

Intraparenchymal Hemorrhage

Etiology • vascular pathology • morphology • clinical correlation

Cerebrovascular pathology

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Learning objectives

- Classify intraparenchymal bleeds by their anatomical distribution.
- Explain vessel-wall injury in hypertensive hemorrhage and cerebral amyloid angiopathy.
- Recognize the morphologic evolution and secondary consequences of a hematoma.
- Differentiate major acquired and inherited causes using clinicopathologic clues.

Definition: Blood within the brain parenchyma

- Primary intraparenchymal hemorrhage follows rupture of a vessel within brain tissue.
- Blood collects inside parenchyma rather than solely in meningeal compartments.
- The presentation can be abrupt, producing a focal neurologic stroke syndrome.

Hemorrhage compartments are anatomically distinct

Compartment	Principal distinction
Epidural	Between skull and dura; usually traumatic
Subdural	Between dura and arachnoid; usually traumatic
Subarachnoid	Within CSF-containing subarachnoid space
Intraparenchymal	Within brain substance; often vascular disease

A compartment-based classification precedes etiologic classification.

Primary bleeding versus hemorrhagic transformation

Primary hemorrhage

- Initial event: Intraparenchymal vessel rupture
- Forms a hematoma within brain tissue
- Deep or lobar pattern offers etiologic clues

Secondary hemorrhagic transformation

- Preceded by an ischemic infarct
- Hemorrhage occurs within injured/infarcted tissue
- May appear as punctate cortical bleeding

Different initiating event

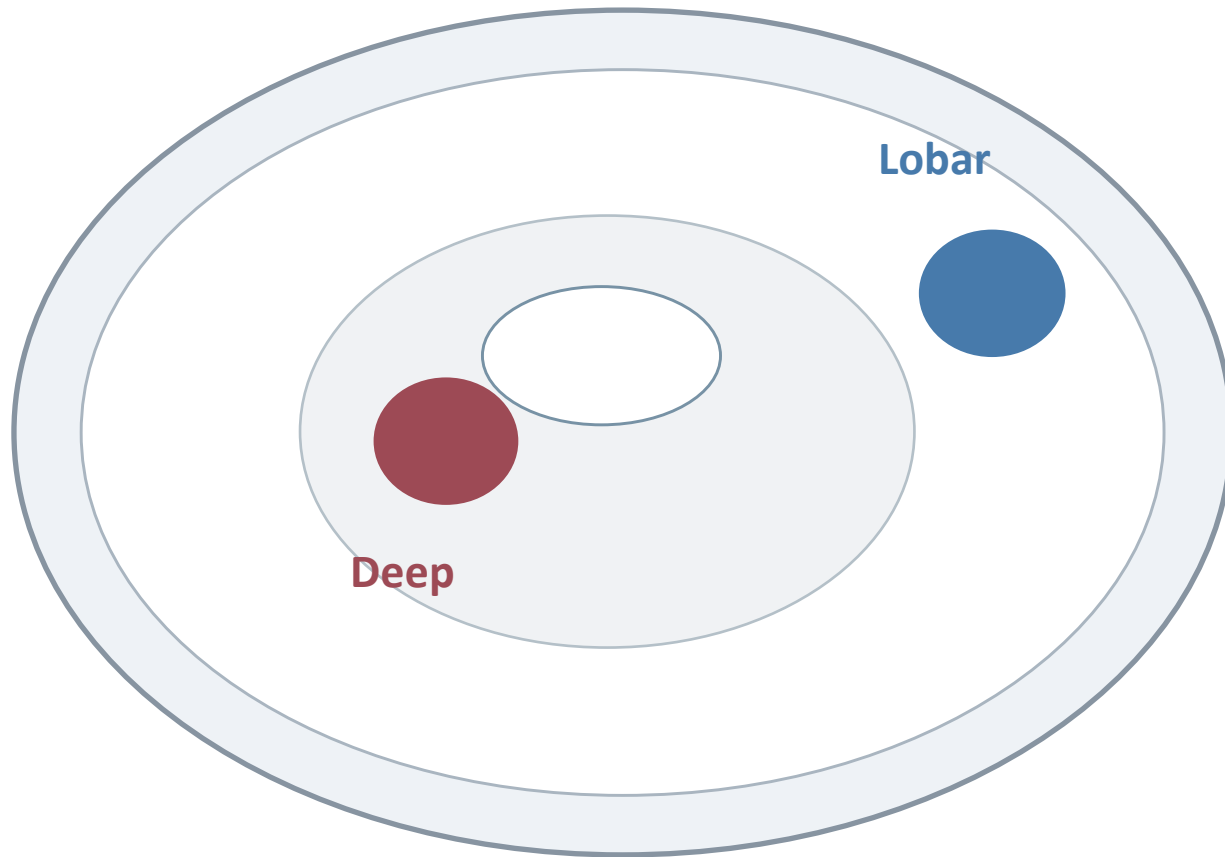
Clinical onset commonly resembles stroke

- Symptoms often begin suddenly, reflecting abrupt bleeding into the parenchyma.
- The focal deficit depends primarily on the region of brain affected.
- Extensive hemorrhage or ventricular extension can cause especially severe injury.

Who develops spontaneous hemorrhage?

- Spontaneous intraparenchymal hemorrhage predominantly in middle to late adult life.
- An incidence peak around 60 years.
- Anatomical distribution and associated vascular pathology are more discriminating than age alone.

Two major distribution patterns

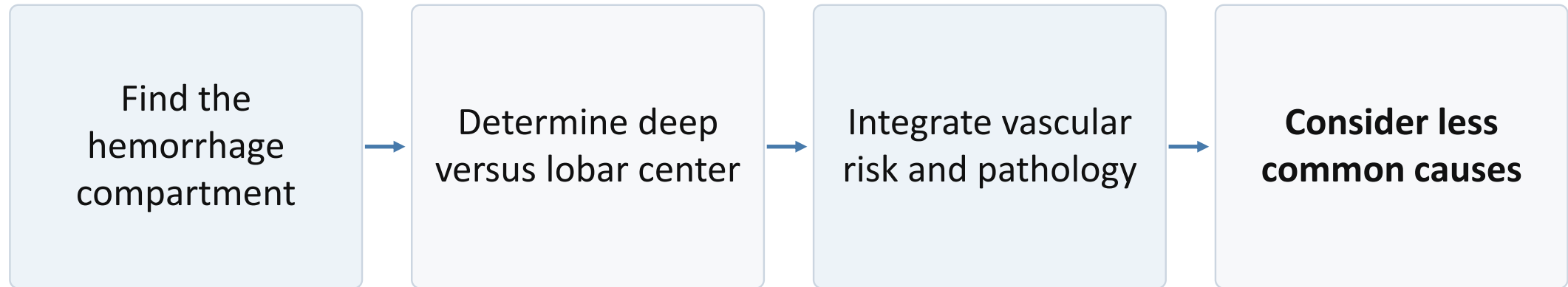


Schematic anatomy — not a clinical scan

Morphologic interpretation

- Deep/ganglionic: Basal ganglia and thalamus
- Lobar: Superficial cerebral hemisphere
- Typical associations: Hypertension versus CAA

Interpretation begins with location



Location is a clue, not independent proof of a single cause.

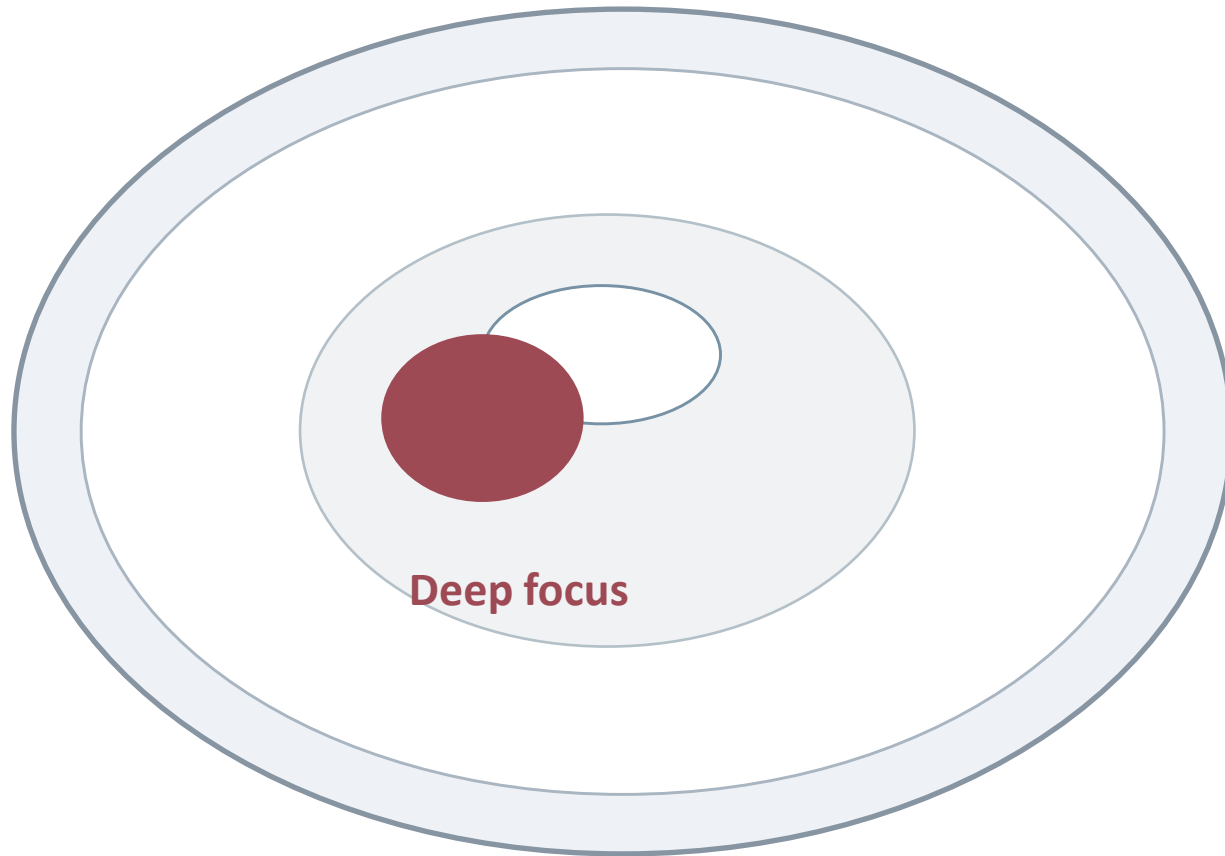
Nontraumatic intraparenchymal bleeding: Etiologies

Major association	Other contributors
Hypertension	Deep small-vessel disease
Cerebral amyloid angiopathy	Superficial/lobar vessel disease
Systemic coagulation disorders	Hemostatic susceptibility
Neoplasms, vasculitis, aneurysms	Local lesion or vessel injury
Vascular malformations	Abnormal vascular structure

Hypertension is dominant in deep hemorrhage

- Chronic hypertension is the most prominent association with deep intraparenchymal bleeding.
- More than half of clinically significant hemorrhages to hypertension.
- The pathological substrate is altered vessel walls, particularly within deep brain regions.

The putamen is a frequent origin

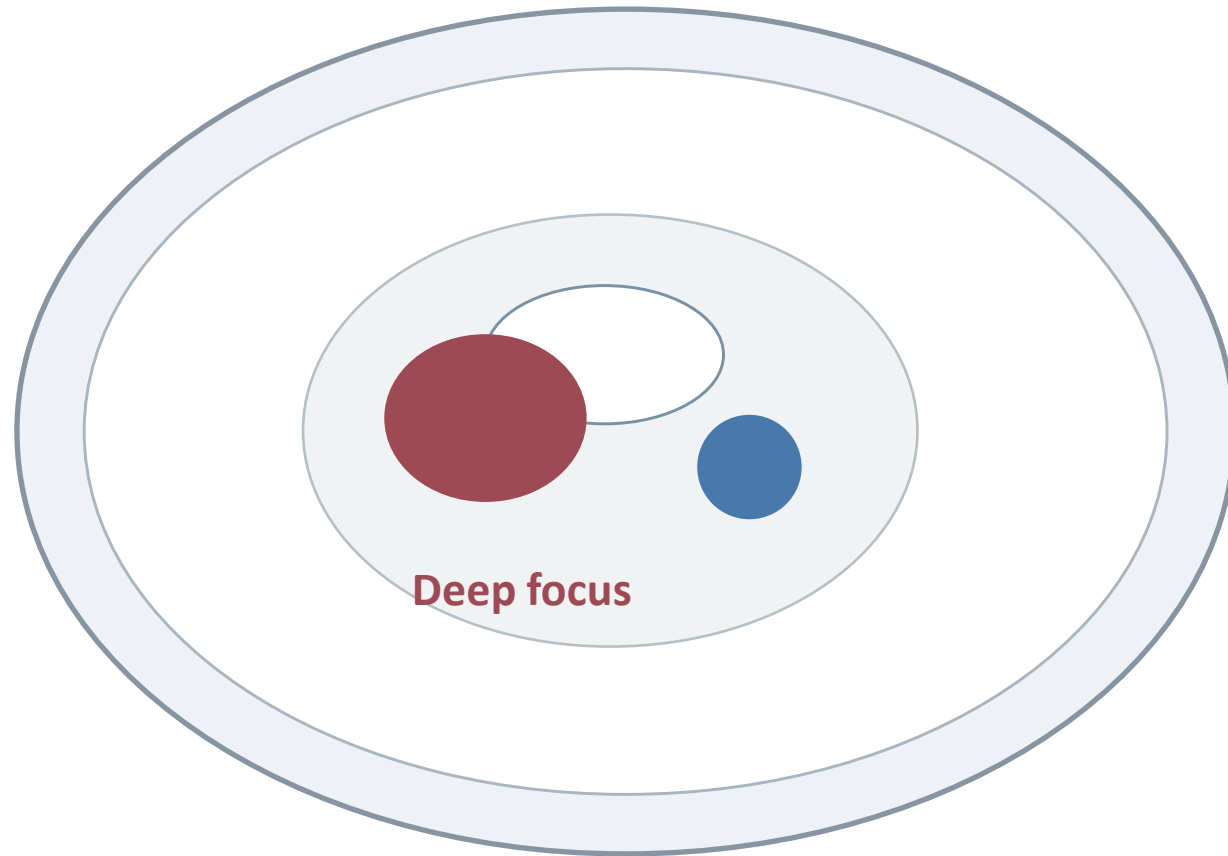


Schematic anatomy — not a clinical scan

Morphologic interpretation

- Putaminal origin in 50–60% of hypertensive intraparenchymal hemorrhages.
- The lesion is centered in deep gray matter.
- Large hematomas can extend beyond the site of origin.

Additional hypertensive hemorrhage sites



Deep focus

Schematic anatomy — not a clinical scan

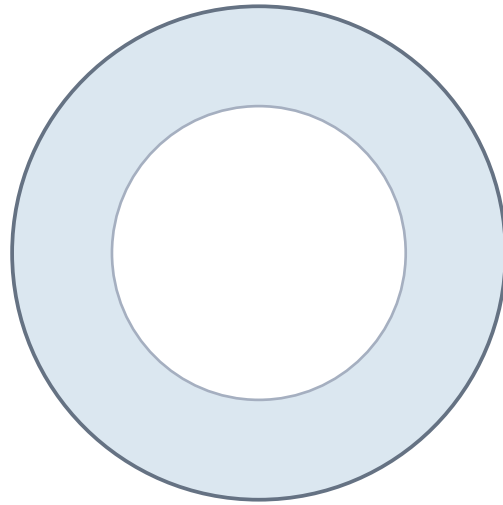
Morphologic interpretation

- Thalamus: Deep hemispheric site
- Pons: Brainstem location
- Cerebellar hemisphere: Posterior fossa location

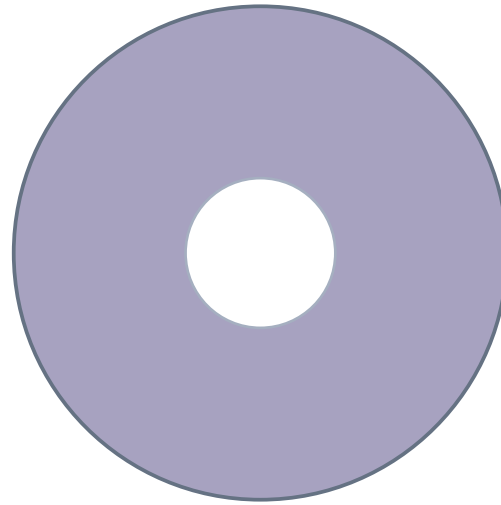
Hypertension damages vessels by caliber

- Large arteries may show accelerated atherosclerosis.
- Small arteries and arterioles undergo hyaline arteriolosclerosis.
- Severe vascular injury can produce proliferative changes and arteriolar necrosis.

Normal small artery versus hyaline arteriolosclerosis



Normal arteriole



Hyaline-thickened wall

Pathological interpretation

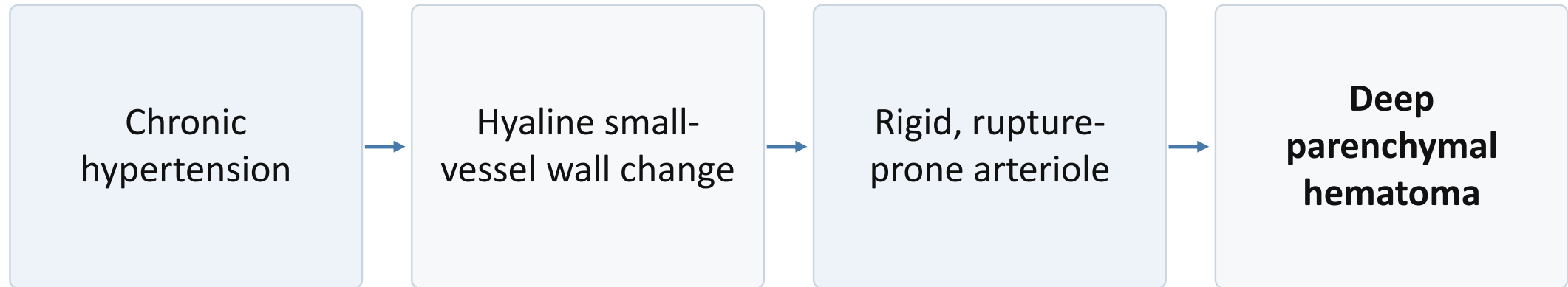
- Normal: Compliant wall with patent lumen
- Hyalinosis: Wall thickening and increased rigidity
- Rigidity predisposes damaged arterioles to rupture

Cross-sectional schematic; Not histology

Hyaline arteriolosclerosis: Defining change

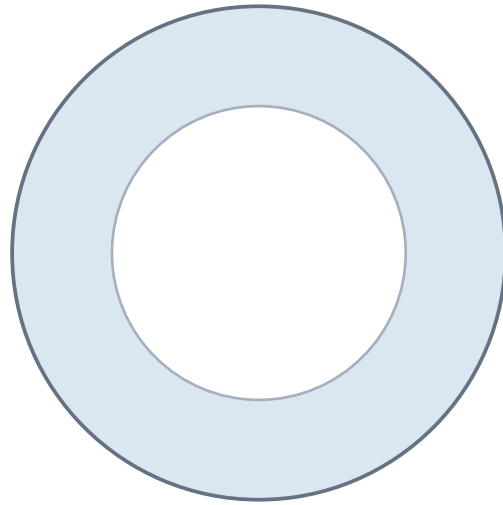
- The arteriolar wall becomes thicker because of hyaline/fibrotic material.
- Although thickened, the vessel is mechanically abnormal rather than protected.
- Basal ganglia and subcortical white-matter vessels.

Pathogenesis of hypertensive hemorrhage

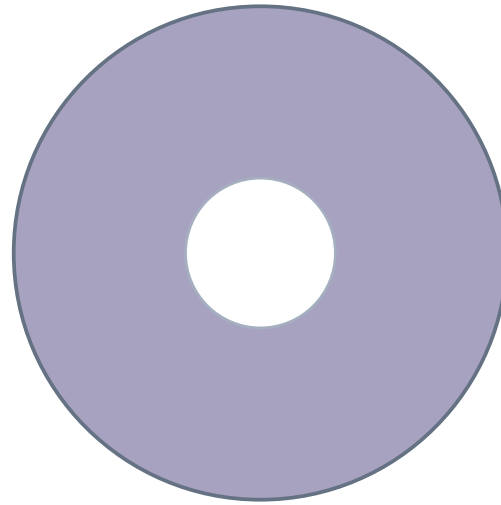


Mechanistic sequence summarized from the Robbins discussion.

Why thickening does not equal strength



Normal arteriole



Hyaline-thickened wall

Cross-sectional schematic; Not histology

Pathological interpretation

- Pathological thickening reduces normal wall compliance.
- Rigid vessel walls are more vulnerable to rupture.
- Microscopic wall disease produces macroscopic parenchymal hemorrhage.

Spectrum of hypertensive vasculopathy

Affected structure	Source-described alteration
Larger arteries	Accelerated atherosclerosis
Small arteries / arterioles	Hyaline arteriolosclerosis
Severely injured arterioles	Proliferation and frank necrosis

These are distinct vessel lesions, not synonymous processes.

One diseased arteriole, two major outcomes

Rupture

- Wall fragility predominates
- Blood enters brain parenchyma
- A primary hemorrhagic lesion forms

Occlusion

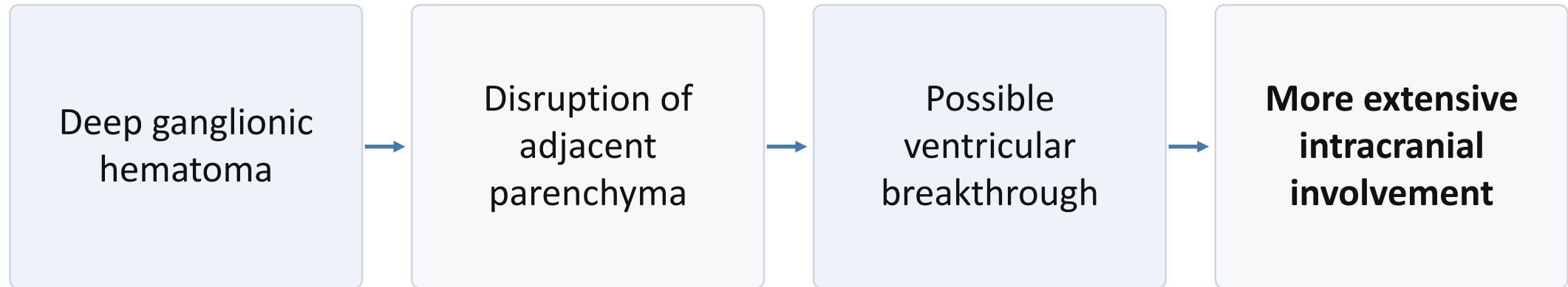
- Vessel lumen becomes blocked
- Small territory becomes ischemic
- A lacunar infarct may develop

Rupture ≠ occlusion

Lacunar infarction is an ischemic counterpart

- Hyaline arteriolosclerosis to both hemorrhage and lacunar infarction.
- When a small affected artery is occluded, its dependent tissue undergoes infarction.
- A lacune is not equivalent to an old intraparenchymal hematoma.

Extension into the ventricular system

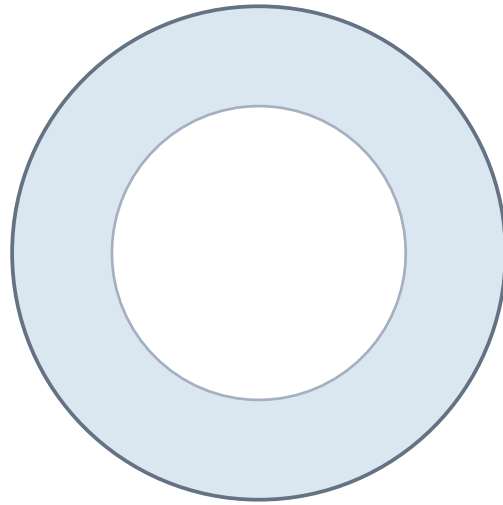


The Robbins illustration depicts ganglionic bleeding entering a lateral ventricle.

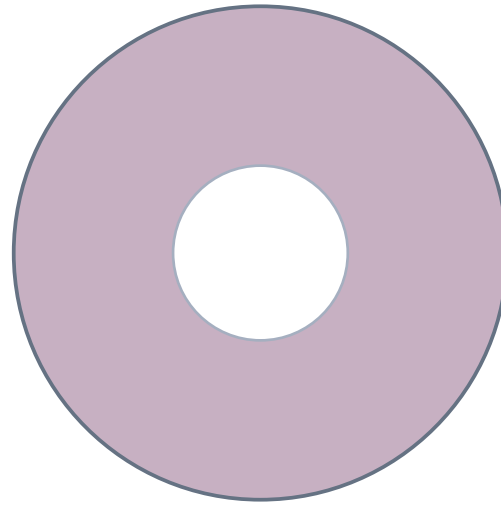
Cerebral amyloid angiopathy: Clinical association

- Cerebral amyloid angiopathy (CAA) is particularly associated with lobar hemorrhages.
- Its defining lesion is amyloid deposition in small- and medium-caliber brain vessels.
- Involved vessels are structurally weakened and prone to hemorrhage.

CAA: Deposition in a vessel wall



Reference vessel



A β -laden vessel

Cross-sectional schematic; Not histology

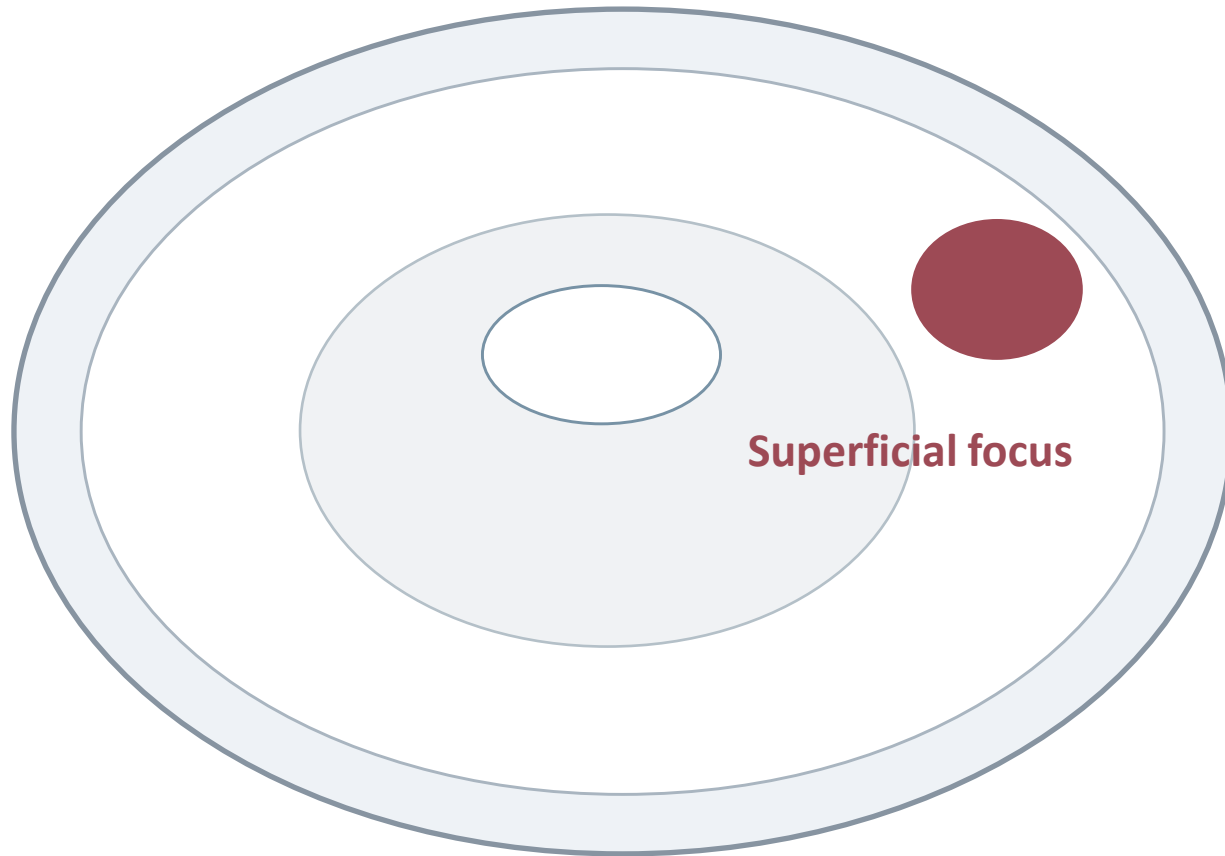
Pathological interpretation

- Amyloid β is deposited within the vessel wall.
- The vessel is rigid and may fail to collapse during histologic sectioning.
- Unlike hypertensive hyalinosis, the deposited material is amyloid.

The key CAA protein is amyloid β

- The vascular peptide as amyloid β (A β).
- The same amyloidogenic peptide class is linked to Alzheimer disease.
- CAA describes vascular amyloid deposition; It is not simply a synonym for parenchymal Alzheimer plaques.

CAA preferentially targets surface vessels



Schematic anatomy — not a clinical scan

Morphologic interpretation

- Leptomeningeal and cortical vessels are prominent sites of disease.
- Cerebellar vessels can also be involved.
- This distribution is distinct from the deep-vessel predominance of hypertension.

CAA and the cerebellum

- CAA can affect vessels within the cerebellum as well as cerebral cortical vessels.
- Its association with lobar hemorrhage reflects predominance in superficial cerebrovascular territories.
- Distribution should be interpreted alongside other etiologic evidence.

Routine H&E: Two hyaline-appearing lesions

Hypertensive arteriolosclerosis

- Fibrotic/hyaline thickening
- Prominent in basal ganglia / white matter
- Often produces deep hemorrhage

CAA

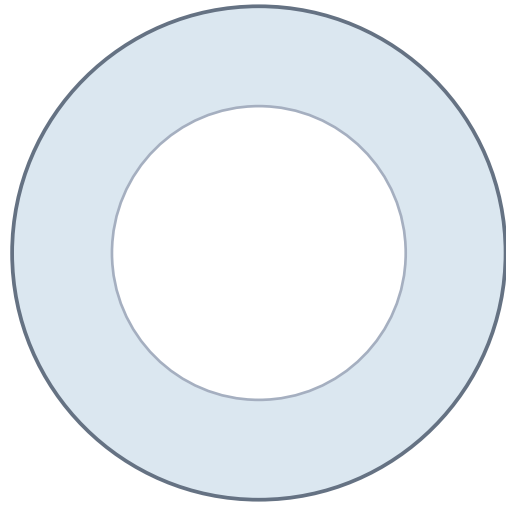
- A β deposition in vessel wall
- Prominent in cortex / leptomeninges
- Often produces lobar hemorrhage

Deposited substance differs

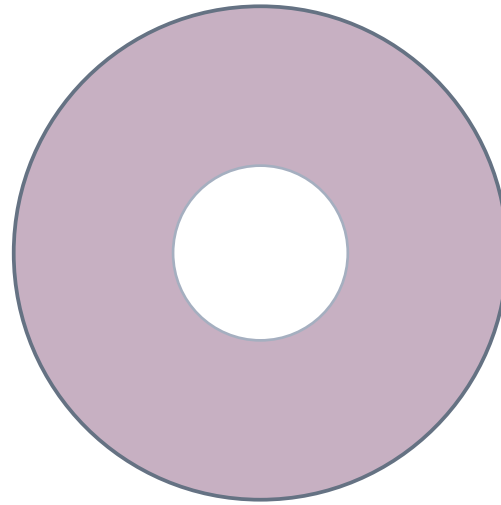
CAA: Pathological confirmation requires specificity

- H&E may show a thickened, hyaline-appearing vessel wall.
- The deposited material is amyloid rather than ordinary collagenous hyaline.
- A β immunohistochemistry demonstrating vascular deposits.

A β deposition can be localized by immunostaining



Reference vessel



A β -laden vessel

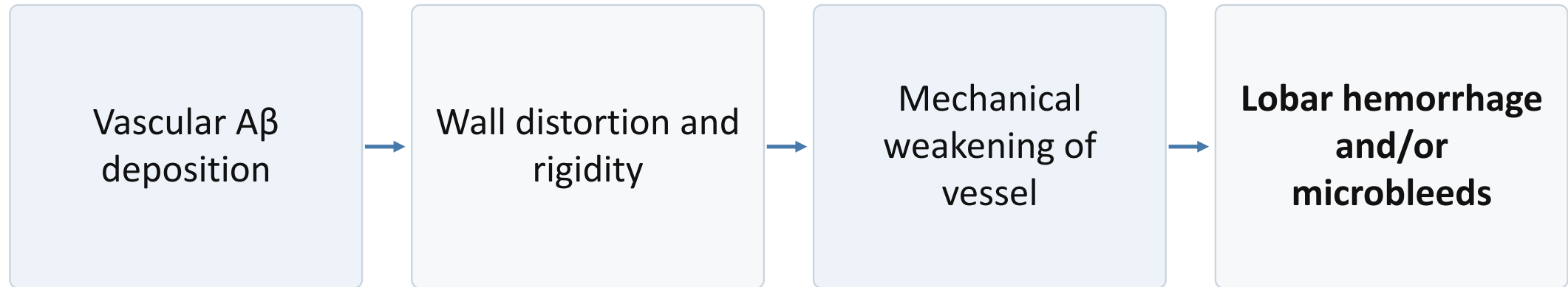
Conceptual stain localization

Cross-sectional schematic; Not histology

Pathological interpretation

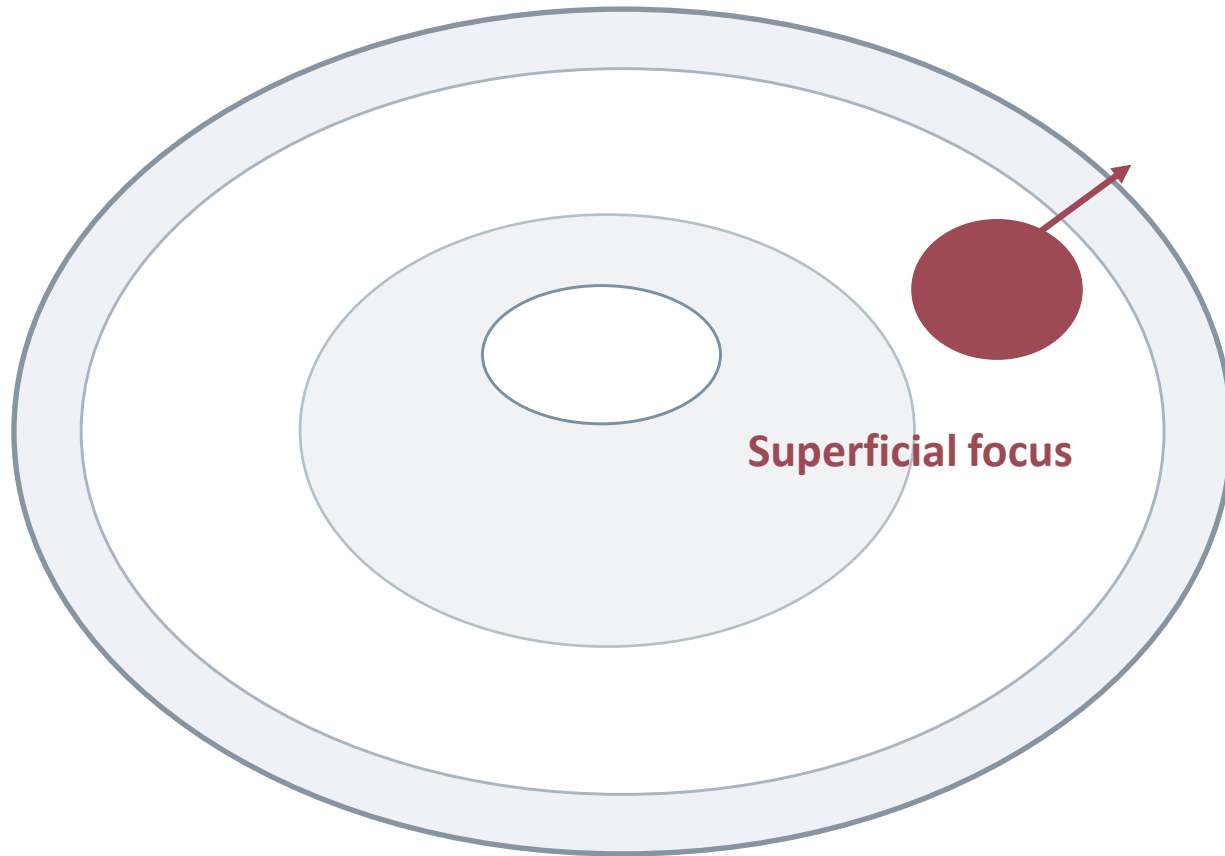
- Vascular A β labeling as evidence of the deposited peptide.
- A labeled vascular wall localizes disease to the vasculature.
- A positive tissue stain must be interpreted in anatomical context.

CAA progression to hemorrhage



Schematic causal model; Not a quantitative temporal pathway.

Lobar hemorrhage may reach the subarachnoid space



Schematic anatomy — not a clinical scan

Morphologic interpretation

- CAA-associated hematomas often involve subcortical white matter.
- Large lobar bleeds may dissect toward the cortical surface.
- The Robbins gross image shows extension into subarachnoid space.

Microbleeds reflect smaller vessel failures

- CAA may produce numerous small hemorrhages, not only a single large hematoma.
- Robbins calls these deposits of blood “microbleeds.”
- The source notes that microbleeds can be demonstrated using imaging techniques.

CAA and Alzheimer pathology share A β

CAA

- Deposits localized in vessel walls
- Weakens vessel integrity
- Associated with hemorrhage

Alzheimer-related A β pathology

- A β is also involved in Alzheimer disease
- Shared peptide does not imply identical lesion
- Different compartment and clinical expression

Same peptide, different location

APOE alleles modify bleeding risk in CAA

- The APOE gene encodes apolipoprotein E.
- Both $\epsilon 2$ and $\epsilon 4$ alleles as associated with increased CAA bleeding risk.
- Genetic association is a susceptibility factor, not a stand-alone diagnosis.

APP mutations can cause hereditary CAA

- Some autosomal dominant CAA forms arise from APP mutations.
- APP encodes the precursor protein from which amyloid β peptides are generated.
- A mutation can favor amyloidogenic vascular deposition and hemorrhagic disease.

Hypertension versus CAA: High-yield distinctions

Feature	Hypertension	CAA
Typical center	Deep/ganglionic	Lobar/subcortical
Characteristic vessels	Basal ganglia, white matter	Cortical, leptomeningeal
Wall lesion	Hyaline arteriolosclerosis	Vascular A β deposition
Additional feature	May cause lacunar infarcts	May cause microbleeds

Cortical versus deep vessel distribution matters

- A thickened vessel wall on H&E is not sufficient to distinguish CAA from hyalinosis.
- Assess the affected vascular territory: Cortex/leptomeninges versus deep nuclei.
- Use amyloid-specific evidence when making a tissue diagnosis of CAA.

When a case does not fit hypertension or CAA

- Consider hereditary cerebral small-vessel disorders.
- Consider systemic bleeding predispositions, vascular malformations, tumors, and vasculitis.
- Location and the accompanying pathology guide the next etiologic hypothesis.

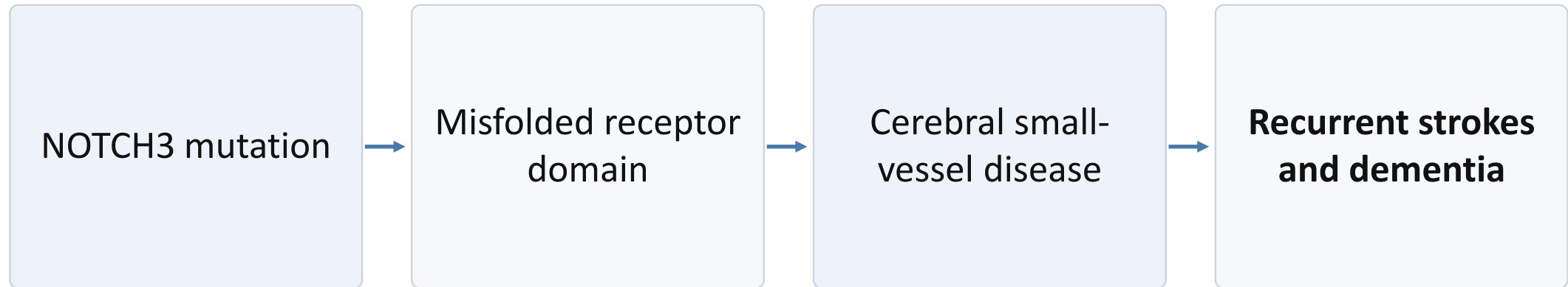
Hereditary small-vessel disorders

Disorder	Major gene	Prominent clinical expression
Hereditary CAA	APP	Amyloid-associated hemorrhage
CADASIL	NOTCH3	Small-vessel strokes; often infarcts
COL4A1-related disease	COL4A1	Hemorrhage and systemic findings

CADASIL is a NOTCH3-associated arteriopathy

- CADASIL is an autosomal dominant hereditary small-vessel disease.
- Pathogenic NOTCH3 mutations lead to misfolding of the receptor's extracellular domain.
- It primarily causes small-vessel strokes and progressive neurologic disease.

CADASIL: Molecular defect to phenotype



Infarcts more often than hemorrhages.

CADASIL: White-matter abnormalities come early

- The earliest detectable imaging changes in cerebral white matter.
- Changes may be identified around age 35 and progress with time.
- The prominent presentation is recurrent small-vessel ischemia rather than lobar hemorrhage.

CADASIL versus CAA

CADASIL

- NOTCH3; Autosomal dominant
- White-matter imaging changes
- Infarcts are more common than hemorrhages

CAA

- Vascular A β ; APP in rare familial cases
- Cortical/leptomeningeal vessel disease
- Lobar bleeds and microbleeds

Different vascular pathology

COL4A1 affects the vascular basement membrane

- COL4A1 encodes a collagen component of the basement membrane.
- Pathogenic variants can cause an inherited cerebral small-vessel disorder.
- COL4A1-related disease with intracerebral hemorrhage.

COL4A1 disease extends beyond the brain

- The source lists cataract, hematuria, and epilepsy among its additional findings.
- The multisystem phenotype reflects a basement-membrane component defect.
- An associated systemic feature may support an inherited vascular disorder.

Inherited disease: Discriminator table

Clue	Consider
Vascular A β and familial lobar bleeding	APP-associated CAA
Early white-matter disease and recurrent infarcts	CADASIL / NOTCH3
Hemorrhage with cataract or hematuria	COL4A1-related disease

These are teaching clues, not stand-alone diagnostic criteria.

Systemic disorders of coagulation

- Systemic coagulation disorders can cause or contribute to spontaneous parenchymal bleeding.
- A bleeding tendency may act alongside pre-existing cerebral vessel pathology.
- Systemic hemostatic dysfunction in the etiologic differential.

Hemorrhage associated with neoplasia

- Primary high-grade gliomas may bleed into their tumor parenchyma.
- Melanoma, choriocarcinoma, and renal-cell carcinoma metastases.
- A neoplastic lesion is an alternative to primary hypertensive or amyloid vasculopathy.

Local nonhypertensive causes

Category	Reason for inclusion
Vasculitis	Inflammatory damage to vascular walls
Aneurysm	Focal vascular lesion can rupture
Vascular malformation	Structurally abnormal vascular channels
Neoplasm	Bleeding within primary or metastatic tumor

Traumatic contusions have a characteristic setting

- Intraparenchymal hemorrhage may result from trauma rather than spontaneous vessel disease.
- Contusions preferentially affect gyral crests that contact the inner skull.
- Frontal and temporal tips and orbitofrontal surfaces as susceptible.

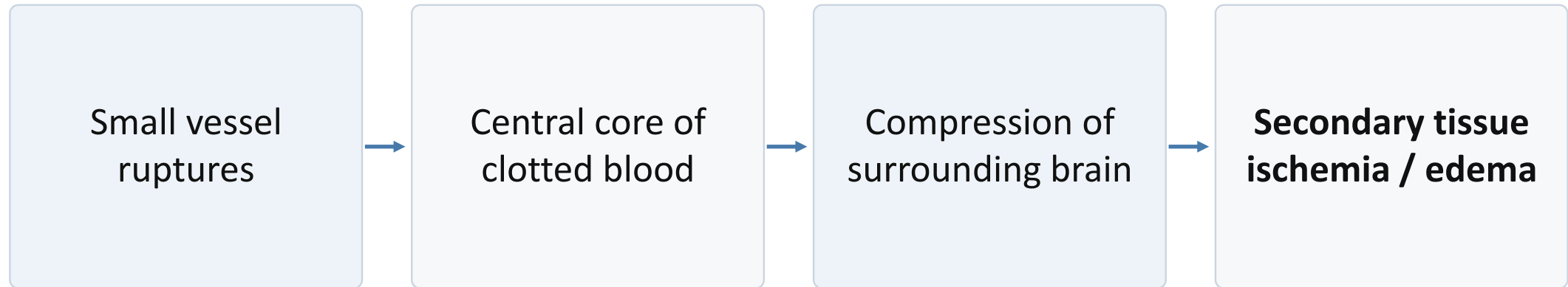
Hemorrhagic infarction is not primary ICH

- Punctate hemorrhages can occur in brain tissue previously injured by ischemia.
- The source describes hemorrhagic conversion along the cortical ribbon.
- Distinguish this pattern from a primary, space-occupying hematoma.

Three major intraparenchymal bleeding patterns

Pattern	Characteristic context
Primary deep hematoma	Hypertensive arteriolar disease
Primary lobar hematoma	CAA, among other causes
Hemorrhagic transformation	Bleeding superimposed on ischemic infarction
Contusion	Trauma at vulnerable brain surfaces

Acute gross morphology of primary hemorrhage

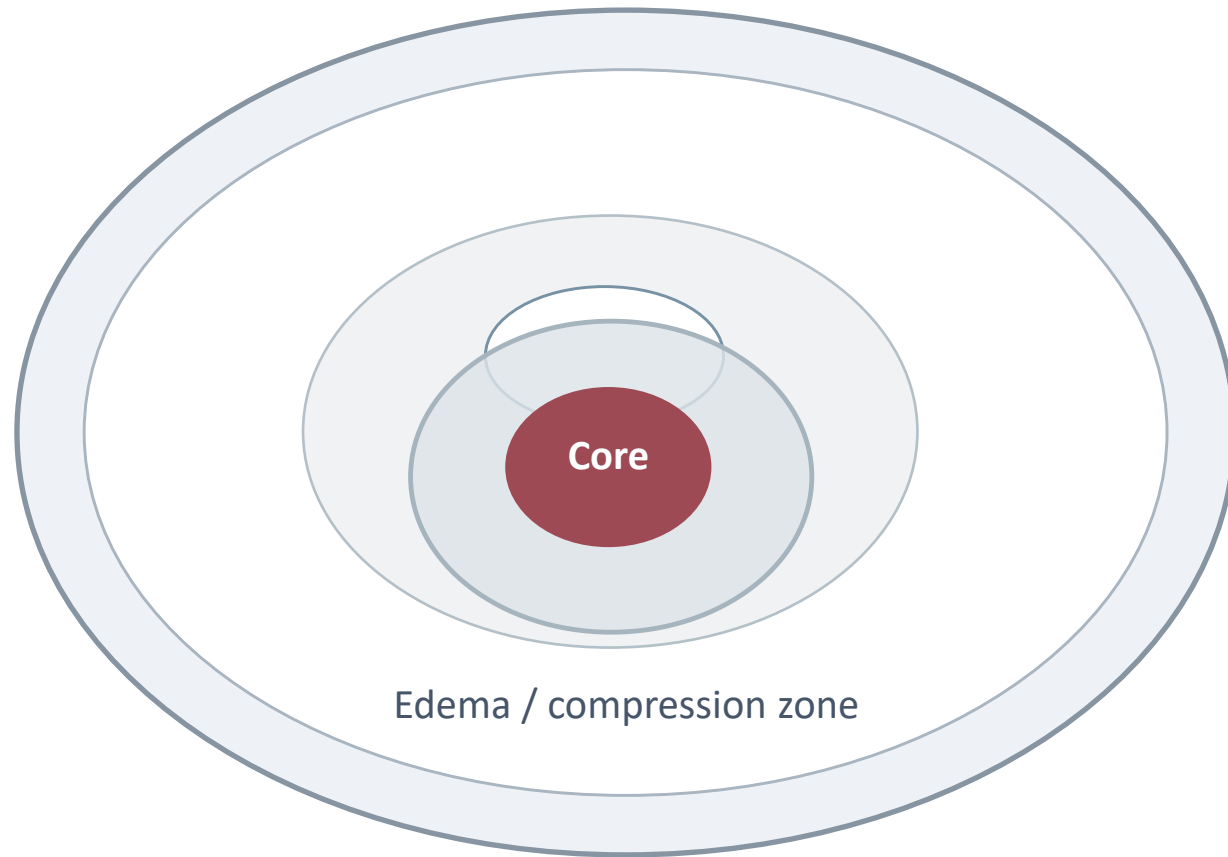


Schematic sequence based on the Robbins morphology box.

The hematoma compresses adjacent brain

- The acute lesion contains a central clot.
- Expanding blood compresses local neural tissue and small vessels.
- Surrounding parenchymal compression contributes to secondary infarction.

Perihematomal injury is not just blood loss



Edema / compression zone

Schematic anatomy — not a clinical scan

Morphologic interpretation

- Blood clot: Physical space occupation
- Adjacent brain: Compression and edema
- Parenchymal response: Secondary ischemic damage

Microscopic consequences of compression

- Perihematomal ischemia causes anoxic changes in neurons.
- Glial cells are also affected by the secondary injury.
- Edema compounds disruption of surrounding brain tissue.

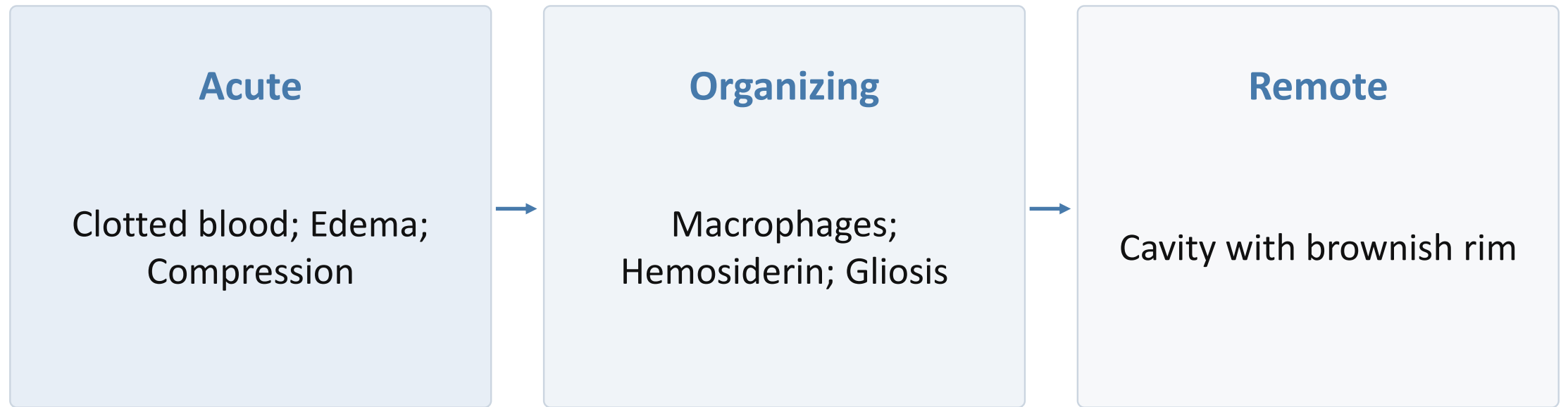
Organized response: Blood breakdown and cleanup

- As the acute phase resolves, macrophages accumulate.
- Macrophages may contain hemosiderin from blood breakdown.
- Lipid-laden macrophages accompany the removal of injured tissue.

Astroglial reaction marks tissue injury

- Reactive astrocytes proliferate at the lesion periphery.
- The cellular progression parallels repair after cerebral infarction.
- Gliosis demarcates the boundary between destroyed and surviving brain.

Morphologic evolution of a hematoma



Phases qualitatively; No exact hemorrhage-specific time intervals are asserted.

Remote hemorrhage leaves destructive sequelae

- Old hematomas may form a cavity after loss of brain parenchyma.
- A peripheral brown discoloration reflects residual blood breakdown products.
- Irreversible cavitory loss differs from simple reabsorption without tissue injury.

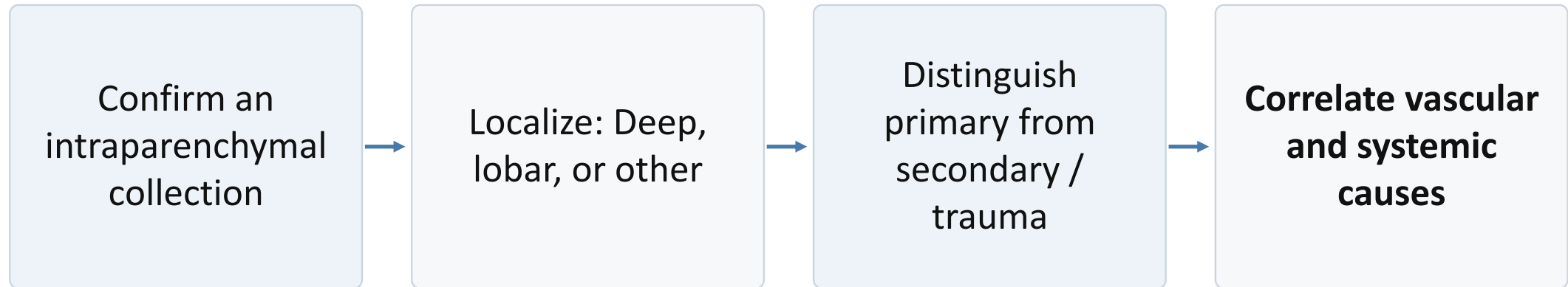
Outcome depends on location and extent

- A large bleed can be devastating because substantial brain tissue is directly disrupted.
- Extension into the ventricular system is another adverse anatomic feature.
- Smaller focal bleeds may be silent or resemble ischemic infarcts clinically.

Hematoma clearance can permit improvement

- Blood and necrotic material may be removed gradually over weeks to months.
- Some neurologic improvement may accompany hematoma resolution.
- Clinical recovery remains constrained by the amount and location of permanent tissue damage.

Clinicopathologic reasoning pathway



Anatomic localization is the organizing principle.

Applied case: Ganglionic hemorrhage

Clinical stem

A 61-year-old with chronic hypertension has sudden focal neurologic deficits and a hematoma centered in the putamen.

Question

Which vascular lesion is the strongest pathological correlate?

Answer

Hyaline arteriolosclerosis of deep small vessels.

Pathological reasoning

Robbins relates chronic hypertension, deep ganglionic hemorrhage, and rigid hyalinized arterioles.

Applied case: Superficial hemorrhage

Clinical stem

An older adult has a spontaneous hematoma in subcortical white matter with extension toward the cortical surface.

Question

Which vascular disorder is a leading etiologic consideration?

Answer

Cerebral amyloid angiopathy.

Pathological reasoning

CAA damages cortical and leptomeningeal vessels and is strongly associated with lobar bleeding.

Applied case: Recurrent infarcts and dementia

Clinical stem

An adult with an autosomal dominant history has progressive white-matter abnormalities, recurrent small-vessel strokes, and cognitive decline.

Question

Which gene-associated small-vessel disease fits best?

Answer

CADASIL associated with NOTCH3.

Pathological reasoning

The textbook contrasts recurrent small-vessel infarcts in CADASIL with CAA-associated lobar hemorrhage.

Applied morphology: Remote lesion

Clinical stem

A remote intraparenchymal lesion shows a cavity and a brown-tinged peripheral zone.

Question

What does this morphology indicate?

Answer

An old hemorrhage with cavitory parenchymal destruction and residual hemosiderin.

Pathological reasoning

Macrophage-mediated cleanup and reactive gliosis accompany long-term posthemorrhagic changes.

Diagnostic synthesis: Pattern to mechanism

Finding	Most pertinent pathological explanation
Deep ganglionic bleed	Hyaline arteriolosclerosis
Lobar bleed / cortical microbleeds	Amyloid β angiopathy
White-matter disease with mostly infarcts	NOTCH3 small-vessel disease
Hemorrhage plus cataract / hematuria	COL4A1 basement-membrane disease
Cavity + brown rim	Remote parenchymal hemorrhage

Core teaching messages

- Deep and lobar hemorrhage distributions reflect different predominant vessel diseases.
- Hypertension injures deep arterioles; CAA deposits A β in cortical/leptomeningeal vessels.
- A hematoma causes compression, edema, secondary infarction, macrophage cleanup, and reactive gliosis.
- Always distinguish spontaneous primary bleeding from trauma and hemorrhagic transformation.

Reference and source boundaries

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Chapter 28, “Intraparenchymal Hemorrhage,” pp. 1139–1141.

Associated source material: “Intracranial Hemorrhage” introductory section and Table 28.1.

Original schematics are conceptual teaching drawings, not patient images or histologic specimens.

Clinical algorithms, acute therapy and externally updated diagnostic criteria are outside this source-grounded lecture.