Invasive Aspergillosis

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Conferinta de Imunosupresie si Antibioterapie
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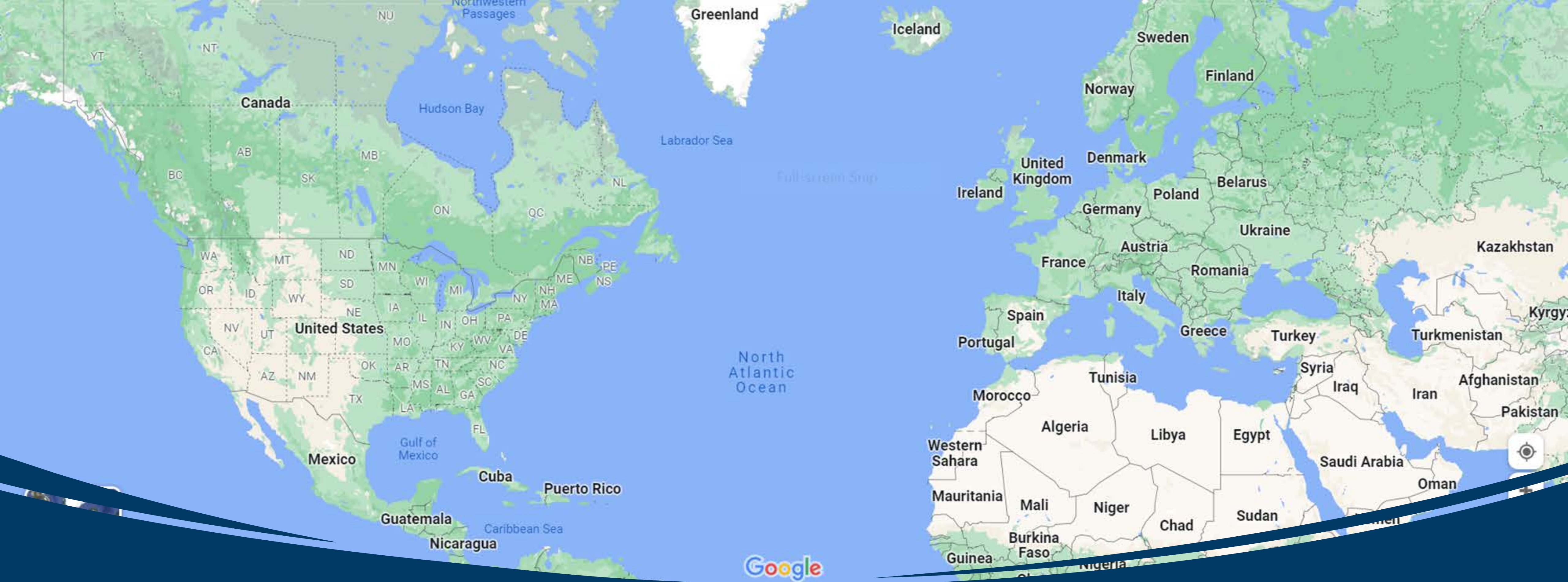
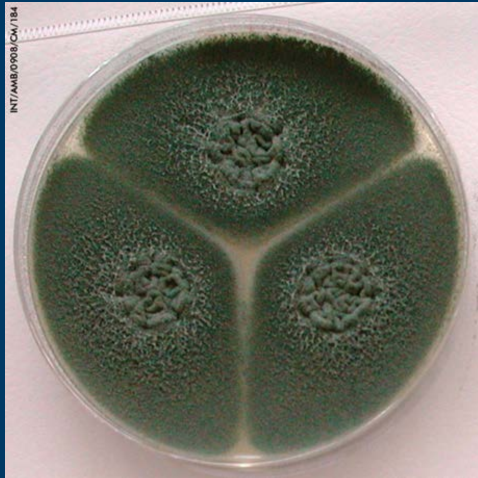


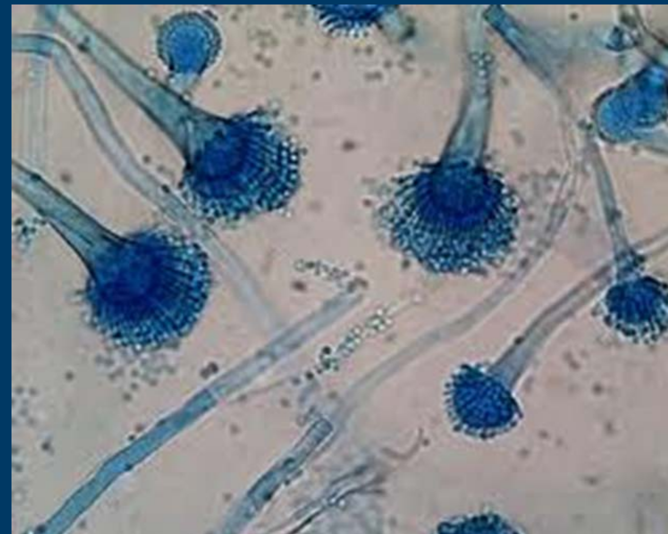
2018 ESCMID&ECMM&ERS
2016 IDSA
2020 ECMM/ISHAM

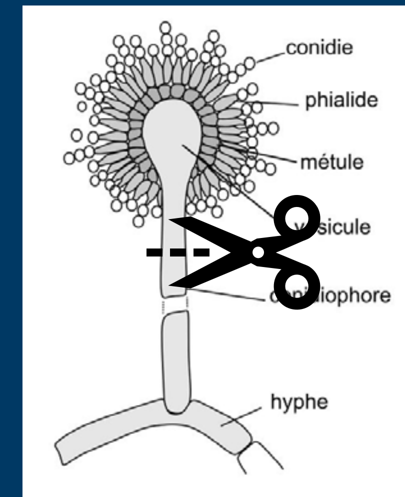
- IA: Invasive Aspergillosis updated guidelines
- CAPA: Covid19-Associated Pulmonary Aspergillosis

Aspergillus spp.

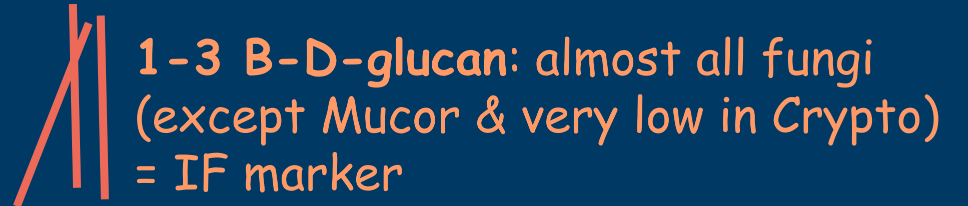
fungicidal use (azoles)
→ A. spp. VCZ-R!

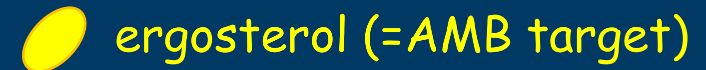


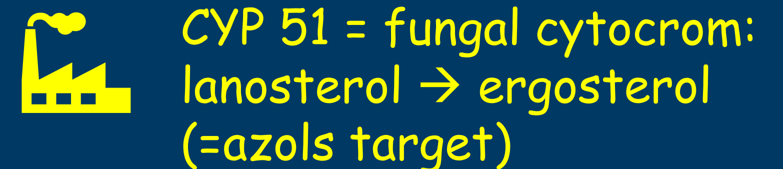


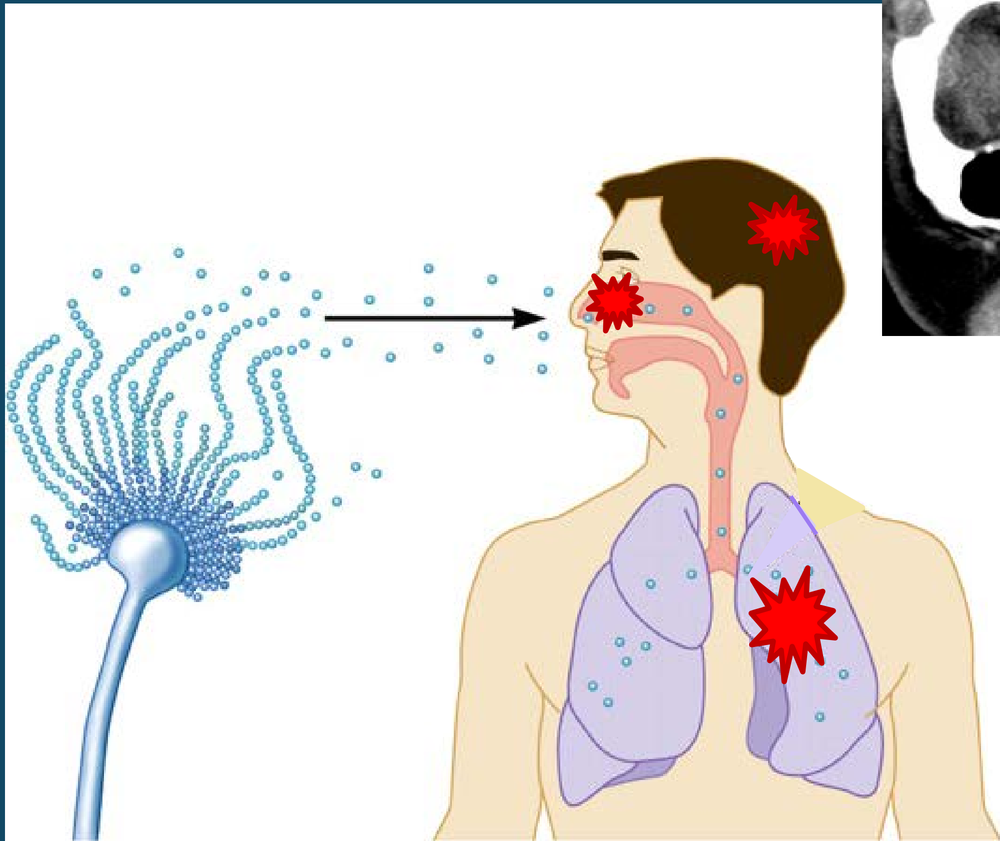


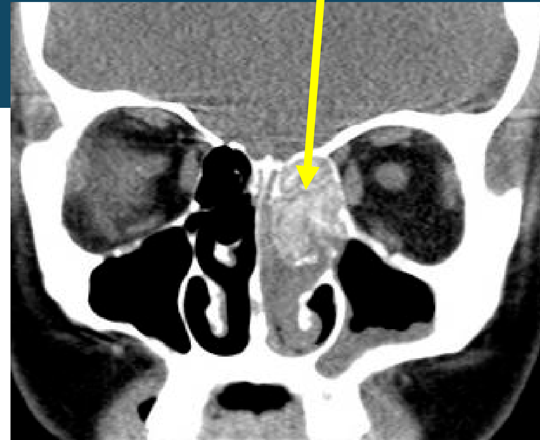
nucleus

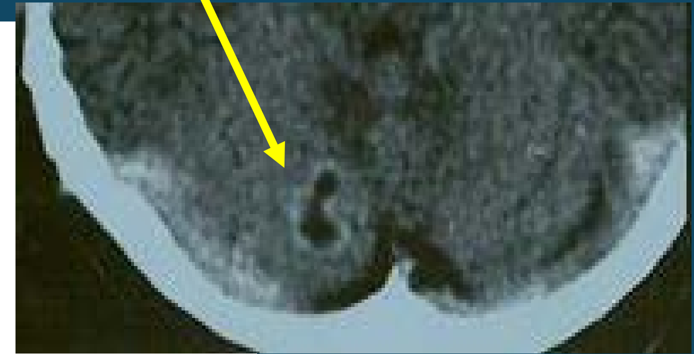


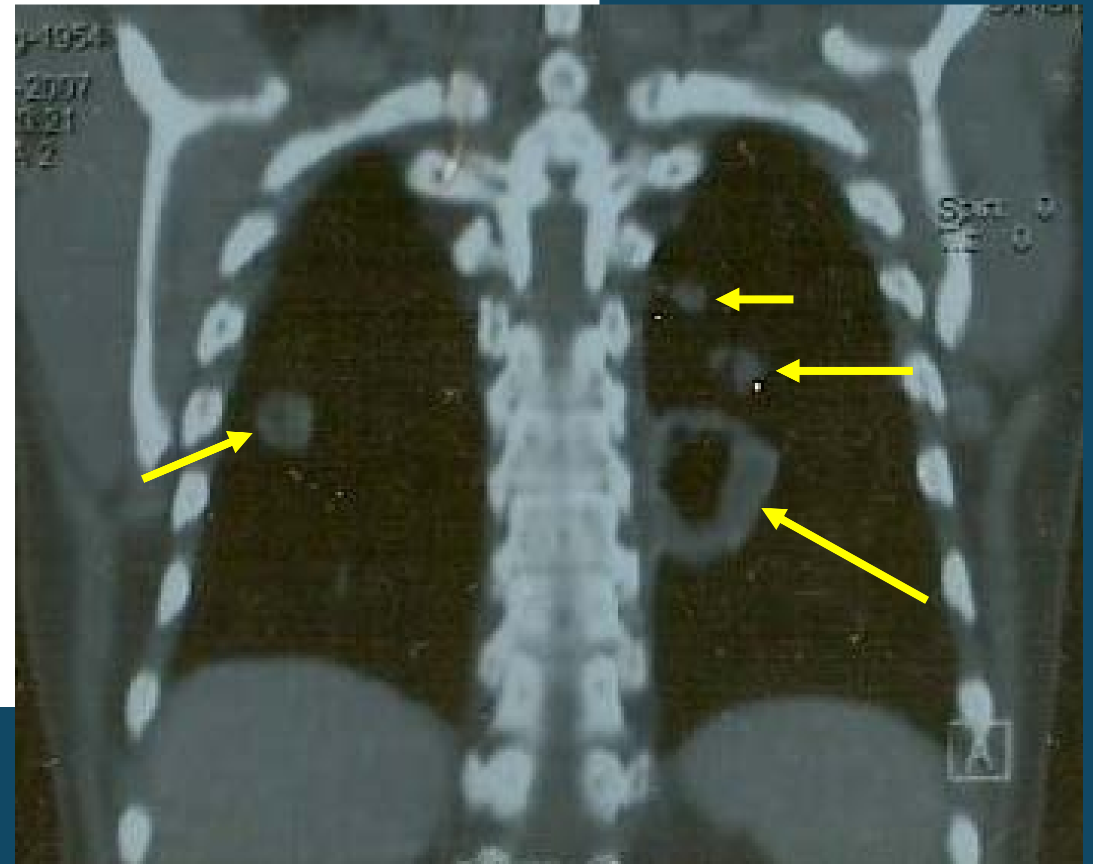




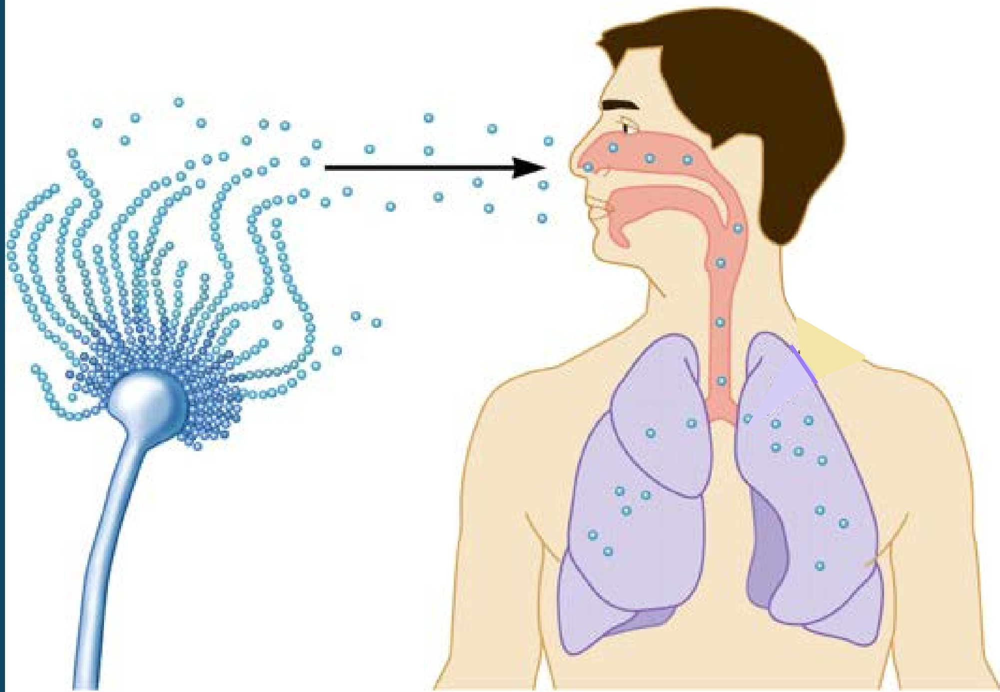








Aspergillus fumigatus- An Overview | Mycology | Microbe Notes
microbenotes.com



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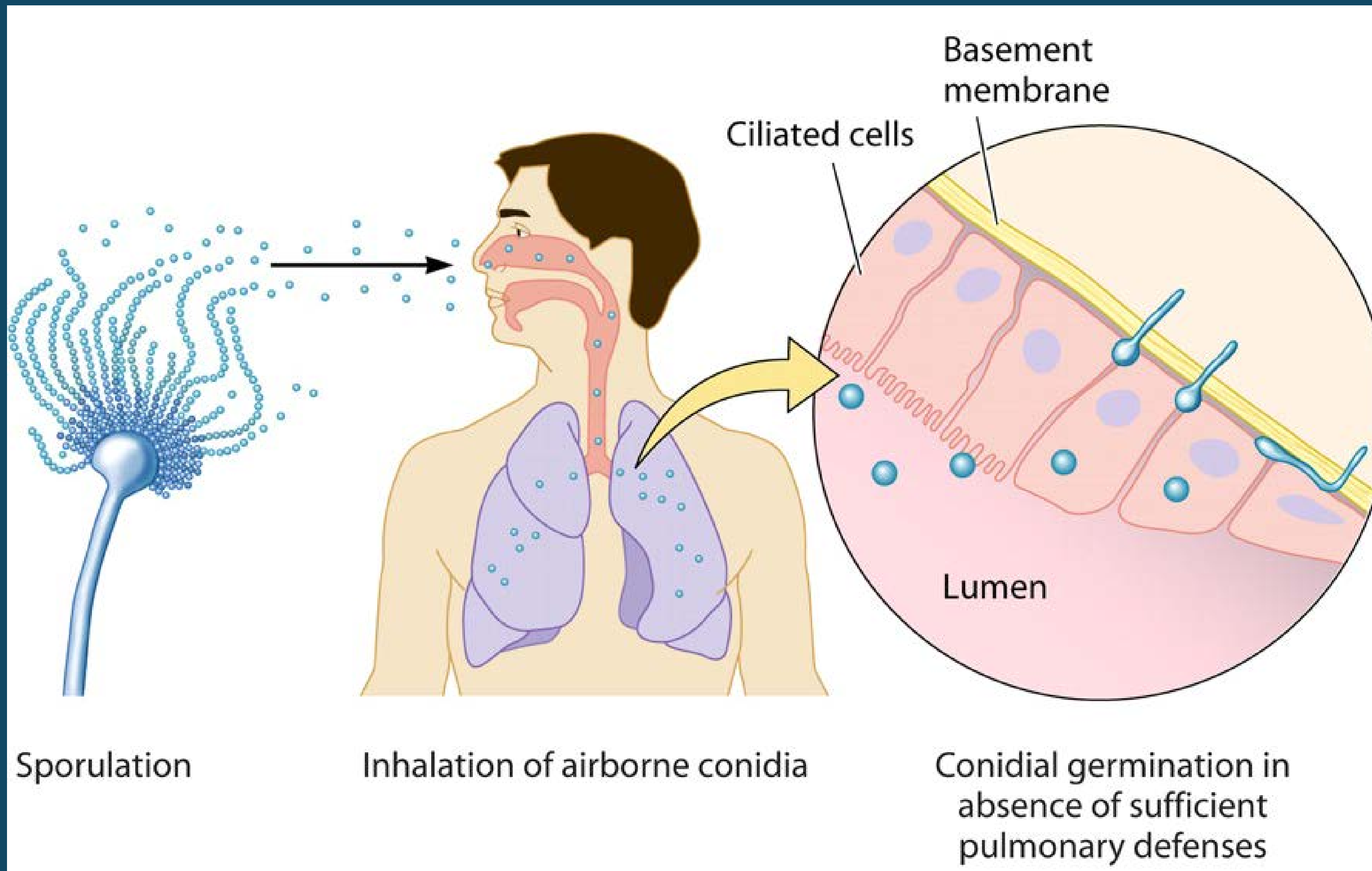
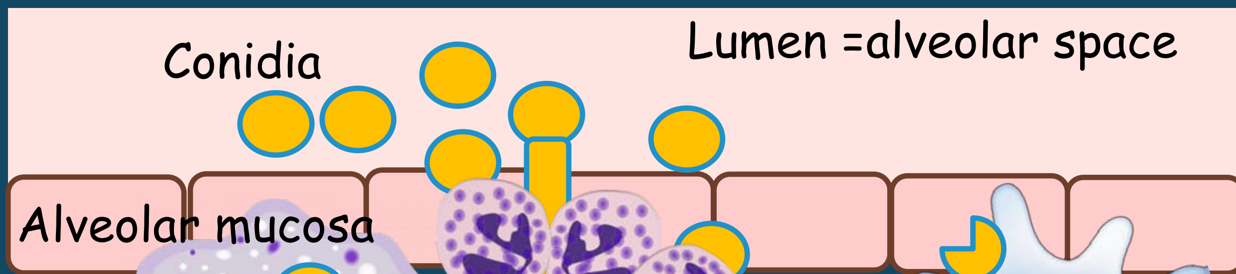
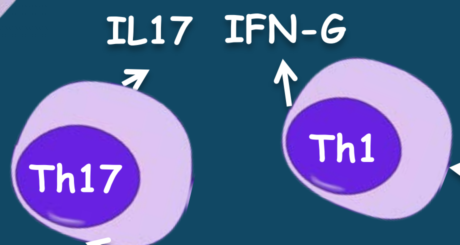
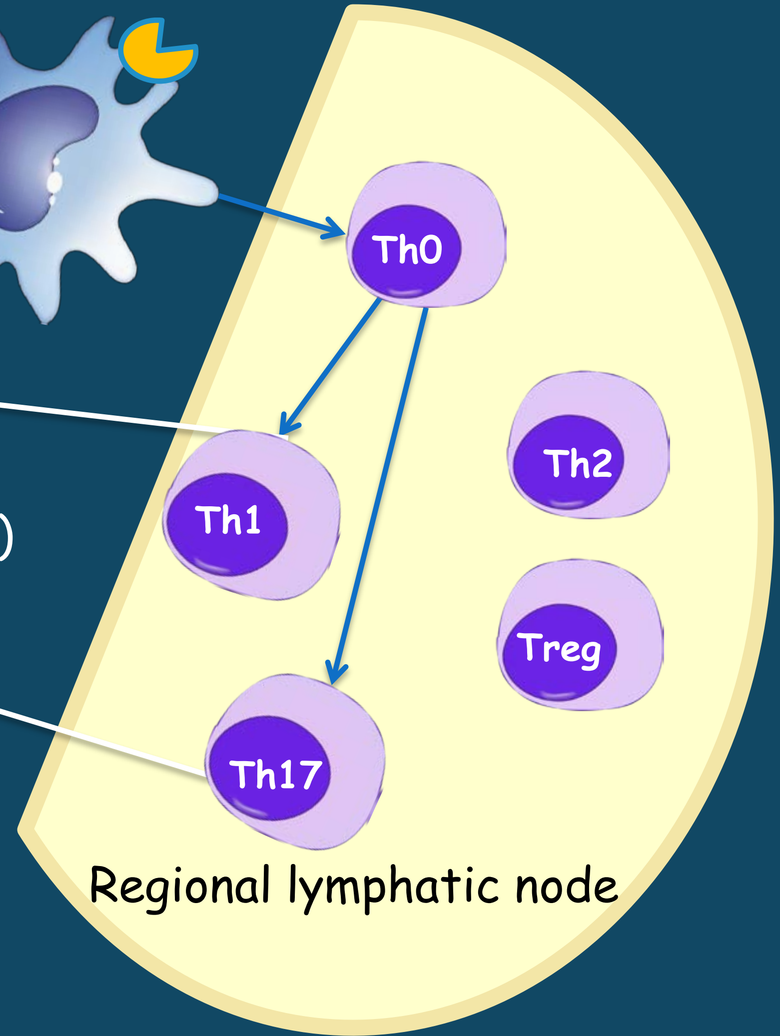


Basement membrane
Ciliated cells
Lumen
Sporulation
Inhalation of airborne conidia
Conidial germination in absence of sufficient pulmonary defenses



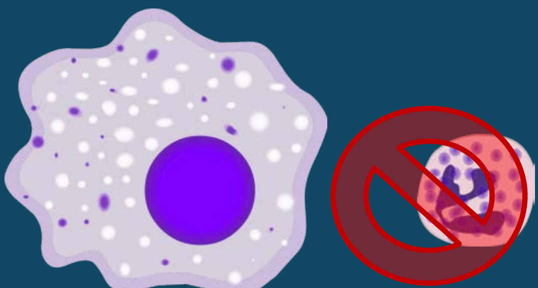




~ days (7-10)

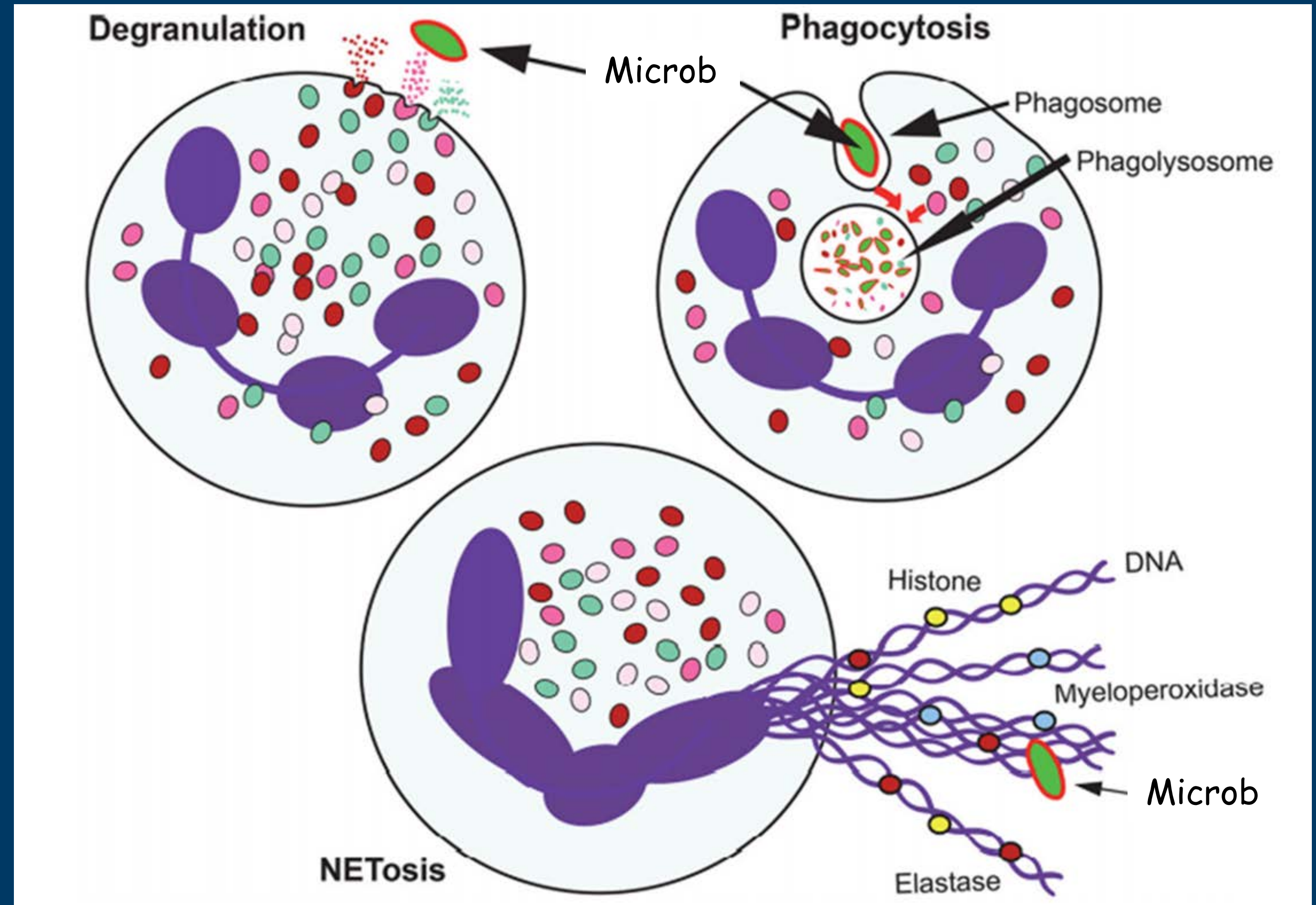
Neutropenia/Impaired Ne:
- ✓ Immunosupp. in hematol cancers
- ✓ Corticoids
- ✓ Diabetes

Limphopenia/ Impaired Ly:
- ✓ Immunosupp. Posttransplant
- ✓ HIV



Who is at risk?

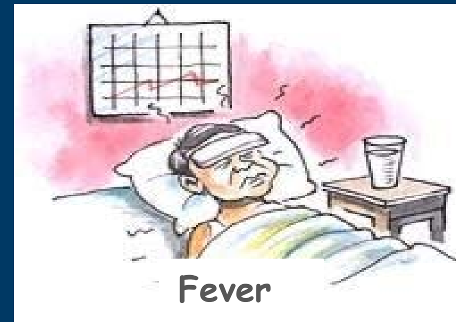
- Highest: AML in induction; allog HSCT in immunosupp.; SOT in intense immunosupp.
- Moderate: COPD, ICU+one of: steroids, burns, liver failure, intense malnutrition, severe bacterial sepsis, increased environmental exposure (poor control of the environment)
- Other: varia immunosupp. conditions (cancers, AIDS, liver cirrhosis, etc. or suppressive tx), influenza, SARS-CoV2



Neutrophil: A Cell with Many Roles in Inflammation or Several Cell Types? Front. Physiol. 2018 Carlos Rosales (Mexico)

Diagnosis

Dg~Possible Hematologic pts: Fever-driven = Empiric



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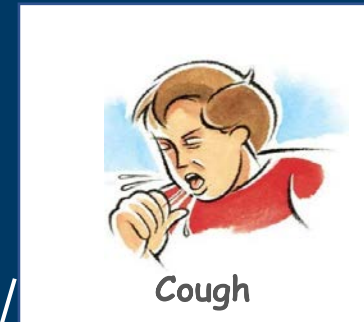
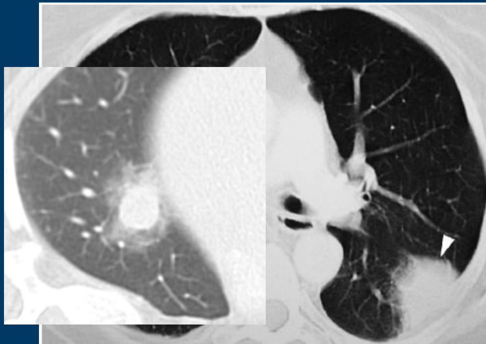
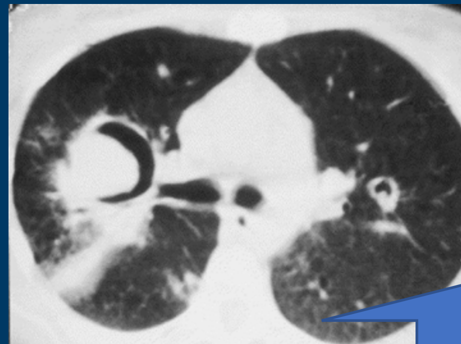
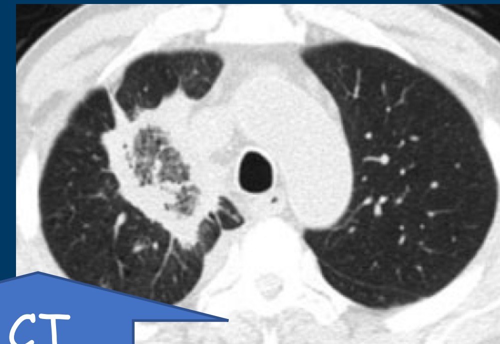
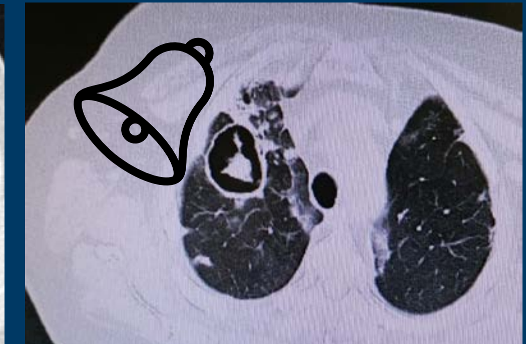


+

- **Clinical data**: unresponsive fever and/or symptoms of lower respiratory tract inf in patients with **risk** factors
- **Imagery** (CT)

CT

Dg~Probable Hematologic pts: Diagnostic-driven = Pre-Emptive

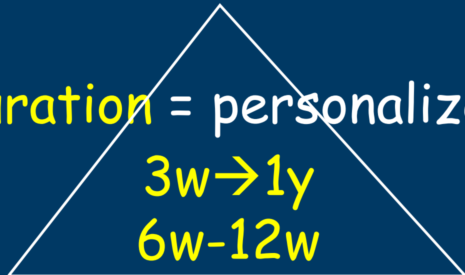
GM /LFD/PCR

- **Histology** Dg=Proven
- **Microbiological** data (serum/blood, BAL, other: biopsies, CSF, sputum, resp. aspirat
  - Direct microscopy (septate, branched 45° hyphae)
  - Cultures: identification to spp. complex
  - Antifungal susceptibility (**5**UFC!)
  - GM (**>0.5** serum, **>1** LBA), PCR, LFD; +/- BDG

Treatment

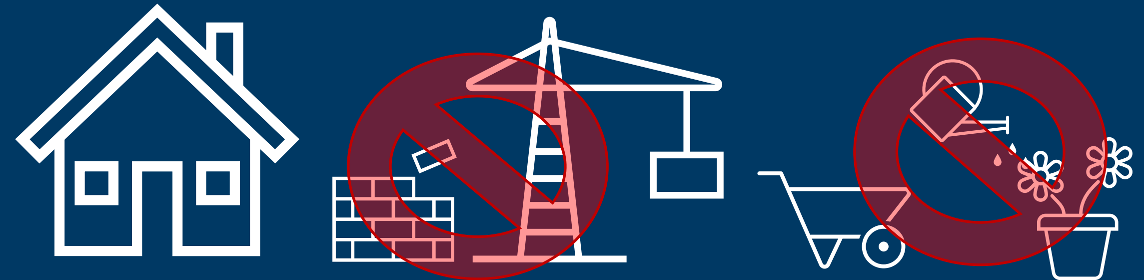
- Antifungals:
  - ➢ Voriconazole or Isavuconazole = I line
  - ➢ AMB (for Azoles-R spp.)
  - ➢ Posaconazole = Prophylaxis

    +TDM especially if VCZ or PCZ suspension!
- Immunosuppression correction = paramount!
- Additional/Special circumstances:
  - ➢ Surgery
  - ➢ Switch to other antifungal class
  - ➢ Combo-therapy
- Duration = personalized: clinical improvement
  imagery resolution&
  immunosupp. revers



Environment Control

- ✓ Room: +ve pressure/ laminar/HEPA
- ✓ Filters for air& water



COVID19: Pro-Fungal triad

SARS-CoV2	Treatment	Co-morbidities

COVID19: Pro-Fungal triad

SARS-CoV2

- **Lymphopenia**, CD4↓
- **Endotelititis** & endothelial injury & thrombosis (inflammation &cytokine storm)
- ↑ **Fe++**
- ↑ **acidosis**
- ↑ **glicemia**

Treatment

- Steroids:
  - ↑**glicemia**/ DM novo/ Decompens DM
  - ↓**phagocytosis** (impaired Ne, MØ)
- AntiIL6, AntiIL1
- Fever(=protective) block!
- AB: e.g.Linezolid iv (G 5%)

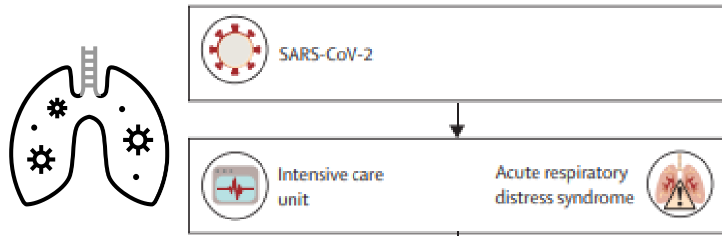
Co-morbidities

- **DM**
- Obesity
- Chronic lung diseases
- Cardiovascular diseases
- Cancers
- Immunosuppressive medication

Defining and managing **CAPA** (COVID-19-associated pulmonary **aspergillosis**): the 2020 ECMM/ISHAM consensus criteria

- Prospective cohort **108** critical pts+ARDS: **44% CAPA** (vs 19%): excess of mortality 16-25% at 30d CAPA vs nonCAPA!

- **Consensus definitions for CAPA: proven, probable, possible**



Histology

Invasive growth

or

or

or

a combination

Proven

Microbiol LBA ser

or

or

index >0·5

or

index ≥1·0

or

2×

or

†

<36 threshold cycle

or

†

plus

or

a combination

Imagery

Pulmonary infiltrate

or

cavitating infiltrate

or

both

Clinical

Refractory fever

or

pleural rub

or

chest pain

or

haemoptysis

or

a combination

Microbiol Aspirat

or

or

index >4·5

or

2×

index >1·2

or

index >1·2

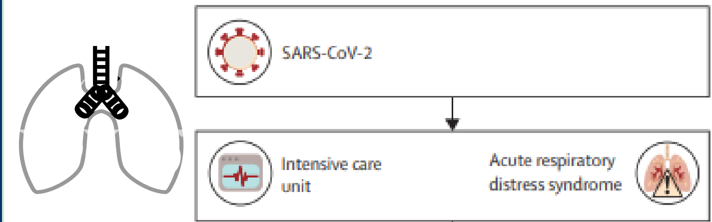
plus

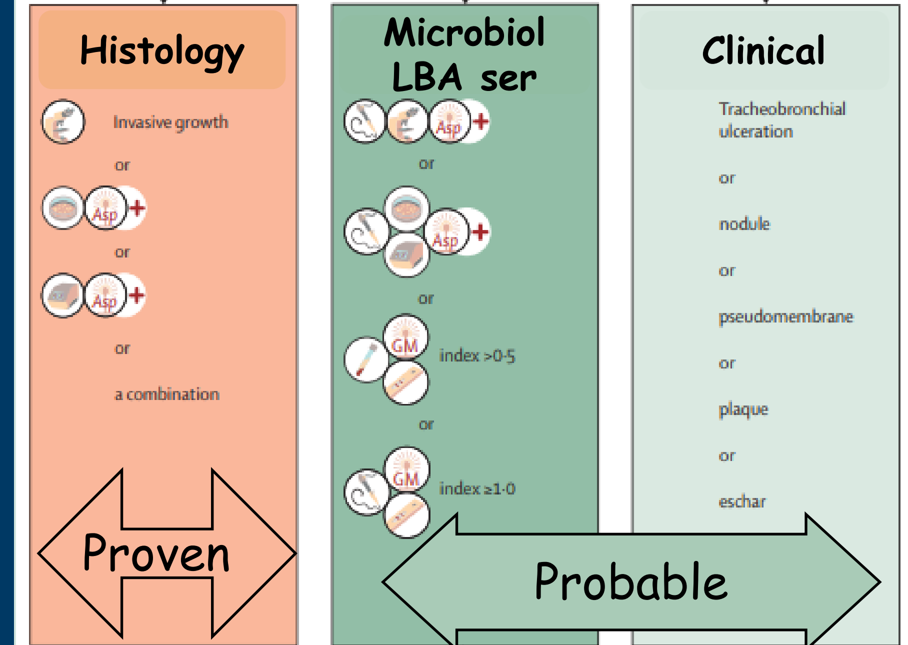
or

a combination

Probable

Possible





Positive | Lung biopsy | Aspergillus | Microscopy

Two tests | CT | Enzyme immunoassay for galactomannan | Culture

Serum | Lateral flow assay* | Bronchoalveolar lavage

Plasma, serum, or whole blood | PCR | Non-bronchoscopic lavage

Defining and managing **CAPA** (COVID-19-associated pulmonary **aspergillosis**): the 2020 ECMM/ISHAM consensus criteria

- **Prevention and management**:
  - Limit steroids use & antiIL6
  - Control DM! Hglicemia!
- **In addition**, for ICU pts:
  - Clinic: fever >/=3d nonresponsive to Ab; Refractory Resp. Insufficiency
  - Serial imagery
  - Serial tests (1-2/w): BDG, **GM (Se=20%):** serum, **BAL**, sup. resp. tract, PCR or LFA/LFD, culture, smears, +/- biopsies: histology!
- Treatment: VCZ, PCZ, ISZ, AMB-L **Resistance!** DDI (+Remdesivir: CYP3A4!)

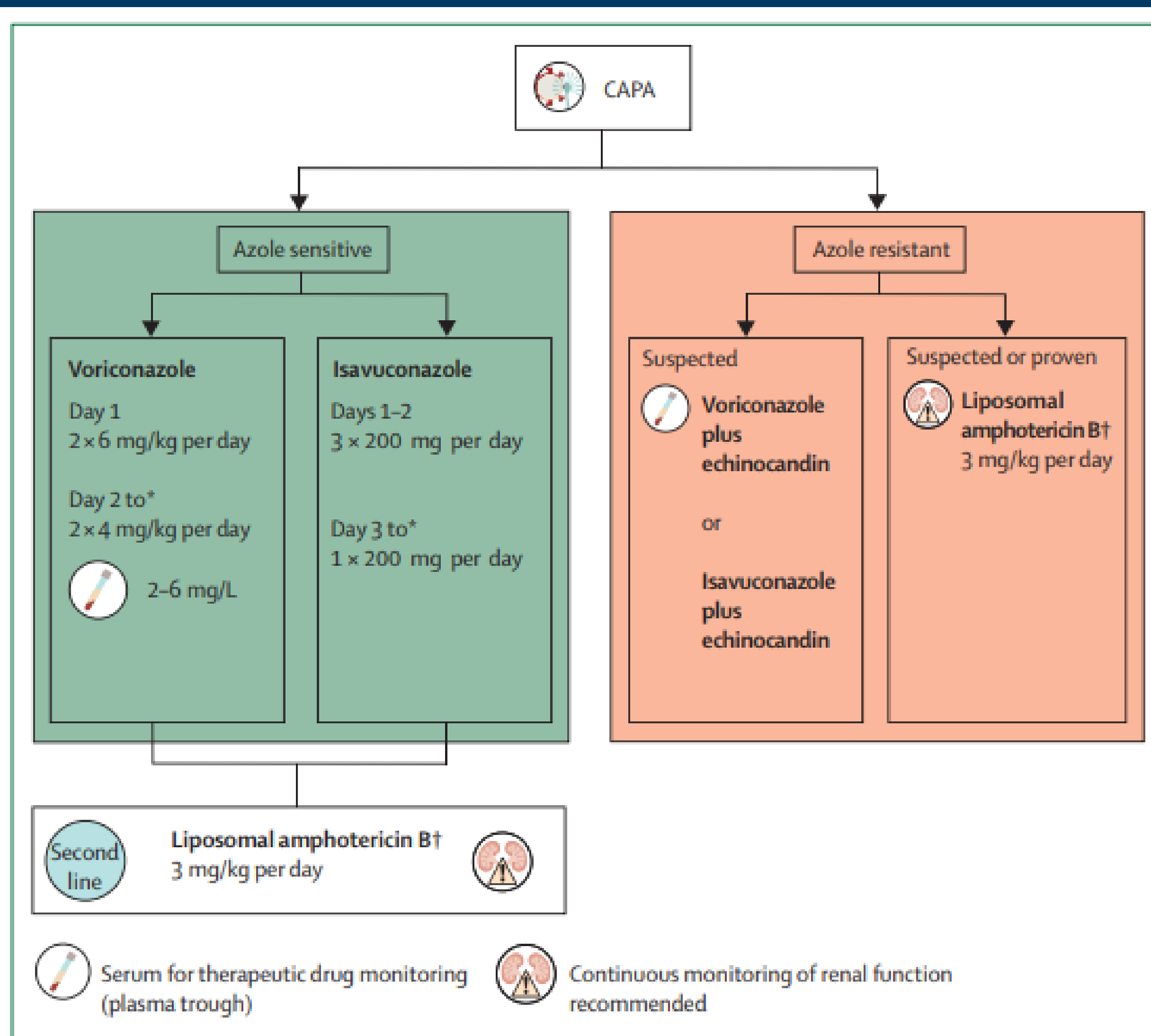


***Figure 3:* Recommended treatment for CAPA**

CAPA=COVID-19-associated pulmonary aspergillosis. *The optimal duration is unknown, but the expert panel suggests 6–12 weeks as a treatment course. In immunocompromised patients (eg, with haematological malignancy or receiving immunosuppressive therapy), longer treatment might be necessary. †Salvage therapy: caspofungin 70 mg loading dose on the first day followed by 50 mg/day. If body weight is more than 80 kg, then 70 mg loading dose on the first day followed by 70 mg/day.

76 yo lady, atrial fibrillation, DM decompensated in Covid19

24 Oct 2021:
Covid19 moderate

28 Oct 2021 (+4days)
Critic: CPAP

18 Nov 2021 (+3weeks)
2l/min O2

3 May 2022
(~6 mo from Dg)

BAL: GM=7.52;
BAL: PCR +++
Blood: GM=1.58
Culture S VCZ, PCZ

Monthly CT; Weekly serum GM

ISZ → VCZ (bad tolerated)→ PCZ (↑GM, ↔ CT) → VCZ again…total: ~6 mo
(!must add LMW Heparin: injectable, twice daily)

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