

Cardiopulmonary Bypass and Collateral Injury

Part I: Pathophysiology

Jeremy L. Herrmann, MD

Section of Cardiothoracic Surgery

Department of Surgery

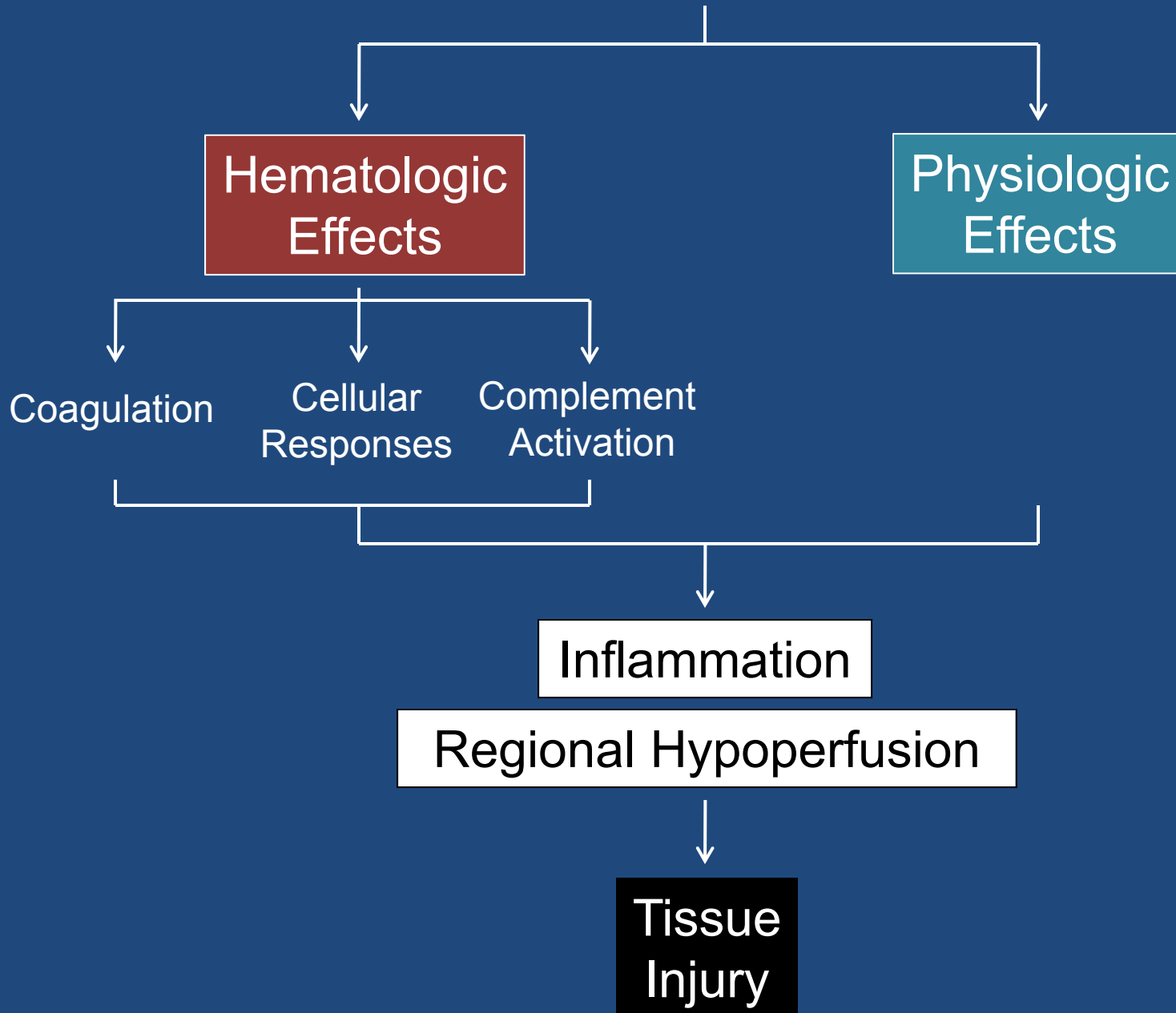
Indiana University School of Medicine

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Talk supervisor: Dan Meldrum, MD



Cardiopulmonary Bypass



Cardiopulmonary Bypass



Hematologic
Effects



Coagulation

- Activation of extrinsic and intrinsic pathways
- Thrombin generation
- Inadequate *in vivo* anticoagulation mechanisms



Hematologic Effects: Coagulation

**Synthetic Surface Contact
(Intrinsic Pathway)**



PK, HMWK

XII → XIIa

(thrombin)

XI → XIa

IX → IXa + VIIIa, PL, Ca⁺⁺

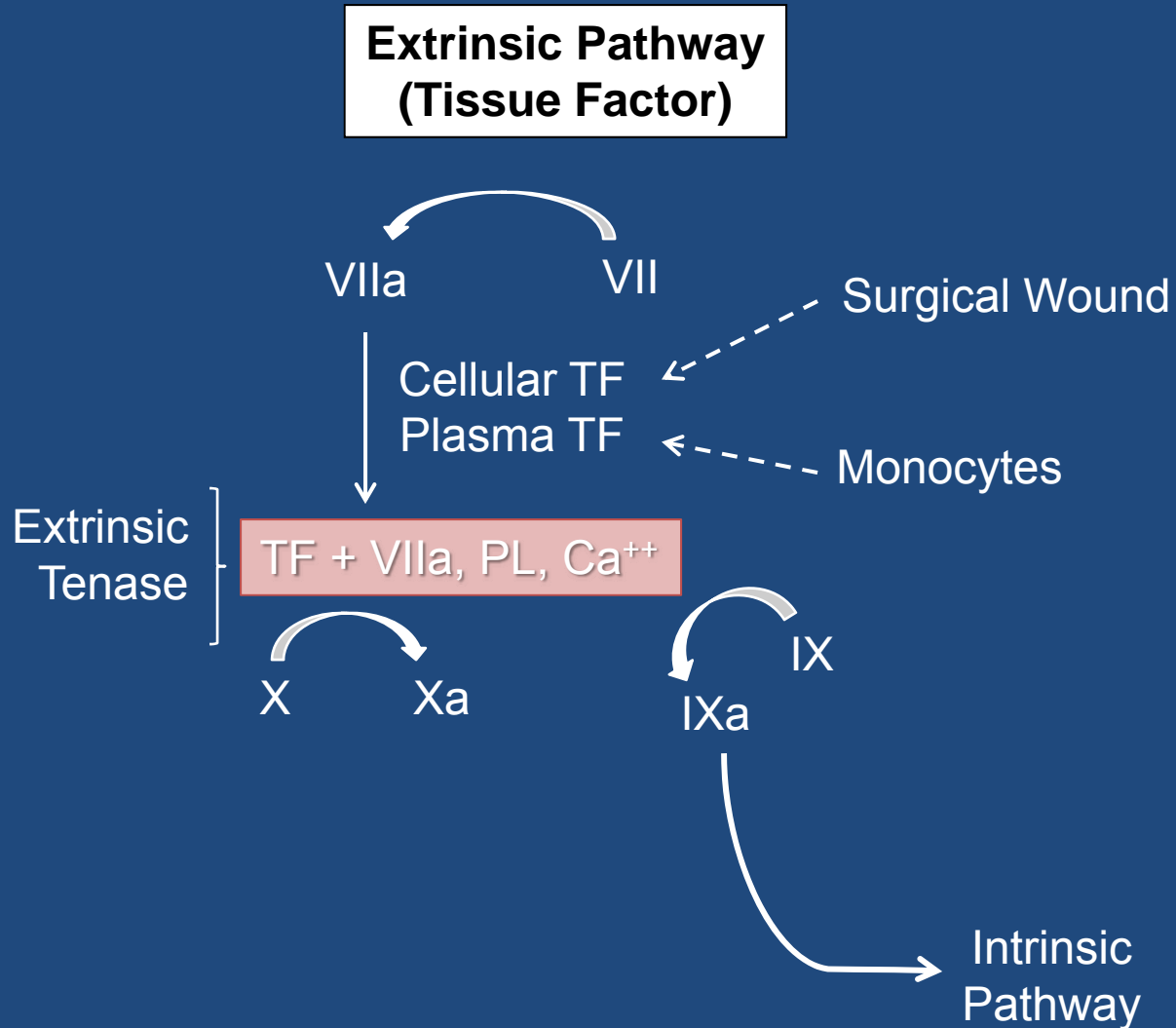
Intrinsic Tenase

X → Xa

Complement activation
Neutrophil activation
Inflammation

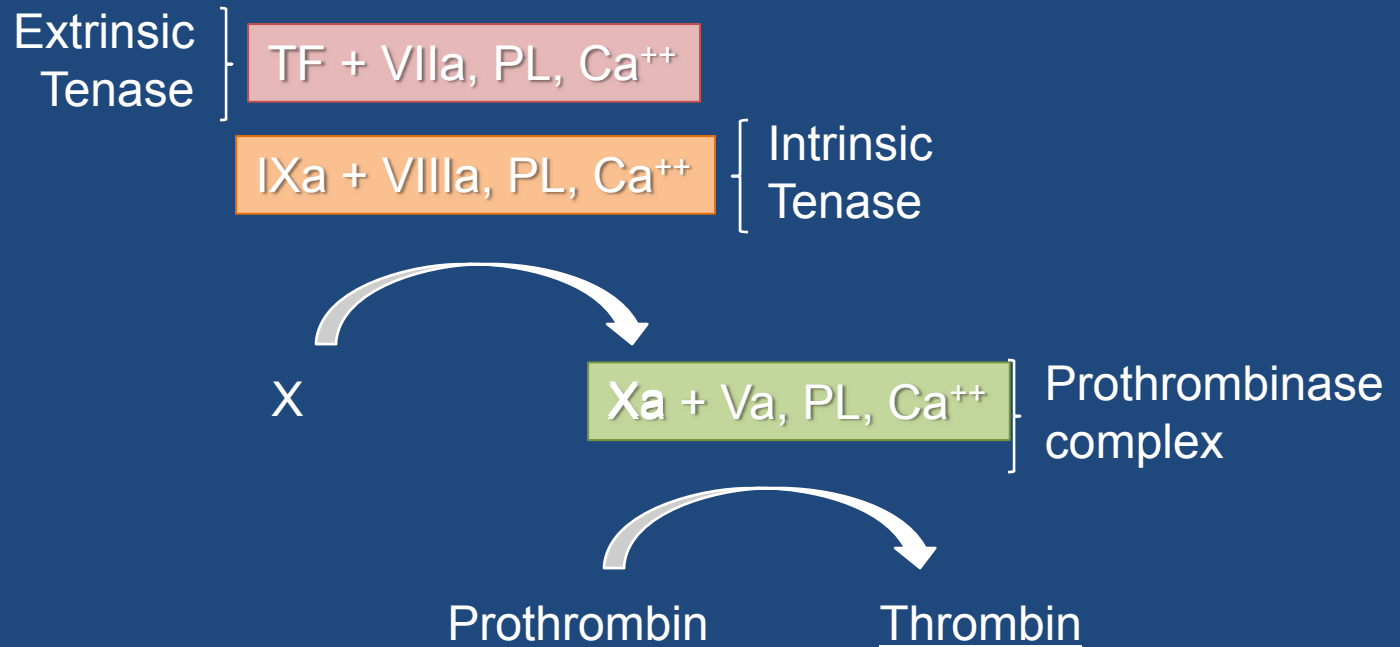


Hematologic Effects: Coagulation



Hematologic Effects: Coagulation

Common Coagulation Pathway



Hematologic Effects: Coagulation

- Procoagulant Effects of Thrombin:
 - Feedback activation of XI and VIII
 - Secondary activation of VII
 - Activation of V in prothrombinase complex
 - Activation of XIII to cross-link fibrin
 - Catalyzes formation of fibrin from fibrinogen
 - Activates thrombin-activated fibrinolysis inhibitor



Hematologic Effects: Coagulation

- Anticoagulant Effects of Thrombin:
 - Stimulates endothelial cell tPA production
 - Stimulates endothelial cell NO and PG synthesis
 - Activates protein C → deactivates V and VIII



Cardiopulmonary Bypass



Hematologic Effects



Cellular Responses

- Neutrophils
- Platelets
- Monocytes
- Endothelial cells



Hematologic Effects: Neutrophil Activation

Activated by

- Kallikrein
 - C5a
- Cytokines (IL-1 β , TNF- α , IL-8)
- Factor XIIa
- Histamine
- LTB₄, PAF, TXA₂

Effects

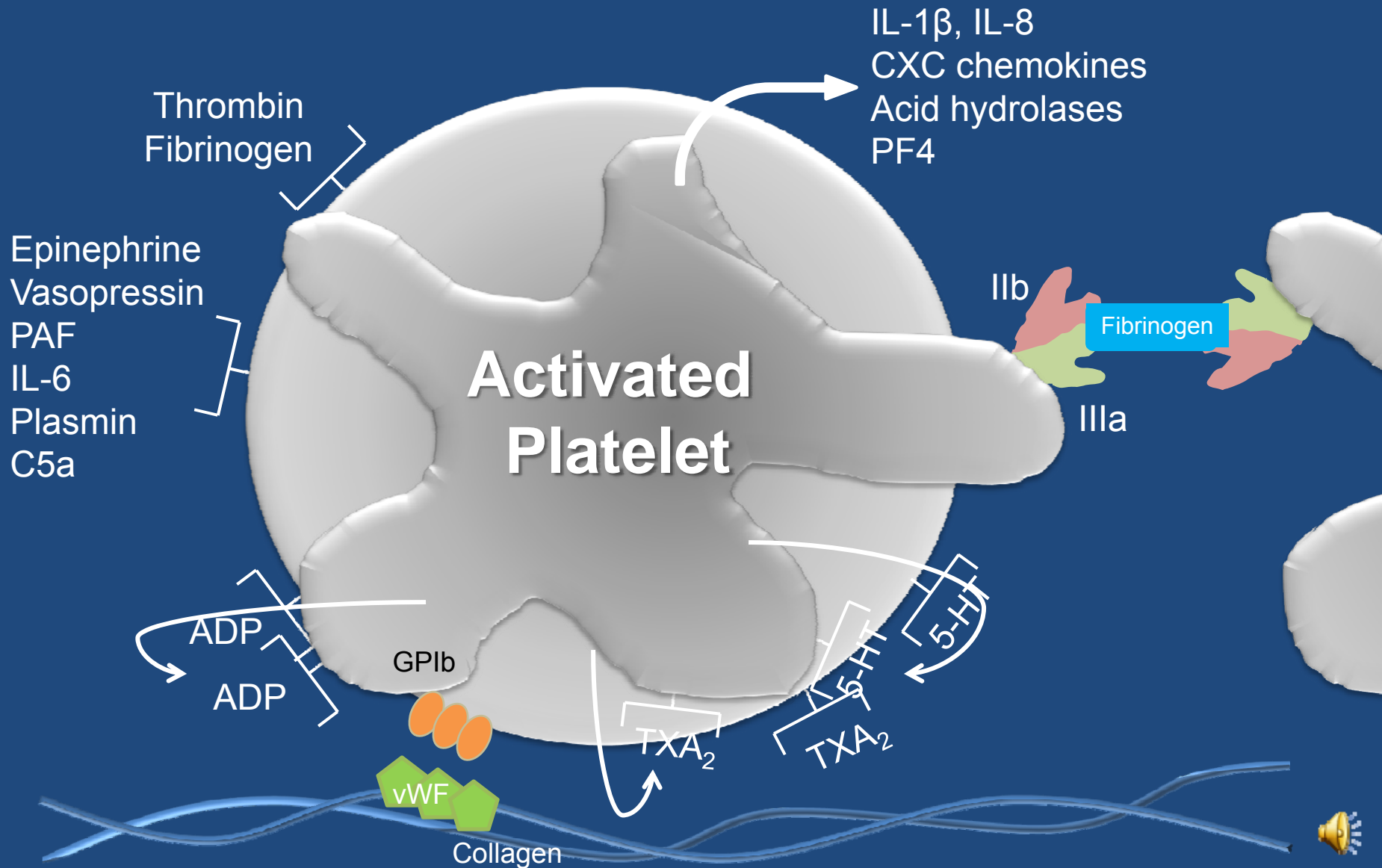
- Respiratory burst (ROS, nitrogen metabolites)
- Vasoactive substances (LTB₄, PAF, TXA₂)
- Proteolytic and cytotoxic substances (lysozyme, MPO, elastase, collagenases, acid hydrolases, phospholipase)



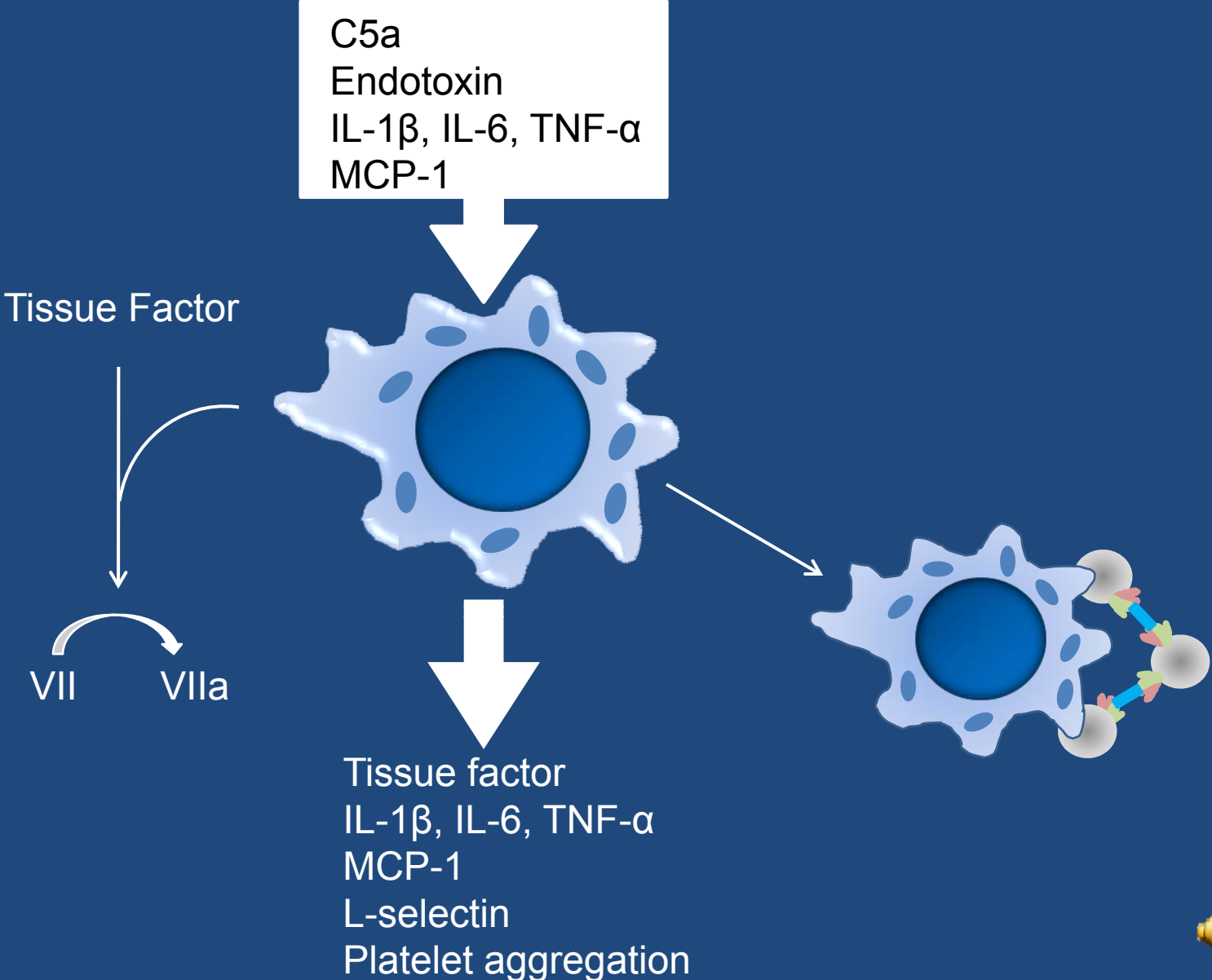
SIRS



Hematologic Effects: Platelet Activation



Hematologic Effects: Monocyte Activation



Hematologic Effects: Endothelial Cells

- Activated by
 - C5a
 - IL-1 β , TNF- α
 - \uparrow P- and E-selectin expression
 - \uparrow ICAM-1 and VCAM-1 expression
 - Thrombin
- Produce PGI₂ and NO – \downarrow shear stress and \uparrow permeability
- Produce proinflammatory cytokines (IL-1 β , IL-6, IL-8, MCP-1, PAF)
- Procoagulant: bind vWF, IXa and Xa
- Anticoagulant: produce t-PA, heparan sulfate, protein S, TFIP



Cardiopulmonary Bypass



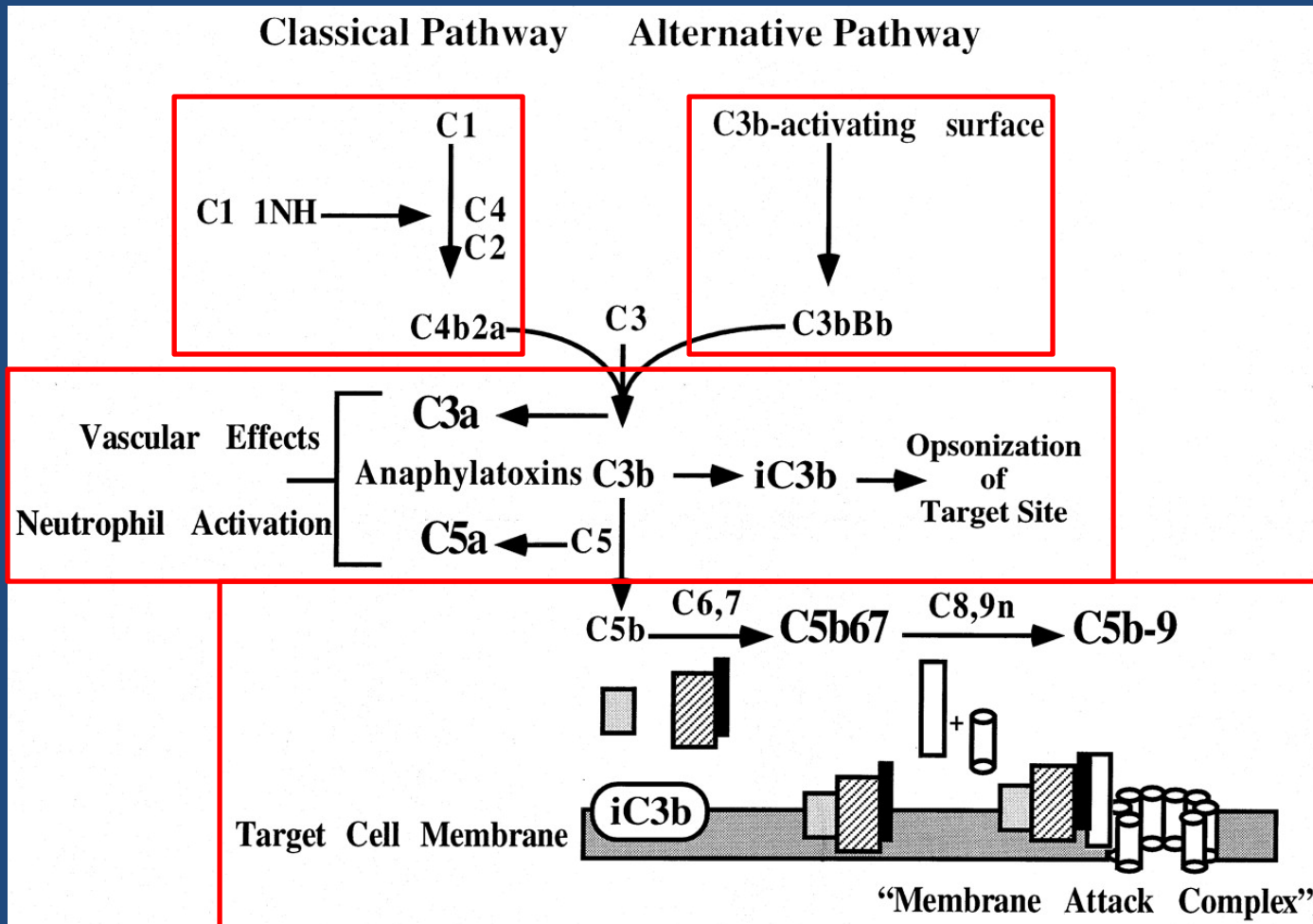
Hematologic
Effects



Complement
Activation



Hematologic Effects: Complement Activation



Park, J. L. et al. Ann Thorac Surg 1999;68:1905-1912



Cardiopulmonary Bypass

Physiologic
Effects

Regional Hypoperfusion

Tissue
Injury



Regional Hypoperfusion

- Caused by
 - Increased interstitial fluid
 - ↓plasma oncotic pressure, ↑venous pressure
 - Nonpulsatile flow
 - Temperature mismatch
 - Systemic and local inflammation
 - pH
 - Excessive hemodilution
 - Microemboli



Sources of Microemboli during CPB

<u>Gas</u>	<u>Foreign</u>	<u>Blood</u>
Bubble oxygenators	Atherosclerotic debris	Fibrin
Air entry into the circuit	Fat, fat droplets	Free fat
Residual air in the heart	Fibrin clot	Aggregated chylomicrons
Loose purse-string sutures	Cholesterol crystals	Denatured proteins
Cardiotomy reservoir	Calcium particles	Platelet aggregates
Rapid rewarming	Muscle fragments	Platelet-leukocyte aggregates
Cavitation	Tubing debris, dust	Hemolyzed red cells
	Bone wax, talc	Transfused blood
	Silicone antifoam	
	Glue, Surgical	
	Cotton sponge fiber	

Adapted from Hammon JW. Extracorporeal Circulation: Organ Damage. Cohn LH, ed. Cardiac Surgery in the Adult. New York: McGraw-Hill, 2008.



Strategies to Reduce Microemboli

- Circuit-Related

- Anticoagulation
- Membrane oxygenator
- Washing collected blood
- Heparin-coated tubing
- Filtering cardiectomy reservoir
- Closed venous drainage
- Leukocyte filters

- Intraoperative

- Removal of residual air in heart and great vessels
- Avoiding atherosclerotic plaques
- Selective filtration of cerebral vessels
- Minimization of aortic cross-clamping
- Use of retrograde cardioplegia (avoid sandblasting effect)



Specific Organ Injury

- Cardiac
- Neurologic
- Pulmonary
- Renal
- Liver
- Pancreas
- Alimentary tract



Cardiac Injury

- Difficult to define CPB-related cardiac injuries
- Heart partially protected during CPB by aortic cross-clamping



Neurologic Injury

- Causes
 - Atheroemboli
 - Systemic microemboli
 - SIRS
- Classification
 - Type I – focal injury, stupor or coma at discharge
 - Type II – deterioration in intellectual function, memory deficit, or seizures



Neurologic Injury

- Roach, et al – Prospective analysis of patients undergoing elective CABG (n=2108)
 - 3.1% type I outcomes
 - proximal aortic atherosclerosis, history neurologic disease, older age
 - 3.0% type II outcomes
 - older age, systolic hypertension, pulmonary disease, excessive alcohol consumption



Neurologic Injury

- Newman, et al – Prospective pre- and post-operative neurocognitive assessment of type II outcomes in patients undergoing CABG (n=261)
 - 53% exhibited cognitive decline at discharge
 - 42% exhibited cognitive decline at 5 yrs
 - Cognitive function at discharge greatest predictor of long-term function

Neurologic Injury

- Selnes, et al – Prospective cognitive analysis of patients undergoing CABG (n=140) and nonsurgical control group with CAD (n=90)
 - Both groups showed trends in decreased cognitive performance between 12-36 mos
 - Surgical group demonstrated slightly better function at 36 mos in certain tests



Pulmonary Injury

CPB Factors:

- Lack of PA blood flow
- Hemodilution
- ↑LA pressure
- Inflammatory cytokines



↑Capillary
permeability



Interstitial edema



↓Compliance
↑Work of breathing
↑AV shunt
↑Infection risk



Renal Injury

- Up to 30% of cardiac surgery patients exhibit some form of acute kidney injury
- Risk factors:
 - Advanced age
 - Diabetes
 - Previous cardiac surgery
 - Congestive heart failure
 - Prolonged operations
 - Postoperative low cardiac output, hypotension
- Incidence of Post-CPB ARF requiring dialysis: 1%
 - increases to 5% after complex procedures
 - Renal failure requiring dialysis increases morbidity and mortality 8-fold



Liver Injury

- Normal liver usually tolerant of CPB
- Liver transaminases may be mildly elevated;
- 10-20% develop mild jaundice
- Persistent and rising bilirubin 2 d after CPB may portend liver failure



Pancreatic Injury

- <1% develop clinical pancreatitis
- 30% develop transient increase in serum amylase or lipase
- Risk factors:
 - h/o pancreatitis
 - perioperative shock
 - prolonged CPB
 - high dose inotropic agents
 - high doses of calcium
- Fulminant pancreatitis rare but usually fatal



Stomach and Intestinal Injury

- Risk factors:
 - Advanced age
 - Emergency surgery
 - Prolonged CPB
 - Postoperative shock or low cardiac output
 - Prolonged vasopressor therapy
 - Elevated venous pressure
- CPB decreases gastric pH – ulcer and gastritis complications effectively prevented pharmacologically



Conclusion

- CPB-related collateral injuries occur through hematologic and physiologic mechanisms
- Hematologic mechanisms include coagulation, blood cell activation, complement activation, and endothelial cell activation/dysfunction
- Both categories of mechanisms result in inflammation, regional hypoperfusion, and ultimately, tissue and organ injury

