

Fungal Infections

Fungal forms · mycosis classes · host defenses · tissue patterns

General and systemic pathology

A morphology-led clinicopathologic approach

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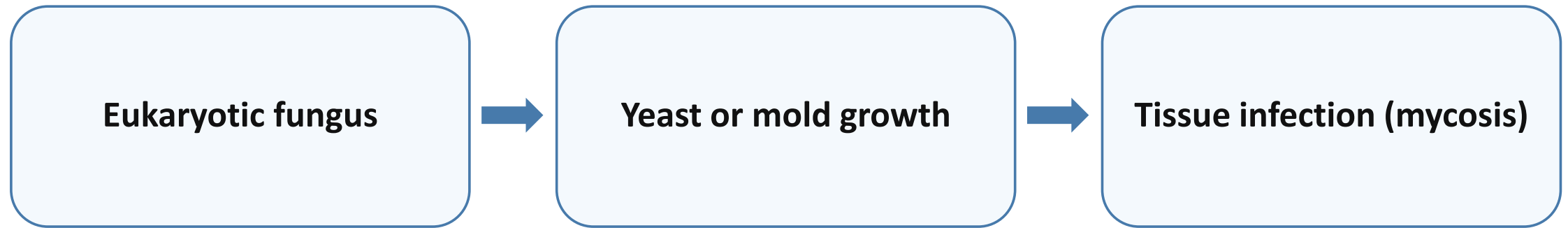
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Learning objectives

- Classify mycoses by site, depth, host state, and epidemiologic context.
- Explain the distinctions between budding yeast, pseudohyphae, mold hyphae, and dimorphic growth.
- Link innate / adaptive immune responses to fungal tissue injury.
- Recognize major organism-associated morphology and formulate appropriate differentials.

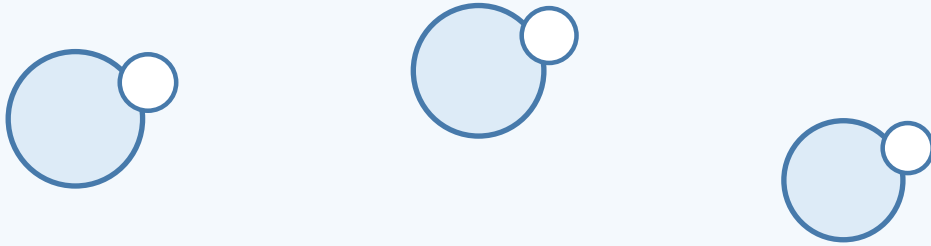
Fungi are eukaryotic pathogens



Fungal pathogens differ structurally from bacteria and are organized as yeast cells or filamentous molds. Cell walls maintain fungal shape; Morphology is a useful first step in tissue recognition.

Yeast growth: Budding cells

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Budding daughter cell attached to yeast

Interpretation

- Round-to-oval cells are the typical yeast form.
- New daughter cells usually arise by budding.
- The budding pattern may help narrow a morphologic differential, but does not always identify species.

Pseudohyphae: Buds that remain attached

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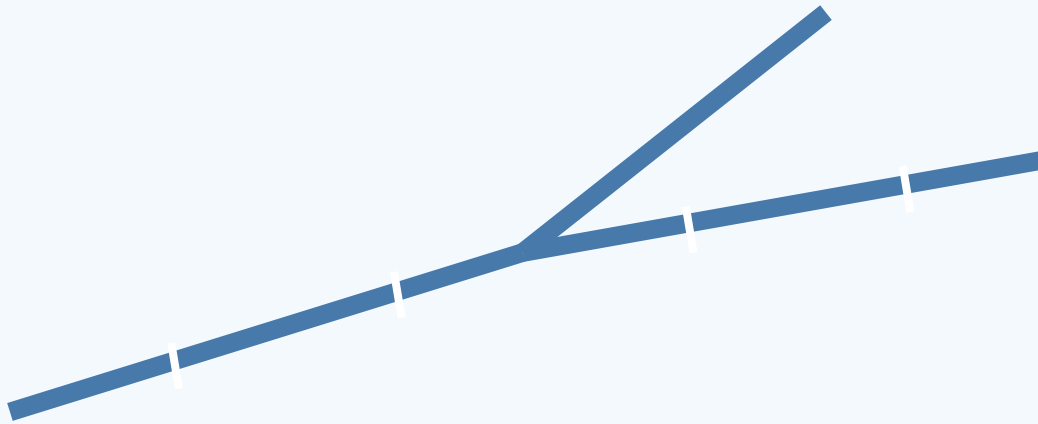
Elongated buds linked at constricted junctions

Interpretation

- Some yeasts, including *Candida albicans*, form elongated daughter buds that fail to separate.
- Linked elongated cells create a pseudohyphal chain.
- Constricted junctions between cells are an important distinguishing feature.

Mold architecture: Apically growing hyphae

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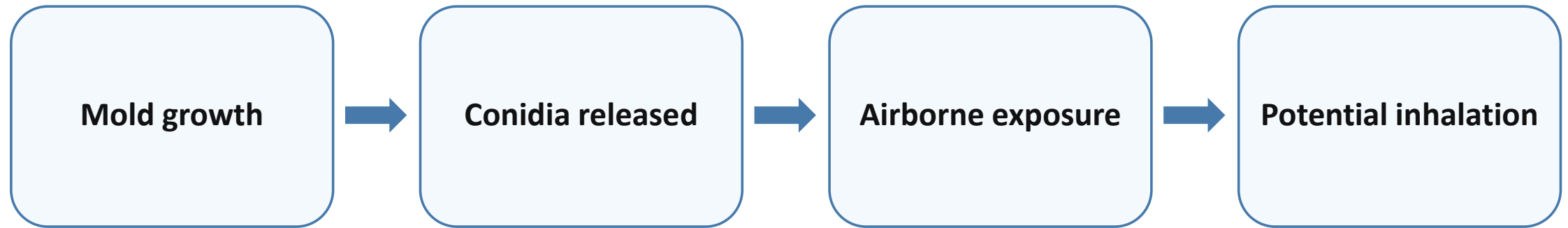


Continuous branching filaments; Septa indicated schematically

Interpretation

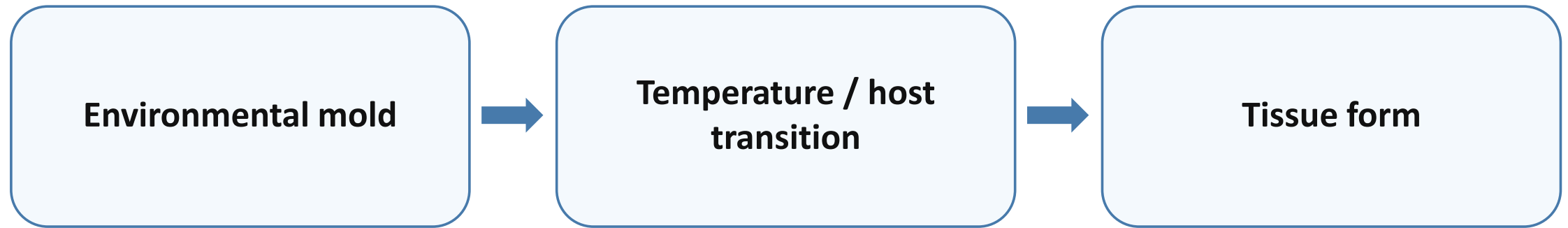
- Molds are made of multicellular filaments called hyphae.
- Filaments extend and divide at their tips, producing a branching network.
- Hyphal configuration becomes especially important in the diagnosis of invasive mold infections.

Conidia enable airborne dispersal



Molds can generate rounded reproductive cells called conidia. Conidia can become airborne and disperse widely.

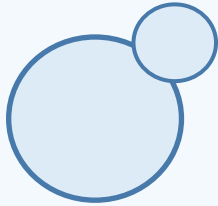
Dimorphism links environment to tissue form



Many medically significant fungi alternate between environmental mold and tissue yeast forms. The Robbins overview describes mold at room temperature and yeast at body temperature as the usual pattern.

Yeast, pseudohyphae, and true hyphae

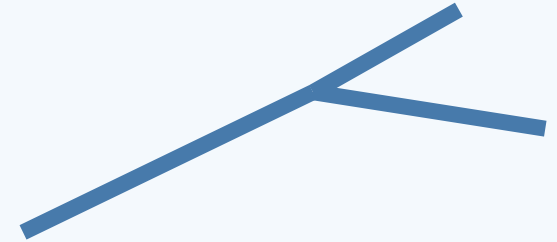
Yeast



Pseudohyphae



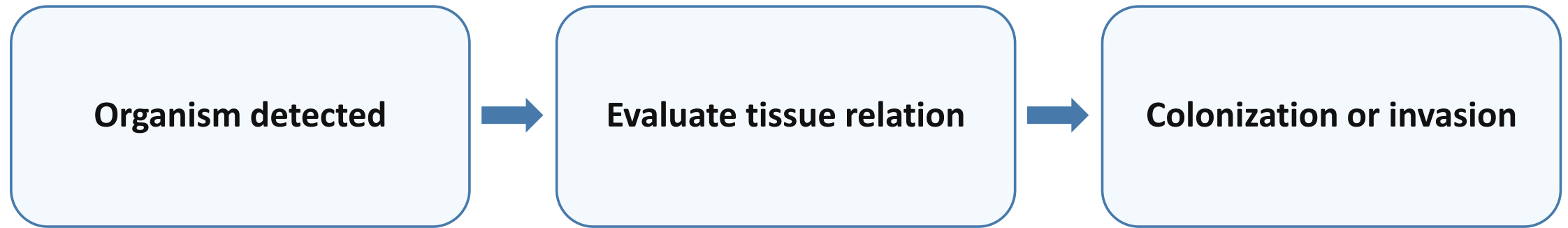
Mold hyphae



Schematic cell forms — topology only; Not a stained preparation

Morphism is a diagnostic clue, but does not independently establish species.

The central diagnostic question is tissue invasion



Finding fungal structures is not equivalent to establishing invasive fungal disease. Noninvasive *Aspergillus* growth in pre-existing cavities with angioinvasive disease.

Four major clinicopathologic types of mycosis

Category	Anatomic / clinical boundary
Superficial / cutaneous	Surface and keratinized skin, hair, nails
Subcutaneous	Skin, deeper soft tissue, lymphatics
Endemic	Systemic infection possible in healthy hosts
Opportunistic	Severe disease with impaired defenses or devices

Superficial and cutaneous mycoses

Surface / keratinized tissues

Viable epidermis / dermis

Subcutaneous tissue

Lymphatic region

- Common infections limited to the superficial or keratinized layers of skin, hair, and nails.
- The site and depth distinguish this category from deep or systemic infections.
- More detailed dermatophyte pathology belongs to the separate skin chapter/topic.

Subcutaneous mycoses

Surface / keratinized tissues

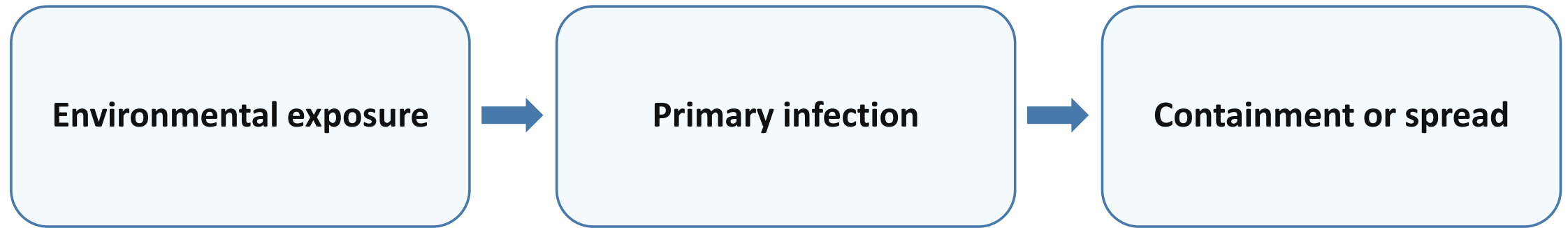
Viable epidermis / dermis

Subcutaneous tissue

Lymphatic region

- Involve the skin, subcutaneous tissue, and lymphatic structures.
- The process extends deeper than superficial keratinized sites.
- Systemic dissemination is uncommon according to the Robbins overview.

Endemic mycoses



Caused by dimorphic fungi associated with particular environmental regions. Can produce serious systemic illness even in an immunocompetent host.

Opportunistic mycoses



Severe systemic fungal disease is favored by immunosuppression. Prosthetic devices and vascular catheters provide additional opportunities for infection.

Classification is not a species list

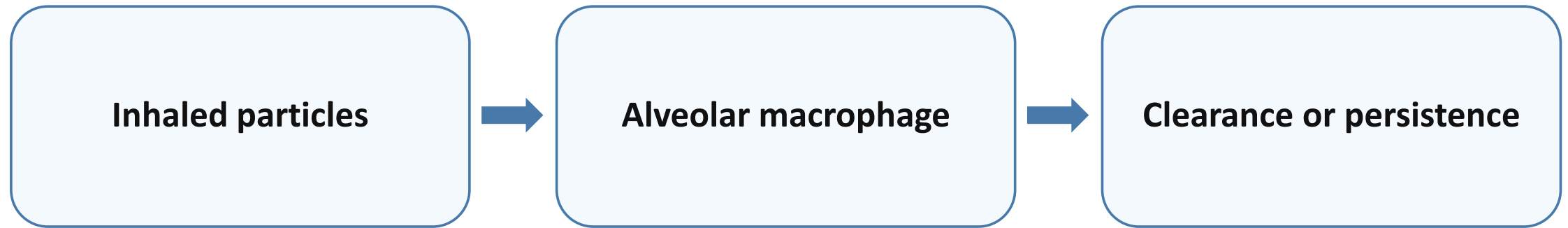
Axis	Practical question
Anatomic extent	Surface, deep tissue, or systemic?
Host condition	Normal defense or altered immunity?
Pathogen biology	Yeast, mold, or dimorphic fungus?
Evidence	Colonization, inflammation, or invasion?

Host-pathogen interaction determines severity



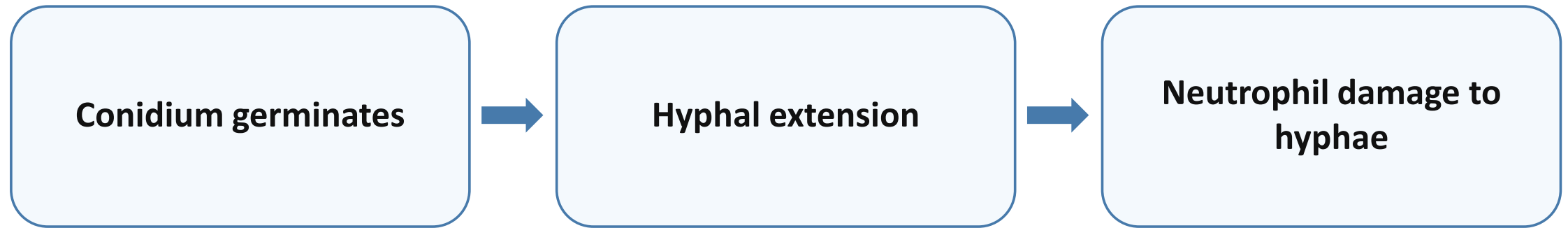
The same fungal organism may be contained, remain localized, or disseminate. Different fungal strategies include adhesive growth, capsules, environmental transition, and biofilms.

Macrophages defend initial portals of entry



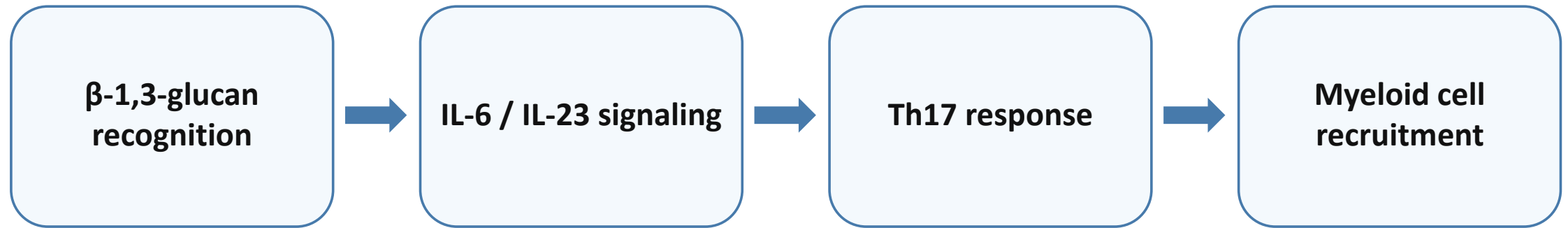
Alveolar macrophages ingest *Aspergillus* conidia and *Histoplasma* propagules after inhalation. Phagocytosis may control exposure, but some fungi survive intracellularly.

Neutrophils are central in invasive molds



Neutrophils injure and kill growing *Aspergillus* and mucormycete hyphae. Profound neutropenia is strongly associated with aggressive invasive mold disease.

Th17 immunity protects against Candida



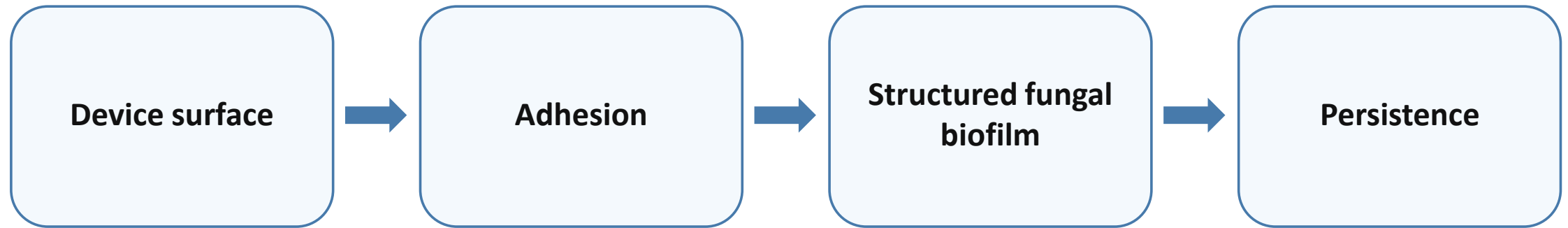
Candida yeast β-1,3-glucan is sensed by dectin on dendritic cells. IL-6 and IL-23 promote Th17 responses; These recruit neutrophils and monocytes.

Th1 immunity restrains Histoplasma



Intracellular Histoplasma can persist in macrophages until T-cell-mediated immunity develops. Th1-derived IFN- γ activates macrophage fungicidal activity.

Biofilms alter device-associated infection

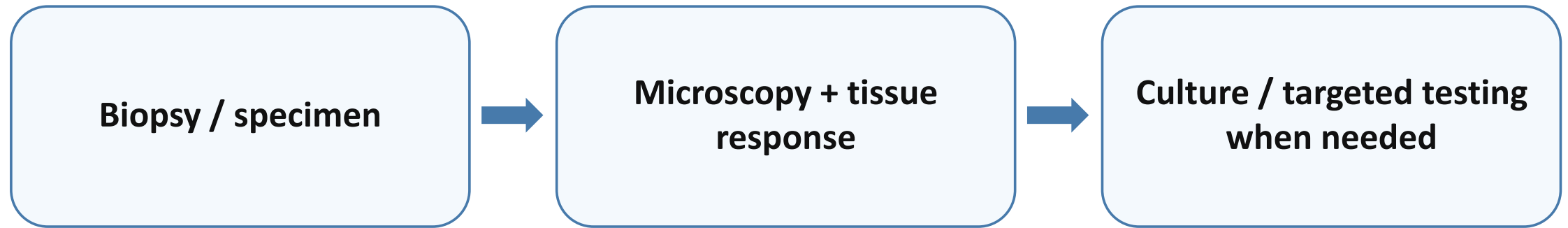


C. Albicans can grow as attached microbial communities with extracellular matrix. Yeast and filamentous forms can coexist in these device-associated biofilms.

Fungal virulence mechanisms vary by organism

Example	Mechanism
Candida	Adhesion, morphologic switching, biofilm
Cryptococcus	Capsule limits phagocytosis; Melanin
Aspergillus	Conidial camouflage; Antioxidant activity
Mucormycetes	Growth favored by increased free iron

Histology is an initial identification method



Fungi can often be recognized in tissue sections by their cellular or filamentous forms. Tissue examination allows direct correlation with inflammation and invasion.

H&E may reveal fungi; Special stains sharpen contrast

Technique	What the source supports
H&E	Fungal forms sometimes visible with tissue context
GMS	Better visualization of many fungi
PAS	Enhances fungal structures; Stains cryptococcal capsule
Mucicarmine	Highlights cryptococcal polysaccharide capsule

Branching pattern is suggestive, not definitive

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Septate / acute-angle

Broad / wide-angle

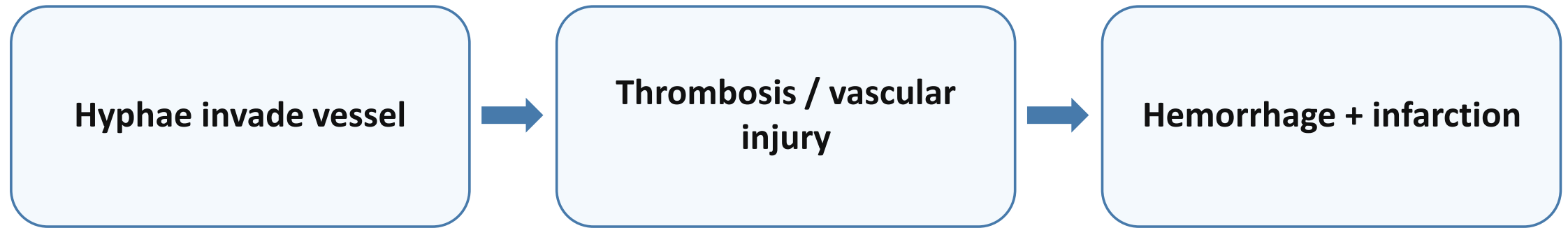
Interpretation

- Septate acute-angle branching raises the possibility of *Aspergillus*.
- Broad, irregular, typically nonseptate hyphae with near-right-angle branching suggest mucormycetes.
- Hyphal overlap and other molds mean morphology alone may not yield a species-level diagnosis.

Tissue reaction can range from absent to florid

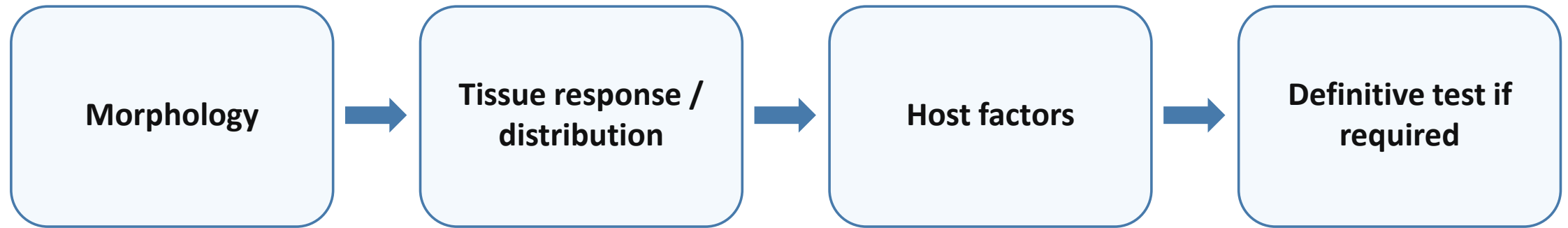
Response	Example in Chapter 8
Minimal inflammation	Cryptococcal masses in major immune suppression
Suppurative	Some invasive Candida foci; Blastomycotic lesions
Granulomatous	Controlled Histoplasma or cryptococcal infection
Necrosis and infarction	Angioinvasive Aspergillus or mucormycetes

Angioinvasion explains hemorrhage and infarction



Invasive *Aspergillus* and mucormycetes can penetrate blood vessel walls. Vascular thrombosis compromises perfusion and promotes necrosis.

A fungal differential needs multiple dimensions



Begin with the organism's tissue form: Budding yeast, hyphae, or spherules. Then evaluate capsule, budding base, septation, and branching.

Candida is usually a human commensal

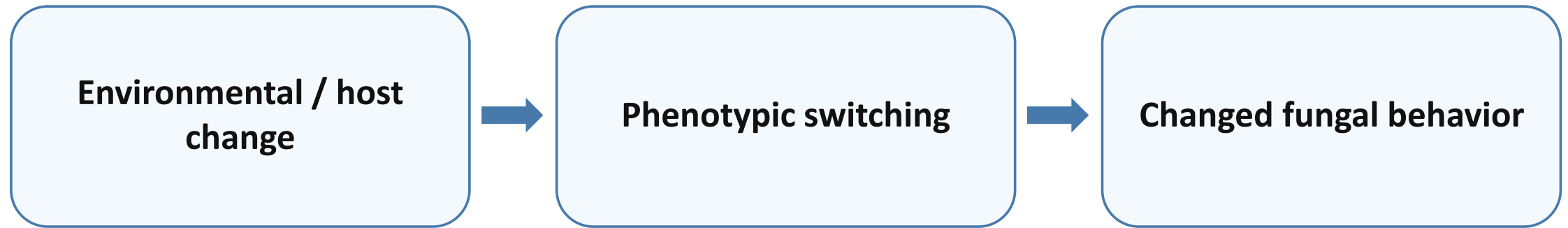


C. Albicans is an important human fungal pathogen and may normally reside on skin and mucosal surfaces. The mouth, gastrointestinal tract, and vagina are recognized commensal sites.

Candida syndromes vary with host context

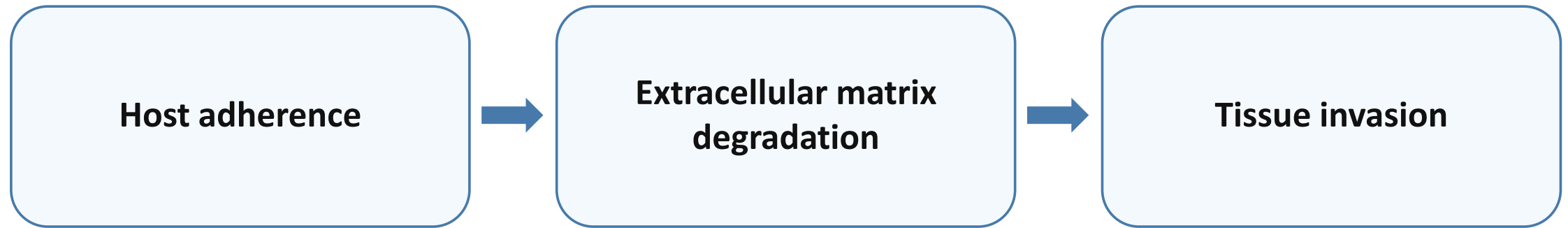
Context	Common consequence
Intact community host	Mucosal / skin infection
Diabetes or burns	Susceptibility to superficial candidiasis
Vascular access devices	Bloodstream entry / dissemination
Profound neutropenia	Severe invasive or disseminated disease

Candida morphologic plasticity aids adaptation



C. Albicans can switch among multiple cellular phenotypes. The Robbins section links switching to temperature, nutrient conditions, antibiotic exposure, and immunity.

Adhesion and enzymes promote Candida invasion



Adhesins bind host extracellular matrix components and epithelial/endothelial cells. Secreted aspartyl proteinases may facilitate tissue invasion by degrading matrix proteins.

Pseudohyphae are a Candida diagnostic clue

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Elongated buds linked at constricted junctions

Interpretation

- Tissue Candida may display budding yeast, pseudohyphae, and sometimes true hyphae.
- Pseudohyphal junctions show constrictions between elongated cells.
- Multiple forms in one field favor interpretation of a mixed morphologic population.

Oral candidiasis produces pseudomembranes

Surface / keratinized tissues

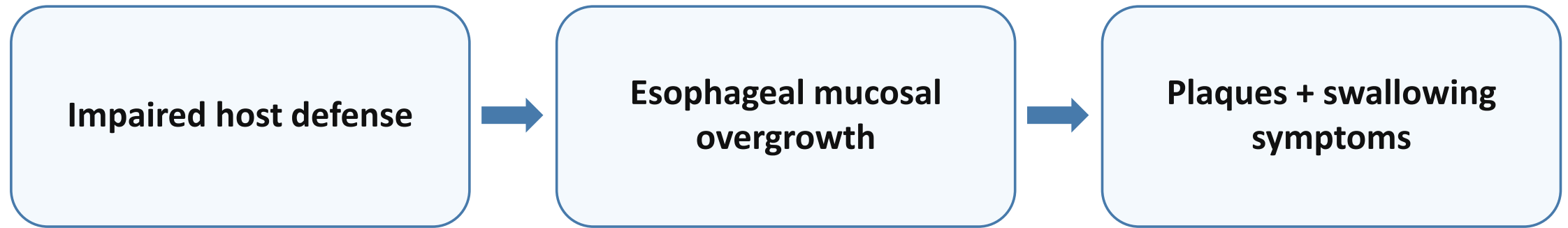
Viable epidermis / dermis

Subcutaneous tissue

Lymphatic region

- Fungal overgrowth forms gray-white superficial material with organisms and inflammatory debris.
- Inflamed mucosa lies beneath the superficial plaques.
- Antibiotics, steroids, debility, and impaired cellular immunity are relevant contexts.

Esophageal candidiasis causes mucosal plaques



Candida esophagitis is associated with advanced HIV disease and hematologic malignancy. Patients can develop swallowing symptoms and retrosternal pain.

Superficial Candida infection has varied sites

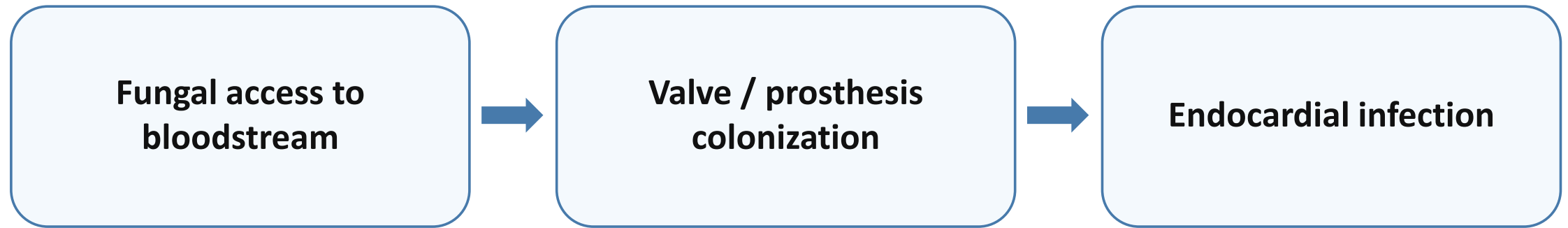
Site	Named example
Vagina	Candida vaginitis
Nail fold	Paronychia
Intertriginous skin	Intertrigo
Infant perineum	Diaper candidiasis

Disseminated Candida follows bloodstream spread



Candidemia can seed multiple distant organs. Renal, myocardial, cerebral, ocular, and hepatic involvement.

Endocarditis is a device-associated complication

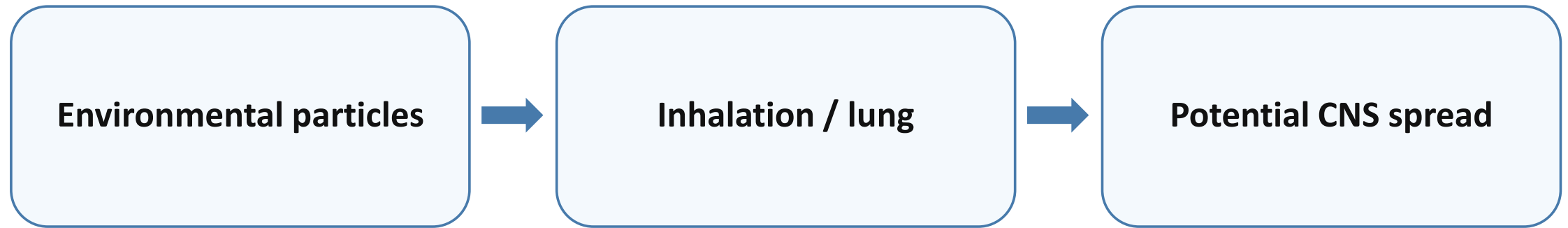


Candida is a major cause of fungal endocarditis in the source discussion. Prosthetic heart valves create a major predisposing setting.

Candida auris challenges infection control

Clinical aspect	Practical interpretation
Colonization	Not synonymous with invasive disease
Healthcare setting	Device-associated outbreaks described
Environment	Persistence on dry and moist surfaces
Therapy	Resistance can span multiple antifungal classes

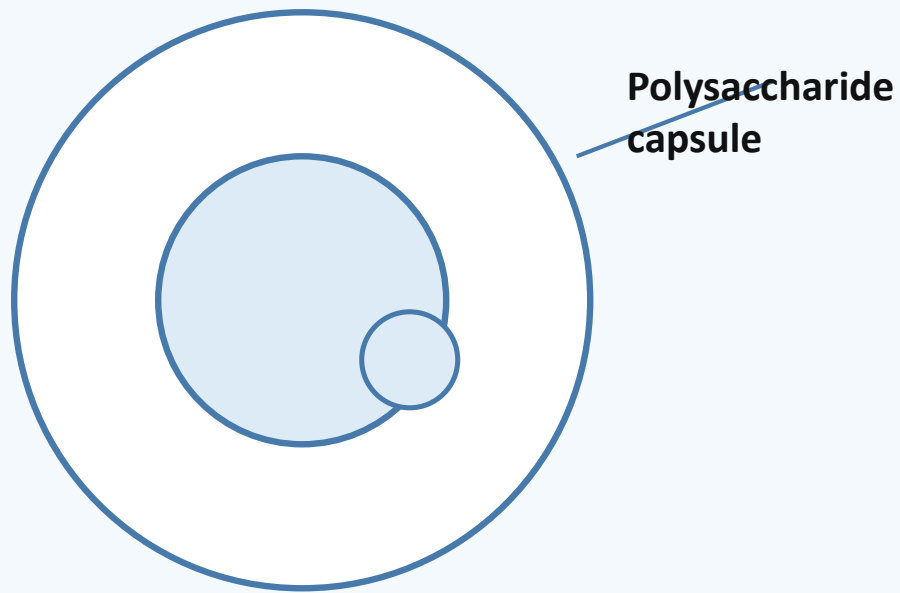
Cryptococcus enters through inhalation



C. Neoformans and C. Gattii are pathogenic encapsulated yeasts. C. Neoformans may be acquired from soil containing pigeon guano.

The cryptococcal capsule blocks host defense

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Encapsulated budding yeast

Interpretation

- A thick polysaccharide capsule impedes phagocytosis.
- Capsular factors can reduce inflammatory-cell recruitment and dendritic-cell functions.
- A weak tissue response may allow organism-rich gelatinous lesions.

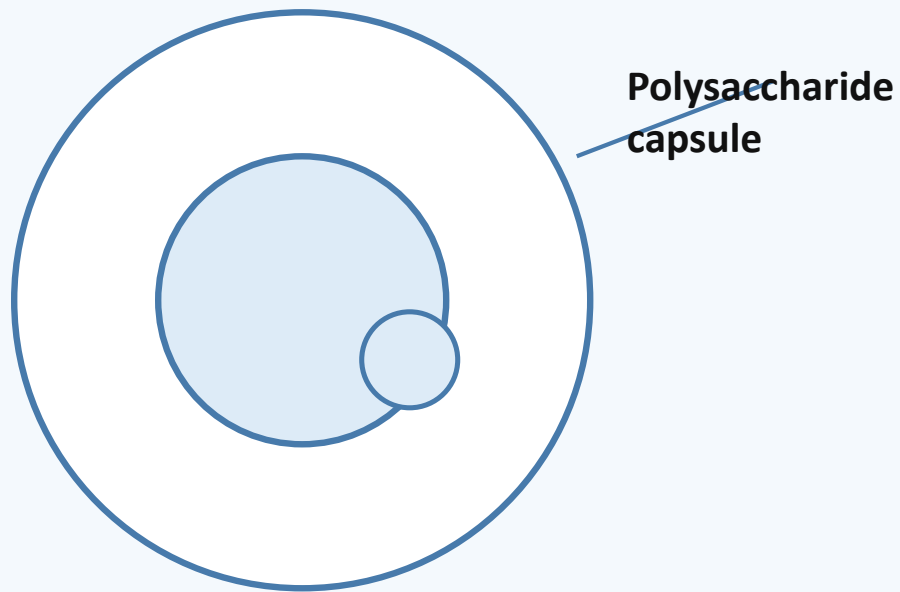
Cryptococcus causes meningoencephalitis



The central nervous system is a major disease site. In markedly immunosuppressed hosts, enlarged perivascular spaces may contain gelatinous fungal masses.

Cryptococcal morphology: Capsule-rich yeast

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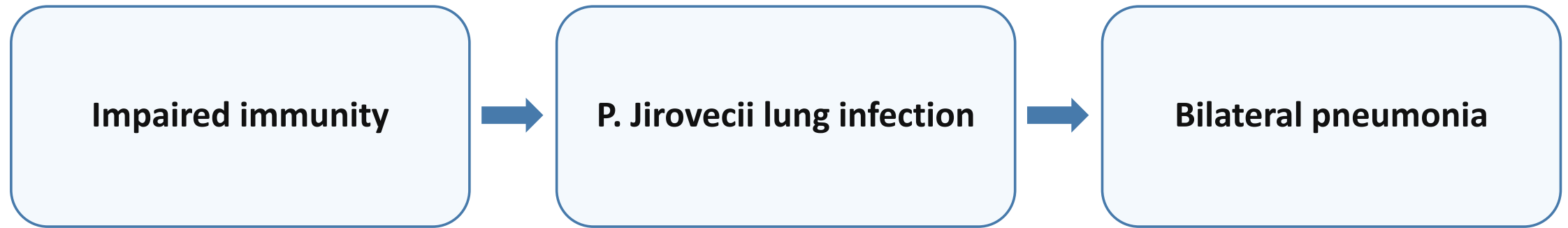


Encapsulated budding yeast

Interpretation

- In human tissue, *Cryptococcus* appears as yeast rather than pseudohyphae or true hyphae.
- The capsule is prominently visualized with mucicarmine and periodic acid–Schiff.
- Capsular antigen may be detected in cerebrospinal fluid or blood.

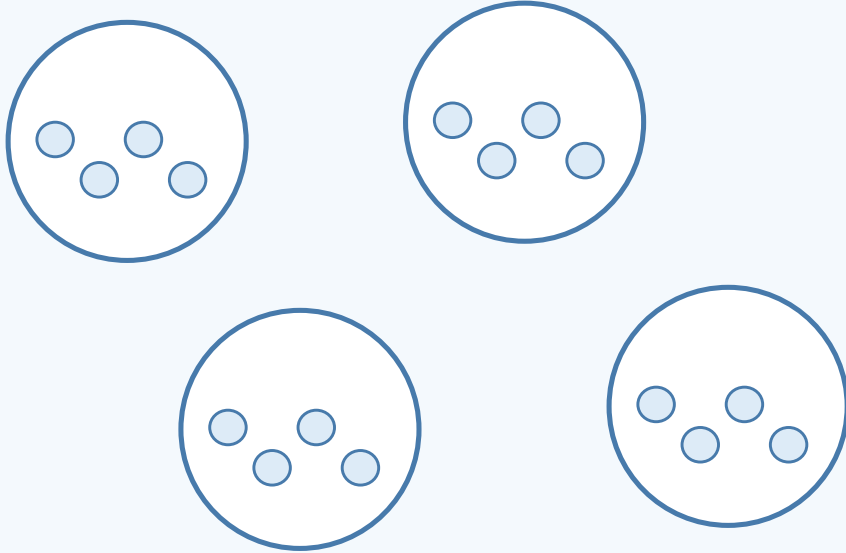
Pneumocystis is a pulmonary opportunist



Pneumocystis jirovecii is classified as a yeast-like fungus. It principally causes potentially progressive bilateral pneumonia in immunocompromised hosts.

Pneumocystis yields foamy alveolar exudate

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Schematic alveolar exudate, not tissue microscopy

Interpretation

- The Robbins description emphasizes interstitial alveolar thickening.
- Alveolar spaces contain eosinophilic, honeycombed or foamy material.
- Cysts can be demonstrated with methenamine silver; Trophic forms are not shown by that stain.

Pneumocystis testing is modality-dependent

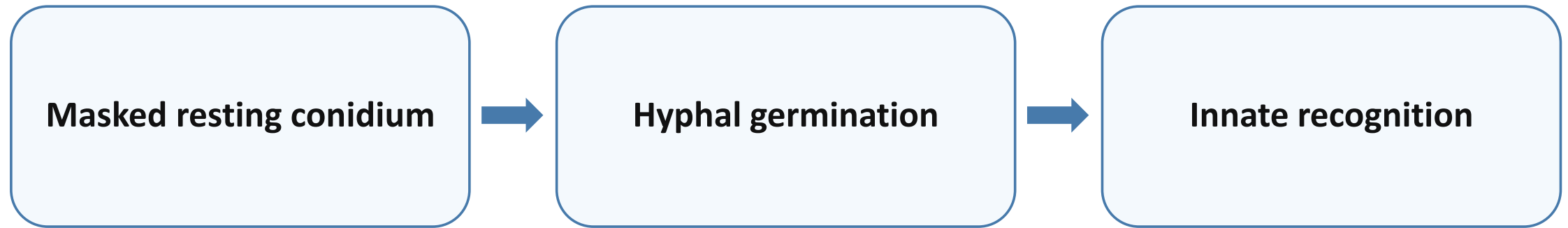
Method	Interpretive point
GMS tissue stain	Cyst / ascus wall highlighted
Immunofluorescence	Organism-targeted visualization
PCR	Sensitive organism nucleic-acid detection
β -D-glucan	Supportive but not species-specific

Aspergillus begins with inhaled conidia



A. Fumigatus is described as the most common pathogenic Aspergillus species. Small airborne conidia can reach the pulmonary alveoli.

Aspergillus conidia evade early detection



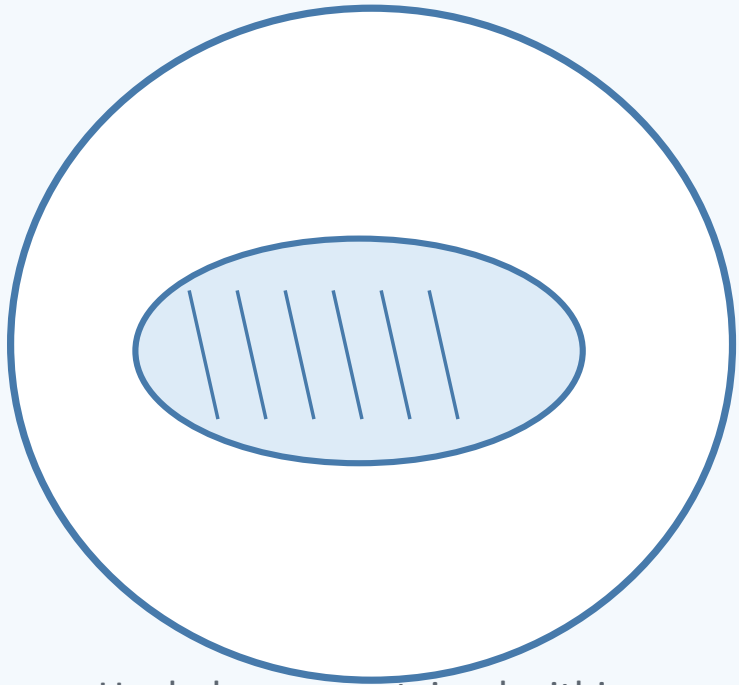
Surface hydrophobic proteins conceal fungal molecular motifs on resting conidia. Germination exposes microbial cell-wall structures to immune recognition.

Aspergillus has allergic, colonizing, invasive forms

Syndrome	Dominant mechanism
Allergic bronchopulmonary disease	Hypersensitivity to airway colonization
Aspergilloma	Fungal ball in pre-existing cavity
Invasive aspergillosis	Hyphal invasion and tissue necrosis

Aspergilloma occupies a pre-existing cavity

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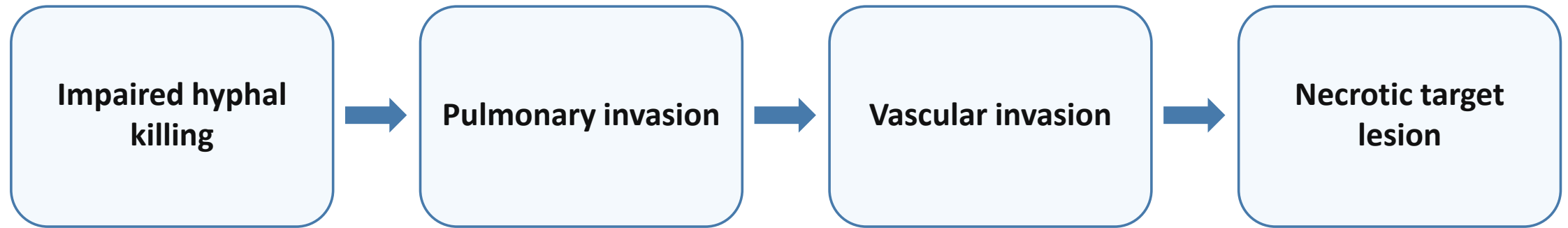


Hyphal mass contained within a pre-existing cavity

Interpretation

- Previous tuberculosis, bronchiectasis, infarction, or abscess may leave a suitable lung cavity.
- Hyphae proliferate within the cavity to form a fungus ball.
- Recurrent hemoptysis is a recognized clinical consequence.

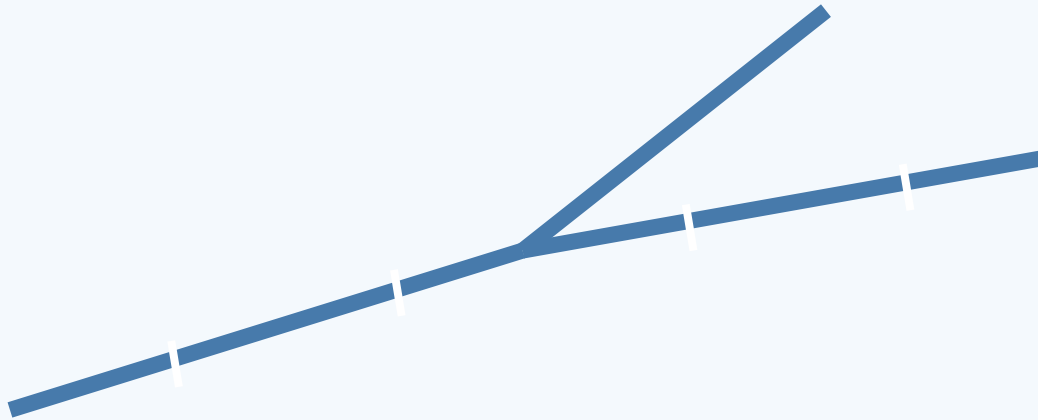
Invasive Aspergillus targets blood vessels



A major risk setting is severe neutropenia or corticosteroid treatment. Angioinvasion causes tissue ischemia, necrosis, and hemorrhage.

Aspergillus-type hyphae: Septate and acute-angle

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Continuous branching filaments; Septa indicated schematically

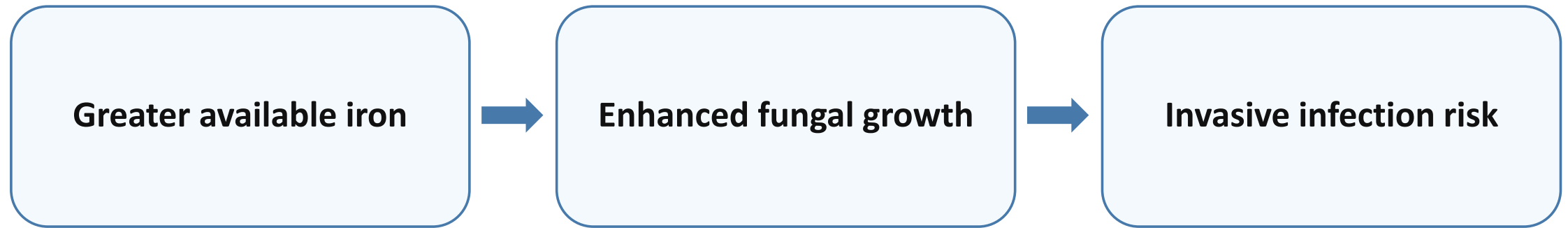
Interpretation

- Septate filaments with branching at approximately acute angles.
- This pattern is a useful morphologic clue in necrotic tissue.
- Without fruiting bodies, morphologically similar fungi can prevent definitive genus identification.

Mucormycosis exploits distinctive host risks

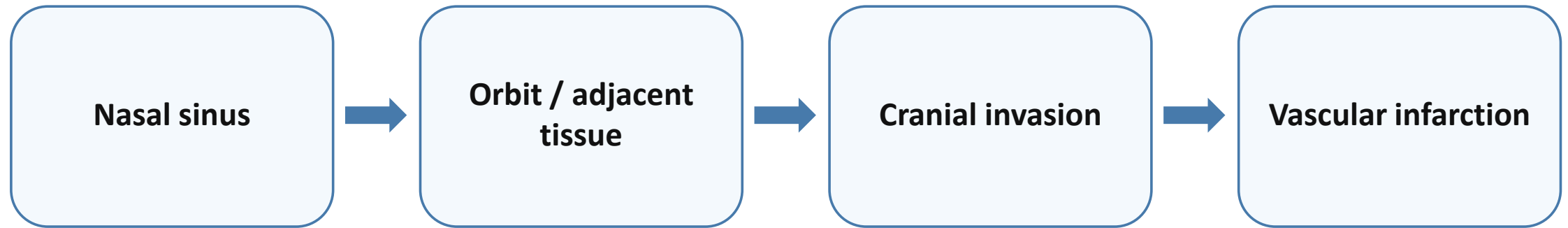
Predisposition	Pathogenetic relevance
Neutropenia	Reduced hyphal killing
Diabetic ketoacidosis	Metabolic / iron-related vulnerability
Corticosteroids	Impaired antifungal defenses
Open wounds / burns	Disrupted physical barrier

Increased free iron favors mucormycete growth



The chapter identifies available free iron as a promoter of mucormycete growth. Ketoacidosis in diabetes is a key clinical setting.

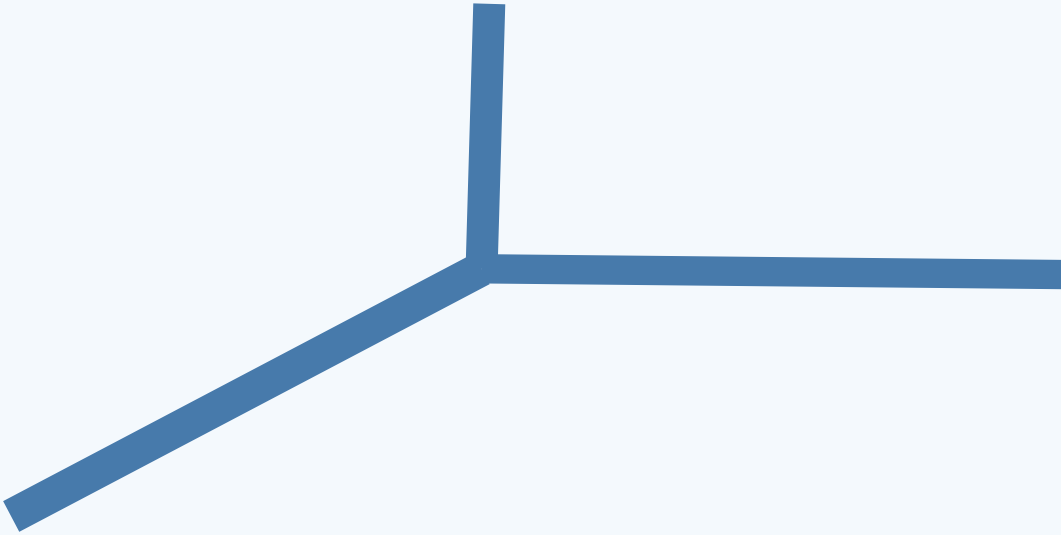
Rhinocerebral mucormycosis follows tissue planes



The organism can progress from nasal sinuses into the orbit and cranial compartment. Hyphae can invade arterial walls, leading to thrombosis and necrosis.

Mucormycete hyphae: Broad and irregular

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Broad irregular, typically nonseptate; Wide-angle branching

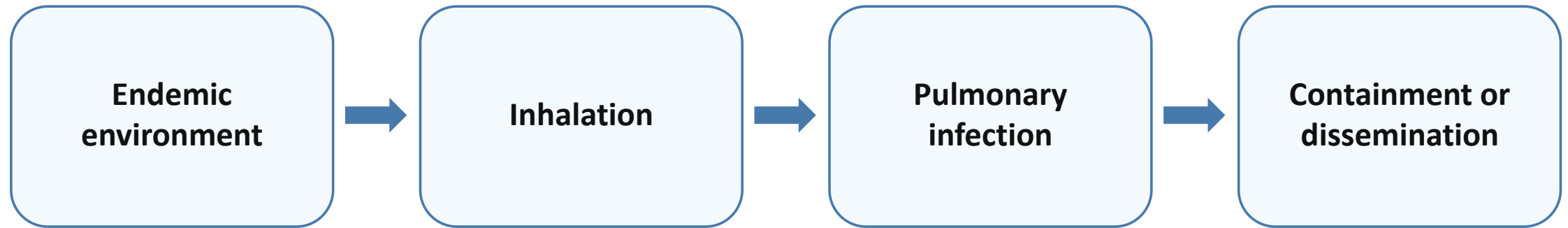
Interpretation

- The source describes nonseptate filaments of variable width.
- Branching is often at wide, approximately right angles.
- Morphology must be combined with necrosis, vascular invasion, and confirmatory studies.

Aspergillus and mucormycetes are not equivalent

Feature	Aspergillus-type mold	Mucormycetes
Hyphae	Narrower; Generally septate	Broader; Irregular; Nonseptate
Branching	Typically acute angle	Often near right angle
Shared finding	May invade vessels	May invade vessels
Key clinical context	Neutropenia / steroids	DKA, iron overload, neutropenia

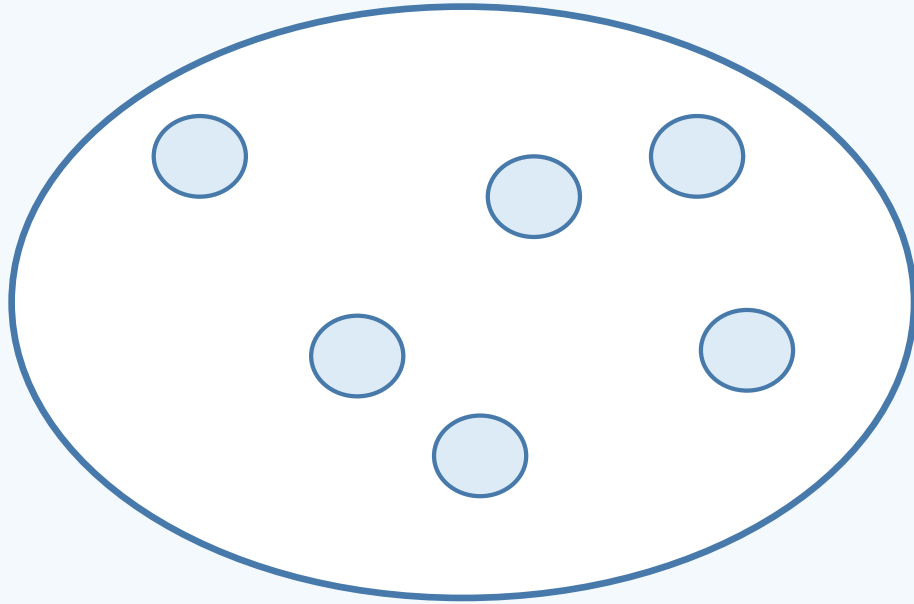
Endemic dimorphic fungi produce systemic disease



These organisms exist in specific geographic environments. Exposure to environmental fungal particles may initiate respiratory infection in healthy hosts.

Histoplasma may reside inside macrophages

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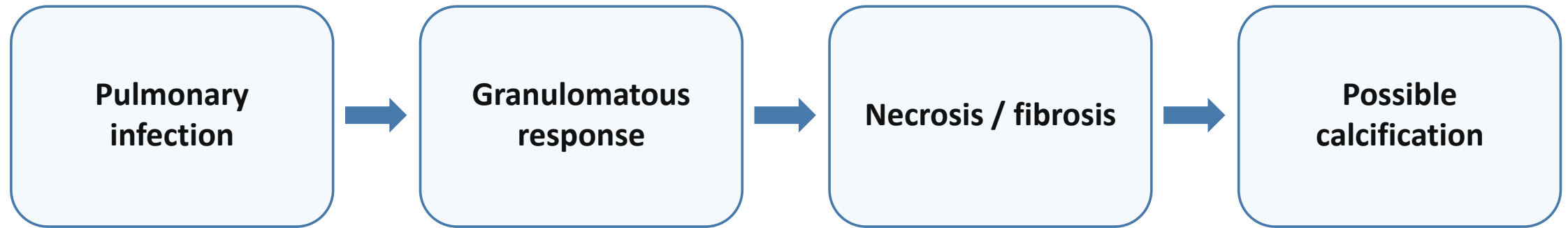


Small yeast forms shown within a phagocyte

Interpretation

- Histoplasma capsulatum is acquired by inhaling contaminated dust.
- Its small yeast forms are often found within macrophages.
- Before effective T-cell immunity, organisms can persist and disseminate from the lung.

Histoplasma lung disease may resemble tuberculosis



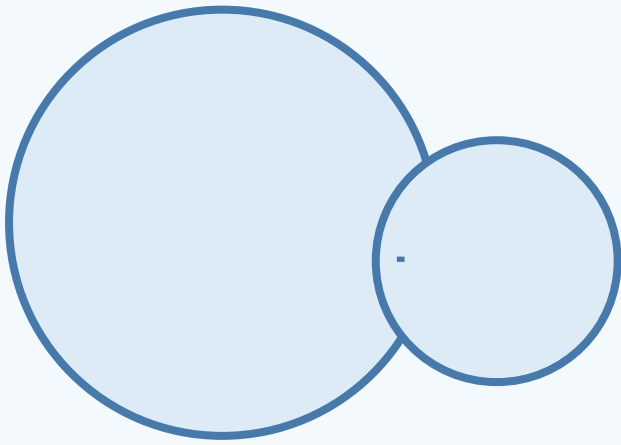
Primary pulmonary infection can be self-limited and occasionally produce a radiographic coin lesion. Chronic progressive disease can affect apical lung regions.

Disseminated histoplasmosis changes morphology

Host state	Dominant pathologic pattern
Relatively intact immunity	Granulomas; Possible necrosis / fibrosis
Depressed cell immunity	Disseminated yeast-laden macrophages
Interpretation	Immune status strongly alters morphology

Blastomyces produces broad-based budding

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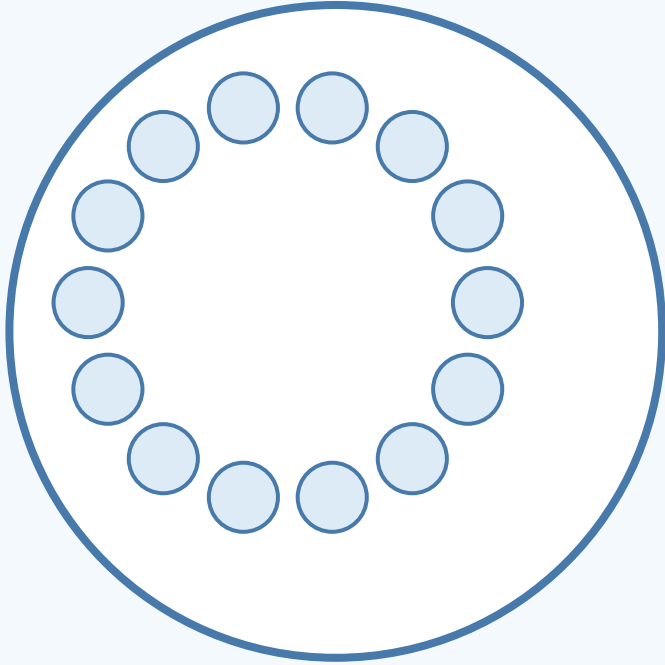
Broad contact between parent and daughter buds

Interpretation

- Blastomyces dermatitidis is a soil-associated dimorphic fungus.
- Tissue forms have thick-walled, round yeast cells with broad-based buds.
- Pulmonary lesions may be suppurative granulomas; Epithelial hyperplasia can mimic squamous carcinoma.

Coccidioides produces endospore-filled spherules

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Large nonbudding spherule with endospores

Interpretation

- Coccidioides tissue morphology features thick-walled, nonbudding spherules.
- Spherules contain endospores and may provoke suppuration when they rupture.
- Invasive disease can involve lung, skin, meninges, bones, and other organs.

Morphologic recognition: Major fungal signatures

Tissue form	Leading consideration
Budding yeast + pseudohyphae	Candida
Encapsulated yeast	Cryptococcus
Intracellular small yeast	Histoplasma
Broad-based budding yeast	Blastomyces
Spherule with endospores	Coccidioides
Septate / acute-angle hyphae	Aspergillus-type mold
Broad / wide-angle hyphae	Mucormycetes

Diagnostic decisions depend on host context

Clinical clue	Most relevant interpretation
Antibiotic exposure + oral plaque	Superficial candidiasis
Neutropenia + necrotic lung focus	Potential invasive mold disease
CNS disease + encapsulated yeasts	Cryptococcosis
Granulomas + environmental exposure	Consider endemic dimorphic fungi

Case application: Oral plaques after antibiotics

- Teaching scenario: A debilitated patient develops white oral plaques after broad-spectrum antibiotics.
- Most likely process: Superficial Candida proliferation with an inflammatory pseudomembrane.

What process explains the plaque?

Surface fungal proliferation plus inflammatory debris

Case application: Neutropenic pulmonary necrosis

- Teaching scenario: Profound neutropenia is followed by a rounded hemorrhagic lung lesion.
- The source's major concern is an angioinvasive mold, particularly *Aspergillus*.

Why is the border hemorrhagic?

Vascular invasion with thrombosis and infarction

Case application: Diabetic sinonasal necrosis

- Teaching scenario: Diabetes with ketoacidosis accompanies rapidly progressive sinonasal disease extending toward the orbit.
- Mucormycosis is strongly suggested by the risk setting and angioinvasive anatomy.

What links the metabolic risk to invasion?

Greater accessible iron and impaired antifungal defense

Case application: Meningitis with capsulated yeast

- Teaching scenario: An immunosuppressed patient develops meningoencephalitis with encapsulated budding yeasts.
- Cryptococcus is the major diagnostic consideration.

Which structure aids immune evasion?

Polysaccharide capsule

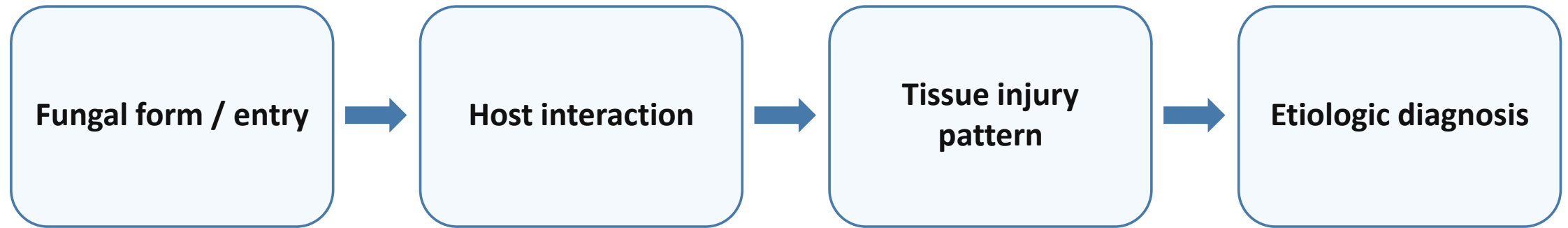
Case application: Lung granuloma with tiny yeast

- Teaching scenario: Granulomatous pulmonary inflammation contains small yeasts in macrophages.
- Histoplasma is a leading possibility in a suitable exposure setting.

Why can granulomas be absent in disseminated disease?

Failure of effective cell-mediated macrophage activation

Synthesis: Trace the path from fungus to injury



Start with the fungal form and route of entry. Determine the relevant defense failure or hypersensitivity response.

Reading and source context

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition (2026), Chapter 8, “Infectious Diseases.”
- Primary overview: “Fungal Infections”; adjacent sections cover Candida, Cryptococcus, Pneumocystis, molds, and endemic dimorphic fungi.
- All cell-form illustrations in this lecture are original schematics, not histologic micrographs.