
Large Vessel Vasculitis

Arterial territories · Immune injury · Morphology · Clinical consequences

Giant cell arteritis and Takayasu arteritis

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Learning objectives

ORIENTATION

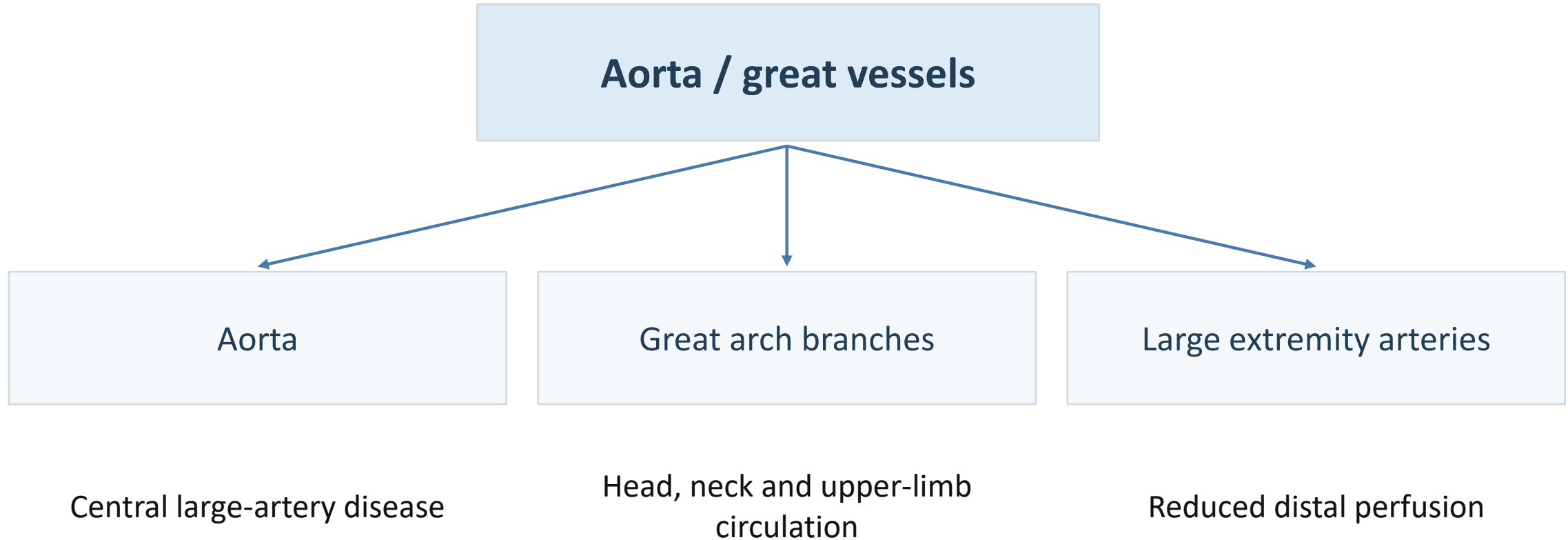
- Identify the arterial territories preferentially affected by large-vessel vasculitis.
- Link immune-mediated arterial wall injury to stenosis, ischemia, and remodeling.
- Recognize the pathology and clinical consequences of giant cell and Takayasu arteritis.
- Interpret overlapping histology and the limits of biopsy sampling.

Large-vessel vasculitis: Operational definition

- Noninfectious vessel-wall inflammation preferentially involving the aorta and its major branches.
- Frequently extends to great arch vessels and large arteries supplying extremities.
- “Large-vessel” describes a predominant pattern—not exclusive restriction to one caliber.

The distribution is preferential, not absolute.

Distribution: The major arterial territories



The aorta and its first-order branches are the defining territories.

Classification is based on predominant vessel caliber

Large-vessel pattern

- Aorta and major branches
- Giant cell arteritis
- Takayasu arteritis

Other patterns

- Medium: Main visceral arteries and branches
- Small: Arterioles, capillaries and venules
- Overlap occurs across categories

The predominant caliber guides classification; It does not define a strict boundary.

Vascular caliber does not impose rigid boundaries

- Giant cell arteritis may affect medium and even smaller arteries in addition to the aorta.
- Takayasu arteritis involves medium and larger arteries, often centered on the aortic arch.
- Distributions overlap; Classification is interpreted with morphology and clinical context.

Clinical-anatomic pattern is more informative than isolated vessel size.

Two major large-vessel vasculitides

Large-vessel vasculitis

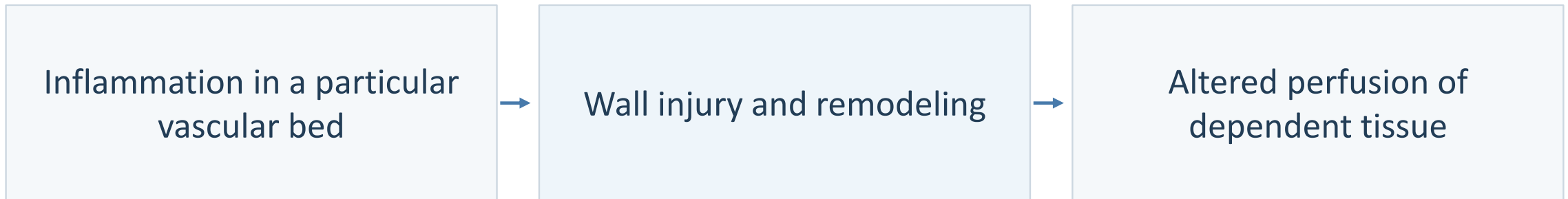
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graph TD; A[Large-vessel vasculitis] --> B[Giant cell arteritis]; A --> C[Takayasu arteritis];
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Giant cell arteritis

Takayasu arteritis

Both may be granulomatous and can involve the aorta.

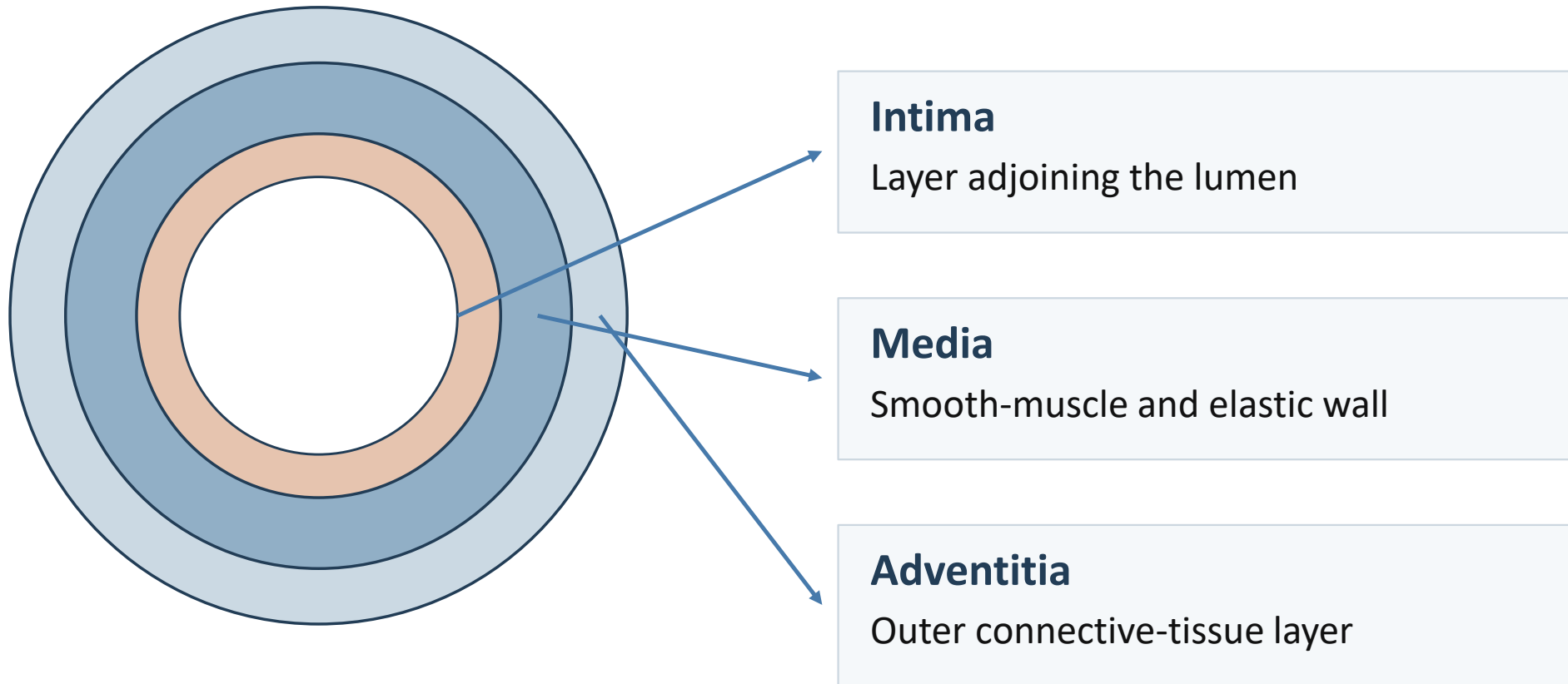
Why vascular location determines manifestations



- Systemic inflammation produces constitutional symptoms.
- Local arterial lesions explain organ-specific ischemia.

An identical wall lesion can produce different symptoms in different territories.

Normal arterial wall: Three functional layers



Arterial cross-section: Original native schematic, not a micrograph.

Immune and infectious mechanisms must be separated

Immune-mediated arteritis

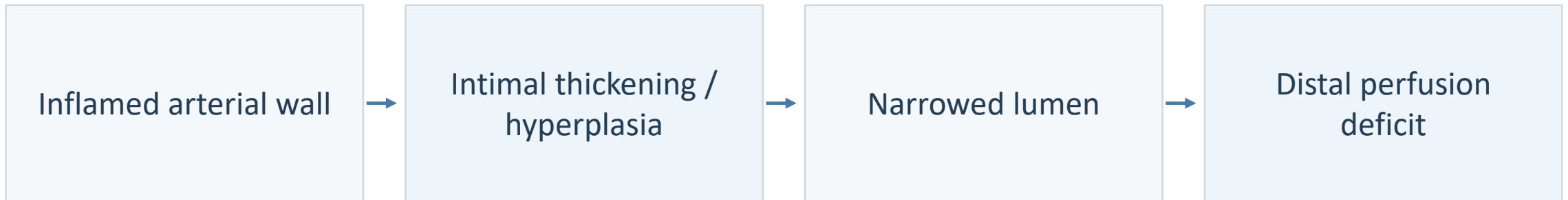
- Vessel-wall inflammation from an immune response
- T-cell and other immune mechanisms contribute
- Immunosuppression is relevant

Infectious arteritis

- Direct microbial invasion of vessel wall
- Potential thrombosis, infarction or aneurysm
- Immunosuppression can be harmful

A vascular inflammatory phenotype alone does not establish etiology.

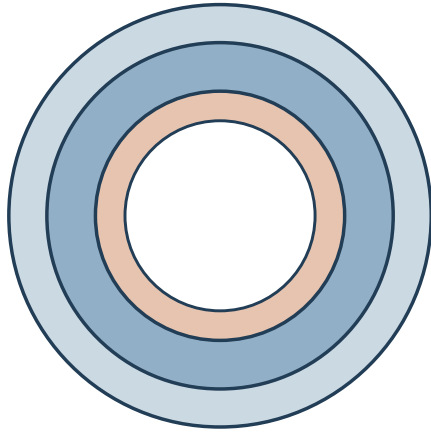
Inflammation causes luminal stenosis



- Vascular pulses weaken when major proximal branches become severely narrowed.

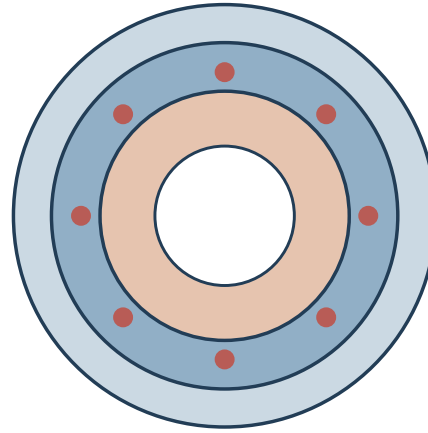
Intimal remodeling converts mural inflammation into flow-limiting disease.

Concentric wall change reduces effective lumen



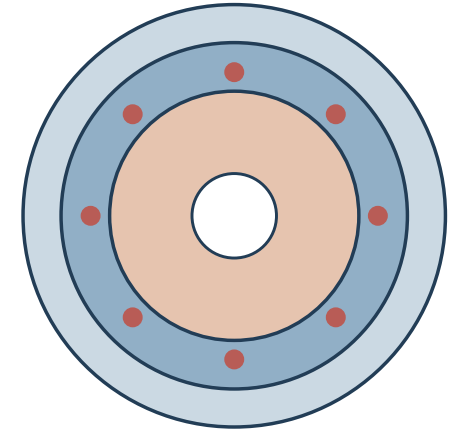
Normal wall

Open central lumen



Thickening

Reduced luminal radius

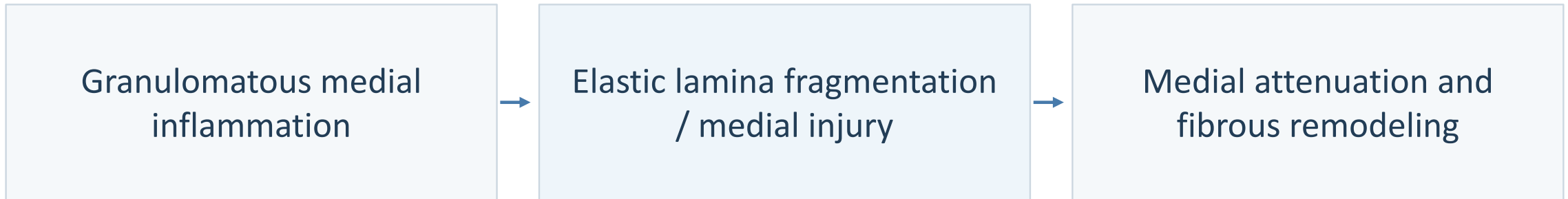


Advanced lesion

Marked narrowing

Schematic geometry; Not a measured stenosis or microscopy image.

Medial and elastic injury alter wall integrity



- Giant cell arteritis damages the internal elastic lamina.
- Takayasu arteritis may cause root dilation with valvular insufficiency.

Wall injury may coexist with stenosis; Morphology is not confined to the intima.

Granulomatous inflammation is a frequent pattern

- Giant cell arteritis classically has granulomatous inflammation, often centered on the internal elastic membrane.
- Takayasu arteritis may exhibit giant cells and patchy medial necrosis.
- Histologic features substantially overlap between these two diseases.

Shared arterial injury: Lesion to phenotype



- Neurologic, visual, limb, renal, and cardiac manifestations reflect the affected bed.

The organ harmed depends on the arterial territory involved.

Large-vessel arteritis: Comparative framework

Feature	Giant cell arteritis	Takayasu arteritis
Typical age pattern	Usually >50 years	Usually <50 years
Principal territories	Head vessels; Also aorta	Aortic arch and major branches
Wall pathology	Often granulomatous	Often granulomatous
Distinctive clue	Temporal symptoms; Ocular risk	Upper-limb weak pulses

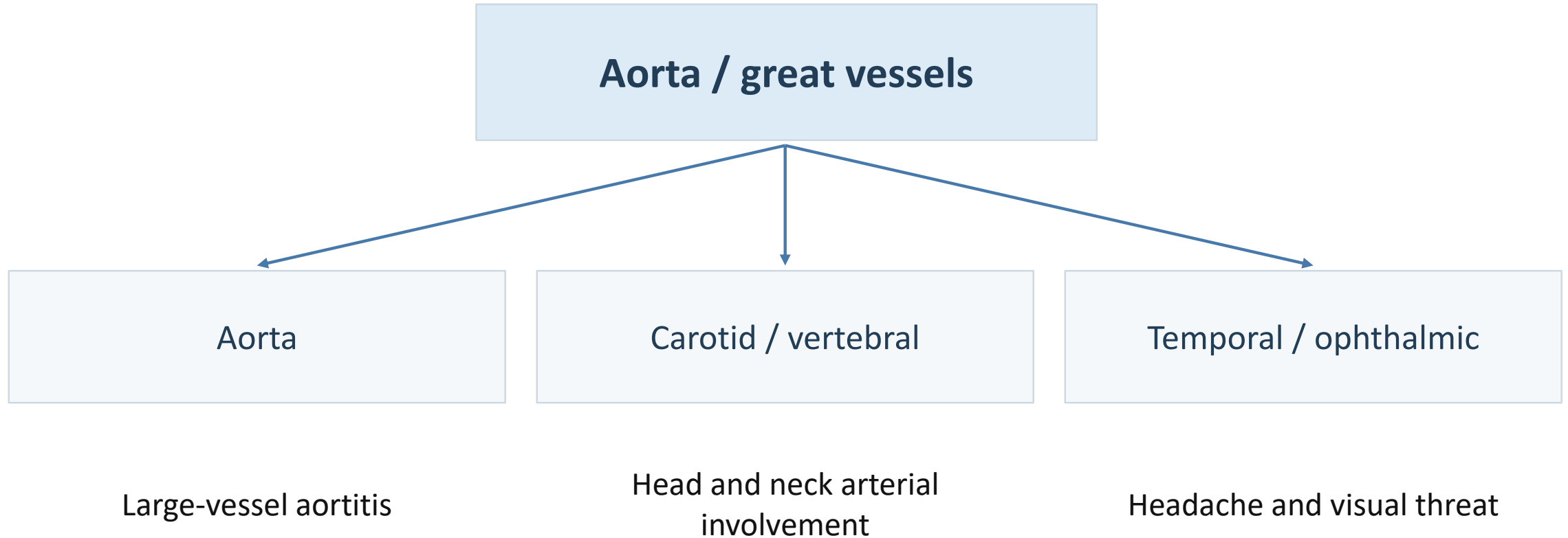
Age and site are helpful patterns; The lesions can overlap.

Giant cell arteritis: Defining features

GIANT CELL ARTERITIS

- Chronic arteritis classically showing a granulomatous inflammatory reaction.
- Affects large and medium arteries, particularly those supplying the head.
- Most prominent in older adults; Uncommon before age 50 years.

Giant cell arteritis: More than temporal arteries



"Temporal" is a convenient biopsy designation, not a complete disease map.

Why the disease retains the name temporal arteritis

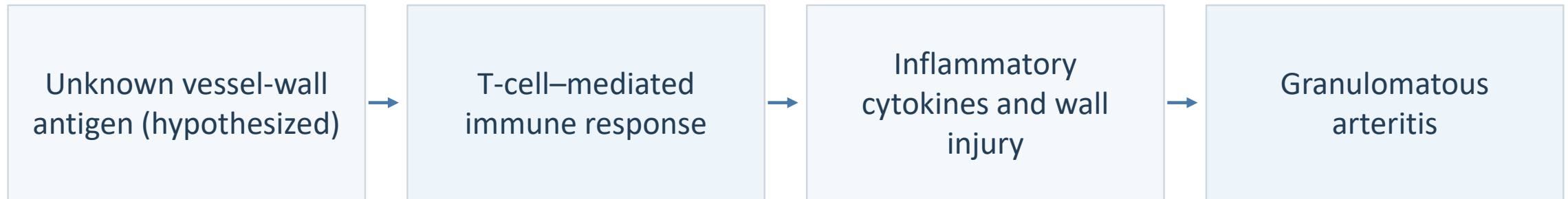
- Temporal arteries are accessible for diagnostic biopsy.
- The disease is not uniquely restricted to superficial temporal vessels.
- A finding in temporal artery may signal involvement of vertebral and ophthalmic arteries.

Ophthalmic involvement is the critical danger

- Arteritis affecting the ophthalmic circulation can precipitate abrupt visual disturbances.
- Clinical effects range from diplopia to complete loss of vision.
- Potential irreversible blindness makes prompt recognition essential.

New visual symptoms in a compatible presentation require urgent evaluation.

Giant cell arteritis: Proposed T-cell pathogenesis



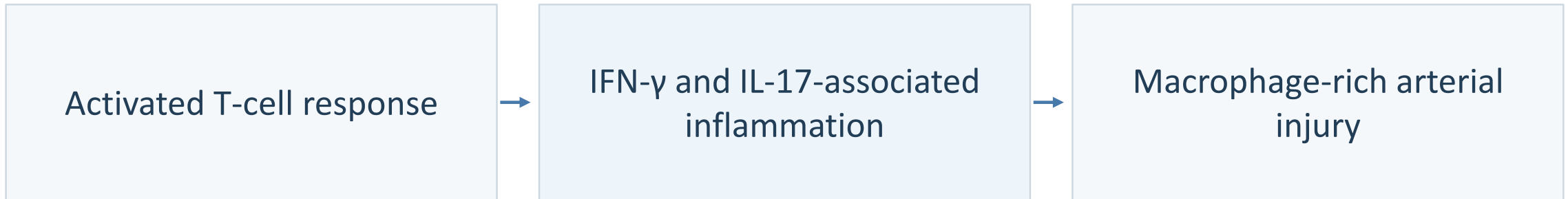
- The exact vessel-wall antigen remains uncharacterized in the supplied text.

The initiating antigen is uncertain; An immune-mediated mechanism is strongly supported.

The initiating antigen is not established

- A T-cell response to an as-yet uncharacterized vessel-wall antigen.
- The predilection for head vessels is not satisfactorily explained.
- Different embryologic vascular origins are presented as a hypothesis—not proven causation.

Inflammatory mediators in giant cell arteritis



- Antiendothelial-cell antibodies also may contribute.
- The text lists mediators but does not establish a complete linear pathway.

Flow is a teaching simplification of supported relationships—not a validated molecular cascade.

Evidence supporting immune causation

Histologic and genetic observations

- Granulomatous arterial inflammation
- Association with some MHC class II haplotypes
- T-cell and macrophage infiltrates

Clinical and mediator observations

- Steroid responsiveness
- Proinflammatory cytokines
- Possible antiendothelial antibodies

Multiple observations converge on immune mediation; No specific antigen is proven.

Active giant cell arteritis: Core microscopy

- Inflammation often predominates in the arterial media.
- Classic lesions form granulomatous reactions around the internal elastic membrane.
- An inflammatory infiltrate includes T cells and macrophages.

Internal elastic lamina injury is central



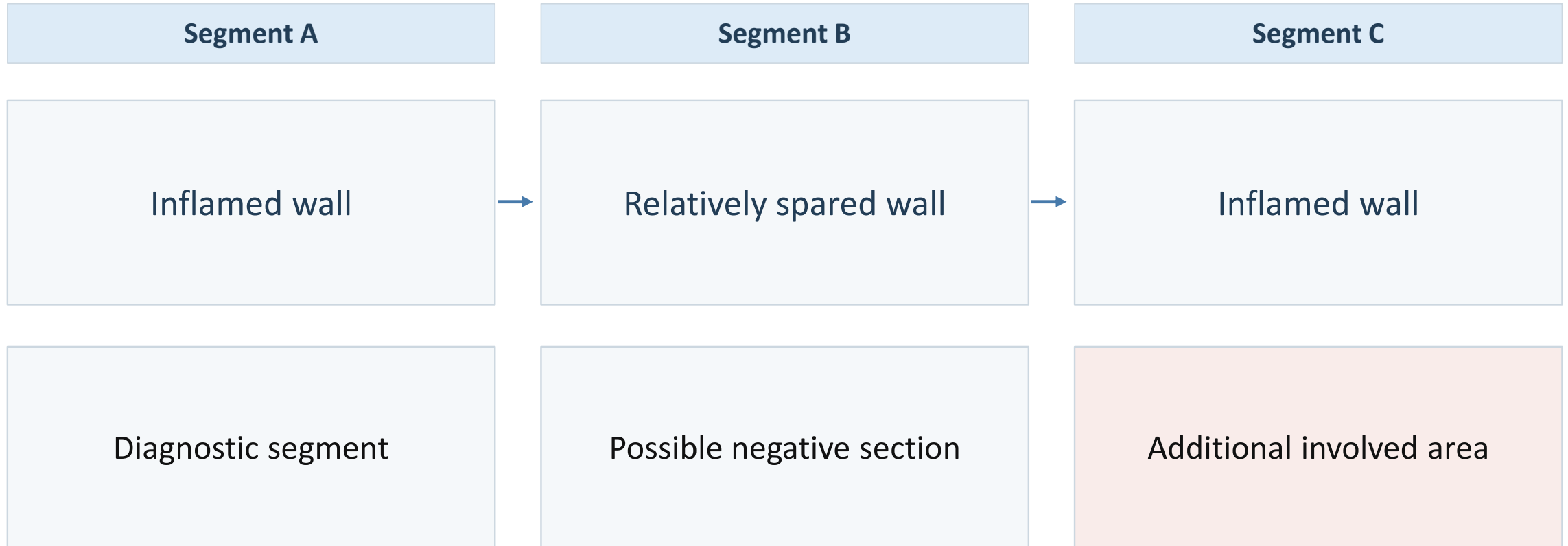
- A structure-specific lesion links inflammation to the characteristic arterial histology.

Microscopic recognition requires seeing the actual elastic boundary—not merely “granulomas.”

Giant cells are characteristic but not mandatory

- Multinucleated giant cells are described in many adequate biopsy specimens.
- Granulomas and giant cells can be scarce or absent despite giant cell arteritis.
- The full distribution and wall injury pattern matter in histologic interpretation.

Patchy involvement produces skip lesions



Schematic segments illustrate sampling heterogeneity, not measured lesion length.

Intimal thickening and thrombosis may compound ischemia

- Involved segments show intimal thickening that reduces vessel diameter.
- Thrombi are occasionally present in the described lesions.
- Either obstruction mechanism can impair flow in a vulnerable arterial bed.

Active versus healed giant cell arteritis

Active lesion

- Medial inflammatory infiltrate
- Granulomatous reaction may be present
- Elastic lamina fragmentation

Healed lesion

- Medial attenuation and scarring
- Persistent intimal thickening
- Adventitial fibrosis

The diagnostic architecture changes as inflammation becomes scar.

Headache and tenderness reflect cranial arteritis

- Localized headache or facial pain may track the superficial temporal artery.
- The involved artery can be painful on palpation.
- Symptoms should be linked to a specific inflamed cranial vascular territory.

Constitutional symptoms may be the only initial clues

- Fever, fatigue and weight loss may accompany the disease.
- Symptoms of systemic inflammation may precede recognizable local ischemia.
- Absence of an obvious focal arterial symptom does not rule out vasculitis.

Giant cell arteritis: Ocular clinicopathologic chain



Abrupt visual dysfunction can reflect arterial disease beyond the temporal biopsy site.

Temporal artery biopsy assesses a patchy disease

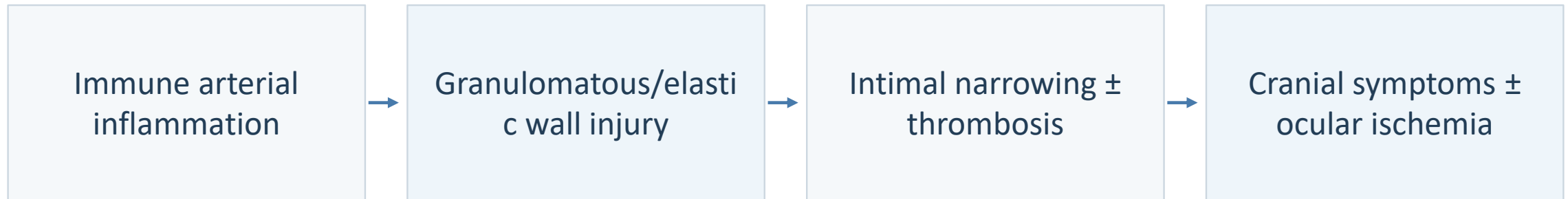
- Histologic diagnosis relies on obtaining an adequately sampled artery segment.
- Skip lesions create a risk that a sampled portion is not representative.
- Biopsy should be interpreted together with the clinical presentation.

A negative temporal artery biopsy is not absolute exclusion

- Even adequate samples may miss patchy arterial inflammation.
- The posterior probability depends on the compatible clinical and vascular findings.
- A negative section cannot erase a strong clinical suspicion by itself.

Histology is important; Sampling error must be understood.

Giant cell arteritis: Consolidate pathology and presentation



- Inflammation and ischemia each contribute to the symptom complex.

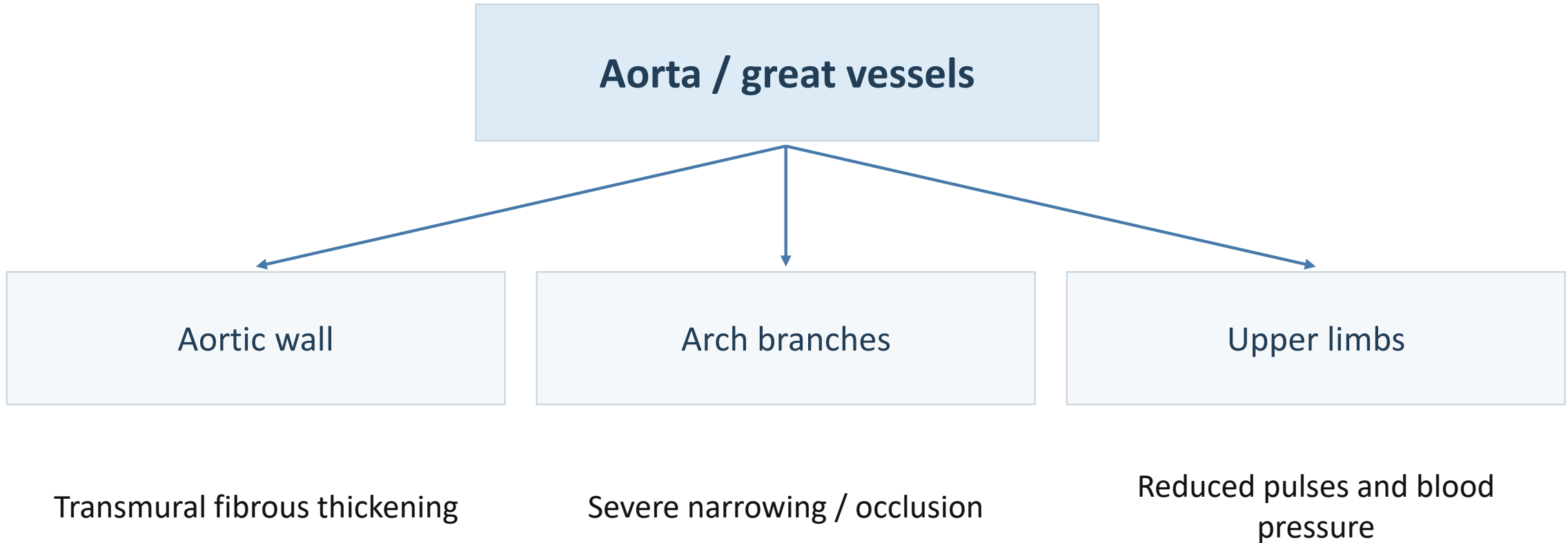
Clinical urgency comes from the threatened ophthalmic circulation.

Takayasu arteritis: Defining features

TAKAYASU ARTERITIS

- Granulomatous arteritis affecting medium and large arteries.
- Predominant involvement of aorta, especially the arch and its great branches.
- Commonly manifests with attenuated upper-extremity pulses—“pulseless disease.”

Takayasu arteritis: The aortic arch pattern



The pattern explains why upper-extremity vascular findings are conspicuous.

Transmural thickening is a major gross feature

- The aortic wall becomes irregularly thickened.
- Involvement can be distributed through the full wall thickness.
- Intimal hyperplasia contributes to critical branch-vessel stenosis.

Age pattern and geography are clinical context

Age

- Usually presents before age 50 years classification
- Compared with giant cell arteritis, patients are typically younger
- Age assists classification but does not define histology

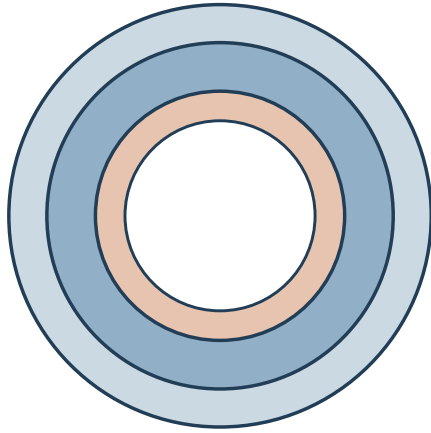
Geography

- Historically associated with Japanese populations
- Occurs across the world
- Associated with some HLA haplotypes

Takayasu pathogenesis is likely T-cell mediated

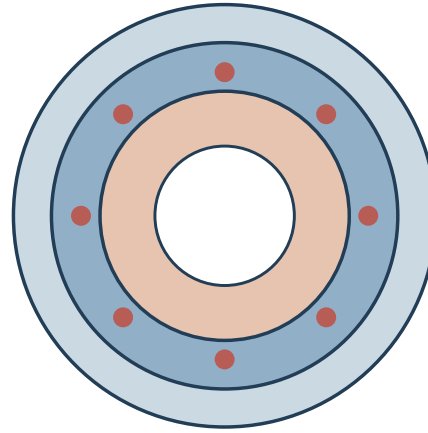
- A probable autoimmune mechanism mediated by T cells.
- Some HLA associations support immune susceptibility.
- The textbook does not identify a definitive initiating antigen.

Takayasu: Wall thickening can obliterate large branches



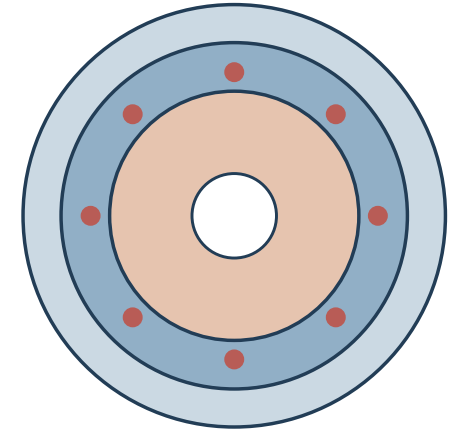
Uninvolved segment

Patent lumen



Intimal hyperplasia

Reduced lumen

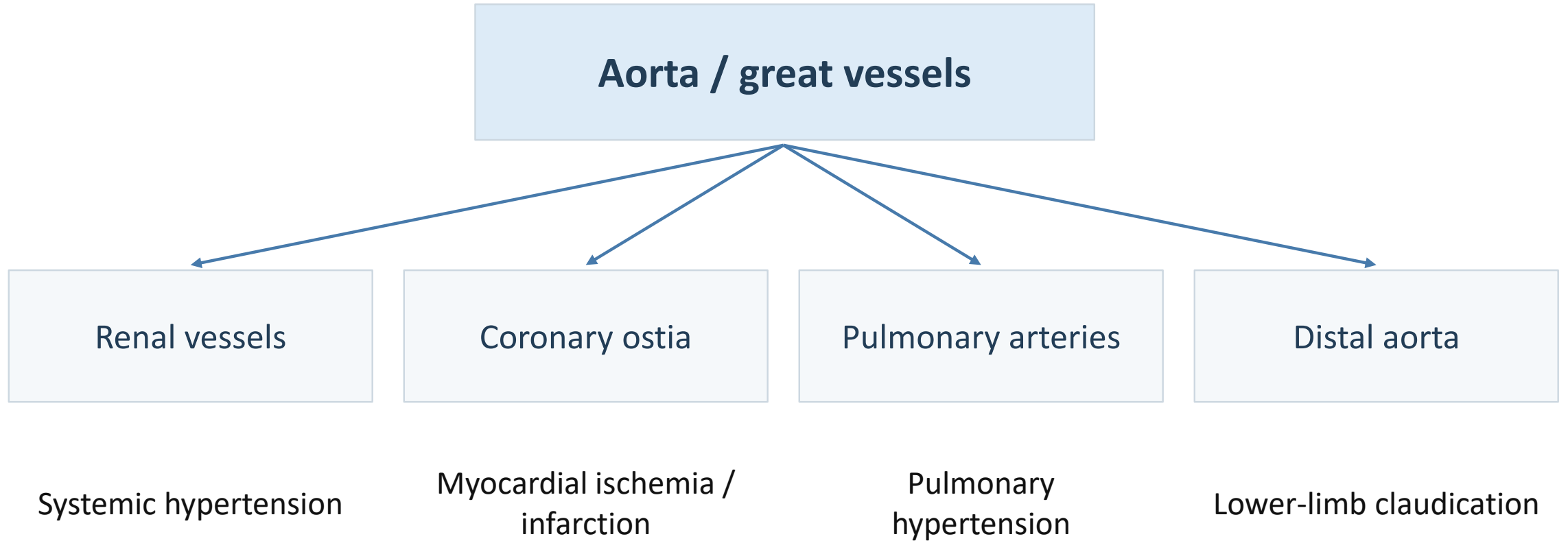


Severe disease

Critical obstruction

Schematic shapes illustrate luminal change; No numeric stenosis estimates.

Takayasu disease may extend beyond the arch



The phenotype broadens when other aortic branches are involved.

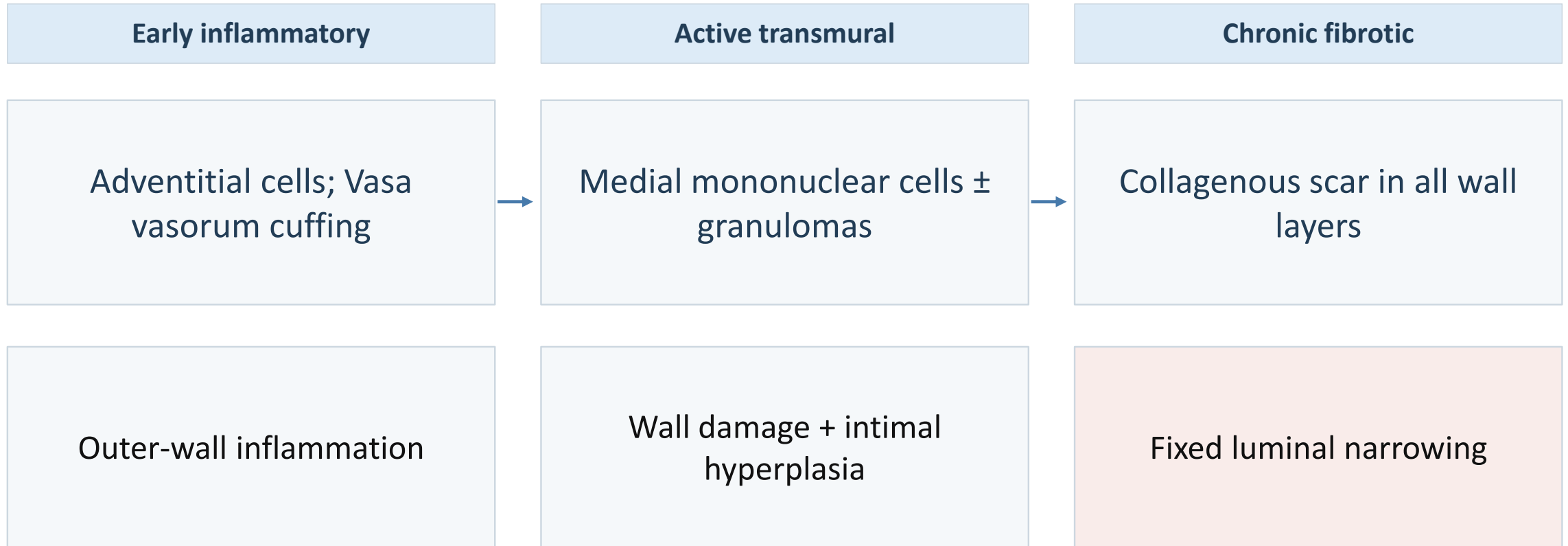
Early Takayasu histology: Adventitial inflammation

- Adventitial mononuclear infiltrates may surround vasa vasorum.
- Perivascular cuffing is one described early/active pattern.
- Inflammation is not restricted to a single mural layer.

Media: Granulomas and focal injury in Takayasu

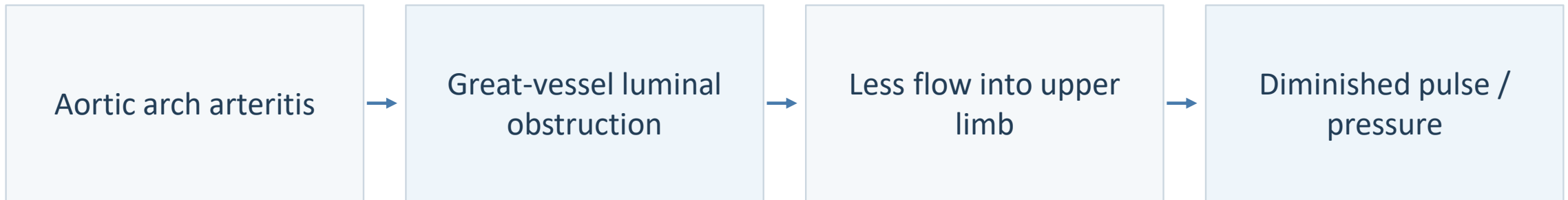
- Intense mononuclear inflammation may extend through the media.
- Granulomatous inflammation may include multinucleated giant cells.
- Patchy medial necrosis is described within the active injury pattern.

Takayasu: Progression to fibrous remodeling



Schematic stages represent patterns, not a fixed timeline.

Pulseless disease: An anatomic explanation



- Marked stenosis or luminal obliteration is the structural correlate.

Peripheral pulse abnormalities can arise from proximal large-artery lesions.

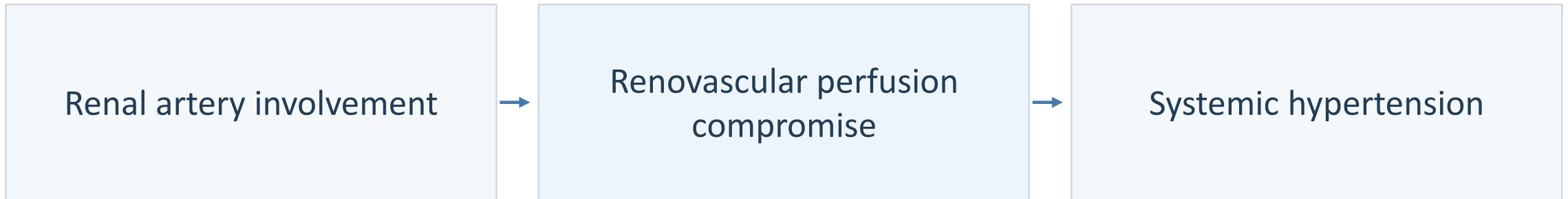
Systemic symptoms may precede vascular insufficiency

- Early fatigue, fever and weight loss are nonspecific.
- As arterial lesions progress, ischemic vascular symptoms increasingly dominate.
- A systemic-to-vascular clinical evolution is described, but course varies.

Ocular and neurologic consequences in Takayasu

- Ocular disturbances include visual defects and retinal hemorrhages.
- Severe disease can be associated with complete visual loss.
- Neurologic deficits arise as major arterial territories become compromised.

Renal arterial stenosis contributes to hypertension



- Systemic hypertension in many affected patients.

A proximal arterial inflammatory lesion can produce a secondary blood-pressure phenotype.

Coronary ostial narrowing threatens the myocardium



This mechanism differs anatomically from primary coronary plaque obstruction.

Pulmonary arterial involvement affects pressure

Pulmonary artery arteritis



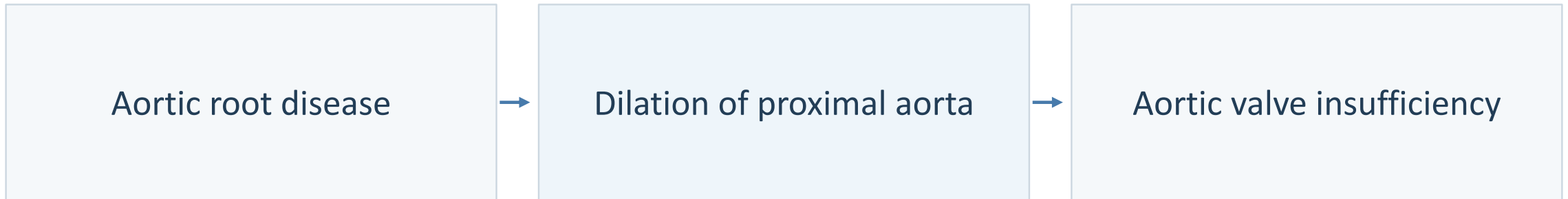
Flow-limiting vessel disease



Pulmonary hypertension

Pulmonary circulation may also participate in large-vessel arteritis.

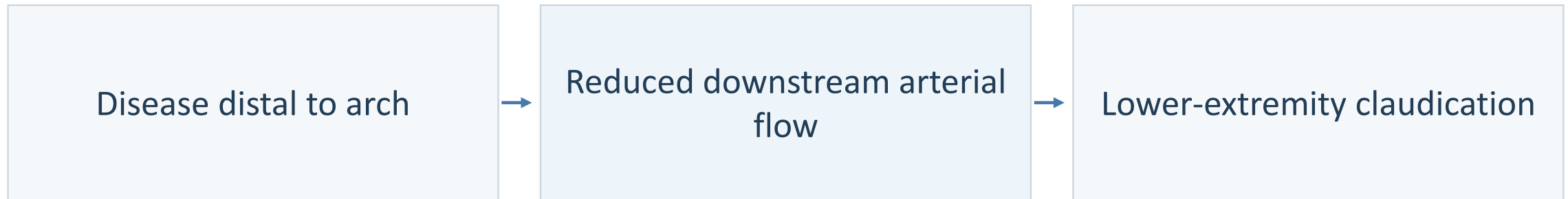
Aortic-root involvement may lead to valve insufficiency



- Dilation is an occasional complication, not the dominant branch-vessel pattern.

Not all large-vessel complications result from stenosis.

Distal aortic disease produces leg symptoms



The same inflammatory disease can produce different limb findings by site.

Takayasu clinical course is heterogeneous

More progressive presentation

- Early constitutional symptoms
- Increasing vascular abnormalities
- Potential end-organ sequelae

Less progressive / quiescent period

- Some patients enter a quieter interval
- Previous injury may leave lasting deficits
- Long-term survival remains possible

Clinical inactivity does not necessarily reverse established structural injury.

The histology of GCA and Takayasu overlaps

Giant cell arteritis

- Medial granulomatous reaction
- Elastic lamina fragmentation
- Intimal narrowing and healed scars

Takayasu arteritis

- Mononuclear $\pm$ granulomatous medial inflammation
- Intimal hyperplasia
- Transmural fibrosis and scarring

Robbins explicitly describes the two histologic patterns as essentially indistinguishable.

Demographics and distribution resolve histologic overlap

- Older age and cranial/temporal symptoms favor giant cell arteritis.
- Younger age and aortic-arch branch obstruction favor Takayasu arteritis.
- Neither granulomas nor giant cells alone reliably distinguishes the two.

Systemic inflammation and focal ischemia coexist

Systemic inflammatory features

- Fever or malaise
- Fatigue and weight loss
- Manifestations may be nonspecific

Arterial territory–specific features

- Headache and visual loss
- Upper-limb pulse deficit
- Hypertension, claudication or organ ischemia

Localize the arterial lesion from the clinical clue

Clue	Probable involved arterial bed	Pathologic consequence
Temple pain	Superficial cranial arteries	Focal arterial inflammation
Reduced arm pulse	Aortic arch branches	High-grade stenosis
Renal hypertension	Renal arteries	Perfusion compromise
Claudication	Distal aorta / limb arteries	Flow limitation
Visual loss	Ocular-supplying arteries	Threatened ocular perfusion

Clinical application: Cranial arteritis

HYPOTHETICAL TEACHING CASE

A patient older than 50 years develops new temporal-region headache, scalp-region arterial tenderness, systemic fatigue, and abrupt diplopia.

Which vascular complication is most urgent to recognize, and why?

Case interpretation: Giant cell arteritis

- Age and cranial symptoms support the giant cell arteritis pattern.
- Ocular dysfunction raises concern for ophthalmic arterial involvement.
- Granulomatous arteritis and elastic lamina injury are expected pathology, but biopsy sampling may miss skip lesions.

Clinical consequences must inform interpretation of a potentially negative biopsy.

Clinical application: Pulseless disease

HYPOTHETICAL TEACHING CASE

A younger adult has fever and fatigue followed by asymmetric weak upper-extremity pulses, low arm blood pressure, and new exertional arm symptoms.

Where should the arterial lesion be localized, and what structural change explains the pulses?

Case interpretation: Takayasu arteritis

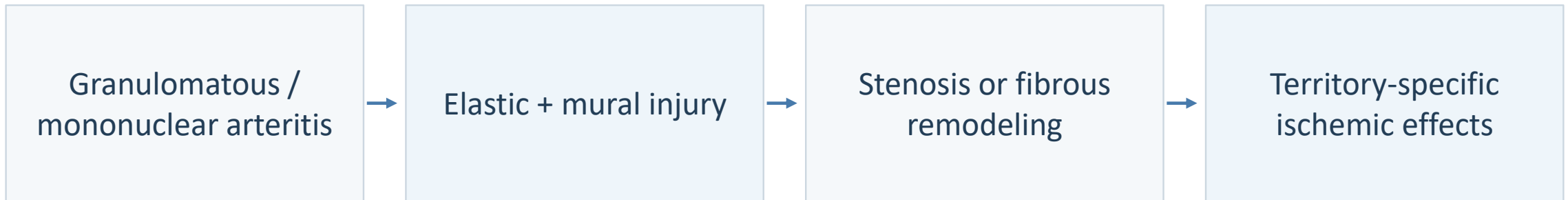
- The aortic arch and its major branches are the favored anatomic pattern.
- Intimal hyperplasia and mural fibrosis can produce severe branch-vessel narrowing.
- Granulomatous histology alone would not separate Takayasu from giant cell arteritis.

Use age, distribution, hemodynamics and histology together.

Etiologic safeguard: Exclude direct infectious arteritis

- Not every inflamed large artery has an immune-mediated vasculitis.
- Direct invasion by bacterial or fungal pathogens as an alternative.
- The immune-versus-infectious distinction matters because immunosuppression can aggravate infection.

Synthesis: From immune injury to clinical pattern



- Giant cell arteritis: Cranial ischemic threat in older adults.
- Takayasu arteritis: Arch-branch obstruction in younger adults.

The arterial wall is the lesion; Vascular territory determines the clinical phenotype.

Further reading and source figures

Robbins, Cotran & Kumar

Pathologic Basis of Disease

Large Vessel Vasculitis and the immediately following sections on Giant Cell Arteritis and Takayasu Arteritis

Refer to the original textbook images for specimen morphology; the drawings in this lecture are explanatory schematics.