

A Comparison of Body Fluids

Chemical Composition of Body Fluids

- Intracellular fluid:**
 - The principal cation is potassium (K^+). (98% of the body's potassium is found inside cells).
 - The principal anion is phosphate (mainly HPO_4^{2-}).
 - Has more than 4x as much protein as plasma
- Extracellular fluid:**
 - The principal cation is sodium (Na^+).
 - The principal anion is chloride (Cl^-).
 - Interstitial fluid has very little protein; plasma contains an appreciable amount of protein.

	Principle Cation	Principle Anion	Protein Content
Intracellular fluid	K^+	HPO_4^{2-}	High
Interstitial fluid	Na^+	Cl^-	Low
Plasma	Na^+	Cl^-	Relatively high

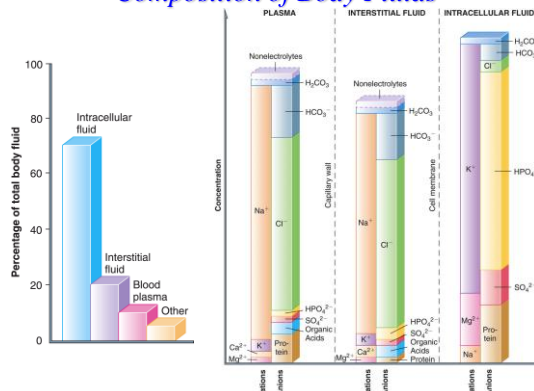
Introduction

- To carry out its functions, a living cell requires a steady supply of reactants, such as nutrients and oxygen (O_2). It also requires a reliable system for removing waste products (such as CO_2 and H_2O).
 - In simple organisms, the process of diffusion and osmosis is enough to bring materials through the cell wall.
 - In more complex organisms, consisting of many closely packed cells, some circulating system is necessary to bring materials into cells and carry away the wastes, otherwise the liquid surrounding the cells would be depleted of reactants and saturated with wastes.

Intracellular and Extracellular Fluids

- The average adult body contains ~42 L of fluids, which make up about 2/3 of the total body weight.
 - Intracellular fluids** — located inside the cells (about 28 L, ~70%). This is the medium in which vital life-maintaining reactions occur
 - Extracellular fluids** — located outside the cells. These fluids provide a constant environment for cells and transports substances to and from cells.
 - Interstitial fluids** — fills the space between tissue cells and moves in lymph vessels (10.5 L, 20%)
 - Plasma** — the liquid portion of the bloodstream (3.5 L, 7%)
 - Other body fluids include urine, digestive juices, and cerebrospinal fluid.

Composition of Body Fluids



Oxygen and Carbon Dioxide Transport

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CONSTITUENTS OF BLOOD

- **Plasma** constitutes 55% of blood fluid. It is mostly water (92%), along with proteins, CO₂, and other materials. Plasma circulates dissolved nutrients, such as glucose, amino acids, and fatty acids, and removes wastes, such as CO₂, urea, and lactate.
- The **blood cells** (45% of blood fluid) are
 - **Red Blood Cells** (erythrocytes) contain *hemoglobin*, which facilitates O₂ transport by reversibly binding O₂ and increasing its solubility in blood. They contain no cell nucleus or other organelles.
 - **White Blood Cells** (leukocytes) are involved in the body's immune responses to infections and foreign materials, and remove discarded cells and debris.
 - **Platelets** (thrombocytes) are responsible for blood clotting (coagulation)

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Hemoglobin

- Blood carries oxygen from the lungs to the tissues. An average adult at rest requires about 350 mL of oxygen per minute.
 - Only about 2% of this oxygen is carried in blood plasma.
 - The remaining 98% of the oxygen is carried by red blood cells using molecules of **hemoglobin**. (Normal human blood contains about 15 g of hemoglobin per 100 mL.)
 - **Oxyhemoglobin** — a combination of oxygen and hemoglobin.
 - **Deoxyhemoglobin** — the non-oxygenated form (often simply referred to as *hemoglobin*).

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BLOOD

- **Blood** is a body fluid that delivers substances such as nutrients and oxygen to the cells and transports metabolic waste products away from the cells.
 - Blood has an density of ~1.06 g/mL, and comprises 8% of the human body weight. The average adult has ~5 liters (1.3 gal) of blood.
 - Blood is circulated around the body through blood vessels by the pumping action of the heart.
 - In animals with lungs, arterial blood carries oxygen from inhaled air to the tissues of the body, and venous blood carries the waste product carbon dioxide from the tissues to the lungs to be exhaled.
 - In vertebrates, blood is composed of **blood cells** suspended in a liquid called **blood plasma**.

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FUNCTIONS OF BLOOD

- Blood performs many important functions within the body:
 - Supplies of oxygen to tissues
 - Supplies nutrients (e.g., glucose, amino acids, and fatty acids)
 - Removes wastes such as CO₂, urea, and lactic acid.
 - Immunological functions, including circulation of white blood cells, and detection of foreign material by antibodies.
 - Coagulation (blood clotting after an open wound in order to stop bleeding)
 - Messenger functions, including the transport of hormones and the signaling of tissue damage
 - Regulation of body pH
 - Regulation of core body temperature
 - Hydraulic functions

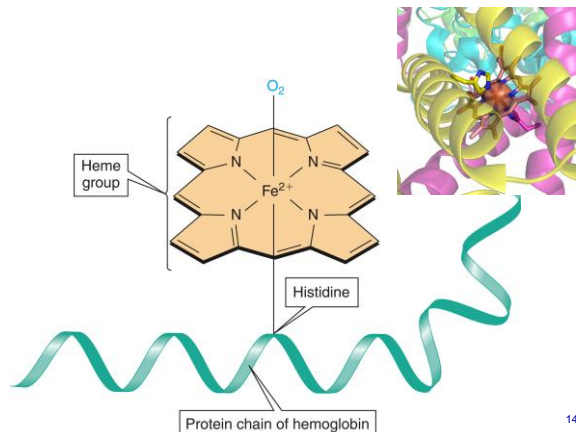
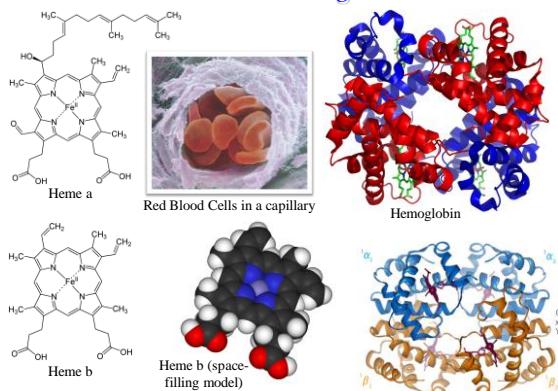
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Heme and Hemoglobin

- Hemoglobin is a conjugated protein containing four protein chains (the **globin** portion of the molecule) and four **heme** groups.
 - The heme group consists of a flat porphyrin-ring with four nitrogen atoms pointing in towards a central cavity, which bind an Fe²⁺ ion.
 - The iron atom is also bound to a histidine group in the protein.
 - The sixth bond to the Fe²⁺ ion is to an O₂ molecule.
- Because there are four heme groups in a hemoglobin molecule, **one hemoglobin can bind a total of four O₂ molecules**.

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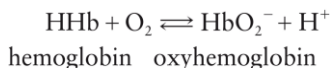
Heme and Hemoglobin



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Oxygen Binding

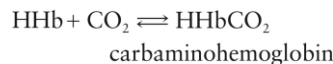
- When one of the four heme groups binds an O_2 , the affinity of the other heme groups for O_2 is *increased*.
 - When an O_2 binds to the Fe^{2+} , the histidine residue is pulled towards the heme group.
 - The resulting strain on the protein is transmitted to the other three heme binding sites, inducing a similar change in conformation, which makes the binding of O_2 easier. The binding of oxygen is thus a cooperative process.
- The reversible binding of O_2 to hemoglobin (HHb) is represented by the equation:



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Carbon Dioxide Binding

- When CO_2 is present, hemoglobin can combine with it to form **carbaminohemoglobin**. This reversible reaction is favored by conditions found in body tissues:

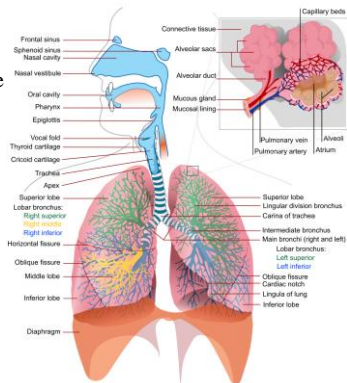


- Carbon dioxide is transported in the blood several different ways:
 - 25% is transported as carbaminohemoglobin.
 - 5% dissolves in plasma and travels in solution.
 - 70% is transported in the form of the bicarbonate ion, HCO_3^- .

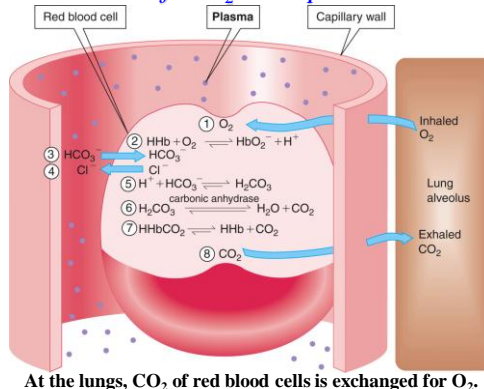
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Mechanisms for O_2 Transport to Tissues

- The transport of O_2 to tissues begins when inhaled air fills the alveoli of the lungs.
- These clusters of small sacs are surrounded by many tiny blood capillaries, through which O_2 is absorbed into the blood.



Mechanism for O_2 Transport to Tissues



At the lungs, CO_2 of red blood cells is exchanged for O_2 .

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Mechanism for O₂ Transport to Tissues

1. O₂ partial pressure is higher in the alveoli than in the red blood cells (RBCs). O₂ diffuses from the alveoli through the capillary wall and into the RBCs.
2. Inside the RBCs, O₂ reacts with hemoglobin to form oxyhemoglobin and H⁺ ions. Oxyhemoglobin formation is favored (according to Le Chatelier's principle) by a high partial pressure of O₂, a slight cooling of the blood, and an increase in pH (decrease of H⁺ ions).
3. Bicarbonate ions (HCO₃⁻) diffuse from the plasma into the RBCs
4. The bicarbonate ions are replaced in the plasma by chloride ions that diffuse out of the blood cells. This **chloride shift** maintains charge balance and osmotic pressure relationships between the plasma and the RBCs.

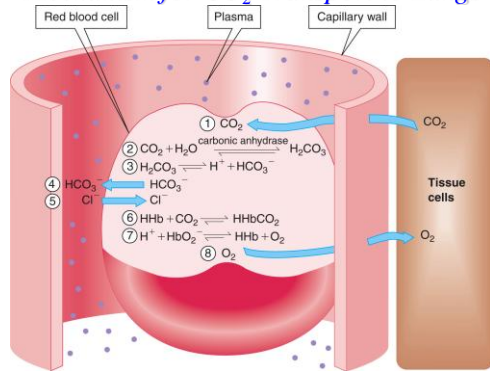
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Mechanism for O₂ Transport to Tissues

5. Protons released by hemoglobin as it is oxygenated (Step 2) react with bicarbonate ions to form carbonic acid (H₂CO₃).
6. An enzyme in the RBCs, carbonic anhydrase, promotes the breakdown of carbonic acid to water and CO₂. The reaction is reversible, but the low pressure of CO₂ in the lungs favors the formation of O₂ and water through Le Chatelier's principle.
7. Carbaminohemoglobin (HHbCO₂), formed from hemoglobin at the cellular level, breaks apart to yield hemoglobin and CO₂.
8. Because the CO₂ pressure is high in the RBCs but low in the alveoli, CO₂ molecules diffuse out of the RBCs and into the lung. The CO₂ and some of the water formed in Step 6 are expelled in the exhaled air.

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Mechanism for CO₂ Transport to Lungs



At the tissue cells, O₂ of red blood cells is exchanged for CO₂. 21

Mechanism for CO₂ Transport to Lungs

- Oxygenated RBCs are carried by the bloodstream into the capillaries surrounding the cells of active tissues. The steps that take place (see previous slide) are essentially the reverse of what happens at the lungs.
1. Tissue cells use oxygen to produce energy. CO₂ and H₂O are formed as byproducts. The concentration of CO₂ is higher in the tissue cells than in the RBCs, so CO₂ diffuses from the tissue cells into the interstitial fluid and then into the RBCs.
 2. Inside the RBCs, CO₂ rapidly reacts with water in the presence of carbonic anhydrase to produce carbonic acid (H₂CO₃).
 3. Carbonic acid dissociates into H⁺ and HCO₃⁻ ions.

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Mechanism for CO₂ Transport to Lungs

4. The bicarbonate ions diffuse into the plasma. The bicarbonate ions in the plasma are the form in which most CO₂ moves from tissue cells to the lungs.
5. The chloride shift takes place in the opposite direction to maintain electrolyte balance.
6. A smaller amount (25%) of CO₂ from Step 1 reacts with hemoglobin to form carbaminohemoglobin (HHbCO₂) for transport to the lungs.
7. This increase in H⁺ concentration inside the RBCs promotes a reaction with oxygemoglobin, which releases O₂.
8. The free O₂ diffuses out of the RBCs through the plasma, capillary membrane, interstitial fluid, and into the tissue cells.

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Chemical Transport to the Cells

Chemical Transport to the Cells

- For substances to be chemically transported in the body, they must become part of the moving bloodstream. They may
 - dissolve in the water-based plasma (sugars, amino acids, ions, and gases to some extent)
 - become chemically bonded to cellular components (O_2 and CO_2)
 - form a suspension in the plasma (lipids).



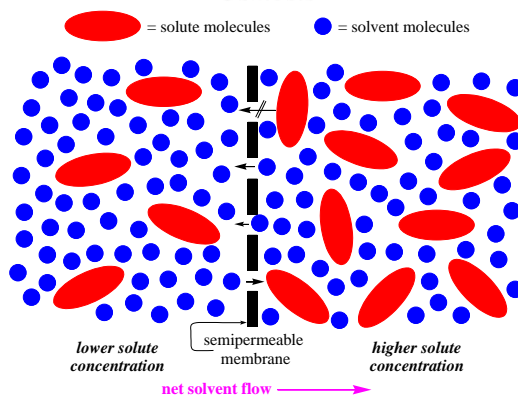
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Osmosis in Cells

- Materials transported in the bloodstream must
 - move through the capillary wall into the interstitial fluid and through the cell membrane into the cell.
 - move through the cell membrane to the interstitial fluid and through the capillary wall into the bloodstream when waste products are removed.
- The walls of the capillaries act as **selectively permeable membranes** (or **semi-permeable membranes**), allowing water with dissolved nutrients to pass in one direction and water containing dissolved wastes to pass in the other direction.
- **Osmosis** is the process in which solvent molecules can pass through a semipermeable membrane in response to a concentration gradient.

Osmosis



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Flow Between Blood and Interstitial Fluid

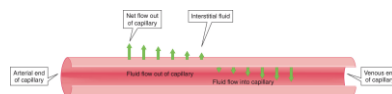
- The movement of water and dissolved materials through the capillary walls is governed by two factors:
 - the *pressure* of blood against the capillary walls
 - the *differences in protein concentration* on each side of the capillary walls.
- Because concentration of proteins in the plasma is higher than that of the interstitial fluid, there is an osmotic pressure of about 18 torr, which would tend to move fluid into the bloodstream.
 - The blood pressure at the arterial end of a capillary is ~32 torr, while at the venous end it is ~12 torr.



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Flow Between Blood and Interstitial Fluid

- At the arterial end, the blood pressure is **higher** than the osmotic pressure, so the tendency is for a net flow to occur *from* the capillary *into* the interstitial fluid, carrying dissolved nutrients, oxygen, hormones, and vitamins needed by the tissue cells.
- At the venous end, the blood pressure is **lower** than the osmotic pressure, so the tendency is for a net flow to occur *from* the interstitial fluid *into* the capillary, carrying the metabolic waste products out of the cell, and into the bloodstream.



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The Constituents of Urine

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Urine

- Urine contains about 96% water and 4% dissolved organic and inorganic waste products.
- Approximately 40-50 g of dissolved solids are contained in daily urine output of an adult.
- The urine of a healthy person has a pH of 4.5-8.0, with 6.6 a reasonable average on an ordinary diet.
 - Fruits and vegetables make urine basic.
 - High-protein foods make urine acidic.
- The composition of urine can be checked using **urinalysis test strips** and other clinical tests for abnormal urine constituents.

Table 25.1 Major Dissolved Solids in Normal Urine

Constituent ^a	Grams per 24 Hours ^b
Amino acids	0.80
Urea	25.0
Creatinine	1.5
Uric acid	0.7
H ⁺	pH 4.5-8.0
Na ⁺	3.0
K ⁺	1.7
NH ₄ ⁺	0.8
Ca ²⁺	0.2
Mg ²⁺	0.15
Cl ⁻	6.3
SO ₄ ²⁻	1.4
H ₂ PO ₄ ⁻	1.2
HCO ₃ ⁻	0-3
Other compounds	2-3

^aThe 24-hour volume and composition of urine vary widely, depending on the fluid intake and diet.
^bThese data are for an average 24-hour specimen with a total volume of 1400 mL.

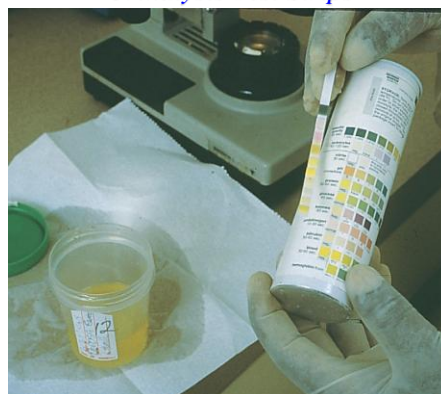
Abnormal Urine Constituents

Table 25.2 Some Abnormal Urine Constituents

Abnormal Constituent	Condition	Causes
Glucose (in large amounts)	Glucosuria	Diabetes mellitus, renal diabetes, alimentary glycosuria
Protein	Proteinuria or albuminuria	Kidney damage, nephritis, bladder infection
Ketone bodies	Ketonuria	Diabetes mellitus, starvation, high-fat diets
Pus (leukocytes)		Kidney or bladder infection
Hemoglobin	Hemoglobinuria	Excessive hemolysis of red blood cells
Red blood cells	Hematuria	Hemorrhage in the urinary tract
Bile pigments (in large amounts)	Jaundice	Blockage of bile duct, hepatitis, cirrhosis

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Urinalysis Test Strips



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Fluid and Electrolyte Balance

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Fluid and Electrolyte Balance

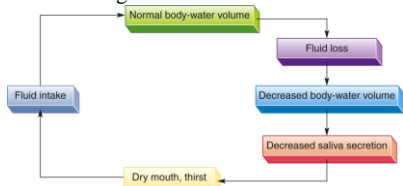
- The body is 45-75% water by weight (depending on a number of factors). Fluid balance within the body is maintained not only by a balance in the total amount but by a normal and stable distribution of fluid in the body's three fluid-containing areas.
- Fluid and electrolyte balance are interdependent, so if one deviates from normal, so will the other.
- For proper fluid balance, fluid output and intake must be equal.
 - Water from food and drink is absorbed into the body from the digestive tract.
 - Water is also derived within the cells from food metabolism.

Table 25.3 Typical Normal Values for Water Entry and Exit

Intake (mL)	
Ingested liquids	1500
Water in foods	700
Water formed by oxidation	200
Total	2400
Output (mL)	
Kidneys (urine)	1400
Lungs (water in expired air)	350
Skin	
By diffusion	350
By perspiration	100
Intestines (in feces)	200
Total	2400

The Thirst Mechanism

- Water intake is regulated in part by the **thirst mechanism**.
 - When the body loses large amounts of water, salivary secretions decrease, and a dry feeling develops in the mouth.
 - This and other sensations are recognized as thirst, and water is drunk to relieve the condition, reestablishing the fluid balance.



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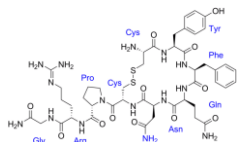
Regulation of Fluid Balance

- Water normally leaves the body through the kidneys (urine), lungs (water vapor in expired air), skin (by diffusion and perspiration), and the intestines (feces).
- Abnormally high fluid losses, and possibly dehydration, can be caused by hyperventilation, excessive sweating, vomiting, or diarrhea.
- Fluid balance in the body is maintained or restored primarily by variations in urine output.
 - Normally, this is about 1400 mL per day, but the total excretion adjusts according to water intake.
 - The primary factor that controls urine production is the rate of water reabsorption from the renal tubules in the kidneys. This rate is regulated chiefly by the pituitary hormone **vasopressin** and by the adrenal cortex hormone **aldosterone**.

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Regulation of Fluid Balance

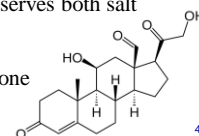
- Vasopressin** (antidiuretic hormone, ADH) is a nonapeptide (9 amino acid) hormone that increases reabsorption of water from renal tubules.
 - In the absence of vasopressin, less water is reabsorbed into the bloodstream, and a large volume of light yellow, dilute urine results.
 - In the presence of vasopressin, the tubules become more permeable to water that is drawn into the capillaries, increasing blood volume; a low volume of dark yellow, concentrated urine results.



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Regulation of Fluid Balance

- Aldosterone** is a steroid hormone produced in the adrenal glands.
 - When bodily fluid levels are dangerously low, the adrenal gland secretes aldosterone, which stimulates the reabsorption of Na^+ from the renal tubules into the blood.
 - Chloride ions follow the sodium ions (chloride shift) to maintain electrical neutrality.
 - Water follows sodium chloride.
 - Aldosterone secretion thus conserves both salt and water in the body.
 - When the fluid level returns to normal, the amount of aldosterone that is secreted decreases.



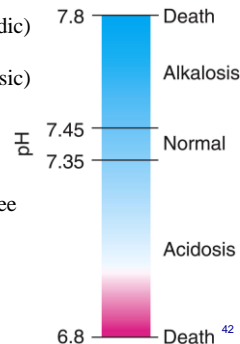
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Acid-Base Balance

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Acid-Base Balance

- Blood pH normally remains in a narrow range between 7.35 and 7.45.
 - A decrease in pH (more acidic) is called **acidosis**.
 - An increase in pH (more basic) is called **alkalosis**.
 - Death can result if the pH falls below 6.8 or rises above 7.8.
- Blood pH is maintained by three systems:
 - buffer
 - respiratory
 - urinary



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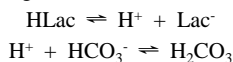
Buffer Control of Blood pH

- A buffer system prevents large changes in the pH of a solution when an acid or base is added.
 - A buffer contains a mixture of a weak acid and its conjugate base (or a weak base and its conjugate acid).
 - When an acid or base is added to the buffer, there is something present which can neutralize it, keeping the pH at a fairly constant level.
- There are three major buffer systems in blood:
 - the bicarbonate buffer (bicarbonate + carbonic acid)
 - the phosphate buffer
 - the plasma proteins

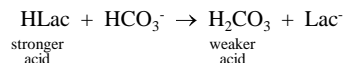
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Buffer Control of Blood pH

- When lactic acid (HLac) enters the bloodstream, it dissociates to produce H⁺ ions and lactate ions (Lac⁻). The liberated H⁺ ions decrease the pH of the blood. The bicarbonate ions of the bicarbonate buffer system react with the excess H⁺ and return the pH to the normal range:



- If we add these equations together, we see that the effect of the buffering is to replace lactic acid in the blood with carbonic acid, which is a weaker acid and releases fewer H⁺ ions to the blood:



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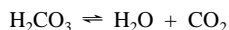
Buffer Control of Blood pH

- Although the bicarbonate system is not the strongest buffer system in the body (the most powerful and plentiful one is the proteins of plasma and cells), it is very important because the concentrations of both bicarbonate and carbonic acid are regulated by the kidneys and the respiratory system.
- Without the respiratory and urinary processes, the capacity of buffers would eventually be exceeded.

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Respiratory Control of Blood pH

- The respiratory system helps control the acidity of blood by regulating the elimination of CO₂ and H₂O. These molecules come from carbonic acid:



- The more CO₂ and H₂O that are exhaled, the more carbonic acid is removed from the blood, thus elevating the blood pH to a more alkaline level.
- The respiratory control of blood pH begins in the brain with respiratory center neurons that are sensitive to blood CO₂ levels and pH.

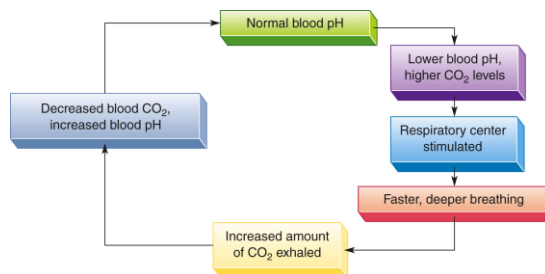
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Respiratory Control of Blood pH

- A significant increase in the CO₂ of arterial blood, or a decrease below 7.38 of arterial blood pH, causes the breathing to increase both in rate and depth, resulting in **hyperventilation**.
 - This increased ventilation eliminates more CO₂, reduces carbonic acid and H⁺ concentrations, and increases the blood pH back to the normal level.
- If the opposite situation, an increase in blood pH above normal causes **hypoventilation**, a reduced rate of respiration.
 - Less CO₂ is exhaled, and the higher concentration of carbonic acid remaining in the blood lowers the pH back to normal.

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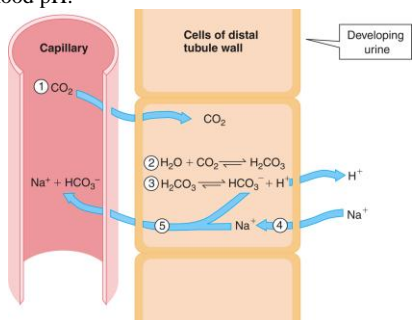
Respiratory Control of Blood pH



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Urinary Control of Blood pH

- The kidneys can excrete varying amounts of acid and base, and therefore play a vital role in regulating blood pH.



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Urinary Control of Blood pH

- CO₂ diffuses from the blood capillaries into the kidney distal tubule cells.
 - Water and CO₂ react to give carbonic acid under the influence of carbonic anhydrase.
 - The H₂CO₃ ionizes to give H⁺ ions and HCO₃⁻ ions. The H⁺ ions diffuse into the developing urine.
 - For every H⁺ ion entering the urine, a Na⁺ ion passes into the tubule cells.
 - The Na⁺ ions and HCO₃⁻ ions enter the bloodstream capillaries.
- The net result of these reactions is the conversion of CO₂ to HCO₃⁻ in the blood. Both the decrease of CO₂ and the increase of HCO₃⁻ tend to increase blood pH levels back to normal.

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Urinary Control of Blood pH

- The developing urine has picked up the hydrogen ions, which now react with buffering ions such as phosphate that are present in urine:

$$H^+ + HPO_4^{2-} \rightarrow H_2PO_4^-$$
- The presence of the phosphate buffer system (H₂PO₄⁻/HPO₄²⁻) usually keeps urine from going much below pH 6, but too great an excess of protons can exceed the buffer capacity of the system and result in very acidic urine.

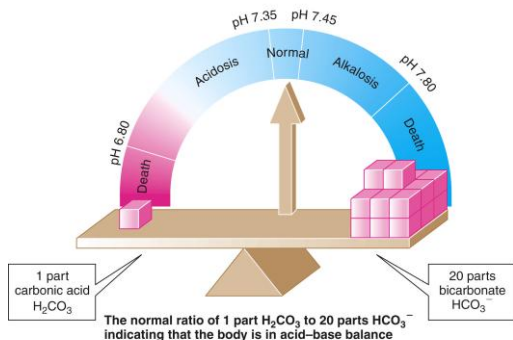
Acidosis and Alkalosis

- When blood pH is normal, components of the bicarbonate buffer are present in plasma in a ratio of 20 parts HCO₃⁻ to 1 part H₂CO₃.
- When respiratory and urinary systems work together to maintain the blood at pH 7.4, they do so primarily by maintaining the HCO₃⁻/H₂CO₃ ratio at 20:1. Any change in the ratio produces a change in pH.
 - An increase in the ratio of bicarbonate to carbonic acid causes the pH to increase (**alkalosis**).
 - A decrease causes the pH to decrease (**acidosis**).

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Acidosis and Alkalosis



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Respiratory Alkalosis

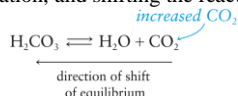
- Respiratory alkalosis** is caused by hyperventilating (breathing rapidly and deeply). Too much CO₂ is exhaled, disturbing the CO₂/H₂CO₃ ratio.
 - According to Le Chatelier's principle, the reaction below shifts to the right, reducing the amount of H₂CO₃ present:

$$H_2CO_3 \rightleftharpoons H_2O + CO_2 \uparrow$$
 direction of shift to restore equilibrium
 - The HCO₃⁻/H₂CO₃ ratio becomes greater than 20:1, causing blood pH to rise to 7.54 or higher within a few minutes.
 - This condition can be combated by breathing into a paper bag, administering CO₂, or treating the cause of the hyperventilation.

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Respiratory Acidosis

- **Respiratory acidosis** is caused by hypoventilation (slow or shallow breathing) resulting from an overdose of narcotics, barbiturates, or anesthetics, from lung diseases such as emphysema and pneumonia, or an object lodged in the windpipe.
 - Too little CO₂ is exhaled, increasing its blood concentration, and shifting the reaction to the left:

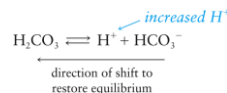


- The concentration of H₂CO₃ increases, the HCO₃⁻/H₂CO₃ ratio becomes less than 20:1, and respiratory acidosis sets in.
- Treatment involves administering isotonic sodium bicarbonate solution.

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Metabolic Acidosis

- **Metabolic acidosis** results from the production of too much H⁺ ions from various metabolic pathways. The diffusion of these substances into the bloodstream causes a shift in the equilibrium:



- This decreases the concentration of HCO₃⁻ and increases the concentration of H₂CO₃, decreasing the HCO₃⁻/H₂CO₃ ratio and decreasing blood pH.
- This is a problem in uncontrolled diabetes, and may occur temporarily after heavy exercise, or with severe diarrhea or an aspirin overdose. Symptoms include hyperventilation, increased urine formation, drowsiness, headache, and disorientation.

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Metabolic Alkalosis

- **Metabolic alkalosis** results when the body has lost acid in some form, perhaps from prolonged vomiting of the acidic stomach contents, or there has been an ingestion of alkaline substances (such as sodium bicarbonate).
 - A decrease in acid concentration within the body or an increase in HCO₃⁻ levels causes the HCO₃⁻/H₂CO₃ ratio to rise above 20:1, increasing blood pH.
 - The respiratory center responds by slowing the breathing (hypoventilation). Other symptoms may include numbness, tingling, and headache.

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Causes of Acid-Base Imbalances

Table 25.4 Some Causes of Blood Acid–Base Imbalance

Condition	Causes
<i>Respiratory</i>	
Acidosis: CO ₂ ↑ pH ↓	Hypoventilation, blockage of diffusion within lungs, respiratory center depressants
Alkalosis: CO ₂ ↓ pH ↑	Hyperventilation, excitement, trauma
<i>Metabolic</i>	
Acidosis: H ⁺ ↑ pH ↓	Kidney failure, prolonged diarrhea, ketone bodies from diabetes mellitus
Alkalosis: H ⁺ ↓ pH ↑	Kidney disease, prolonged vomiting, excessive intake of baking soda

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