

Focal Cerebral Ischemia

Arterial occlusion • cerebral infarction • tissue response

Pathogenesis, vascular mechanisms, gross and microscopic evolution, and
clinicopathologic correlations

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Learning objectives

Mechanism

- Explain how arterial occlusion and collateral flow determine infarct distribution.
- Distinguish embolic, thrombotic, and small-vessel causes.

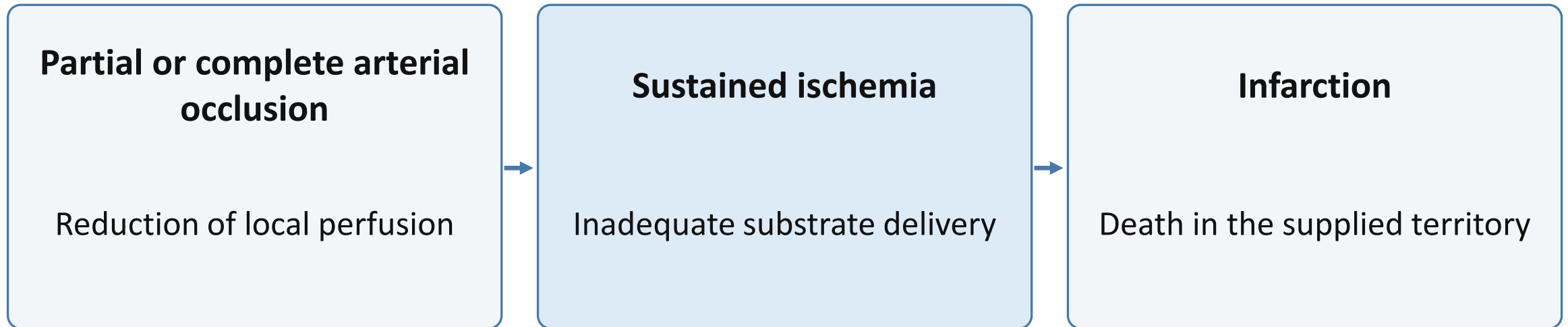
Morphology

- Differentiate pale, hemorrhagic, lacunar, and venous infarcts.
- Sequence acute, subacute, and remote tissue reactions.

Clinical translation

- Relate the anatomic lesion to neurologic deficits.
- Recognize the rationale for urgent evaluation of hemorrhage.

Focal ischemia: The defining event



Extent depends on duration and collateral flow.

Focal versus global cerebral ischemia

Focal

- One territory or localized region
- Often partial/complete arterial occlusion
- Deficit tracks anatomic distribution

Global

- Widespread perfusion failure or hypoxemia
- Generalized vulnerable neural populations
- Separate parent-topic entity

The focus of this lecture is focal arterial ischemia.

Why the brain is highly vulnerable

- Strict reliance on aerobic energy production
- Disproportionately high oxygen demand for its mass
- Ongoing neuronal activity depends on maintained perfusion

Physiologic context

Physiologic parameters:
~1–2% of body mass, ~15%
of resting cardiac output,
and ~20% of oxygen use.

Reduced flow is not identical to hypoxemia

Ischemia

- Insufficient blood flow into tissue
- May result from vessel occlusion or low perfusion pressure
- Deprives tissue of circulating substrates

Hypoxemia

- Reduced oxygen content of blood
- Can occur even without a focal vessel obstruction
- Distinguished from local arterial blockade

The focal lesion here arises from impaired arterial delivery.

Three determinants of infarct extent

Duration

Longer sustained ischemia increases tissue injury.

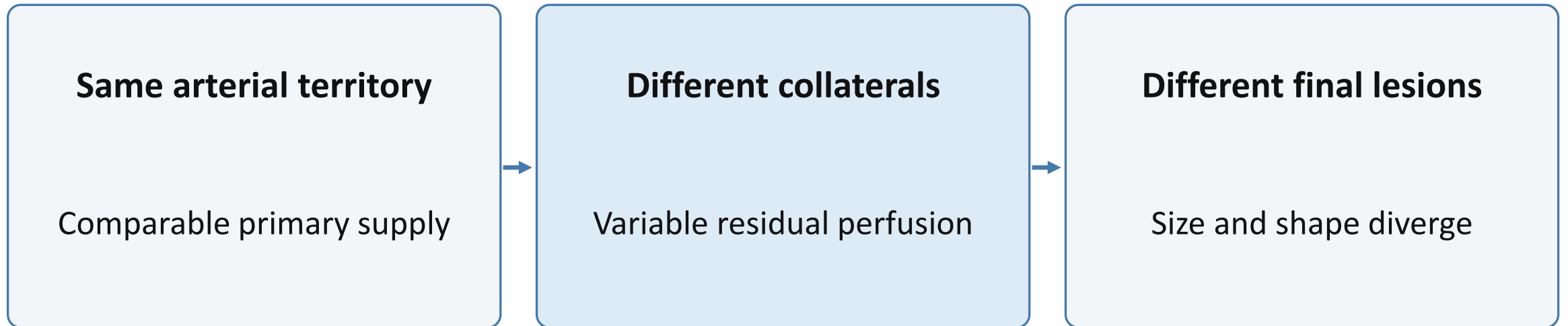
Magnitude

Severity and speed of flow loss alter survival.

Collateral supply

Alternate pathways may preserve threatened tissue.

Why equal occlusions need not look alike



Ischemic duration adds an independent influence.

Collateral circulation: Three routes

Circle of Willis

- Principal collateral source.
- Proximal arterial connections.

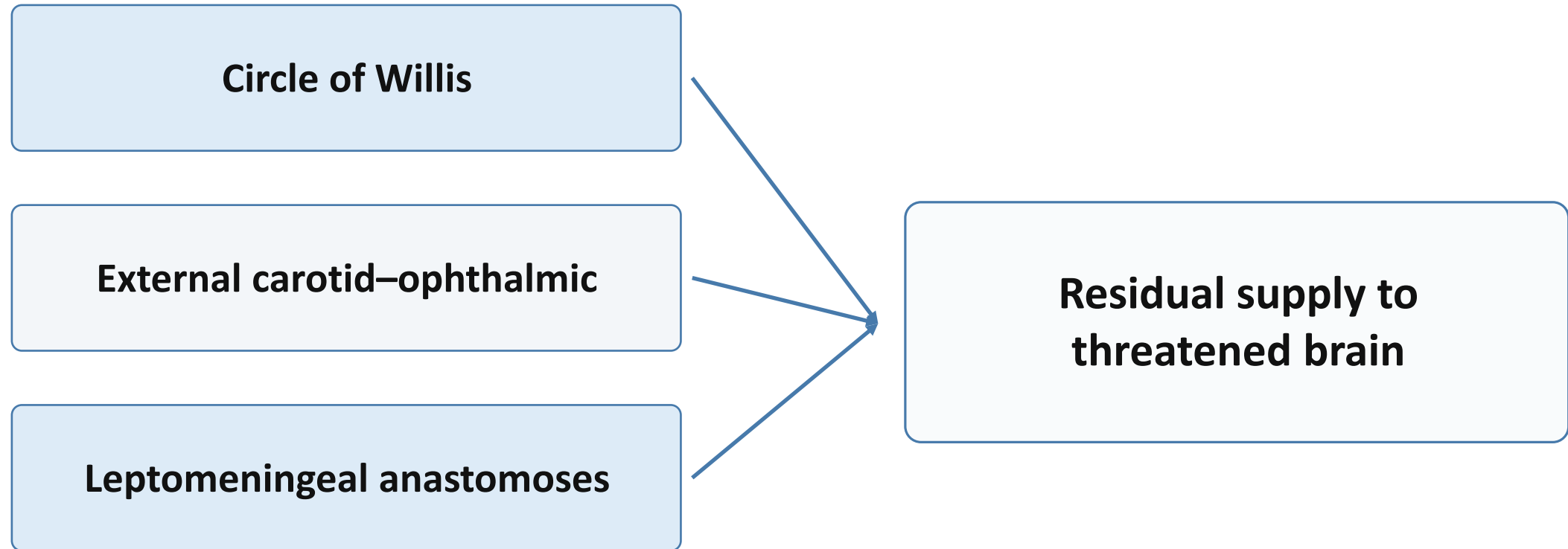
External carotid route

- Ophthalmic artery collateral contribution.
- May supplement intracranial flow.

Leptomeningeal vessels

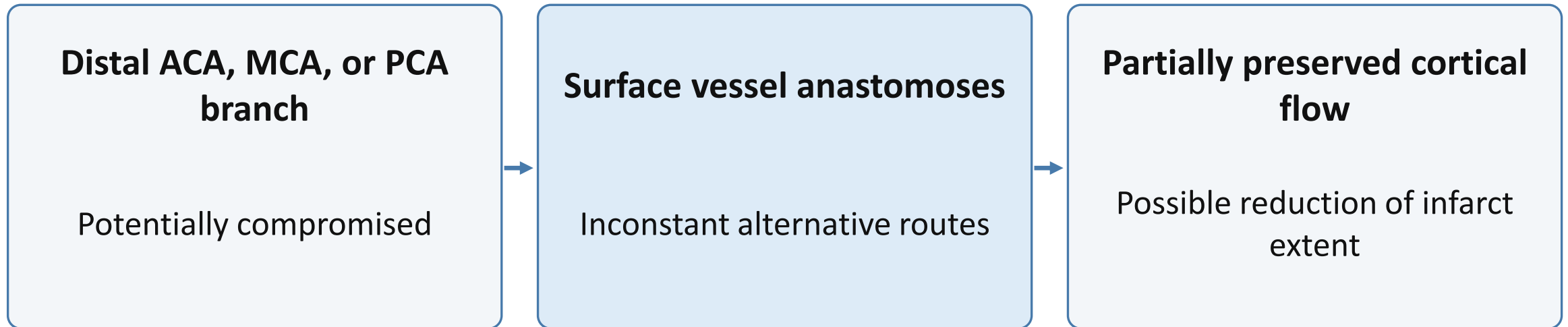
- Variable cortical anastomoses.
- Can support distal arterial branches.

Collateral supply is a network, not a guarantee



Schematic routes; Contributions vary between individuals.

Leptomeningeal anastomoses: Distal rescue



These interterritorial surface collaterals are anatomically variable.

Deep penetrating arteries: Limited reserve

Surface cortex

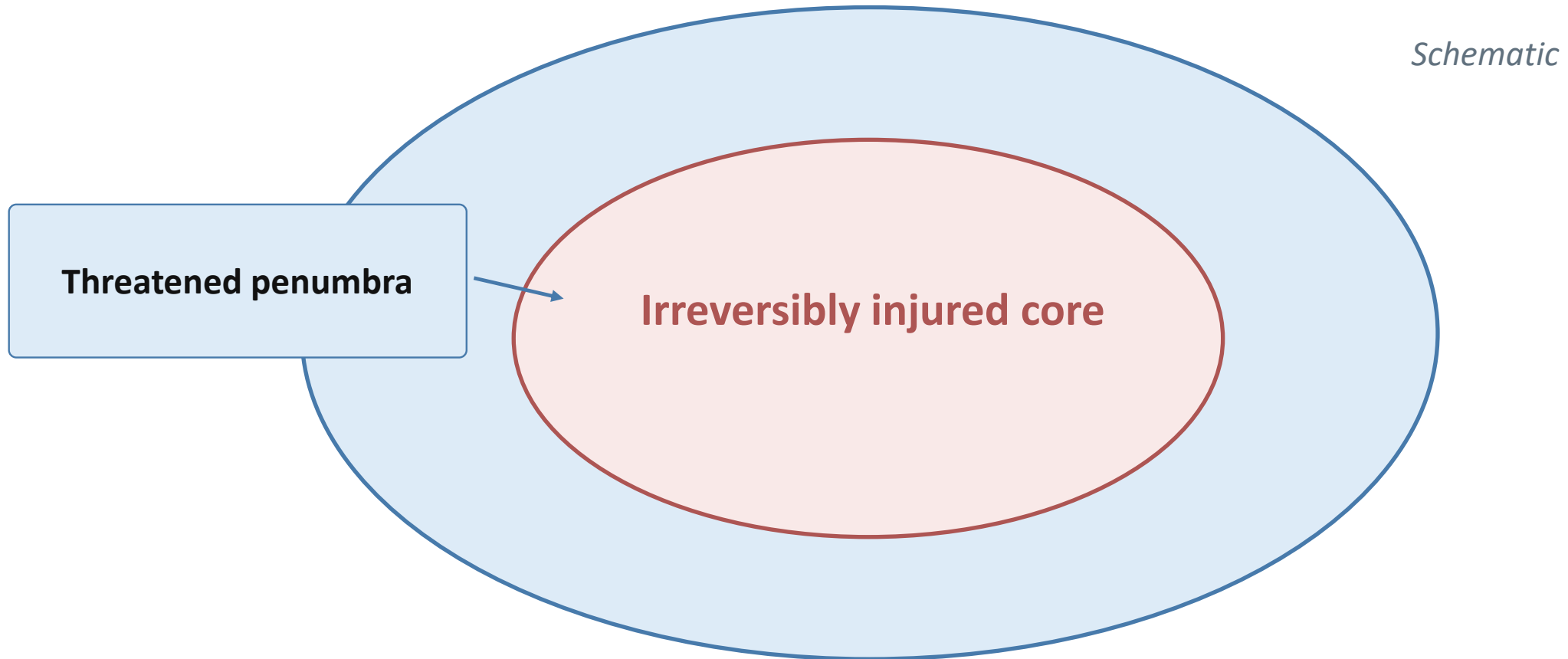
- Distal branches may communicate.
- Leptomeningeal collaterals can be available.
- Variable rescue of distal territory.

Deep structures

- Long, deep penetrating vessels.
- Little or no effective collateral supply.
- Occlusion creates a discrete vulnerable territory.

Deep structures include basal ganglia, thalamus and deep white matter.

Ischemic tissue exists along a gradient



Conceptual distribution; No fixed dimensions or flow thresholds implied.

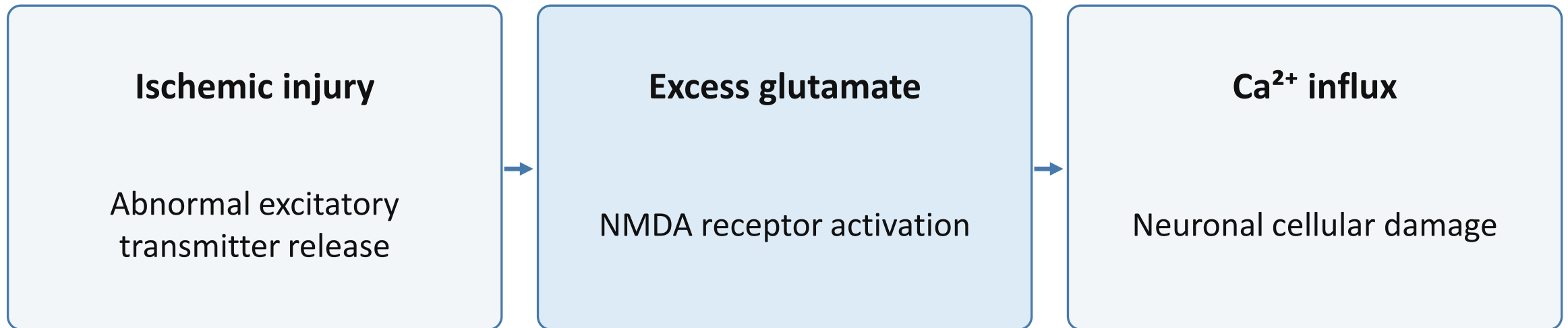
The penumbra is biologically threatened tissue

- Located at the transition between necrotic and preserved brain.
- Degree and duration of hypoperfusion influence its fate.
- Preclinical anti-apoptotic experiments support more than one neuronal death pathway.

Evidence boundary

The cited rescue observations are from animal models—not proof of a specific human treatment.

Glutamate excitotoxicity in ischemia



Excitotoxicity as an additional CNS-specific ischemic mechanism.

Neuronal injury: Necrosis and apoptosis

Necrotic injury

- Visible eosinophilic neuron death.
- Acute structural disruption.
- Subsequent tissue removal.

Apoptotic contribution

- Suggested by preclinical rescue experiments.
- May occur around the injured core.
- Not synonymous with gross infarct appearance.

Both mechanisms are considered without assuming exact proportions.

Three major occlusive etiologies

Embolization

Occlusive material arrives from a remote source.

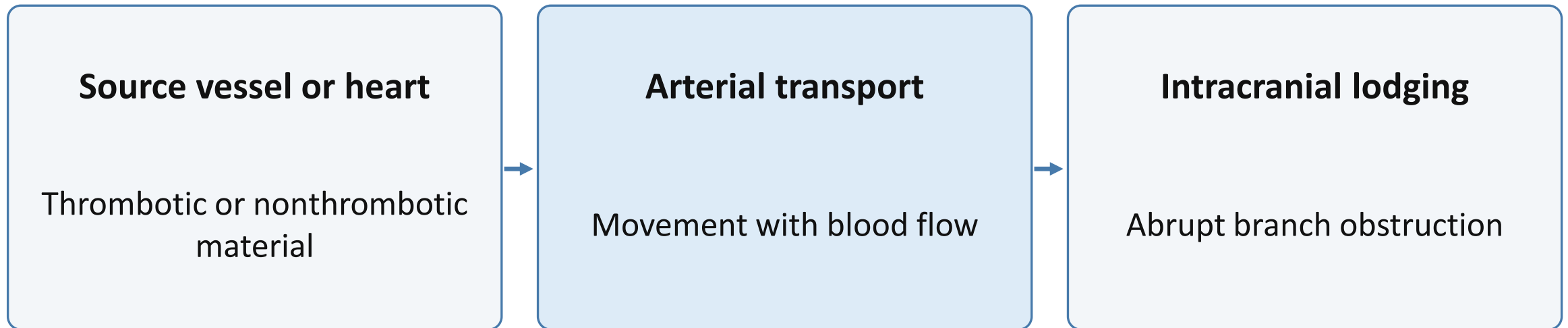
In situ thrombosis

Thrombus develops at a diseased cerebral artery.

Vascular inflammation

Vessel injury leads to narrowing and thrombosis.

Embolization: A remote source, a local infarct



An embolic event usually localizes where vessel caliber or geometry traps material.

Cardiac mural thrombi as embolic sources

- Cardiac mural thrombus is a major source of cerebral emboli.
- Associated settings include myocardial infarction and atrial fibrillation.
- Valvular disease also predisposes to embolization.

Causal link

An embolus from the heart can obstruct an otherwise distant cerebral artery.

Cardiac conditions alter cerebral embolic risk

Myocardial infarction

- Predisposes to mural thrombus.
- A potential source for distant embolization.

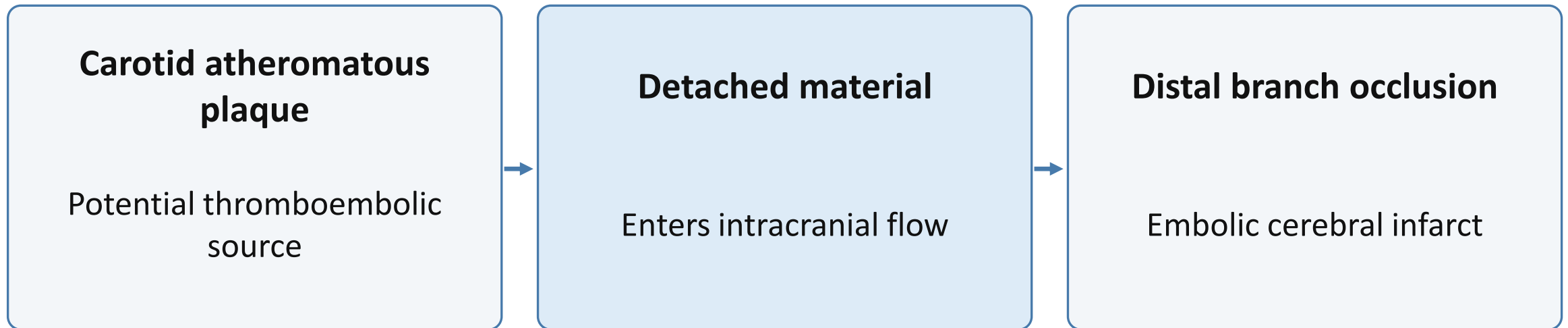
Atrial fibrillation

- An important embolic predisposition.
- The source can remain outside the brain.

Valvular disease

- A recognized cardiac source category.
- Requires distinguishing from local cerebral thrombosis.

Artery-to-artery embolization



Carotid plaques are an important noncardiac source.

Paradoxical and procedure-related emboli

Paradoxical emboli

- Systemic venous thrombus accesses arterial circulation.
- Children with congenital heart disease.

Cardiac procedures

- Cardiac surgery may be followed by thromboembolism.
- Mechanism remains embolic, not necessarily in situ cerebral thrombosis.

Both are less typical than cardiac mural or carotid sources in the source text.

Nonthrombotic emboli

Fat or marrow

Trauma/fracture-associated shower of emboli.

Air

An embolic material explicitly listed.

Tumor

Another nonthrombotic source of arterial obstruction.

Why the middle cerebral artery is often affected

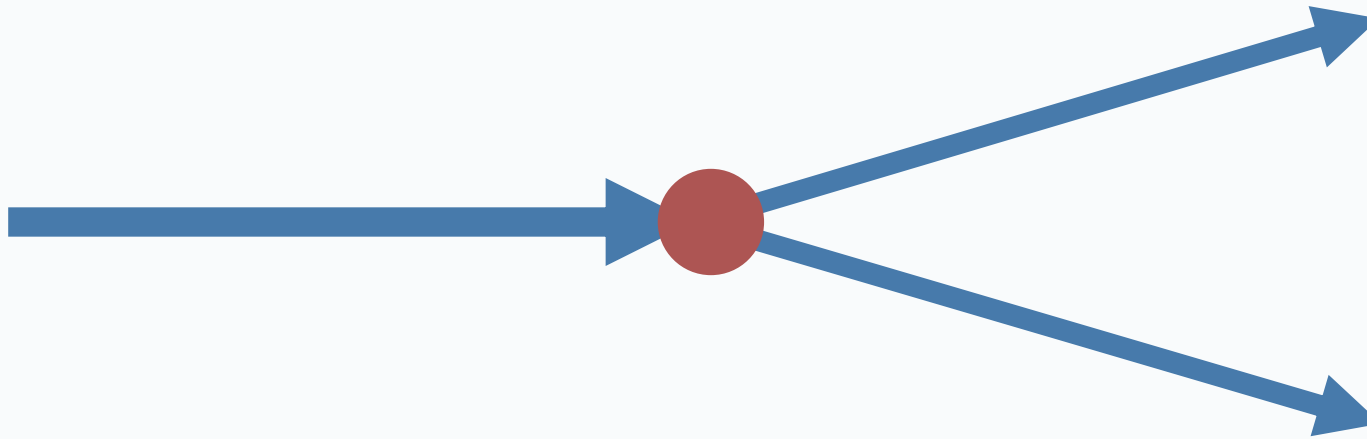
- The MCA is a direct continuation of internal carotid flow.
- Its vascular territory is the most frequent site of embolic infarction in the source.
- Embolic infarction affects both hemispheres with approximately equal frequency.

Distribution matters

Site of vascular obstruction predicts the lesion more closely than the distant embolic source.

Emboli preferentially lodge at branch points

Flowing embolus



Lodging at branching point

Arterial branching and pre-existing narrowing are favored sites of lodging.

Shower embolization is a different pattern

Single major embolus

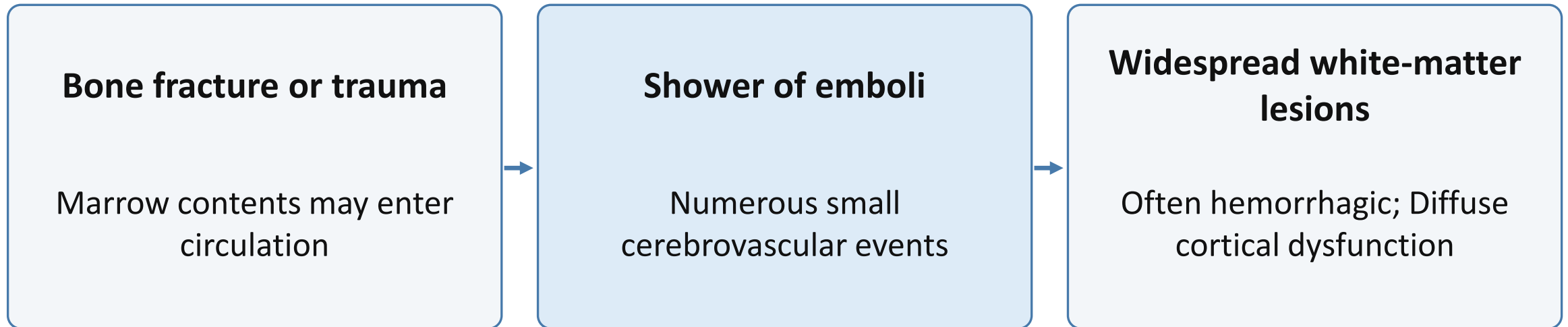
- A dominant occluded artery.
- A localized arterial territory.
- Focal neurologic dysfunction is often evident.

Multiple small emboli

- Many distal vascular occlusions.
- More widespread dysfunction.
- May lack clear localizing signs.

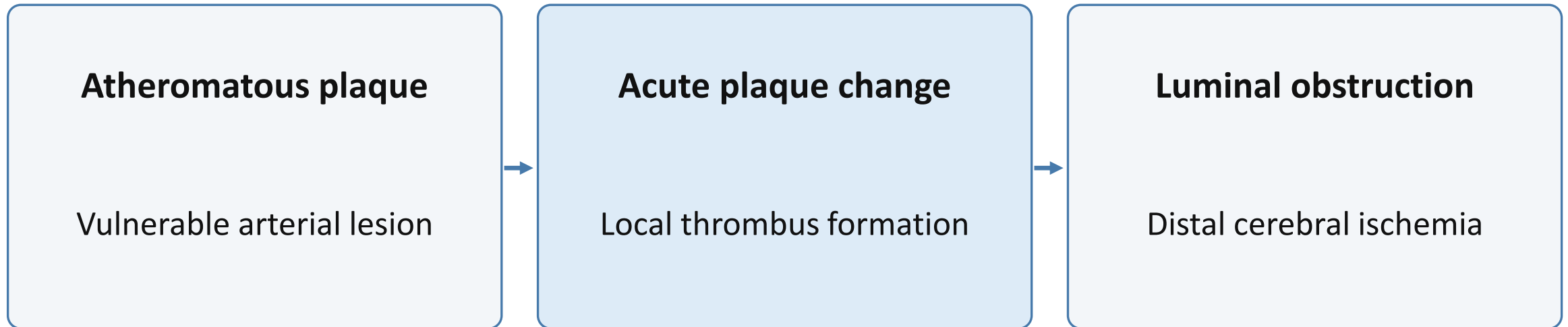
The second pattern is described in fat embolism after fractures.

Marrow/fat embolization after trauma



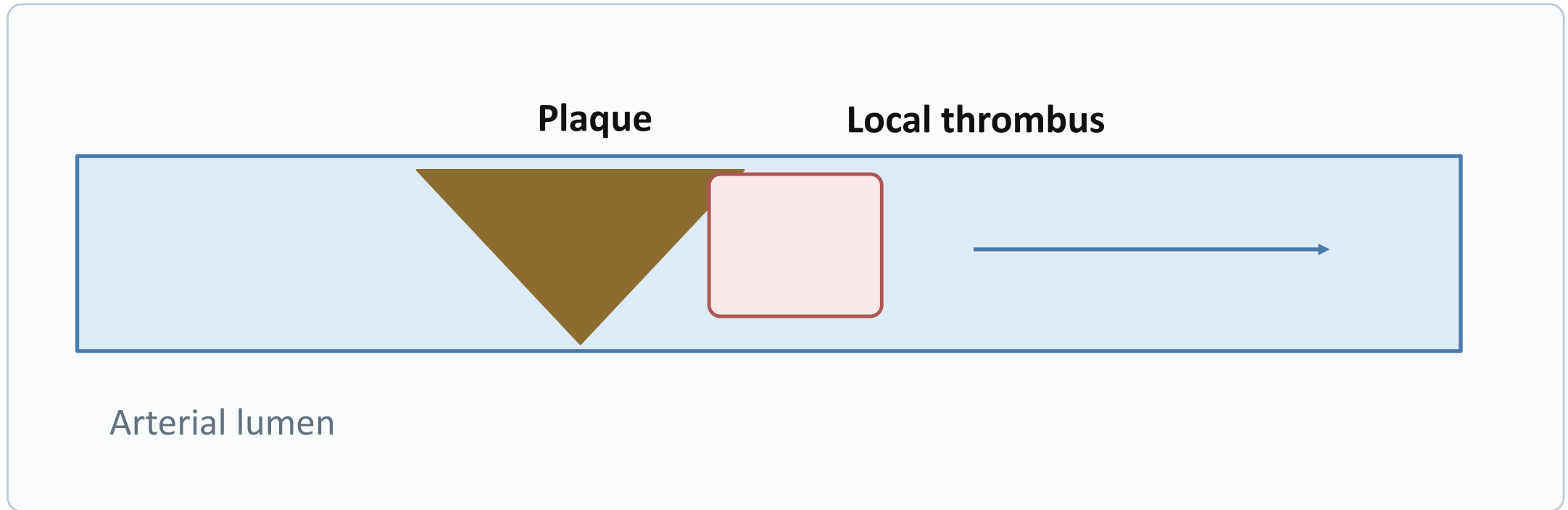
Higher cortical dysfunction and impaired consciousness can occur without focal signs.

In situ arterial thrombosis



The source identifies altered atherosclerotic plaque as the common mechanism.

Vulnerable plaque: Local mechanism



Schematic arterial lumen: Not a pathologic specimen.

Common sites of cerebral atherothrombosis

Carotid bifurcation

- Atherosclerosis-prone branching site.
- May obstruct flow or generate emboli.

MCA origin

- Proximal major intracranial artery.
- Direct downstream arterial territory.

Basilar artery ends

- Both ends are named vulnerable sites.
- Occlusion affects posterior circulation.

Thrombus can evolve in three ways

Progressive narrowing

Increasing local restriction of blood flow.

Anterograde extension

Thrombus propagates along the vessel.

Distal embolization

Fragmentation seeds downstream branches.

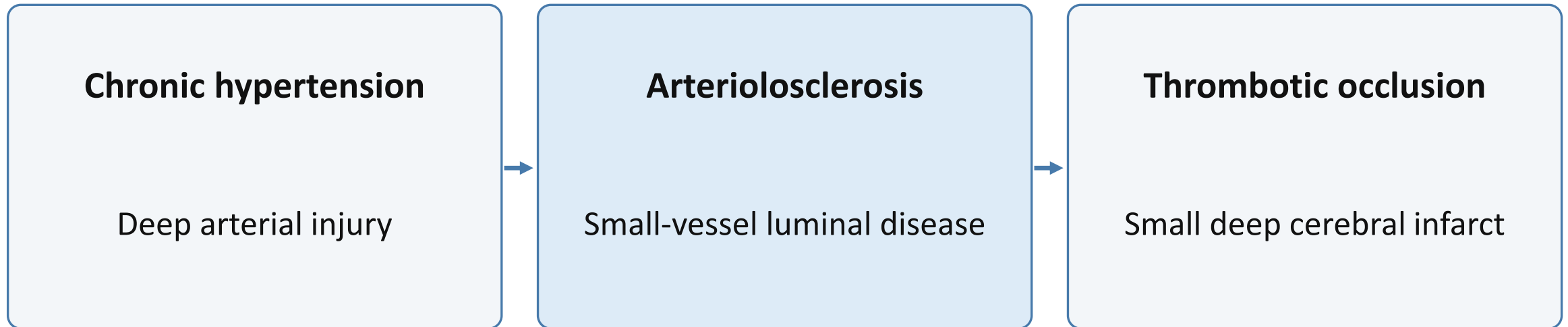
Atherosclerotic disease: Systemic associations

- Hypertension and diabetes commonly coexist with cerebrovascular atherosclerosis.
- Cerebral occlusive disease therefore often reflects systemic vascular pathology.
- Risk association does not specify whether a given infarct is thrombotic or embolic.

Diagnostic interpretation

The vascular lesion and distribution remain essential to mechanism attribution.

Hypertensive small-vessel disease



Arterioles and small arteries supplying deep CNS structures are involved.

Small-vessel caliber in the source

- Implicated arteries as approximately 40–900 μm in diameter.
- Affected vessels supply basal ganglia, hemispheric white matter, and brainstem.
- This is a morphologic small-vessel disease category, distinct from major carotid occlusion.

Scope

The caliber range is explicitly from the textbook; Not a proposed diagnostic cutoff for imaging.

Deep small-vessel territories

Deep gray nuclei

- Putamen and globus pallidus.
- Thalamus and caudate nucleus.

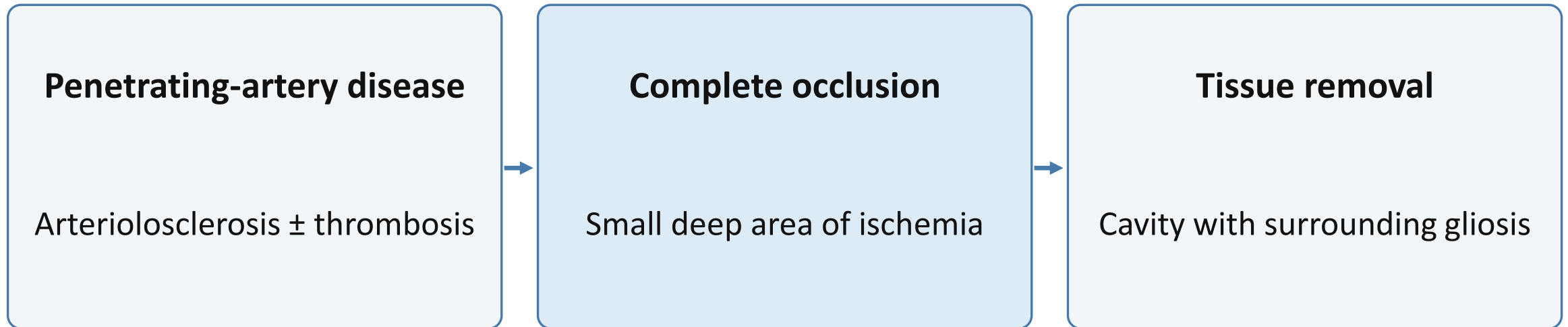
White matter

- Internal capsule.
- Other hemispheric deep white matter.

Brainstem

- Pons is a characteristic location.
- Deficits depend on the tract or nucleus involved.

How a lacune forms



A small lacunar infarct can be clinically silent or severely disabling.

Lacunar infarct: Anatomic distribution

- The source lists putamen, globus pallidus, thalamus, internal capsule, deep white matter, caudate, and pons.
- Several lesions may coexist in deep brain regions.
- Clinical impact is governed by exact location, not merely small size.

Interpretation

A lesion involving critical deep tracts can cause substantial impairment.

Gross and microscopic lacunar morphology

Gross appearance

- Small lake-like cavitory lesion.
- A conventional largest dimension below 15 mm.
- Can be single or multiple.

Microscopic appearance

- Definite loss of brain parenchyma.
- Gliosis around the tissue defect.
- Consistent with a healed small infarct.

The <15 mm definition is the supplied textbook convention.

État criblé is not a lacunar infarct

État criblé

- Widened perivascular spaces.
- No tissue infarction is required.
- Associated with diseased deep small vessels.

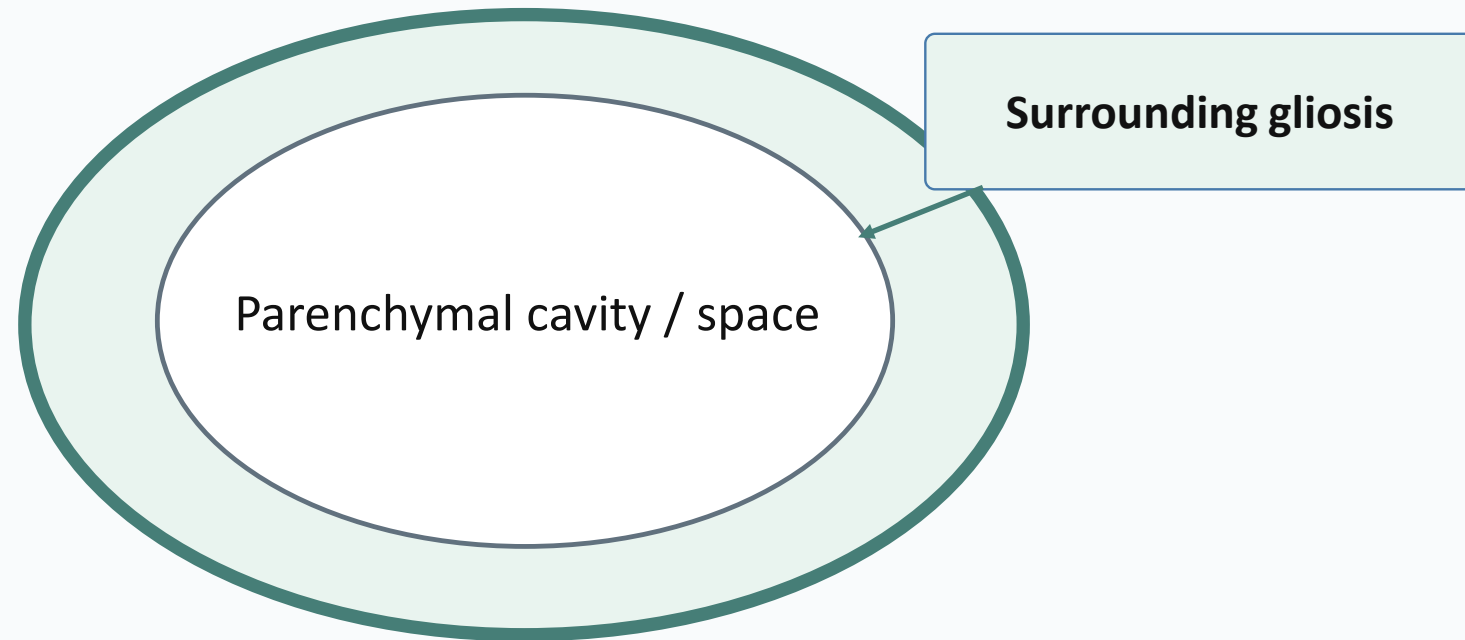
Lacunar infarct

- Ischemic tissue destruction has occurred.
- A true cavitary defect remains.
- Surrounding reactive gliosis is present.

A dilated space should not automatically be labeled an infarct.

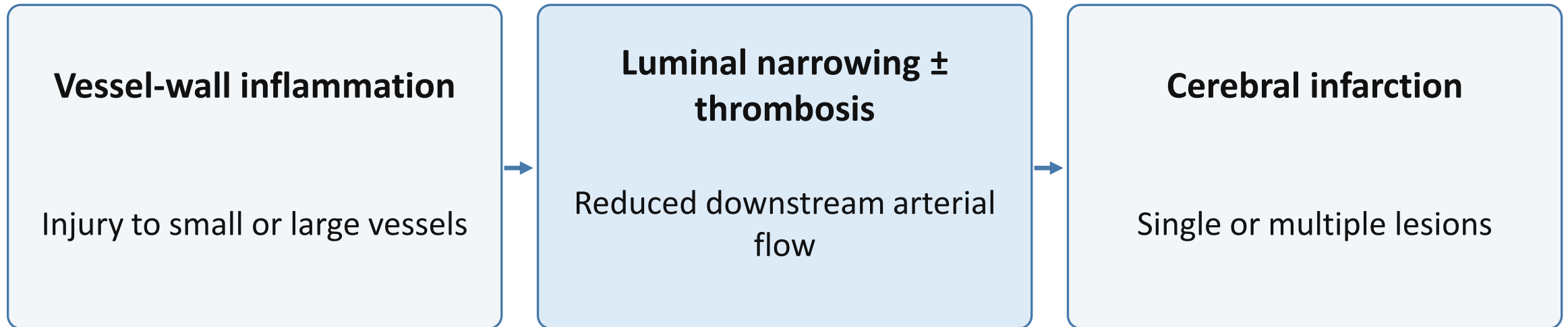
Small-vessel cavities: Interpret the tissue

Schematic



A lacune represents tissue loss; A widened perivascular space does not by itself establish infarction.

Vasculitis can obstruct cerebral flow



Both infectious and noninfectious vascular inflammation are recognized.

Infectious vasculitic causes

Syphilis

- Named classic infectious cause.
- May involve cerebral vessels.

Tuberculosis

- Another named infectious cause.
- Potential vessel inflammation and occlusion.

Opportunistic fungi

- Aspergillosis is a listed example.
- Relevant particularly with immunosuppression.

Noninfectious cerebral vasculitis

Systemic inflammatory disease

- Polyarteritis nodosa is a cited example.
- Other vasculitides may involve brain vessels.
- Infarcts may be multiple.

Primary angiitis of the CNS

- Vasculitis develops in the CNS.
- It may exist without systemic vasculitis.
- Produces cerebral ischemia through vessel injury.

No modern diagnostic criteria are imported beyond the supplied text.

Additional thrombotic/occlusive conditions

Hypercoagulability

- Can promote thrombosis.
- May also contribute to venous events.

Cervical arterial dissection

- Extracranial neck vessels can dissect.
- Downstream cerebral perfusion may suffer.

Substance exposure

- Amphetamines, heroin and cocaine are listed.
- Associated with vascular occlusive events.

Cerebral infarcts: Two morphologic patterns

Nonhemorrhagic

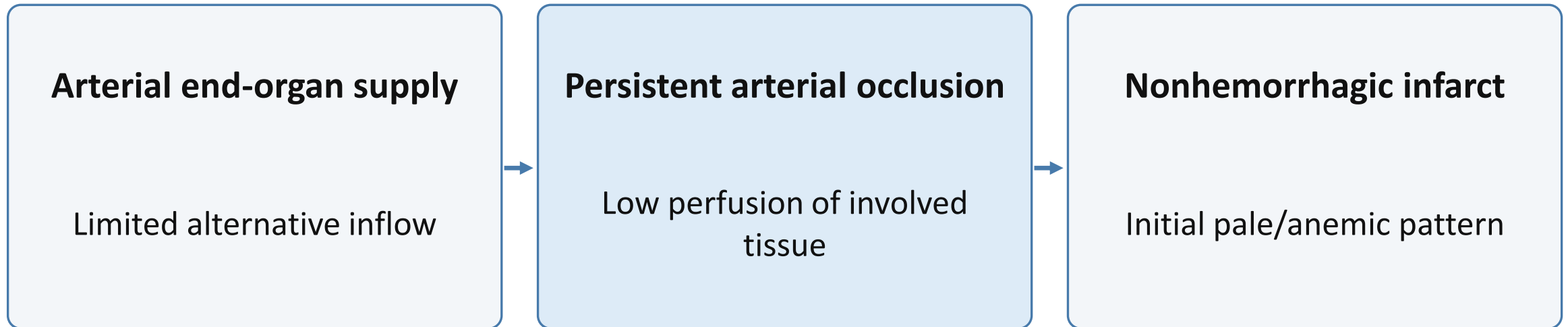
- Often begins pale or anemic.
- Typical initial occlusive pattern.
- Tissue softening and necrosis develop.

Hemorrhagic

- Secondary extravasation of blood.
- Often reflects reperfusion of damaged vessels.
- May be punctate or confluent.

Both are ischemic infarcts; The labels describe secondary hemorrhage.

Why occlusive infarcts usually begin pale



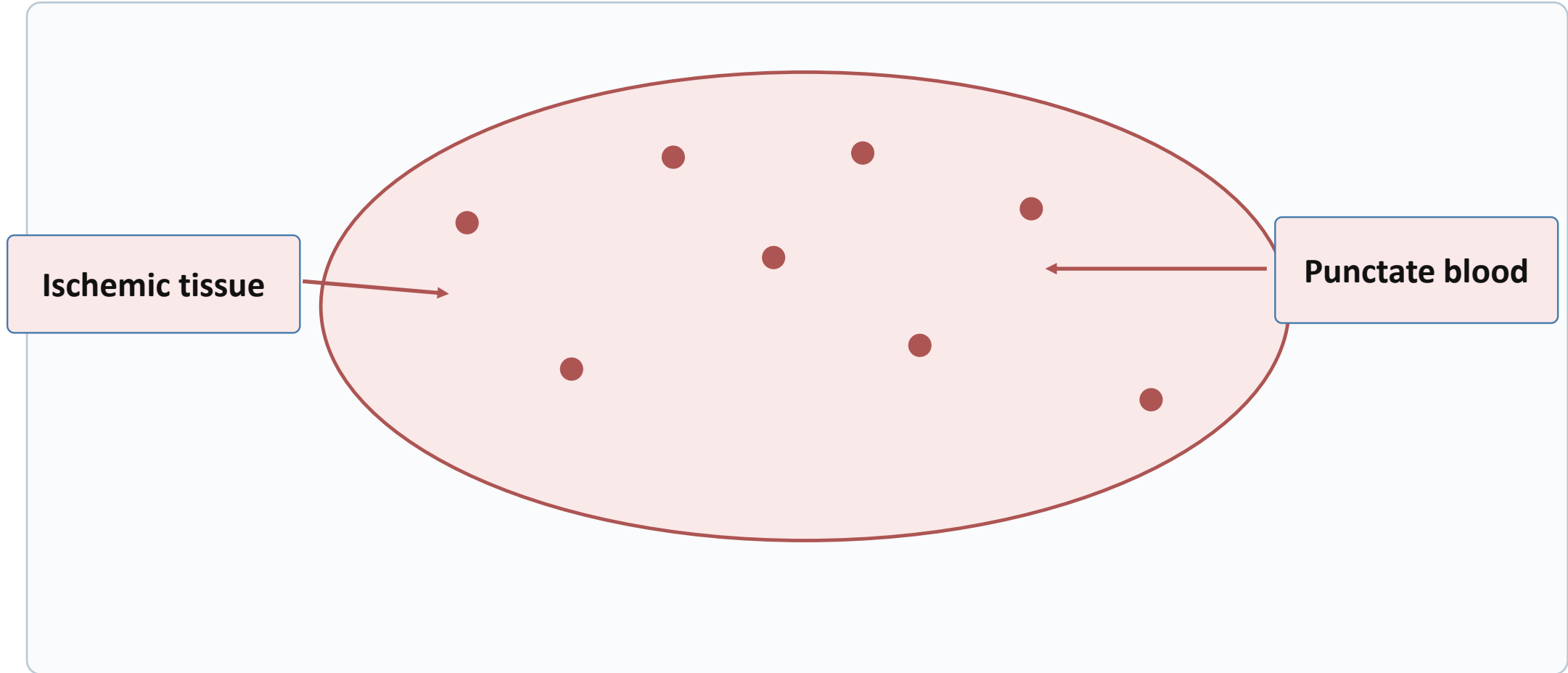
A nonhemorrhagic lesion can later undergo hemorrhagic transformation.

Hemorrhagic transformation: Causal sequence



Reperfusion injury explains secondary hemorrhage within an infarct.

Recognizing the reperfusion lesion



Schematic only. Red marks denote potential punctate secondary hemorrhage—not actual gross pathology.

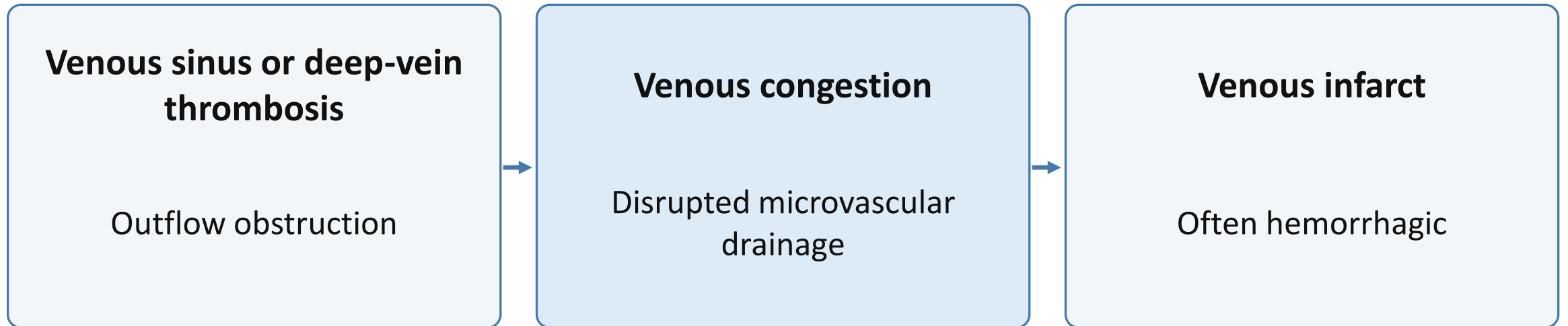
Anticoagulation and hemorrhagic extension

- Hemorrhagic infarcts include extravasated blood with subsequent resorption.
- Extensive intracerebral hematomas may occur in anticoagulated individuals.
- A hemorrhagic component materially changes acute treatment considerations.

Clinical safety

Robbins specifically cautions against thrombolysis when brain hemorrhage is present.

Cerebral venous infarcts



Superior sagittal sinus, other sinuses and deep cerebral veins are cited.

Venous infarction: Predisposing settings

Hypercoagulability

- Systemic propensity to thrombosis.
- A listed contributor to venous occlusion.

Neoplasm

- Cancer-associated clotting tendency can raise risk.
- Context affects diagnostic suspicion.

Local infection

- Another potential prothrombotic setting.
- Outflow obstruction can lead to hemorrhagic infarction.

Arterial and venous mechanisms compared

Arterial occlusion

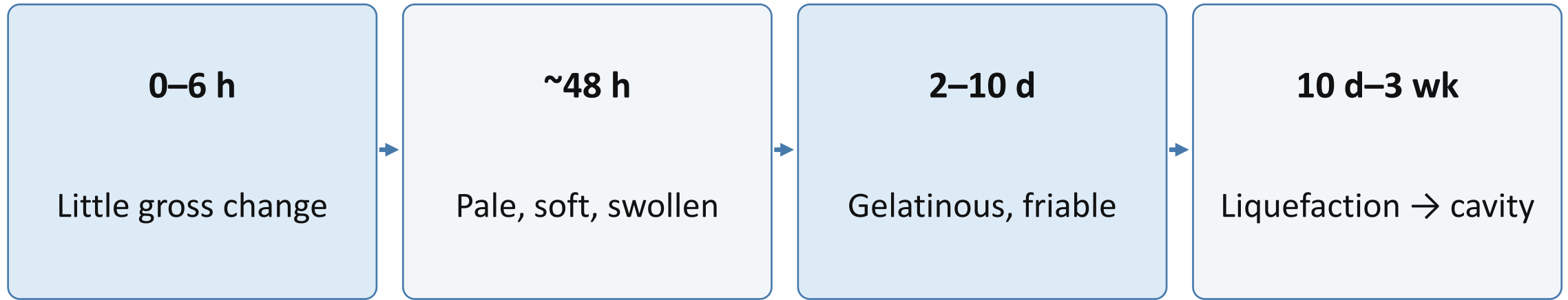
- Failure of inflow.
- Typically initially pale.
- May hemorrhage after reperfusion.

Venous thrombosis

- Failure of outflow.
- Venous infarction is often hemorrhagic.
- Sinus/deep vein obstruction is characteristic.

Gross hemorrhage alone does not identify the original vascular cause.

Gross appearance changes over time



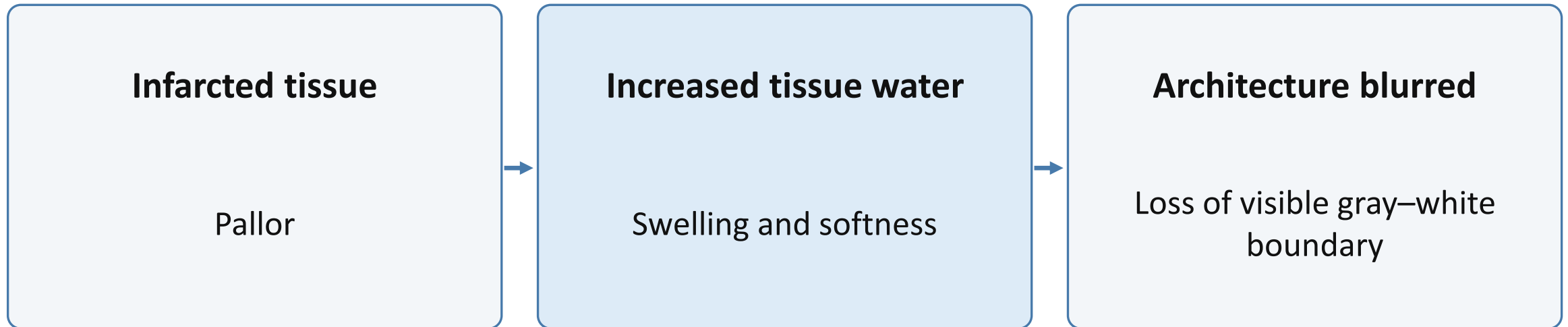
First six hours: Subtle gross appearance

- Even with irreversible injury, little gross change may be visible.
- A visually normal-looking region does not rule out early ischemic injury.
- Histologic changes and gross changes follow different time courses.

Observation

The first hours are a poor interval for gross recognition of infarction.

Around 48 hours: Edema and pallor



The infarct becoming pale, soft and swollen by roughly 48 hours.

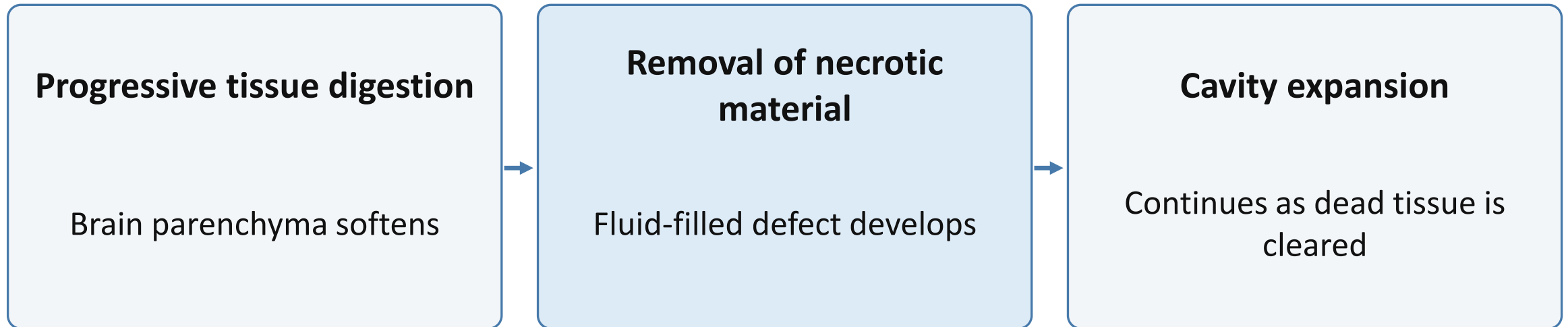
Days 2–10: Friability develops

- Dead tissue becomes gelatinous and friable.
- Infarct boundary becomes easier to appreciate.
- Resolution of adjacent viable-tissue edema sharpens the interface.

Why the border appears

The evolving distinction is partly due to reduction of edema outside the lesion.

Days 10–21: Liquefaction and cavitation



The cavity is the end result of tissue loss, not a restored normal cortex.

Gross evolution integrates two processes

Early injury

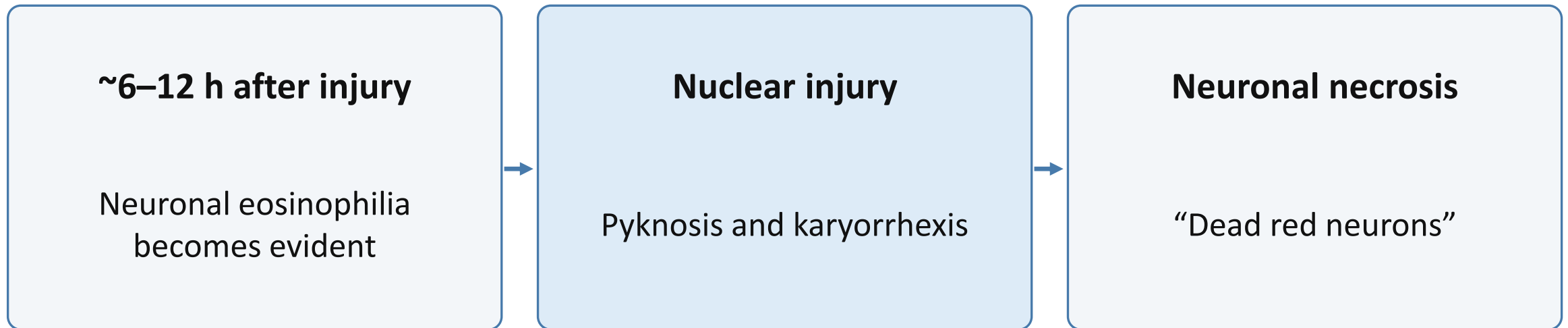
- Loss of perfusion and cell damage.
- Pallor, swelling, and softening.
- Tissue remains present but nonviable.

Later cleanup

- Phagocytosis and liquefaction.
- Removal of damaged parenchyma.
- Development of a residual cavity.

Timing is approximate and varies within and between lesions.

Acute microscopy: Red neurons



Schematic chronology; No photomicrograph has been reproduced.

“Dead red neuron”: Components of the sign

Cytoplasm

- Greater eosinophilia.
- Associated neuronal shrinkage.

Nucleus

- Pyknosis and karyorrhexis.
- Irreversible nuclear injury.

Context

- Acute ischemic neuronal necrosis.
- Needs clinical-anatomic correlation.

Acute edema involves cells and interstitium

Cytotoxic edema

- Cellular swelling during ischemic injury.
- Neurons and glia are vulnerable.
- Coexists with other early changes.

Vasogenic edema

- Fluid accumulation outside cells.
- Occurs concurrently in acute infarcts.
- Contributes to gross swelling.

Both forms are described in the acute infarct phase.

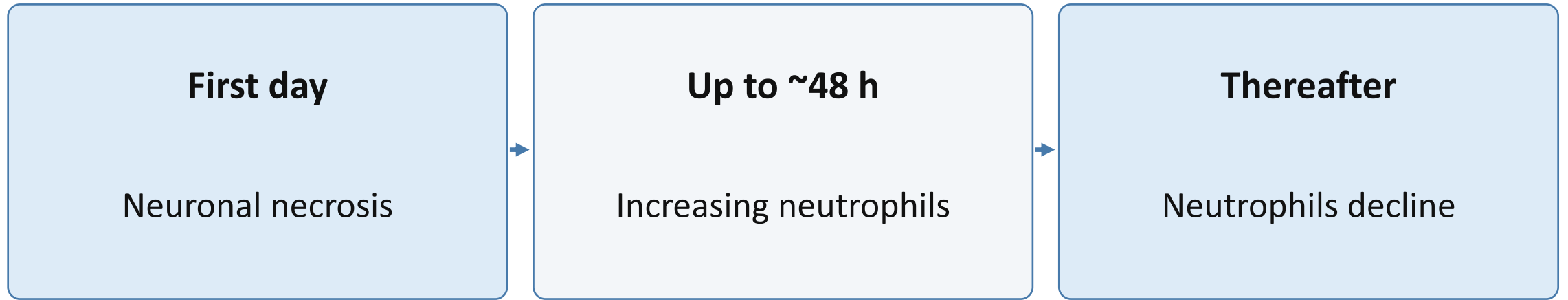
Early glial and myelin injury

- Astrocytes and endothelial cells swell in the acute lesion.
- Normal staining distinction between gray and white matter is lost.
- Myelinated fibers begin to disintegrate.

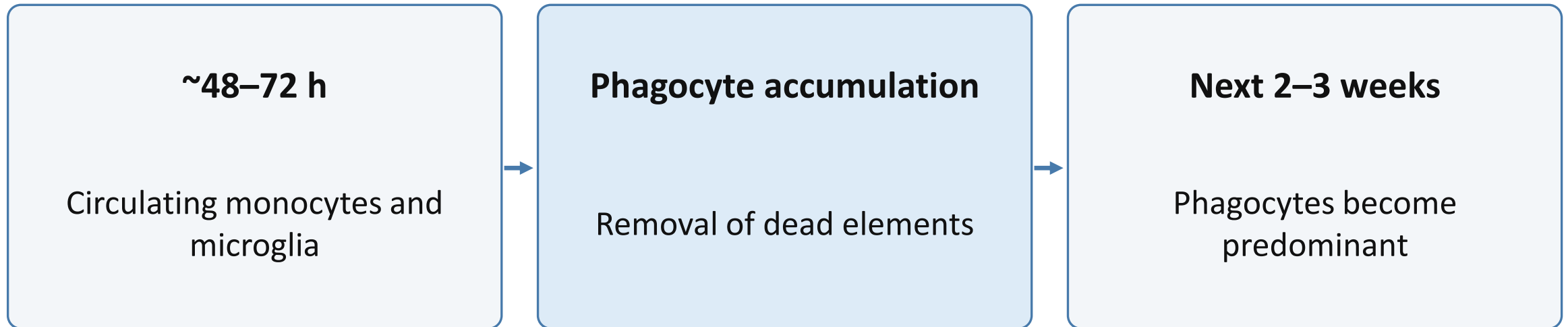
Tissue-level message

Neuronal death is not the only component of infarct evolution.

Neutrophils enter during early infarction



Macrophages and microglia arrive



Macrophage-dominant cleanup distinguishes evolving from very early lesions.

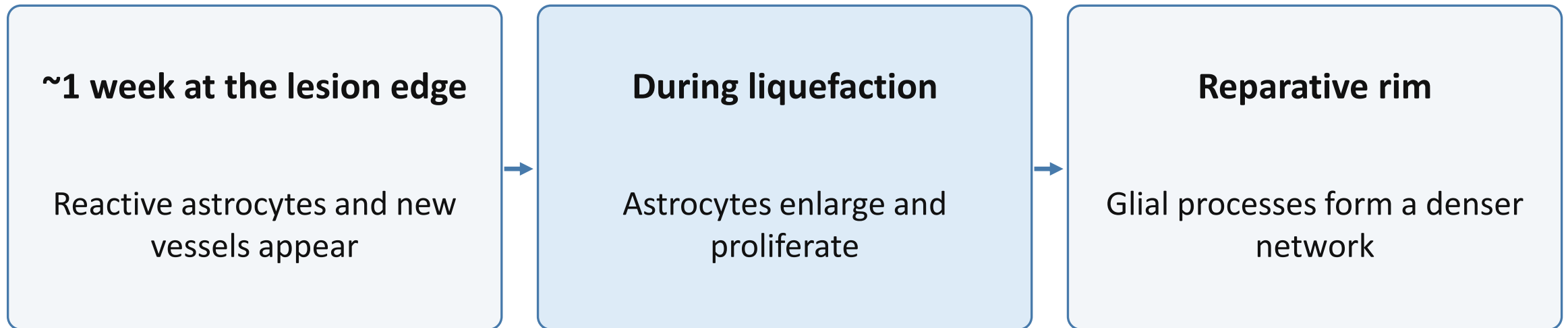
Foamy macrophages signal cleanup

- Macrophages ingest degraded myelin and sometimes blood products.
- Their cytoplasm becomes laden with phagocytosed material.
- They may remain within the lesion for months or years.

Interpretive value

A lipid-laden macrophage population supports an organizing infarct in context.

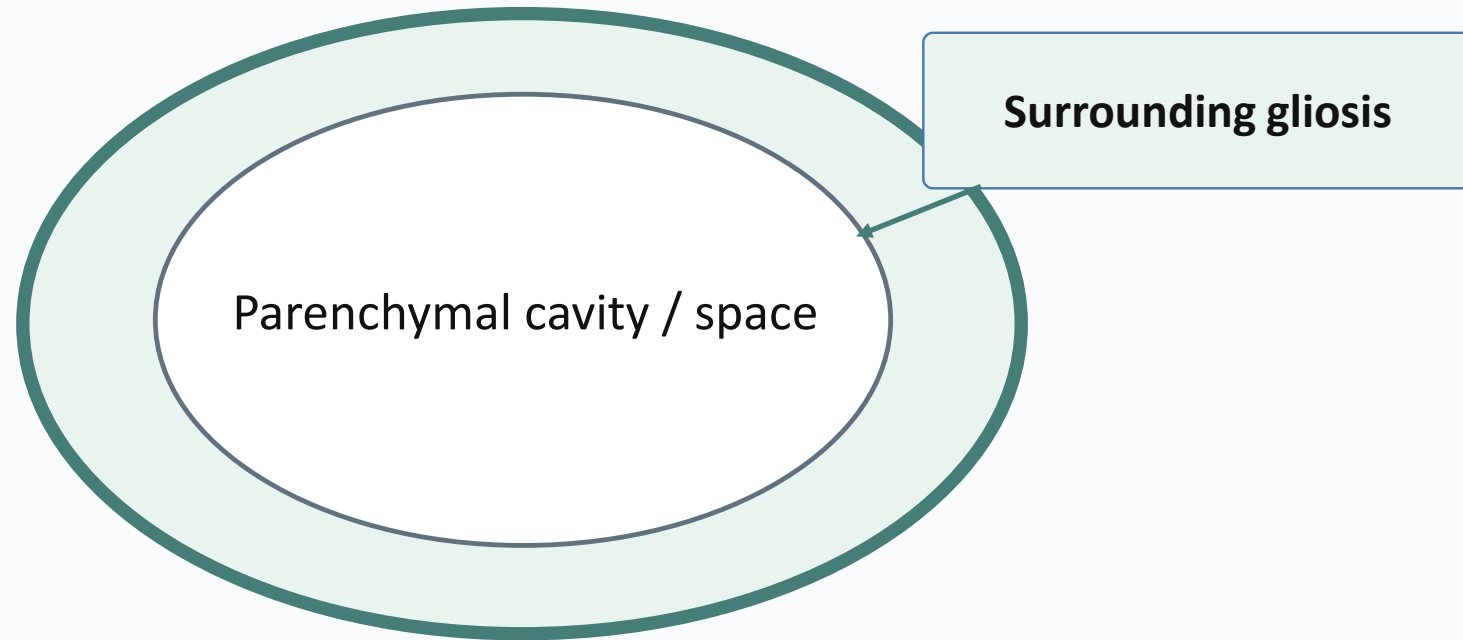
Peripheral astrogliosis and neovascularization



Reparative reactions are especially prominent at the infarct margin.

Remote infarct: Cyst cavity and glial rim

Schematic



Schematic healed infarct: Parenchymal loss surrounded by gliosis and capillaries.

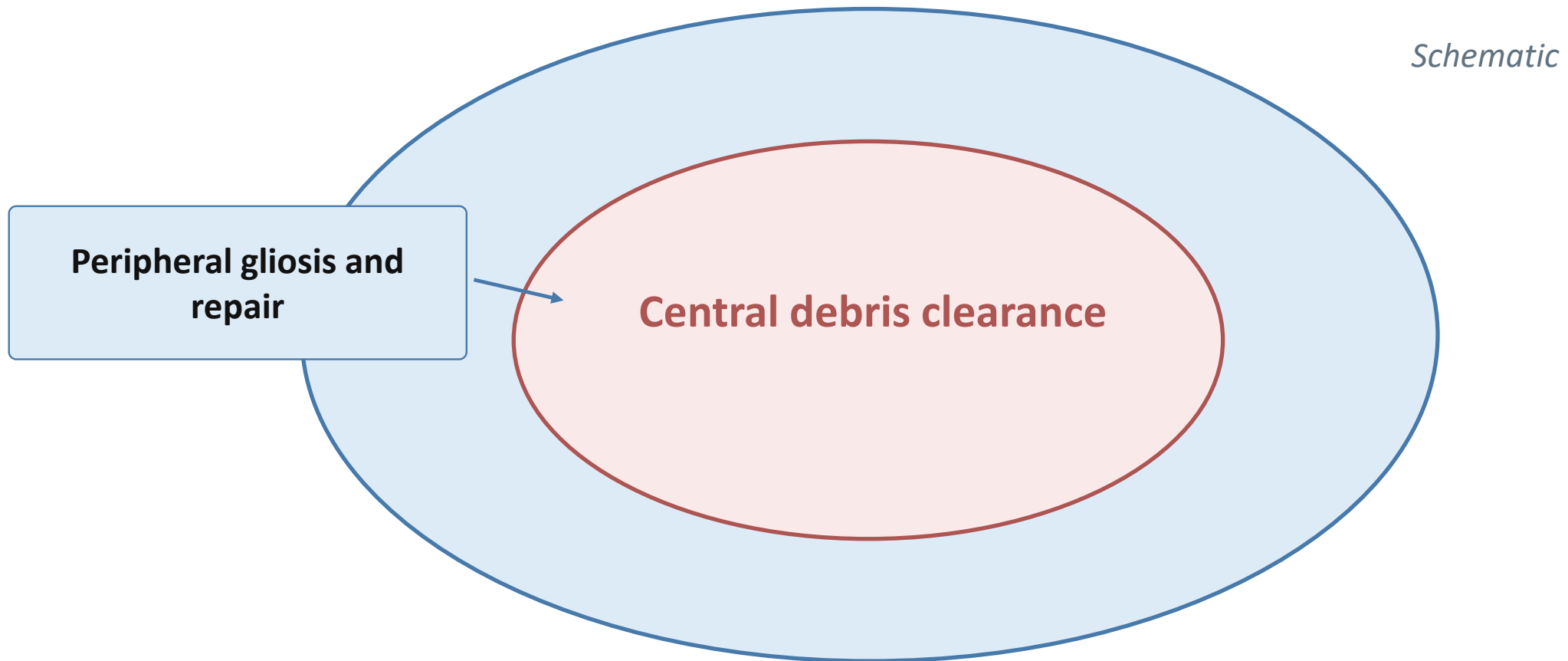
The cortex retains a gliotic boundary

- In a remote cortical infarct, the cavity is separated from meninges by gliotic tissue.
- The residual layer derives from the cortical molecular layer.
- Pia and arachnoid are not directly destroyed by the infarct in this description.

Morphologic point

A fluid-filled parenchymal cavity need not be continuous with subarachnoid space.

Evolution occurs from the edge inward



Schematic process: A single infarct can show different apparent ages in adjacent zones.

Histologic stages: A diagnostic comparison

Stage	Approximate period	Dominant findings
Acute	~6–48 hours	Red neurons, edema, neutrophils
Evolving	~48 hours to weeks	Microglia/macrophages, then astrogliosis
Remote	After months	Cyst cavity with gliotic, vascularized rim

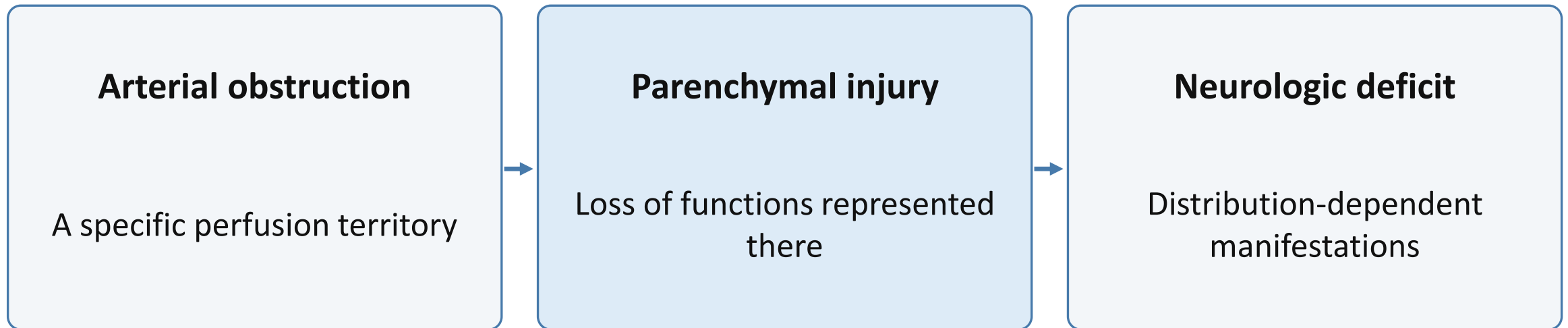
The clock is approximate, not absolute

- Reactions overlap and are spatially heterogeneous.
- The periphery may organize while the center remains in an earlier cleanup phase.
- Use morphology and anatomic context rather than assigning a single exact hour.

Practical principle

Progression from infarct
edge to center.

Clinical deficit reflects the damaged territory



Cause alone does not predict signs; Localization matters.

Symptoms usually develop rapidly

- Neurologic manifestations often start over minutes.
- The deficit may continue to evolve over hours.
- Time course plus focal neurologic distribution prompts urgent vascular assessment.

Clinical correlation

The presentation reflects rapidly evolving tissue damage and its territory.

Clinical severity need not track lesion diameter

Small strategic infarct

- May interrupt essential deep pathways.
- Lacunes can cause severe neurologic dysfunction.

Small nonstrategic infarct

- May remain clinically silent.
- Anatomic location remains decisive.

Robbins explicitly contrasts silent and disabling lacunar infarcts.

Recovery has more than one substrate

At-risk tissue

- Some threatened tissue may recover.
- Penumbra preservation is biologically important.

Surrounding edema

- Edema resolution may improve function.
- Changes can occur without replacing dead neurons.

Longer evolution

- Slow recovery can continue for months.
- Extent depends on initial injury.

Why hemorrhage assessment is urgent

No hemorrhage demonstrated

- A nonhemorrhagic arterial infarct is possible.
- Urgent reperfusion decisions can be relevant.

Brain hemorrhage present

- Management materially differs.
- Thrombolysis is contraindicated with intracranial hemorrhage.

This is pathology-level rationale—not a treatment protocol or eligibility checklist.

Applied case: Sudden focal dysfunction

Clinical vignette

A patient develops an abrupt focal neurologic deficit. A cardiac mural thrombus is identified.

Which pathogenesis best explains a new MCA-territory infarct?

Cardioembolism: A heart-derived thrombus travels distally and obstructs a cerebral artery.

- Mural thrombus provides a distant source.
- MCA territory is a common embolic destination.
- Anatomic localization predicts the deficit.

Applied case: Small deep cavity

Clinical vignette

A patient with longstanding hypertension has a small healed cavitory lesion in the internal capsule.

What vascular process and microscopic rim are expected?

Deep penetrating-artery small-vessel disease causing a lacunar infarct, with surrounding gliosis.

- Hypertension affects penetrating vessels.
- Lacunes are small tissue-loss cavities.
- A strategic deep location can be clinically important.

Applied case: Secondary hemorrhage

Clinical vignette

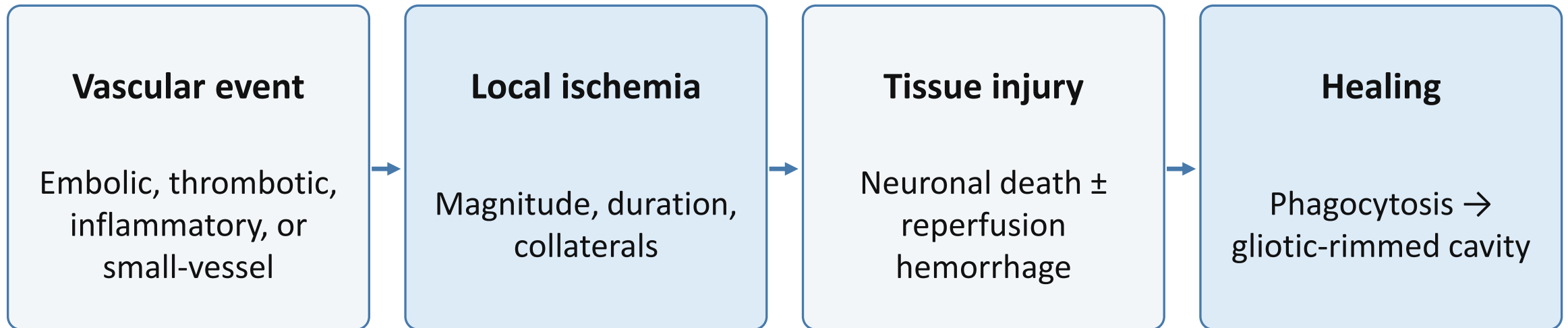
An initially pale arterial infarct later contains punctate hemorrhages after vessel recanalization.

Which mechanism links the two appearances?

Hemorrhagic transformation from reperfusion of previously injured microvessels.

- Prolonged ischemia injures small vessel walls.
- Restored flow permits extravasation.
- This is not synonymous with primary vessel rupture.

Integrated pathogenesis and tissue response



Lesion anatomy determines the neurologic syndrome.

Key distinctions to retain

Mechanism

- Embolus travels;
Thrombus forms locally.
- Surface collaterals differ
from deep vessels.

Morphology

- Pale and hemorrhagic
describe blood content.
- Lacune requires
parenchymal tissue loss.

Timeline

- Red neurons early;
Macrophages later.
- Remote lesions cavitate
with gliosis.

Primary reference and source boundaries

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

Chapter 28 · The Central Nervous System

Focal cerebral ischemia; adjacent hypoxia/ischemia and cerebrovascular disease
context

No chapter PDF or licensed textbook micrographs were supplied. Illustrations here are original
editable schematics, not diagnostic images.