

Hypertensive Vascular Disease

Mechanisms, vascular remodeling, and target-organ injury

Mechanisms • Morphology • Clinicopathologic correlation

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Learning objectives

- Explain how cardiac output, peripheral resistance, and renal sodium handling govern arterial pressure.
- Distinguish essential from secondary hypertension and identify major etiologic categories.
- Recognize hyaline and hyperplastic arteriolosclerosis, malignant hypertension, and organ injury.

Pressure homeostasis: Two clinically important extremes

Low arterial pressure

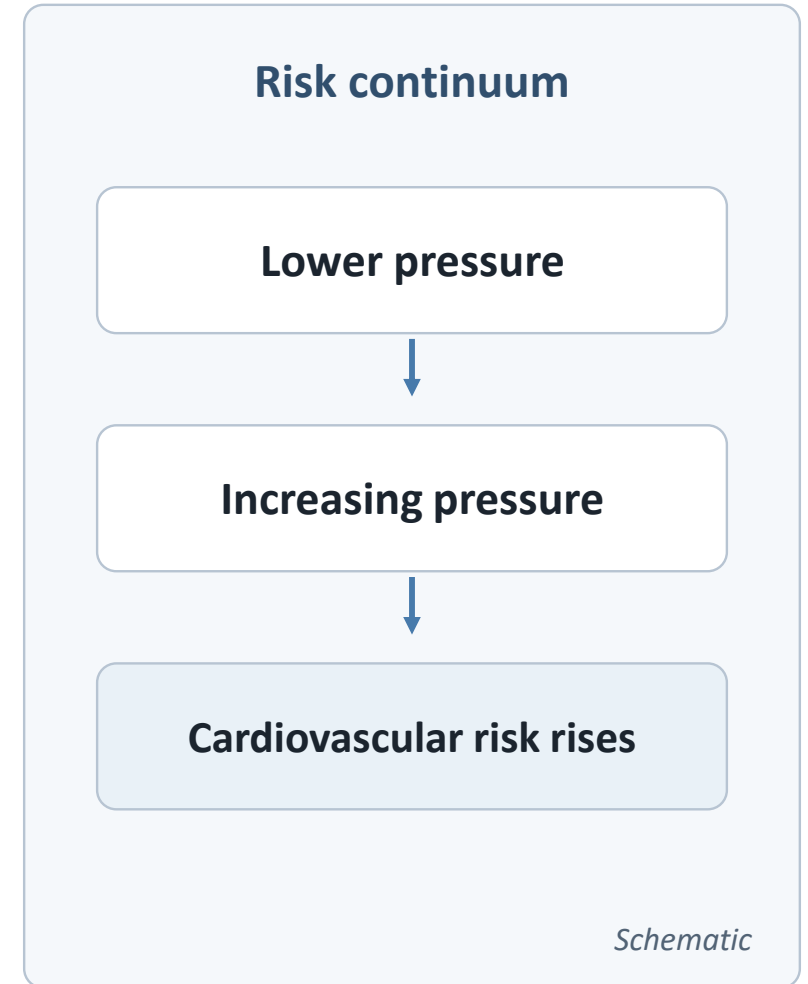
- Inadequate tissue perfusion
- Functional impairment of vulnerable organs
- Prolonged deficit may cause tissue death

High arterial pressure

- Progressive vascular wall injury
- Increased atherosclerotic risk
- Target-organ dysfunction

Arterial pressure is a continuous biologic variable

- Blood pressure is continuously distributed in populations, rather than separated into natural normal and abnormal clusters.
- Cardiovascular risk increases as blood pressure rises: A threshold is useful for decisions, but does not create risk de novo.
- Risk depends on both the attained pressure and the accompanying clinical context.



Blood-pressure descriptions

Category	Systolic	Diastolic	Interpretive point
Normotensive example	<120 mm Hg	<80 mm Hg	Descriptive values in Robbins
Borderline elevated	120–130 mm Hg	—	Textbook wording; overlap at 130
Overt hypertension	≥130 mm Hg	or ≥90 mm Hg	Robbins definition; not universal clinical guidance

Systolic and diastolic pressure both matter

- Systolic pressure reflects the peak pressure imposed on arterial walls during ventricular ejection.
- Diastolic pressure reflects arterial pressure during cardiac relaxation.
- Robbins explicitly identifies both measurements as contributors to cardiovascular risk.

Two pressure components

Systole: Peak pressure



Diastole: Lower pressure



Both inform risk

Schematic

The risk context modifies interpretation

- A single pressure cutoff does not reliably determine every patient's future vascular risk.
- Coexisting factors, illustrated by diabetes in the source, can modify clinical thresholds and absolute risk.
- Keep textbook descriptors separate from whichever formal clinical guideline is used in practice.

Interpretive framework

Pressure reading



Coexisting risk factors



Clinical risk assessment

Schematic

Hypertension is common and becomes more consequential with age

- That roughly one-third to one-half of adults in many populations meet its stated hypertension definition.
- Both hypertension prevalence and vulnerability to complications rise with age.
- Population estimates depend on the population studied and the diagnostic definition applied.

Hypertension may remain clinically silent for years

- Even very elevated pressure can exist without obvious symptoms for a prolonged period.
- Absence of symptoms does not exclude injury to small vessels, heart, brain, or kidneys.
- The first recognizable clinical event may reflect established target-organ disease.

Clinically silent progression

Elevated pressure over years



Few or no symptoms



Organ injury may accumulate

Schematic

Two major etiologic groups

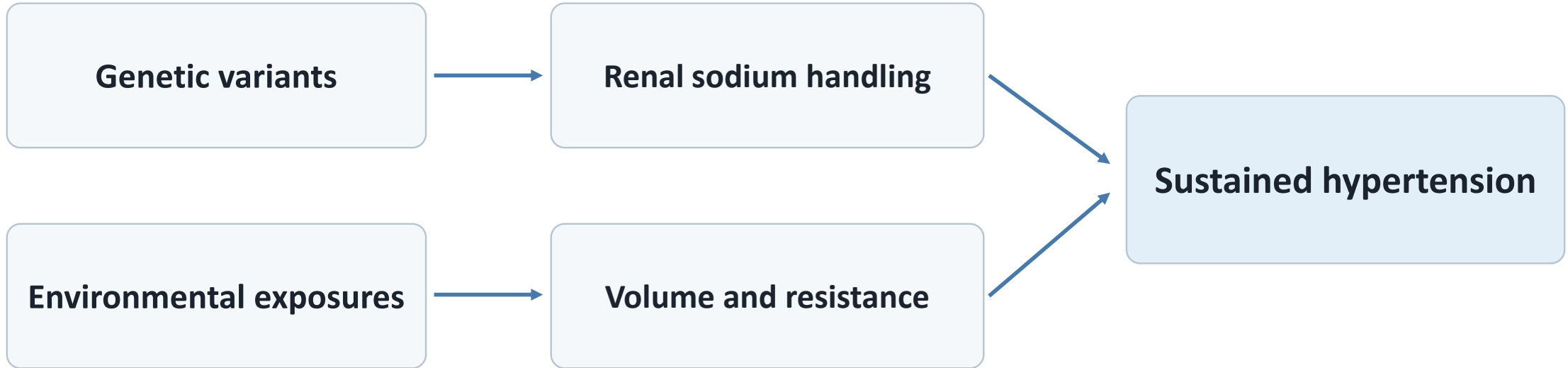
Essential hypertension

- Approximately 90%–95% of cases
- No single identifiable cause
- Polygenic and environmental contributions

Secondary hypertension

- Approximately 5%–10% of cases
- Identifiable underlying disorder
- Renal, endocrine, or other causes

From inherited predisposition to sustained pressure



Essential hypertension is a network-level phenotype rather than a one-gene disease.

Secondary hypertension: Etiologic map

Renal	Endocrine	Cardiovascular / other
Renal artery stenosis	Primary aldosteronism	Aortic coarctation
Chronic kidney disease	Cushing syndrome	Aortic rigidity / volume expansion
Acute glomerulonephritis	Pheochromocytoma	Sleep apnea or neurologic causes
Polycystic kidney disease	Thyrotoxicosis	Pregnancy-induced hypertension

Renal disease can drive systemic hypertension

- Reduced perfusion from renal artery stenosis may initiate a renin-mediated pressor response.
- Renal parenchymal disease can disrupt sodium balance and vascular regulation.
- Renal vascular injury can also be a consequence of long-standing hypertension, creating a bidirectional relationship.

Two-way renal relationship

Renal disease



Altered pressure control



Renal vascular injury

Schematic

Endocrine causes act through distinct pressor pathways

- Primary aldosteronism promotes renal sodium and water retention.
- Pheochromocytoma produces a catecholamine-associated hypertensive state.
- Cushing syndrome, thyroid disease, and selected hormone exposures are listed causes.

Endocrine pressor signals

Mineralocorticoid excess



Catecholamine excess



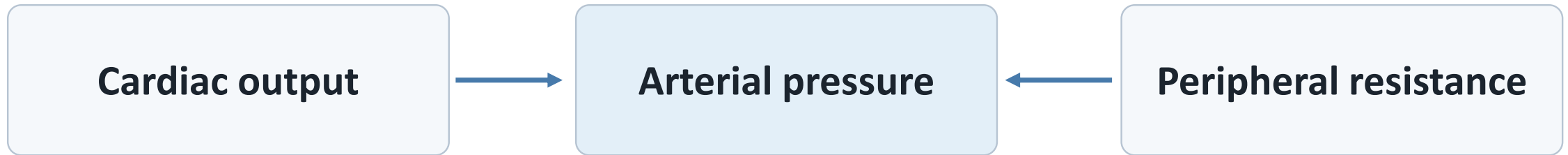
Increased arterial pressure

Schematic

Additional causes differential

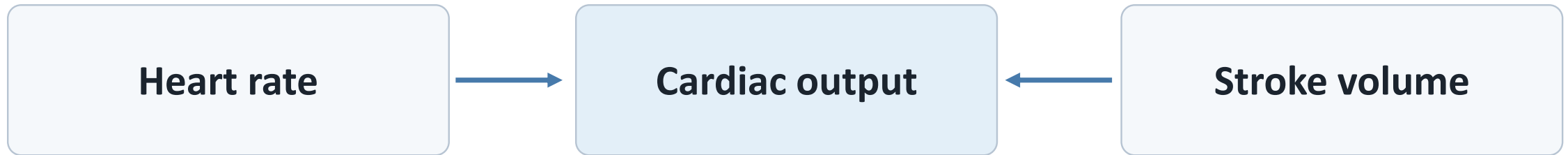
Category	Examples	Practical reasoning
Cardiovascular	Aortic coarctation; increased cardiac output	Altered vascular structure or flow
Neurologic	Increased intracranial pressure; acute stress	Neural and sympathetic effects
Sleep-disordered breathing	Sleep apnea	Secondary contributor listed in Robbins
Pregnancy-associated	Preeclampsia	Distinct clinical context
Drug / hormonal exposures	Glucocorticoids, estrogens, sympathomimetics	Review exposure history

Determinants of arterial pressure



Arterial pressure depends on BOTH cardiac output and systemic vascular resistance.

Determinants of cardiac output



Stroke volume is influenced by ventricular filling and myocardial contractility.

Why renal sodium handling changes cardiac output

- Renal sodium retention leads to retention of water and expansion of intravascular volume.
- Blood volume determines ventricular filling and thereby strongly influences stroke volume.
- The kidney couples long-term salt balance to the cardiac component of blood pressure.

Cardiac-output linkage

Sodium retention



Water retention



Volume and stroke volume

Schematic

The arterioles are key resistance vessels

- Peripheral vascular resistance is regulated predominantly in small arteries and arterioles.
- Vascular smooth-muscle contraction acutely changes arteriolar caliber.
- Neural, hormonal, and local metabolic signals influence arteriolar tone.

Resistance-vessel regulation

Arteriolar smooth muscle



Lumen diameter



Peripheral resistance

Schematic

Vasomotor mediators shape resistance

Predominant vasoconstrictors

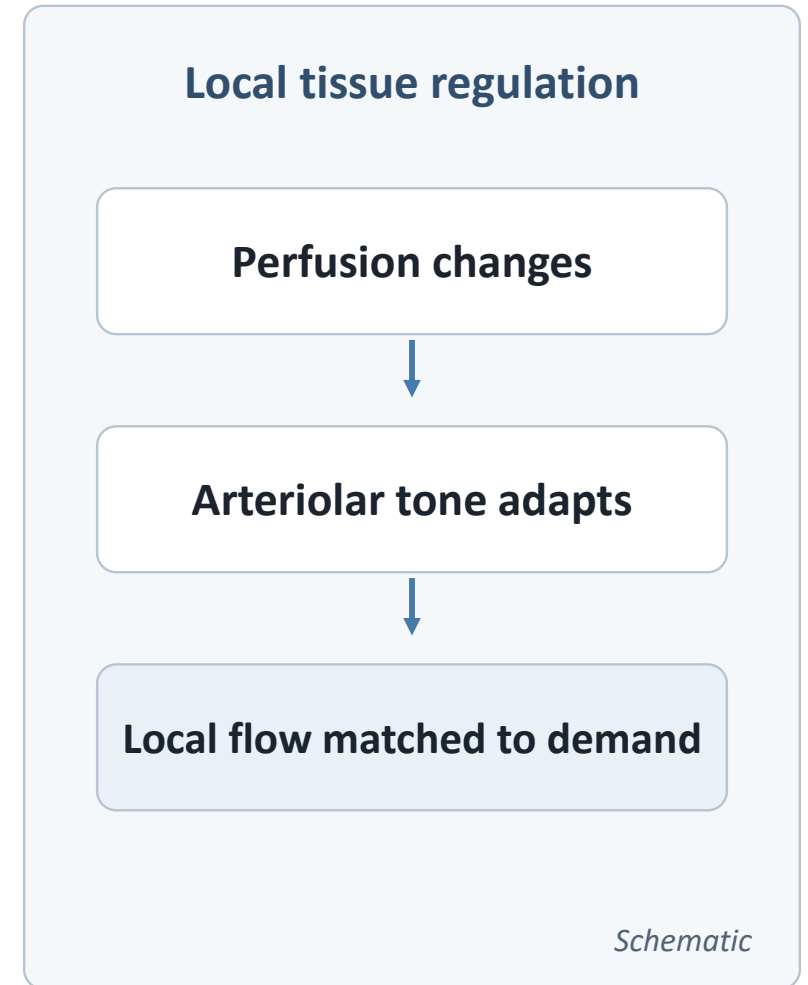
- Angiotensin II
- Catecholamines
- Endothelin

Predominant vasodilators

- Nitric oxide
- Kinins
- Prostaglandins

Autoregulation couples regional flow to local demand

- Resistance vessels respond to variations in regional blood flow and perfusion pressure.
- Increased flow may produce protective local vasoconstriction, limiting hyperperfusion.
- Tissue pH and hypoxia help tailor perfusion to changing metabolic needs.



Hormonal regulation integrates three organs

- Kidney: Renin secretion and adjustable sodium excretion.
- Adrenal cortex: Aldosterone-mediated renal sodium retention.
- Heart: Natriuretic peptides that favor vasodilation and sodium excretion.

Organ-level interaction

Kidney: Renin / sodium



Adrenal: Aldosterone



Heart: ANP / BNP

Schematic

Small adjustments in sodium excretion matter

- Filtration of about 170 L plasma and 23 mol of salt each day.
- With an illustrative 100 mEq daily dietary sodium intake, about 99.5% of filtered sodium must be reabsorbed.
- Fine regulation of the remaining sodium reabsorption sets long-term net sodium balance.

Fine control of salt balance

High filtered sodium load



Precisely regulated
reabsorption



Daily excretion matches intake

Schematic

Juxtaglomerular renin release: Three stimuli

- Reduced pressure in the renal afferent arteriole.
- Elevated circulating catecholamine signaling.
- Reduced sodium delivery to the distal renal tubule.

Juxtaglomerular stimulus

Low afferent pressure



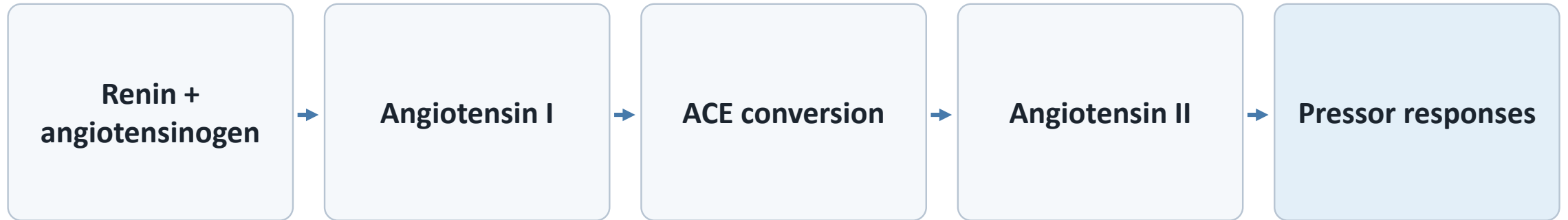
Catecholamines / low distal
 Na^+



Renin release

Schematic

Renin–angiotensin cascade



Renin first cleaves angiotensinogen; ACE generates angiotensin II from angiotensin I.

Three pressor actions of angiotensin II

- Causes vascular smooth-muscle contraction and increases resistance.
- Stimulates adrenal aldosterone secretion.
- Increases renal tubular sodium reabsorption.

Angiotensin II effectors

Arteriolar constriction



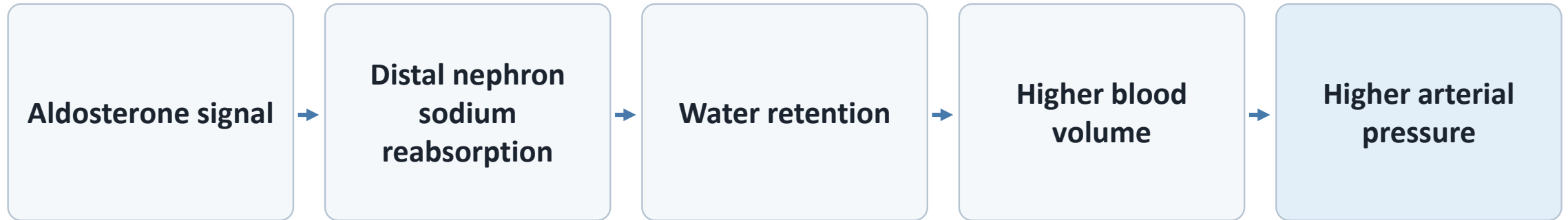
Aldosterone secretion



Tubular Na⁺ retention

Schematic

Aldosterone: Sodium to blood volume



The principal pressor effect emphasized is expansion of extracellular and circulating volume.

Natriuretic peptides counter sodium retention

- Atrial natriuretic peptide is secreted by atrial myocardium; BNP rises particularly with ventricular volume overload.
- These peptides favor systemic vasodilation and renal sodium excretion/diuresis.
- Elevated circulating ANP or BNP can reflect volume overload, as in congestive heart failure.

Counter-regulatory response

**Volume-stretched
myocardium**



ANP / BNP release



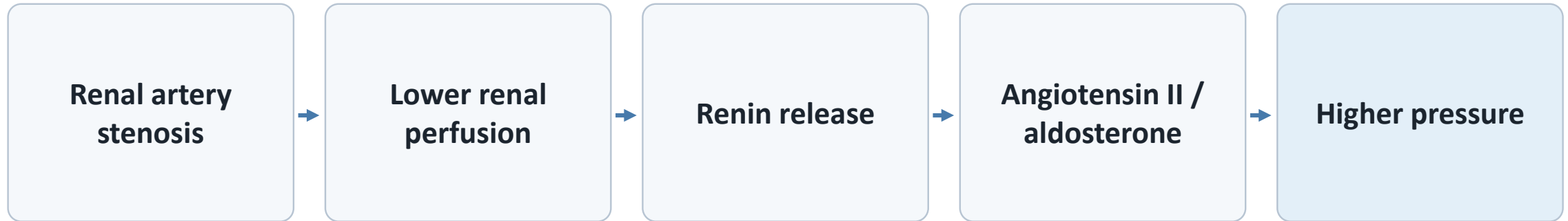
Vasodilation and natriuresis

Schematic

Counter-regulatory pressure systems

Feature	RAAS predominance	Natriuretic peptide predominance
Trigger	Reduced renal perfusion / sodium delivery	Cardiac volume stretch
Resistance	Angiotensin II raises tone	Vasodilation
Sodium balance	Aldosterone promotes retention	Natriuresis / diuresis
Net directional effect	Tends to increase arterial pressure	Tends to decrease arterial pressure

Renovascular hypertension: Causal sequence



The stenotic kidney may interpret local hypoperfusion as systemic underfilling.

Primary aldosteronism: A sodium-retentive cause

- Primary aldosteronism is listed among the frequent identifiable endocrine causes.
- It may be idiopathic or associated with an aldosterone-secreting adrenal adenoma.
- Enhanced distal sodium reabsorption expands volume and contributes to hypertension.

Mineralocorticoid pathway

Aldosterone elevation



Distal sodium retention



Volume expansion

Schematic

Rare monogenic hypertensive phenotypes

- Single-gene disorders can perturb aldosterone metabolism or renal epithelial sodium transport.
- Some steroidogenic enzyme defects produce an excess mineralocorticoid effect.
- Liddle syndrome exemplifies ENaC-related increased distal nephron sodium reabsorption.

Rare inherited mechanisms

Steroidogenic enzymes



ENaC sodium transport



Potential monogenic
hypertension

Schematic

Essential hypertension has a polygenic substrate

- Twin and family/adoption observations support heritable variation in blood pressure.
- More than 500 blood-pressure-associated variants from genome-wide association studies.
- Each contribution must be interpreted within interacting environmental and physiologic networks.

Essential-disease substrate

Many associated alleles



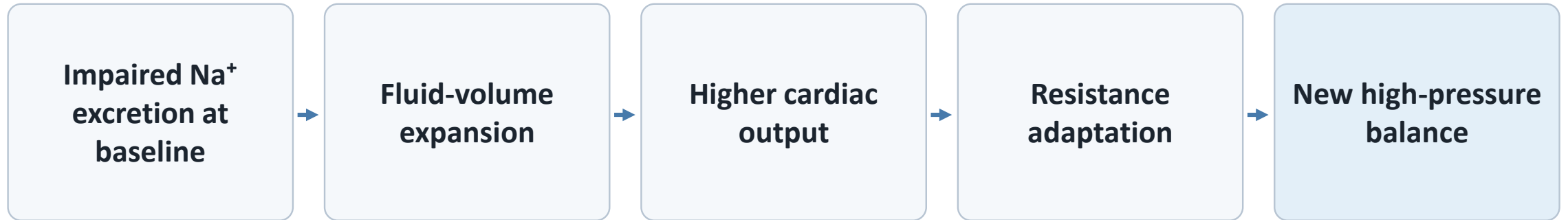
Environmental exposures



Shared BP physiology

Schematic

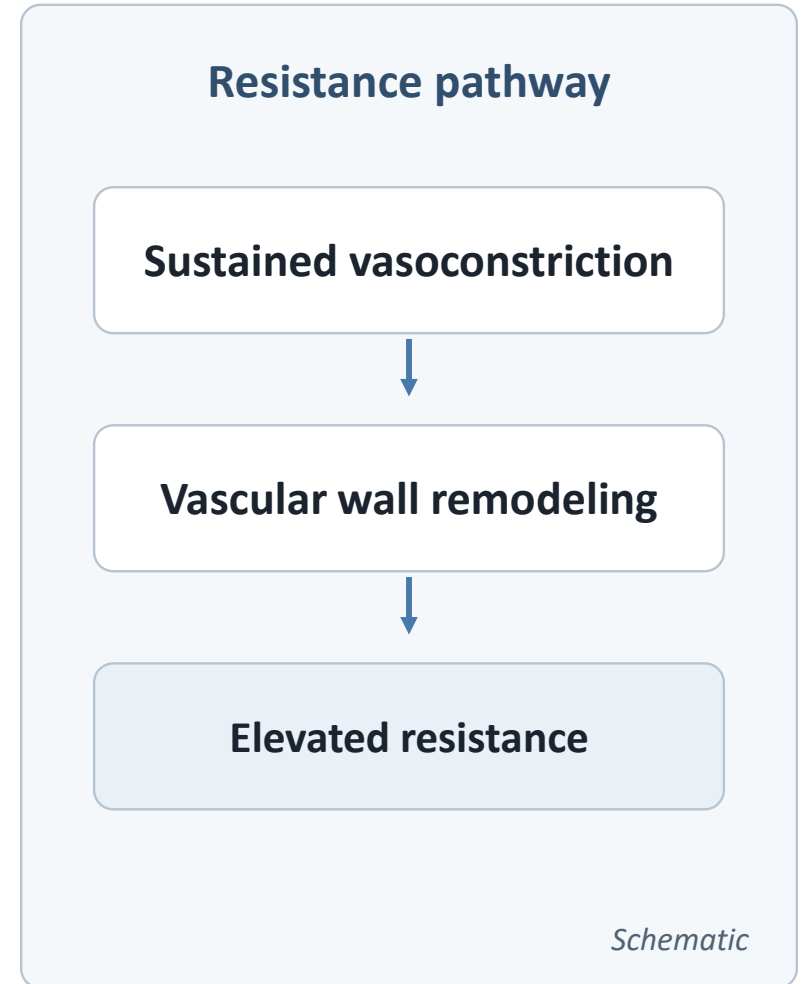
Pressure natriuresis can reset at higher pressure



Sodium excretion again matches intake, but only at an elevated pressure set point.

Increased vascular resistance reinforces hypertension

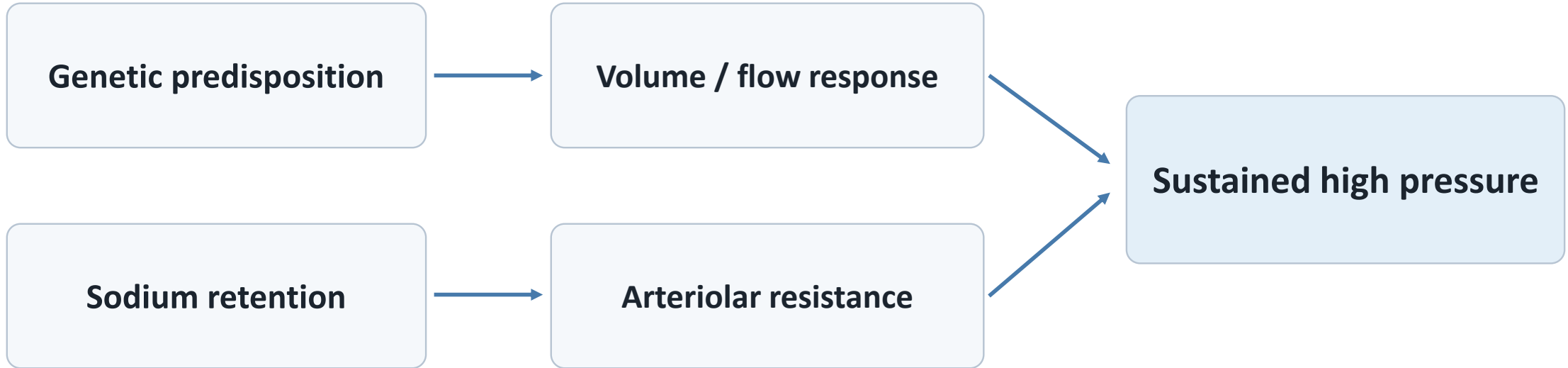
- Sustained vasoconstrictor influences elevate arteriolar tone.
- Structural changes of resistance-vessel walls may further increase resistance.
- Volume-dependent and resistance-dependent influences can reinforce one another.



Environmental factors highlighted by Robbins

Factor	Pathophysiologic connection
High dietary sodium	Greater sodium burden when excretory adjustment is impaired
Obesity	Complex interaction with volume and neurohormonal regulation
Physical inactivity	Associated with essential-hypertension risk
Smoking	Vascular and cardiovascular risk contribution
Stress	Neural and hormonal pressure influences

Convergence of essential-hypertension pathways



Genetic and environmental influences converge on sodium and vascular regulation.

Mechanistic comparison: Essential vs secondary

Essential disease

- No single initiating lesion can be assigned
- Multiple genetic and environmental influences
- Common final pathways: Sodium, volume, resistance

Secondary disease

- An identifiable driver exists
- Renal stenosis, endocrine disorder or other cause
- Specific causal pathway may be established

Vascular injury can be both cause and consequence

- Chronic hemodynamic stress promotes endothelial dysfunction and structural adaptation.
- Small-vessel luminal narrowing compromises distal perfusion.
- Reduced renal perfusion may further sustain pressor pathways.

Positive-feedback potential

Vascular injury



Luminal restriction

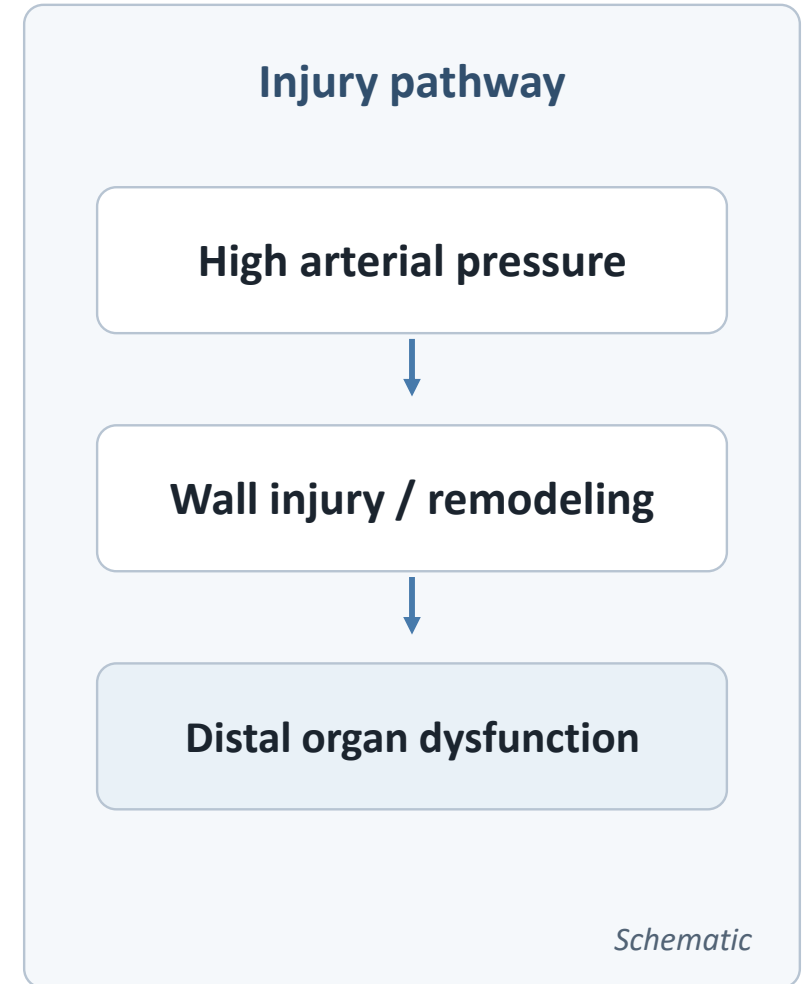


Renal perfusion changes

Schematic

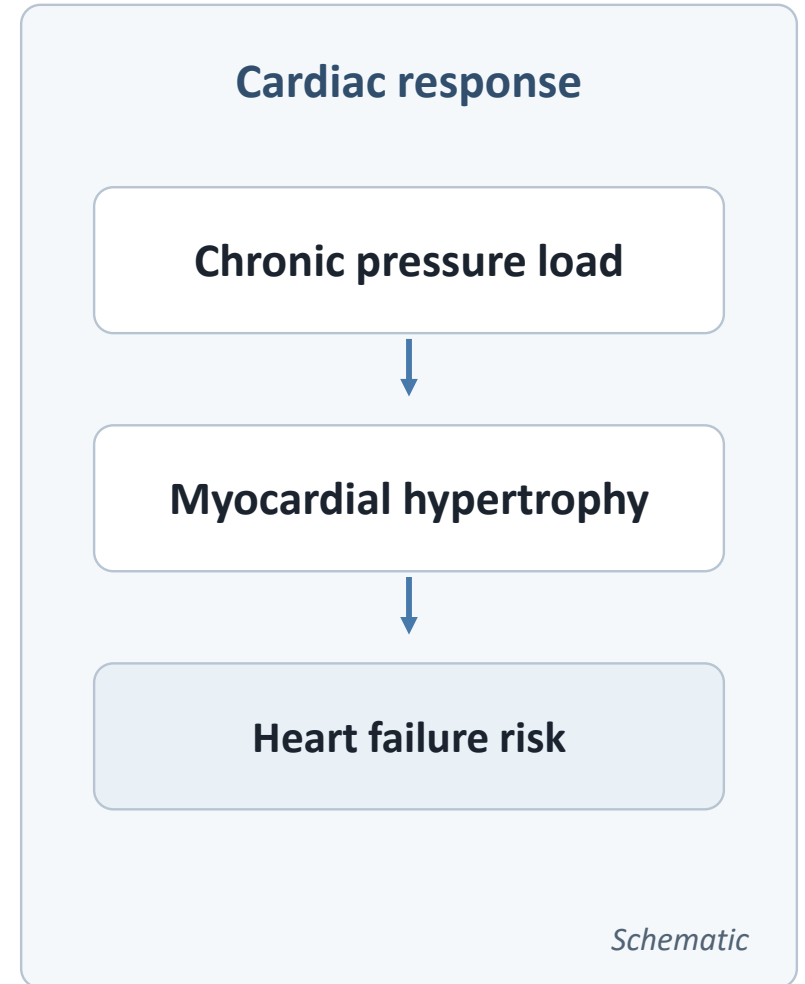
Why hypertension produces target-organ damage

- Increased pressure accelerates atherogenesis in susceptible large and medium arteries.
- Arterial and arteriolar remodeling can narrow vessel lumens and cause ischemia.
- Sudden severe pressure elevation may produce vascular wall necrosis and acute organ failure.



Cardiac consequences: Pressure overload

- Long-standing hypertension is associated with cardiac hypertrophy.
- Progressive cardiac dysfunction may culminate in heart failure.
- Atherosclerotic cardiovascular disease contributes additional ischemic risk.



Brain and cerebrovascular complications

- Elevated pressure contributes to cerebrovascular hemorrhage.
- Hypertension increases atherosclerotic and ischemic cerebrovascular risk.
- Chronic vascular disease is associated with multi-infarct dementia.

Cerebrovascular injury

Vascular wall injury



Occlusion / hemorrhage

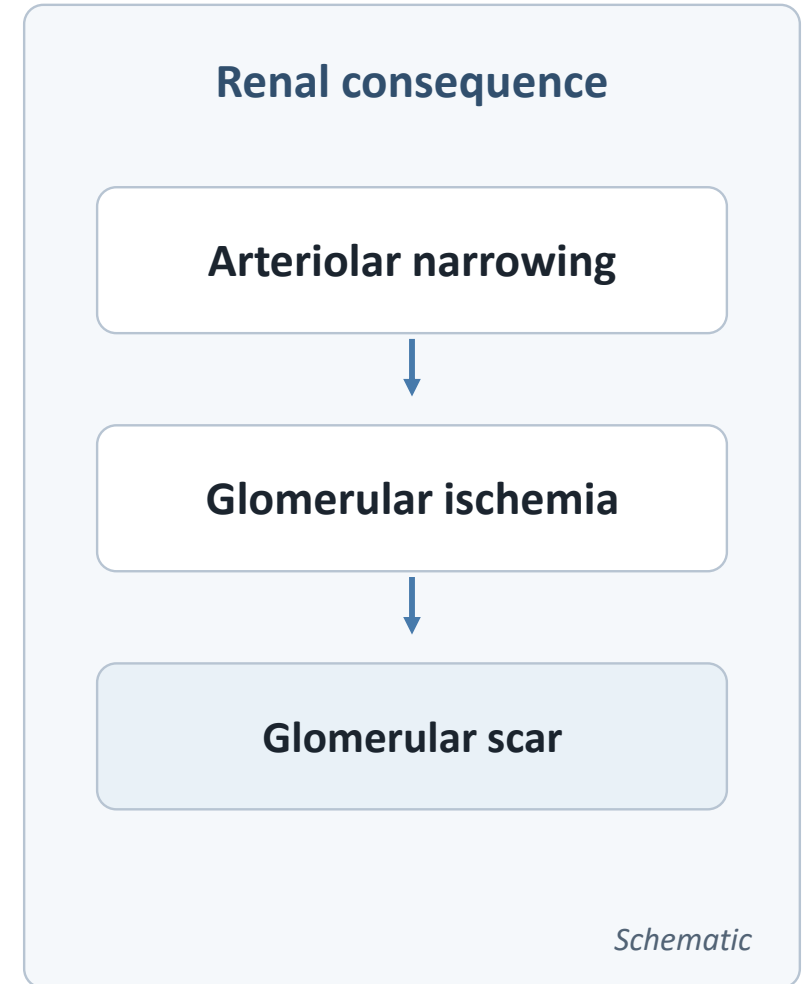


Neurologic consequences

Schematic

Kidney injury: Microvascular to parenchymal disease

- Arteriolar wall thickening narrows renal microvascular lumens.
- Diffuse loss of renal blood supply can cause glomerular scarring.
- Chronic nephrosclerosis may progress to renal functional impairment.



Large- and medium-artery consequences

- Hypertension accelerates atherogenesis and the associated ischemic burden.
- Chronic hemodynamic stress contributes to arterial wall degeneration.
- Aortic dissection and cerebrovascular hemorrhage are important consequences listed.

Major-artery consequence

Chronic arterial stress



Atherogenesis and
degeneration



Major-artery complications

Schematic

Organ-based map of hypertensive disease

Tissue	Illustrative injury	Pathology linkage
Heart	Hypertrophy; heart failure	Pressure load and ischemic disease
Brain	Stroke; multi-infarct damage	Vascular injury and occlusion / rupture
Kidney	Nephrosclerosis; renal failure	Arteriolar narrowing and glomerular scarring
Aorta	Dissection	Degenerative wall injury
Retina	Hemorrhages and exudates in severe disease	Small-vessel target-organ injury

Chronic vs rapidly progressive disease

Long-standing hypertension

- Often clinically silent
- Cumulative vascular and organ remodeling
- Hyaline arteriolosclerosis is common

Malignant hypertension

- Rapidly escalating, very high pressure
- Acute kidney and retinal injury
- Hyperplastic changes with necrosis may occur

Malignant hypertension: Source-defined phenotype

- Rapidly rising, severe blood pressure—often >180 mm Hg systolic and >120 mm Hg diastolic.
- Associated renal failure and retinal hemorrhages/exudates are defining features in the source.
- Papilledema may be present but is not obligatory in the described syndrome.

Organ-threatening phenotype

Marked and rising pressure



Retinal / renal injury

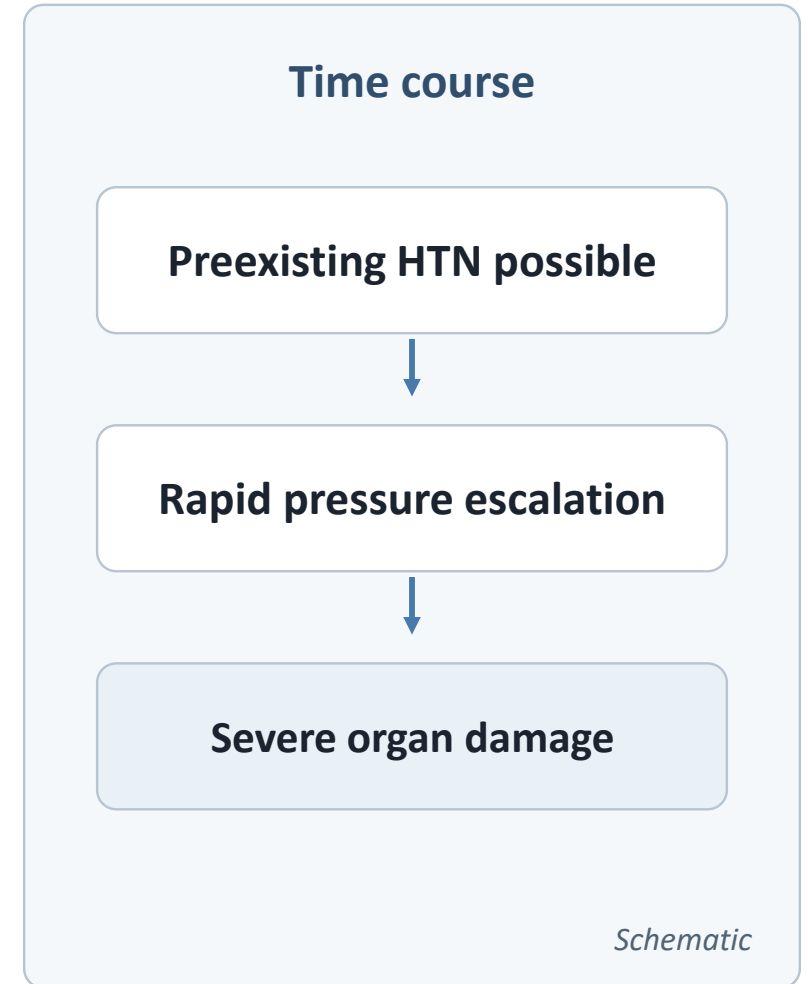


Destructive microvascular
lesions

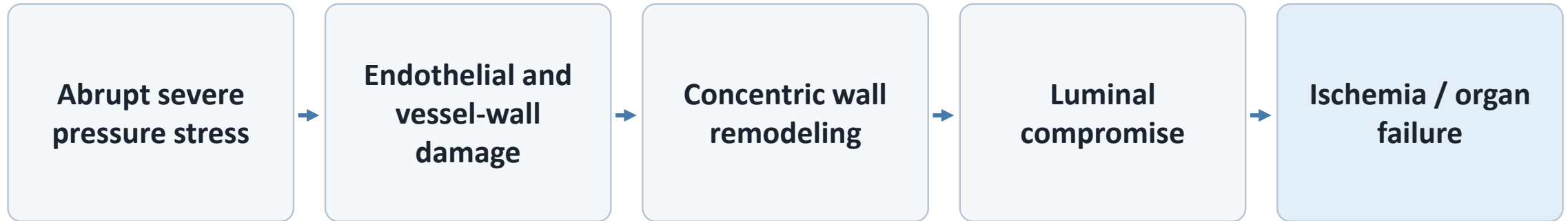
Schematic

Malignant hypertension can complicate prior disease

- The syndrome may develop in previously normotensive individuals.
- More commonly, it supervenes on preexisting hypertension described historically as “benign.”
- The malignant descriptor reflects rapidly progressive organ-threatening injury, not neoplasia.



Severe-pressure microvascular injury sequence



Fibrinoid injury and necrosis may accompany the hyperplastic lesion in malignant disease.

Retina and kidney are defining target organs

- Retinal hemorrhages and exudates are named manifestations of the malignant syndrome.
- Papilledema may occur and should be separately recognized.
- Renal failure signals severe renal vascular and parenchymal injury.

Target-organ evidence

**Retinal hemorrhages /
exudates**



Renal dysfunction



Malignant syndrome

Schematic

Pulmonary hypertension is a distinct vascular setting

- Pulmonary pressure elevation has causes including left-heart disease, congenital defects, valvular disease, lung disorders and thromboembolism.
- Pulmonary arterioles can display intimal fibrosis and medial hyperplasia.
- These findings should not be substituted for systemic hypertensive arteriolosclerosis without the relevant context.

Pulmonary vascular bed

Pulmonary vascular pressure



Intimal / medial remodeling



Distinct etiologic work-up

Schematic

Hypertension-related arteriolar lesion spectrum

- Hyaline arteriosclerosis: Amorphous eosinophilic wall thickening with luminal loss.
- Hyperplastic arteriosclerosis: Concentric laminated wall thickening in severe hypertension.
- Necrotizing arteriolitis: Destructive vascular wall lesion, especially emphasized in renal disease.

Three named lesions

Hyaline thickening



Concentric hyperplasia

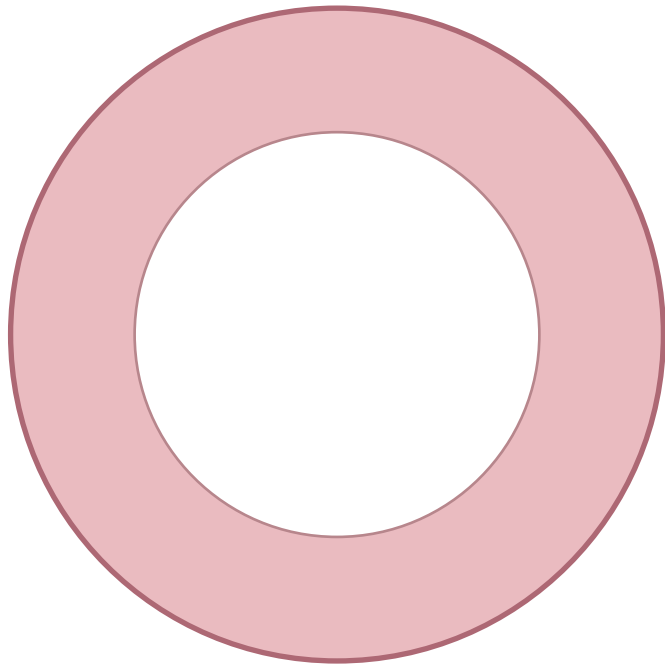


Necrotizing damage

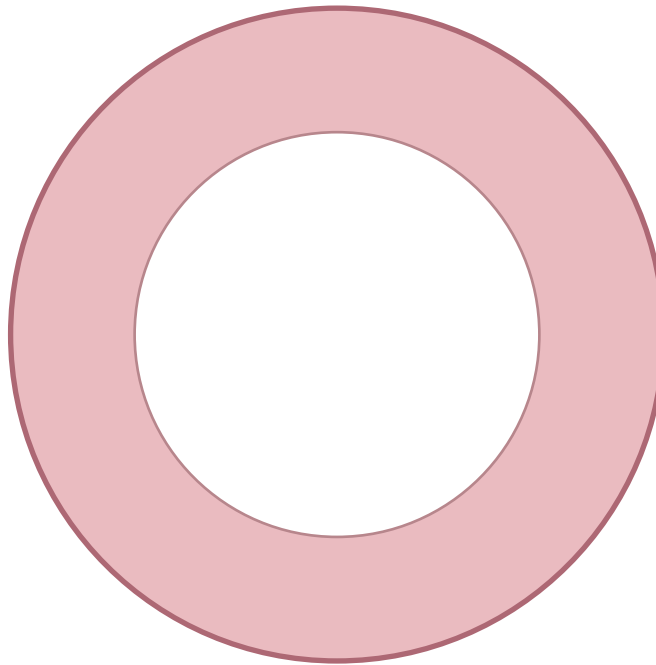
Schematic

Normal arteriole: The baseline for comparison

Reference arteriole



Normal anatomy

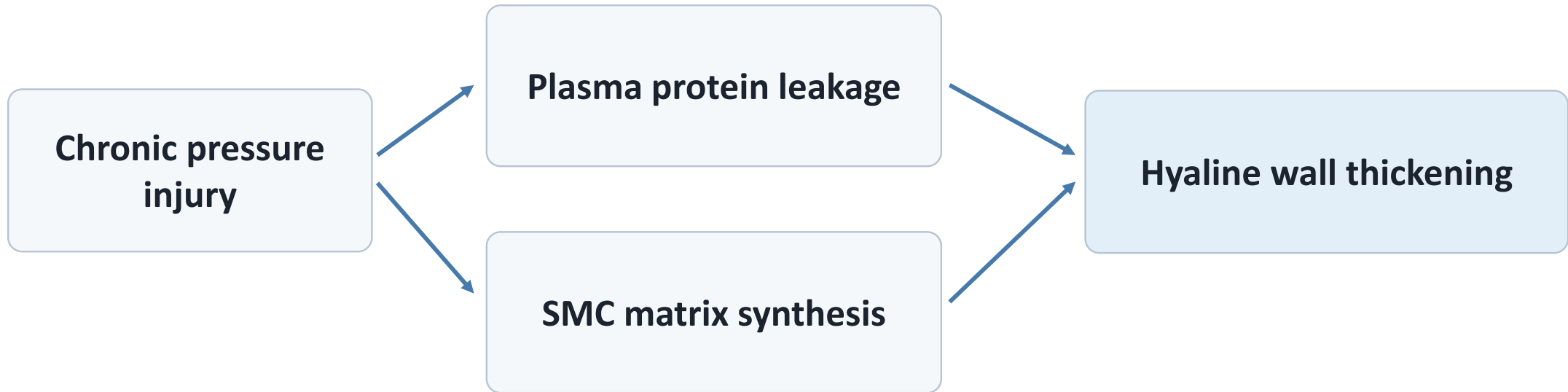


Recognition points

- Patent lumen bounded by a relatively thin muscular wall
- Endothelium at the blood–wall interface
- Useful reference for recognizing pathological wall-to-lumen ratios

Schematic cross-sections; Not photomicrographs

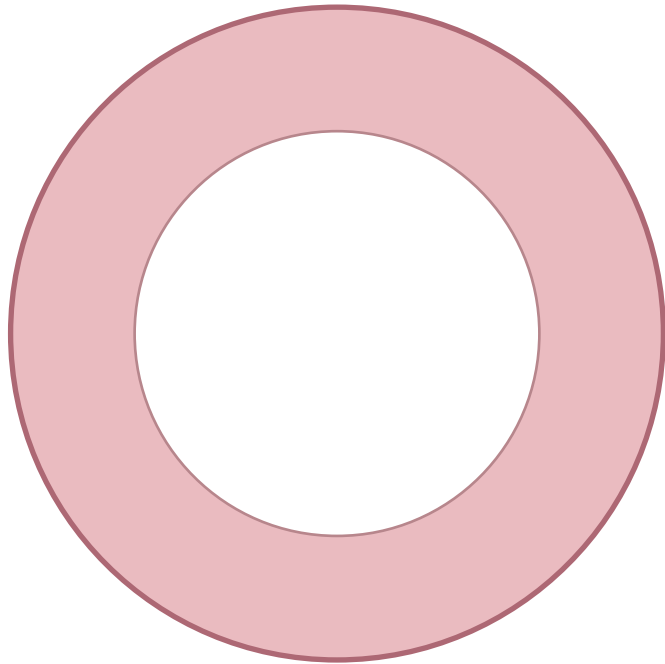
Hyaline arteriolosclerosis: Two contributors



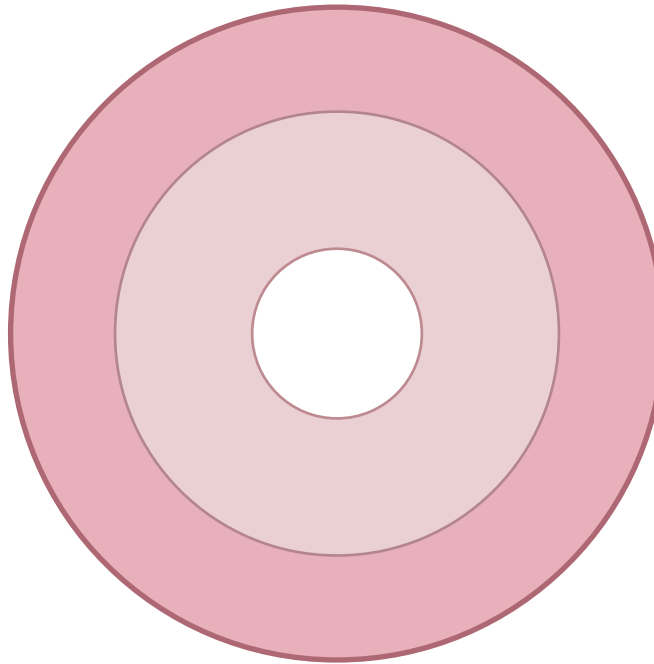
Two parallel processes contribute to the homogeneous, thickened wall and narrowed lumen.

Hyaline arteriolosclerosis: Diagnostic schematic

Reference arteriole



Hypertension-associated lesion



Recognition points

- Homogeneous eosinophilic-appearing material accumulates in arteriolar walls
- Wall thickening is predominantly acellular / glassy
- Luminal narrowing reduces downstream tissue perfusion

Schematic cross-sections; Not photomicrographs

Hyalinosi is not exclusive to hypertension

- Arteriolar hyalinosi may be encountered with advancing age even without hypertension.
- It is more generalized and severe in patients with hypertension and diabetes.
- Attribution requires the broader clinical and renal parenchymal context.

Clinicopathologic context

Older age



Hypertension / diabetes



Arteriolar hyalinosi

Schematic

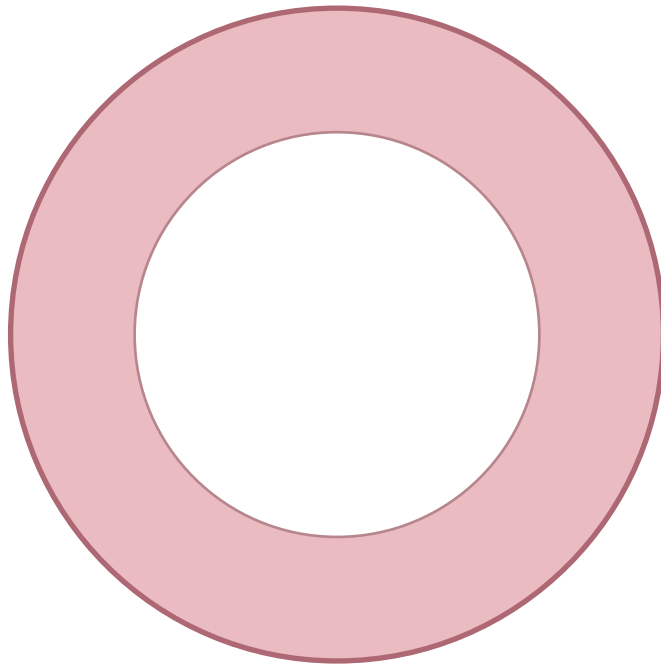
Chronic hypertensive nephrosclerosis



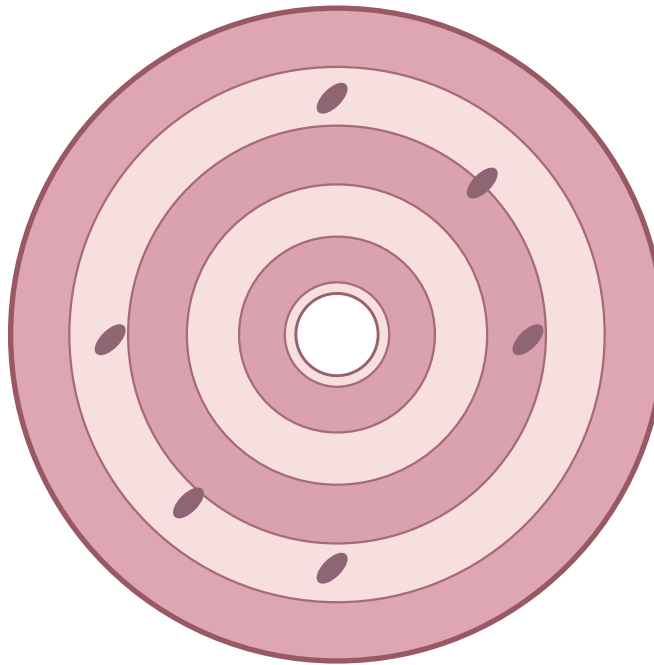
The microvascular lesion explains why apparently indolent pressure elevation causes cumulative renal disease.

Hyperplastic arteriolosclerosis: Diagnostic schematic

Reference arteriole



Hypertension-associated lesion



Recognition points

- Concentric, laminated “onion-skin” wall thickening
- Smooth-muscle cells and reduplicated basement membranes form the layers
- Severe luminal narrowing accompanies severe hypertension

Schematic cross-sections; Not photomicrographs

Why onion-skin laminations form

- Sustained severe hemodynamic injury stimulates vessel-wall cellular and matrix responses.
- Concentric smooth-muscle proliferation and basement-membrane reduplication create stacked lamellae.
- The narrowing lumen is a functional consequence, not a merely decorative histologic feature.

Microscopic architecture

SMC accumulation



**Basement membrane
reduplication**

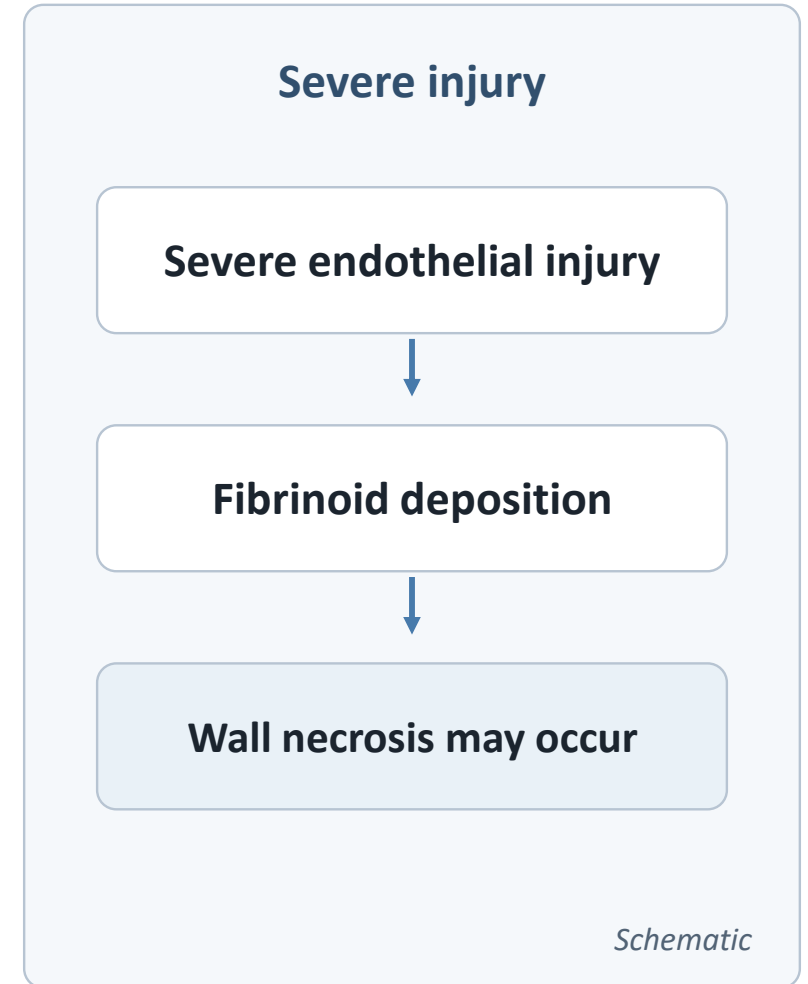


Concentric wall laminations

Schematic

Fibrinoid deposits indicate destructive injury

- In malignant hypertension, hyperplastic change may be accompanied by fibrinoid deposition.
- Vascular wall necrosis marks acute, severe microvascular damage.
- Fibrinoid necrosis should be distinguished morphologically from chronic, non-necrotizing hyaline material.



Necrotizing arteriolitis: An important renal lesion

- Necrotizing arteriolitis as a third hypertension-related small-vessel lesion.
- It is highlighted particularly in the kidney.
- This lesion belongs to the severe injury spectrum and is distinct from simple luminal hyalinosis.

Necrotizing spectrum

Severe pressure-associated injury



Arteriolar wall necrosis



Renal microvascular dysfunction

Schematic

Small-vessel lesions compared

Feature	Hyaline	Hyperplastic	Necrotizing
Typical setting	Chronic HTN; also aging/diabetes	Severe HTN	Severe destructive injury
Dominant change	Glassy eosinophilic wall material	Concentric lamellated thickening	Wall necrosis
Key source mechanism	Protein leakage + matrix synthesis	SMC proliferation + basement membrane	Fibrinoid injury / necrosis
Clinical link	Chronic ischemia; nephrosclerosis	Marked luminal narrowing	Acute organ-threatening microvascular injury

Do not confuse patterns of arteriosclerosis

Pattern	Principal arterial level / change	Relation to hypertension
Arteriolosclerosis	Small arteries and arterioles	Hyaline / hyperplastic forms
Atherosclerosis	Intimal atheromatous plaques	Hypertension accelerates risk
Mönckeberg medial sclerosis	Medial calcification, often little lumen change	Different process
Fibromuscular intimal hyperplasia	Repair-associated intimal SMC / ECM thickening	Mechanical/inflammatory injury response

A pathology report must be interpreted in context

- Arteriolar hyalinosis is a descriptive morphologic finding, not a unique test for hypertension.
- Concentric arteriolar proliferation should prompt attention to severity and acute vascular injury.
- Glomerulosclerosis, tubulointerstitial change, diabetes, and large-vessel disease may modify interpretation.

Diagnostic integration

Morphologic lesion



Clinical context



Integrated pathology
interpretation

Schematic

Application: Prolonged, silent hypertension

Clinical / pathology stem

A patient has had years of minimally symptomatic elevated pressure. Renal microscopy shows diffuse homogeneous pink thickening of arteriolar walls and small lumina.

Which vascular lesion best explains reduced renal perfusion?

Interpretation

Hyaline arteriosclerosis: Wall protein leakage and SMC-derived matrix contribute to narrowing and chronic nephrosclerosis.

Application: Renovascular hypertension

Clinical / pathology stem

A patient has narrowing of a main renal artery. The affected kidney experiences reduced afferent perfusion despite high systemic pressure.

What renal signal amplifies systemic pressure?

Interpretation

Renin release → angiotensin II → vasoconstriction and aldosterone-mediated sodium retention.

Application: Abrupt severe hypertension

Clinical / pathology stem

A patient develops rapid, marked pressure elevation together with renal dysfunction and retinal hemorrhages. Renal arterioles are concentrically laminated.

Name the syndrome and explain the characteristic arteriolar lesion.

Interpretation

Malignant hypertension; Hyperplastic arteriolosclerosis is an onion-skin lesion and may accompany fibrinoid injury.

Integrated pathologic reasoning

- Identify the pressure pattern and whether an underlying cause is recognizable.
- Connect renal sodium regulation and arteriolar resistance to persistent pressure elevation.
- Interpret arteriolar morphology alongside target-organ findings and clinical tempo.

Three-part interpretation

Pressure phenotype



Etiologic pathway



Morphology + organ injury

Schematic

Selected sources and diagnostic-image references

Source	Role
Robbins, Cotran & Kumar, Pathologic Basis of Disease, 11th ed., Ch 11, pp 445–448	Primary source for lecture text and diagrams
Wikimedia Commons: “Histopathology of renal arteriolar hyalinosis” (M. Häggström; CC0)	Authentic specimen reference; NOT embedded
Wikimedia Commons: “Onion-skin renal arteriole” (Pacolarosa; CC BY-SA 3.0)	Authentic specimen reference; NOT embedded