

Mucormycosis (Zygomycosis)

Opportunistic fungal disease • Innate immunity • Angioinvasion

An integrated morphologic and clinicopathologic lecture

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraisakhri.com

Pathology learning objectives

- Classify mucormycosis as an opportunistic mycosis caused by environmental molds.
- Explain how phagocyte defenses and iron availability influence invasive infection.
- Recognize the characteristic fungal morphology and destructive vascular pathology.
- Connect the entry site with rhinocerebral, pulmonary, gastrointestinal, and wound disease.

Identify the fungus

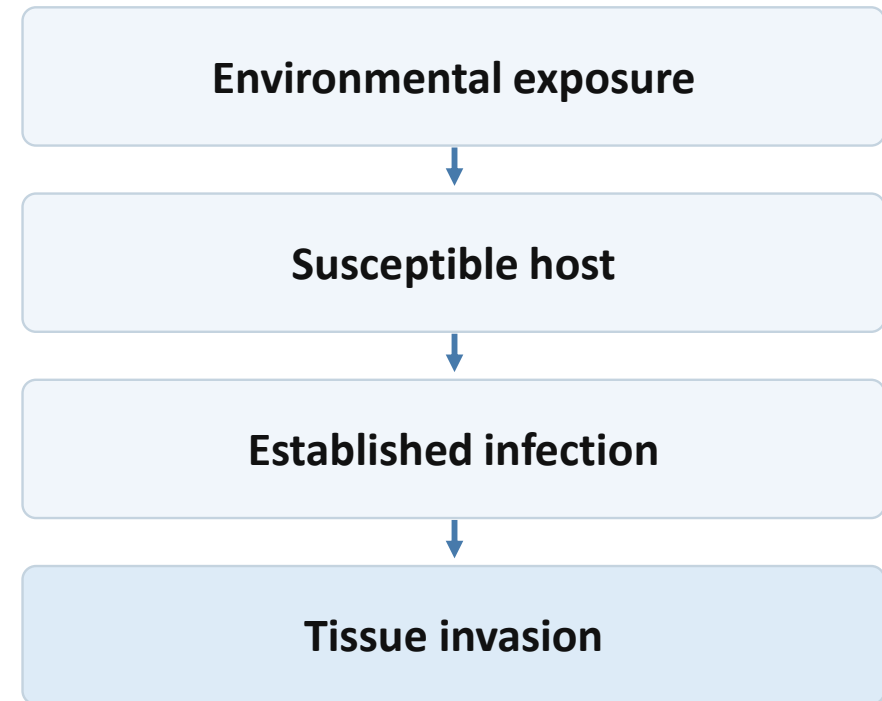
Explain host defenses

**Recognize
angioinvasion**

Interpret organ injury

Mucormycosis is an invasive opportunistic mycosis

- Mucormycotina are widespread environmental fungi.
- Exposure alone does not imply tissue-invasive disease.
- A vulnerable host allows fungal growth and destructive invasion.



Mucorales agents encountered

- The disease name encompasses infections due to multiple environmental genera.
- Mucor, Rhizopus, Rhizomucor, and Cunninghamella.
- Morphologic recognition in tissue generally precedes species-level identification.

Mucor spp.

Rhizopus spp.

Rhizomucor spp.

Cunninghamella spp.

Historical terminology: Zygomycosis

- Robbins titles the section “Mucormycosis (Zygomycosis).”
- It explicitly identifies zygomycosis as a former name.
- The lecture uses mucormycosis for the invasive disease described in the source.

Former term

Zygomycosis

Current term

Mucormycosis

Mold growth provides the morphologic context

- Fungal molds form multicellular filaments called hyphae.
- Molds extend by growth and division at hyphal tips.
- Tissue hyphae are the key structures in mucormycosis morphology.

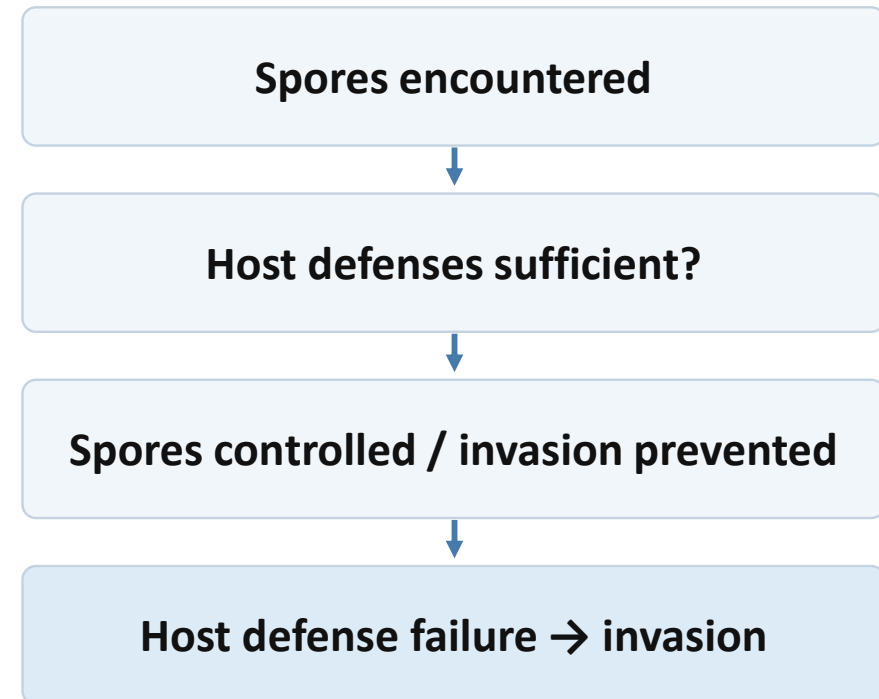
**Yeasts:
Round/oval
cells**

**Molds:
Filamentous
hyphae**

**Mucormycetes:
Invasive
hyphae**

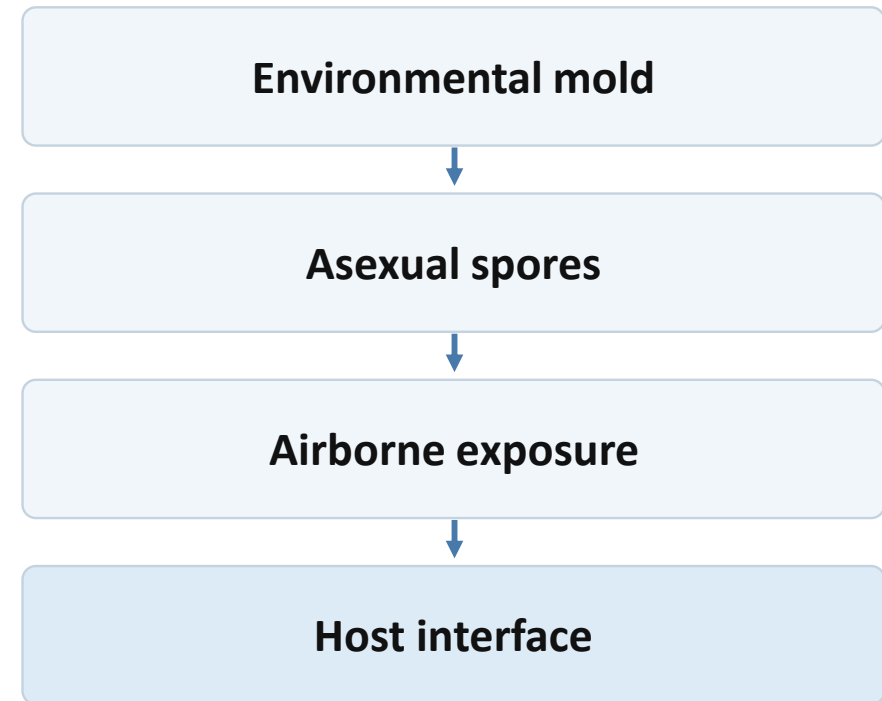
Opportunistic infection depends on the host

- The textbook places mucormycosis among opportunistic mycoses.
- Immunocompetent hosts usually resist these environmental fungi.
- Impaired host defenses permit spores to establish infection.



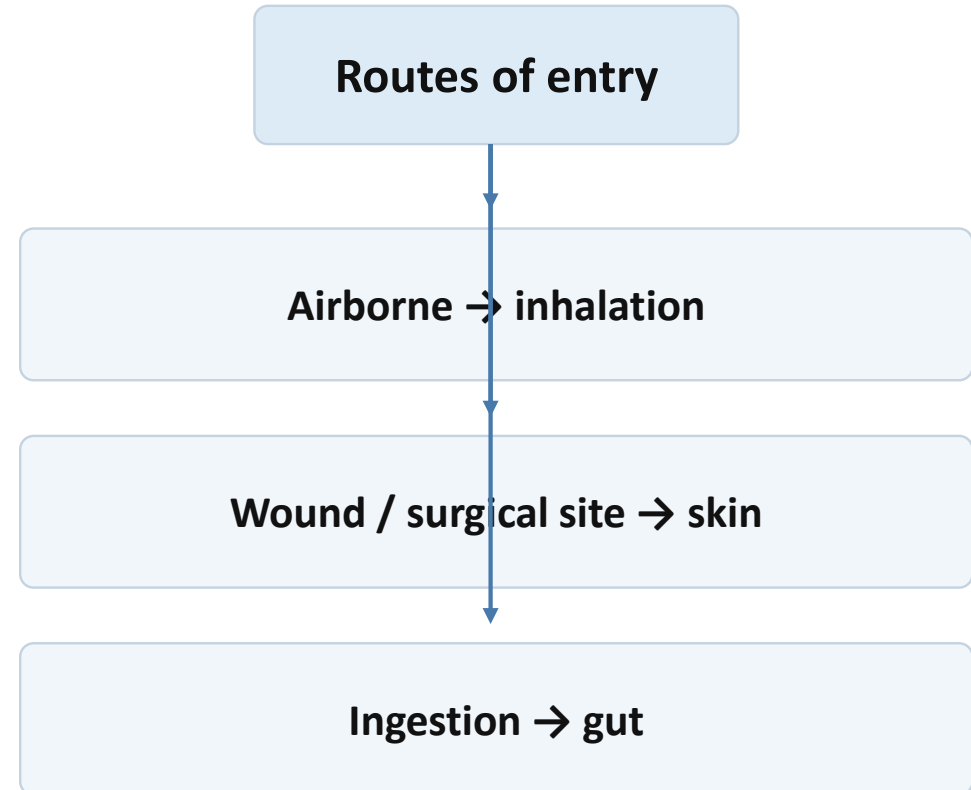
Aerosolized spores make exposure common

- Mucormycotina produce asexual spores dispersed in air.
- Dust and air can carry infective propagules.
- The severity of infection depends strongly on host context, not simply exposure.



Three principal entry routes

- Inhalation of spores is the most common portal of entry.
- Percutaneous contamination can follow injury or an operative procedure.
- Ingestion provides an additional route to infection.



Entry route influences anatomic distribution

- Sinuses, lungs, and gastrointestinal tract are the principal organ sites.
- Entry by air, wound contamination, or ingestion suggests different starting locations.
- Subsequent vascular invasion can extend injury beyond the original focus.

Portal	Potential focus
Inhalation	Sinuses or lungs
Ingestion	Gastrointestinal tract
Percutaneous	Wound / skin

Major susceptibility factors

- Deficits in phagocyte number or function.
- Metabolic changes affecting available iron also promote infection.
- Damage to the cutaneous barrier enables direct inoculation.

Neutropenia

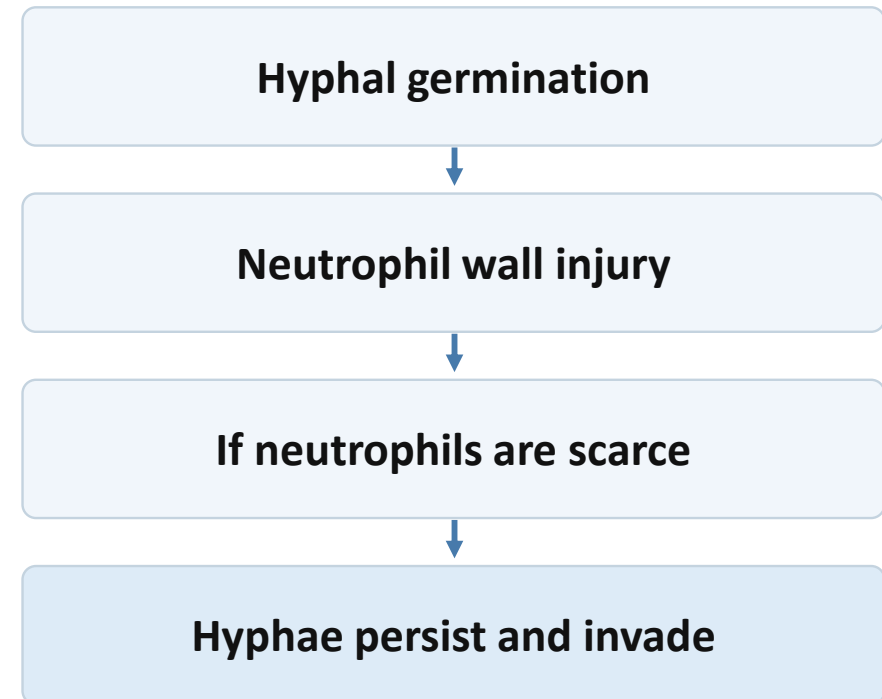
Corticosteroids

**Diabetes / iron
overload**

Wounds / trauma

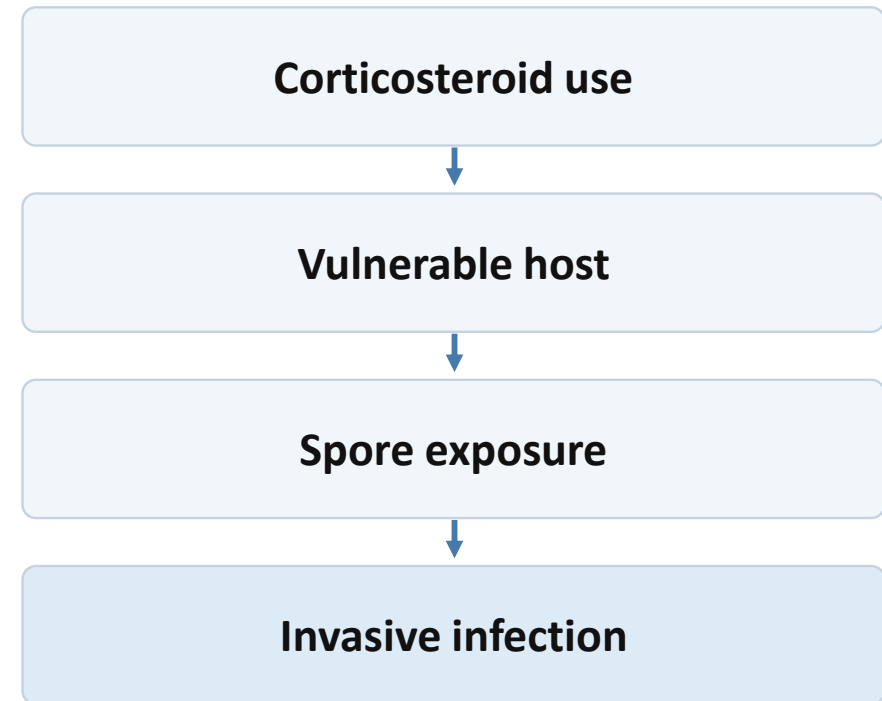
Neutropenia removes an essential hyphal defense

- Neutrophils directly injure fungal hyphal walls after germination.
- Reduced neutrophil number compromises this defense.
- Invasive growth becomes more likely when viable hyphae persist.



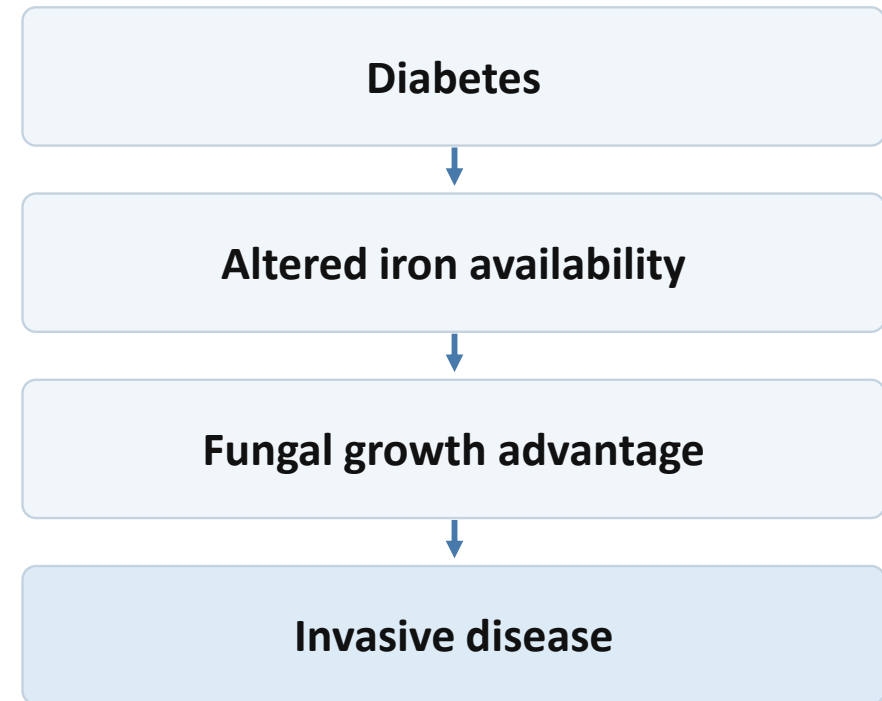
Corticosteroid exposure increases susceptibility

- Corticosteroid use is named as a major predisposing condition.
- It belongs to the immune-suppression component of the risk profile.
- Interpret risk in conjunction with other host factors and exposure routes.



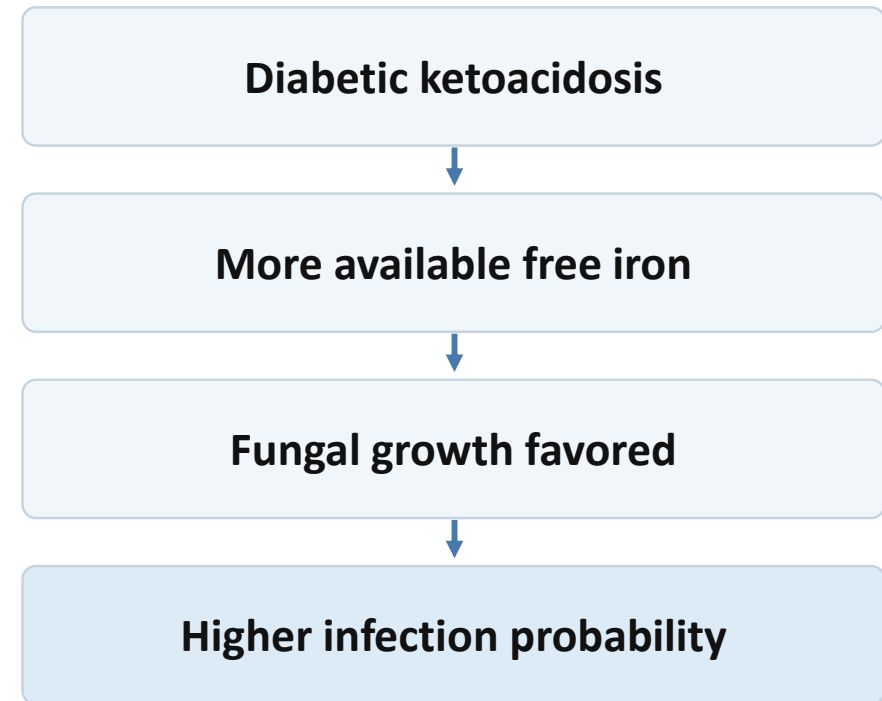
Diabetes mellitus is a major host context

- Diabetes mellitus is one of the major predisposing factors.
- The textbook links diabetes to altered free-iron availability.
- Diabetic ketoacidosis is particularly associated with rhinocerebral disease.



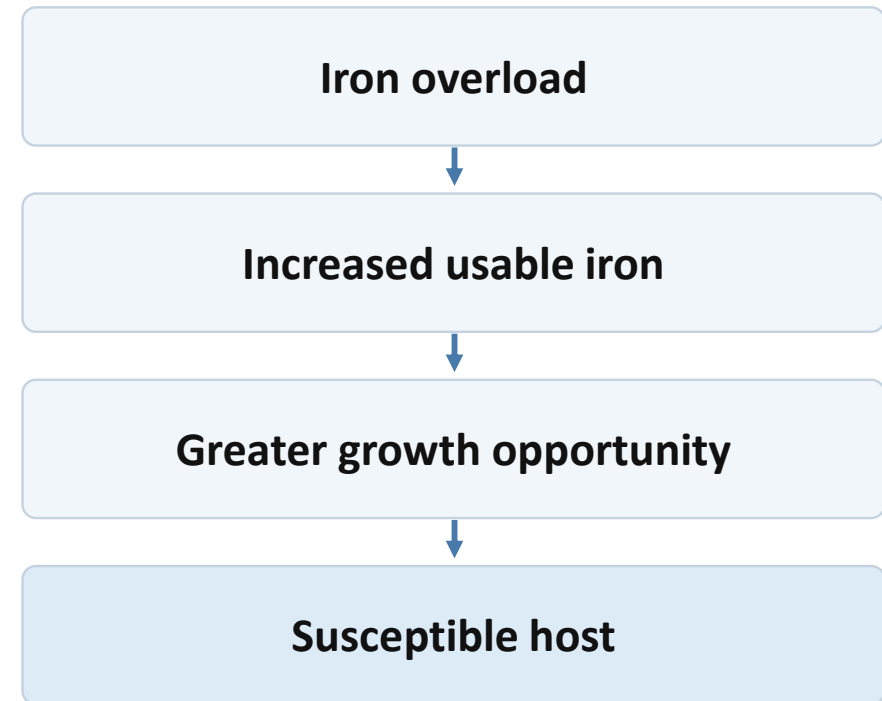
Ketoacidosis increases accessible iron

- Diabetic ketoacidosis with increased free iron.
- The proposed mechanism involves diminished normal iron binding.
- Free iron promotes Mucormycotina growth.



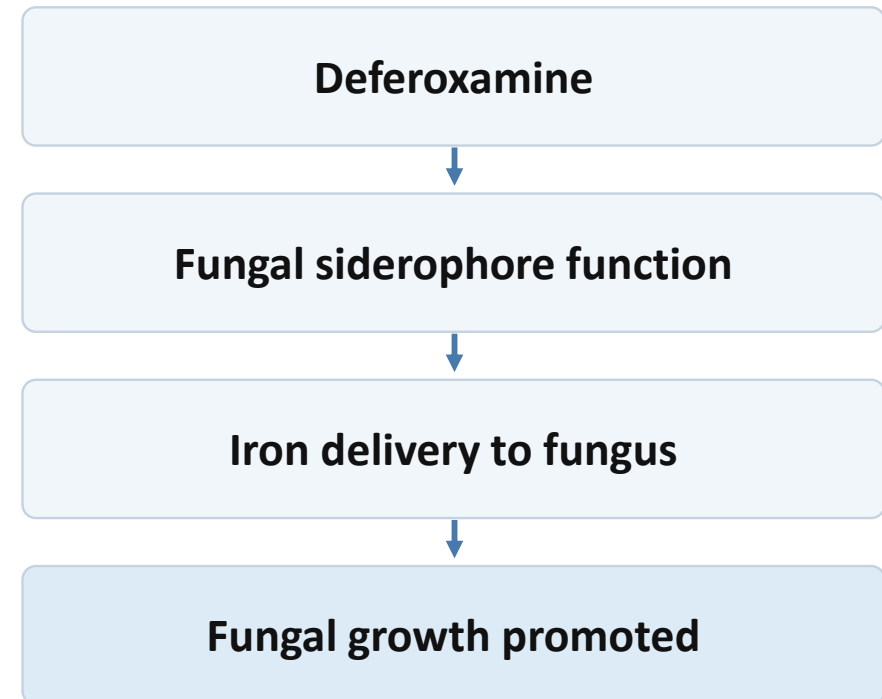
Iron overload is a separate risk factor

- Iron overload appears among the major predisposing conditions.
- Mucormycotina benefit from available free iron.
- The risk relates to usable iron, not merely the presence of iron in tissue.



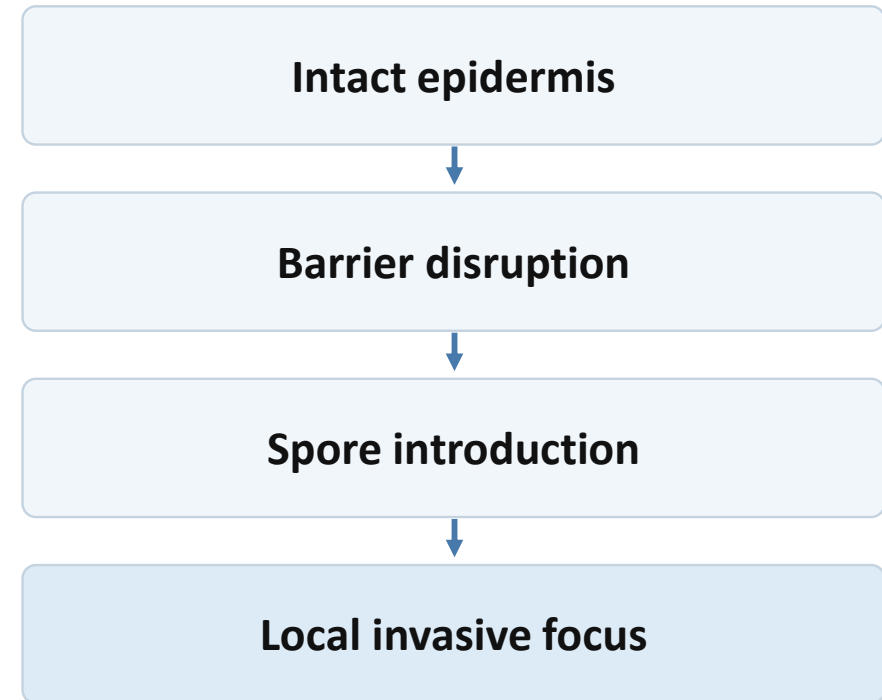
Deferoxamine can facilitate fungal iron access

- Chronic deferoxamine chelation as a special risk.
- Deferoxamine can serve as a siderophore for these fungi.
- This explains why chelation does not necessarily deprive them of iron.



Barrier breakdown creates a cutaneous portal

- Burns, surgical wounds, and trauma disrupt the skin barrier.
- Spores can enter directly at these vulnerable sites.
- This pathway is distinct from the usual airborne route.



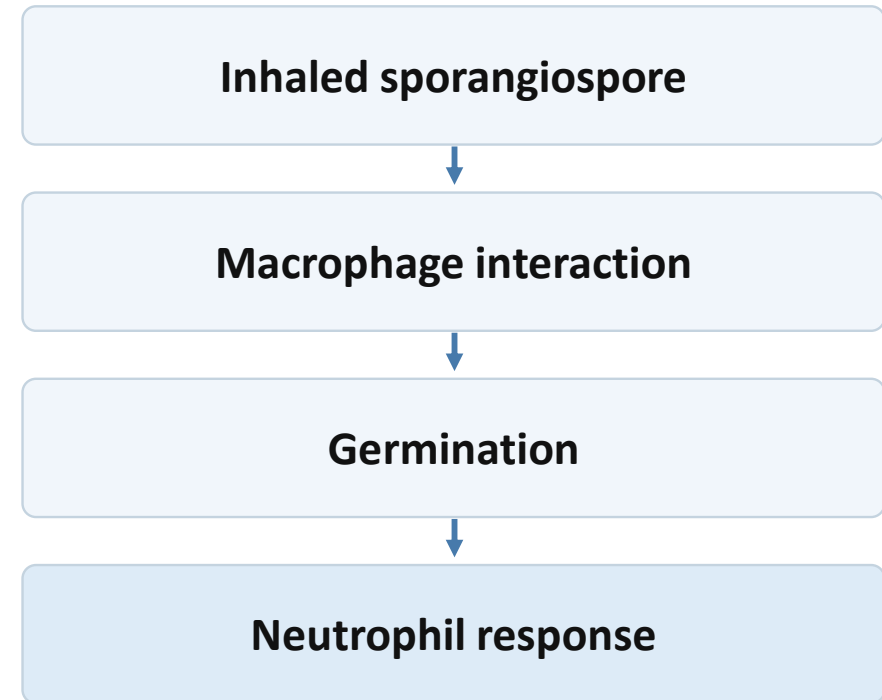
The risk factors act through different pathways

- Neutropenia primarily compromises direct hyphal killing.
- Metabolic and chelation states alter fungal access to iron.
- Wounds create a direct route through a disrupted surface barrier.

Host problem	Principal vulnerability
Neutropenia	Reduced hyphal killing
Diabetes / iron	Enhanced fungal growth
Barrier injury	Direct inoculation

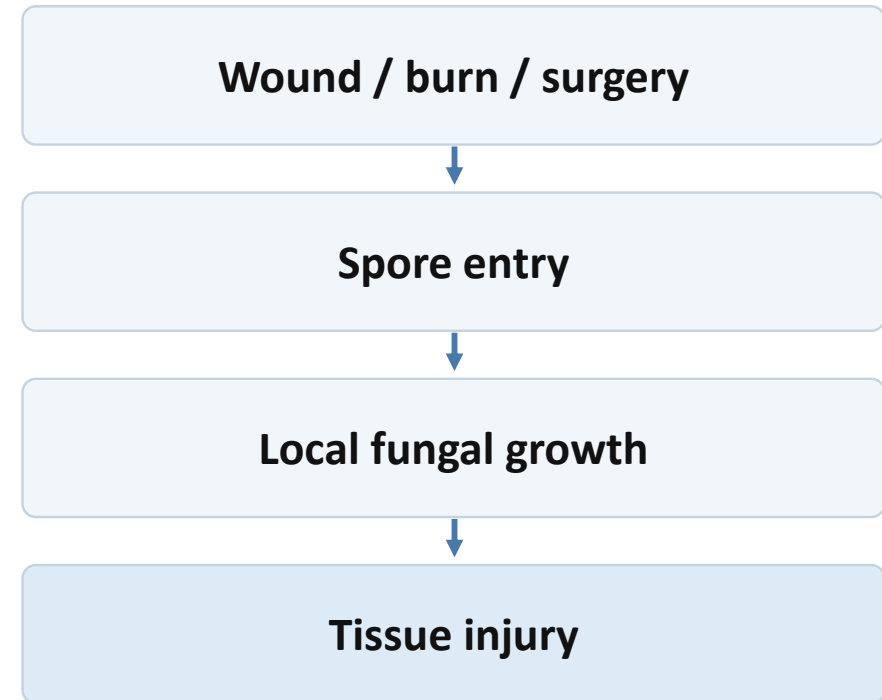
Inhaled spores meet innate defenses

- Inhalation is the most common entry route.
- Germinating spores normally encounter tissue macrophages.
- Neutrophils become critical when fungi develop hyphae.



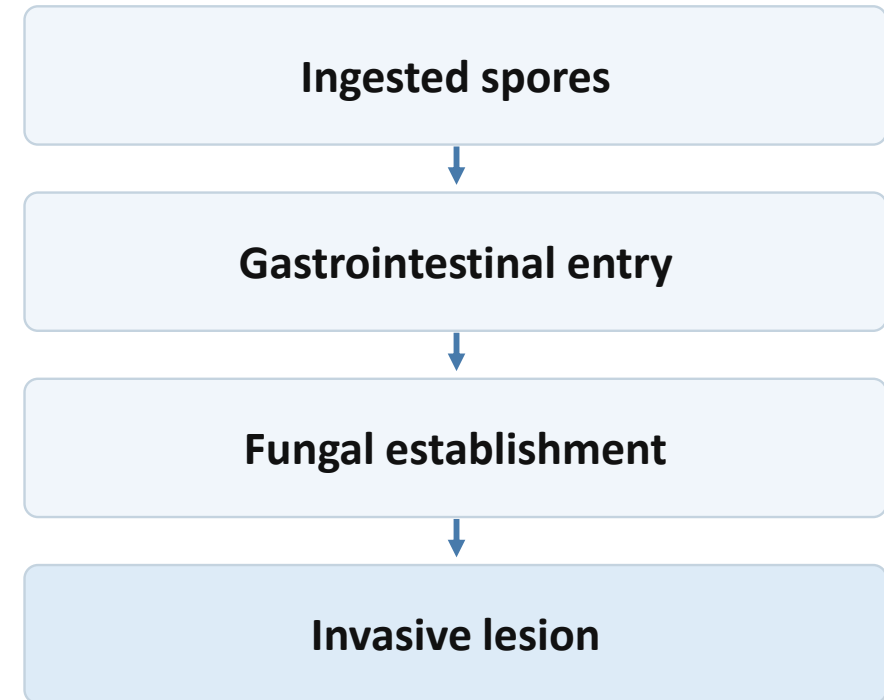
Percutaneous exposure bypasses surface protection

- Trauma or a surgical wound provides a break in the cutaneous barrier.
- The wound can be exposed to environmental spores.
- The resulting focus can undergo local tissue invasion and necrosis.



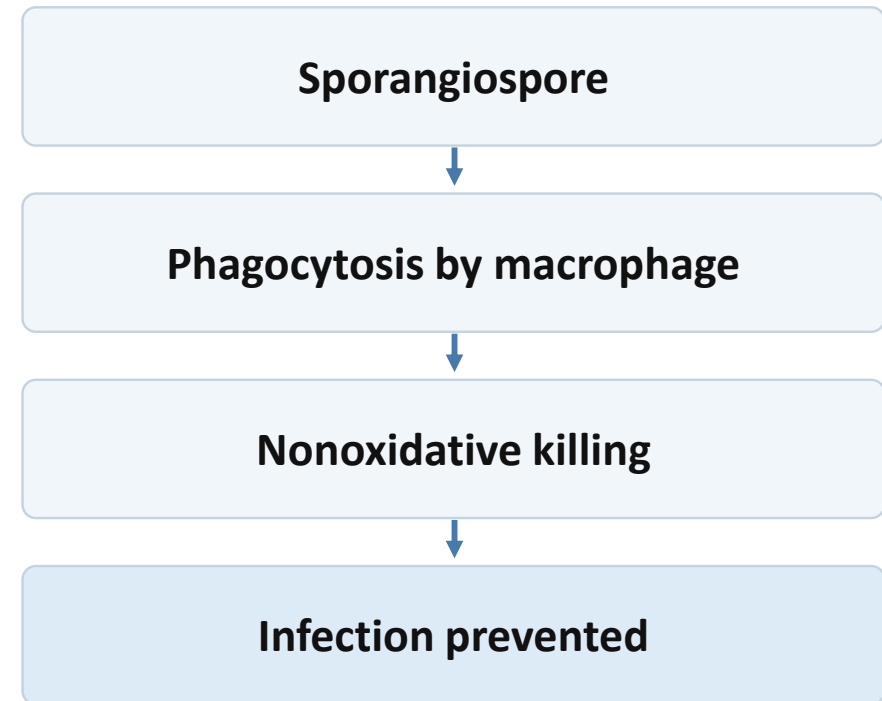
Ingestion can seed gastrointestinal disease

- Ingestion is a recognized alternative mode of entry.
- The gastrointestinal tract is a primary site of fungal invasion.
- Interpret organ involvement in light of the route of exposure.



Macrophages are the first defensive barrier

- Macrophages phagocytose germinating sporangiospores.
- Early killing to nonoxidative mechanisms.
- Effective macrophage function helps prevent establishment.



Germination changes the host–pathogen interface

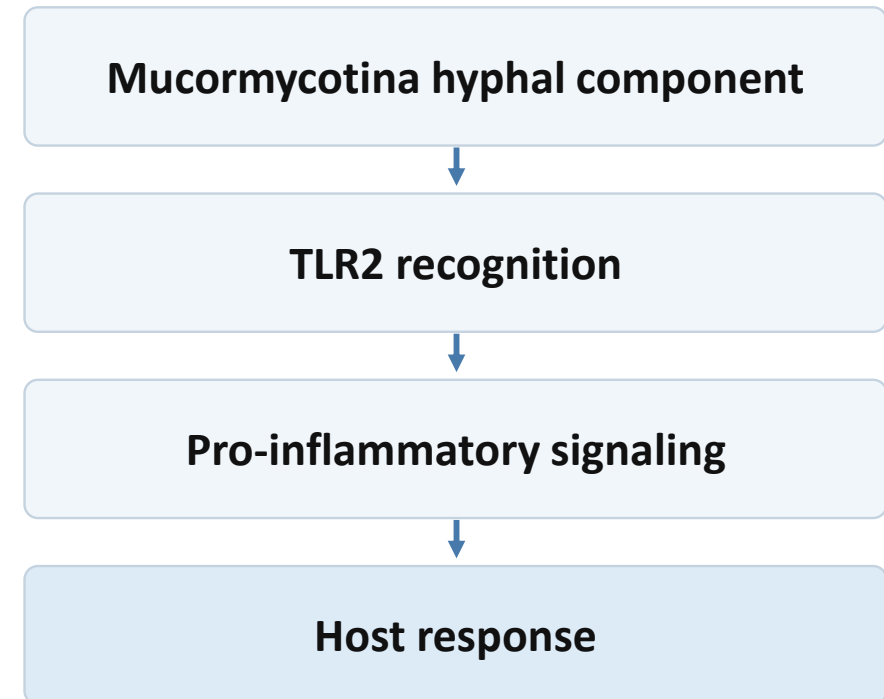
- The source distinguishes sporangiospores from mature hyphae.
- Macrophages act early during spore germination.
- Neutrophils are particularly important after hyphae develop.

**Early: Germinating
spores**

Later: Invasive hyphae

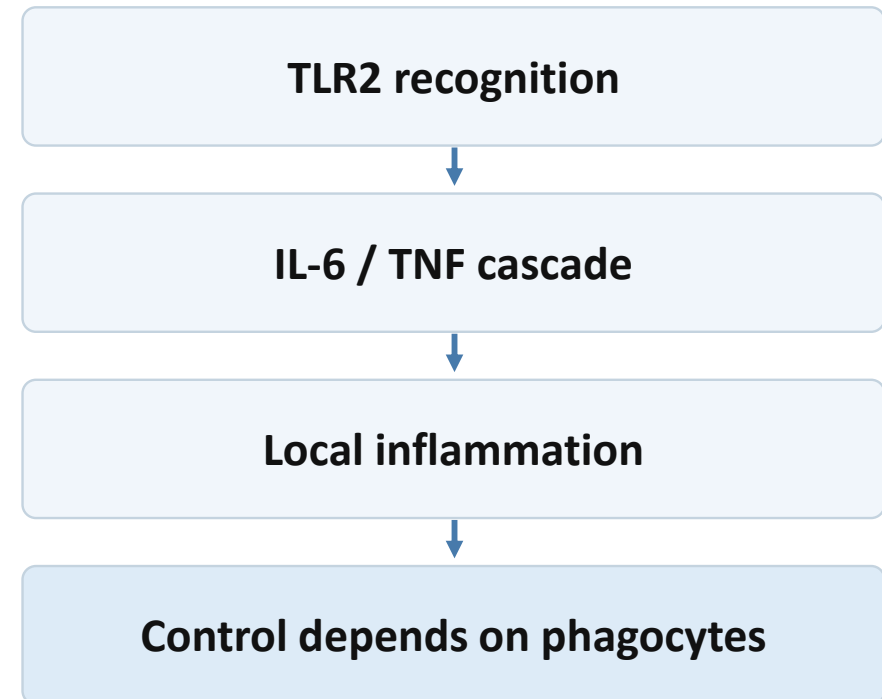
TLR2 detects fungal hyphal components

- Fungal hyphal components are recognized through TLR2.
- This recognition triggers a pro-inflammatory response.
- The innate reaction recruits and activates antifungal host defenses.



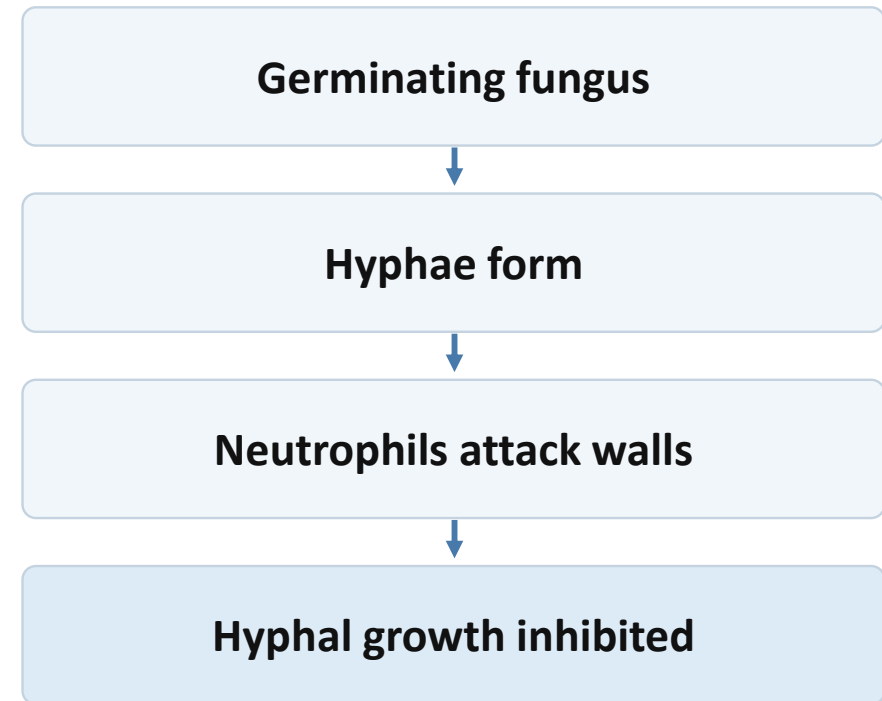
Inflammatory mediators include IL-6 and TNF

- Robbins explicitly names IL-6 and tumor necrosis factor (TNF).
- Both belong to the response induced by recognition of hyphal components.
- Inflammation alone is not evidence that fungal growth is controlled.



Neutrophils directly damage hyphal walls

- Neutrophils have a key role once sporangiospores germinate.
- Their antifungal effect includes direct hyphal-wall damage.
- This action limits ongoing filamentous tissue invasion.



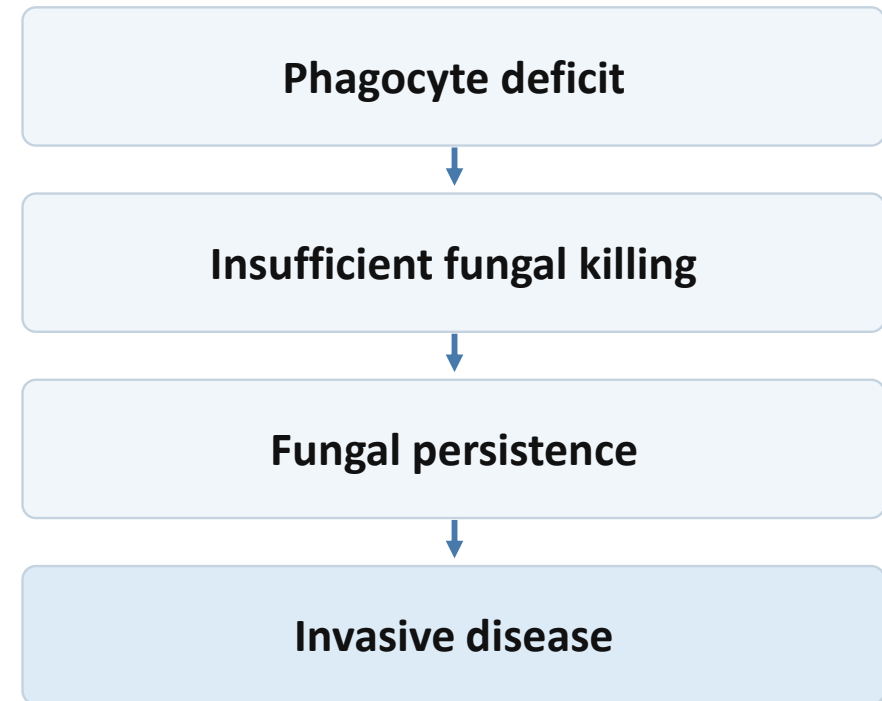
Two coordinated phases of innate resistance

- Macrophages act at the germinating-spore stage.
- Neutrophils are emphasized at the hyphal stage.
- Compromise of either population facilitates establishment and invasion.

Defense	Principal target
Macrophages	Germinating sporangiospores
Neutrophils	Germinated hyphae
Both impaired	Greater invasive risk

Compromised phagocytes permit fungal persistence

- Reduced cell number or impaired cell function raises the probability of infection.
- Persistent fungal growth increases the likelihood of tissue invasion.
- Host failure is the central switch from exposure to disease.



Aggressiveness varies between Mucor species

- The source reports species-related variation in resistance to phagocytosis.
- Susceptibility to neutrophil-mediated damage also varies.
- The reasons for these interspecies differences remain unknown.

Spore phagocytosis resistance



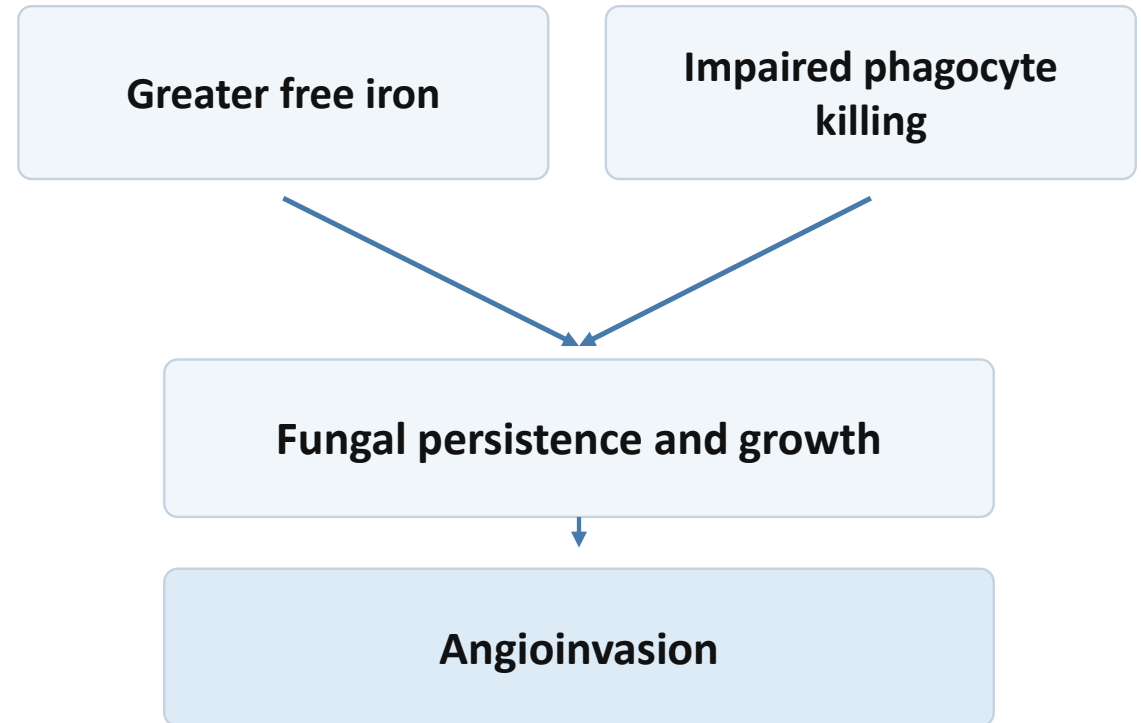
Hyphal resistance



Different clinical aggressiveness

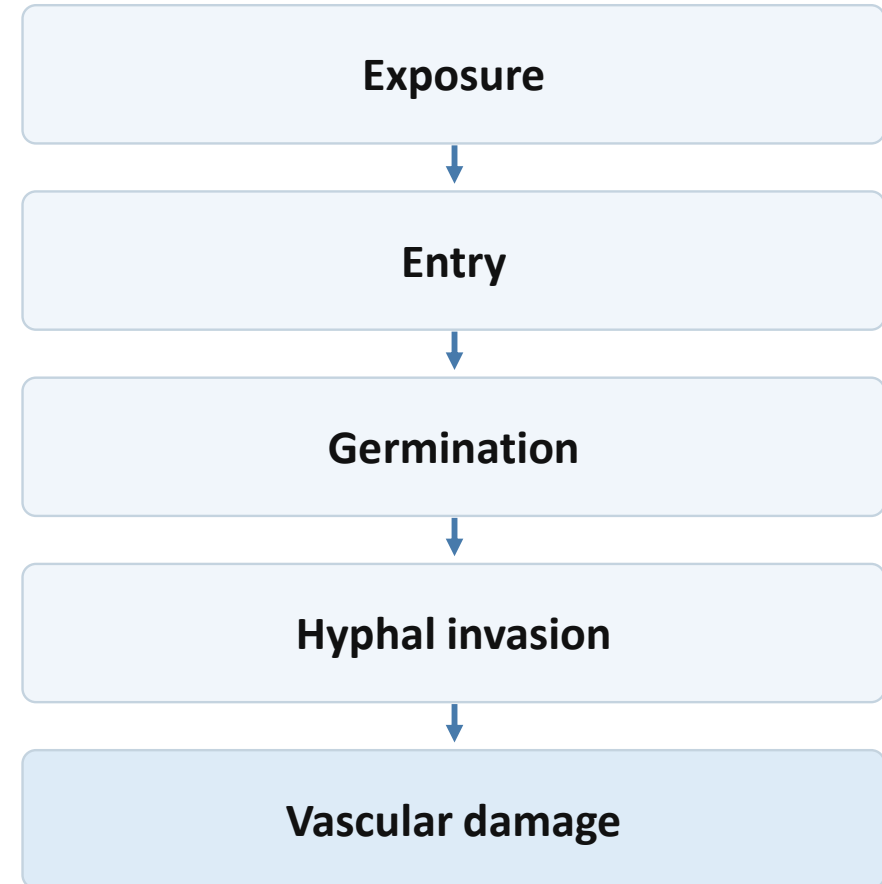
Free iron and defective defenses reinforce risk

- Greater available iron can favor fungal growth.
- Reduced phagocyte protection can fail to restrict germination and hyphae.
- Either mechanism makes tissue invasion more likely in a susceptible host.



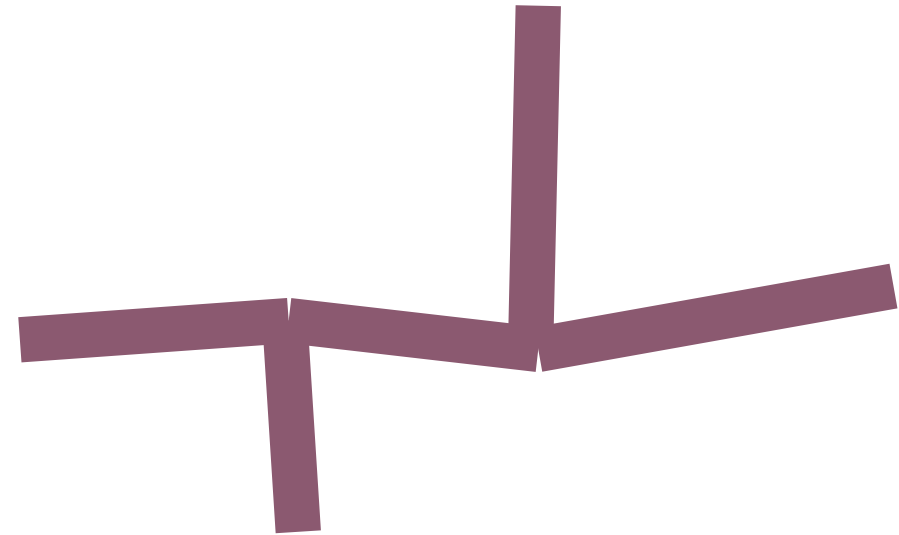
Pathogenesis is a sequence, not a single event

- Environmental spores encounter a permissive portal and host.
- Germination overcomes early innate defenses.
- Developing hyphae can invade tissue and blood vessels.



Tissue morphology identifies the invasive mold

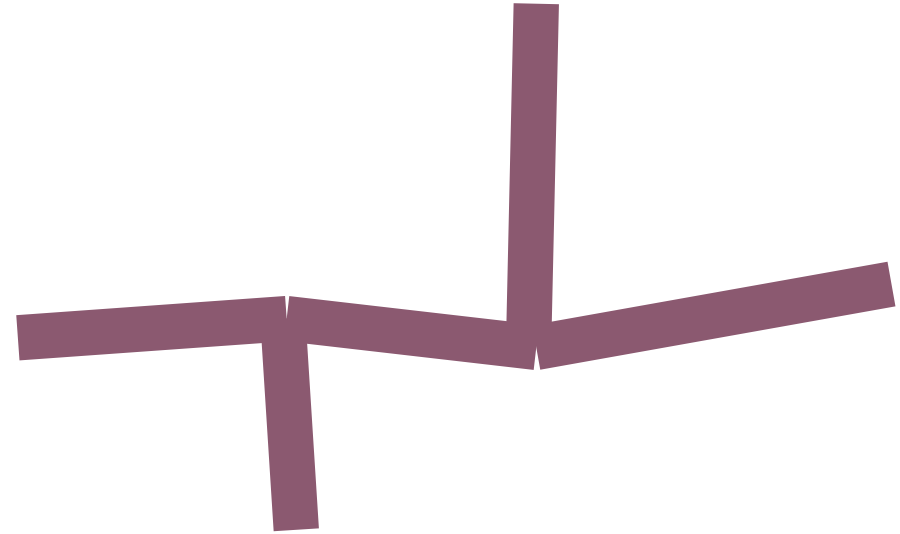
- The hallmark is broad, variably sized hyphae that lack regular septation.
- Branches are often nearly perpendicular to the parent filament.
- Recognition should include the tissue response and vessels, not hyphae alone.



Original schematic — not a tissue micrograph

The hyphal caliber is variable

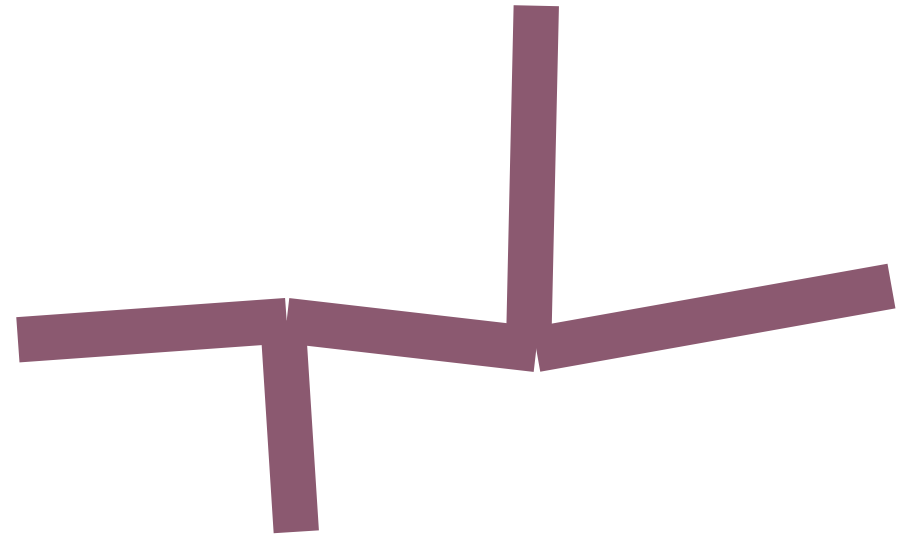
- Hyphal widths of approximately 6–50 μm .
- Width may vary appreciably along the same filament.
- A uniform, narrow filament is less typical of the described pattern.



Original schematic — not a tissue micrograph

Nonseptate architecture is a diagnostic clue

- Nonseptate fungal hyphae.
- Aseptate or sparsely septate appearance contrasts with regularly septate *Aspergillus*.
- Interpret septation together with branching and vessel invasion.



Original schematic — not a tissue micrograph

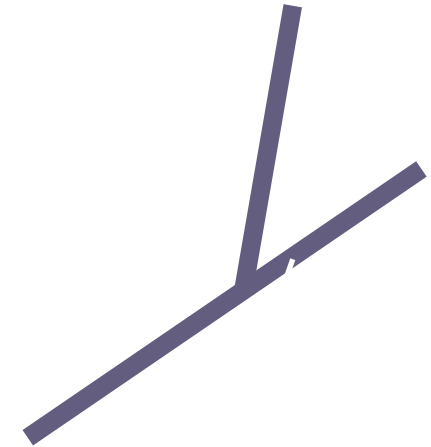
Near-right-angle branching distinguishes the pattern

- Mucormycetes frequently exhibit approximately 90° branches.
- Aspergillus in the adjacent Robbins section forms acute-angle branches.
- Branching geometry is supportive, not a substitute for full morphologic assessment.



~90°

Mucormycetes



~40°

Aspergillus

Mucormycetes versus Aspergillus: Tissue hyphae

- The genera using hyphal width, septation, and branching.
- Mucormycetes are broad and variably sized; Aspergillus filaments are narrower.
- The distinction matters in tissue sections with angioinvasive fungi.

Feature	Mucormycetes	Aspergillus
Hyphae	6–50 µm; Variable	5–10 µm
Septa	Nonseptate	Septate
Branching	Near 90°	Acute (~40°)

H&E and fungal stains reveal the hyphae

- Invasive hyphae are visible with H&E.
- Special fungal stains may also demonstrate the filaments.
- Assess architecture, adjacent necrosis, and vascular involvement.

Hematoxylin & eosin

Special fungal stains

Three morphologic observations belong together

- Hyphal caliber: Broad and uneven.
- Hyphal structure: No regular septa.
- Branch pattern: Commonly near 90°.

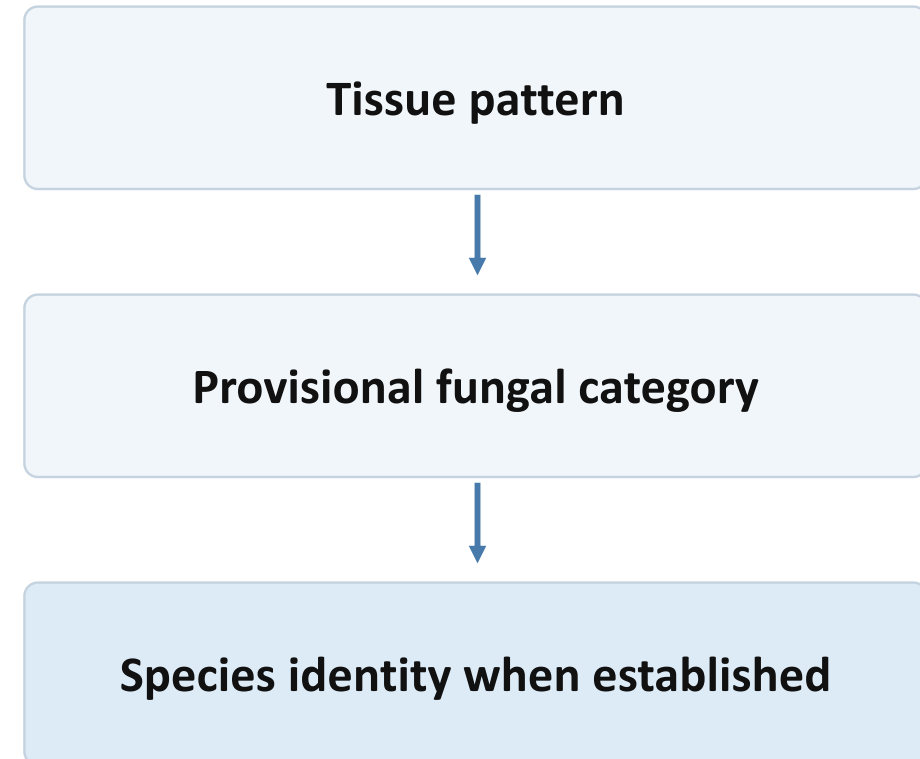
Variable width

Nonseptate

Near-right-angle

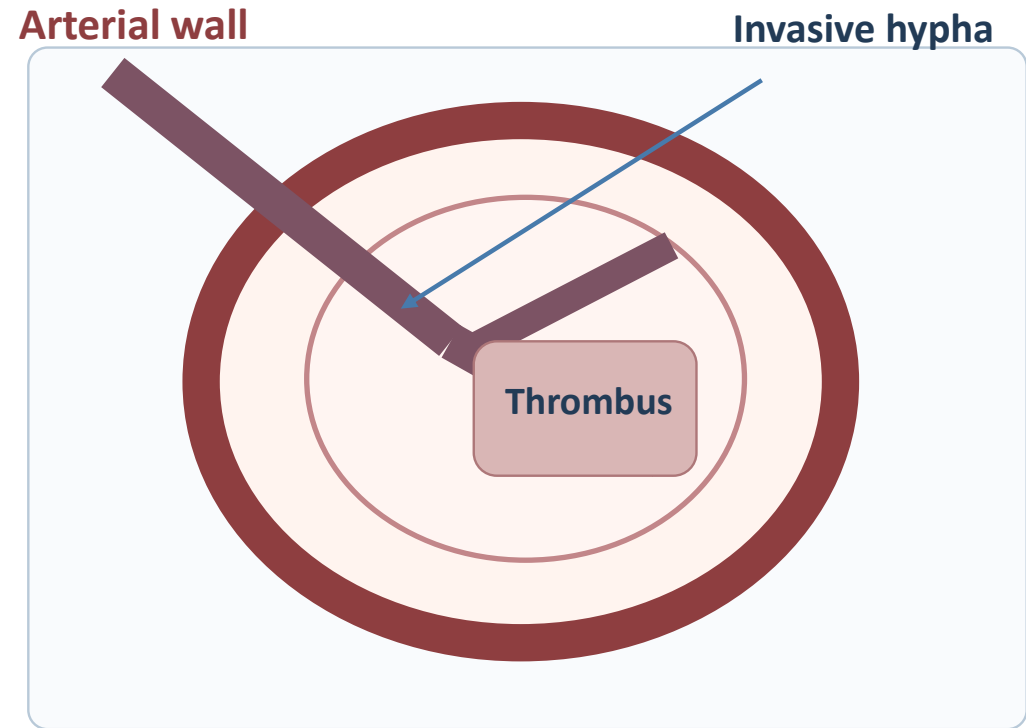
Tissue morphology has identification limits

- Microscopic tissue patterns can support a fungal diagnosis.
- The general fungal-infection section notes that culture may be required for some species.
- Report observed structures separately from unverified species-level assignment.



Angioinvasion defines the destructive lesion

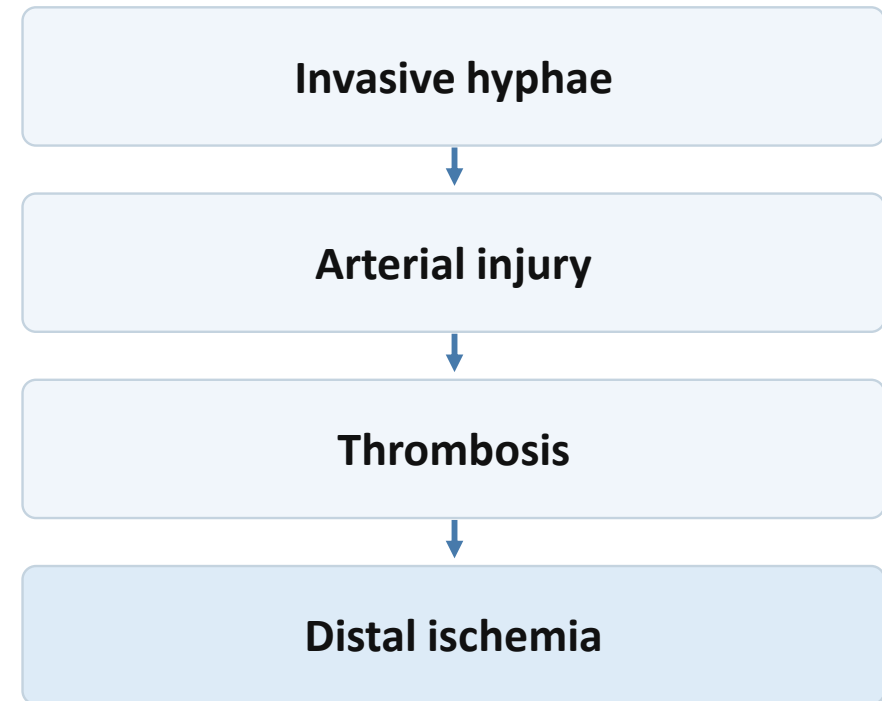
- The fungi invade arterial walls rather than staying on mucosal surfaces.
- Invasion damages vascular integrity and can promote thrombosis.
- The consequent ischemia contributes to tissue necrosis.



Schematic cross-section

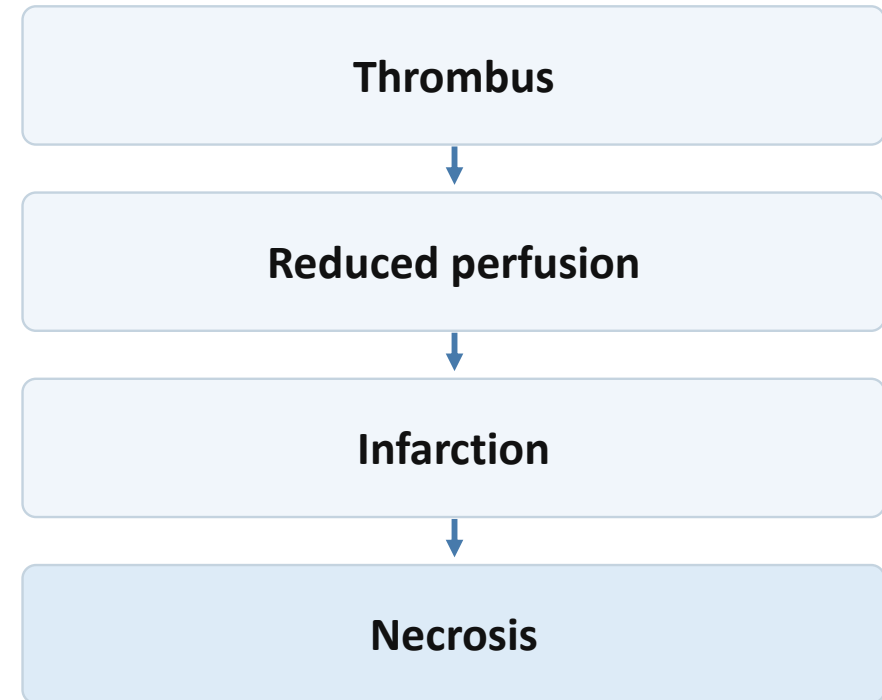
Fungal vascular invasion promotes thrombosis

- Hyphae penetrate or grow within vessel walls.
- The involved artery can thrombose.
- Reduced downstream perfusion creates infarction risk.



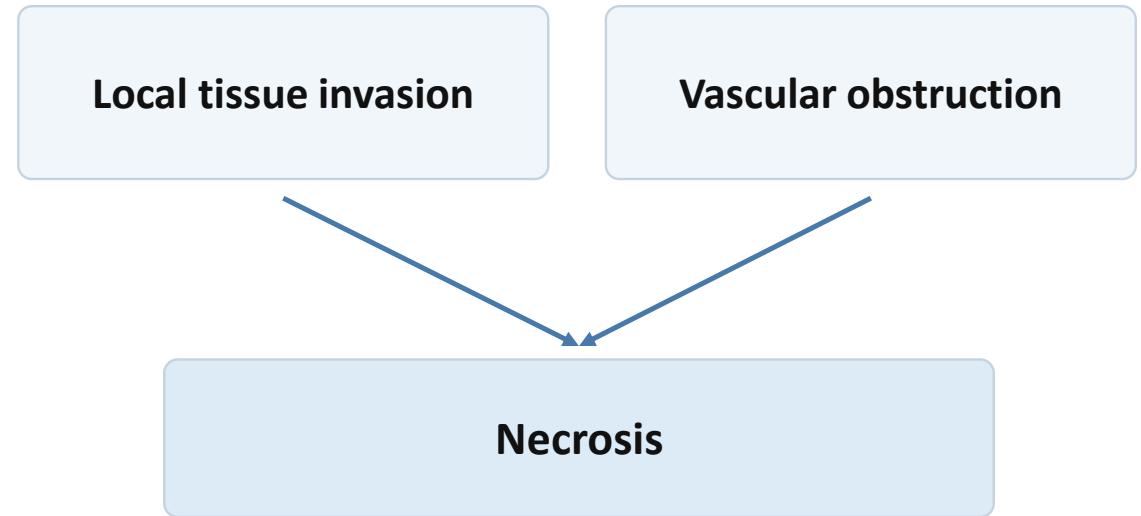
Thrombosis links microscopic invasion to infarction

- Vascular obstruction compromises blood supply to tissue.
- Distal tissue undergoes infarction when perfusion fails.
- This vascular mechanism explains tissue destruction extending beyond visible fungal growth.



Necrosis is a consequence of vascular and tissue invasion

- The fungus directly invades local tissues.
- Arterial thrombosis adds ischemic injury.
- The combination underlies the destructive character of mucormycosis.



Primary organ sites reflect the portal of entry

- The nasal sinuses are a characteristic site after airborne exposure.
- The lungs may be involved primarily or secondarily.
- The gastrointestinal tract can be involved following ingestion.

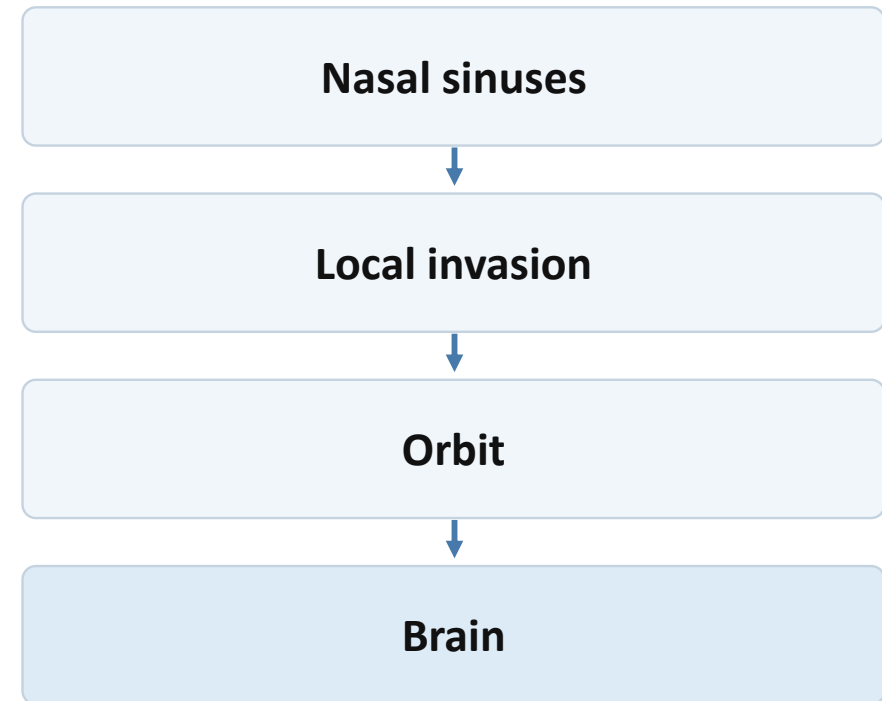
Nasal sinuses

Lungs

Gastrointestinal tract

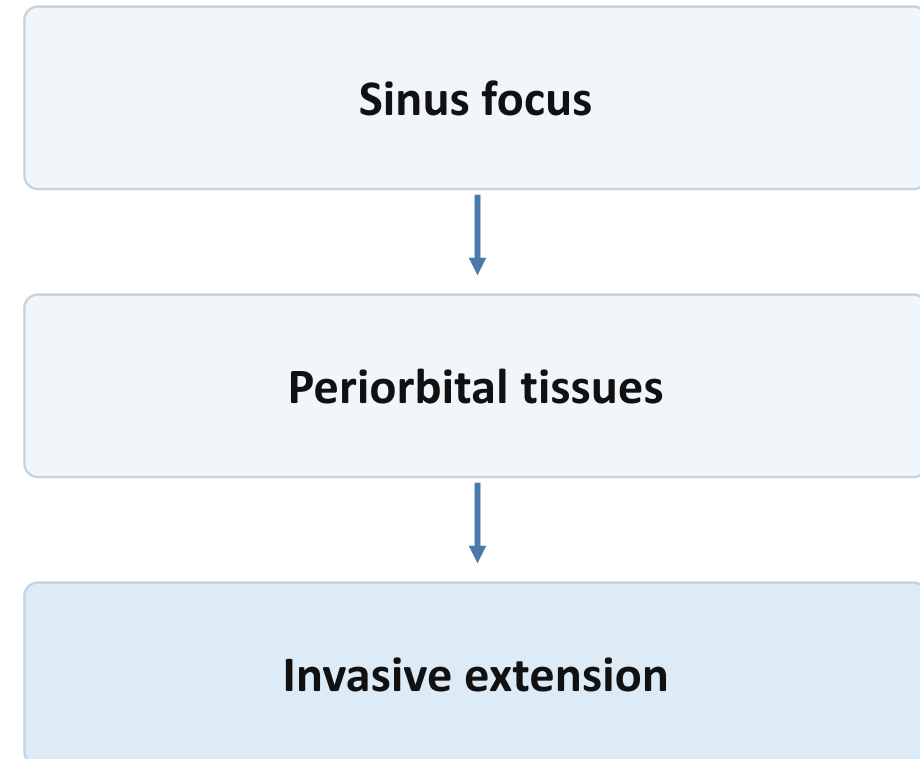
Sinus disease may extend into adjacent tissues

- Rhino-sinus infection may begin in the nasal sinuses.
- Locally invasive growth can penetrate contiguous structures.
- Robbins particularly links rhinocerebral disease with diabetic ketoacidosis.



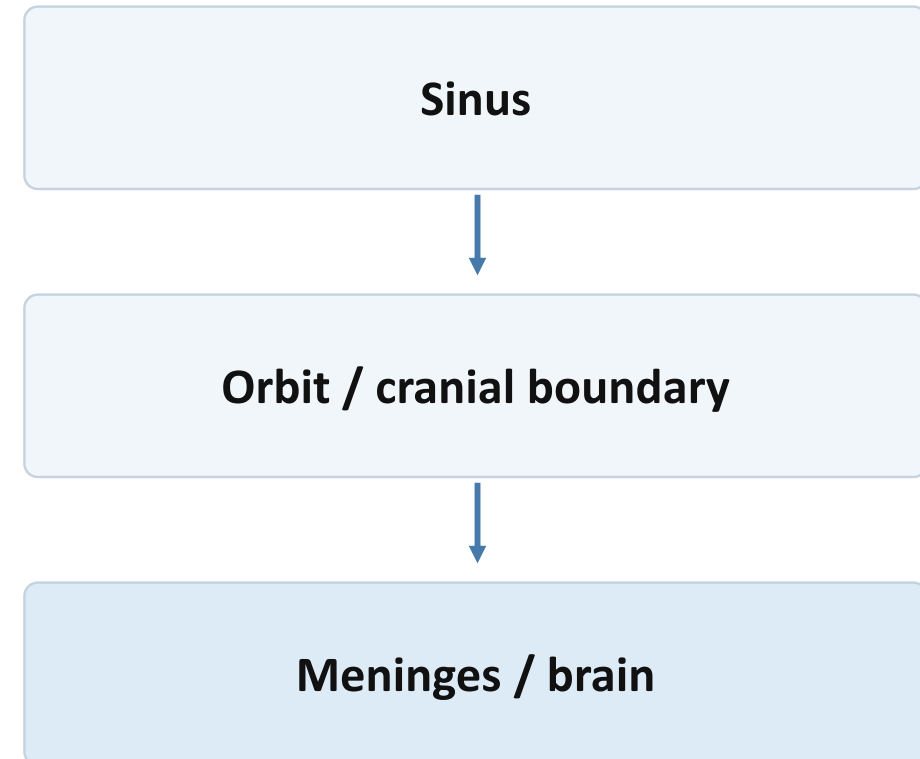
Orbital involvement follows spread from the sinuses

- The sinus focus can penetrate periorbital tissues.
- Spread is by contiguous invasion rather than merely airborne deposition.
- Orbital extension signals anatomically advanced local disease.



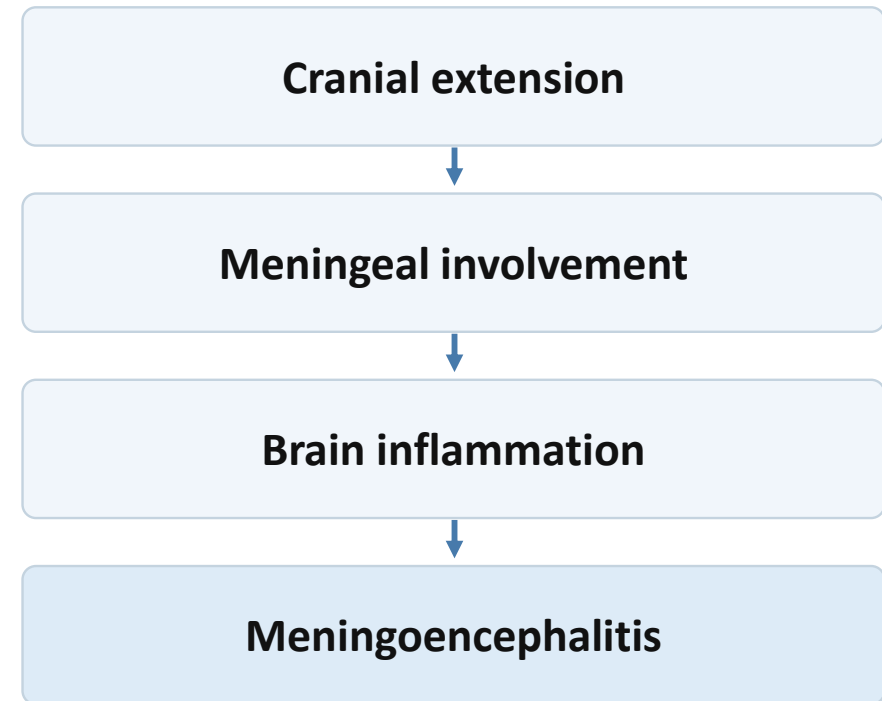
Intracranial invasion extends the disease spectrum

- The organism may breach the cranial vault.
- Intracranial extension can lead to meningoencephalitis.
- The route follows destructive invasion from the original sinus focus.



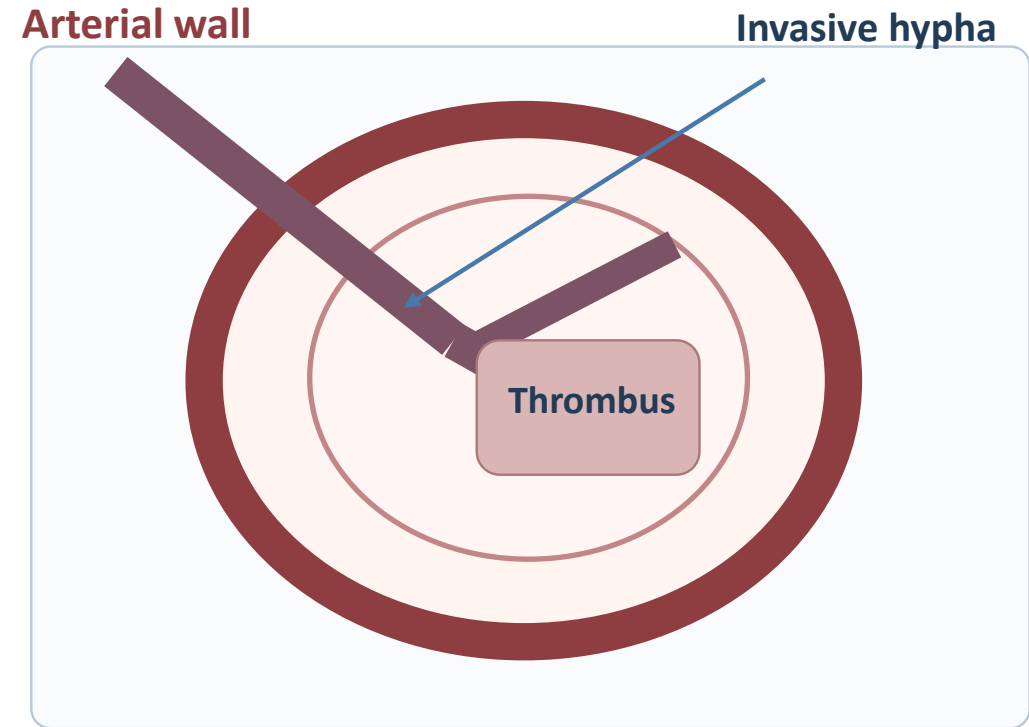
Rhinocerebral mucormycosis can cause meningoencephalitis

- Fungal entry into the cranial compartment involves neural tissues.
- The textbook specifically identifies meningoencephalitis.
- This is a consequence of local extension and severe invasive disease.



Cerebral infarcts can complicate rhinocerebral disease

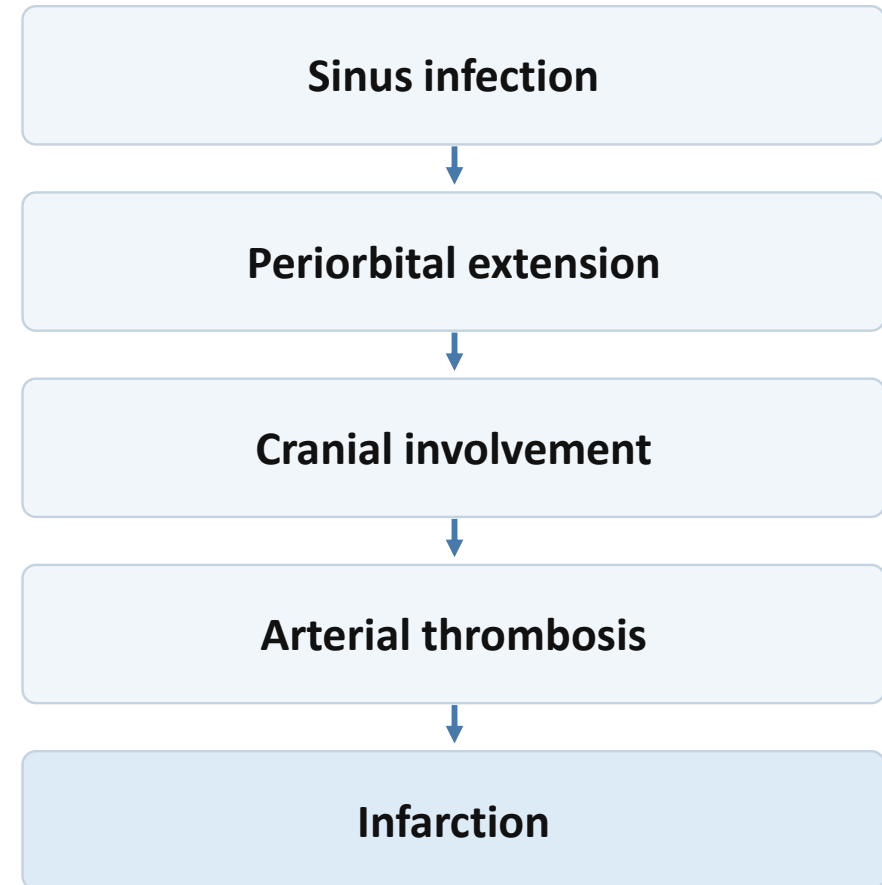
- Fungi may invade cerebral arteries.
- Arterial thrombosis impairs cerebral blood flow.
- Cerebral infarction may accompany the infectious meningoencephalitis.



Schematic cross-section

Rhinocerebral injury follows a coherent cascade

- The likely chain begins with sinus infection.
- Contiguous invasion can reach orbital and intracranial structures.
- Arterial infection and thrombosis create infarctive complications.



Pulmonary disease has two described pathways

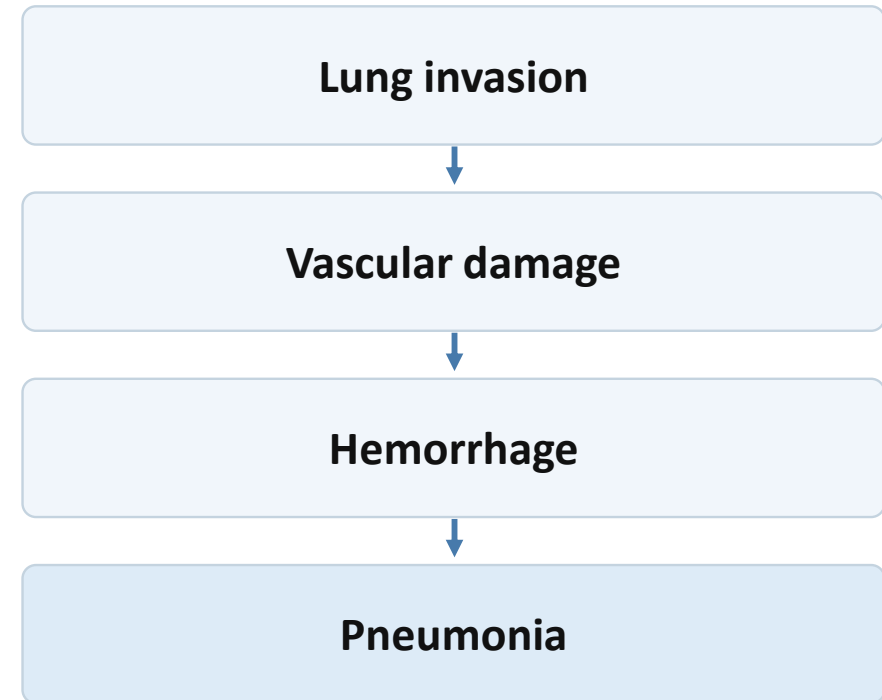
- Pulmonary mucormycosis may be primary in severe immunodeficiency.
- Lung involvement may also arise secondary to rhinocerebral disease.
- In both settings, vascular injury shapes the morphologic lesions.

**Primary pulmonary
disease**

**Secondary lung
involvement**

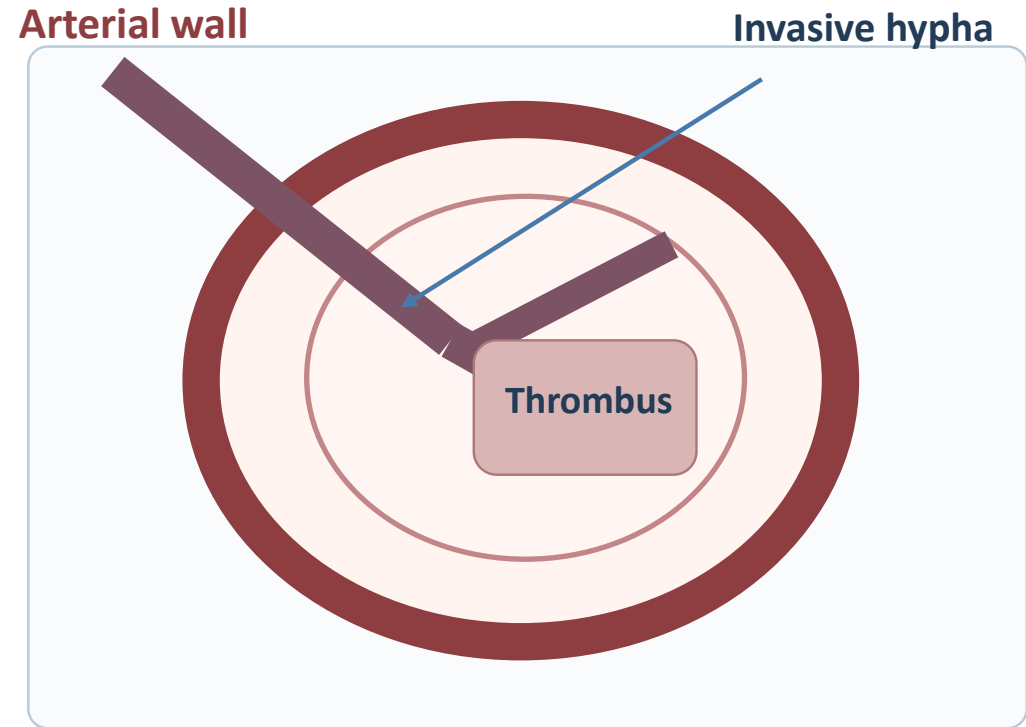
Pulmonary lesions include hemorrhagic pneumonia

- Hemorrhagic pneumonia in lung infection.
- Tissue destruction coexists with bleeding.
- Vascular invasion accounts for much of the accompanying ischemic damage.



Pulmonary thrombi reflect vascular invasion

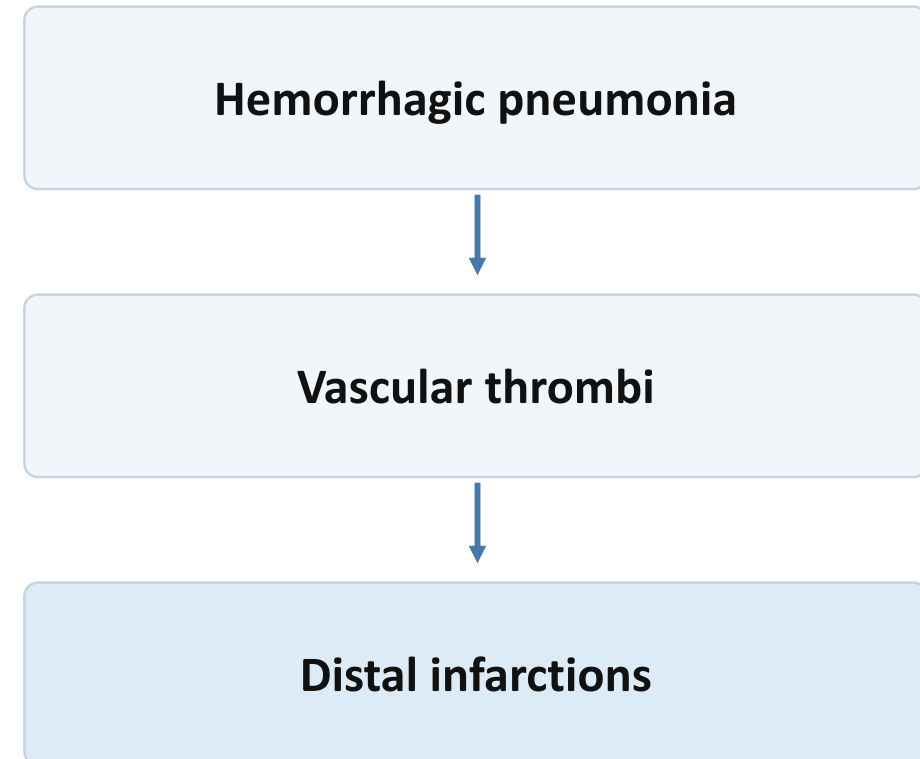
- Infected pulmonary tissue contains vascular thrombi.
- Vessel obstruction disrupts normal perfusion.
- Pulmonary morphology must be read as parenchymal and vascular injury.



Schematic cross-section

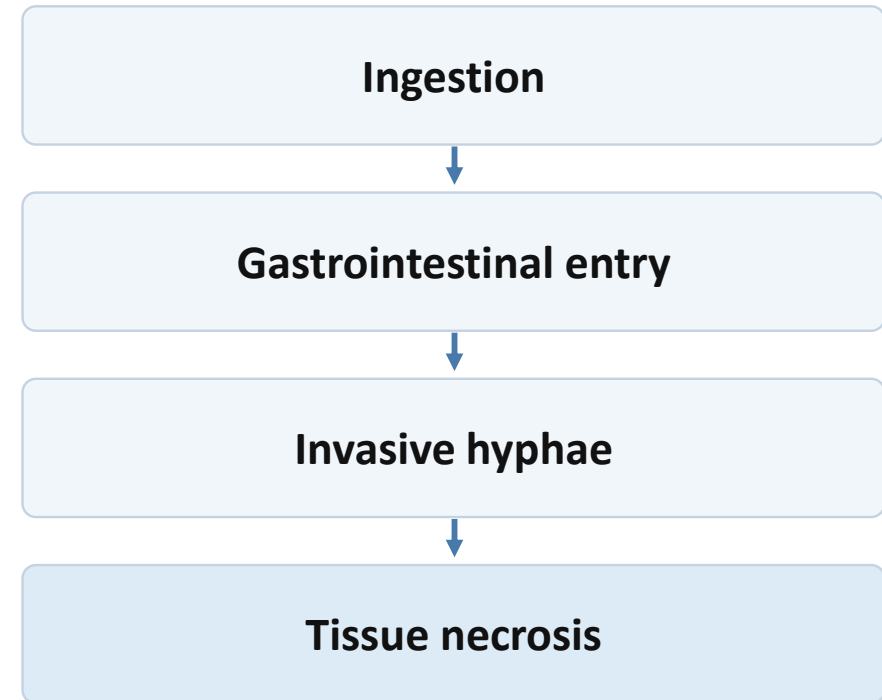
Distal lung infarcts complete the pulmonary triad

- Pulmonary thrombi block blood flow to downstream tissue.
- Distal infarctions with hemorrhagic pneumonia.
- Recognize pneumonia, thrombi, and infarction as linked findings.



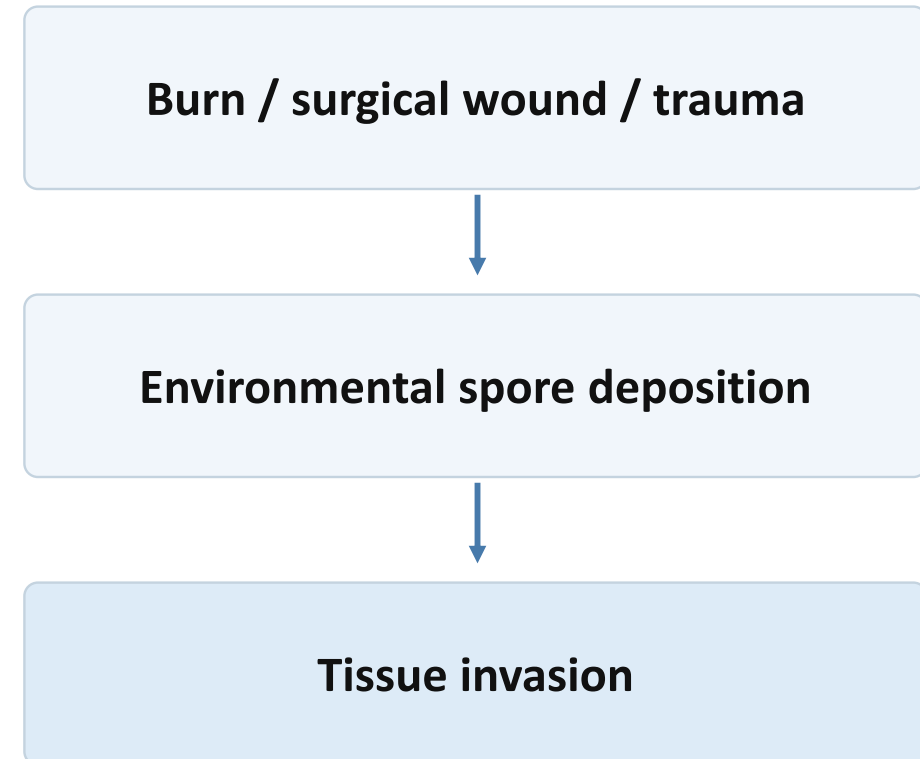
Gastrointestinal infection relates to ingestion

- The gastrointestinal tract is one of three main invasion sites.
- Ingestion is a possible route of entry.
- Invasive disease can be understood through the same hyphal and vascular mechanisms.



Cutaneous infection begins at a disrupted barrier

- Burns, surgery, or trauma allow direct fungal introduction.
- The presenting tissue context differs from sinus or pulmonary inhalation.
- Histologic investigation still focuses on invasive hyphae and injured tissue.



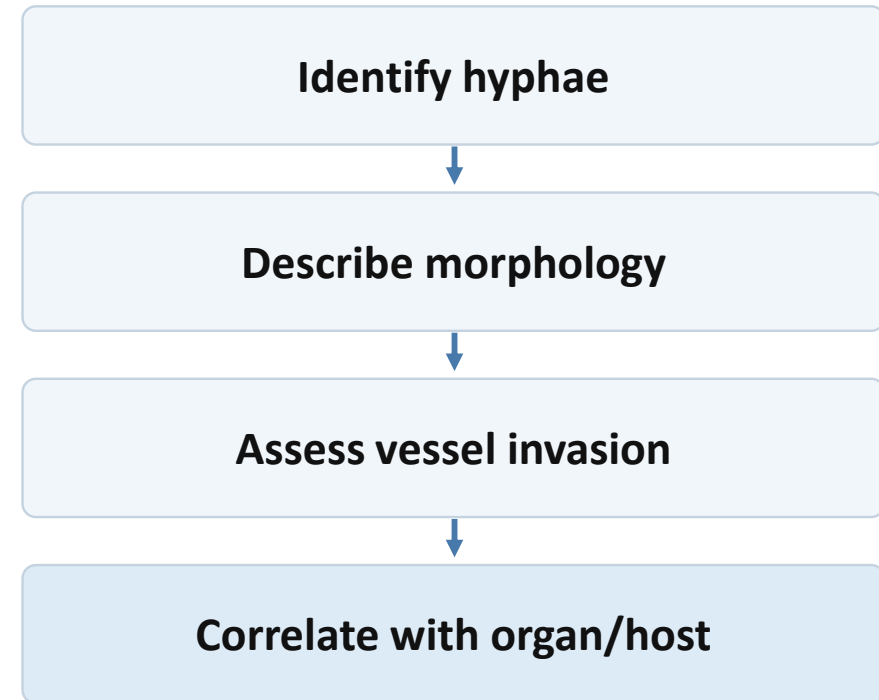
Anatomic form and underlying host state correlate

- Diabetic ketoacidosis is highlighted with rhinocerebral spread.
- Severe immunodeficiency is highlighted in primary pulmonary involvement.
- Barrier disruption is the distinctive context for wound inoculation.

Pattern	Textbook-linked setting
Rhinocerebral	Diabetic ketoacidosis
Primary pulmonary	Severe immunodeficiency
Cutaneous entry	Barrier breach

A tissue-based diagnostic reasoning sequence

- Establish whether there are invasive fungal hyphae in involved tissue.
- Characterize width, septation, and branching in the section.
- Look for vascular invasion, thrombosis, and necrosis.



Describe the finding before inferring the organism

- Observation: Broad, nonseptate, variable-width, branching hyphae.
- Interpretation: Morphologic pattern consistent with mucormycetes.
- Do not claim a species from morphology alone when not established.

**Observed
tissue findings**

**Interpretive
diagnosis**

**Species-level
identification**

Case: Ketoacidosis with destructive sinus disease

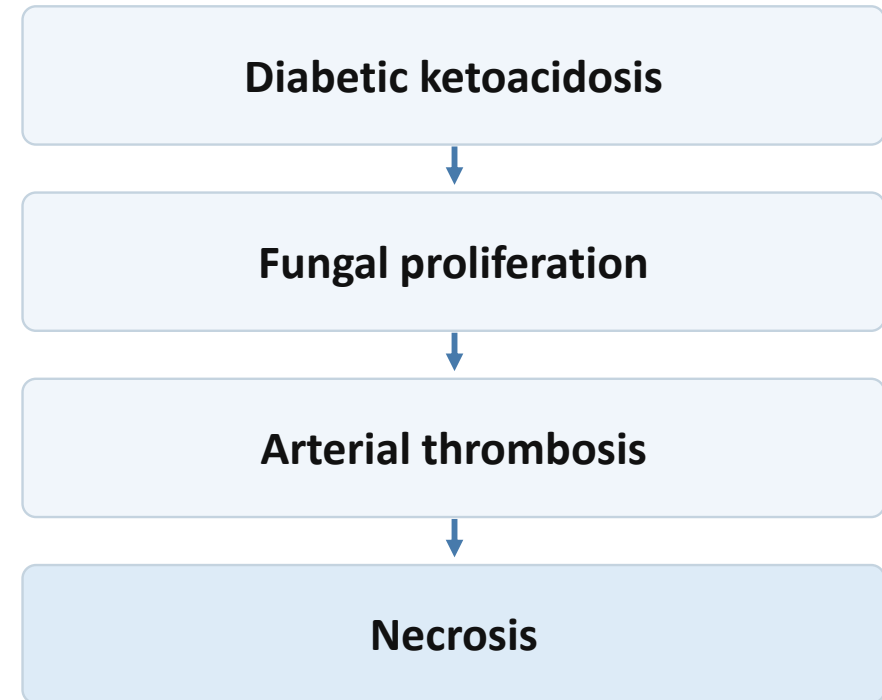
- A patient with diabetic ketoacidosis has invasive sinus disease.
- Biopsy shows broad, nonseptate hyphae in necrotic tissue.
- The tissue contains vessels infiltrated by fungal elements.

Clinicopathologic question

What mechanism explains the necrosis?

Case reasoning: Rhinocerebral pathogenesis

- The described hyphal pattern supports mucormycosis.
- Diabetic ketoacidosis favors accessible free iron.
- Angioinvasion and arterial thrombosis cause ischemic tissue necrosis.



Case: Severe immunodeficiency with pulmonary lesions

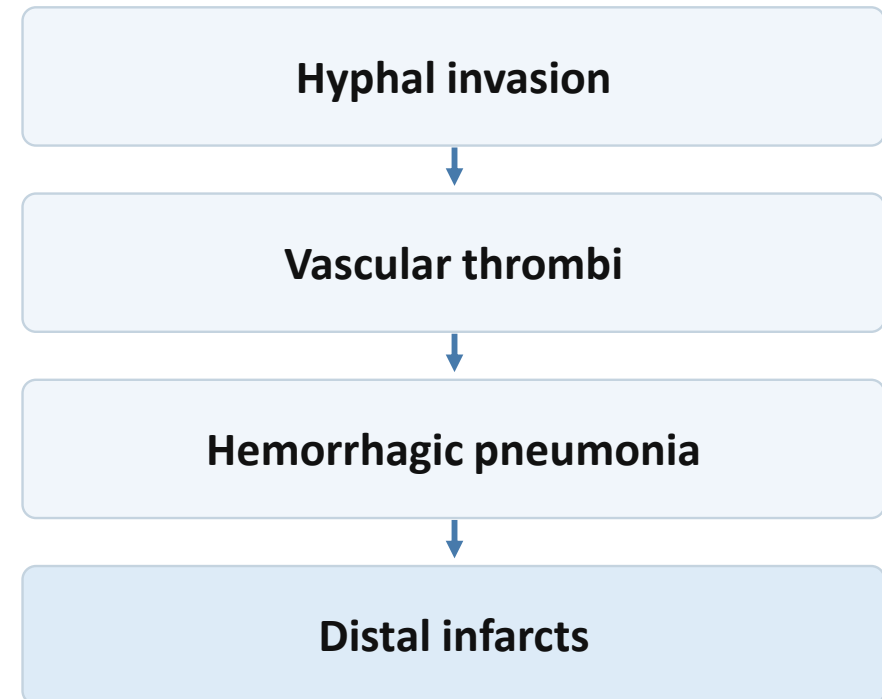
- A severely immunodeficient patient develops fungal lung disease.
- The lung contains hemorrhagic pneumonia and vascular thrombi.
- Broad irregular nonseptate hyphae are present in tissue.

Clinicopathologic question

How do the lung lesions fit together?

Case reasoning: Pulmonary vascular injury

- The hyphal morphology is compatible with mucormycetes.
- Vascular invasion explains thrombus formation.
- Hemorrhagic pneumonia with distal infarction is the textbook pattern.



Case: Trauma followed by a fungal tissue lesion

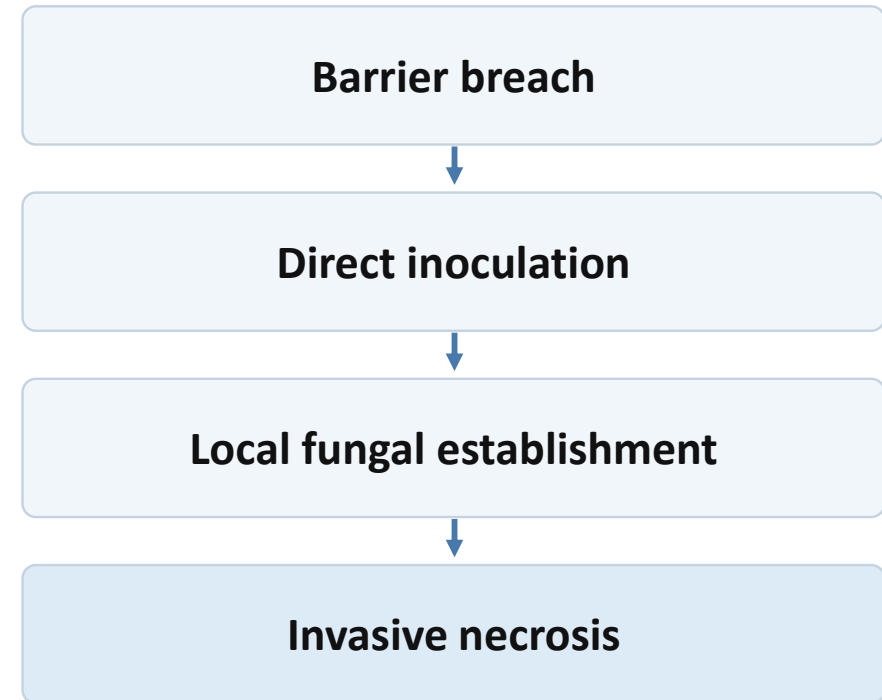
- A wound follows an episode of local tissue trauma.
- A tissue section reveals broad, nonseptate invasive hyphae.
- The clinical question is why this patient acquired the infection.

Clinicopathologic question

What route of entry is most relevant?

Case reasoning: Disruption of the skin barrier

- Trauma creates a portal for direct environmental inoculation.
- Wound exposure can bypass normal cutaneous protection.
- Once established, the same invasive fungal pathology may follow.



Aspergillus is the principal hyphal differential

- Both infections may invade vessels and produce infarction.
- Mucormycetes: Nonseptate, broad, variably sized, often near-right-angle branches.
- Aspergillus: Narrower, septate filaments with predominantly acute-angle branches.

**Mucormycetes: Broad /
90°**

**Aspergillus: Septate /
acute**

Integrated pathology: one causal model

- Exposure plus a susceptible host permits spores to germinate.
- Invasive hyphae are associated with vascular thrombosis.
- Ischemia and necrosis explain severe organ damage.

