Composition and Distribution of Body Fluids

- Case Study Part 1
  - Patient recently became violent
  - Currently calm, confused and disorientated
  - Patient is a psychiatric patient taking chlorpromazine (Thorazine)
  - Has been sent to the medical unit for hyponatremia
  - Water has been restricted and saline has been administered intravenously
  - Serum sodium is currently normal
## Composition and Distribution of Body Fluids

<table>
<thead>
<tr>
<th></th>
<th>Yesterday</th>
<th>Today</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium mEq/L</td>
<td>116</td>
<td>138</td>
</tr>
<tr>
<td>Potassium mEq/L</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Chloride mEq/L</td>
<td>84</td>
<td>104</td>
</tr>
<tr>
<td>Bicarbonate mEq/L</td>
<td>20</td>
<td>24</td>
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<tr>
<td>Glucose mg/dL</td>
<td>80</td>
<td>90</td>
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<tr>
<td>BUN mg/dL</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>Creatinine mg/dL</td>
<td>0.7</td>
<td>1.2</td>
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</table>
Composition and Distribution of Body Fluids

- Case Study Part 2 (several months later) - Hot night, patient on psychiatric unit with the following:
  - Patient had collapsed, cutting his head requiring stitches
  - Did not lose consciousness
  - BP at the time, 60/42
  - Pulse 72
  - Taking both chlorpromazine (to control his violence) and propranolol (Inderal, for hypertension)
  - Upon questioning reported that he was very thirsty but was not allowed to drink, fountain turned off at night
  - Blood test showed a serum sodium of 165 mEq/L
  - Meds were removed and he was allowed to drink, BP rose to 110/70
Composition and Distribution of Body Fluids

• Case Discussion – Part 1

  – In the first episode, what blood chemistry parameters was/were very abnormal?
    • Too little sodium, hyponatremia (his 116 mEq/L, normal 135 – 145)
  – Based upon the medications that the patient was taking, why is the above finding not surprising?
    • Chlorpromazine – anticholinergic – What effect does this have on salivation?
    • How did the patient respond to this?
      – Drank excessive fluids
    • What effect does this have on the movement of water between cells, especially brain cells?
      – Causes them to swell, resulting in cerebral dysfunction
      – Because of the above it is important to correct the problem slowly by restricting fluids. If a concentrated saline solution is administered what effect could this have?
Composition and Distribution of Body Fluids

• Case Discussion - Part 2

  – This patient’s water intake had been carefully monitored? However, in many instances water loss can be difficult to monitor, why?

  – What did the patient’s blood levels of sodium indicate? Why?

  – What effect did this have on the patient’s brain cells?

  – Why was the patients blood pressure low?
Composition and Distribution of Body Fluids

- Why didn’t the patient’s compensatory mechanisms for raising blood pressure work?

  - Propranolol – beta blocking agent
    - Decreases strength of cardiac contractions
    - Prevents compensatory increase in heart rate

  - Chlorpromazine
    - Blocked alpha andrenergic receptors which regulate vascular smooth muscle cells
Composition and Distribution of Body Fluids

• Regulation of Intracellular Fluids

  – Cell Volume Regulation

    • Role of the Sodium Pump

      – Prevents cell swelling by moving sodium out of the cell that diffuses in

      – If ATP synthesis is impaired:

        » What would you expect to see in cells effected?

        » How could a pathologist use the above fact to determine if a person that died suddenly was the result of a heart attack?

    • Role of Sodium Permeability

      – If the permeability of the membrane is increased it could possibly overwhelm the sodium pump, resulting in swelling

        » Some snake venoms work this way, referred to as being hemolytic poisons
Composition and Distribution of Body Fluids

- Role of Extracellular Fluid Osmolarity

Effects of Hypotonic, Isotonic, and Hypertonic Solutions on Red Blood Cells

- Hypotonic solution (a)
- Isotonic solution (b)
- Hypertonic solution (c)
Composition and Distribution of Body Fluids

- Adaptation

*Note: Diagrams illustrate the process of cell volume changes in response to hypotonic and hypertonic media.*

**Diagram Description:**

- **B:** A brain cell of normal volume is shown to swell in a hypotonic medium.
- **C:** The swollen cell adapts by extruding potassium ions, reducing its volume.
- **D:** When suddenly placed back in an isotonic medium, the cell returns to its original volume.
- **E:** In contrast, a brain cell is shown to shrink in a hypertonic medium.
- **F:** The shrunken cell produces osmolytes such as sorbitol, increasing its volume.
- **G:** When suddenly placed back in an isotonic medium, the cell swells to greater volume.

*Note: Adaptation is a mechanism that allows cells to adjust to changes in osmotic pressure.*
Composition and Distribution of Body Fluids

- Regulation of Plasma Osmolarity

  • Water Balance – water intake must equal water excreted
    
    - Normally
      
      » 2 l of water ingested each day
      
      » Fluid loss
        
        Insensible loss about 1 l, skin and lungs
        
        Urine, 1 l
    
    - Regulation of ADH (Vasopressin)
      
      » Osmoreceptors – when stimulated the result of concentrated extracellular fluids
        
        Hypothalamus generates the sensation of thirst
        
        Hypothalamus tells posterior pituitary gland to secrete ADH, which causes tubule cells to become more permeable to water vasoconstriction
Composition and Distribution of Body Fluids

- Water Intoxication (Increased Intracellular Fluids)

  • Increased Water Intake – as in psychogenic polydipsia
    - Symptoms – usually the consequence of hyponatremia
      » Lethargy
      » Confusion
      » Delirium
      » Convulsions
      » Coma

  • Decreased Water Output
    - Renal damage resulting in renal insufficiency
    - Syndrome of Inappropriate ADH
      » Frequently lung tumors
      » Head trauma
Composition and Distribution of Body Fluids

- Dehydration (Decreased Intracellular Fluids) – typically results in hypernatremia
  - Decreased Water Intake
    - Various reasons
  - Increased Water Loss
    - Urine
    - Sweat
    - Skin
    - Lungs
    - ADH insufficiency – Diabetes Insipidus

- Diabetic Coma
  - What is the effect on brain cells of extremely high levels of glucose (900 mg/dL)?
    - Cell shrink at first
  - Then produce idiogenic osmoles (sorbitol)

- What would happen if the patient above was given insulin too rapidly and why?
Composition and Distribution of Body Fluids

• Regulation of Extracellular Fluids

  – Sodium Balance – [intake = output]
    • What happens upon an increase in sodium intake?
      – Water follows increasing fluid volume
      – Weight increases as a result
    • What is the body’s response to the increased fluid volume?
      – Body adapts by increasing water loss
      – Weight drops
    • What is the time for this to take place?
      – Typically three (3) days
Composition and Distribution of Body Fluids
– Decreased Extracellular Fluids (Diarrhea and or Vomiting)

• Rapidly deplete extracellular fluid

• Symptoms:
  – Anorexia
  – The result of decreased volume
    » Dizzy
    » Faint
    » Fatigue
    » Cramps
    » Oliguira
    » ↑BUN
    » ↑Creatine
    » ↑BUN/Creatinine
    » ↑Hematocrit
Composition and Distribution of Body Fluids

• Regulation of Blood Volume

  – Decreased Blood Volume (Hemorrhage)

    • Upon the loss of a considerable amount of blood what would initially happen to the following?
      
      – Hematocrit
      – Sodium concentration
      – Blood Pressure

    • Would the above blood lab findings initially lead you in the right direction?

    • How would the body respond to these changes?

    • Upon the body compensating how will it effect the hematocrit and hemoglobin levels of this individual?

    • What would be the best treatment for this individual?
Composition and Distribution of Body Fluids

• Sequestration of Fluids in the Third Space (Ascites)

  – Cirrhosis of the liver

    • Portal hypertension causes

      – Fluid loss to the abdomen

      – With fluid being lost to the abdomen CO decreases, then what?

        » Retention of fluids and eventually CHF

    • Effect of pressing on abdomen

    • Treat with diuretics
Water Balance

- Case Study – Polyuria and Polydipsia

  - Mr. D has pains in his neck following a car accident, x-rays showed nothing

  - Taking ibuprofen for the pain

  - Psych nurse reports that he has been drinking abnormally large amounts and urinating large amounts frequently

  - Patient reports that the thirst has only been since the accident

  - Examination revealed muscle spasms in the neck

  - Given a neck brace, weighed, blood sample taken, and asked not to drink anything and to collect all urine and record the time it was produced
Water Balance

- Nurse was asked to remove all water sources, take blood pressure and pulse every hour

- Results

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<td>50</td>
<td>12</td>
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<tr>
<td>6:45 pm</td>
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<td>7:10 pm</td>
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<td>8:30 pm</td>
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<td>110</td>
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<tr>
<td>10:05 pm</td>
<td>139</td>
<td>130</td>
<td>7</td>
<td>313</td>
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</tbody>
</table>
Water Balance

- Results after 5 units vasopressin S.Q.

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<tr>
<td>11:30 pm</td>
<td></td>
<td>330</td>
<td>15</td>
<td>293</td>
</tr>
<tr>
<td>1:15 am</td>
<td></td>
<td>580</td>
<td>.7</td>
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- Case Discussion

- The cause of Mr. D’s problem was whiplash from the car accident, what was his real problem?

  - Damage to the pituitary stalk, preventing the secretion of ADH, diabetes insipidus
Water Balance

- Two types of diabetes insipidus

  - Pituitary diabetes insipidus – lack of ADH
  
  - Nephrogenic diabetes insipidus – target cells are resistant to ADH
  
  - Why couldn’t Mr. D concentrate his urine to the maximum of 1200 mOsm/l?

    - Washed away much of the sodium chloride and urea from the renal medulla over the past several days
Water Balance

- Case Study – Prostatic Hypertrophy
  - Mr. N, 65, patient in a nursing home, paranoid schizophrenia, complaint: stomach pains and can’t pass urine
  - Currently taking
    - Chlorpromazine
    - Prazosine an alpha andrenergic blocker
    - Finasteride a 5-alpha reductase inhibitor
  - Patient appears anxious, holding his lower belly, complaining that his stomach feels as if it is about to burst
  - Upon palpation, found bladder to be very distended, well above the pubis
Water Balance

- Rectal exam of the prostate revealed an enlarged prostate that was smooth and firm

- Told doctors that he has had hesitancy and dribbling, with frequent night night trips to the bathroom

- A Foley catheter was inserted immediately and 1200 ml of urine was drained (cloudy)

- Some of this urine was sent to the lab for culture and antibiotic sensitivity

- Blood tests showed
  
  - Normal acid phosphatase
  - Normal PSA

- After infection resolved a urologist performed a transurethral prostatectomy
Water Balance

- Case Discussion
  - As a male ages, after 50 years old, the prostate enlarges normally
  - 40% of males will have symptoms of the prostate impinging on the urethra, decreasing urinary flow
    - Frequently a sense of urgency and hesitancy
    - Many times difficult to stop urine flow, dribbling
  - With urine being left behind in the bladder predisposes the male to bacterial infections, inflammation leads to further obstruction
  - Mr. N was having two problems
    - Bladder infection
    - Micturition reflex impaired by chlorpromazine, an acetylcholine blocker
Water Balance

- The Prazosin he was taking was used to relax the smooth muscle of the posterior urethra and prostate gland (believed that the alpha receptors are increased in cases of prostatic hypertrophy)

- Treatment
  
  - Foley catheter is used if it can pass the obstruction
  - Suprapubic catheter is used if obstruction cannot be passed
  - Permanent solution, transurethral prostatectomy (10% of all males over 60)

- Cause of BPH, testosterone being converted to dihydrotestosterone (DTH) by 5 alpha reductase) results in hyperplasia of prostate cells
Water Balance

– Cancer of the Prostate

  • Very common
  • Blood levels of acid phosphatase elevated, once metastasis has occurred
  • Prostate is hard with irregular nodules
  • Elevated levels of PSA

– Treatment of Prostate Cancer

  • May include castration
  • Administration of estrogens (suppress GnRH)
  • Radioactive seeds
  • Radical prostatectomy
Sodium and Potassium Balance

• Case Study – The Kidney in Congestive Heart Failure

  – Mr. F, having difficulty breathing and legs are swollen
  – His prescriptions have been empty for some time (Digoxin and Lasix)
  – BP 110/90
  – Pulse 100 b/min
  – Respiratory rate 24 b/min
  – Over the last 6 months has gained 20 pounds, much of it in his legs (swollen with pitting edema)
  – Wet rales throughout both lung fields
  – An audible gallop heart sound (third)
Sodium and Potassium Balance

- Abdomen tender in the right upper quadrant from a congested liver

- Blood test revealed
  - Sodium 125 meq/l (135 – 145)
  - Potassium 8.3 meq/l (3.5 – 5.0)

- ECG and another blood test
  - Physician asked for another blood test and an ECG
  - ECG normal
  - Blood test
    - Sodium 133
    - Potassium 4.2
Sodium and Potassium Balance

• Case Discussion

  – Remember heart adjusts sodium not based upon sodium concentration rather by sensing blood pressure (extracellular volume)

  – What was the situation in this case?

    • Low blood pressure not the result of too little sodium, rather a weakened left ventricle

  – How would Mr. F’s physiology respond?

    • Retain fluid, which ultimately was deposited in lung and peripherally

  – If Mr. F was retaining sodium, why was his sodium levels on the low side?

    • Dilution
Sodium and Potassium Balance

- Hyperkalemia – at first glance Mr. F’s potassium levels appear dangerously high, what could happen?
  
  - Ventricular fibrillation

- How could we rule out hyperkalemia?
  
  - Look at ECG (normal)

  - High potassium levels could be the result of hemolysis (improper storage) of RBC’s – second blood test revealed normal levels
Sodium and Potassium Balance

• **Effect of Diuretics on Potassium Excretion**
  
  – Loop diuretics (furosemide) and thiazides result in a secretion of potassium for two reasons
    
    • Increased sodium arriving at the collecting ducts
    
    • Increased flow rate in kidney tubules in general
    
    • Results in hypokalemic metabolic alkalosis
Sodium and Potassium Balance

1. Potassium ions are freely filtered at the glomerulus.

2. About two-thirds of the filtered potassium load is reabsorbed in the proximal tubule by passive transport.

3. One quarter of the filtered potassium load is reabsorbed in the thick ascending limb of Henle.

4. Less than one-tenth of the filtered potassium load enters the distal tubule.

5. Virtually all potassium excreted in urine results from potassium secreted by principal cells in exchange for sodium reabsorption under the influence of aldosterone.

6. On a potassium-deficient diet, some potassium is actively transported from tubular fluid to blood by potassium-hydrogen ion ATPases in the luminal membrane of intercalated cells.
Sodium and Potassium Balance

1. Furosemide is secreted into tubular fluid

2. The $2\text{Cl}^-$, $\text{Na}^+$, $\text{K}^+$ symporter in TAL is inhibited by furosemide as it binds to chloride sites.

3. More sodium is reabsorbed in collecting duct in exchange for potassium and hydrogen ions.

4. Sodium, potassium, hydrogen ions, and water are lost in urine.

5. Hypokalemic metabolic alkalosis results.

6. Furosemide induced NaCl loss in urine

7. Contraction alkalosis, i.e., increased bicarbonate concentration
Sodium and Potassium Balance

- Potassium Sparing Diuretics
  
  - Spironolactone – slow acting
    
    - Acts by competing with aldosterone

  - Amiloride – faster acting but not that strong, usually combined with loop diuretics
    
    - Blocks sodium specific channels of the principle cells
Physiology of Diuretics

- **Action of Mannitol**

  1. Mannitol is filtered at the glomerulus.
  2. Its concentration increases progressively along the proximal tubule as sodium is reabsorbed by active transport and water follows passively.
  3. Because proximal tubule fluid remains isosmotic with respect to interstitial fluid and peritubular blood, the progressive increase in osmotic activity of mannitol is balanced by a decrease in osmotic activity and concentration of sodium.
  4. The decrease in tubular sodium concentration causes sodium to leak backward from peritubular fluid through (leaky) tight junctions.
  5. Thus, mannitol limits water and sodium reabsorption in the proximal tubule.
Acid Base Balance

- Case Study – Diabetic Ketoacidosis
  - Male, late 20’s, brought to hospital by a friend appearing confused and stuporous
  - Friend informs the staff that needle marks are the result of insulin injections, commented that he has been urinating a lot
  - Mr. Y was breathing heavily, scent of fruity acetone
  - Degree of needle marks and sclerotic veins indicated previous heroine use
  - Skin was dry and tented
  - Eyes recessed, pupils normal size
  - Neck veins collapsed
  - Pulse weak and rapid, blood pressure low
  - Infected toe from an ingrown toenail
Acid Base Balance

- ABG’s
  - pH 7.32
  - PaCO₂ 20 mmHg
  - PaO₂ 120 mmHg
  - HCO₃⁻ 10 meq/l
  - Base excess –8 meq/l

- Blood Chemistry
  - Sodium 135 meq/l
  - Potassium 6.5 meq/l
  - Chloride 95 meq/l
  - Glucose 750 mg/dl
  - BUN 56 mg/dl
  - Creatinine 2 mg/dl
  - Ketones 4+ (1:1 dilution)
Acid Base Balance

- Case Discussion

  - Could rule out heroine overdose, how?
    - Recent needle marks intramuscular
    - Breathing rapid, not depressed
    - Pupils normal, not constricted

  - Mr. Y typical juvenile diabetes mellitus (Type I, Insulin Dependent, or brittle diabetes mellitus)

  - With too little insulin body cannot use glucose and turns to fatty acids for energy production

    - Metabolism of fatty acids by the liver produces acidic ketone bodies
      - Acetoacetate
      - Beta-hydroxybutyrate
      - Acetone
Acid Base Balance

- It takes time for the kidneys to do this so other, extrarenal mechanisms, must be brought into play

- Extrarenal Buffering of $H^+$
  - Bicarbonate
  - Phosphate
  - Sulfate
  - Proteins

- Kussmaul Breathing – hyperventilation showing, deep labored inspiration and a grunting exhalation, what causes this and how does it work?

- Why does it take a while for the Kussmaul breathing to “kick in”?

- Renal Bicarbonate Reabsorption during Metabolic Acidosis / Renal Acid Excretion During Metabolic Acidosis
• Loss of hydrogen ions in the urine and gain of bicarbonate ions into the blood causes an increase in blood pH
Acid Base Balance

- Kidneys try to rid the body of these excess H+ increasing the production of ammonium by making glutaminase and glutamate dehydrogenase
Acid Base Balance

- Potassium Balance in Diabetic Ketoacidosis
  - What mechanisms result in a loss of potassium from the body? Why did Mr. Y actually have elevated serum levels of potassium?
    - Cells exchange $K^+$ for $H^+$ in an attempt to maintain plasma pH
    - Insulin is needed for $K+$ to enter cells (necessary for $Na^+/K^+$ pump)
    - Plasma osmolarity increases because of increased glucose causing cells to shrink, increases $K+$ conc. in cells which leaks out (raises plasma $K^+$)
  
- The result of all three of the above causes increased $K+$ then increased aldosterone – which results in?
Acid Base Balance

- Sodium Balance in Diabetic Ketoacidosis

1. When the capacity of the sodium-glucose symporters is exceeded in diabetes, glucose concentration of tubular fluid rises as volume declines due to sodium transport.

2. As sodium concentration in tubular fluid declines due to the rise in glucose concentration, sodium ions back-diffuse across leaky, tight junctions.

3. This causes sodium, glucose, and water loss in urine.

Urine: Increased sodium, increased glucose, increased water
Acid Base Balance

- Physiologic Approach to Treatment
  
  • Isotonic Saline, what is this attempting to correct?
    
    - Restore extracellular volume
    
    - Increase venous return
    
    - Increase renal perfusion
  
  • Insulin, must be done slowly, why?
    
    - Idiogenic osmoles
  
  • Potassium
    
    - Do blood level checks and add over time as needed