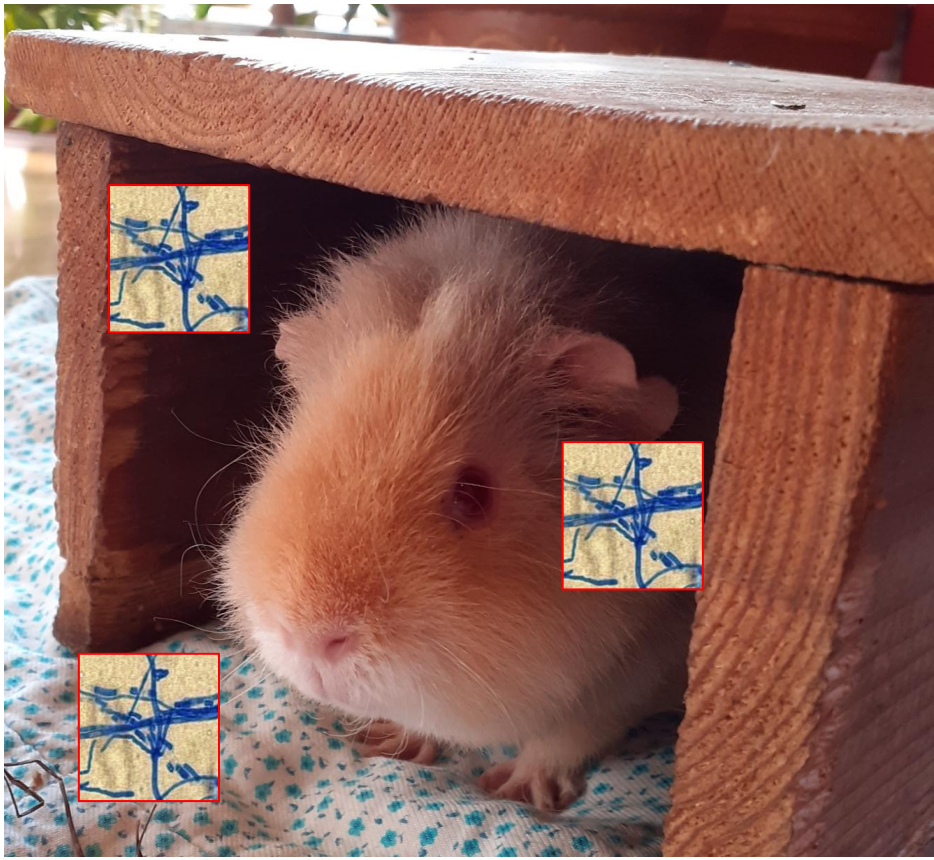
- Acute disease course, severe inflammatory reaction

Mycopathologia 185(1)2020

Anthropophilic dermatophytes Transmission

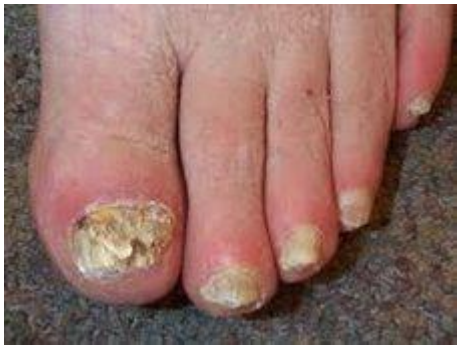


Zoophilic dermatophytes - transmission

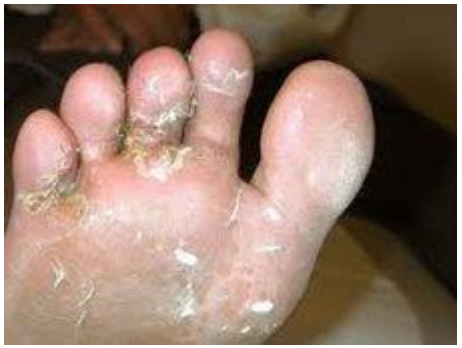


Dermatophytoses – clinical forms

Tinea unguium
dermnentz.org

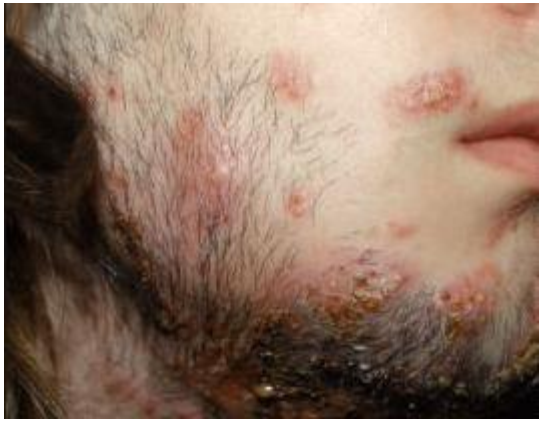


Tinea pedis
natural-health-news.com

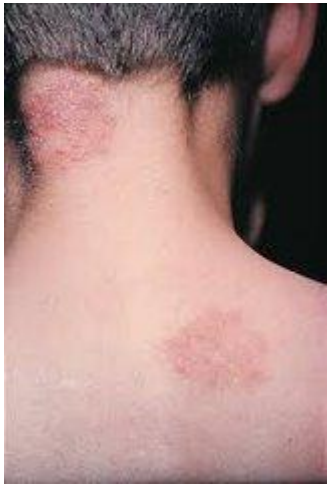


Tinea barbae

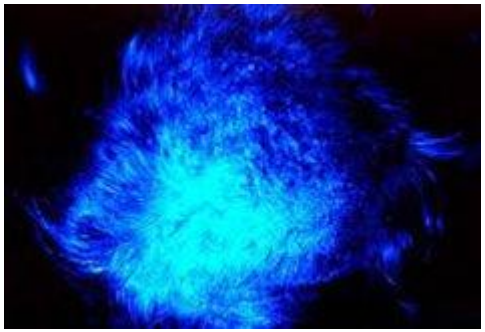
By Maddyportelli - Own work, CC BY-SA 4.0, https://commons.wikimedia.org/w/index.php?curid=48807927



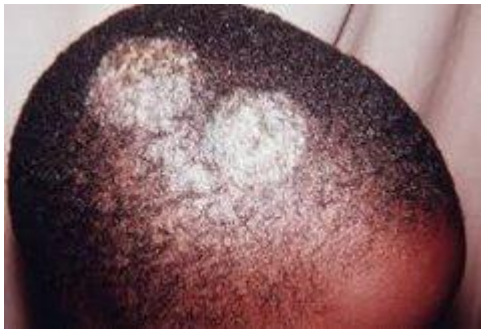
Tinea corporis
sciencedirect.com



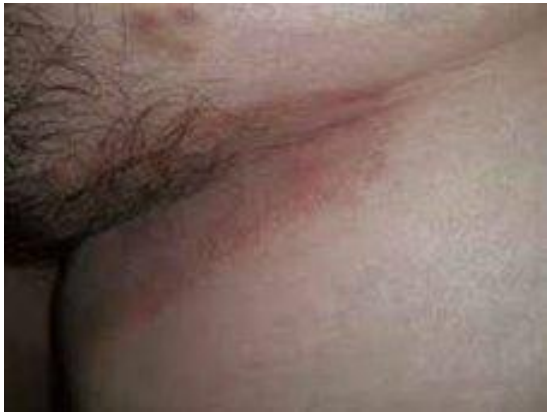
Tinea capitis
Woodova lampa
medscape



Tinea capitis
medicinenet.com



Tinea cruris
mitchmedical.us



Dermatophytoses - treatment

Local antifungals if one nail except 1st toenail affected

Other cases – systemic treatment

- **Terbinafin**
- **Itraconazole**

Minimum 4 weeks in zoophilic dermatophytes, if toenail affected – several months

Resistance to antifungals in dermatophytes

Trichophyton indotineae

- Anthropophilic, *Trichophyton mentagrophytes/interdigitale* complex
- Tinea corporis, cruris, faciei
- Terbinafin resistance - **point mutations in squalenepoxidase gene**
- Origin in Indian subcontinent, global spread including Czechia

Trichophyton rubrum

- Terbinafin resistance - **point mutations in squalenepoxidase gene**
- Global spread from Asia
- Not detected in Czechia (2021)

Kolarczyková D et al. Mycoses. 2024;67:e13708
Uhrlaß S et al. J. Fungi 2022, 8, 757.