

Pathology lecture

Vasculitis

Vessel-wall injury, classification, morphology and clinicopathologic patterns

Inflammatory vascular injury · major patterns · clinical correlation

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Learning objectives

- Explain why vessel-wall inflammation produces ischemia, thrombosis, aneurysm and systemic symptoms.
- Distinguish infectious invasion from immune-mediated vasculitis.
- Classify major noninfectious forms by vessel caliber and immunopathogenesis.
- Recognize defining morphologic and clinical patterns of representative vasculitides.

Vasculitis is inflammation of the vessel wall

- The defining lesion is inflammation within the vascular wall—not merely inflammation around a vessel.
- Presentations reflect the vascular territories damaged.
- Disease may remain localized to one organ or be systemic across several vascular beds.
- General inflammatory symptoms often coexist with organ-specific injury.

Local versus systemic distribution

Single-organ pattern

A vascular bed in one tissue is principally affected

Limited at presentation does not establish lifelong localization

Systemic pattern

Several organ vascular beds are involved

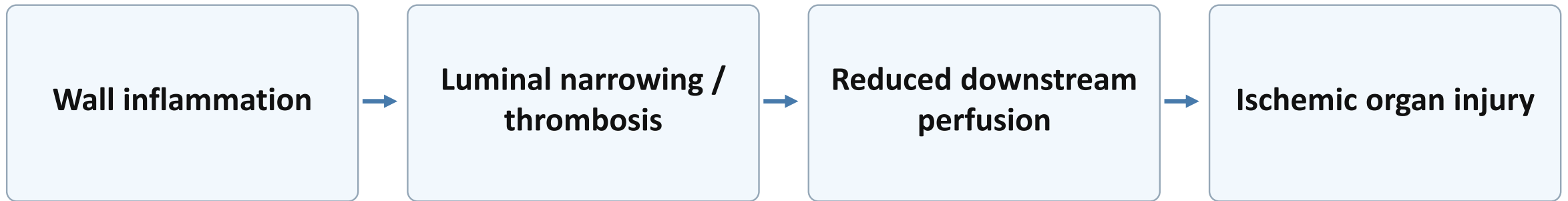
Constitutional symptoms and multiple organ syndromes may coexist

The anatomic distribution explains why one umbrella term contains clinically dissimilar diseases.

Constitutional manifestations reflect inflammation

- Fever and malaise are manifestations of systemic inflammatory activity.
- Myalgias and arthralgias may accompany vessel-wall injury.
- Absence of striking systemic symptoms does not exclude an organ-threatening localized process.
- Specific manifestations depend on whether perfusion, vascular integrity or both are compromised.

Inflammation connects the vessel lesion to organ injury



Necrotizing arteritis can also weaken the vessel wall, producing aneurysm or rupture.

Four clinically important consequences

Stenosis

Wall thickening reduces luminal diameter

Pulse deficits; Tissue hypoperfusion

Thrombosis

Endothelial injury promotes occlusion

Infarction; Organ dysfunction

Aneurysm

Inflammation weakens the wall

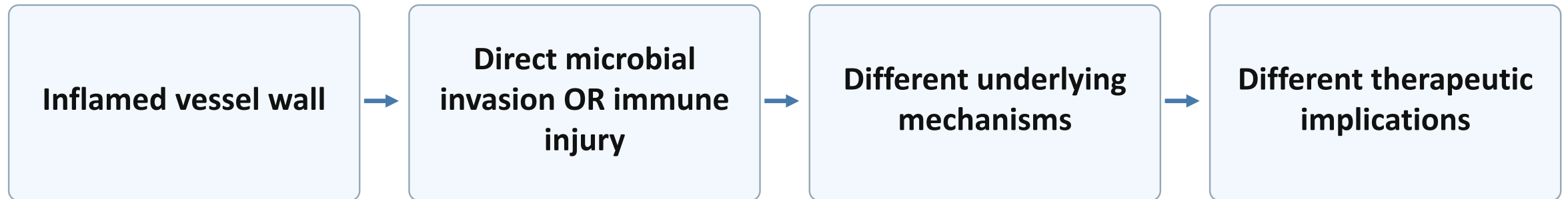
Risk of rupture or local thrombosis

Hemorrhage

Disruption of vessel integrity

Tissue or alveolar bleeding

First etiologic branch: Infection or immunity?



Infection can also trigger a secondary immune-mediated vasculitis; Categories are not mutually exclusive.

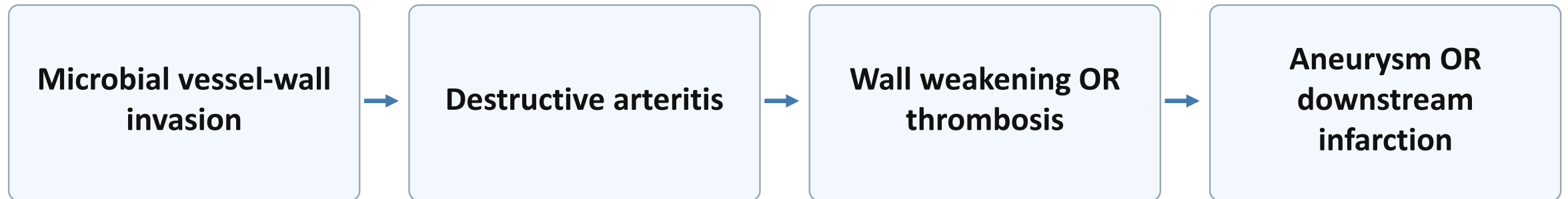
Why identifying infection matters

- Immunosuppression is appropriate for some immune-mediated processes.
- The same intervention may worsen vasculitis caused by an invasive pathogen.
- Microbes may damage a vessel directly or trigger immune complexes without invading the wall.
- Physical injury, irradiation and toxins are additional causes of vascular inflammation.

Direct microbial invasion: Typical settings

- Bacteria such as *Pseudomonas* may invade arterial walls.
- Fungi including *Aspergillus* and *Mucor* species can be angioinvasive.
- Spread can occur locally from infected tissue or abscesses.
- Less commonly, hematogenous seeding follows septicemia or infected emboli from endocarditis.

Direct infection can cause two distinct complications



Example: Meningeal vessel thrombosis during bacterial meningitis can contribute to brain infarction.

Direct infectious versus secondary immune vasculitis

Question	Direct infectious vasculitis	Infection-triggered immune vasculitis
Where is the injury initiated?	Pathogen invades vascular wall	Antigen–antibody response injures wall
Illustrative mechanism	Fungal or bacterial angioinvasion	Circulating microbial immune complexes
Important distinction	Treat invasive infection	Establish immunologic mechanism
Clinical hazard	Thrombosis; infected aneurysm	Systemic immune-mediated injury

The presence of infection in a patient is not proof of direct microbial vascular invasion.

Classifying noninfectious vasculitis

- Vessel caliber: Large, medium or small is the first organizing principle.
- Tissue preference and distribution provide additional discrimination.
- Immune deposits, autoantibodies and granulomas refine classification.
- Overlap is common; An affected artery does not always fit its nominal caliber category.

Vessel caliber predicts the broad clinical pattern

Large

Aorta and its major
branches

Aortic and great-vessel
disease

Medium

Major visceral arteries and
branches

Aneurysms, stenoses, regional
ischemia

Small

Arterioles, capillaries and
venules

Skin, lung capillary and renal
glomerular injury

Size categories describe predominant—not exclusive—vascular involvement.

Large-, medium- and small-vessel overview

Predominant caliber	Representative entities	Typical vessel-level consequence
Large	Giant cell arteritis; Takayasu arteritis	Great-vessel narrowing or wall damage
Medium	Buerger disease; PAN; Kawasaki disease	Arterial thrombosis or aneurysm
Small	MPA; GPA; EGPA; immune-complex forms	Capillaritis; glomerulonephritis; purpura

The entity lists are representative, not exhaustive.

Classification has important overlap

- Giant cell arteritis can affect arteries smaller than the aorta.
- Medium-vessel diseases can involve small arteries and branch vessels.
- Small-vessel vasculitis may also involve medium-sized arteries.
- Distribution, serology and pathology must be integrated rather than treating caliber as an absolute rule.

Four immune pathways recur across vasculitides

Immune complexes

Deposits recruit complement and inflammatory cells

Vessel-wall deposits may be demonstrable

ANCA antibodies

Neutrophil activation leads to proteolytic vascular injury

Typically pauci-immune vessels

Anti-endothelial antibodies

May contribute to vascular inflammatory targeting

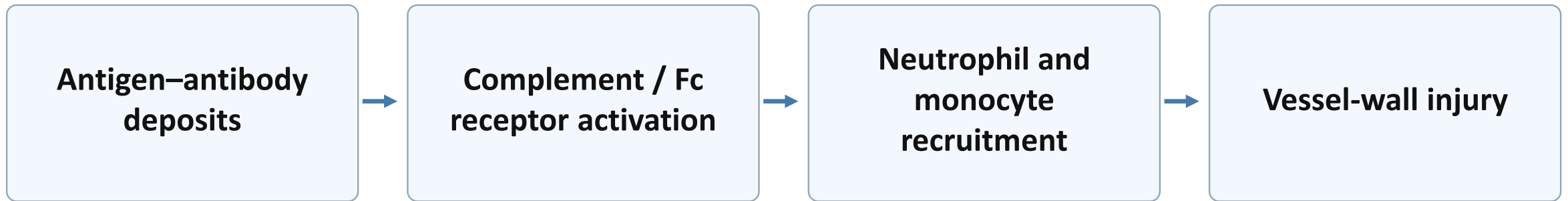
Implicated in selected entities

Autoreactive T cells

T-cell/cytokine pathways foster granulomatous arteritis

Prominent in large-vessel disorders

Immune-complex vasculitis: Injury cascade

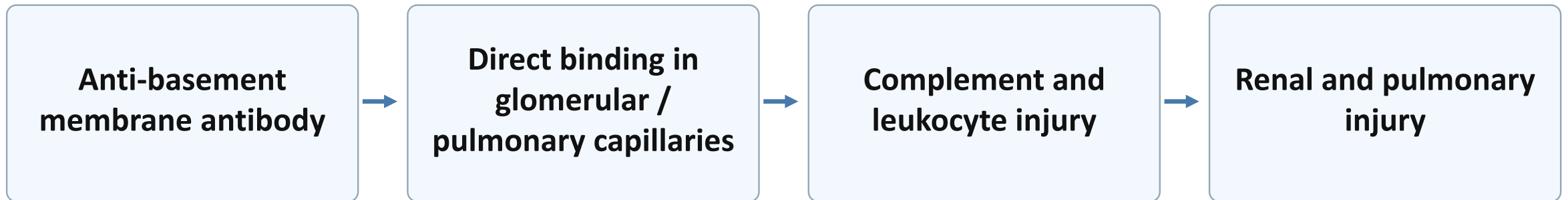


The responsible antigen is often unidentified; Complexes may arrive via blood or form locally.

Immune deposits are a major diagnostic discriminator

- Immune-complex forms show moderate or extensive immunoglobulin and/or complement deposition.
- Immune-complex glomerulonephritis often accompanies the vascular lesions.
- ANCA-associated forms generally lack conspicuous tissue immunoglobulin deposits.
- Patterns of deposition help distinguish mechanisms, but must be interpreted with lesion age.

Anti-GBM disease: Antibody binds in situ



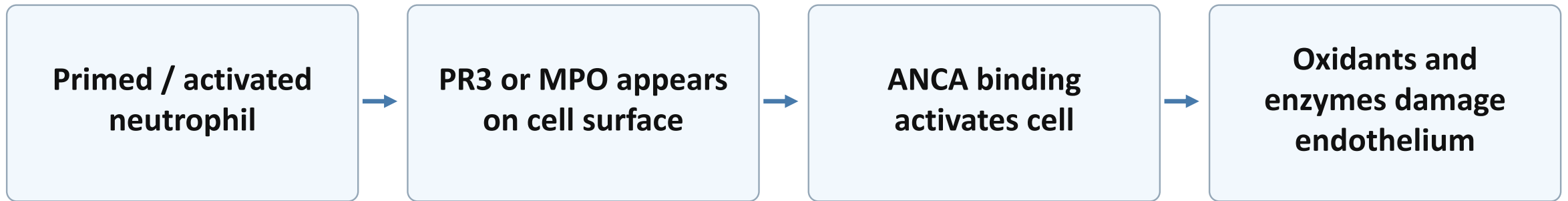
Unlike classic deposited immune complexes, the antibody reacts directly with structural basement-membrane targets.

ANCA antigens: Use target specificity

Antibody	Main target	Robbins-linked patterns
PR3-ANCA	Proteinase 3 in neutrophil granules	Granulomatosis with polyangiitis
MPO-ANCA	Myeloperoxidase in granules	Microscopic polyangiitis; eosinophilic GPA
Legacy staining	c-ANCA / p-ANCA patterns	Target-specific nomenclature is preferred

Association is not disease identity: Serology must be interpreted with clinicopathologic findings.

ANCA-mediated neutrophil injury



ANCAs target primarily intracellular antigens that can become accessible on activated cells.

Why ANCA-associated lesions are pauci-immune

- Antibodies bind neutrophil antigens rather than forming classic circulating immune complexes.
- Vessel wall may be necrotic despite few demonstrable antibody or complement deposits.
- PR3/MPO antibody testing supports diagnosis, but is not a substitute for tissue/clinical correlation.
- Clinical severity and relapse risk may track with antibody activity, but are not inferred from a single result.

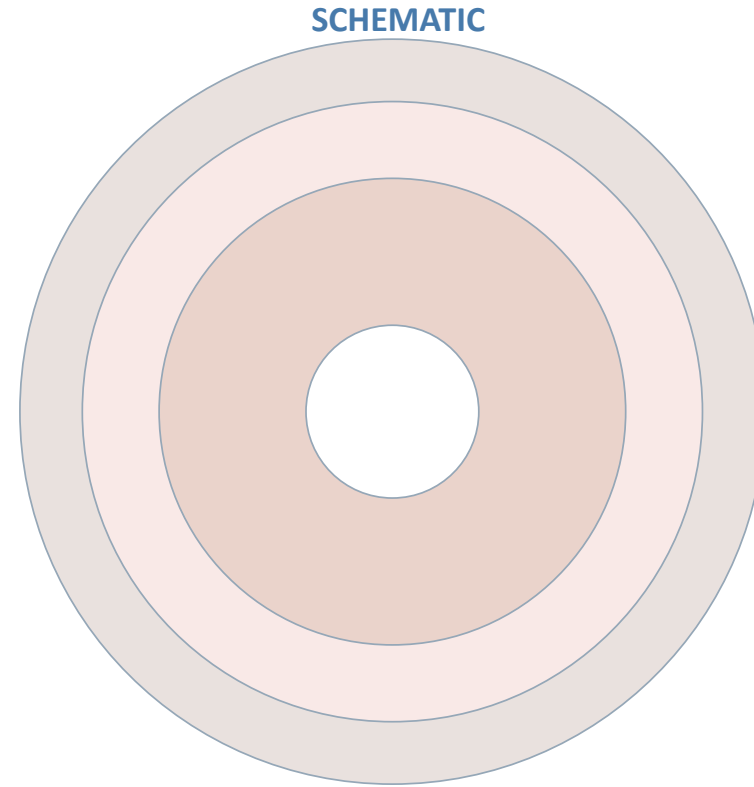
Granulomatous versus nongranulomatous injury

Pattern	Morphologic clue	Representative contexts
Granulomatous arteritis	Macrophages ± giant cells near injured wall	GCA; Takayasu arteritis
Necrotizing vasculitis	Fibrinoid wall necrosis with inflammation	PAN; MPA
Granulomatous necrosis	Necrotizing respiratory granulomas	GPA
Eosinophil-rich lesions	Eosinophils with necrotizing granulomas	EGPA

Morphology overlaps and may be incomplete in limited specimens.

Schematic: Inflammatory stenosis

- Wall inflammation and intimal thickening diminish the open lumen.
- Less flow to dependent tissue explains ischemic manifestations.

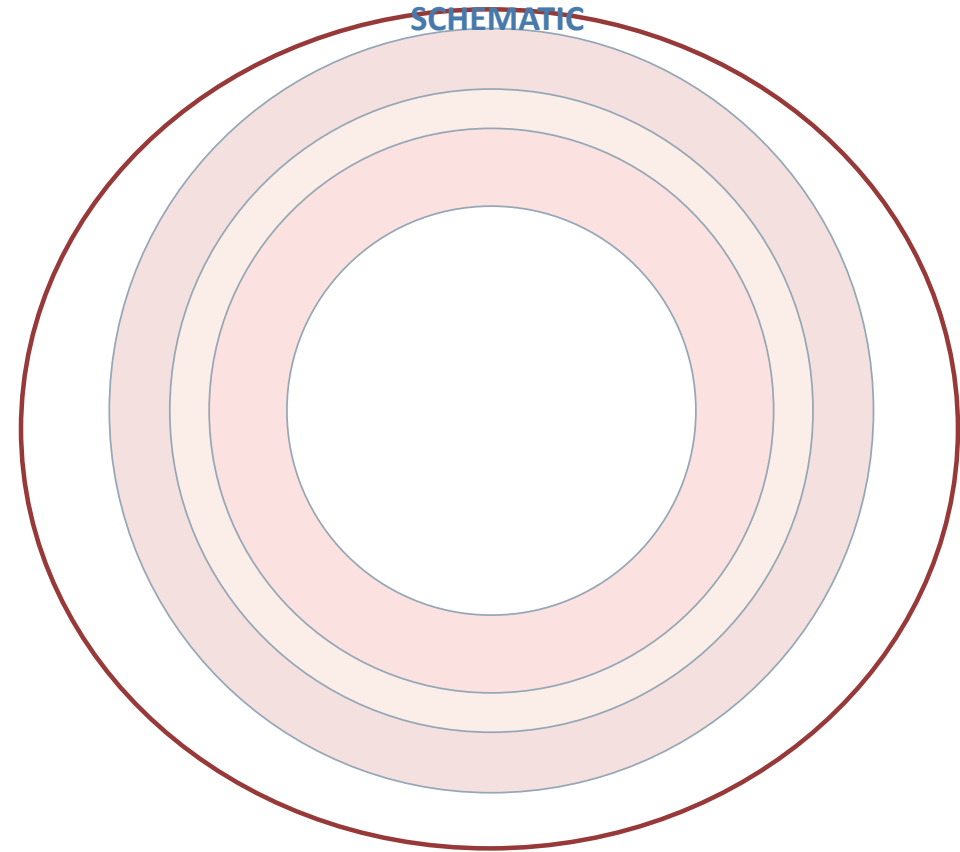


Narrowed lumen

Original editable cross-section; Not a histologic specimen or to scale.

Schematic: Destructive vessel injury

- Transmural injury can destroy structural support and permit aneurysmal dilation.
- Thrombosis may coexist with inflammatory arterial wall damage.



Wall damage / remodeling

Original conceptual drawing; Not an anatomic measurement or clinical image.

Segmental lesions create sampling pitfalls

- Giant cell arteritis often has skip lesions along the same artery.
- PAN typically affects only part of an arterial circumference.
- Multiple stages of PAN injury may occur in different vessel segments.
- The location and length of biopsy determine which part of the disease is actually seen.

Link the vascular bed to symptoms

Cranial arteries

Temporal headache; Ophthalmic ischemia

Visual loss in GCA

Aortic branches

Pulse or pressure asymmetry

Takayasu arteritis

Visceral arteries

Abdominal pain; Hypertension

PAN

Glomerular / lung capillaries

Hematuria; Hemoptysis

Small-vessel vasculitis

A rational pathology-based approach

- Establish evidence of inflammation involving a vascular wall.
- Determine predominant caliber, anatomic territories and lesion pattern.
- Assess for immune deposits and ANCA-associated or granulomatous features.
- Search for infectious context before attributing the lesion to autoimmunity.

Histology requires pattern recognition, not one finding

- Fibrinoid necrosis establishes destructive injury but is not specific to a single vasculitis.
- Neutrophil fragmentation (leukocytoclasia) occurs in several small-vessel mechanisms.
- Granulomas and giant cells can be focal or absent in a limited biopsy.
- Active inflammation, healed scarring and vascular remodeling may coexist.

Large-vessel arteritis: Shared phenotype

- Giant cell arteritis and Takayasu arteritis are principal large-vessel forms.
- Both can produce granulomatous inflammation and chronic arterial wall remodeling.
- Aorta and major branches are especially relevant; Medium arteries may also be affected.
- Clinical age and distribution often distinguish entities whose histology overlaps.

Giant cell arteritis: Characteristic distribution

- Chronic arteritis, often granulomatous, commonly targets cranial arterial branches.
- Temporal arteries are accessible for biopsy but are not uniquely susceptible.
- The aorta, carotid/vertebral branches and ophthalmic circulation can be involved.
- Often occurs after age 50 and threatens visual function.

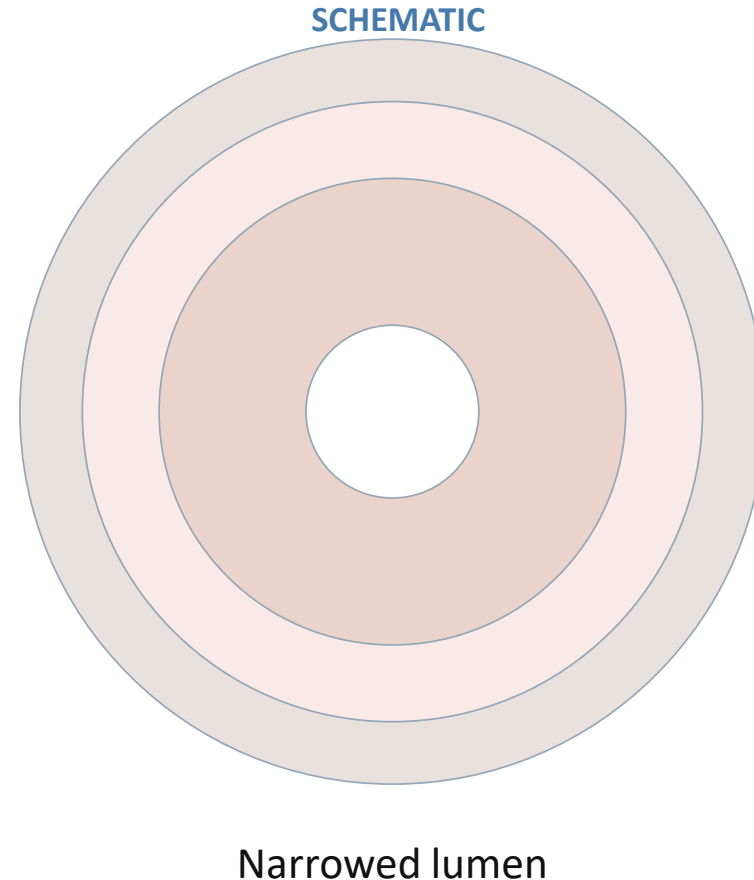
Giant cell arteritis: Proposed immune mechanism



This mechanism is described as likely, not definitively established; Tissue tropism remains unexplained.

Giant cell arteritis: Wall remodeling

- Granulomatous inflammation commonly centers on the internal elastic lamina.
- Elastic fragmentation and intimal thickening accompany luminal compromise.
- Healed lesions may show wall scarring and adventitial fibrosis.



Editable conceptual cross-section; Assess real morphology on authentic histology.

Giant cell arteritis: Skip lesions

- Inflammation is discontinuous along a potentially involved artery.
- Adequate biopsy sampling improves the chance of detecting a diagnostic focus.
- Multinucleated giant cells are useful but not obligatory in each specimen.
- A negative biopsy does not definitively exclude GCA when the clinical syndrome is compelling.

Giant cell arteritis: Clinical pattern

Systemic

Fatigue; Fever; Weight loss

Inflammation may precede
focal complaints

Cranial

New headache; Facial
pain; Tender temporal
artery

Cranial arterial inflammation

Ocular

Diplopia or abrupt vision
loss

Ophthalmic vascular
involvement

Possible permanent blindness makes ocular involvement an urgent clinical concern.

GCA: Ophthalmic injury is the critical complication

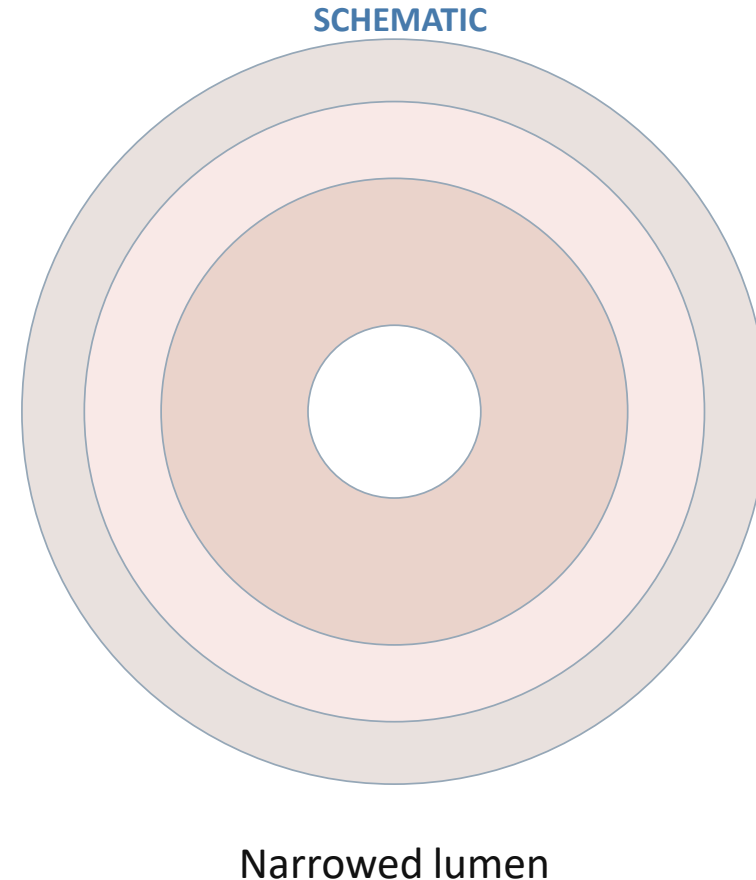
- Temporal disease may coexist with vertebral and ophthalmic artery involvement.
- Visual symptoms can develop abruptly and permanent vision loss can follow.
- Do not use a negative limited biopsy to dismiss a strongly supported clinical syndrome.
- Prompt evaluation and treatment are emphasized by Robbins because ischemic blindness may be irreversible.

Takayasu arteritis: Clinical identity

- Granulomatous arteritis of aorta and major branches, often presenting before age 50.
- The aortic arch and great vessels are especially prone to severe narrowing.
- Markedly weak upper-extremity pulses explain the term “pulseless disease.”
- Immune-mediated T-cell mechanisms are considered likely.

Takayasu arteritis: Aortic-branch stenosis

- Transmural fibrous thickening and intimal hyperplasia narrow large arteries.
- Arch branch obstruction explains asymmetric or diminished upper-extremity pulses.



Illustrative cross-section of stenosis; Not an angiogram.

Takayasu: Inflammation becomes fibrosis

- Early lesions can include adventitial mononuclear inflammation near vasa vasorum.
- Medial infiltrates and granulomatous inflammation may include giant cells.
- Chronic lesions scar across intima, media and adventitia.
- Aortic root involvement occasionally produces dilation and aortic valve insufficiency.

Takayasu: Organ consequences of branch disease

Upper limbs

Weak pulses; Reduced blood pressure

Great-vessel stenosis

Brain / eyes

Neurologic deficits; Visual problems

Cranial circulation compromise

Renal vessels

Systemic hypertension

Renal arterial narrowing

Coronary / pulmonary

Myocardial ischemia; Pulmonary hypertension

Relevant ostial or pulmonary arterial involvement

Giant cell arteritis versus Takayasu arteritis

Characteristic	Giant cell arteritis	Takayasu arteritis
Age profile	Usually >50 years	Usually <50 years
Emphasized vessels	Cranial arteries ± aorta	Aortic arch and major branches
Clinical clue	Headache; potential vision loss	Weak pulses; pressure asymmetry
Histology	Often granulomatous	Often granulomatous; may overlap

Age patterns guide classification but are not histologic diagnostic criteria.

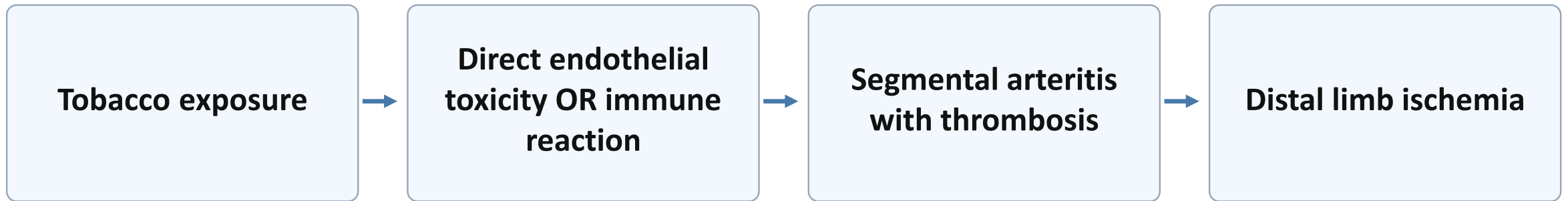
Medium-vessel arteritis: Recurring pathology

- Predominantly involves muscular arteries and their branches.
- Consequences include arterial stenosis, thrombosis, infarction or aneurysm.
- Three major Robbins examples are Buerger disease, polyarteritis nodosa and Kawasaki disease.
- The disease-specific distribution and host context are diagnostically informative.

Buerger disease: Segmental thrombosing vasculitis

- Thromboangiitis obliterans targets distal medium arteries, especially tibial and radial arteries.
- Acute and chronic inflammation accompanies luminal thrombosis.
- Classically affects young individuals with heavy tobacco exposure.
- Reduced distal perfusion explains acral ischemia and tissue injury.

Buerger disease: Tobacco-linked vascular injury



The source presents competing mechanistic explanations; Neither is conclusively established.

Buerger disease: Signature morphology

- Occlusive thrombi may contain neutrophilic microabscesses.
- Granulomatous inflammation surrounds intrathrombotic microabscesses.
- Adjacent veins and peripheral nerves may participate in the inflammatory process.
- Organization, recanalization and fibrosis may occur in longstanding lesions.

Buerger disease: Ischemic and neural symptoms

Vasospasm

Raynaud phenomenon

Often an early complaint

Claudication

Exercise-induced instep foot pain

Distal perfusion failure

Neural pain

Severe rest pain

Associated nerve involvement

Tissue loss

Ulcers or gangrene

Progressive ischemia

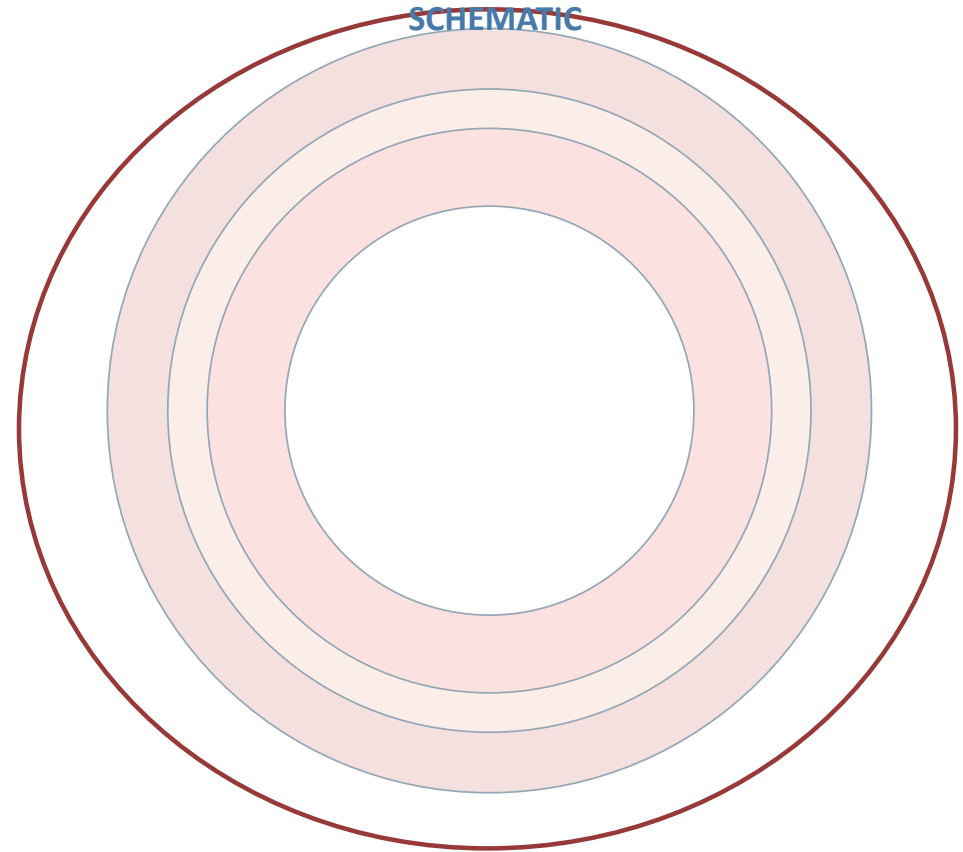
The value of early smoking abstinence in limiting further attacks.

Polyarteritis nodosa: Distribution is decisive

- PAN is a systemic necrotizing arteritis of medium and small muscular arteries.
- Renal and visceral arterial beds are prominent targets.
- Pulmonary arterial circulation and glomerular capillaries are characteristically spared.
- ANCA association is absent in classic PAN; Hepatitis B immune complexes may contribute in some patients.

PAN: Segmental transmural necrotizing injury

- Transmural inflammation and fibrinoid necrosis affect segments of the arterial wall.
- Thrombus and aneurysm may complicate structurally injured segments.
- Part of the wall circumference may remain uninvolved.



Wall damage / remodeling

Original editable arterial lesion schematic, not a histologic image.

PAN: Lesions of different ages coexist

- Active lesions contain mixed inflammatory cells with fibrinoid necrosis and sometimes thrombus.
- Healing lesions show fibrous wall thickening extending into the adventitia.
- Active and healed lesions may occur in neighboring vessels.
- A branch-point predilection and segmental involvement contribute to uneven perfusion.

PAN: Clinicopathologic consequences

Renal arteries

Accelerating hypertension

Ischemia rather than primary glomerulitis

Mesenteric arteries

Abdominal pain; Bloody stools

Intestinal vascular injury

Peripheral nerves

Motor-predominant neuropathic deficits

Vasa nervorum injury

Muscle

Diffuse myalgias

Muscular arterial involvement

PAN versus microscopic polyangiitis

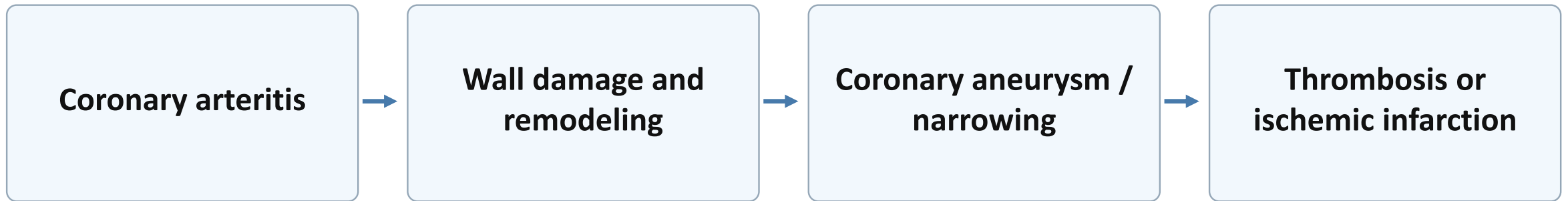
Feature	PAN	MPA
Vessel caliber	Small and medium arteries	Arterioles, capillaries, venules
Glomerular involvement	Glomerular capillaries spared	Necrotizing GN frequent
Pulmonary capillaritis	Not characteristic	Common
ANCA association	Not associated	Often MPO-ANCA
Lesion chronology	Mixed stages coexist	Lesions often same age

These are discriminating patterns, not an exhaustive diagnostic rule set.

Kawasaki disease: An acute childhood arteritis

- Febrile systemic illness largely affecting infants and young children.
- Mucocutaneous inflammation and cervical lymphadenopathy are characteristic.
- Medium- and large-artery involvement can include coronary arteries.
- In susceptible hosts, infection-triggered immune responses are proposed, not proven as a single cause.

Kawasaki coronary injury: A causal sequence



Coronary complications, rather than noncardiac vascular findings, drive much of its clinical significance.

Kawasaki disease: Wall changes

- Dense transmural inflammation can resemble the arteritis of PAN.
- Fibrinoid necrosis tends to be less prominent than in PAN.
- Arterial injury may leave aneurysmal dilation or healed obstructive intimal lesions.
- That treatment reduces clinically important coronary sequelae.

Kawasaki disease: Mucocutaneous syndrome

- Conjunctival and oral erythema accompany fever.
- Hands and feet may be edematous, with palmar or plantar erythema.
- Desquamating rash and cervical lymph node enlargement are characteristic.
- Coronary artery complications range from ectasia to aneurysm and thrombosis.

Small-vessel vasculitis: An immunologic split

- Capillaries, venules, arterioles and intraparenchymal small arteries predominate.
- Immune-complex disease generally has vessel-wall antibody and complement deposits.
- ANCA-associated disease is characteristically pauci-immune.
- Both mechanisms may produce glomerular or pulmonary microvascular lesions.

Small-vessel vasculitis: Deposition pattern

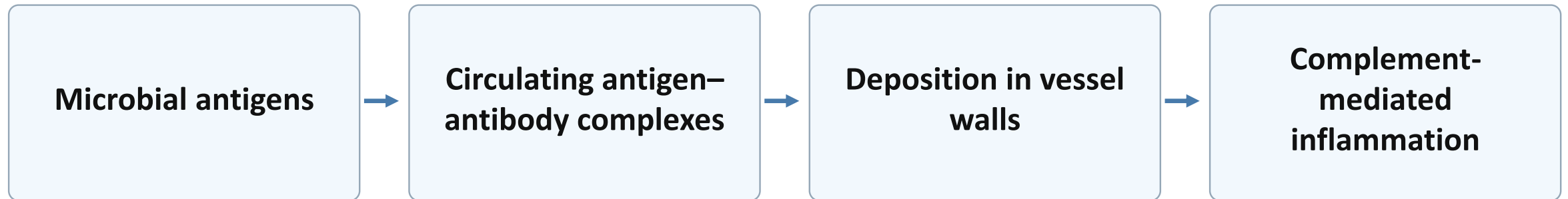
Assessment	Immune-complex pattern	ANCA-associated pattern
Tissue immunoglobulin	Moderate to extensive deposits	Few or no deposits
Complement injury	Frequently contributes	Antibody activation of neutrophils
Common organs	Skin; kidney; systemic beds	Kidney; lung; skin and others
Example	IgA/cryoglobulinemic vasculitis	MPA; GPA; EGPA

Direct anti-GBM binding is mechanistically distinct despite immunoglobulin deposition.

Drug-triggered immune-complex vasculitis

- A drug may act as a hapten bound to an endogenous carrier protein.
- Foreign therapeutic proteins can themselves be antigenic.
- Antigen–antibody complexes recruit inflammatory cells to small vessels.
- Cutaneous lesions are common; Removing the offending agent is an important etiologic intervention.

Infection can cause vasculitis without invading the wall



Hepatitis B surface antigen-antibody complexes are a Robbins example linked to a subset of PAN.

Systemic autoimmune diseases may inflame vessels

- Systemic lupus erythematosus can generate DNA/anti-DNA immune complexes.
- Rheumatoid vasculitis tends to occur in longstanding severe rheumatoid arthritis.
- Anti-endothelial antibodies and cellular mechanisms may coexist with immune complexes.
- The context of systemic disease helps interpret vascular lesions.

IgA and cryoglobulinemic vasculitis

Entity	Immunologic basis described in Robbins	Interpretive anchor
IgA vasculitis	Complexes involving abnormally glycosylated IgA	Small-vessel immune-complex injury
Cryoglobulinemic vasculitis	Immunoglobulins that precipitate below body temperature	Vascular immune deposits
Common implication	Vessel-wall Ig/complement deposition	Look for systemic associations

Subclassification and test interpretation extend beyond this introductory pathology comparison.

Anti-GBM disease has direct antigen binding

- Autoantibodies recognize glomerular and pulmonary capillary basement membranes.
- Unlike circulating antigen–antibody immune complexes, binding is directly to target basement membrane.
- Complement activation and leukocyte injury can nevertheless resemble other antibody-mediated disease.
- Kidney and lung involvement follows the anatomic distribution of the antigen.

Microscopic polyangiitis: Phenotype

- MPA is a necrotizing vasculitis dominated by small vessels.
- Necrotizing glomerulonephritis and pulmonary capillaritis are prominent.
- MPO-ANCA association is common, while immune deposits are usually sparse.
- Many different organ vascular beds may be involved.

MPA: Histology and leukocytoclasia

- Segmental fibrinoid necrosis occurs in capillary-scale and small arterial vessels.
- Granulomatous inflammation is absent in its typical morphology.
- Fragmented neutrophil nuclei may create a leukocytoclastic pattern.
- Leukocytoclasia is not specific: Immune-complex vasculitis can look similar.

MPA: Small vessels, multisystem symptoms

Lung

Hemoptysis

Pulmonary capillaritis

Kidney

Hematuria; Proteinuria

Glomerular injury

Skin

Palpable purpura

Superficial small-vessel inflammation

Other organs

Bowel symptoms; Weakness

Variable microvascular territories

GPA: Three interlocking lesions

Respiratory granulomas

Necrotizing lesions in
upper and/or lower
airways

Sinonasal and lung
abnormalities

Necrotizing vasculitis

Small- to medium-sized
vessels

Systemic vascular injury

Glomerulonephritis

Focal necrosis often with
crescents

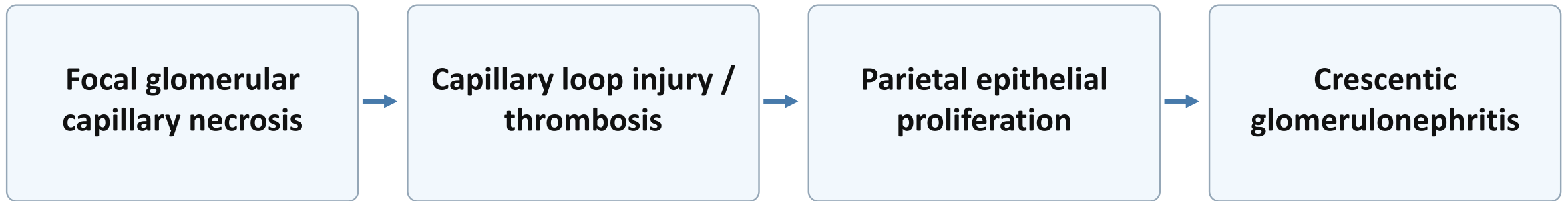
Renal disease

Limited disease may initially be restricted to the respiratory tract.

GPA: Upper airway and lung morphology

- Upper airway lesions may show granulomatous sinusitis or mucosal ulceration.
- Lung involvement may produce nodules or cavitating granulomatous lesions.
- Multifocal necrotizing granulomatous vasculitis can be accompanied by alveolar hemorrhage.
- Organizing lesions may progressively fibrose.

GPA glomerular injury progresses in severity



This is a conceptual severity sequence, not a required temporal pathway in every patient.

GPA: Serology complements morphology

- PR3-ANCA is strongly associated with GPA in the supplied Robbins description.
- Granulomatous respiratory pathology and necrotizing glomerulonephritis remain central to recognition.
- A single positive antibody result does not by itself establish the full disease phenotype.
- The source connects antibody activity with treatment response and disease recurrence.

EGPA: Asthma, eosinophilia and vasculitis

- Eosinophilic granulomatosis with polyangiitis is a necrotizing vasculitis of small vessels.
- Asthma, allergic rhinitis and pulmonary infiltrates are common contexts.
- Peripheral eosinophilia accompanies eosinophil-rich vascular and extravascular lesions.
- Extravascular necrotizing granulomas distinguish the classic morphology.

EGPA contrasted with other ANCA vasculitides

Characteristic	MPA	GPA	EGPA
Granulomas	Absent	Necrotizing	Eosinophil-rich
Respiratory pattern	Capillaritis	Granulomatous nodules	Asthma / allergic disease
Serologic link	MPO-ANCA	PR3-ANCA	MPO-ANCA in a subset
Organ clue	Renal + lung	Airways + kidney	Cardiac eosinophilic injury

Neither ANCA positivity nor one histologic feature substitutes for the full phenotype.

EGPA: Systemic injury beyond the airway

- Purpura, gastrointestinal bleeding and renal abnormalities can occur.
- Eosinophil-rich myocardial inflammation can damage cardiac muscle.
- Cardiomyopathy is a major clinical risk in the Robbins account.
- The combination of eosinophils and granulomas is a particularly useful morphologic clue.

Behçet syndrome affects arteries and veins

- Multisystem inflammatory disease may cause vasculitis in both arterial and venous beds.
- Recurrent oral ulcers, often with genital ulcers, are prominent clinical clues.
- Vascular involvement may include arterial aneurysm and venous thrombosis.
- The precise trigger is unknown; Abnormal Th17-associated immune responses are proposed.

Behçet syndrome: Organ manifestations

Mucosa

Recurrent oral $\pm$ genital ulcers

Common distinguishing clue

Eye

Uveitis or hypopyon

Threatens ocular function

Central nervous system

Inflammatory brainstem lesions

Potentially severe deficits

Vascular

Aneurysm or venous thrombosis

Both arteries and veins involved

Integrated comparison: Major arterial vasculitides

Disease	Distinguishing setting	Prominent injury
Giant cell arteritis	Older adult; headache/vision complaint	Cranial arterial granulomatous injury
Takayasu	Younger patient; weak pulses	Aortic branch stenosis
Buerger	Heavy tobacco exposure; distal symptoms	Thrombosing limb arteritis
PAN	Systemic visceral and renal arteries	Necrotizing arteritis; infarction
Kawasaki	Febrile mucocutaneous childhood illness	Coronary arteritis / aneurysm

This comparison is a diagnostic orientation, not a formal classification score.

Integrated comparison: Small-vessel entities

Entity	Immunopathology	Distinguishing clue
Immune-complex vasculitis	Ig / complement deposits	Drugs, infection, autoimmunity, IgA
Microscopic polyangiitis	Pauci-immune; MPO-linked	Necrotizing GN; capillaritis
Granulomatosis with polyangiitis	Pauci-immune; PR3-linked	Necrotizing respiratory granulomas
Eosinophilic GPA	Pauci-immune subset; eosinophils	Asthma; eosinophilic granulomas
Anti-GBM disease	Direct basement membrane binding	Glomerular and pulmonary capillaries

Use morphologic and clinical distribution in addition to the immunologic category.

Five discriminators before labeling a vasculitis

- Is the mechanism direct infection, immune injury or physical/chemical damage?
- Which vessel caliber and organ distribution predominate?
- Is injury granulomatous, necrotizing, eosinophil-rich or thrombosing?
- Do tissue deposits support an immune-complex process or pauci-immune injury?
- Does the clinical pattern align with available serology and tissue findings?

Clinical application: New headache and visual symptoms

CLINICAL STEM

An older adult develops new temporal headache and abrupt visual disturbance. Arterial biopsy samples a short segment and shows no giant cells.

Interpretation: Giant cell arteritis remains a serious possibility.

Cranial distribution and vision risk support urgent assessment; Skip lesions and occasional absence of giant cells limit the exclusionary value of one biopsy.

Clinical application: A pulmonary–renal presentation

CLINICAL STEM

A patient has hemoptysis, hematuria and necrotizing glomerular injury. Tissue shows little immunoglobulin deposition; Respiratory granulomas are not demonstrated.

Interpretation: Consider an ANCA-associated pauci-immune small-vessel vasculitis.

The pulmonary–renal distribution and pauci-immune pattern support the group. MPA versus GPA requires the rest of the clinical, morphologic and serologic phenotype.

Clinical application: Painful ischemic toes

CLINICAL STEM

A young heavy smoker develops severe distal rest pain, superficial thrombophlebitis and ischemic toe ulcers.

Interpretation: Thromboangiitis obliterans (Buerger disease) is an important consideration.

Tobacco association, distal thrombosing disease and associated venous/neural involvement produce the characteristic clinicopathologic pattern.

Clinical application: Visceral ischemia without GN

CLINICAL STEM

A patient has difficult hypertension, abdominal pain and motor neuropathy; Visceral arterial biopsy shows segmental transmural necrotizing arteritis, but no glomerular capillaritis.

Interpretation: The pattern favors polyarteritis nodosa over MPA.

PAN affects medium/small muscular arteries, whereas the hallmark small-vessel glomerular and lung capillary lesions point toward MPA.

Synthesis: Mechanism, caliber and morphology

- Definition: The common denominator is inflammation within vascular walls.
- Etiology: Distinguish direct infection from immune-mediated injury and other triggers.
- Anatomy: Caliber and organ distribution determine the dominant clinical syndrome.
- Pathology: Immune deposition, granulomas, necrosis and thrombosis separate major patterns.
- Integration: Diagnosis requires tissue, clinical context and appropriately interpreted antibodies.

Primary teaching source

Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026). Section: Vasculitis.

Sections: Vasculitis; Infectious and Noninfectious Vasculitis; Large, Medium and Small Vessel Vasculitis.

The schematic drawings and comparison diagrams in this lecture are original, editable teaching constructs—not clinical images.