

Lung transplantation

Indications • infection • rejection • pathology

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Learning objectives

- Identify major indications and understand the choice of single versus bilateral transplantation.
- Differentiate infection from rejection using timing, clinical presentation, and pathology.
- Recognize the morphological patterns of acute and chronic rejection.
- Explain why bronchiolitis obliterans causes irreversible allograft dysfunction.

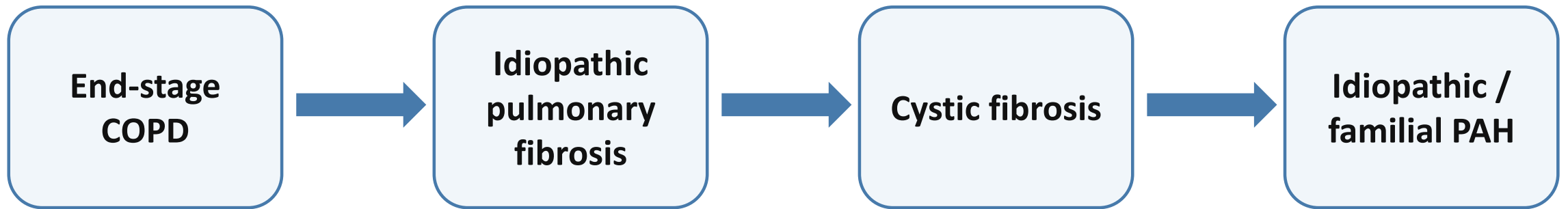
Lung transplantation restores gas-exchange capacity

- Transplantation replaces one or both severely diseased recipient lungs with donor allograft tissue.
- It is considered for terminal, nonneoplastic pulmonary disease.
- The graft is functionally valuable but immunologically nonself: Rejection and infection dominate long-term care.

Eligibility depends on more than lung severity

- The underlying pulmonary condition should be advanced and nonneoplastic.
- Other serious illness may preclude the lifelong immunosuppression that transplantation requires.
- Recipient assessment therefore balances pulmonary benefit against systemic treatment burden.

Four common transplant indications



Indications listed; Not a ranked frequency comparison.

End-stage COPD: Loss of functional reserve

- Severe COPD is a common indication for lung transplantation in the source.
- Obstructive physiology and destructive parenchymal disease limit ventilatory reserve.
- The transplant decision concerns the overall severity of established lung disease, not an isolated histologic sign.

Idiopathic pulmonary fibrosis: Progressive restriction

- Idiopathic pulmonary fibrosis is among the major transplant indications.
- Fibrosis progressively alters lung architecture and compromises respiratory function.
- Transplantation addresses the organ-level consequence rather than reversing fibrosis in the native lung.

Cystic fibrosis: Structural disease and infection

- Cystic fibrosis is a major indication in patients with terminal pulmonary disease.
- Chronic suppurative airway disease creates an infectious reservoir in the recipient lungs.
- This has a direct surgical implication: Both infected lungs require replacement.

Pulmonary arterial hypertension as an indication

- Idiopathic or familial pulmonary arterial hypertension is explicitly listed as an indication.
- The primary physiological burden is pulmonary vascular disease.
- The correct operation depends on overall cardiopulmonary assessment; The source does not provide a selection algorithm.

Single versus bilateral transplantation

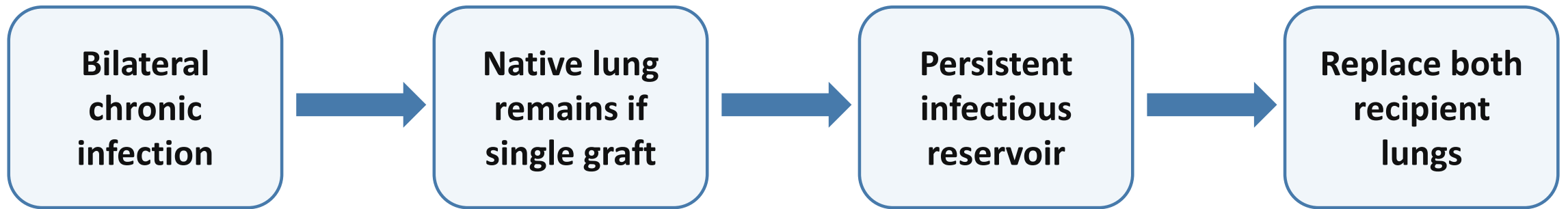
Single lung

- One donor may benefit two different recipients.
- A strategy with a donor-organ allocation advantage.

Bilateral lungs

- Associated with better outcomes in the source.
- Needed when the native lungs contain bilateral chronic infection.

Why bilateral infection changes the operation



Illustrative rationale from the cystic fibrosis / bronchiectasis examples.

The donor-allocation trade-off

- Single-lung transplantation can use lungs from one donor to treat two recipients.
- Bilateral transplantation provides both donor lungs to one recipient.
- The textbook associates bilateral transplantation with superior recipient outcomes, but does not quantify the effect.

Early surgical and graft complications

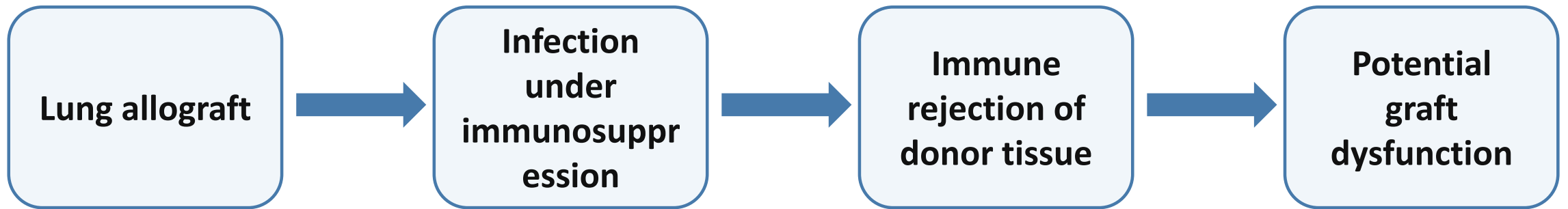
Anastomotic / vascular

- Anastomotic dehiscence
- Vascular thrombosis

Immediate graft dysfunction

- Primary graft dysfunction
- The source notes improvement with surgical and preservation techniques.

Two major threats to the lung allograft



Infection and rejection may produce overlapping symptoms; Neither can be inferred from symptoms alone.

The immunosuppression paradox

Desired effect

- Suppress alloreactive lymphocytes.
- Reduce tissue-damaging graft immune responses.

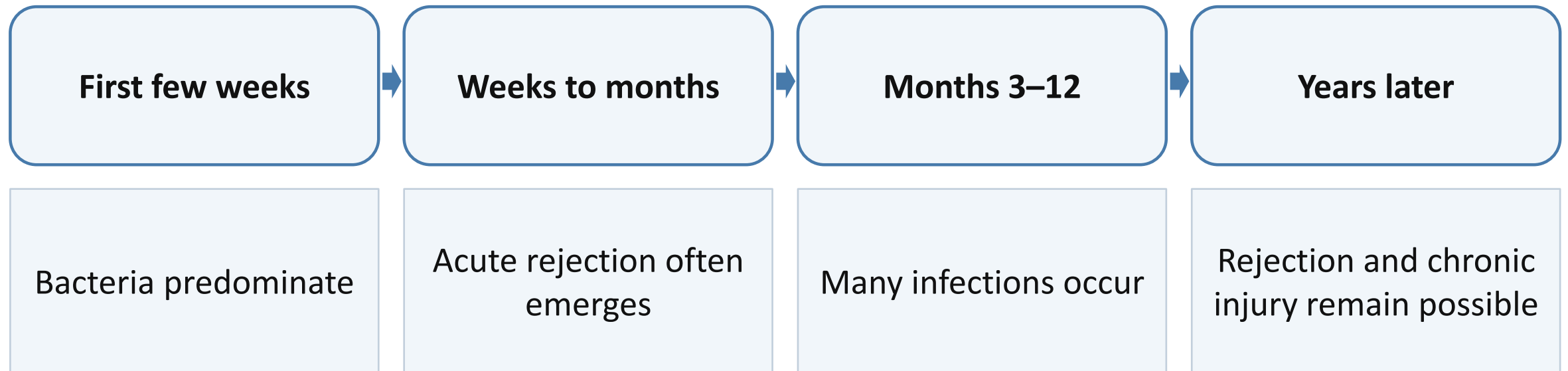
Consequent vulnerability

- Reduced defenses against pathogens.
- Opportunistic pulmonary infections become important.

Infections resemble those of other immunocompromised hosts

- Transplant immunosuppression expands the range of potential pulmonary pathogens.
- Usual respiratory pathogens remain important alongside opportunistic agents.
- More than one infectious organism may contribute to an infiltrate.

Infection risk is time-dependent



Approximate textbook periods; Patterns overlap and are not exclusive.

Early infections: Bacterial predominance

- Bacterial infections are the most common infectious events in the first weeks after transplantation.
- This timing is a useful prior probability, not a microbiologic diagnosis.
- Clinical and imaging manifestations still require evaluation for alternative causes.

Most infections arise during months 3–12

- Most post-transplant infections in the third through twelfth months.
- Both conventional and opportunistic organisms remain relevant.
- Timing should guide the differential without excluding infection outside this window.

Bacterial spectrum in immunocompromised lungs

Examples listed in the parent section

- *Pseudomonas aeruginosa*
- *Mycobacterium* species

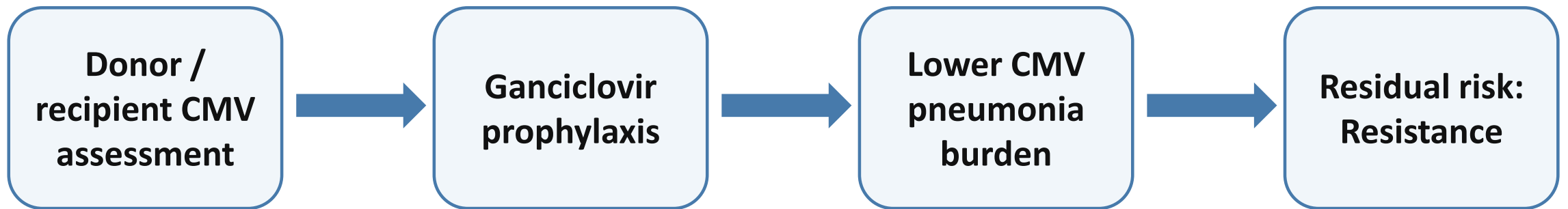
Additional examples

- *Legionella pneumophila*
- *Listeria monocytogenes*

CMV pneumonia after transplantation

- Cytomegalovirus is an opportunistic viral pneumonia relevant to transplant recipients.
- Lower frequency and severity with antiviral prophylaxis and donor–recipient CMV-status matching.
- Antiviral-resistant CMV strains are nevertheless described.

CMV prevention is not elimination

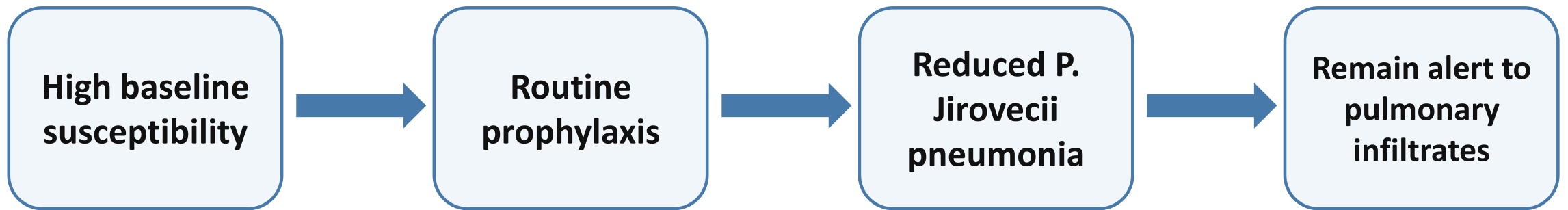


Source describes a reduction in frequency/severity, not complete prevention.

Pneumocystis jirovecii pneumonia

- P. Jirovecii is a major opportunistic pneumonia pathogen in immunocompromised hosts.
- Post-lung-transplant pneumonia due to this organism as rare with routine prophylaxis.
- The usual prophylactic agent named is trimethoprim–sulfamethoxazole.

The prophylaxis–incidence relationship



Qualitative conceptual relationship; No incidence values are implied.

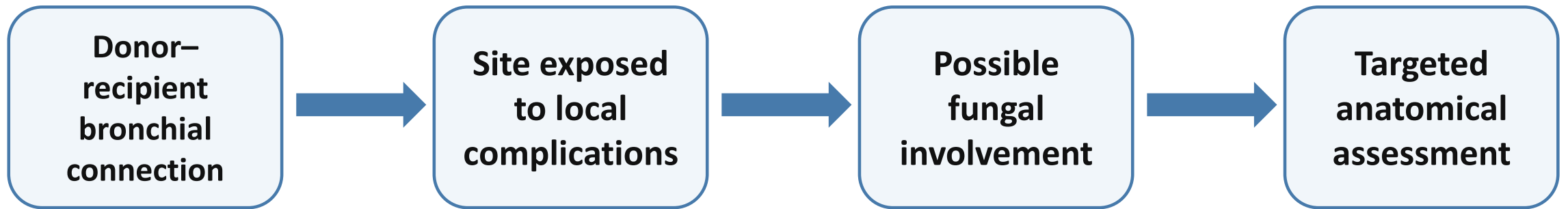
Fungal disease: Aspergillus

- Aspergillus species are among the major fungi implicated in post-transplant lung infection.
- Infection can involve the lung parenchyma and/or bronchial anastomotic site.
- The affected site matters when correlating imaging and bronchoscopic findings.

Fungal disease: Candida

- Candida species are also listed among fungal pathogens after lung transplantation.
- Potential sites include the bronchial anastomosis and/or transplanted lung.
- The excerpt does not provide microbiologic diagnostic criteria; Organism recovery alone should not be overinterpreted.

The bronchial anastomosis is a distinct site



Schematic clinical-anatomic reasoning; Not a published management protocol.

Focal versus diffuse pulmonary infiltrates

Pattern	Textbook examples	Interpretive caution
Diffuse	CMV; P. jirovecii; drug reaction	Not specific for infection
Focal	Gram-negative bacteria; S. aureus; fungi	Not exclusive to infection
Either pattern	Malignancy listed in the differential	Correlate clinically

Noninfectious infiltrates still matter

- In immunocompromised hosts, drug reactions and malignant involvement can produce lung infiltrates.
- In a lung allograft, rejection adds a critical noninfectious cause.
- Radiology can identify an infiltrate without defining its pathogenesis.

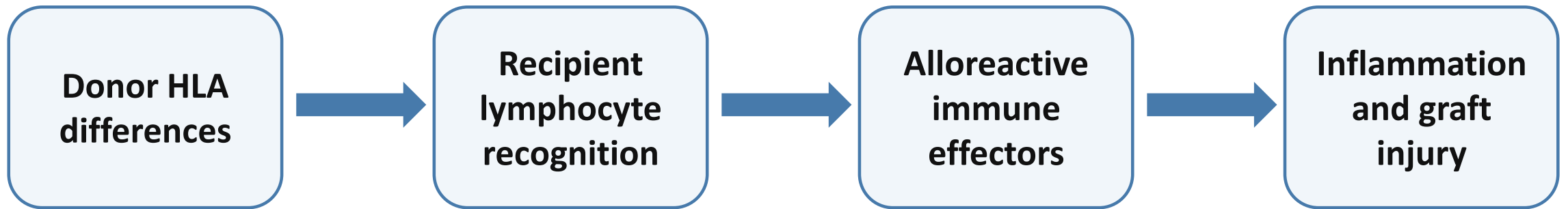
Mixed processes are possible

- The parent section notes that more than one infectious agent can be present.
- Infection and rejection also have overlapping clinical presentations.
- Avoid interpreting a single clinical clue as proof of only one process.

Acute rejection: Clinical syndrome

- Acute rejection commonly causes fever, dyspnea, cough, and radiologic infiltrates.
- The same findings can arise from pulmonary infection.
- Transbronchial biopsy to help establish the diagnosis.

Rejection begins with alloantigen recognition

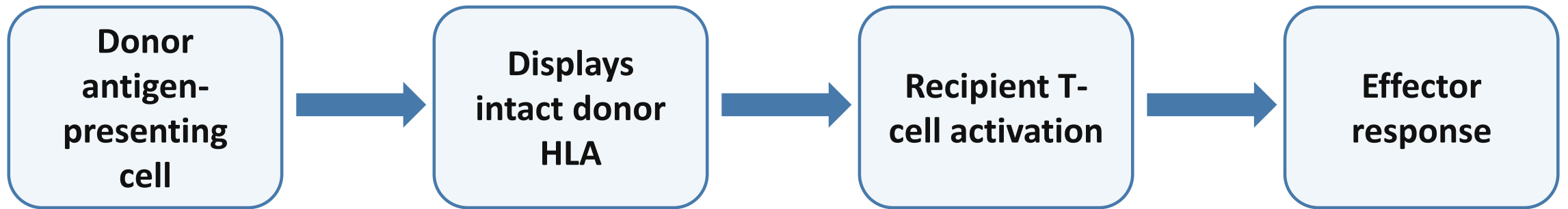


Schematic of general transplant immunobiology applied to the lung.

HLA disparity explains alloimmunity

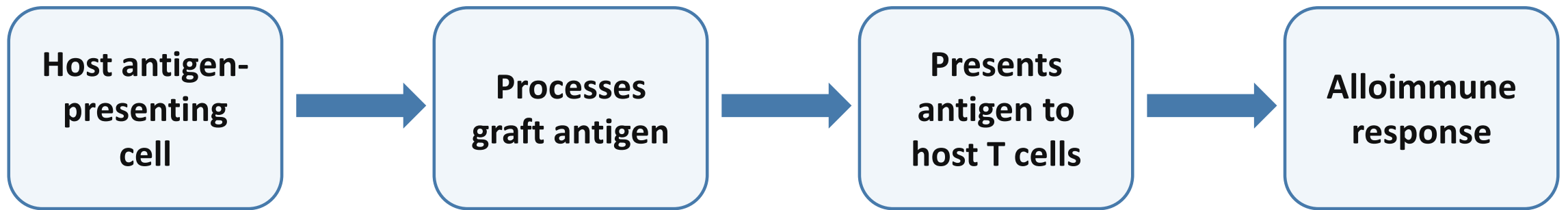
- Highly polymorphic HLA alleles differ between most donor–recipient pairs.
- Recipient T cells can interpret donor alloantigens as foreign.
- The alloreactive repertoire is large; Immunosuppression is required for graft survival.

Direct alloantigen presentation



Source describes direct presentation as particularly important in acute CTL-mediated rejection.

Indirect alloantigen presentation



Source discusses a potentially greater role of this route in chronic rejection.

Two T-cell effector arms

CD8+ T cells

- Develop into cytotoxic T lymphocytes.
- Can directly injure graft cells.

CD4+ T cells

- Differentiate into cytokine-producing effectors.
- Recruit and activate inflammatory responses.

B cells and alloantibodies

- B lymphocytes can recognize donor HLA and other polymorphic antigens.
- T-cell help supports generation of anti-donor antibodies.
- The general transplant-immunology section identifies both cellular and humoral rejection mechanisms.

Immunosuppression targets alloimmune pathways

Drug class / agent	Textbook action	Pathologic rationale
Glucocorticoids	Reduce inflammation	Limit graft-damaging inflammation
Mycophenolate mofetil	Inhibits lymphocyte proliferation	Reduce effector expansion
Tacrolimus	Calcineurin inhibition	Reduce T-cell activation

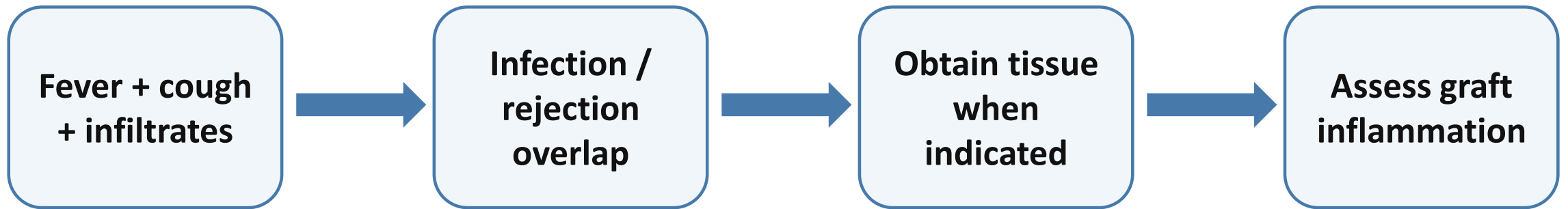
Acute rejection is not limited to early months

- Lung acute rejection is most commonly seen weeks to months after transplantation.
- It may present years after surgery, particularly if immunosuppression is reduced.
- Time from transplantation therefore modifies—but does not eliminate—the diagnosis.

Clinical overlap: Rejection versus infection

Finding	Acute rejection	Infection
Fever	May occur	May occur
Cough / dyspnea	May occur	May occur
Pulmonary infiltrates	May occur	May occur
Discriminating test in source	Transbronchial biopsy often used	Etiologic assessment needed

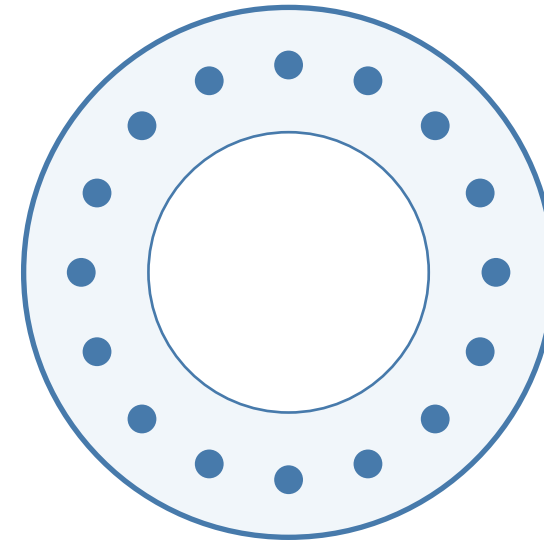
Why biopsy becomes important



A teaching workflow based on source rationale; Local clinical protocols may differ.

Acute rejection: Perivascular inflammation

- Mononuclear inflammatory cells aggregate around small blood vessels.
- The inflammatory infiltrate is a principal acute rejection pattern.

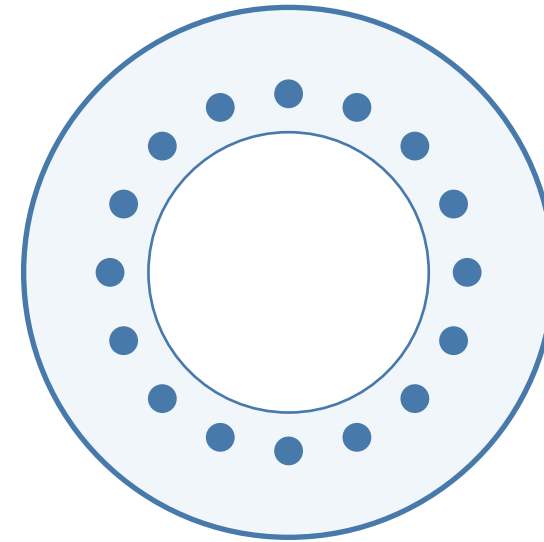


Schematic inflammatory cuff

Schematic — not a histologic micrograph.

Acute rejection: Airway submucosal inflammation

- Inflammation can be located in the submucosa of small airways.
- Perivascular and airway-centered patterns may coexist.



Schematic inflammatory cuff

Schematic — not a histologic micrograph.

Cell composition in acute rejection

Predominant

- Lymphocytes
- Plasma cells

Less numerous

- Neutrophils
- Eosinophils

Morphology is a pattern, not a symptom label

- Acute rejection is defined by tissue inflammatory patterns in a compatible setting.
- A patient's fever or infiltrate is not sufficient to infer perivascular lymphocytes.
- Tissue findings should be interpreted with infection assessment and clinical context.

What a transbronchial biopsy can demonstrate

- Inflammatory cuffs around sampled small vessels.
- Small-airway submucosal inflammatory infiltrates, if the airway is represented.
- A limited sample must be interpreted with awareness of lesion distribution.

Acute cellular airway inflammation and treatment

- Acute cellular airway rejection as generally responsive to therapy.
- Airway inflammation is considered a possible antecedent to later fibrotic obliteration.
- Response in the acute phase contrasts with the poor reversibility of established obliteration.

Chronic rejection: Progressive graft injury

- Chronic rejection is a major long-term complication of lung transplantation.
- It is associated with cough, dyspnea, and irreversible loss of lung function.
- The most characteristic pathologic lesion is bronchiolitis obliterans.

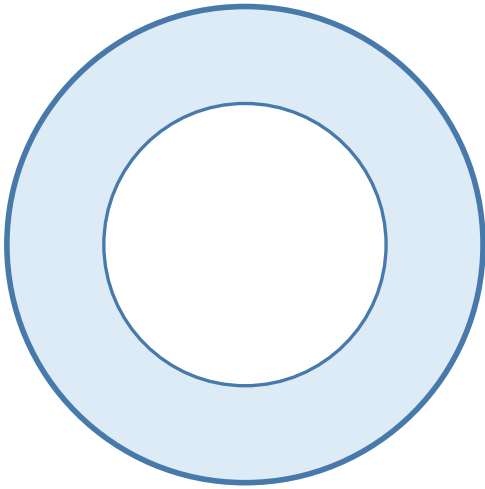
Long-term burden of chronic rejection

- The Robbins text reports significant chronic rejection in at least half of patients at 3–5 years.
- This is the textbook's reported estimate, not a newly calculated contemporary registry rate.
- Functional surveillance and recognition of progressive obstruction are therefore important.

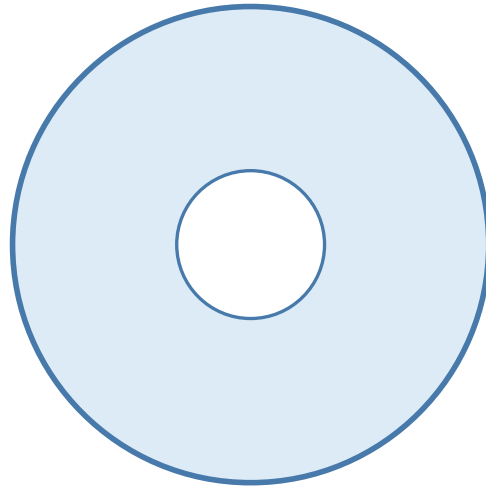
Bronchiolitis obliterans: Core lesion

- The small-airway lumen is narrowed or completely occluded by fibrosis.
- Active inflammation may be present or absent.
- Fibrotic remodeling—not merely transient inflammation—explains persistent dysfunction.

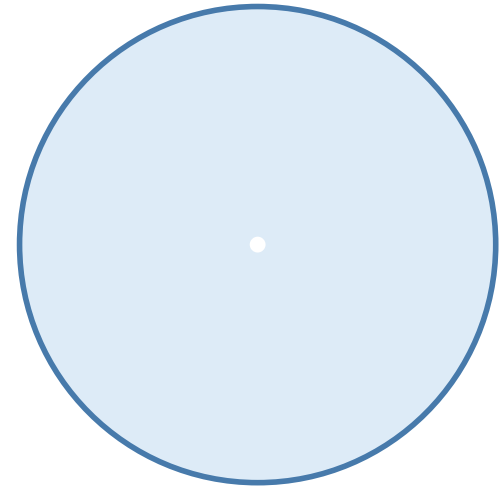
Normal airway to luminal obliteration



Patent lumen

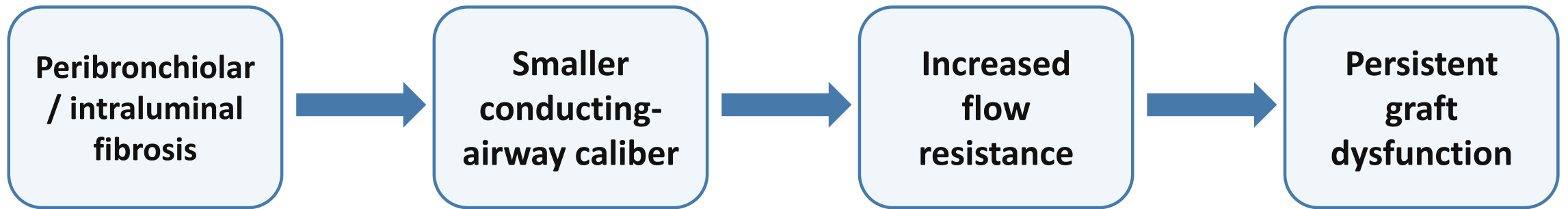


Partially narrowed lumen



Fibrotic occlusion

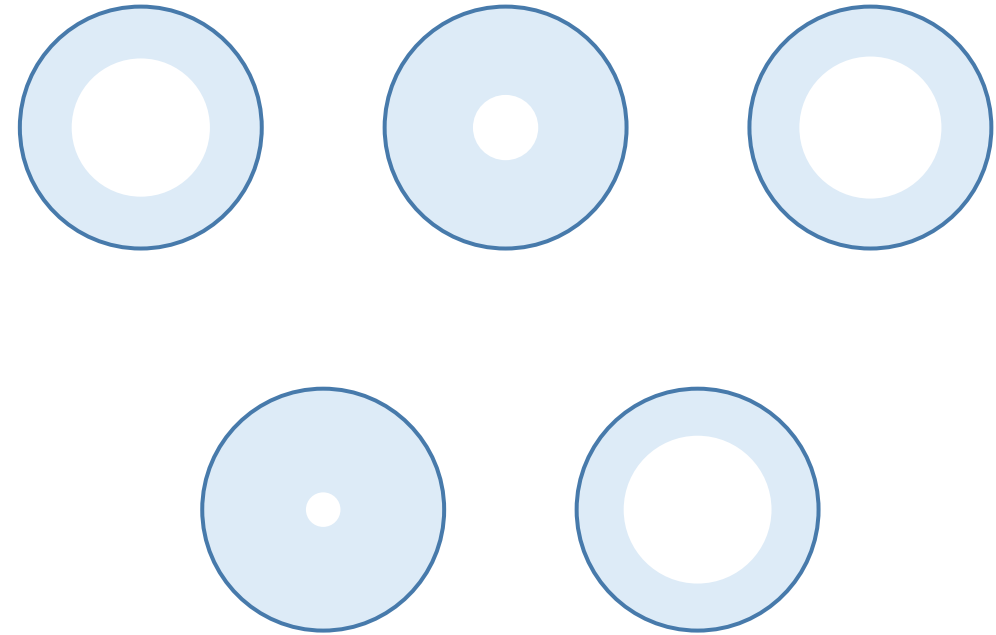
Why the fibrotic bronchiole obstructs airflow



Physiologic interpretation of the Robbins morphologic description.

Bronchiolitis obliterans is patchy

- Affected bronchioles may be interspersed with relatively preserved airways.
- A transbronchial sample may miss the diagnostic lesion.



Variable airway narrowing across one conceptual sample

Sampling schematic, not observed tissue or a sensitivity estimate.

Consequences of longstanding chronic rejection

Small airways

- Bronchiolitis obliterans.
- Patchy fibrous luminal occlusion.

Broader architecture

- Bronchiectasis may develop.
- Pulmonary fibrosis may develop.

Chronic rejection: Clinical–pathologic alignment

Clinical finding	Tissue correlate	Reasoning
Cough / dyspnea	Chronic airway and parenchymal damage	Reduced ventilatory function
Irreversible functional loss	Fibrotic small-airway occlusion	Fixed structural lesion
Biopsy may miss lesion	Patchy bronchiolitis obliterans	Sampling limitation

Chronic fibrosis is difficult to reverse

- Established bronchiolitis obliterans cannot be reversed.
- Progression may sometimes be slowed or halted for a period.
- This underlines the distinction between controlling inflammation and removing a mature fibrotic lesion.

Acute and chronic rejection: Pathology

Feature	Acute rejection	Chronic rejection
Dominant change	Cellular inflammatory infiltrates	Fibrotic narrowing of bronchioles
Typical location	Perivascular / airway submucosa	Small-airway lumen
Clinical trajectory	May improve with therapy	Often irreversible dysfunction
Sampling issue	Biopsy aids diagnosis	Patchy lesion may be missed

Infection and rejection: Integrated interpretation

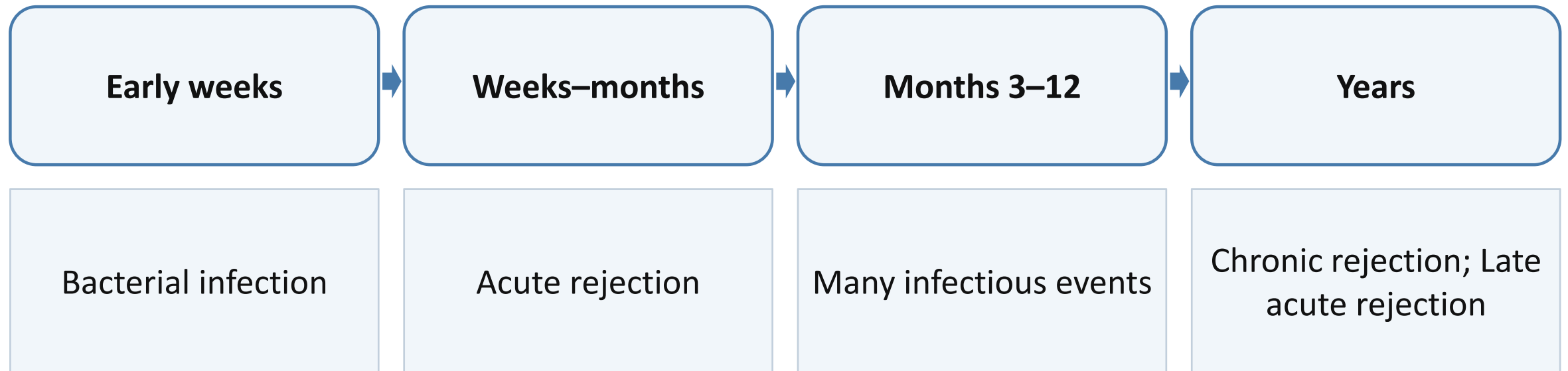
Infection

- Opportunistic and conventional pathogens.
- Temporal patterns vary with prophylaxis.
- Anastomotic involvement possible with fungi.

Rejection

- Immune recognition of donor alloantigens.
- Acute: Inflammatory infiltrates.
- Chronic: Bronchiolar fibrosis.

What the calendar can—and cannot—tell you



All periods overlap. The calendar narrows the differential; It never establishes a diagnosis.

EBV-associated B-cell lymphoma

- EBV-associated B-cell lymphoma is an infrequent complication described after lung transplantation.
- It most often arises within the transplanted lung.
- A mass or infiltrate in an immunosuppressed recipient cannot automatically be labeled infection or rejection.

Survival data require source context

- An overall median lung-transplant survival of six years.
- The excerpt also associates better outcomes with younger recipients and bilateral transplantation.
- This textbook figure is not a separately verified current survival estimate and should be interpreted accordingly.

Case 1: Infiltrates two weeks after transplantation

- A recipient develops fever, cough, and a new pulmonary infiltrate two weeks after surgery.
- Question: Which infectious category has the strongest timing association?
- Expected reasoning: Bacterial infection predominates in the earliest weeks, but rejection remains possible.

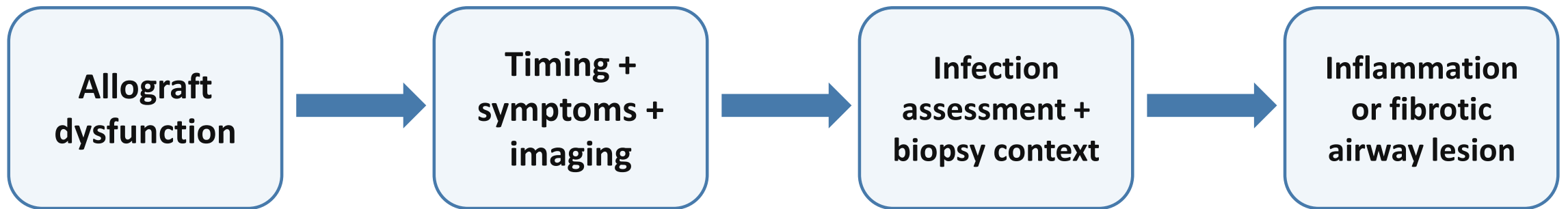
Case 2: Dyspnea four months after transplantation

- Four months after transplantation, a patient develops fever, dyspnea, and radiologic infiltrates.
- Question: Why is symptom-based discrimination unsafe?
- Expected reasoning: Acute rejection and infection overlap; Biopsy can be diagnostically important.

Case 3: Progressive decline several years later

- A recipient has progressive cough, breathlessness, and sustained worsening of pulmonary function years later.
- Question: Which structural lesion is most characteristic of chronic rejection?
- Expected reasoning: Patchy bronchiolitis obliterans with fibrous small-airway occlusion.

Diagnostic synthesis: Link syndrome to tissue



An educational synthesis, not a comprehensive contemporary clinical diagnostic algorithm.

Five distinctions to retain

- The transplant indications include end-stage COPD, IPF, CF, and idiopathic/familial PAH.
- Bilateral chronic infection requires replacing both lungs.
- Early bacterial infection, opportunistic infection, and rejection overlap in time.
- Acute rejection is inflammatory; Chronic rejection is characteristically fibrotic.
- Bronchiolitis obliterans is patchy, often difficult to sample, and irreversible once established.

References and scope

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. 2026. Chapter 15: The Lung; “Lung Transplantation,” pp. 650–651.
- Robbins, Cotran & Kumar. Chapter 15: “Pneumonia in the Immunocompromised Host,” p. 650.
- Robbins, Cotran & Kumar. Chapter 6: “Rejection of Tissue Transplants,” pp. 208–211.
- Anatomical and mechanistic schematics in this lecture are original editable teaching diagrams, not clinical specimens.