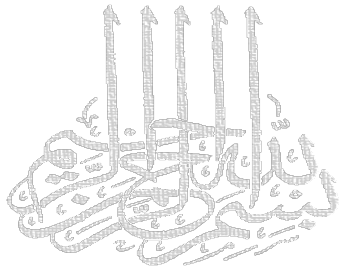


icu REACH
Spreading Knowledge · Improving Outcome

Pathophysiology of Brain Death

Give Life

Outline

- Intracranial pathalopgy leading to brain death
- Increased intracranial pressure and brain herniation
- Gross pathology of brain herniation
- Micropathalogy of brain death
- Pathophysiology of brain death
- Autonomic storm
- Hormonal abnormality

Speed Limit!

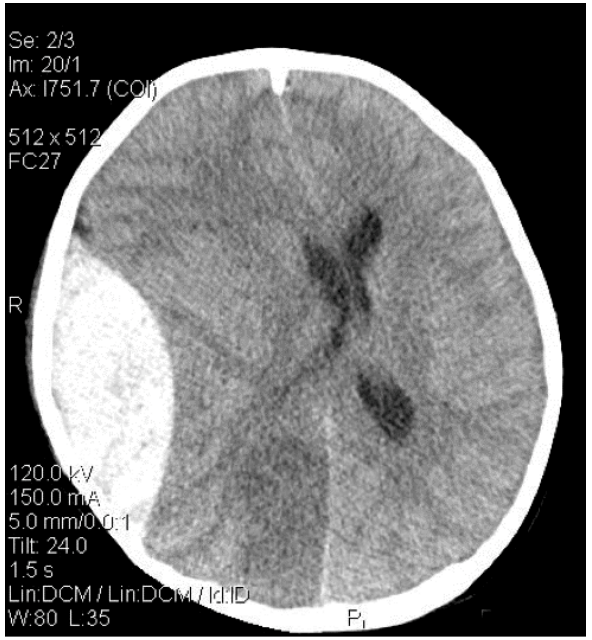

SCHOOL
SPEED LIMIT
25
CHILDREN ARE PRESENT
YOUR SPEED
42

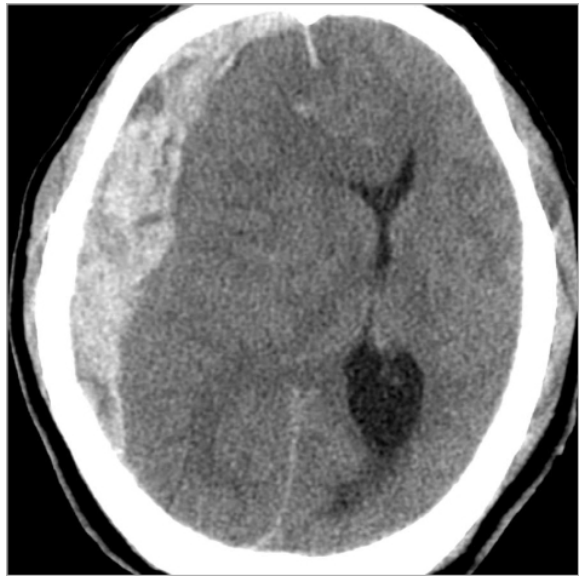

SPEED LIMIT
30
YOUR SPEED
49

Deadly Car Accidents

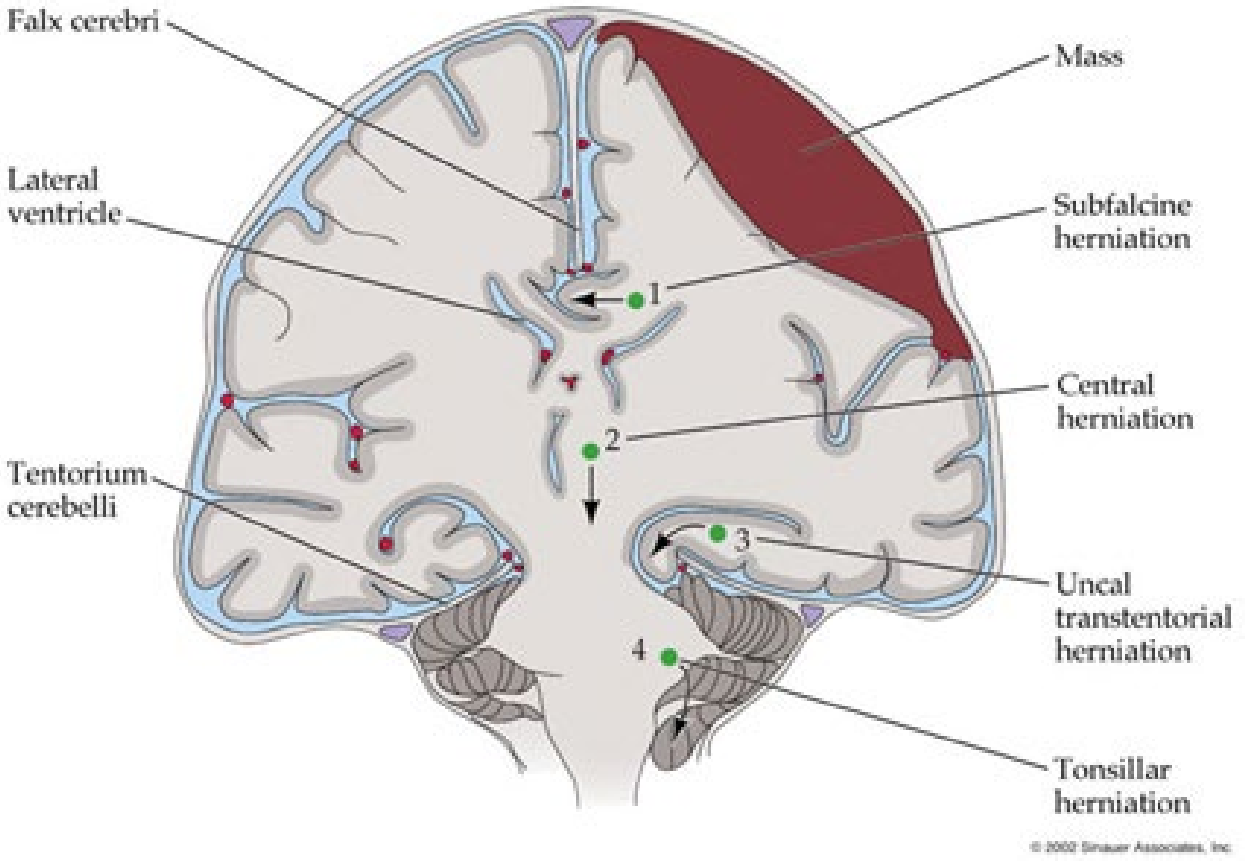
Catastrophic Brain Injuries

Intracranial Pathology





Brain Herniation Occurs due to Elevated Intracranial Pressure



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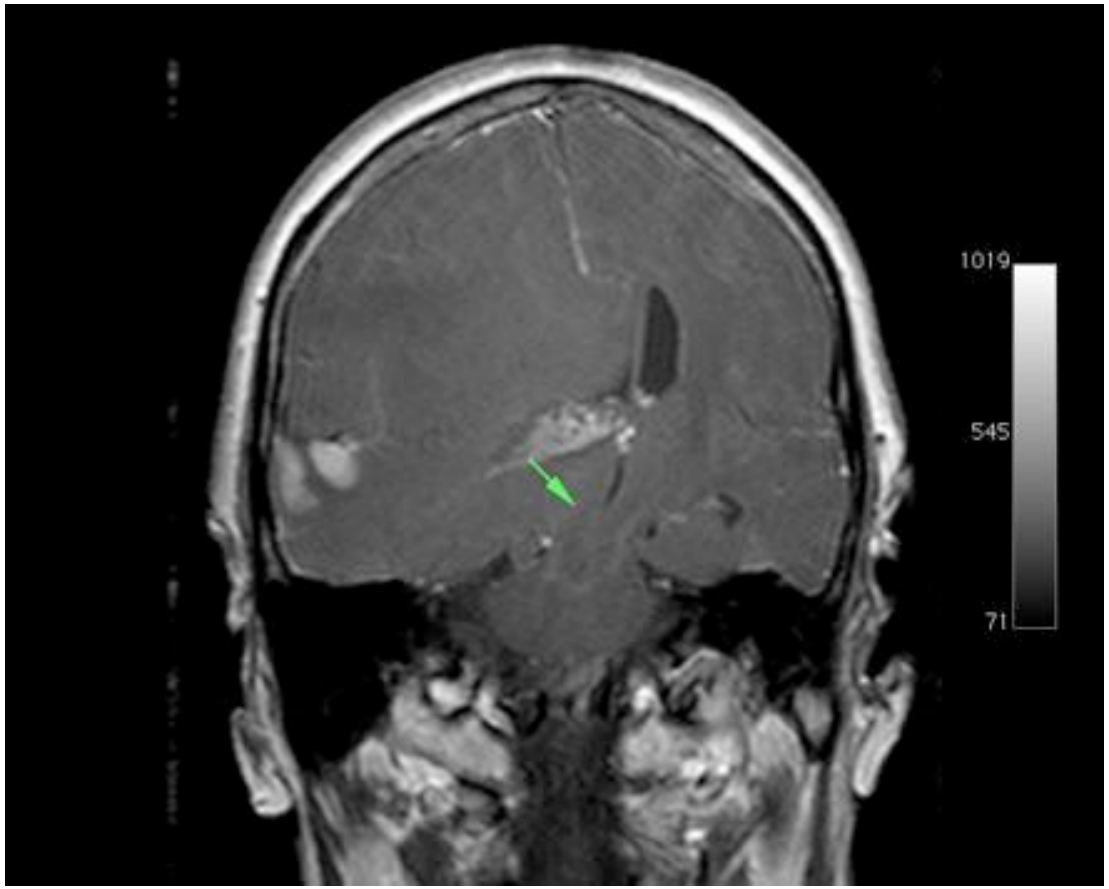
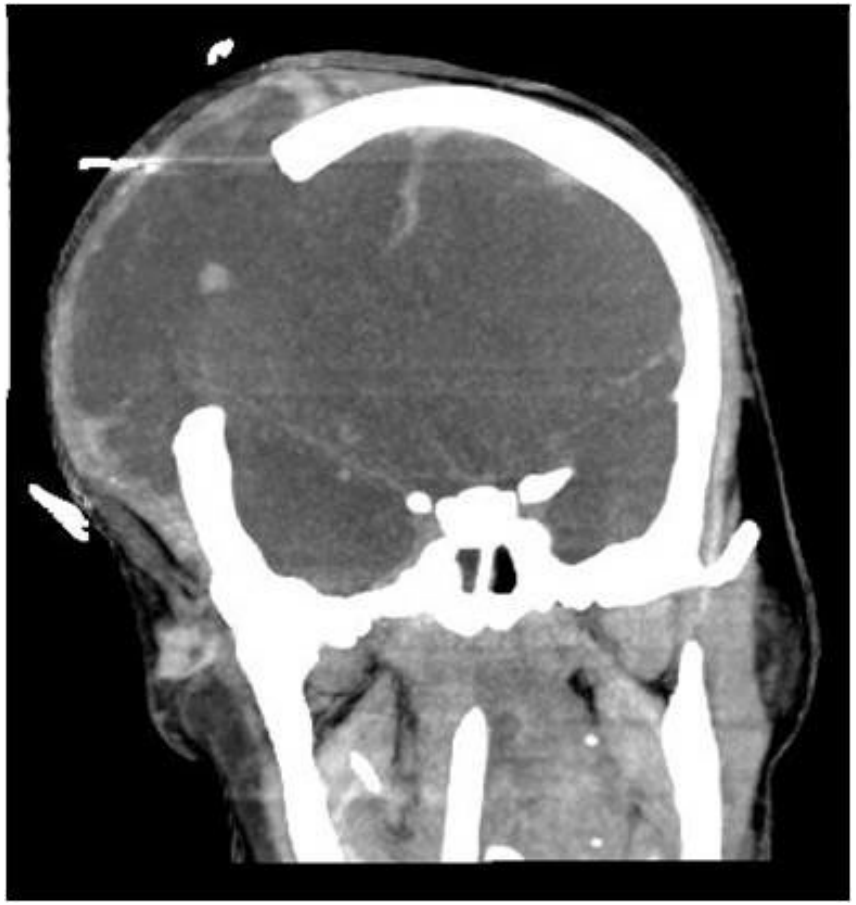
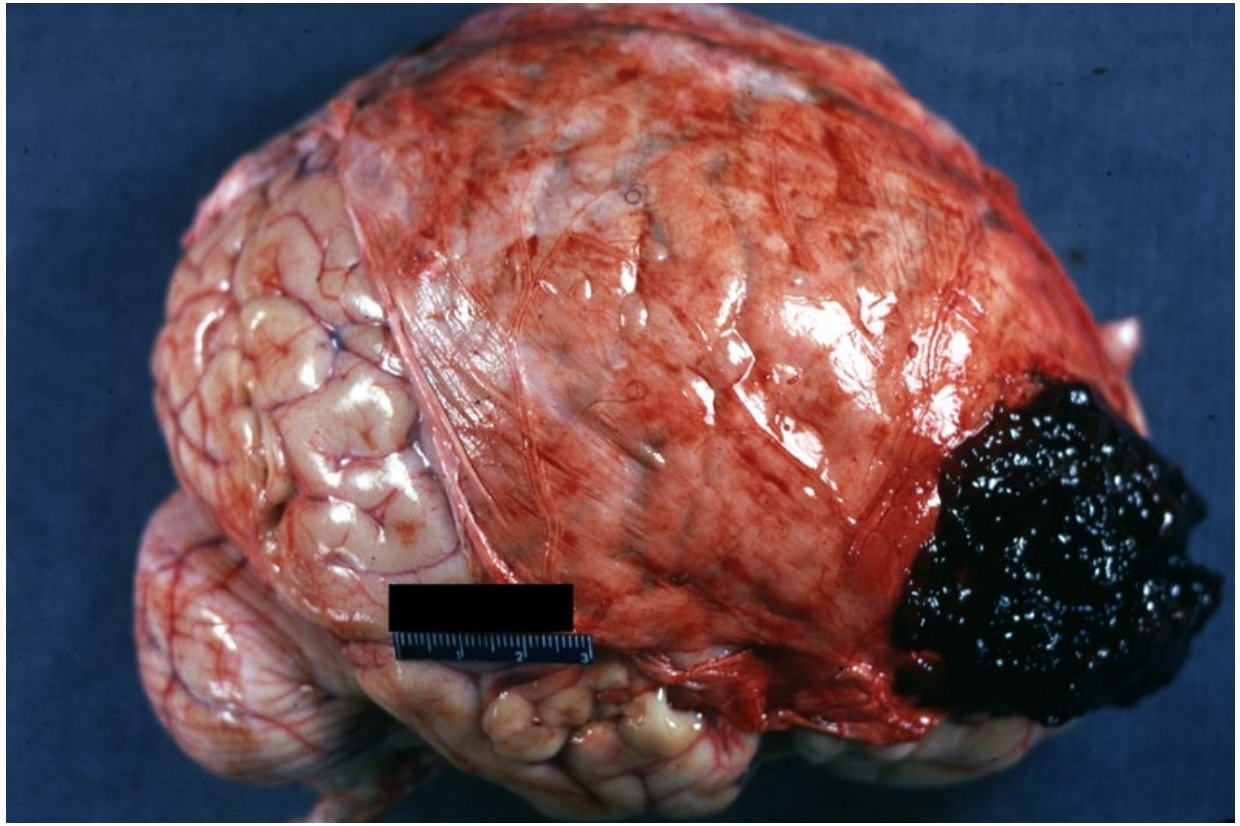
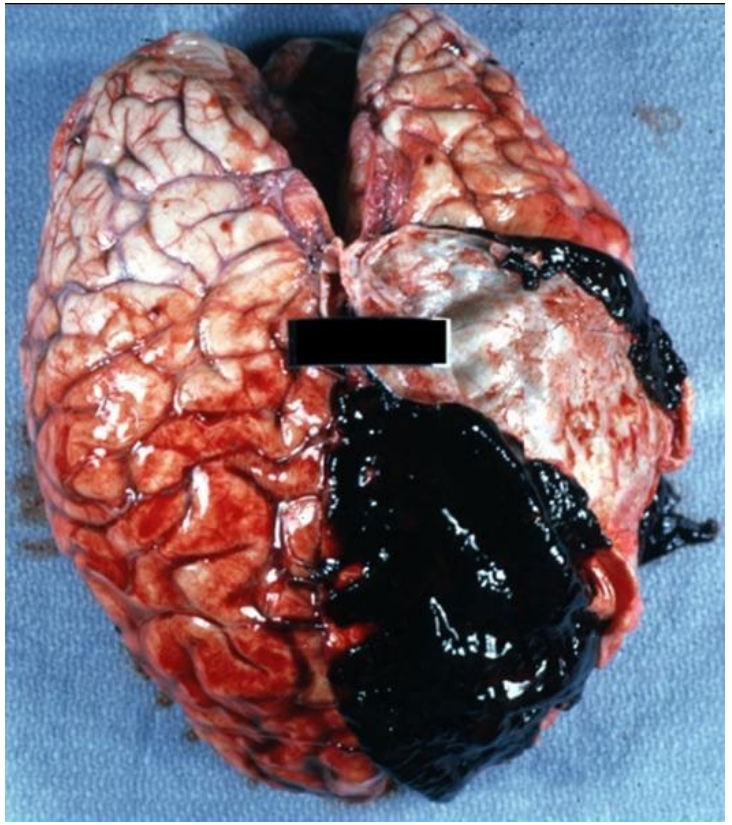




Gross Pathology

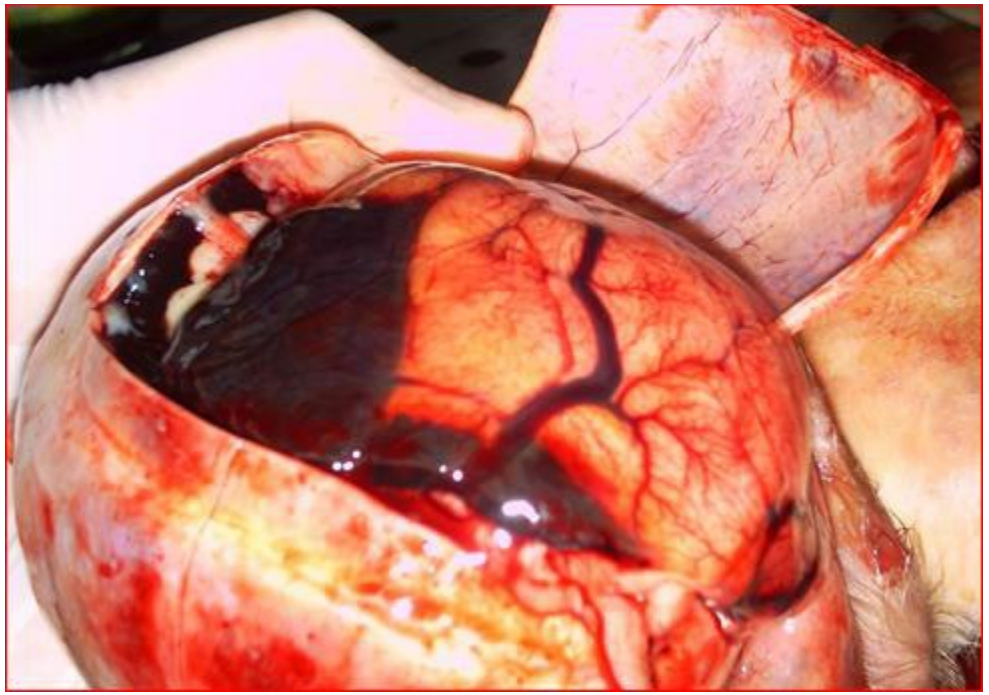


Epidural Hematoma



Subdural Hematoma

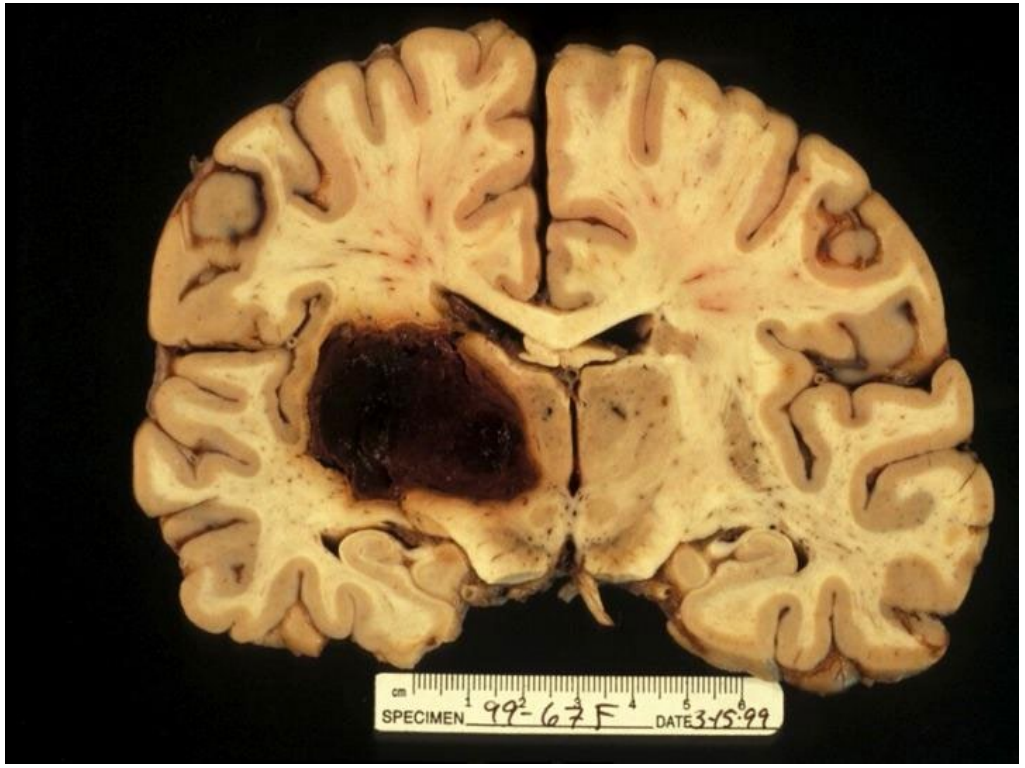
Gross Pathology

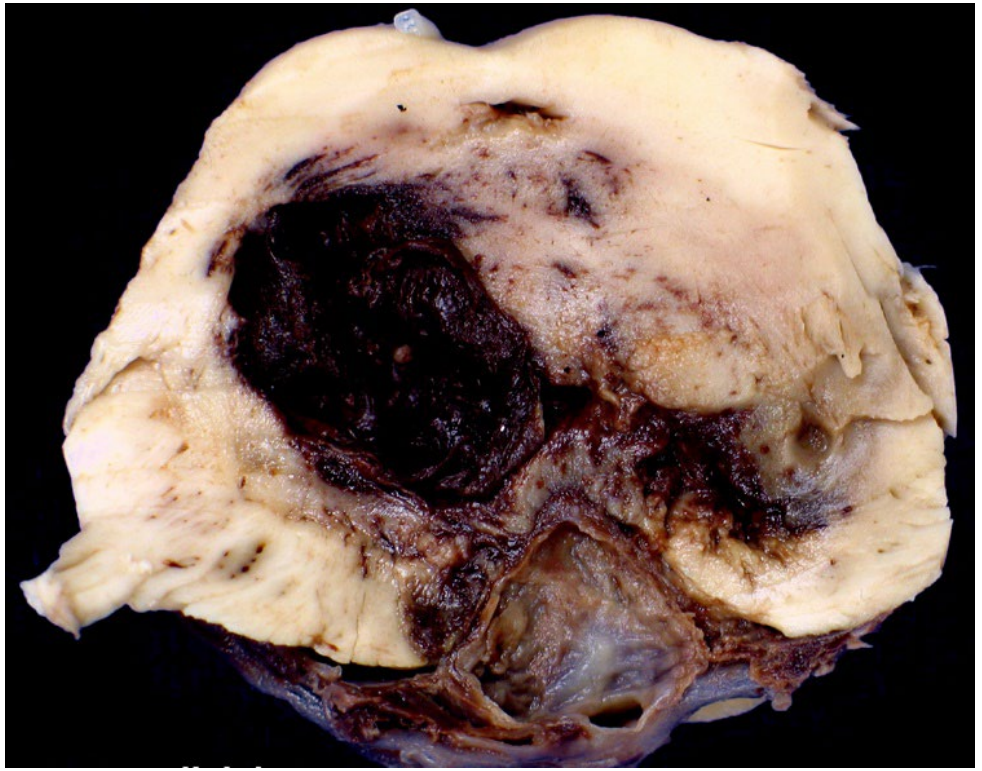


Subarachnoid Hemorrhage

Ruptured Aneurysm

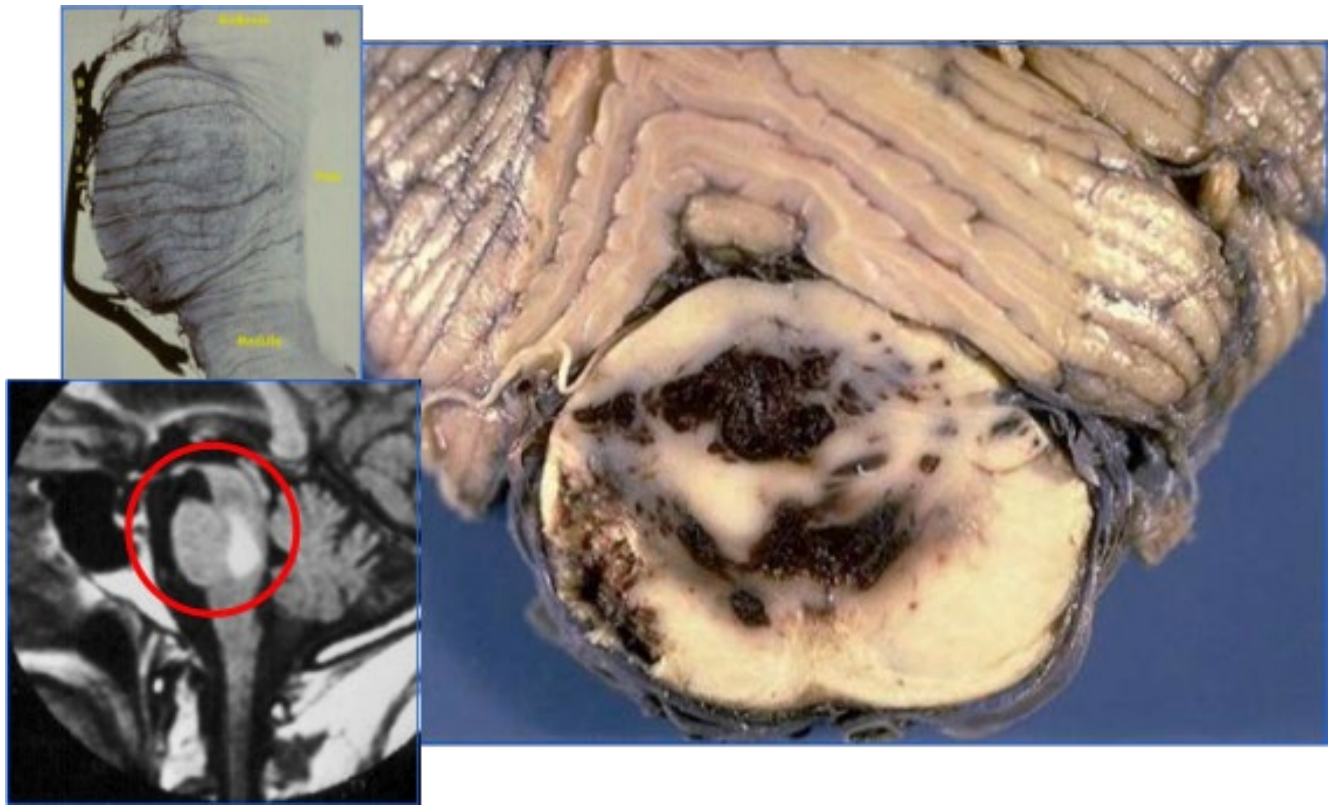
Gross Pathology

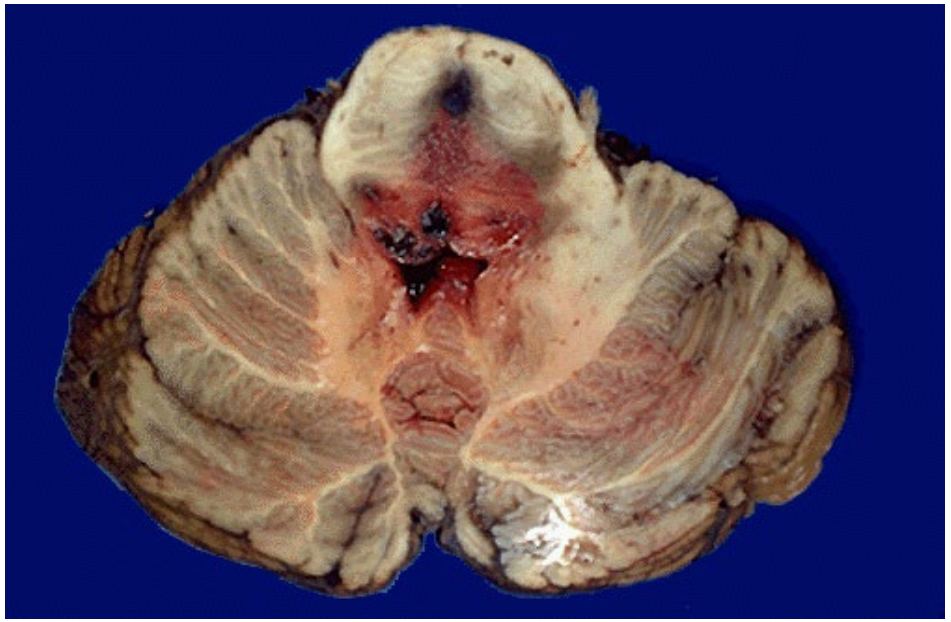




Cerebral Hemorrhage

Gross Pathology





Duret Hemorrhage

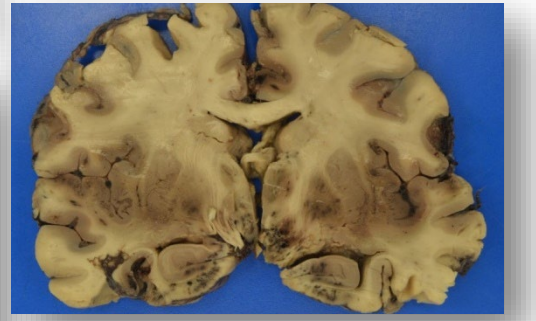
The end result of temporal medial lobe herniation is compression of the brainstem (midbrain and pons) and stretching of small arterial branches to cause Duret hemorrhages, as seen here in the pons

Gross pathology

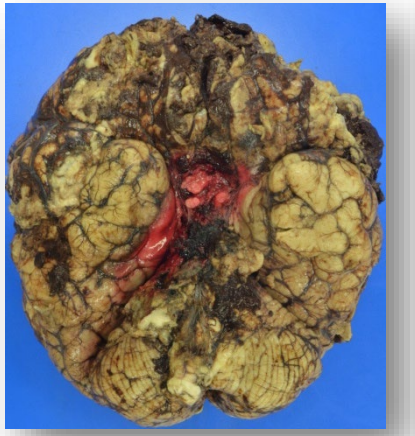
- Transtentorial herniation leads to compression of the brainstem with stretching and laceration of pontine perforating branches of the basilar artery or thrombosis and venous infarction. These lead to duret hemorrhages

- Brain will increasingly take on a dusky, congested, and discolored appearance once intracranial blood flow has arrested

Gross pathology specimens of tonsillar transtentorial herniation



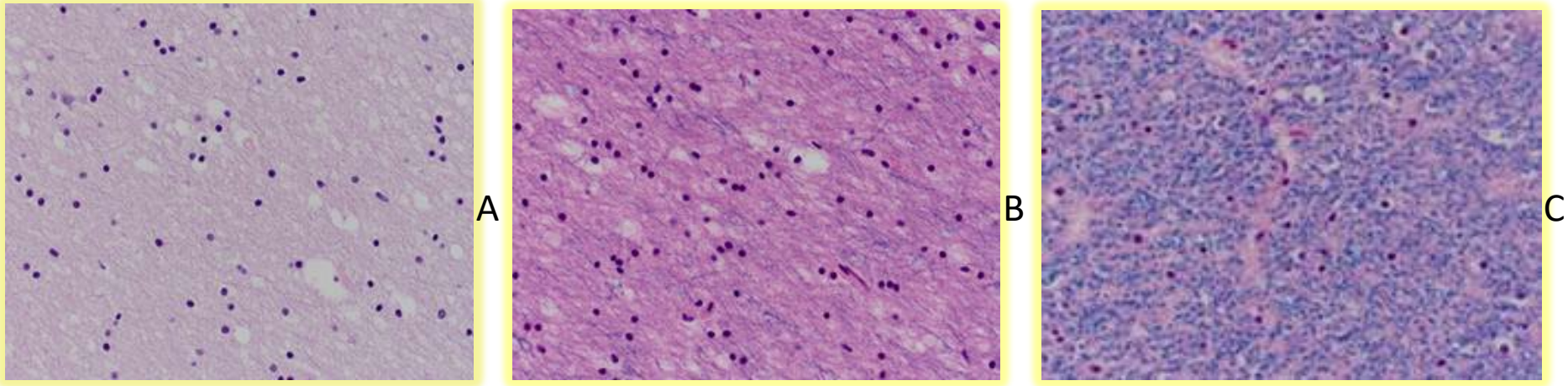
Gross pathology demonstrating uncal herniation



Duret hemorrhages

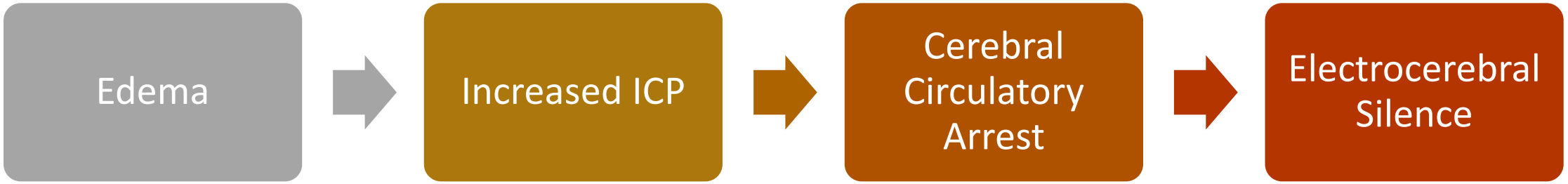
Micropathology

- Diffuse cytotoxic edema occurs throughout the gray and white matter, with intracellular edema occurring within the astrocytes in gray matter and within the oligodendroglial cell bodies, astrocytes, myelin sheaths, and axons in white matter
- Interstitial edema occurs in periventricular tissues presumably from CSF reabsorption and increased transependymal flow
- Autolysis is a phenomenon that occurs with anoxia related to release of intracellular compounds, which can be a result of delayed fixation, and can occur along with changes from brain death

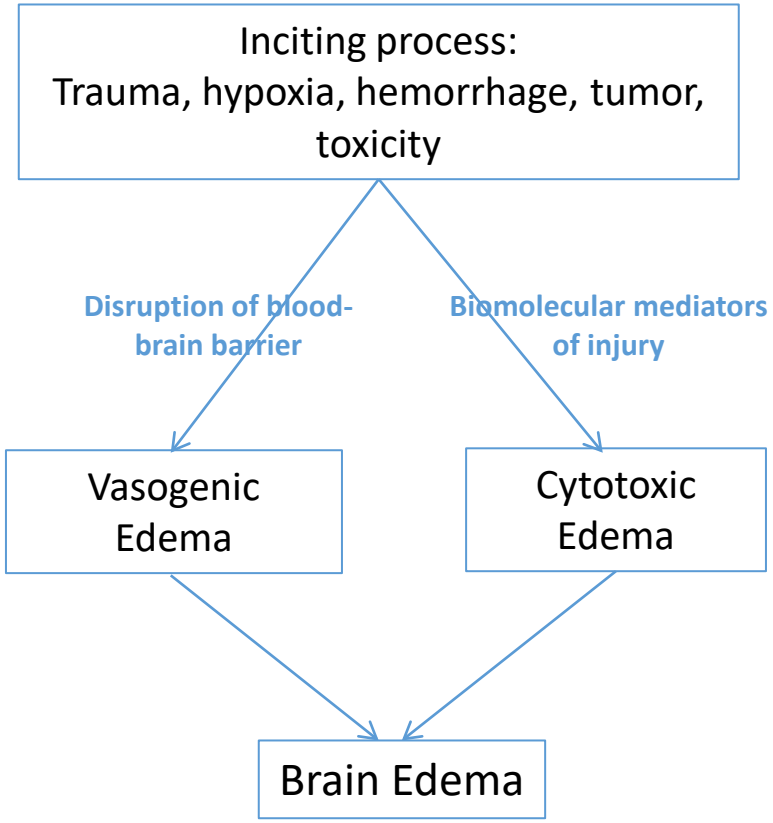


Micropathology slides show A) vacuolation of white matter and B) decreased myelin staining (LFB stain). Compare this with C) normal controls (LFB stain).

Pathophysiology of Brain Death

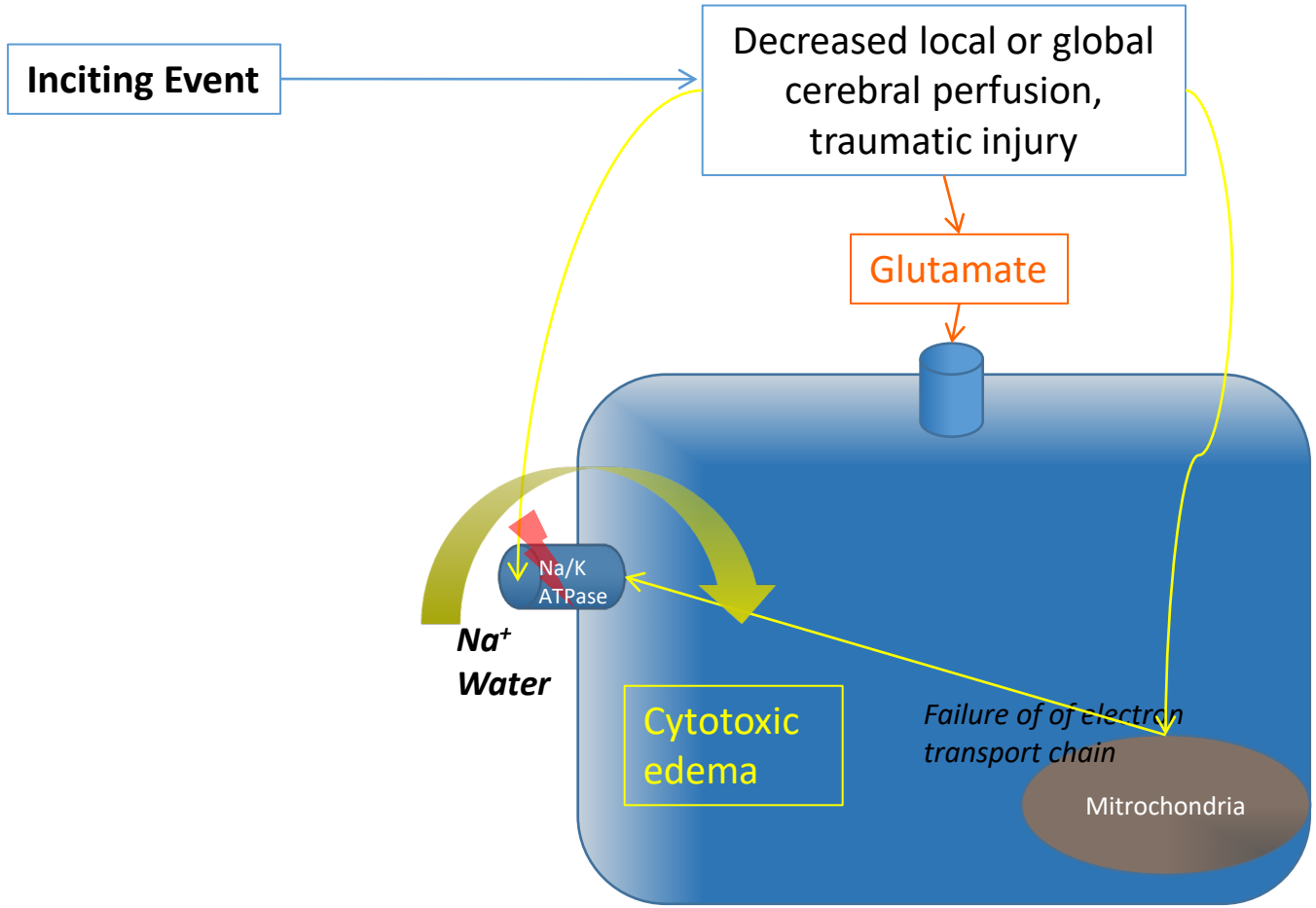


Mechanism of Brain Edema

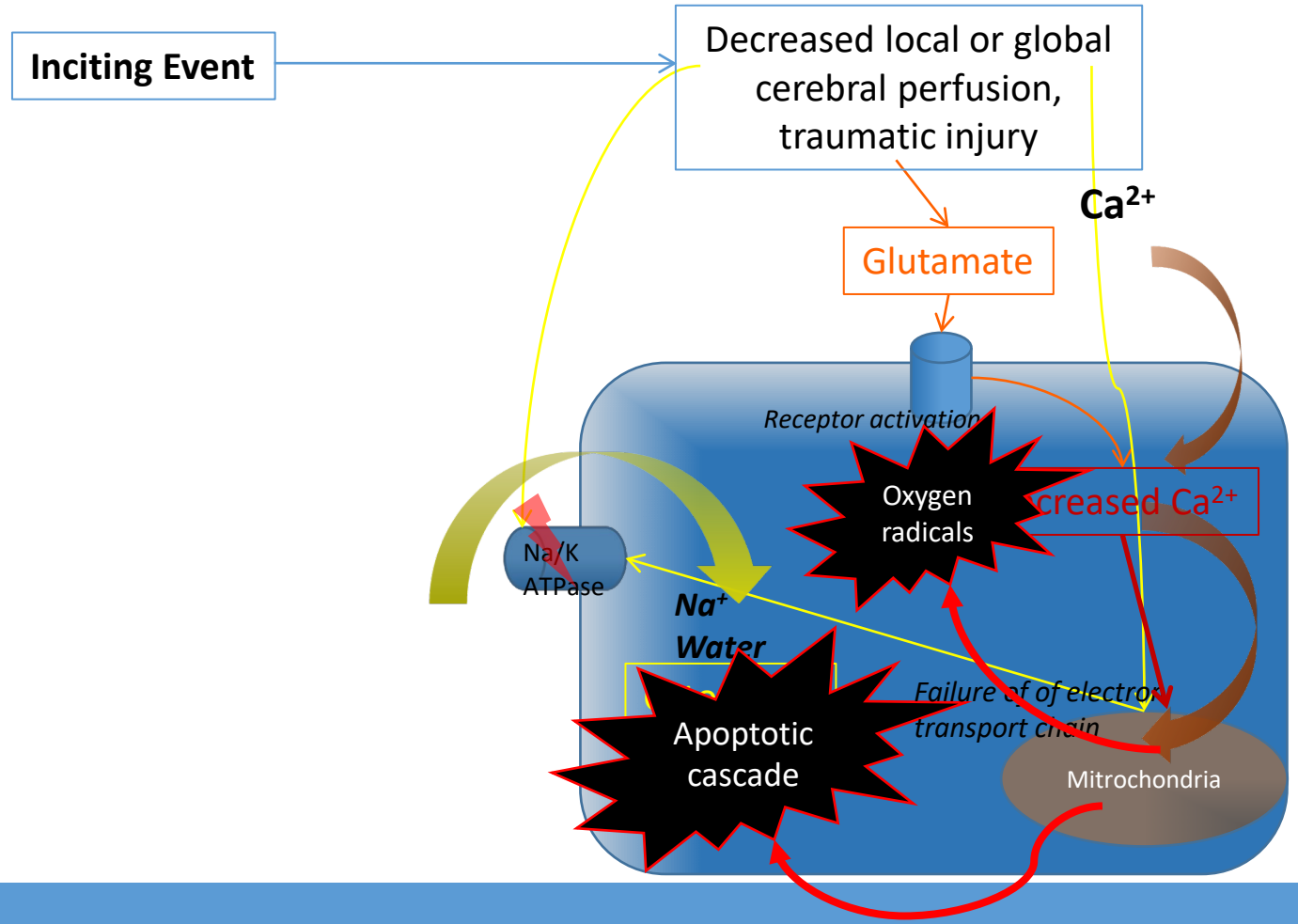


- Vasogenic edema
  - Extracellular edema caused by influx of water when blood-brain barrier is disrupted
  - Decreased cerebral perfusion causes alteration in blood gases with increased pCO_2 and causing secondary arterial vasodilation, contributing to extracellular water and edema.
- Cytotoxic edema
  - Intracellular edema of glial cells
  - Metabolically mediated
- The combination of vasogenic and cytotoxic edema increases brain volume, and have the potential to increase intracranial pressure.
- Edema is greatest by 24 to 72 hours after the event.

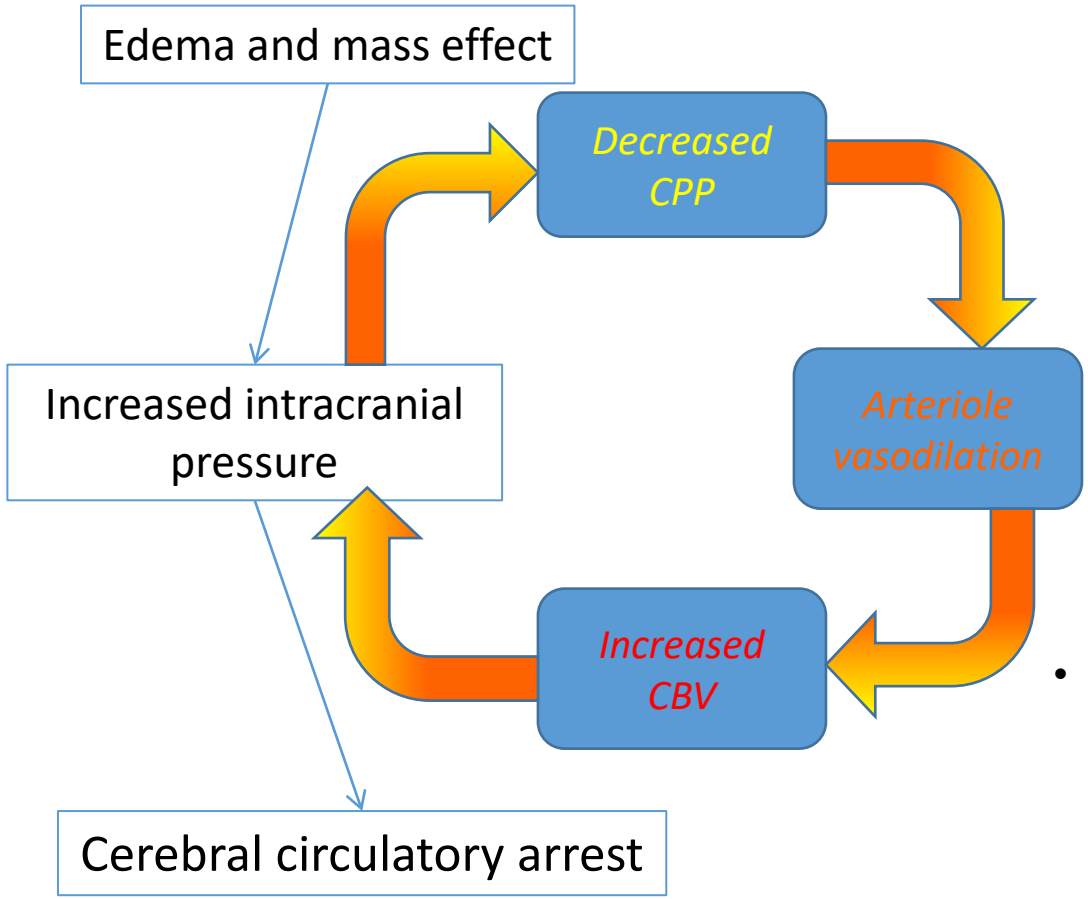
Cytotoxic Edema and Cell Death



Cytotoxic Edema and Cell Death



Increased Intracranial Pressure



Cerebral perfusion pressure (CPP) is the driving arterial pressure gradient across cerebral vasculature, and is related to mean arterial pressure (MAP) and ICP

CPP=MAP-ICP

Autoregulation is the process of maintaining cerebral blood flow over varying cerebral perfusion pressures. *Arteriole vasodilation* is the response to maintain cerebral blood flow over decreased cerebral perfusion pressures.

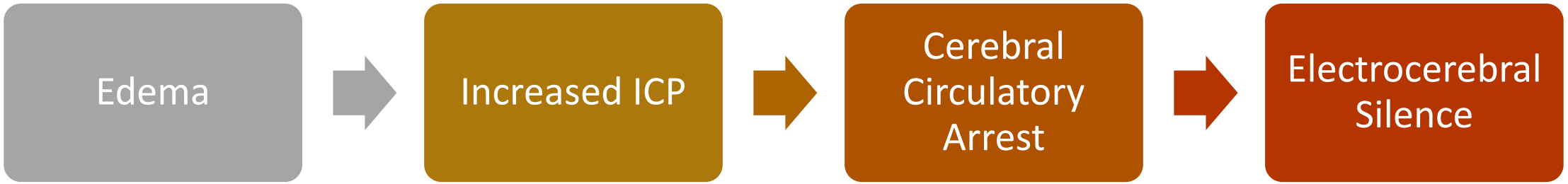
- This vasodilation leads to an *increase in cerebral blood volume*

A vicious cycle may ensue in which increases in CBV cause further increases in ICP, and the cycle begins again by decreasing CPP

Intracranial Pressure and Intracranial Volume Regulation

- Total intracranial volume = Blood + CSF + Brain tissue + Water
- The rigid cavity of the skull leaves very limited ability to compensate for swelling, edema, or mass effect.
- Compensatory mechanisms for increased brain volume include decreasing CSF (decreased production, increased absorption, shunting to spinal subarachnoid space) or shunting venous blood
- The main compensatory process for restoring equilibrium is CSF reabsorption. When most of the CSF has been reabsorbed, the brain will occupy the areas previously occupied by CSF, leading to herniation

Pathophysiology of Brain Death



Eventually venous congestion results, causing further increases in ICP.
As edema develops, a threshold is reached in which ICP rises exponentially to small changes in edema.

When intracranial pressure exceeds diastolic pressure, there is loss of perfusion

Early Donor Hear Failure following Transplantation

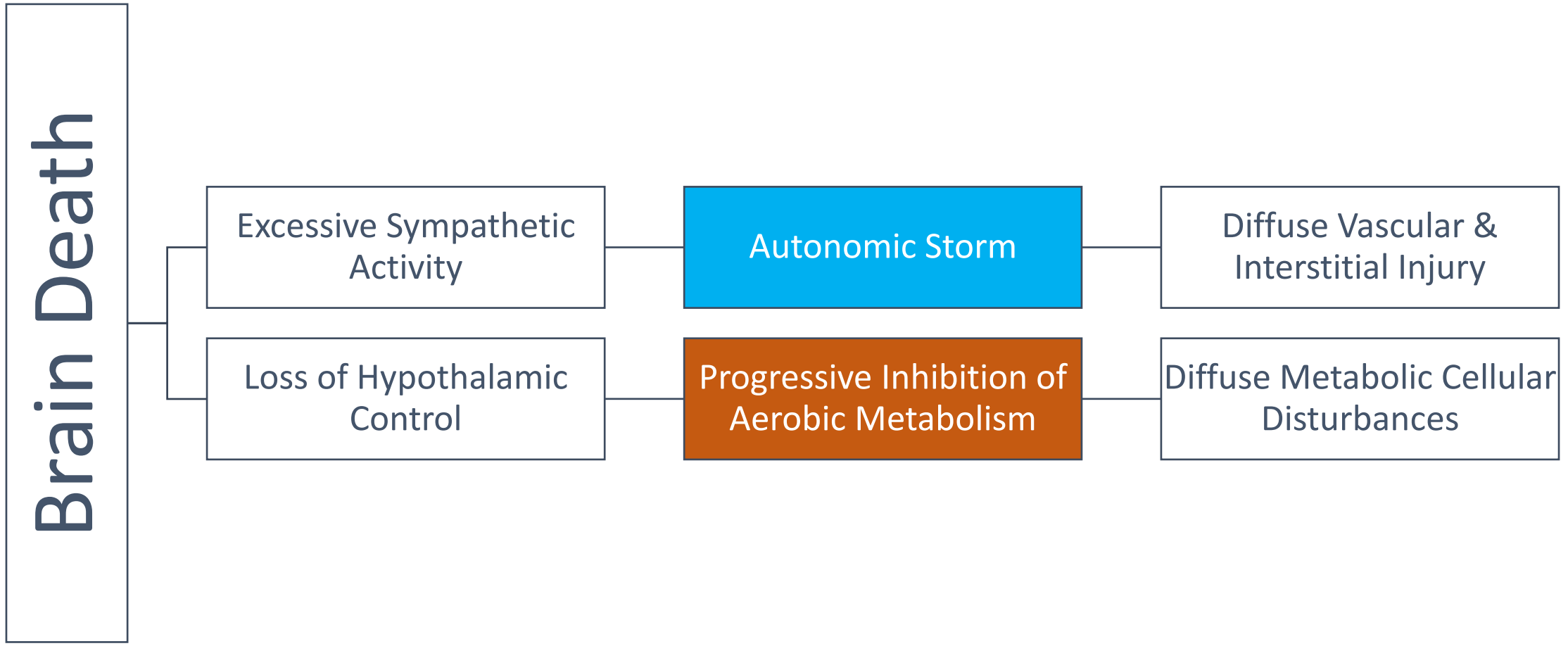
The possible Role of Myocardial Injury During Brain Death

20% of donor hearts from brain dead potential organ donors were deemed unsuitable for transplantation due to Irreversible hemodynamic deterioration

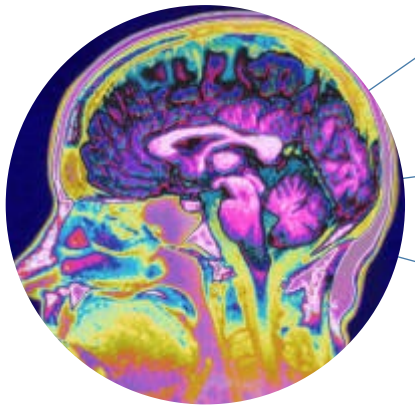
Significant number of hearts that, although appearing functionally satisfactory before excision from the donor, did not function adequately after tranplantation

Novitzky, D. et al Clin Transplant. 1987;1:108-13

Changes Associated Brain Death



Physiologic Changes Associated with Severe Brain Injury and Brain Death



Autonomic (sympathetic) storm

- Cusshing's triad
- Catecholamine surge
- Increased systemic vascular resistance
- Severe hypertension
- Stunned myocardium
- Cardiac arrhythmias

Loss of sympathetic tone

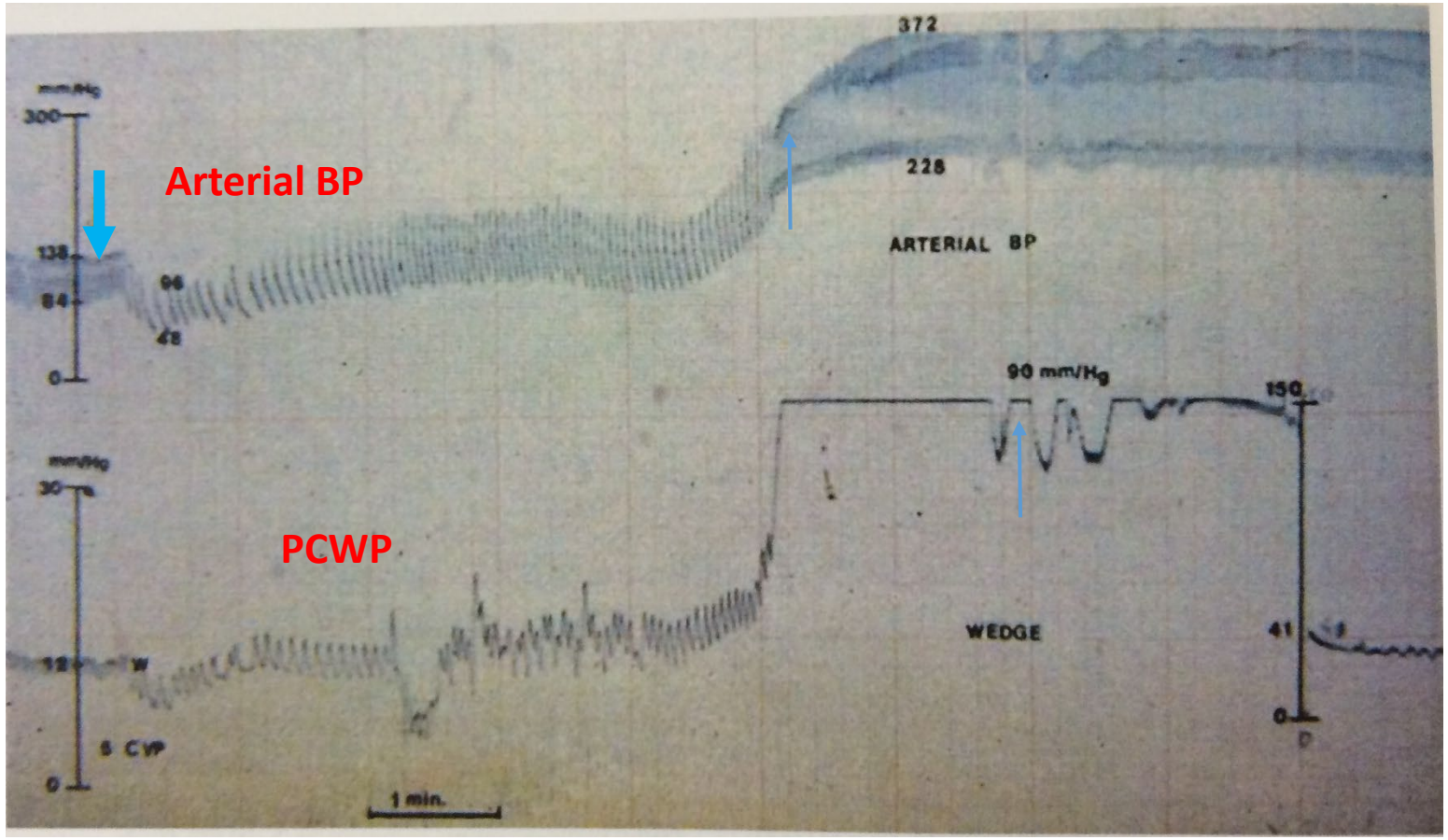
- Hypotension
- Hypothermia

Disruption of pituitary axis

- Decreased T3, Arg-VP, cortisol and insulin
- Anaerobic metabolism
- Endothelial activation
- Cytokines, immune, etc.

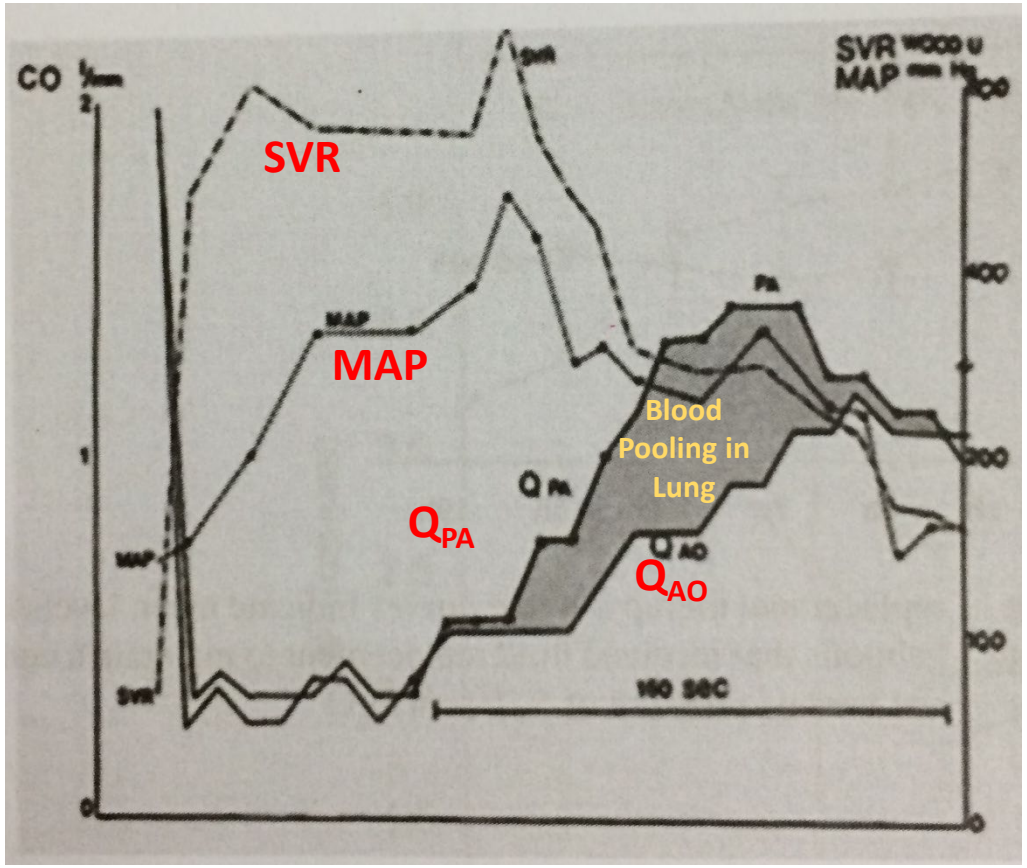
Autonomic Storm

Hemodynamic Changes after Induction of Brain Death in the Baboon



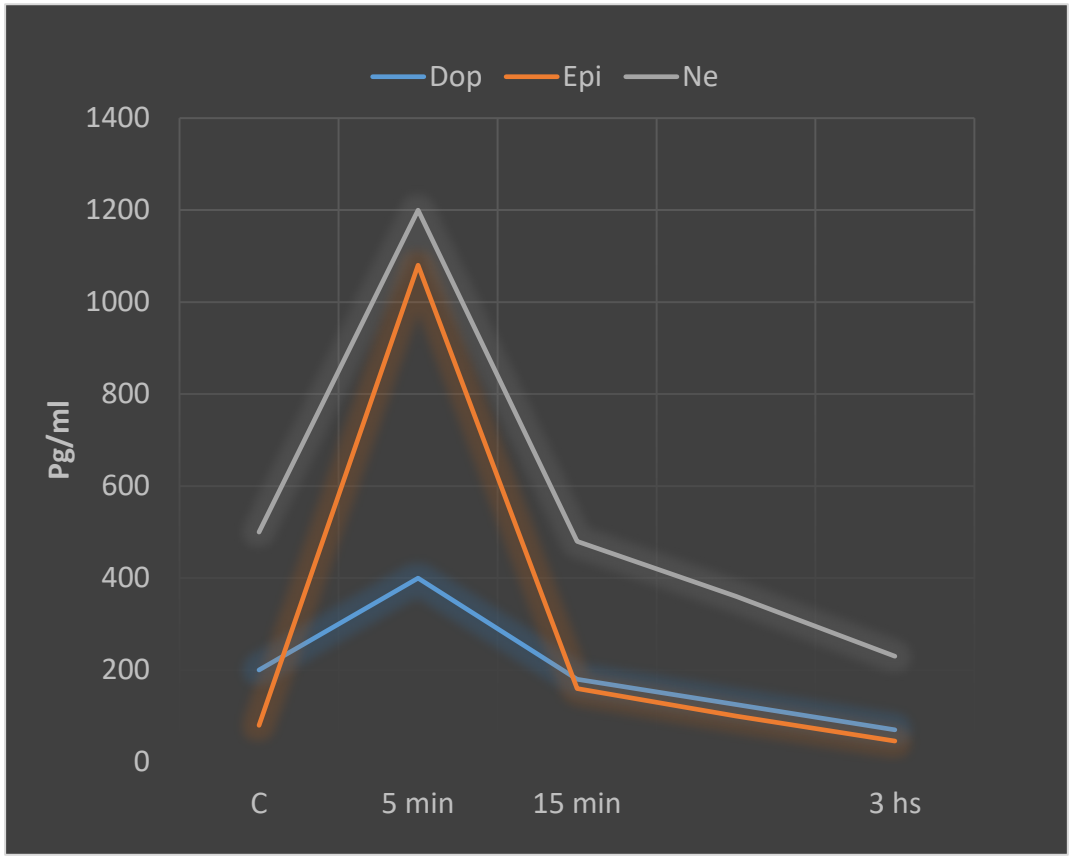
Novitzky D. et al. Cryobiology. 1987;24:1-10

Hemodynamic Changes after Induction of Brain Death in the Baboon



Novitzky D. et al. Cryobiology. 1987;24:1-10

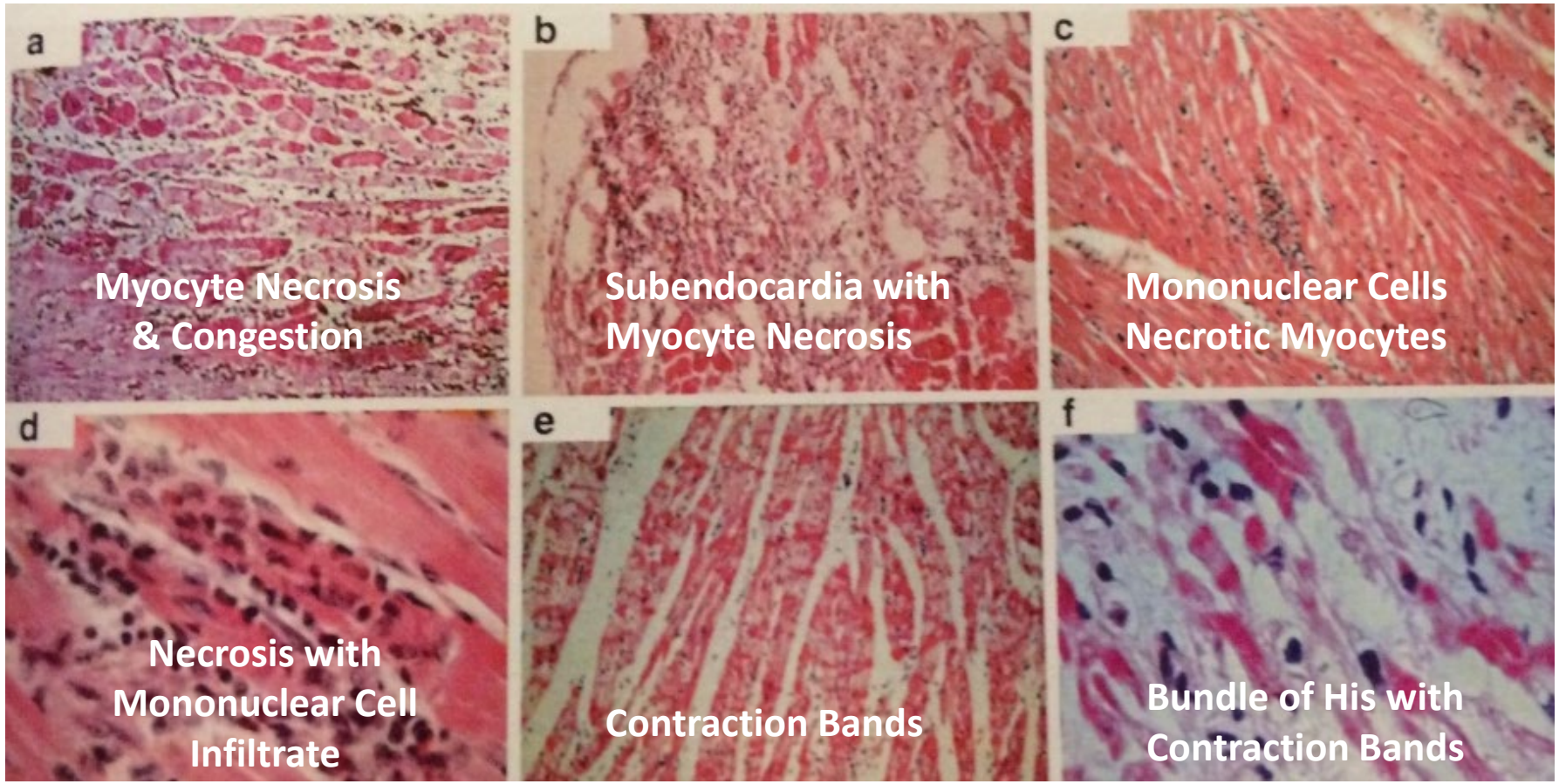
Changes in Norepinephrine, Epinephrine and Dopamine Levels after Experimental Brain Death in the Baboon



C	5min	15min	3h
Norepinephrine	P<0.01	ns	P<0.05
Epinephrine	P<0.001	ns	ns
Dopamine	P<0.05	ns	ns

Novitzky D. et al. Cryobiology. 1987;24:1-10

Microscopic Sections from Baboon Heart after Induction of Brain Death



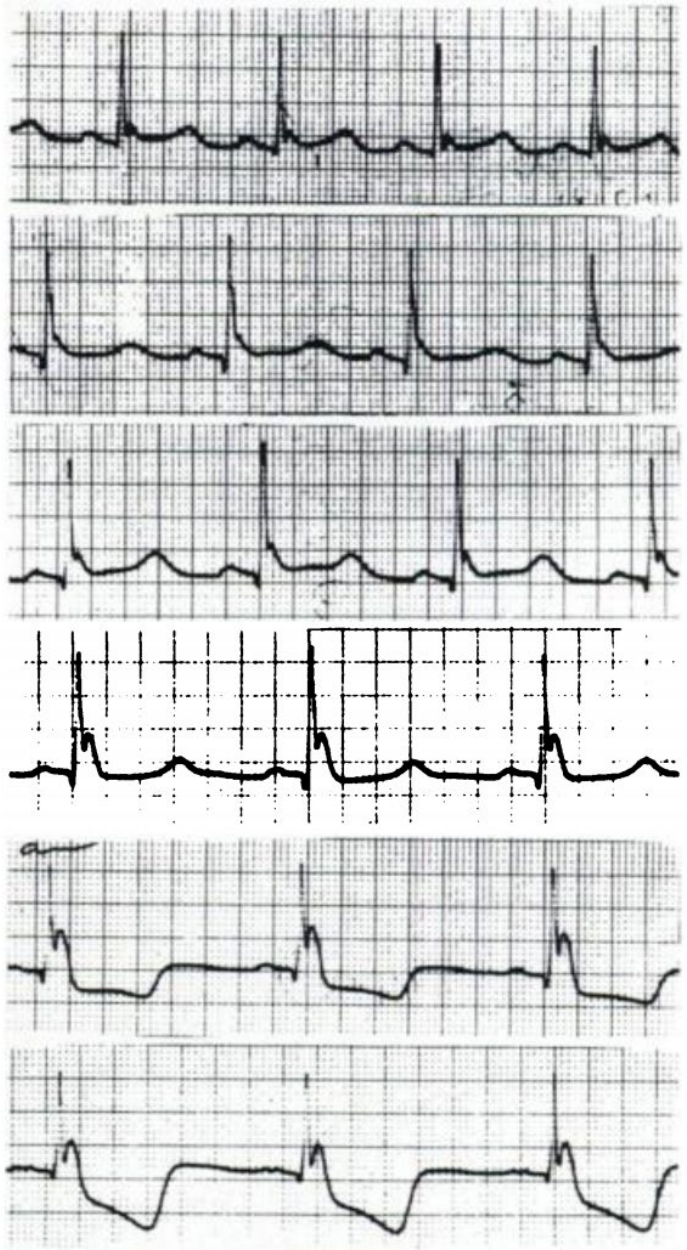
Novitsky D. et al. **J Heart Transplantation 1984; 4: 63–9.**

Electrocardiographs Findings in Brain Death; Description and Presumed Mechanism

Table 2—*Electrocardiographic Findings in 28 Cases of Brain Death

ECG findings	No of cases
Broadening of the terminal part of the QRS complex (J wave)	24
Prolonged QT interval	21
ST depression, negative T waves	16
ST elevation	5
Flat T waves	9
Giant T waves	1
Prolonged PR interval	2
Broad and notched P waves	1
Arrhythmia	1
Normal tracing	1

Drory, Y. CHEST,67: 4, APRIL,1975



Electrocardiographs Findings in Brain Death: Drory, Y. CHEST,67: 4, APRIL,1975

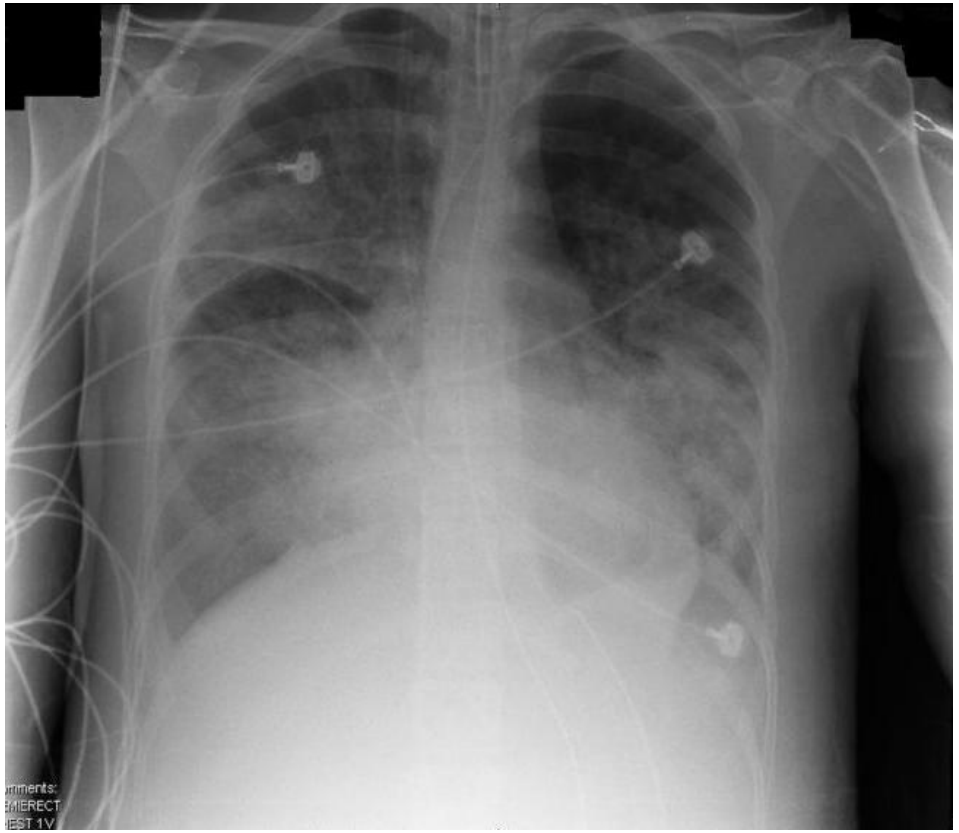
Electrocardiographs Findings in Brain Death; Description and Presumed Mechanism

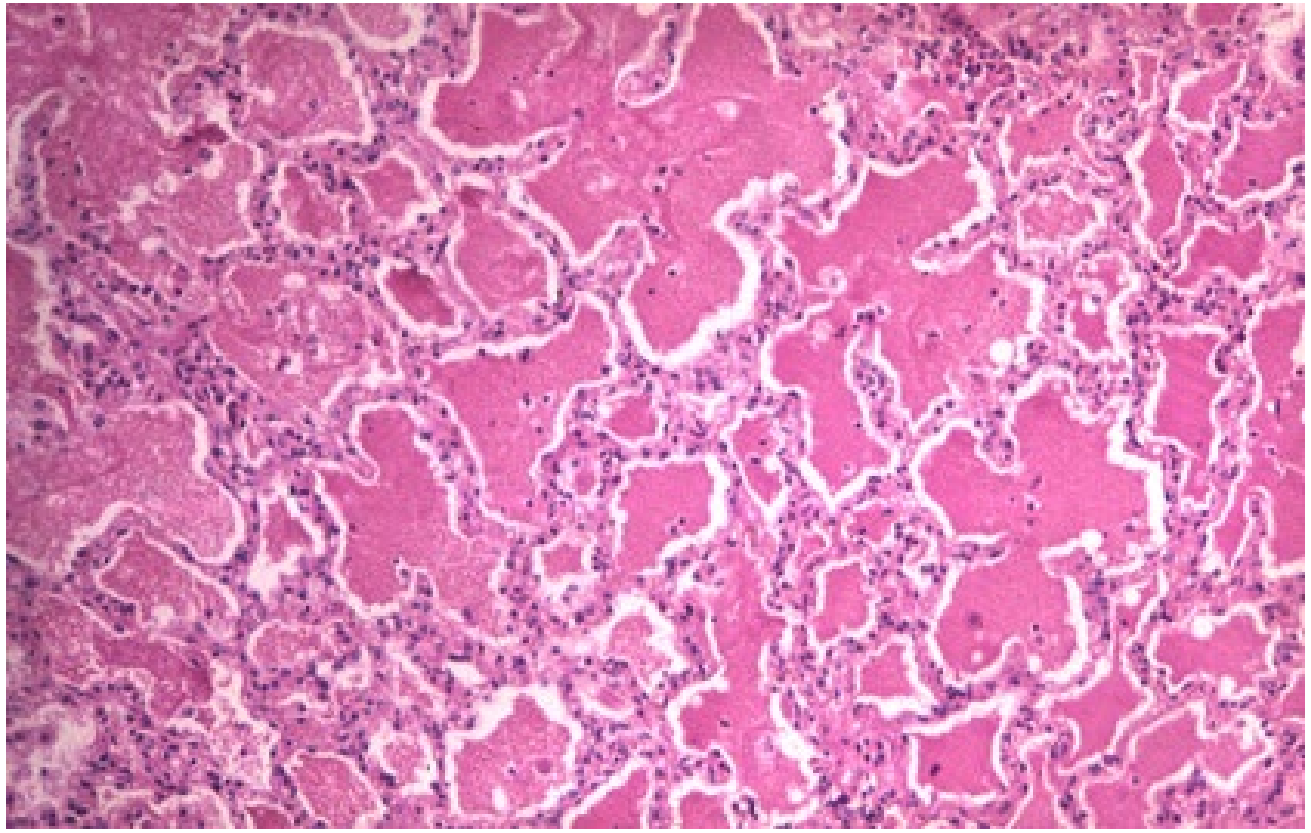
Table 3—*Electrocardiographic Changes in the Terminal Stage in 12 Cases of Brain Death*

ECG finding	No of cases
Gradual depression of sinus activity	11
Sinus arrhythmia	3
Supraventricular premature beats	3
Atrial fibrillation with progressive depression of atrioventricular conduction*	7
A-V junctional or idioventricular rhythm	2
Intermittent ventricular tachycardia	1
Ventricular fibrillation	2
Partial or complete A-V block	4
Intraventricular conduction disturbances	3
ST-T changes	
Terminal ST elevation preceded by ST depression	5
ST depression	1
Decrease or disappearance of J waves	6
Diminution of voltage	8

Drory, Y. CHEST,67: 4, APRIL,1975

Pulmonary Edema in Brain Death





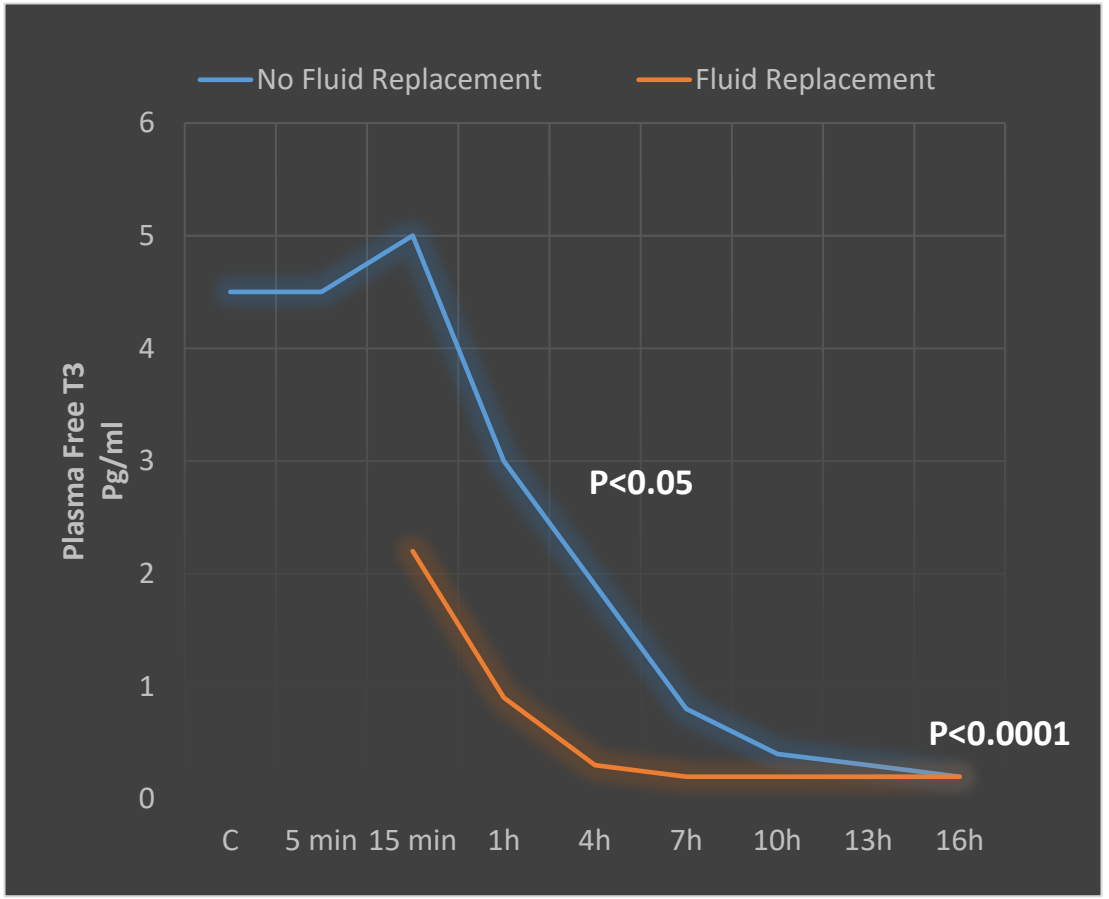
Novitzky D. et al. Cryobiology. 1987;24:1-10

Autonomic Storm

- The body's attempt to compensate for the increase in intracranial pressure
- Significant increase in systemic vascular resistance
- Acute transient left systolic and diastolic dysfunction
- Various forms of myocardial necrosis
- Decreases Cardiac output
- Increased left atrial and pulmonary capillary wedge pressures
- Blood pooling within the lung and pulmonary edema

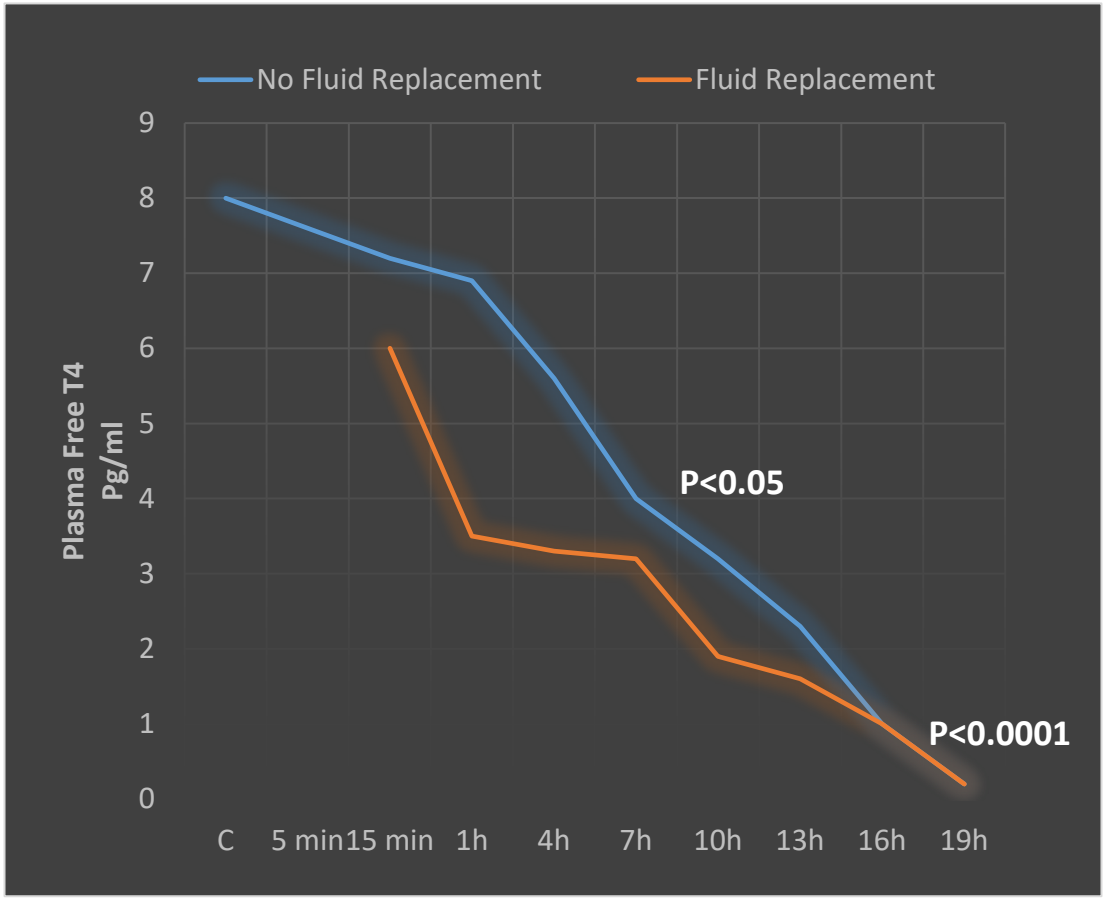
Hormonal Changes

Changes in Plasma Free T3 Levels after Experimental Brain Death in the Baboon



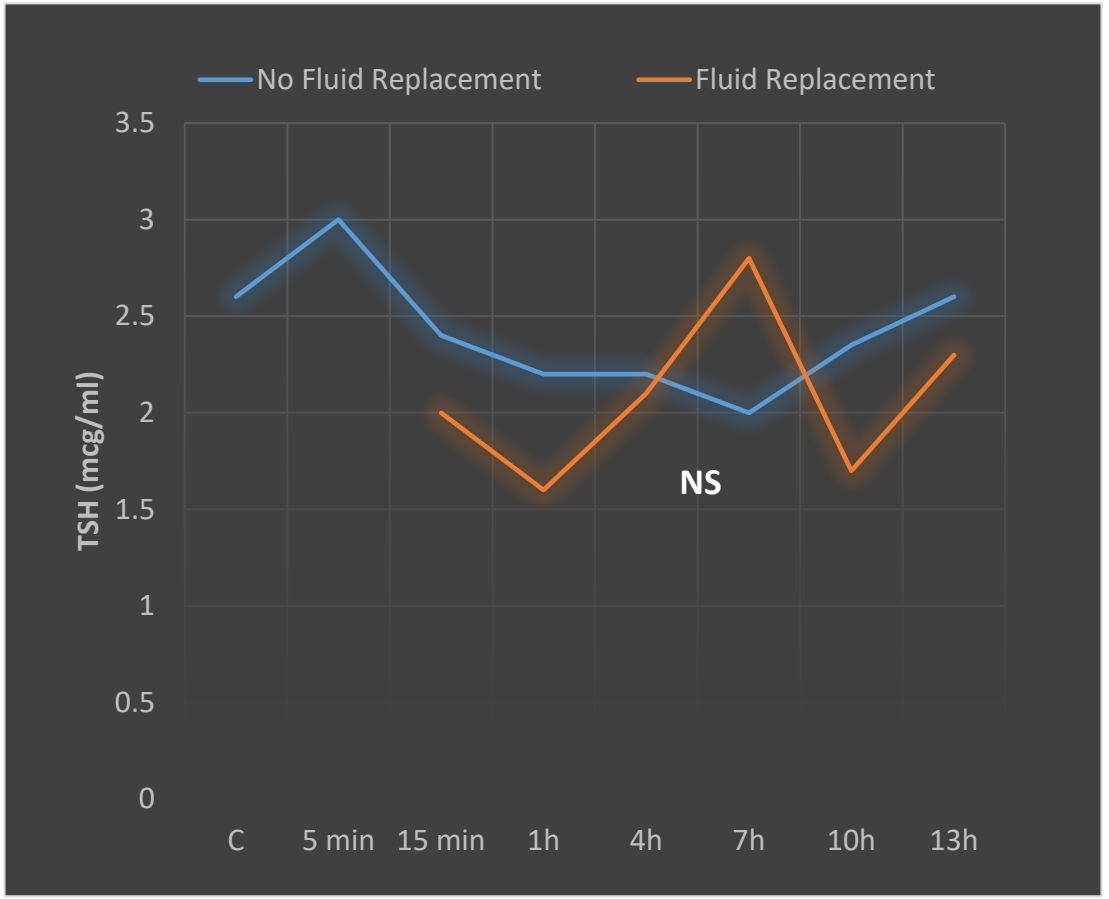
Novitzky D. et al. Cryobiology. 1987;24:1-10

Changes in Plasma Free T4 Levels after Experimental Brain Death in the Baboon



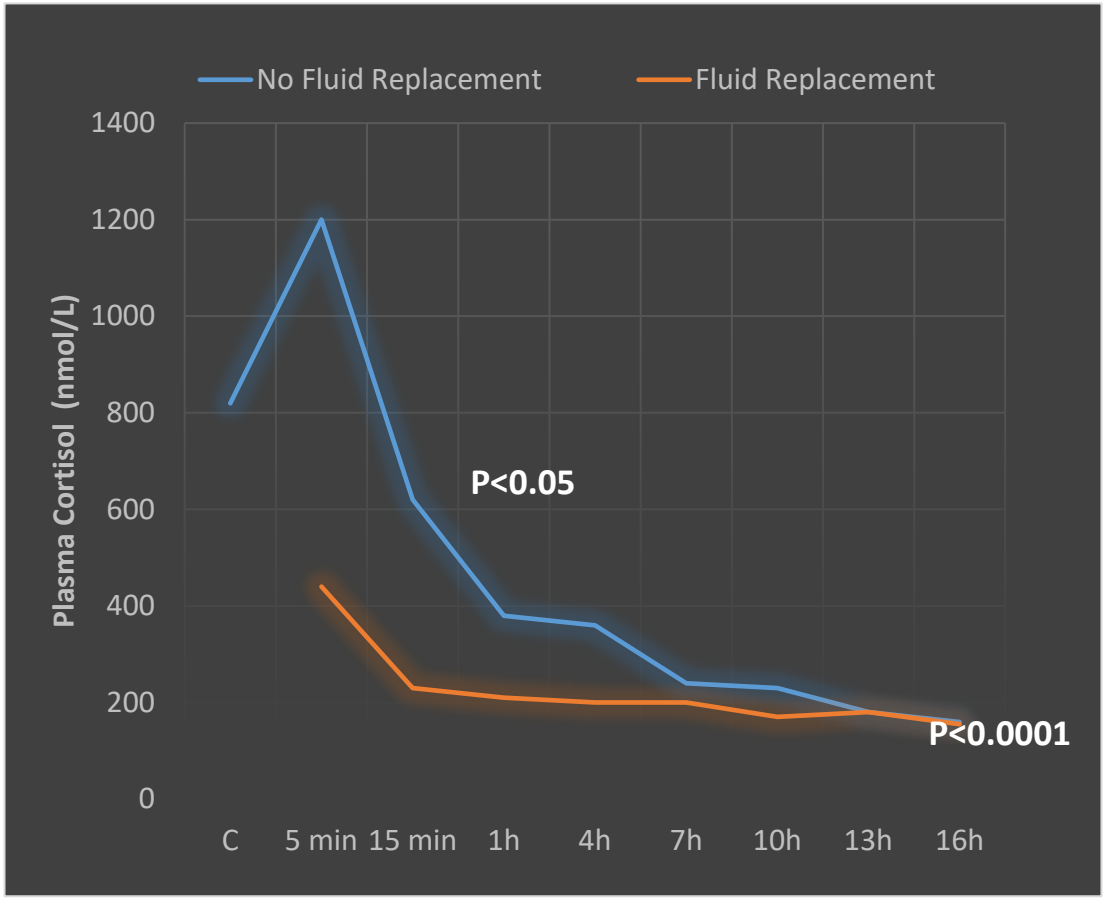
Novitzky D. et al. Cryobiology. 1987;24:1-10

Changes in Plasma THS Levels after Experimental Brain Death in the Baboon



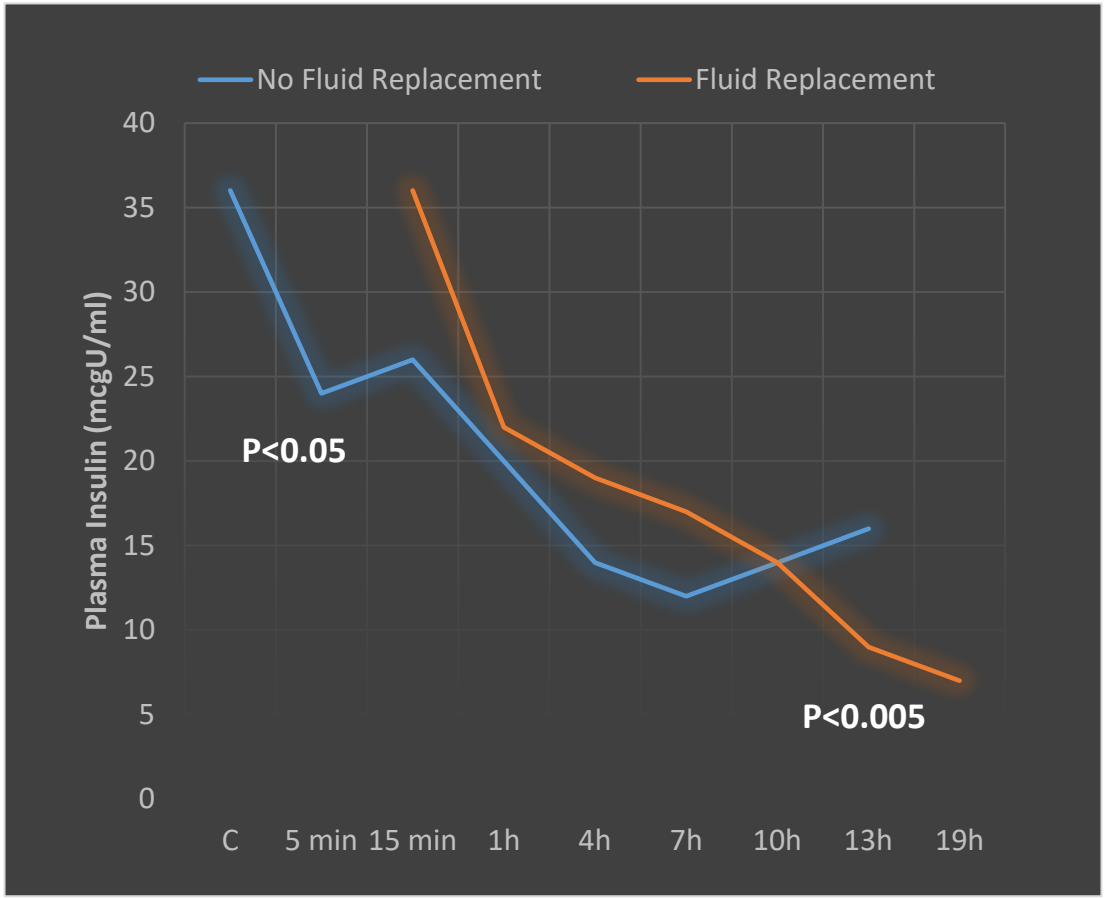
Novitzky D. et al. Cryobiology. 1987;24:1-10

Changes in Plasma Cortisol Levels after Experimental Brain Death in the Baboon



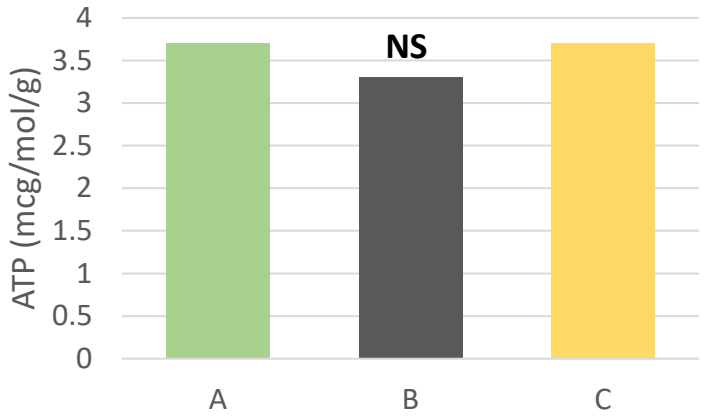
Novitzky D. et al. Cryobiology. 1987;24:1-10

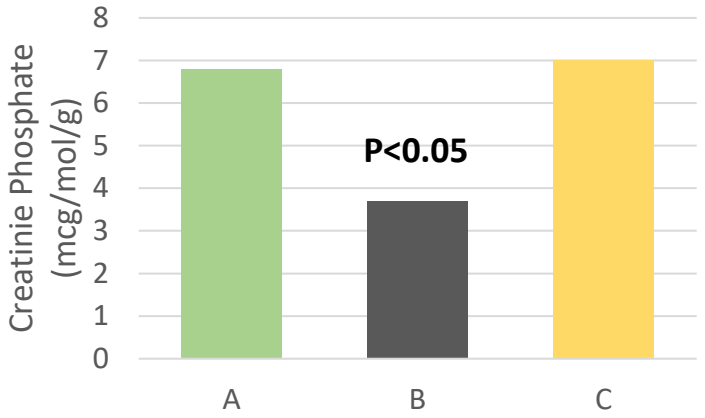
Changes in Plasma Insulin Levels after Experimental Brain Death in the Baboon



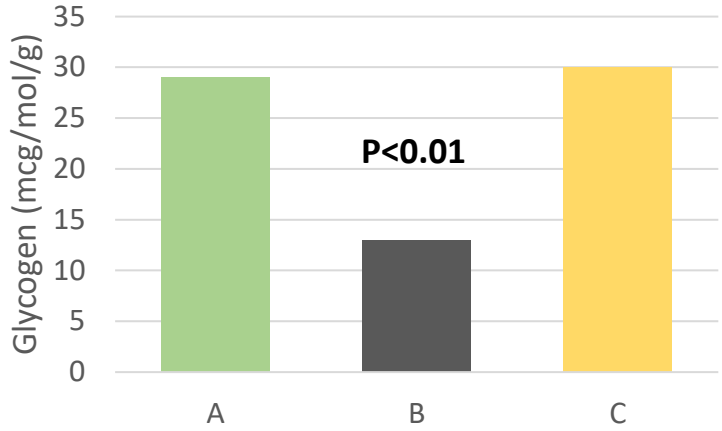
Novitzky D. et al. Cryobiology. 1987;24:1-10

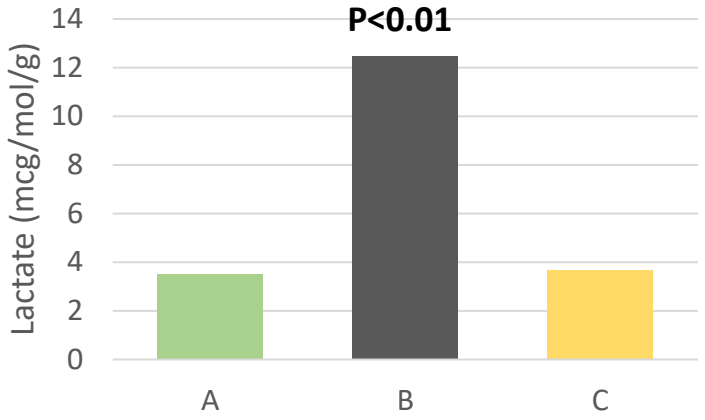
Effect of Brain Death on Myocardial Energy Stores





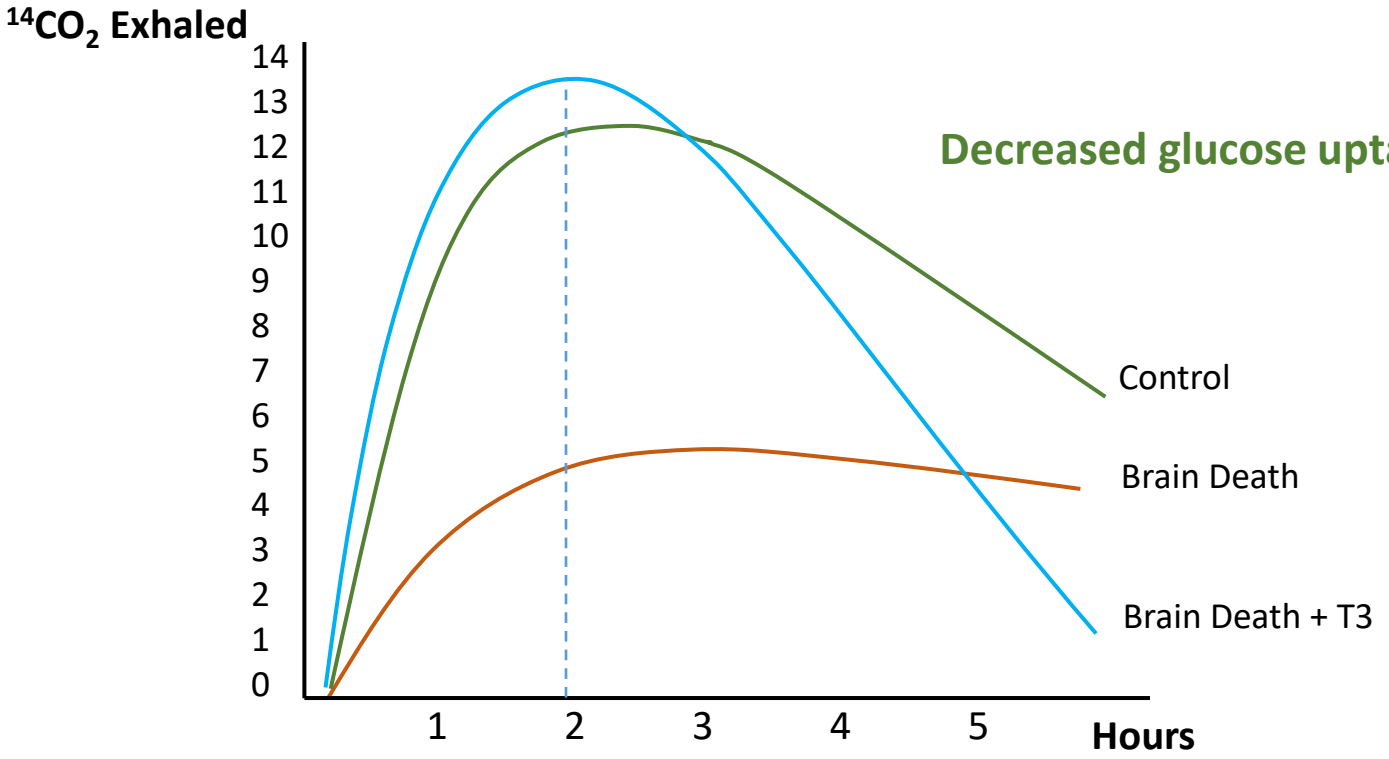
(A) freshly Excised Heart. (B) Heart taken from brain-dead pigs (c) hearts taken from brain –dead pigs and received hormonal therapy





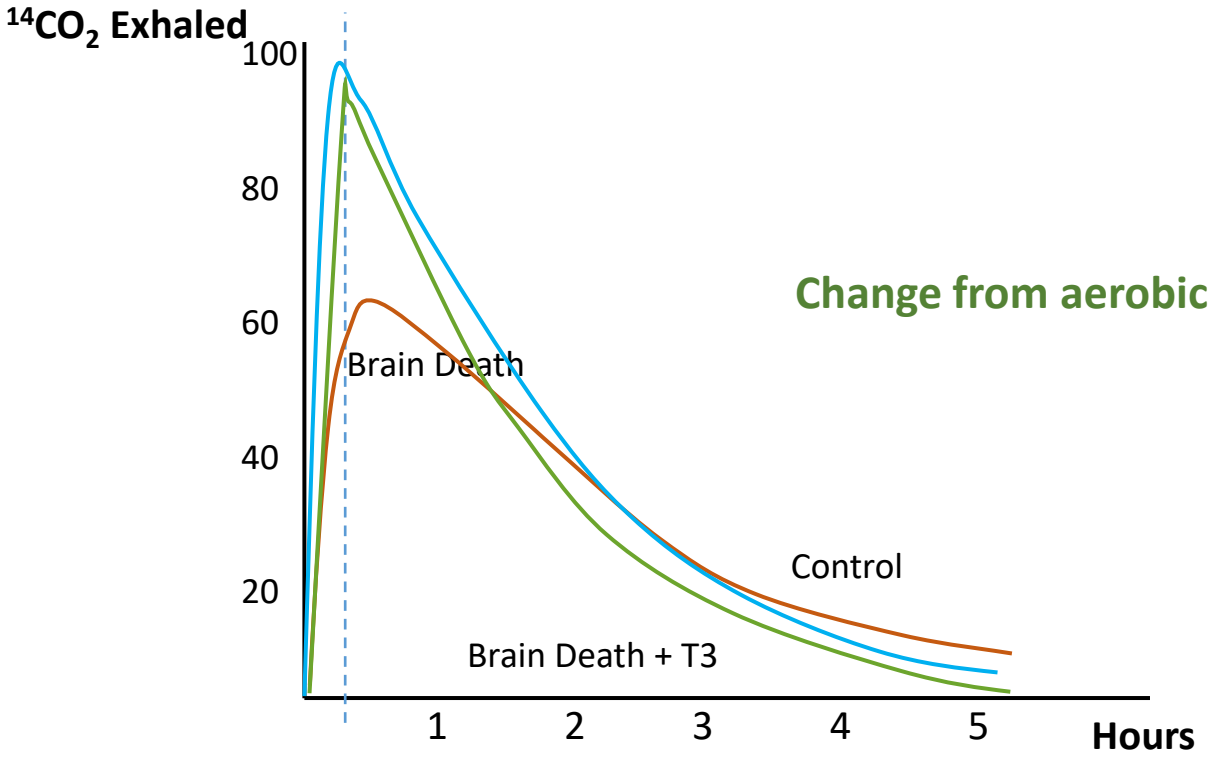
Cooper et alAnn R Coll Sur Engl. 1989;71:261-6

^{14}C Glucose Injection



Novitzky D. et al. Cryobiology. 1987;24:1-10

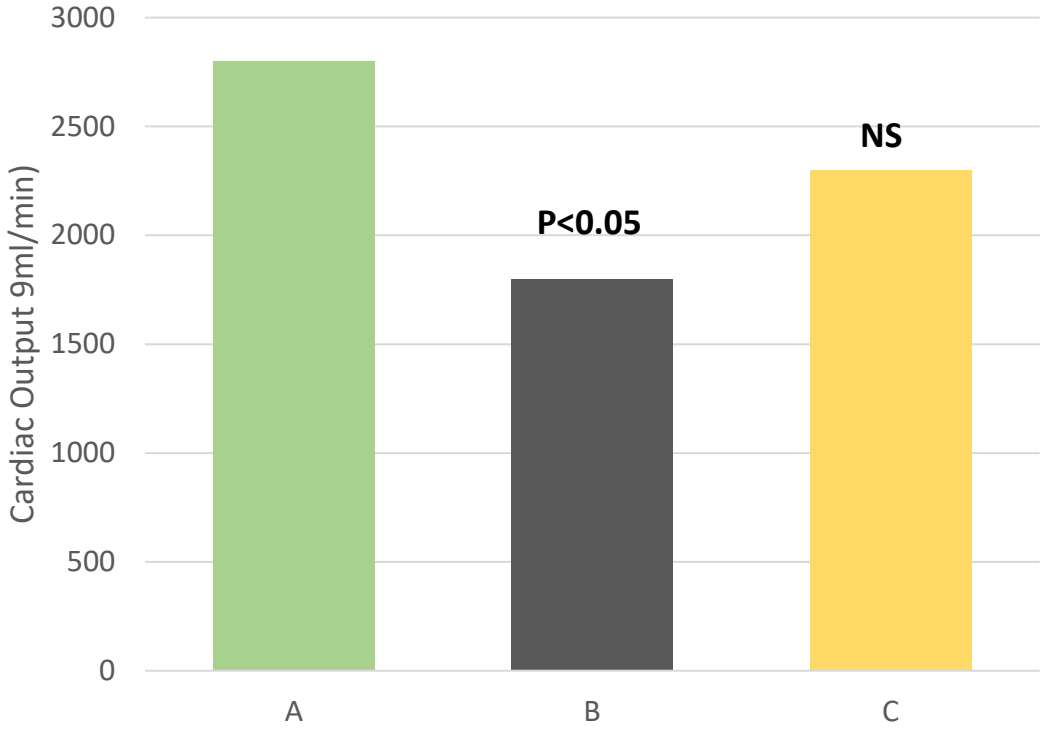
^{14}C Pyruvate Injection

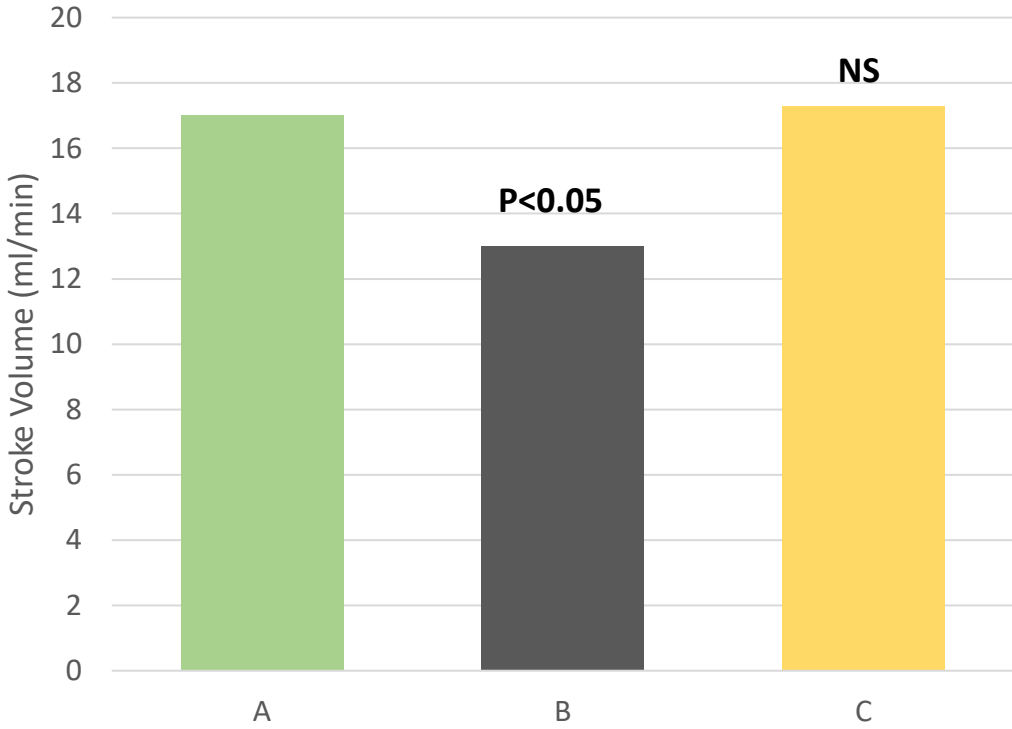


Change from aerobic to anaerobic metabolism

Novitzky D. et al. Cryobiology. 1987;24:1-10

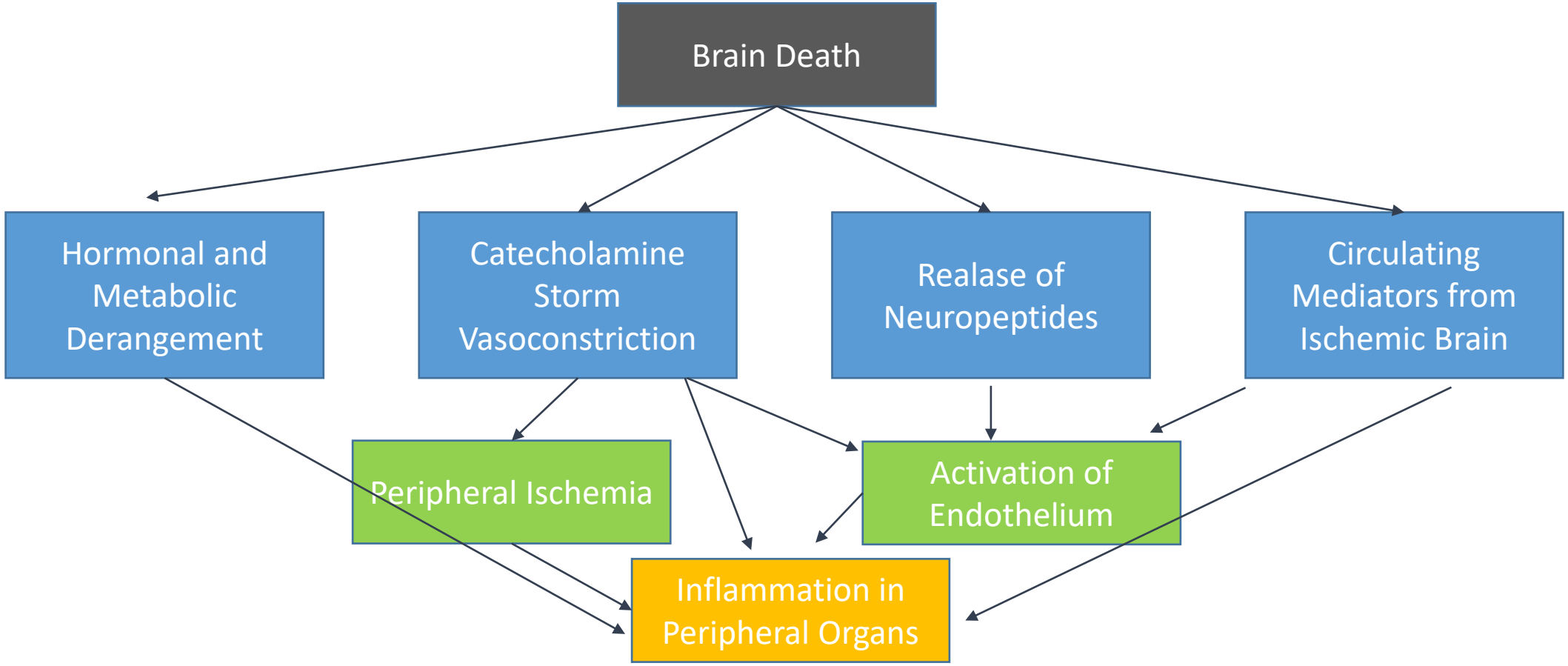
Effect of Brain Death on Cardiac Output and Stroke Volume



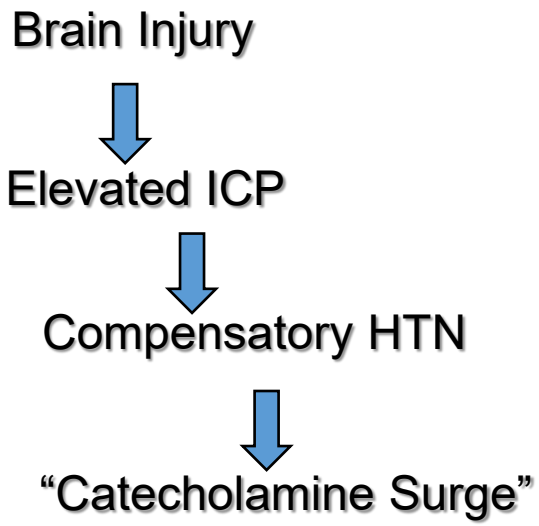


Cooper et al. Ann R Coll Sur Engl. 1989;71:261-6

The Inflammatory response to Brain Death



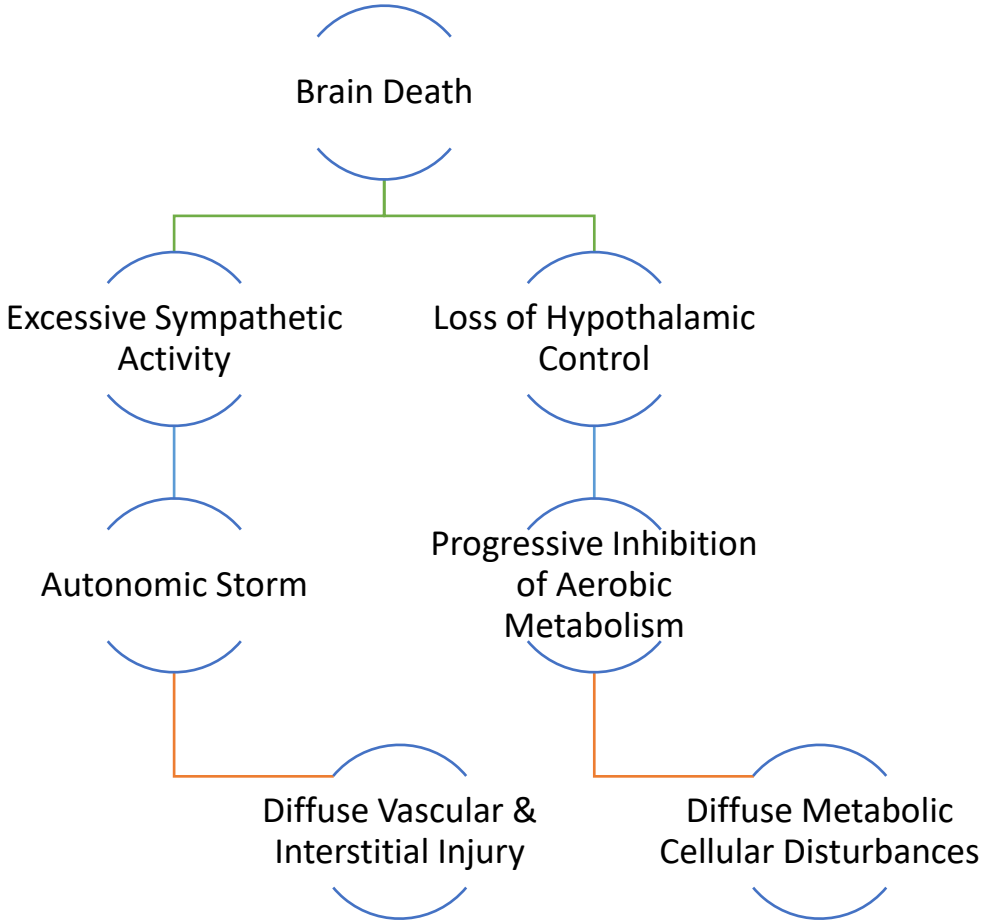
Physiology Associated with Severe Brain Injury



- Peripheral vasoconstriction
- Tachycardia - Arrhythmias
- Central redistribution of blood
  - Pulmonary edema
- Myocardial dysfunction
- Endothelial dysfunction
- Platelet activation-micro thrombi-DIC
- Cytokine – Inflammatory activation (SIRS)

Experimental studies demonstrate circulating epinephrine concentrations increase on the order of 200 to 1000-fold in association with increase in ICP

Summary


Brain Death
Excessive Sympathetic Activity
Loss of Hypothalamic Control
Autonomic Storm
Progressive Inhibition of Aerobic Metabolism
Diffuse Vascular & Interstitial Injury
Diffuse Metabolic Cellular Disturbances

Thank You