ELECTROLYTES

Course: Clinical Chemistry (PHAR 431)

Textbook:
Bishop ML, Fody EP, Schoeff LE (2013). Clinical Chemistry: principles, techniques and correlations, 7th ed.
Chapter 16

Electrolytes

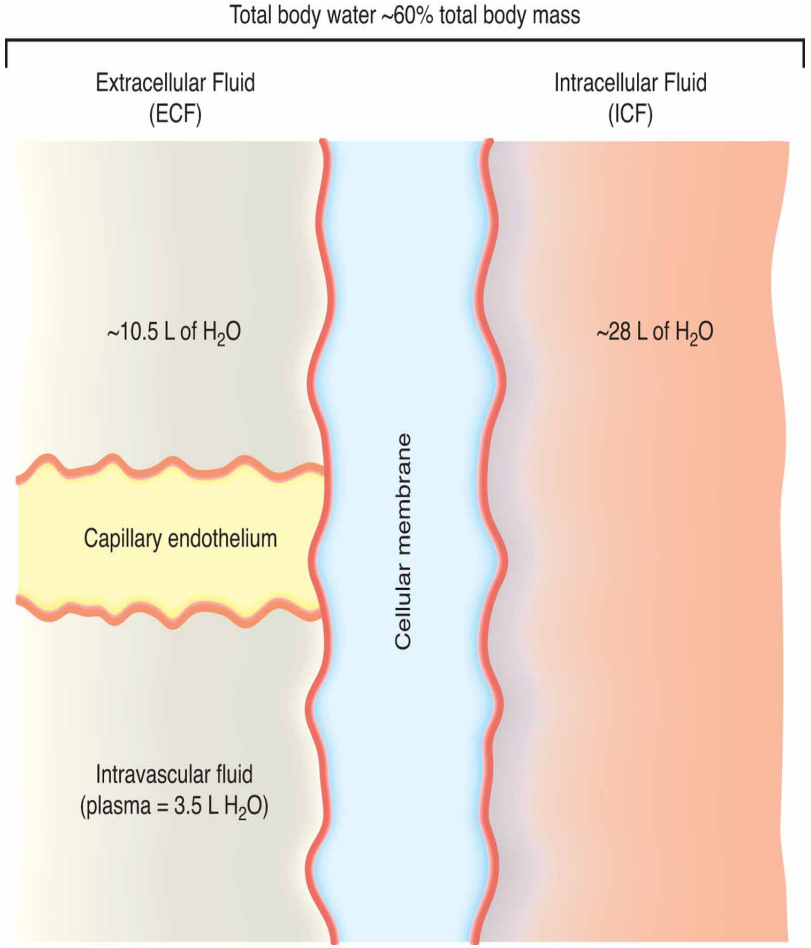
- Electrolytes: are ions capable of carrying an electric charge, anions or cations
- Electrolytes are essential components in:
  - Volume and osmotic regulation (Na^+, Cl^-, K^+)
  - Myocardial rhythm and contractility (K^+, Mg^{2+}, Ca^{2+},
  - Cofactors in enzyme activation: Mg^{2+}, Ca^{2+}, Zn^{2+}
  - Regulation of adenosine triphosphate (ATP) ion pump: Mg^{2+}
  - Acid-base balance: HCO_3^-, K^+, Cl-
  - Blood coagulation: Ca^{2+}, Mg^{2+}
  - Neuromuscular excitability: K^+, Ca^{2+}, Mg^{2+}
  - Production and use of ATP: Mg^{2+}, PO_4^-

Water

- Water content of human body is 40-75%
- Declining values with age and obesity
- Water functions to
  - Transport nutrients to cells
  - Determine cell volume
  - Remove waste products (urine)
  - Act as body's coolant (sweat)

Water

- Water is found in
  - **Intracellular fluid (ICF):** 2/3 of body water
  - **Extracellular fluid (ECF):** 1/3 & includes intravascular fluid (plasma) and interstitial cell fluid



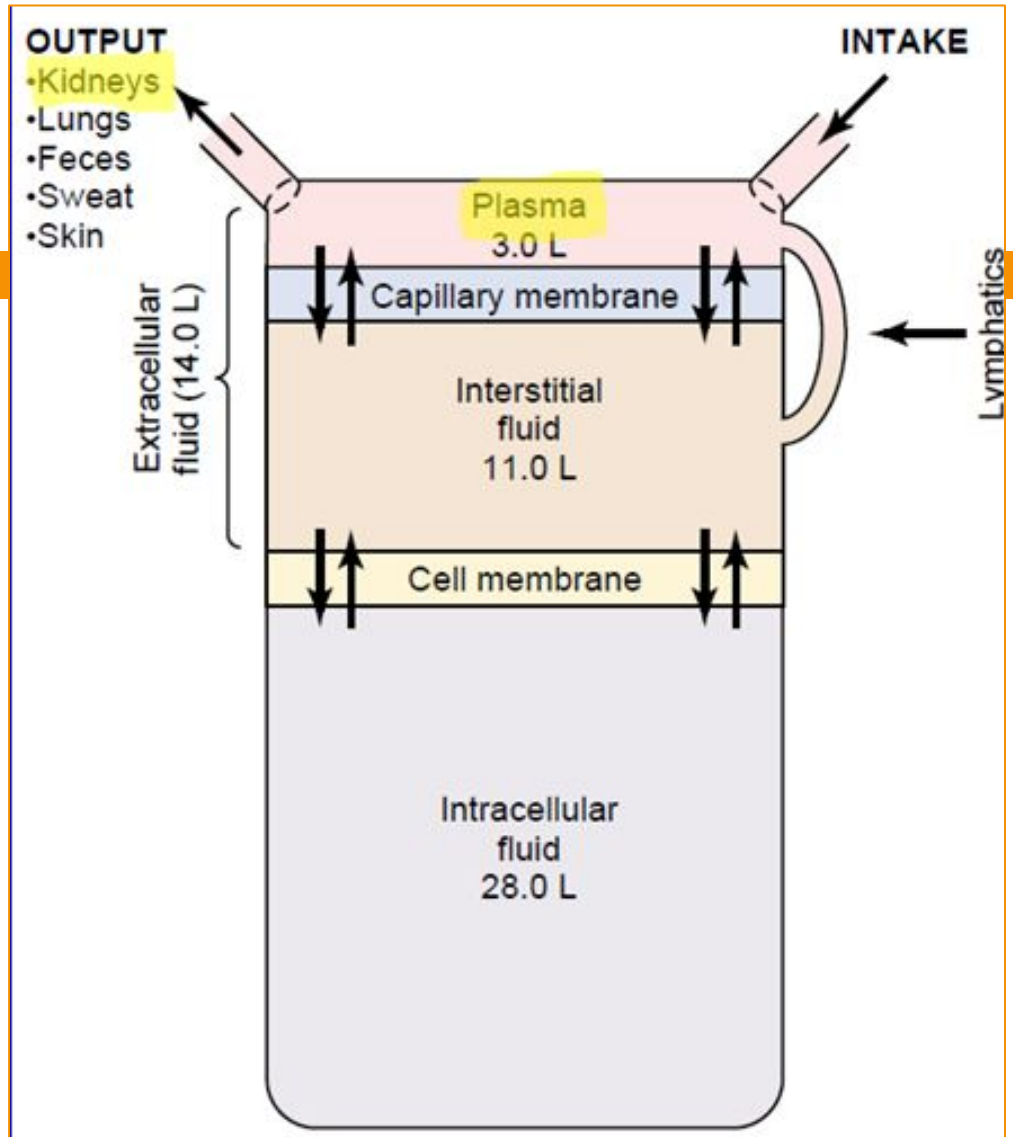


Figure 25–1

Summary of body fluid regulation, including the major body flu compartments and the membranes that separate these compa ments. The values shown are for an average 70-kilogram perso

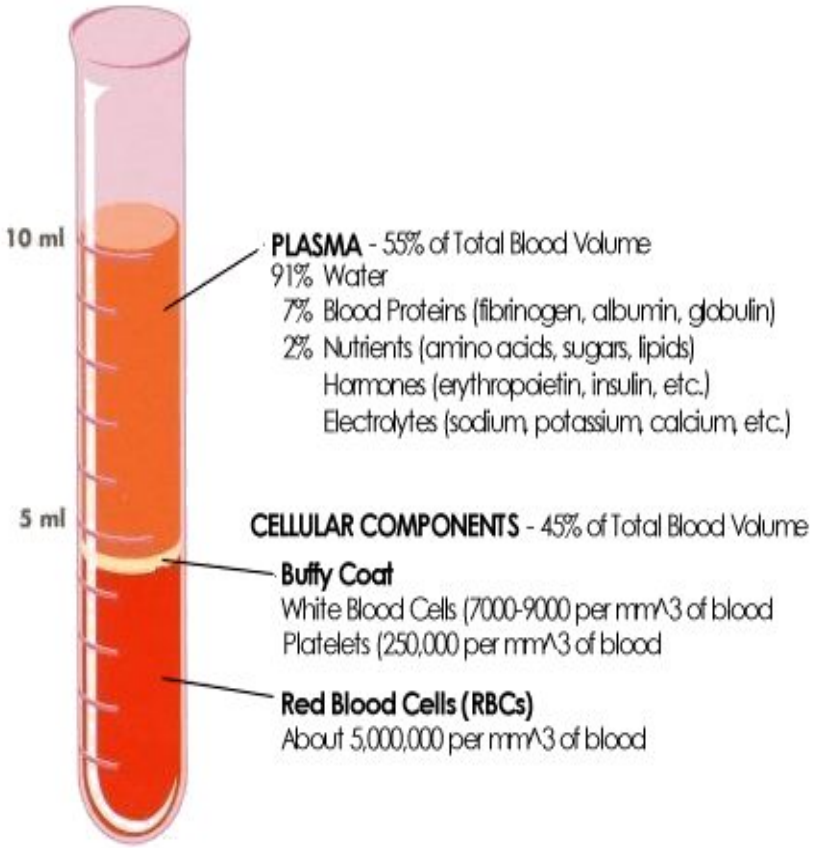
Distribution of body water in the adult*

Compartment	% of body weight	Volume (L)	% of total body water
ECF			
Plasma	5	3.5	8
Interstitial	15	10.5	25
ICF	40	28	67
Total	60	42	100

*For the average 70-kg person.

Body Fluid Composition

- Plasma
  - 55% of total blood volume
  - Analytes measured directly
  - Consists of ions, molecules, proteins
- Serum



Water Balance

- Ions exist in all of these fluids, but the concentration varies depending on individual ion and compartment

- The body uses active and passive(diffusion) transport principles to keep water and ion concentration in place

Water Balance

- Plasma proteins
  - ALBUMIN
  - Draws water INTO the vessels
- Hydrostatic pressure
  - Drives water OUT of the vessels
- These two forces create OSMOTIC or ONCOTIC PRESSURE
- In cases of reduced plasma proteins (e.g. proteinuria) oncotic pressure is reduced → excess water in tissues (edema)

Water balance

- Sodium has a pulling effect on water
  - More Na outside cells than inside, the water is pulled out of cells into the extracellular fluid.
  - Na^+ determines osmotic pressure of extracellular fluid

- Proteins (*especially albumin*) inside the capillaries strongly pull/keep water inside the vascular system
  - Albumin provides oncotic pressure.
  - By keeping Na^+ & albumin in their place, the body is able to regulate its hydration.

- When there is a disturbance in osmolality,
  - the body responds by regulating water intake and urinary control of water loss or retention, not by changing electrolyte balance

Water Balance & Osmolality

- **Osmolality:** a physical property of a solution based on solute concentration
  - Water concentration is regulated by thirst and urine output
  - Thirst and urine production are regulated by plasma osmolality

Water Balance & Osmolality

- Increased osmolality stimulates two responses that regulate water
  - Hypothalamus stimulates the sensation of thirst
  - Posterior pituitary secrets arginine vasopressin hormone (AVP) or ADH (antidiuretic hormone)
    - AVP increases H_2O re-absorption by renal collection ducts
- In both cases, plasma water increases

Osmolality

- Osmolality
  - concentration of solute/kg
  - reported as mOsm/kg

- another term:
  - Osmolarity - mOsm/L - not often used (inaccurate, esp. hyperlipidemia and hyperproteinemia)

Osmolality

- **Calculated osmolality**
  - uses glucose, blood urea nitrogen (BUN), & Na values
  - Two formulas: Calculated Osmolality =
    - 1.86 (Na) + [glucose/18] + [BUN/2.8] + 9
    - 2 (Na) + [glucose (mg/dL) /20] + [BUN (mg/dL) / 3]

- ***Osmolal gap***
  - Indicates the presence of osmotically active substances other than Na, glucose or BUN
  - Difference between calculated and determined osmolality
  - Formula:
    - [**Determined** Osm/kg] – [**calculated** Osm/ kg] = osmolal gap
    - Should be less than 5-10 units difference

TABLE 16-1	REFERENCE RANGES FOR OSMOLALITY
Serum	275–295 mOsm/kg
Urine (24 h)	300–900 mOsm/kg
Urine/serum ratio	1.0–3.0
Random urine	50–1200 mOsm/kg
Osmolal gap	5–10 mOsm/kg

Formulas in Action

https://www.youtube.com/watch?v=VofGdSeafTA

- A 40-year-old woman suffers from vomiting and diarrhea. What would be her osmolality based on the below data?
  - Sodium= 145 mmol/L (=145 mEq/L)
  - Glucose= 750 mg/dL
  - BUN= 25 mg/dL

Regulation of Blood Volume

- Renin-angiotensin-aldosterone system responds to a decreased blood volume
- Angiotensin II causes vasoconstriction and secretion of Aldosterone
  - Aldosterone stimulates sodium reabsorption and potassium ion secretion

Renin-Angiotensin-Aldosterone System

- Series of events
  - Body detects decreased blood volume/ pressure
  - Renin converts angiotensinogen to angiotensin I
  - Angiotensin I converted to angiotensin II by ACE
  - Angiotensin II causes
    - Vasoconstriction
    - Secretion of aldosterone
    - Stimulates AVP secretion and thirst
    - Enhances Na^+ and Cl^- reabsorption

https://www.youtube.com/watch?v=bY6fWVgFCrQ

Regulation of Blood Volume

- Other factors that affect blood volume
- Atrial Natriuretic peptide (ANP): released in response to volume expansion, promotes Na excretion in kidney
- Glomerular filtration rate (GFR): increases with volume expansion and decreases with volume depletion
- Volume receptors: stimulate release of AVP

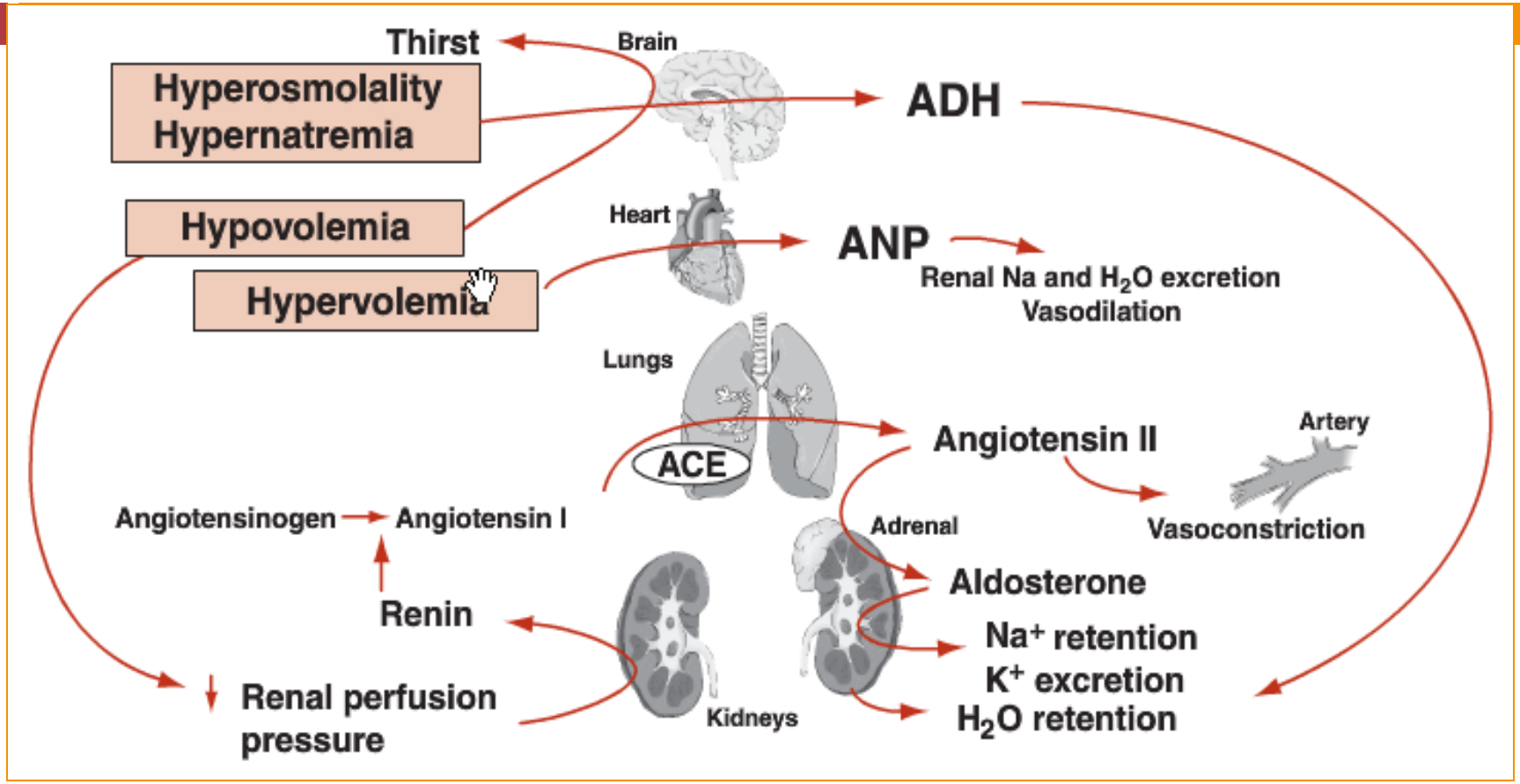


FIGURE 16-1 Responses to changes in blood osmolality and blood volume. ANP, atrial natriuretic peptide; ADH, antidiuretic hormone; ACE, angiotensin-converting enzyme. The primary stimuli are shown in *boxes* (e.g., hypovolemia).

Electrolytes

- General dietary requirements
  - Most need to be consumed only in small amounts as utilized
  - Excessive intake leads to increased excretion via kidneys
  - Excessive loss may result in need for corrective therapy
    - loss due to vomiting / diarrhea; therapy required - IV replacement, Pedialyte, etc.

Pedialyte: is a medical-grade hydration solution

Electrolyte Panel

- Panel consists of:
  - sodium (Na)
  - potassium (K)
  - chloride (Cl)
  - bicarbonate (in its ion form = HCO_3^-)

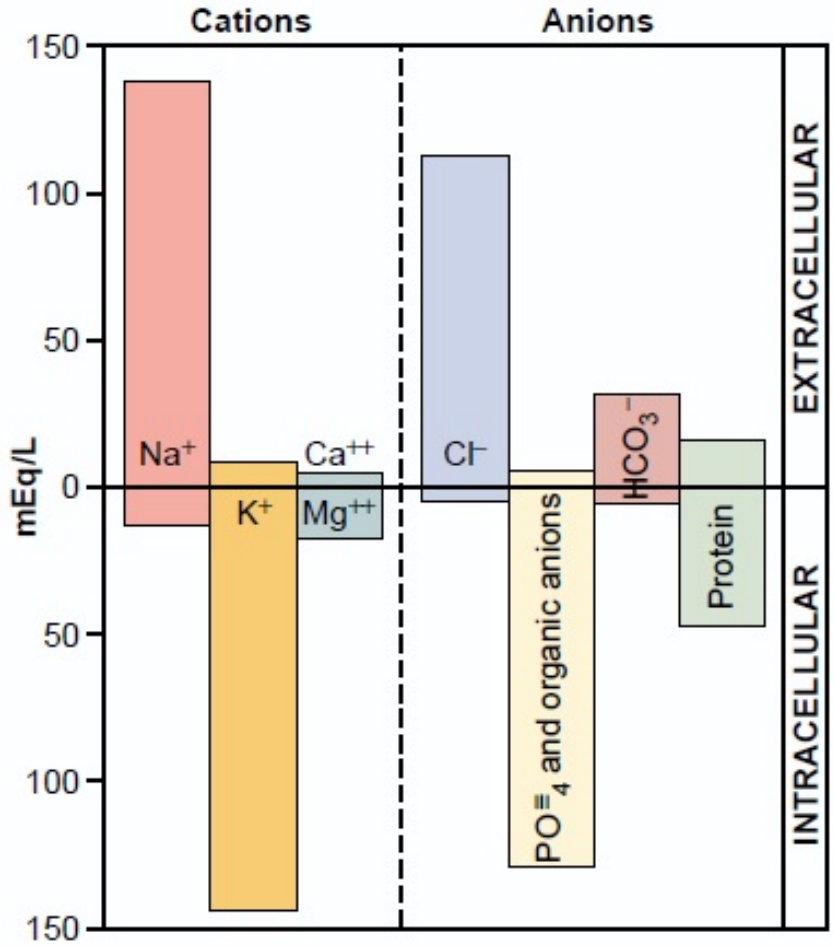


Figure 25–2

Major cations and anions of the intracellular and extracellular fluids. The concentrations of Ca^{++} and Mg^{++} represent the sum of these two ions. The concentrations shown represent the total of free ions and complexed ions.

Analytes of the Electrolyte Panel

- **Sodium (Na)–**
  - The major cation of extracellular fluid
  - Most abundant extracellular cation (90% of the 154 mmol/L of inorganic cations in plasma)
  - Diet
    - Average person ingests 3 g of Na as Cl, sulfate or other salts
    - Easily absorbed from many foods
  - Body of average-sized adult contains 80g Na, of which 35g in ECF
- Influence on regulation of body water
  - Osmotic activity
    - **Sodium determines osmotic activity**
    - Main contributor to plasma osmolality

Functions: Sodium

- Neuromuscular excitability
  - extremes in concentration can result in neuromuscular symptoms

- Na-K ATPase Pump
  - ***pumps 3Na out and 2K into cells***
  - Without this active transport pump, the cells would fill with Na^+ and subsequent osmotic pressure would rupture the cells

Regulation of Sodium

- Concentration depends on 3 factors:
  - intake of water in response to thirst
  - excretion of water affected by AVP in response to changes in blood volume or osmolality
  - Blood volume status which affects Na excretion through Aldosterone, Angiotensin II and ANP
- Renal regulation of sodium
  - Kidneys can conserve or excrete Na+ depending on ECF and blood volume
    - by aldosterone
    - and the renin-angiotensin system
      - this system will stimulate the adrenal cortex to secrete aldosterone

Reference Ranges: Sodium

- Serum, plasma
  - 136-145 mmol/L
- Urine (24 hour collection)
  - 40-220 mmol/day, varies with diet
- CSF
  - 136 -150 mmol/L

Sodium

- Urine testing & calculation:
  - Because levels are often increased, a dilution of the urine specimen is usually required.
  - Once a number is obtained, it is multiplied by the dilution factor and reported as (mmol/d) in 24 hr.

CASE STUDY 16-1

A 32-year-old woman was admitted to the hospital following 2½ days of severe vomiting. Before this episode, she was reportedly well. Physical findings revealed decreased skin turgor and dry mucous membranes. Admission study results were as follows:

SERUM

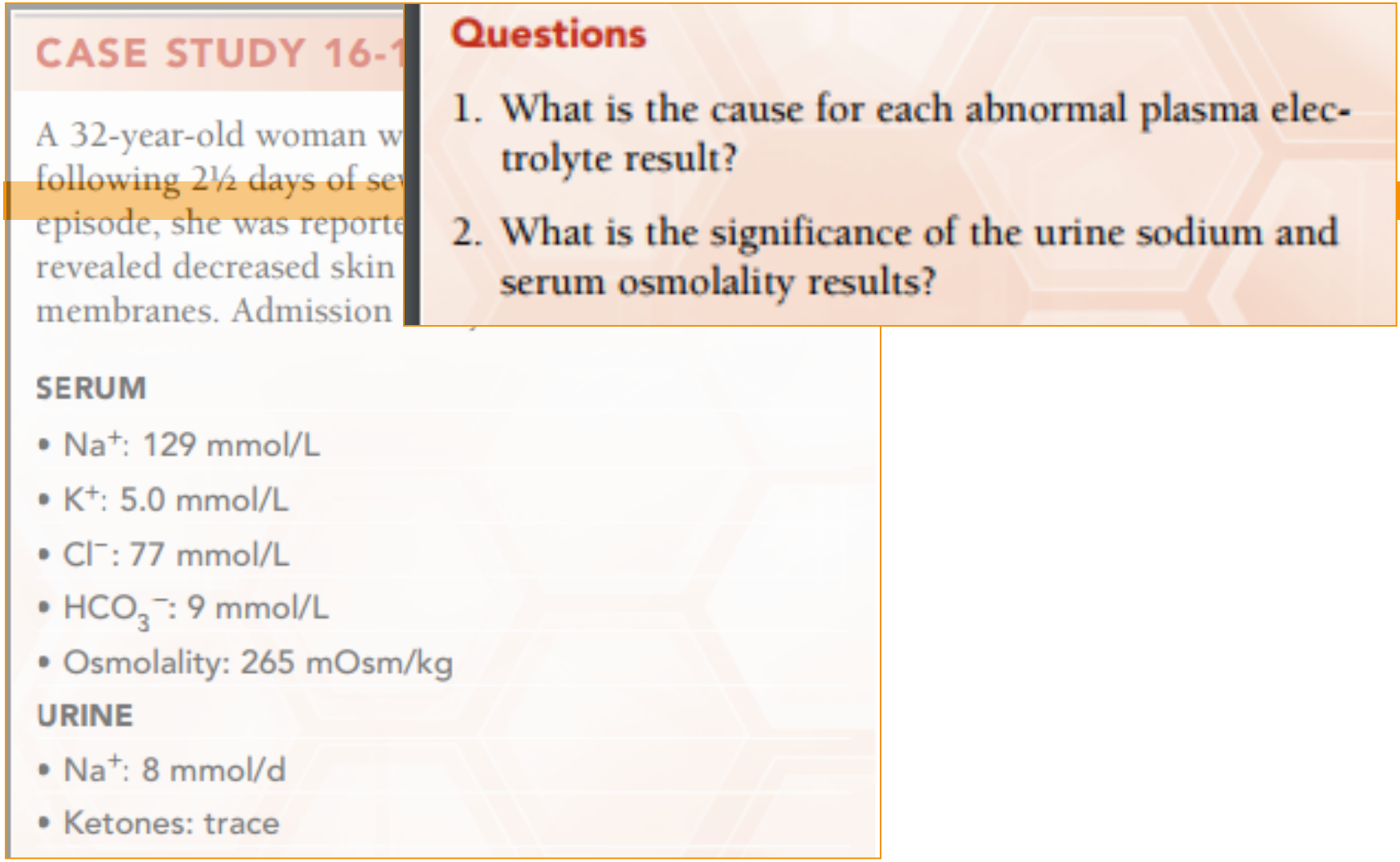
- Na^+: 129 mmol/L
- K^+: 5.0 mmol/L
- Cl^-: 77 mmol/L
- HCO_3^-: 9 mmol/L
- Osmolality: 265 mOsm/kg

URINE

- Na^+: 8 mmol/d
- Ketones: trace

Questions

1. What is the cause for each abnormal plasma electrolyte result?
2. What is the significance of the urine sodium and serum osmolality results?



1. Vomiting caused lowering of all electrolytes
2. Sodium loss in NON-RENAL

Loss of osmolality is due to loss of sodium

Hypovolemia explains the decreased skin turgor and dry mucus membrane

Clinical applications

- **Hyponatremia: < 135 mmol/L**
  - Causes of:
    - Increased Na^+ loss
    - Increased water retention
    - Water imbalance
    - Levels < 130 mmol/L are clinically significant
- **Hypernatremia: > 150 mmol/L**
  - Causes of:
    - Excess water loss
    - Increased intake/retention
    - Decreased water intake

Hyponatremia

1. Increased Na^+ loss
   - Aldosterone deficiency (hypoadrenalism)
   - Diabetes mellitus
     - In diabetic ketoacidosis, Na is excreted with ketones. Also Na is lost by replacement of water because of thirst
   - Potassium deficiency
     - K is normally excreted in urine
     - In serum K deficiency, tubules will save K and secrete Na instead
   - Loss of gastric contents
   - Severe burns
   - Prolonged vomiting & diarrhea
   - Some diuretics like thiazides
   - Urine Na usually < 20 mmol/d

Hyponatremia

2. Increased water retention
   - Dilution of plasma Na+
     - Renal failure
     - Nephrotic syndrome (loss of plasma proteins)
     - Hepatic cirrhosis
     - Congestive heart failure (CHF)
     - Urine Na>=20 mmol/d in acute or chronic renal failure
     - Urine <20 mmol/d, water retention is likely due to nephrotic syndrome, hepatic cirrhosis or CHF

Hyponatremia

3. Water imbalance
   - Excess water intake like in polydipsia (increased thirst)
   - Chronic condition
   - SIADH causes an increase in water retention because of increased AVP (ADH) production. A defect in AVP regulation has been associated with pulmonary disease, malignancies, central nervous system (CNS) disorders, infections (e.g., *Pneumocystis carinii* pneumonia), or trauma.

SIADH: syndrome of inappropriate antidiuretic hormone secretion > continued secretion of AVP despite normal or increased plasma volume.

TABLE 16-3 CLASSIFICATION OF HYPONATREMIA BY OSMOLALITY

WITH LOW OSMOLALITY
Increased sodium loss
Increased water retention
WITH NORMAL OSMOLALITY
Increased nonsodium cations
Lithium excess
Increased γ-globulins—cationic (multiple myeloma)
Severe hyperkalemia
Severe hypermagnesemia
Severe hypercalcemia
Pseudohyponatremia
Hyperlipidemia
Hyperproteinemia
Pseudohyperkalemia as a result of in vitro hemolysis
WITH HIGH OSMOLALITY
Hyperglycemia
Mannitol infusion

Sodium

Note:

- Increased lipids or proteins may cause false decrease in results. This would be classified as artifactual/pseudo-hyponatremia

Clinical Symptoms of **Hypo**natremia

- Depends on the serum level
  - Can affect
    - GI tract (Na 125-130 mmol/L)
    - Neurological (Na <125 mmol/L)
      - Nausea, vomiting, headache, seizures, coma
- Serum Na <120 mmol/L for 48 hrs or less is a medical emergency!!

Treatment of **Hypo**natremia

- Restriction of water intake
- Hypertonic saline or other pharmacologic solutions
- AVP receptor antagonist (Conivaptan) is effective in euvolemic and hypervolemic hyponatremia

Hypernatremia

1. Excess water loss
   - Profuse sweating, breathing
   - Prolonged diarrhea
   - Severe burns
   - Renal tubular disorder
   - Diabetes insipidus: either because the kidney cannot respond to AVP (nephrogenic diabetes insipidus) or because AVP secretion is impaired (central diabetes insipidus).

Hypernatremia

2. Increased intake/retention
   - Excessive IV therapy
   - Hyperaldosteronoism
   - Administration of hypertonic solutions of Na such as $NaHCO_3$ or dialysis solutions
3. Decreased water intake
   - Elderly
   - Infants
   - Mental impairment

Clinical Symptoms of Hypernatremia

- Involve the CNS
  - Altered mental status
  - Lethargy
  - Irritability
  - Vomiting
  - Nausea
  - Serum Na+ >160 mmol/L is associated with a mortality rate of 60% to 75%

Specimen Collection: Sodium

- Serum, plasma, and urine are all acceptable for Na+ measurements.
- Plasma: lithium heparin, ammonium heparin, and lithium oxalate are suitable anti-coagulants
- Serum (slight hemolysis is OK, but not gross)
- Timed and random urine
- Sweat
- GI fluids
- Liquid feces (would be only time of excessive loss)

Determination of sodium

- Specimen: serum, plasma, urine
- When plasma is used lithium heparin is suitable as anticoagulant
- Hemolysis does not cause a significant change in serum or plasma levels
- Methods:
  - Chemical methods, (almost outdated, low precision))
  - Ion-selective electrode: most routinely used

Analytes of the Electrolyte Panel

- **Potassium (K^+)**
  - the major cation of **intracellular** fluid
    - Only 2% of potassium is in the plasma
    - Potassium concentration inside cells is 20 X greater than it is outside.
    - This is maintained by the Na-K pump
      - exchanges 3 Na for 1 K
  - The kidney can't decrease K excretion to zero as it can with Na
  - Diet
    - easily consumed by food products such as bananas
    - ~2-3 gm of K are ingested and excreted daily in the form of salts

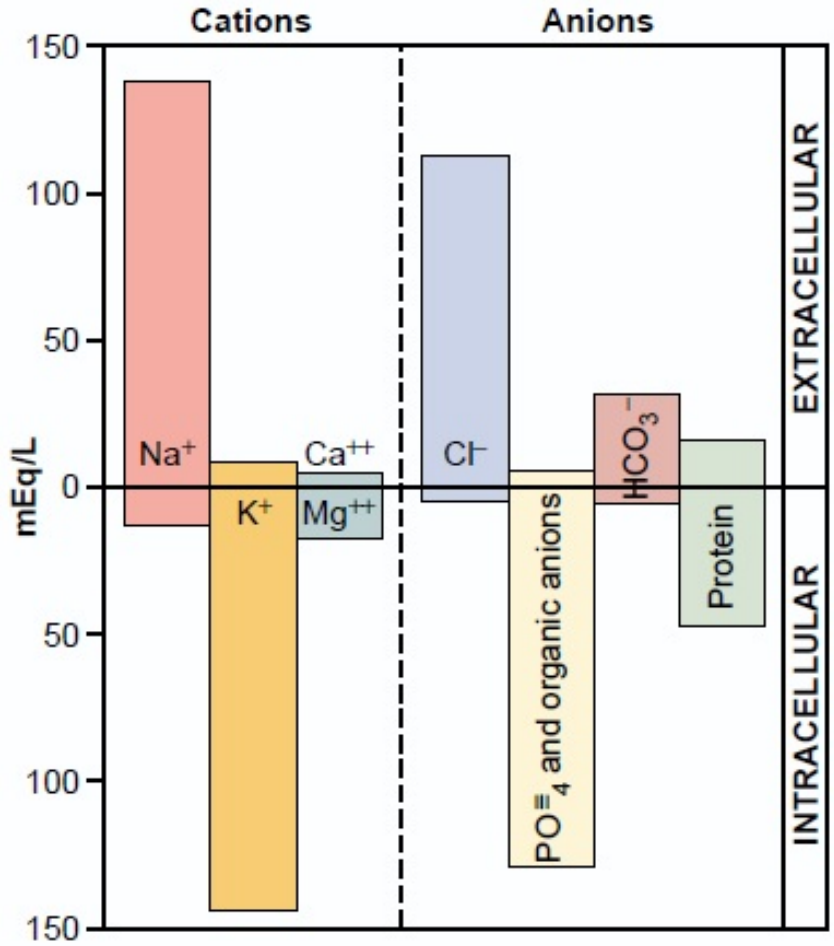


Figure 25–2

Major cations and anions of the intracellular and extracellular fluids. The concentrations of Ca^{++} and Mg^{++} represent the sum of these two ions. The concentrations shown represent the total of free ions and complexed ions.

Function: Potassium

- Critically important to the functions of
  - Neuromuscular cells
  - Acid-base balance
  - Intracellular fluid volume
  - Controls heart muscle contraction
  - Promotes muscular excitability
    - Decreased K (<3 mmol/L) increases muscle irritability and can cause cessation of heartbeat in systole (contraction)
    - Increased K (>7.5mmol/L) may seriously inhibit irritability of muscles including the heart to the point of paralysis or cessation of heartbeat

Regulation of Potassium

- K loss frequently occurs as Na-K ATPase pump is inhibited by hypoxia, hypomagnesemia, digoxin overdose
- Insulin promotes acute K entry into skeletal muscle cells and liver by increasing Na-K ATPase activity
- Catecholamines, such as epinephrine (β 2-stimulator), promote cellular entry of K+, whereas propanolol (β -blocker) impairs cellular entry of K+.

Regulation of Potassium //cont'd

- Kidneys: Responsible for regulation. Potassium is readily excreted, but gets reabsorbed in the proximal tubule - under the control of ALDOSTERONE

Reference Ranges: Potassium

- Serum (adults)
  - 3.5 - 5.1 mmol/L
- Newborns
  - 3.7 - 5.9 mmol/L
- Urine (24 hour collection)
  - 25 - 125 mmol/L

Disorders of Potassium Homeostasis

- **Hypokalemia**
  - < 3.5 mmol/L
  - Causes
    - Non-renal loss
    - Renal Loss
    - Cellular Shift
    - Decreased intake
- **Hyperkalemia**
  - >5.1 mmol/L
  - Causes
    - Decreased renal excretion
    - Cellular shift
    - Increased intake
    - Artifactual / False elevations

Hypokalemia

1. Non-renal loss
   - Excessive fluid loss (diarrhea, vomiting, diuretics)
   - Increased Aldosterone promote Na reabsorption … K is excreted in its place
   - Some diuretics

Hypokalemia

2. Renal Loss
   - Nephritis, renal tubular acidosis, hyperaldosteronism, Cushing's Syndrome (a tumor secreting ACTH)
3. Cellular Shift
   - Alkalosis, insulin overdose
4. Decreased intake

Clinical Symptoms of Hypokalemia

- Neuromuscular weakness
- Cardiac arrhythmia
- Constipation

Hyperkalemia

1. Decreased renal excretion
   - Renal disease
   - Adrenal cortical insufficiency or Addison's disease leading to low Aldosterone and low cortisol

2. Cellular Shift
   - Metabolic and renal acidosis
   - Chemotherapy, leukemia, muscle/cellular injury
   - Hydrogen ions compete with potassium to get into the cells
   - Conditions of shock or circulatory failure

Hyperkalemia

3. Increased intake
   - Insulin IVs promote rapid cellular potassium uptake

4. Artifactual
   - Sample hemolysis
   - Prolonged tourniquet use
   - Excessive fist clenching

Clinical Symptoms of Hyperkalemia

- Muscle weakness
- Tingling
- Numbness
- Mental confusion
- Cardiac arrhythmias
- Cardiac arrest

Treatment of hypo- & hyper-kalemia

- Hypokaleia: Oral KCl replacement over several days or IV replacement
- Hyper-kalemia: Ca is given to reduce the threshold potential of myocardial cells

Specimen Collection: Potassium

- Non-hemolyzed serum
- heparinized plasma
- 24 hr urine

- Determination of K: ISE

Analytes of the Electrolyte Panel

- **Chloride (Cl^-)**
  - The major anion of **extracellular** fluid
  - Chloride moves passively with Na^+ or against HCO_3^- to maintain neutral electrical charge
  - Chloride usually follows Na
    - if one is abnormal, so is the other

Function: Chloride

- Body hydration/water balance
- Osmotic pressure
- Electrical neutrality

Regulation of Chloride

- Regulation via diet and kidneys
  - In the kidney, Cl is reabsorbed in the renal proximal tubules, along with sodium.
  - Deficiencies of either one limits the reabsorption of the other.

Reference Ranges: Chloride

- Serum, plasma
  - 98 -107 mmol/L
- 24 hour urine
  - 110-250 mmol/L
  - varies with diet
- *CSF*
  - 120 - 132 mmol/L
  - Often CSF Cl is decreased when CSF protein is increased, as often occurs in bacterial meningitis.

Determination: Chloride

- Specimen type
  - Serum
  - Plasma
  - 24 hour urine
  - CSF
  - Sweat
    - Sweat Chloride Test
      - Used to identify cystic fibrosis patients
        - Increased salt concentration in sweat
        - Pilocarpine= chemical used to stimulate sweat production
        - Iontophoresis (ionization)= mild electrical current that stimulates sweat production

Disorders of Chloride Homeostasis

- **Hypochloremia**
  - Decreased blood chloride
  - Causes
    - Conditions where output exceeds input

- **Hyperchloremia**
  - Increased blood chloride
  - Causes
    - Conditions where input exceeds output

Hypochloremia

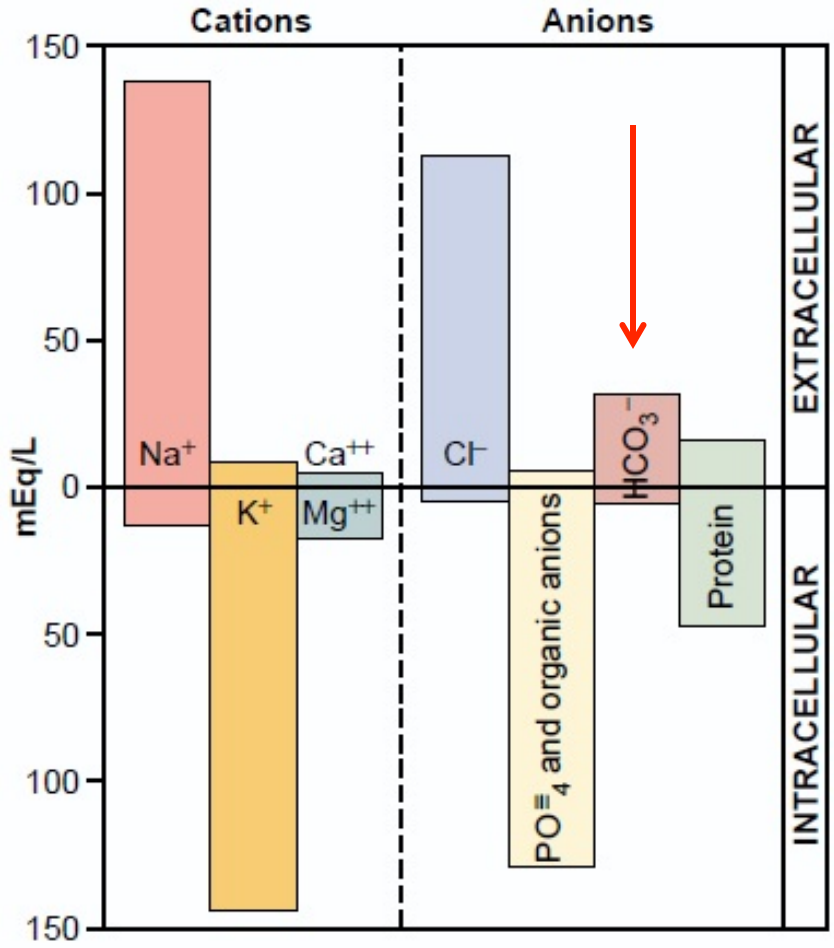
- Decreased serum Cl
  - loss of gastric HCl
  - salt loosing renal diseases such as pyelonephritis
  - metabolic alkalosis/compensated respiratory acidosis
    - increased $HCO3^-$ and decreased Cl^-
- Diabetic ketoacidosis
- Aldosterone deficiency

Hyperchloremia

- Increased serum Cl
  - dehydration (relative increase)
  - excessive intake (IV)
  - congestive heart failure
  - renal tubular disease
  - metabolic acidosis
    - decreased HCO_3^- & increased Cl^-

Sample collection for chloride

- Serum or plasma may be used, with lithium heparin being the anticoagulant of choice.
- Hemolysis does not cause a significant change in serum or plasma values as a result of decreased levels of intracellular Cl^-.
- Marked hemolysis, levels may be decreased as a result of a dilution effect.
- Whole blood samples may be used with some analyzers.
- The specimen of choice in urine Cl^- analyses is 24-hour collection because of the large diurnal variation.
- Sweat is also suitable for analysis.



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Major cations and anions of the intracellular and extracellular fluids. The concentrations of Ca^{++} and Mg^{++} represent the sum of these two ions. The concentrations shown represent the total of free ions and complexed ions.

Analytes of the Electrolyte Panel

- **Carbon dioxide/bicarbonate (HCO_3^-)**
  - 2nd most abundant anion of **extra**cellular fluid
  - **Total plasma: $CO_2 = HCO_3^- + H_2CO_3^- + CO_2$**

    - HCO_3^- (bicarbonate ion)
      - accounts for 90% of total plasma CO_2 at physiol pH
    - $H_2CO_3^-$ (carbonic acid)
    - Dissolved CO2

Function: Bicarbonate ion

- CO2 is a waste product
  - continuously produced as a result of cell metabolism,
  - the ability of the bicarbonate ion to accept a hydrogen ion makes it an efficient and effective means of buffering body pH
  - dominant buffering system of plasma

$$CO_2 + H_2O \xleftrightarrow{CA} H_2CO_3 \xleftrightarrow{CA} H^+ + HCO_3^-$$

CA: carbonic anhydrase in RBCs.

Regulation of Bicarbonate ion

- Bicarbonate is regulated by secretion / reabsorption of the renal tubules
- Acidosis: decreased renal excretion. A decrease in blood pH occurs when the ratio of HCO3-/H2CO3 falls below 20:1
- Alkalosis: increased renal excretion

Regulation of Bicarbonate ion

- Kidney regulation requires the enzyme carbonic anhydrase - which is present in renal tubular cells & RBCs

Reaction: $CO_2 + H_2O \leftrightharpoons H_2CO_3 \rightarrow H^+ + HCO^-_3$

Pulmonary Control

Renal Control

Reference Range: Bicarbonate ion

- ***Total*** Carbon dioxide (venous)
  - 23-29 mmol/L
    - includes bicarb, dissolved and undissociated H_2CO_3 - carbonic acid (bicarbonate)

- Bicarbonate ion (HCO_3^-)
  - 22-26 mmol/L

Specimen Collection: Bicarbonate ion

- heparinized plasma
- arterial whole blood
- fresh serum
- Anaerobic collection preferred

Determination of CO_2

- Two methods
- ISE: uses acid reagent to convert all forms of CO_2 to CO_2 gas and measured by pCO_2 electrode

- Enzymatic: alkalinizes all forms of CO_2 to HCO_3^-, which is then used to carboxylate PEP
- PEP + HCO_3^- → oxaloacetate + $H_2PO_4^-$
- Oxaloacetate + NADH + H^+ → malate and NAD^+

CASE STUDY 16-2

A 60-year-old man entered the emergency department after 2 days of "not feeling so well." History revealed a myocardial infarction 5 years ago, when he was prescribed digoxin. Two years ago, he was prescribed a diuretic after periodic bouts of edema. An ECG at time of admission indicated a cardiac arrhythmia. Admitting lab results are shown in Case Study Table 16-2.1.

CASE STUDY TABLE 16-2.1 LABORATORY RESULTS

VENOUS BLOOD

Digoxin: 1.4 ng/mL, therapeutic 0.5–2.2 (1.8 nmol/L, therapeutic 0.6–2.8)

Na^+: 137 mmol/L

K^+: 2.5 mmol/L

Cl^-: 100 mmol/L

HCO_3^-: 25 mmol/L

Mg^{2+}: 0.4 mmol/L

Ion/free Ca^{2+}: 1.0 mmol/L

Ref. ranges:

Serum Mg2+: 0.6-1.0 mmol/L

Serum Ion Ca2+: 1.16-1.32 mmol/L

HCO3-: 22-29 mmol/L

Questions

1. Because the digoxin level is within the therapeutic range, what may be the cause for the arrhythmia?
2. What is the most likely cause for the hypomagnesemia?
3. What is the most likely cause for the decreased potassium and ionized calcium levels?
4. What type of treatment would be helpful?

Electrolyte balance

- **Anion gap** – an estimate of the difference between *unmeasured* anions and unmeasured cations
- There is never a "gap" between total cationic charges and anionic charges
- AG is calculated by the concentrations difference between commonly measured cations (Na+K) and commonly measured anions (Cl+HCO3-)

Anion Gap: two methods

- **Anion Gap Calculations**

1. ***Na - (Cl + CO_2 or HCO_3^-)***

- ***Reference range: 7-16 mmol/L***

This is equivalent to the unmeasured anions minus unmeasured cations: $(PO_4^- - 2SO_4^-) - (K^+ + Ca^{2+} + Mg^{2+})$

2. ***(Na + K) - (Cl + CO_2 or HCO_3^-)***

   - ***Reference range: 10-20 mmol/L***

- Why measuring AG?
- An indications of an increase in one or more of the unmeasured anions
- Quality control for the electrolytes analyzer

Functions of the Anion Gap

- Causes in normal patients
  - what causes the anion gap?
  - 2/3 plasma proteins & 1/3 phosphate & sulfate ions, along with organic acids

- Elevated ***AG*** is caused by
  - uncontrolled diabetes or starvation (due to lactic & keto acids)
  - uremia/ renal disorders: leads to increased PO4- and SO4- retention
  - Hypernatremia, lactic acidosis
  - Poisoning with ethanol, methanol, ethylene glycol, or salicylates
  - lab error

Functions of the Anion Gap

- Low ***AG*** is caused by
  - a decrease AG is rare, more often it occurs due to test/instrument error
  - Hypoalbuminemia (decrease in unmeasured anions)
  - Severe hypercalcemia (increase in unmeasured cations)

CASE STUDY 16-5

A 15-year-old girl in a coma was brought to the emergency department by her parents. She has diabetes and has been insulin dependent for 7 years. Her parents stated that there have been several episodes of hypoglycemia and ketoacidosis in the past and that their daughter has often been "too busy" to take her insulin injections. The laboratory results obtained on admission are shown in Case Study Table 16-5.1.

Questions

1. What is the diagnosis?
2. Calculate the anion gap. What is the cause of the anion gap result in this patient?
3. Why are chloride and bicarbonate decreased? What is the significance of the elevated potassium value?
4. What is the significance of the plasma osmolality?

CASE STUDY TABLE 16-5.1
LABORATORY RESULTS

		RESULT	REFERENCE RANGE
Venous blood	Na^+	145 mmol/L	136–145 mmol/L
	K^+	5.8 mmol/L	3.4–5.0 mmol/L
	Cl^-	87 mmol/L	98–107 mmol/L
	HCO_3^-	8 mmol/L	22–29 mmol/L
	Glucose	1,050 mg/dL	70–110 mg/dL
	Urea nitrogen	35 mg/dL	7–18 mg/dL
	Creatinine	1.3 mg/dL	0.5–1.3 mg/dL
	Lactate	5 mmol/L	0.5–2.2 mmol/L
	Osmolality	385 mOsm/kg	275–295 mOsm/kg
Arterial blood	pH	7.11	7.35–7.45
	po_2	98 mm Hg	83–100 mm Hg
	pco_2	20 mm Hg	35–45 mm Hg
Urine		Normal	
	Glucose	4+	Negative
	Ketones	4+	Negative

End

CASE STUDY 16-4

Consider the following laboratory results from three adult patients (Case Study Table 16-4.1):

CASE STUDY TABLE 16-4.1
LABORATORY RESULTS

			REFERENCE RANGES		
CASE	ION CA^{2+} 1.16–1.32 mmol/L	TOTAL MG^{2+} 0.63–1.0 mmol/L	PO_4^- 0.87–1.45 mmol/L	HEMATOCRIT 35–45%	INTACT PARATHYROID HORMONE 13–64 ng/L
A	1.44	0.90	0.85	42	100
B	1.08	0.50	0.90	40	25
C	1.70	0.98	1.43	30	12

Questions

1. Which set of laboratory results (Case A, B, or C) is most likely associated with each of the following diagnoses?
   - Primary hyperparathyroidism
   - Malignancy
   - Hypomagnesemic hypocalcemia

Electrolyte Summary

- ***cations (+)***
  - ***Na 142***
  - ***K 5***
  - ***Ca 5***
  - ***Mg 2***

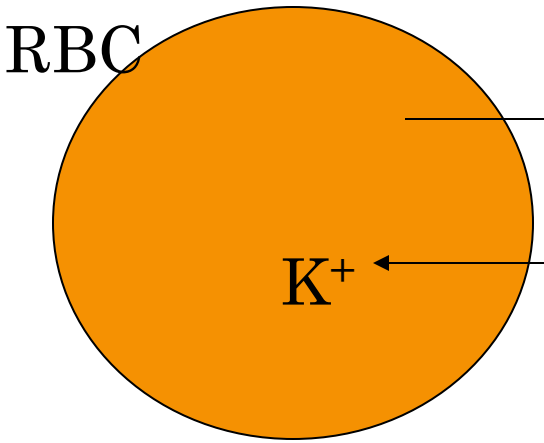
  154 mmol/L

- ***anions (-)***
  - ***Cl 105***
  - ***HCO3- 24***
  - ***HPO4- 22***
  - ***SO4-2 1***
  - ***organic acids 6***
  - ***proteins 16***

  154 mmol/L

Mechanism of hypokalemia

- Increased plasma pH (decreased Hydrogen ion)



K^+ moves into RBCs to preserve electrical balance,
causing plasma potassium to decrease. (Sodium also shows a slight decrease)

References

- Bishop, M., Fody, E., & Schoeff, I. (2010). *Clinical Chemistry: Techniques, principles, Correlations*. Baltimore: Wolters Kluwer Lippincott Williams & Wilkins.
- http://thejunction.net/2009/04/11/the-how-to-authority-for-donating-blood-plasma/
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CASE STUDY 16-1

A 32-year-old woman was admitted to the hospital following 2½ days of severe vomiting. Before this episode, she was reportedly well. Physical findings revealed decreased skin turgor and dry mucous membranes. Admission study results were as follows:

SERUM

- Na^+: 129 mmol/L
- K^+: 5.0 mmol/L
- Cl^-: 77 mmol/L
- HCO_3^-: 9 mmol/L
- Osmolality: 265 mOsm/kg

URINE

- Na^+: 8 mmol/d
- Ketones: trace

Questions

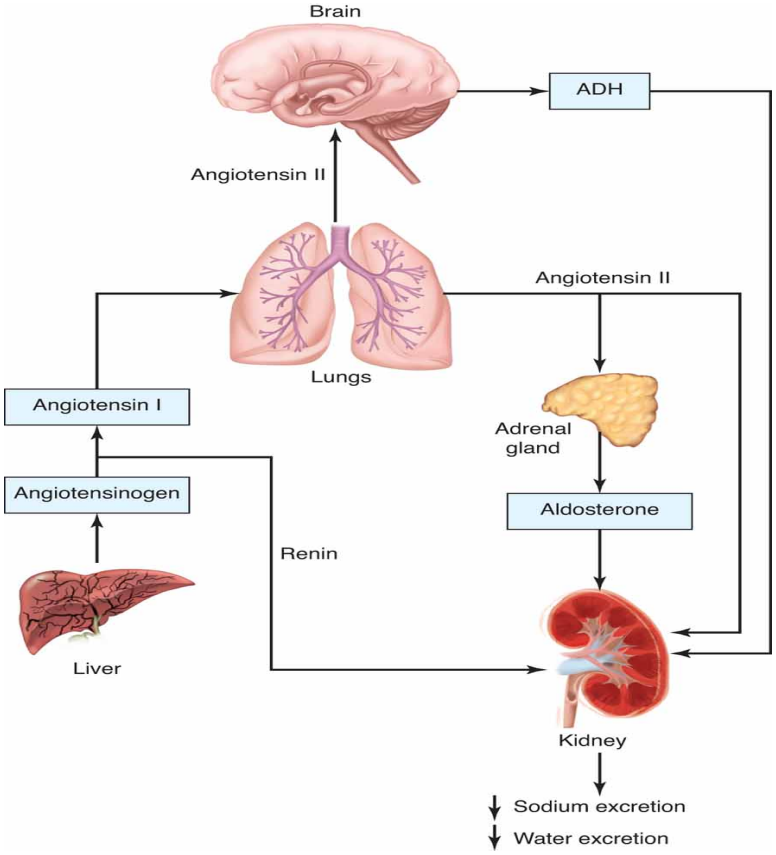
1. What is the cause for each abnormal plasma electrolyte result?
2. What is the significance of the urine sodium and serum osmolality results?

Electrolytes

- Electrolytes
  - Substances whose molecules dissociate into ions when they are placed in water.
  - Osmotically active particles
  - Classification of ions: by charge
    - CATIONS (+)
      - In an electrical field, move toward the cathode
      - Sodium (Na), Potassium (K), Calcium(Ca), Magnesium(Mg)
    - ANIONS (-)
      - In an electrical field, move toward the anode
      - Chloride(Cl), Bicarbonate, PO_4, Sulfate

Renin-Angiotensin-Aldosterone System

- Series of events
  - Body detects decreased blood volume/ pressure
  - Renin converts angiotensinogen to angiotension I
  - Angiotension I converted to angiotension II by ACE
  - Angiotension II causes
    - Vasoconstriction
    - Secretion of aldosterone
    - Stimulates AVP secretion and thirst
    - Enhances NaCl reabsorption



References

- Sunheimer, R., & Graves, L. (2010). *Clinical Laboratory Chemistry*. Upper Saddle River: Pearson .