

Fat Embolism

From marrow injury to microvascular dysfunction

Pathogenesis · morphology · clinicopathologic correlations

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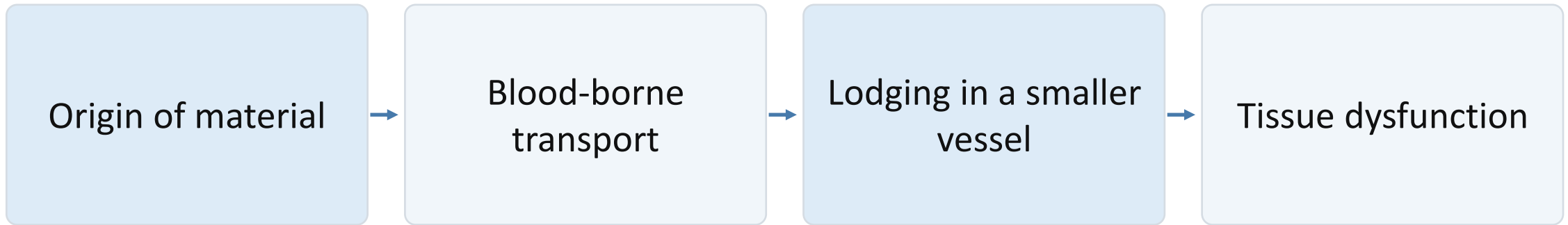
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Learning objectives

At the end of this lecture, explain:

- How fat and marrow enter vessels following tissue injury.
- Why microscopic embolization differs from fat embolism syndrome.
- How mechanical occlusion and toxic inflammation damage microvessels.
- What the clinical manifestations and histologic pitfalls signify.

Embolism describes a traveling intravascular mass



An embolus can be solid, liquid, or gaseous; Most are detached thrombi.

Fat is one of several nonthrombotic embolic materials

Thrombotic embolus

- A detached intravascular thrombus
- Typical source: Venous thrombus in pulmonary thromboembolism
- Thrombus is the embolized material

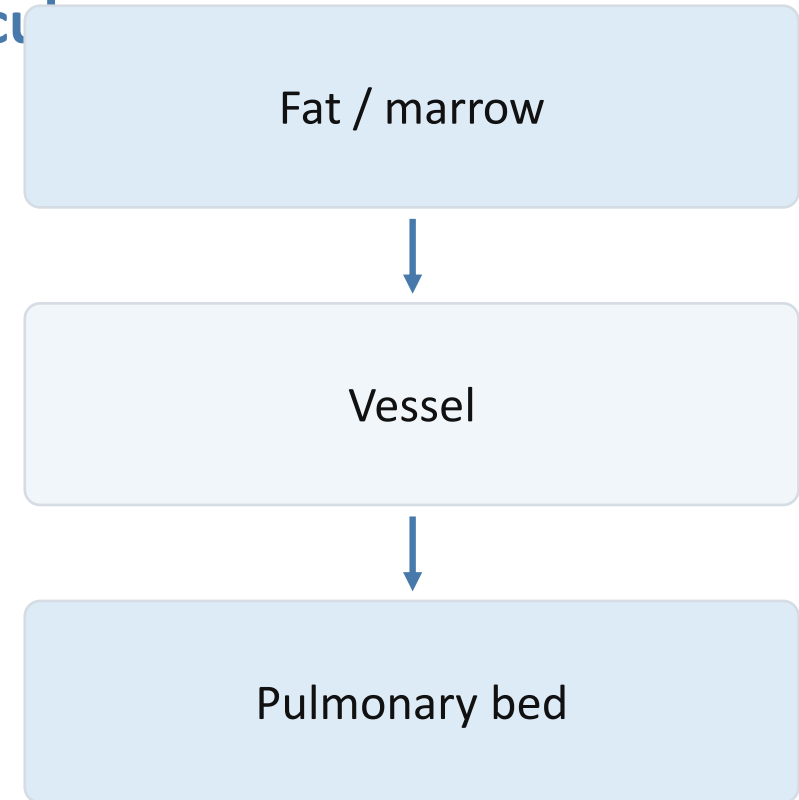
Fat or marrow embolus

- Microscopic fat globules may travel within blood
- Hematopoietic marrow tissue may accompany fat
- Entry commonly follows skeletal injury

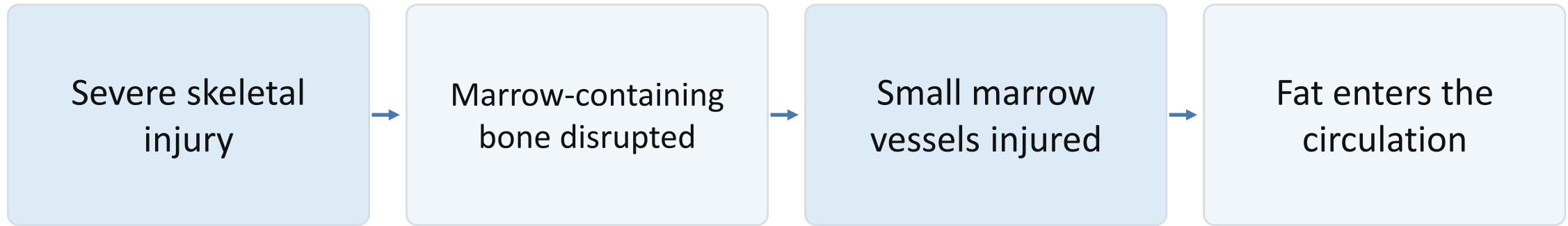
Fat embolism is an anatomic phenomenon

Microscopic fat globules are present within the vasculature

- The embolized material may include bone marrow cells.
- The pulmonary circulation is an important destination.
- Its detection does not by itself establish clinical fat embolism syndrome.



Long-bone fracture is the classic initiating event



Long-bone fractures provide the characteristic clinical setting.

Soft-tissue trauma and burns are less common settings

Usual setting

- Fractures of long bones
- Particularly severe skeletal injury
- Marrow and vascular compartments disrupted

Less common settings

- Soft-tissue trauma
- Burn injuries
- Evidence of embolization may follow tissue damage

Marrow contains two potentially embolized components

Emboli can consist of adipose material with accompanying hematopoietic cells.

- Fat forms globules or droplets within vessels.
- Hematopoietic elements provide a recognizable cellular component.
- This mixture has an important morphologic signature.

Adipose component

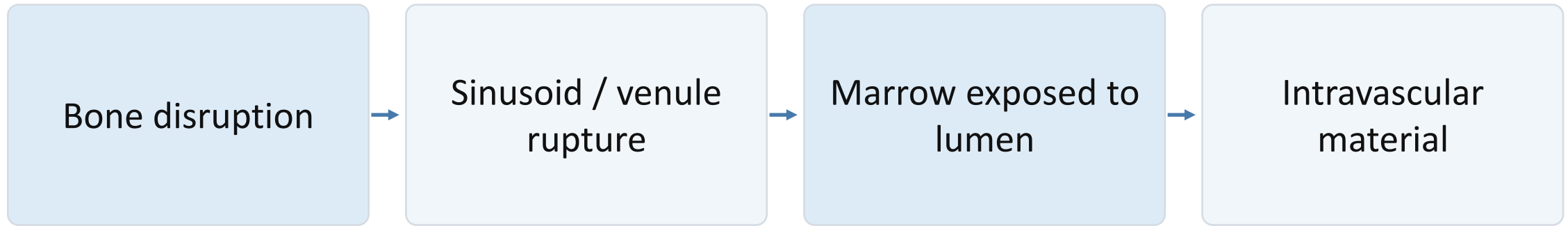


Hematopoietic cells



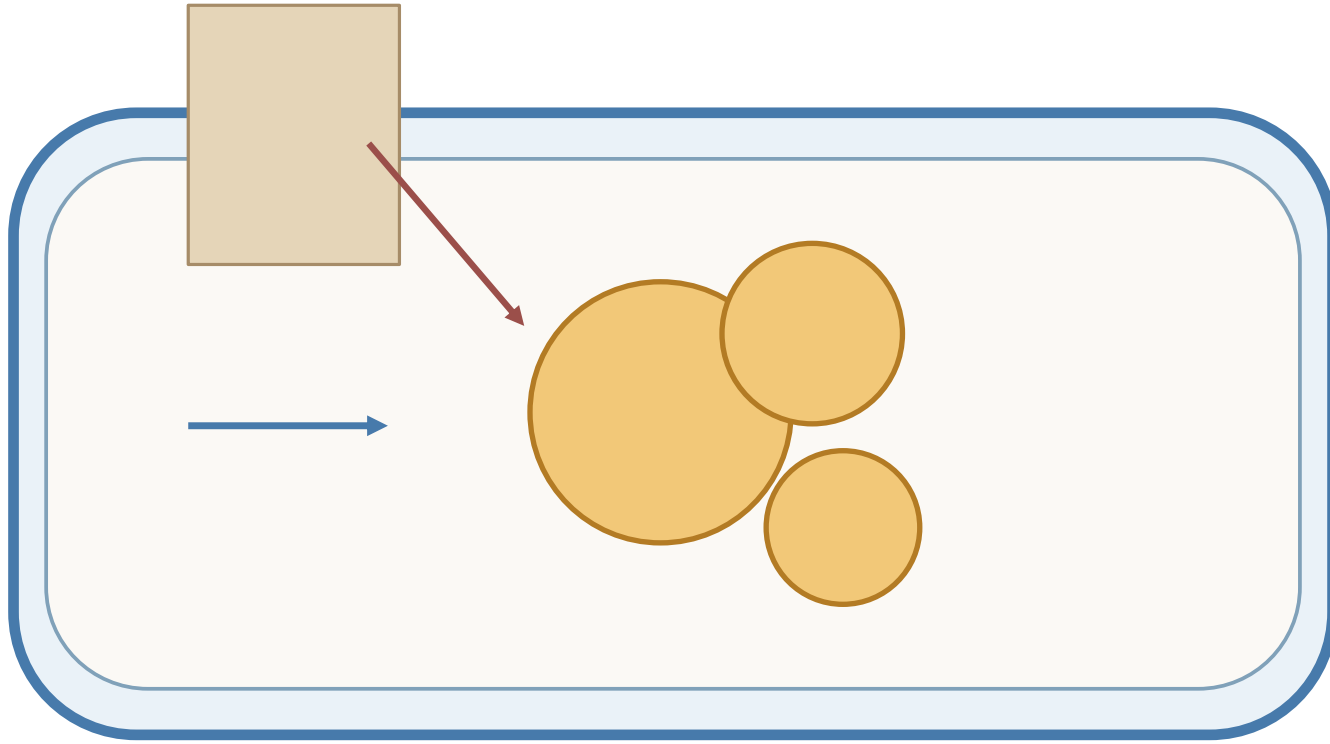
Mixed marrow embolus

Damage to marrow sinusoids creates vascular access



That injuries rupture sinusoids or small venules in marrow.

Marrow and fat herniate into injured vessels

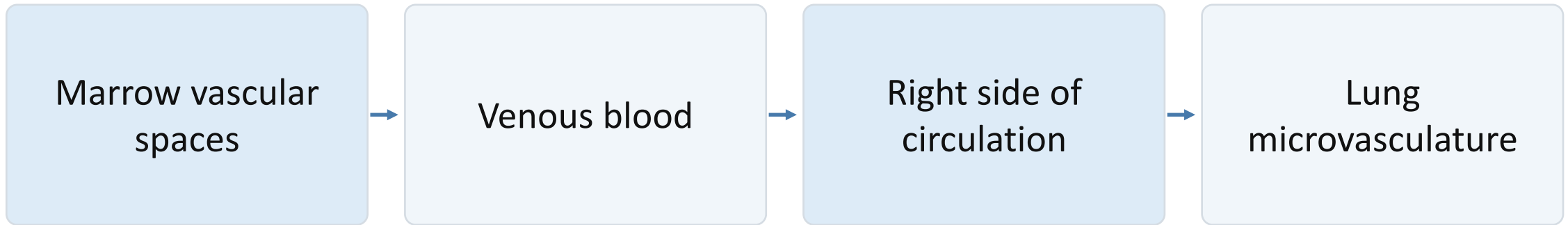


Entry of marrow material

- Disrupted vascular boundary allows tissue to enter blood.
- The resulting embolic material may contain both fat and marrow cells.
- Transport follows the direction of blood flow.

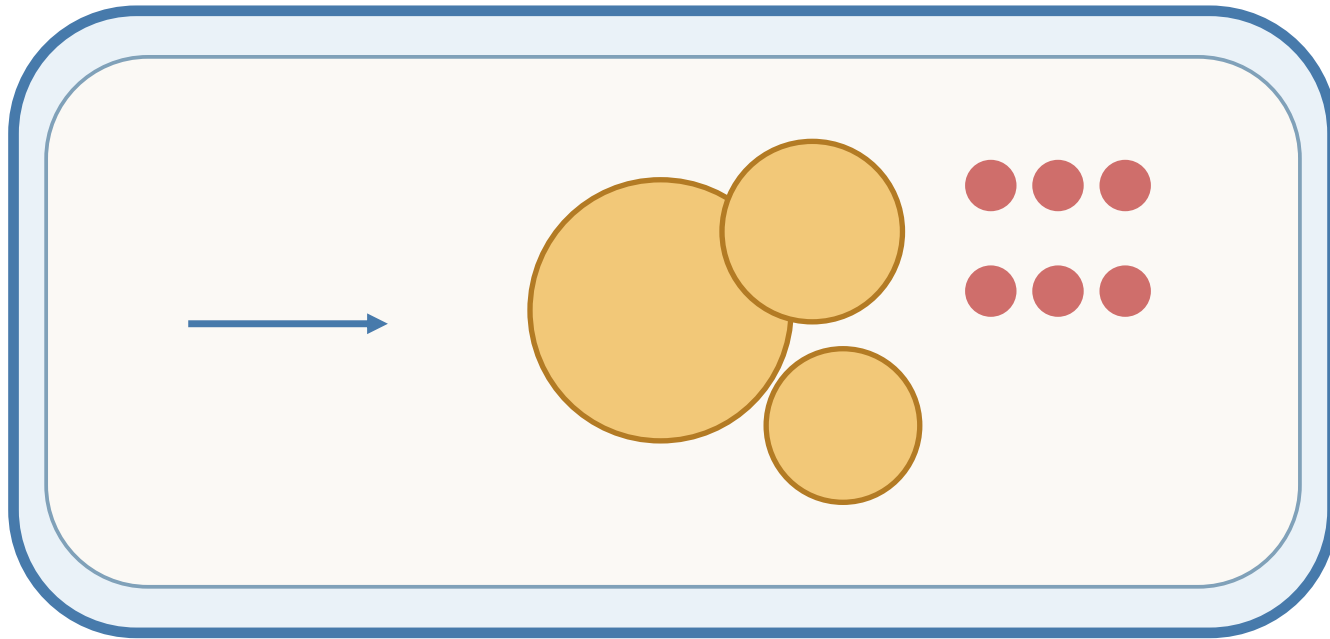
Native schematic — not histology

Venous transport explains pulmonary localization



The source text describes fat and marrow material traveling to the lung.

Emboli lodge where vessels become too small



Fat / cellular microembolus

- Emboli are carried downstream from the site of origin.
- Small vessel caliber can prevent passage.
- Occlusion can be partial or complete.

Native schematic — not histology

An embolus may contain fat without marrow cells

Fat microglobules

- Small lipid droplets in vascular lumina
- May be difficult to demonstrate in paraffin sections
- Specialized tissue preparation can be required

Marrow-containing embolus

- Lipid vacuoles and hematopoietic cells
- Additional marrow elements facilitate recognition
- May coexist with early thrombotic organization

Microscopic fat embolization is frequent after major injury

~90%

Severe skeletal injuries

Fat embolism in approximately 90% of individuals with severe skeletal injury.

- This figure describes embolization, not symptomatic syndrome.
- It must not be interpreted as a syndrome incidence estimate.

Fat embolization and fat embolism syndrome differ

Fat embolization

- Vascular presence of fat microglobules
- Common after severe skeletal trauma
- Can be clinically silent

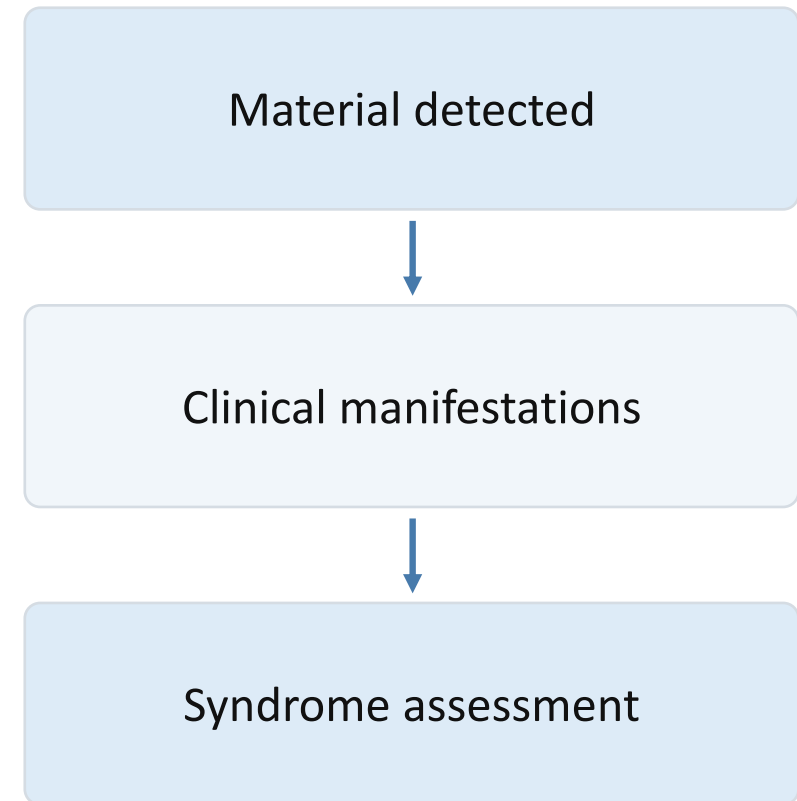
Fat embolism syndrome

- Symptomatic minority of patients
- Pulmonary, neurologic, and hematologic effects
- Can be life-threatening

A histologic finding is not equivalent to clinical disease

Two levels of inference must remain separate.

- Morphologic observation: Intravascular fat or marrow.
- Clinical interpretation: A multisystem syndrome after injury.
- The source specifically reserves “syndrome” for symptomatic patients.



Four organ-system signals define the syndrome

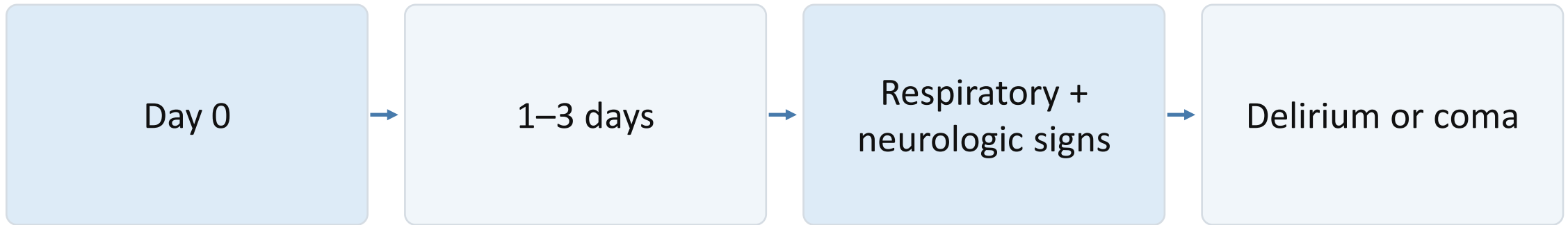
Pulmonary insufficiency

Neurologic symptoms

Anemia

Thrombocytopenia

Symptoms usually begin 1–3 days after injury



Timing is a key clinical association description.

Clinical manifestations may begin suddenly

A recognizable post-injury change may include:

- Tachypnea or dyspnea
- Tachycardia
- Irritability or restlessness
- Subsequent neurologic deterioration in severe cases

Tachypnea is an early respiratory manifestation

Increased respiratory rate may accompany the onset

- The symptom follows a characteristic post-injury interval.
- Pulmonary microcirculatory obstruction is one implicated process.
- Endothelial toxicity compounds the vascular injury.

Microvascular emboli

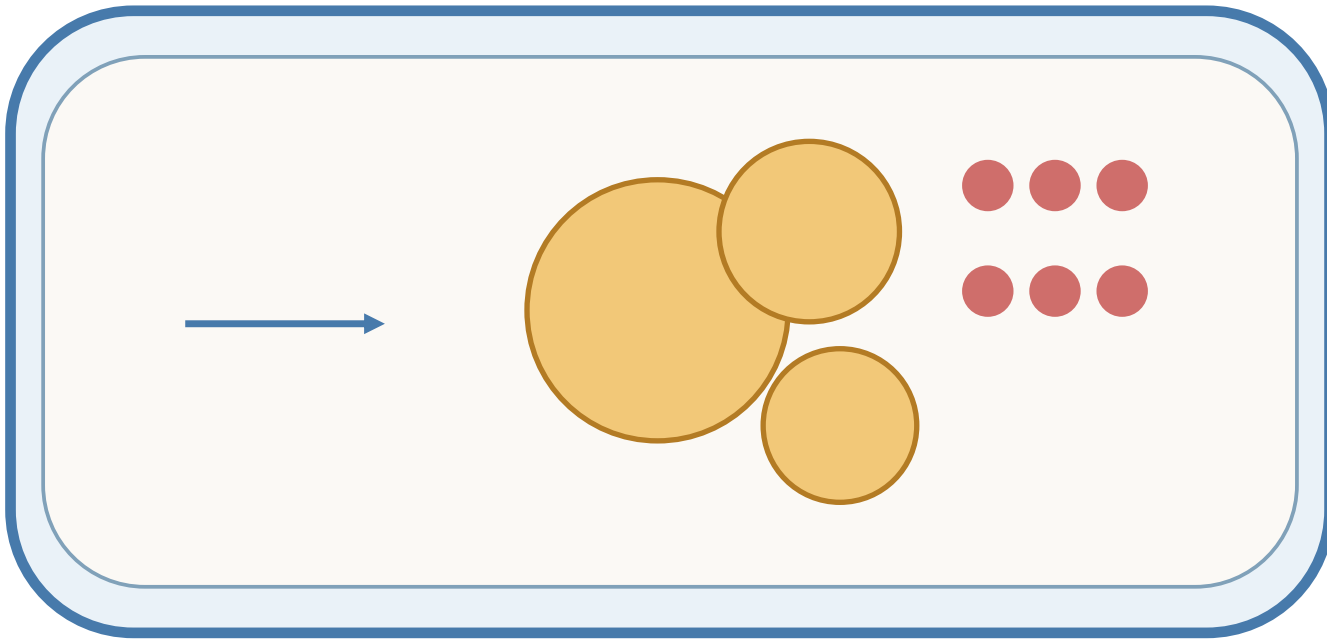


Pulmonary dysfunction



Tachypnea

Dyspnea accompanies pulmonary insufficiency



Pulmonary microvascular injury

- Fat and cell aggregates can obstruct pulmonary microvessels.
- Free fatty acid injury and inflammatory mediators add injury.
- Dyspnea reflects clinically evident pulmonary dysfunction.

Native schematic — not histology

Tachycardia may accompany early deterioration

Tachycardia with the typical onset.

- It occurs alongside tachypnea and dyspnea.
- It is not uniquely diagnostic of fat embolism syndrome.
- It should be read within the injury-and-timing context.

Irritability and restlessness are neurologic clues

Early changes

- Irritability
- Restlessness
- Can appear with respiratory symptoms

Severe progression

- Delirium
- Coma
- Marks neurologic deterioration

Neurologic dysfunction may progress

Irritability



Restlessness



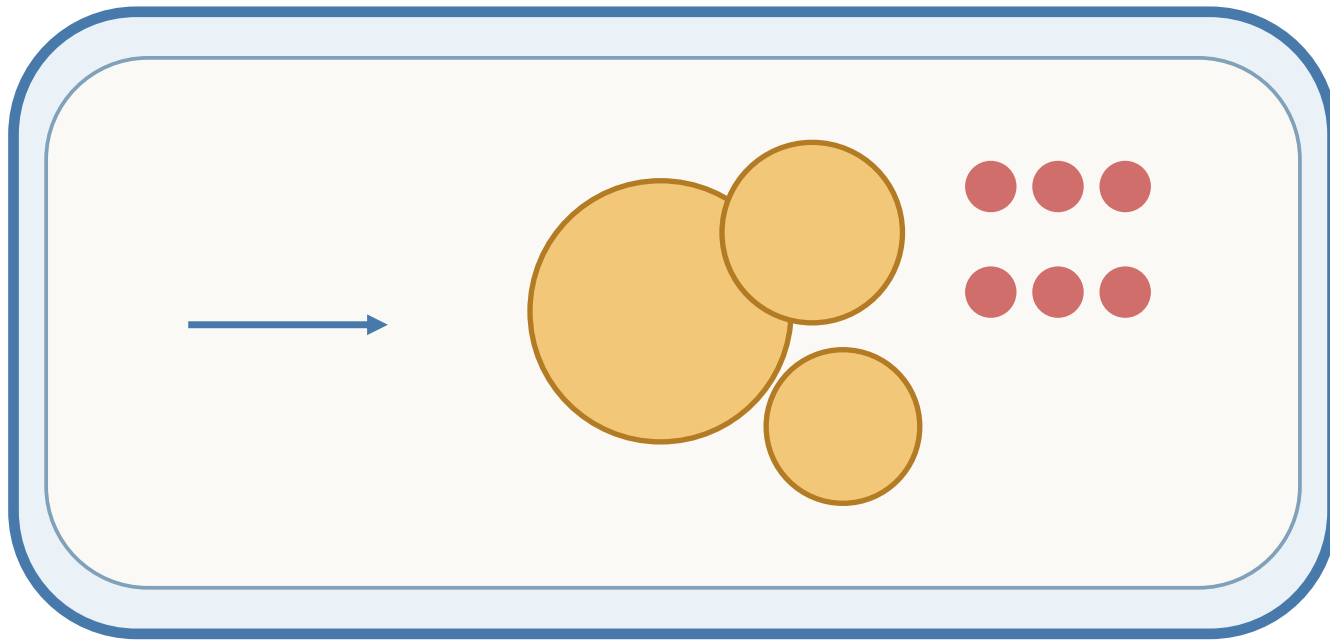
Delirium



Coma

This is a possible clinical progression, not an inevitable sequence in every patient.

Cerebral microvascular obstruction contributes to symptoms



Native schematic — not histology

Cerebral microvascular injury

- Fat microemboli can involve cerebral microcirculation.
- Red-cell and platelet aggregates can contribute to occlusion.
- This provides a mechanism linking emboli with neurologic injury.

Respiratory and cerebral injury share a microvascular basis

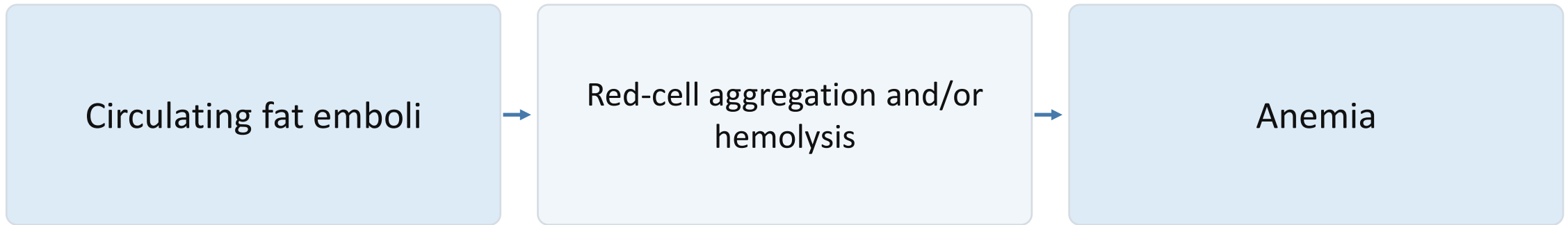
Pulmonary circulation

- Obstruction by fat and cellular aggregates
- Local endothelial injury
- Clinical pulmonary insufficiency

Cerebral circulation

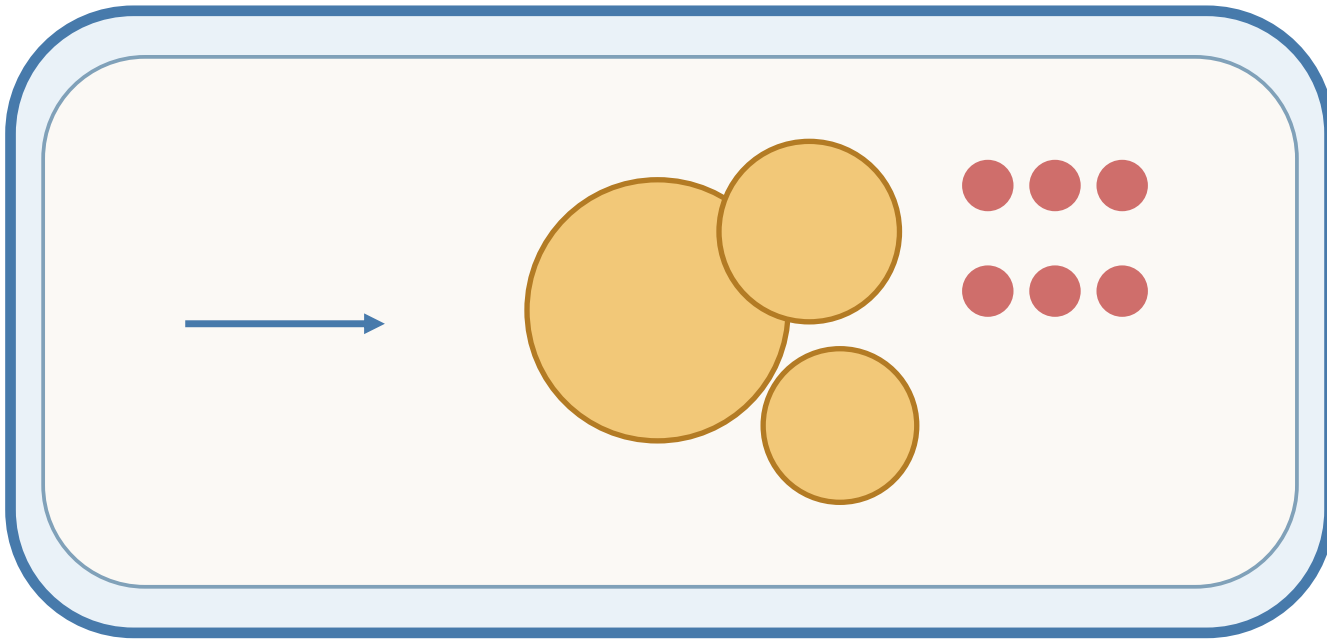
- Microvascular occlusion
- Vascular injury
- Neurologic dysfunction

Anemia can arise from red-cell injury



Red-cell aggregation and/or hemolysis as explanations.

Platelets can adhere to circulating fat globules

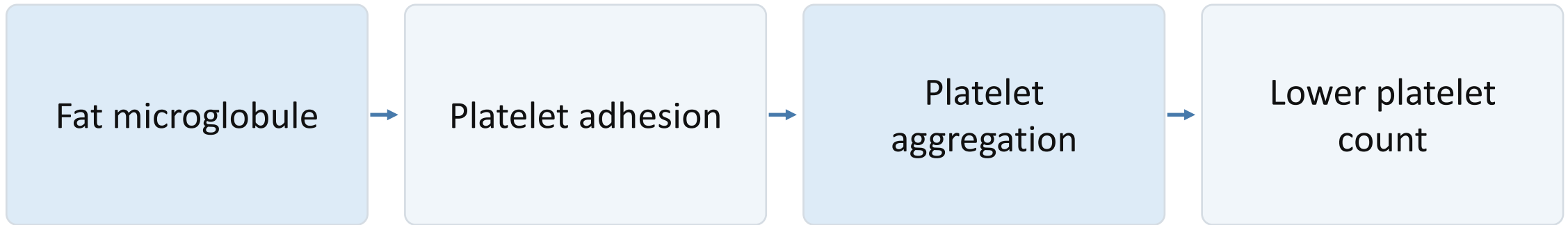


Platelet adhesion / aggregation

- Fat globules provide surfaces for platelet adhesion.
- Subsequent platelet aggregation is described.
- This contributes to a falling circulating platelet count.

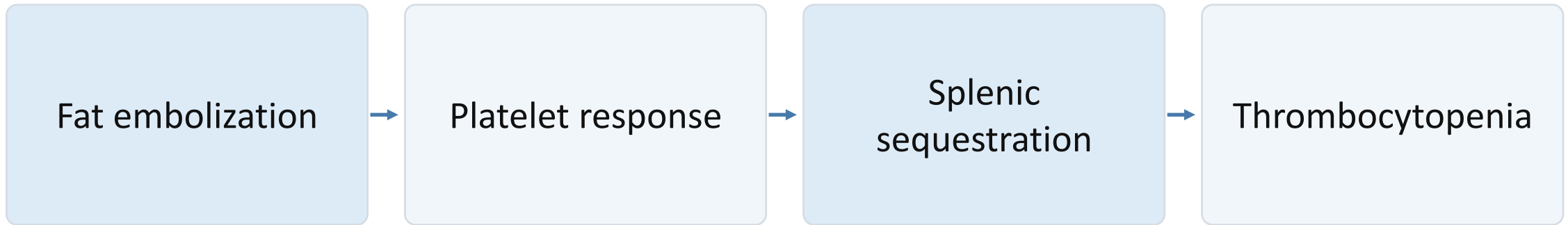
Native schematic — not histology

Platelet aggregation is one route to thrombocytopenia



Platelet consumption into aggregates is one proposed mechanism.

Splenic sequestration is an alternative platelet pathway



Splenic sequestration alongside platelet aggregation.

Thrombocytopenia may have two contributing mechanisms

Platelet adhesion / aggregation

- Adhesion to fat globules
- Aggregation of adherent platelets
- Intravascular platelet depletion

Splenic sequestration

- Redistribution into splenic pool
- Reduction in circulating platelets
- Also proposed

Petechial rash is an important cutaneous clue

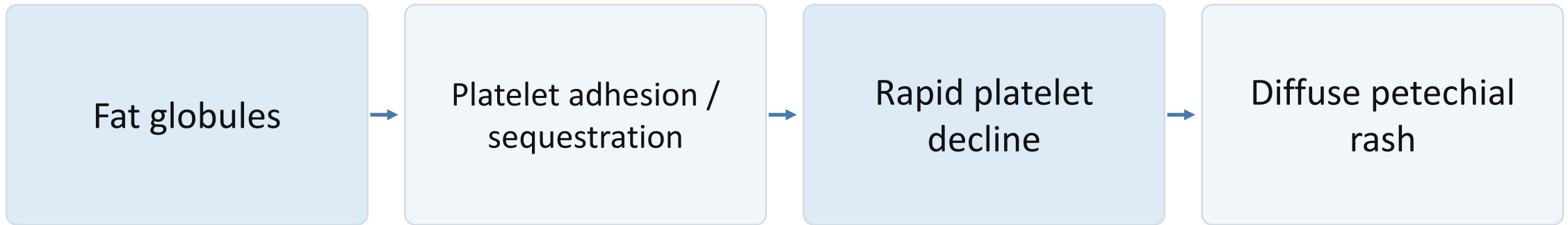
20–50%

Petechial rash

A diffuse petechial rash in 20%–50% of fat embolism syndrome cases.

- Petechiae are useful diagnostically when present.
- Absence of a rash does not exclude the syndrome.

Rapid thrombocytopenia helps explain petechiae



The source links the rash to rapid thrombocytopenia.

Petechiae should be interpreted with accompanying signs

After skeletal trauma, a patient develops dyspnea, restlessness and a new diffuse petechial rash.

Which co-occurring laboratory finding does Robbins connect to the rash?

Rapid thrombocytopenia, associated with platelet adhesion/aggregation and possibly splenic sequestration.

Fat embolism syndrome can be fatal

5–15%

Case fatality

Fatal outcomes in 5%–15% of fat embolism syndrome cases.

- This percentage is for the symptomatic syndrome.
- It must not be assigned to all patients with microemboli.

Two mechanisms operate together

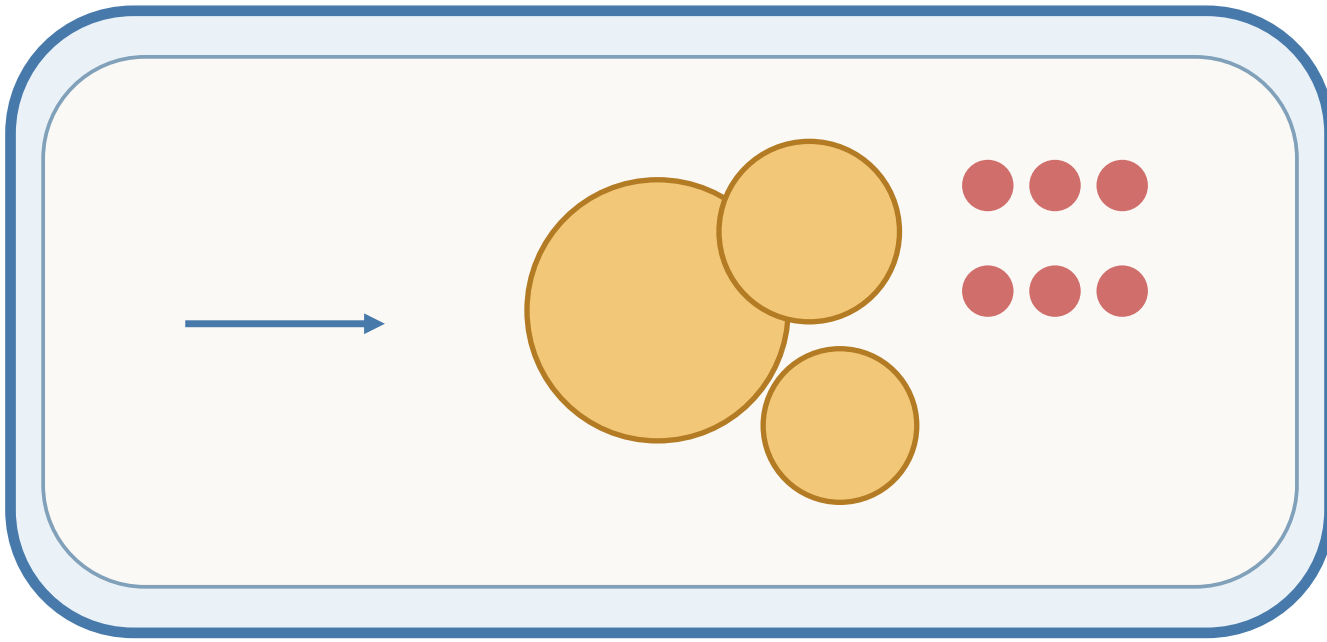
Mechanical obstruction

- Fat globules and cellular aggregates
- Lung and brain microvessel occlusion

Biochemical injury

- Free fatty acid–mediated toxicity
- Platelet and granulocyte activation

Mechanical injury starts with intravascular blockage



Fat / cellular microembolus

- Fat microemboli physically occupy small vessels.
- Associated red-cell and platelet aggregates increase obstruction.
- Pulmonary and cerebral vascular beds are emphasized.

Native schematic — not histology

Cellular aggregates increase the embolic burden

Fat globules

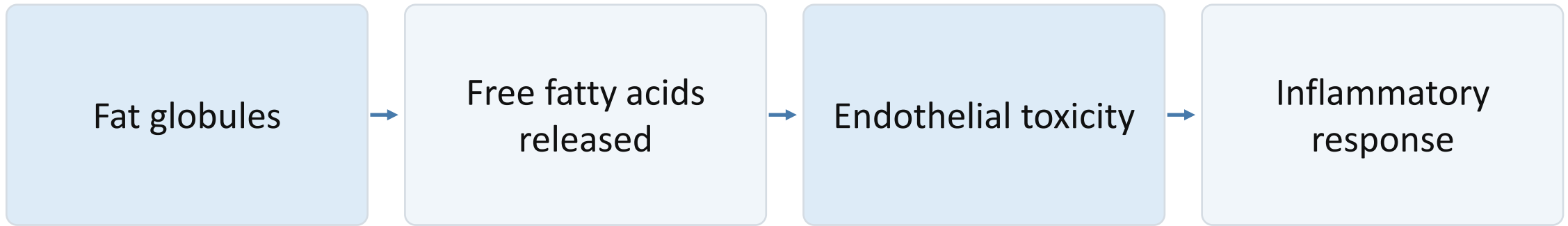
Red-cell aggregates

Platelet aggregates

Small-vessel obstruction

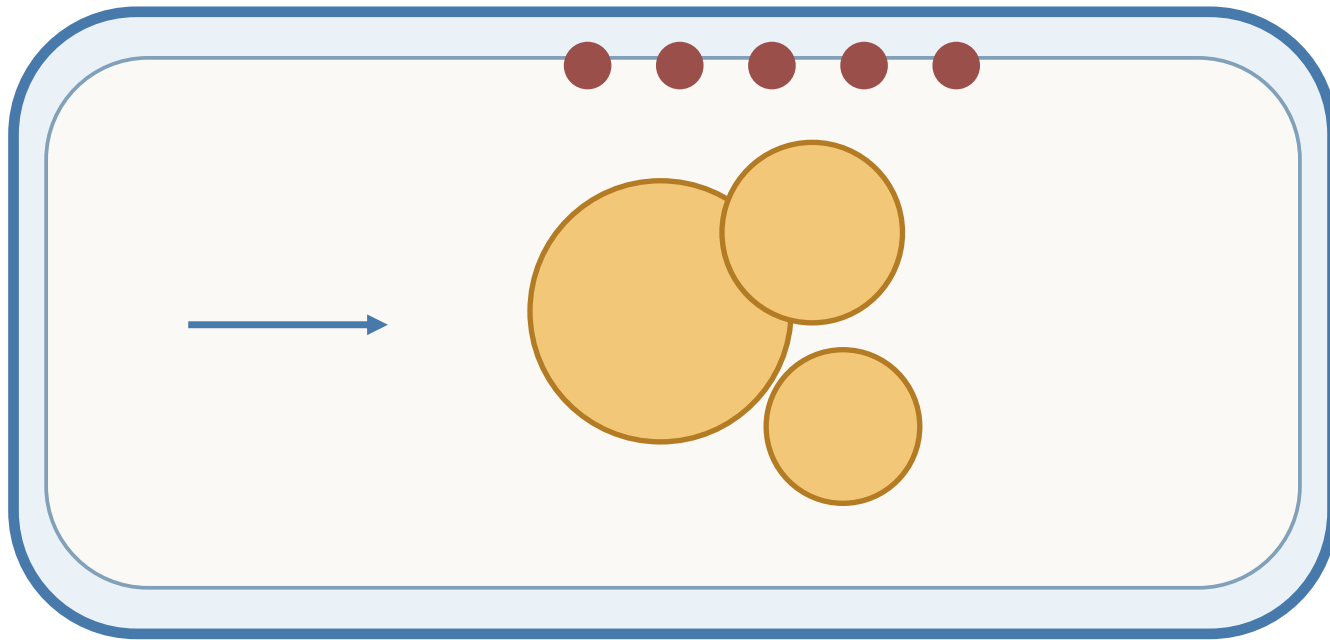
These components can act together within the microvasculature.

Biochemical injury is not simply an obstructed lumen



The source attributes direct local toxic injury to released fatty acids.

Free fatty acids amplify endothelial damage



Fatty acid endothelial toxicity

- Fat globules are a source of free fatty acids.
- Released fatty acids locally injure the endothelium.
- This exacerbates mechanical microvascular obstruction.

Native schematic — not histology

Platelet activation extends vascular injury

Fat embolization



Platelet activation



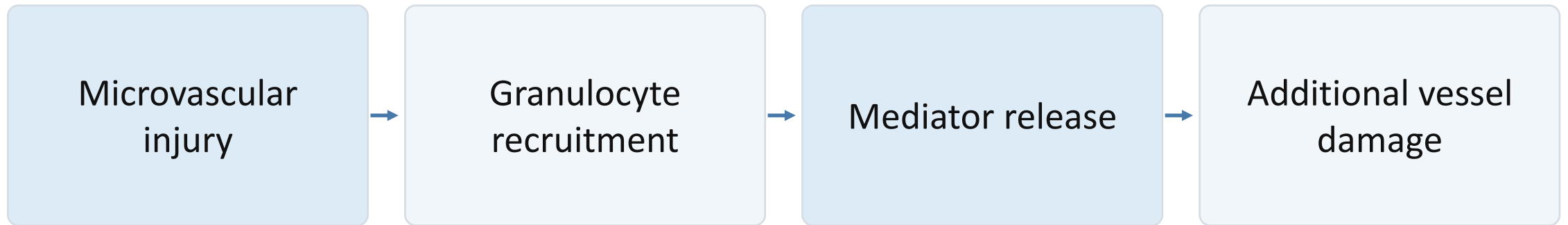
Platelet aggregates



Amplified vascular
insult

Activation is part of the biochemical pathway, alongside physical occlusion.

Granulocyte recruitment adds inflammatory mediators



Robbins specifically mentions granulocyte recruitment.

Granulocytes release three named mediator classes

Mediator	Role within the textbook model
Free radicals	Part of inflammatory vascular assault
Proteases	Granulocyte-associated damaging mediators
Eicosanoids	Lipid mediators accompanying granulocyte recruitment

Mechanical and biochemical pathways converge

Block the microcirculation

- Fat, red-cell and platelet aggregates
- Physical limitation of vascular flow

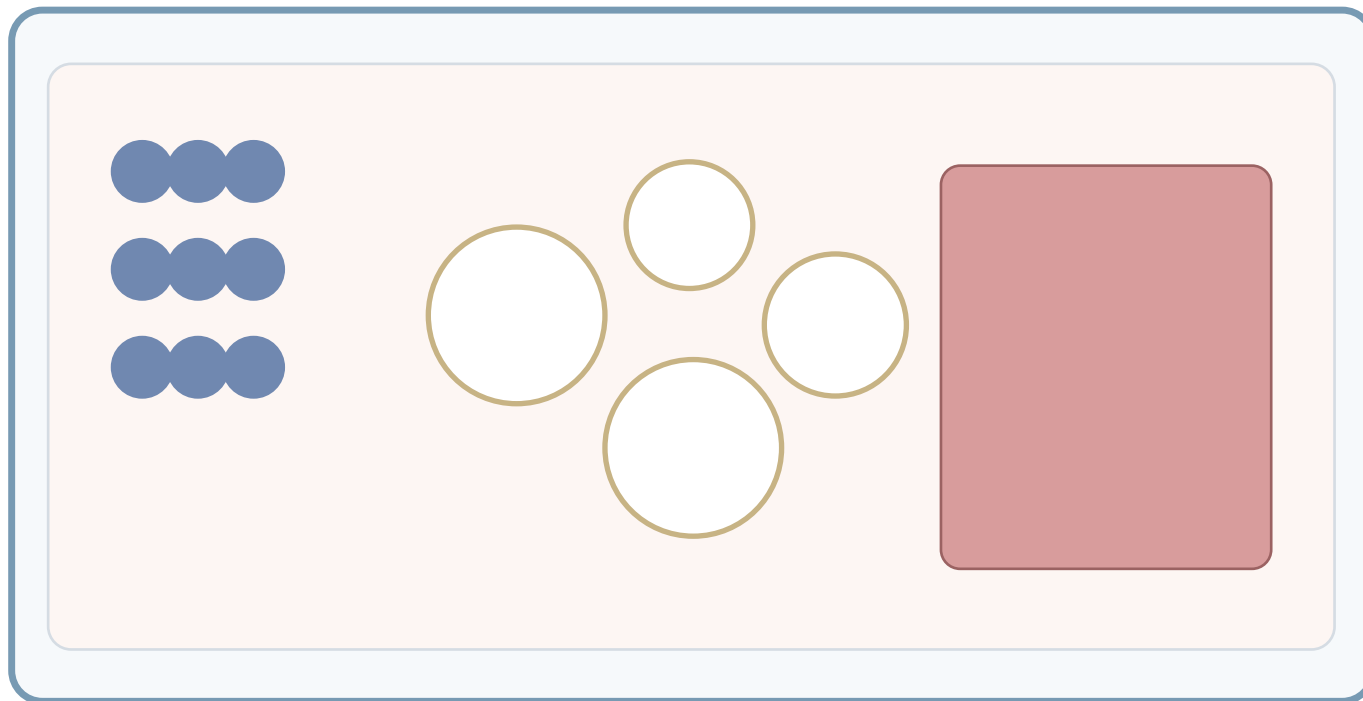
Damage the microcirculation

- Free fatty acid toxicity
- Activated platelets and granulocyte mediators

Vascular injury links pathology to organ dysfunction

Embolic / cellular material	Vascular process	Clinical correlate
Fat + cell aggregates	Pulmonary occlusion	Pulmonary insufficiency
Fat + cell aggregates	Cerebral occlusion	Neurologic symptoms
Platelet interaction	Aggregation / sequestration	Thrombocytopenia
Red-cell effect	Aggregation / hemolysis	Anemia

The pulmonary marrow embolus has three components



Morphologic overview

- Hematopoietic marrow cells
- Vacuolated areas representing marrow fat
- An associated early organizing thrombus

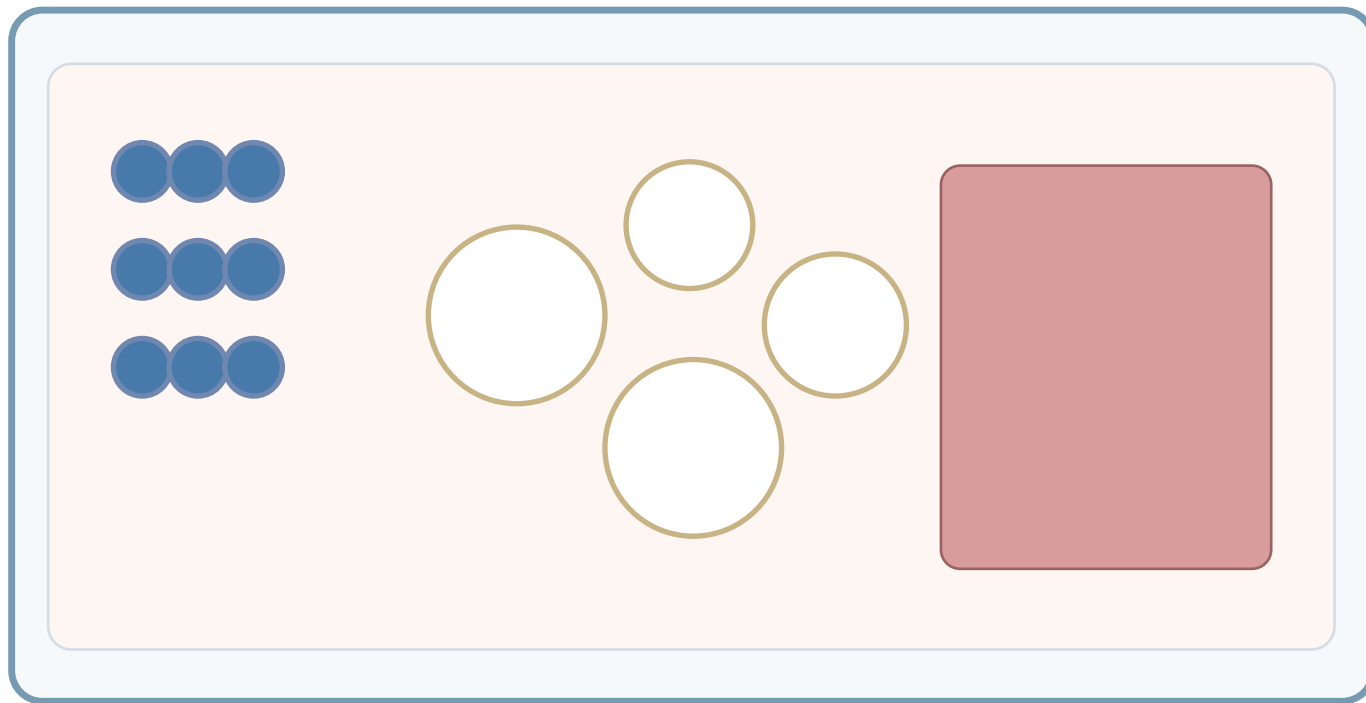
Marrow cells

Marrow fat

Organizing thrombus

Interpretive vector schematic — not a tissue image

Hematopoietic cells identify marrow derivation



Marrow cells

Marrow fat

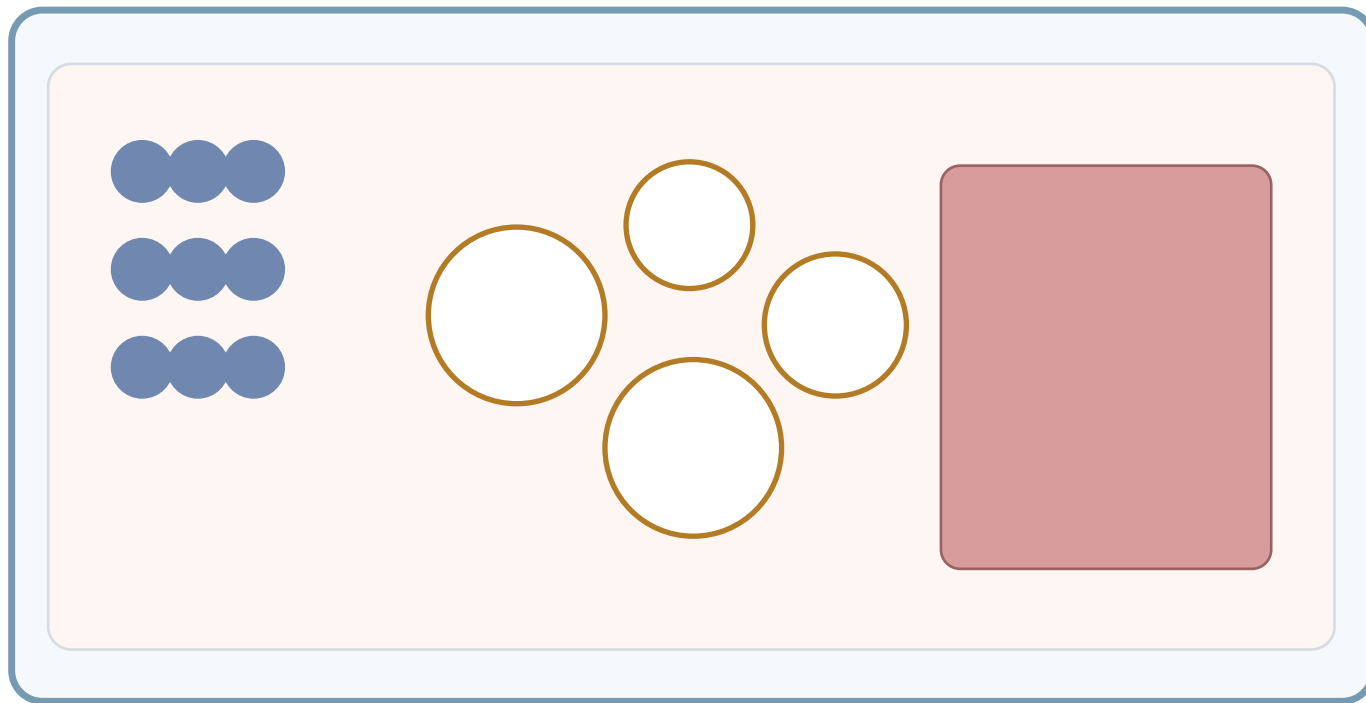
Organizing thrombus

Hematopoietic component

- The textbook figure shows cellular marrow elements in an embolus.
- Their presence supports the interpretation of marrow embolization.
- This is different from an isolated fat microglobule.

Interpretive vector schematic — not a tissue image

Empty-looking vacuoles can represent extracted fat



Marrow cells

Marrow fat

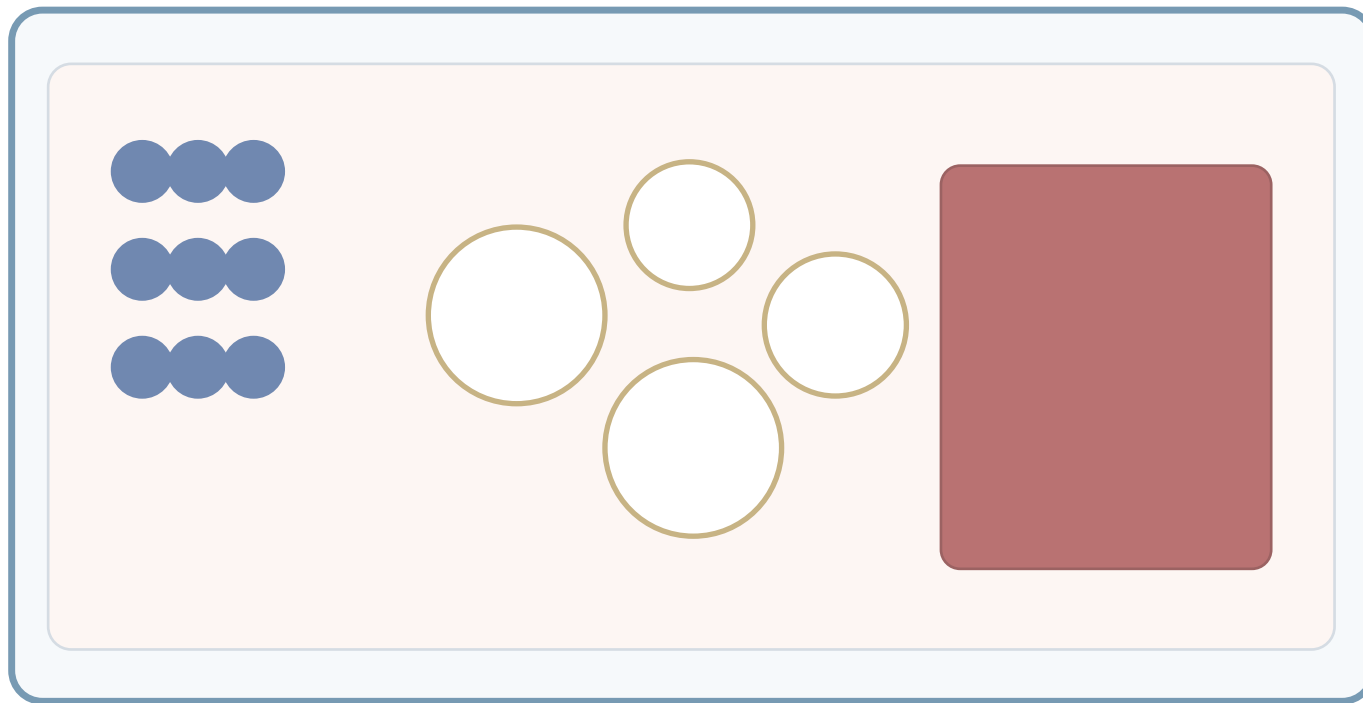
Organizing thrombus

Fat-containing vacuoles

- Clear spaces are described as marrow fat in the source figure.
- Routine processing can remove lipids.
- Vacuoles are interpreted using adjacent tissue context.

Interpretive vector schematic — not a tissue image

An organizing thrombus may accompany the embolus



Marrow cells

Marrow fat

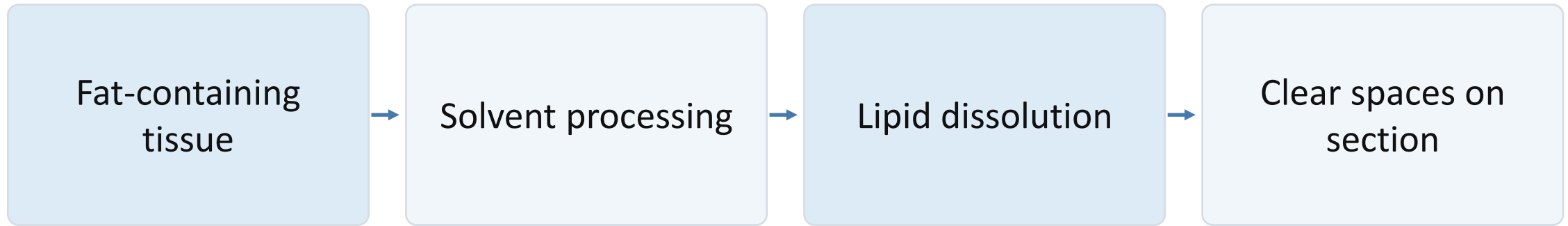
Organizing thrombus

Thrombotic component

- The reference figure shows a relatively uniform red region.
- Its caption identifies that region as early organizing thrombus.
- The embolic complex can contain fat, marrow, and thrombogenic material.

Interpretive vector schematic — not a tissue image

Routine paraffin processing can remove lipid



Solvents used in routine embedding can extract fat.

Why an isolated fat microglobule may be missed

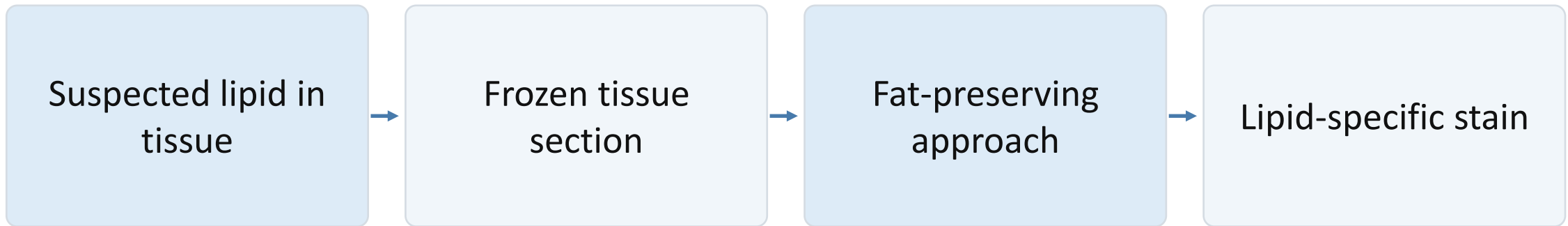
Routine paraffin preparation

- Lipids can be dissolved during processing
- Isolated fat may be difficult to demonstrate
- A clear vacuole is not itself a direct lipid stain

Specialized lipid-preserving examination

- Frozen-section approach
- Stain for fat
- Can help demonstrate residual fat droplets

Frozen sections help preserve demonstrable lipids

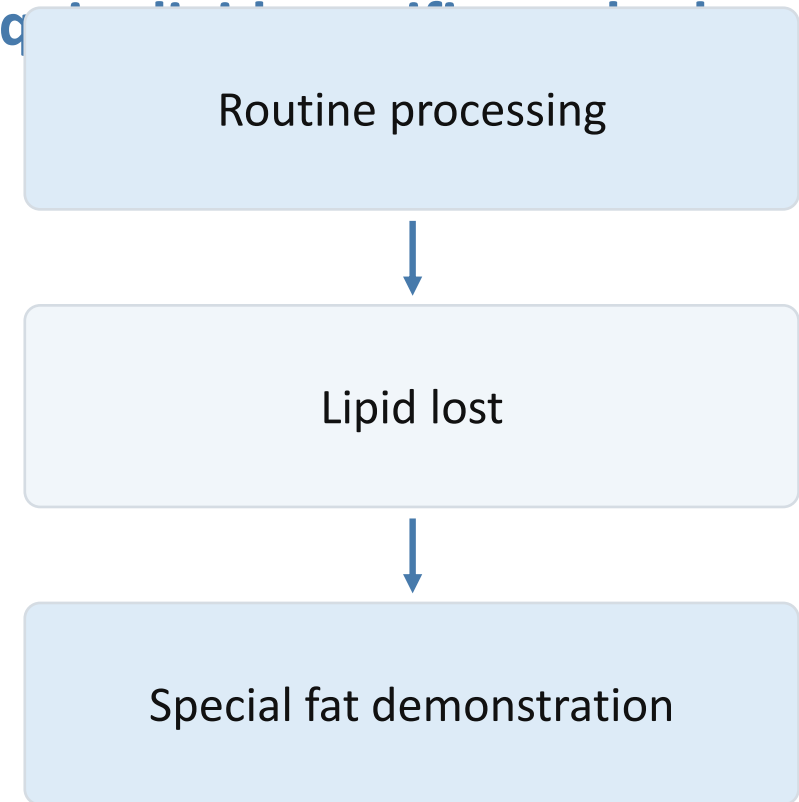


Frozen sections and fat stains as specialized techniques.

A stain for fat addresses the processing problem

Demonstration of isolated fat microglobules may require special processing techniques

- The source does not name a particular fat stain.
- The critical distinction is preservation versus solvent extraction.
- Technique selection is part of morphologic interpretation.



Marrow elements can aid recognition when lipid is absent

With marrow elements

- Hematopoietic cells may remain recognizable
- Suggests marrow material in a vessel
- Source figure illustrates this pattern

Without marrow elements

- Only fat microglobules may be suspected
- Routine embedding can obscure lipid
- Specialized methods may be necessary

Fat embolism cannot be reduced to one microscope feature

Correlate two different forms of evidence.

- Morphology establishes intravascular fat or marrow material.
- Clinical syndrome establishes symptomatic organ dysfunction after injury.
- Textbook symptoms and the 1–3-day interval provide a clinical pattern.
- Morphology and clinical syndrome are related but not identical.

Compare fat emboli and thromboemboli structurally

Feature	Fat / marrow embolus	Typical thromboembolus
Embolic material	Fat droplets $\pm$ marrow cells	Dislodged thrombus
Common context	Severe skeletal injury	Venous thrombosis
Typical destination	Pulmonary microvasculature	Pulmonary arteries
Dominant teaching mechanism	Obstruction + toxic injury	Vascular obstruction

Case: Deterioration after a long-bone fracture

Day 2 after severe long-bone injury: Sudden tachypnea, dyspnea, tachycardia and restlessness. Platelet count is falling.

Which linked findings make fat embolism syndrome plausible?

Compatible skeletal trigger, 1–3-day delay, pulmonary signs, neurologic signs, and thrombocytopenia.

Case: Isolated fat in a lung microvessel

A lung specimen following severe skeletal trauma contains microscopic intravascular fat droplets; No respiratory syndrome was documented.

Does the histology alone establish fat embolism syndrome?

No. Fat embolization is an anatomic finding; Robbins reserves the syndrome for symptomatic patients.

Case: Marrow embolus on histology

A pulmonary vessel contains hematopoietic marrow cells, clear vacuoles, and an adjacent uniform thrombus-like region.

How should the three morphologic compartments be interpreted?

Marrow cells, extracted marrow fat, and possible early organizing thrombus—matching the textbook's figure description.

Case: The negative routine fat stain problem

After routine paraffin embedding, an embolus suspected of containing fat no longer shows intact lipid droplets.

What tissue-processing principle explains this limitation?

Organic solvents can dissolve fat. Frozen sections and stains for fat may be needed to demonstrate microglobules.

Common interpretive errors

Misstatement	Textbook-consistent interpretation
~90% develop clinical syndrome	~90% may have fat emboli after severe skeletal injury
A rash is mandatory	Petechiae appear in 20%–50% of cases
Pure mechanical blockage explains all injury	Fatty acids and inflammatory mediators add damage
No lipid in paraffin excludes fat embolism	Routine processing may dissolve lipid

Mechanism-to-phenotype synthesis

Starting event	Intermediate mechanism	Result
Skeletal injury	Fat / marrow into blood	Emboli to lung
Fat + cell aggregates	Lung / brain microvessel obstruction	Respiratory / neurologic effects
Fatty acid release	Toxic endothelial injury	Inflammatory vascular damage
Platelet / RBC effects	Aggregation, sequestration or hemolysis	Low platelets / anemia

Five facts to retain

The defining clinicopathologic structure is:

- Fat embolization is frequent after severe skeletal trauma.
- Only a minority develop the symptomatic syndrome.
- The usual interval to onset is 1–3 days.
- Obstruction and biochemical vascular injury coexist.
- Histologic fat detection is altered by routine solvent processing.