Human Physiology/Homeostasis

Human Physiology — Cell physiology →

Homeostasis — Cells — Integumentary — Nervous — Senses — Muscular — Blood — Cardiovascular — Immune — Urinary — Respiratory — Gastrointestinal — Nutrition — Endocrine — Reproduction (male) — Reproduction (female) — Pregnancy — Genetics — Development — Answers

Overview

The human organism consists of trillions of cells all working together for the maintenance of the entire organism. While cells may perform very different functions, all the cells are quite similar in their metabolic requirements. Maintaining a constant internal environment with all that the cells need to survive (oxygen, glucose, mineral ions, waste removal, and so forth) is necessary for the well-being of individual cells and the well-being of the entire body. The varied processes by which the body regulates its internal environment are collectively referred to as homeostasis.

What is Homeostasis?

Homeostasis in a general sense refers to stability, balance or equilibrium. It is the body's attempt to maintain a constant internal environment. Maintaining a stable internal environment requires constant monitoring and adjustments as conditions change. This adjusting of physiological systems within the body is called *homeostatic regulation*.

Homeostatic regulation involves three parts or mechanisms: 1) the ***receptor***, 2) the ***control center*** and 3) the ***effector***.

The ***receptor*** receives information that something in the environment is changing. The ***control center*** or ***integration center*** receives and processes information from the ***receptor***. And lastly, the ***effector*** responds to the commands of the ***control center*** by either opposing or enhancing the stimulus. This is an ongoing process that continually works to restore and maintain homeostasis. For example, in regulating body temperature there are temperature *receptors* in the skin, which communicate information to the brain, which is the *control center,* and the *effector* is our blood vessels and sweat glands in our brain.

Because the internal and external environment of the body are constantly changing and adjustments must be made continuously to stay at or near the set point, homeostasis can be thought of as a *synthetic equilibrium.*

Positive and Negative Feedback

When a change of variable occurs, there are two main types of feedback to which the system reacts:

- ***Negative feedback***: a reaction in which the system responds in such a way as to reverse the direction of change. Since this tends to keep things constant, it allows the maintenance of homeostasis. For instance, when the concentration of carbon dioxide in the human body increases, the lungs are signaled to increase their activity and expel more carbon dioxide. Thermoregulation is another example of negative feedback. When body temperature rises (or falls), receptors in the skin and the hypothalamus sense a change, triggering a command from the brain. This command, in turn, effects the correct response, in this case a decrease in body temperature.
- **Home Heating System Vs. Negative Feedback**'

When you are at home, you set your thermostat to a desired temperature. Let's say today you set it at 70 degrees. The thermometer in the thermostat waits to sense a temperature change either too high above or too far below the 70 degree set point. When this change happens the thermometer will send a message to the "Control Center", or thermostat, Which in turn will then send a message to the furnace to either shut off if the temperature is too high or kick back on if the temperature is too low. In the home-heating example the air temperature is the "NEGATIVE

FEEDBACK." When the Control Center receives negative feedback it triggers a chain reaction in order to maintain room temperature.

- ***Positive feedback***: a response is to amplify the change in the variable. This has a destabilizing effect, so does not result in homeostasis. Positive feedback is less common in naturally occurring systems than negative feedback, but it has its applications. For example, in nerves, a threshold electric potential triggers the generation of a much larger action potential. Blood clotting and events in childbirth are other types of positive feedback.
- ***'Harmful Positive Feedback'***

Although Positive Feedback is needed within Homeostasis it also can be harmful at times. When you have a high fever it causes a metabolic change that can push the fever higher and higher. In rare occurrences the body temperature reaches 113 degrees and the cellular proteins stop working and the metabolism stops, resulting in death.

Summary: Sustainable systems require combinations of both kinds of feedback. Generally with the recognition of divergence from the homeostatic condition, positive feedbacks are called into play, whereas once the homeostatic condition is approached, negative feedback is used for "fine tuning" responses. This creates a situation of "metastability," in which homeostatic conditions are maintained within fixed limits, but once these limits are exceeded, the system can shift wildly to a wholly new (and possibly less desirable) situation of homeostasis.

Homeostatic systems have several properties

- They are ultra-stable, meaning the system is capable of testing which way its variables should be adjusted.
- Their whole organization (internal, structural, and functional) contributes to the maintenance of balance.
- Physiology is largely a study of processes related to homeostasis. Some of the functions you will learn about in this book are not specifically about homeostasis (e.g. how muscles contract), but in order for all bodily processes to function there must be a suitable internal environment. Homeostasis is, therefore, a fitting framework for the introductory study of physiology.

Where did the term "Homeostasis" come from?

The concept of homeostasis was first articulated by the French scientist Claude Bernard (1813-1878) in his studies of the maintenance of stability in the "milieu interior." He said, "All the vital mechanisms, varied as they are, have only one object, that of preserving constant the conditions of life in the internal environment" (from *Leçons sur les Phénonèmes de la Vie Commune aux Animaux et aux Végétaux*, 1879). The term itself was coined by American physiologist Walter Cannon, author of *The Wisdom of the Body* (1932). The word comes from the Greek *homoios* (same, like, resembling) and *stasis* (to stand, posture).

Cruise Control on a car as a simple metaphor for homeostasis

When a car is put on cruise control it has a set speed limit that it will travel. At times this speed may vary by a few miles per hour but in general the system will maintain the set speed. If the car starts to go up a hill, the systems will automatically increase the amount of fuel given to maintain the set speed. If the car starts to come down a hill, the car will automatically decrease the amount of fuel given in order to maintain the set speed. It is the same with homeostasis- the body has a set limit on each environment. If one of these limits increases or decreases, the body will sense and automatically try to fix the problem in order to maintain the pre-set limits. This is a simple metaphor of how the body operates—constant monitoring of levels, and automatic small adjustments when those levels fall below (or rise above) a set point.

Pathways That Alter Homeostasis

A variety of homeostatic mechanisms maintain the internal environment within tolerable limits. Either homeostasis is maintained through a series of control mechanisms, or the body suffers various illnesses or disease. When the cells in the body begin to malfunction, the homeostatic balance becomes disrupted. Eventually this leads to disease or cell malfunction. Disease and cellular malfunction can be caused in two basic ways: either, *deficiency* (cells not getting all they need) or *toxicity* (cells being poisoned by things they do not need). When homeostasis is interrupted in your cells, there are *pathways* to correct or worsen the problem. In addition to the internal control mechanisms, there are external influences based primarily on lifestyle choices and environmental exposures that influence our body's ability to maintain cellular health.

- **Nutrition:** If your diet is lacking in a specific vitamin or mineral your cells will function poorly, possibly resulting in a disease condition. For example, a menstruating woman with inadequate dietary intake of iron will become anemic. Lack of hemoglobin, a molecule that requires iron, will result in reduced oxygen-carrying capacity. In mild cases symptoms may be vague (e.g. fatigue), but if the anemia is severe the body will try to compensate by increasing cardiac output, leading to palpitations and sweatiness, and possibly to heart failure.
- **Toxins:** Any substance that interferes with cellular function, causing cellular malfunction. This is done through a variety of ways; chemical, plant, insecticides, and/or bites. A commonly seen example of this is drug overdoses. When a person takes too much of a drug their vital signs begin to waver; either increasing or decreasing, these vital signs can cause problems including coma, brain damage and even death.
- **Psychological:** Your physical health and mental health are inseparable. Our thoughts and emotions cause chemical changes to take place either for better as with meditation, or worse as with stress.
- **Physical:** Physical maintenance is essential for our cells and bodies. Adequate rest, sunlight, and exercise are examples of physical mechanisms for influencing homeostasis. Lack of sleep is related to a number of ailments such as irregular cardiac rhythms, fatigue, anxiety and headaches.
- **Genetic/Reproductive:** Inheriting strengths and weaknesses can be part of our genetic makeup. Genes are sometimes turned off or on due to external factors which we can have some control over, but at other times little can be done to correct or improve genetic diseases. Beginning at the cellular level a variety of diseases come from mutated genes. For example, cancer can be genetically inherited or can be caused due to a mutation from an external source such as radiation or genes altered in a fetus when the mother uses drugs.
- **Medical:** Because of genetic differences some bodies need help in gaining or maintaining homeostasis. Through modern medicine our bodies can be given different aids, from anti-bodies to help fight infections, or chemotherapy to kill harmful cancer cells. Traditional and alternative medical practices have many benefits, but like any medical practice the potential for harmful effects is present. Whether by nosocomial infections, or wrong dosage of medication, homeostasis can be altered by that which is trying to fix it. Trial and error with medications can cause potential harmful reactions and possibly death if not caught soon enough.

The factors listed above all have their effects at the cellular level, whether harmful or beneficial. Inadequate beneficial pathways (deficiency) will almost always result in a harmful waiver in homeostasis. Too much toxicity also causes homeostatic imbalance, resulting in cellular malfunction. By removing negative health influences, and providing adequate positive health influences, your body is better able to self-regulate and self-repair, thus maintaining homeostasis.

Homeostasis Throughout the Body

Each body system contributes to the homeostasis of other systems and of the entire organism. No system of the body works in isolation, and the well-being of the person depends upon the well-being of all the interacting body systems. A disruption within one system generally has consequences for several additional body systems. Here are some brief explanations of how various body systems contribute to the maintenance of homeostasis:

Nervous System

Since the nervous system does not store nutrients, it must receive a continuous supply from blood. Any interruption to the flow of blood may bring brain damage or death. The nervous system maintains homeostasis by controlling and regulating the other parts of the body. A deviation from a normal set point acts as a stimulus to a receptor, which sends nerve impulses to a regulating center in the brain. The brain directs an effector to act in such a way that an adaptive response takes place. If, for example, the deviation was a lowering of body temperature, the effector acts to increase body temperature. The adaptive response returns the body to a state of normalcy and the receptor, the regulating center, and the effector temporarily cease their activities. Since the effector is regulated by the very conditions it produced, this process is called control by negative feedback (fig. 2). This manner of regulating normalcy results in a fluctuation between two extreme levels. Not until body temperature drops below normal do receptors stimulate the regulating center and effectors act to raise body temperature. Regulating centers are located in the central nervous system, consisting of the brain and spinal cord (fig. 3a, 3b). The hypothalamus is a portion of the brain particularly concerned with homeostasis; it influences the action of the medulla oblongata, a lower part of the brain, the autonomic nervous system, and the pituitary gland.

The nervous system has two major portions: the central nervous system and the peripheral nervous system (table 3). The peripheral nervous system consists of the cranial and spinal nerves. The autonomic nervous system is a part of peripheral nervous system and contains motor neurons that control internal organs. It operates at the subconscious level and has two divisions, the sympathetic and parasympathetic systems. In general, the sympathetic system brings about those results we associate with emergency situations, often called fight or flight reactions, and the parasympathetic system produces those effects necessary to our everyday existence.

Endocrine System

The endocrine system consists of glands which secrete hormones into the bloodstream. Each hormone has an effect on one or more target tissues. In this way the endocrine system regulates the metabolism and development of most body cells and body systems. To be more specific, the Endocrine system has sex hormones that can activate sebaceous glands, development of mammary glands, alter dermal blood flow and release lipids from adipocytes and MSH can stimulate melanocytes on our skin. Our bone growth is regulated by several hormones, and the endocrine system helps with the mobilization of calcitonin and calcium. In the muscular system, hormones adjust muscle metabolism, energy production, and growth. In the nervous system, hormones affect neural metabolism, regulate fluid/electrolyte balance and help with reproductive hormones that influence CNS development and behaviors. In the Cardiovascular system, we need hormones that regulate the production of RBC's, which elevate and lower blood pressure. Hormones also have anti-inflammatory effects and stimulate the lymphatic system. In summary, the endocrine system has a regulatory effect on basically every other body system.

Integumentary System

The integumentary system (the skin) is involved in protecting the body from invading microbes (mainly by forming a thick impenetrable layer), regulating body temperature through sweating and vasodilation, or shivering and piloerection (goose bumps), and regulating ion balances in the blood. Stimulation of mast cells also produce changes in blood flow and capillary permeability which can effect the blood flow in the body and how it is regulated. It also helps synthesize vitamin D which interacts with calcium and phosphorus absorption needed for bone growth, maintenance, and repair. Hair on the skin guards entrance into the nasal cavity or other orifices preventing invaders of getting further into our bodies. Our skin also helps maintain balance by excretion of water and other solutes (i.e.) the keratinized epidermis limits fluid loss through skin. It also provides mechanical protection against environmental hazards. We need to remember that our skin is integumentary; it is our first line of defense.

Skeletal System

As the structural framework for the human body, the skeletal system consists mainly of the 206 or so bones of the skeletal system but also includes cartilages, ligaments, and other connective tissues that stabilize and interconnect them. Bones work in conjunction with the muscular system to aid in posture and locomotion. Many bones of the skeleton function as levers, which change the magnitude and direction of forces generated by skeletal muscle. Protection is a pivotal role occupied by the skeletal system, as many vital organs are encased within the skeletal cavities (cranial, and spinal "or dorsal"), and bones form much of the structural basis for other body cavities (ex: thoracic and pelvic cavities). The skeletal system also serves as an important mineral reserve. For example, if blood levels of calcium or magnesium are low and the minerals are not available in the diet, they will be taken from the bones. Also, the skeletal system provides calcium needed for all muscular contraction. Finally, red blood cells, lymphocytes and other cells relating to the immune response are produced and stored in the bone marrow.

Muscular System

The muscular system is one of the most versatile systems in the body. The muscular system contains the heart, which constantly pumps blood through the body. The muscular system is also responsible for involuntary (e.g. goosebumps, digestion, breathing) and voluntary (e.g. walking, picking up objects) actions. Muscles also help protect organs in the body's cavities.

Cardiovascular System

The cardiovascular system, in addition to needing to maintain itself within certain levels, plays a role in maintenance of other body systems by transporting hormones (heart secretes ANP and BNP) and nutrients (oxygen, EPO to bones,etc.), taking away waste products, and providing all living body cells with a fresh supply of oxygen and removing carbon dioxide. Homeostasis is disturbed if the cardiovascular or lymphatic systems are not functioning correctly. Our skin, bones, muscles, lungs, digestive tract, and nervous, endocrine, lymphatic, urinary and reproductive systems use the cardiovascular system as its "road" or "highway" as far as distribution of things that go on in our body. There are many risk factors for an unhealthy cardiovascular system. Some diseases associated are typically labeled "uncontrollable" or "controllable." The main uncontrollable risk factors are age, gender, and a family history of heart disease, especially at an early age.

Lymphatic System

The lymphatic system has three principal roles. First is the maintenance of blood and tissue volume. Excess fluid that leaves the capillaries when under pressure would build up and cause edema. Secondly, the lymphatic system absorbs fatty acids and triglycerides from fat digestion so that these components of digestion do not enter directly into the blood stream. Third, the lymphatic system is involved in defending the body against invading microbes, and the immune response. This system assists in maintenance, such as bone and muscle repair after injuries. Another defense is maintaining the acidic pH of urine to fight infections in the urinary system. The tonsils are our bodies "helpers" to defend us against infections and toxins absorbed from the digestive tract. The tonsils also protect against infections entering into our lungs.

Respiratory System

The respiratory system works in conjunction with the cardiovascular system to provide oxygen to cells within every body system for cellular metabolism. The respiratory system also removes carbon dioxide. Since CO2 is mainly transported in the plasma as bicarbonate ions, which act as a chemical buffer, the respiratory system also helps maintain proper blood pH levels, a fact that is very important for homeostasis. As a result of hyperventilation, CO2 is decreased in blood levels. This causes the pH of body fluids to increase. If acid levels rise above 7.45, the result is respiratory alkalosis. On the other hand, too much CO2 causes pH to fall below 7.35 which results in respiratory acidosis. The respiratory system also helps the lymphatic system by trapping pathogens and protecting deeper tissues within. Note that when you have increased thoracic space it can provide abdominal pressure through the contraction of respiratory muscles. This can assist in defecation. Remember the lungs are the gateway for our breath of life.

Digestive System

Without a regular supply of energy and nutrients from the digestive system, all body systems would soon suffer. The digestive system absorbs organic substances, vitamins, ions, and water that are needed all over the body. In the skin, the digestive tract provides lipids for storage in the subcutaneous layer. Note that food undergoes three types of processes in the body: digestion, absorption, and elimination. If one of these is not working, you will have problems that will be extremely noticeable. Mechanics of digestion can include chemical digestion, movements, ingestion absorption, and elimination. In order to maintain a healthy and efficient digestive system, we have to remember the components involved. If these are disturbed, digestive health may be compromised.

Urinary System

Toxic nitrogenous wastes accumulate as proteins and nucleic acids are broken down and used for other purposes. The urinary system rids the body of these wastes. The urinary system is also directly involved in maintaining proper blood volume (and indirectly blood pressure) and ion concentration within the blood. One other contribution is that the kidneys produce a hormone (erythropoietin) that stimulates red blood cell production. The kidneys also play an important role in maintaining the correct water content of the body and the correct salt composition of extracellular fluid. External changes that lead to excess fluid loss trigger feedback mechanisms that act to inhibit fluid loss.

Reproductive System

The Reproductive System is unique in that it does little to contribute to the homeostasis of the organism. Rather than being tied to the maintenance of the organism, the reproductive system relates to the maintenance of the species. Having said that, the sex hormones do have an effect on other body systems, and an imbalance can lead to various disorders (e.g. a woman whose ovaries are removed early in life is at much higher risk of osteoporosis).

Thermoregulation

The living bodies have been characterized with a number of automated processes, which make them self-sustainable in the natural environment. Among these many processes are that of reproduction, adjustment with external environment, and instinct to live, which are gifted by nature to living beings.

The survival of living beings greatly depends on their capability to maintain a stable body temperature irespective of temperature of surrounding environment. This capability of maintaining body temperature is called thermoregulation.

Body temperature depends on the heat produced minus the heat lost. Heat is lost by radiation, convection, and conduction, but the net loss by all three processes depends on a gradient between the body and the outside. Thus, when the external temperature is low, radiation is the most important form of heat loss. When there is a high external temperature, evaporation is the most important form of heat loss. The balance of heat produced and heat lost maintains a constant body temperature. However, temperature does vary during the day, and this set point is controlled by the hypothalamus.

Body temperature is usually about 37.4°C, but does vary during the day by about 0.8°C. The lowest daily temperature is when the person is asleep. Temperature receptors are found in the skin, the great veins, the abdominal organs and the hypothalamus. While the ones in the skin provide the sensation of coldness, the hypothalamic (central core) temperature receptors are the most important. The core body temperature is usually about 0.7-1.0°C higher than axillary or oral temperature.

When body temperature drops due to external cold, an important component of protection is vasoconstriction of skin and limb blood vessels. This drops the surface temperature, providing an insulating layer (such as the fat cell layer) between the core temperature and the external environment. Likewise, if the temperature rises, blood flow to the skin increases, maximizing the potential for loss by radiation and evaporation. Thus, if you dilated the skin blood vessels by alcohol ingestion this might give a nice warm glow, but it would increase heat loss (if the external temperature was still low). The major adjustment in cold is to shiver to increase heat production.

Besides the daily variation in body temperature, there are other cyclic variations. In women, body temperature falls prior to ovulation and rises by about 1°C at ovulation, largely due to progesterone increasing the set point. Thyroid hormone and pyrogens also increase the set point. The basal metabolic rate is about 30 calories/sq m/h. It is higher in children than in adults, partly as a result of different surface area to body mass ratio. Due to this relationship, young children are more likely to drop their temperature rapidly; there is greater temperature variation in children than in adults. It is increased by thyroid hormone and decreased by thyroid hormone lack. Different foods can affect BMR and the Respiratory Quotient of foods differ. Carbohydrate 1.0; Protein = 1.0; Fats = 0.7.

Body Composition

	Extracellular Fluid	Cellular Fluid
Volume	plasma – 3 litres interstitial – 10 litres	30 litres
Osmolality (mOsm)	290	290
Na^{+} (mmol/l)	140	15
Ca^{2+} (mmol/l)	2.2	$< 10^{-6}$
Cl^{-} (mmol/l)	110	10
HCO_3^{-} (mmol/l)	30	10
K^{+} (mmol/l)	4	150
Mg^{2+} (mmol/l)	1.5	15
PO_4^{3+} (mmol/l)	2	40
pH	7.4	7.1
Potential Difference (mV)		-70

The blood pressure in large arteries is about 120/80 mmHg. By the time this comes to the capillaries it has partly lost its pulsatile nature and has a pressure of about 35 mmHg. The pressure falls rapidly along the capillary to 15 mmHg at the venous end. This hydrostatic pressure tends to force fluid out of the capillary into the interstitium but balance is maintained by the colloid osmotic pressure (due to protein, principally albumin) of 26 mmHg. Net water movement is small (about 2%) and thus colloid osmotic pressure is the same at the arterial and venous end of the capillary.

At the arterial end of the capillary there is a net outward force of about 11 mmHg while at the venous end the net inward force is about 9 mmHg (ie. -9). There is an imbalance between water movement out and movement back in which leads to an imbalance of about 3 litres/day, which is removed as lymph. There is some albumin in the interstitial tissue and it varies in different organs but the concentration may be up to 10 or 20% of plasma. This gives an interstitial oncotic pressure which causes movement of fluid into the interstitium. However the bulk movement of water is not the way nutrients get to cells. Nutrients diffuse down their concentration gradient as the capillary is very permeable to all small molecules.

The extracellular volume is approximately thirteen litres in a seventy kg person. Ten litres are in the interstitial space and three litres in plasma. The capillaries are the interface between the two compartments and are permeable to most substances with a molecular weight less than 20,000. Thus nutrients can readily diffuse across the wall and go from blood to cell. Despite the high permeability of the capillary water is maintained inside due to the oncotic pressure and only about 2% of the plasma flowing through the capillary moves across the wall.

The blood volume is about 5 litres of which about 3 litres are plasma and about 2 litres red blood cells. The red blood cell volume (haematocrit) is about 43% and the relationship between plasma and blood volume and haematocrit is Blood Volume = Plasma Volume 100/(100 - Ht). Most of the blood is usually in the veins (70%).

Capillaries differ in their permeability throughout the body. Brain capillaries are relatively impermeable. In order of less permeability:

Brain < Muscle < Glomerulus < Liver sinusoids.

The capillaries, while having a large surface area, only contain about 7% of the blood volume. The arteries and arterioles contain about 15%. Most of the blood is in the veins.

Body Fluid Distribution

The cell membrane is a bilipid layer that is permeable to water and lipid soluble particles. However, it is impermeable to charged particles. It is the osmolality controlling factor. Osmolality in the cell and interstitial fluid are the same but the anionic and cationic compositions differ. Made of albumin, the capillary membrane is permeable to everything except proteins. The membranes in different tissues differ. There are fenestrae to promote better flow of fluids. Particles weighing over 40,000 have low permeability. It is the oncotic pressure controlling factor. Capillaries in the brain are relatively impermeable while capillaries in liver sinusoids and glomeruli are extremely permeable.

	Water (litres)	Sodium (mmol)	Potassium (mmol)
Total	43	3700	4000
Intracellular	30	400	
Bone	-	1500	300
Extracellular	13	1820	52
Plasma	3	420	12
Interstitial	10	1400	40
Usual Intake	1.5	180	70
Range	0.7-5	5-400	50-400

Dehydration and Volume Depletion

Plasma osmolality is about 290 mosmol/l contributed mainly by sodium (140 mmol/l) and it's accompanying anions. In dehydration water is lost from the body. The rise in osmolality that occurs in the plasma (also sodium rises) causes water to initially move out of the cells along the osmotic gradient. Thus cell volume is initially reduced but cell homeostatic processes subsequently return it towards normal by taking up solute.

In dehydration water is removed from the plasma and thus haematocrit and albumin which have not been lost will have a higher concentration. In volume depletion water and electrolytes are both lost and thus there will be little effect on either sodium concentration or osmolality. As osmolality is not altered there will be no force to pull water out of the cells and cell volume is not affected.

In volume depletion due to blood loss the haematocrit acutely is the same but the resultant fall in blood pressure causes fluid to come out of the interstitium into the vascular compartment and albumin and haematocrit both decrease. When there is volume depletion due to electrolyte and water loss by vomiting or diarrhoea there will be little or no effect on plasma osmolality or sodium concentration. However there will be a small increase in haematocrit and plasma albumin because the volume is lost from the extracellular space and as blood cells and albumin are not lost this increases the concentration.

In volume depletion forces are activated that retain sodium and water in the body. The sodium retention works to a major extent by the renin-angiotensin-aldosterone system which is activated by a fall in blood pressure caused by volume depletion. In dehydration, the high osmolality activates ADH secretion which causes water retention. As there is also volume depletion, this activates the renin-angiotensin-aldosterone system which causes sodium to be retained. This retention would tend to cause a rise in sodium concentration which is already high but the water retention would correct this. There is no effective receptor that monitors and controls Na concentration by altering sodium excretion. Sodium retaining hormones are predominantly regulated by the volume and blood pressure. Initially in blood loss the haematocrit is not altered but falls as fluid comes in from the interstitial space.

Water Balance

Vasopressin is the principal compound controlling water balance by decreasing water output by the kidney. It perceives the need by monitoring plasma osmolality and if this is high, vasopressin is secreted. Vasopressin is formed in the hypothalamus and travels down axons to the posterior pituitary where it is stored.

Plasma osmolality is the usual factor regulating vasopressin release but other factors alter the release. Pain and emotion release vasopressin together with the other posterior pituitary hormone oxytocin. Alcohol inhibits the release of vasopressin and thus causes a diuresis. A low plasma volume also releases vasopressin which in high concentration can cause vasoconstriction. These different factors can overcome the usual physiological control of osmolality.

Osmoreceptors in the hypothalamus monitor the plasma osmolality and send a signal down the axon that releases vasopressin from the posterior pituitary gland. Vasopressin travels by the blood to the kidney and binds to a receptor on the basolateral membrane and by a series of cellular events alters the permeability of the luminal membrane to water, thereby increasing the water permeability of the collecting duct and due to osmotic gradients created in the kidney causes water to be retained by the body (ie. an antidiuresis) which provides the other name for vasopressin of antidiuretic hormone.

Vasopressin released by the pituitary binds to a receptor on the basolateral membrane and activates adenyl cyclase which increases cyclic AMP levels in the kidney. This by a series of reactions, some of which involve calcium, cause microfilaments to contract and insert preformed water channels (aquaporins) into the luminal membrane increasing water permeability.

A high plasma osmolality is the important physiological stimulus causing vasopressin release. Urea in plasma in a normal person only has a concentration of 6 mmol/l and thus contributes to only a small part of plasma osmolality.

Even if plasma urea is elevated to 30 mmol/l it would not have a significant effect on vasopressin release as membranes (including those of the osmoreceptor cells) are permeable to urea. If there is excessive ADH water is retained and the osmolality and sodium concentration would fall (hyponatraemia). If there is no ADH water is lost and osmolality and sodium concentration would rise klkølk (hypernatraemia). While ADH is released if the plasma volume falls the most important factor to restore volume is retention of sodium by the renin-angiotensin-aldosterone and other salt retaining systems.

Sodium Balance

	Amount	Concentration
Amount in body	3700 mmol	
Intracellular	400 mmol	15 mmol/l
Extracellular	1800 mmol	140 mmol/l
Plasma	420 mmol	140 mmol/l
Interstitial	1400 mmol	140 mmol/l
Bone	1500 mmol	
Amount in diet		
Hunter Gatherer	20 mmol/day	
Western	180 mmol/day	
Japanese	300 mmol/day	
Obligatory Need	< 5 mmol/day	

Sodium is an important cation distributed primarily outside the cell. The cell sodium concentration is about 15 mmol/l but varies in different organs and with an intracellular volume of 30 litres about 400 mmol are inside the cell. The plasma and interstitial sodium is about 140 mmol/l with an extracellular volume of about 13 litres, 1800 mmol are in the extracellular space. The total body sodium, however, is about 3700 mmol as there is about 1500 mmol stored in bones.

The usual sodium intake of an Australian diet is about 180 mmol/d but varies widely (50-400 mmol/day) depending on habit and cultural influences. The body has potent sodium retaining mechanisms and even if a person is on 5 mmol Na+/day they can maintain sodium balance. Extra sodium is lost from the body by reducing the activity of the renin angiotensin aldosterone system which leads to increased sodium loss from the body. Sodium is lost through the kidney, sweat and faeces. In states of sodium depletion aldosterone levels increase and in states of sodium excess aldosterone levels decrease. The major physiological controller of aldosterone secretion is the plasma angiotensin II level which increases aldosterone secretion. A high plasma potassium also increases aldosterone secretion because besides retaining Na+ high plasma aldosterone causes K+ loss by the kidney. Plasma Na+ levels have little effect on aldosterone secretion.

A low renal perfusion pressure stimulates the release of renin, which forms angiotensin I which is converted to angiotensin II. Angiotensin II will correct the low perfusion pressure by causing constriction of blood vessels and by increasing sodium retention by a direct effect on the proximal renal tubule and by an effect operated through aldosterone. The perfusion pressure to the adrenal gland has little direct effect on aldosterone secretion and the low blood pressure operates to control aldosterone via the renin angiotensin system.

In addition to aldosterone and angiotensin II other factors influence sodium excretion. Thus in high sodium states due either to excess intake or cardiac disease (+ others) atrial peptide is secreted from the heart and by a series of actions causes loss of sodium by the kidney. Elevated blood pressure will also tend to cause Na+ loss and a low blood pressure usually leads to sodium retention. Aldosterone also acts on the sweat ducts and colonic epithelium to conserve sodium. When aldosterone has been activated to retain sodium the plasma sodium tends to rise. This immediately causes release of ADH which causes water to be retained, thus retaining Na+ and H2O in the right proportion to restore plasma volume.

Potassium Balance

	Amount	Concentration
Amount in body	4000 mmol	
Intracellular	3000 + mmol	110 mmol/l
Extracellular	52 mmol	4 mmol/l
Plasma	12 mmol	4 mmol/l
Interstitial	40 mmol	4 mmol/l
Bone	300 mmol	
Amount in diet		
Hunter Gatherer	200 – 400 mmol/day	
Western	50 – 100 mmol/day	
Obligatory Need	30 – 50 mmol/day	

Potassium is predominantly an intracellular ion and most of the total body potassium of about 4000 mmol is inside the cells and the next largest proportion (300-500 mmol) is in the bones. Cell K+ concentration is about 150 mmol/l but varies in different organs. Extracellular potassium is about 4.0 mmol/l and with an extracellular value of about 13 litres, 52 mmol (ie. less than 1.5%) is present here and only 12 mmol in the plasma.

In an unprocessed diet potassium is much more plentiful than sodium and is present as an organic salt while sodium is added as NaCl. In a hunter gatherer K+ intake may be as much as 400 mmol/d while in the Western diet it is 70 mmol/d or less if a person has a minimal amount of fresh fruit and vegetables. Processing of foods replaces K+ with NaCl. While the body can excrete a large K+ load it is unable to conserve K+. On a zero K+ intake or in a person with K+ depletion there will still be a loss of K+ of 30-50 mmol/d in the urine and faeces.

If there is a high potassium intake, eg. 100 mmol, this would potentially increase the extracellular K+ level 2 times before the kidney could excrete the extra potassium. The body buffers the extra potassium by equilibrating it within the cells. The acid base status controls the distribution between plasma and cells. A high pH (ie. alkalosis >7.4) favours movement of K+ into the cells whilst a low pH (ie. acidosis) causes movement out of the cell. A high plasma potassium increases aldosterone secretion and this increases the potassium loss from the body, restoring balance. This change of distribution with the acid base status means that the plasma K+ may not reflect the total body content. Thus a person with an acidosis (pH 7.1) and a plasma K+ of 6.5 mmol/l could be depleted of total body potassium. This occurs in diabetic acidosis. Conversely a person who is alkalotic with a plasma K+ of 3.4 mmol/l may have normal total body potassium.

Calcium and Phosphate Balance

	Amount	Concentration
Amount in body		
Interstitial (0.9%)	270 mmol	9 mmol/l
Cytoplasm	<1 mmol	10^{-6} mmol/l
Cell organelles	270 mmol	9 mmol/l
Extracellular (0.1%)	30 mmol	2.2 mmol/l
Plasma	7 mmol	2.2 mmol/l
Interstitial	23 mmol	2.2 mmol/l
Bone (99%)	27.5 mol (1.1 kg)	
Amount in diet	1200 mg/day	40 mmol/day
Amount absorbed	300 mg/day	10 mmol/day
Amount excreted	300 mg/day	10 mmol/day
Obligatory Need	100 mg/day	3 mmol/day
Bone => Plasma	500 mmol/day	

Calcium is a very important electrolyte. 99% or more is deposited in bone but the remainder is importantly associated with nerve conduction, muscle contraction, hormone release and cell signalling. The plasma concentration of Ca++ is 2.2 mmol/l and phosphate 1.0 mmol/l. The solubility product of Ca and P is close to saturation in plasma. The concentration of Ca++ in the cytoplasm is < 10-6 mmol/l but the concentration of Ca++ in the cell is much higher as calcium is taken up (and is able to be released from) cell organelles.

In the Australian diet there is about 1200 mg/d of calcium. Even if it was all soluble it is not all absorbed as it combines with phosphates in the intestinal secretions. In addition absorption is regulated by active Vitamin D and increased amounts increase Ca++ absorption. Absorption is controlled by Vitamin D while excretion is controlled by parathyroid hormones. However, the distribution from bone to plasma is controlled by both the parathyroid hormones and vitamin D. There is a constant loss of calcium by the kidney even if there was none in the diet. The excretion of calcium by the kidney and its distribution between bone and the rest of the body is primarily controlled by parathyroid hormone.

Calcium in plasma exists in 3 forms. Ionized, non ionized and protein bound. It is the ionized calcium concentration that is monitored by the parathyroid gland and if low, parathyroid hormone secretion is increased. This acts to increase ionized calcium levels by increasing bone reabsorption, decreasing renal excretion and acting on the kidney to increase the rate of formation of active Vitamin D, and thereby increase gut absorption of calcium.

The usual amount of phosphate in the diet is about 1 g/d but not all is absorbed. Any excess is excreted by the kidney and this excretion is increased by parathyroid hormone. Parathyroid hormone also causes phosphate to come out of bone. Plasma phosphate has no direct effect on parathyroid hormone secretion. However if it is elevated it combines with Ca++ decreasing the ionized Ca++ in plasma, thereby increasing parathyroid hormone secretion.

Case Study

Heat stroke and Heat exhaustion

If you have ever performed heavy manual labor or competed in an athletic event on a sweltering hot day, chances are you may have experienced symptoms of heat exhaustion. Typically these include an elevated core body temperature (above 104F or 40C), profuse sweating, pale color, muscle cramps, dizzines, and in some extreme circumstances, fainting or loss of consciousness.

Heat exhaustion occurs as a consequence of disruption of the body's own system of thermoregulation, the means by which it adjusts temperature. Sweating is the principal means through which the body cools itself down, but diverting blood from other regions toward the skin also serves this purpose. Although sweat allows excess heat to dissipate as the moisture reaches the skin surface, it can also have dangerous implications for blood pressure and volume. As sweating increases, blood volume can drop precipitously, meaning that the brain and other body systems are at risk for insufficient oxygen and nutrient supplies. Furthermore, diverting blood away from other systems and towards the skin compounds the changes in blood volume and blood pressure induced through sweating.

Heat stroke is a far more serious condition. This happens when the body's temperature rises out of control due to the failure of the thermoregulating system. If the body is unable to reduce its temperature due to outside or physical influences, the brain will start to malfunction. Delirium and loss of consciousness set in. The center of the brain controlling the sweat glands will stop functioning, halting the production of sweat. This causes the body's temperature to rise even faster. Furthermore, with the increase of the body's temperature, the metabolic process will speed up causing even more heat in the body. If left untreated this will result in death. One of the easiest ways to spot heat stroke is the skin. If it is flushed due to the increase of blood flow but dry because the sweat glands have stopped secreting, the individual will need prompt medical attention.

Other Examples

- Thermoregulation
  - The skeletal muscles can shiver to produce heat if the body temperature is too low.
  - Non-shivering thermogenesis involves the decomposition of fat to produce heat.
  - Sweating cools the body with the use of evaporation.
- Chemical regulation
  - The pancreas produces insulin and glucagon to control blood-sugar concentration.
  - The lungs take in oxygen and give off carbon dioxide, which regulates pH in the blood.
  - The kidneys remove urea, and adjust the concentrations of water and a wide variety of ions.

Main examples of homeostasis in mammals are as follows:

- The regulation of the amounts of water and minerals in the body. This is known as osmoregulation. This happens primarily in the kidneys.
- The removal of metabolic waste. This is known as excretion. This is done by the excretory organs such as the kidneys and lungs.
- The regulation of body temperature. This is mainly done by the skin.
- The regulation of blood glucose level. This is mainly done by the liver and the insulin and glucagon secreted by the pancreas in the body.

Most of these organs are controlled by hormones secreted from the pituitary gland, which in turn is directed by the hypothalamus.

Review Questions

Answers for these questions can be found here

1. Meaning of Homeostasis:

A) contributor and provider

B) expand

C) same or constant

D) receiver

2. What is the normal pH value for body fluid?

A) 7.15-7.25

B) 7.35-7.45

C) 7.55- 7.65

D) 7.00-7.35

E) 6.5-7.5

3. An example of the urinary system working with the respiratory system to regulate blood pH would be

A) When you hold your breath the kidneys will remove CO_2 from your blood

B) If you exercise a lot your urine will become more acidic

C) If you have emphysema the kidneys will remove fewer bicarbonate ions from circulation

D) If you hyperventilate the kidneys will counteract the alkalinity by adding hydrogen ions into the blood stream

E) None of the above-the urinary system never works with the respiratory system

4. The urge to breathe comes in direct response to:

A) How long it has been since you last took a breath

B) The oxygen concentration of your surrounding environment

C) The buildup of nitrogen within your blood stream

D) The pH of your blood

E) The buildup of blood pressure that occurs when you don't breathe

5. In response to a bacterial infection my body's thermostat is raised. I start to shiver and produce more body heat. When my body temperature reaches 101 degrees, I stop shivering and my body temperature stops going up. This is an example of:

A) Negative feedback

B) A malfunctioning control system

C) Positive feedback

D) A negative impact

6. Which of the following is an example of a positive feedback?

A) Shivering to warm up in a cold winter storm

B) A cruise control set on your car applies more gas when going up a hill

C) You sweat on a hot summer's day and the blood vessels in your skin vasodilate

D) You get cut and platelets form a clot. This in turn activates the fibrin clotting system and more blood forms clots

7. Where is the body's "thermostat" found?

A) Within the nervous system, in the Hypothalamus

B) Within the integumentary system, in the skin

C) Within the brain, in the corpus callosum

D) Within the Urinary system, in the kidneys

8. What system has little to contribute to the homeostasis of the organism?

A) Urinary System

B) Reproductive System

C) Respiratory System

D) Nervous System

9. Select the *phrase(s)* below that best describe(s) homeostasis.

A) Fluctuating within a homeostatic range

B) Maintaining a constant internal environment

C) Dynamic equilibrium

D) Deviating

Review Answers

- 1=C
- 2=B
- 3=C
- 4=D
- 5=A
- 6=D
- 7=A
- 8=B
- 9=B

Glossary

- **Control Center or Integration Center:** receives and processes information from the receptor
- **Effector:** responds to the commands of the control center by either opposing or enhancing the stimulus
- **Homeostasis:** refers to stability, balance or equilibrium
- **Negative Feedback:** a reaction in which the system responds in such a way as to reverse the direction of change
- **Positive Feedback:** a response is to amplify the change in the variable
- **Receptor:** receives information that something in the environment is changing

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