

# COVID-19-Associated Fungal Disease

Since the global spread of COVID-19, reports of secondary infections with fungal organisms, particularly *Aspergillus spp.*, have emerged.

Diagnostic criteria have been proposed for COVID-19-associated pulmonary aspergillosis (CAPA).



## CAPA DIAGNOSTIC CRITERIA

Unlike invasive pulmonary aspergillosis (IPA), no additional immune-suppressing event beyond COVID-19 and associated therapies is required.



SARS-CoV-2 + ICU

COVID diagnosis can be 2 weeks prior to CAPA or within 96 hours after

### PROVEN CAPA

Histopathology with tissue invasion

OR

Detection from sterile site by any of the following means:

- Culture
- Histology
- PCR

### PROBABLE CAPA TRACHEOBRONCHITIS

Tracheobronchitis (eschar, pseudomembrane, ulceration)

AND

BAL with fungal elements OR  
Positive fungal culture OR  
Positive BAL PCR OR  
BAL GM  $\geq 1.0$  index OR  
Serum GM  $\geq 0.5$  index

### PROBABLE CAPA PULMONARY DISEASE

Unexplained pulmonary infiltrate or cavitating lesion

AND

BAL with fungal elements OR  
Positive fungal culture OR  
Positive BAL PCR OR  
Two positive serum PCRs OR  
BAL GM  $\geq 1.0$  index OR  
Serum GM  $\geq 0.5$  index



## RISK FACTORS FOR CAPA

- Solid organ transplant recipients
- Prolonged corticosteroids (>3 weeks at any dose)

AND

## TRADITIONAL RISK FACTORS FOR IPA

- Neutropenia ( $<500/\text{mm}^3$ ) for >10 days
- Hematologic malignancy
- Allogeneic stem cell transplant recipients
- Treatment with T- or B-cell inhibitors
- Inherited immune deficiency syndromes



## TREATMENT OF CAPA

**First line:** Voriconazole or isavuconazole

**Salvage therapy:** Echinocandin plus voriconazole

**Duration:** Unknown, but most recommend 6-12 weeks

**When to start therapy:** At time of suspected diagnosis. **Do not wait** for confirmatory microbiologic, radiographic, or histopathologic evidence. Antifungal therapy can be stopped if diagnostic criteria not met.

**When to suspect CAPA:** Refractory fever for  $\geq 3$  days, fever after >48 hours of defervescence, hemoptysis or worsening pleuritic chest pain

## INCIDENCE OF CAPA

- 5%-35% of ICU patients with COVID-19 ARDS have been reported to have CAPA
- This may be an overestimation of the true incidence, as it is likely that cases of colonization have been counted as true infection
- Using stringent diagnostic criteria, **the true incidence is believed to be around 5%**—similar to the incidence of non-COVID ARDS
- Immune-modulating therapies such as corticosteroids and IL-6 inhibitors may increase the risk

## OTHER FUNGAL DISEASE RELATED TO COVID-19

### Mucormycosis

- <10 cases of associated mucormycosis reported
- Risk factors: Diabetes, renal disease, immune suppression

### Invasive candidiasis (IC)

- Unclear if the incidence of IC has been impacted
- No unique risk for IC secondary to COVID

### Endemic fungi

- Reports of increased incidence of endemic fungal infections, particularly coccidioidomycosis
- Unknown if increased risk secondary to COVID or COVID therapies