

Nontuberculous mycobacterial infections

Etiology · host susceptibility · pathogenesis · morphology · clinicopathologic
diagnosis

A pathology lecture organized around host–organism interactions

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning objectives

- Identify the major NTM pathogens and their environmental reservoirs.
- Connect pulmonary and disseminated disease to distinct host vulnerabilities.
- Explain neutrophil-mediated injury, macrophage-rich morphology, and diagnostic pitfalls.
- Interpret species identification in clinical and pathologic context.

NTM: A group defined by exclusion

Genus *Mycobacterium*

```
graph TD; A[Genus Mycobacterium] --> B[M. Tuberculosis]; A --> C[Nontuberculous mycobacteria]; A --> D[M. Leprae];
```

M. Tuberculosis

Excluded: Tuberculosis

**Nontuberculous
mycobacteria**

Focus of this lecture

M. Leprae

Excluded: Leprosy

Acid-fastness reflects the mycobacterial cell wall

- Mycobacteria contain unusual lipid-rich cell walls.
- Mycolic acids contribute to resistance to acid–alcohol decolorization.
- An acid-fast stain identifies a property of the genus—not the species.



Mycobacterial bacilli

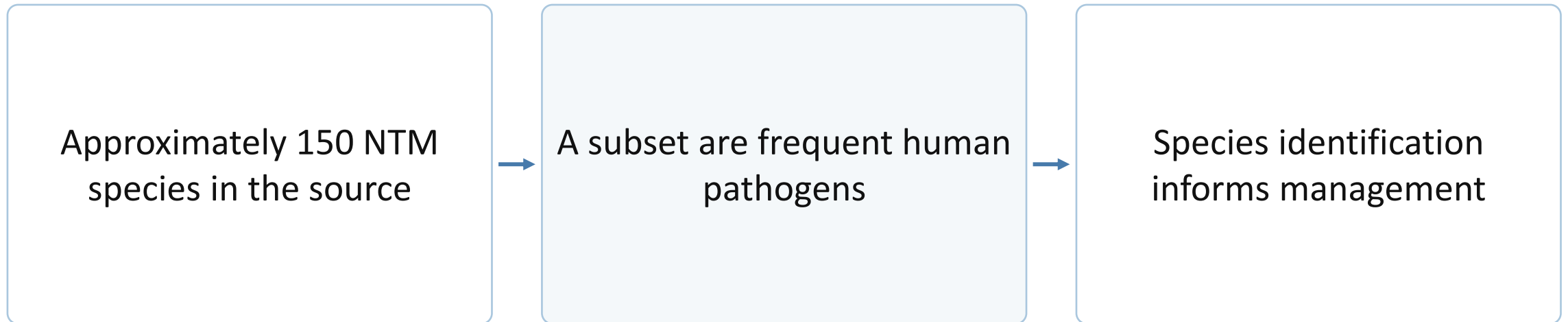


Schematic · not a stained specimen

NTM disease has become more prevalent worldwide

- An increase in NTM disease prevalence worldwide.
- The source provides no current numerical incidence or prevalence series.
- Interpret changing frequency separately from the clinical spectrum of disease.

The NTM group comprises many species



Species diversity does not imply equal pathogenicity.

Three major pathogens anchor the clinical discussion

**Mycobacterium avium
complex**

MAC

M. Abscessus complex

Rapidly growing NTM complex

M. Kansasii

Distinct species

MAC is a clinically defined species complex

Mycobacterium avium complex (MAC)

```
graph TD; MAC[Mycobacterium avium complex (MAC)] --> MA[M. Avium]; MAC --> MI[M. Intracellulare]; MAC --> MC[M. Chimaera];
```

M. Avium

Member

M. Intracellulare

Member

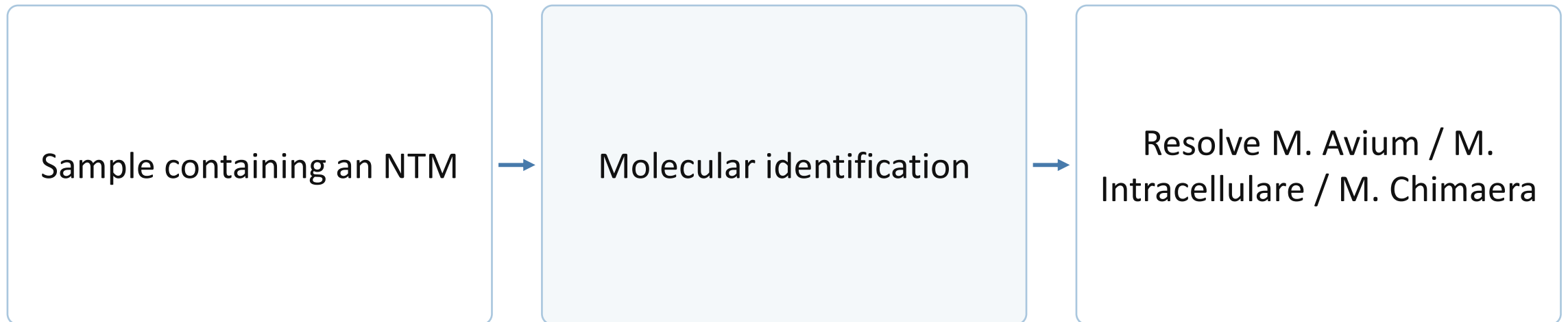
M. Chimaera

Molecularly distinguished member

Traditional identification may not resolve MAC members

Historical limitation	Implication
Physical / biochemical tests	M. avium and M. intracellulare are difficult to separate
Similar clinical features	Grouping as MAC remains clinically useful
Species-level uncertainty	Avoid claiming identification beyond the assay

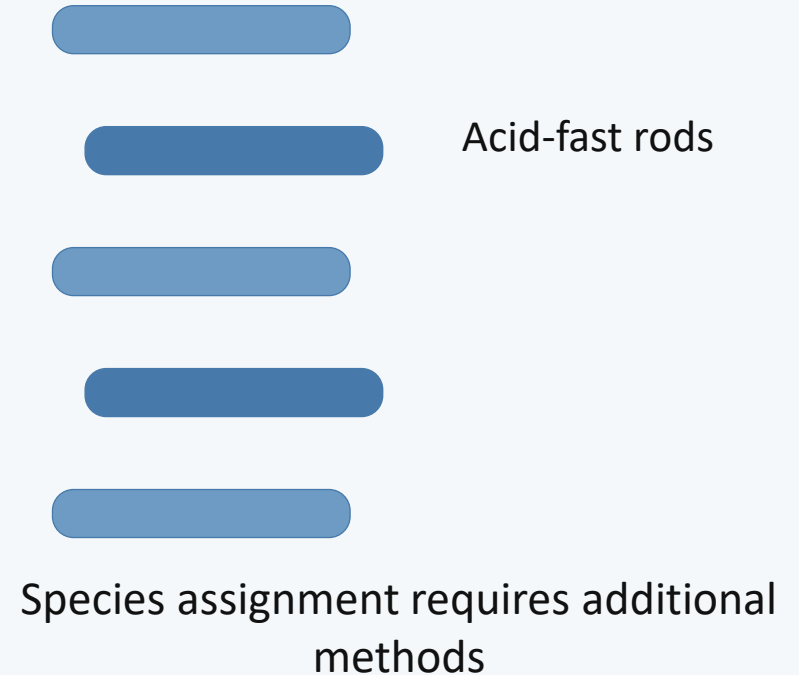
Molecular methods refine MAC identification



The source states molecular methods better distinguish these MAC species.

Species identity matters because therapy differs

- Different treatments for leading NTM pathogens.
- Report the identified species or complex rather than “AFB positive” alone.
- This lecture does not specify drug regimens or guideline algorithms.



Environmental reservoirs: Soil and water

Water

Ubiquitous environmental
source

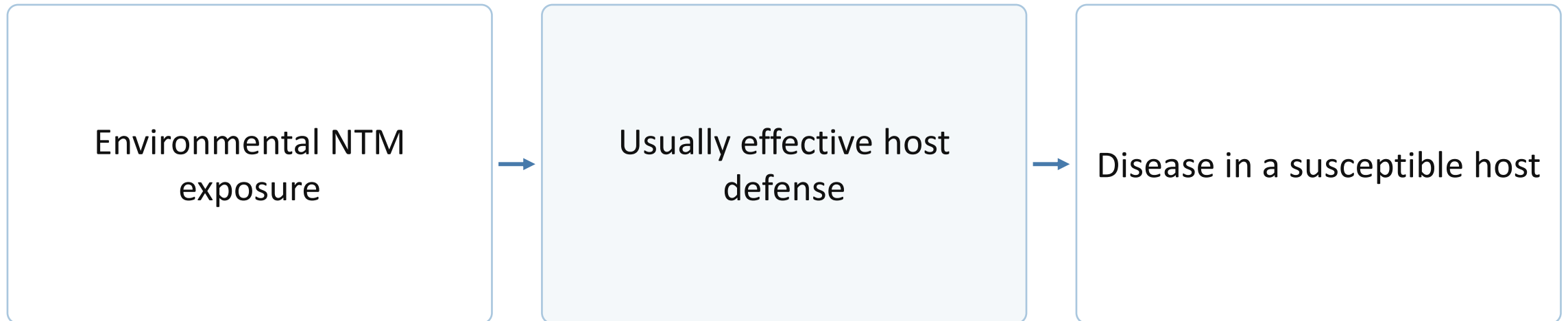
Soil

Ubiquitous environmental
source

Human exposure

Does not automatically equal
clinical disease

Exposure and disease are distinct concepts



The diagram represents susceptibility—not a deterministic sequence.

Person-to-person transmission is uncommon

- NTM usually arise from environmental reservoirs, not ordinary interpersonal spread.
- The source describes little human-to-human transmission.
- Do not import the epidemiologic model of contagious pulmonary tuberculosis.

Cystic fibrosis is a transmission exception

- A small number of person-to-person transmission cases in cystic fibrosis.
- This exception does not overturn the predominantly environmental transmission pattern.
- The source does not specify transmission rates or infection-control protocols.

Four major clinical NTM syndromes

Chronic pulmonary disease

Most frequent presentation

Lymphadenitis

Lymph-node involvement

Cutaneous disease

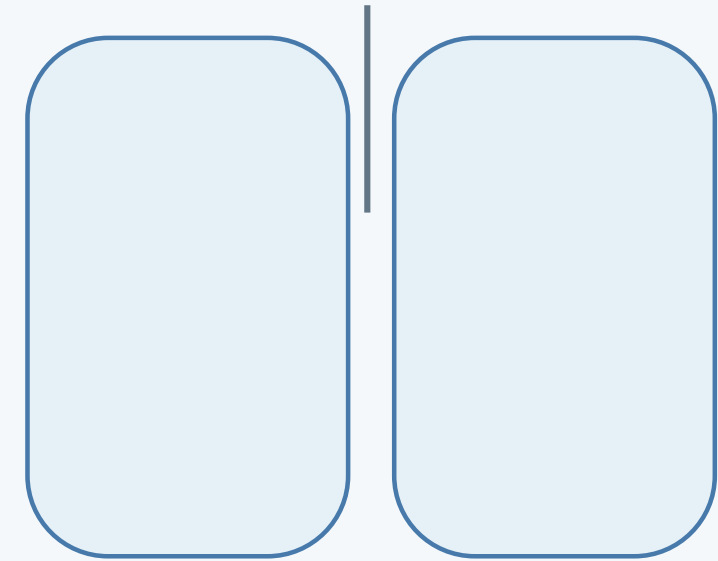
Skin / soft tissue

Disseminated disease

Multiorgan infection

The lung is the predominant disease site

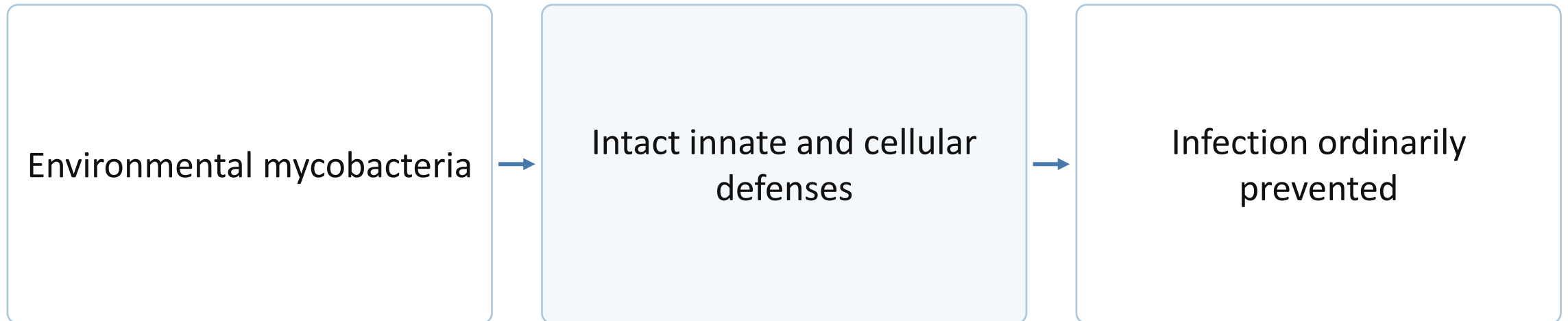
- Chronic pulmonary infection is the commonest clinical presentation.
- Structural lung disorders are prominent predispositions.
- Pulmonary phenotype differs from disseminated MAC in profound T-cell deficiency.



Pulmonary disease predominates

Distribution schematic · not radiologic imaging

Host defense usually prevents NTM infection



The susceptibility spectrum matters more than exposure alone.

Structural lung damage creates susceptibility

Bronchiectasis

Damaged and dilated bronchi

Cystic fibrosis

Abnormal airway secretions

Primary ciliary dyskinesia

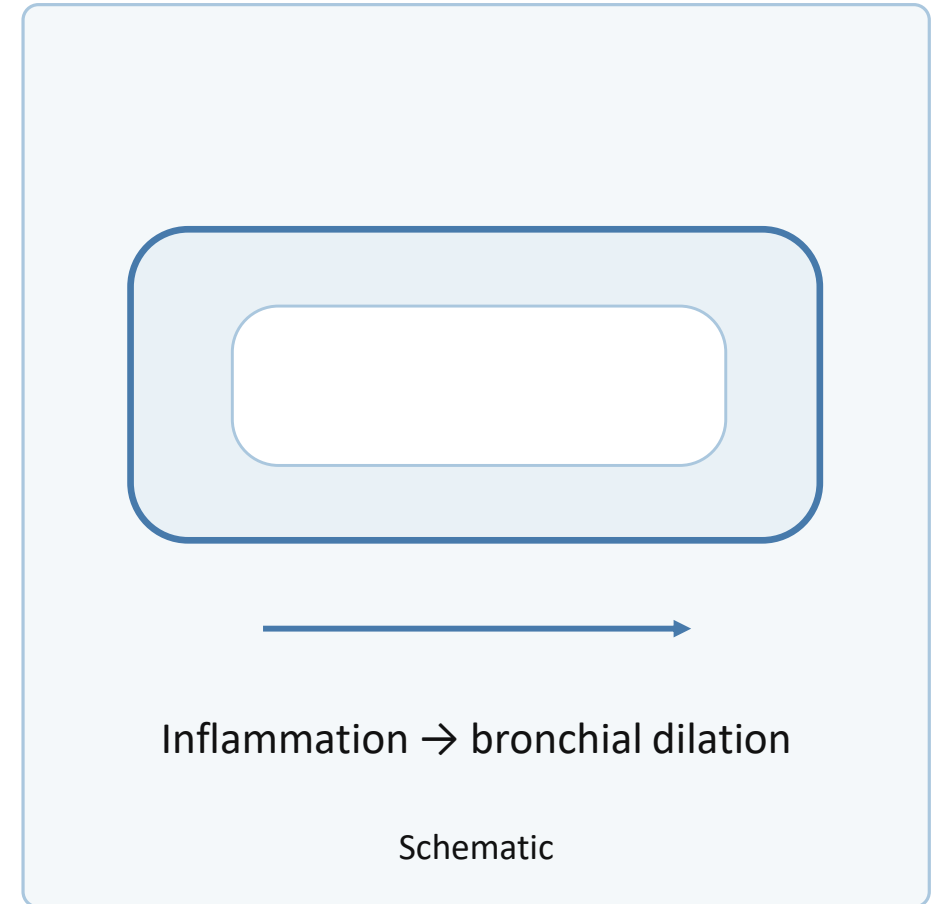
Impaired ciliary clearance

COPD / pneumoconiosis

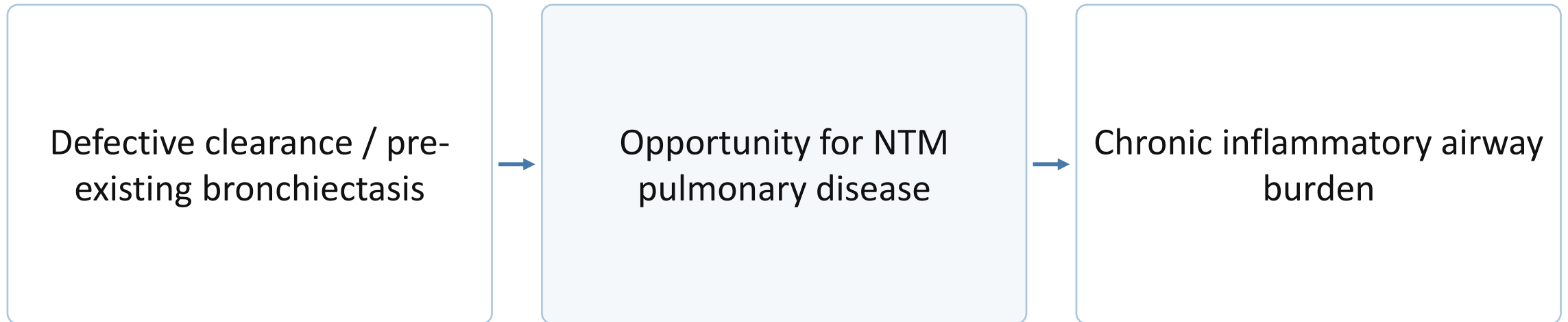
Chronic structural lung injury

Bronchiectasis: Permanent bronchial dilation

- In the Robbins lung chapter, infection and inflammation damage bronchial wall smooth muscle and elastic tissue.
- Defective airway clearance fosters ongoing infection.
- NTM infection is one possible complication in structurally abnormal lungs.



Bronchiectasis and NTM can reinforce lung injury



Conceptual amplification model; Causation in any individual patient requires clinical evidence.

Cystic fibrosis supplies a distinct airway substrate



Robbins also lists NTM among CF-associated opportunistic pulmonary pathogens.

Primary ciliary dyskinesia compromises clearance

- Dysfunctional motile cilia impair mucociliary transport.
- Recurrent infections and bronchiectasis follow the clearance defect.
- This constitutes a structural susceptibility pathway for NTM.



Impaired motile cilia

Schematic

COPD and pneumoconiosis are relevant risk contexts

Predisposing condition	Clinicopathologic framing
Chronic obstructive pulmonary disease	Pre-existing altered lung architecture / function
Pneumoconiosis	Chronic occupational lung injury / structural disease
Practical interpretation	Consider the diseased lung when interpreting NTM isolation

Immune suppression creates another vulnerability axis

HIV infection

T-cell immunodeficiency may be severe

Transplantation

Immunosuppressive state

TNF inhibitor therapy

Altered antimycobacterial host response

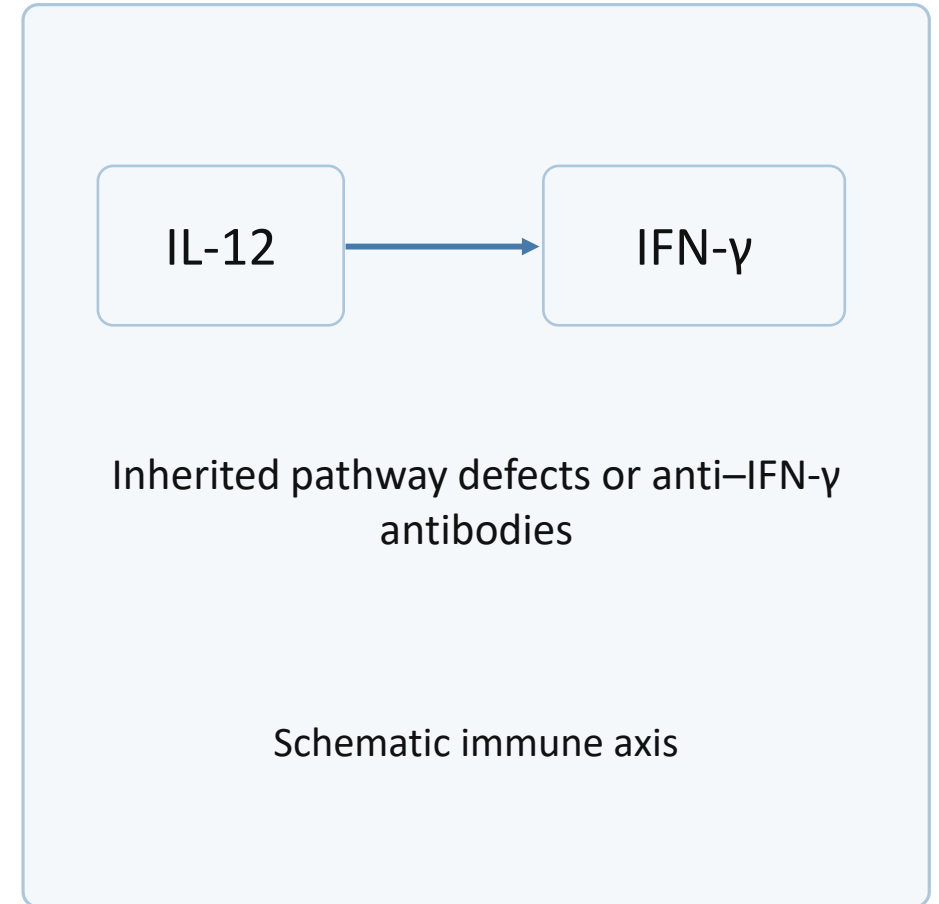
Profound T-cell deficiency changes disease distribution



In this setting, macrophage-rich tissue infection may contain very large numbers of bacilli.

Rare defects implicate IL-12 / IFN- γ immunity

- Inherited defects in the IL-12/IFN- γ pathways.
- Rare anti-IFN- γ autoantibodies are another predisposing condition.
- These features highlight the importance of the cellular immune axis.

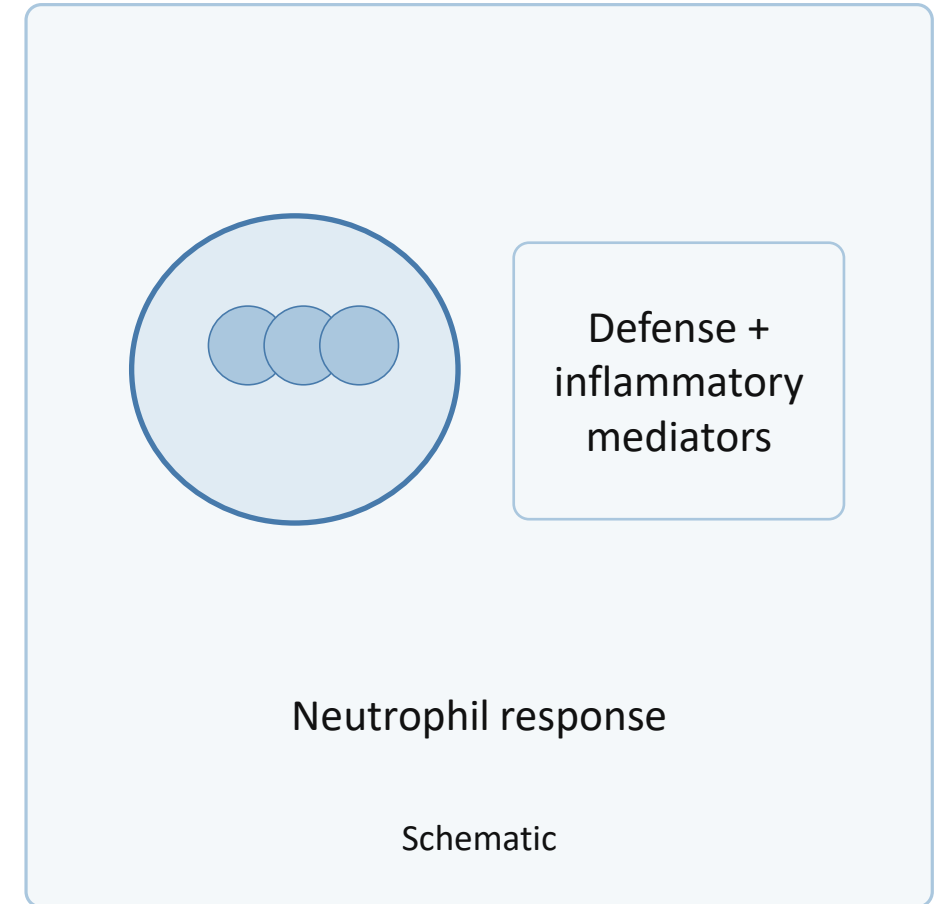


Two broad host routes lead to NTM disease

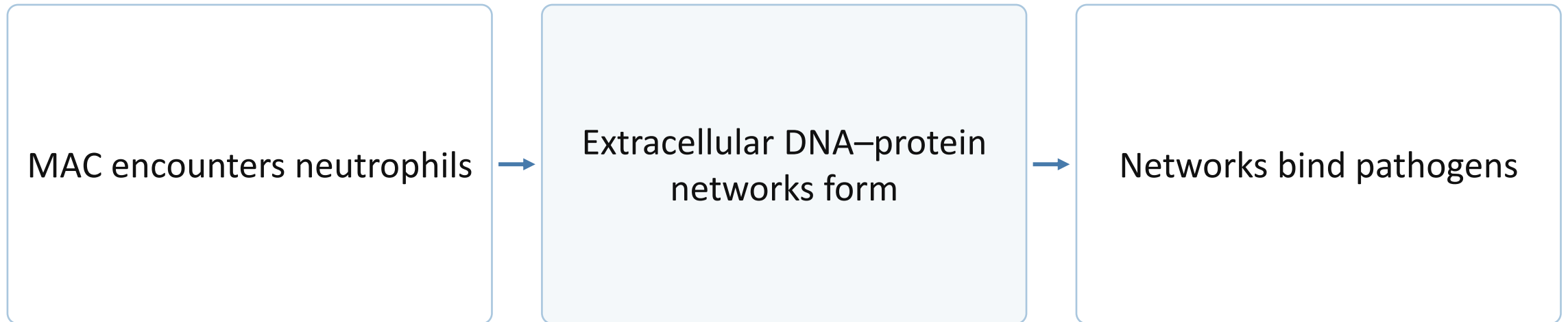
Predominant host vulnerability	Typical disease context
Damaged airways / impaired clearance	Chronic pulmonary infection
Major T-cell immunodeficiency	Disseminated MAC infection
Procedure / injured tissue	Rapidly growing NTM wound infection

Neutrophils participate in antimycobacterial defense

- Neutrophils as critical host-defense cells.
- The same cell population can release inflammatory mediators.
- Inflammation may worsen tissue disease while responding to pathogens.



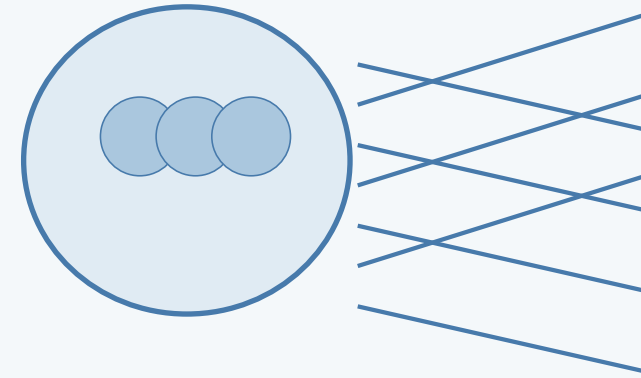
MAC induces neutrophil extracellular traps



NET = neutrophil extracellular trap; A host-defense response.

NETs are extracellular DNA–protein frameworks

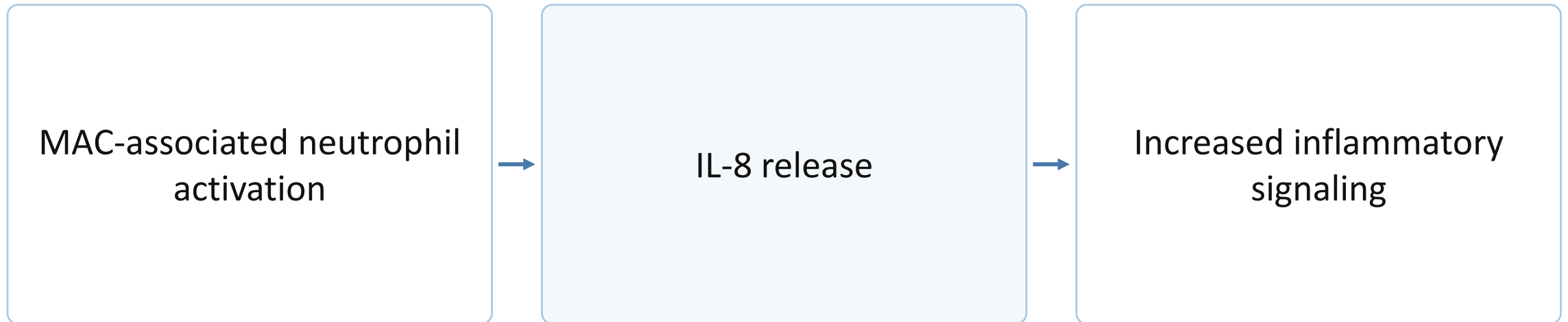
- NETs consist of extracellular strands of DNA and proteins.
- Their role in binding pathogens.
- They are mechanistically distinct from granulomas and from bacilli.



Extracellular DNA–protein network

Schematic

IL-8 release amplifies local inflammatory signaling



The source links IL-8 release to the neutrophil response in NTM lung disease.

Neutrophil metalloproteinases contribute to injury

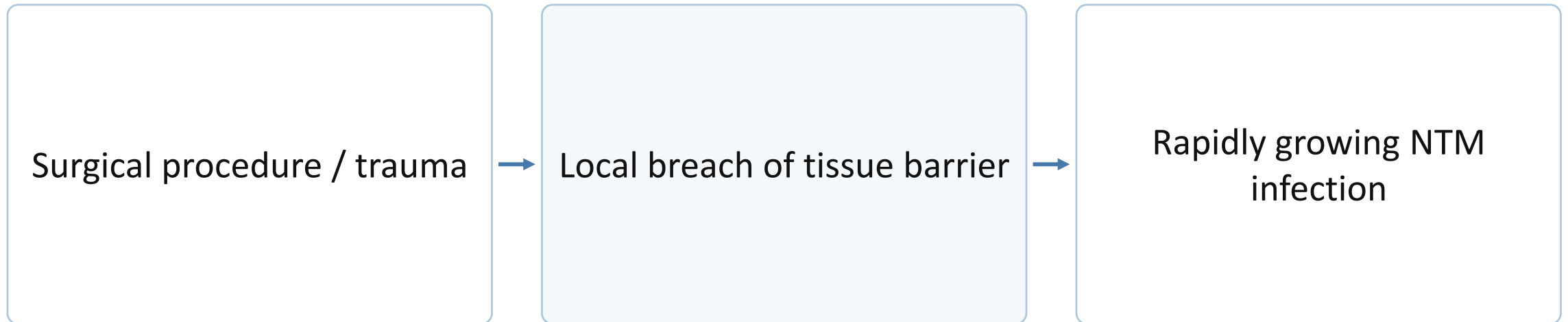


Host-mediated injury accompanies the antimicrobial response.

Neutrophil defense and tissue injury coexist

Host-protective activity	Potential pathologic consequence
NET formation binds pathogens	Extracellular inflammatory material in affected tissue
IL-8 release	Amplified inflammatory signaling
Matrix metalloproteinases	Contribution to destructive airway inflammation

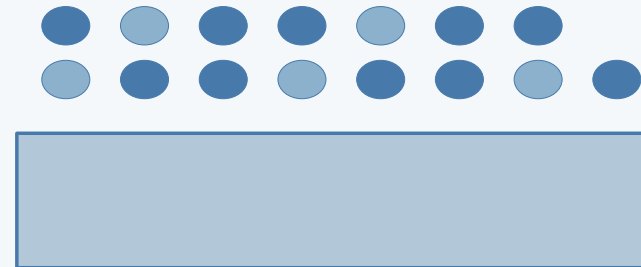
Rapidly growing NTM: Postsurgical or traumatic infection



An association; No particular procedure or species-specific rate is asserted.

Medical-device biofilms provide a source of NTM

- NTM biofilms on medical devices are a documented infection source.
- Surface-associated bacteria create a device-linked infection context.
- Microbiologic evaluation requires attention to the implicated device.



Surface-associated NTM biofilm

Schematic—not device imaging

Biofilm-associated infection is a different pathway

Pulmonary NTM disease	Device-associated NTM infection
Background lung susceptibility	Presence of a colonized material surface
Chronic airway symptoms / radiologic changes	Local or device-linked presentation
Source may be environmental	Biofilm is a documented infection source

Disseminated MAC: Systemic clinical phenotype

- Marked T-cell immunodeficiency predisposes to widespread dissemination.
- MAC organisms proliferate in several organs.
- Patients commonly develop fever, drenching night sweats and weight loss.

Disseminated MAC affects multiple organ systems

Lungs

Extensive organism proliferation

Gastrointestinal tract

Extensive organism proliferation

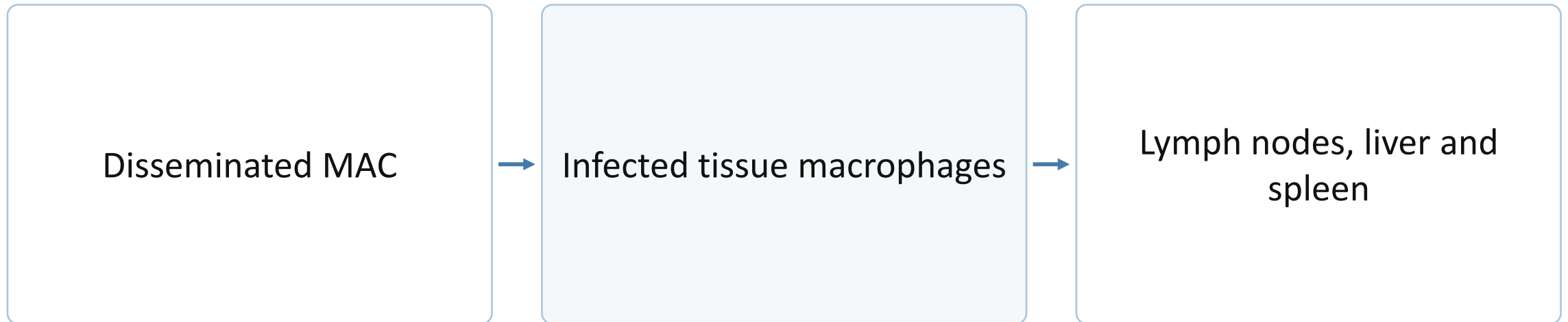
Lymph nodes

Macrophage-system involvement

Liver / spleen

Macrophage-system involvement

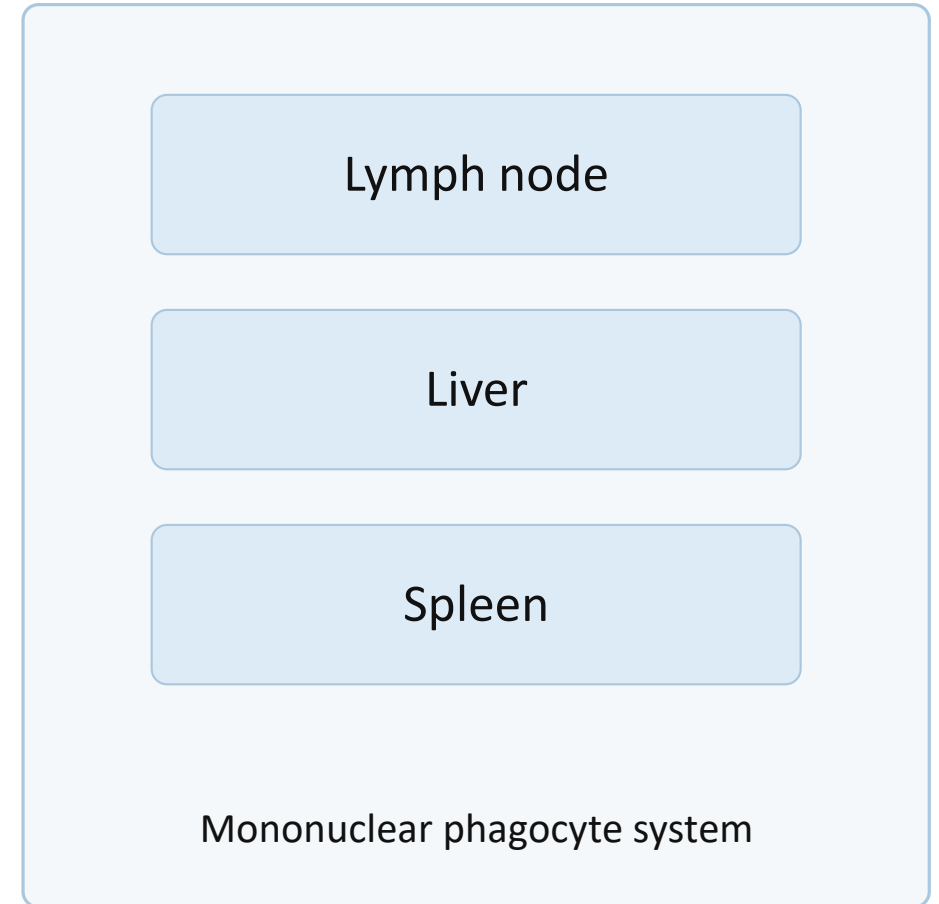
Dissemination targets the mononuclear phagocyte system



Multiorgan macrophage infiltration underlies characteristic pathology.

Macrophage accumulation enlarges affected organs

- Involved lymph nodes can enlarge.
- Liver and spleen enlargement may accompany dissemination.
- The organ changes are linked to extensive macrophage involvement.



Affected organs may show yellowish pigmentation

- Possible yellowish discoloration of involved organs.
- The cause is the large burden of bacteria within swollen macrophages.
- Color alone is neither diagnostic nor sufficient for species identification.

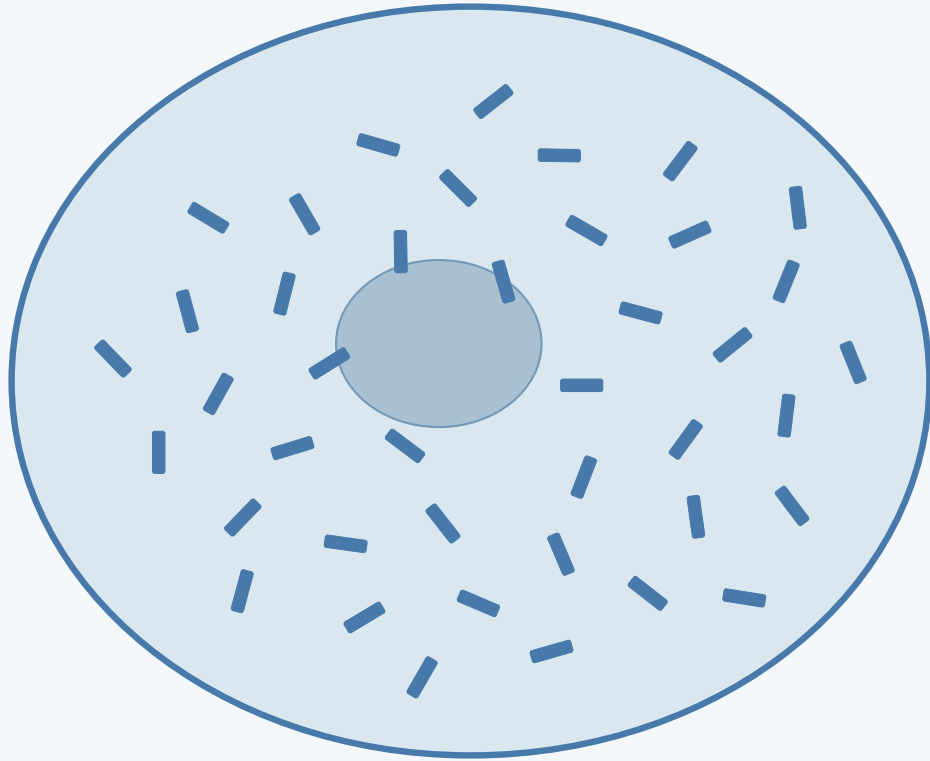
Lymph node

Liver

Spleen

Possible yellowish discoloration

Macrophages may be packed with acid-fast bacilli



Macrophage containing numerous acid-fast organisms

Schematic morphology—not a histology image

- Hallmark described for MAC in patients with HIV.
- Abundant acid-fast bacilli lie within macrophages.

Granulomas may be sparse in severe MAC disease

Feature	Robbins description in HIV-associated MAC
Organism burden	Often abundant within macrophages
Granulomas	Rare
Lymphocytes	Rare
Tissue destruction	Rare

Heavy bacillary burden need not mean destructive lesions

- In advanced immunodeficiency, heavy intracellular infection may dominate histology.
- Granulomas, lymphocytes and tissue destruction can be minimal.
- Interpret bacterial burden together with the host's immune state.

T-cell competence helps explain morphology

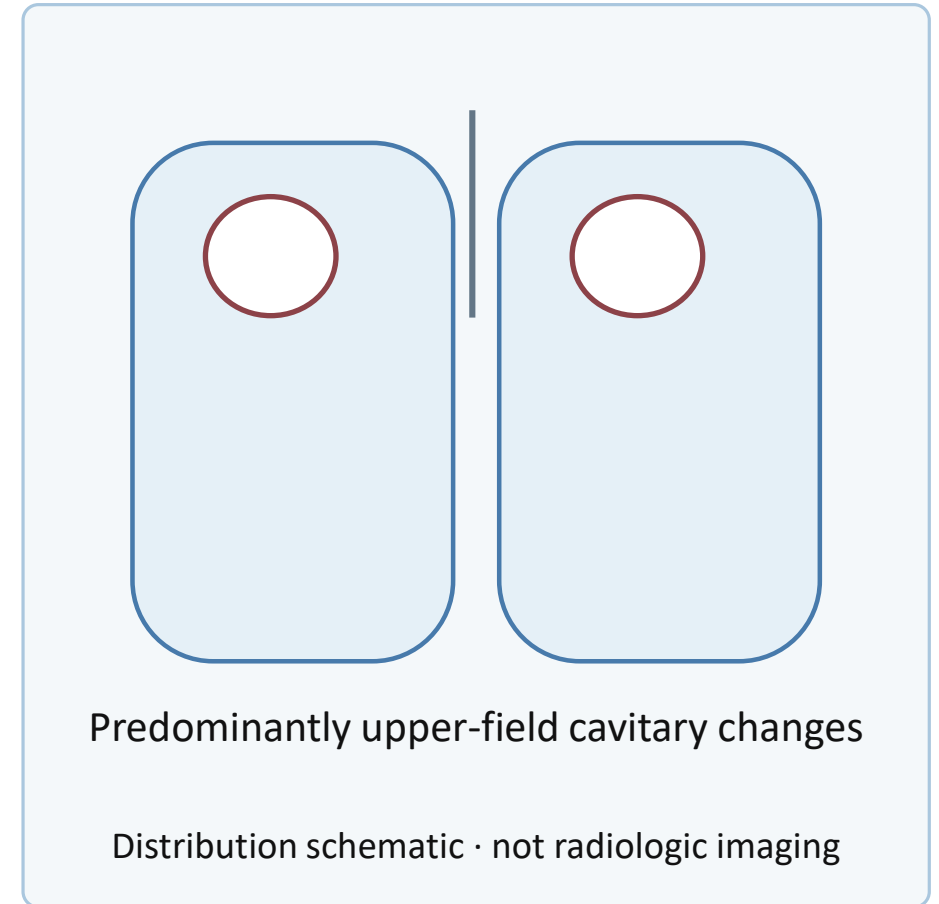
Severe immune deficiency: disseminated MAC	T-cell-mediated response: TB context
Organism-laden macrophages may predominate	Granulomatous response is characteristic
Granulomas can be rare	Caseating or noncaseating granulomas occur
NTM-specific source observation	Contrast drawn from neighboring tuberculosis section

Pulmonary MAC presents with a productive cough

- Without HIV or another severe immunodeficiency, MAC mainly involves the lung.
- The illness may cause a productive cough.
- Fever and weight loss occur in some patients.

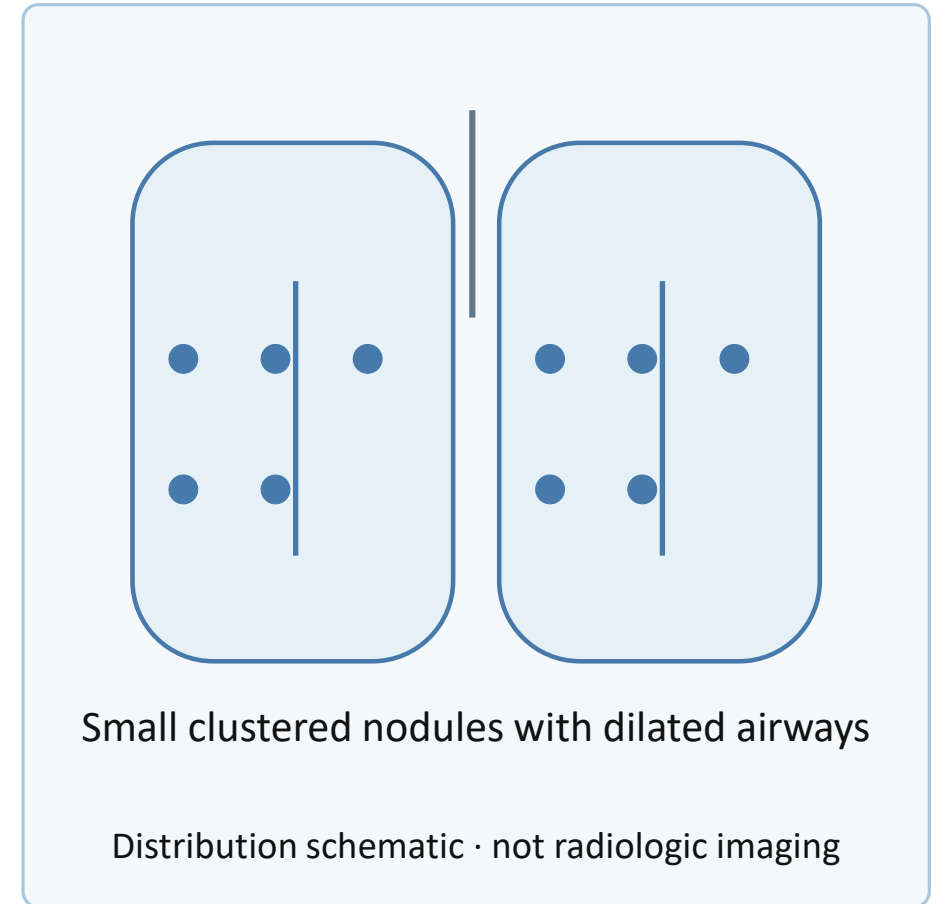
Pulmonary imaging may show upper-lobe fibrocavitary disease

- Fibrocavitary lesions as one pulmonary pattern.
- These are described primarily in the upper lobes.
- The schematic conveys distribution, not CT or radiographic evidence.



An alternative pattern is nodular bronchiectasis

- Bronchiectasis can coexist with multiple small pulmonary nodules.
- Multifocal clusters of small nodules.
- This contrasts with the predominantly upper-lobe fibrocavitary pattern.



Two imaging phenotypes support pulmonary recognition

Fibrocavitary phenotype	Nodular-bronchiectatic phenotype
Fibrocavitary lesions	Bronchiectasis
Predominantly upper-lobe distribution	Multifocal clusters of small nodules
One possible radiographic pattern	Another possible radiographic pattern

Lymphadenitis is a recognized NTM manifestation

- NTM disease is not restricted to the lung.
- Lymphadenitis is one of the four clinical presentations listed by Robbins.
- The supplied NTM section does not provide node-specific histologic criteria.

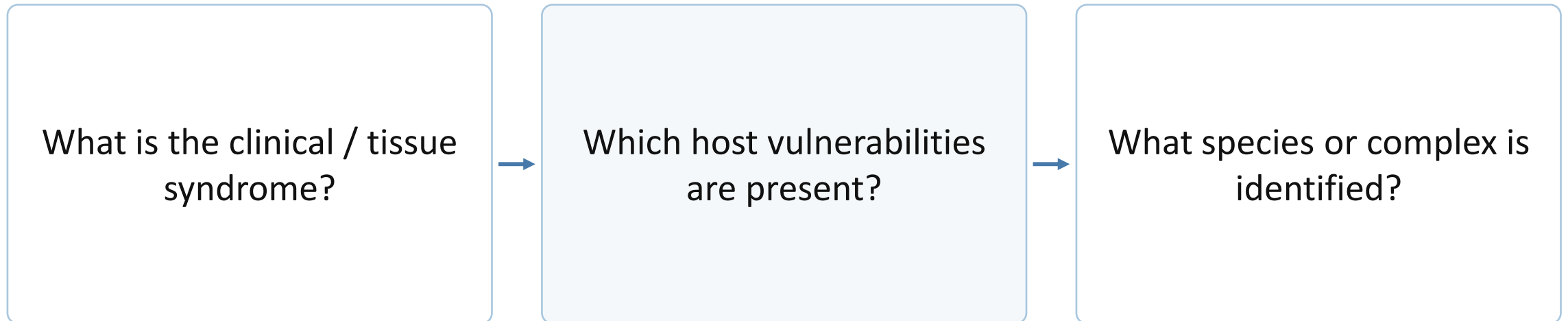
Cutaneous disease is part of the NTM spectrum

- NTM can manifest as cutaneous infection.
- Rapidly growing NTM may be associated with postsurgical or traumatic infection.
- The source does not distinguish specific skin morphologies by species.

Organ pattern and host context should be read together

Presentation	Context highlighted in Robbins
Chronic pulmonary disease	Structural lung damage and impaired clearance
Disseminated MAC	Marked T-cell immunodeficiency
Skin / procedure-related infection	Postoperative or posttraumatic infection with rapid growers
Device-linked infection	Biofilm on a medical device

An NTM evaluation has three distinct questions



Interpretation integrates phenotype, susceptibility and microbiology.

Acid-fast morphology does not assign a species

- The acid-fast cell-wall property is shared across mycobacteria.
- An acid-fast stain cannot, by itself, assign MAC vs *M. Abscessus* vs *M. Kansasii*.
- Molecular differentiation has particular value within MAC.

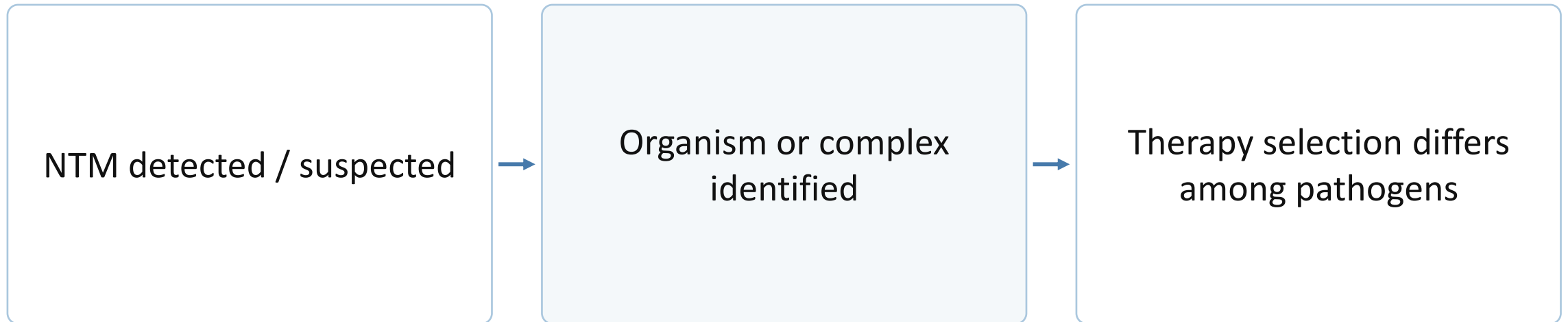


Mycobacterial bacilli



Schematic · not a stained specimen

Microbiologic speciation is clinically consequential



Robbins stresses species identification; Regimen details lie outside the supplied source.

A diagnosis needs more than pathogen vocabulary

Finding	What it supports—and does not establish
Acid-fast organisms	Mycobacterial morphology; not a species
Abnormal chest imaging	Pulmonary phenotype; not organism identity
MAC species identified	Microbiologic identity; clinical context still matters
Macrophage-rich tissue with AFB	Typical in advanced HIV-associated MAC; assess host

Case: Chronic cough in a damaged airway

Clinical scenario

A person with established bronchiectasis develops persistent productive cough. Imaging shows small clustered nodules and bronchiectatic airways.

Which NTM pattern is most relevant?

A nodular-bronchiectatic pulmonary pattern. Correlate with microbiologic identification; The vignette alone cannot prove NTM disease.

Case: Advanced HIV and systemic symptoms

Clinical scenario

A patient with profound T-cell immunodeficiency develops fever, drenching night sweats, weight loss and hepatosplenomegaly.

What organism–morphology pairing fits?

Disseminated MAC; Tissues may contain swollen macrophages packed with acid-fast bacilli, often with few granulomas.

Case: Infection following an invasive procedure

Clinical scenario

A patient develops a persistent local soft-tissue infection after a surgical procedure. Organism workup suggests a nontuberculous mycobacterium.

Which NTM group deserves consideration?

Rapidly growing NTM, given the source association with postsurgical and posttraumatic infection. Definitive identification is required.

Case: Infection around a medical device

Clinical scenario

An NTM-associated infection is investigated in a patient with an implanted device; The device surface is suspected as a reservoir.

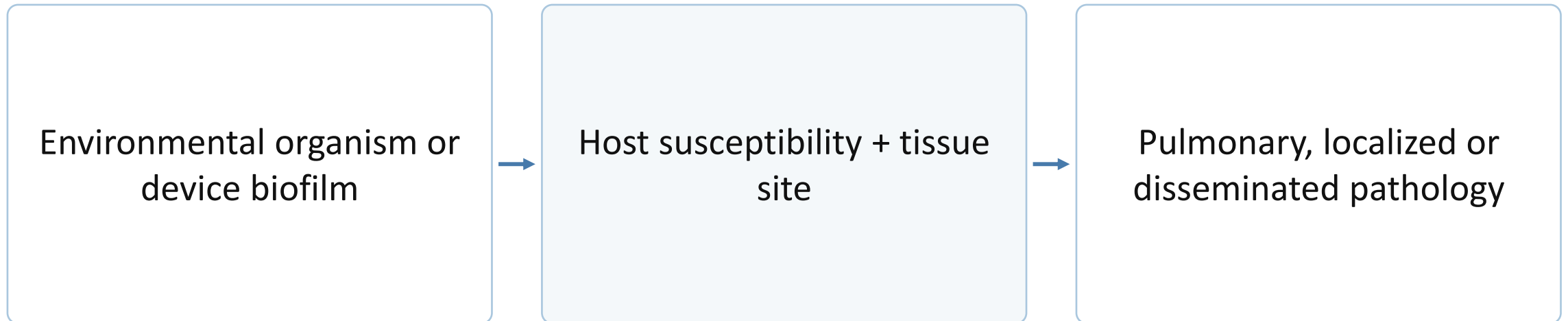
Which biological process explains the source?

Biofilm development on medical devices is a well-documented source of NTM infection.

Avoid four common interpretive errors

- Do not equate all acid-fast organisms with *M. Tuberculosis*.
- Do not treat MAC members as universally distinguishable by older biochemical methods.
- Do not expect conspicuous granulomas in profoundly immunodeficient MAC disease.
- Do not assume that NTM typically spreads between people.

Integrating NTM pathobiology



Species identity modifies clinical interpretation and treatment selection.

Five points for clinicopathologic practice

- MAC, M. Abscessus complex and M. Kansasii are leading NTM pathogens.
- Environmental acquisition predominates; Interpersonal spread is uncommon.
- Damaged lungs and impaired cellular immunity produce different syndromes.
- MAC can produce massive macrophage-associated AFB in advanced HIV.
- Species-level identification is necessary because treatment differs.

Selected references

Robbins, Cotran & Kumar: Pathologic Basis of Disease (11th edition).

Core textbook section: “Nontuberculous Mycobacterial Infections.”

Related sections used for context: “Mycobacterial Infections” and “Bronchiectasis.”

Additional pathophysiology context: cystic fibrosis pulmonary disease.

Complete chapter, page and slide-level source mapping is provided in the presenter notes.