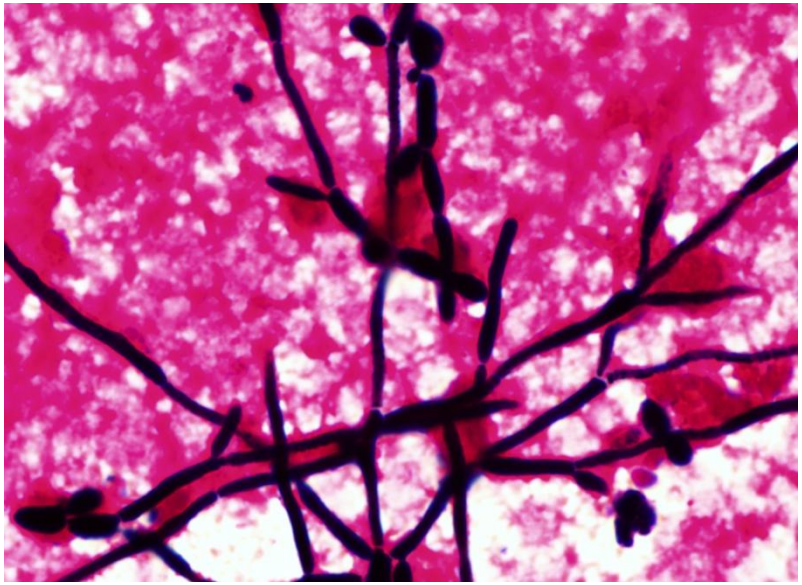
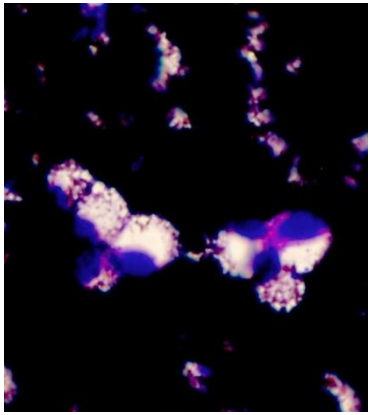
Mycology II

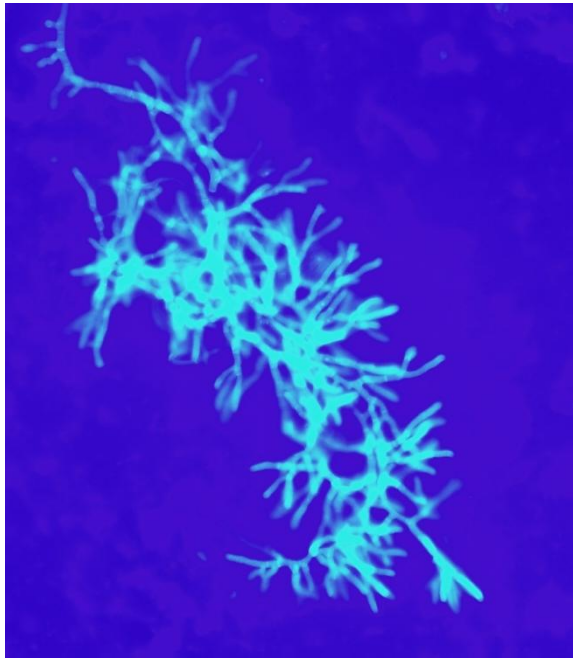
Candidiasis
Cryptococcosis
Aspergillosis
Mucormycosis
Pneumocystis jirovecii pneumonia

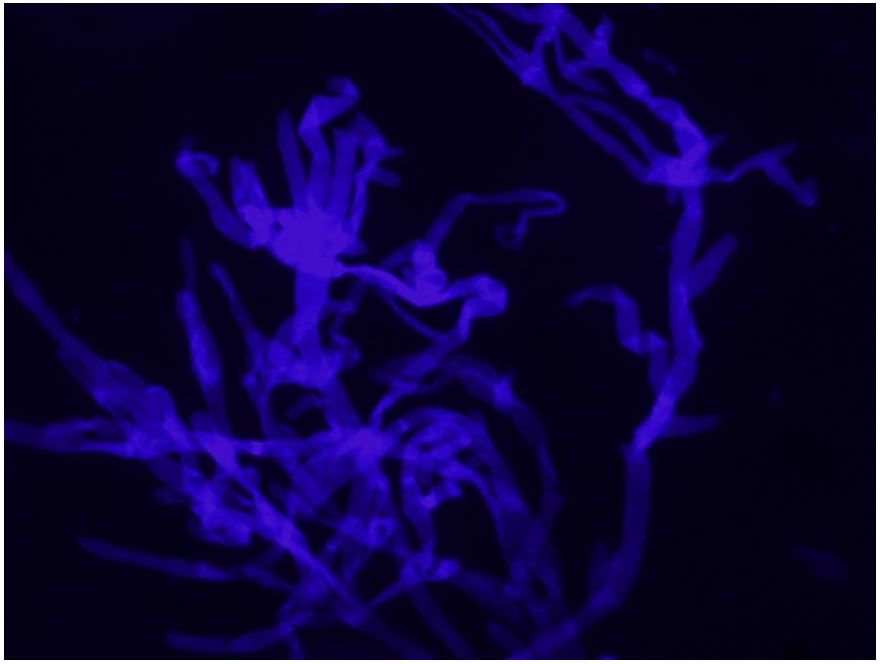
7. 10. 2025

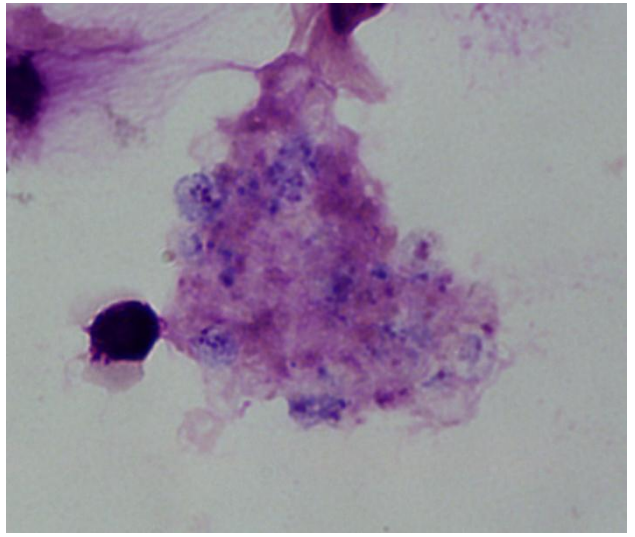
2. LF UK











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

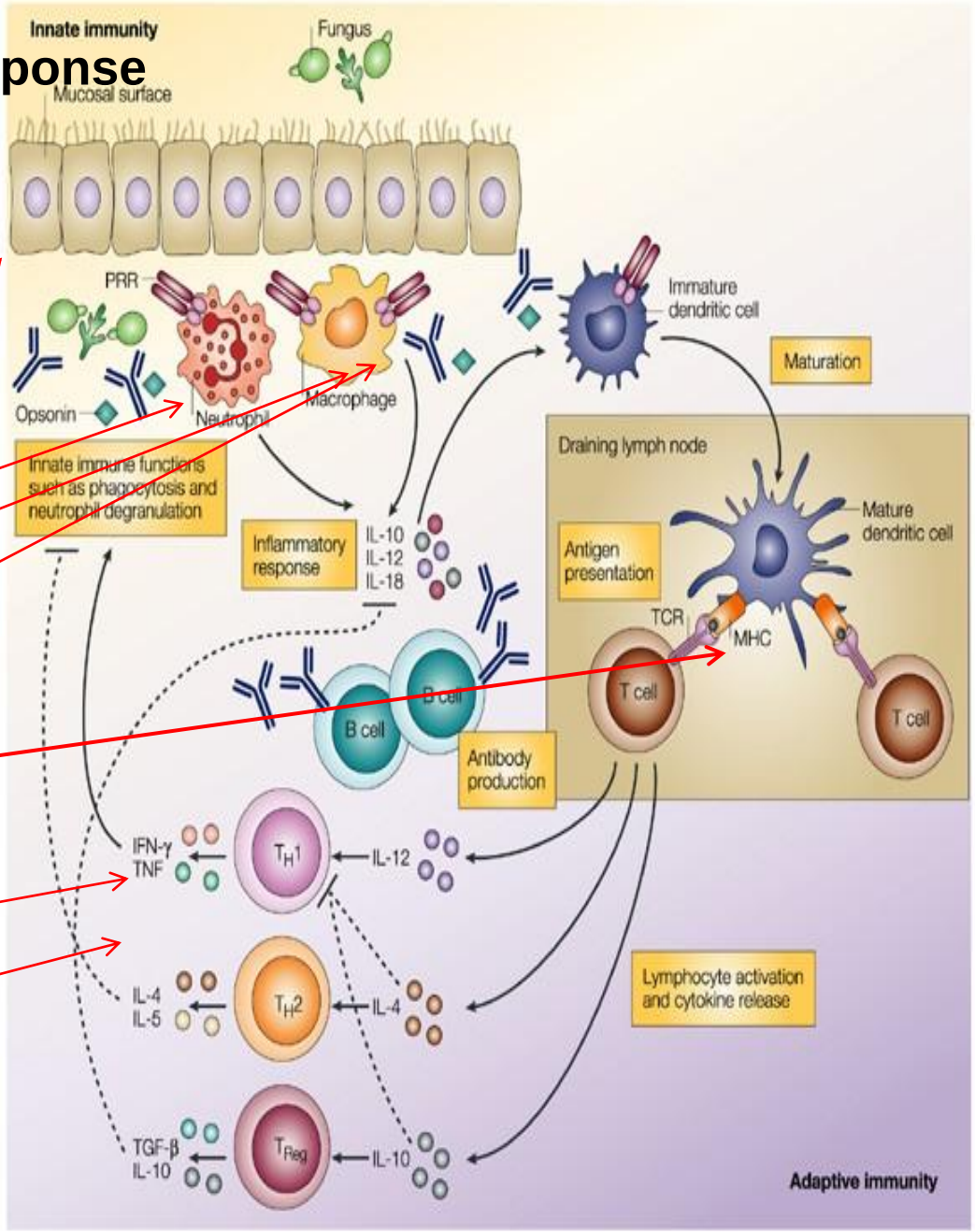
Intravenous catheters

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



Candidiasis

Mostly **endogenous** fungal infection except HAI (C. auris, other)

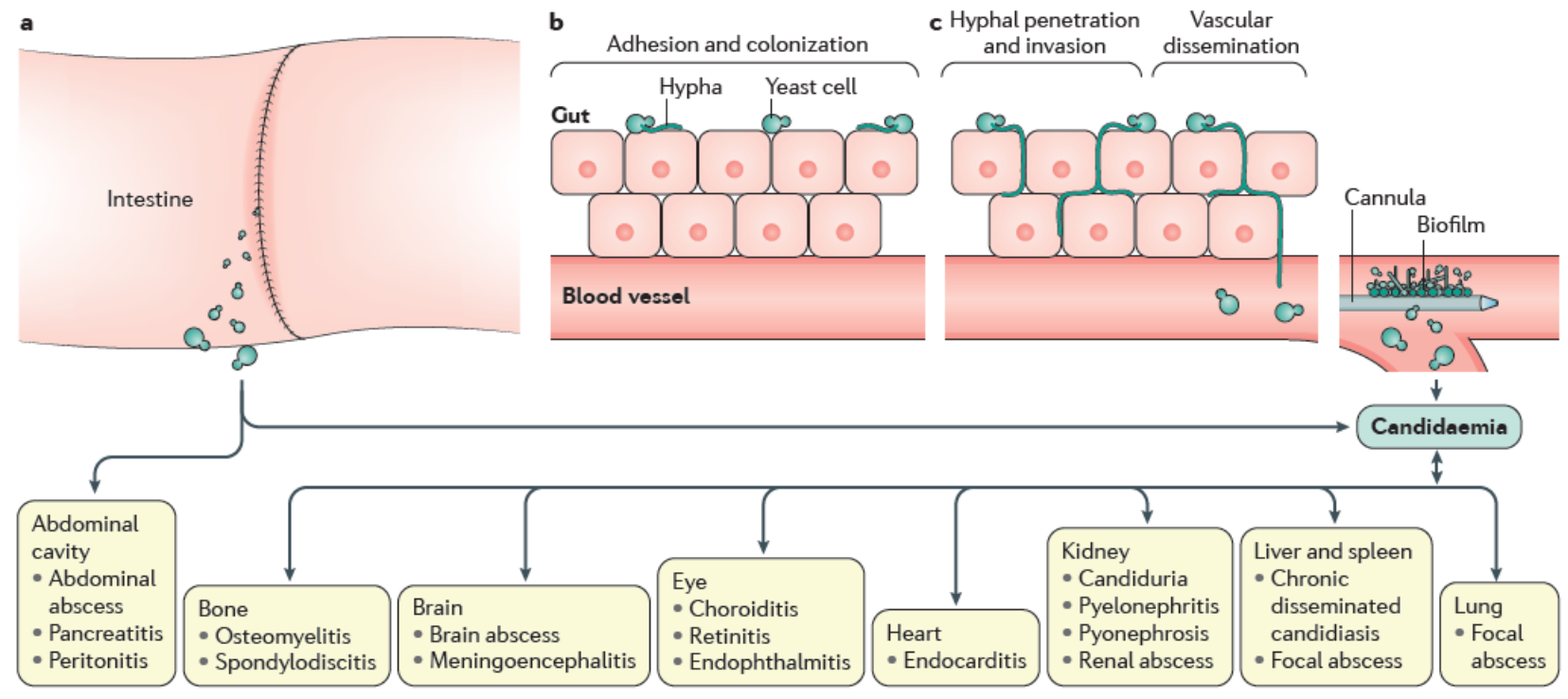
Superficial infections - Th 17 lymphocytes
Visible mucosal/cutaneous lesions
•Mucosal candidiasis – thrush, vaginal candidiasis
•Mucocutaneous candidiasis – rare innate immune defficiencies (STAT3 HIES, STAT1-G
•Oesophagitis

Invasive infections – myeloid phagocytes

RF
•Major GIT surgery
•Intravascular catheters (parenteral nutrition)
•Neutropenia/cellular immune deficiency
•Broad spectrum antibiotics
•Premature newborns

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

Candidiasis – pathogenesis



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

Candidasis – causative agents

Candida albicans, Candida glabrata, Candida tropicalis, Candida parapsilosis and Candida krusei

Candida – virulence factors

- Morphotype change (yeast – pseudeohyphae – hyphae)
- Adherence and invasion of *Candida* spp. in endothelial and epithelial cells
- Biofilm formation

Candida – immune recognition and response

PRRs – myeloid phagocytes
TLR
The C-type lectin receptor (CLR) family of receptors – cascade activation – interleukin synthesis – Th1 and Th17 immune response
T-independent response

Neutrophiles - oxidative + non-oxidative killing

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 that is unresponsive to antibacterial treatment

Invasive candidiasis – diagnostic options

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

Invasive candidasis – 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 condition

- **Allergic bronchopulmonary aspergillosis** - paranasal sinuses or bronchial mucosa colonization followed by allergic reaction
- **Aspergilloma -** previously formed cavity (paranasal sinuses, lungs (tumor necrosis, bronchiectasis, evacuated abscess…), adhesion of inhaled conidia, hyphae formation, finally cavity filled with fungal thallus, no invasion to surrounding tissue
- **Chronic pulmonary aspergillosis (CPA) –** chronic pulmonary disease, tissue invasion
- **Invasive aspergillosis** – conidia inhalation and adhesion, growing hyphae invade surrounding tissue, angioinvasion, tissue necrosis and destruction, hematogenous dissemination (CNS, heart, GIT, kidneys, liver)

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Aspergillosis – clinical manifestation, diagnosis, treatment

Colonization, bronchial obstruction, allergic bronchopulmonary aspergillosis - cough, asthma
Antiallergic and symptomatic therapy in most cases

Aspergilloma if bleeding is a threat, surgery and antifungal therapy is indicated

Invasive aspergilosis
Fever refractory to antibiotic treatment, pulmonary infiltrates, hemoptysis, pleuritis.

Complex diagnostic procedure (history, immunology, imaging, microbiology, histopathology)

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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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

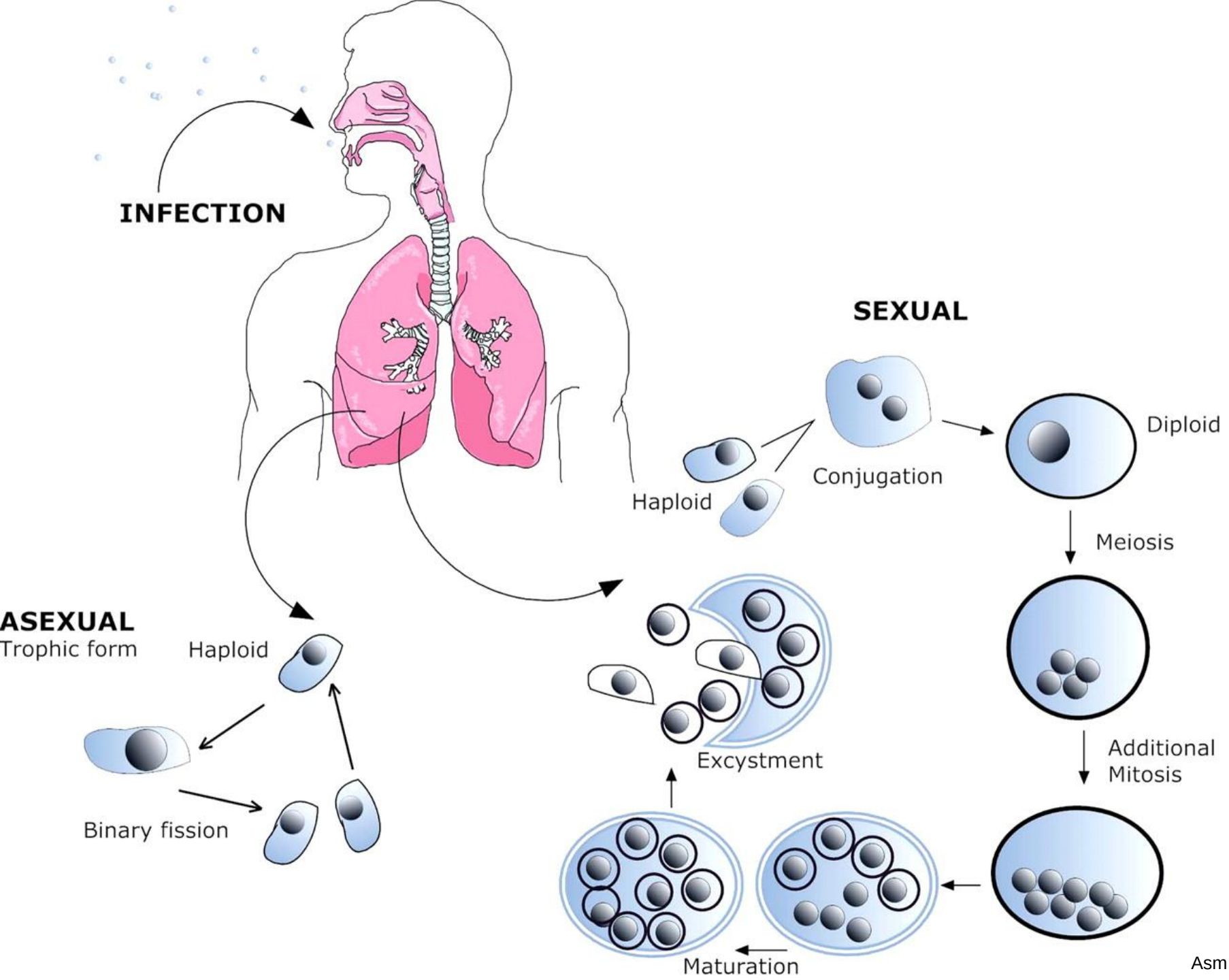
Ascomycetous fungus previously classified as protozoon

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)


INFECTION
SEXUAL
Haploid
Conjugation
Diploid
Meiosis
ASEXUAL
Trophic form
Haploid
Binary fission
Excystment
Additional
Mitosis
Maturation

Thank you for your attention