

Chronic Pneumonia

Etiology • Host response • Morphology • Diagnosis

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Chronic pneumonia: Learning objectives

- Define the clinicopathologic syndrome and distinguish it from acute pneumonia.
- Relate persistent organisms and cell-mediated immunity to granulomatous injury.
- Recognize characteristic lesions of tuberculosis, NTM, nocardiosis, and endemic mycoses.
- Select tissue-based investigations without overinterpreting morphology alone.

Chronic pneumonia is a clinicopathologic pattern

- Most often a localized pulmonary lesion in an immunocompetent patient.
- Regional lymph node involvement may be present or absent.
- The typical tissue reaction is granulomatous inflammation.
- The category includes bacterial and fungal causes—not a single organism.

Persistent infection differs from acute pneumonia

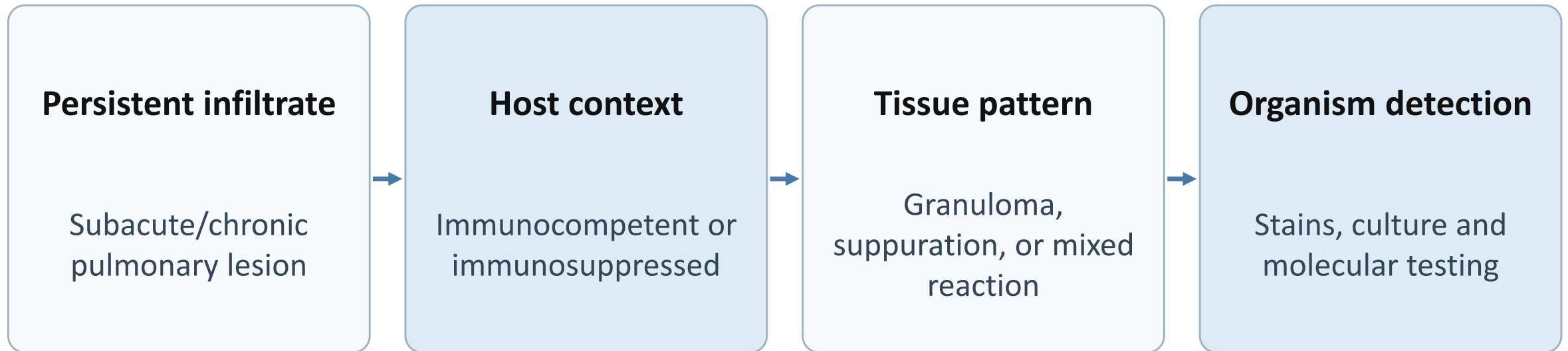
Acute bacterial pneumonia

- Rapid alveolar accumulation of neutrophil-rich exudate.
- Often diffuse lobar or patchy bronchopneumonia.
- Consolidation reflects exudate within air spaces.

Chronic pneumonia

- Persistent local lesions develop over a longer course.
- Granulomas frequently contain the offending organism.
- Necrosis, scarring, nodules, or cavities may evolve.

Clinical context narrows the etiologic differential



Schematic

Principal infectious causes

Group	Representative agents	Predominant clue
Mycobacteria	M. tuberculosis; nontuberculous mycobacteria	Granulomatous inflammation
Actinomycetes	Nocardia; Actinomyces	Chronic or suppurative lesions
Endemic fungi	Histoplasma; Blastomyces; Coccidioides	Granulomatous or mixed reaction

What the host response tells the pathologist

- An organized granuloma usually implies a functioning cellular immune response.
- Necrosis may reflect immune-mediated injury, persistence, and local destruction.
- Suppurative inflammation does not rule out a chronic infectious cause.
- Severe immunodeficiency can prevent classic granuloma formation.

Chronic lesion: Three morphologic questions

At low magnification

- Is the process focal, multifocal, or diffuse?
- Is there central necrosis, cavitation, or fibrosis?
- Are bronchi, vessels, or pleura affected?

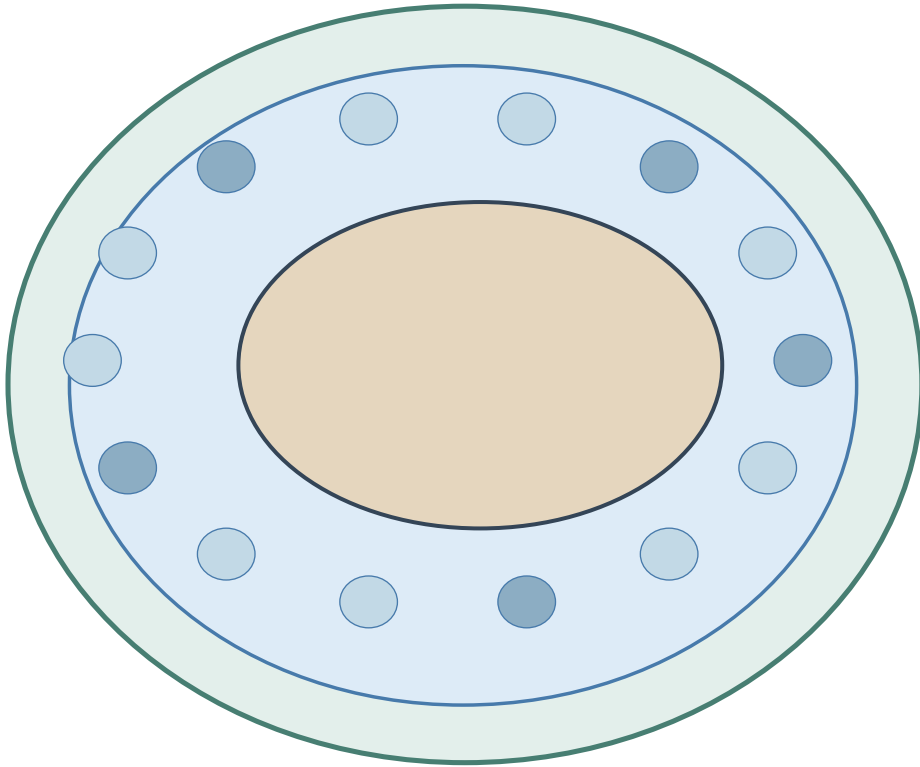
At higher magnification

- Are epithelioid histiocytes and giant cells present?
- Are neutrophils prominent at the center?
- Can microorganisms be demonstrated?

Granuloma: An organized chronic response

- Granulomas are aggregates of activated epithelioid macrophages.
- Lymphocytes are commonly present at their periphery.
- Multinucleated giant cells may form by macrophage fusion.
- A granuloma attempts to contain material that is difficult to eradicate.

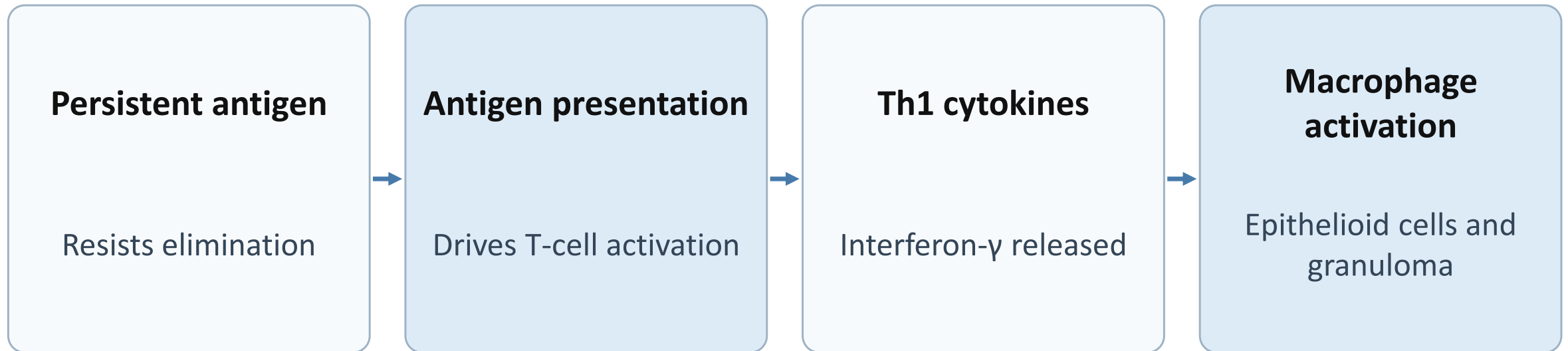
Anatomy of an immune granuloma



Schematic — not histologic evidence

- Central persistent stimulus $\pm$ necrosis
- Epithelioid histiocytes / giant cells
- Outer lymphocytes and fibroblasts

T-cell-mediated granuloma formation



Schematic

Caseating versus noncaseating granulomas

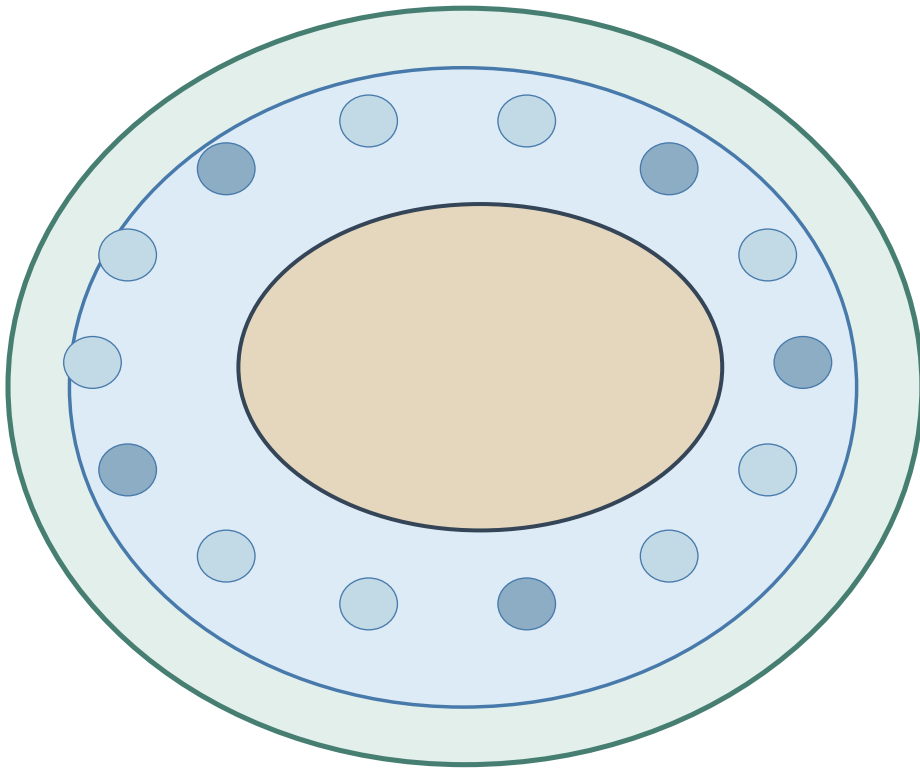
With caseous necrosis

- Granular, acellular central debris may be present.
- A characteristic finding in tuberculosis.
- Also occurs in certain fungal infections.

Without caseous necrosis

- Central necrosis is absent on the section examined.
- Does not exclude tuberculosis or infection.
- Sarcoidosis and other mimics remain possible.

Caseation is a tissue pattern, not an etiology



Schematic — not histologic evidence

- Necrotic core: Cellular architecture lost
- Inflammatory and granulomatous rim
- Requires microbiological correlation

Granulomatous and suppurative responses

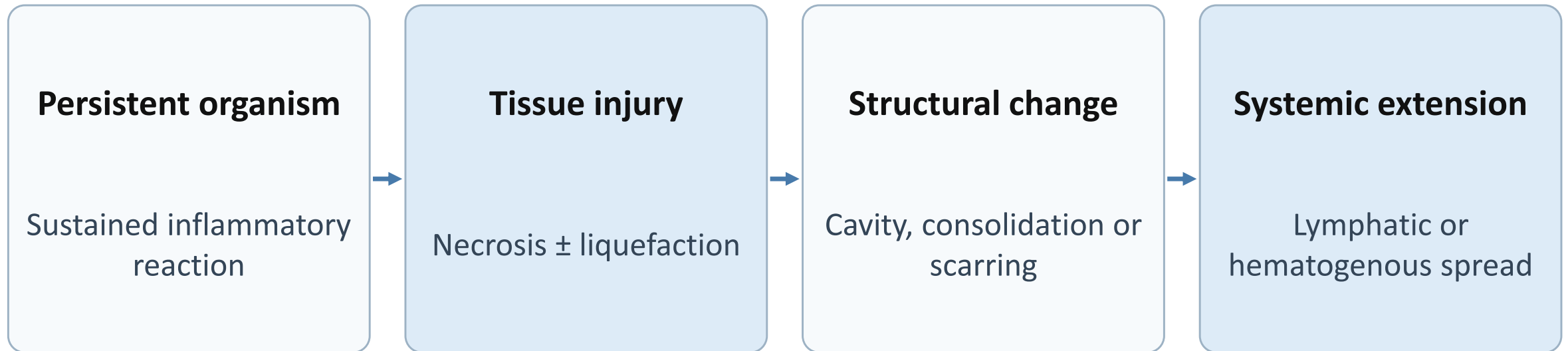
Granulomatous pattern

- Macrophage-rich immune containment.
- Caseation or fibrosis may develop.
- Prominent in tuberculosis and histoplasmosis.

Suppurative pattern

- Neutrophil-rich destructive inflammation.
- Central liquefaction or abscesses may occur.
- Important in nocardiosis and blastomycosis.

Possible fates of a chronic pulmonary lesion



Schematic

Why organisms must be identified

- Granuloma architecture overlaps across infectious and noninfectious disorders.
- Caseation is suggestive, not proof, of tuberculosis.
- Special stains may identify bacteria or fungi within affected tissue.
- Culture and molecular studies distinguish morphologically similar infections.

Tissue-based investigation: Complementary roles

Method	Main contribution	Interpretive caution
H&E morphology	Classifies inflammation, necrosis and injury	Usually not etiologically specific
Special stains	Visualizes acid-fast bacilli or fungal forms	Negative stain does not exclude infection
Culture	Can identify a viable pathogen	Depends on sample handling and growth
Molecular studies	Detects species-specific nucleic acid	Interpret with lesion and clinical context

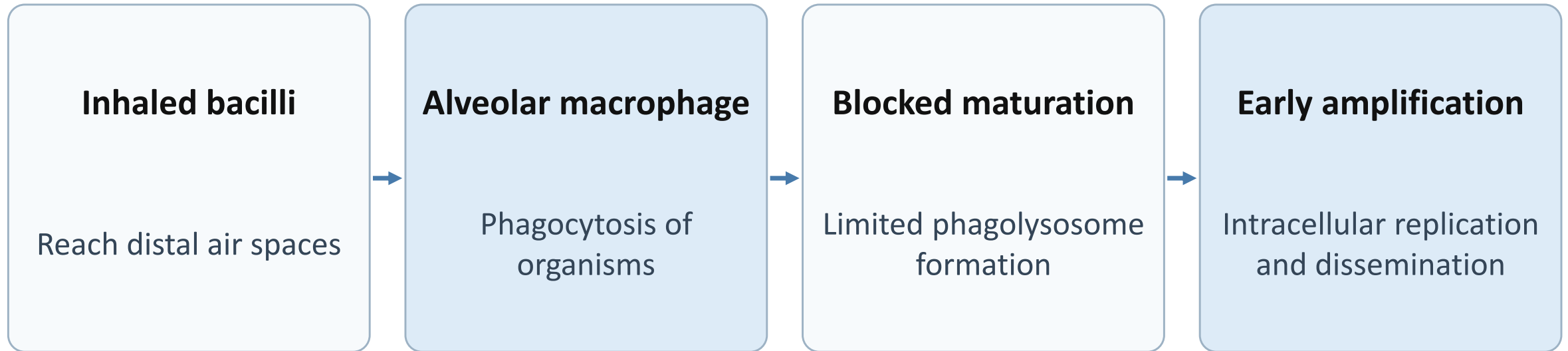
Specimen handling affects diagnostic yield

- A biopsy for histology demonstrates tissue response and may reveal organisms.
- A separate appropriately collected sample may be required for microbiology.
- Sample a viable interface as well as necrotic areas when feasible.
- Share the differential diagnosis with the microbiology laboratory.

Tuberculosis: Prototype chronic pneumonia

- M. Tuberculosis causes chronic pulmonary and potentially systemic disease.
- Transmission is usually airborne from a patient with active pulmonary disease.
- Clinical states include infection without disease and active disease.
- Cell-mediated immunity both contains bacilli and injures lung tissue.

Initial M. Tuberculosis infection

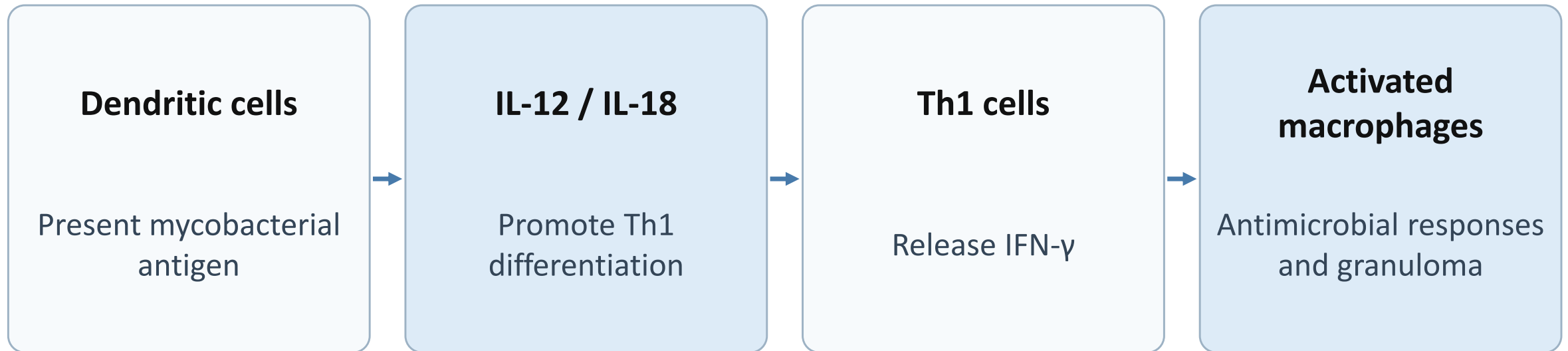


Schematic

Why tuberculosis survives in macrophages

- The bacillus interferes with phagosome maturation and fusion with lysosomes.
- Intracellular survival permits early multiplication before adaptive immunity.
- Antigen-presenting cells recruit antigen-specific T-cell responses.
- Successful host defense requires macrophage activation rather than antibodies alone.

Th1 immunity is pivotal in tuberculosis



Schematic

Protective and destructive effects of Th1 immunity

Containment

- IFN- γ activates macrophage antimicrobial functions.
- Nitric oxide, reactive oxygen species and autophagy contribute.
- Granuloma formation restricts infection.

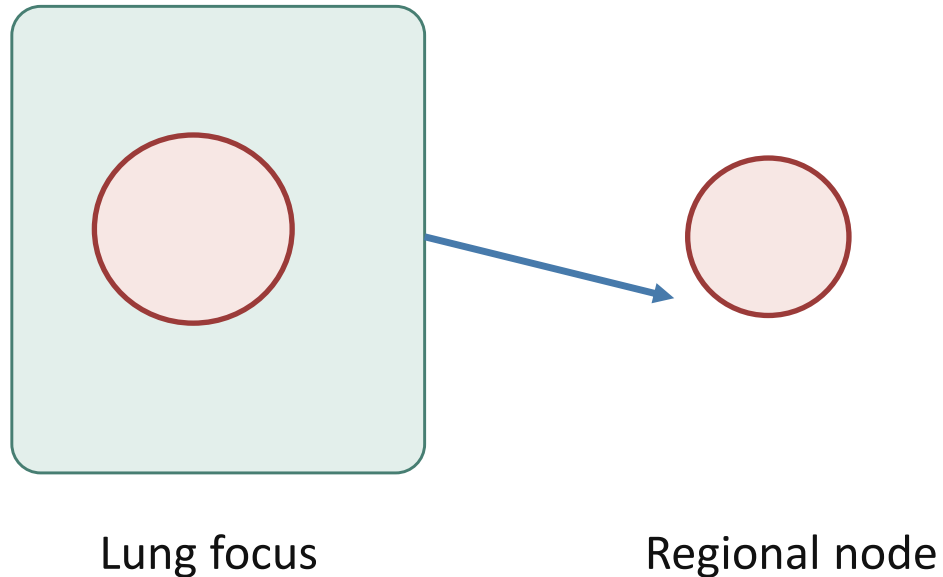
Collateral injury

- Sustained cellular immune activation damages tissue.
- Caseous necrosis may become extensive.
- Necrotic foci can progress to cavitation.

TNF helps maintain granulomatous containment

- Activated macrophages secrete TNF and chemokines.
- These mediators recruit additional monocytes to infected lesions.
- Granuloma maintenance contributes to control of latent infection.
- TNF-antagonist treatment increases risk of tuberculosis reactivation.

Primary tuberculosis: Pulmonary focus and nodes



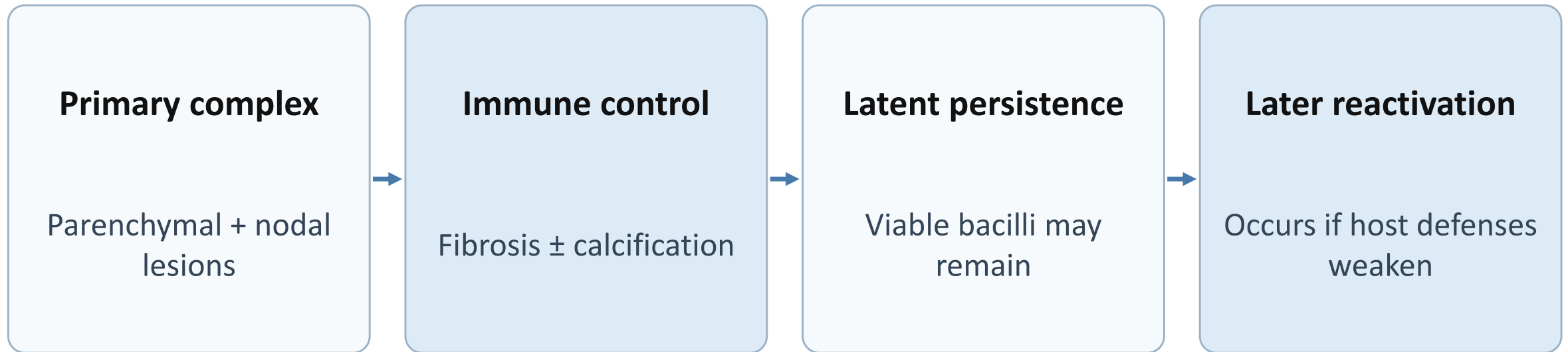
Schematic — not histologic evidence

- Subpleural pulmonary focus (Ghon focus)
- Draining lymphatics to regional nodes
- Ghon complex = focus plus nodal disease

Primary tuberculosis: Early morphologic course

- Initial implantation is often near the pleura in a lower upper lobe or upper lower lobe.
- A small gray-white focus of consolidation develops.
- The center often undergoes caseous necrosis.
- Regional lymph nodes can show similar caseating inflammation.

Primary infection: Possible outcomes



Schematic

The histologic tubercle

- An epithelioid macrophage aggregate often surrounds caseous necrosis.
- Multinucleated giant cells and peripheral lymphocytes may be seen.
- Some tuberculous granulomas are noncaseating.
- Bacillary yield varies across lesions and stages.

Primary versus secondary pulmonary tuberculosis

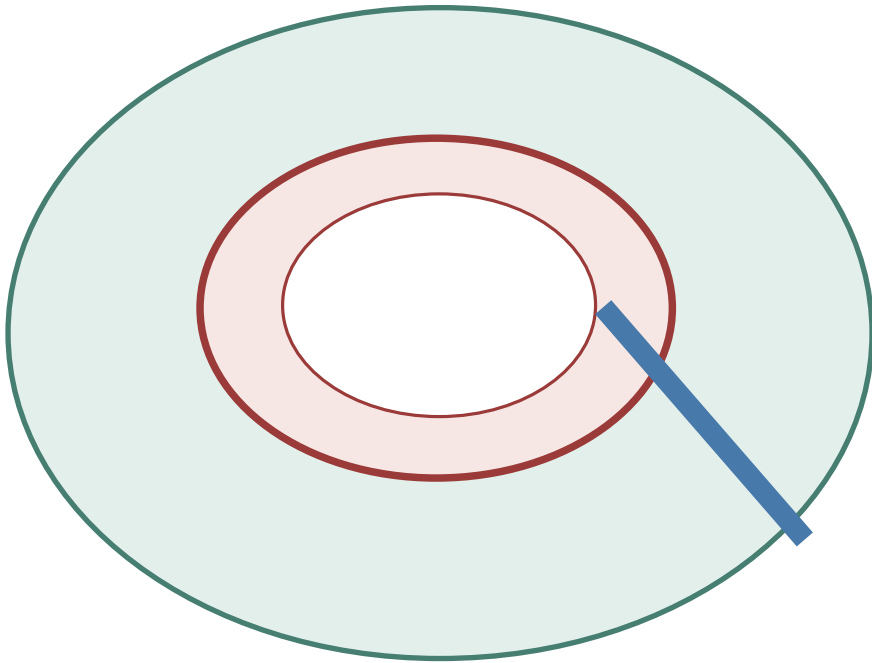
Primary disease

- Often a peripheral focus with regional nodal involvement.
- May heal as a fibrocalcific complex.
- Commonly recognized as the initial encounter.

Secondary (postprimary) disease

- Classically favors apical lung parenchyma.
- Fibrosis and central caseation are common.
- Progressive lesions can erode into bronchi and cavitate.

Secondary tuberculosis and cavitation



Schematic — not histologic evidence

- Apical focus with central caseation
- Bronchial erosion drains necrotic material
- Cavity contributes to infectious sputum and bleeding

Consequences of progressive cavitory tuberculosis

- Cavitation follows drainage of caseous necrotic material into airways.
- Involvement of blood vessels can cause hemoptysis.
- Bronchogenic spread creates additional pulmonary foci.
- Healing can leave fibrosis and distorted lung architecture.

Routes of progression in tuberculosis

Route	Pulmonary consequence	Possible systemic consequence
Bronchogenic	New air-space foci; endobronchial disease	Laryngeal involvement
Lymphatic / venous	Numerous small pulmonary nodules	Miliary involvement
Arterial bloodstream	Variable pulmonary involvement	Disseminated organ lesions
Contiguous extension	Pleural inflammation or effusion	Local tissue extension

Immune competence changes tuberculosis morphology

Adequate T-cell response

- Organized granulomas and tissue caseation.
- Fibrosis and local containment are possible.
- Cavitation may accompany destructive disease.

Advanced immunodeficiency

- Granuloma architecture may be poorly formed.
- Macrophages may harbor numerous bacilli.
- Disseminated infection becomes more likely.

Tuberculous infection cannot be inferred from H&E alone

- Granulomatous inflammation suggests a limited etiologic differential.
- Acid-fast stains are indicated even when granulomas lack caseation.
- Culture or molecular testing establishes organism identity.
- A paucibacillary lesion may be stain-negative despite active infection.

Nontuberculous mycobacteria (NTM)

- NTM are mycobacteria outside the *M. Tuberculosis* complex and *M. Leprae*.
- Human pathogens include *M. Avium* complex, *M. Abscessus* complex, and *M. Kansasii*.
- The environment—water and soil—is an important reservoir.
- Unlike tuberculosis, person-to-person transmission is generally uncommon.

Who is vulnerable to pulmonary NTM disease?

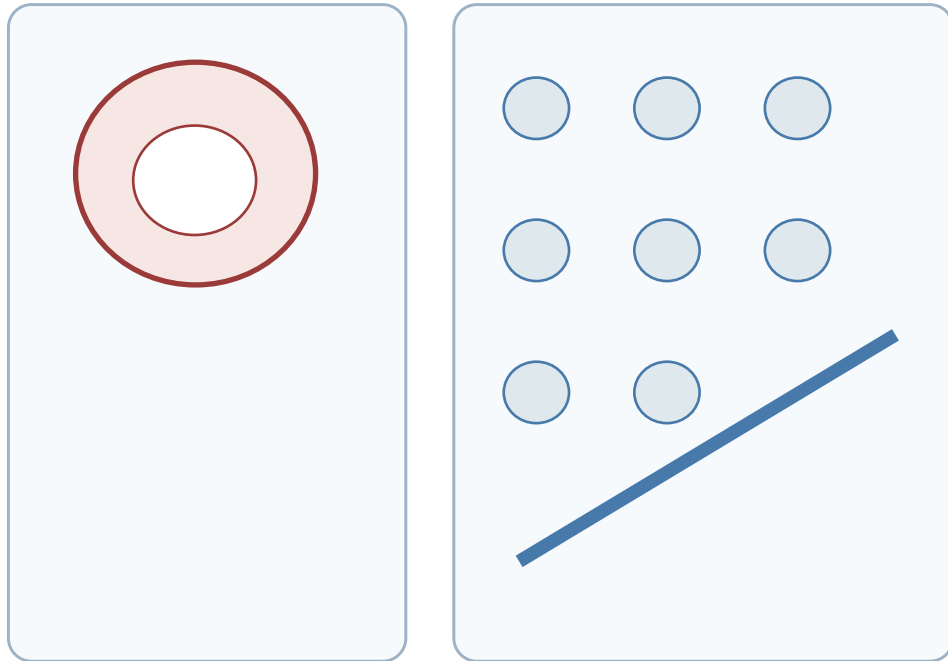
Structural lung disease

- Bronchiectasis or cystic fibrosis.
- Chronic obstructive pulmonary disease.
- Primary ciliary dyskinesia or pneumoconiosis.

Host defense impairment

- HIV infection and transplantation.
- TNF antagonists.
- Rare IL-12 / IFN- γ pathway disorders.

Two patterns of pulmonary NTM disease



Schematic — not histologic evidence

- Fibrocavitary lesions often affect upper lobes
- Nodular bronchiectasis produces small clustered nodules
- Imaging pattern alone is not a species diagnosis

NTM requires organism-level interpretation

- Species identification is important because organism-specific treatment differs.
- Culture isolation must be related to clinical and radiologic disease.
- Chronic productive cough, fever, and weight loss may occur.
- Advanced immunodeficiency may produce disseminated MAC infection.

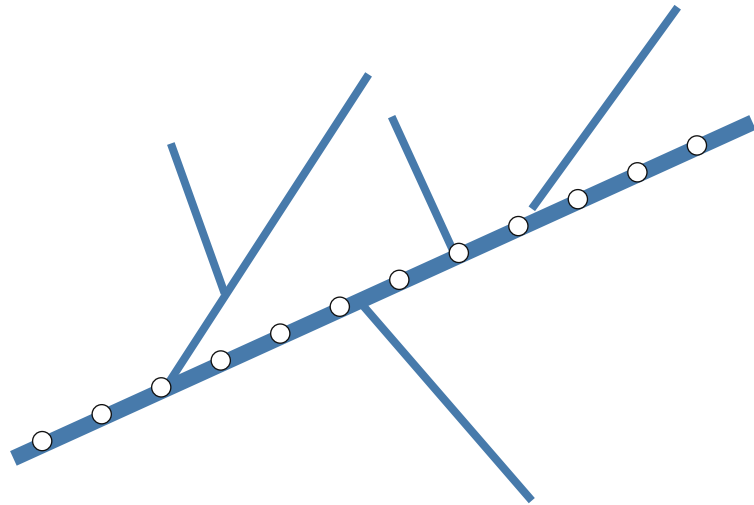
Tuberculosis versus pulmonary NTM

Feature	Tuberculosis	NTM
Typical source	Person with active disease	Environmental water / soil
Transmission	Airborne human-to-human	Usually environmental acquisition
Host context	Any immune status	Structural lung disease or impaired defenses common
Pathologic reaction	Granulomatous $\pm$ caseation	Granulomatous/chronic lesions; pattern overlaps

Nocardia: Chronic infection by filamentous bacteria

- Nocardia species are aerobic gram-positive, soil-associated bacteria.
- They form branching, filamentous structures resembling fungal hyphae.
- Pulmonary disease often follows an indolent course.
- Glucocorticoid use, HIV infection, and diabetes increase vulnerability.

Nocardia: Branching filamentous morphology



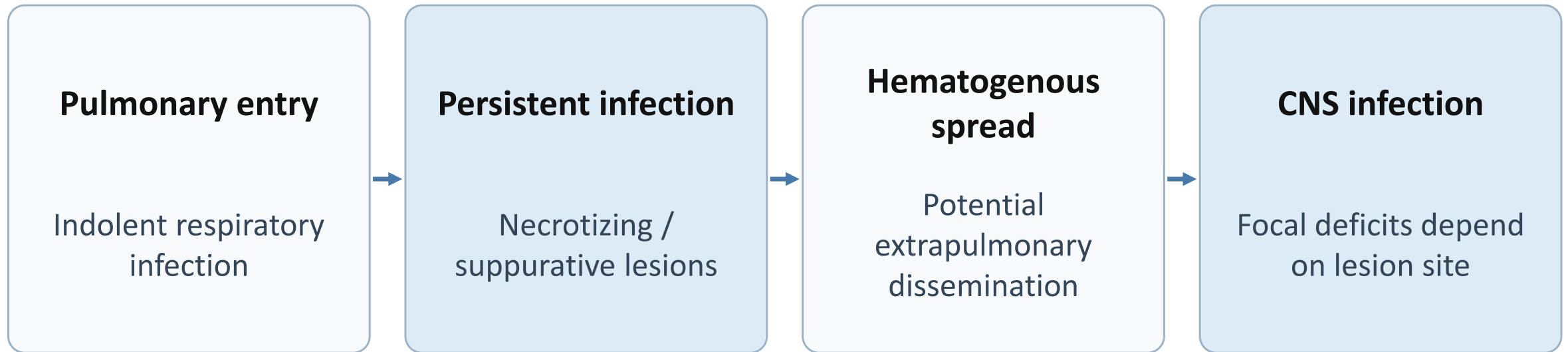
Schematic — not histologic evidence

- Slender branching Gram-positive organisms
- Irregular, beaded staining
- Modified acid-fast stain can be positive

Nocardial lung pathology is often suppurative

- Nocardia causes a neutrophil-rich inflammatory reaction.
- Central liquefaction can create abscess-like lesions.
- Granulation tissue and fibrosis may surround destructive foci.
- The lesion can imitate tuberculosis or pulmonary malignancy.

Nocardial dissemination: A clinical warning



Schematic

Nocardia versus Actinomyces: Key laboratory clue

Feature	Nocardia	Actinomyces
Filamentous Gram-positive bacteria	Yes	Yes
Modified acid-fast stain	Often positive	Negative
Interpretation	Possible pulmonary nocardiosis	Separate consideration in chronic suppuration

Do not confuse bacterial filaments with fungal hyphae

- Branching architecture is not proof that an organism is a mold.
- Nocardia is a bacterium despite superficial resemblance to mycelia.
- Gram stain and modified acid-fast staining can resolve key distinctions.
- Culture and species identification remain important.

Endemic dimorphic fungi: Pulmonary entry

- Major organisms are Histoplasma, Blastomyces, and Coccidioides.
- Geographic and environmental exposures alter pretest probability.
- Pulmonary infection follows inhalation of environmental forms.
- Tissue morphology differs markedly among these organisms.

Dimorphism must be interpreted by organism

Histoplasma and Blastomyces

- In tissue: Yeast forms.
- Environmental phase: Mold with hyphae.
- Host immunity influences persistence or dissemination.

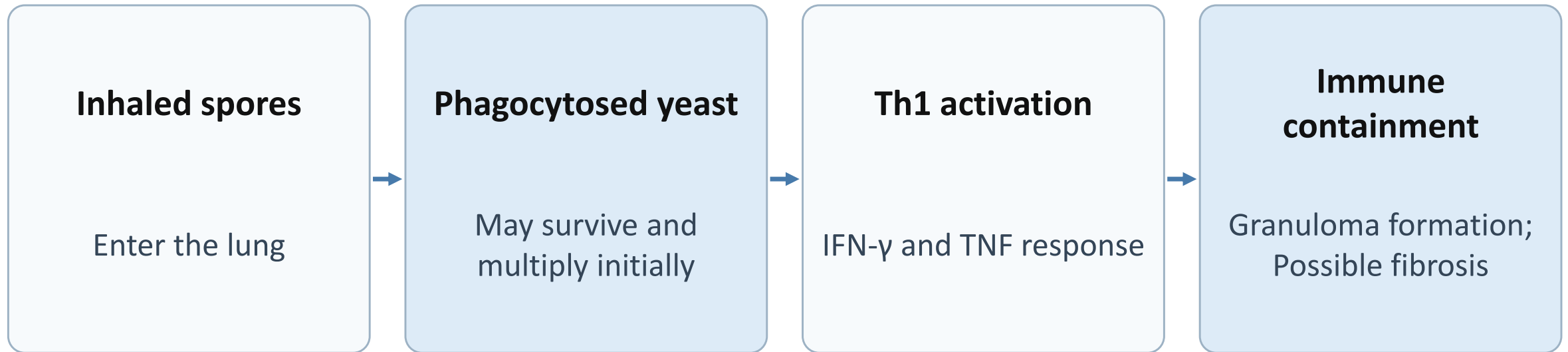
Coccidioides

- In tissue: Large endospore-filled spherules.
- Not classified by a typical budding yeast in tissue.
- Spherule rupture can induce suppuration.

Histoplasma: Environmental acquisition

- Infection follows inhalation of microconidia from contaminated soil dust.
- Bird or bat droppings are an important exposure clue.
- The Ohio and Mississippi River Valleys among endemic areas.
- Organisms are found predominantly within phagocytic cells.

Histoplasma: T-cell–macrophage defense

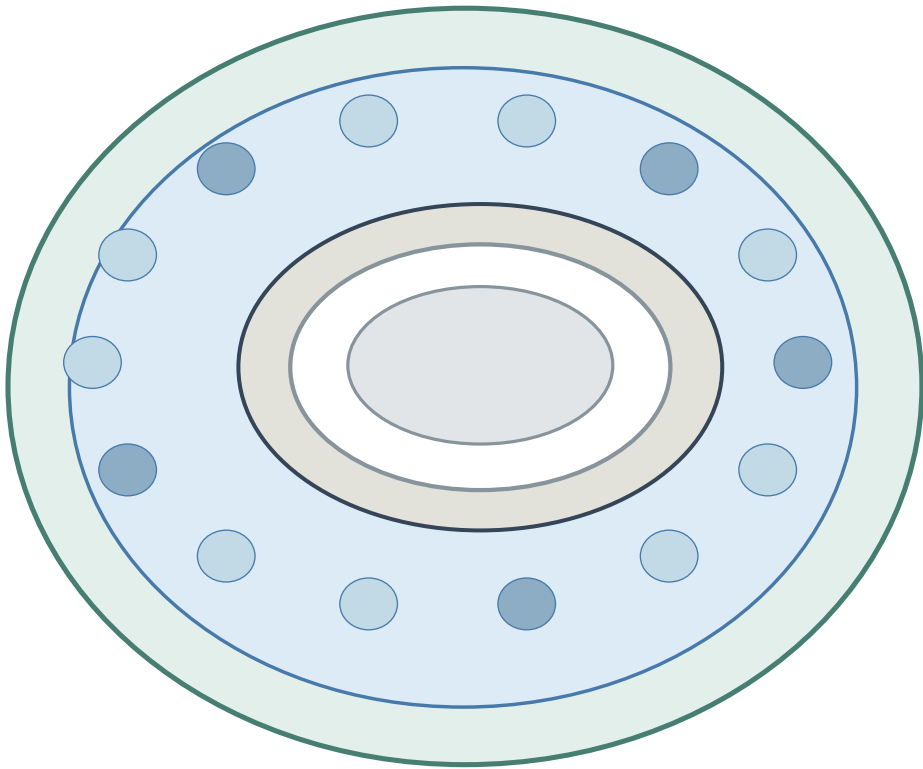


Schematic

Histoplasmosis has several pulmonary courses

- Self-limited primary infection may leave a small pulmonary nodule.
- Chronic progressive lesions can involve the lung apices.
- Clinical symptoms may resemble tuberculosis.
- Severe cell-mediated immune impairment favors widespread dissemination.

Histoplasma granuloma: Necrosis to calcification



Schematic — not histologic evidence

- Pulmonary granulomas often develop necrosis
- Resolution may produce fibrosis and concentric calcification
- Small yeasts may persist in tissue

Histoplasma: Critical microscopic clue

- Numerous small thin-walled yeasts may be found within macrophages.
- Yeast forms in the approximately 3–5 μm range.
- Disseminated disease may show yeast-filled phagocytes without granulomas.
- Special fungal stains assist in demonstrating organisms.

Localized versus disseminated histoplasmosis

Effective cellular immunity

- Granulomatous lesions may necrose.
- Fibrosis and calcification can follow.
- Persistent small pulmonary lesions may remain.

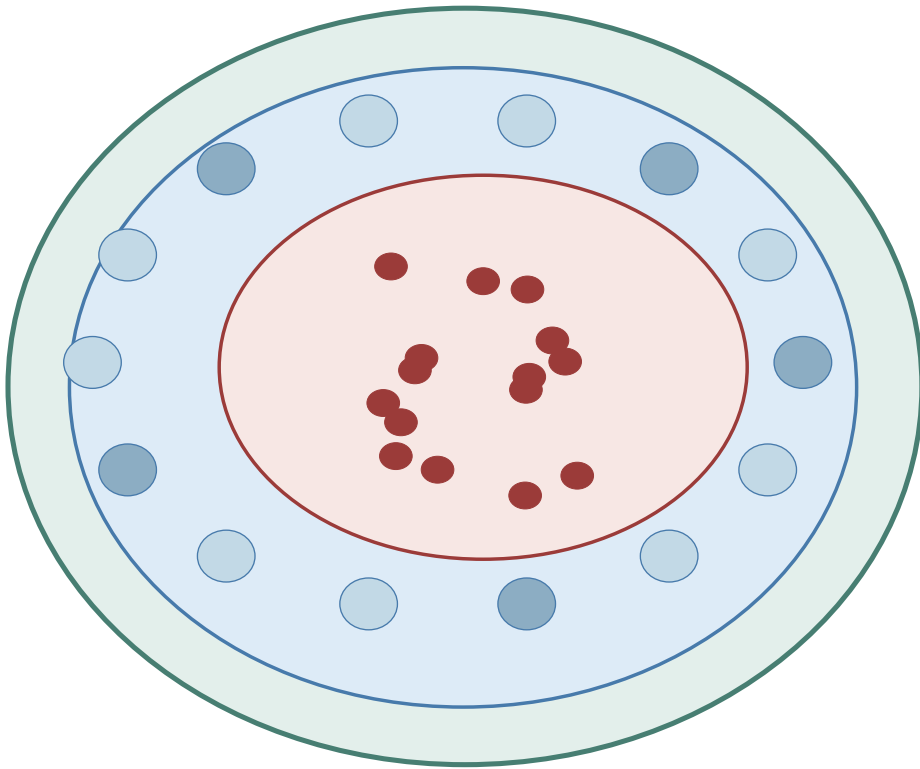
Deficient cellular immunity

- Granulomas may fail to organize.
- Yeast-laden macrophages accumulate widely.
- Extrapulmonary disease becomes important.

Blastomyces: Clinical-pathologic spectrum

- *Blastomyces dermatitidis* is a soil-associated dimorphic fungus.
- Pulmonary infection may resolve or progress to a chronic lesion.
- Disseminated disease can involve extrapulmonary sites.
- A rare primary cutaneous infection follows direct inoculation.

Blastomyces: Suppurative granulomas



Schematic — not histologic evidence

- Granulomatous macrophage response
- Prominent neutrophilic suppuration
- Thick-walled yeast with broad-based budding

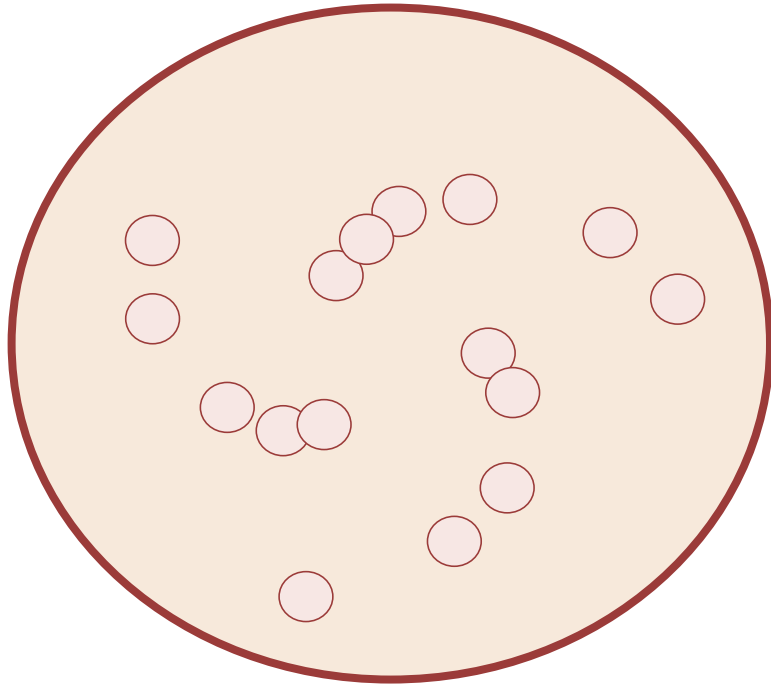
Blastomyces morphology: Distinguish the yeast

- Rounded yeast typically measures approximately 5–15 μm in tissue.
- A thick, double-contoured wall is characteristic.
- Broad-based budding is a defining morphologic clue.
- Skin or laryngeal epithelial hyperplasia can mimic squamous carcinoma.

Coccidioides: Pulmonary infection after inhalation

- *Coccidioides immitis* and *C. Posadasii* are relevant species.
- Exposure is linked to endemic arid regions of the Americas.
- Many infections remain asymptomatic.
- A small subset causes progressive pulmonary or disseminated disease.

Coccidioides in tissue: Spherules, not budding yeast



Schematic — not histologic evidence

- Large thick-walled tissue spherule
- Internal endospores; No broad-based bud
- Rupture releases endospores and recruits neutrophils

Coccidioidal inflammation is morphologically variable

Unruptured spherules

- Granulomatous inflammation may predominate.
- Tissue reaction can resemble other fungal granulomas.
- Identification of spherules is highly informative.

Ruptured spherules

- Endospore release triggers a pyogenic response.
- Granulomatous and suppurative components may coexist.
- Mixed histology is not contradictory.

Coccidioides: Sites of progressive disease

- Progressive infection may involve lung parenchyma and regional nodes.
- Disseminated foci can develop in meninges, skin and bone.
- Reduced T-cell immunity increases the risk of dissemination.
- Pregnancy is identified by Robbins as another risk context.

Distinguish the three endemic fungi in tissue

Organism	Typical tissue form	Characteristic reaction
Histoplasma	Small yeast, often inside macrophages	Necrotizing granulomas; absent in severe dissemination
Blastomyces	Thick-walled, broad-based budding yeast	Suppurative granulomas
Coccidioides	Endospore-filled spherule	Granulomatous, pyogenic, or mixed

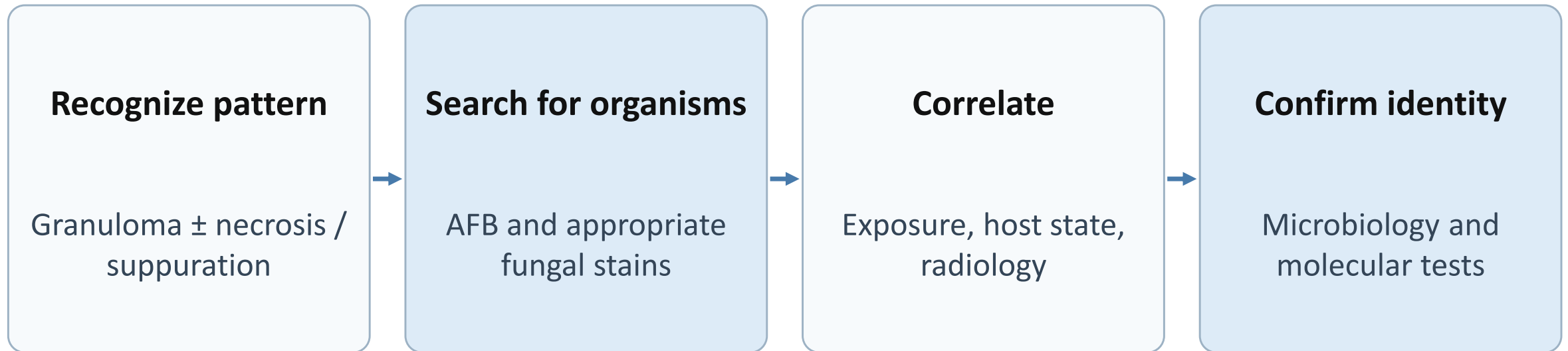
Tissue differential for chronic granulomatous pneumonia

Finding	Leading consideration	Necessary next step
Caseating granuloma	Tuberculosis; endemic fungal disease	AFB and fungal stains; culture / molecular study
Suppurative granuloma	Blastomyces; Nocardia; other infection	Evaluate yeast/filament morphology and stains
Noncaseating granuloma	Infections; sarcoidosis among mimics	Do not exclude infection on necrosis alone
Few granulomas in immune suppression	Disseminated infection possible	Search carefully for abundant organisms

The noninfectious differential is essential

- Sarcoidosis may cause pulmonary granulomas without an infectious agent.
- Foreign material can induce granulomatous reactions.
- Necrotizing or suppurative injury may overlap with noninfectious processes.
- Positive organism identification is decisive when morphology overlaps.

A pathology-centered diagnostic algorithm



Schematic

How not to overread a negative stain

A negative tissue stain means

- Organisms were not demonstrated in those sections.
- Low numbers or sampling may impair visualization.
- A targeted microbiologic evaluation may still be required.

A positive specific morphology means

- Fungal tissue forms may be strongly suggestive.
- Acid-fast bacilli identify a group, not necessarily species.
- Clinical and microbiologic interpretation remain necessary.

Case discussion: An apical cavitory lesion

An adult with cough, weight loss and an apical cavitory pulmonary lesion undergoes tissue sampling. The biopsy contains necrotizing granulomas.

Diagnostic questions

- What is the priority infectious consideration?
- Can the H&E appearance alone prove the diagnosis?

Tuberculosis is a leading consideration; Request acid-fast testing and appropriate microbiologic confirmation. Fungal causes remain in the differential.

Case discussion: A suppurative lung mass

An immunosuppressed adult presents with a slowly progressive pulmonary mass. Sections show central liquefaction, neutrophils and surrounding fibrosis.

Diagnostic questions

- Which filamentous bacterium merits examination?
- What second organ system warrants clinical attention?

Nocardia is a relevant possibility; Seek branching organisms with Gram/modified acid-fast stains, and consider the potential for CNS dissemination.

Case discussion: Small yeasts in macrophages

A patient with prolonged fever and a pulmonary infiltrate has biopsy specimens with phagocytes containing numerous small yeast forms. Organized granulomas are sparse.

Diagnostic questions

- Which endemic mycosis best matches the tissue clue?
- What feature of host defense might explain weak granuloma formation?

Histoplasma is a leading consideration. Severe impairment of cell-mediated immunity can blunt granuloma organization.

Case discussion: Broad-based budding

A lung biopsy shows neutrophils mixed with granulomas. Round, thick-walled yeast cells with broad-based buds are identified.

Diagnostic questions

- Which fungal cause does the morphology suggest?
- Why might a purely granulomatous description be misleading?

Blastomyces is strongly suggested; Its characteristic inflammatory pattern is suppurative granulomatous rather than exclusively epithelioid.

Case discussion: An endospore-filled body

A pulmonary biopsy demonstrates large thick-walled spherules containing internal small structures. Neutrophils cluster around a ruptured form.

Diagnostic questions

- Name the likely pathogen group.
- Explain the coexistence of suppuration and granulomas.

Coccidioides is favored; Rupture releases endospores and may superimpose a pyogenic reaction.

Integrated pathologic reporting principles

- Describe the inflammatory pattern and the extent of necrosis.
- Record whether organisms are visible and which stains were used.
- Separate a suggestive morphology from proven microbiologic identity.
- Flag diagnostic alternatives when the reaction is nonspecific.

Five morphology-to-organism clues

Clue	Most useful association
Caseating, epithelioid granuloma	Tuberculosis; other granulomatous infection
Branching, beaded Gram-positive filaments	Nocardia
Small yeasts inside macrophages	Histoplasma
Broad-based budding thick-walled yeast	Blastomyces
Endospore-containing spherule	Coccidioides

Core synthesis: Mechanisms to diagnosis

- Chronic pneumonia often involves persistent intracellular or difficult-to-clear microbes.
- Th1–macrophage immunity promotes containment and contributes to tissue damage.
- Necrosis, suppuration, fibrosis and cavitation reflect different lesion pathways.
- Morphology directs testing; Organism identification establishes the etiology.

References and source boundaries

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. 2026.
- Pulmonary infections: chronic pneumonia and its etiologic groups.
- Mycobacterial infections, nocardiosis, and endemic mycoses.
- Granulomatous inflammation and inflammatory tissue injury.