

# Medium Vessel Vasculitis

Thromboangiitis obliterans • Polyarteritis nodosa • Kawasaki disease

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Vascular injury, morphology and clinicopathologic consequences

**Dr Abu Suraih Sakhri**

MBBS, MD (Pathology)

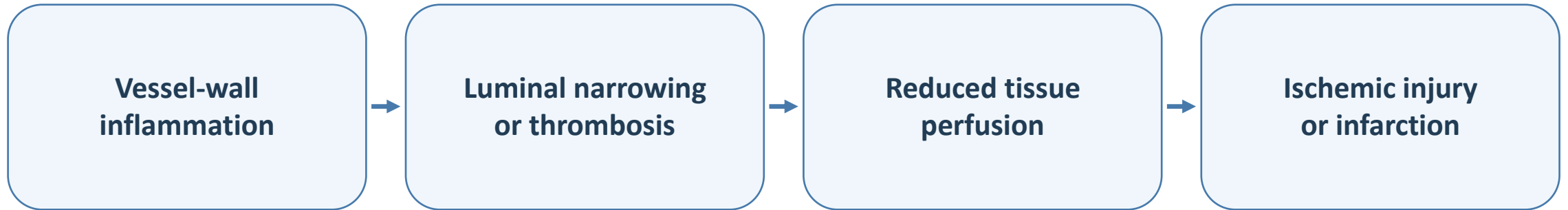
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## Learning objectives

- Define medium vessel vasculitis and recognize overlap between vessel-size categories.
- Distinguish Buerger disease, polyarteritis nodosa, and Kawasaki disease by their target vessels and clinical context.
- Explain how thrombosis, necrotizing arteritis, and aneurysms generate characteristic complications.
- Interpret representative clinical scenarios using morphology and distribution.

Emphasis: Mechanisms → arterial lesions → organ dysfunction.

# Vasculitis: An inflammatory vascular injury



The affected vascular bed determines the clinical phenotype.

## What defines the medium-vessel group?

- Predominantly affects medium-sized muscular arteries and their branches.
- Includes visceral arteries, limb arteries, and coronary arteries depending on the entity.
- Inflammatory stenoses and aneurysms are characteristic structural consequences.
- “Medium vessel” identifies a predilection, not an absolute vessel-size boundary.

The three core entities differ more in distribution and morphology than in caliber alone.

## Three major disorders—three target patterns

### **Buerger disease**

Distal extremity arteries;  
Thrombosis; Associated  
venous and nerve  
involvement.

### **Polyarteritis nodosa**

Systemic muscular arteries;  
Renal and visceral beds;  
Necrotizing arteritis.

### **Kawasaki disease**

Childhood mucocutaneous  
illness; Coronary-artery  
arteritis and aneurysms.

Anatomical preference is a major diagnostic discriminator.

# Vasculitis is not only a question of size

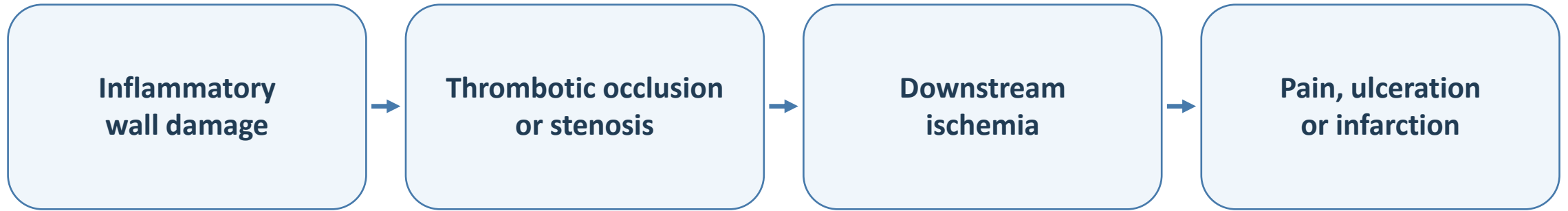
## Classification axes

- Predominant artery caliber
- Target tissue and vascular bed
- Histologic pattern and immune mechanism

## Practical constraint

- Substantial overlap in affected vessel sizes
- Clinical and pathologic exceptions occur
- Interpret classification with organ distribution

# How an inflamed artery injures tissue



Aneurysm formation reflects weakening rather than merely narrowing the arterial wall.

# Stenosis and aneurysm are different outcomes

## Flow-limiting lesion

- Intimal thickening or luminal thrombosis
- Decreased distal perfusion
- Ischemia, pain, infarction

## Wall-weakening lesion

- Destructive inflammation of arterial wall
- Focal dilatation / aneurysm
- Potential thrombosis, hemorrhage or rupture

## First-pass differential: Medium-vessel vasculitis

| Feature               | Buerger disease         | PAN                             | Kawasaki disease               |
|-----------------------|-------------------------|---------------------------------|--------------------------------|
| Typical context       | Young heavy smoker      | Young adults; any age           | Infants / young children       |
| Dominant distribution | Distal limbs            | Renal / visceral arteries       | Coronary arteries              |
| Signature lesion      | Inflammatory thrombosis | Segmental necrotizing arteritis | Transmural arteritis; aneurysm |
| Key threat            | Distal gangrene         | Visceral / renal ischemia       | Myocardial infarction          |

## Buerger disease: Defining lesion

- Also termed thromboangiitis obliterans.
- Segmental acute and chronic inflammation with thrombosis of medium arteries.
- Especially affects tibial and radial arteries.
- Vascular insufficiency is predominantly distal and limb-centered.

The combination of arteritis + occlusive thrombus is essential.

# Buerger disease targets distal arterial beds

## Affected muscular arteries

### Tibial arteries

Distal lower-limb ischemia

### Radial arteries

Distal upper-limb ischemia

### Adjacent veins

Superficial nodular phlebitis

### Nearby nerves

Intense pain

### Distal tissues

Ulceration and gangrene

### Tobacco exposure

Strong exposure association

## Tobacco exposure is a central association

- Classically occurs in young heavy cigarette smokers.
- A strong relationship with cigarette use.
- Tobacco exposure may injure the endothelium directly or modify vessel-wall proteins.
- The relationship supports prevention but does not establish one proven molecular mechanism.

Association is strong; The exact initiating pathogenesis is incompletely resolved.

# Buerger pathogenesis: Two proposed routes

## Direct toxicity hypothesis

- A tobacco constituent causes idiosyncratic endothelial injury
- Endothelial dysfunction favors vascular inflammation

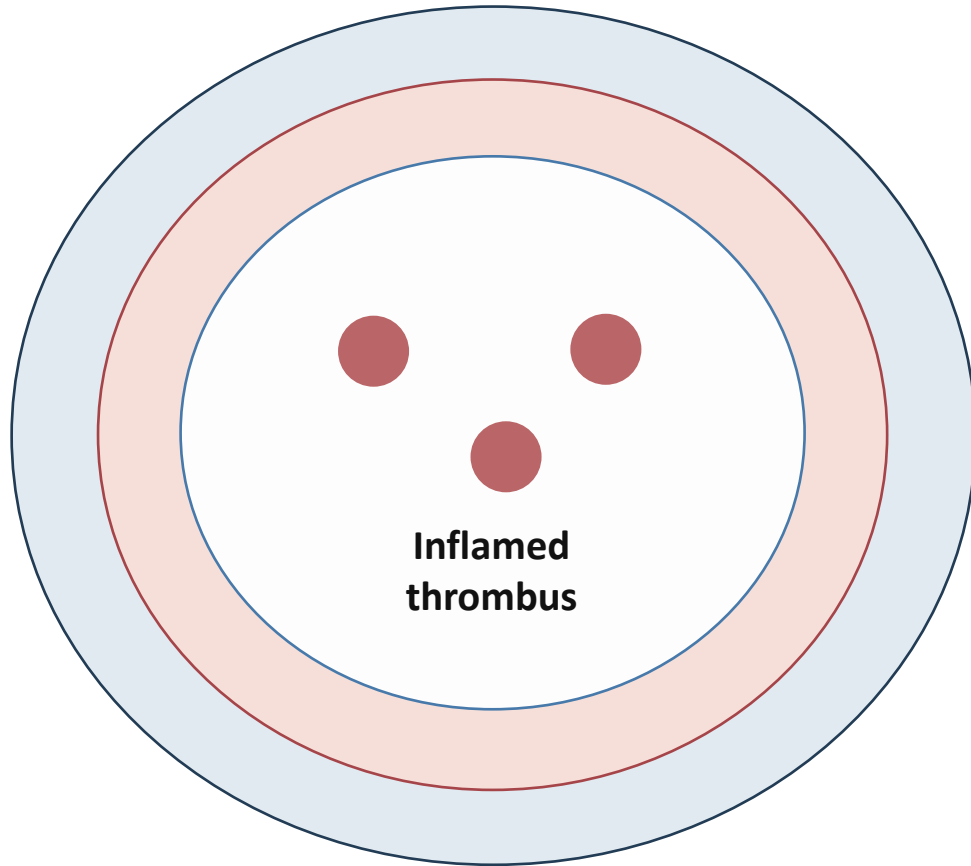
## Immune hypothesis

- Tobacco-derived agents alter vascular wall proteins
- Host immune response targets the modified structures

## Functional endothelial findings in Buerger

- Some affected persons exhibit hypersensitivity to injected tobacco extracts.
- Endothelium-dependent vasodilation after acetylcholine challenge may be impaired.
- Associations with certain MHC haplotypes support susceptibility.
- Neither observation alone constitutes a diagnostic test in this lecture.

# Buerger morphology: Artery and occlusive thrombus



## Arterial wall

Acute and chronic inflammation

## Lumen

Inflammatory thrombus

## Thrombus center

Possible neutrophilic microabscesses

## Evolution

Organization and recanalization

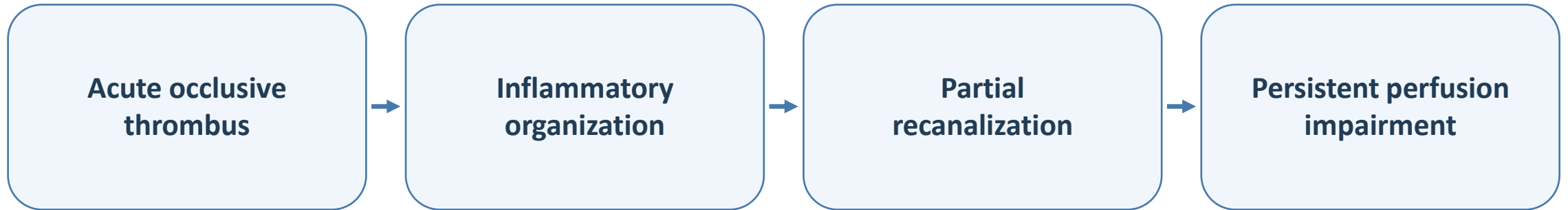
Original schematic — not histology

## Microabscesses are within the thrombus

- Characteristic thrombi may contain small aggregates of neutrophils.
- Granulomatous inflammation can surround these microabscesses.
- Vessel-wall inflammatory cells coexist with the intraluminal lesion.
- This morphology is illustrated figure but not reproduced here.

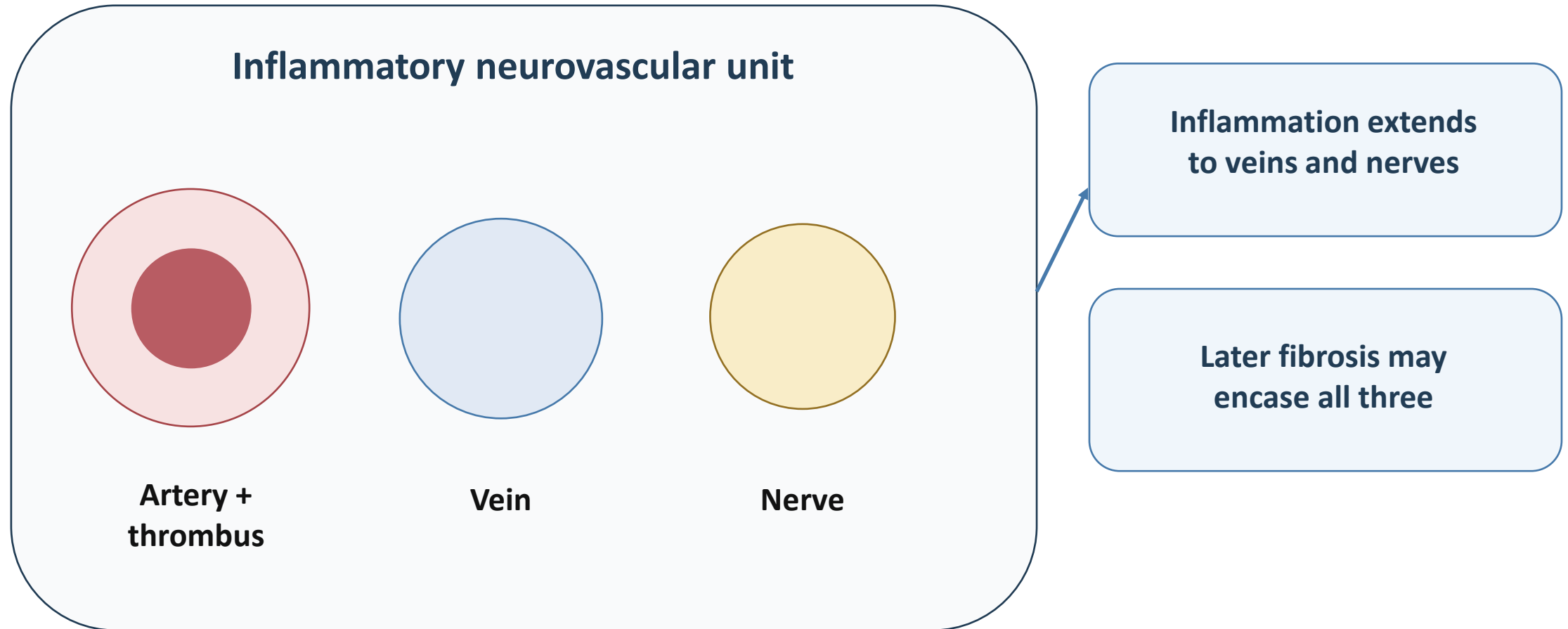
Distinguish thrombus-associated microabscesses from a generic mural inflammatory infiltrate.

# Thrombus evolution can change the lumen



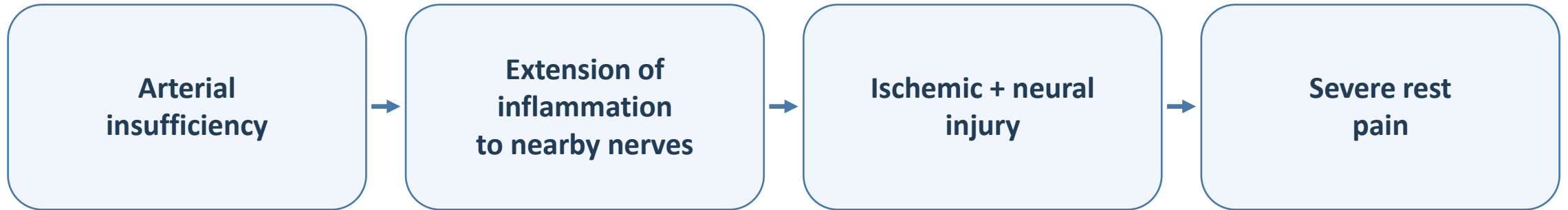
Recanalization does not imply full restoration of distal vascular function.

# Buerger uniquely extends beyond arteries



Original simplified schematic — not histology

## Nerve involvement helps explain disproportionate pain



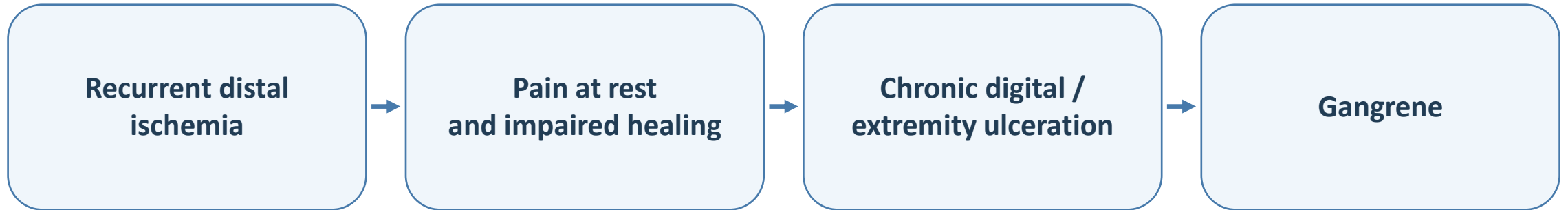
The source explicitly links unusually intense pain to neural involvement.

## Early clues in Buerger disease

- Raynaud phenomenon may precede fixed tissue injury.
- Instep claudication causes exertional foot pain.
- Superficial nodular phlebitis can accompany arterial disease.
- These findings suggest disease in distal neurovascular territories.

An early symptom complex is not the same as established gangrene.

## Late tissue injury in Buerger disease



The lesion evolves from reversible symptoms toward structural tissue loss.

# Smoking abstinence: Stage matters

## Early course

- Abstinence may ameliorate further attacks
- Prevents continued smoke-related exposure

## Established lesions

- Fixed vascular injury may persist despite abstinence
- Cessation is not equivalent to reversal of organized lesions

# Buerger: Integrated phenotype

## Exposure

Heavy cigarette smoking is the main epidemiologic association.

## Anatomy

Distal limb arteries;  
Associated superficial veins and nerves.

## Outcome

Occlusion produces claudication, rest pain, ulcers, gangrene.

This vascular-neural-thrombotic pattern distinguishes it from systemic visceral PAN.

## Clinical application: Distal ischemia

A young heavy cigarette smoker develops exercise-induced instep pain, painful digits, and recurrent superficial nodular phlebitis. Subsequent symptoms include severe pain at rest.

**Which disease and which vascular relationships best account for the presentation?**

## Case resolution: Distal thromboangiitis

- Most consistent entity: Thromboangiitis obliterans (Buerger disease).
- Distal muscular artery thrombosis accounts for ischemic claudication.
- Inflammation extending into veins explains nodular phlebitis.
- Adjacent nerve involvement contributes to severe pain.

No single symptom establishes the diagnosis; The pattern is the teaching point.

## PAN: Systemic necrotizing muscular arteritis

- Polyarteritis nodosa (PAN) affects small- to medium-sized muscular arteries.
- It preferentially involves renal and visceral arterial beds.
- The pulmonary circulation is characteristically spared.
- Clinical injury results from ischemia and infarction of supplied organs.

PAN is an arterial disease; It does not classically target glomerular capillaries.

# PAN has an organ-selective distribution

## Affected muscular arteries

### Kidney

Renal arteries → hypertension

### Heart

Coronary branches → ischemia

### Liver

Hepatic arterial involvement

### Gastrointestinal tract

Pain / hemorrhagic injury

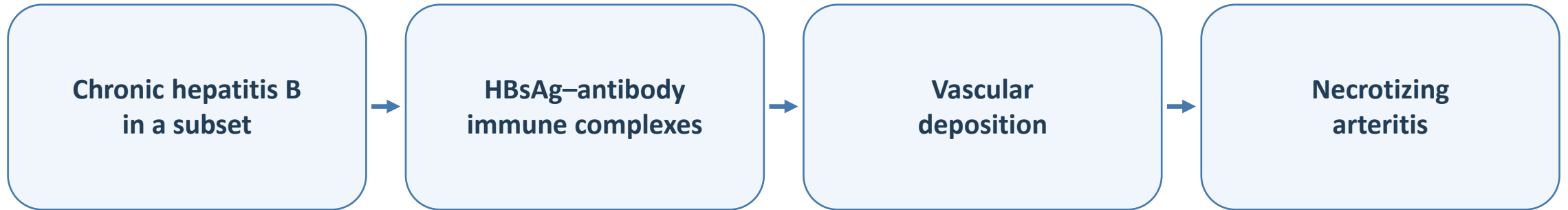
### Peripheral nerves

Neuritis, often motor

### Muscle

Diffuse myalgia

## A subset of PAN is associated with hepatitis B



The textbook estimates an HBV association in approximately one-third; This is not presented as a contemporary population estimate.

## Most PAN cases are not explained by HBV

- The source links roughly one-third of PAN cases to chronic hepatitis B.
- It describes the cause in remaining patients as unknown.
- An immune-complex model explains the HBV-associated subset.
- Avoid assigning that specific trigger to every PAN patient.

Etiologic heterogeneity is compatible with a recognizable arterial lesion.

# PAN is not an ANCA-associated vasculitis

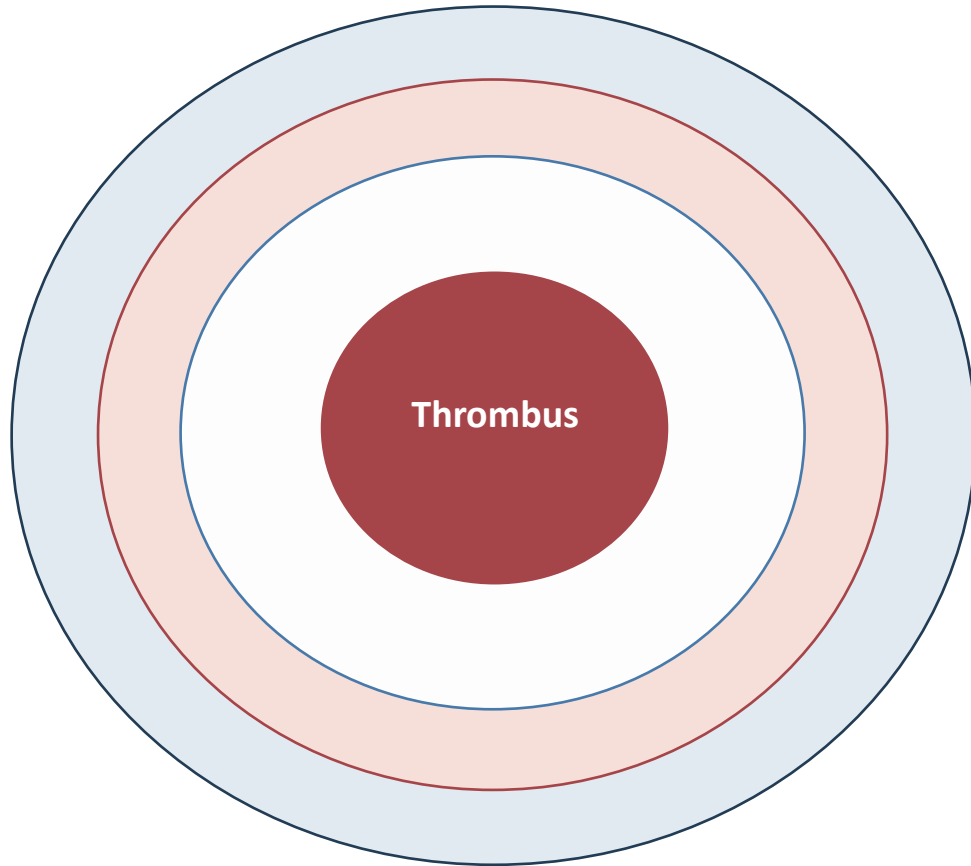
## PAN (Robbins)

- No association with antineutrophil cytoplasmic antibodies
- Predominantly muscular arteries
- No classic glomerular capillaritis

## ANCA-associated small-vessel group

- PR3-ANCA and MPO-ANCA patterns are important
- Often involves arterioles or capillaries
- Glomerulonephritis and pulmonary capillaritis may occur

# The PAN lesion is segmental and transmural



## **Segmental**

Only part of artery circumference may be involved

## **Transmural**

Inflammatory injury crosses the wall

## **Necrotizing**

Fibrinoid necrosis in active disease

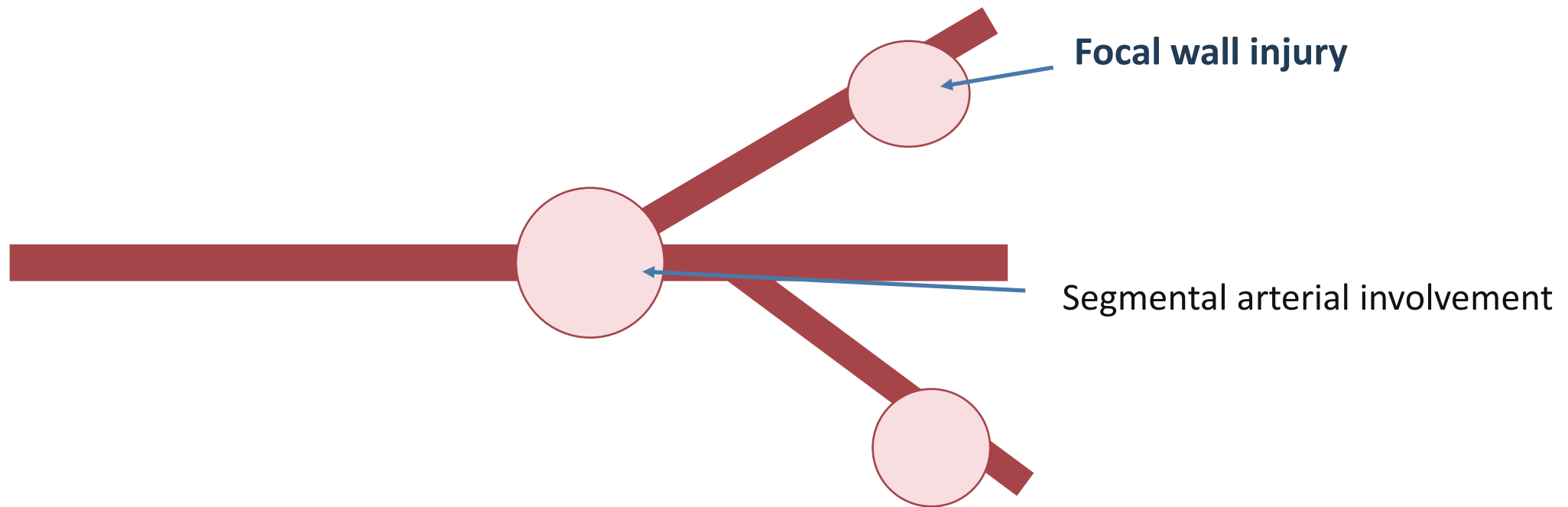
## **Luminal**

Thrombosis may coexist

Original schematic — not histology

## PAN often targets arterial branch points

Lesions favor arterial branches and may involve only part of a wall

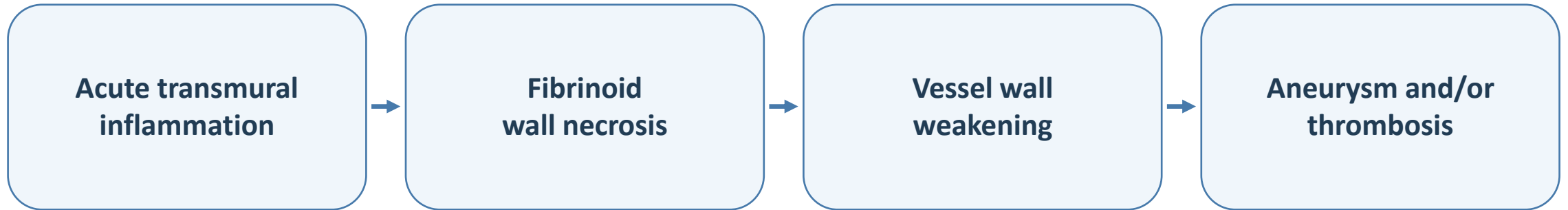


Schematic arterial tree, not angiography

## Active PAN: A mixed inflammatory infiltrate

- Acute lesions show transmural arterial inflammation.
- Neutrophils, eosinophils and mononuclear cells may coexist.
- Fibrinoid necrosis is a frequent accompaniment.
- Lumen thrombosis adds an immediate flow-limiting component.

## Fibrinoid necrosis signals destructive wall injury



Fibrinoid necrosis denotes wall destruction, not simply a thrombus.

# Multiple lesion ages coexist in PAN

## Active lesions

- Leukocyte-rich inflammation
- Fibrinoid necrosis
- Possible thrombotic occlusion

## Healed / older lesions

- Fibrous thickening extends toward adventitia
- Remodeling and persistent stenosis
- Different stages may coexist in one organ

# Downstream injury depends on perfusion loss

## Reduced flow

Ischemic atrophy when perfusion remains chronically insufficient.

## Abrupt occlusion

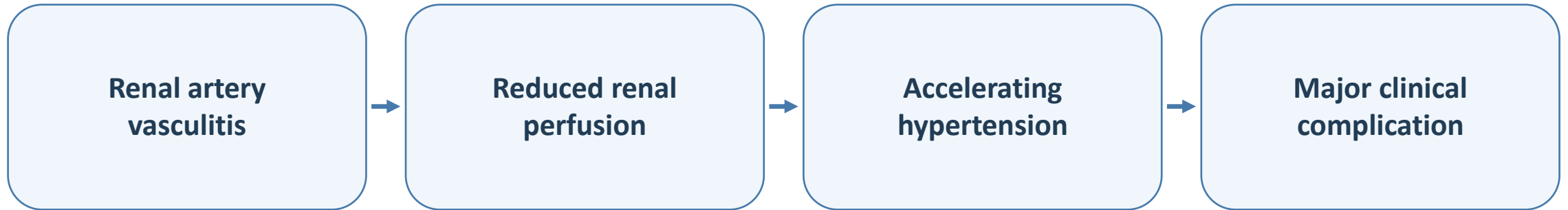
Infarcts and focal ulcerations after severe arterial compromise.

## Wall disruption

Hemorrhage may accompany destructive arteritis or aneurysm.

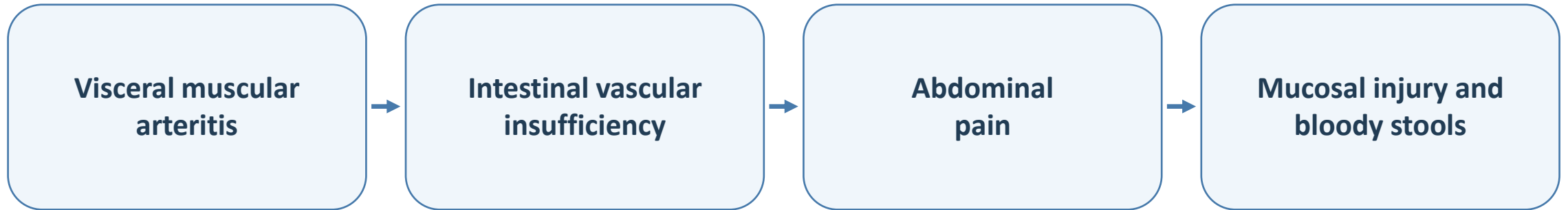
The pathologic consequences follow directly from arterial geometry and injury.

## Renal PAN: Arterial injury → hypertension



The renal-artery pattern is distinct from primary glomerular capillaritis.

# Gastrointestinal PAN: Ischemic abdominal illness



Pain and gastrointestinal bleeding may reflect the same ischemic mechanism.

## PAN can cause peripheral neuritis

- Peripheral nerves are vulnerable to ischemia from affected feeding arteries.
- Peripheral neuritis is a typical presentation.
- The motor component is described as predominant.
- Coexisting myalgias and visceral symptoms suggest systemic arterial involvement.

## PAN can remit and relapse

- Clinical disease can be episodic, with symptom-free intervals.
- Different vascular territories may be affected at different times.
- Mixed-age lesions provide a morphologic counterpart to continued injury.
- An unremarkable interval does not erase the structural arterial damage.

# PAN severity derives from vital-organ ischemia

## Organ threat

- Renal involvement: Important contributor to mortality
- Visceral disease: Ischemic bowel injury
- Cardiac disease: Arterial ischemia

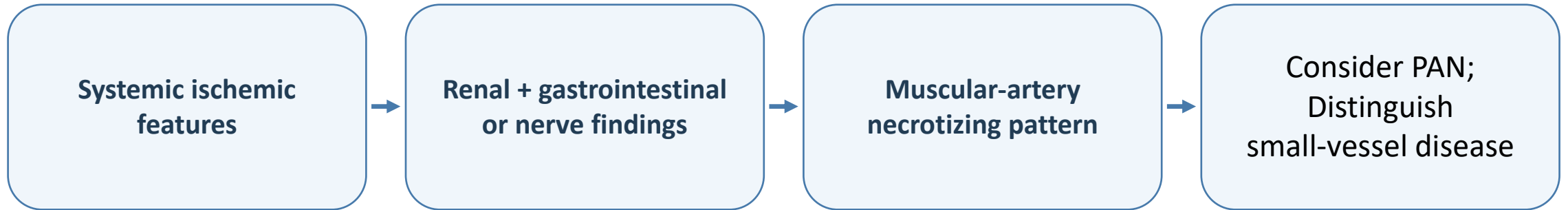
## Source-reported outcome

- Untreated PAN is commonly fatal account
- Immunosuppression substantially improves survival
- Up to 80% five-year survival with treatment

## PAN versus microscopic polyangiitis

| Discriminator          | Polyarteritis nodosa             | Microscopic polyangiitis              |
|------------------------|----------------------------------|---------------------------------------|
| Primary vessel pattern | Medium / small muscular arteries | Small vessels incl. capillaries       |
| Glomerular involvement | No classic glomerular vasculitis | Necrotizing glomerulonephritis common |
| Pulmonary circulation  | Usually spared                   | Pulmonary capillaritis may occur      |
| ANCAs                  | No association                   | Often MPO-ANCA                        |

# PAN diagnostic reasoning starts with distribution



This is a teaching pathway, not formal diagnostic or classification criteria.

## Clinical application: Visceral and renal ischemia

A young adult develops rapidly accelerating hypertension, abdominal pain with bloody stools, diffuse myalgias, and motor-predominant peripheral neuritis.

**Which vasculitis pattern and vascular lesions best unite these findings?**

## Case resolution: Polyarteritis nodosa

- The combination favors systemic PAN.
- Renal muscular-artery lesions explain hypertension.
- Visceral ischemia accounts for pain and bloody stools.
- Necrotizing, segmental arteritis may produce thrombosis, aneurysm and infarction.

A multisystem ischemic syndrome can have a unifying arterial origin.

## Kawasaki disease: Childhood medium-vessel arteritis

- An acute febrile illness, generally of infancy and childhood.
- 80% of patients are younger than five years.
- Large- to medium-sized arteries may be involved.
- Coronary arteritis determines much of the clinical importance.

The dominant threat is coronary rather than renal or distal-limb ischemia.

# A coronary-centered vascular phenotype

## Affected muscular arteries

### Coronary arteries

Arteritis and wall injury

### Coronary aneurysm

Focal arterial dilation

### Coronary thrombosis

Luminal occlusion

### Myocardium

Potential infarction

### Cardiovascular outcome

Occasional sudden death

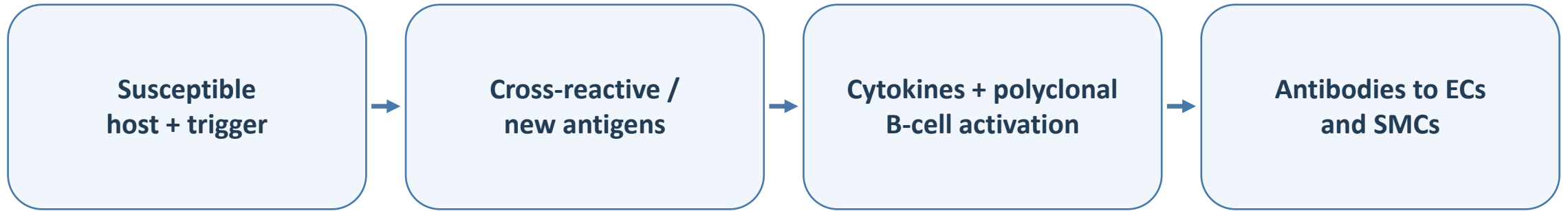
### Healed arteries

Obstructive intimal thickening

## Kawasaki etiology remains incompletely resolved

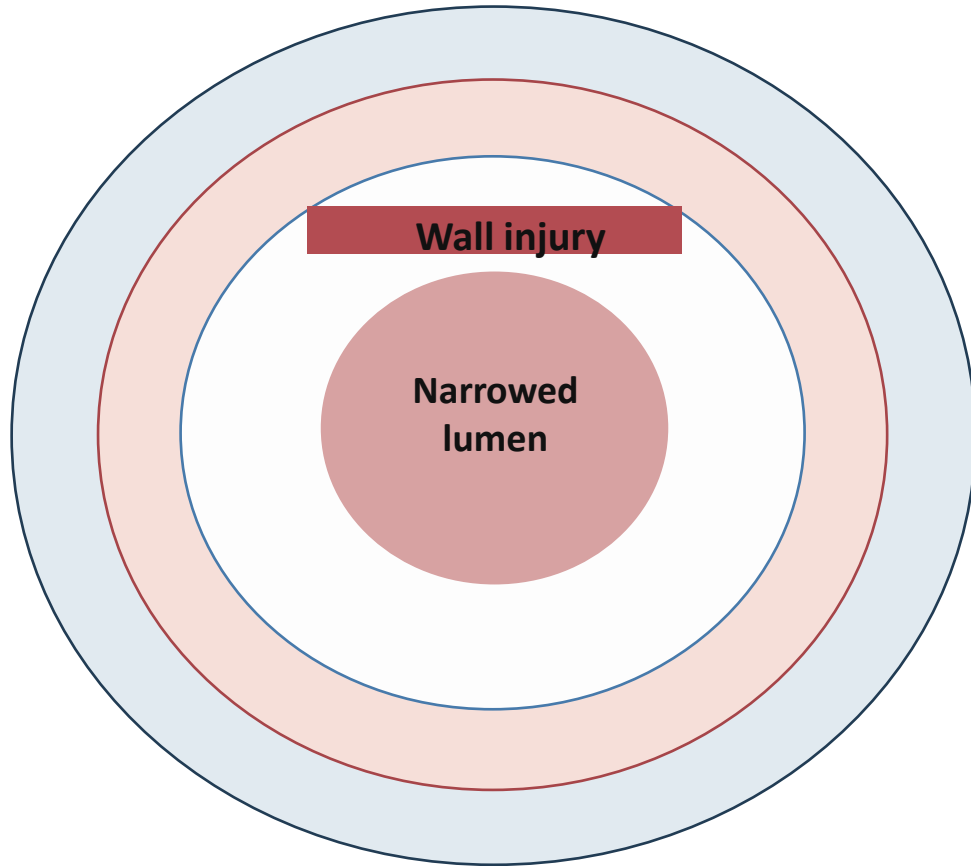
- A trigger following infection is proposed, often framed as viral.
- Host genetic susceptibility is considered relevant.
- Immune cross-reactivity as a candidate mechanism.
- This hypothesis is not an identified single infectious cause.

# Proposed immune sequence in Kawasaki disease



This is the mechanism proposed by Robbins, not an established universal pathway.

# Kawasaki histology is transmural



## Arteritis

Dense transmural inflammatory infiltrate

## Necrosis

Often less fibrinoid necrosis than in PAN

## Wall integrity

Injury permits aneurysm formation

## Healing

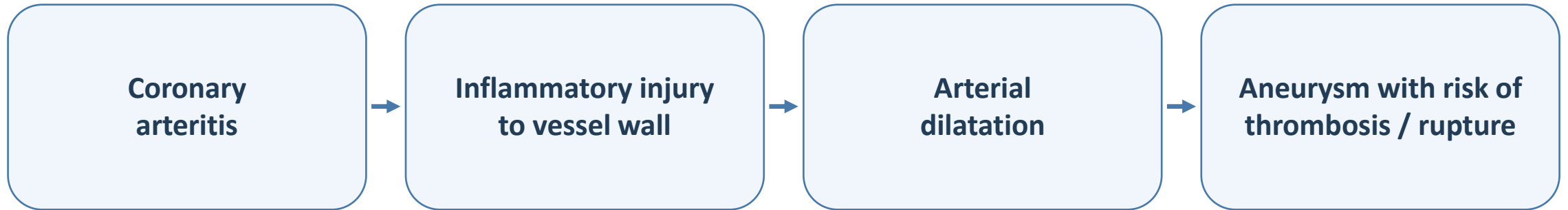
Obstructive intimal thickening may remain

Original schematic — not histology

## PAN and Kawasaki share an arterial injury pattern

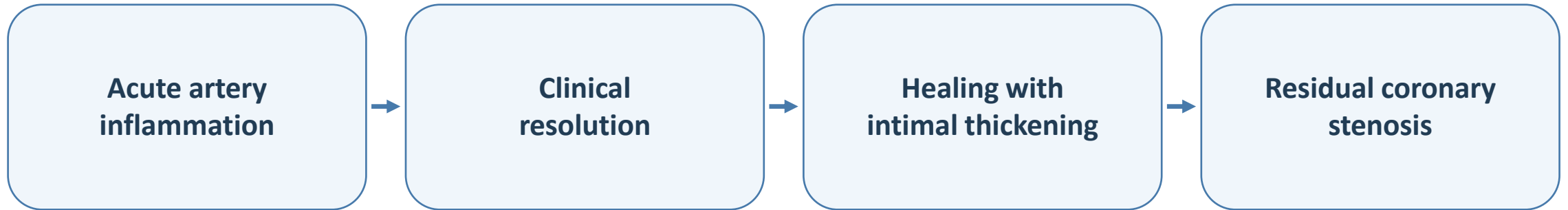
| Feature            | PAN                              | Kawasaki disease              |
|--------------------|----------------------------------|-------------------------------|
| Inflammation       | Segmental transmural necrotizing | Dense transmural inflammatory |
| Fibrinoid necrosis | Common in active lesions         | Usually less conspicuous      |
| Aneurysms          | May accompany thrombosis         | Major coronary complication   |
| Clinical context   | Systemic visceral / renal        | Febrile childhood syndrome    |

# Kawasaki coronary aneurysms: Mechanism



Coronary arterial inflammation can persist as a mechanical vascular hazard.

## Healed Kawasaki lesions may obstruct flow



Self-limited fever does not guarantee normalization of the affected artery.

# Mucocutaneous lymph node syndrome

## Mucosal / ocular

Conjunctival and oral erythema; Oral mucosal changes.

## Extremities / skin

Edema of hands and feet;  
Palm/sole redness;  
Desquamating rash.

## Lymph nodes

Cervical lymph-node enlargement in a febrile child.

The clinical grouping provides a clue to possible coronary risk.

# Extremity findings evolve with the illness

## Early inflammatory signs

- Hand and foot edema
- Erythema of palms and soles

## Subsequent epithelial change

- Desquamating rash
- Cutaneous changes accompany systemic fever

# Coronary complications explain major morbidity

## **Ectasia / aneurysm**

Loss of normal coronary caliber after inflammatory wall injury.

## **Thrombotic occlusion**

Intraluminal clot can compromise myocardial perfusion.

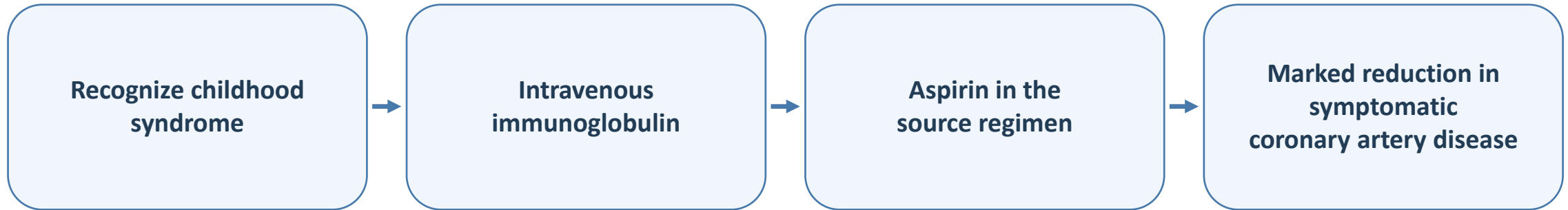
## **Myocardial damage**

Infarction or sudden death can follow severe coronary involvement.

## Untreated coronary sequelae are not rare

- The source estimates cardiovascular sequelae in approximately 20% of untreated patients.
- The spectrum includes clinically silent coronary arteritis and coronary ectasia.
- Large coronary aneurysms can rupture or thrombose.
- These textbook figures describe an untreated cohort, not treated contemporary rates.

# Therapy changes Kawasaki coronary outcomes



Therapeutic statement reflects Robbins; No dose or contemporary guideline is inferred.

# Kawasaki-like MIS-C: Related description, not identity

## Textbook observation

- A Kawasaki-like inflammatory syndrome has been described after SARS-CoV-2 infection
- Term used: Multisystem inflammatory syndrome in children (MIS-C)

## Interpretive boundary

- Phenotypic similarity does not prove identical disease mechanisms
- Do not substitute MIS-C diagnostic criteria for Kawasaki disease

## Clinical application: Febrile mucocutaneous syndrome

A preschool child develops fever, conjunctival and oral erythema, swelling of hands and feet, erythematous palms and soles, desquamation, and cervical lymphadenopathy.

**Which artery group makes this clinical syndrome especially important?**

## Case resolution: Evaluate the coronary risk

- The constellation is characteristic of Kawasaki disease in the source.
- Coronary arterial inflammation is the central pathology concern.
- Wall damage can create aneurysms with thrombosis or rupture.
- Intravenous immunoglobulin with aspirin reduces symptomatic coronary complications.

## Three diseases: Three dominant modes of damage

| Question               | Buerger             | PAN                       | Kawasaki              |
|------------------------|---------------------|---------------------------|-----------------------|
| Who / context?         | Young heavy smoker  | Systemic presentation     | Febrile young child   |
| Where?                 | Distal limb vessels | Visceral / renal arteries | Coronary arteries     |
| Dominant lesion?       | Inflamed thrombus   | Necrotizing arteritis     | Transmural arteritis  |
| Primary tissue threat? | Gangrene            | Organ infarction          | Myocardial infarction |

# Matching an artery to its clinical signal

## Distal extremity

Claudication + rest pain +  
superficial phlebitis suggest  
Buerger.

## Renal and visceral

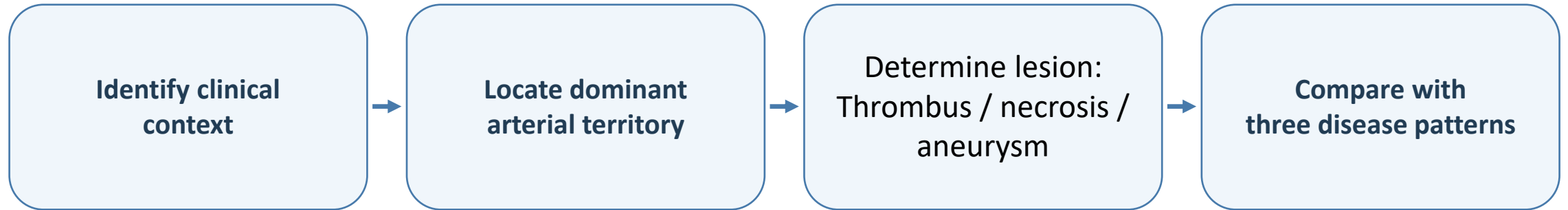
Hypertension + bowel  
ischemic symptoms suggest  
PAN.

## Coronary in childhood

Mucocutaneous fever +  
coronary hazard suggest  
Kawasaki.

Distribution carries more discriminating information than inflammation alone.

## A source-based reasoning pathway



Schematic reasoning aid, not a validated diagnostic algorithm.

## Avoid common category mistakes

- Medium-vessel diseases can affect arteries outside the nominal size class.
- PAN should not be treated as equivalent to ANCA-associated capillaritis.
- Kawasaki and PAN share transmural inflammation but differ in clinical setting and coronary predilection.
- Buerger disease affects associated nerves and veins; It is not simply distal atherosclerosis.

# Lesion morphology at a glance

| Morphologic question              | Buerger disease                | PAN                              | Kawasaki disease                      |
|-----------------------------------|--------------------------------|----------------------------------|---------------------------------------|
| Is thrombosis prominent?          | Yes: inflamed, often occlusive | May accompany necrosis           | Possible in damaged coronary arteries |
| Is fibrinoid necrosis central?    | Not the defining feature       | Characteristic in active lesions | Less prominent than PAN               |
| Can vessel damage cause aneurysm? | Not emphasized in source       | Yes                              | Yes, especially coronary              |
| Can healed lesions narrow lumen?  | Organized thrombus             | Fibrous wall thickening          | Obstructive intimal thickening        |

# Interpretations must separate evidence levels

## Established in supplied source

- Three principal diseases within medium-vessel group
- Characteristic vessel distribution and morphology
- Textbook clinical complications and treatment effects

## Not established by available files

- Current external guideline algorithms or new classifications
- Modern incidence, trial estimates or cohort-specific rates
- Authentic microscopy images or licensed textbook figure reproductions

## Integration exercise: Three short presentations

| Presentation                             | Most likely disorder | Reason                                  |
|------------------------------------------|----------------------|-----------------------------------------|
| Smoker; instep claudication + phlebitis  | Buerger              | Distal vascular-neural syndrome         |
| Hypertension; bloody stools + neuritis   | PAN                  | Systemic visceral + renal ischemia      |
| Febrile child; oral + extremity findings | Kawasaki             | Mucocutaneous syndrome; coronary hazard |

## Final synthesis: Phenotype reflects vessel injury

- Buerger: Tobacco-associated thrombosing inflammation of distal limb neurovascular bundles.
- PAN: Segmental necrotizing muscular-artery injury with systemic ischemic consequences.
- Kawasaki: Childhood transmural arteritis with potentially serious coronary aneurysms.
- Classify by pattern; Explain presentations through vascular anatomy and morphology.

Identify the artery → understand the lesion → predict the organ at risk.

## Primary source and scope

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026).
- Chapter 11, Blood Vessels: vasculitis and medium-vessel vasculitis, printed pp. 463–468.
- Classification context: Table 11.4; morphology captions: Figs. 11.22, 11.25 and 11.26.
- Figures not reproduced: original Chapter 11 PDF and authenticated image assets were not supplied.