

**IN THE NAM OF GOD ▶**



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# **MUCORMYCOSIS AND COVID -19**



# MUCORMYCOSIS ▶



- Mucormycosis, previously called zygomycosis, refers to several different diseases caused by infection with fungi belonging to the order Mucorales.
- Most mucormycosis infections are life-threatening.

- Risk factors such as diabetic ketoacidosis & neutropenia are present in most cases.
- Successful mucormycosis treatment requires correction of the underlying risk factor(s), antifungal therapy (traditionally with a polyene), and aggressive surgery.



# Etiology and Pathophysiology

- Risk factors:
  - Diabetes mellitus → especially ketoacidosis
  - Patients with cancer, especially → neutropenic & receiving broad-spectrum antibiotics
  - Patients with immunosuppressive agents → steroids & TNF-alpha blockers
  - Patients with hematologic cancer → CMV inf. & GVHD

# Etiology and Pathophysiology

- Prior receipt of voriconazole
- Extreme malnutrition → GI
- Deferoxamine use (older iron chelators)
- Trauma & contaminated medical supplies over wounds → cutaneous mucormycosis.



# Etiology and Pathophysiology

- Nonsterile tape & contaminated wooden splints with trauma/surgery
- Presence of a preexisting wound or IV line.
- Patients with burns
- No identifiable risk factors.

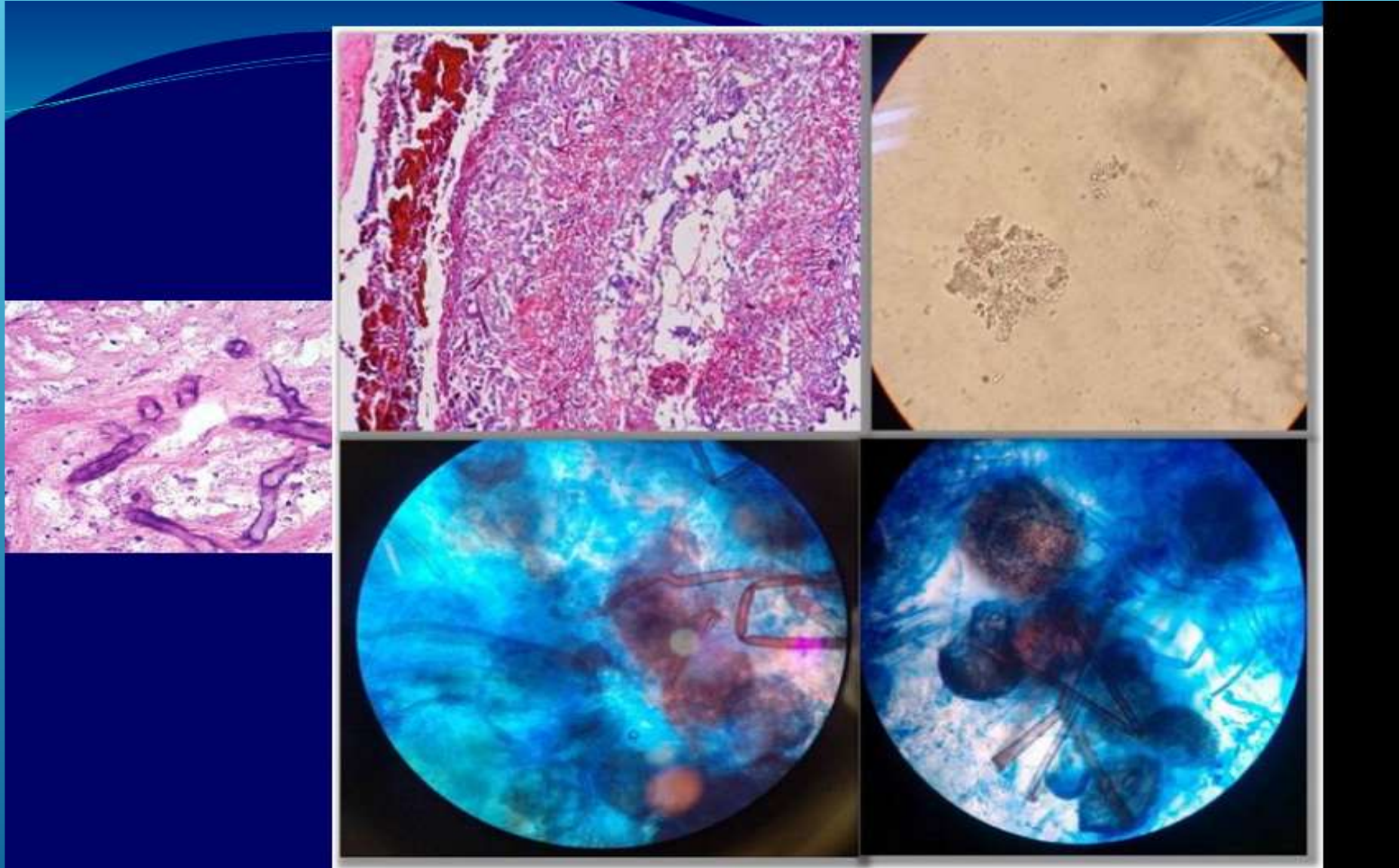
# Pathophysiology

- Mucorales are ubiquitous fungi that are commonly found in soil and in decaying matter.
- Rhizopus can be found in moldy bread.
- The major route of infection → inhalation of conidia
- Other routes:
  - Ingestion
  - Traumatic inoculation



# Pathophysiology

- **fungal hyphae invade blood vessels, producing tissue infarction, necrosis, and thrombosis.**
- When spores are deposited in:
  - Nasal turbinates → rhinocerebral disease
  - Lungs → pulmonary
  - Ingested → GI disease
  - Interrupted skin → cutaneous disease



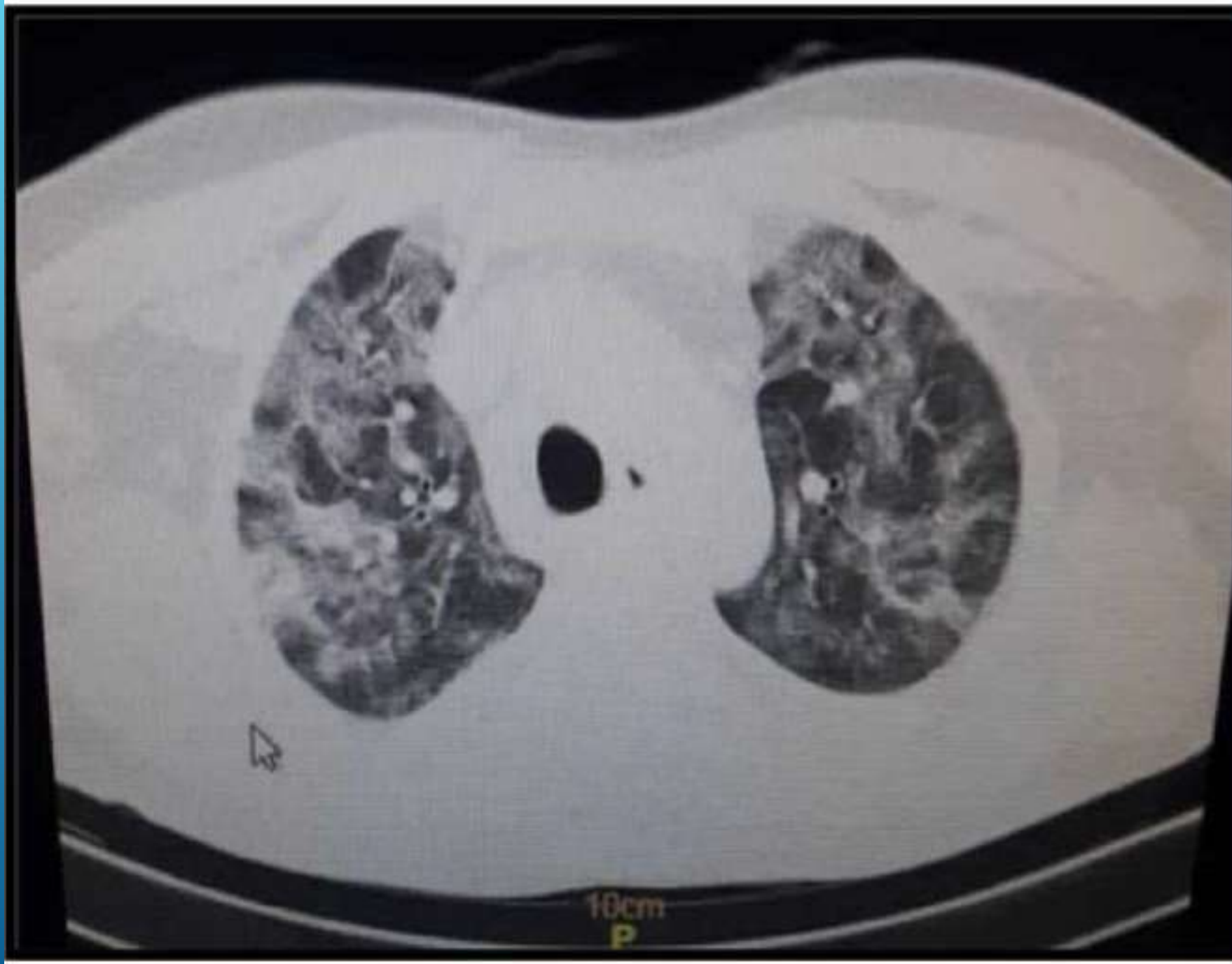


# History and Physical Examination

- Rhinocerebral disease
- Pulmonary disease
- Cutaneous disease
- Gastrointestinal
- Disseminated disease
- Central nervous system





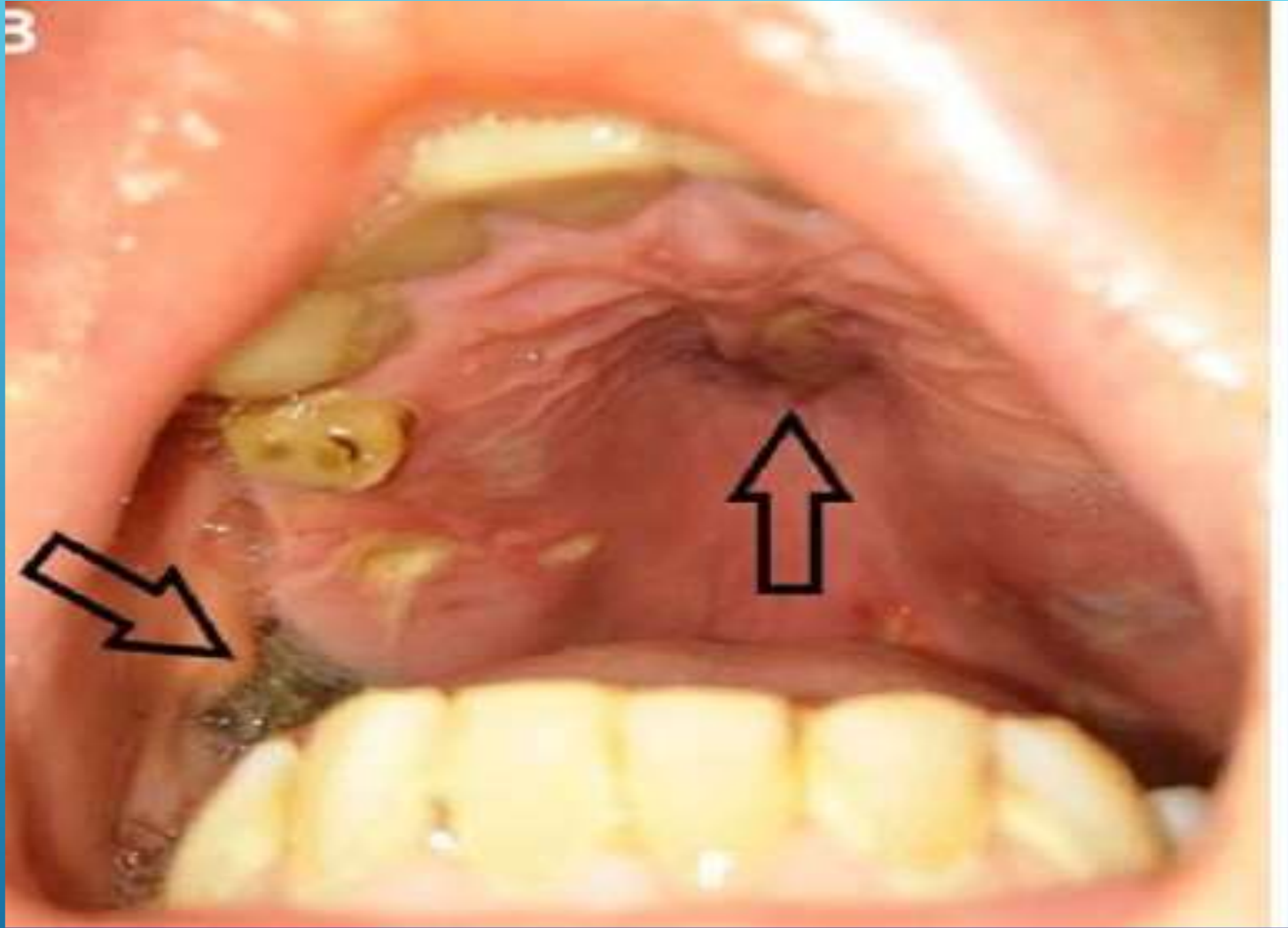














# Prognosis

- Prognosis and survival depend on early diagnosis and timely initiation of treatment.
- Mortality varies between 40%-80%, despite advances in treatment
- Mortality depends on the site of infection.

# Prognosis

- Higher mortality of 80% → disseminated disease to CNS
- Rhino-orbital-cerebral → mortality rate of 25% to 62%
- Rapid diagnosis, and early surgical debridement, lead to lower mortality

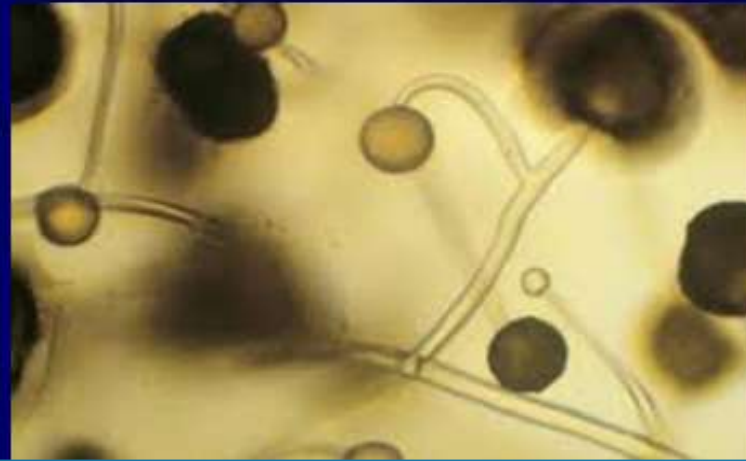
# Laboratory Tests

- Complete blood cell
- Chemistry panel
- Molecular based testing



# Diagnosis

- Imaging
- Non-pigmented hyphae showing tissue invasion must be shown in tissue sections stained with haematoxylin-eosin, periodic acid-Schiff stain or Grocott-Gomori's methenamine-silver stain or both.
- Histopathologically, Mucorales hyphae have a variable width of 6–16  $\mu\text{m}$ , but may be up to 25  $\mu\text{m}$ , and are non-septate or pauci-septate



# COVID-19 and Mucormycosis

- COVID-19 disease can be complicated by:
  - Secondary bacterial infection
  - Invasive fungal infection (COVID-19-associated pulmonary aspergillosis, Pneumocystosis, and mucormycosis)



Criteria for the clinical diagnosis of mucormycosis are still considered to be gold standard and include:

- Black, necrotic turbinate's easily mistaken for dried, crusted Blood
- Blood-tinged nasal discharge and facial pain, both on the same side

**Criteria for the clinical diagnosis of mucormycosis are still considered to be gold standard and include:**

- **Soft peri-orbital or peri-nasal swelling with discoloration and induration**
- **Ptosis of the eyelid, proptosis of the eyeball and complete ophthalmoplegia & Multiple cranial nerve palsies unrelated to documented lesions**



A number of triggers that may precipitate mucormycosis in people with COVID-19 in relation to corticosteroids:

- Presence of DM with or without DKA increases the risk of contracting mucormycosis and DM is often associated with an increased severity of COVID-19,
- Uncontrolled hyperglycemia and precipitation of DKA is often observed due to corticosteroid intake.
- Low pH due to acidosis is a fertile media for mucor spores to germinate.

- Low pH due to acidosis is a fertile media for mucor spores to germinate.
- Steroid use reduces the phagocytic activity of WBC (both first line and second line defense mechanism), causes impairment of bronchoalveolar macrophages migration, ingestion, and phagolysosome fusion, making a diabetic patient exceptionally vulnerable to mucormycosis.



- COVID-19 often causes endothelialitis, endothelial damage, thrombosis, lymphopenia, and reduction in CD4 and CD8 T-cell level and thus predisposes to secondary or opportunistic fungal infection,
- Free available iron is an ideal resource for mucormycosis.



- Hyperglycemia causes glycosylation of transferrin & ferritin, & reduces iron binding allowing increased free iron.

- Increase in cytokines in patients with COVID-19 especially interleukin-6, increases free iron by increasing ferritin levels due to increased synthesis and decreased iron transport.
- Concomitant acidosis increases free iron by the same mechanism and additionally by reducing the ability of transferrin to chelate iron,



# COVID-19 and Mucormycosis

- The most common clinical manifestation was rhino-orbital form.
- Case fatality at 12 weeks was 45.7% with no difference in mortality among COVID-19 and non-COVID-19 patients.
- Case reports describe patients who were diagnosed with rhinocerebral mucormycosis and COVID-19 simultaneously
- Patient who was diagnosed with GI mucormycosis five days after admission for COVID-19 treated with both steroids and tocilizumab



- COVID-19 has a predisposition to cause extensive lung damage, which promotes colonization and infection of invasive fungi of airway, sinuses, and lung.
- Alteration in T cell immunity, use of steroids, and broad-spectrum antibiotics are additional risk factors for acquiring invasive fungal infection.

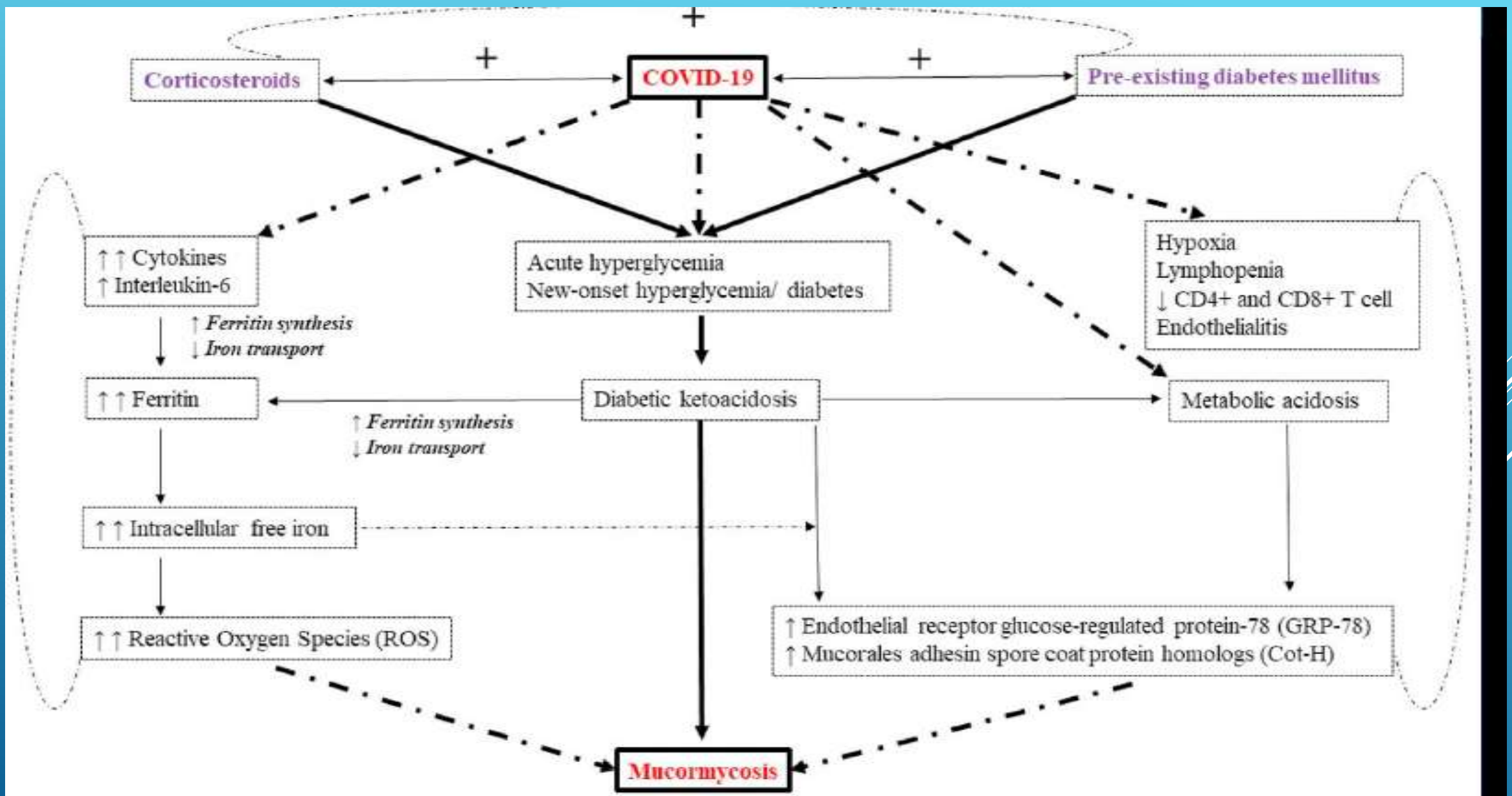
- COVID-19 disrupts iron metabolism, resulting in high ferritin state and increasing intracellular iron, which causes tissue damage.
- This causes more iron to be released into the circulation, and it is this increase in free iron that is a risk factor for mucormycosis.



- Patients with diabetes and infected with SARS-CoV2 are at increased risk for mucormycosis
- A retrospective study conducted in India from Sep -Dec 2020, reported a 2.0 fold rise in 2020 compared to 2019 of COVID-19 mucormycosis



- One review of case reports of mucormycosis in patients with COVID-19 included 101 cases:
  - 80 % had pre-existing diabetes mellitus
  - 76 % received glucocorticoids
- The majority of cases were from India
  - 90 % of cases involved the nose and sinuses
- Overall mortality was 31 %
- Clinicians should be aware of the potential for rhinocerebral mucormycosis as a complication of COVID-19, especially in patients with underlying diabetes mellitus.



**THANKS FOR ATTENTION ▶**

