

A microscopic image of fungi, likely Aspergillus, showing numerous hyphae and spores. The hyphae are long, thin, and branching, while the spores are smaller, oval-shaped structures. The entire image has a blue tint.

Medical Mycology I.

6. 10. 2025
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

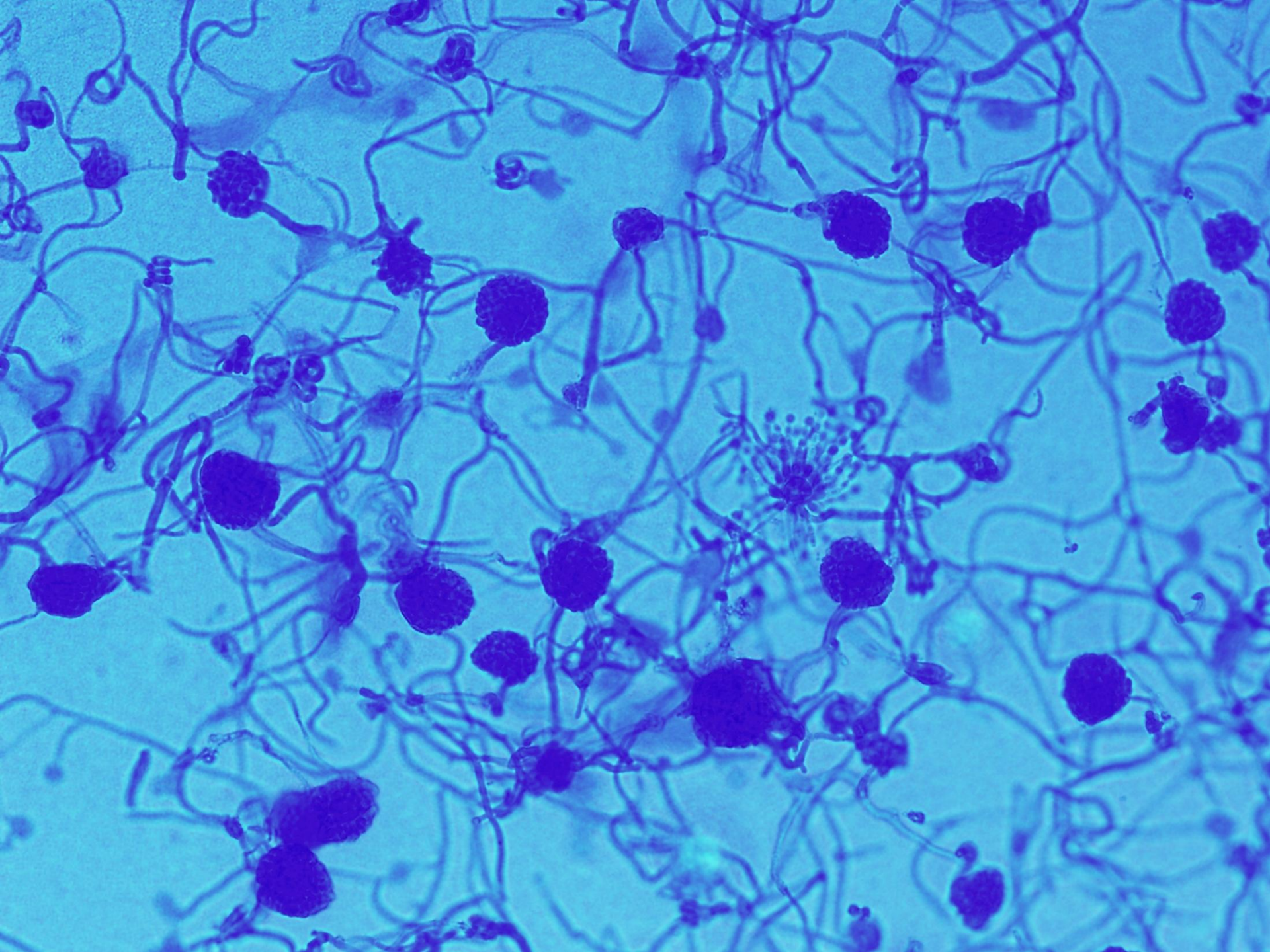
Unicellular: yeast, multicellular: Hyphae ➡ thallus

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

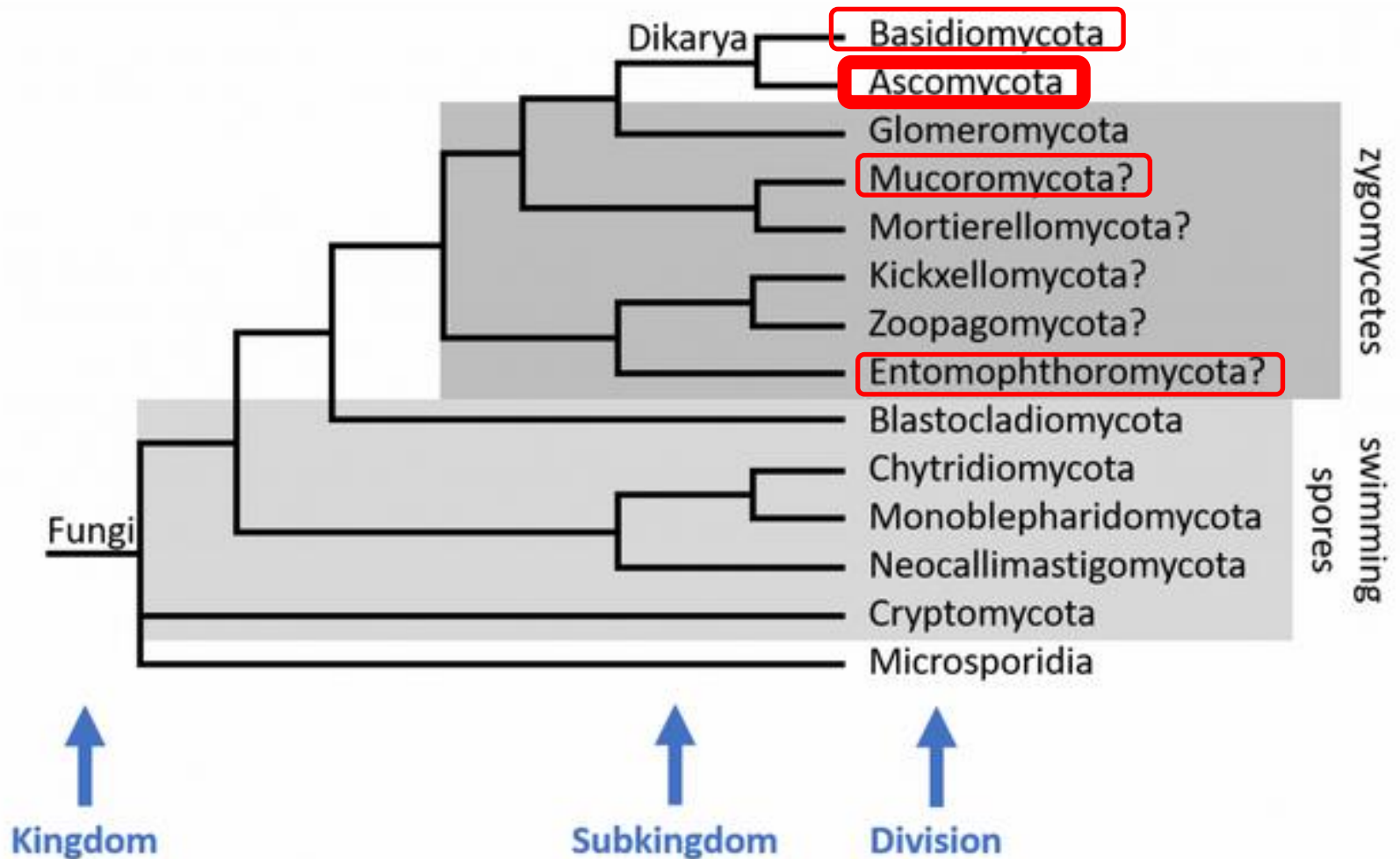
Cell membrane - **ergosterole**

Replication – sexual, parasexual, asexual

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



Fungal taxonomy and medical mycology



Fungal taxonomy in medicine

Classification of fungi based on phenotypic characteristics



Different forms – different taxon names



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?

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

WHO Fungal Priority Pathogens list (2022)

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

Climate change, environmental effects and pathogenicity potential in fungi

Thermotolerance

New human fungal pathogens

Candida auris

Weather variability

Adaptation to stress effects

Increased virulence, easier spread

Fungal plant pathogens

Fungicidal substances in agriculture

Antifungal resistance

***Aspergillus fumigatus*, azoles**

Changes in geographical spread of fungi

Changes in fungal diseases epidemiology

***Coccidioides*, USA**

Natural disasters

Effects of climate changes on humans – UV light – T lymphocytes, cytokines, complement

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

Antifungals

Substances able to harm fungi 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

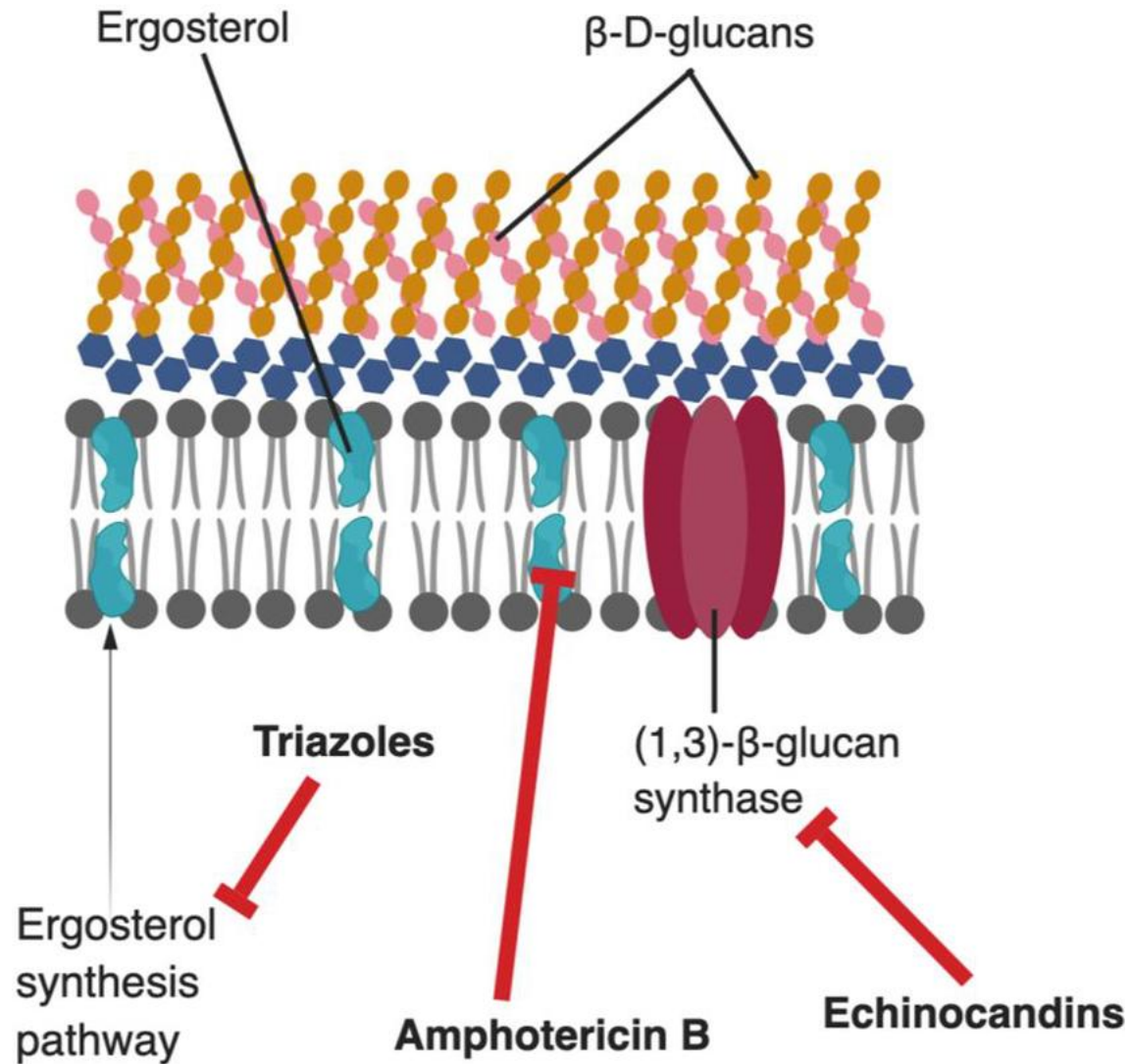
Cell wall	echinokandins, ibrexafungerp
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Cytoplasmatic membrane	polyenes, azoles, terbinafin
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Mikrotubules	griseofulvin
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Nucleic acid synthesis	5 – fluorocytosin
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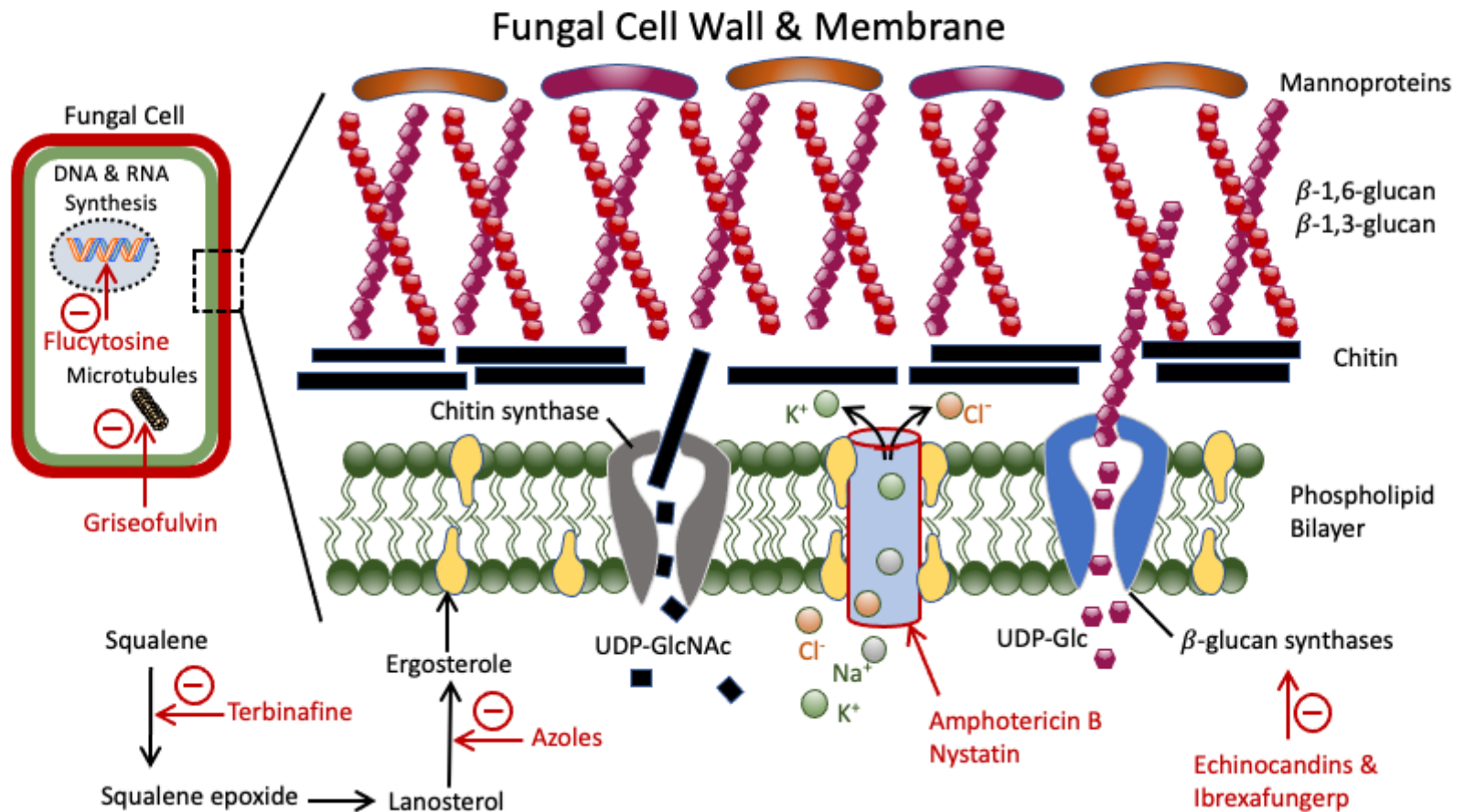
Antifungals – mechanism of action



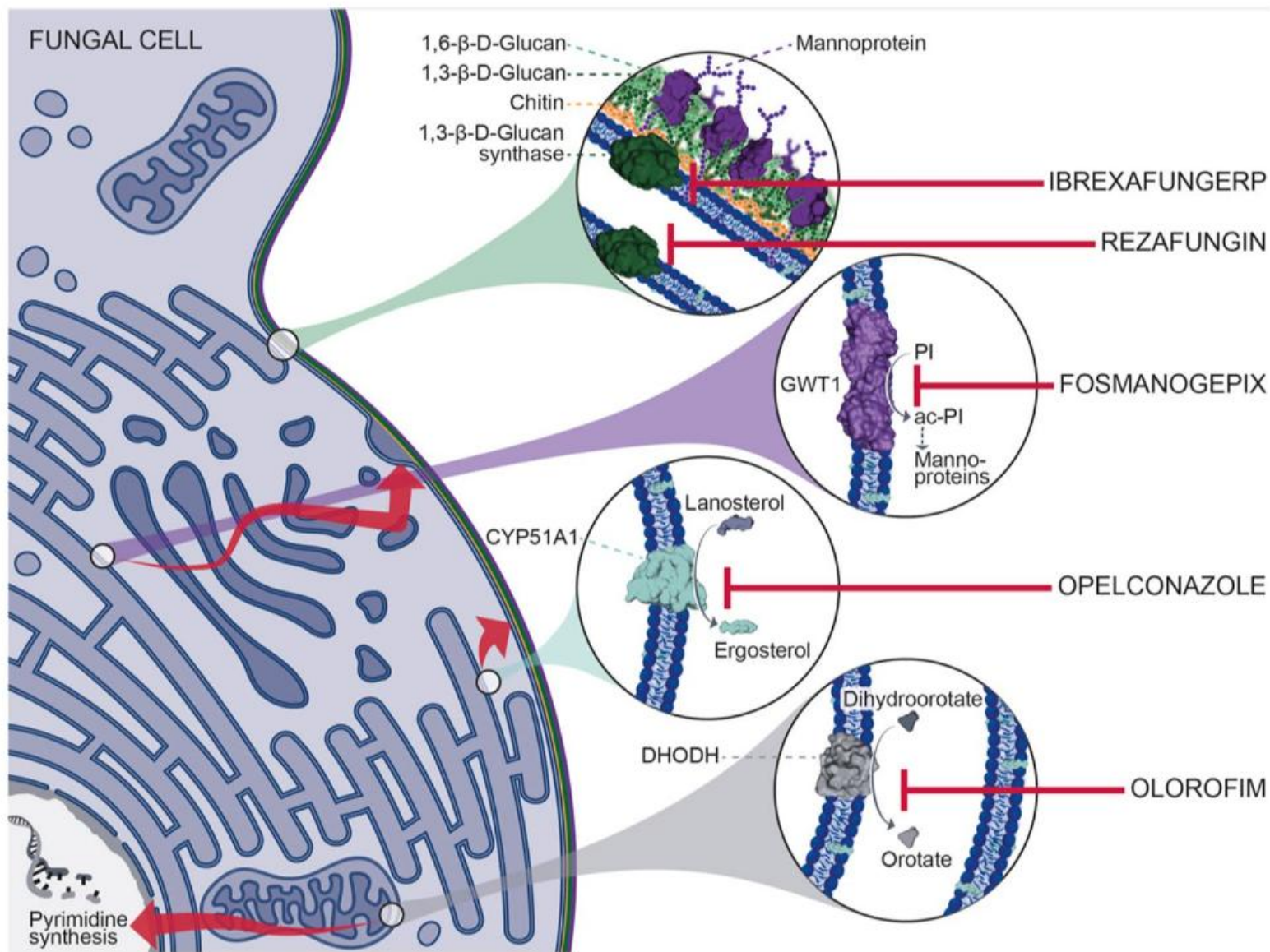
Antifungals – mechanism of action

Antifungal Molecular Targets

Antifungal Sites of Action



Antimykotika – mechanismus účinku



Echinocandins

Caspofungin, micafungin, anidulafungin, rezafungin

Inhibit beta-D-glucan (cell wall 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 echinocandin exposition (prophylaxis, treatment)
- Minimal adverse effects

Polyenes

Amphotericin B

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

Nystatin – topical

Mechanism of action

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

AMB 1st choice - **mucormycosis, disseminated cryptococcosis (+5-FC)**

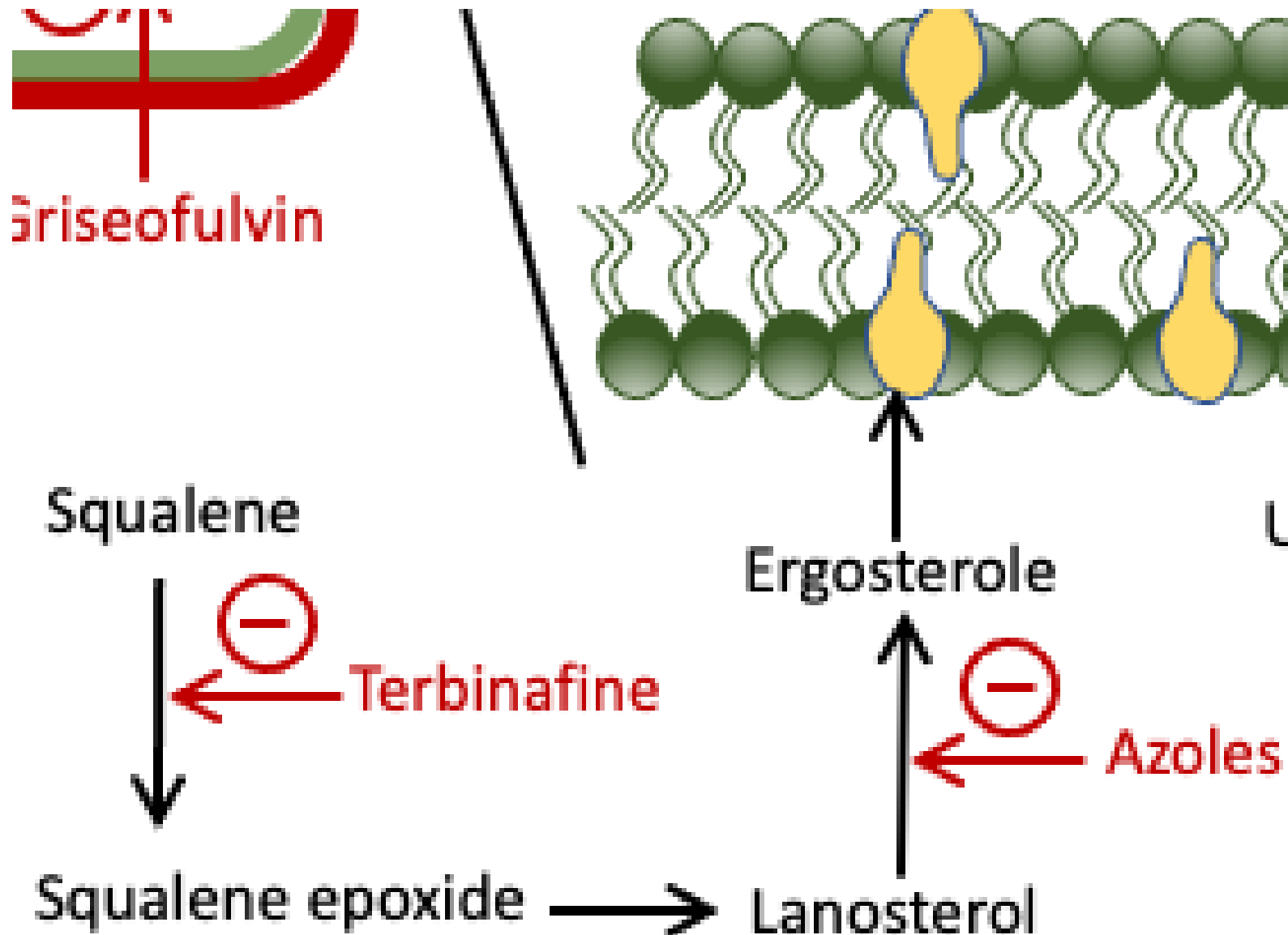
Azole resistant aspergillosis

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, hypocalcemia, hypomagnesemia

Ergosterole synthesis inhibitors



Azoles

Imidazoles – topical

Triazoles – systemic treatment

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

Mechanism of action

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

Azoles

Fluconazole

Disseminated cryptococcal infection – consolidation and maintenance
Invasive candidiasis

Targeted therapy in susceptible strains

UTI, ocular, intracranial candidiasis

Mucosal/mucocutaneous candidiasis, esophagitis - systemic therapy

No effect in moulds

Výsledek mikroskopie:

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](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
- Photosensitivity
- Severe cutaneous hypersensitivity
- Dysrhythmia, QTc interval elongation

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

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

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

Terbinafin

Dermatophytosis

Terbinafine resistance

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

5-fluorocytosin (flucytosin, 5-FC)

Mechanism of action

- DNA and RNA synthesis inhibition after intracellular conversion to 5-fluorouracil
- Conversion does not occur in human cells

Disseminated cryptococcal infection

- Initial treatment (+L-AMB)
- Rapid resistance development - monotherapy

Adverse effects

- Haematopoiesis impairment
- Hepatotoxicity

Antimykotika - rezistence

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

Fungi with acquired antifungal resistance of critical epidemiological significance

Candida auris

- Environmental origin, **thermotolerant**
- 5 different clades, **simultaneous global spread**
- Highly tolerant to environmental effects, long-term survival on human skin and surfaces
- Most strains resistant to fluconazole, acquired resistance to echinocandins and amphotericin B

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

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 marneffe*
 - *Cryptococcus gattii*
-
- Causative agents of **endemic systemic fungal infections**
 - Americas, Asia, Africa, Europe – imported cases

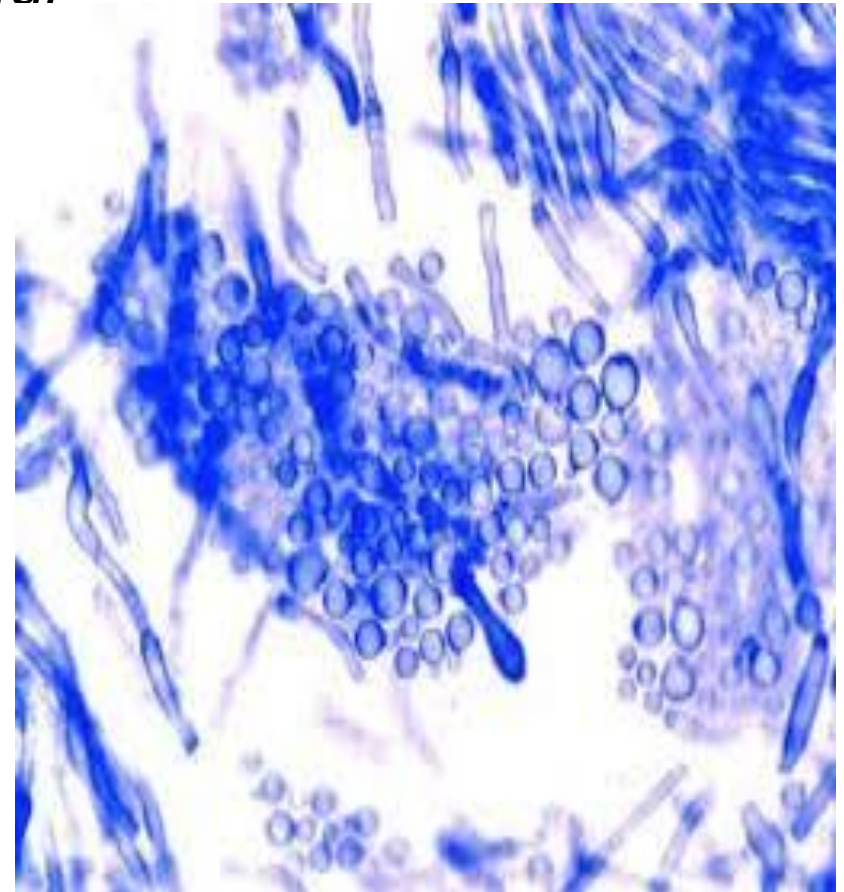
Superficial fungal infections

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

Dermatomykóza – other fungal species (yeasts and environmental moulds)

Dermatophytes

Keratinophilic, keratinolytic fungi

Temperature optimum 28 – 30 °C

Invade stratum corneum a keratinized layers of hair and nails

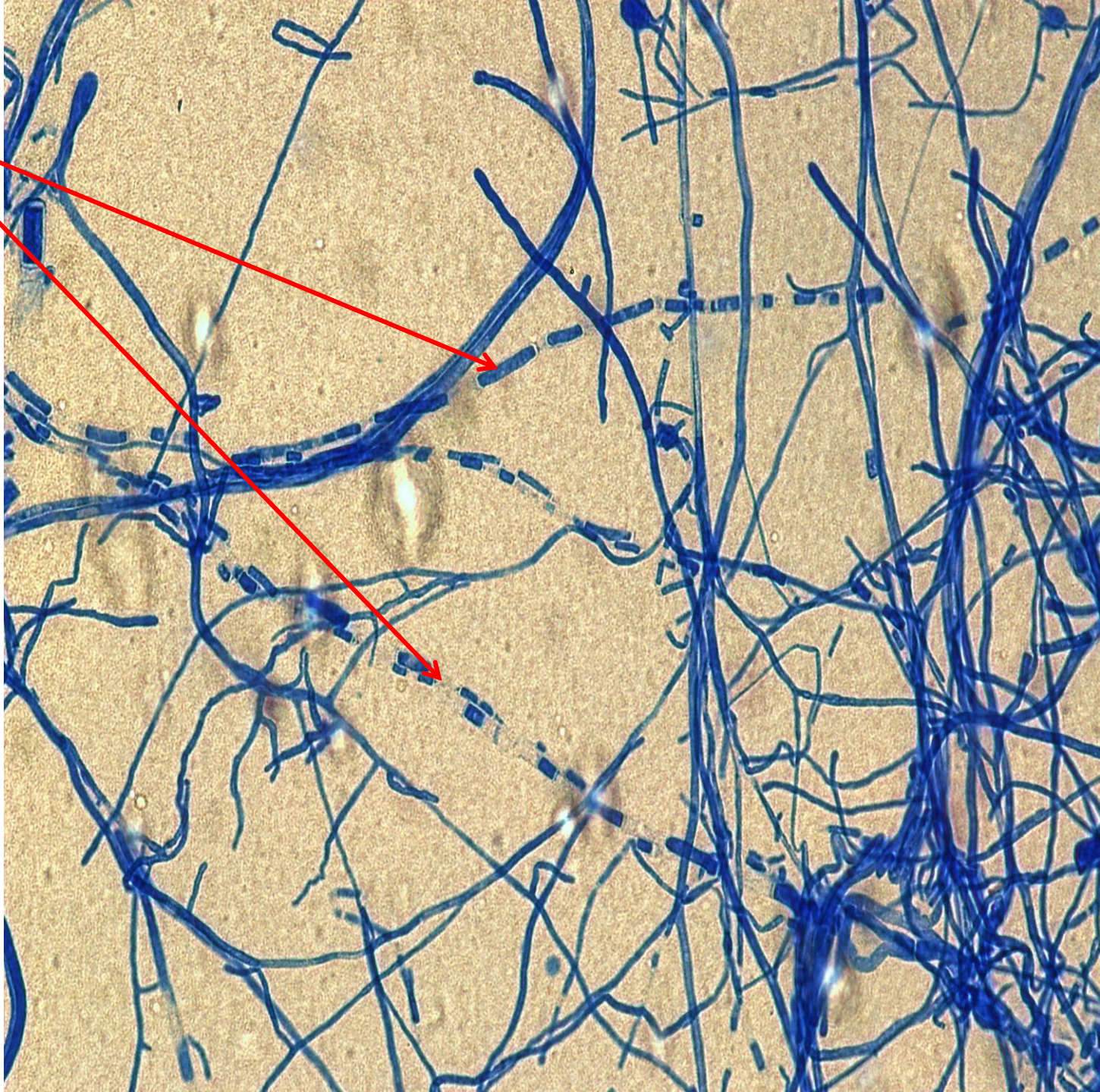
Name of disease - tinea + anatomic localisation

Infectious particles (propagules) – **artroconidia – particles formed by breaking of the hyphae**

Transmitted by desquamated epidermal cells

Fomites, contaminated surfaces

Arthroconidia



Dermatophytes – ecology, epidemiology

Antropophilic – Adapted to human 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

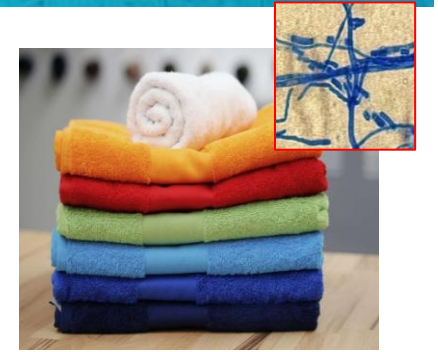
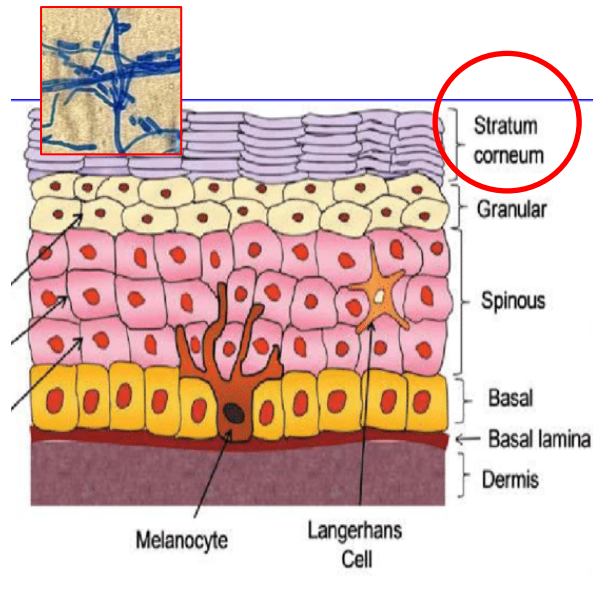
Trichophyton mentagrophytes complex, *Trichophyton benhamiae*, *Microsporum* sp.

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

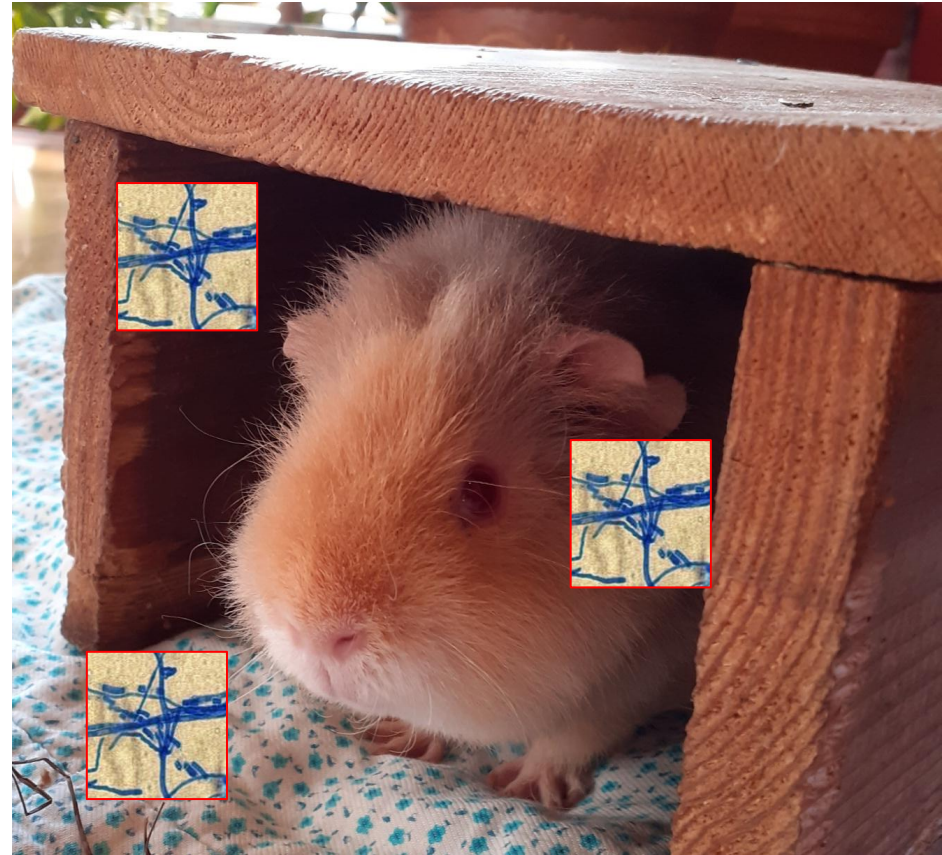
- Acute disease course, severe inflammatory reaction

Anthropophilic dermatophytes

Transmission



Zoophilic dermatophytes - transmission



Dermatophytoses – clinical forms

Tinea unguium
dermntentz.org



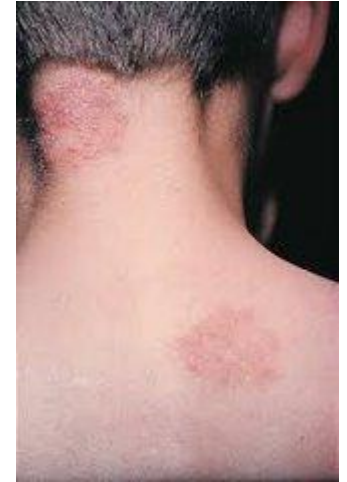
Tinea barbae

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



Tinea corporis

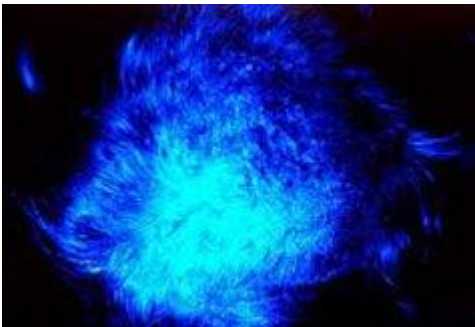
sciencedirect.com



Tinea pedis
natural-health-news.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)

