

# Inflammatory Response to Major Vascular Operations

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## What You Must Know to Prevent Disasters

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## Disclosure

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I do not have any potential conflict of interest.

# Ischemia / Reperfusion Syndrome



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THE UNIVERSITY OF TEXAS AT DALLAS  
CONTROVERSIES & UPDATES  
IN VASCULAR SURGERY  
JANUARY 22-24 2015



# Ischemia / Reperfusion Syndrome

- Pathophysiology
  - Ischemia
  - Tissue hypoxia
  - Reperfusion
  - Activation of cytokines
  - Exaggerated inflammatory response
  - Generation of free oxygen radicals
  - Tissue damage
  - Organ dysfunction

# Ischemia / Reperfusion Syndrome

- Interest to Vascular Surgery
  - Refractory hypotension following repair of ruptured aortic aneurysm or other major vascular procedure
  - Brain ischemia
    - Stroke
    - Ischemic penumbra
    - Hyperperfusion syndrome
  - Visceral ischemia
  - Delayed onset paraplegia following repair of ThAAA
  - Compartment syndrome
  - Multiple trauma

# Ischemia / Reperfusion Syndrome

- Common scenario
  - 78 y/o man presents to the ED with back and abdominal pain, hypotension and evidence of a ruptured AAA





# Ischemia / Reperfusion Syndrome

- Common scenario
  - Brought to surgery and undergoes open repair of the ruptured aneurysm
  - Post-operatively stable but remains hypotensive (70/50) despite fluid resuscitation, ventilator support and inotropes
  - Usual next step: *vasopressors*

# Ischemia / Reperfusion Syndrome

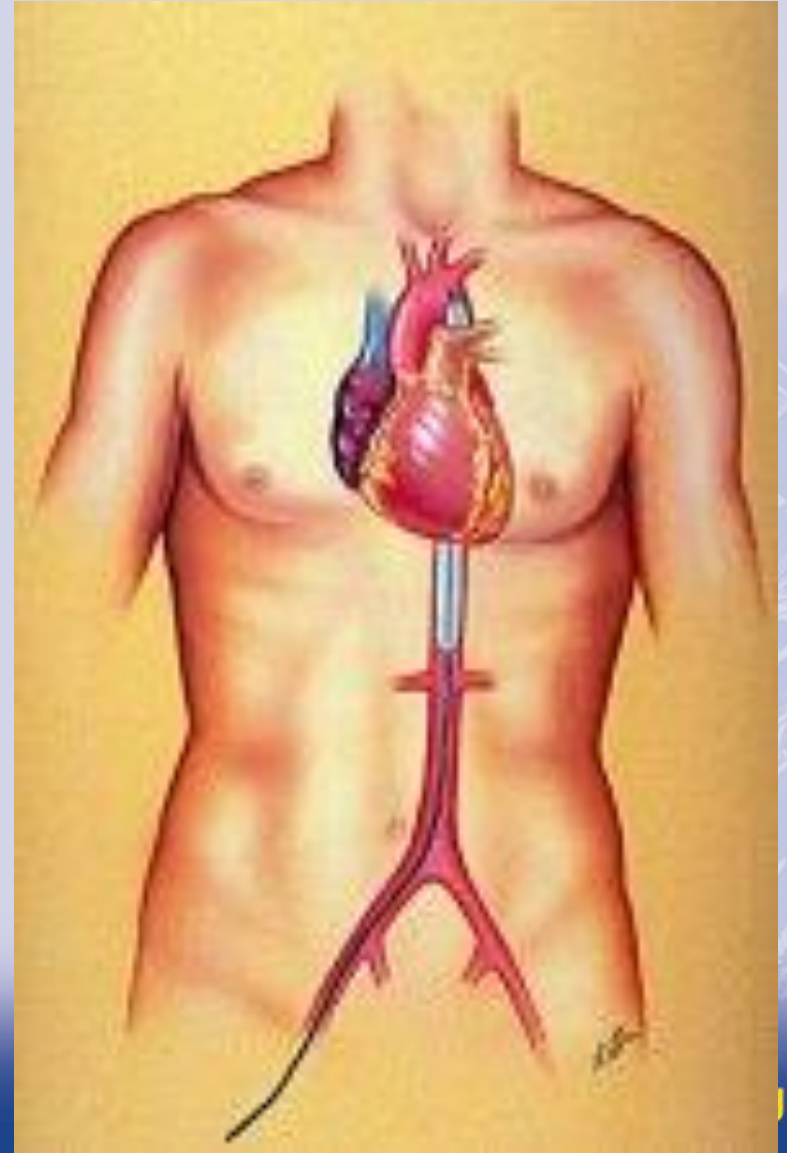
- Mechanism of dysfunction
  - Hypotension
  - Decreased tissue perfusion with progressive oxygen debt
  - Multiple organ dysfunction
    - ***Depression of cardiac function***
    - Worsening of tissue perfusion
    - Attempting to raise BP with vasopressors only worsens the oxygen deficit at the cellular level

# Ischemia / Reperfusion Syndrome

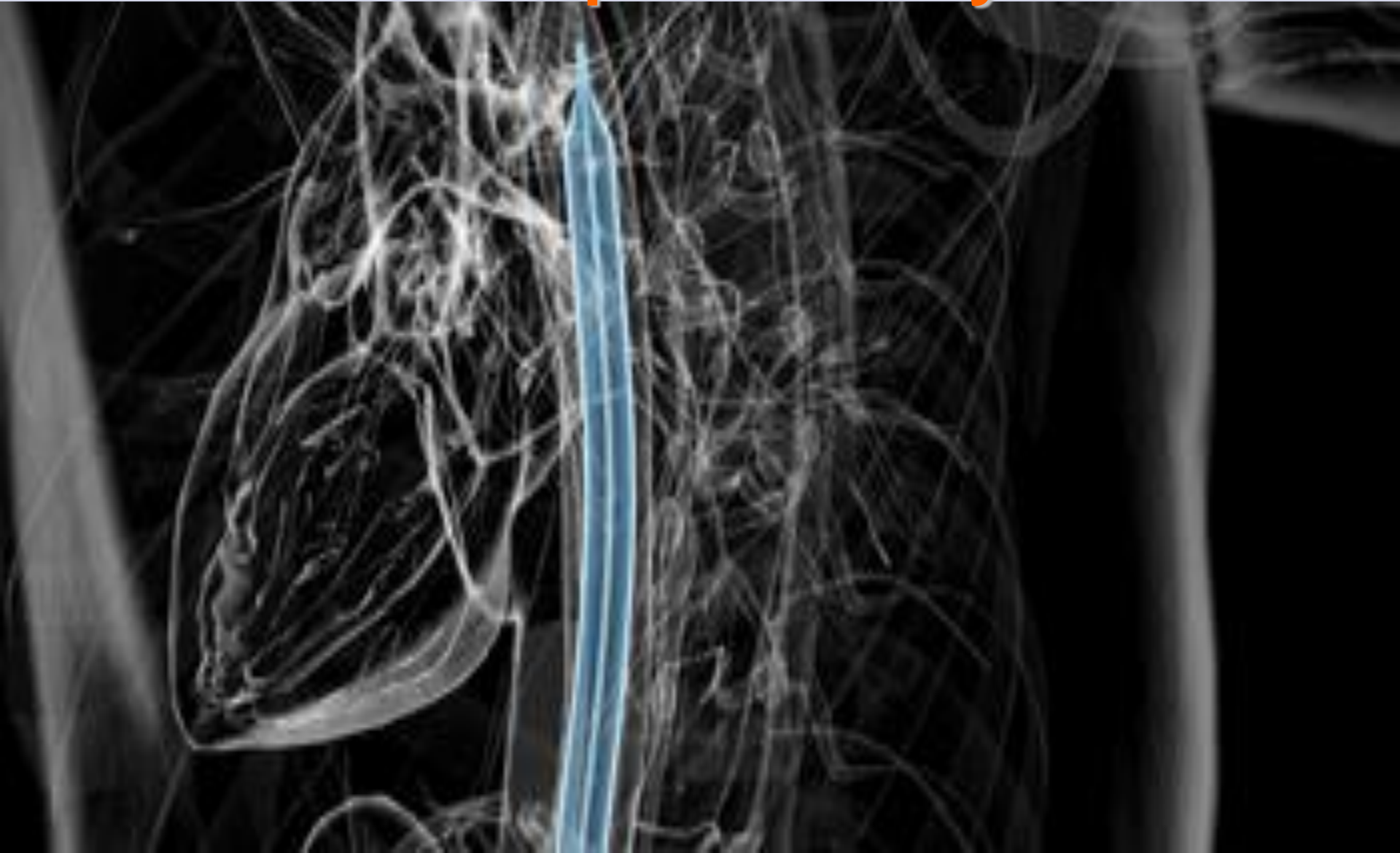
- Previously published our experience with the use of intra-aortic balloon counterpulsation for hemodynamic support in these high risk patients\*
- Inserted percutaneously through the groin and passed through the graft and into the thoracic aorta
- Set at 1:1 counterpulsation
- After stability achieved, IABP removed after rapid wean

\*Intra-aortic Balloon Counterpulsation as Adjunct to Aneurysmectomy in High-Risk Patients. Mayo Clinic Proceedings, Sept. 1981, Vol. 56

# Ischemia / Reperfusion Syndrome



# Ischemia / Reperfusion Syndrome



# Ischemia / Reperfusion Syndrome

- Immediately post-op
  - BP 70/50
  - Cardiac index 1.1 L/min/m<sup>2</sup>
  - Despite adequate fluid replacement and correction of acid-base imbalance
- 2 hours post-IABP insertion
  - Cardiac index 3.7 L/min/m<sup>2</sup>

# Ischemia / Reperfusion Syndrome

## Post-op Course

- Remained stable at 1/1 counterpulsation
- No anticoagulation
- Weaned progressively 1/2, 1/4, 1/8 over next 24 hours and IABP removed
- Remainder of hospital course uneventful

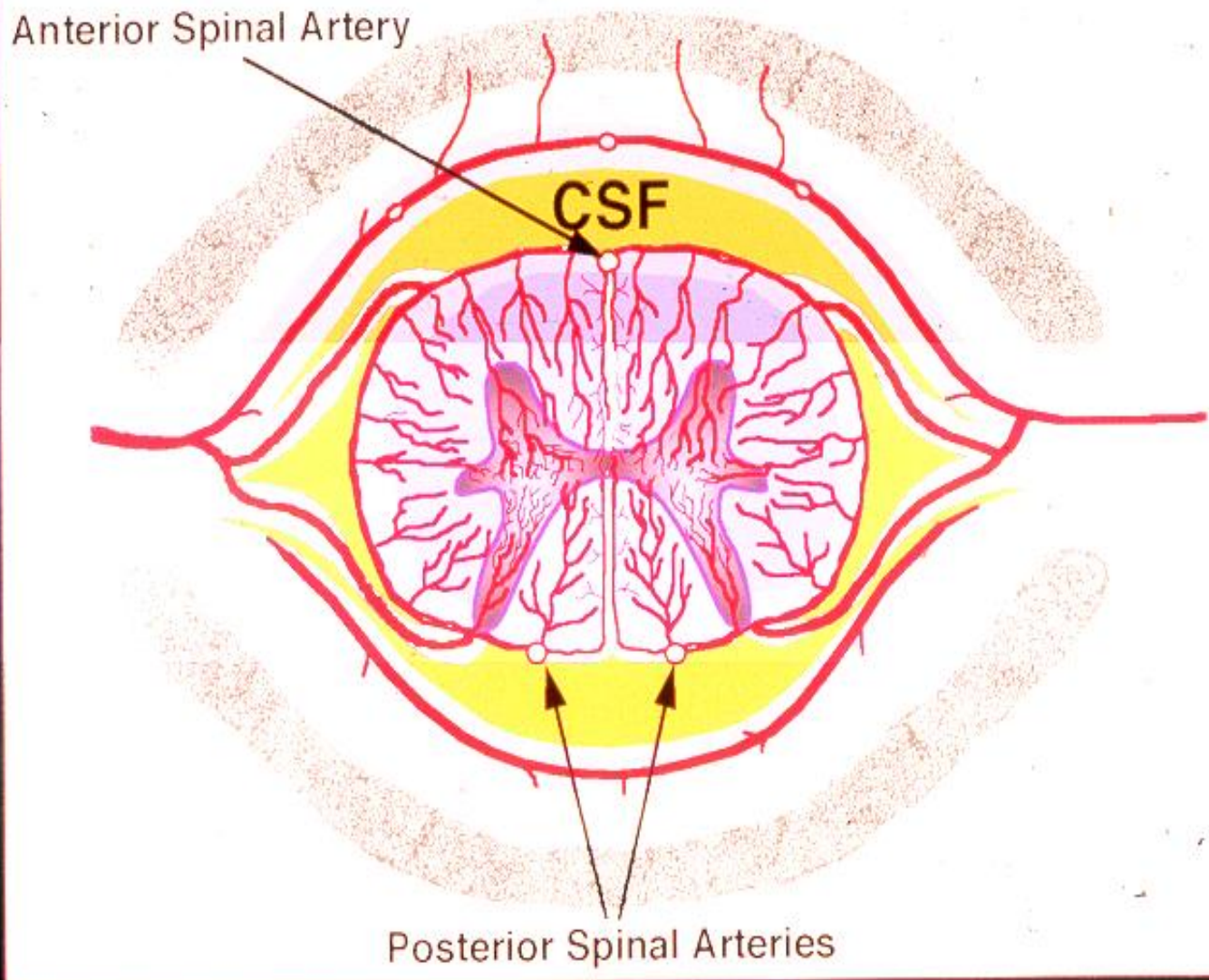
# Ischemia / Reperfusion Syndrome

- Therapeutic mechanism
  - Severe hypotension between time of rupture and time of repair resulted in severe tissue hypoxia
  - Cardiac dysfunction related to myocardial tissue oxygen debt further worsens the oxygen debt
  - IABP improves subendocardial perfusion and increases oxygen delivery to myocardium as well as to the other organs
  - IABP is perhaps the most expeditious way to improve oxygen delivery to all tissues of the body in this situation



# Ischemia / Reperfusion Syndrome

- Delayed-onset Paraplegia
  - Occurs usually 12-72 hours post-op
  - Due to:
    - Intermediate level of cord ischemia intra-operatively with progressive post-op cord edema and increasing CSF pressure
    - Prolonged gut ischemia with intra-operative activation of cytokines and secondary spinal cord injury (apoptosis, direct cytokine injury, non-reflow phenomenon)



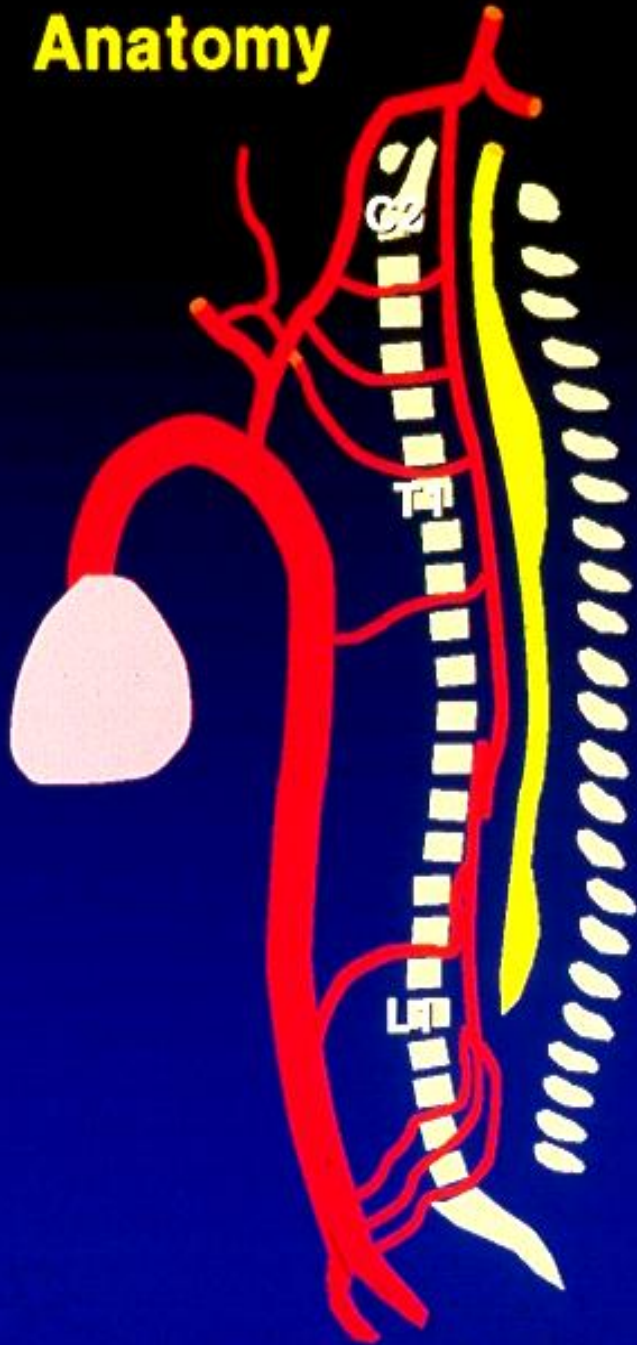
**Spinal Cord Perfusion = Spinal Artery Pressure - CSF Pressure**

# Ischemia / Reperfusion Syndrome

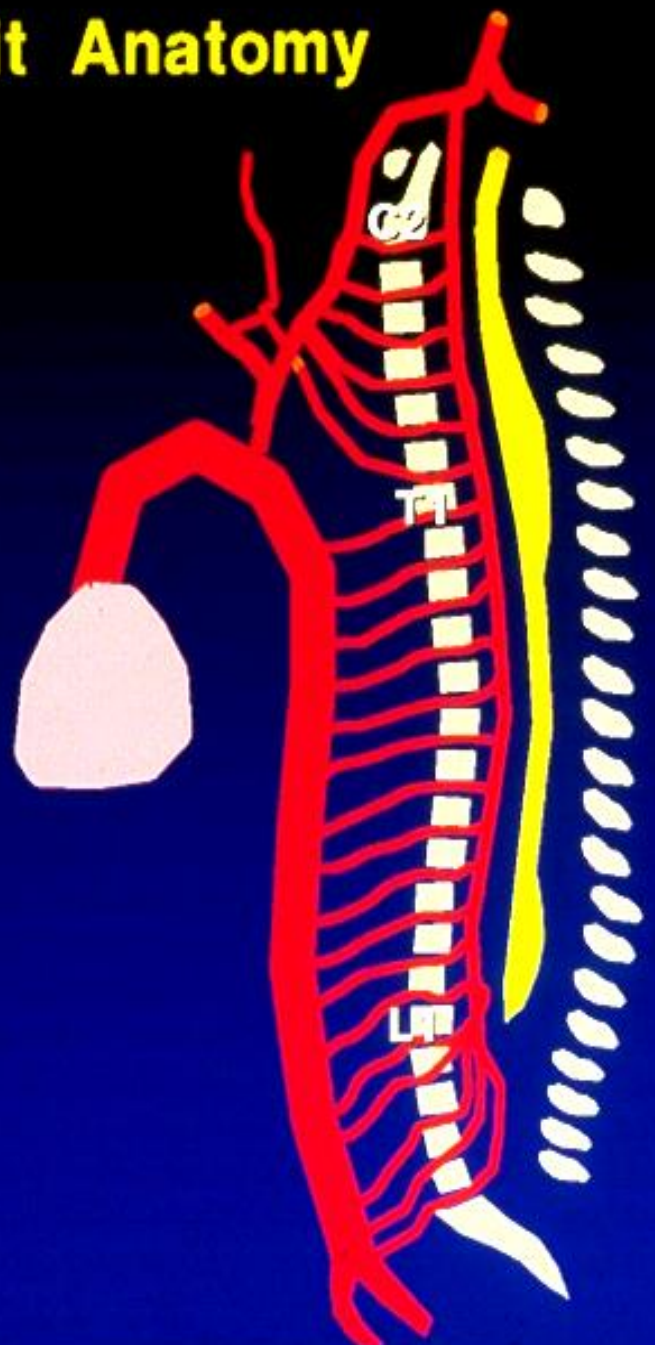
## □ CSF Drainage

- CSF drainage reduced the incidence of neurologic deficit and increased the safe ischemia time after thoracic aortic occlusion in dogs
  - McCollough, Hollier, 1987
- CSF drainage reduced the incidence of acute neurologic deficit in humans
  - Moore, Hollier, 1989

## Human Anatomy



## Rabbit Anatomy



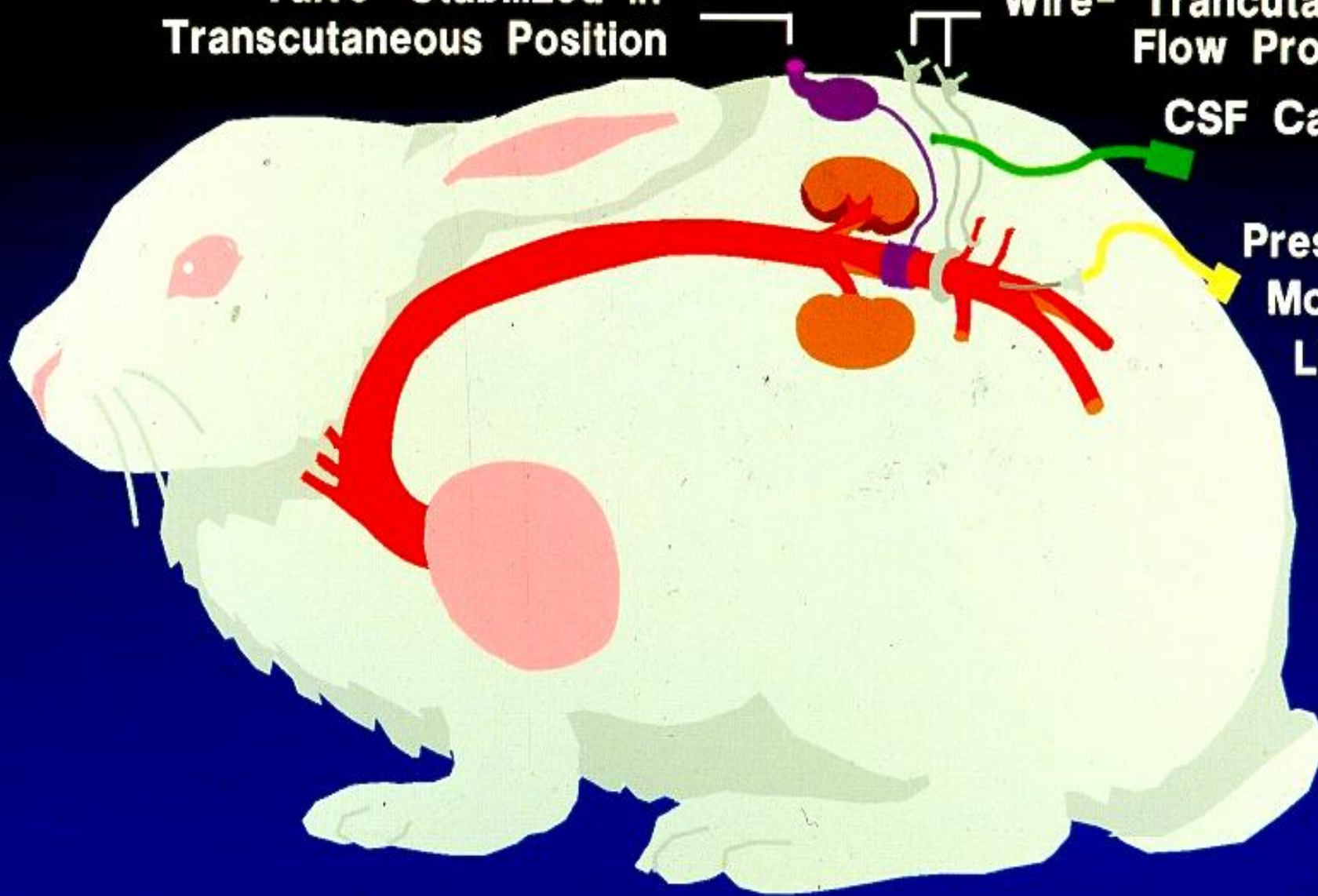
# RABBIT PARAGLEGIA MODEL UTILIZING DUNN OCCLUDER

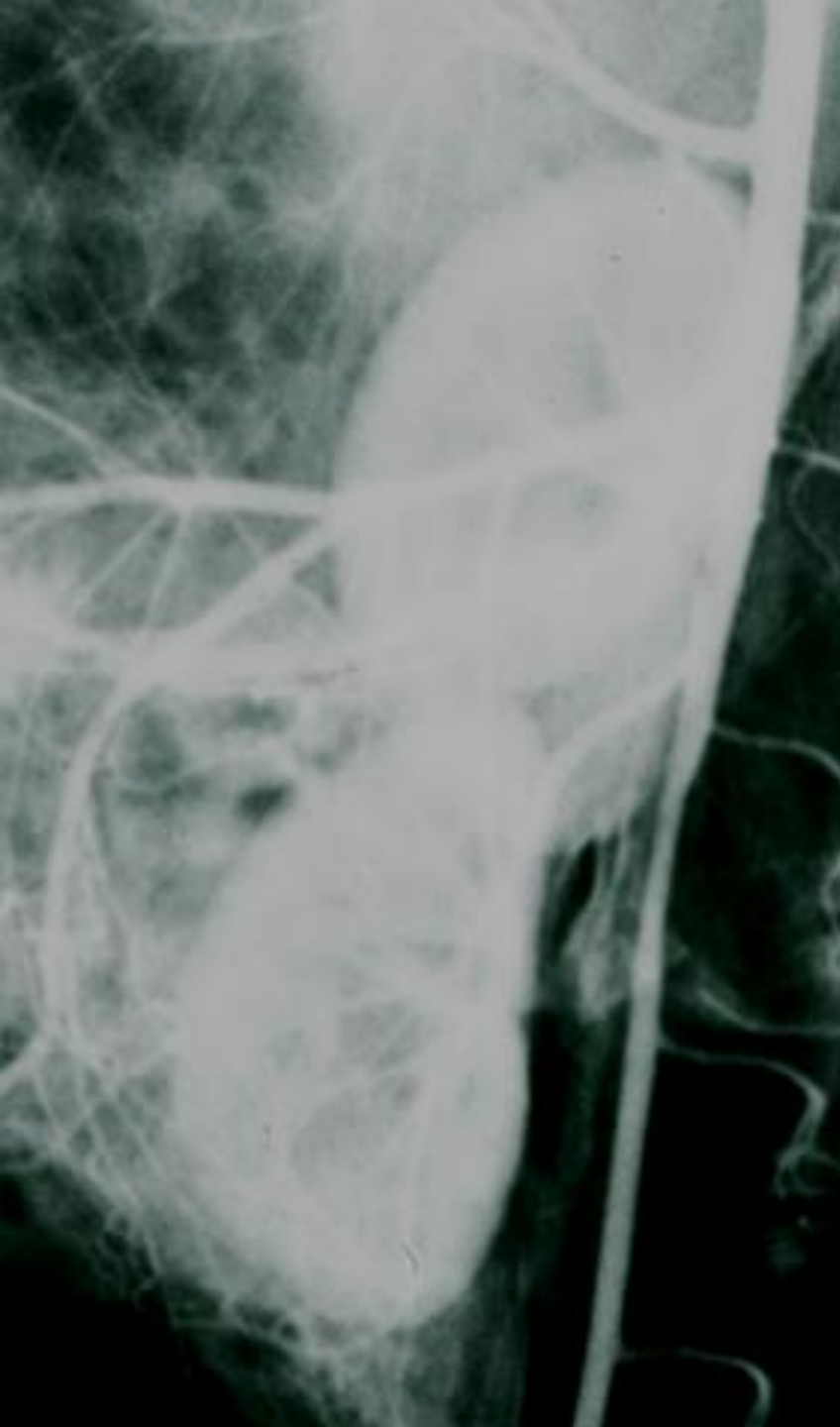
Valve- Stabilized in  
Transcutaneous Position

Wire- Transcutaneous  
Flow Probe

CSF Catheter

Pressure  
Monitor  
Line





## **DELAYED-ONSET PARAPLEGIA Results**

<b>Group</b>	<b>Duration of Ischemia</b>	<b>Normal</b>	<b>Acute Paraplegia</b>	<b>Delayed Onset</b>
<b>I</b>	<b>10-16 min</b>	<b>100%</b>		
<b>II</b>	<b>17-26 min</b>	<b>33.3%</b>	<b>9.1%</b>	<b>57.6%</b>
<b>III</b>	<b>&gt; 27 min</b>		<b>100%</b>	

# RABBIT PARAGLEGIA MODEL UTILIZING DUNN OCCLUDER

Valve- Stabilized in  
Transcutaneous Position

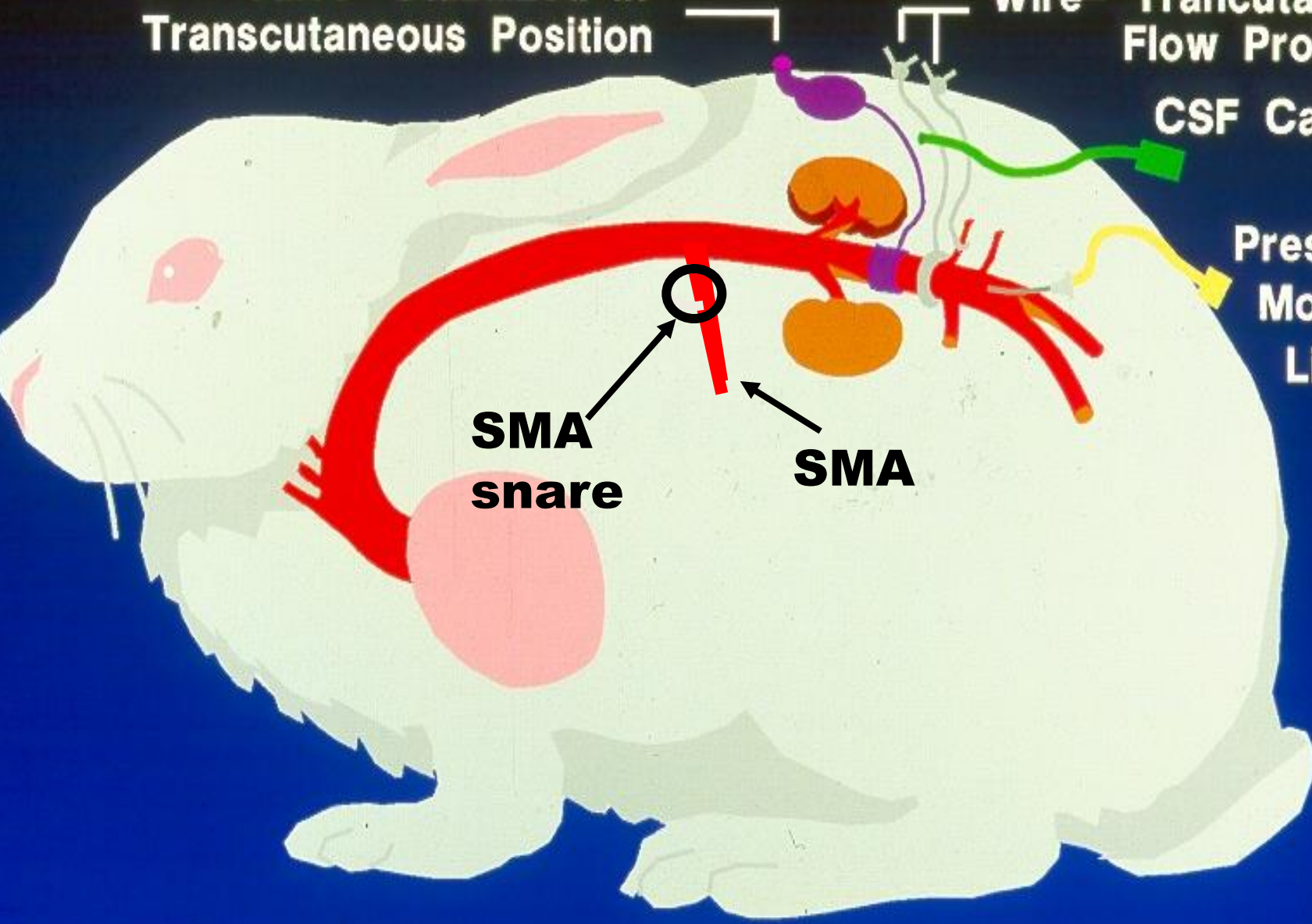
Wire- Transcutaneous  
Flow Probe

CSF Catheter

Pressure  
Monitor  
Line

SMA  
snare

SMA





# Results - Control

## Aortic occlusion alone - 12 minutes

- Neurologic Deficit 20%
  - Delayed onset paraplegia (1/10)
  - Acute paraplegia (1/10)

# Results – Group II

Aorta 12 mins.

***SMA 12 mins.***

- Neurologic deficit 81%
  - Acute paraplegia 4/11
  - Delayed paraplegia 5/11

P<0.05

# Results - Group III

Aorta 12 mins.

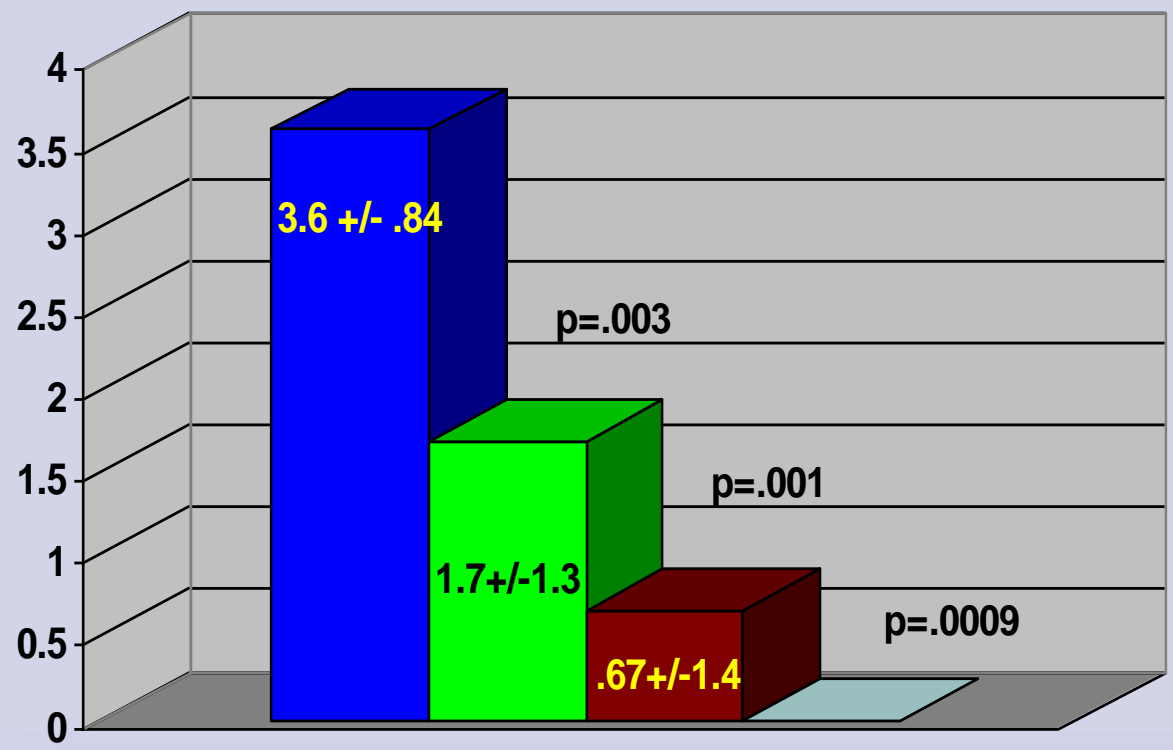
***SMA 18 mins.***

- Neurologic Deficit 100%
  - Acute paraplegia 6/10
  - Delayed paraplegia 4/10

P<0.05

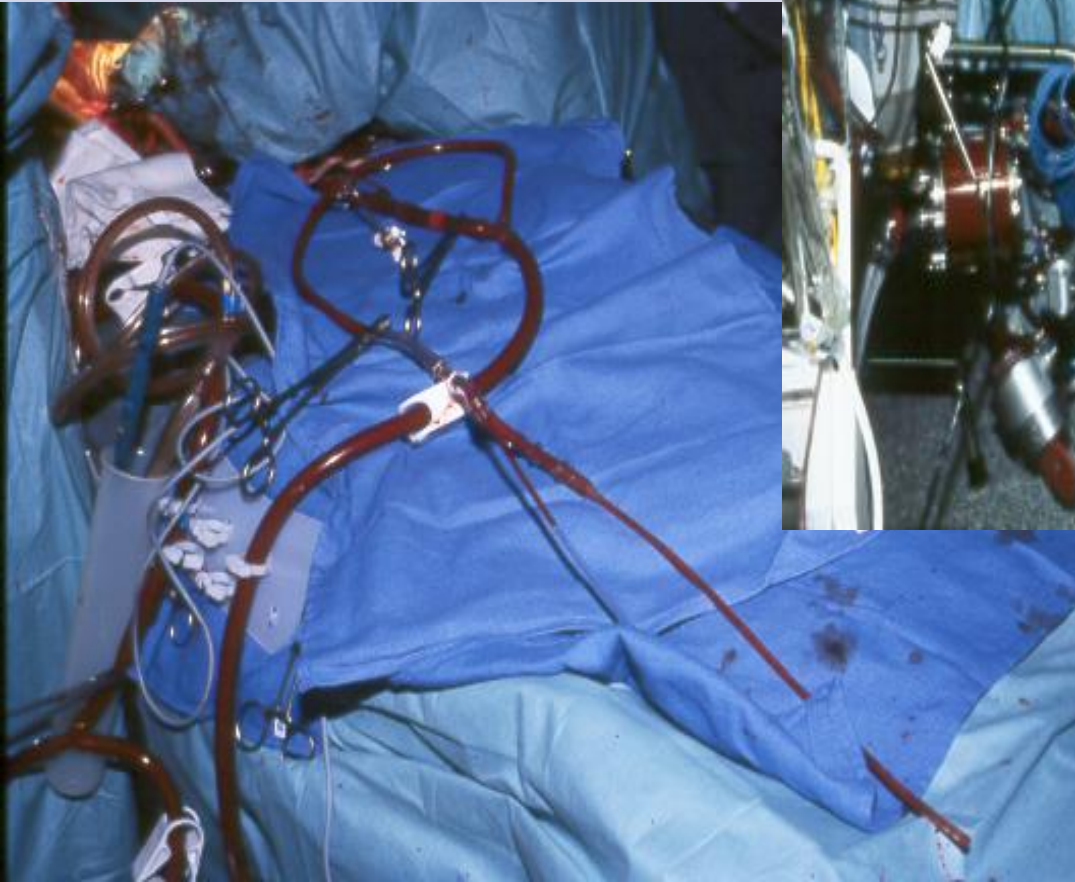
# Ischemia / Reperfusion Syndrome

## Tarlov Scores



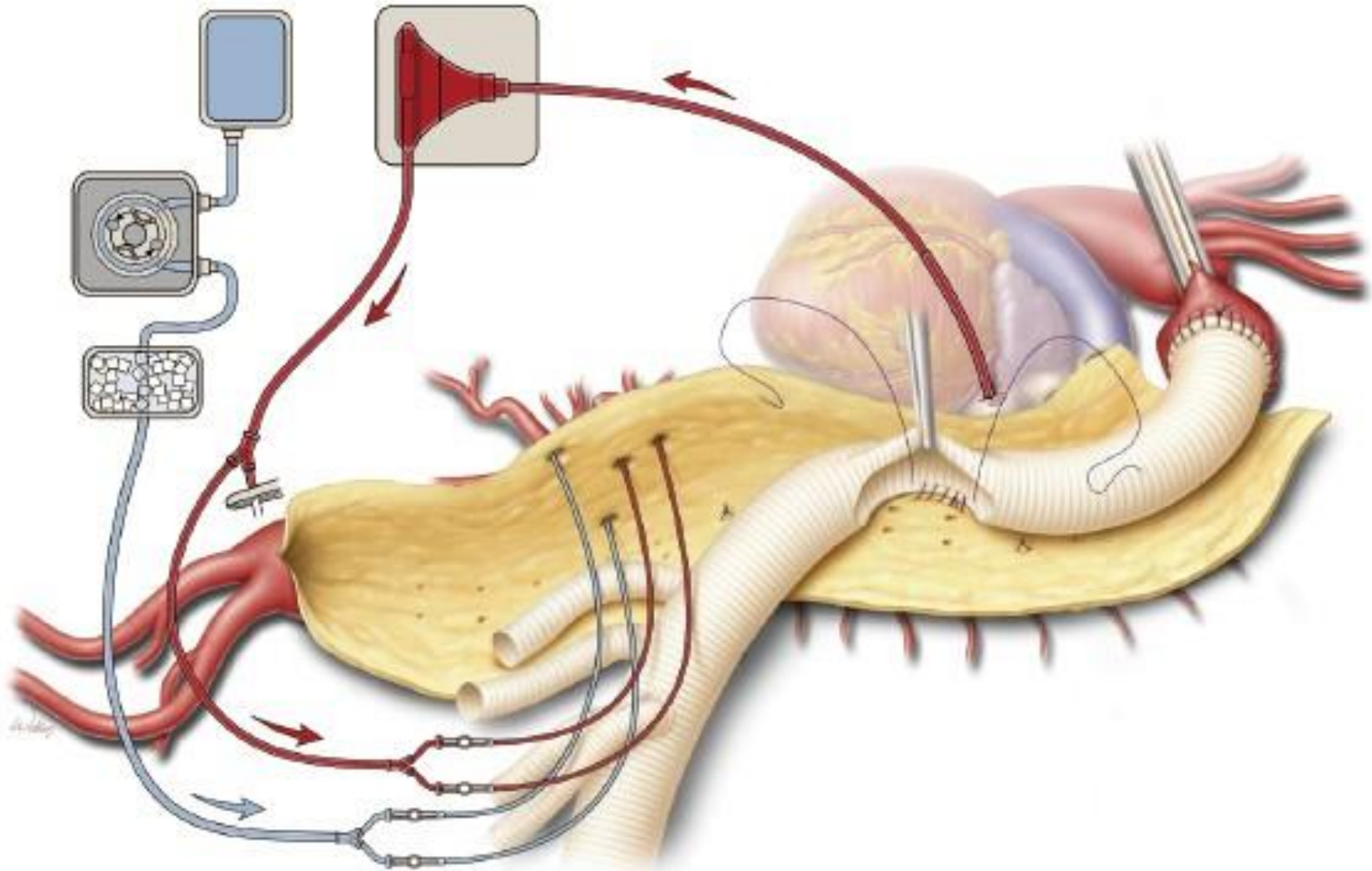
- Aorta 12 mins.
- Aorta 12 mins. SMA 10 mins.
- Aorta 12 mins. +SMA 12 mins
- Aorta 12 mins. + SMA 18

# Atrio-femoral or femoro-femoral bypass



# Axillo-femoral bypass graft

# Visceral Perfusion



**Visceral Perfusion  
Catheters**

**To prox. TA**

**Femoral "Shunt"  
sutured to left iliac**



# Visceral Perfusion





# Ischemia / Reperfusion Syndrome

- Visceral Ischemia / reperfusion
  - Activates injury cascade
    - Leucocyte and cytokine activation
    - Increase in TNF alpha, IL-1 beta, C3A
    - Production of adhesion molecules
  - Neurologic injury
  - Fibrinolysis
  - Pulmonary dysfunction
  - Cardiac dysfunction

## Ischemia / Reperfusion Syndrome

- The duration and severity of visceral ischemia is the single most important factor associated with post-operative multiple system organ dysfunction following repair of thoracoabdominal aortic aneurysms.

# Ischemia / Reperfusion Syndrome



# Ischemia / Reperfusion Syndrome

## Paraplegia following THAAA repair

- Decreased spinal cord perfusion during the procedure
  - (Recognize that even aorto-pulmonary bypass itself activates cytokines)
- Reperfusion activates cytokines resulting in spinal cord edema
  - Closed space (Starling resistor)
  - Cord swelling increases CSF pressure
  - Results in further decrease in cord perfusion
  - Activated cytokines and adhesion molecules further compromise microvascular perfusion

# Ischemia / Reperfusion Syndrome

- Ischemia / reperfusion syndrome is the most common cause of death in the intensive care unit
- In Severest Form:
  - Previously called “*multiple organ failure*” ( MOF) or “*multisystem organ failure* (MSOF)

# Ischemia / Reperfusion Syndrome

- Hypoxia cascade
  - Inadequate tissue oxygen delivery and inadequate cellular oxygen supply
  - Generalized inflammatory response with activated cytokines increases endothelial permeability with resultant edema and vessel obstruction by adherent neutrophils and platelets

# Ischemia / Reperfusion Syndrome

- Conventional Therapies
  - Volume resuscitation (fluid, blood, colloids)
  - Inotropic agents to improve cardiac performance and increase oxygen delivery
  - Improve oxygen input with ventilator support
    - Permissive hypercapnia and inverse ratio ventilation
  - Vasopressors (Levophed <“leave ‘em dead”>)
    - Further decreases capillary perfusion and cellular oxygenation