1. Why is water critical for survival?
   
   1. A large proportion of our body is made up of water
      – 50-60% total body weight
      – 99% of extracellular fluid (ECF)
      – Essential component of cytosol (intracellular fluid, ICF)
   2. All cellular operations rely on water for:
      Diffusion medium for gases, nutrients, waste products

2. Why do all cellular operations rely on water?

   Water acts as a diffusion medium for gases, nutrients, and waste products

3. Of what must the body maintain normal volume and composition?

   1. ICF
   2. ECF = all other body fluids
      • Major - IF, plasma
      • Minor - lymph, CSF, serous and synovial fluids

4. What is intracellular fluid (ICF)?

   The cytosol; the fluid within the cell membrane

5. What is extracellular fluid (ECF)?

   All other body fluids outside the cell membrane, includes
   1. Major - IF, plasma
   2. Minor - lymph, CSF, serous and synovial fluids

6. ICF is (accounts for) 2/3 of the total body H₂O.

7. ECF is (accounts for) is 1/3 of the total body H₂O.

8. The ICF acts as a water reserve.

9. What aspects of the body fluid must be maintained?

   1. Volume (fluid balance)
   2. Ionic concentration (electrolyte balance)
   3. pH (acid-base balance)
10. Define fluid (water) balance.

The amount of H2O gained each day equals the amount of H2O lost each day.

11. In body fluid balance, balancing efforts involve/affect almost all body systems.

12. In fluid (water) balance, what is regulated?

Regulates content and exchange of body water between ECF and ICF.

13. What contributes/influences the amount of water gained each day?

1. GI tract (from food, liquid) *Primary source
2. Catabolism [For example, from metabolic activity like the H2O produced during electron transport (oxidative phosphorylation)]

14. What contributes/influences the amount of water lost each day?

1. Urine *Primary route
2. Evaporation (from skin, lungs)
3. Feces

15. Define electrolyte (ion) balance.

The amount of ions (electrolytes) gained each day equals the amount of ions lost each day to the environment outside the body; balances gains and losses of all electrolytes (ions that can conduct electrical current in solution).

16. What contributes/influences the gain of ions?

GI (from food, liquid)

17. What contributes/influences the loss of ions?

1. Urine
2. Sweat
3. Feces

18. Define acid-base (pH) balance.

The production of H+ ions is precisely offset by the loss of H+ ions from the body; balanced production and loss of H+; exists when pH of body fluids remain WNL (within normal limits).
19. What contributes/influences the gain of hydrogen ions?

GI (from food and liquid)
Metabolism

20. What contributes/influences the loss of hydrogen ions?

Kidneys (secrete H+ ← free H+ ions are acidic)
Lungs (eliminate CO2 ← mildly acidic)

21. ECF components (plasma and IF) are very similar. However, there are major differences between ECF and ICF.

22. Why is ICF very different than ECF?

Because of cell membrane
  – Is selectively permeable
  – Has specific channels for ions
  – Uses active transport to move things into/out of cell

23. How does water exchange between ECF and ICF occur?

Water exchange between ECF and ICF occurs across cell membranes by:
  1. Diffusion
  2. Osmosis
  3. Carrier-mediated transport

24. List the cations and anions in the ECF.

  1. Na+
  2. Cl-
  3. HCO3-

25. What is the dominant cation in ECF?

Na+ (sodium)

26. List the cations and anions in the ICF.

  1. K+ (98% of body content)
  2. Mg++
  3. HPO4--
  4. Negatively charge proteins
27. What is the dominant cation in ICF?

K+ (potassium)

28. List the principles of fluid and electrolyte regulation.

1. All homeostatic mechanisms that monitor and adjust body fluid composition respond to changes in ECF, not ICF
2. No receptors directly monitor fluid or electrolyte balance – monitor secondary indicators
3. Cells cannot move water by active transport
4. Body’s content of water and electrolytes:
   - Increases if gains exceed losses
   - Decreases if losses exceed gains
5. Fluid balance and electrolyte balance are interrelated

29. What do all homeostatic mechanisms that monitor and adjust body fluid composition respond to?

They respond to changes in ECF, not ICF because:
   - A change in ECF spreads throughout body and affects many or all cells
   - A change in ICF in one cell does not affect distant cells

30. No receptors directly monitor fluid or electrolyte balance, but receptors can monitor fluid balance and, electrolyte balance, so homeostatic adjustments to monitor fluid and electrolyte balance occur in response to changes in plasma volume and osmotic concentration.

31. What receptors help monitor fluids and electrolytes and what does each monitor?

   1. Baroreceptors – for plasma volume/pressure
   2. Osmoreceptors – for osmotic (solute) concentration

*Note: Solute = ions, nutrients, hormones, all other materials dissolved in body fluids*

32. How do cells move water?

Passively in response to osmotic gradients (Cells cannot move water by active transport)

33. Fluid balance and electrolyte balance are interrelated. (When H2O is lost, plasma volume ↓ s & electrolyte concentrations ↑. When electrolytes are gained or lost, there is an associated H2O gain or loss due to osmosis.)

34. The body’s water content of water and electrolytes increases if gains exceed losses and decreases if losses exceed gains.
35. List the primary hormones for fluid and electrolyte balance.

1. ADH
2. Aldosterone
3. Natriuretic peptides (e.g., ANP)

36. List the characteristics of ADH.

- Produced by osmoreceptor neurons in supraoptic nuclei in hypothalamus (and released by posterior pituitary)
- Osmoreceptors monitor osmotic concentrations in ECF
- Osmotic concentration increases/decreases when:
  - Na+ increases/decreases or
  - H2O decreases/increases
- Increased osmotic concentration → increased ADH
- → Water conservation
  - Increases water absorption → decreased osmotic concentration (by diluting Na)
  - Stimulates thirst center in hypothalamus → increased fluid intake

37. Where is ADH produced?

Produced by osmoreceptor neurons in supraoptic nuclei in hypothalamus (and released by posterior pituitary)

38. What do osmoreceptors monitor? What happens when what they monitor increases or decreases?

- Osmoreceptors monitor osmotic concentrations in ECF
- Osmotic concentration increases/decreases when:
  - Na+ increases/decreases or
  - H2O decreases/increases

39. Increased osmotic concentration results in increased ADH levels/secretion.

40. What is the action of ADH?

Stimulates water conservation at the kidneys, which
1. Increases water absorption → decreased osmotic concentration (by diluting Na)
2. Stimulates thirst center in hypothalamus → increased fluid intake
41. List the characteristics of aldosterone.

- Mineralocorticoid secreted by adrenal cortex
- Produced in response to:
  - Decreased Na+ or increased K+
  - In blood arriving at:
    - Adrenal cortex
    - Kidney (renin-angiotensin system)
- Plays a major role in Na+ reabsorption and K+ loss along DCT and collecting system (Conserves Na+ ions)

42. Aldosterone is secreted by the adrenal cortex.

43. What is Aldosterone produced in response to?

1. Decreased Na+ or increased K+
2. In blood arriving at:
   - Adrenal cortex
   - Kidney (renin-angiotensin system)

44. List what rennin is released in response to.

Renin is released in response to:
- Decreased Na+ or increased K+ in renal circulation
- Decreased plasma volume or BP at JGA
- Decreased osmotic concentration at DCT

45. Renin ultimately results in the activation of angiotensin II in the lung capillaries.

46. What endocrine organs does angiotensin II stimulate and what does each produce?

1. Adrenal cortex $\rightarrow$ increased aldosterone
2. Posterior pituitary $\rightarrow$ ADH
3. Increased BP (hence it’s name)

47. What is the end result of angiotensin II (the renin – angiotensin system) actions?

Increased BP (hence it’s name)

48. What is the effect of aldosterone in the DCT and collecting system of the kidneys?

In DCT and collecting system of kidneys $\rightarrow$
- Increased Na+ absorption (and associated Cl- and H2O absorption)
- Increased K+ loss
49. What is the effect of aldosterone on the salt receptors on the tongue?

Increased sensitivity of salt receptors on tongue → crave salty foods

50. Natriuretic peptides (ANP) are produced/released by cardiac muscle cells/fibers stretched by: increased BP or blood volume.

51. What are the 4 important functions of angiotensin II?

1. Stimulates adrenal production of aldosterone (Na+ retention & enhances H2O reabsorption at kidneys)
2. Stimulates secretion of ADH (stimulates H2O at the kidneys enhancing effects of aldosterone)
3. Stimulates thirst (increases fluid consumption and elevates blood volume)
4. Constricts blood vessels (increases BP)

52. How do natriuretic peptides (ANP) oppose angiotensin II?

Oppose angiotensin II and cause diuresis
   → Decreased ADH → increased H2O loss at kidneys
   → Decreased aldosterone → increased Na+ and H2O loss at kidneys
   → Decreases thirst → decreased H2O intake

53. Natriuretic peptides (ANP) oppose angiotensin II and cause diuresis.

54. The net result of the effects of natriuretic peptides (ANP) is decreased stretching of cells.

55. What happens to the plasma volume and electrolyte concentrations, when the body loses water?

   • Plasma volume decreases
   • Electrolyte concentrations increase

56. What happens when the body loses electrolytes?

   • Electrolyte concentrations decrease
   • Water also lost

57. Dehydration means water depletion.

58. What causes dehydration?

   • Inadequate water intake
   • Fluid loss, e.g., vomiting, diarrhea
   • Inadequate ADH (hypothalamic/pituitary malfunction)
59. What does dehydration lead to?

1. Too high Na+ = hypernatremia
2. Thirst, wrinkled skin
3. Decreased blood volume and BP
4. Fatal circulatory shock

60. What is hypernatremia?

Condition where Na+ ion concentration is too high

61. Overhydration means water excess.

62. What causes overhydration?

1. Excess water intake (>6-8 L/24 hours)
   - Seen in hazing rituals (water torture)
   - Marathon runners/paddlers
   - Ravers on ecstasy who overcompensate for thirst
2. Chronic renal failure
3. Excess ADH

63. What does overhydration lead to?

1. Too low Na+ = hyponatremia
2. Increased blood volume and BP
3. CNS symptoms (water intoxication); can proceed to convulsions, coma, death

64. What two fluid and electrolyte balance disorders involve K+?

1. Hypokalemia
2. Hyperkalemia

65. What is hyponatremia?

Condition where Na+ ion concentration is too low

66. What is hypokalemia?

Condition where K+ ion concentration is too low

67. What are the causes and results of hypokalemia?

- Caused by diuretics, diet, chronic alkalosis (plasma pH >7.45)
- Results in muscle weakness and paralysis
68. What is hyperkalemia?

Condition where K+ ion concentration is too low

69. What are the causes and results of hyperkalemia?

- Caused by diuretics (that block Na+ reabsorption), renal failure, chronic acidosis (plasma pH<7.35)
- Results in severe cardiac arrhythmias

70. What are most common problems with electrolyte balance caused by?

Caused by imbalance between gains/losses of Na+ in
  - Uptake across digestive epithelium
  - Excretion in urine and perspiration

71. Problems with potassium balance are less common, but more dangerous.

72. Acid-base balance is the control of pH.

73. What happen when the body generate acids (H+) during metabolic processes?

  Decrease pH

74. What is the normal pH range of ECF?

  7.35 – 7.45

75. The values of normal plasma pH are limited to a range between 7.35 – 7.45.

76. Define acidosis.

  A pH of <7.35 = acidosis (more common than alkalosis)

77. Define alkalosis.

  A pH of >7.45 = alkalosis

78. What pH range is lethal?

  <6.8 or >7.7 = lethal
79. Why are deviations outside the normal pH range dangerous?

They:
1. Disrupt cell membranes
2. Alter protein structure (remember hemoglobin?)
3. Change activities of enzymes

80. Acid-base balance affects all body systems especially CNS and CVS.

81. The CNS and CVS are especially sensitive to pH fluctuations. Which is more lethal acidosis or alkalosis?

Acidosis more lethal than alkalosis

82. What happens in acidosis?

- CNS deteriorates → coma → death
- Cardiac contractions grow weak and irregular → heart failure
- Peripheral vasodilation → decreased BP and circulatory collapse

83. What is the most important factor affecting the pH of ECF? Explain.

Carbonic acid (H2CO3) is the most important factor affecting pH of ECF because it is quicker to buffer the pH of the ECF than the protein buffer systems are.

84. What is the relationship between PCO₂ and pH?

Because most of the CO₂ in solution is converted to H₂CO₃ and most of the H₂CO₃ dissociates, the PCO₂ and pH are inversely related.

- ↑ PCO₂ → ↓ pH
- ↓ PCO₂ → ↑ pH

85. Where and how are H⁺ gained?

- At digestive tract
- Through cellular metabolic activities

86. Where and how are H⁺ eliminated?

- At kidneys by secretion of H⁺ into urine
- At lungs by forming H₂O and CO₂ from H⁺ and HCO₃-

87. The sites of H⁺ elimination are far from the sites of production.
As H⁺ ions travel through the body, they must be neutralized to avoid tissue damage. How is this accomplished? Explain.

It is accomplished through buffer systems. Buffer systems are compounds dissolved in body fluids that stabilize the pH by providing or removing H+ ion, thereby rendering them harmless (neutral).

List 3 buffer systems in body fluids.

1. Phosphate buffer system
2. Protein buffer systems
3. Carbonic acid-bicarbonate buffer system

Where is the phosphate buffer system located?

In ICF and urine

Where are the protein buffer systems located and what do they include?

- Found in ICF and ECF
- Include:
  - Hb buffer system (RBCs only)
  - Amino acid buffers (in proteins)
  - Plasma protein buffers (albumins, globulins...)

Of the 3 buffer systems, which is the most important in the ECF?

Carbonic acid-bicarbonate buffer system

Explain the carbonic acid – bicarbonate buffer system.

With some exceptions, body cells continually generate CO2. Most of the CO2 is converted to carbonic acid (H2CO3), which then dissociates into a H+ ion and a HCO3- ion. The carbonic acid – bicarbonate buffer system consists of H2CO3 and its dissociation products and its primary function is to prevent changes in pH caused by acids in the ECF. Because the following reaction is reversible, any change in one of the components affects the concentrations of the other components in the reaction.

\[
\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^- 
\]

This means that if H+ ion concentrations rise, most of them will be removed (neutralized temporarily) by HCO3-. HCO3- acts as a weak base that buffers the excess H+ ions by associating with the H+ ions to form H2CO3 (carbonic acid), which then dissociates into CO2 and H2O that can be excreted at the lungs. This will raise pH in an effort to bring it to normal levels. On the other side of the coin, the carbonic acid – bicarbonate system can also lower a rising or high (alkaline) pH by removing H+ ions from the plasma. This causes the reaction to shift to the right as H2CO3 dissociates into H+ ions and HCO3- ions causing a decrease in pH/increase in acidity.
94. What must be balanced for homeostasis of acid-base balance to be preserved?

H+ gains and losses must be balanced

95. What must happen to excess H⁺ so that acid-base balance is maintained? How is this accomplished?

Excess H⁺ must be:
1. Tied up by buffers
   • Temporary; H⁺ not eliminated, just not harmful
2. Permanently tied up in H₂O molecules
   • Associated with CO₂ removal at lungs
3. Removed from body fluids
   • Through secretion at kidneys

Accomplished by:
• Respiratory mechanisms
• Renal mechanisms

96. List the conditions affecting acid-base balance.

1. Disorders affecting buffers, respiratory or renal function
   – Emphysema, renal failure
2. Cardiovascular conditions
   – Heart failure or hypotension
   – Can affect pH, change glomerular filtration rates, respiratory efficiency
3. Conditions affecting CNS
   – Neural damage/disease that affects respiratory and cardiovascular reflexes that regulate pH

97. What disorders affect buffers, respiratory or renal function?

Emphysema, renal failure

98. What cardiovascular conditions affect acid-base balance?

Heart failure or hypotension

99. Cardiovascular conditions can affect pH, change glomerular filtration rates, and affect respiratory function.

100. List the phases that serious abnormalities in acid-base balance have and describe each.

   – Acute (initial) phase
     • pH moves rapidly out of normal range
   – Compensated phase
     • If condition persists
     • Physiological adjustments move pH back into normal range
     • Cannot be completed unless underlying problem corrected
101. List the types of compensation in the compensated phase.

   1. Respiratory
   2. Renal

102. List the characteristics of respiratory compensation.

   • Changes respiratory rate
     – Increasing/decreasing respiratory rate changes pH by lowering/raising PCO2
     – Helps stabilize pH of ECF
   • Occurs whenever pH moves outside normal limits
   • Has a direct effect on carbonic acid-bicarbonate buffer system

103. In respiratory compensation, what does increased PCO₂ lead to?

   Increased PCO₂ →
   – Increased H₂CO₃ → increased H⁺ → decreased pH (acidosis)
   – Increased respiratory rate → more CO₂ lost at lungs → CO₂ decreases to normal levels

104. In respiratory compensation, what does decreased PCO₂ lead to?

   Decreased PCO₂ →
   – Decreased H₂CO₃ → decreased H⁺ → increased pH (alkalosis)
   – Decreased respiratory rate → less CO₂ lost at lungs → CO₂ increases to normal levels

105. List the characteristics of renal compensation.

   • Changes renal rates of H⁺ and HCO₃⁻
     – Secretion
     – Reabsorption
   • In response to changes in plasma pH
     – Increased H⁺ or decreased HCO₃⁻ →
       • Decreased pH (acidosis) → more H⁺ secreted and/or less HCO₃⁻ reabsorbed
     – Decreased H⁺ or increased HCO₃⁻ →
       • Increased pH (alkalosis) → less H⁺ secreted and/or more HCO₃⁻ reabsorbed

106. Renal compensation changes renal rates of H⁺ and HCO₃⁻ during secretion and reabsorption.

107. Renal compensation occurs in response to changes in plasma pH. Answer the 3 questions below.

   a. What is renal compensation? Control of blood pH by kidneys that involves H⁺ removal

   b. What occurs when H⁺ is increased or HCO₃⁻ is decreased?

     – Increased H⁺ or decreased HCO₃⁻ →
       • Decreased pH (acidosis) → more H⁺ secreted and/or less HCO₃⁻ reabsorbed
c. What occurs when H+ is decreased or HCO3- is increased?

- Decreased H+ or increased HCO3- →
  - Increased pH (alkalosis) → less H+ secreted and/or more HCO3- reabsorbed

108. What are conditions resulting from disturbance of the acid-base balance named for? Give examples.

- Conditions named for:
  - Uncompensated or
    - Compensated
  - Primary source of problem
    - Respiratory or metabolic
    - Mixed (both)
  - Primary effect
    - Acidosis or alkalosis

109. List the cause of respiratory acid-base disorders, what acid-base disorders cause and what they lead to.

- Result from imbalance between:
  - CO2 generated in peripheral tissues (ECF)
  - CO2 excreted at lungs
- Cause abnormal CO2 levels in ECF
- Respiratory
  - Acidosis
  - Alkalosis

110. List the characteristics of respiratory acidosis.

- Most common challenge to acid-base equilibrium
- Primary sign is hypercapnia (increased PCO2)
- Develops when respiratory system cannot eliminate all CO2 generated by peripheral tissues
- Usual cause is hypoventilation
- Acute situation may be immediate, life-threatening condition
  - Requires bronchodilation or mechanical breathing assistance (ventilator)
  - pH can get as low as 7.0

111. What is the primary sign of respiratory acidosis?

Hypercapnia (increased PCO2)
112. Respiratory acidosis develops when the respiratory system cannot eliminate all the CO₂ generated by peripheral tissues. What does the previous statement mean?

Respiratory acidosis develops when plasma pH is decreased due to an increased PCO₂.

113. When respiratory acidosis is acute it may be an immediate, life-threatening condition that requires bronchodilation or mechanical breathing assistance (ventilator).

114. With respiratory acidosis, how low can the pH get?

pH can get as low as 7.0.

115. List the characteristics of respiratory alkalosis.

- Relatively uncommon
- Primary sign is high pH
- Develops when increased respiratory activity (hyperventilation) lowers plasma PCO₂ to below normal levels (hypocapnia)
- Seldom of clinical significance
- pH can get as high as 7.8 – 8.0

116. What is the primary sign of respiratory alkalosis?

Primary sign is high pH.

117. When does respiratory alkalosis develop?

Develops when increased respiratory activity (hyperventilation) lowers plasma PCO₂ to below normal levels (hypocapnia).

118. With respiratory alkalosis, how high can the pH get?

pH can get as high as 7.8 – 8.0.

119. What do metabolic acid-base disorders result from?

- Production of acids during metabolic processes
- Conditions that affect concentration of HCO₃⁻ in ECF

120. What do metabolic acid-base disorders lead to?

- → Metabolic
  - Acidosis
  - Alkalosis
121. What does metabolic acidosis result from?

- Results from:
  - Production of large numbers of acids
    - $\text{H}^+$ overloads buffer systems
  - Inability to excrete $\text{H}^+$ at kidneys
  - Severe HCO$_3^-$ loss

122. List the major causes of metabolic acidosis and briefly explain each one.

1. Production of large number of acids
   - Lactic acidosis from anaerobic respiration
     - After strenuous exercise
     - From prolonged tissue hypoxia (O2 starvation)
   - Ketoacidosis from generation of ketone bodies during metabolism
     - When peripheral tissues cannot obtain adequate glucose from bloodstream and begin metabolizing lipids and ketone bodies), e.g.,
       - Starvation
       - Complication of poorly controlled diabetes mellitus

2. Inability to excrete $\text{H}^+$ at kidneys
   - With severe kidney damage (glomerulonephritis)
   - Caused by diuretics that interfere with $\text{H}^+$ secretion into urine

3. Severe HCO$_3^-$ loss
   - From chronic diarrhea
   - Loss interferes with buffer system ability to remove $\text{H}^+$

123. The most frequent cause of metabolic acidosis is the production of a large number of acids. List 2 examples of metabolic acidosis and explain each.

1. Lactic acidosis from anaerobic respiration
   - After strenuous exercise
   - From prolonged tissue hypoxia (O2 starvation)

2. Ketoacidosis from generation of ketone bodies during metabolism
   - When peripheral tissues cannot obtain adequate glucose from bloodstream and begin metabolizing lipids and ketone bodies), e.g.,
     - Starvation
     - Complication of poorly controlled diabetes mellitus
124. What causes metabolic alkalosis to occur and why?

- Occurs after repeated vomiting
  - Stomach continues to generate HCl to replace lost acids
  - Is associated with increased HCO3- in ECF
  - HCO3- + H+ → H2CO3
    - Reduces H+ → alkalosis

125. How are acidosis and alkalosis detected?

- Blood tests for:
  - pH
  - PCO2
  - HCO3-
- Recognition of acidosis or alkalosis
- Classification as respiratory or metabolic

126. How are acidosis and alkalosis classified?

Classified as respiratory or metabolic