

Local Immune Complex Disease

Arthus reaction · localized type III hypersensitivity

From antigen deposition to necrotizing vasculitis

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Learning objectives

- Define the Arthus reaction as a localized immune complex–mediated vasculitis.
- Trace antigen exposure, immune complex formation, inflammation, necrosis, and thrombosis.
- Connect neutrophils, complement, and fibrinoid necrosis to vessel-wall injury.
- Distinguish localized Arthus injury from systemic immune complex disease and other mechanisms.

The defining lesion

The Arthus reaction is acute, localized immune complex vasculitis.

- The classic experimental site is the skin.
- Vessel-wall injury can produce localized tissue necrosis.
- A superimposed thrombus adds an ischemic component to injury.

Local versus systemic immune complex disease

Local: Arthus reaction

- Antigen is introduced into a limited tissue site.
- Large complexes form locally in vascular walls.
- Cutaneous vasculitis and tissue necrosis predominate.

Systemic: Serum sickness

- Circulating complexes form after an antibody response.
- Complexes deposit in vessels and susceptible organs.
- Multi-organ manifestations can follow deposition.

Necessary experimental components

Prior immunization

- Host already has circulating antibody against the antigen.

Local antigen

- Antigen is injected intracutaneously at one site.

Accessible vessels

- Antigen can diffuse to local vascular walls.

Arthus reaction: The source sequence



- Thrombosis may superimpose on vessel damage and aggravate ischemia.

Why prior immunization matters

- The experimental host already contains circulating antibodies specific for the injected antigen.
- Antibody is therefore present when antigen arrives at the vascular wall.
- This permits a localized antigen–antibody reaction without first waiting for a new primary antibody response.

Antigen and antibody begin in different locations

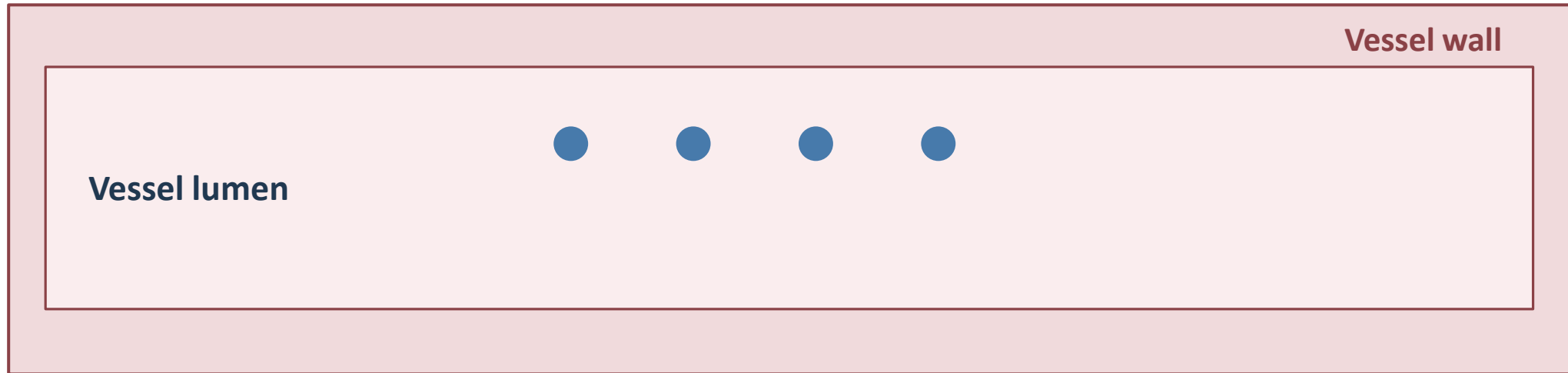
Locally introduced antigen

- Antigen enters the skin at the injection site.
- It diffuses outward toward local blood vessels.
- Its spatial distribution helps localize the lesion.

Preformed specific antibody

- Specific antibody is already present in blood.
- It encounters antigen as antigen reaches vessel walls.
- Binding creates immune complexes in situ.

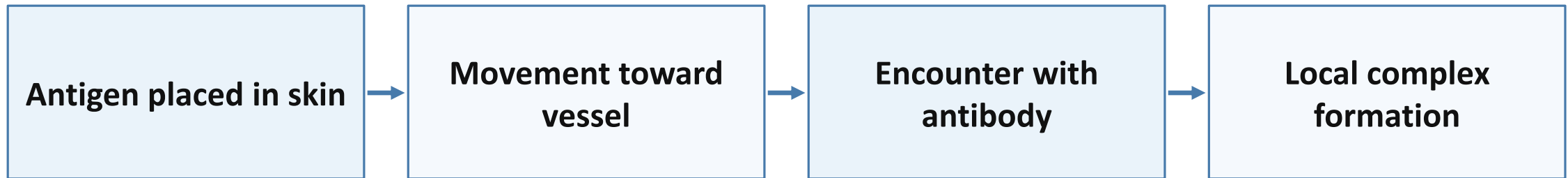
The local microvascular setting



Antigen reaches the wall of a local blood vessel, where specific antibody is available.

Schematic (not histology)

Antigen diffusion creates a focal reaction

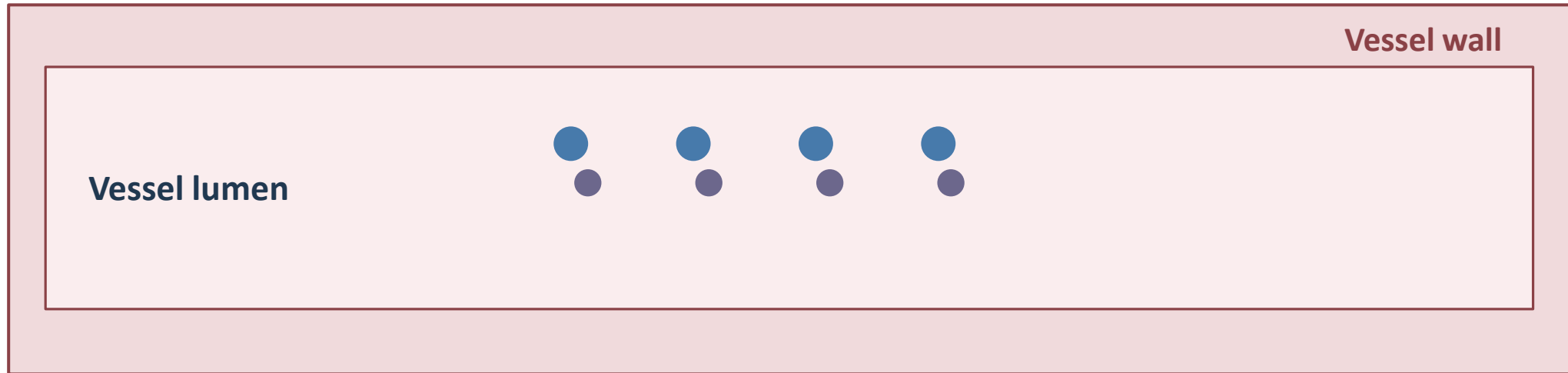


- The location of the antigen–antibody encounter explains the localized tissue distribution.

Where immune complexes form

- The Arthus model emphasizes formation of large immune complexes locally in vessel walls.
- This is an example of immune complexes formed at a tissue site, rather than only in the circulation.
- The shared pathologic endpoint of type III reactions is inflammation wherever complexes deposit.

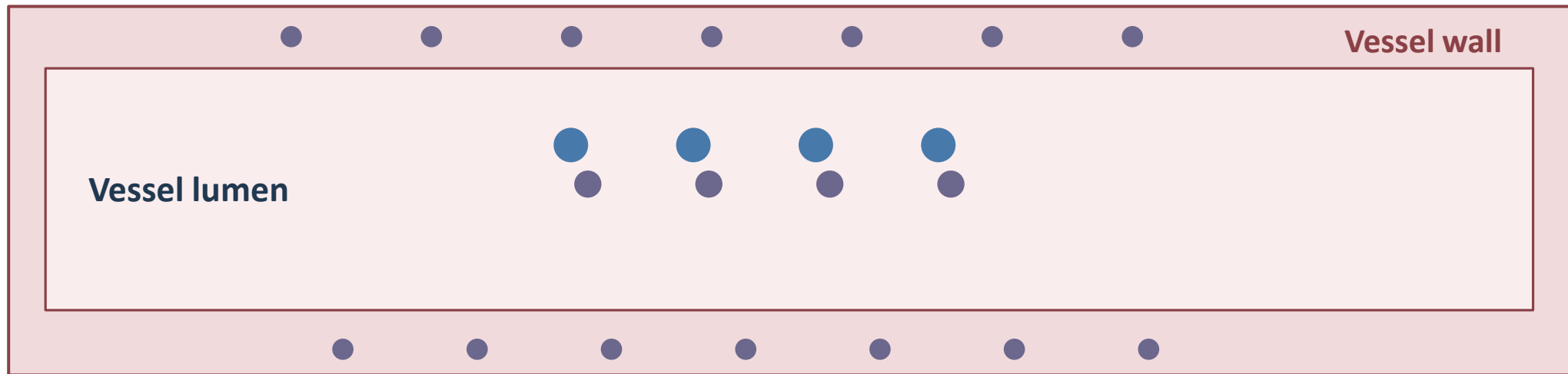
Large complexes form near the vessel wall



Blue antigen and purple antibody symbols illustrate binding; The diagram is conceptual.

Schematic (not histology)

Complexes deposit within vascular walls



Deposited immune complexes convert an antigen–antibody reaction into a vessel-wall lesion.

Schematic (not histology)

Immune complex formation is not yet tissue necrosis

Immunologic event

- Antigen binds specific antibody.
- Large antigen–antibody complexes form.
- Complexes become localized in the vessel wall.

Pathologic consequence

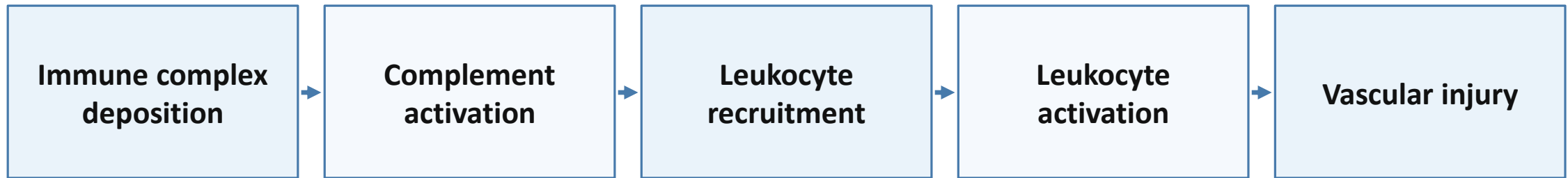
- Deposited complexes initiate acute inflammation.
- Inflammatory cells injure the vessel wall.
- Fibrinoid necrosis and thrombosis may result.

Type III hypersensitivity as the mechanism

Antigen–IgG complexes damage tissues mainly through inflammation at sites of deposition.

- Complexes may arise in the circulation or locally in tissues.
- Antigens may be foreign proteins, microbial products, or self antigens.
- Distribution of deposits influences the clinical pattern of injury.

Deposited complexes activate an inflammatory cascade



- Complement and Fc receptor engagement amplify the inflammatory response.

Three linked effector processes

Complement

- C3a and C5a increase vascular permeability.
- C5a is chemotactic.

Cell recruitment

- Granulocytes and monocytes migrate to sites of deposits.
- Neutrophils dominate acute vasculitis.

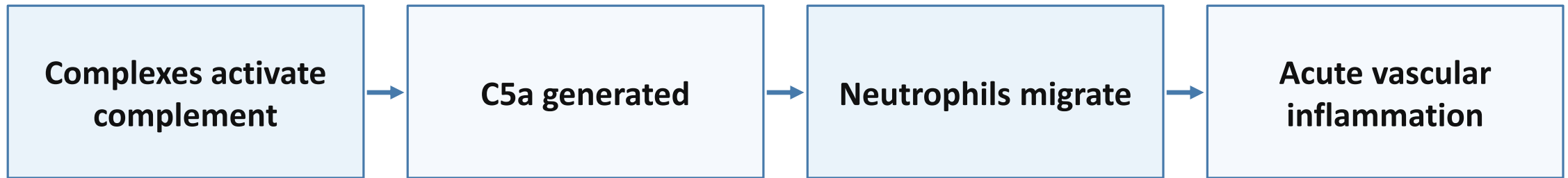
Tissue injury

- Leukocytes release proteases and reactive oxygen species.
- Structural vessel elements are damaged.

Complement connects deposits to vessel injury

- Immune complexes activate complement at the site of deposition.
- C5a contributes chemotactic signals that recruit inflammatory leukocytes.
- C3a and C5a contribute to increased vascular permeability, supporting local inflammation.

C5a drives leukocyte recruitment



- Chemotaxis explains why immune complex–injured vessel walls become neutrophil-rich.

Chemotaxis and activation are distinct steps

Recruitment

- C5a directs leukocyte migration toward deposited complexes.
- Inflammatory cells accumulate near injured vessels.

Activation

- Leukocyte Fc and complement receptors engage immune material.
- Activated cells release enzymes and reactive oxygen intermediates.

Leukocyte receptors in antibody-mediated inflammation

Fc receptors

- Recognize the Fc region of deposited IgG.
- Help activate recruited leukocytes.

Complement receptors

- Recognize complement fragments such as C3b.
- Provide additional activation signals.

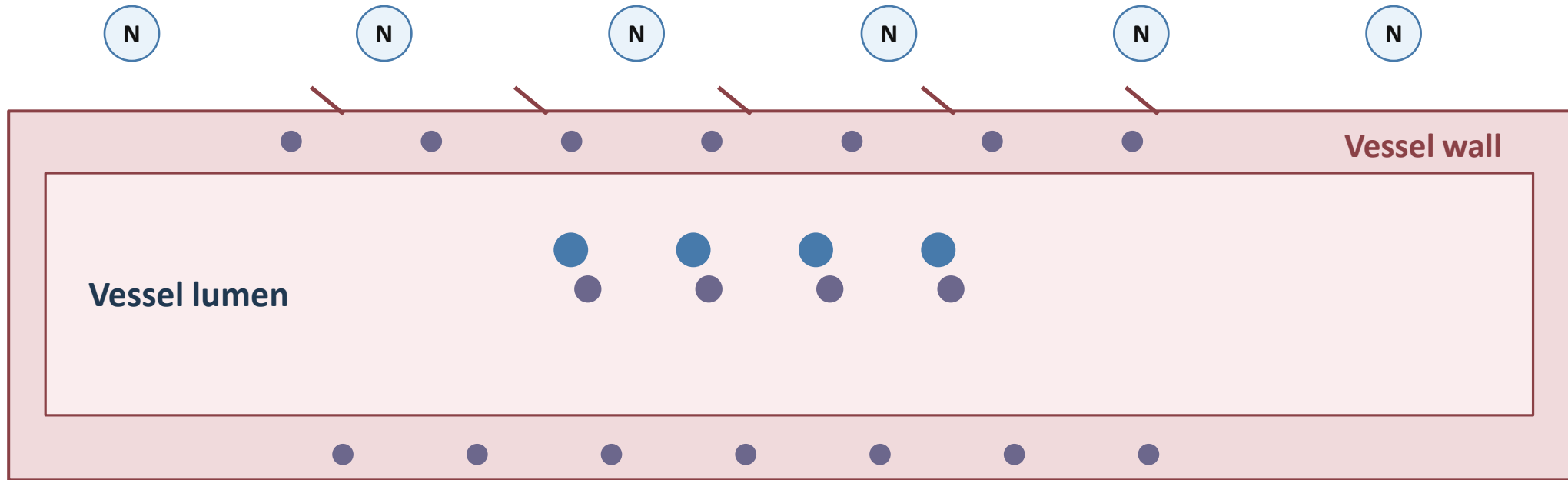
How proteases damage vascular tissue

- Activated leukocytes release lysosomal enzymes including proteases.
- Proteases can digest basement membrane, collagen, and elastin.
- This is a mechanism of structural vessel-wall destruction, rather than merely antibody binding.

Reactive oxygen species add to injury

- Activated leukocytes generate reactive oxygen species.
- These reactive intermediates contribute to damage at sites of antibody-mediated inflammation.
- In the Arthus reaction, this inflammation is spatially concentrated around deposited complexes.

Neutrophilic inflammation surrounds the vessel



N = recruited neutrophils; The diagram denotes immune-complex–associated vessel injury.

Schematic (not histology)

From inflammation to fibrinoid necrosis



- The pathologic endpoint is necrosis of the vessel wall with intense inflammation.

The central histologic pattern

Acute vasculitis with neutrophilic infiltration and vessel-wall necrosis.

- Neutrophils are a major component of the acute inflammatory infiltrate.
- Necrosis is located in the affected vessel wall.
- Fibrinoid material appears as smudgy eosinophilic tissue destruction on routine microscopy.

Vasculitis: Cellular and structural components

Inflammatory component

- Intense neutrophilic infiltration.
- Complement-mediated recruitment.
- Leukocyte activation and enzyme release.

Wall injury component

- Necrosis of affected vascular wall.
- Fibrinoid appearance of damaged tissue.
- Potential superimposed thrombosis.

Fibrinoid necrosis: Why it looks eosinophilic

- The necrotic vessel wall contains material from damaged tissue and deposited plasma constituents.
- Immune complexes, complement, and plasma proteins contribute to the eosinophilic appearance.
- This produces a smudgy zone of tissue destruction described as fibrinoid necrosis.

Components of the fibrinoid zone

Necrotic wall

- Destruction of vascular tissue underlies the change.

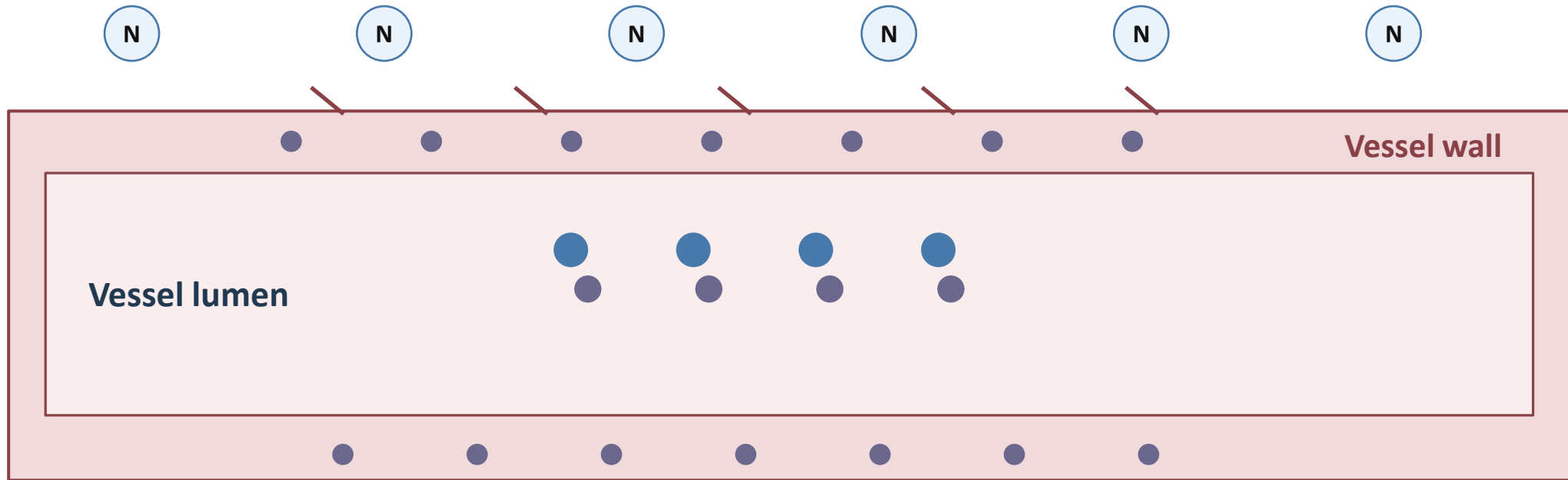
Immune material

- Immune complexes and complement occur at sites of injury.

Plasma proteins

- Extravasated plasma constituents add to eosinophilic material.

Wall necrosis and the lumen are linked



The vascular wall is the target of injury; Luminal obstruction can become a second insult.

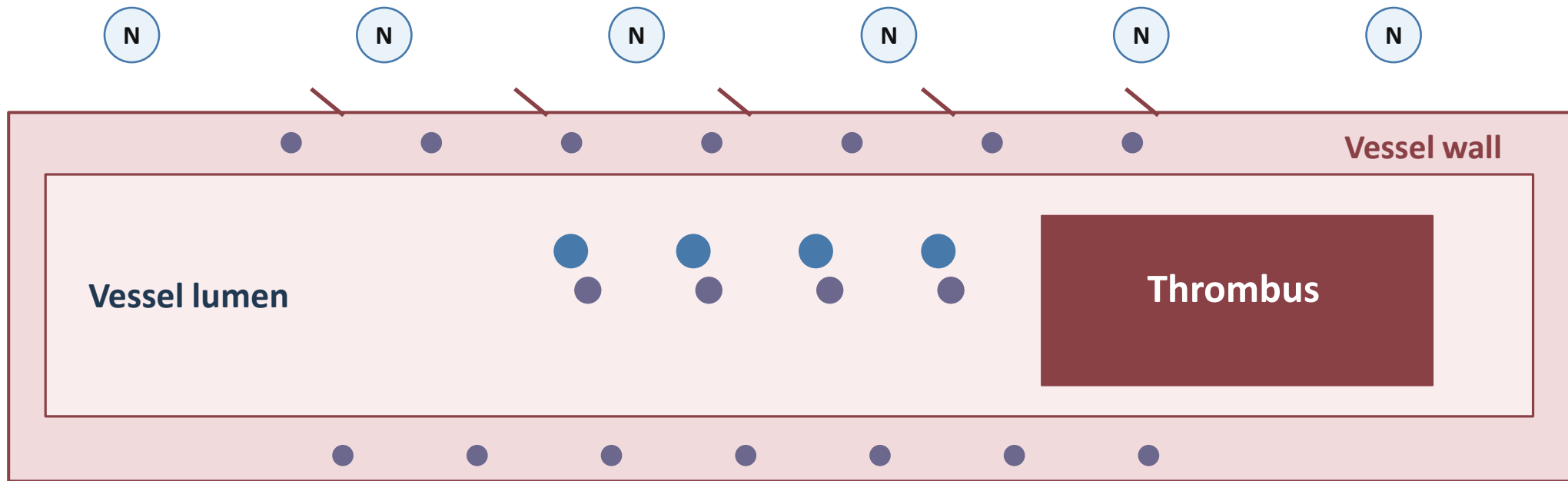
Schematic (not histology)

Thrombosis aggravates ischemic injury

Thrombus formation is not the initiating antigen–antibody event.

- Vessel-wall necrosis follows local immune complex–associated vasculitis.
- Superimposed thrombosis compromises the damaged vessel further.
- Ischemic injury is intensified when thrombosis develops.

Thrombosis superimposed on vasculitis

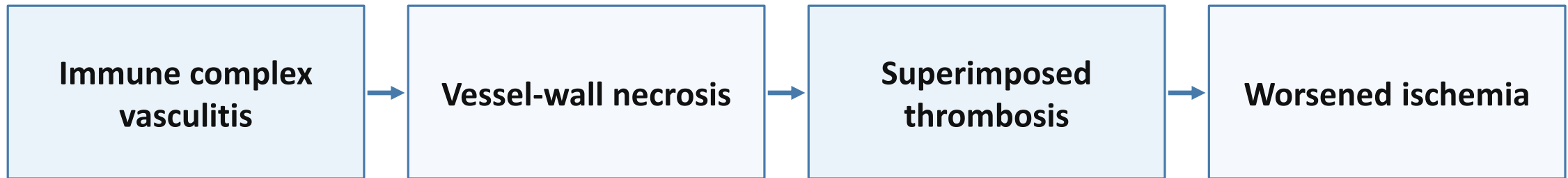


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Worsened ischemic injury

The model separates vessel-wall inflammation from additional luminal thrombosis.

Schematic (not histology)

Why tissue necrosis becomes pronounced



- Two connected processes—wall destruction and impaired perfusion—compound local tissue injury.

Identify two forms of damage

Direct inflammatory injury

- Complement and leukocytes injure the vessel wall.
- Fibrinoid necrosis is the characteristic morphologic pattern.

Secondary ischemic injury

- Thrombosis is superimposed on necrotizing vasculitis.
- Reduced tissue perfusion worsens local damage.

From microscopic observation to mechanism

Microscopic finding	Supported inference	Mechanistic link
Neutrophils in vessel wall	Acute inflammation	Complement recruitment
Necrotic vessel wall	Vasculitic injury	Leukocyte mediators
Smudgy eosinophilic material	Fibrinoid necrosis	Necrotic tissue + deposits
Luminal thrombus	Secondary ischemic component	Superimposed thrombosis

In situ and circulating immune complexes

In situ complex formation

- Antigen is present or becomes established at a tissue site.
- Antibody binds antigen locally.
- The Arthus model illustrates localized vascular deposition.

Circulating complexes

- Antigen and antibody combine within the blood.
- Complexes subsequently deposit at susceptible sites.
- Serum sickness provides the systemic prototype.

Arthus reaction versus serum sickness

Feature	Arthus reaction	Serum sickness
Antibody condition	Preformed specific antibody	Antibody response after systemic antigen
Complex generation	Localized at vascular walls	Initially in circulation
Distribution	Focal, commonly skin	Systemic; vessels and organs
Pathologic focus	Acute cutaneous vasculitis	Vasculitis and organ injury

Why immune complex distribution matters

- The site at which antigen and antibody meet influences the initial location of complexes.
- Deposited complexes induce inflammation in their immediate tissue environment.
- This explains how the same type III effector mechanism can have focal or systemic expression.

Sites often affected in systemic disease

Glomeruli

- High-pressure filtration helps concentrate complexes.
- Nephritis can result.

Joints

- Complex deposition can involve synovial sites.
- Arthritis may result.

Small vessels

- Deposits initiate acute vessel-wall inflammation.
- Vasculitis may result.

Other examples contextualize type III injury

Immune complex disorder	Antigen listed by Robbins	Manifestation
Systemic lupus erythematosus	Nuclear antigens	Nephritis, skin lesions, arthritis
Poststreptococcal GN	Streptococcal antigens	Nephritis
Polyarteritis nodosa	HBV antigens in some cases	Systemic vasculitis
Reactive arthritis	Bacterial antigens (e.g., Yersinia)	Acute arthritis

What antigen identity does—and does not—tell us

Antigen identity

- Foreign injected proteins can drive experimental Arthus lesions.
- Type III disorders may also involve microbial or self antigens.

Anatomic distribution

- Deposition determines the inflamed tissue.
- A focal skin lesion differs from glomerular or systemic vasculitis.

Type II versus type III antibody-mediated injury

Feature	Type II	Type III
Antigen location	Fixed cell or matrix target	Soluble or tissue-planted antigen
Antibody pattern	Binds pre-existing target	Forms antigen–antibody complexes
Injury examples	Opsonization, inflammation, dysfunction	Inflammation at deposit sites
Illustration	Basement membrane antibody reaction	Arthus localized vasculitis

A tissue contains IgG deposits: Is every antibody lesion type III?

Does antibody-related inflammation automatically prove immune complex disease?

Mechanism

- No. Type II and type III can both involve antibodies and complement.

Reasoning

The key distinction is antibody binding to fixed targets versus complexes formed with antigen.

Type III versus type IV hypersensitivity

Dimension	Type III (Arthus)	Type IV (T-cell mediated)
Key mediator	Antigen–antibody complexes	T-cell cytokines / cytotoxicity
Initiating context	Complex deposition in tissue	Antigen-recognizing T lymphocytes
Principal injury	Complement and leukocyte inflammation	T-cell–driven inflammation or killing
Teaching prototype	Arthus reaction	Delayed-type hypersensitivity

Avoid conflating Type III and Type IV

An antigen challenge in skin can lead to mechanistically different reactions.

- Arthus: Preexisting antibodies + vascular immune complexes + acute vasculitis.
- T-cell-mediated hypersensitivity: Cytokines from T cells drive tissue inflammation.
- The site of exposure alone does not classify the hypersensitivity mechanism.

What morphology can establish

- Acute vasculitis can be recognized through inflammatory injury to the vessel wall.
- Neutrophilic inflammation and fibrinoid necrosis support an acute necrotizing pattern.
- Morphology should be connected to the antigen–antibody mechanism; A pattern alone does not identify a specific inciting antigen.

Immune deposits across organs: Avoid overgeneralization

Renal example

- Immunofluorescence may show granular immunoglobulin and complement deposits.
- Electron microscopy may show electron-dense deposits along the GBM.

Arthus skin model

- The provided passage specifies necrotizing cutaneous vasculitis.
- It does not state a specific skin IF/EM pattern or diagnostic threshold.

How would you interpret fibrinoid necrosis?

Is fibrinoid necrosis equivalent to a unique proof of an Arthus reaction?

Mechanism

- No. Fibrinoid necrosis as a principal morphology of immune complex vascular injury.

Reasoning

Interpret tissue pattern alongside local antigen exposure and preexisting antibody.

What the supplied Robbins passage does not quantify

- It provides no numerical diagnostic threshold for the local Arthus reaction.
- It does not supply a validated clinical grading system or sensitivity/specificity data.
- It does not document a particular time-to-onset or standardized treatment protocol for human cutaneous Arthus reactions.

Mechanism exercise: Previously immunized host

A previously immunized animal receives intracutaneous antigen. What must occur before vasculitis?

Mechanism

- Specific antibody binds the introduced antigen and large immune complexes form locally in vessel walls.

Reasoning

This is the initiating local immunologic event in the Robbins Arthus model.

Mechanism exercise: Complement activation

Why does a vessel containing immune complexes attract neutrophils?

Mechanism

- Deposited complexes trigger complement; C5a recruits leukocytes to the inflamed vascular site.

Reasoning

The accumulated neutrophils contribute to acute vasculitic injury.

Mechanism exercise: Destroyed wall

Which processes explain fibrinoid necrosis rather than mere immune deposition?

Mechanism

- Leukocyte activation and release of enzymes and reactive oxygen intermediates damage the vessel wall.

Reasoning

Deposited complexes initiate injury but are not the entire pathologic event.

Mechanism exercise: Deteriorating ischemia

A localized necrotizing vasculitis develops luminal thrombosis. Why is injury amplified?

Mechanism

- The thrombus adds impaired perfusion to preexisting inflammatory vessel-wall destruction.

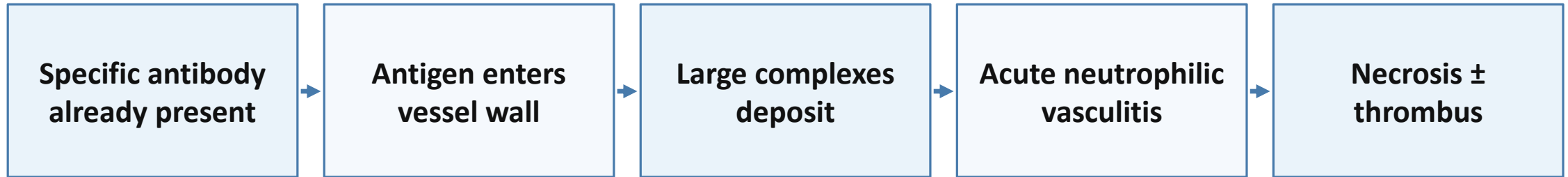
Reasoning

Robbins explicitly identifies superimposed thrombosis as a factor worsening ischemia.

Five findings in a mechanistic chain

Observation / context	Pathologic meaning	Place in sequence
Prior antigen sensitization	Specific circulating antibody	Prerequisite
Local antigen introduction	Antigen diffuses into vascular wall	Trigger
Deposited large complexes	Local antigen–antibody interaction	Immune phase
Neutrophilic necrotizing vasculitis	Inflammatory vessel damage	Effector phase
Associated thrombosis	Additional reduction of perfusion	Amplifier

Reconstruct the entire Arthus lesion



- Anatomic concentration of complexes explains localization; Effector injury explains pathology.

Core clinicopathologic synthesis

Focal immune complex formation drives focal vascular inflammation.

- Trigger: Local antigen challenge in an immunized host.
- Mechanism: Antibody complexes, complement, and recruited leukocytes.
- Morphology: Acute necrotizing vasculitis with fibrinoid change.
- Amplification: Thrombosis worsens ischemic tissue injury.

Interpretation pitfalls to avoid

Do not assume

- Every antibody-associated vasculitis is Arthus.
- Fibrinoid necrosis alone identifies the antigen.
- The renal granular IF description directly applies to skin.

Instead establish

- Evidence for a local antigen–antibody reaction.
- Relationship of complex deposition to inflammation.
- Specific morphology and anatomic distribution.

High-yield distinctions

Question	Best source-grounded answer
What makes it local?	Complexes form at the local antigen-exposure site.
What injures the wall?	Complement-driven, neutrophil-rich inflammation.
Why eosinophilic necrosis?	Necrotic tissue with complex, complement, and plasma protein.
Why ischemia worsens?	Superimposed thrombosis.
What is the systemic analog?	Serum sickness with circulating complexes.

Reference and scope

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th edition (2026).
- Topic section: Local Immune Complex Disease; contextual mechanisms from Type III hypersensitivity and antibody-mediated inflammation.
- Morphology context: immune complex–associated vasculitis and fibrinoid necrosis.
- All diagrams in this lecture are original, editable schematics—not clinical or histopathologic specimens.