

Cerebrovascular Disease

Vascular mechanisms · cerebral injury · clinicopathologic patterns

A pathology lecture

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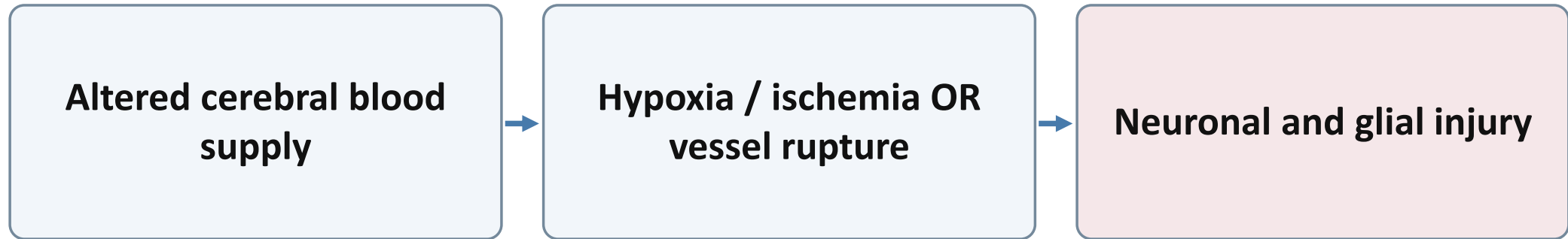
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Learning outcomes

- Separate ischemic injury from primary hemorrhage and explain their convergent neuronal damage.
- Relate vascular occlusion, collateral flow, and ischemic duration to infarct distribution.
- Recognize evolving cerebral infarction morphology and the major hemorrhagic patterns.
- Explain aneurysms, vascular malformations, and cumulative vascular cognitive injury.

Two major pathways to cerebrovascular injury



- Both mechanisms can ultimately produce tissue infarction or parenchymal destruction.

Ischemic and hemorrhagic stroke

Predominantly ischemic mechanism

- Reduced perfusion or oxygen delivery to neural tissue.
- Localized arterial obstruction or generalized circulatory failure.
- Infarction reflects sustained irreversible damage.

Predominantly hemorrhagic mechanism

- Rupture of intracranial arteries or other vessels.
- Extravasated blood displaces and injures parenchyma.
- Secondary compression and ischemic tissue injury can coexist.

What is meant by stroke?

- An acute neurological syndrome attributed to a vascular mechanism.
- The Robbins text describes a duration-based definition: Symptoms persisting beyond 24 hours.
- The clinical deficit is determined chiefly by the injured anatomic territory.
- Mechanisms include arterial occlusion and vessel rupture.

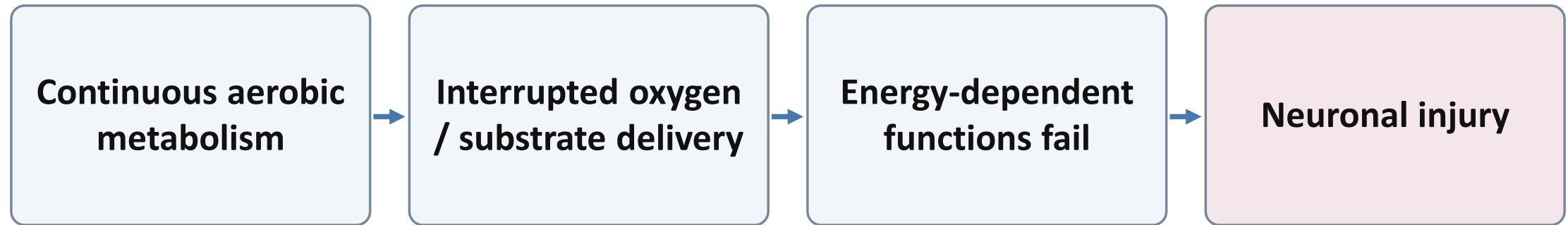
Transient ischemic attack in the source

- The traditional symptom-duration threshold: Resolution within 24 hours.
- A transient syndrome indicates reversible clinical dysfunction, not necessarily a harmless event.
- The book's operational description is presented here as a source-specific definition, not a contemporary diagnostic guideline.

The brain has extraordinary metabolic demand

- Approximately 1%–2% of total body weight, but about 15% of resting cardiac output.
- Approximately 20% of body oxygen consumption is attributed to the brain.
- Continual aerobic ATP supply makes nervous tissue susceptible to interrupted perfusion.

Why perfusion failure rapidly threatens neurons



- Severity depends on residual perfusion, collateral vessels, and duration of the insult.

Cerebral autoregulation

- Vascular resistance adjusts to maintain relatively stable cerebral blood flow.
- This compensation operates across a substantial range of perfusion pressures.
- Severe hypotension or vascular occlusion may overwhelm compensatory capacity.

Hypoxemia is not identical to ischemia

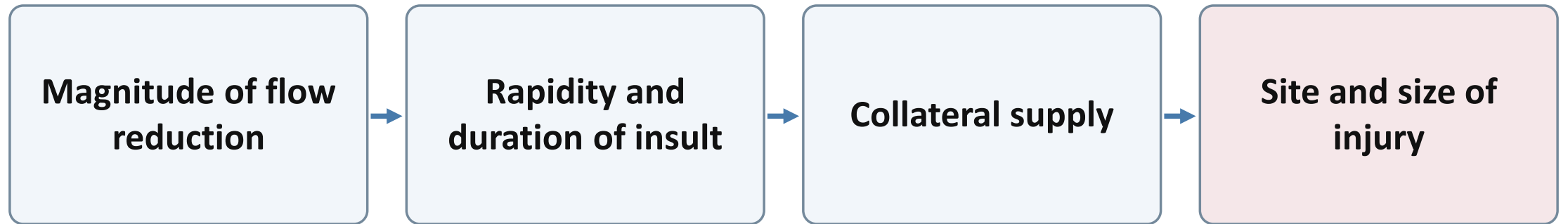
Hypoxemia

- Reduced oxygen content of circulating blood.
- Oxygen delivery falls even if some perfusion is maintained.
- Example in the source: Carbon monoxide poisoning.

Ischemia

- Insufficient blood flow to the brain or a region.
- Caused by low perfusion pressure, vessel obstruction, or both.
- May be global or confined to a vascular territory.

Four determinants of infarct expression



- These variables determine both lesion morphology and clinical consequences.

CNS excitotoxicity after ischemia



- CNS-specific amplification occurs alongside general mechanisms of ischemic cell damage.

Infarct core versus penumbra

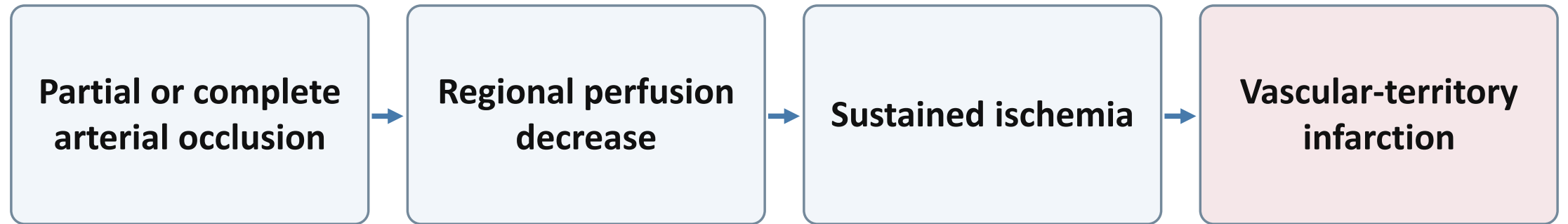
Irreversibly injured core

- Severely compromised perfusion with established cell death.
- Morphology reflects time from the ischemic insult.

Ischemic penumbra

- Adjacent hypoperfused tissue remains at risk.
- Viability may persist and recovery is possible with timely restoration of flow.
- Apoptotic pathways may contribute to neuronal loss.

Focal cerebral ischemia: Territorial injury



- Infarct geometry depends on arterial territory, collateral routes, and time.

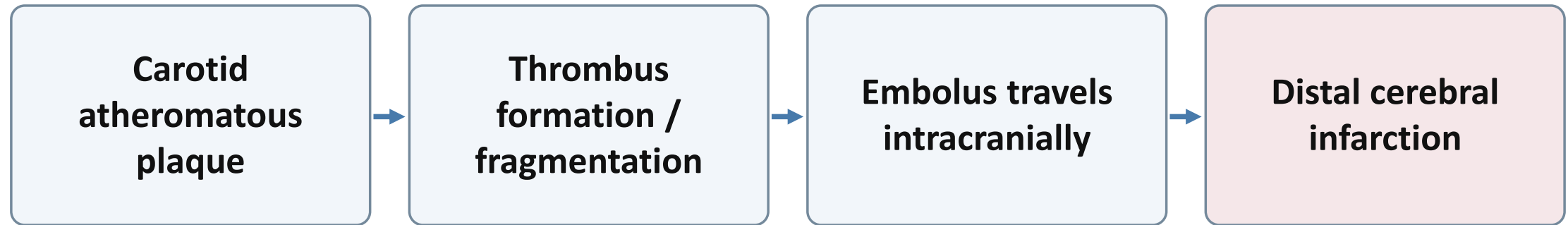
Major mechanisms of arterial occlusion

Mechanism	Typical initiating process	Relevant consequence
Embolization	Material travels from heart or proximal artery	Abrupt distal territorial occlusion
In-situ thrombosis	Occlusion develops at diseased arterial wall	Reduced luminal flow or distal embolization
Vasculitic injury	Inflammatory narrowing or thrombosis	Single or multiple cerebral infarcts
Small-vessel disease	Hypertensive penetrating-arteriole damage	Lacunar infarction or hemorrhage

Cardiac sources of cerebral emboli

- Mural thrombi associated with myocardial infarction may embolize to cerebral arteries.
- Atrial fibrillation and valvular disease are important predisposing conditions.
- Other embolic material can include tumor, fat, or air.
- The occlusion site often lies at a branch point or pre-existing stenosis.

Artery-to-artery thromboembolism



- The carotid arteries are major extracranial sources of atherothrombotic cerebral emboli.

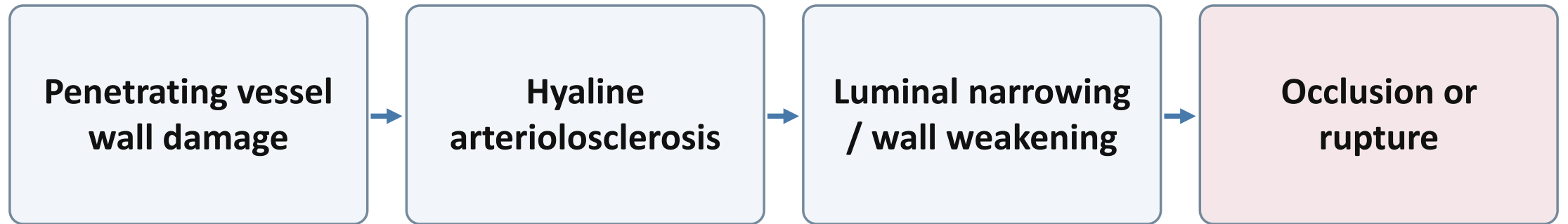
Why the MCA territory is often affected

- The middle cerebral artery is a direct continuation of internal carotid arterial flow.
- It is the cerebral arterial distribution most often involved by embolic infarcts in the source.
- Deficits vary with the involved cortical and deep structures.
- An embolus may obstruct a branch point or stenotic segment.

Large-artery thrombosis: Characteristic sites

- Thrombotic disease commonly complicates unstable atherosclerotic plaques.
- Important locations include carotid bifurcation, MCA origin, and ends of the basilar artery.
- Thrombus can propagate locally or fragment into downstream emboli.
- Hypertension and diabetes often coexist with atherosclerotic cerebrovascular disease.

Small-vessel injury in chronic hypertension

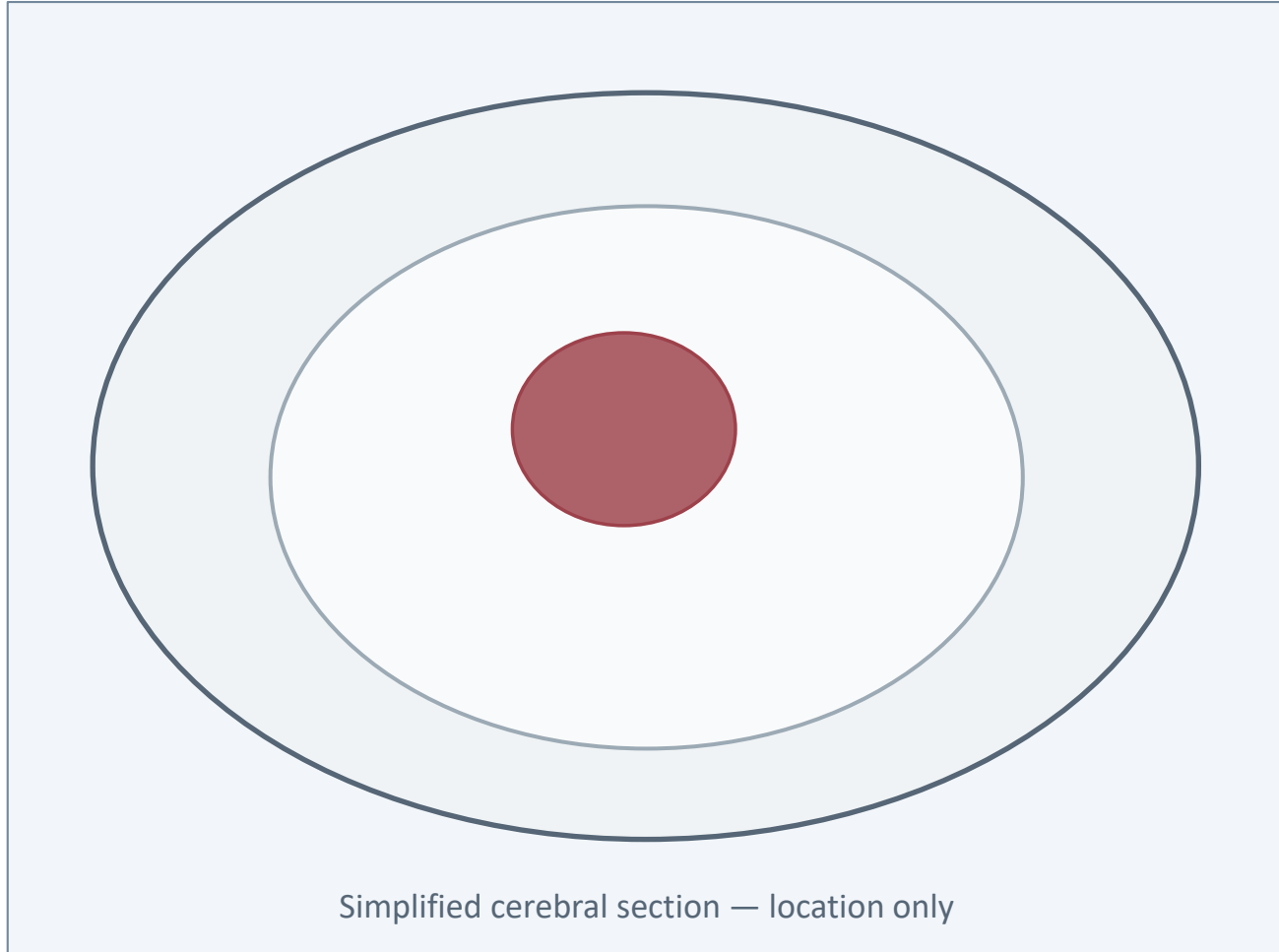


- The same vessel disease can therefore underlie lacunar infarction or deep brain hemorrhage.

Deep perforators have limited collateral supply

- Penetrating vessels feed basal ganglia, thalamus, deep white matter, and brainstem.
- Leptomeningeal collaterals primarily connect cortical arterial territories.
- Small-vessel occlusion may consequently injure a discrete deep region.
- Clinical severity can be substantial despite a small lesion.

Lacunar infarction: Deep location



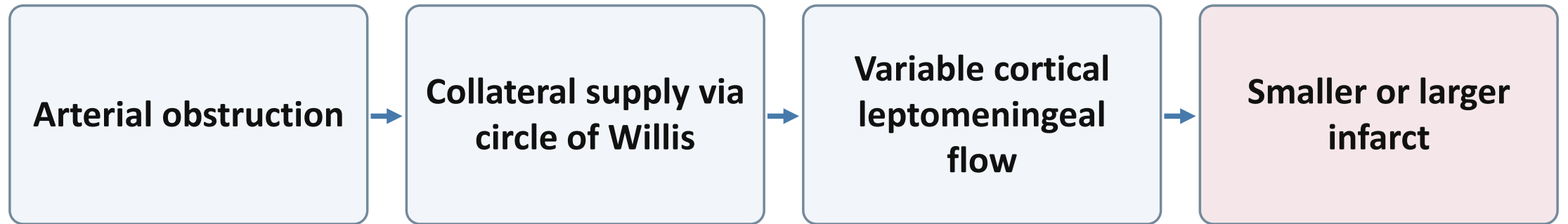
A lacune is a small cavitory infarct.

- Typical locations include putamen, thalamus, internal capsule and pons.
- Microscopy shows tissue loss bordered by gliosis.

Lacunes: Pathological size and outcome

- The source describes an arbitrary gross cutoff of less than 15 mm in greatest dimension.
- They are often multiple in chronic hypertensive small-vessel disease.
- Depending on location, they may be silent or produce severe impairment.
- Enlarged perivascular spaces without infarction are termed état criblé.

How collateral circulation influences injury



- Deep perforating territories have comparatively few alternatives to their parent vessel.

Additional focal ischemic etiologies

- Primary CNS angiitis and systemic inflammatory vasculitides can compromise arterial lumina.
- Infectious vasculitis may occur, including in immunosuppressed patients.
- Hypercoagulable states and cervical arterial dissection may precipitate stroke.
- The source also lists selected vasoactive substance exposures.

Pale infarction and hemorrhagic transformation

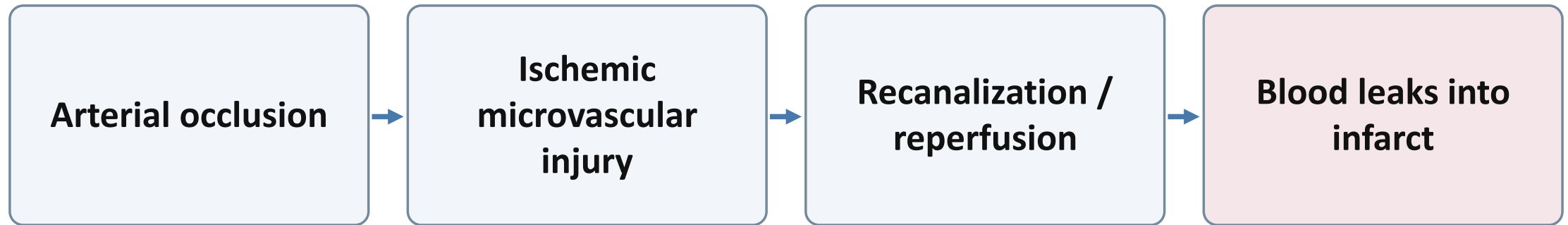
Nonhemorrhagic infarct

- Most occlusive infarcts begin with little extravasated blood.
- Early gross appearance can be pale and swollen.
- Ischemia remains the underlying lesion mechanism.

Hemorrhagic infarct

- Previously ischemic vessels are damaged.
- Reperfusion can cause punctate or confluent extravasation.
- Blood may appear within the territory of a recent infarct.

Mechanism of hemorrhagic transformation



- This secondary hemorrhage is distinct from rupture of a previously intact deep parenchymal vessel.

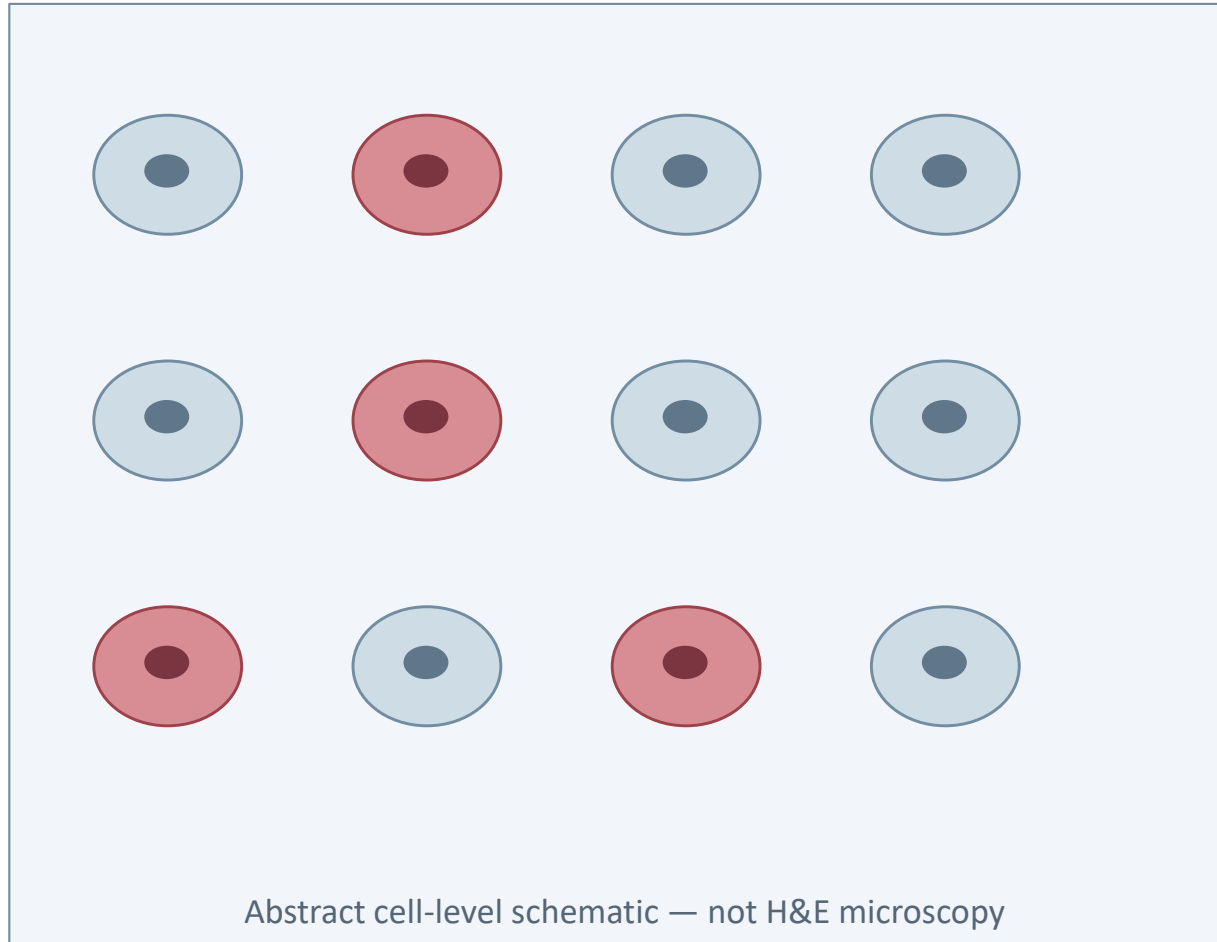
Primary hemorrhage versus hemorrhagic infarction

Feature	Primary parenchymal hemorrhage	Hemorrhagic transformation
Initiating event	Vessel rupture with a hematoma	Occlusion and ischemic infarction
Role of blood	Primary space-occupying lesion	Secondary extravasation into infarct
Pattern	Commonly central blood clot	Often punctate hemorrhage in infarct territory
Background	Hypertension, amyloid angiopathy, etc.	Reperfusion after vessel obstruction

Gross evolution of nonhemorrhagic infarction

0–6 hours	~48 hours	2–10 days	10 d–3 wk
Little visible gross change Irreversible injury may already exist	Pale, soft and swollen Gray–white margin obscured	Gelatinous and friable Infarct margin becomes clearer	Liquefactive breakdown Progressive cavity formation

Acute neuronal injury: The “red neuron”

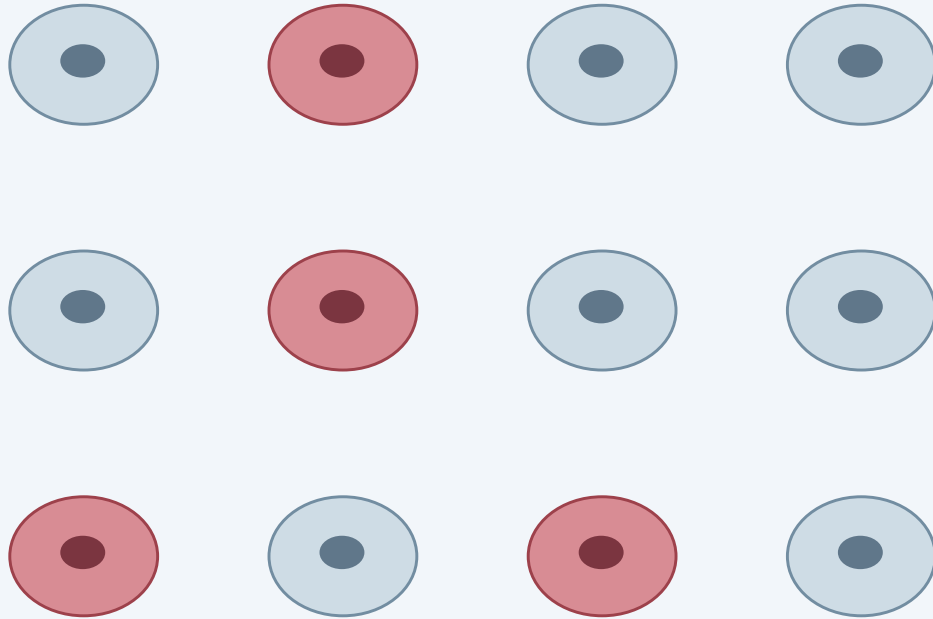


- After roughly 6–12 hours, neurons develop deeply eosinophilic cytoplasm.
- Nuclear pyknosis and karyorrhexis follow.
- Neuronal necrosis coexists with cellular swelling and edema.

Early microscopy beyond neuronal necrosis

- The normal staining distinction of gray and white matter deteriorates.
- Endothelial cells and astrocytes swell; Myelinated fibers begin disintegrating.
- Neutrophils progressively enter for up to about 48 hours.
- The neutrophilic response is less conspicuous than in myocardial infarction.

Subacute infarction: Phagocytic response



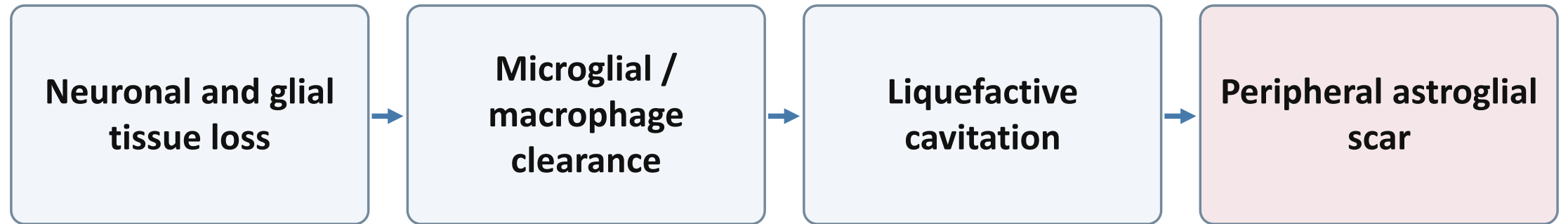
Abstract cell-level schematic — not H&E microscopy

- At about 48–72 hours, monocyte-derived macrophages and activated microglia appear.
- Phagocytes dominate the lesion over the next 2–3 weeks.
- Foamy cells ingest myelin products and sometimes blood remnants.

Gliososis and vascular repair at the infarct edge

- Reactive astrocytes and newly formed vessels can be seen from about 1 week.
- Astrocytes enlarge, proliferate, and elaborate interlacing processes.
- The injury is cleared from its periphery inward.
- Different regions of one lesion may show different stages at one time.

Healed cerebral infarction



- After several months, a cystic cavity remains with a dense gliotic rim and new capillaries.

Microscopic evolution of cerebral infarction

Phase	Dominant pathological findings
Acute	Red neurons, edema, glial swelling; subsequent neutrophils
Subacute	Foamy macrophages, activated microglia, reactive astrocytes and vessels
Remote	Cystic tissue loss bordered by a dense glial scar

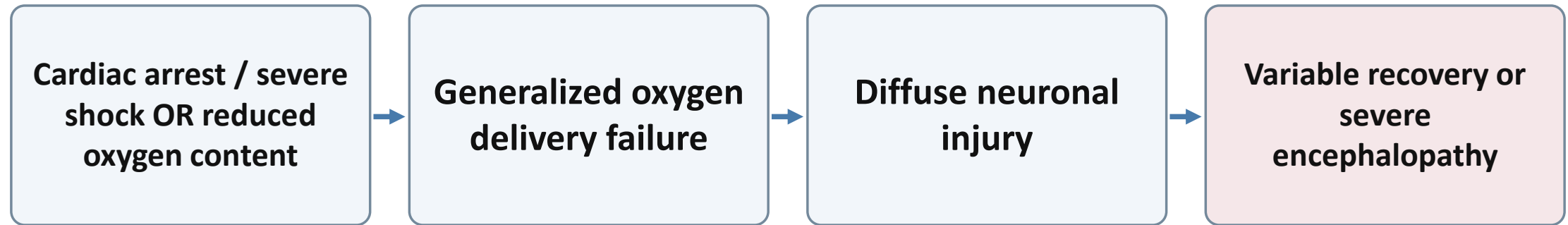
Clinical deficit follows anatomy

- Neurological signs arise from the structures injured, not simply the embolic or thrombotic source.
- Deficits often appear over minutes and can evolve over hours.
- Edema and ischemic penumbra may contribute to temporarily impaired function.
- Recovery can occur over months, but established tissue necrosis is not restored.

Why the infarct boundary matters clinically

- The infarct core contains nonviable parenchyma.
- The penumbra and edematous adjacent brain can be functionally impaired but potentially viable.
- Timely diagnosis and restoration of flow can prevent additional permanent injury.
- Primary hemorrhage must be distinguished before therapies that increase bleeding risk.

Global cerebral hypoxia / ischemia



- Unlike a focal arterial occlusion, global injury can involve both hemispheres and multiple structures.

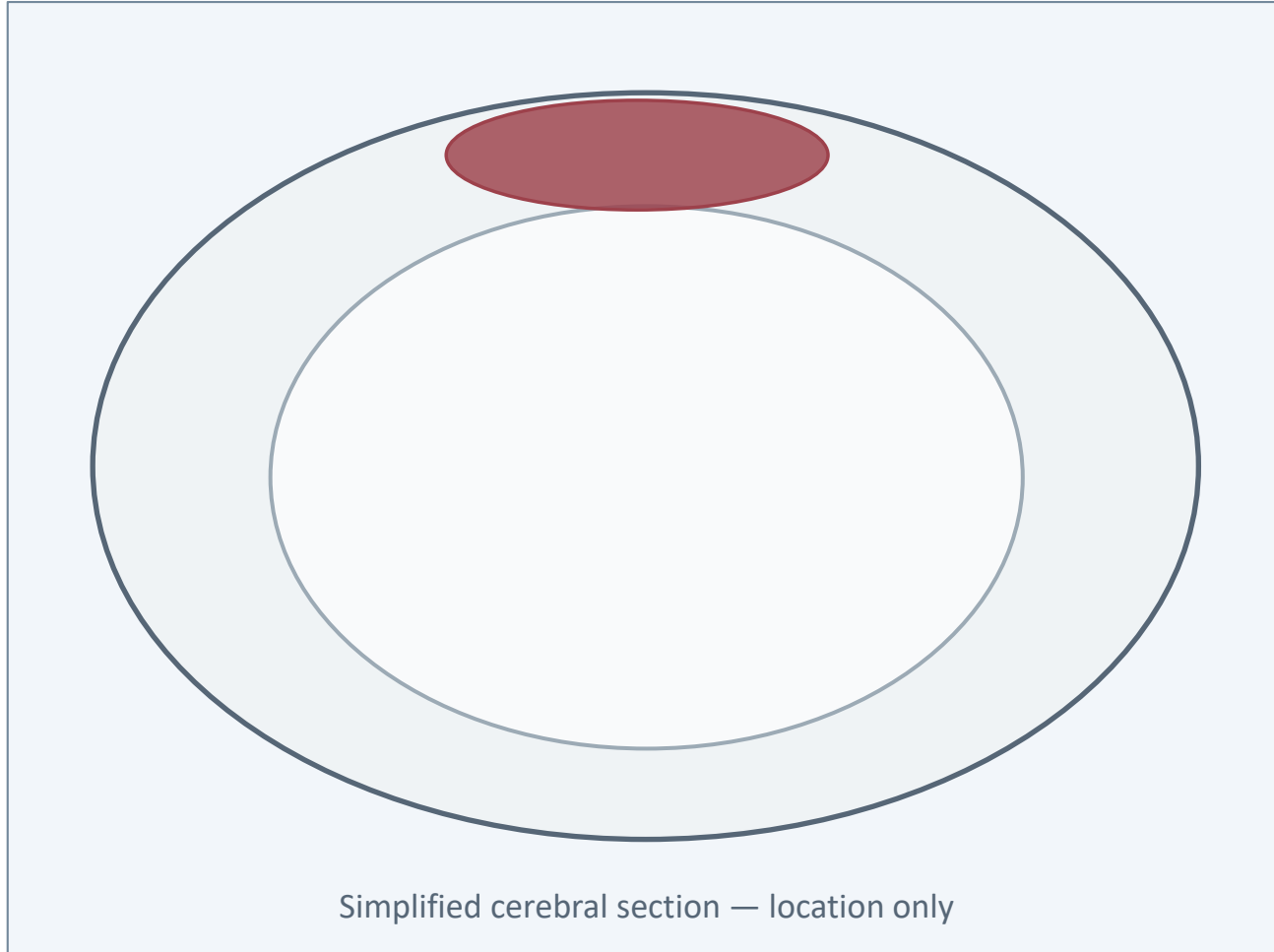
Global insults: Major contexts

- Generalized perfusion loss can follow cardiac arrest, shock, or profound hypotension.
- Reduced blood oxygen-carrying capacity can produce global hypoxic injury.
- Outcome depends on the intensity and duration of oxygen deprivation.
- Milder episodes may result in transient confusion and recovery.

Selective neuronal vulnerability

- Neurons are generally more sensitive than glia to global hypoxia–ischemia.
- Especially vulnerable: Hippocampal CA1 pyramidal neurons.
- Cerebellar Purkinje cells are also selectively susceptible.
- Cortical layers III and V contain particularly sensitive pyramidal neurons.

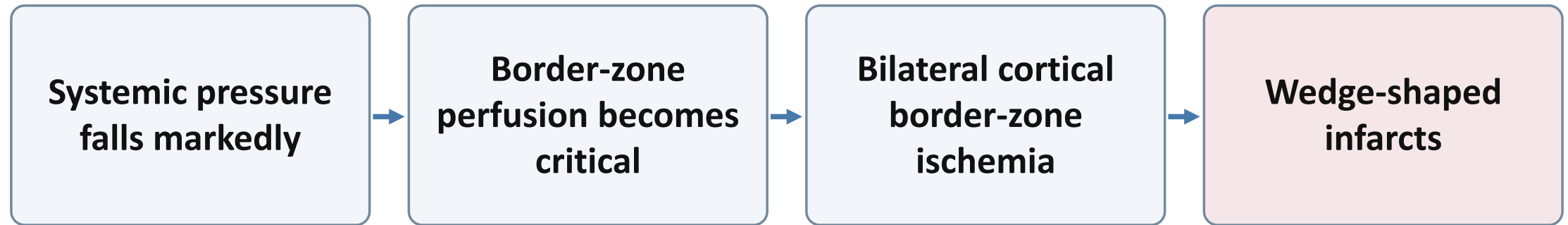
Watershed infarcts occur at arterial borders



Distal arterial boundary zones have relatively marginal flow.

- The anterior–middle cerebral artery border is particularly vulnerable.
- Severe systemic hypotension may produce bilateral lesions.

Mechanism of watershed injury



- Secondary hemorrhagic transformation can be present; The source emphasizes ACA–MCA border regions.

Global ischemia: Gross morphology

- Diffuse cerebral edema causes swollen, broad gyri and narrowed sulci.
- Gray-white differentiation becomes difficult to identify on cut surfaces.
- Microscopically, changes follow stages resembling those of focal infarction.
- Early red neurons precede macrophage recruitment and gliosis.

Global ischemia: Histopathological course

6–12 h	24 h–2 wk	After ~2 wk
Acute red neurons	Tissue necrosis	Removal of necrosis
Early cytotoxic injury	Phagocytes + gliosis	Cysts + residual gliosis

Laminar cortical necrosis

- Hypoxic injury may affect cortical layers unevenly.
- Selective loss of neurons in some layers and preservation of others creates a laminar pattern.
- The tissue response includes neuronal loss and reactive gliosis.
- This represents a morphological pattern of cortical global ischemic injury.

Consequences of severe global injury

- Widespread neuronal death may cause sustained loss of meaningful responsiveness.
- Severe diffuse injury may involve cerebral cortex and brainstem.
- The chapter describes clinical brain death using irreversible neurologic injury criteria.
- Brain death is a clinical determination; Histology alone does not establish it.

Ischemic lesions: The essential distinctions

Territorial · lacunar · border-zone · diffuse

- Territorial infarcts reflect focal arterial occlusion and variable collateral flow.
- Lacunar lesions reflect deep perforating small-vessel injury.
- Watershed lesions reflect vulnerable border-zone flow during severe hypotension.

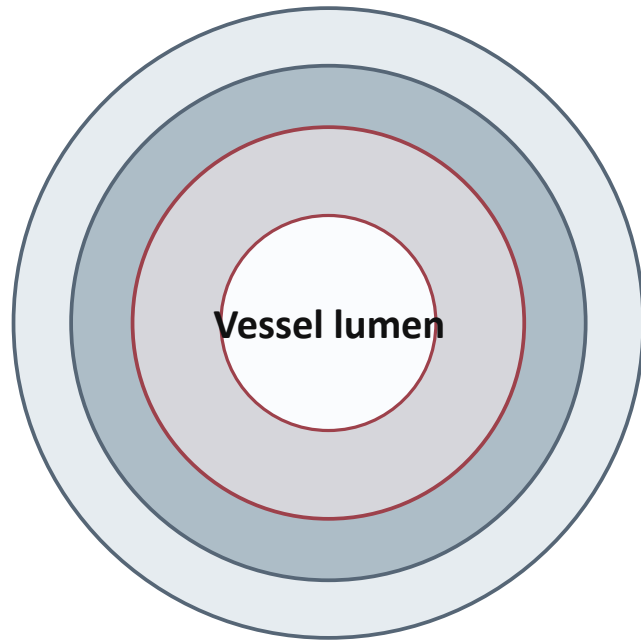
Where can intracranial blood accumulate?

Compartment	Typical context	Pathologic consequence
Epidural	Most often trauma	Extra-axial compression
Subdural	Most often trauma	Extra-axial blood collection
Subarachnoid	Trauma or aneurysmal / vascular lesion	Blood within CSF-containing space
Intraparenchymal	Hypertension, CAA, lesions, tumors	Tissue destruction and hematoma

Primary intraparenchymal hemorrhage

- Rupture of a small vessel deposits blood directly within the brain parenchyma.
- The hematoma can compress adjacent tissue, producing edema and secondary ischemic damage.
- Two major spontaneous patterns are deep ganglionic and superficial lobar hemorrhage.
- The underlying vessel disease is a strong clue to location and morphology.

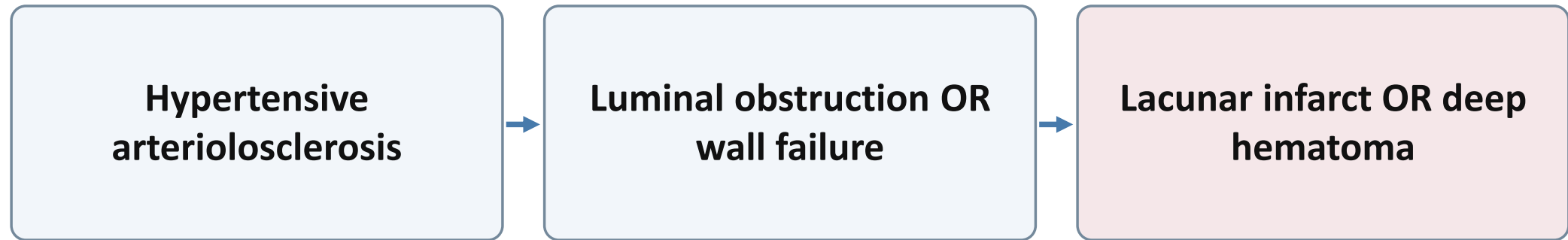
Hypertensive hyaline arteriolosclerosis



Schematic wall section

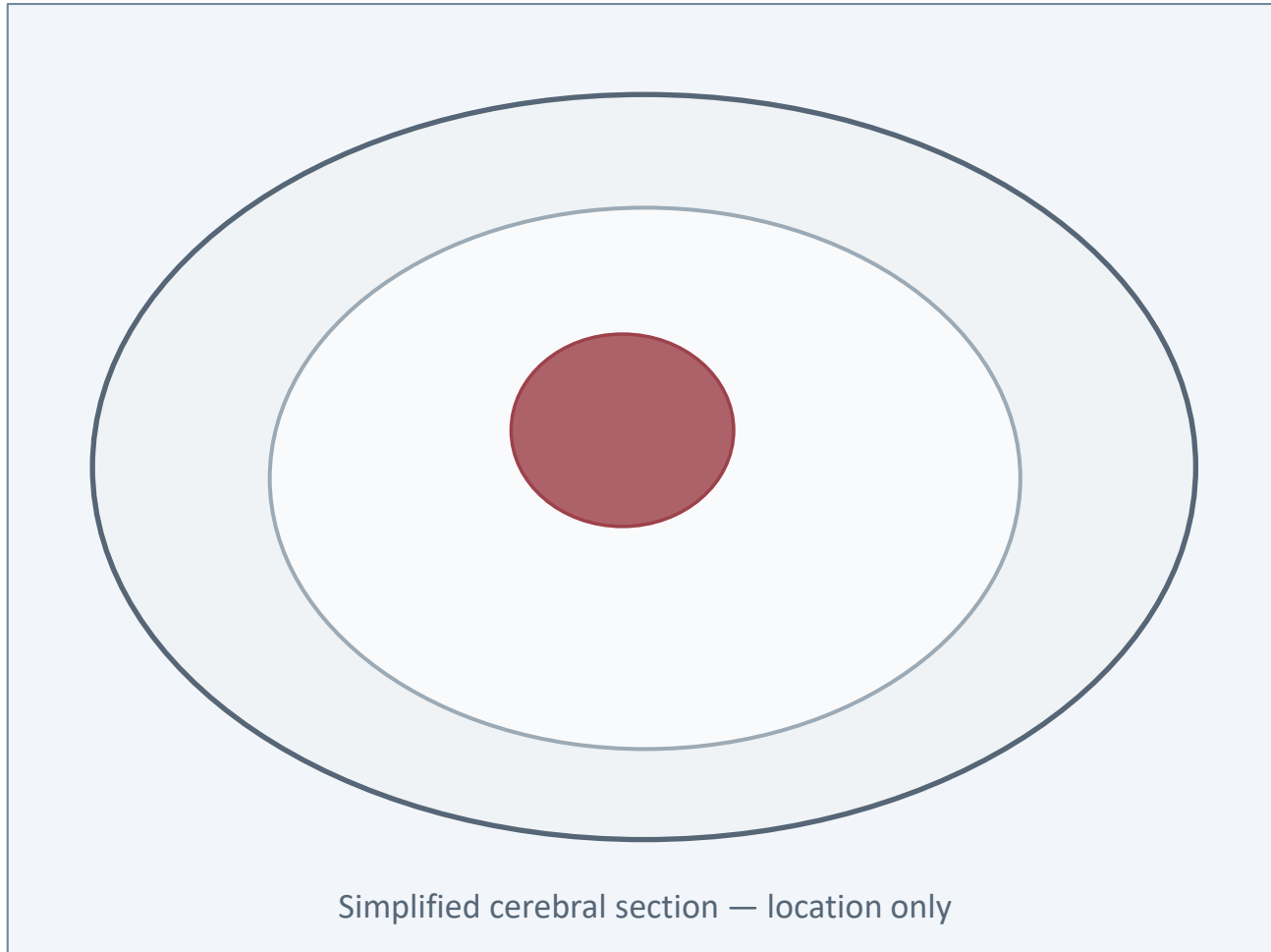
- Chronic hypertension causes thickening and fibrosis of small penetrating arteriolar walls.
- Affected walls become rigid and structurally vulnerable.
- Occlusion can cause a lacune; Rupture can produce deep hemorrhage.
- The process preferentially injures basal ganglia and deep white-matter vessels.

One arteriolar disease, two outcomes



- Vessel-wall pathology connects the ischemic and hemorrhagic manifestations of chronic hypertension.

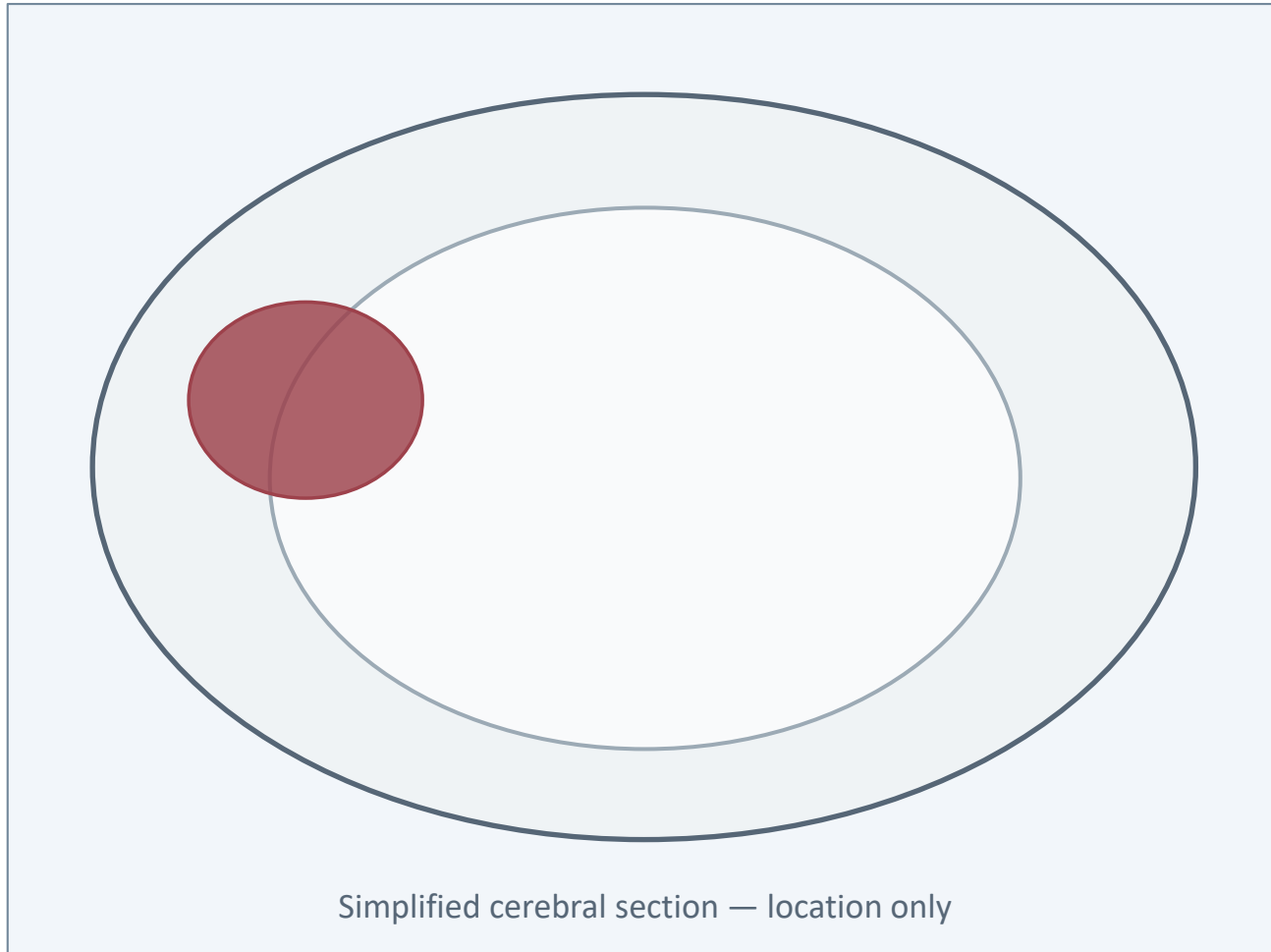
Hypertensive hemorrhage: Deep location



The putamen and thalamus are common sites.

- Cerebellum and pons can also be affected.
- A large hematoma may rupture into the ventricular system.

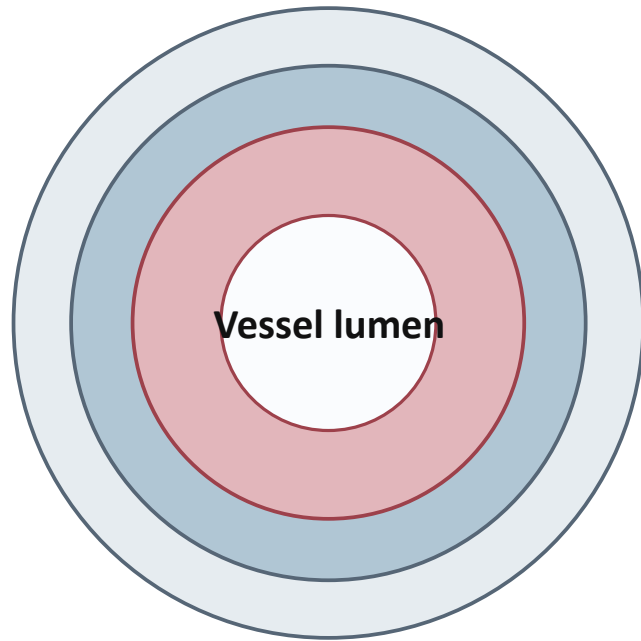
Cerebral amyloid angiopathy: Lobar hemorrhage



β -amyloid accumulates in meningeal and cortical arterial walls.

- Rigid, amyloid-laden vessels are prone to bleeding.
- A characteristic consequence is superficial or lobar hemorrhage.

Cerebral amyloid angiopathy: Vessel-wall injury



Schematic wall section

- Amyloid deposition involves leptomeningeal, cortical and cerebellar vessels.
- Accumulation is β -amyloid rather than the collagen of ordinary hyaline sclerosis.
- Vessel-wall fragility may cause lobar hemorrhage and multiple microbleeds.
- CAA is distinct from hypertensive basal ganglia arteriolosclerosis.

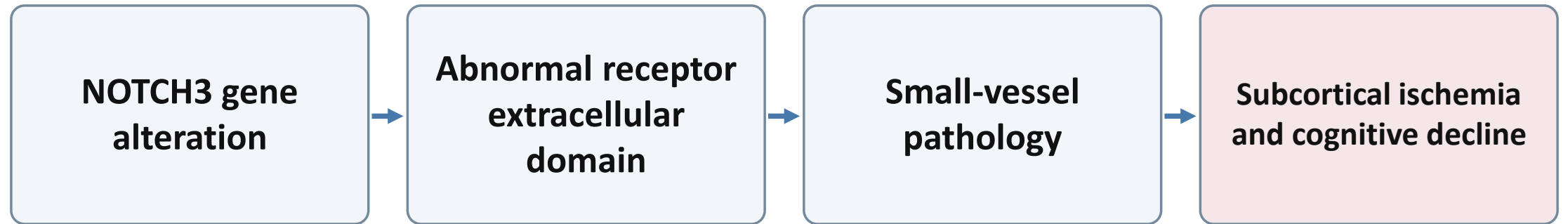
CAA: Genotype and pathological risk

- The source associates APOE ϵ 2 and ϵ 4 alleles with increased bleeding risk.
- Some hereditary CAA variants involve APP mutations.
- Vessel-wall β -amyloid can be highlighted by appropriate amyloid studies.
- On ordinary H&E, CAA and hyaline vascular thickening may look similar.

Other inherited small-vessel diseases

- CADASIL is associated with autosomal dominant pathogenic NOTCH3 variants.
- It can manifest with recurrent small-vessel strokes, white-matter injury and dementia.
- The source also describes COL4A1-associated small-vessel disease.
- COL4A1-related injury can involve brain hemorrhage and extra-neural manifestations.

CADASIL: Molecular defect to clinical injury

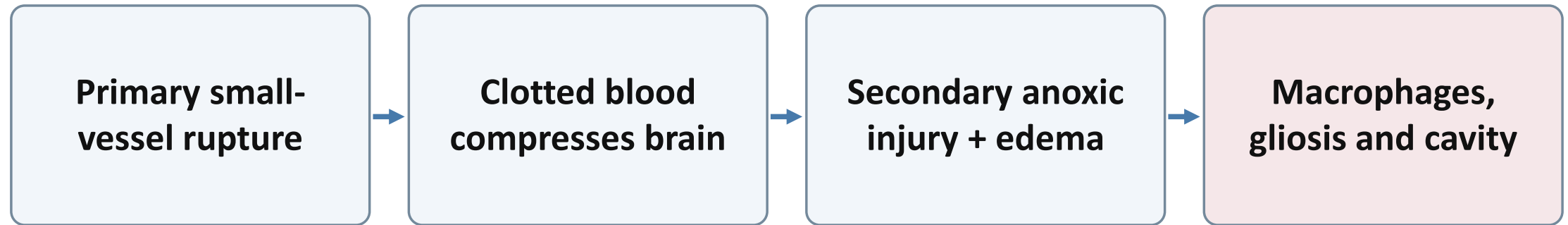


- This inherited arteriopathy is distinct from sporadic hypertensive or amyloid-related disease.

COL4A1-associated cerebrovascular pathology

- Type IV collagen contributes to vascular basement membranes.
- Pathogenic COL4A1 variants can be associated with cerebral vessel fragility.
- Reported accompanying manifestations include cataract, hematuria and epilepsy.
- Inherited small-vessel pathology should be considered apart from conventional vascular risk factors.

Evolution of a primary intracerebral hematoma



- The final defect may have a hemosiderin-stained rim after prior bleeding.

Morphology of remote hemorrhage

- The early lesion contains a central coagulum of blood surrounded by compressed tissue.
- Hemosiderin-laden and lipid-laden macrophages accumulate during clearance.
- Reactive astrocytes form a gliotic lesion rim.
- Old destructive hemorrhages may leave a cavity with brown discoloration.

Deep ganglionic versus lobar hemorrhage

Deep / ganglionic

- Hypertensive arteriolosclerosis is the canonical association.
- Putamen, thalamus, pons, or cerebellum may be involved.
- Ventricular extension can complicate major bleeds.

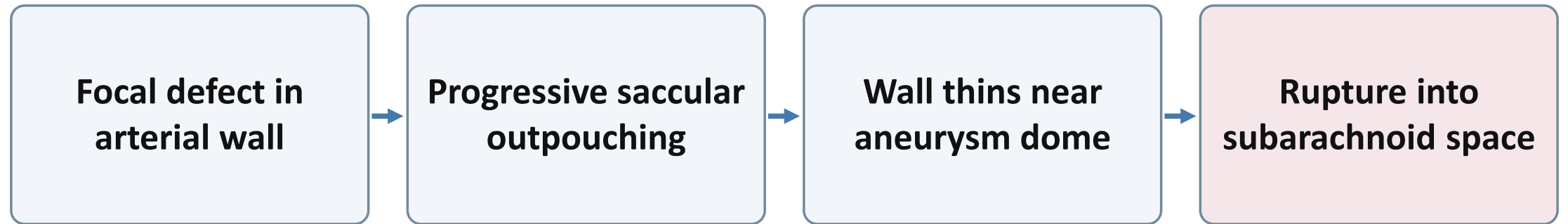
Lobar / superficial

- Cerebral amyloid angiopathy is a principal association.
- Cortical and subcortical territories are affected.
- Adjacent subarachnoid extension or microbleeds may coexist.

Subarachnoid hemorrhage: Vascular mechanism

- Blood enters the cerebrospinal-fluid-containing subarachnoid space.
- Ruptured saccular intracranial aneurysm is a leading spontaneous cause.
- Vascular malformations, hematologic disorders and trauma are alternative etiologies.
- An arterial source produces abrupt pressure-related symptoms and complications.

Saccular aneurysm at an arterial branch point



- Aneurysms may also bleed into nearby brain tissue.

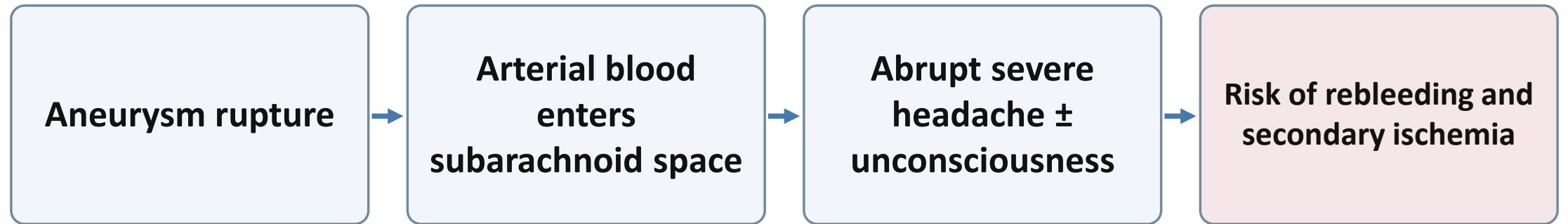
Aneurysm predisposition

- Aneurysms often develop near major arterial branching points in the anterior circulation.
- Underlying attenuation of vascular media and internal elastic lamina is important.
- Familial susceptibility and selected connective-tissue disorders increase risk.
- Smoking, hypertension and hemodynamic wall stress contribute.

Saccular aneurysm: Gross structural features

- A rounded, thin-walled, shiny outpouching arises near the circle of Willis.
- Size and neck width vary; Sac walls can contain mural thrombus or calcification.
- Smooth muscle and internal elastic lamina are absent from the sac itself.
- Rupture typically occurs at or near its dome.

Ruptured aneurysm: Early clinical sequence



- The pathology lecture focuses on mechanism and consequences, not acute management algorithms.

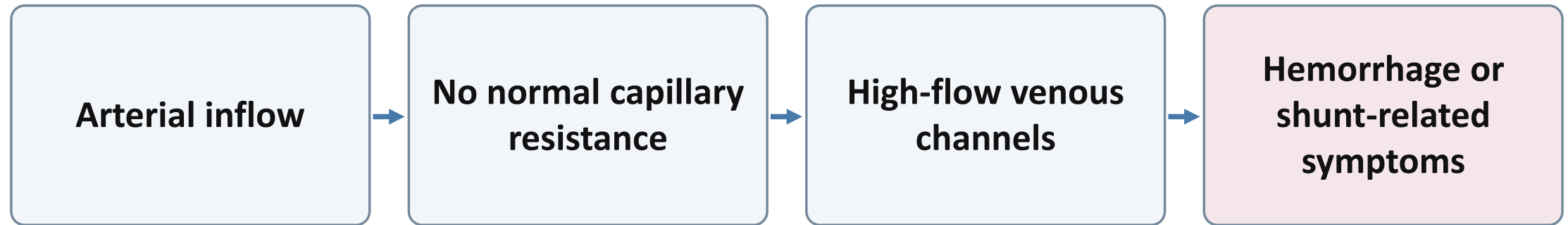
Secondary injury after subarachnoid blood

- Blood bathing cerebral arteries can provoke arterial vasospasm.
- Vasospasm may reduce blood flow and cause additional ischemic injury.
- Meningeal fibrosis in the healing phase can obstruct CSF circulation or resorption.
- Thus, delayed injury is not limited to the initial hemorrhage volume.

Cerebral vascular malformations

Type	Basic architecture	Major teaching consequence
Arteriovenous malformation	High-flow abnormal arteries and veins	Hemorrhage, seizure, hemodynamic shunt
Cavernous malformation	Back-to-back low-flow vascular spaces	Focal bleeding or seizures
Capillary telangiectasia	Small capillary-level abnormality	Distinct structural category
Venous angioma	Abnormal venous drainage pattern	Distinct structural category

Arteriovenous malformation: Direct shunting



- Large lesions can cause clinically significant altered hemodynamics.

AVM morphology and clinical presentation

- Grossly, AVMs form tangled, enlarged, wormlike vascular channels.
- Abnormal vessels are separated by reactive gliotic tissue and may show old bleeding.
- Patients may present with seizures or intracranial hemorrhage.
- Prominent high-flow lesions can create substantial arteriovenous shunting.

AVM versus cavernous malformation

Arteriovenous malformation

- High-flow artery–vein connections with shunting.
- Vascular channels may display arterial wall abnormalities.
- Intervening gliotic tissue and previous hemorrhage may be present.

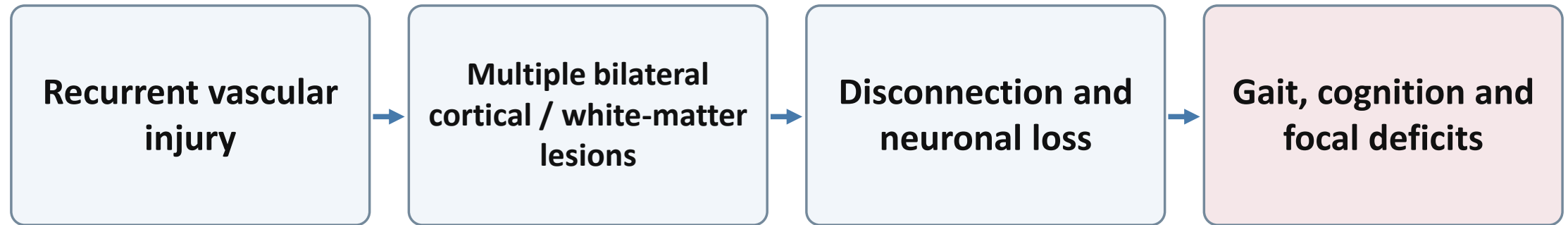
Cavernous malformation

- Back-to-back, distended vascular channels with collagenized walls.
- Usually little or no brain tissue between the abnormal channels.
- Low-flow lesion without a typical AV shunt.

Molecular pathology of vascular malformations

- The source reports activating somatic KRAS mutations in many arteriovenous malformations.
- Familial cavernous malformations can involve CCM-complex genes.
- Progressive cavernous lesions may additionally acquire activating PIK3CA changes.
- Somatic driver alterations support a disease mechanism involving endothelial signaling.

Cumulative infarction and vascular dementia



- Underlying mechanisms may include atherosclerosis, thromboembolism and chronic arteriolosclerosis.

Subcortical vascular dementia / Binswanger pattern

- Predominant subcortical white-matter vascular injury forms a recognizable distribution.
- The Robbins chapter uses Binswanger disease for this subcortical arteriolosclerotic pattern.
- Cognitive impairment may coexist with gait disturbance and pseudobulbar signs.
- Other white-matter diseases must be differentiated radiologically and clinically.

Integrating location, mechanism, and morphology

Lesion	Dominant mechanism	Morphological clue
Large territorial infarct	Arterial embolus / thrombosis	Territorial softening → cavitation
Lacune	Deep small-vessel occlusion	Small gliosis-rimmed cavity
Watershed infarct	Generalized hypoperfusion	Border-zone wedge-shaped lesion
Deep hematoma	Hypertensive arteriolosclerosis	Ganglionic clot and compression
Lobar hematoma	Cerebral amyloid angiopathy	Cortical/subcortical bleeding
Subarachnoid bleed	Often ruptured saccular aneurysm	Blood in subarachnoid space

Clinicopathologic problem: Sudden focal deficit

An acute arterial deficit is not defined solely by the mechanism

- Which vascular territory corresponds to the neurological findings?
- Is there arterial occlusion with infarction or primary bleeding?
- How might collateral perfusion alter the extent of injury?

Clinicopathologic problem: Deep cerebral hematoma

A deep putaminal hemorrhage points toward small-vessel disease

- Link long-standing hypertension to arteriolar wall thickening.
- Explain the alternative endpoints: Luminal closure or rupture.
- Predict an adjacent zone of edema and secondary parenchymal injury.

Clinicopathologic problem: Explosive headache

Blood in the subarachnoid space suggests a ruptured vascular lesion

- Consider a saccular aneurysm at an intracranial branch point.
- Distinguish the initial bleed from vasospasm-related delayed ischemia.
- Explain how later meningeal fibrosis can disturb CSF dynamics.

Pathology synthesis

Vascular injury is defined by mechanism + location + time

- Regional occlusion, global flow failure, and vascular rupture produce different initial lesions.
- Cerebral ischemia characteristically evolves toward liquefaction and gliotic cavitation.
- Vessel pathology links the ischemic and hemorrhagic presentations of cerebrovascular disease.

Source and visual provenance

Primary textbook

Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026). Chapter 28, The Central Nervous System, pp. 1136–1143.

Teaching scope

Introductory Cerebrovascular Disease section, supplemented by contiguous focal/global ischemia, hemorrhage, vascular malformation, and vascular dementia sections from the same chapter.

Diagrams are authored editable schematics, not diagnostic specimens.