Overview

- Total Body Fluid
- Intravascular Volume Depletion
- Fluid resuscitation vs. Maintenance IV Fluid
- Osmolarity of IV Fluids
- Hypertonic Saline
  - Hyponatremia
- Hypotonic Fluid
  - Hypernatremia
- Hypokalemia and Hyperkalemia
- Other Electrolytes (Mg, PO₄, Ca) and shortages

To answer Question 1, think about…

- How do we recognize intravascular volume depletion?
- How do IV fluids distribute in total body fluid?
- What IV fluids can be used to optimize intravascular volume?

Conflicts of Interest

- I have no conflicts to disclose.

Question 1 (Fluid Resuscitation)

A 74yo female presents with a 3-day history of cough, fever to 102, and lethargy. Vitals/Labs: BP 72/40, HR 115, CXR: LUL infiltrate, WBC 18,000, Hgb 12.5, BUN/Cr 28/1.7 (baseline Cr 1.2), BG 82, UO 10ml/hr, wt 72kg. PMH: CAD. After 500ml NS IV bolus, BP is 80/46. Which one of the following is the most appropriate treatment?

A. Furosemide 40mg IV
B. 0.9% NaCl 300ml/hr + Norepinephrine for SBP > 90
C. 1000ml fluid bolus with D5 / 0.9% NaCl
D. 500ml fluid bolus with 0.9% NaCl
E. 500ml fluid bolus with 5% Albumin

Total Body Fluid

- 60% Intracellular (IC)
- 40% Extracellular (EC)
- 75% Interstitial
- 25% Intravascular
Intravascular Space

- Not exactly “extracellular” because there are cells in this space (RBC’s)
- The extracellular fluid in the intravascular space is known as plasma, and is about ~ 3 L
- There’s an additional ~ 2L of fluid in RBC’s, making the total blood volume about 5L
- Intravascular fluid is analogous to the fluid in your car’s gas tank

Intravascular Volume Depletion

- Intravascular volume depletion due to:
  - Hemorrhagic shock (blood loss)
  - Septic shock (fluid redistribution)
  - Cardiogenic shock (usually fluid overload)
- Intravascular volume depletion causes reduced myocardial function and subsequent organ hypoperfusion

The Starling Curve

Measures of Intravascular Volume (e.g., CVP, LVEDP, MAP)

Intravascular Volume Depletion

- S/S: SBP < 80, HR > 100, BUN:Cr > 10:1, ↓ UO, dizziness, altered mental status
- Perhaps the best sign of intravascular fluid depletion is the patient’s response to a fluid bolus
- S/S usually occur when 15% (~750ml) lost
- Need prompt intravascular fluid replacement through central line to maintain organ perfusion
  - Crystalloids
  - Colloids

Question 2 (Fluid Resuscitation)

Which of the following IV fluids provides the most intravascular volume replacement?

A. NS 1000ml
B. D5W 1000ml
C. 25% Albumin 200ml
D. 5% Albumin 500ml

Distribution of IV Crystalloid

- 0.9% NaCl or LR
  - Sodium and chloride do not freely enter cells
  - Distributed evenly in extracellular space
    - 75% Interstitial and 25% Intravascular = 250ml per L infused
- D5W
  - Dextrose is metabolized to H2O and CO2
  - Water crosses any membrane, will distribute evenly in TBW
    - 60% intracellular, 40% extracellular...then 25% of EC intravascular = 100ml per L infused
- NS or LR recommended for fluid resuscitation
**NS vs. LR**
- LR is an isotonic solution consisting mostly of Na and Cl, but also lactate, K⁺, and Ca²⁺
- LR and NS are equivalent with respect to fluid resuscitation
- Lactate is metabolized to bicarbonate and can be useful for metabolic acidosis, however lactate metabolism is impaired during shock, thus it’s an ineffective source of bicarbonate
- LR is historically preferred in trauma patients, but no evidence suggest superiority over NS for fluid resuscitation

**Distribution of IV Colloid**
- Colloids are too large to cross capillary membrane, so all volume infused remains in intravascular space
- PRBC fills intravascular space and carries O₂
- Pooled human plasma
  - e.g., 5% albumin, plasma protein fraction or plasmanate
- Semi-synthetic glucose polymer (Dextran)
- Semi-synthetic hydroxyethyl starch (hetastarch)
- For products above, 500ml infused = 500ml intravascular volume replacement

**Distribution of IV Colloid**
- Unlike 5% albumin, 25% albumin causes fluid redistribution
- 100ml IV = 500ml intravascular volume replacement
- Theoretical risk of cellular dehydration (so monitor for organ dysfunction)
- Possibly useful in patients with ascites or pleural effusions where fluid redistribution is goal

**Crystalloids vs. Colloids**
- Crystalloids (NS, LR) are recommended
- Colloids “seem” better than crystalloids based on distribution properties
  - No evidence to demonstrate improved outcomes
  - Higher cost

**Limited evidence, but colloids used in certain situations…**
- Consider albumin after fluid resuscitation with crystalloid (usually 4-6 L) has failed to achieve hemodynamic goals or when clinically significant edema limits further administration of crystalloid
  - e.g., pulmonary edema causing hypoxia
- Avoid hetastarch due to risk of kidney injury and coagulopathy

**Limited evidence, but colloids used in certain situations…**
- Consider albumin in patients who have required large volume of resuscitation fluid AND albumin < 2.5 g/dL
- Consider albumin (preferably 25%) + loop diuretic if clinically significant edema AND albumin < 2.5 g/dL AND diuretics alone ineffective
  - e.g., pulmonary edema or effusion causing respiratory failure
How much fluid?

- For fluid resuscitation, administer 500-1000ml through a large-bore central catheter as fast as possible, then re-evaluate.
  - Continue as long as S/S of volume depletion improve (BP, HR, CVP, UO, etc)
- For daily fluid maintenance, many use 1500 ml for first 20kg, then 20ml/kg thereafter (~2500ml/day) OR 20-40 ml/kg/day
  - Adjust based on I/O’s, weight, estimated insensible loss (e.g., skin when febrile)

Maintenance IV Fluid

- Goal is prevent dehydration and maintain normal fluid and electrolyte balance
- Not for intravascular volume depletion
- Typical maintenance IV fluid is D5 0.45% NaCl + KCl 20 - 40meq/L
  - Omit KCl if elevated K or kidney failure
- 0.9% NaCl, LR, or colloids are NOT appropriate maintenance IV fluids
- Evaluate IV fluids daily and d/c if taking sufficient fluid orally or through feeding tube

Question 1: Answer

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C. 1000ml fluid bolus with D5 / 0.9% NaCl
D. 500ml fluid bolus with 0.9% NaCl
E. 500ml fluid bolus with 5% Albumin

Question 2: Answer

Which of the following IV fluids provides the most intravascular volume replacement?

A. NS 1000ml ~ 250ml
B. D5W 1000ml ~ 100ml
C. 25% Albumin 200ml ~ 1000ml
D. 5% Albumin 500ml ~ 500ml

Question 3 (Osmolarity)

Calculate the osmolarity of D5W

MW = 180 gm/mol

A. 74 mosm/L
B. 154 mosm/L
C. 278 mosm/L
D. 550 mosm/L

Plasma Osmolarity

- Plasma osmolarity (Posm) 275-290 mOsm/kg
- Primary determinant of Posm is sodium salts (hence 2 x 140 = 280 ~ Posm)
- Major changes in serum Na can result in changes in Posm
- Changes in Posm cause fluid shifts across cell membranes
  - Increased Posm causes cellular dehydration
  - Decreased Posm causes cellular overhydration (cell swelling)
Changes in Posm
- Posm maintained in normal range by thirst and secretion of ADH from posterior pituitary.
- Rapid change in Posm or in serum Na can cause permanent neurologic damage in CNS cells.
- Chronic / slow changes in serum Na or Posm are usually well tolerated and asymptomatic.
  - In chronic hyponatremia, cerebral swelling is avoided by osmotic adaptation (i.e., solutes move out of cerebral cells to lower the cellular osmolarity...this prevents the osmotic shift of water into the cerebral cells).
  - Avoid the instinct to quickly correct chronic hyponatremia.

Osmolarity of IV Fluids
- Isotonic
  - No osmotic gradient, no fluid shift.
- Hypotonic IV Fluid
  - Cell overhydration can occur if < 150 mOsm/L.
  - RBC swelling = hemolysis.
  - Brain cell swelling = cerebral edema / herniation.
- Hypertonic IV Fluid
  - Cell dehydration / shrinkage.

Calculate Osmolarity of IV Fluid
- 0.9% NaCl = 0.9 gm/100ml = 9gm/L.
- MW of NaCl = 58.5gm.
- Osmotic Coefficient NaCl = 0.93

\[
\begin{align*}
0.9 \text{ gm} &\times 1 \text{ mol} \times 1000 \text{ mosm} \\
9 \text{ L} &\times 58.5 \text{ gm} &\times 1 \text{ osm} \\
0.93 &\times 1 \text{ mol} \\
&= 287 \text{ mOsm/L (isotonic)}
\end{align*}
\]

Question 3: Answer
- Calculate the osmolarity of D5W.
  - MW = 180 gm/mol.
  - (Osmotic coefficient is not applicable).
  - A. 74 mosm/L
  - B. 154 mosm/L
  - C. 278 mosm/L \((D5W \text{ is Isotonic})\)
  - D. 550 mosm/L

Question 4 (Hypertonic Saline)
- A 72yo female is admitted to the hospital with confusion and visual hallucinations that started 1 day prior. Her serum Na was 118 on admission. Wt is 60kg. Vital signs are stable. She started taking HCTZ 25mg daily 3 weeks prior. The medical resident calls the pharmacy and asks what is the recommended concentration of saline to administer?
  - A. 23.4% NaCl
  - B. 3% NaCl
  - C. 0.9% NaCl
  - D. 0.45% NaCl.

Osmolarity: It gets easier
- Osmolarity of D5W / NS = 278 + 286 = 564.
- Even though this is relatively hypertonic, it has not been associated with clinically significant shifts of fluid.
**Hypertonic Saline**

- Typically 3%, 7.5%, or 23.4%
- Osmolarity ~ 1000, 2500, 8000 respectively
- Administer via central line
- Use
  - Traumatic Brain Injury to reduce elevated ICP and/or increase BP (3%, 7.5%, 23.4%)
  - Acute symptomatic Hyponatremia (usually 3%)
    - Acute = symptom onset within 48h or less
    - Symptomatic = lethargy, psychosis, seizure, coma

**Symptoms of Hyponatremia**

<table>
<thead>
<tr>
<th>Serum Sodium</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>120-125</td>
<td>Nausea, malaise</td>
</tr>
<tr>
<td>115-120</td>
<td>Headache, lethargic, obtundation, unsteadiness, confusion</td>
</tr>
<tr>
<td>110-115</td>
<td>Delirium, seizure, coma, respiratory arrest, death</td>
</tr>
</tbody>
</table>

**Hypertonic Saline is NOT for:**

- Chronic asymptomatic hyponatremia
  - i.e. SIADH is usually chronic and treated with fluid restriction
- Hyponatremia secondary to DKA
  - As glucose is corrected and as intravascular volume is restored, serum Na will correct
- Hyponatremia associated with CHF
  - Usually chronic and asymptomatic
  - If symptomatic, caution regarding volume overload with hypertonic saline

**Safe Use of Hypertonic Saline for Symptomatic Hyponatremia**

- Goal is a SMALL but QUICK rise in Na by 0.75-1 meq/L/hr to a “safe” concentration of 120 mEq/L, then slow to 0.5 mEq/L/hr
- Can be achieved using 3% NaCl 1-2 ml/kg/hr or 250ml bolus over 30 min
- Treat until:
  - Symptoms stop
  - Safe, serum Na range (120-125 mmol/L)
  - Obtained max safe amt of change in serum Na

**Correcting Serum Sodium**

- Max change is 10-12 mmol/L in 24 hours
- Rapid correction of serum sodium can cause central pontine myelinolysis or osmotic demyelination syndrome
  - Characterized by paraparesis, quadriplegia, coma
  - Permanent neurologic damage
  - Highest risk is patients with chronic hyponatremia
- Watch for the “knee-jerk” response to hyponatremia: some things don’t need fixing

**Other Complications of HS**

- Hypokalemia
- Hyperchloremic acidosis
  - Avoid by using 1:1 or 2:1 ratio of NaCl and NaAcetate
- Hypernatremia
- Phlebitis if administered in peripheral vein
- Heart failure (caution if treating hyponatremia in patients with HF)
- Coagulation / platelet dysfunction
- Hypotension if administered rapidly (fluid shift)
Avoid this Error

- 150 mEq Sodium Bicarbonate mixed in 850 ml IV Fluid (typically to prevent RCN).
- If mixed in 0.9% NaCl, the result is equivalent to 3% sodium (hypertonic).
- I suggest using D5W instead.
- Sterile water could be used as well, but I avoid this due to risk of error.

Important Considerations for Patients with Hyponatremia

- Correct Potassium Depletion
- Identify type of hyponatremia (3 types) based on volume
- Treatment is based on type (i.e., volume status) and symptoms

Check K+ if Hyponatremia

- Hypokalemia can cause an intracellular shift of sodium to maintain cell electroneutrality.
- If hypokalemia and hyponatremia occur together, first correct hypokalemia.
- As potassium is replaced, serum sodium will increase due to extracellular shift of sodium.

3 Types of Hyponatremia

<table>
<thead>
<tr>
<th>Description</th>
<th>Hypovolemic Hyponatremia</th>
<th>Normovolemic Hyponatremia</th>
<th>Hypovolemic Hyponatremia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caused by excess Na and fluid but fluid excess predominates</td>
<td>Normal total body Na with excess fluid volume (i.e., dilutional)</td>
<td>Deficit of both Na and fluid but total Na is decreased more than total body water</td>
<td></td>
</tr>
<tr>
<td>SIADH</td>
<td>Fluid loss (e.g., emesis, diuretics, fever), third spacing, renal loss (e.g., diuretics)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Example

- Heart failure, cirrhosis, nephrotic syndrome
- SIADH
- Fluid loss (e.g., emesis, diuretics, fever), third spacing, renal loss (e.g., diuretics)

For Hyponatremia

- If acute, symptomatic hyponatremia treat as previously discussed
- Until intravascular volume is restored, will continue to secrete ADH causing water reabsorption which perpetuates hyponatremia. Once volume restored, ADH secretion will decrease, causing water to be excreted. This could lead to rapid correction of serum Na; careful monitoring is required to prevent overly rapid correction.
3 Types of Hyponatremia

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</tr>
</thead>
<tbody>
<tr>
<td>Fluid loss (e.g., emesis, diarrhea, fever), third spacing, renal loss (e.g., diuretics)</td>
<td>Fluid resuscitation with crystalloid (0.9% NaCl, NOT hypertonic saline)</td>
<td></td>
</tr>
</tbody>
</table>

Once restore intravascular volume, may still need to replace Na (in mEq) deficit: 0.5 (LBW) x (140-Na) for women 0.5(LBW) x (140-Na) for men

Administer 25-50% during first 24 hours based on symptoms and serial serum Na concentrations.

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Question 4: Answer

A 72yo female is admitted to the hospital with confusion and visual hallucinations that started 1 day prior. Her serum Na was 118 on admission. Wt is 60kg. Vital signs are stable. She started taking HCTZ 25mg daily 3 weeks prior. The medical resident calls the pharmacy and asks what is the recommended concentration of saline to administer?

A. 23.4% NaCl
B. 3% NaCl acute, symptomatic, hyponatremia
C. 0.9% NaCl use 0.9% if S/S volume depletion
D. 0.45% NaCl

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Question 5 (Hypertonic Saline)

Which of the following is an appropriate dose of hypertonic saline for this patient (wt 60kg)?

A. 30ml/hr
B. 90ml/hr
C. 180ml/hr
D. 500ml bolus over 15 minutes

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Question 5 Answer

Which of the following is an appropriate dose of hypertonic saline for this patient (wt 60kg)?

A. 30ml/hr
B. 90ml/hr (1-2 ml/kg/hr initially, then adjust based on rate of change of serum sodium)
C. 180ml/hr
D. 500ml bolus over 15 minutes

---

Question 6 (Hypertonic Saline)

Which of the following is an appropriate treatment goal in using hypertonic saline during the 1st 24 hours of admission? (Initial serum Na 118)

A. Increase serum Na to 122
B. Increase serum Na to 132
C. Increase serum Na to 140
D. Increase serum Na to 148

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Question 6: Answer

Which of the following is an appropriate treatment goal in using hypertonic saline during the 1st 24 hours of admission? (Initial serum Na 118)

A. Increase serum Na to 122 (a safe range)
B. Increase serum Na to 132
C. Increase serum Na to 140
D. Increase serum Na to 148

These exceed the max change recommend in 24 hrs
Pseudohyponatremia
- As discussed to this point, hyponatremia is associated with a reduction in plasma osmolality.
- In some cases, hyponatremia associated with normal or elevated plasma osmolality - known as pseudohyponatremia because Na content is not actually reduced, but rather shifted from extracellular compartment into the cells to maintain plasma osmolality in a normal range.
  - Severe hyperlipidemia
  - Severe hyperglycemia (e.g., DKA)
- When correct underlying cause, Na will correct (i.e., shift out of cells).

Vaptans: Efficacy
- Vasopressin receptor antagonists
- IV Conivaptan, oral tolvaptan
- AVP secreted by hypothalamus to regulate osmolality
  - Facilitate aquaresis (electrolyte-free water excretion)
  - Increase serum Na
  - Alleviate symptoms and reduce weight in CHF
- Safe and efficacious for normovolemic (SIADH), or hypervolemic hyponatremia (CHF, Cirrhosis)
  - Facilitate aquaresis (electrolyte-free water excretion)
  - Increase serum Na
  - Alleviate symptoms and reduce weight in CHF
  - No evidence in prospective RCT’s regarding mortality or improving clinical outcomes (e.g., fall prevention, avoid hospitalization, reduce hospital length of stay).

Vaptans: Safety
- Substrates and inhibitors of CYP450 3A4 isoenzymes, therefore monitor for drug interactions with other 3A4 inhibitors that could increase the effect and lead to a rapid increase in serum Na.
- Fluid restriction in combination with a vaptan during the first 24 hours can also increase the risk of overly-rapid correction of serum Na.
  - If needed, fluid restriction can be used after 24 hours of vaptan administration.

Question 7 (Hypotonic Fluid and Hypernatremia)
A 55yo female with CVA, wt 50kg, on hospital day 4.
Receiving enteral nutrition through a nasogastric (NG) feeding tube with Jevity 60ml/hr x 4d. Serum sodium over the last 4 days was 142, 149, 156, and 160 today. She is also receiving NS 100ml/hr x 4d. She has had no change in her mental status over the last 4 days. Other labs are normal. Which of the following orders is most appropriate to correct her serum sodium?
A. 200ml water per FT q 6 hours
B. D5 / 0.2% NaCl to infuse at 100ml/hr
C. Sterile Water IV 100ml/hr
D. D5W IV 100ml/hr

Question 8 (Hypotonic Fluid and Hypernatremia)
What is the most likely cause of her elevated serum sodium?
A. Too much sodium in tube feeding
B. Insufficient free water
C. Inappropriate use of 0.9% NaCl
D. Diabetes Insipidus due to CVA

Hypotonic Fluid
- Avoid IV fluid with osmolarity < 150 mOsm/L
- Albumin 25% diluted with sterile water to make albumin 5% is hypotonic with an osmolarity of about 60 mOsm/L
  - Associated with hemolysis and death
- 0.2% NaCl is hypotonic with an osmolarity of 68 mOsm/L
  - Generally ordered in error
  - Eliminate risk by changing to D5 / 0.2% NaCl, or D2.5 / 0.2% NaCl
  - Note: 5% dextrose = 50gm/L = 170 kcal/L
Appropriate Use of Hypotonic IV Fluid

Hypernatremia

- Na > 145 mEq/L
- Usually associated with an increase in plasma osmolality
- Osmotic gradient causes water movement out of cells into the extracellular space
- Prevented by release of ADH and thirst
  - Mostly occurs in adults with altered mental status with an impaired thirst response or do not have access or ability to ask for water
  - Also occurs in infants
- Causes
  - Loss of water (fever, burns, infection, renal loss, GI loss)
  - Insufficient water (receiving calorics-dense enteral nutrition)
  - Retention of Na (administration of Na)

Hypernatremia Symptoms

- Related to dehydration of brain cells
- Symptoms depend on rate and degree of increase in plasma osmolality
  - Similar to hyponatremia, cerebral cells can have osmotic adaptation (take up solutes, thus limiting osmotic gradient)
- Earlier symptoms include lethargy, weakness, and irritability
- Can progress to twitching, seizures, coma, and death (usually if Na > 155)
- Cerebral dehydration can cause cerebral vein rupture with subsequent intracerebral or subarachnoid hemorrhage

Prevent Hypernatremia

- If receiving calorics-dense enteral nutrition (e.g., 1.5-2 kcal/ml), prevent by providing about 1 ml H2O per kcal
- Check the TF product label for water content
- Most products will supply about 700-850 ml H2O per liter, so the patients will require an additional 150-300 ml of water daily for a 1 kcal/ml product (more if 1.5-2 kcal/ml)
- Administer as water flushes through tube feedings if possible
  - E.g., 50-100ml water flush every 6-8 hrs
  - Especially in patients who can’t communicate thirst

Is Hypernatremia a good reason to use hypotonic saline?

- Generally patients with hypernatremia need water, not NaCl (i.e., 0.2% NaCl)
- But we NEVER give water IV
- So if possible, give water enterally
- Or if NPO, give free water IV (DSW)
  - Dextrose is metabolized to CO2 and water, is isotonic, and can thus be given IV
- Follow same serum Na goals as previously discussed (max change 10-12mmol/L/d)

Hypernatremia Treatment: Estimating Water Deficit

- If hypernatremic, replace water deficit slowly
  - Water Deficit in women = \((0.4 \times \text{Wt}) \times [(\text{Na}/140)-1]\)
  - Water Deficit in men = \((0.5 \times \text{Wt}) \times [(\text{Na}/140)-1]\)
Treatment of Hypernatremia

- Monitor serum sodium every 1-4 hours
- When replacing water deficit (with enteral water or intravenous D5W), if serum Na is decreasing too fast, can administer D5W/0.2% NaCl or D5W/0.45% NaCl to slow the rate of decrease

Example:

- Female patient weighing 50kg with Na = 160
- Water deficit = (0.4 x 50kg) x [(160/140) - 1]
  - Approximately 3 L water deficit
  - Administer over several days, while monitoring rate of change of serum sodium
- Prevent hypernatremia
  - After water deficit is corrected, prevent hypernatremia from developing by increasing daily water to approximately 1 ml water per calorie provided

Question 7: Answer

A 55yo female with CVA, wt 50kg, on hospital day 4. Receiving enteral nutrition through a nasogastric (NG) feeding tube with Jevity 60ml/hr x 4d. Serum sodium over the last 4 days was 142, 149, 156, and 160 today. She is also receiving NS 100ml/hr x 4d. She has had no change in her mental status over the last 4 days. Other labs are normal. Which of the following orders is most appropriate to correct her serum sodium?

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C. Sterile Water IV 100ml/hr
D. D5W IV 100ml/hr

Question 8: Answer

What is the most likely cause of her elevated serum sodium?

A. Too much sodium in tube feeding
B. Insufficient free water (a medical error)
C. Inappropriate use of 0.9% NaCl
D. Diabetes Insipidus due to CVA

What to do with those orders for “quarter saline”?

- This is a potentially fatal error
- Generally ordered in error
- Eliminate risk by changing to
  - D5W (best case scenario if need IV)
  - D5/0.2% NaCl (a recommendation that’s more likely to succeed)
  - D2.5 / 0.2% NaCl (for those who complain about risk of hyperglycemia with 5% dextrose)
  - Addition of KCl will also increase osmolarity
  - Enteral water (best case scenario)

Question 9: Hyperkalemia

A 55yo male with DM and CKD presents with a K+ of 7.2 mEq/L, Ca 9 mg/dL, albumin 3.5, Gluc 302 mg/dL, and peaked T waves on EKG. Which is most appropriate to give first?

A. Reg insulin 10 units IV + 30g glucose IV
B. 10% Ca gluconate 10ml IV over 5 min
C. Kayexalate 15g now
D. Na bicarbonate 50 mEq IV over 5 min
**Potassium (K⁺)**

- The primary intracellular cation
- The perfect balance of K⁺ is maintained between IC and EC by:
  - β₂-stimulation promotes cellular uptake
  - Insulin promotes cellular uptake
  - Plasma K⁺ concentration can cause passive shifts in or out of cells

**Hypokalemia (K<3.5 meq/L)**

- Seldom caused by reduced K⁺ intake because of ↓ kidney excretion
- Causes of hypokalemia
  - A shift of K⁺ into cells can occur with
    - ↑ pH
    - Insulin or carbohydrate load
    - β₂ stimulation (stress, drugs)
    - Hypothermia
  - GI loss
  - Urinary loss
  - ↓ Mg⁺⁺ causes ↑ renal loss of K⁺ (so correct Mg)

**Symptoms of Hypokalemia**

- Generally occur when plasma K⁺ is < 3 mEq/L
- Muscle weakness
  - Most commonly in lower extremities, but can progress to trunk, upper extremities, and respiratory muscles
  - Muscle weakness in GI tract can manifest as ileus, abdominal distention, N, V, constipation
- EKG changes (e.g., flattened T waves)
- Arrhythmias (bradycardia, heart block, VT, VF)
- Digoxin toxicity (even if normal dig level)
- Rhabdomyolysis can occur because hypokalemia can cause reduced blood flow to skeletal muscle

**Treatment of Hypokalemia**

- How much?
  - There is no calculation to estimate K⁺ loss based on a plasma K⁺ concentration
  - K⁺ replacement is guided by plasma K⁺
- How fast?
  - 10-20 mEq/hr, max 20-40 mEq/hr (regardless of route) requires continuous EKG monitoring
- Route?
  - Oral KCl (60-80 meq/d) should be considered if no symptoms and K⁺ > 2.5 -ish
  - If peripheral IV, max concentration is 60 meq/L

**Treatment of Hypokalemia**

- Dosage form
  - KCl is preferred if metabolic alkalosis because these patients typically lose Cl through diuretics or GI loss
  - Potassium acetate IV or potassium bicarbonate orally is preferred for patients with a metabolic acidosis
  - Avoid mixing intravenous K in dextrose, which can cause insulin release with subsequent intracellular shift of K

**Suggested K Replacement**

<table>
<thead>
<tr>
<th>Plasma K</th>
<th>Treatment (if normal kidney fxn)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-3.5</td>
<td>Oral KCl 60-80 mEq/day if no signs or symptoms</td>
<td>Recheck K daily; Doses &gt; 60 mEq should be divided to avoid GI effects</td>
</tr>
<tr>
<td>2.5-3</td>
<td>Oral KCl 120 mEq/day or IV 60-80 mEq administered at 10-20 mEq/hr if signs or symptoms</td>
<td>Monitor K every 2 hours</td>
</tr>
<tr>
<td>2.2.5</td>
<td>IV KCl 10-20 mEq/hr</td>
<td>Consider continuous EKG monitoring</td>
</tr>
<tr>
<td>&lt; 2</td>
<td>IV KCl 20-40 mEq/hr</td>
<td>Requires continuous EKG monitoring</td>
</tr>
</tbody>
</table>
Hyperkalemia: Causes

- Increased intake
- Shift from intracellular to extracellular compartment
  - Acidosis
  - Insulin deficiency
  - β-adrenergic blockade
  - Digoxin overdose
  - Rewarming after hypothermia (e.g., after cardiac surgery or cardiac arrest hypothermia protocol)
  - Succinylcholine
- Reduced urinary excretion
  - Kidney dysfunction
  - Volume depletion
  - Hypoaldosteronism
  - Drugs (K-sparing diuretics, ACEIs, ARBs)

Hyperkalemia: Symptoms

- Muscle weakness or paralysis is caused by changes in neuromuscular conduction and typically occurs when plasma K > 8
- Abnormal cardiac conduction can first manifest as peaked, narrowed T waves (usually if K > 6), widening of the QRS
- Can progress to ventricular fibrillation and asystole
- Not all patients will experience EKG changes, and the initial manifestation of hyperkalemia can be VF, thus consider emergent treatment even if no EKG changes if K > 6.5

Evaluating Hyperkalemia (K>5)

- Is it real? Does it fit the clinical scenario?
  - Artificially elevated if traumatic venipuncture (hemolysis)
  - Artificially elevated if serum, rather than plasma drawn (due to K+ release during coagulation)
- Is pt experiencing severe muscle weakness or EKG changes (narrowed/peaked T) or is K+ > 6.5 meq/L (VF can be first sign)?
  - No – cation-exchange resin (Kayexalate)
  - Yes...

Hyperkalemia Urgent Treatment

1. Calcium gluconate 1-2gm IV over 2-10 minutes can prevent hyperkalemia-induced arrhythmias (quick onset, short duration)
   - Avoid if dig toxicity because can worsen dig effects
2. Drugs that cause an intracellular shift of K+:
   - Insulin 10 units (with optional 25-50gm glucose to prevent hypoglycemia) – effect w/60min
   - Sodium bicarbonate 50mEq – effect w/30-60 min; efficacy is disputed
   - Albuterol 10-20mg neb – effect w/90 min; 40% won’t respond

Hyperkalemia Treatment: Focus on Calcium

- Calcium gluconate can be administered peripherally and is preferred over calcium chloride because of reduced risk of tissue necrosis
  - Calcium chloride can be used if central IV access is available
  - Adjust dose because 10 ml provides 3 x’s more calcium than 10% calcium gluconate
- Onset is within minutes, but short duration (30-60 min)
- Will not reduce plasma K, but will antagonize effect of K in cardiac conduction cells

Hyperkalemia Treatment: Focus on Insulin

- Caution: risk of insulin errors when used in emergent situations
  - Errors involving calculations (100 units/ml)
  - Errors involving preparation
  - Errors involving syringes (using 4 or 10 ml syringe instead of an insulin syringe)
After Urgent Treatment, ↑ K excretion with...

- Diuretics to ↑ renal excretion
  - Loop or thiazide diuretics
  - Ineffective if advanced kidney disease
- Cation-exchange resin (Kayexalate®) 15g PO q6h PRN or as 30-50g retention enema (although less effective than oral)
  - Exchange Na for K resulting in GI excretion of K
  - Caution in kidney or heart failure due to Na retention
  - Do not use 70% sorbitol as vehicle (oral or rectal) due to risk of colonic necrosis and other serious GI effects; mix in water or syrup
  - For enema, mix in 100-200ml water warmed to body temp and retain for 30-60 min or up to 3 hrs; irrigate colon after enema
  - Not for urgent use due to slow onset (2-6h) and unpredictable effect
- Dialysis when other measure ineffective

Focus on Kayexalate & Sorbitol

- Safety: Many reports to FDA of bowel injury with both oral and rectal administration of Kayexalate mixed in sorbitol
- Linked to deposition of drug crystals in GIT, damaging mucosa and causing necrosis
- Most reports involve 70% sorbitol, not 33% (current premixed suspension)
- Risk of colonic necrosis is rare with 33% formulation
- But, a recent systematic review found that formulations without sorbitol also associated with colonic necrosis

More on Kayexalate...

- There are no controlled trials demonstrating efficacy
- FDA approved in 1958...before required to demonstrate efficacy

Question 9: Answer

A 55yo male with DM and CKD presents with a K+ of 7.2 mEq/L, Ca 9 mg/dL, albumin 3.5, Gluc 302 mg/dL, and peaked T waves on EKG. Which is most appropriate to give first?

A. Reg insulin 10 units IV + 30g glucose IV- use after Ca, but without the glucose
B. 10% Ca gluconate 10ml IV over 5 min fast for cardiac instability!
C. Kayexalate 15g now – too slow for acute situation
D. Na bicarbonate 50 mEq IV over 5 min – less effective in patients with CKD

Other Electrolytes

- Magnesium
- Phosphate
- Calcium

Hypomagnesemia

- Normal 1.4-1.8 mEq/L or 1.7-2.3 mg/dL
- Hypomagnesemia usually associated with impaired intestinal absorption (ulcerative colitis, diarrhea, pancreatitis, chronic laxative abuse), inadequate intake, hypokalemia, or increased renal excretion (diuretic use)
  - Common in hospitalized patients
  - Associated with alcoholism and delirium tremens
- Often occurs concurrently with hypokalemia and hypocalcemia
Hypomagnesemia

- Symptoms of hypomagnesemia include tetany (muscle contractions), hypertension, seizures, arrhythmias
- Oral magnesium is fine for asymptomatic patients, but limited by diarrhea
- Symptomatic patients can be treated with 1-4 gm (8-32 mEq) Mg sulfate SLOWLY (i.e., 1 gm/hr) to avoid hypotension and increased renal elimination
  - Can follow with infusion of 0.5 mEq/kg/day
- Administer IV push if emergency (torsades)
- Half of administered Mg is eliminated renally, so replace slowly over 3-5 days
- Reduce doses by half in advanced kidney disease

Hypermagnesemia

- Mg > 2 mEq/L
- Rarely occurs and generally associated with kidney disease
- Signs and symptoms rarely occur unless Mg > 4-5 mEq/L include:
  - N, V, bradycardia, hypotension
  - Heart block, asystole, respiratory failure, death
- Treatment:
  - Discontinue all Mg-containing medications
  - Asymptomatic patients with normal kidney function can be treated with 0.9% NaCl and loop diuretics
  - Symptomatic patients treat with 100-200mg elemental Ca IV over 5-10 minutes for cardiac stability
  - If all else fails, hemodialysis

Hypophosphatemia

- Normal 2.5-4.5 mg/dL
- Causes
  - Increased renal elimination (diuretics, glucocorticoids, Na bicarbonate)
  - Rapidly refeeding patients with chronic malnutrition
  - Respiratory alkalosis
  - Treatment of DKA (PO4 shifts into cells)
- Symptoms of hypophosphatemia include CNS effects (confusion, delirium, seizures, coma), respiratory failure, heart failure, and arrhythmias

Preventing Hypophosphatemia

- Prevent hypophosphatemia by adding 10-30 mmol/L to IV in patients at risk
  - Malnourished (anorexia, poor intake, cancer, chronically ill, malabsorption, unintentional weight loss)
  - Alcoholism
  - DKA
  - Oral products (K-phos) are ok for asymptomatic patients, but poorly absorbed
  - Symptomatic patients should be treated with 15-30 mmol sodium phosphate or potassium phosphate IV over 3-6 hours

IV Phosphate Shortage

- Reduce daily amount phosphate in parenteral nutrition
- Reserve phosphates for pediatric and neonatal patients requiring PN
- Reserve for those patients with a therapeutic need for phosphate (e.g., DKA)
- IV fat emulsions contain 15 mmol/L of phosphate as egg phospholipids…probably sufficient for most

Hyperphosphatemia

- Typically occurs in patients with chronic kidney disease or hypoparathyroidism
- Most patients are asymptomatic, but they can have signs and symptoms including hypocalcemia, EKG changes, paresthesias, and vascular calcifications
- Treatment is beyond scope of this presentation
Hypocalcemia

- Normal 8.5-10.5 mg/dL or 1.1-1.3 mmol/L ionized
- 99% of total body stores of calcium is in bone
- Extracellular fluid contains less than 1% of total body calcium, and about half of extracellular Ca is bound to plasma protein (primarily albumin)
  - Only the unbound (or ionized) form is active and regulated by parathyroid hormone, phosphorus, vitamin D, and calcitonin
- Hypocalcemia occurs in patients with CKD, hypoparathyroidism, vitamin D deficiency, alcoholism, hyperphosphatemia, large blood transfusions, or those undergoing continuous renal replacement therapy (Ca chelates with citrate in stored blood or CRRT)

Hypocalcemia and Albumin

- Factors that cause an increase in Ca binding to albumin (metabolic alkalosis) can cause reduction in ionized Ca leading to symptomatic hypocalcemia
- Correction for low albumin
  - Low albumin causes a falsely low total serum calcium concentration
  - For every 1 g/dL decrease in albumin < 4 g/dL, add 0.8 mg/dL to total serum calcium concentration

Hypocalcemia: Symptoms and Treatment

- Symptoms of hypocalcemia include tetany, muscle spasms, hypoactive reflexes, anxiety, hallucinations, lethargy, hypotension, seizures
- Don’t treat asymptomatic hypocalcemia associated with low albumin (ionized Ca usually normal)
- Asymptomatic hypocalcemia can be treated with oral calcium 2-4 g/day (may also need vitamin D)

Hypocalcemia Treatment

- Symptomatic hypocalcemia is treated with 200-300mg elemental Ca administered intravenously over 5-10 minutes, followed by a continuous infusion
  - Equivalent to CaCl₂ 1g (270mg elemental Ca) through central IV catheter; Avoid CaCl₂ via peripheral IV…can cause limb ischemia
  - Equivalent to 2-3 g CaGlucenate (180-270 mg elemental Ca): preferred for peripheral IV administration
- Do not infuse Ca at a rate faster than 60mg elemental Ca per minute; rapid administration can cause hypotension, bradycardia, or asystole
  - Ideally, bolus over 1-2 hours, then 0.5-2 mg/kg/hr

IV Calcium Shortage

- If calcium gluconate shortage, do not add calcium chloride to parenteral nutrition (can administer separately if needed)
- Consider multi-electrolyte products for addition to parenteral nutrition
- If calcium chloride is diluted in 50-100ml IV fluid, can it be given peripherally?
  - I can’t find an answer, but in an emergent situation, will need to weigh risks and benefits

Hypercalcemia

- Serum Ca > 10.5 mg/dL
- Usually related to malignancy or hyperparathyroidism
- Treatment is beyond scope of this presentation
**Electrolyte Shortages**

- Consider oral or enteral route when possible
- Prioritize patients to vulnerable populations
  - Neonates or pediatrics
  - Short bowel
  - Malabsorption syndromes
- Minimize use of electrolyte / mineral additives in maintenance IV fluid
- Reconsider electrolyte protocols, especially with a focus on avoiding IV replacement in asymptomatic patients
  - Increase awareness of signs and symptoms of deficiencies
- Reduce electrolytes in parenteral nutrition; use standardized, premixed parenteral nutrition when possible

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**Review Question 1 (Fluid)**

James is hospitalized for pneumonia and sepsis. After 2 days of antibiotics and IV fluid of NS 100ml/hr his WBC has decreased and he is afebrile. BP 108/64, UO 45 ml/hr, tolerating an oral diet, K 3.4, Gluc 78, other labs are WNL. Which of the following is most appropriate?

A. Change IV fluid to D5W / 0.45% NaCl + KCl 20meq/L
B. Change IV fluid to D5W / 0.9% NaCl + KCl 40meq/L
C. Add KCl 40meq/L to his current IV of NS
D. Discontinue IV fluid and give oral MicroK 60meq

**Review Question 1: Answer**

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C. Add KCl 40meq/L to his current IV of NS
D. Discontinue IV fluid and give oral MicroK 60meq

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**Review Question 2 (Fluid Resuscitation)**

A 20yo male patient has just arrived to the emergency room. He is unconscious and was found thrown from his car. BP 72/39, HR 166, Hgb 8.2g/dL. Which of the following is the ideal fluid for this patient?

A. LR
B. NS
C. PRBC
D. 5% Albumin

**Review Question 2: Answer**

A 20yo male patient has just arrived to the emergency room. He is unconscious and was found thrown from his car. BP 72/39, HR 166, Hgb 8.2g/dL. Which of the following is the ideal fluid for this patient?

A. LR
B. NS
C. PRBC
D. 5% Albumin

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**Review Question 3: Calcium**

You receive an order for calcium gluconate 3g IV over 1 hour. There is currently a shortage of calcium gluconate. After checking labs and with the nurse, you find out the following about this patient: Ca 6.9 (NL 8.5-10.5 mg/dL), Creatinine 1.2, albumin 2.1. Per RN: VSS, patient is constipated in AF but no CNS or muscular symptoms. Which of the following is the most appropriate recommendation to the prescriber?

A. Recommend no calcium supplementation
B. Change to CaCl₂ 1gm IV over 2 hrs through central IV
C. Change to CaCl₂ 1gm IV push through peripheral IV
D. Change to calcium carbonate 1gm orally
Review Question 3: Answer

You receive an order for calcium gluconate 3g IV over 1 hour. There is currently a shortage of calcium gluconate. After checking labs and with the nurse, you find out the following about this patient: Ca 6.9 (NL 8.5-10.5 mg/dL), Creatinine 1.2, albumin 2.1. Per RN: VSS, patient is constipated, in AF but no CNS or muscular symptoms. Which of the following is the most appropriate recommendation to the prescriber?

A. Recommend no calcium supplementation. (Corrected Ca 8.5)
B. Change to CaCl₂ 1gm IV over 2 hrs through central IV
C. Change to CaCl₂ 1gm IV push through peripheral IV
D. Change to calcium carbonate 1gm orally (won't harm)

Review Question 4 (HS)

An elderly male is hospitalized for worsening SOB over the last 2 weeks due to CHF. Pertinent info includes Na 125 meq/L, BP 132/84, HR 105, BNP 850, Cr 1.7, CXR pulm congestion, Wt 85kg (up 3kg). The patient is not experiencing nausea, HA, or mental status change. An order is written for 23.4% NaCl 30ml x 1 IV. Which of the following is the best recommendation?

A. Change to 3% NaCl 50ml + furosemide 40mg IV
B. Change to 0.9% NaCl 75ml/hr + furosemide 40mg IV
C. Dispense order as written
D. D/C order and consider fluid restriction

Review Question 5 (HS)

A 32yo female is admitted for DKA. Pertinent labs include glucose 1350, Na 121, K 3.6. Which of the following treatments is most appropriate to correct her low serum Na?

A. Sodium Bicarbonate
B. Potassium
C. Insulin (and also intravascular fluid resuscitation with 0.9% NaCl)
D. 3% NaCl

Review Question 6 (Hypotonic)

There is a shortage of 5% albumin, so the pharmacy will compound it from 25% albumin. Which of the following is the most appropriate diluent?

A. Sterile water
B. 0.25% NaCl
C. D5W
D. LR
Review Question 6: Answer

There is a shortage of 5% albumin, so the pharmacy will compound it from 25% albumin. Which of the following is the most appropriate diluent?

A. Sterile water
B. 0.25% NaCl (but NS would be ok)
C. D5W
D. LR

Review Question 7 (Hypotonic)

You receive an order for 0.2% NaCl for a 55yo male patient. Pertinent labs include Na 149 meq/L. Which of the following is the most appropriate recommendation to the prescriber?

A. Change to D5 / 0.2% NaCl most likely to succeed
B. Change to 0.45% NaCl
C. Change to D5W most logical - need water not Na
D. Change to sterile water IV

Review Question 8 (Hyponatremia)

An elderly female is admitted to the hospital for a worsening cellulitis and feeling tired for 3 days. Her BP is 84/40, HR 118, temp 102, urine output is negligible for the last 2 hours, weight 70kg (normally 72kg), Na 122 meq/L, K 3.9 meq/L, albumin 2g/L. Her lungs are clear, CXR is normal, EKG shows NSR, and she is saturating at 98% on room air. Her PMH includes COPD, CHF, and CAD. She is drowsy, but responsive. Which of the following is most appropriate?

A. 3% NaCl IV at 70ml/hr
B. NS 500ml bolus
C. Albumin 25% 100ml to infuse over 2 hours
D. KCL 40mEq IV over 2 hrs

Extra Question 1

A 63kg female has been receiving tube feedings over the last 4 days. Her Na today is 160 meq/L. What is her estimated water deficit that will be needed to correct her serum sodium?

A. 2L
B. 4L
C. 6L
D. 8L
Estimating water deficit

- Estimate Water Deficit in patients with hypernatremia:
  - 0.5 \times Wt \times \left(\frac{Na}{140}\right) - 1 \text{ for men}
  - 0.4 \times Wt \times \left(\frac{Na}{140}\right) - 1 \text{ for women}

- Replace water deficit slowly following guidelines for safe changes in serum Na

Extra Question 1: Answer

A 63kg female has been receiving tube feedings over the last 4 days. Her Na today is 160 meq/L. What is her estimated water deficit that will be needed to correct her serum sodium?

A. 2L
B. 4L \quad 0.4 \times 63 \times \left(\frac{160}{140}-1\right) = 3.6 \text{ L}
C. 6L
D. 8L

Extra Question 2

A 72 yo female is unable to communicate following a recent stroke. She is started on Ultracal tube feedings (contains 1kcal/ml) to infuse at 64 ml/hr. Ultracal provides 830ml free water per liter of formula. How much additional water should be administered to prevent hypernatremia?

A. 130ml
B. 260ml
C. 450ml
D. 600ml

Extra Question 2: Answer

A 72 yo female is unable to communicate following a recent stroke. She is started on Ultracal tube feedings (contains 1kcal/ml) to infuse at 64 ml/hr. Ultracal provides 830ml free water per liter of formula. How much additional water should be administered to prevent hypernatremia?

A. 130ml
B. 260ml
C. 450ml
D. 600ml

Preventing Hypernatremia during Tube Feeding: Add Water

- Be proactive to prevent hypernatremia in patients who can’t ask for water
- Need approximately 1ml water for every 1 kcal
- 64ml/hr = 1536 kcal/day and ml/day
  - Receiving 830 H2O/L x 1.54L = 1278 ml/day
  - Needs addl 1536 ml – 1278 = 258 ml/day

Extra Question 3

How should the water from question 2 above be administered?

A. Drink it
B. 60-70ml bolus Q6H via NG tube
C. D5W to infuse at 11 ml/hr
D. Sterile water to infuse at 11 ml/hr
Extra Question 3: Answer

How should the water from question 2 above be administered?

A. Drink it
B. 60-70ml bolus Q6H via NG tube
C. D5W to infuse at 11 ml/hr
D. Sterile water to infuse at 11 ml/hr

Extra Question 4

A male patient is admitted to the ICU following a closed head injury. The physician has ordered 23.4% NaCl 30ml over 20 minutes every 4 hours for an elevated intracranial pressure (ICP). Current ICP is 40 mmHg. Which is the most appropriate recommendation.

A. Enter order as written
B. Recommend 3% NaCl instead
C. Recommend change to q4h PRN ICP
D. Recommend change to q10 min PRN

Extra Question 4: Answer

A male patient is admitted to the ICU following a closed head injury. The physician has ordered 23.4% NaCl 30ml over 20 minutes every 4 hours for an elevated intracranial pressure (ICP). Current ICP is 40 mmHg. Which is the most appropriate recommendation.

A. Enter order as written
B. Recommend 3% NaCl instead
C. Recommend change to q4h PRN ICP
D. Recommend change to q10 min PRN

Extra Question 5

You receive an order to change all of Mr. Smiths IV’s from D5W to NS. He is recovering from sepsis and is currently receiving steroids. Between his antibiotics and other IV’s, this totals to about 300ml of D5W per day currently. His blood glucose has been 200-300 mg/dL. He receives a sliding scale of insulin that gives 2 units insulin for a glucose > 200 mg/dL. What recommendation is the most appropriate?

A. Do not change IV’s to D5W because the glucose effect on BG is negligible.
B. He should receive a scheduled insulin dose in addition to the sliding scale.
C. Re-evaluate the need for steroids.
D. All of the above.

Extra Question 5: Answer

You receive an order to change all of Mr. Smiths IV’s from D5W to NS. He is recovering from sepsis and is currently receiving steroids. Between his antibiotics and other IV’s, this totals to about 300ml of D5W per day currently. His blood glucose has been 200-300 mg/dL. He receives a sliding scale of insulin that gives 2 units insulin for a glucose > 200 mg/dL. What recommendation is the most appropriate?

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B. He should receive a scheduled insulin dose in addition to the sliding scale.
C. Re-evaluate the need for steroids.
D. All of the above.

Thank You

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