

Preeclampsia and Eclampsia

Placental disease and maternal microvascular injury

Clinicopathologic mechanisms · placental morphology · complications

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Learning goals

- Explain the two linked stages: Abnormal placentation and maternal endothelial injury.
- Recognize placental maternal vascular malperfusion lesions and their pathogenesis.
- Connect systemic endothelial dysfunction with renal, neurologic, hepatic and hematologic effects.
- Distinguish preeclampsia, eclampsia and HELLP syndrome and interpret clinical scenarios.

A systemic disease with a placental origin

Placenta

Inadequate physiologic spiral-artery remodeling

Relative uteroplacental underperfusion

Maternal vessels

Circulating antiangiogenic influence

Diffuse endothelial dysfunction

Target organs

Hypertension and protein leakage

Microthrombi and organ dysfunction

Clinical syndrome: Core boundaries

- Typically recognized after 20 weeks of gestation, most often in the last trimester.
- New hypertension occurs with proteinuria or another maternal organ/uteroplacental manifestation.
- Eclampsia denotes convulsions attributable to the hypertensive pregnancy disorder.
- Severe disease threatens both maternal organ function and placental–fetal perfusion.

Hypertensive disorders: Pattern recognition

Condition	Defining clinical pattern
Gestational hypertension	New hypertension after 20 weeks without additional preeclampsia findings.
Preeclampsia	New hypertension with proteinuria and/or organ or uteroplacental dysfunction.
Preeclampsia with severe features	Preeclampsia with specified severe BP or end-organ findings (ACOG).
Eclampsia	New-onset convulsions not explained by another cause in this setting.
HELLP spectrum	Hemolysis, elevated liver enzymes, low platelets; serious preeclampsia manifestation.

Timing: Early placental insult, later maternal disease

Early implantation

Extravillous trophoblast invasion and vessel remodeling



Placental adaptation

Low-resistance uteroplacental blood flow must increase with gestation



Late maternal syndrome

Defective perfusion → placenta-derived mediators → systemic manifestations

Risk context emphasized

- Occurs in approximately 3–5% of pregnancies account.
- More often reported in first pregnancies (primiparity).
- Underlying hypertension, kidney disease or coagulopathy may be associated with earlier presentation.
- Molar pregnancy may also be associated with an unusually early onset.

Why proteinuria is not essential for diagnosis

- Modern frameworks do not require proteinuria when new hypertension accompanies qualifying organ dysfunction.
- Renal insufficiency, thrombocytopenia, liver injury, pulmonary edema and neurologic features must be assessed.
- Clinical classification should not depend on edema alone: It is nonspecific in pregnancy.
- Textbook language highlights edema and proteinuria; This slide uses contemporary criteria.

ACOG thresholds: Hypertension and proteinuria

Assessment	Threshold or interpretation
New hypertension	Systolic ≥ 140 mm Hg or diastolic ≥ 90 mm Hg on two occasions ≥ 4 h apart, ordinarily after 20 weeks.
Severe-range pressure	Systolic ≥ 160 mm Hg or diastolic ≥ 110 mm Hg.
24-hour urinary protein	≥ 300 mg per 24 hours.
Spot urine protein/creatinine	≥ 0.3 mg/mg.
Absence of proteinuria	Does not exclude preeclampsia if eligible organ dysfunction is present.

ACOG: Major severe-feature findings

Organ domain	Clinically significant finding
Pressure	Systolic ≥ 160 or diastolic ≥ 110 mm Hg.
Hematologic	Platelet count $< 100,000/\mu\text{L}$.
Renal	Creatinine > 1.1 mg/dL or doubling from baseline without another renal disease.
Hepatic	Transaminases > 2 times normal; persistent severe RUQ/epigastric pain may be relevant.
Pulmonary	Pulmonary edema.
Neurologic	New persistent headache unresponsive to medication or visual symptoms.

Eclampsia: Neurologic escalation

- Seizures mark severe neurologic involvement in the preeclampsia spectrum.
- Severe headache and visual symptoms may precede convulsions but are not obligatory.
- Eclampsia may progress to coma and maternal death.
- Alternative causes of seizures must be considered clinically.

HELLP is a multisystem vascular complication

H — hemolysis

Microangiopathic red-cell injury

Reflects small-vessel damage and consumption

EL — enzymes

Hepatic enzyme elevation

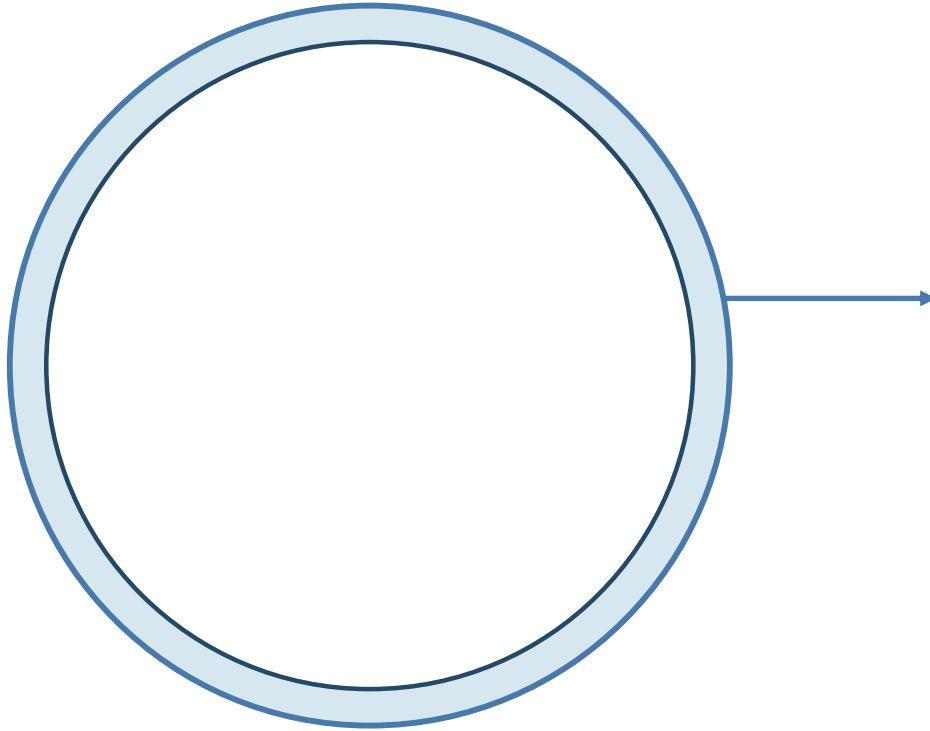
Can accompany hepatic microthrombi, necrosis or hemorrhage

LP — platelets

Thrombocytopenia

Platelet consumption in systemic endothelial/coagulation injury

Normal spiral-artery remodeling produces low resistance



Physiologic pregnancy

- Extravillous trophoblast enters vessel wall
- Smooth muscle coat is lost
- Broad, low-resistance uteroplacental channel
- Adequate maternal perfusion of intervillous space

Schematic cross-section, not histology

Physiologic conversion of the placental bed

Extravillous invasion

Fetal trophoblast enters decidua and maternal spiral-artery walls



Wall remodeling

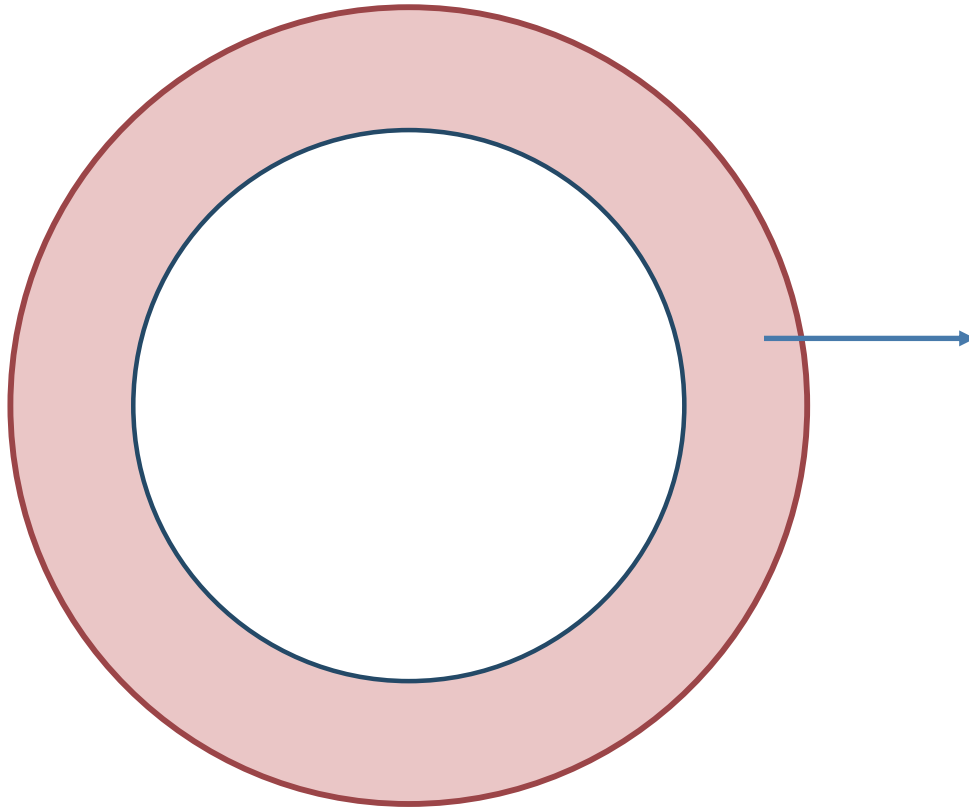
Vascular muscle is lost and trophoblast replaces endothelial lining



High-capacity flow

Dilated, low-resistance maternal vessels perfuse intervillous space

Failed spiral-artery transformation in preeclampsia

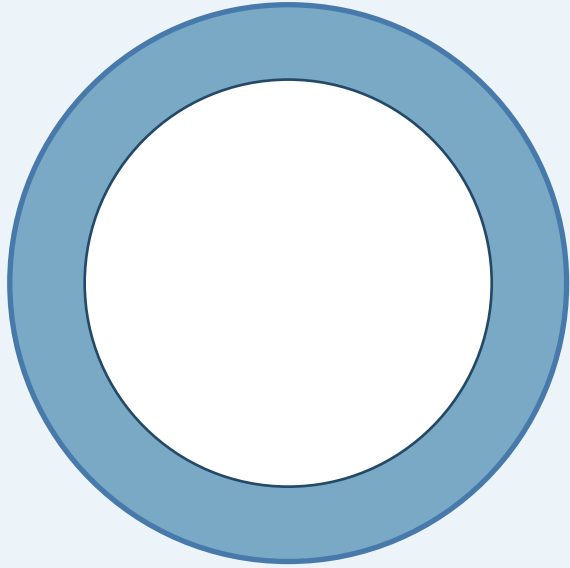


Preeclampsia

- Inadequate extravillous trophoblast invasion
- Persistence of arterial smooth muscle
- Relatively narrow, high-resistance lumen
- Reduced capacity to meet late-gestational flow demand

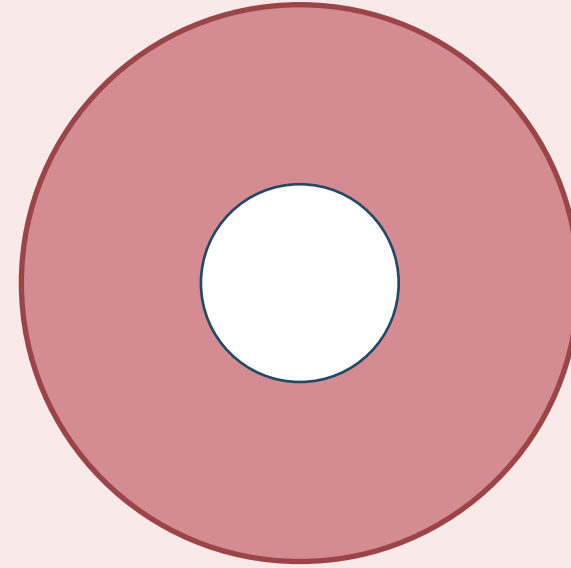
Schematic cross-section, not histology

Spiral arteries: Normal versus failed transformation



Physiologic remodeling

Muscle loss · expanded lumen



Inadequate remodeling

Persistent media · higher resistance

The central placental hemodynamic defect

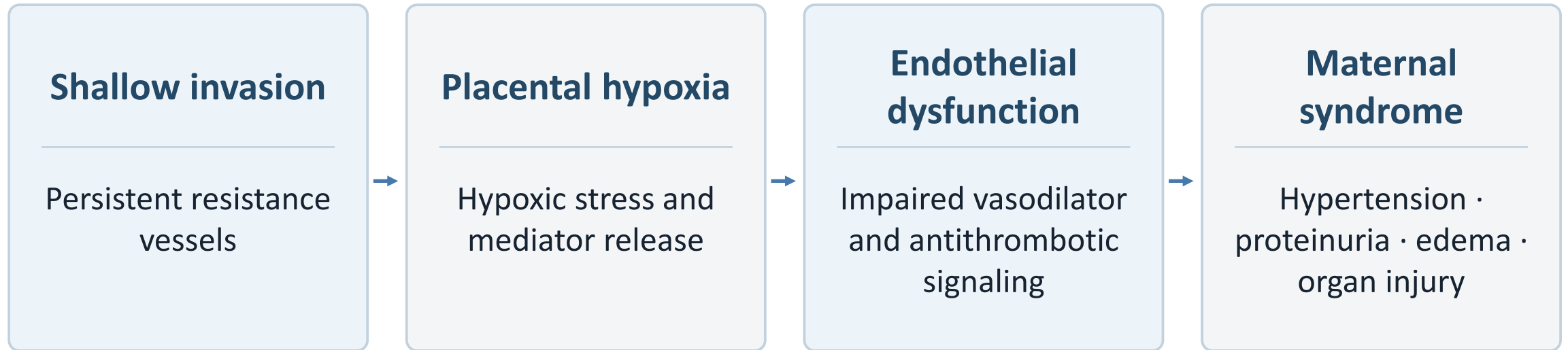
- Shallow trophoblast implantation leaves maternal spiral arteries inadequately remodeled.
- Narrow, relatively muscular vessels limit adaptive delivery of maternal blood.
- Later gestation increases flow requirements beyond what these vessels can support.
- The resulting placental underperfusion is a proposed initiating stimulus.

A two-stage model connects placenta and mother



Conceptual model: Placental pathology begins before overt maternal symptoms

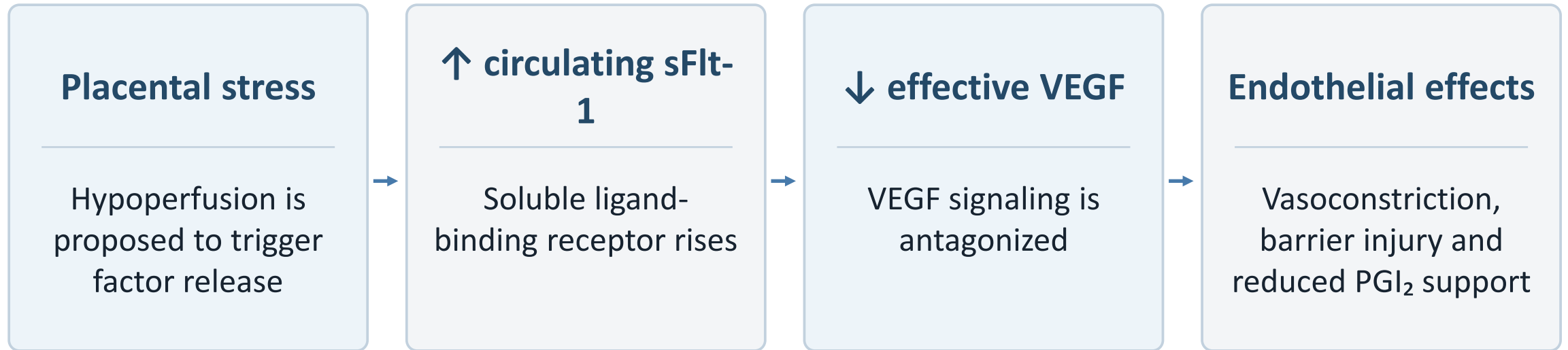
From trophoblast to clinical presentation



SFlt-1: Soluble VEGF receptor activity

- Placenta-derived soluble fms-like tyrosine kinase 1 (sFlt-1) is elevated model.
- It binds/antagonizes vascular endothelial growth factor (VEGF) signaling.
- Reduced VEGF-dependent endothelial support contributes to dysfunction.
- The source treats this as a major proposed mechanistic bridge, not a sole cause.

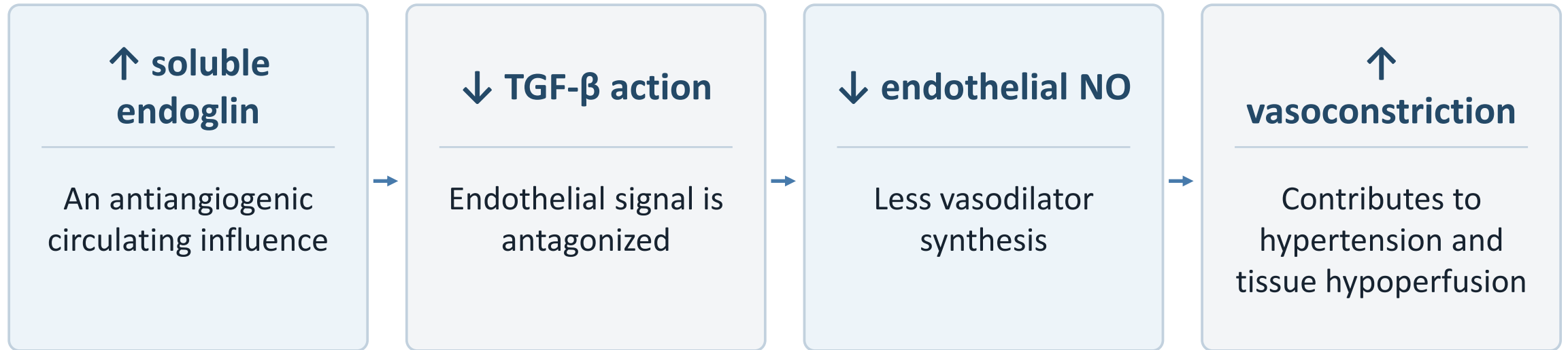
SFlt-1 links placenta to endothelial dysfunction



Soluble endoglin antagonizes TGF- β signaling

- Soluble endoglin is another placenta-derived antiangiogenic factor emphasized by Robbins.
- It antagonizes transforming growth factor- β (TGF- β) signaling.
- TGF- β normally contributes to endothelial nitric oxide production.
- Consequent reduction in vasodilatory signaling may increase systemic vascular tone.

Endoglin–TGF- β –nitric oxide axis



Why prostacyclin matters for thrombosis

- VEGF stimulates endothelial production of prostacyclin (PGI₂).
- PGI₂ has vasodilatory and antithrombotic properties.
- VEGF antagonism by sFlt-1 may reduce PGI₂ generation.
- Reduced antithrombotic protection and procoagulant release favor microthrombosis.

Antiangiogenic imbalance converges on injury

SFlt-1 → VEGF blockade

Less PGI₂-supported
antithrombotic signaling



Endoglin → TGF- β block

Less nitric oxide-mediated
vasodilation



Endothelial dysfunction

Hypertension + leak +
microvascular thrombosis

Three endothelial consequences explain the phenotype

Increased tone

Generalized vasoconstriction

Systemic hypertension and
organ hypoperfusion

Barrier failure

Increased vascular
permeability

Proteinuria and fluid
extravasation

Prothrombotic state

Thrombi in
arterioles/capillaries

Tissue ischemia, hemolysis
and platelet use

Evidence supporting a placental mediator model

- Clinical manifestations commonly improve following placental delivery.
- Maternal sFlt-1 and soluble endoglin levels are markedly increased in the source description.
- Experimental overexpression in pregnant rats induces hypertension, proteinuria and HELLP-like effects.
- Animal experiments support causality but do not establish identical biology in every patient.

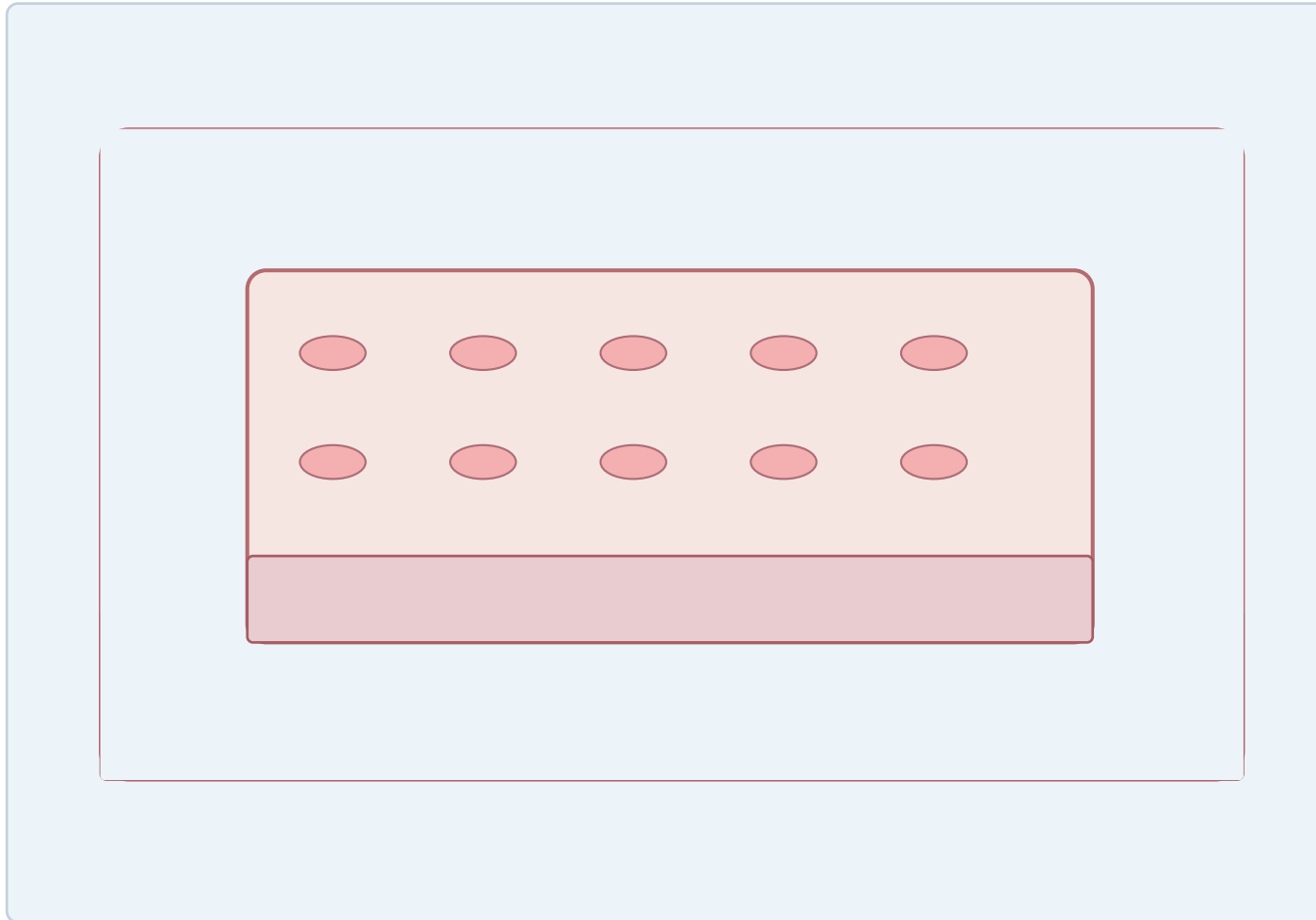
Heterogeneity and mechanistic caution

- The source describes a predominant pathway, not a uniform molecular cause of all disease.
- Placental vascular pathology and clinical severity do not map one-to-one in every pregnancy.
- Antiangiogenic factors are mechanistically informative; They do not replace a clinical diagnosis.
- Avoid treating a schematic sequence as a unique, fully proved causal chain.

Placental pathology: Maternal vascular malperfusion

- Maternal vascular malperfusion (MVM) is inadequate maternal supply to the intervillous space.
- In preeclampsia, MVM appears as a constellation of placental and decidual lesions.
- The findings include a small placenta, infarction, ischemic villous changes, hematoma and decidual arteriopathy.
- Each finding supports a vascular pattern but should be interpreted in clinical and gestational context.

Placental hypoplasia reflects impaired perfusion



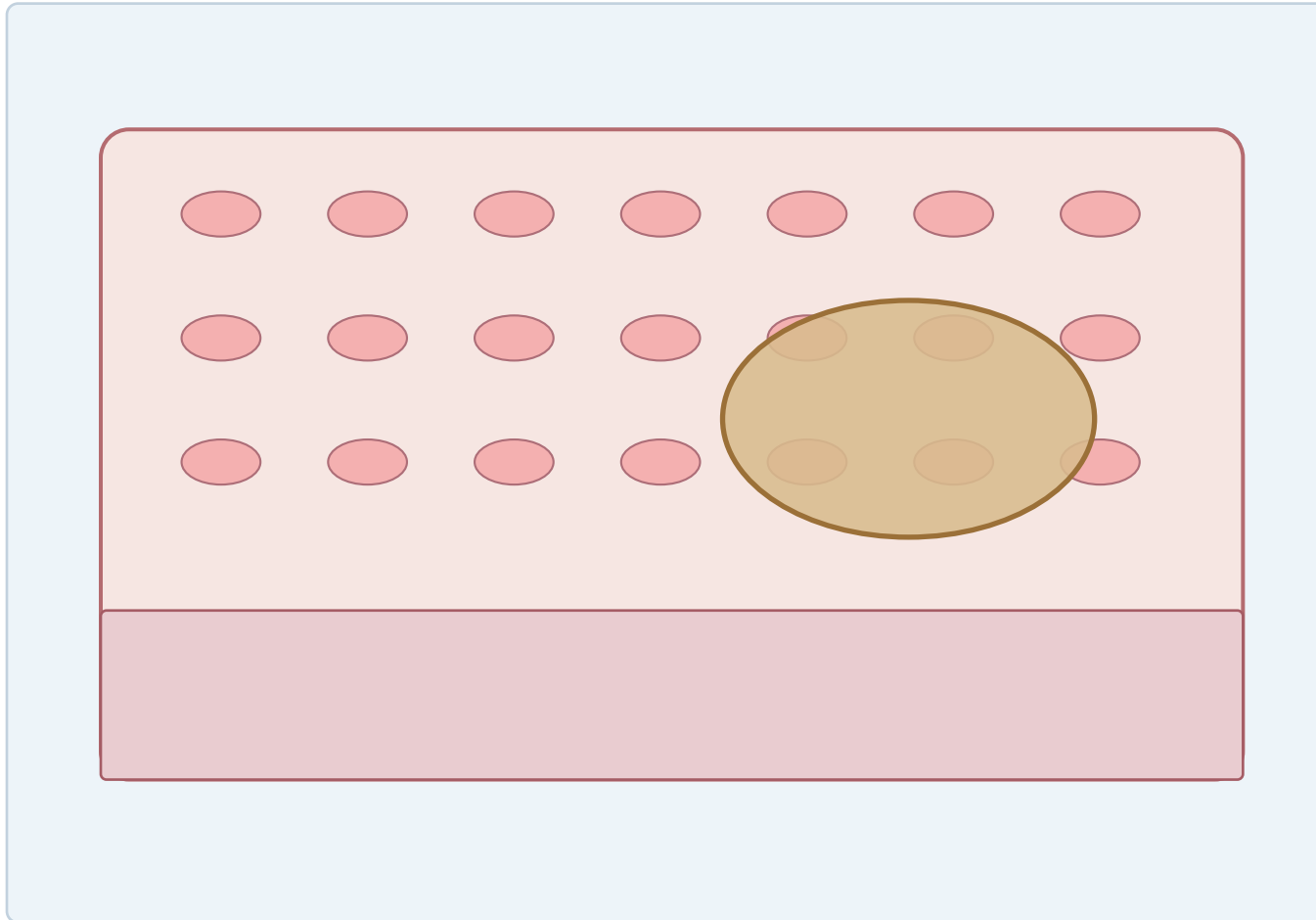
Schematic, not gross pathology

Placental hypoplasia

Reduced placental mass is one feature of maternal vascular malperfusion.

Interpret weight against gestational age rather than in isolation.

Placental infarction: Consequence of ischemia



Schematic, not gross pathology

Placental infarct

An ischemic focus of villous necrosis follows impaired maternal perfusion.

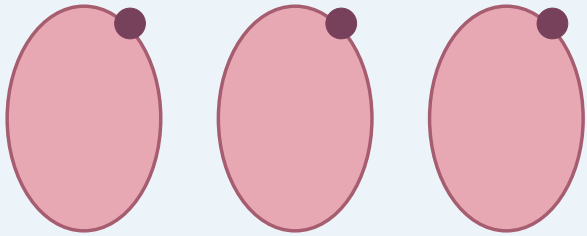
Infarcts may be extensive or multiple in preeclampsia.

Villous stress and accelerated maturation

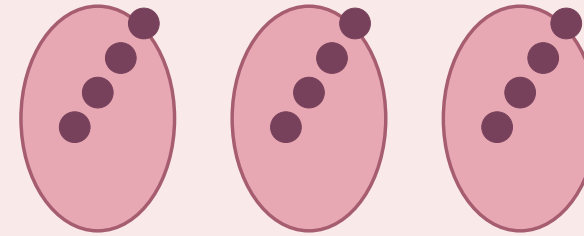
- Chorionic villi exposed to inadequate maternal perfusion show ischemic stress.
- The source specifically describes increased syncytial knots.
- Smaller, shrunken distal villi can accompany altered intervillous spacing.
- The microscopic pattern should be interpreted with gestational age and sampling context.

Increased syncytial knots: Schematic villous change

Typical villous contour



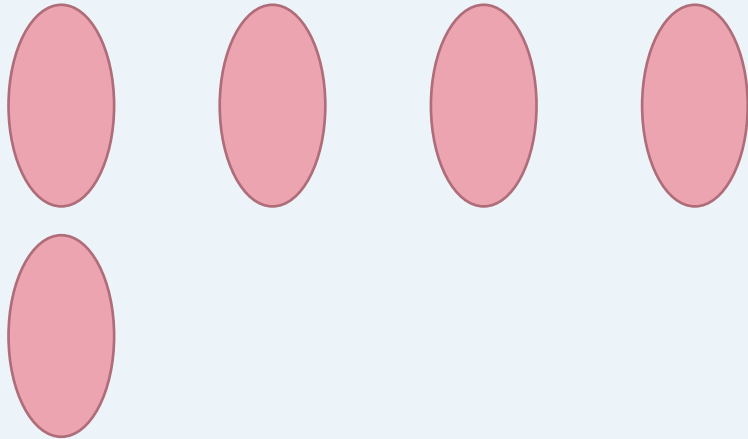
Exaggerated knotting



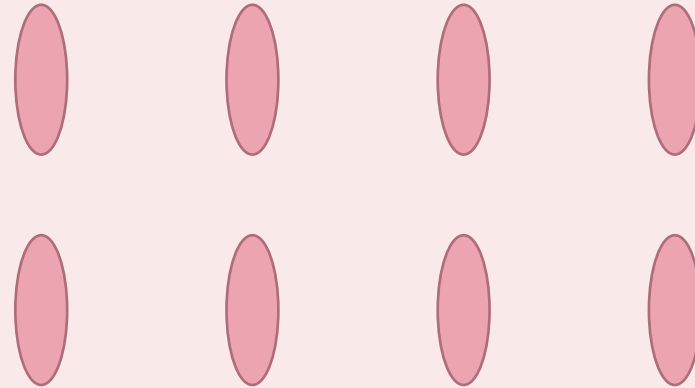
Illustrative schematic; Not a photomicrograph

Distal villous hypoplasia: Altered villous architecture

Appropriate villous development

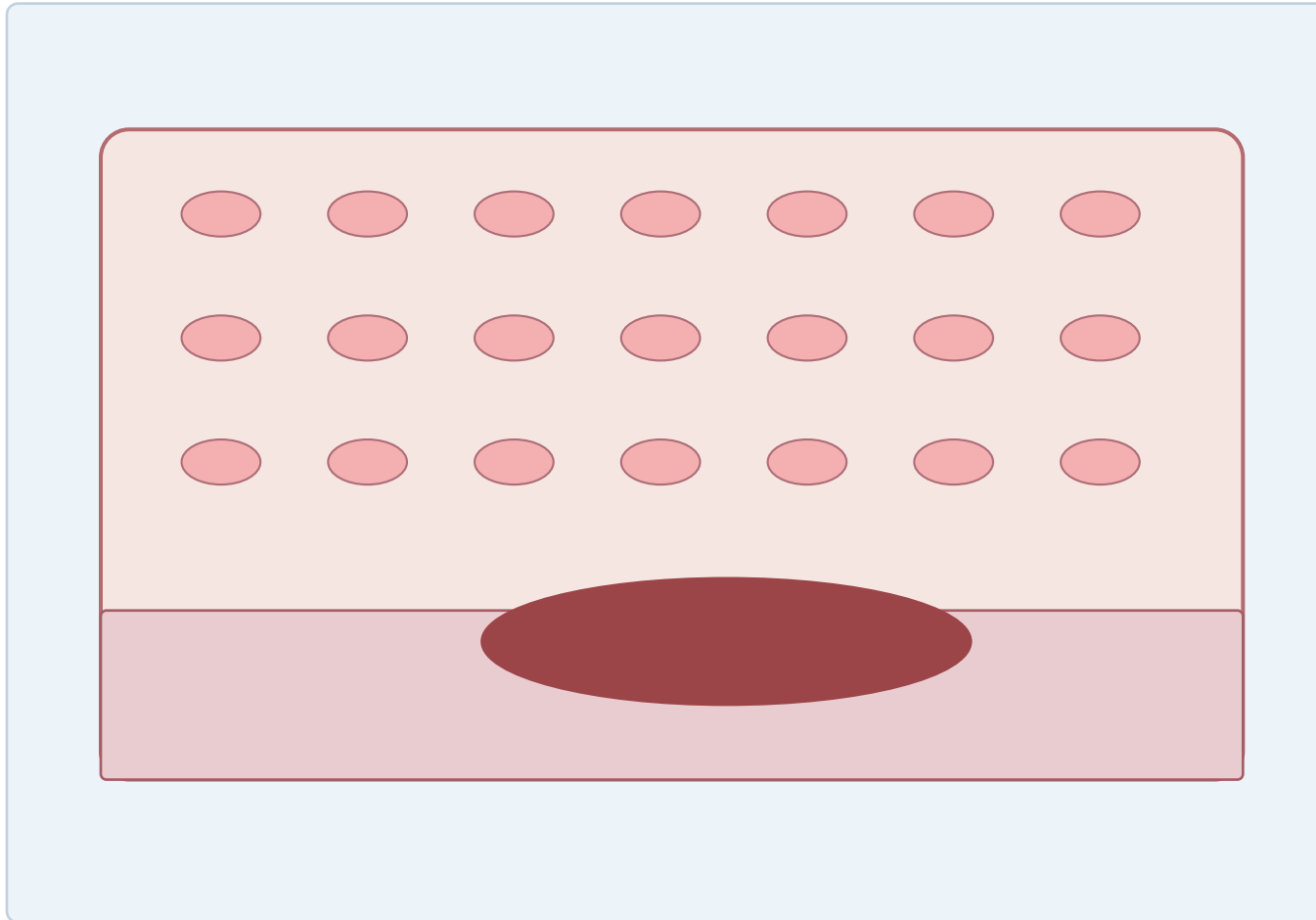


Distal villous hypoplasia



Schematic of relative villous form, not a diagnostic slide

Retroplacental hematoma and vessel instability



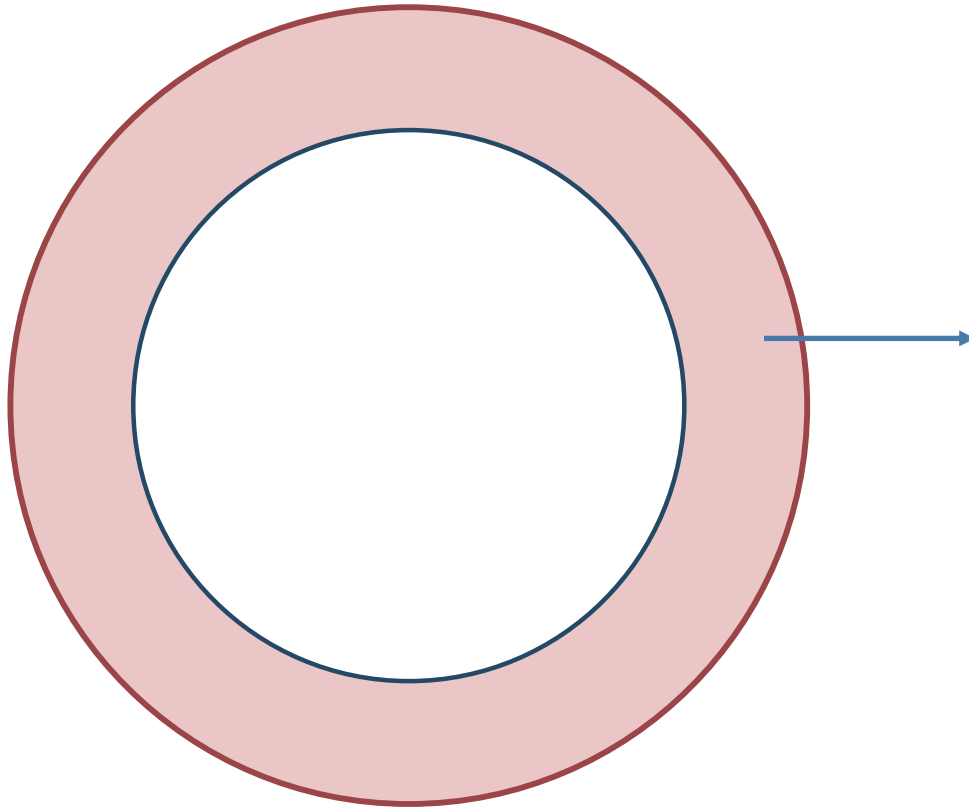
Schematic, not gross pathology

Retroplacental hematoma

Hemorrhage accumulates between maternal surface and uterine wall.

May reflect vessel instability and accompany placental abruption.

Decidual arteriopathy: Unremodeled maternal vessel



Preeclampsia

- Inadequate extravillous trophoblast invasion
- Persistence of arterial smooth muscle
- Relatively narrow, high-resistance lumen
- Reduced capacity to meet late-gestational flow demand

Schematic cross-section, not histology

Acute atherosclerosis: Characteristic vessel injury

- Decidual spiral arteries may show intimal lipid deposition (acute atherosclerosis).
- Associated findings include fibrinoid necrosis and inadequate physiologic remodeling.
- The lesion is part of the decidual vascular injury spectrum in MVM.
- Atherosclerosis should not be treated as specific to preeclampsia in isolation.

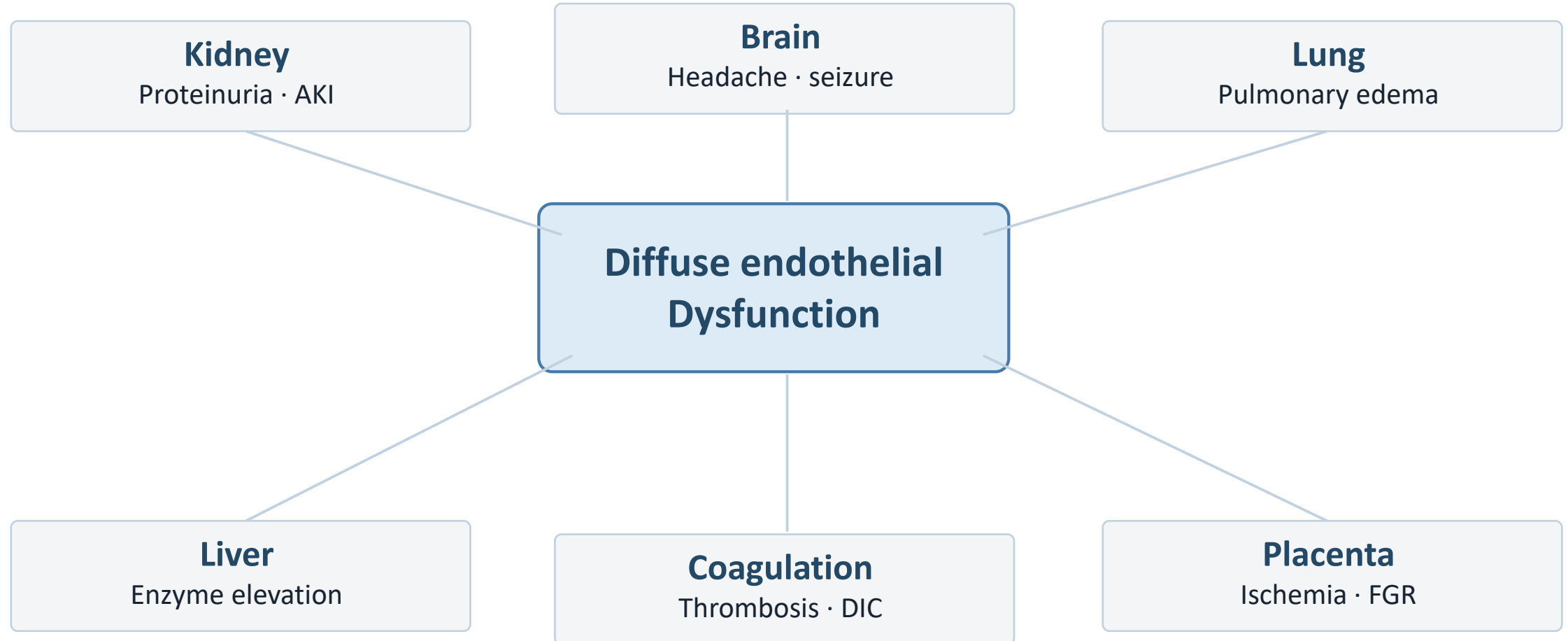
Placental vascular lesions: Mechanism and finding

Lesion	Morphologic correlate	Mechanistic interpretation
Hypoplasia	Placenta small for gestational age	Reduced placental growth/perfusion
Infarction	Foci of ischemic villous necrosis	Reduced maternal blood supply
Distal villous hypoplasia	Small distal villi; expanded maternal space	Abnormal villous development
Retroplacental hematoma	Blood between placenta and uterine wall	Uteroplacental vessel bleeding
Decidual arteriopathy	Thrombi, failed remodeling, fibrinoid damage, atherosclerosis	Maternal inflow vasculopathy

Interpreting pathology without overdiagnosis

- Neither a single placental infarct nor an isolated syncytial knot proves preeclampsia.
- The useful diagnosis is a coherent maternal vascular malperfusion pattern.
- Gestational age, placental weight, sampling and clinical hypertensive history remain important.
- The placenta demonstrates injury; Maternal clinical criteria establish the syndrome.

One endothelial injury pattern, multiple target organs



Hypertension: Vessel tone is the key link

Antiangiogenic signals

SFlt-1/endoglin influence
endothelium



Loss of vasodilation

Less nitric oxide/ PGI_2 support



Systemic resistance

Arteriolar tone increases →
maternal hypertension

Renal proteinuria: Glomerular barrier injury

Maternal endotheliopathy

Systemic microvascular
dysfunction



Renal vascular injury

Glomerular barrier becomes
abnormal



Protein leakage

Urinary protein excretion
increases

Renal involvement extends beyond proteinuria

- Acute renal failure can complicate severe preeclampsia.
- Renal injury is part of the syndrome even when urinary protein is not dominant.
- Maternal perfusion and microvascular injury are both relevant mechanisms.
- Creatinine assessment is necessary when severe disease is suspected.

Edema reflects endothelial permeability

Endothelial dysfunction

Barrier regulation deteriorates



Vascular fluid leakage

Fluid extravasates into
interstitial spaces



Tissue fluid accumulation

Peripheral edema and, in
severe disease, pulmonary
edema

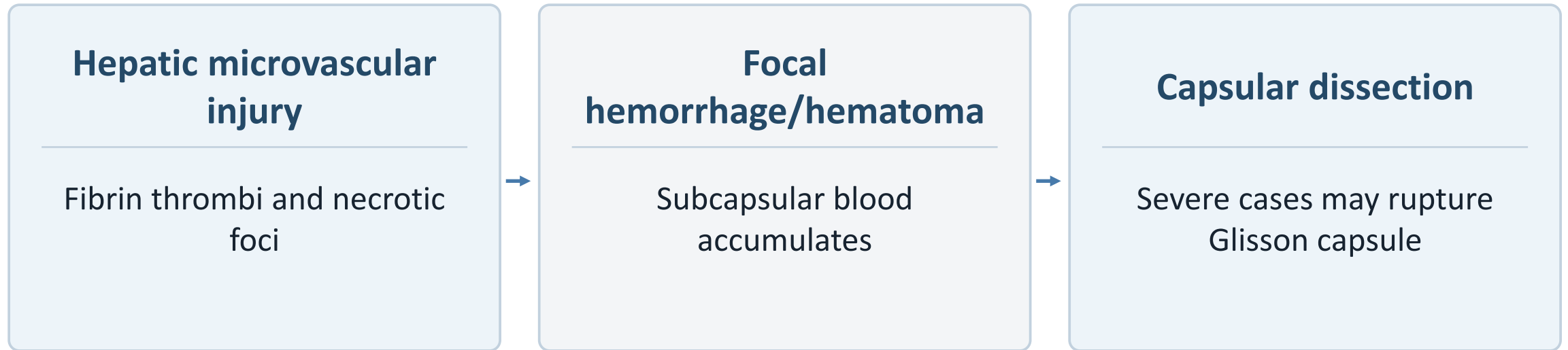
Neurologic warning signs and eclampsia

- Headache and visual disturbances indicate possible severe disease.
- Seizures signify major central nervous system involvement.
- Stroke is among the principal causes of life-threatening maternal morbidity.
- Absence of a preceding symptom does not ensure freedom from seizure risk.

Hepatic injury: Microthrombi and necrosis

- Chapter 22 describes fibrin thrombi in portal capillaries with focal hemorrhagic necrosis.
- Chapter 18 emphasizes periportal sinusoidal fibrin and hemorrhage into the space of Disse.
- Hepatocellular injury can elevate aminotransferases.
- Severe hepatic dysfunction or coagulopathy signals potentially lethal disease.

Subcapsular hepatic hemorrhage can rupture



A dangerous complication; Not a routine finding in uncomplicated disease

HELLP syndrome: Mechanistic integration

- Hemolysis: Erythrocyte injury in a microangiopathic circulation.
- Elevated liver enzymes: Hepatic ischemic/hemorrhagic injury.
- Low platelets: Consumption associated with vascular/coagulation activation.
- The constellation warrants recognition as serious preeclampsia-spectrum disease.

Microthrombi connect coagulation and bleeding

Endothelial activation

Loss of antithrombotic
endothelial function



Small-vessel thrombi

Thrombi particularly involve
placenta, liver, kidneys and
brain



Consumption and injury

Thrombocytopenia, ischemia
and, in severe cases, DIC

Pulmonary edema: Permeability meets hemodynamics

- Generalized endothelial barrier injury permits fluid movement into extravascular compartments.
- Pulmonary edema is a severe systemic manifestation.
- Fluid-management decisions require specialist clinical assessment.
- Respiratory symptoms should not be dismissed as normal pregnancy discomfort.

Fetal consequences originate in placental supply

- Abnormal uteroplacental inflow restricts effective placental nutrient and oxygen exchange.
- Fetal growth restriction may accompany placental underperfusion.
- Placental infarction and abruption can acutely compromise fetal status.
- Early delivery itself carries neonatal risks that must be weighed against maternal risk.

Clinicopathologic distinctions

Feature	Gestational HTN	Preeclampsia / eclampsia
Maternal blood pressure	Elevated after 20 weeks	Elevated; may reach severe range
Proteinuria	Not required / typically absent	May occur, but not required
Organ dysfunction	Absent by definition	Can involve kidney, liver, platelets, lung, CNS
Seizures	Not defining	Eclampsia when attributable to disorder
Placental MVM	Not diagnostic	Common associated pathology

Differential diagnosis: Hepatic and microangiopathic disease

- Preeclampsia/HELLP may share thrombocytopenia and transaminitis with other syndromes.
- Acute fatty liver of pregnancy can cause severe hepatic dysfunction with microvesicular steatosis.
- Thrombotic microangiopathies require their own clinical/laboratory evaluation.
- Placental findings assist context but cannot independently separate every maternal syndrome.

Maternal evaluation: Connect testing to mechanisms

Assessment	Question answered
Serial blood pressure	Is hypertension persistent or severe?
Urinary protein assessment	Is glomerular barrier injury evident?
Platelet count / blood film	Is platelet consumption or hemolysis present?
Creatinine	Is renal function impaired?
Liver enzymes	Is hepatocellular injury present?
Symptoms / respiratory status	Are neurologic or pulmonary severe features present?
Fetal assessment	Is uteroplacental function compromised?

Management decision rests on maternal and fetal risk

Assess gestational age

Preterm or term pregnancy



Determine severity

Severe features, HELLP,
eclampsia, fetal compromise?



Delivery versus monitoring

Maternal stabilization and
delivery, or close expectant
care if appropriate

Term and preterm management principles

Term pregnancy

- Delivery is generally the treatment of choice.
- Maternal blood pressure and severe features require assessment.
- Manage possible seizures and complications.

Preterm pregnancy

- Without severe features, selected patients may be monitored closely.
- Severe features or fetal compromise may require earlier delivery.
- Maternal stabilization and fetal maturity are balanced.

Indications for urgent delivery account

- Eclampsia and preeclampsia with severe features.
- HELLP syndrome.
- Fetal compromise or rapidly evolving maternal organ injury.
- Clinical stabilization is essential while arranging definitive obstetric management.

Delivery removes the major placental driver

- Removal of the placenta typically leads to rapid clinical improvement.
- That hypertension and proteinuria usually settle within 1–2 weeks.
- Postpartum-onset or persistent hypertension may still occur, requiring surveillance.
- Resolution after delivery supports, but does not individually prove, placental causality.

Long-term vascular implications persist

- That some survivors later develop hypertension and microalbuminuria.
- The textbook associates a prior preeclampsia pregnancy with approximately doubled long-term cardiovascular risk.
- Pregnancy can therefore reveal underlying or future vascular susceptibility.
- Long-term cardiovascular risk review matters after apparent obstetric recovery.

Case: New hypertension without proteinuria

Clinical vignette

At 32 weeks, a previously normotensive pregnant patient develops sustained blood pressure of 162/112 mm Hg, severe headache and visual disturbance. Urinary protein is not detected.

Interpretation

- Does lack of proteinuria exclude preeclampsia?
- Which features indicate danger?
- What maternal systems need evaluation?

Case: Pathology–fetal correlation

Clinical vignette

A placenta from a pregnancy complicated by hypertension and fetal growth restriction is small for gestational age, with multiple infarcts, distal villous hypoplasia and unremodeled decidual arteries.

Interpretation

- Identify the injury pattern.
- Which maternal vessels initiate the process?
- Why is fetal growth affected?

Case: Hepatic warning pattern

Clinical vignette

At 34 weeks, a patient with pregnancy-associated hypertension has worsening right upper quadrant pain, elevated aminotransferases, hemolysis and falling platelet count.

Interpretation

- What syndrome is suggested?
- What hepatic lesions explain pain/injury?
- Why is the situation time-critical?

Pathogenesis, morphology and clinical expression

Initiating / mediator event	Pathology	Clinical expression
Inadequate spiral-artery remodeling	Placental MVM, infarction	Fetal growth restriction
sFlt-1 / endoglin excess	Endothelial dysfunction	Hypertension, edema, proteinuria
Reduced PGI ₂ / procoagulant signals	Microvascular thrombosis	HELLP, ischemic injury
Hepatic microvascular injury	Periportal fibrin and necrosis	Transaminitis, RUQ pain, hematoma

High-yield synthesis: Five causal connections

Placental bed

Shallow invasion

Persistent high-resistance
spiral arteries

Angiogenic imbalance

↑ sFlt-1 · ↑ endoglin

Less VEGF/TGF- β protective
signaling

Systemic organs

Vasoconstriction · leak ·
thrombosis

Kidney, brain, liver, lung and
placenta affected

Final diagnostic and morphologic cautions

- Do not make edema or proteinuria mandatory criteria under modern classification.
- Do not diagnose preeclampsia from an isolated placental lesion without clinical findings.
- Do not assume all preeclampsia follows one identical antiangiogenic mechanism.
- Identify HELLP, severe hypertension and neurologic symptoms promptly.

References and source transparency

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition (2026): Chapter 22, pages 937–939.
- Additional Robbins context: maternal vascular malperfusion (Chapter 22) and hepatic pathology (Chapter 18, pages 786–787).
- ACOG Practice Bulletin 222 (2020, reaffirmed 2026): diagnostic and management guidance.
- ISSHP 2021 recommendations: international clinical criteria and recognition of nonproteinuric disease.