Mycology II

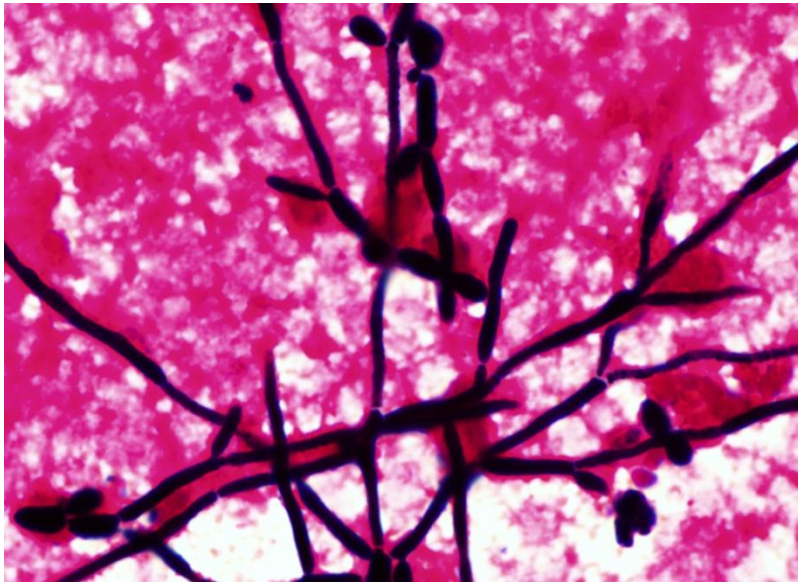
Candidiasis
Cryptococcosis
Aspergillosis
Mucormycosis
Pneumocystis jirovecii pneumonia

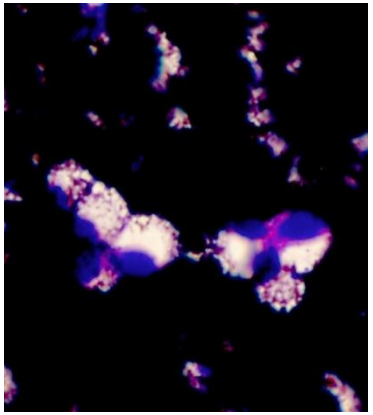
14. 5. 2026

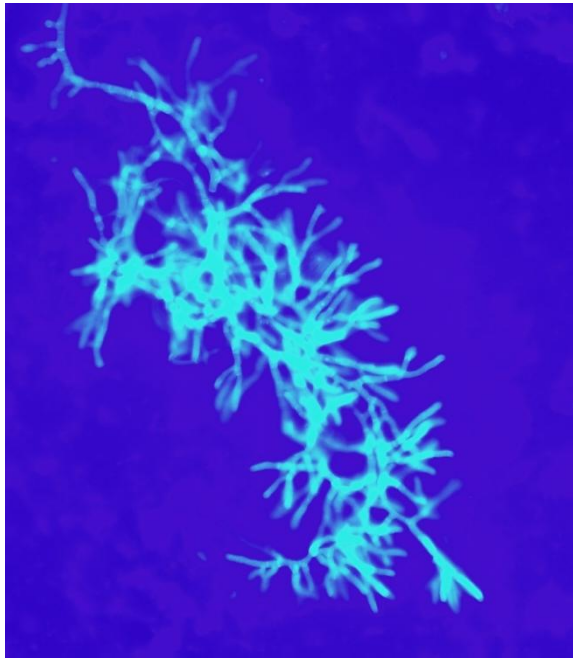
2. LF UK

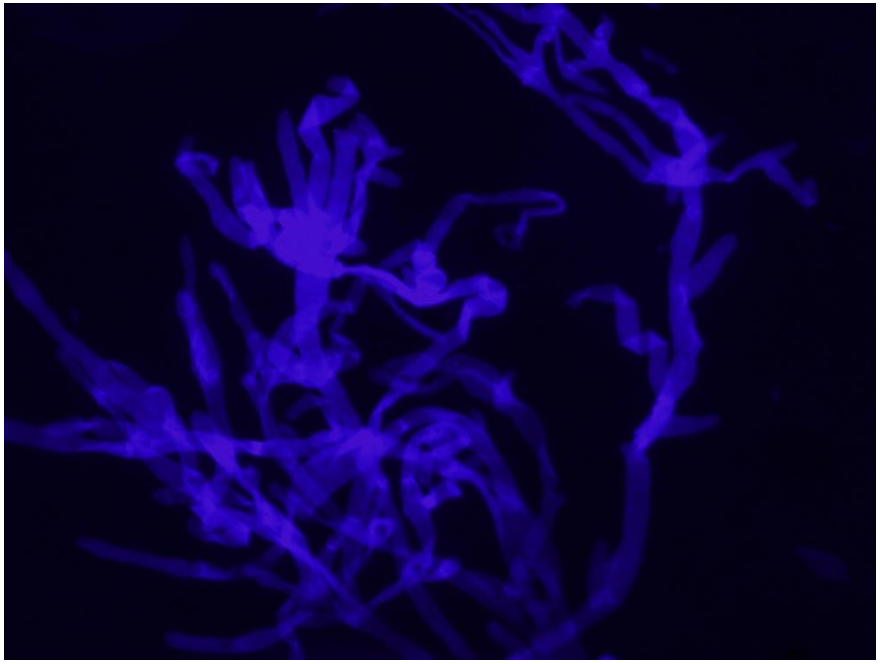
FNMH
Fakultní nemocnice
Motol a Homolka

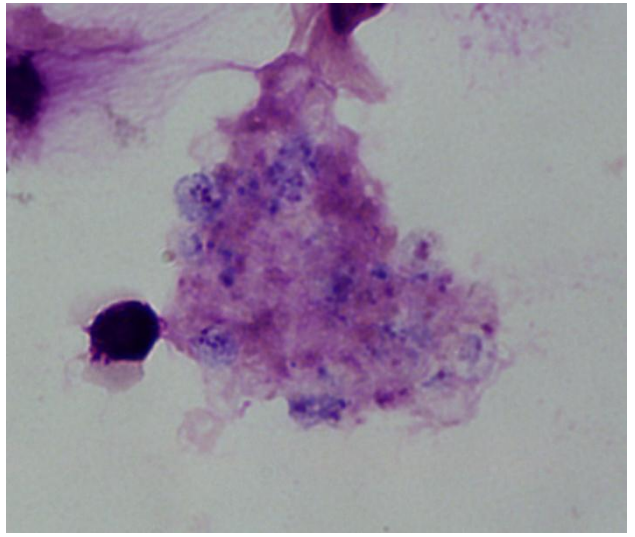
2. LÉKAŘSKÁ FAKULTA UNIVERZITA KARLOVA











Opportunistic fungal infections

Fungal infections affecting humans with **specific risk factors**

Cellular immune response impairment
Impairment of cutaneous or mucosal barrier

- Endogenous
- Exogenous

Never happen without risk factors in the host

Fungal infections – immune response

Major surgery, burn wounds, major skin and soft tissue wounds, ATB

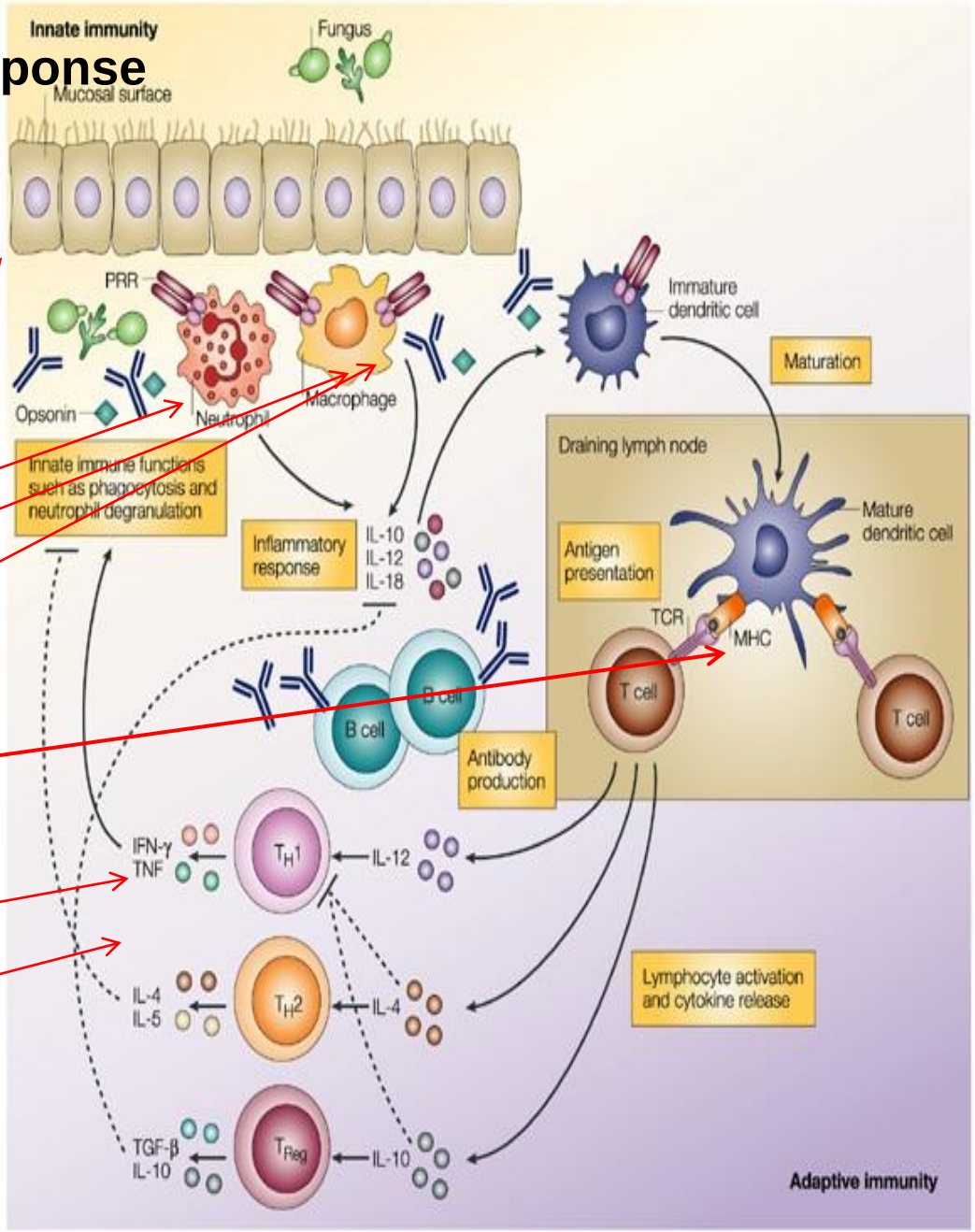
Intravenous catheters

Diabetes mellitus: decreased functions (chemotaxis, phagocytosis, killing) of diabetic polymorphonuclear cells and diabetic monocytes/macrophages compared to cells of controls

Glucocorticoids

Immunosupressants administered after bone marrow and solid organ transplantation or autoimmune diseases

AIDS



Candidasis

Diseases caused by *Candida* sp. and related species
Most cases endogenous
Candida albicans, Candida auris, Candida parapsilosis, Candida glabrata, Candida tropicalis, Candida krusei

Candida – virulence factors

- Thermotolerance - růst při 37 °C
- Adhaerence – epithelial and endothelial cells
- Hydrophobic cell surface
- Morphotype change (yeast – pseudeohyphae – hyphae)
- Biofilm formation

Candida – immune recognition and response

Myeloid phagocytes

•TLR
•C-type lectin receptor (CLR) family of receptors – cascade activation - Th1 and Th17 response
•T-independent response

Neutrophiles - oxidative + non-oxidative killing

Cutaneous and mucosal candidiasis

RF
Th 17 immune response impairment
•HIV
•Innate chronic mucocutaneous candidiasis
•Immunosupressive therapy
•Diabetes mellitus

Mucosa and skin
•Mechanic – diapers, dental prostheses
•ATB
•Glucocorticoids, cytostatics

Superficial candidiasis
Visible mucosal/cutaneous lesions
•Mucosal candidiasis – thrush, vaginal candidiasis
•Mucocutaneous candidiasis – rare innate immune defficiencies (STAT3 HIES, STAT1-GOF)
•Oesophagitis – systemic treatment!

Invasive candidiasis

Bloodstream or organ infection caused by *Candida sp*.
Haematogenous dissemination

RF

Mucosal or skin barrier disruption

- Major GIT surgery
- Intravascular catheters (parenteral nutrition)
- Broad spectrum antibiotics

Myeloid phagocytes deficiency

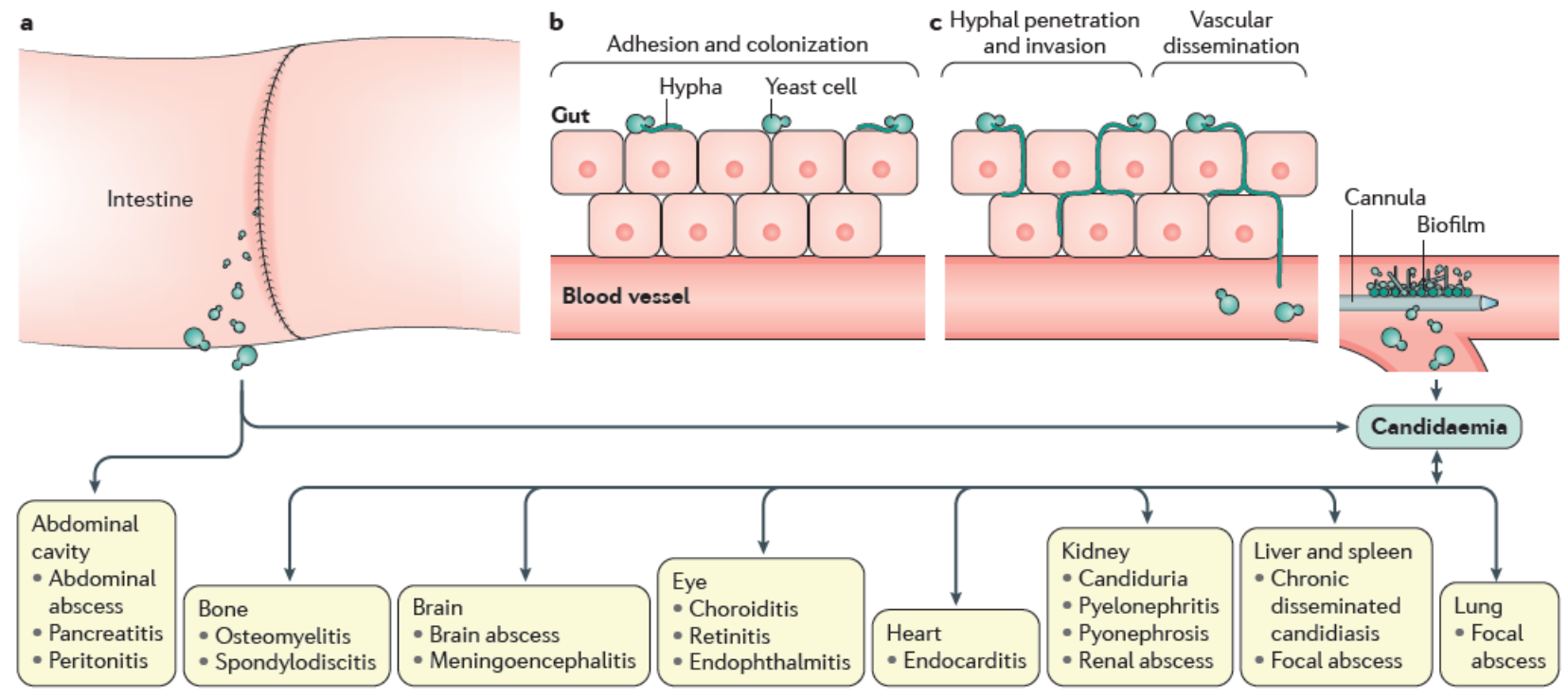
Neutropenia/cellular immune deficiency

Premature newborns

Clinical forms

- Bloodstream infections - candidaemia
- Organ candidiasis with/without candidaemia
- Disseminated candidiasis
- Candida UTI with/without candidaemia

Invasive candidiasis – pathogenesis



Pappas PG et al. Nature reviews | **disease primers volume 4 | article number 18026 | 1**

Invasive candidiasis – clinical manifestation

Mild symptoms to severe sepsis, organ-specific (neutropenic)

Invasive candidiasis should be suspected in patients with known risk factors who have an unexplained fever unresponsive to antibacterial treatment

Invasive candidiasis – microbiological diagnosis

- Microscopy, culture, antifungal susceptibility testing – blood, tissue
- Beta-D-glucan detection (serum)
- Mannan/antimannan detection (serum)
- PCR (panfungal – tissue, targeted)

Invasive candidiasis – treatment

1st line echinocandins

Targeted/step-down fluconazole/other azoles if susceptible

Amphotericin B (UTI, neonates, salvage)

Candida – antifungal resistance

- Echinocandins – FKS1/FKS2 mutations
- Azoles - ERG11 mutations
- Amphotericin B – *C. auris*

Cryptococcus neoformans

Infection source – contaminated soil, dust (bird droppings), **inhalation**

Risk factors

- Cellular immunodeficiency (macrophage – CD4+T-cell cooperation)

Pathogenicity factors

- Polysaccharide capsule
- Melanin
- Body temperature 37 °C survival and growth

Pathogenesis - after inhalation blastoconidia are engulfed by alveolar macrophages, but they survive, dissemination in macrophages via blood and lymph, predilected localization: CNS

Clinical manifestation: meningoencephalitis, disseminated disease in mos cases, subacute/chronic course

Treatment amphotericin B + 5-FC, high-dose fluconazole, long-term

Aspergillosis

Source: environment - soil, pot flowers, food, household (conidia, inhalation)

Risk factors

- Neutropenia (neutrophiles able to destruct conidia)
- T lymphocytes/macrophage impairment (leading to restricted ability to destruct hyphae)
- ICU treatment, mechanical ventilation, lung tissue destruction (viruses – influenza, SARS-CoV2)
- Chronic pulmonary disease

Causative agents: ***A. fumigatus***, *A. niger, A. flavus, A. terreus*

Pathogenicity factors

- Adherence – fibronectin, laminin (conidia)
- Gliotoxin (inhibits macrophage activity and and T- cell proliferation)
- Enzymes - catalase, phospholipase, elastase, proteases

Lionakis MS et al. Nature Reviews Immunology | Volume 23 | July 2023 | 433–452
Pathakumari B et al. Biomedicine & Pharmacotherapy 130 (2020) 11055
Ullmann AJ et al. / *Clin Microbiol Infect* 24 (2018) e1 - e38

Aspergillosis – clinical forms

depends on host´s predisposing factors

- **Allergic bronchopulmonary aspergillosis** - paranasal sinuses or bronchial mucosa colonization followed by allergic reaction
- **Aspergilloma -** cavity of any origin filled with fungal hyphae (paranasal sinuses, pulmonary (tumor necrosis, bronchiectasia, evacuated abscess) no tissue invasion
- **Chronic pulmonary aspergillosis (CPA) –** chronic pulmonary disease, slow tissue invasion, fibrosis and loss of pulmonary functions
- **Invasive pulmonary aspergillosis** – subacute
- **Tracheobronchitis** – COVID-19, influenza
- **Disseminated aspergillosis** - rapid progression, angioinvasion, tissue necrosis and destruction, bleeding, organ dissemination

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Aspergillosis – clinical manifestation, diagnosis, treatment

Allergic bronchopulmonary aspergillosis
•Cough, asthma
•Antiallergic and symptomatic therapy in most cases

Aspergilloma
•threat if bleeding,
•surgery and antifungal therapy

Invasive aspergilosis
•Fever refractory to antibiotic treatment
•Pulmonary infiltrates, hemoptysis, pleuritis, loss of pulmonary functions
•**Complex diagnostic procedure** (history, immunology, imaging, microbiology, histopathology)

Microbiological diagnosis
•Microscopy, culture, AFST – site of infection (tissue, BAL)
•Galactomannan detection – BAL, CSF, serum – neutropenic
•Targeted PCR

Systemic antifungal therapy - **voriconazole, isavuconazole if susceptible**
ARAF – voriconazole + echinocandin, liposomal amphotericin B

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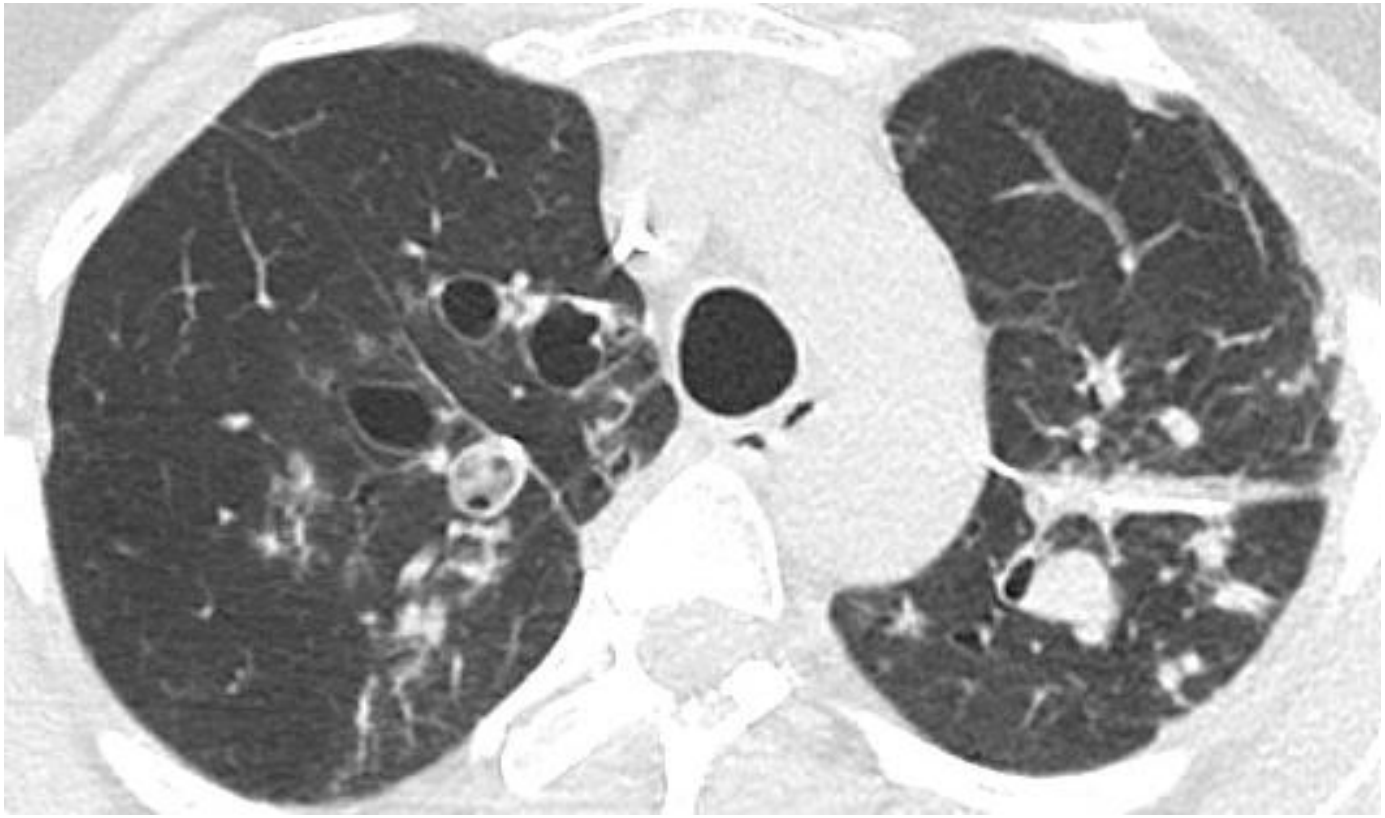
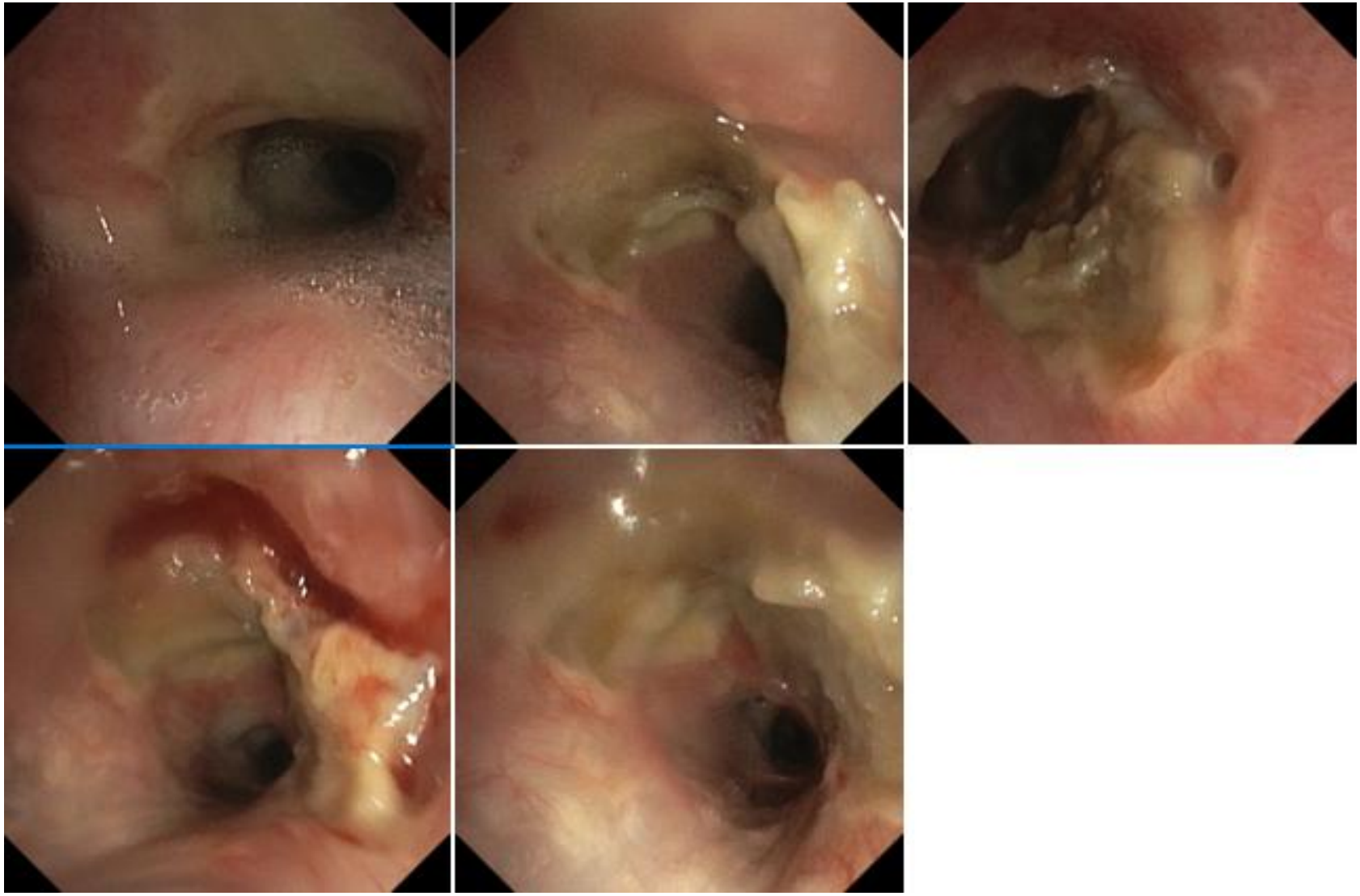
Chronic pulmonary aspergillosis (CPA)

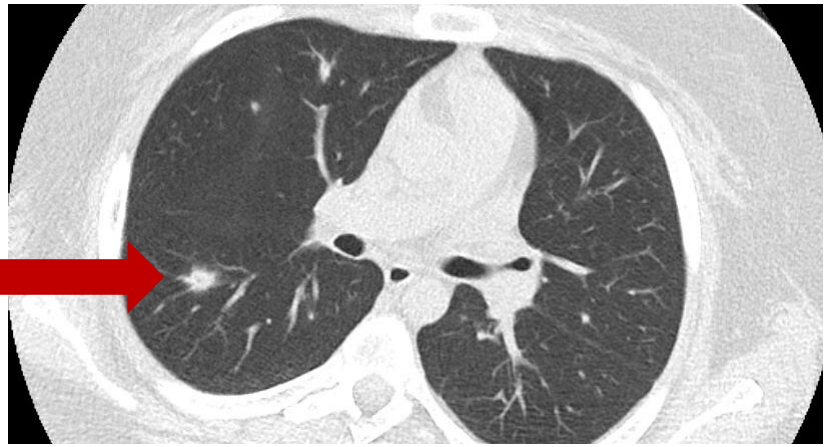


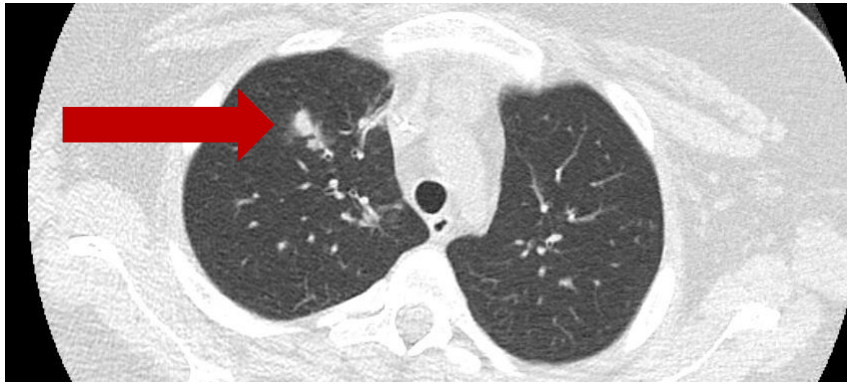
Aspergilus tracheobronchitis

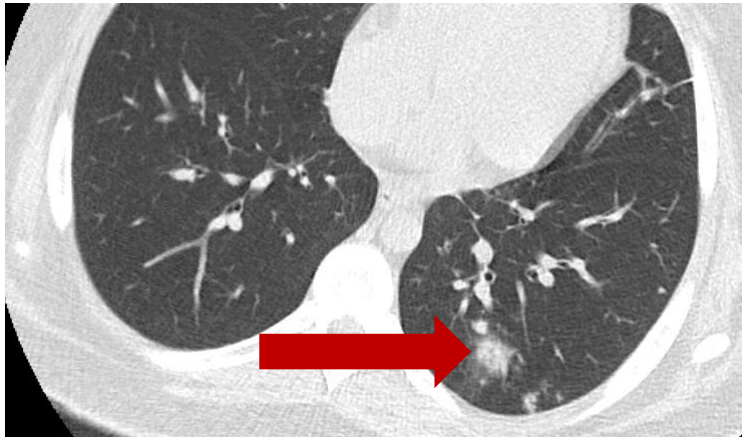


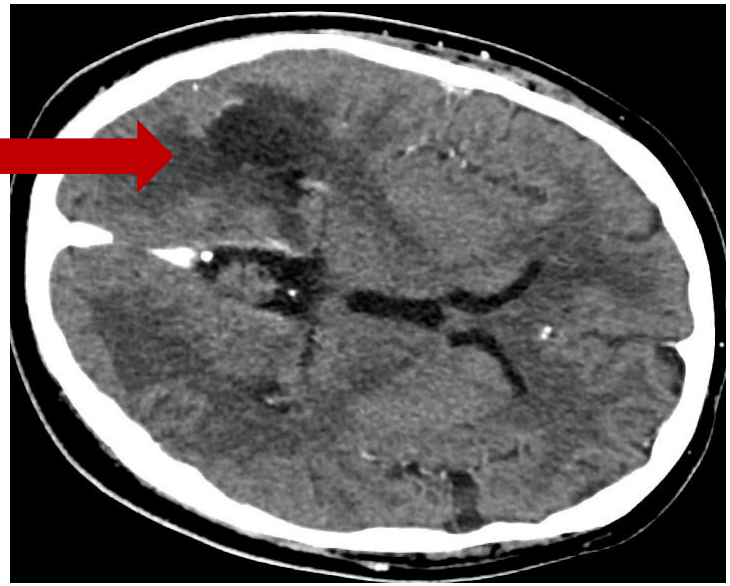
Disseminated aspergillosis

Sérum			CAND,ASP,ser,glukan
Candida (antigen mannan): negativní			
Aspergillus (antigen galaktomannan): 4 index - pozitivní			
beta-D-glukan: 165,5 pg/ml - POZITIVNÍ			
Sérum			CAND,ASP,ser
Candida (antigen mannan): negativní			
Aspergillus (antigen galaktomannan): 4,73 index - pozitivní			









Mucormycosis (zygomycosis)

Rhizopus, Mucor, Lichtheimia, Rhizomucor – environment (soil), sporangiospores

Risk factors

- Cellular immunity impairment – severe neutropenia
- Diabetes mellitus, ketoacidosis
- Renal impairment, hemodialysis, iron chelators administration
- Corticosteroid therapy

Pathogenicity factors

Angioinvasivity – adhaerence to endothelial surfaces (receptor-ligand, up- regulated by glucosis and iron abundance)
Immunomodulation

Mucormycosis - pathogenesis

Sporangiospores are inhaled or contaminate bandages or any wound coverage
Rapid growth and tissue destruction, necrosis and haemorrhage due to angioinvasion

Clinical forms

Rhinocerbral – RF diabetic ketoacidosis
Pulmonary – rapidly progressing haemorrhagic-necrotizing pneumonia
Disseminated - angioinvazsion, rapid dissemination, fatal bleeding
Skin (always suspect dissemination!) or posttraumatic wound infection (burn wounds, hurricane and tsunami associated trauma)

Therapy – surgery whenever possible

Amphotericin B lipid complex, isavuconazole

Pneumocystis jirovecii

Ascomycetous fungus previously classified as protozoon

Both sexual and asexual life cycle occurs in **alveolar tissue**

Risk factors
AIDS
Immaturity, premature birth
Cellular immunity impairment

Clinical manifestation
interstitial pneumonia, granulomatous inflammatory process, diffuse alveolar damage
Respiratory distress, low oxygen saturation, dyspnea, long-term course with gradual deterioration of lung functions

Co-trimoxazole both fot treatment (high-dose) and prophylaxis (low-dose)

P. jirovecii

Life cycle

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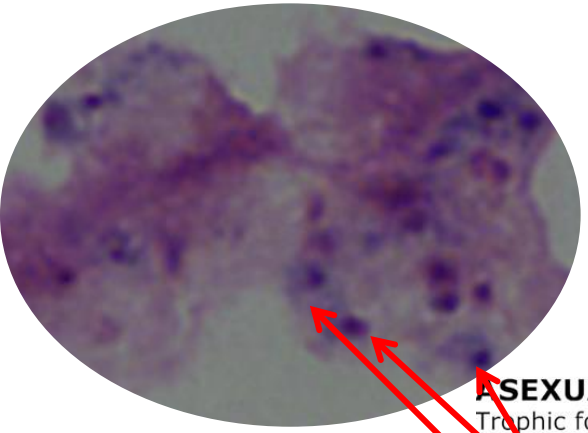
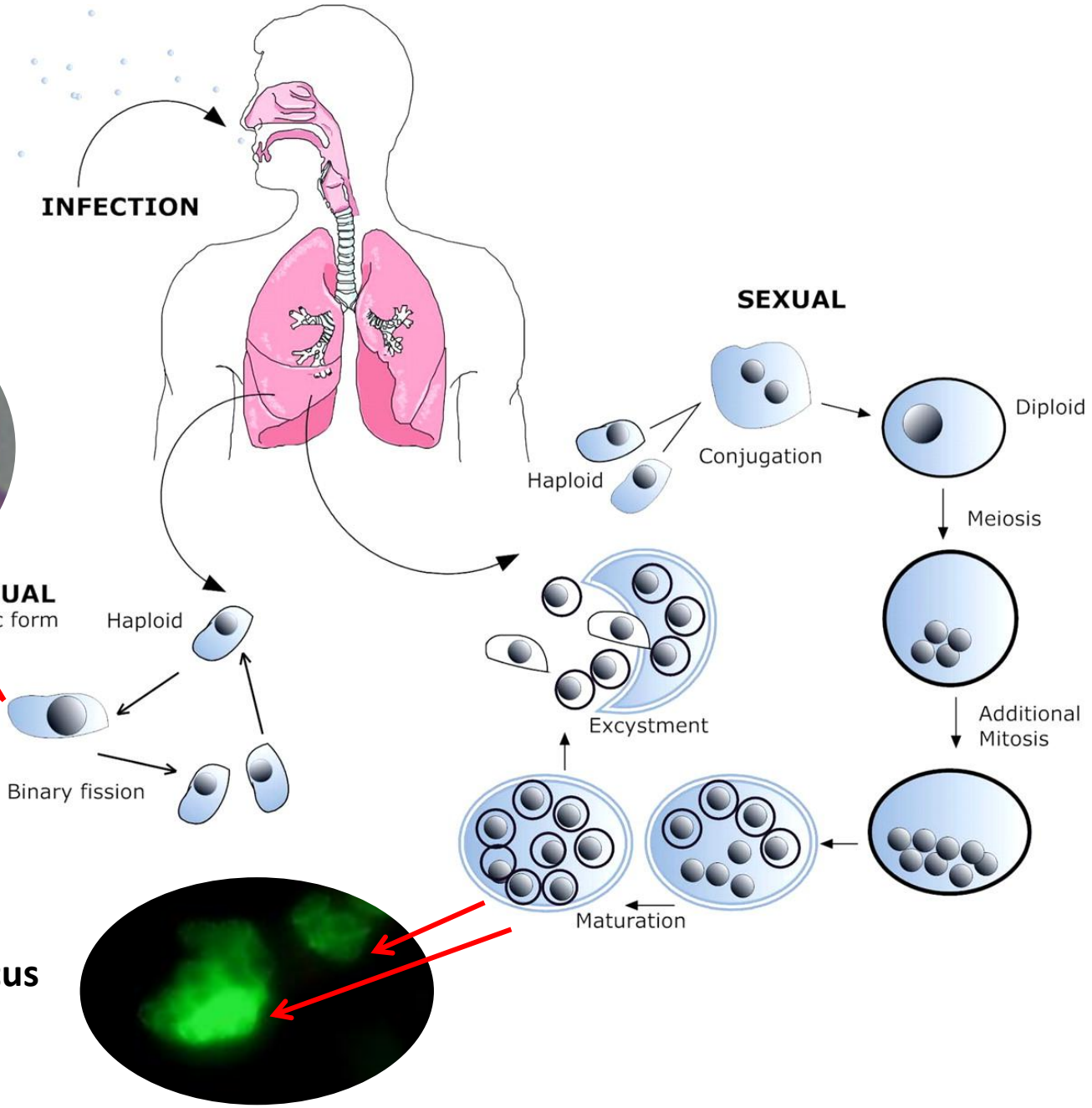


Trophic form
Giemsa



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