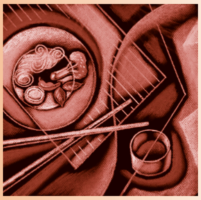

Water Physiology

Essentiality, Metabolism, and Health Implications

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Water is the most abundant molecule in the human body that undergoes continuous recycling. Numerous functions have been recognized for body water, including its function as a solvent, as a means to remove metabolic heat, and as a regulator of cell volume and overall function. Tight control mechanisms have evolved for precise control of fluid balance, indicative of its biological importance. However, water is frequently overlooked as a nutrient. This article reviews the basic elements of water physiology in relation to health, placing emphasis on the assessment of water requirements and fluid balance. Current recommendations are also discussed. Nutr Today. 2010;45(6S):S27–S32

Life on earth has evolved as a consequence of the presence of water. Although some alternative theories have been suggested for the generation of life in nonaqueous environments, virtually all known living systems depend on water for survival. Water has many properties that seem indispensable for the functioning of cells.[1] It is an excellent solvent for ions, required for nerve signaling, enzyme activity, mineralization of organic compounds, and the properties of DNA. It is also a master of weak intermolecular interactions, such as hydrogen bonds, necessary for the protein binding in their substrates, and hydrophobic reactions, necessary for protein structure. The high specific heat of water, in relation to other substances, makes it capable of absorbing or losing heat without a large temperature change, thus protecting living cells from massive temperature changes that could cause cell impairment or even death.

Metabolism

Absorption

Water movement through the gastrointestinal wall has great significance, not only for the delivery of ingested fluids but also for the digestion of other nutrients and as a defense from pathogens. In fact, there is equilibrium between intestinal water secretion (through the pancreatic juices, bile, gastric secretion, and saliva) and water absorption that should be maintained within narrow limits, because disturbances in this equilibrium result in diarrhea or constipation. Water movement across the intestinal epithelium may occur paracellularly through the tight junctions and transcellularly through cell membranes. Experiments in canine intestinal segments have shown that the potential for water absorption differs among the various parts of the intestine. Specifically, the large intestine has a greater capacity to absorb a hypotonic solution compared with the jejunum or the ileum, whereas a negative net water flux is observed in the duodenum in the presence of a hypotonic solution.[2] However, most of the water entering the intestine is absorbed in the small intestine. From a total of approximately 8 L, about 6.5 L is absorbed through the small intestine, whereas the absorptive function of the large intestine is limited to about 1.3 L.[3] Although water may diffuse to some extent through cellular membranes, the hydrophobic properties of their lipid bilayer do not allow the degree of absorption required. Instead, the greater part of absorbed water is transferred through channel systems, such as the aquaporins.[4] Water movement in the gastrointestinal tract is regulated by osmotic gradients and is linked to ionic movements. Specifically, absorption of water is linked primarily to the movement of sodium ions, whereas secretion is linked to the movement of chloride ions.[5] This linkage to ionic movements is less essential to the large intestine, where absorption of even distilled water may occur.[6]

Distribution of Water in Body Fluid Compartments

The fluid compartments of the human body include the intracellular fluid, accounting for 55% of total body water, and the extracellular fluid compartment. The latter can be further subdivided into the intravascular fluid compartment or plasma (7.5% of total body water), the rapidly equilibrating interstitial fluid and lymph (20%), and some smaller compartments (the slowly equilibrating interstitial fluid of dense connective tissue and cartilage, the inaccessible interstitial fluid in the bones, and the transcellular fluid, which is produced by the secretory cells).[7] Water distribution across the capillary endothelium is controlled by the balance of filtration forces (that tend to move water from the plasma to the interstitial space) and reabsorption forces, as first described by Starling.[8] The main filtration forces are the hydrostatic pressure that is caused by the pumping of the heart and a less potent colloid osmotic pressure of a negligible amount of protein that is trapped in the interstitial space. The major reabsorption pressure is the plasma osmotic pressure that is attributed to the solute molecules in the plasma.

Integrated Regulation of Body Fluid Balance

Water homeostasis is maintained by mechanisms that sense changes in intravascular volume and plasma osmolality.[9] Changes in the intravascular volume are sensed by peripheral volume and pressure receptors that induce the release of the antidiuretic hormone, arginine vasopressin, from the neurohypophysis. In addition, neuron-like cells, the osmoreceptors, located within the central nervous system, sense changes in plasma osmolality and also trigger antidiuretic hormone release and the induction of thirst. A second important humoral factor in body fluid regulation is angiotensin II. This hormone may act directly, by stimulating the release of antidiuretic hormone in the central nervous system, or indirectly, by stimulating aldosterone release, which in turn induces sodium conservation, a subsequent increase in plasma osmolality, and expansion of the extracellular volume. Antidiuretic hormone is the key factor in renal water handling, promoting water reabsorption in the nephron. Specifically, antidiuretic hormone binds to its receptor in the basolateral membrane of the principal collecting duct cells, initiating a cascade of reactions that lead to the translocation of the aquaporin 2 water channels from intracellular vesicles to the apical membrane, rendering this membrane permeable to water.[10]

Human Requirements and Recommendations

Human Body Water Content

In healthy adult humans, total body water represents an average of 59% for males and 56% for females, according to body mass. Large variation is observed across and within age groups, with infants having higher values of water content.[11] These variations may be attributed solely to differences in body composition, because it has been recognized that the hydration status of fat-free body mass is not altered by age or sex.[12] These relatively high amounts of body fluids are continuously recycled, with equilibrium being established when fluid intake matches fluid loss. In fact, a water deficit may occur over the course of a few hours when intake is reduced or losses are increased.

Human Body Water Functions

Body fluids serve a variety of functions in the human body, including a key role in the digestion, absorption and transportation of other nutrients, formation and stability of cell structures, removal of waste products and toxins, as a solvent for biochemical reactions, thermoregulation of the human body, and lubrication of cavities such as joints. Cell physiologists also have discovered new functions of cellular water. Because water is the main constituent of the cells, cellular water and fluxes of water between extracellular and intracellular compartments are the primary factors affecting cell volume, which in turn regulates a wide variety of cellular functions, such as epithelial transport, metabolism, excitation, hormone release, migration, cell proliferation, or even cell death.[13]

Given the numerous biological functions of water, as well as the fact that it is a main constituent of the human body, it is a surprising fact that water is often ignored as a nutrient. Most textbooks consider protein, carbohydrate, and fat as the macronutrients because these nutrients provide energy. However, if we consider the quantities of water and the energy-producing nutrients needed for an average person, it becomes clear that water is the quintessential macronutrient. However, many problems and considerations have arisen in the study of water in terms of human physiology and nutrition.

Defining Water Requirements

Defining the nutritional status of water as a nutrient, usually referred to as fluid balance or hydration status and subsequently fluid needs, is a challenging task. The main reason for this is that there is no reserve of water in the human body, and thus, fluids must be continuously recycled. Ideally, fluid balance may be determined by measuring fluid gain (via nutrition and metabolic water production) and fluid losses (via the urinary system, the respiratory tract, the skin, and the gastrointestinal system) under controlled environmental conditions and over a set, relatively small amount of time. Such studies have yielded fluid needs in the range of 1.6 to 3.2 L, depending on the environmental conditions and the physical activity performed by the subjects.[14] More recently, isotope-labeled water has been used to measure body fluid turnover and water needs by following the decline in hydrogen isotope over time. This technique offers the advantage of measuring fluid balance under real conditions of daily living and has produced similar results to those of water balance studies.[15]

Fluid dynamics may vary considerably within the same person over a period of a day, or even a few hours. Therefore, on many occasions, hydration status (ie, the water status of the body at a specific time point) may be of more interest than overall fluid balance. Many markers have been proposed for the assessment of hydration status, including hematologic indices (such as plasma osmolality and sodium concentrations) and urinary indices (ie, urine osmolality, urine color, and specific gravity); the assessment of total body water by bioelectrical impedance; and cardiovascular function measures (such as heart rate, blood pressure, and orthostatic tolerance).[16] These markers may provide a reasonable estimation of a deficiency (dehydration) or an overload (overhydration) of fluid in the body; however. they cannot provide estimates of actual water needs.

Water Deficiency

A general problem in the study of water as a nutrient is that there is a scarcity of studies examining the effect of long-term water deficiency and its complications in the human body. Acute mild dehydration (a 4% change in body weight) provokes unfavorable effects in the cardiovascular function as plasma volume drops. These effects include an increase in stroke volume and a concomitant increase in heart rate, to maintain constant cardiac output.[17] In the periphery, dehydration decreases skin blood flow and sweating,[18] thus compromising thermoregulation and increasing body core temperature.[19] However, these levels of water deficiency are fixed rapidly by a decrease in body water loss and the stimulation of thirst, 2 mechanisms that will be discussed later.

Long-term effects of water deprivation have not been described in detail. The only experiments describing severe dehydration conditions were performed in 1944. In one of these experiments, involving a 6-day period of water and/or food deprivation in healthy male soldiers, it was found that body fluid loss follows a biphasic manner: during the first 48 hours, the loss of fluid occurred predominantly from the extracellular space and subsequently from the intracellular space, with the net effect being equal for both spaces at the end of the experiment.[20] Lassitude was pronounced, and the authors reported that the subjects were "irritable and foolishly argumentative." Ingestion of a hypotonic sodium solution when subjects were already dehydrated resulted in a reduction of water loss, and the same effect was observed when subjects ingested carbohydrates, whereas total fasting increased the negative water balance. These notions highlight the importance of water in retaining internal homeostasis. In the case of salt ingestion, retention of water would be necessary to maintain plasma electrolytes in normal ranges, whereas in the case of carbohydrate ingestion, their protein-sparing effect decreased the need for removal of the nitrogen products of protein break down, as occurred in the case of total fasting.

Another study of water deprivation with balanced energy intake for 3 to 4 days, published at the same time, described decreased efficiency and unhealthy appearance after dehydration, a slight change in voice, sunken and pale face, and cyanosed lips as characteristics of water deprivation that vanished a few hours after restoration of fluid.[21] This study reported that there was practically no increase in the plasma proteins or hematocrit, indicating that the volume of the blood was maintained at the expense of some other fluid compartment. Dehydration led to an increased production of urea, indicating that water deprivation is accompanied by catabolism of body tissues, even if the energy needs are met.

Although a clear picture of human physiology under chronic and severe dehydration has not been obtained, the aforementioned studies indicate that chronic dehydration represents a threat to body homeostasis and health. Numerous later studies, mainly epidemiological in nature, have explored the association between hydration status and health. Although not consistent, hydration status and fluid intake have been associated with many chronic diseases, such as urolithiasis, urinary tract infections, bladder and colon cancer, constipation, bronchopulmonary disorders, hypertension, cerebral infarct, fatal coronary heart disease, venous thromboembolism, mitral valve prolapse, diabetic ketoacidosis, dental diseases, gallstones, glaucoma, and dental diseases.[22] This era of science provides continuous, promising research.

The period that is compatible with life, under conditions of full water deprivation, is not known. Some anecdotal cases of accidental incidents, such as the runner Mauro Prosperi, who lost his way in a sandstorm during the Marathon des Sables, have shown that water deprivation may be sustained for more than 9 days, with losses of body water as high as 13 kg. In critically ill, end-point patients, refusal to take rehydration and nutrition has been considered as a method of euthanasia that takes several days to a few weeks until death occurs.[23] This observation is certainly not applicable to healthy humans, because death may not be attributed solely to dehydration; however, it may indicate that life may be sustained for several weeks under full water deprivation in healthy humans.

Toxicity

Most nutrients display toxicity if their intake exceeds a critical threshold that represents the tolerable upper intake level. For water, no such threshold has ever been established, assuming that the functioning kidney removes the excess fluid. However, in some circumstances, massive fluid intake may indeed provoke toxicity. In psychiatric patients, particularly those with schizophrenia, polydipsia (excess intake of fluids) occurs frequently and may lead to dilutional hyponatremia, a condition also known as water intoxication. Although this kind of hyponatremia is usually associated with an inability to excrete water because of kidney and/or antidiuretic hormone disturbances, some patients are reported to drink such a large fluid volume that they exceed the ability of the kidney to excrete water.[24] This kind of hyponatremia leads to brain edema, causing neurological symptoms such as nausea, vomiting, delirium, ataxia, seizures, and coma, which in turn worsen the psychiatric symptoms of these patients.[25] Water intoxication with hyponatremia may appear also in many other clinical conditions accompanied by a primary defect in the renal excretion of free water and a subsequent expansion of extracellular fluid, but these cases are not related to fluid consumption.[26] Based on the dietary intake data from the third National Health and Nutrition Examination Survey (1988–1994), the top 99th percentile of men aged 31 to 50 years was consuming 8.1 L of fluids per day, and 5% of that age group, more than 6.4 L/d. In a recent study, 44 men aged 55 to 75 years increased their water intake by 2 L/d for 2 months, resulting in an improved lower urinary tract function.[27] In summary, because hyponatremia is extremely rare, no tolerable upper limit has been set by the Institute of Medicine.[14]

An interesting condition of water intoxication is exertional hyponatremia, occurring in some athletes during long ultraendurance events (>3 hours). This type of water toxicity is associated with a fluid intake during exercise that exceeds fluid losses via the sweat, without a concomitant replacement of sodium lost.[28] Decreased free water clearance from the kidney, because of redistribution of cardiac output to the active muscle and the skin capillary bed, as well as inappropriate secretion of antidiuretic hormone may contribute to this kind of water toxicity.[29] However, no adverse effects have been reported as a result of chronically high intakes of fluids, when intake approximates losses.

Recommendations

The first official and specific guideline for water intake was reported in 1964 by the Food and Nutrition Board of the National Academies of Science of the United States.[30] This report recommended that a reasonable standard for calculating water allowance is 1 mL/kcal of food. In the 1989 recommendations of the same body, it was stated that because of the low risk of water intoxication, water requirements may increase to 1.5 mL/kcal, to cover variations in activity level, sweating, and solute load.

A systematic approach to water requirements appeared only recently, in the latest version of the Dietary Reference Intakes.[14] These recommendations include absolute values (in liters per day) as recommendations, in terms of adequate intake across all age groups, total water intake (a combination of drinking water, beverages, and food), and water intake by drinking water and beverages, assuming that food contributes to water intake by approximately 19% (Table). Adequate intakes for water vary from 0.7 L/d of total water in infants to

Table. Dietary Reference Intakes (Adequate Intakes) for Water[a]

	Males			Females		
Age Group	Total Water	From Beverages	From Food	Total Water	From Beverages	From Food
0–6 mo	0.7	0.7	0.0	0.7	0.7	0.0
7–12 mo	0.8	0.6	0.2	0.8	0.6	0.2
1–3 y	1.3	0.9	0.4	1.3	0.9	0.4
4–8 y	1.7	1.2	0.5	1.7	1.2	0.5
9–13 y	2.4	1.8	0.6	2.1	1.6	0.5
14–18 y	3.3	2.6	0.7	2.3	1.8	0.5
19+ y	3.7	3.0	0.7	2.7	2.2	0.5
Pregnancy[b]				3.0	2.3	0.7
Lactation[b]				3.8	3.1	0.7

[a]Values are expressed in liters per day.
[b]In pregnancy and lactation, dietary reference intakes have been set in the age range of 14 to 50 years.
Data were obtained from the Institute of Medicine.[14]

3.7 and 2.7 L/d in male and female adults, respectively. Special recommendations are provided for pregnancy and breast-feeding. Recently, the European Food Safety Authority prepared a report on water requirements [EFSA Panel Dietetics Products, Nutrition (NDA); Scientific Opinion on Dietary Reference Values for Water. *EFSA J*. 2010;8(3):1459; available online at www.efsa.europa.eu]. As in the recommendations provided by the National Academies of Science of the United States, the European committee provides adequate intakes for water in terms of absolute values for many age groups; however, the panel considers the requirements of adolescents beyond the age of 14 years, as well as the requirements of the elderly as being the same as those of adults. Proposed intakes for adults were set at 2.5 and 2.0 L/d for males and females, respectively. Interestingly, these values are considerably lower than those proposed for the population of the United States.

Conclusions

Water is the most abundant and the most frequently recycled element in the human body. Its numerous functions, in combination with the fact that several mechanisms exist for the tight regulation of fluid balance, suggest that water should be considered as the most significant nutrient in human nutrition. Future research in water physiology should focus on the association between fluid balance or intake and disease, at both molecular and epidemiological levels, and the establishment of more effective methodologies to assess fluid balance and water requirements.

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