New Mexico Donor Services

an extraordinary commitment to science, health and hope

A Division of
DCI Donor Services

Management of the Complex Organ Donor Patient

Objectives

- Anticipate the pharmacologic needs of the brain injured patient
- Diagnose Death by Neurologic Criteria
- Appropriately treat electrolyte imbalance

Understanding Brain Death

- Can someone who is brain dead breathe without the support of the breathing machine? Yes No Unsure
- Can someone who is brain dead ever wake up (recover)? Yes No Unsure
- Will someone who is brain dead react (grimace, move away, of blink) if someone touches their eyeball?

  Yes No Unsure
- Can a person be brain dead even if their heart is beating? Yes No Unsure
- Is brain death different from a coma or a vegetative state? Yes No Unsure

Uniform Determination of Death Act

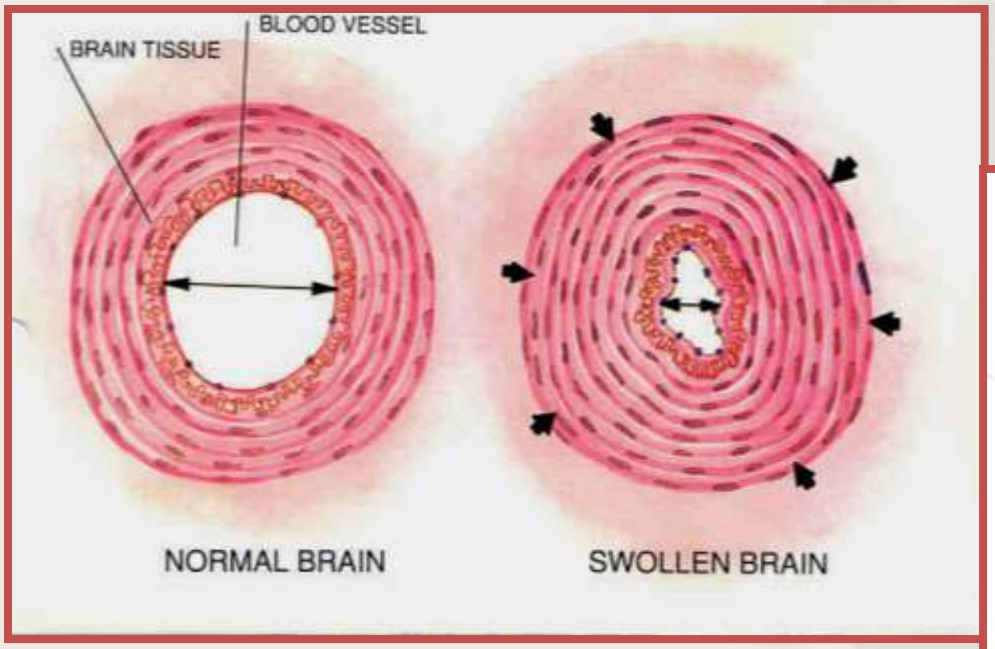
- An individual who has sustained either
  - Irreversible cessation of circulatory and respiratory functions, or
  - Irreversible cessation of all functions of the entire brain, including the brain stem, is dead.
- A determination of death must be made with accepted medical standards.

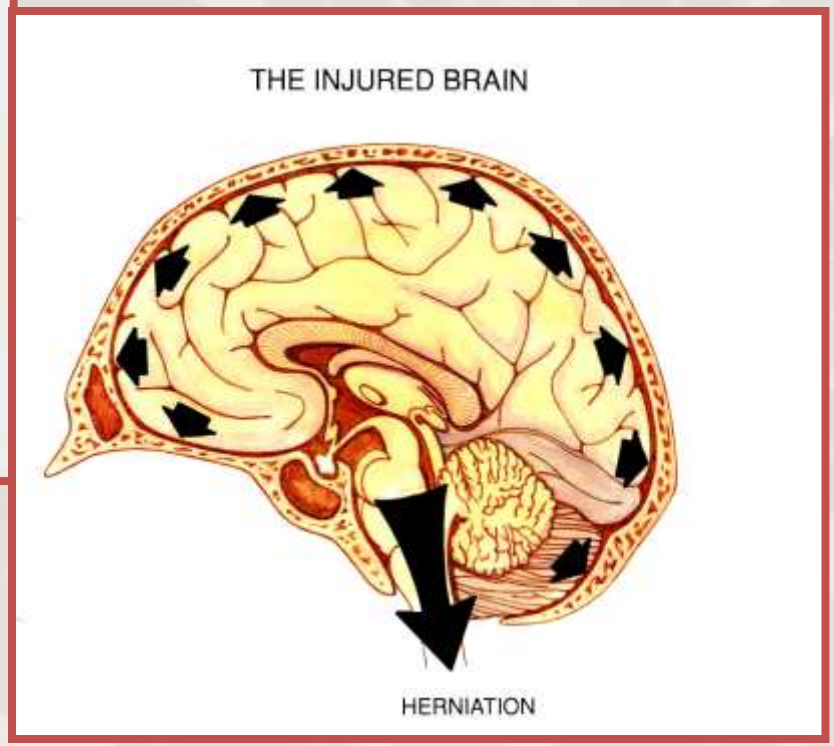
AAN Practice Parameter to determine brain death

3 Clinical findings necessary to confirm irreversible cessation of all functions of the entire brain, including the brain stem.

1. Coma with a known cause
2. Absence of brainstem reflexes
3. Apnea

Cerebral Blood Flow





Pathophysiology

- Hemodynamic Changes
  - Cushing's Reflex
    - Rise in BP & HR as a response to a rise in ICP
    - Catecholamine "storm"
      - Rise in SVR
      - Hypoperfusion, ischemia, hypoxia, metabolic acidosis
      - Embarrassment of coronary circulation and resulting ischemia
        - » Rise in troponin
      - Rise then fall of PVR
        - » Neurogenic pulmonary edema
  - Hypotension

Diagnosis of Brain Death

- Cerebral Function
  - Unresponsive
  - No movement
    - Spinal reflexes = simple reflex arc in which the impulse is not processed in the brain
- Clinical (brain stem) Exam
- Confirmatory Test

Clinical Exam

- Examination of function of Cranial Nerves II-X
- Examination of function of:
  - Midbrain
  - Pons
  - Medulla

Additional Considerations for Coma

- Exclude the presence of CNS-depressant drug effect by history, drug screen, calculation of clearance using 5 times the drug's half-life, or, if available, drug plasma levels below the therapeutic range
- The legal alcohol limit for driving is 0.08% which is a practical threshold below which a brain death examination could proceed
- There should be no severe electrolyte, acid-base, or endocrine disturbance

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Neuroendocrine Imbalance in the Brain Dead Organ Donor

Diabetes Insipidus

Diabetes Insipidus: Etiology

- Normally the regulation of urine production occurs in the hypothalamus, which produces arginine vasopressin (or antidiuretic hormone, ADH). After synthesis, ADH is transported to the posterior pituitary where it is stored for release.

- When these structures are infarcted after brain death, there is a rapid depletion of ADH leading to diabetes insipidus (DI) in ~60-80% of brain dead organ donors.

Reference: Smith M. Physiologic changes during brain stem death: lessons for management of the organ donor. *Journal of Heart and Lung Transplantation*. 2004;23:S217-222.

Diabetes Insipidus: Diagnosis

- DI is characterized by excessive diuresis, severe hypovolemia, and hypernatremia.
- Differential diagnosis of polyuria:

Variable	DI	Mannitol Therapy	Hyperglycemia
Serum Na (mmol/L)	> 150	> 150	> 150
Serum Osmo (mOsm)	> 300	> 300	> 300
Serum Osmolar Gap (mOsm)	Normal	> 10-15	> 10-15
Urine Output (ml/h)	> 300	> 200	> 200
Urine Na (mmol/L)	**< 10**	50-70	50-70
Urine Osmo (mOsm/L)	**< 200**	> 300	> 300
Urine Spec Gravity	**< 1.005**	> 1.020	> 1.020
Urine Glucose	Absent	Absent	Present

Diabetes Insipidus: Complications

- Hypotension due to dehydration
- Electrolyte abnormalities secondary to free water loss:
  - Hypernatremia
  - Hypokalemia
  - Hypocalcemia
  - Hypophosphatemia
- Severe dehydration may cause renal cellular swelling that, in turn, can cause capsular rupture of the kidneys

Diabetes Insipidus: Treatment

- Correct hypovolemia
  - 1:1 fluid replacement with D5W
  - 1:1 fluid replacement with D5 ¼ NS
- Correct free water deficit and hypernatremia
  - Free water deficit (L) = TBW* x ([serum Na/140] – 1)

    TBW = Total Body Water

    TBW (men) = 0.6 x weight (kg)

    TBW (women) = 0.5 x weight (kg)
  - http://www.medcalc.com/freewater.html
- Hormone replacement therapy
  - 0.5 - 2 mcg DDAVP IV Q2h PRN
  - 0.01 – 0.04 U/min Vasopressin IV gtt
  - ??Note: Do not administer within _ hrs of OR??

- GOAL: hourly urine output 0.5 – 2 ml/kg

Impaired Thermoregulation

Impaired Thermoregulation: Etiology

- Results from the lack of hypothalamic body temperature control
- Brain dead patients become POIKILOTHERMIC, meaning that their core temperature drifts progressively downward towards ambient temperature
- The trend towards hypothermia is exacerbated by:
  - Administration of large volumes of intravenous fluids at room temperature
  - ↓ metabolic rate and loss of muscular activity
  - Profound peripheral dilatation

Impaired Thermoregulation: Complications

Hypothermia

- Arterial vasoconstriction
- Oxygen-dissociation curve shifts to the left, leading to ↓ tissue oxygen delivery
- Temperatures < 34^{o}C affect enzymatic processes associated with normal coagulation and platelet function, leading to coagulopathy
- Myocardial depression, ↓ CO
- Impairs ability of kidneys to maintain tubular concentration gradients, leading to cold diuresis
- Temperatures < 28 ^{o}C can lead to ventricular irritability and refractory dysrhythmias

Hyperthermia/Rapid rewarming

- Vasodilatation and hypotension
- ↑ metabolic demands, tissue oxygen consumption
- Tachycardia

Reference: Powner DJ, Reich HS. Regulation of coagulation abnormalities and temperature in organ donors. *Progress in Transplantation*. 2000;10:146-153

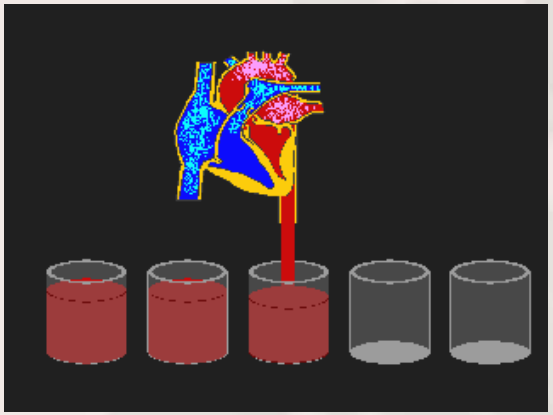
Impaired Thermoregulation: Treatment

- Hypothermia
  - ↑ ambient room temperature
  - Warming blanket
  - Use fluid warmer for IV fluids and blood products
- Hyperthermia
  - ↓ ambient room temperature
  - Cooling blanket, ice packs
  - Note: Pharmacologic treatment (e.g. Tylenol) is ineffective in the brain dead patient

- GOAL*: Core temperature = 35.4 – 37.7 ^{o}C (96 – 100^{o} F)

*Reference: Powner DJ, Reich HS. Regulation of coagulation abnormalities and temperature in organ donors. *Progress in Transplantation*. 2000;10:146-153

Cardiac Output



- Volume of blood pumped by the left ventricle (LV) per minute

  Cardiac Output (CO) = Stroke Volume (SV) x Heart Rate (HR)

- Measurements:
  - CO = SV x HR, normal 4-8 L/min
  - Cardiac Index (CI) = CO/BSA, normal 2.5-4 L/min/m^2
  - Ejection Fraction (EF) = (SV/EDV) x 100%, normal 55-75%
- Stroke Volume is determined by:

  Preload
  Afterload
  Contractility

Preload

- Stretch on myofibrils, measured as the pressure in the ventricle at the end of diastole
- Measurements:
  - RV preload = CVP, normal 2-6mmHg
  - LV preload = PCWP, normal 4-12mmHg
- ↑ preload = ↑ myocardial O_2 consumption

	Increased Preload	Decreased Preload
Causes	Heart failure, hypervolemia, excessive vasoconstriction, mitral/aortic valve insufficiency	***Hypovolemia***, loss of vasomotor tone, ↑ intrathoracic pressure, cardiac tamponade, RV failure, tachycardia
Treatment	Diuretics, venous vasodilators	Volume/blood replacement

Afterload

- Pressure against which the ventricle must pump to open semilunar (aortic and pulmonic) valves
- Measurements:
  - RV afterload: PVR, normal 30-250 dynes/sec/cm^{-5}
  - LV afterload: SVR, normal 900-1400 dynes/sec/cm^{-5}
- ↑ afterload = ↑ myocardial O_2 consumption, ↓stroke volume (SV) and cardiac output (CO)

	Increased Afterload	Decreased Afterload
Causes	HTN, pulmonary HTN, excessive vasoconstriction	***Vasodilatation***
Treatment	Arterial/pulmonary vasodilators, oxygen	Vasopressors

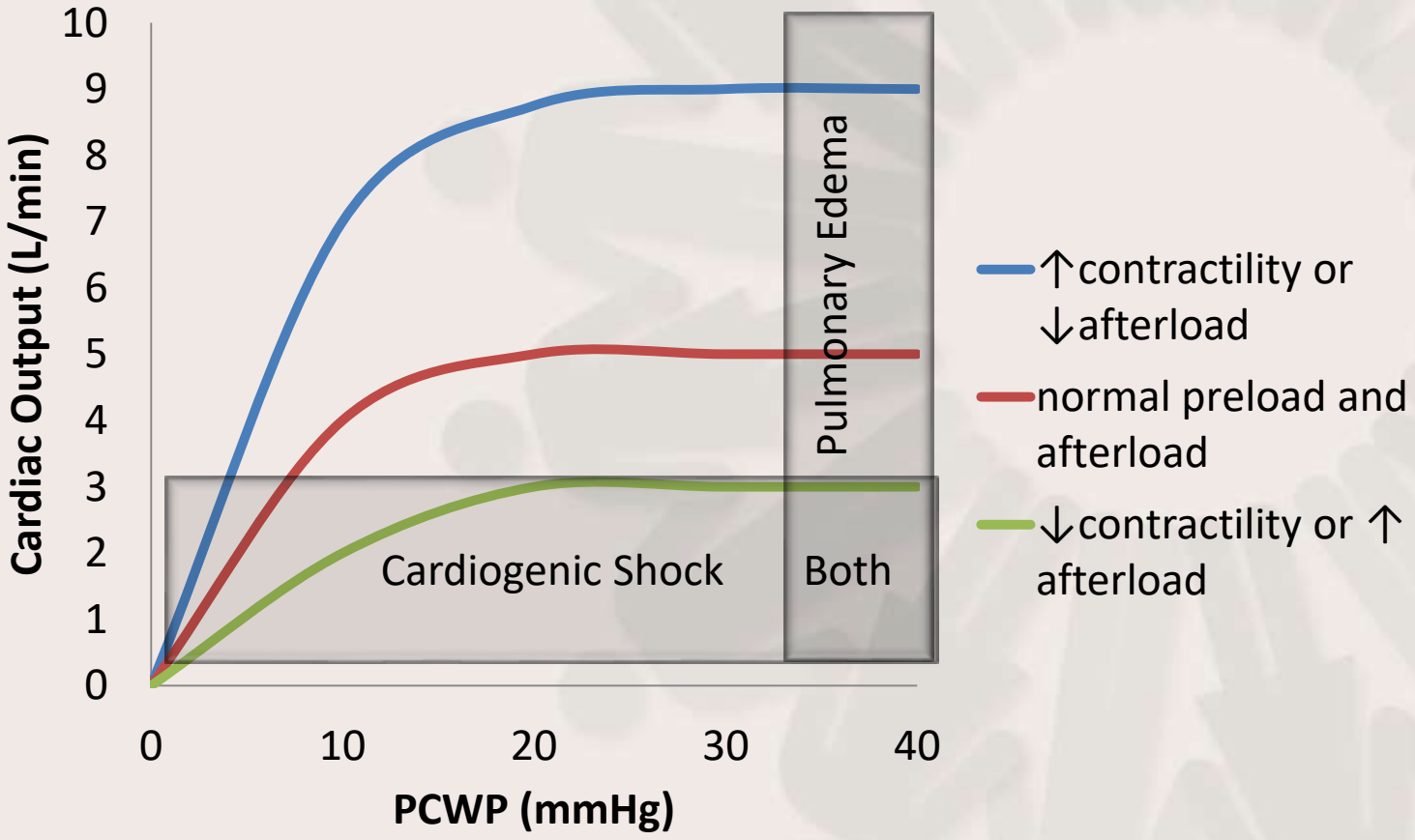
Contractility

- Contractile force of the heart
- Measurements:
  - RV contractility: RVSWI, normal 7-12 g/m
  - LV contractility: LVSWI, normal 35-85 g/m
- ↑ contractility = ↑ myocardial O_2 consumption, ↑SV and CO (within physiologic limits)

	Increased Contractility	Decreased Contractility
Causes	SNS stimulation, inotropes, hypercalcemia	***Brain death process***, trauma, MI, metabolic depression, arrthymias
Treatment	Beta-blockers, calcium-channel blockers	T_4 therapy, inotropes, phosphorus/calcium replacement

Frank-Starling's Law of the Heart:

- Within physiologic limits, the greater the stretch on the myofibrils (preload), the greater the force of subsequent contraction



EKG Findings, Clinical Implications, and Treatments

Location	Coronary Artery	EKG Findings	Clinical Implications	Specific Treatments
Anteroseptal Wall	LAD	• V_1 through V_4 • Q waves and ST segment elevations	LV failure, significant hemodynamic compromise; CHF, pulmonary edema, cardiogenic shock, intraventricular conduction disturbances	• Vasopressors for BP • coronary artery vasodilators to ↓ afterload, ↑ CO, and ↓ myocardial O_2 consumption • pacemaker
Lateral Wall	L Circumflex	• I, aVL, V_5, V_6 • Q waves and ST segment elevations	Evaluate for posterior wall involvement; some hemodynamic changes, SA/AV dysrhythmias	• cardiac monitoring • pacemaker
Posterior Wall	L Circumflex	• V_1 and V_2 • tall upright R waves with ST segment depression	Evaluate for lateral wall involvement; some hemodynamic changes, SA/AV dysrhythmias	• treatment of bradycardia/heart block • pacemaker
Inferior Wall	RCA	• II, III, aVF • Q waves and ST segment elevation	Evaluate for RV involvement; some hemodynamic changes, potential for significant SA/AV dysrhythmias	• treatment of bradycardia/heart block • fluid restrict/diuretics • Nipride to ↓ afterload • pacemaker
Right Ventricular Wall	RCA	• Right precordial chest leads (RV_{1-6}) • Q waves and ST segment elevations	Evaluate for inferior wall involvement; some hemodynamic changes, potential for significant SA/AV dysrhythmias	• meds to ↑ contractility and ↓ RV afterload • fluids to ↑ preload (to ↑ CO) • pacemaker

It's all Greek…

- The sympathetic nervous system (SNS) has a positive chronotropic (↑HR), inotropic (↑ contractility), and dromotropic (↑conductivity) effects.
- SNS (adrenergic) receptors and effects:

Receptor	Location	Effects
$Alpha_1$ α_1	Vascular smooth muscle (arterioles and veins)	Systemic vasoconstriction
$Alpha_2$ α_2	Vascular smooth muscle (coronary and renal arterioles)	Vasoconstriction of coronary and renal vessels
$Beta_1$ β_1	Heart, kidney	↑HR, ↑ contractility, ↑conductivity
$Beta_2$ β_2	Vascular smooth muscle (arterioles), bronchial smooth muscle, liver, AV node	Vasodilatation, bronchodilitation, stimulation of glycogenolysis, ↑conductivity
Dopaminergic	Renal and mesenteric artery bed	Vasodilation

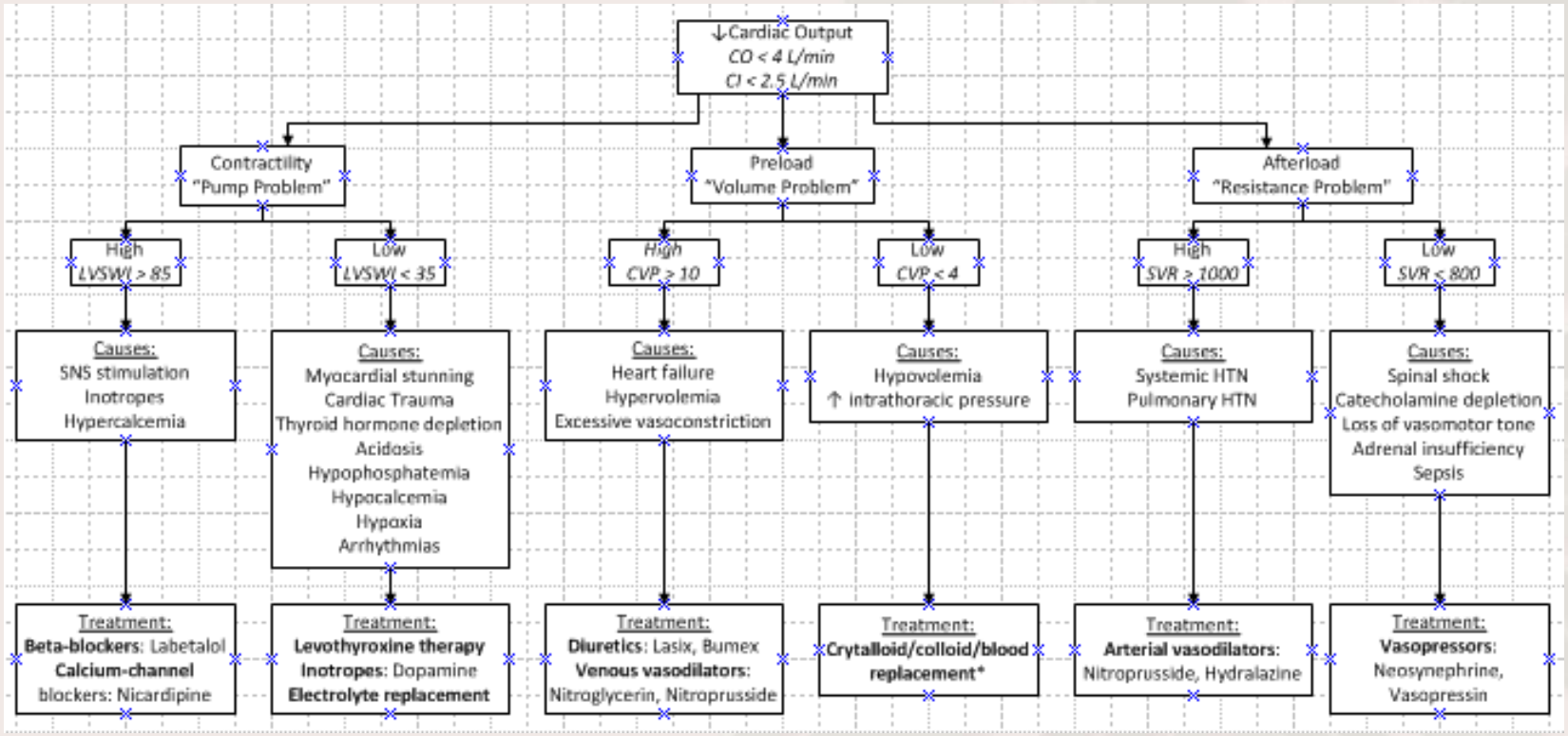
SNS effects of "Pressors"

or: Why a Pressor is not always a Pressor

- Mechanism of action on the adrenergic receptor:

Drug	Alpha effect	$Beta_1$ effect	$Beta_2$ effect
Phenylephrine	++++	+	0
Norepinephrine	++++	++	0
Epinephrine	++++	++++	++
Dopamine	++ >5mcg/kg/min +++ >10mcg/kg/min	++++ <10mcg/kg/min	+
Dobutamine	+	++++	++

Hemodynamic Treatment Algorithm



Swan Ganz Interpretation

- Normal Values

Parameter	Normal Value
Mean Arterial Pressure (MAP)	60-100 mmHg
Central Venous Pressure (CVP)	2-6 mmHg
Pulmonary Artery Systolic Pressure (PA_S)	20-30 mmHg
Pulmonary Artery Diastolic Pressure (PA_D)	10-20 mmHg
Pulmonary Artery Mean Pressure(PA_M)	10-15 mmHg
Pulmonary Capillary Wedge Pressure (PCWP)	4-12 mmHg
Cardiac Output (CO)	4-8 L/min
Cardiac Index (CI)	2.5-4 L/min/m^2
Stroke Volume (SV)	60-100 ml/beat
Systemic Vascular Resistance (SVR)	900-1400 dynes/sec/cm^{-5}
Pulmonary Vascular Resistance (PVR)	30-250 dynes/sec/cm^{-5}
Venous Oxygen Saturation (SVO_2)	60-80%
Left Ventricular Stroke Work Index (LVSWI)	35-85 g/m
Right Ventricular Stroke Work Index (RVSWI)	7-12 g/m

Electrolytes

Where did they go?

Sodium

Hyponatremia
$Na^+ < 125mEq/L$

Most Common Etiology:

- Hyperglycemia causes shift of water into the extracellular space → dilution of serum sodium. For every 100mg/dL ↑ in glucose, serum sodium ↓ 1.6mEq/L
- Excessive DDAVP/Vasopressin administration- effectively mimics SIADH (syndrome of inappropriate antidiuretic hormone)
- Others: Cerebral salt wasting, hemorrhage, GI loss, open wounds, adrenal insufficiency, hypothyroidism, renal failure

Most Common Clinical Manifestations:

- Most often CNS-related (i.e. cerebral edema, headache, lethargy, depressed reflexes, seizures, coma)… therefore not assessed in the brain dead organ donor!
- End-organ effect: intracellular edema

Treatment of Hyponatremia

- D/C hypotonic fluid administration (e.g. D5W), including IV medications
- D/C administration of DDAVP/Vasopressin
- Administer hypertonic fluids[1]:
  1. Calculate sodium deficit:

     Na deficit (mEq) = TBW* x (140 – measured serum Na)
  2. Calculate effect of treatment:

     1L NS: Δ serum Na = (154mEq/L – measured serum Na)/(TBW* + 1)

     1L 3% NaCl: Δ serum Na = (512mEq/L – measured serum Na)/(TBW* + 1)

     (Note: Administer 3% NaCl @ 1-2ml/kg/hr)

  *TBW (men) = 0.6L/kg x weight (kg)

  TBW (women) = 0.5L/kg x weight (kg)
- Administer sodium bicarbonate ($NaHCO_3$) with coexisting acidosis (pH <7.35)
  - One amp (50mL) of $NaHCO_3$ contains 44-54mEq Na

1. Kraft MD, Btaiche IF, Sacks GS, Kudsk KA. Treatment of electrolyte disorders in adult patients in the intensive care unit. American Journal of Health-System Pharmacy. 2005;62: 1663-1682.

Hypernatremia
$Na^+ > 155mEq/L$

Most Common Etiology:

- Diabetes Insipidus resulting from the rapid depletion of ADH (antidiuretic hormone) after infarction of the hypothalamus and posterior pituitary. DI occurs in 60-80% of brain dead organ donors and results in excessive free water loss.
- Administration of hypertonic fluids and/or mannitol for treatment of cerebral edema, or aggressive fluid resuscitation with NS/hypertonic fluids.

Most Common Clinical Manifestations:

- Most often CNS-related (i.e. lethargy, irritability, hyperreflexia, seizures, coma)… therefore not assessed in the brain dead organ donor!
- End-organ effect: Serum $Na^+ > 155mEq/L$ has been shown to adversely affect liver graft function outcomes due to intracellular edema and altered function[1].

1. Powner DJ. Factors during donor care that may affect liver transplantation outcome. Progress in Transplantation. 2004;14:241-249.

Treatment of Hypernatremia

- D/C hypertonic fluid administration (e.g. 3% NaCl, NS), including IV medications
- Treat DI: 1 mcg DDAVP IV Q2h PRN, .01-.04 units/min Vasopressin IV gtt
- Administer hypotonic fluids[1]:
  1. Calculate free water deficit:

     Free water deficit (in L) = TBW* x ([serum Na/140] - 1)
  2. Evaluate volume status to determine IV fluid choice
  3. Calculate effect of treatment:

     1L D5W: Δ serum Na=(0mEq/L – serum Na)/(TBW*+1)

     1L 0.225% NS: Δ serum Na=(38.5mEq/L – serum Na)/(TBW*+1)

     1L 0.45% NS: Δ serum Na=(77mEq/L – serum Na)/(TBW*+1)

     *TBW (men) = 0.5L/kg x weight (kg)

     TBW (women) = 0.4L/kg x weight (kg)
- For hypervolemic hypernatremia (caused by excessive hypertonic fluid administration, *not* DI), administer Lasix and D5W
  - Lasix alone will aggravate the hypernatremia because a Lasix-induced diuresis is equal to one-half isotonic saline solution
- 500mL H_2O via NG/OG (clamp x 1hr, then drain)

1. Kraft MD, Btaiche IF, Sacks GS, Kudsk KA. Treatment of electrolyte disorders in adult patients in the intensive care unit. American Journal of Health-System Pharmacy. 2005;62: 1663-1682.

Potassium

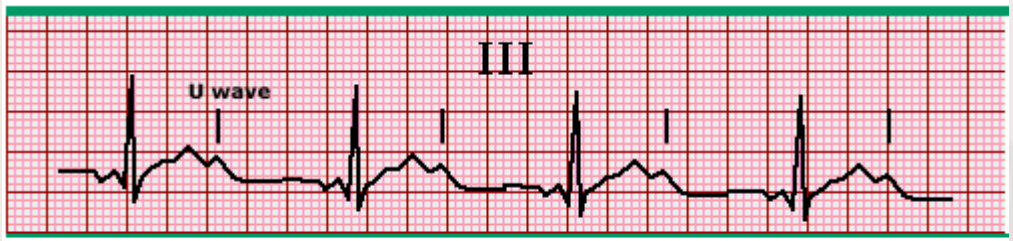
Hypokalemia
$K^+ < 4.0$ mEq/L

Most Common Etiology:

- Intracellular shifts of potassium due to: metabolic alkalosis, administration of beta-adrenergic agonists (e.g. albuterol, insulin), thyroxine therapy
- Increased losses of potassium due to: administration of potassium-wasting diuretics (e.g. Lasix) and corticosteroids, magnesium depletion
- Other: alcoholism, chronic malnutrition

Most Common Clinical Manifestations:

- EKG changes: T-wave flattening or inversion, U waves, ST-segment depression



An increase in the amplitude of U waves, which occur at the end of the T wave, are characteristic of hypokalemia.

- Arrhythmias: PACs or PVCs

Treatment of Hypokalemia

- Correct confounding factors:
  - Metabolic alkalosis
  - Hypomagnesemia- Mg is important in the regulation of intracellular K. Hypomagnesemia may result in refractory hypokalemia, likely due to accelerated renal K loss or impairment of Na-K pump activity.
- Replacement therapy:
  - Potassium Chloride (infuse @ 10-40 mEq/hr through central line)
  - Potassium acetate with coexisting acidosis (pH < 7.35)

K^+ level	Replacement Dosing
3.5 – 3.9 mEq/L	20 mEq KCl or K acetate IVPB over 1 hr*
< 3.5 mEq/L	40 mEq KCl or K acetate IVPB over 1-2 hrs*
* Infuse through central line, otherwise ↓ infusion rate to 10 mEq/hr	

  - Potassium Phosphate with coexisting hypophosphatemia (see PO_4 replacement dosing)

1. Kraft MD, Btaiche IF, Sacks GS, Kudsk KA. Treatment of electrolyte disorders in adult patients in the intensive care unit. American Journal of Health-System Pharmacy. 2005;62: 1663-1682.

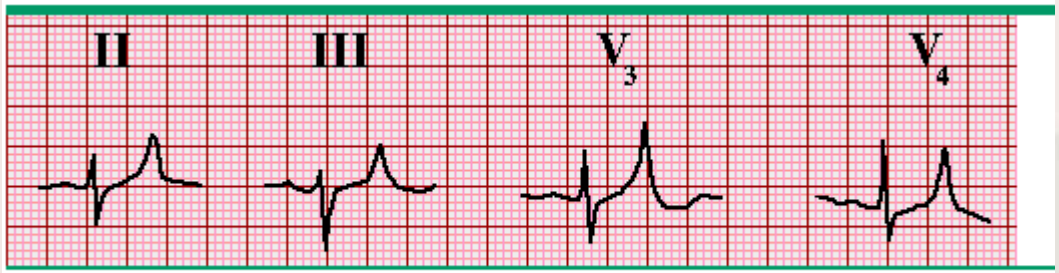
Hyperkalemia
$K^+ > 5.0$ mEq/L

Most Common Etiology:

- Extracellular shifts of potassium due to: metabolic acidosis, muscular injury (e.g. trauma, rhabdomyolysis), administration of succinylcholine or beta-adrenergic blockers
- Impaired potassium excretion due to: acute renal failure, hypoaldosteronism administration of potassium-sparing diuretics, ACE-inhibitors, or NSAIDs

Most Common Clinical Manifestations:

- EKG changes: tall, peaked T-waves and shortened QT interval followed by progressive lengthening of QRS complex and PR interval



A tall peaked and symmetrical T wave is the first change seen on the ECG in a patient with hyperkalemia.

- Arrhythmias: bradycardia, Vfib

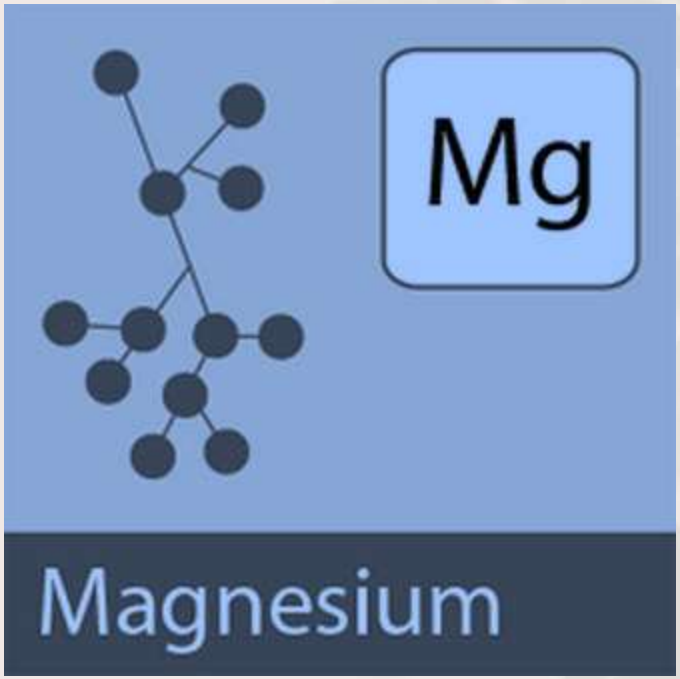
Treatment of Hyperkalemia

- Correct metabolic acidosis
- For symptomatic hyperkalemia, consider pharmacologic options:

Treatment	Effect
1-2g Calcium gluconate IV	Antagonizes cardiac conduction abnormalities
50-100 mEq Sodium bicarbonate IV	Increases serum pH, redistributes K^+ into cells
5-10 units Insulin, 50mL 50% dextrose IV	Increases insulin release, redistributes K^+ into cells
20-40mg Lasix IV	Increases renal K^+ loss
Hemodialysis x 2-4hrs	Removes K^+ from plasma

1. Kraft MD, Btaiche IF, Sacks GS, Kudsk KA. Treatment of electrolyte disorders in adult patients in the intensive care unit. American Journal of Health-System Pharmacy. 2005;62: 1663-1682.

Magnesium



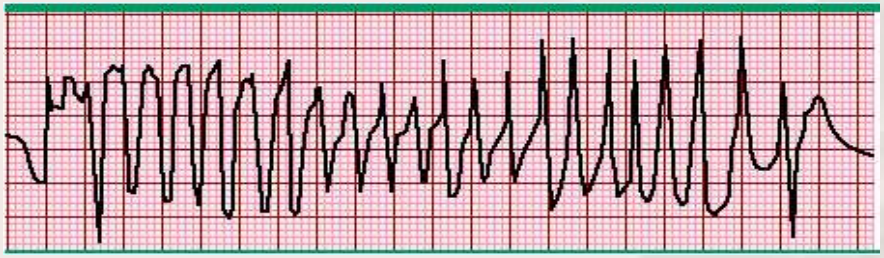
Hypomagnesemia
$Mg^{2+} < 2.0$ mg/dL

Most Common Etiology:

- Hypokalemia often causes concurrent low magnesium secondary to accelerated renal loss or poor Na/K pump function
- Massive transfusion of blood products preserved with citrate.
- Other: trauma, burns, surgery, sepsis, GI loss, renal loss, malnutrition, alcoholism

Most Common Clinical Manifestations:

- EKG changes: prolonged QT and PR interval, widening QRS complex
- Arrhythmias: ventricular arrhythmias, torsades de pointes



Treatment of Hypomagnesemia

- Replacement therapy
  - Magnesium Sulfate (infuse @ 1-2g/hr)

Mg^{2+} level	Replacement Dosing
1.6 – 1.9 mg/dL	2 g Mag Sulfate IVPB over 1 hr
< 1.6 mg/dL	4 g Mag Sulfate IVPB over 2 hrs

1. Kraft MD, Btaiche IF, Sacks GS, Kudsk KA. Treatment of electrolyte disorders in adult patients in the intensive care unit. American Journal of Health-System Pharmacy. 2005;62: 1663-1682.

Hypermagnesemia
$Mg^{2+} > 4$ mg/dL

Most Common Etiology:

- Renal insufficiency

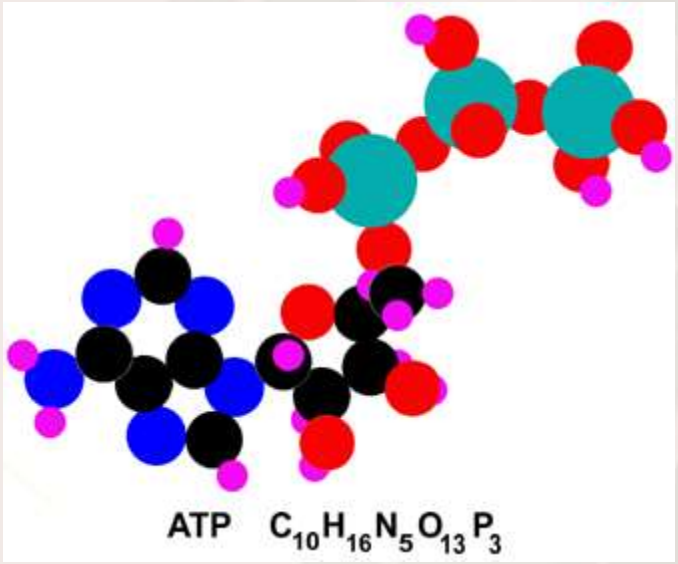
Most Common Clinical Manifestations:

- Bradycardia and hypotension at levels > 4-6 mg/dL(magnesium acts as a calcium channel blocker)
- EKG changes at levels > 6-12mg/dL: widening QRS complex, lengthening of PR and QT intervals, AV block
- Complete heart block and cardiac arrest at levels > 18mg/dL

Treatment of Hypermagnesemia

- Loop diuretics
- Hemodialysis
- IV calcium chloride 0.5-1g over 5-10 minutes via central line to reverse the cardiovascular and neuromuscular effects
- ***Rare occurrence during donor management!***

Phosphorus



What's the big deal?

- Phosphorus is the main intracellular anion and has many important functions including:
  - bone composition
  - cell membrane composition
  - nerve conduction
  - muscle function
- It provides energy-rich bonds in the form of ATP and is ***required in all physiological, homeostatic, and metabolic functions that require energy***, such as:
  - ATP synthesis
  - 2,3-diphosphoglycerate synthesis and function (necessary for oxygen release from hemoglobin and delivery to tissues),
  - glucose utilization and glycolysis
  - muscular function (especially the myocardium and diaphragm)

Hypophosphatemia
$PO_4^{3-} < 2.2$ mg/dL

Most Common Etiology:

- Depletion of phosphorus stores due to increased cellular demand (hypermetabolism) and malnutrition in the critically ill patient.
- Increased uptake stimulated by ↑ circulating levels of insulin, epinephrine, **thyroxine therapy**
- Metabolic/respiratory alkalosis leading to an intracellular shift of phosphorus
- Other: hyperparathyroidism, malnutrition, alcoholism, vitamin D deficiency, diabetic ketoacidosis, GI loss, sepsis, burns

Most Common Clinical Manifestations:

- Tissue hypoxia, ↓ myocardial contractility, impaired diaphragmatic contractility, ↓ systemic vascular resistance
- Decreased function of leukocytes and platelets
- End-organ effect: Global tissue hypoxia, poor heart function, increased need for vasopressors

Treatment of Hypophosphatemia

- Correct confounding factors: metabolic alkalosis
- Replacement Therapy
  - If $K^+ < 4.0$, use Potassium Phosphate
  - If $K^+ > 4.0$, Na < 150, use Sodium Phosphate

PO_4^{3-} level	Replacement Dosing
1.5 – 2.2 mg/dL	0.32 mmol/kg IVPB over 4 hrs
< 1.5 mg/dL	0.5 mmol/kg IVPB over 4 hrs
1.47 mEq K per 1 mmol KPO_4 (or ~ 44 mEq K in 30 mmol KPO_4) 1.33 mEq Na per 1 mmol $NaPO_4$ (or ~ 40 mEq Na in 30 mmol $NaPO_4$)	

- Monitor for hypocalcemia related to redistribution
- Wait at least one hour after infusion to recheck phosphorus level

Hyperphosphatemia
PO_4 > 4.5 mg/dL

Most Common Etiology:

- Excess phosphorus stores/decreased secretion due to renal insufficiency
- Metabolic/respiratory acidosis leading to extracellular shift of phosphorus
- Tissue breakdown during rhabdomyolysis leading to extracellular shift of phosphorus
- Other: hypoparathyroidism, vitamin D toxicity, tumor lysis

Most Common Clinical Manifestations:

- Hypocalcemia due to calcium-phosphate precipitation
- End-organ effect: Precipitation *(which occurs when serum Ca x serum Phos > 55-60mg/dL)* can lead to Ca-Phos deposits into soft tissues causing organ damage

Treatment of Hyperphosphatemia

- Dialysis
- Administration of phosphate binders
- ***Not necessary to treat during donor management!***

Calcium

Interesting Stuff About Calcium

- Calcium functions in bone metabolism, blood coagulation, platelet adhesion, neuromuscular activity, endocrine and exocrine secretory functions, and electrophysiology of the heart and smooth muscles

- Approximately 40-50% of calcium in the blood is bound to plasma proteins, primarily albumin. For serum albumin levels < 4g/dL:

  Corrected serum Ca = serum Ca + (0.8 x [4-serum albumin])

- Ionized calcium is the biologically active form of calcium and is a better indicator of the functional status of calcium metabolism.

Hypocalcemia

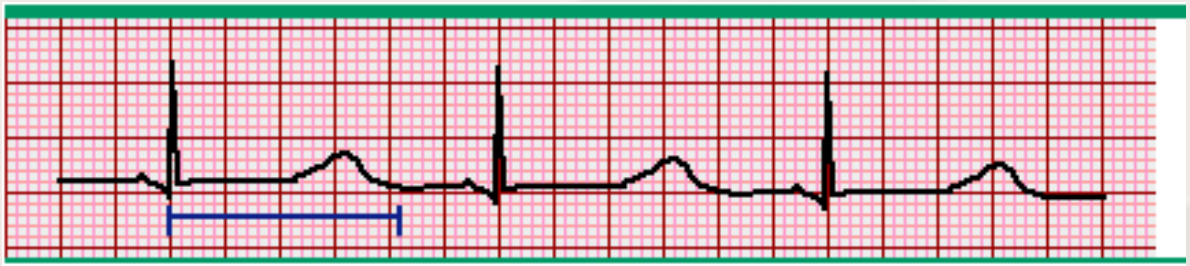
$iCa^{2+} < 1.10$ mmol/L

Most Common Etiology:

- Increased intravascular calcium binding: ↑lactate levels, ↑citrate from massive blood transfusions, acute metabolic/respiratory alkalosis , phosphorus replacement
- Other: hypoalbuminemia, hypomagnesemia, hyperphosphatemia, pancreatitis, hypoparathyroidism, sepsis

Most Common Clinical Manifestations:

- EKG changes: prolonged QT interval



QT interval prolongation is the hallmark of hypocalcemia. In this example, the corrected QT interval is >0.6 seconds (normal ≤0.44 seconds).

- Tetany

Treatment of Hypocalcemia

- Correct confounding factors: metabolic alkalosis
- Replacement therapy:
  - 1 g Calcium Chloride IV over 30 minutes
  - If CalCl unavailable, use 1 g Calcium Gluconate IV over 30 minutes

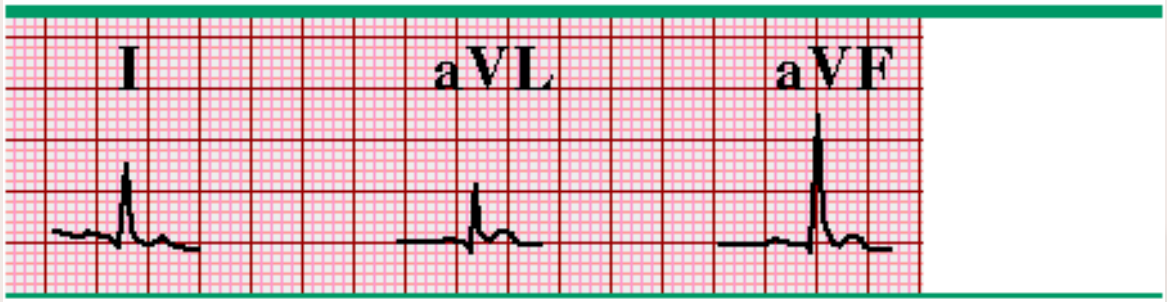
Hypercalcemia
$iCa^{2+} > 1.40$ mmol/L

Most Common Etiology:

- Malignancy, hyperparathyroidism, vitamin D toxicity, adrenal insufficiency, rhabdomyolysis, renal failure

Most Common Clinical Manifestations:

- EKG changes: shortened QT interval, bradycardia



A short QT interval (<0.36 seconds), primarily secondary to a decrease in the ST segment duration, is characteristic of hypercalcemia. The initial portion of the T wave has an abrupt upslope.

Treatment of Hypercalcemia

- Fluid replacement
- Hemodialysis
- ***Rare occurrence during donor management!***

Hyperglycemia

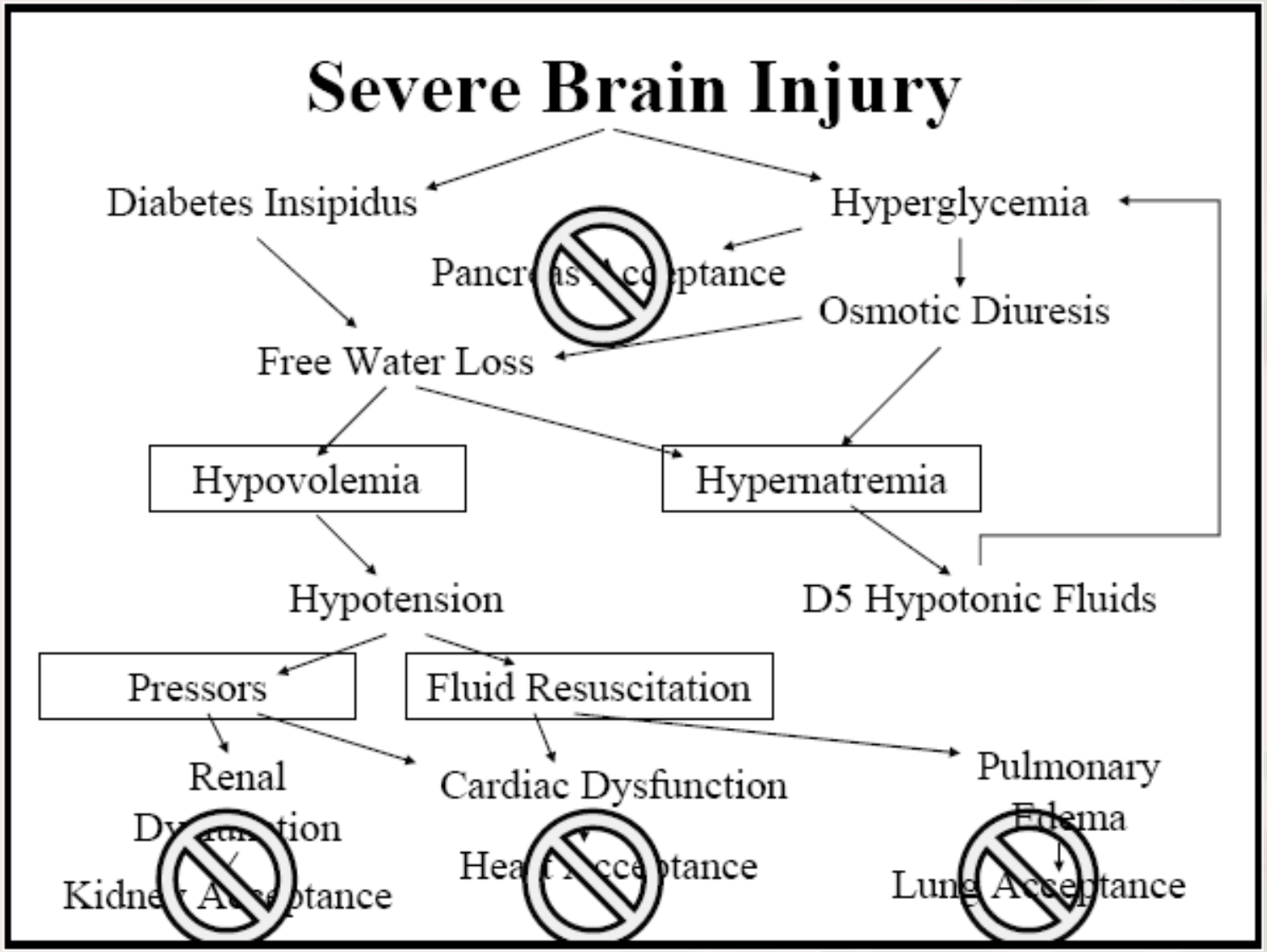
Hyperglycemia: Etiology

- Release of glucocorticoids from physiologic stress response
- Reduced insulin levels due to catecholamine release or inotrope infusion
  - In animal models, insulin levels declined to 50% of normal within 3 hours and 20% of normal within 13 hours after brain death*
- Resuscitation with glucose-containing fluids
- Administration of steroids

*Reference: Novitzky D, Cooper DKC, Rosendale JD, Kauffman HM. Hormonal therapy of the brain-dead organ donor: experimental and clinical studies. *Transplantation*. 2006;82:1396-1401.

Hyperglycemia: Complications

- Hyperosmolar state → osmotic diuresis → dehydration and extracellular shift of electrolytes
  - Hypernatremia
  - Hypokalemia
  - Hypophosphatemia
  - Hypomagnesemia
  - Hypocalcemia
- Ketosis → metabolic acidosis
- Domino effect on donor management and successful organ placement…



Taken from "How Sweet it is: Intensive Glycemic Control in the ICU," presentation at NATCO by Michael Marvin, MD (Director of Liver Transplant, University of Louisville Jewish Hospital)

Hyperglycemia: Treatment

- Consider changing glucose concentration of IV fluids
- Electrolyte replacement
- IV Insulin drip
  - Refer to Insulin Infusion Orders

- GOAL: Blood glucose <150 mg/dL

Adult Organ Donor Insulin Infusion Orders

Goal: Titrate insulin drip to keep blood glucose (BG) **80-110 mg/dL.**

1. Check BG prior to insulin drip initiation. If BG > 110 mg/dL, start insulin drip at **2 units/hr**.
2. Target for correction of hyperglycemia is 50-100 mg/dL drop in BG per hour.
3. Check BG **hourly**.

Titration Order: To determine correction factor for insulin drip:

1. Calculate change in BG from previous hour:
   - Current BG level – last BG level
   - Result is (+) if BG is rising, (-) if BG is falling
2. From the calculation above, determine appropriate "change in BG from previous hour" in the first column below.
3. Read across to appropriate "current BG" column to find correction factor constant.

Change in BG from previous hour	Current BG < 60 mg/dL	Current BG 60-80 mg/dL	Current BG 81-120 mg/dL	Current BG 121-180 mg/dL	Current BG > 180 mg/dL
≥ + 100				Current rate x 2.0	Current rate x 2.0
+ 51 to +99			Current rate x 1.5	Current rate x 1.7	Current rate x 1.8
+1 to +50	Stop	Current rate x 1.0	Current rate x 1.2	Current rate x 1.4	Current rate x 1.5
0 to -49	Stop	Current rate x 0.9	Current rate x 1.1	Current rate x 1.2	Current rate x 1.3
-50 to -99	Stop	Current rate x 0.7	Current rate x 0.9	Current rate x 1.0	Current rate x 1.0
≥ - 100	Stop	Stop	Current rate x 0.7	Current rate x 0.8	Current rate x 0.9

Thyroid Hormone Replacement

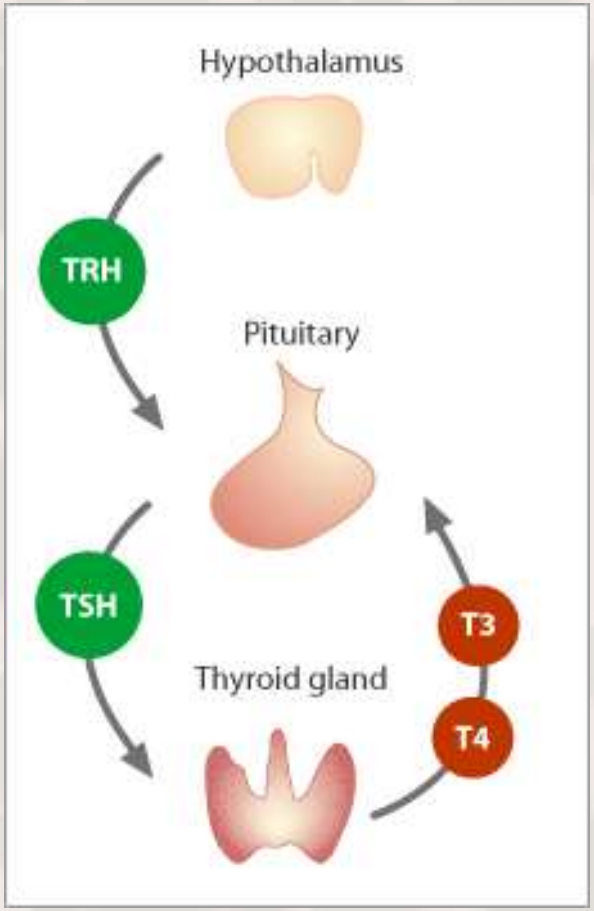
Normal Thyroid Physiology

Hypothalamus produces thyrotropin releasing hormone (TRH)

TRH stimulates the production of thyroid-stimulating hormone (TSH) by the pituitary gland

TSH stimulates the production of tetratraiodothyronine (T_4) by the thyroid gland

T_4 is metabolically converted to triiodothyronine (T_3) in many tissues, especially the liver and kidneys



Reference: Powner DJ, Hernandez M. A review of thyroid hormone administration during adult donor care. *Progress in Transplantation*. 2005;15:202-207

What does thyroid hormone replacement do?

Normal Physiologic Effects of T_3 [1]

- ↑ basal metabolic rate
- ↑ myocardial diastolic relaxation, enhanced systolic function, increased expression of beta-adrenergic receptors, increased rates of depolarization and repolarization of the SA node, increased number of beta-adrenergic receptors in the heart, and amplification of catecholamine action at a postreceptor site
- In animal models, plasma levels of T_3 and T_4 have been shown to fall 50% within one hour after brain death and become undetectable within 9-16 hrs [3]

Proposed benefits of thyroxine [2]

- positive inotropic and chronotropic effects, heightened adrenergic sensitivity
- reduced requirement for exogenous catecholamines, which are associated with poor graft function and reduced graft survival
- prevention of cardiovascular deterioration, which is associated with a shift of cellular metabolism from aerobic to anaerobic, with resulting depletion of glycogen and myocardial high-energy stores and the accumulation of lactate

References: 1. Gardner DG, Shoback D, eds. Greenspan's Basic and Clinical Endocrinology, 8th ed.
2. Salim A, Vassiliu P, Velmahos GC, et al. The role of thyroid hormone administration in potential organ donors. *Archives of Surgery*. 2001;136:1377-1380.
3. Novitzky D, Cooper DKC, Rosendale JD, Kauffman HM. Hormonal therapy of the brain-dead organ donor: experimental and clinical studies. *Transplantation*. 2006;82:1396-1401.

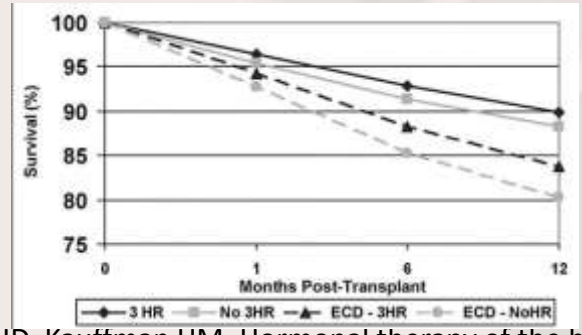
What does the research say?

- Thyroid hormone replacement therapy remains a controversial component of donor management. A limited number of studies have been conducted with human donors, and these show inconsistent results. Those studies which are supportive of T_3/T_4 replacement therapy usually also include administration of steroids, insulin, and vasopressin and propose its benefit as "rescue" treatment for donors who have required higher doses of inotropic or vasopressor medications.
- Powner's article review*:
  - The number of appropriately designed interventional studies found was insufficient to allow a formal meta-analysis
  - Of the 10 studies reviewed: 5 supported the use of thyroid hormone during some phase of donor care, 4 did not, and 1 was equivocal.
  - Hypertension resulting from thyroid administration was noted in 5 patients from 2 studies, necessitating discontinuation of therapy. In all cases, the HTN thereafter resolved and caused no direct organ injury.
  - Conclusion: Additional prospective randomized studies are needed and may contribute substantially to future recommendations. Until then, the use of a thyroid hormone replacement protocol and its dosing should be decided by the individual OPO.

*Reference: Powner DJ, Hernandez M. A review of thyroid hormone administration during adult donor care. *Progress in Transplantation*. 2005;15:202-207

What does the research say?

- OPTN/UNOS retrospective analysis from 2000-2001 on use of 3-drug hormonal resuscitation (HR)*
  - mean number of organs transplanted per donor 22.5% greater with use of 3-drug HR (3.8 vs. 3.1)
  - use of 3-drug HR associated with the following statistically significant increased
  - probabilities of an organ being transplanted from a donor: kidney 7.3%, heart 4.7%, liver 4.9%, lung 2.8%, pancreas 6.0%
  - one-month graft loss for heart recipients was 3.8% when donor received 3-drug HR compared to 7.9% when they received none
  - for heart recipients, analysis showed 46% reduced odds of death within 30 days and a 48% reduced odds of early graft dysfunction when 3-drug HR used
  - for kidney recipients, analysis showed significantly improved one-year kidney graft survival with both SCDs and ECDs when the donor received 3-drug HR
  - for liver recipients, analysis showed no significant difference in one-year survival



*Reference: Novitzky D, Cooper DKC, Rosendale JD, Kauffman HM. Hormonal therapy of the brain-dead organ donor: experimental and clinical studies. *Transplantation*. 2006;82:1396-1401.

Thank You

Questions

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