

# Shock

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Circulatory failure, septic mechanisms, and multiorgan injury

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## Learning objectives

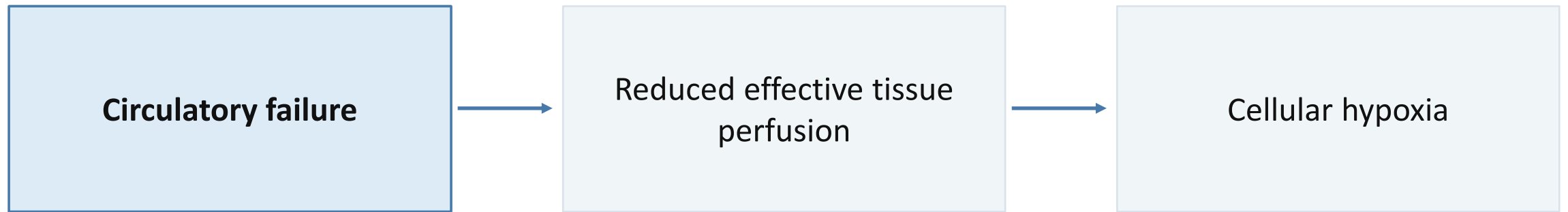
Define shock as systemic circulatory failure with impaired tissue perfusion.

Distinguish cardiogenic, hypovolemic, and septic shock by mechanism.

Trace immune, endothelial, coagulation, and metabolic pathways in septic shock.

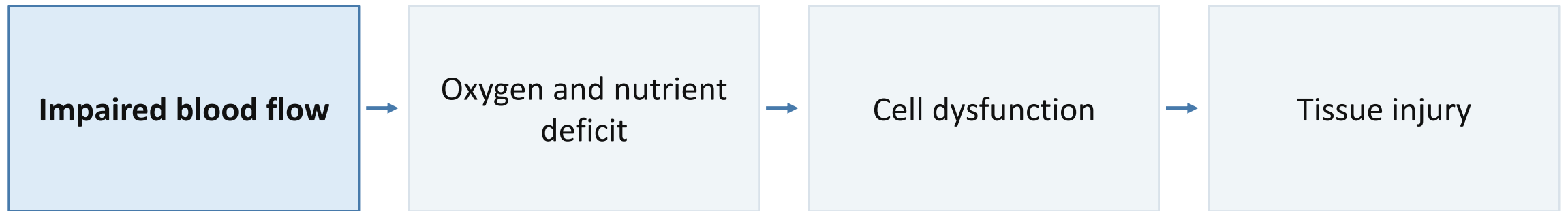
Explain how these pathways culminate in cellular hypoxia and organ dysfunction.

# Shock is circulatory failure with cellular hypoxia



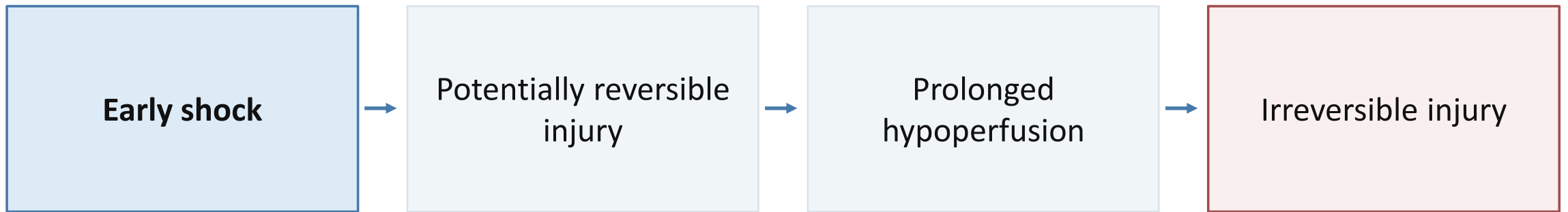
The defining lesion is inadequate tissue oxygen delivery and/or utilization.

# Hypoperfusion links the circulation to tissue injury



Shock describes a systemic pathophysiologic state, not one specific etiologic disease.

## Early injury may be reversible



Duration and severity of the perfusion deficit determine cellular fate.

# Major clinical settings that precipitate shock

## **Massive hemorrhage**

Blood-volume depletion

## **Severe trauma / burns**

Fluid loss and inflammatory injury

## **Myocardial infarction**

Loss of pump function

## **Pulmonary embolism**

Obstruction to cardiac outflow

## Three principal etiologic categories

### **Cardiogenic**

Myocardial pump or  
mechanical outflow failure

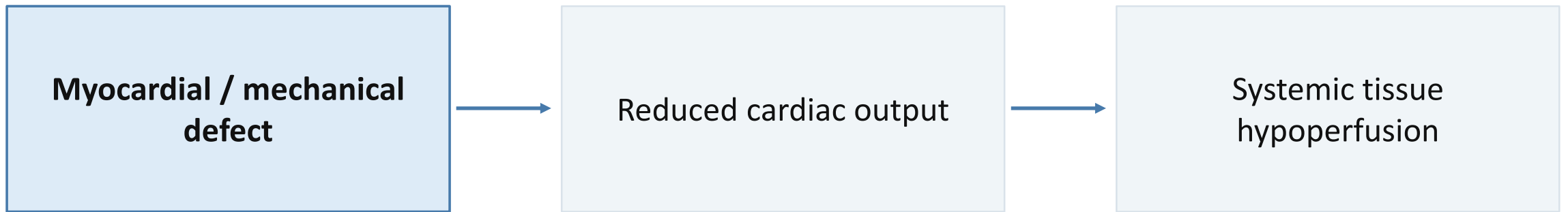
### **Hypovolemic**

Inadequate circulating  
blood or plasma volume

### **Septic**

Dysregulated infection  
response with vascular and  
cellular dysfunction

# Cardiogenic shock: Failure of cardiac output



A primary cardiac mechanism results in circulatory failure.

# Cardiogenic shock can have distinct causes

## **Intrinsic myocardial injury**

Acute myocardial infarction

## **Electrical dysfunction**

Ventricular arrhythmia

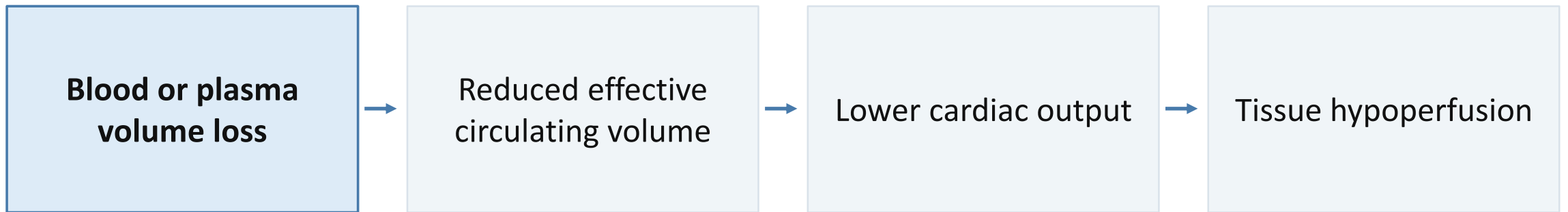
## **Extrinsic compression**

Cardiac tamponade

## **Obstructed outflow**

Massive pulmonary embolism

# Hypovolemic shock starts with volume depletion



# Routes to hypovolemia

## Hemorrhage

Loss of whole blood

## Vomiting / diarrhea

Extracellular fluid loss

## Extensive burns

Plasma and fluid loss

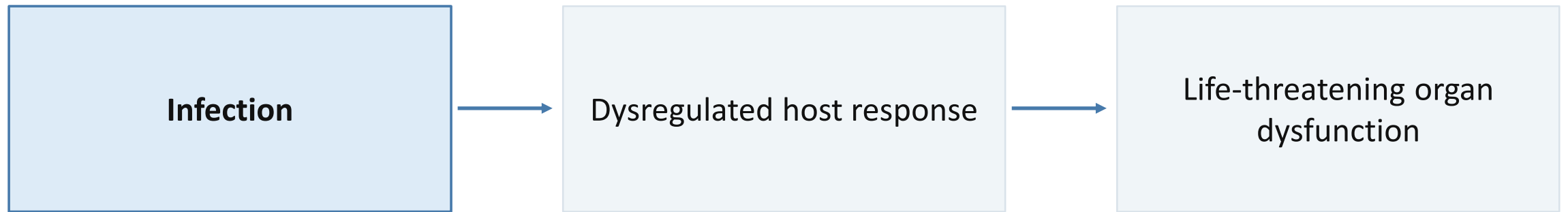
## Trauma

Hemorrhage and fluid loss

## Three types of shock: Compare the initiating defect

| Type        | Dominant initiating disturbance         | Examples                                     |
|-------------|-----------------------------------------|----------------------------------------------|
| Cardiogenic | Pump failure / outflow restriction      | MI; tamponade; arrhythmia; PE                |
| Hypovolemic | Insufficient circulating blood / plasma | Bleeding; burns; gastrointestinal fluid loss |
| Septic      | Systemic response to infection          | Severe microbial infection                   |

# Sepsis is organ dysfunction from a dysregulated response



The organ injury results from the host–microbe interaction, not simply microbial presence.

## Septic shock denotes a particularly severe sepsis subset

### Sepsis

Life-threatening organ dysfunction due to dysregulated infection response

### Septic shock

Profound circulatory, cellular, and metabolic abnormalities with increased mortality risk

# SIRS and sepsis are not synonymous

## SIRS

Systemic inflammatory response can arise from sterile insults

## Sepsis

Requires infection with dysregulated host response and organ dysfunction

Burns, trauma, and pancreatitis can cause nonmicrobial systemic inflammation.

# Uncommon shock mechanisms involve acute vasodilation

## Neurogenic shock

Spinal cord injury may produce acute vasodilation

## Anaphylactic shock

IgE-mediated hypersensitivity may produce acute vasodilation

Both can cause hypotension and tissue hypoperfusion.

# Classifying shock directs attention to the initiating lesion

## CLINICOPATHOLOGIC APPLICATION

A patient with ventricular arrhythmia and low output: Pump failure.

A patient with severe hemorrhage: Volume deficit.

A patient with infection and organ dysfunction: Evaluate the septic pathway.

**Which mechanism is responsible for reduced effective perfusion?**

# Septic shock reflects several mutually reinforcing processes

## Inflammatory activation

Cytokines, leukocytes, complement

## Endothelial dysfunction

Leakage, vasodilation, flow disturbance

## Procoagulant state

Microvascular fibrin thrombi

## Metabolic disturbance

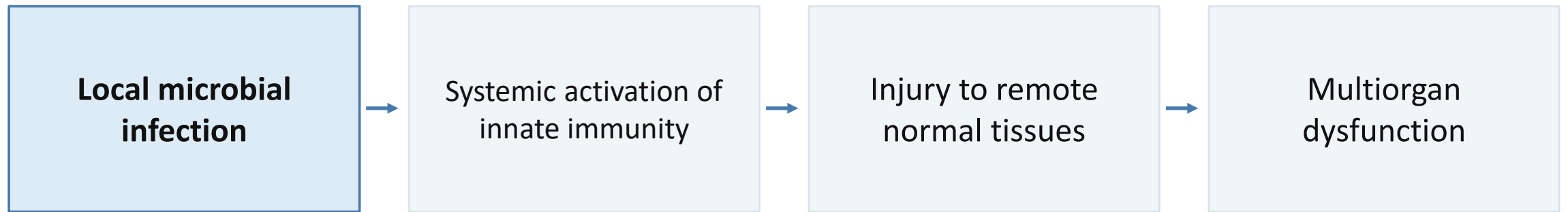
Impaired fuel handling and oxygen use

## Diverse microbial agents can initiate sepsis

| Bacteria                                   | Fungi             | Viruses                                          |
|--------------------------------------------|-------------------|--------------------------------------------------|
| Gram-positive and gram-negative infections | Fungal infections | Certain severe viral infections can cause sepsis |

The mechanism depends on shared host-response pathways rather than one pathogen.

## Septic injury extends beyond the infected site



Failure of normal containment permits a generalized, tissue-damaging host response.

# Innate immunity recognizes both microbes and tissue damage

## **PAMPs**

Pathogen-associated molecular patterns  
derived from microbes

## **DAMPs**

Damage-associated molecular patterns  
released by injured host cells

# Multiple sensors trigger the septic inflammatory response

## **Toll-like receptors**

Recognize diverse  
microbial / damage signals

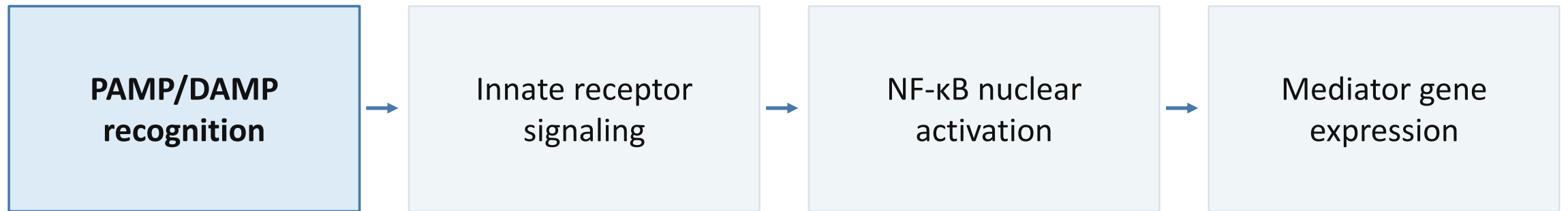
## **G protein–coupled receptors**

Detect some bacterial  
peptides

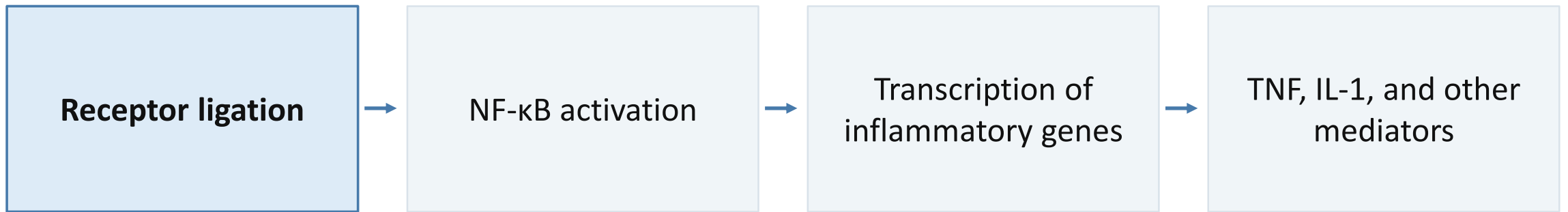
## **C-type lectins (e.g., Dectins)**

Detect fungal antigens

# Microbial recognition activates inflammatory gene programs



# NF- $\kappa$ B links cell sensing to cytokine production



This is one important pathway in a more complex network.

# Major soluble mediators in septic inflammation

## Cytokines

TNF; IL-1; IL-12; IL-18

## Interferons

IFN- $\gamma$

## Late alarmin-like mediator

HMGB1

## Acute-phase markers

C-reactive protein; Procalcitonin

# Reactive oxygen and lipid mediators amplify injury

## Reactive oxygen species

Contribute to cellular and oxidative injury

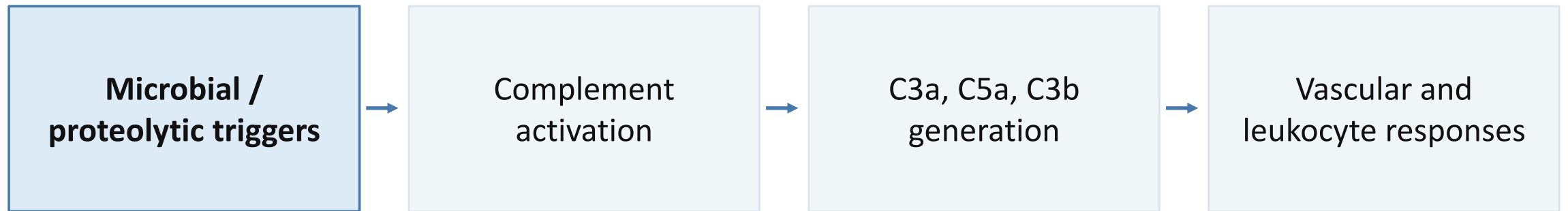
## Prostaglandins

Participate in inflammatory vascular responses

## Platelet-activating factor

Promotes vascular and inflammatory activation

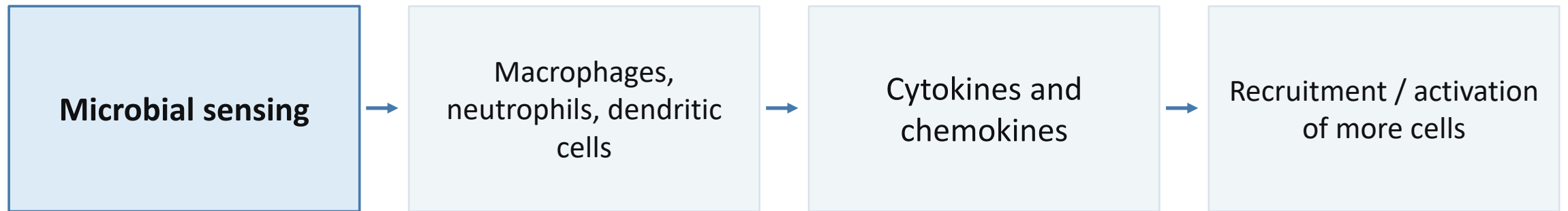
## Complement reinforces the systemic inflammatory state



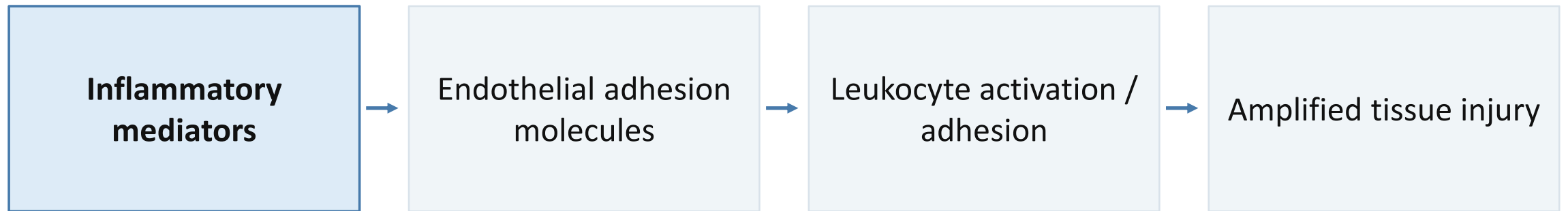
## Complement fragments have different effector roles

| Fragment | Dominant function              | Septic relevance                       |
|----------|--------------------------------|----------------------------------------|
| C3a      | Anaphylatoxin                  | Inflammatory vascular response         |
| C5a      | Anaphylatoxin; chemoattractant | Recruitment / activation of leukocytes |
| C3b      | Opsonin                        | Microbial recognition and clearance    |

## Innate cells extend and amplify mediator release



# Endothelial–leukocyte signaling propagates inflammation



# Inflammation and coagulation activate each other



Thrombin can signal through protease-activated receptors.

# Pro- and anti-inflammatory pathways are concurrent

## Proinflammatory arm

Microbial clearance signals plus risk of host tissue damage

## Counterregulatory arm

Mechanisms limiting inflammation but risking immune dysfunction

Dominance varies with host and pathogen factors.

# Proposed mechanisms of immune suppression

## Antiinflammatory mediators

IL-10; Soluble TNF receptor; IL-1 receptor antagonist

## Immune-cell loss

Lymphocyte apoptosis

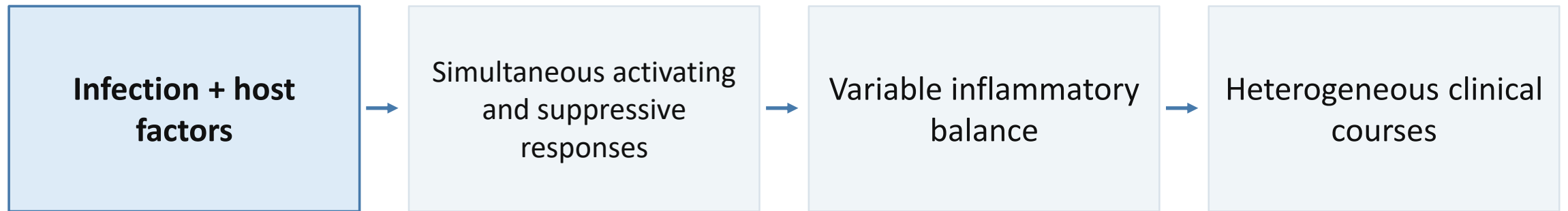
## Reduced responsiveness

Cellular anergy

## Cytokine shift

Relative shift toward anti-inflammatory responses

# The host response is dynamic rather than uniform



Avoid a rigid model of an exclusively early “hyperinflammatory” phase.

# Endothelial injury is central to septic shock

## Barrier dysfunction

Protein-rich vascular leakage

## Vasomotor dysfunction

NO and other mediators

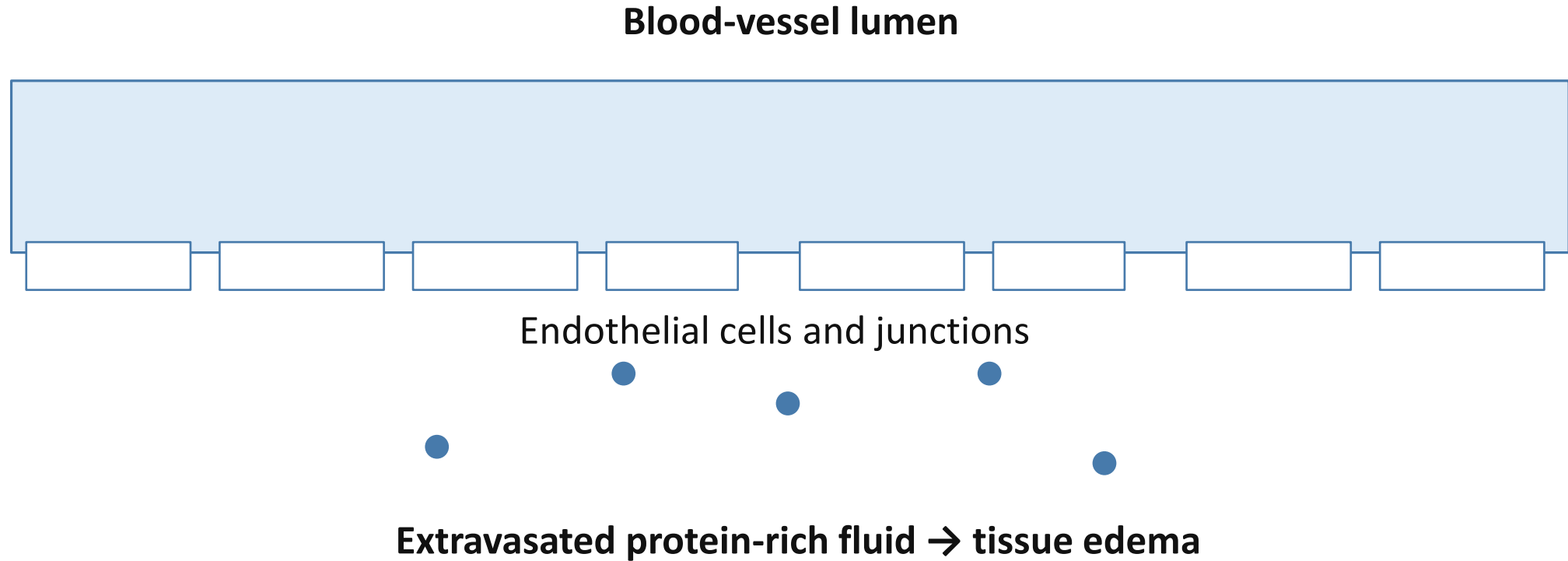
## Microvascular dysfunction

Uneven capillary flow

## Coagulation dysfunction

Loss of anticoagulant restraint

# Cytokines weaken endothelial junctions

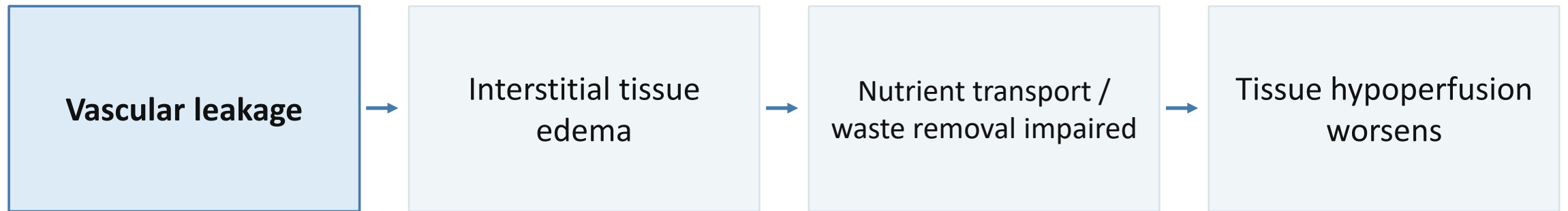


Schematic of increased vascular permeability—not histologic evidence.

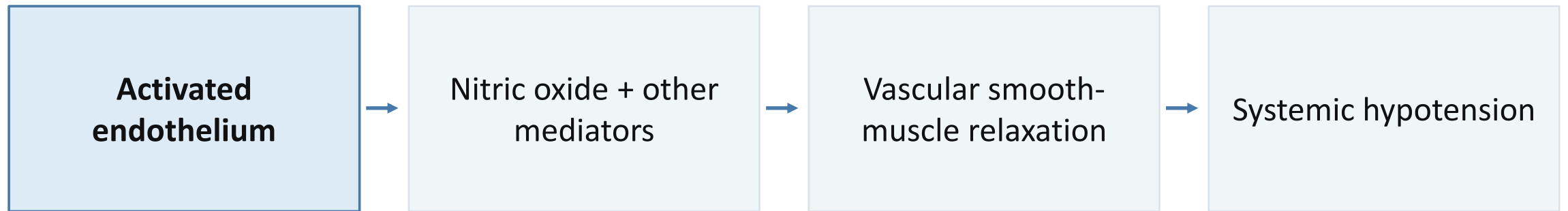
## Loss of barrier function causes interstitial edema



## Edema impairs microvascular exchange

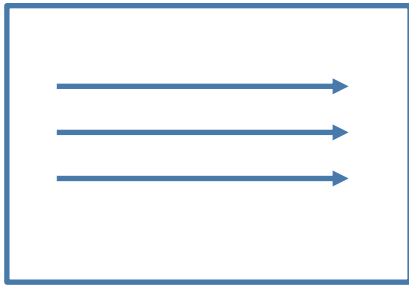


# Vasoactive mediators contribute to hypotension

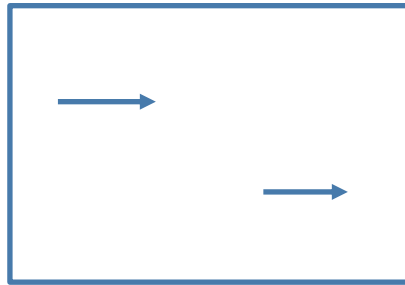


# Septic capillary flow becomes heterogeneous

**Flowing capillary**



**Intermittent flow**

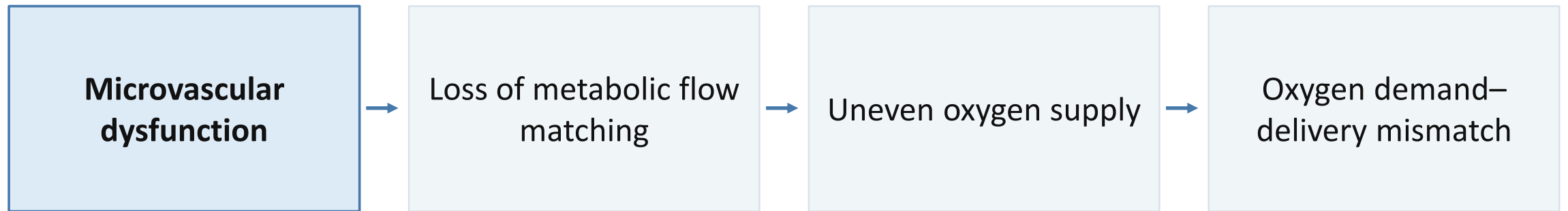


**Poorly perfused capillary**

→ Low flow

Schematic depiction of heterogeneous microvascular flow.

# Loss of local autoregulation causes oxygen mismatch



## Four pathways turn the vessel into an injury amplifier

### Leakage

Fluid leaves the vascular space

### Vasodilation

Effective perfusion pressure declines

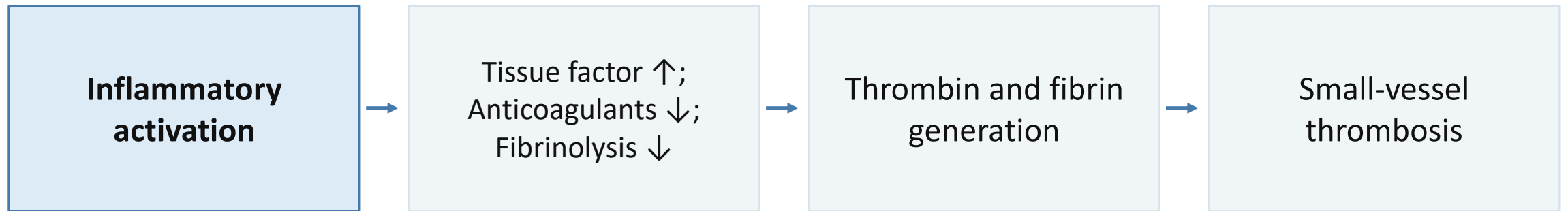
### Flow heterogeneity

Some beds are underperfused

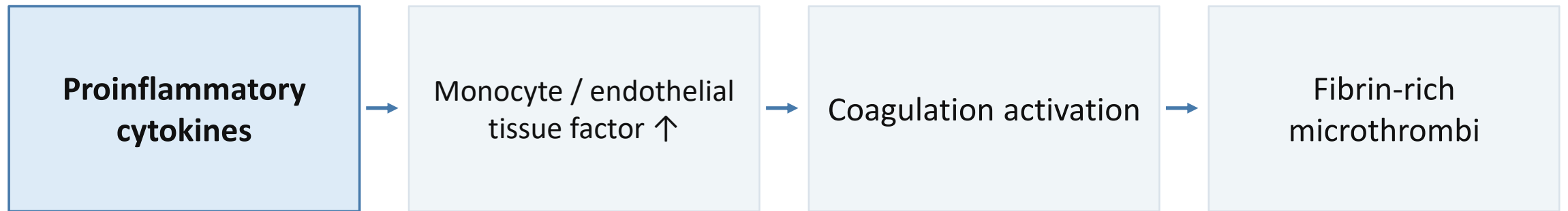
### Thrombosis

Small-vessel lumens are obstructed

# Sepsis produces a systemic procoagulant milieu



# Tissue factor expression promotes thrombin generation



# Anticoagulant pathways are downregulated

## TFPI

Reduced tissue factor pathway inhibition

## Thrombomodulin

Reduced endothelial anticoagulant activity

## Protein C

Reduced anticoagulant protection

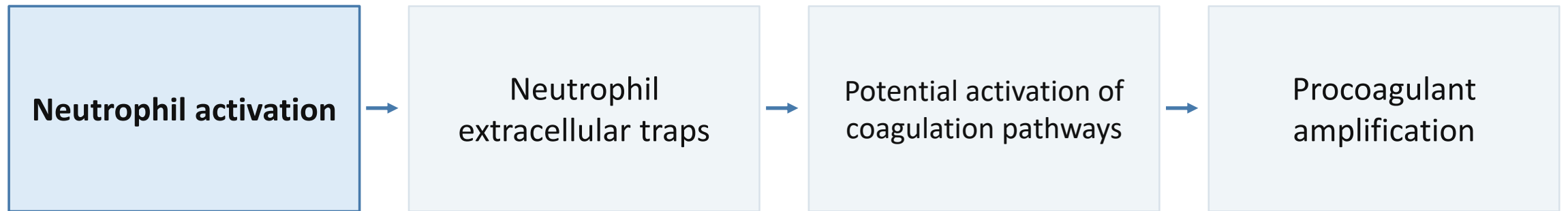
## Net effect

Thrombin activity favors clot formation

## PAI-1 restricts fibrin removal

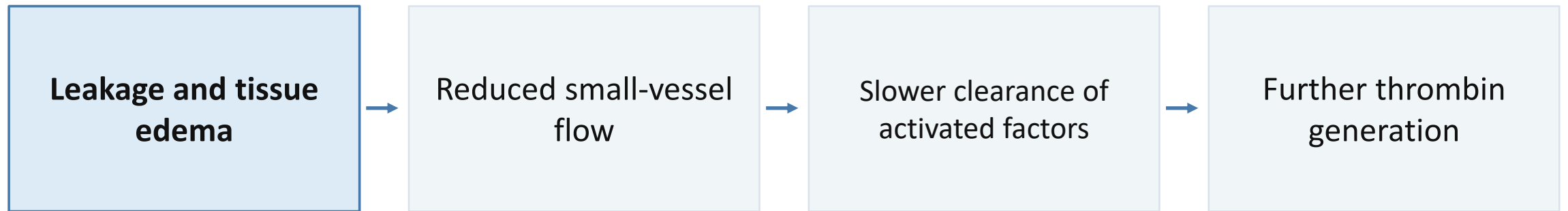


# NETs are a proposed contributor to thrombosis



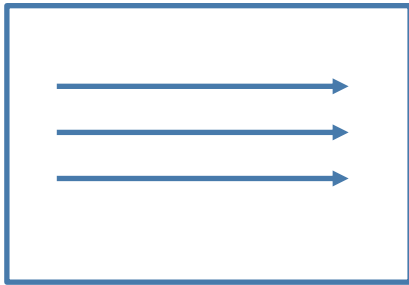
A possible role supported by some studies—not a universally quantified effect.

## Stasis enhances local coagulation

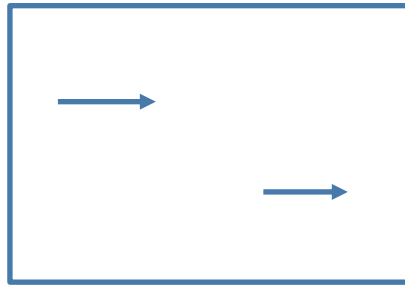


# Microthrombi restrict capillary perfusion

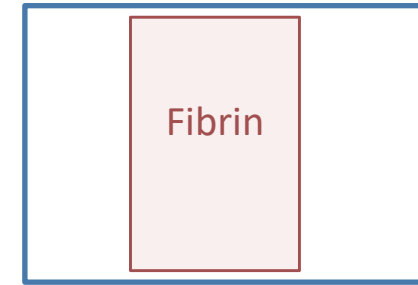
**Patent vessel**



**Fibrin-rich obstruction**



**Downstream low flow**



Schematic of septic microvascular thrombosis, not a specimen.

# DIC combines microthrombosis with bleeding

## Thrombotic component

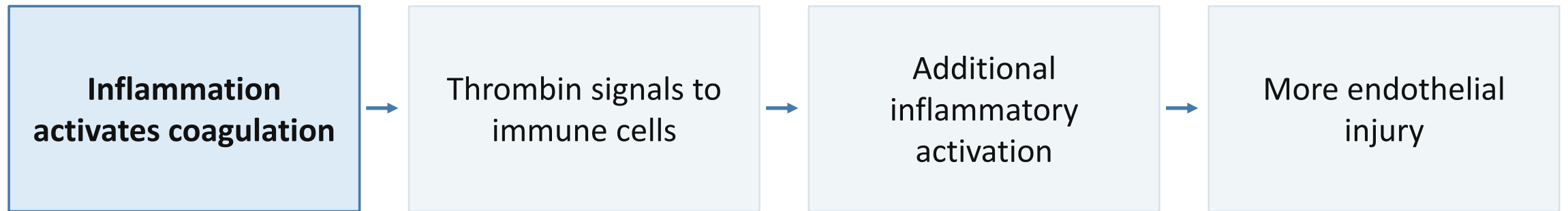
Fibrin-rich thrombi impair organ  
microcirculation

## Hemorrhagic component

Consumption of platelets and coagulation  
factors favors bleeding

DIC is a severe potential complication, not obligatory in every case.

## Coagulation and inflammation form a feedback loop



# Metabolic abnormalities compound septic injury

## Insulin resistance

Reduced response to insulin

## Hyperglycemia

Glucose increases during stress

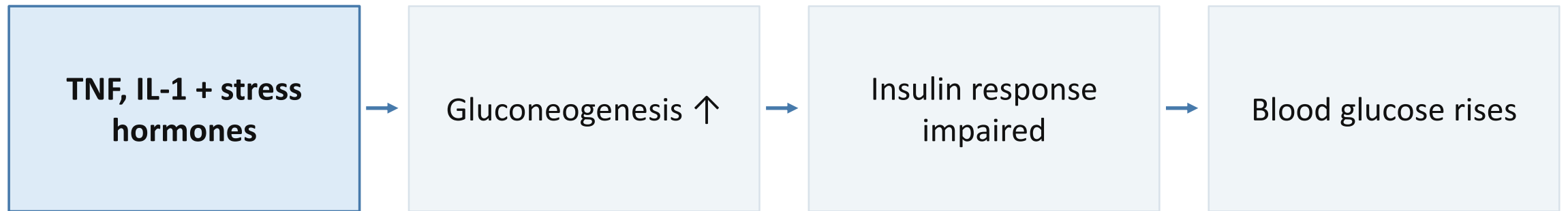
## Lipid abnormalities

Circulating triglycerides may rise

## Lactic acidosis

Hypoxia impairs oxidative ATP production

# Inflammatory and stress signals favor hyperglycemia



# Impaired insulin action has multiple contributors

## Cytokine effects

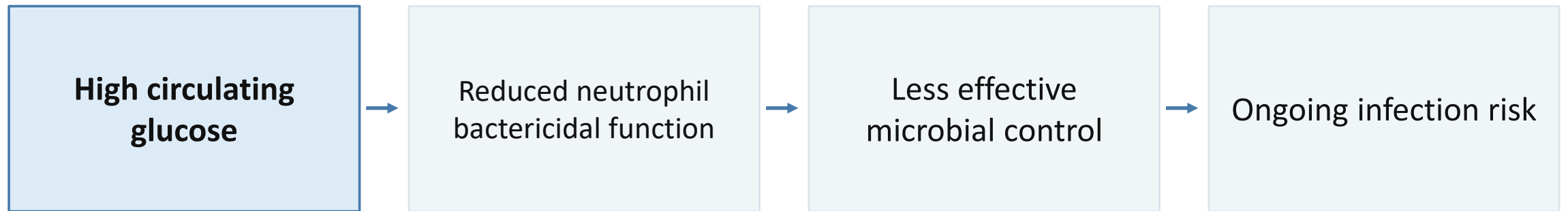
Inflammation can decrease insulin secretion and responsiveness

## Tissue insulin resistance

Abnormal glucose handling in liver and other tissues

The source describes impaired GLUT-4 surface expression as a proposed mechanism.

# Hyperglycemia can worsen antibacterial defense

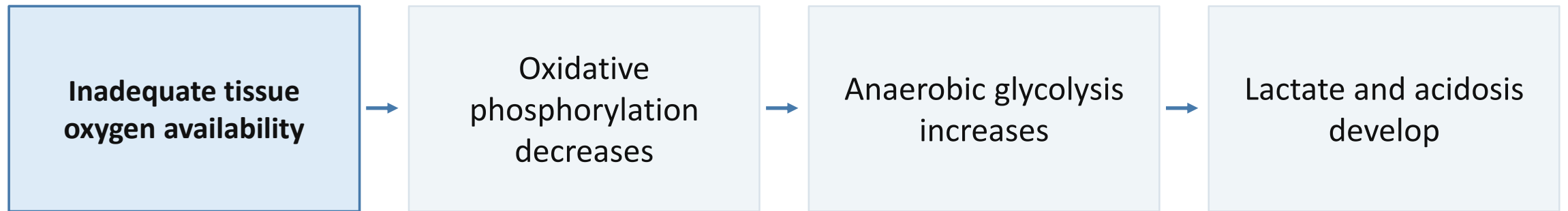


Hyperglycemia also promotes endothelial adhesion molecule expression.

## Sepsis can elevate glucose, triglycerides, and lactate

| Metabolite    | Direction described | Mechanistic interpretation                  |
|---------------|---------------------|---------------------------------------------|
| Glucose       | Increased           | Inflammatory / stress insulin resistance    |
| Triglycerides | Increased           | Systemic metabolic disruption               |
| Lactate       | Increased           | Reduced oxidative metabolism during hypoxia |

# Cellular hypoxia drives lactate accumulation



## Adrenal dysfunction may aggravate severe sepsis



In severe DIC, adrenal hemorrhagic necrosis can occur; This is not a universal septic finding.

# Organ failure reflects impaired delivery and utilization

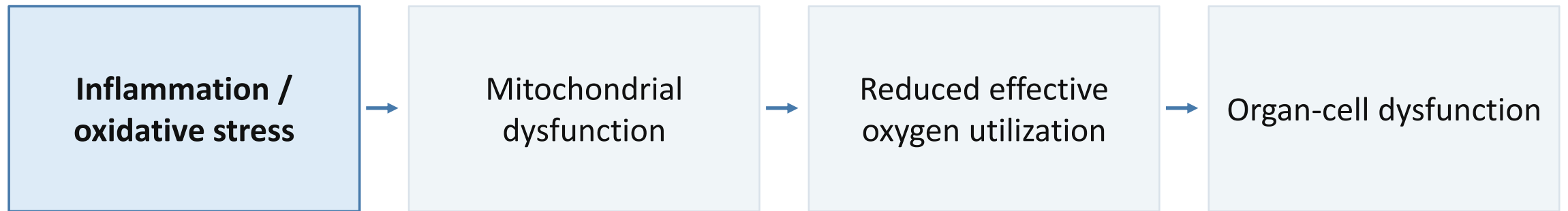
## Supply failure

Hypotension, edema, heterogenous flow,  
thrombosis

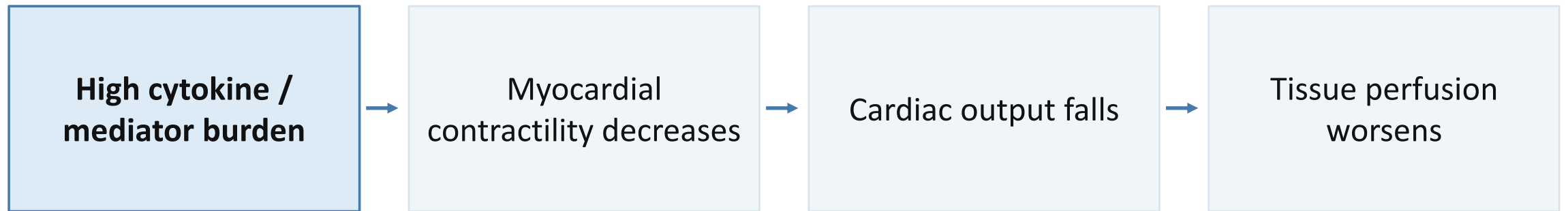
## Cellular utilization failure

Oxidative stress and mitochondrial  
damage

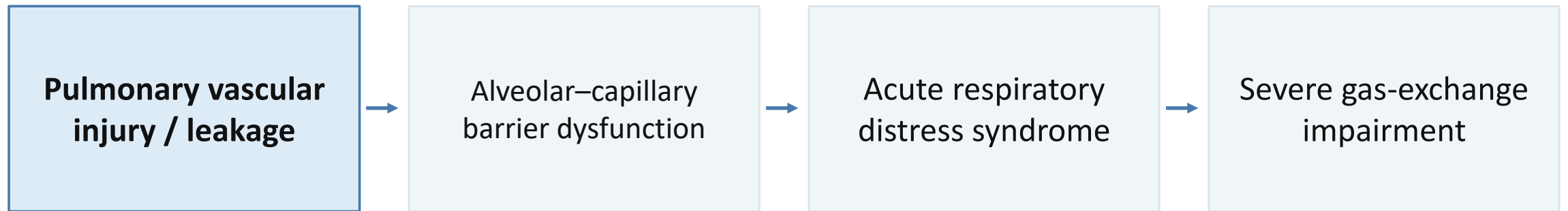
# Oxidative mitochondrial injury can limit oxygen use



# Inflammatory mediators can depress cardiac output



# Endothelial injury can produce pulmonary failure



## Multiple organs may fail together

### **Kidneys**

Impaired renal function

### **Liver**

Hepatic dysfunction

### **Lungs**

Respiratory injury / ARDS

### **Heart**

Impaired myocardial contraction

# Septic shock integrates four injury mechanisms

## Inflammatory injury

Cytokines, innate cells, complement

## Vascular injury

Leakage, vasodilation, flow heterogeneity

## Microthrombosis

TF, lost anticoagulants, fibrin persistence

## Metabolic failure

Hyperglycemia, lactate, mitochondrial  
dysfunction

# Severity reflects pathogen and host characteristics

## Pathogen-related

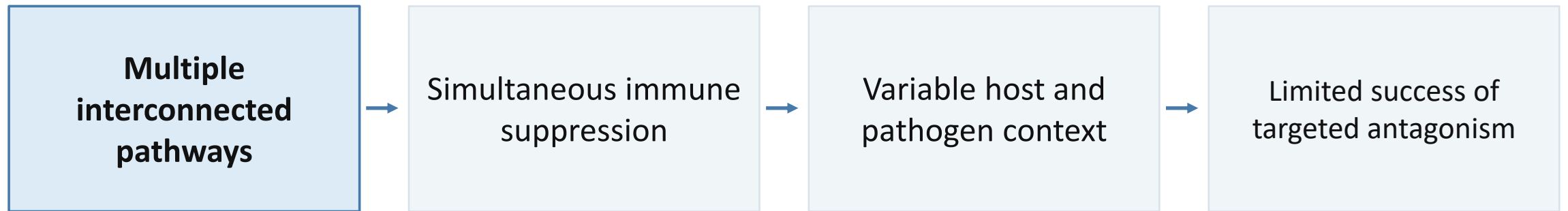
Infectious burden and virulence

## Host-related

Immune state, comorbid conditions,  
mediator patterns

Outcome reflects interacting processes, not one measurable mediator alone.

# Single-mediator blockade has major limitations



The complexity of septic signaling and its therapeutic consequences.

# Source-described management addresses underlying causes

## **Treat infection**

Antibiotics for the  
underlying microbial cause

## **Support circulation**

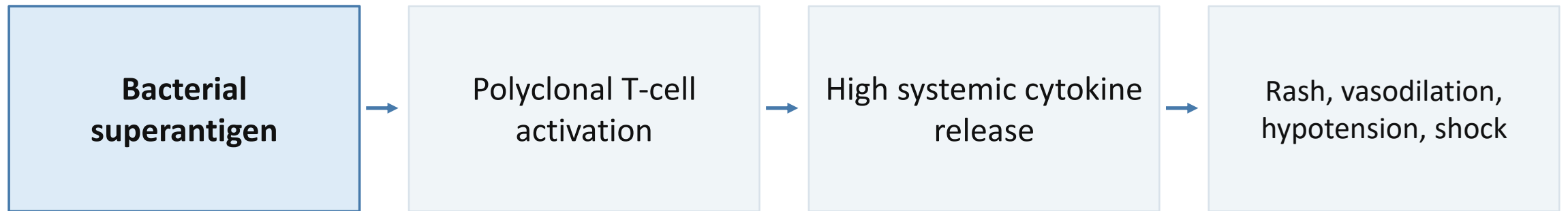
Intravenous fluids and  
pressors

## **Limit tissue hypoxia**

Supplemental oxygen and  
supportive measures

Conceptual textbook overview; Not an up-to-date treatment protocol.

# Bacterial superantigens can trigger shock-like syndromes



# Application: Impaired cardiac pump

## CLINICOPATHOLOGIC APPLICATION

Clinical setting: Acute myocardial infarction.

Primary abnormality: Intrinsic myocardial dysfunction.

Predicted consequence: Falling cardiac output and systemic hypoperfusion.

**Why is this cardiogenic, not hypovolemic, shock?**

# Application: Extensive blood loss

## CLINICOPATHOLOGIC APPLICATION

Clinical setting: Severe hemorrhage after trauma.

Primary abnormality: Reduced blood volume.

Predicted consequence: Inadequate circulating volume and cardiac output.

**Which upstream defect should the explanation identify?**

# Application: Infection with organ dysfunction

## CLINICOPATHOLOGIC APPLICATION

Clinical setting: Major bacterial infection with worsening organ function.

Mechanism: Dysregulated immune–vascular–coagulation response.

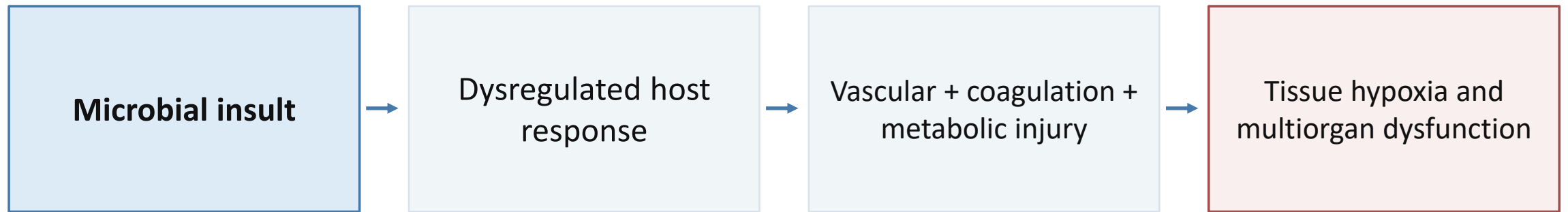
Potential consequences: Hypotension, edema, microthrombi, metabolic injury.

**Why is this more than a localized inflammatory response?**

## Distinguish the three syndromes mechanistically

| Clinical clue                             | Most fitting type              | Why                             |
|-------------------------------------------|--------------------------------|---------------------------------|
| Acute infarction with pump failure        | Cardiogenic                    | Primary impaired cardiac output |
| Major fluid or blood loss                 | Hypovolemic                    | Reduced effective volume        |
| Infection with systemic organ dysfunction | Sepsis / septic shock spectrum | Dysregulated host response      |

# Integrated model of septic shock



## References and source boundaries

Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th edition (2026), Chapter 4, pp. 117–120.

The classification follows Table 4.3; pathway concepts follow the septic-shock text and Figure 4.20.

Original editable diagrams are explanatory schematics, not reproductions of textbook figures.

No external clinical guidelines, protocols, or current epidemiologic estimates were added.