24 Water, Electrolyte, and Acid-Base Balance

Objectives

In this chapter we will study

• various forms of diabetes, especially gestational diabetes and diabetes insipidus;
• abnormalities in sodium balance—hypernatremia and hyponatremia;
• abnormalities in potassium balance—hyperkalemia and hypokalemia; and
• the diagnosis of various forms of acid-base imbalance.

Diabetes

When people say “diabetes,” they usually mean diabetes mellitus. There are other, less common forms of diabetes, however, that have nothing to do with insulin. The one thing they have in common is an abnormally high volume of urine output; the word diabetes means “passing through,” and diabetics of all kinds pass a great deal of water. A general definition of diabetes, embracing all its varieties, is chronic polyuria resulting from a metabolic disorder. (Thus, it does not include the temporary polyuria induced by drinking a lot of water or beer.) In this chapter, we examine the other forms of diabetes in a little more depth.

Diabetes Mellitus

Diabetes mellitus (DM) results from the hyposecretion of insulin (type I, or IDDM) or target cell insensitivity to insulin (type II, or NIDDM). Its signs include polyuria, polydipsia (intense thirst), polyphagia (intense hunger), hyperglycemia (elevated blood glucose), glycosuria (glucose in the urine), and ketonuria (ketones in the urine). These conditions have numerous devastating effects on the body, leading to such consequences as blindness, gangrene, renal failure, and early death if untreated.

Gestational Diabetes

Gestational diabetes (GDM) is a form of diabetes mellitus that develops in pregnant women. It is also called type III diabetes mellitus. Overall, it occurs in 1% to 3% of pregnant women, but the incidence is significantly higher in some groups, including people of Mexican, Indian, American Indian, Asian, and Pacific Islander descent. Pregnancy reduces a mother’s insulin sensitivity as a way of “sparing” blood glucose for the nourishment of the fetus. Gestational diabetes occurs when this mechanism overcompensates for the needs of the fetus, so the mother experiences hyperglycemia and glycosuria, and of course the glycosuria osmotically produces polyuria. Unrecognized and untreated GDM is a common cause of fetal deformity and miscarriage, so it is advisable to screen all pregnant women for GDM. When diagnosed, GDM is managed with dietary modification, weight control, exercise, and small doses of insulin. Also, fetal development is not allowed to go beyond full term (42 weeks) because of the high rate of mortality in overdue fetuses. Newborns with diabetic mothers are at high risk of numerous disorders and are therefore given extra forms of neonatal assessment. Even when a woman has preexisting DM, it places the life of her fetus in jeopardy, and the treatment of DM in pregnancy is a very delicate matter.

Diabetes Insipidus

Diabetes insipidus results from the hyposecretion or inaction of antidiuretic hormone (ADH). Physicians used to taste a patient’s urine to test for glucose; thus the name diabetes insipidus refers to the urine’s lack of sweetness. Central diabetes insipidus results from a lack or deficiency of ADH, usually as a result of cranial trauma or surgical removal of the pituitary. Nephrogenic diabetes insipidus (NDI) results from a lack of ADH receptors in the collecting ducts of the kidney, thus making ADH ineffective. NDI is sometimes hereditary but more often a side effect of certain antibiotics, anesthetics, and other drugs. The hereditary form affects principally males and is thought to be an X-linked recessive trait. This form develops shortly after birth. Its signs include abnormally frequent urination and increased feeding frequency, the latter owing to the baby’s dehydration and intense thirst. Since the urine is hypotonic, the
body’s sodium concentration becomes elevated. If the parents do not recognize the condition, this hypernatremia can lead to vomiting, fever, convulsions, and sometimes brain damage and permanent mental retardation. Even once the disease has been diagnosed, a child grows slowly because of episodes of dehydration throughout infancy and childhood.

Both forms of diabetes insipidus are diagnosed with a water deprivation test. Water is withheld from the patient for 12 to 14 hours. Then the patient is allowed to drink, and the osmolarity of the subsequent urine samples is measured. Patients with diabetes insipidus have an extremely low urine osmolarity (less than 200 mOsm/L) and specific gravity (1.00 to 1.005). NDI is further diagnosed from the fact that this osmolarity shows little or no change even when the patient is given ADH. The highest priority in treatment is to replace the lost water and restore the patient’s fluid volume and osmolarity. Diabetes insipidus is treated essentially the same as hypernatremia, described next. A child with hereditary NDI must be taught about the condition at an appropriate age and cautioned to drink ample water.

**Abnormalities in Sodium Balance**

This section and the next provide insights into the pathology of sodium and potassium excesses and deficiencies. Because of the especially critical role of sodium and potassium in the heartbeat, other muscle contractions, and nerve function, these two ions command the greatest attention in discussions of electrolyte balance.

**Hypernatremia**

Hypernatremia is a serum Na$^+$ concentration above 145 mEq/L. One cause of hypernatremia is the increased intake or retention of sodium. The source of excess sodium is rarely dietary, but more often fluid therapy—for example, I.V. sodium bicarbonate. Hypernatremia can also result from excess sodium retention owing to the hypersecretion of aldosterone. This is sometimes a secondary effect of ACTH hypersecretion, as in Cushing syndrome. The other basic cause of hypernatremia is insufficient water intake or excessive water loss without a proportionate loss of sodium. Excessive water loss can have several root causes: sweating, diabetes insipidus, the use of loop and osmotic diuretics, infant diarrhea, respiratory loss (especially when a respiratory infection or fever induces tachypnea, or accelerated breathing), a blunted sense of thirst, lack of access to potable water (as in exposure at sea or in a desert), infirmity or immobility (inability to get a drink for oneself), and coma (resulting in the inability to move or express the need for water). Hypernatremia is especially common in elderly hospital patients, who suffer high mortality as a result. A caregiver must be especially attentive to the needs of patients who cannot easily move or express their needs.

The signs and symptoms of hypernatremia result mainly from the hypertonic state of the extracellular fluid and resulting shrinkage of nerve cells. They include confusion, neuromuscular excitability, seizures, and coma. Hypernatremia is diagnosed by the measurement of serum Na$^+$ concentration, a high urine specific gravity (> 1.030), elevated hematocrit, and elevated concentration of plasma protein. It is treated primarily by giving water or 5% dextrose in water, orally if a patient is conscious and able to swallow and intravenously otherwise. This dilutes the sodium and restores normal osmolarity. However, both oral and intravenous rehydration must be done gradually (over 48 hours) to prevent excessively rapid rehydration and cerebral edema. Diuretics are sometimes given to promote Na$^+$ excretion, often with isotonic dextrose and KCl to compensate for the fluid loss.

**Hyponatremia**

Hyponatremia is a serum Na$^+$ concentration below 135 mEq/L. One cause is reduced renal excretion of water, as seen in renal failure, congestive heart failure, and cirrhosis. The kidneys retain more water, which dilutes the Na$^+$ of the extracellular fluid. Another cause is excessive Na$^+$ loss—for example, through vomiting, diarrhea, sweating, and burns—and replacement of the lost fluid with plain water (producing dilutional hyponatremia).

The signs and symptoms of hyponatremia stem largely from the swelling of neurons as they take up fluid from the hypotonic ECF. Neurological signs include lethargy, headache, confusion, stupor, neuromuscular excitability, seizures, and coma. Nonneurological signs include weight gain, edema, ascites, and distended jugular veins. Note that the neurological signs are similar to those for hypernatremia, so they alone are insufficient for a final diagnosis. Differential diagnosis is achieved by a finding of low serum Na$^+$ concentration and a low
urine specific gravity (< 1.010). Hyponatremia is treated by restricting water intake, replacing sodium, and correcting the underlying cause. Hyponatremia sometimes results from drugs such as thiazide diuretics, and may require a change of medication.

Abnormalities in Potassium Ion Balance

Whereas sodium is the primary extracellular cation, potassium is the primary intracellular cation. As little as 2% of the body’s potassium is found in the extracellular fluid; most is found in skeletal muscle. In fact, total body potassium can be used as an estimator of lean body mass. Even though most potassium is within the cells, changes in serum potassium adequately measure the body’s potassium balance unless the individual has a disease that alters membrane function, total body mass, or the acid-base balance of the body.

Hyperkalemia

Hyperkalemia is a serum potassium concentration above 5.0 mEq/L. This condition is relatively rare because the kidneys are very efficient at excreting excess K⁺, but it can result from excessive potassium intake (for example, in patients on I.V. fluid therapy or people who overuse potassium salt substitutes), inadequate potassium excretion (in renal failure or aldosterone hyposecretion), or maldistribution of potassium between the intracellular and extracellular fluids (ECF and ICF). Maldistribution can come about by several means. Normally, 98% of the body’s potassium is in the ICF. Hemolytic anemia, massive crush injuries, burns, extensive surgery, and transfusion with stored blood (containing old, leaky RBCs) can release large quantities of K⁺ from the ICF into the ECF and cause sudden, potentially fatal hyperkalemia. Acidosis typically induces hyperkalemia because excess H⁺ enters cells and K⁺ exits them to compensate, thus raising the K⁺ concentration in the ECF. Insulin promotes K⁺ uptake by cells, so an insulin deficiency can also cause excess K⁺ to accumulate in the ECF. Medications such as potassium-sparing diuretics, β-blockers, NSAIDS, and ACE inhibitors also sometimes cause hyperkalemia.

Hyperkalemia can produce confusing and seemingly contradictory signs and symptoms, depending in part on how rapidly the K⁺ concentration rises. Common effects include muscular weakness, neuromuscular excitability, and in severe cases, ventricular fibrillation and cardiac arrest. A rather grim application of this fact is that high-potassium injections are used in veterinary euthanasia and in capital punishment by lethal injection.

Hyperkalemia can be diagnosed from a combination of patient history (for example, trauma, blood transfusion, insulin deficiency, or Addison disease), characteristic abnormalities of the electrocardiogram, and measurement of serum K⁺ concentration. Mild hyperkalemia can be treated with dietary modification and, if the disorder is a side effect of medication, by changing medications. Insulin and glucose can be given to lower the K⁺ level by inducing cellular uptake; drugs are available to reduce neuromuscular excitability until the K⁺ concentration is restored to normal; and hemodialysis is used if the hyperkalemia results from renal failure.

Hypokalemia

Hypokalemia is a serum K⁺ concentration of less than 3.5 mEq/L. The fundamental causes of hypokalemia are inadequate intake, excessive loss, or maldistribution of potassium between the ECF and the ICF. Dietary deficiency is rare, but hypokalemia is not uncommon in people with depressed appetites and poor nutrition, as occurs in alcoholism and anorexia nervosa. Excessive losses of K⁺ can be due to heavy sweating, vomiting, diarrhea, and laxative abuse. Diarrhea can increase the fecal loss of K⁺ from the normal rate of 5 to 10 mEq/day to as much as 200 mEq/day. Excessive urinary loss can result from aldosterone hypersecretion. (Aldosterone promotes Na⁺ retention and K⁺ excretion.) Hypokalemia also occurs if an excess of K⁺ transfers from the ECF to the ICF. In alkalosis, for example, H⁺ ions diffuse out of the cells into the ECF, and K⁺ diffuses from the ECF into the cells to replace the H⁺. Thus, the ECF concentration of K⁺ falls below normal. Insulin can induce severe and even fatal hypokalemia if a patient takes it without also taking potassium supplements. The reason is that diabetic ketoacidosis causes H⁺ to enter cells, and K⁺ leaves the cells to compensate for the H⁺ inflow. The K⁺ that leaves is excreted in the urine, so the ECF K⁺ concentration remains normal, but the body’s total K⁺ stores are depleted. Then, when insulin is given and the ketoacidosis is corrected, K⁺ re-enters the cells and the ECF becomes hypokalemic.
Hypokalemia makes cells less excitable. This is reflected in such clinical signs as muscle weakness, loss of muscle tone, depressed reflexes, and irregular heartbeat. Involvement of the respiratory muscles can bring about depressed ventilation or even respiratory arrest. A loss of smooth muscle tone produces constipation, nausea, vomiting, and intestinal bloating.

Hypokalemia can be diagnosed from the patient’s history, characteristic alterations of the electrocardiogram, and measurement of the serum K⁺ concentration. It is treated by correcting the causes of potassium loss and having the patient eat potassium-rich foods such as bananas and vegetables. If necessary, I.V. potassium can be administered, but it must be given slowly because potassium irritates blood vessels and because overly rapid administration of I.V. potassium can induce a dangerous state of hyperkalemia.

Diagnosing Acid-Base Imbalances

Acidosis and alkalosis can be either respiratory or metabolic in origin. For example, emphysema causes respiratory acidosis because the diseased lungs cannot expel CO₂ as fast as the body produces it. Diabetes mellitus produces metabolic acidosis because incomplete fat oxidation generates ketones (keto acids). Hyperventilation causes respiratory alkalosis because the lungs expel CO₂ faster than the body produces it. Chronic vomiting causes metabolic alkalosis because stomach acid is lost from the body.

When there is a respiratory dysfunction that upsets acid-base balance, the kidneys can sometimes compensate for it and restore homeostasis; if the kidneys do not respond, the condition is uncompensated. Conversely, if the acid-base imbalance is caused by a renal or metabolic disorder, the respiratory system may or may not compensate for it (by adjusting respiratory rate); thus we can have compensated or uncompensated metabolic acidosis or alkalosis. This very simplified summary does not consider conditions beyond the scope of this manual, such as mixed disturbances in which a person might have both metabolic alkalosis and respiratory acidosis. But this introduction at least gives you a general idea of the reasoning process used in diagnosing acid-base disorders.

An important aspect of the clinical assessment of an acid-base imbalance is to determine its origin (respiratory or metabolic) and whether it is compensated or uncompensated. This informs a clinician of what underlying condition may call for treatment, and whether the body is restoring homeostasis on its own or whether clinical intervention (such as I.V. fluid) is necessary to restore a normal pH. Such determinations can be made from measurements of the pH of arterial blood and the PCO₂ and HCO₃⁻ concentration of venous blood.

Table 24.1 shows the normal values of these three variables and what is to be expected in each major form of acid-base imbalance. It is important to see beyond the table entries, however, to the physiological rationale for each, as explained after the table. If you understand the rationale, you can fill in such a table by reason rather than rote memorization.

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<thead>
<tr>
<th>Table 24.1</th>
<th>Forms of Acid-Base Imbalance</th>
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<tr>
<td>Normal Values</td>
<td>pH 7.35–7.45</td>
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<tr>
<td><strong>Acidosis</strong></td>
<td></td>
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<tr>
<td>Compensated respiratory</td>
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<td>Uncompensated respiratory</td>
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Table 24.1 shows eight major possibilities:

1. **Compensated respiratory acidosis** The pH is low by virtue of the definition of acidosis. The PCO₂ is high because the lungs are not expelling CO₂ as fast as the body produces it. CO₂ acidifies the blood, so this is the cause of the acidosis. The kidneys are attempting to compensate for this acid load by retaining bicarbonate (which buffers acid), so the bicarbonate level is elevated. This situation is typical of long-term pulmonary dysfunctions such as emphysema and pneumoconiosis (see chapter 22 of this manual).

2. **Uncompensated respiratory acidosis** The pH is low and the PCO₂ is high for the reasons stated in 1. The bicarbonate level is not elevated, however, indicating that the kidneys are not compensating for the respiratory dysfunction. This condition may be seen in cases of short-term asphyxia or holding the breath, letting CO₂ accumulate but not allowing enough time for renal compensation to take effect.

3. **Compensated metabolic acidosis** The pH is low because of some metabolic acid load. The PCO₂ is low because the respiratory system is “blowing off” CO₂ faster than the body produces it, attempting to compensate for the acidosis. This is typical of conditions like diabetes mellitus, which loads the body with acidic ketone bodies.

4. **Uncompensated metabolic acidosis** The pH and bicarbonate concentrations are low, but there is nothing unusual in the PCO₂ because the respiratory system is not compensating for the imbalance. This could occur in response to the use of an acidic drug or to fluid and electrolyte imbalances that put the body into a state of acidosis, accompanied by an inability of the respiratory system to adjust the ventilation rate (for example, because of depression of the respiratory center by drugs or anesthesia, or pulmonary diseases that reduce lung function).

5. **Compensated respiratory alkalosis** The pH is high (by definition of alkalosis), and the PCO₂ is low because the respiratory system is expelling CO₂ faster than the body produces it. To compensate, the urinary system excretes extra bicarbonate, so the blood bicarbonate concentration is reduced.

6. **Uncompensated respiratory alkalosis** The pH is high and the PCO₂ is low, but the bicarbonate level is normal because the urinary system is not compensating for the respiratory dysfunction. This is typical of hyperventilation, which rapidly expels CO₂ but does not last long enough to activate renal compensation.

7. **Compensated metabolic alkalosis** The pH is high by definition, and the PCO₂ is high because the respiratory system is retaining CO₂ (not expelling it as fast as it is produced). CO₂ lowers the blood pH and compensates for the metabolic condition. This may occur in chronic vomiting, as in pregnant women with severe morning sickness (hyperemesis gravidarum).

8. **Uncompensated metabolic alkalosis** The pH is high, but the PCO₂ is normal; the respiratory system has not adjusted CO₂ elimination to compensate for the metabolic dysfunction. This could also result from chronic vomiting, among other disorders, accompanied by such compromises in pulmonary function as noted in 4.

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**Case Study 24  The Very Thirsty Baby**

Charles, a 4-month-old Asian boy, is brought to his pediatrician by his mother. Charles has two older sisters, and his mother has noticed that he is nursing much more frequently than they did. She thinks this heavy nursing is the cause of the excessive amounts of urine he is producing. She reports that he wants to nurse every hour, and she has to change his diaper about every 30 minutes. In addition, because of the frequency of nursing, she is using an infant formula to supplement her milk in order to meet Charles’s demands.

When reviewing the records of Charles’s two sisters, the pediatrician notes that none of these symptoms were reported for either sister. The pediatrician completes a physical examination and notes the following:
Vital signs:
Rectal temperature = 98.9°F (37.2°C)
Heart rate = 85 beats/min
Respiratory rate = 13 breaths/min
Has lost some weight since last visit.

Reflexes: All within normal range, but slightly excitable.

Skin and mucous membranes: Lack of skin turgor; sunken fontanels; mucous membranes dry.

Based on the results of the physical examination, the pediatrician asks to take both blood and urine samples for analysis. The mother agrees, and the results are as follows:

Blood:
Hematocrit (Hct) = 59%
Serum sodium = 139 mEq/L
Serum potassium = 5 mEq/L
Serum bicarbonate = 21 mEq/L
Serum chloride = 109 mEq/L

Urine:
Specific gravity = 1.001
pH = 6.8
Glucose, protein, lipids, blood all absent

Based on these results, the pediatrician suspects that Charles’s kidneys are not correctly conserving water. He orders another blood test, which shows an elevated ADH level, and renal function tests, which show a normal glomerular filtration rate and renal plasma flow. Suspecting that Charles is suffering from nephrogenic diabetes insipidus, the pediatrician orders a water deprivation test, which shows no change in urine osmolarity over the course of the test. This indicates lack of ADH responsiveness by the kidneys. Based on these results, Charles is diagnosed with nephrogenic diabetes insipidus.

Based on this case study and other information in this chapter, answer the following questions.

1. Why is nephrogenic diabetes insipidus not seen in Charles’s sisters? Why is it not seen in either of his parents? If Charles later has a baby brother, would you expect the baby to have this disorder? Explain.

2. What aspects of the history, physical examination, and laboratory tests support the diagnosis of nephrogenic diabetes insipidus?

3. If you were the pediatrician and Charles’s mother asked you if he was going to need insulin injections and dietary restrictions, what would you tell her?

4. As Charles gets older, what type of counseling should he receive to help him control this disorder?

5. What will be the consequences if Charles disregards this counseling?

6. Why do some patients with nephrogenic diabetes insipidus have elevated levels of ADH?

7. With respect to its pathogenesis, does nephrogenic diabetes insipidus more nearly resemble type I or type II diabetes mellitus? Explain.

8. A patient with hyponatremia would be given
a. rapid infusion of hypotonic saline.
b. rapid infusion of hypertonic potassium chloride.
c. slow infusion of hypertonic saline.
d. slow infusion of hypotonic potassium chloride.
e. antidiuretics.

9. Jack goes into cardiac arrest but is revived in 3 minutes by the paramedics. They administer intravenous sodium bicarbonate to correct the acidosis that developed during the cardiac arrest. He then begins to exhibit excessive neuromuscular excitability and starts to have seizures. Explain (a) why his cardiac arrest produced a state of acidosis, (b) why sodium bicarbonate would correct the acidosis, (c) why he developed hypernatremia, and (d) what could be done next to correct the hypernatremia.

10. Below are blood values from three patients. Identify which of the eight categories of acid-base balance each patient has.

Patient A: pH = 7.62, PCO₂ = 55 mmHg, HCO₃⁻ = 32 mEq/L
Patient B: pH = 7.25, PCO₂ = 48 mmHg, HCO₃⁻ = 34 mEq/L
Patient C: pH = 7.10, PCO₂ = 42 mmHg, HCO₃⁻ = 8 mEq/L
**Selected Clinical Terms**

central diabetes insipidus  Chronic polyuria due to hyposecretion of antidiuretic hormone.

compensated acidosis and alkalosis  Acid-base imbalances in which the respiratory system adjusts pulmonary ventilation to compensate for a metabolic dysfunction or the kidneys adjust acid-base excretion to compensate for a respiratory dysfunction.

diabetes  Any chronic polyuria of metabolic origin; when this word is used without a qualifier, it usually refers to diabetes mellitus.

dilutional hyponatremia  A deficiency of sodium in the ECF resulting from excessive sodium loss and replacement of lost body fluids by ingestion of a hypotonic drink such as plain water.

nephrogenic diabetes insipidus  Chronic polyuria due to renal insensitivity to antidiuretic hormone.

uncompensated acidosis and alkalosis  Acid-base imbalances in which the respiratory system is unable to compensate for a metabolic dysfunction or the kidneys are unable to compensate for respiratory dysfunction, so that acid-base homeostasis cannot be restored without clinical intervention.