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, or 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
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.

Diabetes Insipidus: Diagnosis

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>DI</th>
<th>Mannitol Therapy</th>
<th>Hyperglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Na (mmol/L)</td>
<td>&gt; 150</td>
<td>&gt; 150</td>
<td>&gt; 150</td>
</tr>
<tr>
<td>Serum Osmo (mOsm)</td>
<td>&gt; 300</td>
<td>&gt; 300</td>
<td>&gt; 300</td>
</tr>
<tr>
<td>Serum Osmolar Gap (mOsm)</td>
<td>Normal</td>
<td>&gt; 10-15</td>
<td>&gt; 10-15</td>
</tr>
<tr>
<td>Urine Output (ml/h)</td>
<td>&gt; 300</td>
<td>&gt; 200</td>
<td>&gt; 200</td>
</tr>
<tr>
<td>Urine Na (mmol/L)</td>
<td>&lt; 10</td>
<td>50-70</td>
<td>50-70</td>
</tr>
<tr>
<td>Urine Osmo (mOsm/L)</td>
<td>&lt; 200</td>
<td>&gt; 300</td>
<td>&gt; 300</td>
</tr>
<tr>
<td>Urine Spec Gravity</td>
<td>&lt; 1.005</td>
<td>&gt; 1.020</td>
<td>&gt; 1.020</td>
</tr>
<tr>
<td>Urine Glucose</td>
<td>Absent</td>
<td>Absent</td>
<td>Present</td>
</tr>
</tbody>
</table>
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)
  – [Link](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 POIKILOATHERMIC, 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°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°C can lead to ventricular irritability and refractory dysrythmias

**Hyperthermia/Rapid rewarming**

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

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 °C (96 – 100°F)

Cardiac Output

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

\[
\text{Cardiac Output (CO)} = \text{Stroke Volume (SV)} \times \text{Heart Rate (HR)}
\]

- Measurements:
  - \( \text{CO} = \text{SV} \times \text{HR} \), normal 4-8 L/min
  - Cardiac Index (CI) = \( \frac{\text{CO}}{\text{BSA}} \), normal 2.5-4 L/min/m²
  - Ejection Fraction (EF) = \( \frac{\text{SV}}{\text{EDV}} \) 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 O₂ consumption

<table>
<thead>
<tr>
<th>Causes</th>
<th>Increased Preload</th>
<th>Decreased Preload</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure, hypervolemia, excessive vasoconstriction, mitral/aortic valve insufficiency</td>
<td><strong>Hypovolemia</strong>, loss of vasomotor tone, ↑ intrathoracic pressure, cardiac tamponade, RV failure, tachycardia</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>Diuretics, venous vasodilators</td>
<td>Volume/blood replacement</td>
</tr>
</tbody>
</table>
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)

<table>
<thead>
<tr>
<th>Causes</th>
<th>Increased Afterload</th>
<th>Decreased Afterload</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTN, pulmonary HTN, excessive vasoconstriction</td>
<td>Arterial/pulmonary vasodilators, oxygen</td>
<td>Vasodilatation</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td>Vasopressors</td>
</tr>
</tbody>
</table>
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 O₂ consumption, ↑SV and CO (within physiologic limits)

<table>
<thead>
<tr>
<th>Causes</th>
<th>Increased Contractility</th>
<th>Decreased Contractility</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNS stimulation, inotropes, hypercalcemia</td>
<td>Brain death process, trauma, MI, metabolic depression, arrhythmias</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>Beta-blockers, calcium-channel blockers</td>
<td>T₄ therapy, inotropes, phosphorus/calcium replacement</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>LOCATION</th>
<th>CORONARY ARtery</th>
<th>EKG FINDINGS</th>
<th>CLINICAL IMPLICATIONS</th>
<th>SPECIFIC TREATMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANTEROSEPTAL WALL</td>
<td>LAD</td>
<td>• $V_1$ through $V_4$</td>
<td>LV failure, significant hemodynamic compromise; CHF, pulmonary edema, cardiogenic shock, intraventricular conduction disturbances</td>
<td>• Vasopressors for BP&lt;br&gt;• coronary artery vasodilators to ↓ afterload, ↑ CO, and ↓ myocardial $O_2$ consumption&lt;br&gt;• pacemaker</td>
</tr>
<tr>
<td>LATERAL WALL</td>
<td>L Circumflex</td>
<td>• I, aVL, $V_5$, $V_6$</td>
<td>Evaluate for posterior wall involvement; some hemodynamic changes, SA/AV dysrhythmias</td>
<td>• cardiac monitoring&lt;br&gt;• pacemaker</td>
</tr>
<tr>
<td>POSTERIOR WALL</td>
<td>L Circumflex</td>
<td>• $V_1$ and $V_2$</td>
<td>Evaluate for lateral wall involvement; some hemodynamic changes, SA/AV dysrhythmias</td>
<td>• treatment of bradycardia/heart block&lt;br&gt;• pacemaker</td>
</tr>
<tr>
<td>INFERIOR WALL</td>
<td>RCA</td>
<td>• II, III, aVF</td>
<td>Evaluate for RV involvement; some hemodynamic changes, potential for significant SA/AV dysrhythmias</td>
<td>• treatment of bradycardia/heart block&lt;br&gt;• fluid restrict/diuretics&lt;br&gt;• Nipride to ↓ afterload&lt;br&gt;• pacemaker</td>
</tr>
<tr>
<td>RIGHT VENTRICULAR WALL</td>
<td>RCA</td>
<td>• Right precordial chest leads ($RV_{1-6}$)</td>
<td>Evaluate for inferior wall involvement; some hemodynamic changes, potential for significant SA/AV dysrhythmias</td>
<td>• meds to ↑ contractility and ↓ RV afterload&lt;br&gt;• fluids to ↑ preload (to ↑ CO)&lt;br&gt;• pacemaker</td>
</tr>
</tbody>
</table>
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:

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Location</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha₁</td>
<td>Vascular smooth muscle (arterioles and veins)</td>
<td>Systemic vasoconstriction</td>
</tr>
<tr>
<td>Alpha₂</td>
<td>Vascular smooth muscle (coronary and renal arterioles)</td>
<td>Vasoconstriction of coronary and renal vessels</td>
</tr>
<tr>
<td>Beta₁</td>
<td>Heart, kidney</td>
<td>↑ HR, ↑ contractility, ↑ conductivity</td>
</tr>
<tr>
<td>Beta₂</td>
<td>Vascular smooth muscle (arterioles), bronchial smooth muscle, liver, AV node</td>
<td>Vasodilatation, bronchodilatation, stimulation of glycogenolysis, ↑ conductivity</td>
</tr>
<tr>
<td>Dopaminergic</td>
<td>Renal and mesenteric artery bed</td>
<td>Vasodilation</td>
</tr>
</tbody>
</table>
SNS effects of “Pressors”
or: Why a Pressor is not always a Pressor

- Mechanism of action on the adrenergic receptor:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Alpha effect</th>
<th>Beta&lt;sub&gt;1&lt;/sub&gt; effect</th>
<th>Beta&lt;sub&gt;2&lt;/sub&gt; effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenylephrine</td>
<td>+++</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>+++</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>+++</td>
<td>++++</td>
<td>++</td>
</tr>
<tr>
<td>Dopamine</td>
<td>++ &gt;5mcg/kg/min +++ &gt;10mcg/kg/min</td>
<td>+++ &lt;10mcg/kg/min</td>
<td>+</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>+</td>
<td>++++</td>
<td>++</td>
</tr>
</tbody>
</table>
Hemodynamic Treatment Algorithm
## Swan Ganz Interpretation

### Normal Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Arterial Pressure (MAP)</td>
<td>60-100 mmHg</td>
</tr>
<tr>
<td>Central Venous Pressure (CVP)</td>
<td>2-6 mmHg</td>
</tr>
<tr>
<td>Pulmonary Artery Systolic Pressure (PA$_S$)</td>
<td>20-30 mmHg</td>
</tr>
<tr>
<td>Pulmonary Artery Diastolic Pressure (PA$_D$)</td>
<td>10-20 mmHg</td>
</tr>
<tr>
<td>Pulmonary Artery Mean Pressure (PA$_M$)</td>
<td>10-15 mmHg</td>
</tr>
<tr>
<td>Pulmonary Capillary Wedge Pressure (PCWP)</td>
<td>4-12 mmHg</td>
</tr>
<tr>
<td>Cardiac Output (CO)</td>
<td>4-8 L/min</td>
</tr>
<tr>
<td>Cardiac Index (CI)</td>
<td>2.5-4 L/min/m$^2$</td>
</tr>
<tr>
<td>Stroke Volume (SV)</td>
<td>60-100 ml/beat</td>
</tr>
<tr>
<td>Systemic Vascular Resistance (SVR)</td>
<td>900-1400 dynes/sec/cm$^5$</td>
</tr>
<tr>
<td>Pulmonary Vascular Resistance (PVR)</td>
<td>30-250 dynes/sec/cm$^5$</td>
</tr>
<tr>
<td>Venous Oxygen Saturation (SVO$_2$)</td>
<td>60-80%</td>
</tr>
<tr>
<td>Left Ventricular Stroke Work Index (LVSWI)</td>
<td>35-85 g/m</td>
</tr>
<tr>
<td>Right Ventricular Stroke Work Index (RVSWI)</td>
<td>7-12 g/m</td>
</tr>
</tbody>
</table>
Electrolytes

Where did they go?
Sodium
Hyponatremia
$Na^+ < 125\text{mEq/L}$

**Most Common Etiology:**
- Hyperglycemia causes shift of water into the extracellular space $\rightarrow$ 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 fluids¹:
  1. Calculate sodium deficit:
     \[
     \text{Na deficit (mEq)} = \text{TBW}^* \times (140 - \text{measured serum Na})
     \]
  2. Calculate effect of treatment:
     \[
     1L \text{ NS: } \Delta \text{ serum Na} = (154\text{mEq/L} - \text{measured serum Na})/(\text{TBW}^* + 1)
     \]
     \[
     1L \text{ 3\% NaCl: } \Delta \text{ serum Na} = (512\text{mEq/L} - \text{measured serum Na})/(\text{TBW}^* + 1)
     \]
     \[(\text{Note: Administer 3\% NaCl @ 1-2ml/kg/hr})\]
     \[*\text{TBW (men)} = 0.6L/kg \times \text{weight (kg)}\]
     \[\text{TBW (women)} = 0.5L/kg \times \text{weight (kg)}\]
- Administer sodium bicarbonate (NaHCO₃) with coexisting acidosis (pH <7.35)
  - One amp (50mL) of NaHCO₃ contains 44-54mEq Na

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\(^1\).

---

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:
     
     \[
     \text{Free water deficit (in L)} = \text{TBW}^* \times (\frac{[\text{serum Na}/140] - 1}{})
     \]
  2. Evaluate volume status to determine IV fluid choice
  3. Calculate effect of treatment:
     
     \[
     1L \text{ D5W}: \Delta \text{ serum Na} = \frac{(0\text{mEq/L} - \text{serum Na})}{(\text{TBW}^* + 1)}
     \]
     
     \[
     1L 0.225\% \text{ NS}: \Delta \text{ serum Na} = \frac{(38.5\text{mEq/L} - \text{serum Na})}{(\text{TBW}^* + 1)}
     \]
     
     \[
     1L 0.45\% \text{ NS}: \Delta \text{ serum Na} = \frac{(77\text{mEq/L} - \text{serum Na})}{(\text{TBW}^* + 1)}
     \]

     *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, \textit{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\(_2\)O via NG/OG (clamp x 1hr, then drain)

Potassium
Hypokalemia
$K^+ < 4.0 \text{ mEq/L}$

**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
- 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)
  – Potassium Phosphate with coexisting hypophosphatemia (see PO₄ replacement dosing)

<table>
<thead>
<tr>
<th>K⁺ level</th>
<th>Replacement Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5 – 3.9 mEq/L</td>
<td>20 mEq KCl or K acetate IVPB over 1 hr*</td>
</tr>
<tr>
<td>&lt; 3.5 mEq/L</td>
<td>40 mEq KCl or K acetate IVPB over 1-2 hrs*</td>
</tr>
</tbody>
</table>

* Infuse through central line, otherwise ↓ infusion rate to 10 mEq/hr

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
- Arrhythmias: bradycardia, Vfib
Treatment of Hyperkalemia

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

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

Magnesium
Hypomagnesemia
\[ \text{Mg}^{2+} < 2.0 \text{ mg/dL} \]

**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)

<table>
<thead>
<tr>
<th>Mg²⁺ level</th>
<th>Replacement Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.6 – 1.9 mg/dL</td>
<td>2 g Mag Sulfate IVPB over 1 hr</td>
</tr>
<tr>
<td>&lt; 1.6 mg/dL</td>
<td>4 g Mag Sulfate IVPB over 2 hrs</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>$PO_4^{3-}$ level</th>
<th>Replacement Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 – 2.2 mg/dL</td>
<td>0.32 mmol/kg IVPB over 4 hrs</td>
</tr>
<tr>
<td>&lt; 1.5 mg/dL</td>
<td>0.5 mmol/kg IVPB over 4 hrs</td>
</tr>
</tbody>
</table>

- 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  
$\text{PO}_4 > 4.5 \text{ mg/dL}$

**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

Most Common Etiology: $i\text{Ca}^{2+} < 1.10 \text{ mmol/L}$

- 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
- Tetany

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

![EKG Image]

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

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...
Severe Brain Injury

Diabetes Insipidus → Hyperglycemia
  ↓
Pancreas → Osmotic Diuresis
  ↓
Free Water Loss
  ↓
Hypovolemia
  ↓
Hypotension
  ↓
Pressors
  ↓
Renal Dysfunction
  ↓
Kidney Acceptance

Fluid Resuscitation
  ↓
Cardiac Dysfunction
  ↓
Heart Acceptance

Hypernatremia
  ↓
D5 Hypotonic Fluids
  ↓
Pulmonary Edema
  ↓
Lung Acceptance

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:** Titrated 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.

<table>
<thead>
<tr>
<th>Change in BG from previous hour</th>
<th>Current BG &lt; 60 mg/dL</th>
<th>Current BG 60-80 mg/dL</th>
<th>Current BG 81-120 mg/dL</th>
<th>Current BG 121-180 mg/dL</th>
<th>Current BG &gt; 180 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ +100</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+51 to +99</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+1 to +50</td>
<td>Stop</td>
<td>Current rate x 1.0</td>
<td>Current rate x 1.2</td>
<td>Current rate x 1.4</td>
<td>Current rate x 1.5</td>
</tr>
<tr>
<td>0 to -49</td>
<td>Stop</td>
<td>Current rate x 0.9</td>
<td>Current rate x 1.1</td>
<td>Current rate x 1.2</td>
<td>Current rate x 1.3</td>
</tr>
<tr>
<td>-50 to -99</td>
<td>Stop</td>
<td>Current rate x 0.7</td>
<td>Current rate x 0.9</td>
<td>Current rate x 1.0</td>
<td>Current rate x 1.0</td>
</tr>
<tr>
<td>≥ -100</td>
<td>Stop</td>
<td>Stop</td>
<td>Current rate x 0.7</td>
<td>Current rate x 0.8</td>
<td>Current rate x 0.9</td>
</tr>
</tbody>
</table>
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 tetrataiiodothyronine (T₄) by the thyroid gland

T₄ is metabolically converted to triiiodothyronine (T₃) in many tissues, especially the liver and kidneys

What does thyroid hormone replacement do?

Normal Physiologic Effects of $T_3$\textsuperscript{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 \textsuperscript{3}

Proposed benefits of thyroxine \textsuperscript{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, 8\textsuperscript{th} ed.
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.

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

Thank You

Questions

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