Physiology, Water Balance Tobias A, Ballard BD, Mohiuddin SS. Publication Details Introduction The fluids of the body are primarily composed of water, which in turn contains a multitude of substances.[1] One such group of substances includes electrolytes such as sodium, potassium, magnesium, phosphate, chloride, etc. Another group includes metabolites, such as oxygen, carbon dioxide, glucose, urea, etc. A third important group of substances contained within the water of our body, which includes proteins, most of which are vital for our existence. Examples of proteins include coagulation factors, immunoglobulins, albumin, and various hormones.[1] As the distribution of the fluid in the body and the substances found within is critical for the maintenance of intracellular and extracellular functions pivotal to survival, the body has developed mechanisms to control compartment composition tightly. However, various clinical pathologies can alter the fluid composition and its constituents in the multiple compartments of the human body, which can have deleterious effects on our health and often require intensive interventions to monitor and maintain normal physiological conditions.[2] This article will primarily cover the physiologic composition of water in the human body, differentiate the various compartments in the body and their associated volumes and compositions, depict how to measure the different volumes, and delve into the clinical relevance associated with disturbances of the normal physiological conditions. Cellular At a cellular level, the distribution of the various fluid compartments in the body is paramount for the maintenance of health, function, and survival. For the average 70 kg man, 60% of the total body weight is comprised of water, equaling 42L. The body's fluid separates into two main compartments: Intracellular fluid volume (ICFV) and extracellular fluid volume (ECFV). Of the 42L of water found in the body, two-thirds of it is within the intracellular fluid (ICF) space, which equates to 28L. The ECFV is comprised of two spaces: The interstitial fluid volume (ISFV) and the plasma volume (PV). One-third of the total body water is the ECFV, which is equivalent to 14L. Out of the extracellular fluid volume, 75% or 10.5L of the volume is present in the interstitial space, and 25% of that water is in the plasma, which is equivalent to 3.5L.[3] Each space works in unison with each other and has different functions paramount for normal physiological function. The intracellular fluid is comprised of at least ten separate minuscule cellular packages. For the sake of simplicity and to make the analysis of the intracellular space viable, the concept of a united intracellular "compartment" has been created as these collections have important unifying similarities such as location, composition, and behavior, which provides practical utility in the study of physiology.[4] The interstitial fluid consists of fluid, which lies in the space between and around bodily tissue. Although technically a "virtual" space, the interstitial fluid bathes all the cells in the body and links between intracellular fluid and the intravascular compartment. ISF contains nutrients, oxygen, waste, chemical messengers, and contains a small amount of protein. The ISF also contains the lymphatic system, which returns protein as well as excess ISF into the circulation.[5] Plasma is the only fluid compartment that exists as a real fluid collection all in one space. It differs from the interstitial fluid by its higher protein content and its function in transportation. Plasma is a component of blood and is said to be the "interstitial fluid of the blood" as it bathes the suspended red and white cells, which also reside in the blood.[6] Mechanism Several principles control the distribution of water between the various fluid compartments. To understand the different principles, it is essential to realize the following: ingestion and excretion of water and electrolytes are under tight regulation to maintain consistent total body water (TBW) and total body osmolarity (TBO). To manage these two parameters, body water will redistribute itself to maintain a steady-state so that the osmolarity of all bodily fluid compartments is identical to total body osmolarity. Several different factors mediate the redistribution of water between the two ECF compartments: hydrostatic pressure, oncotic pressure, and the osmotic force of the fluid. Combining these two components yields the Starling equation: $Jv = Kfc [(Pc - Pi] - n (Op-Oi)]$.[7] This equation determines the rate of fluid across the capillary membrane (Jv) and takes the difference between the hydrostatic pressures of the capillary fluid (Pc) and the interstitial fluid (Pi), as well as the oncotic pressure of the capillary fluid (Op) and the interstitial fluid (Oi). It also takes into account the osmotic force between the two compartments (n). Additionally, there is a relationship between the interstitial fluid and intracellular fluid. These two environments very closely influence each other, as the membrane of the cell separates them. Generally, nutrients diffuse into the cell with waste products coming out into the interstitial space. Ions are typically barred from crossing the membrane but can occasionally cross via active transport or under specific conditions. Water can move freely across the membrane and is directed by the osmotic gradient between the two spaces. Changes in the intracellular fluid volume result from alterations in the osmolarity of the ECF but do not respond to isosmotic changes in extracellular volume.[8] However, any flow of water in or out of the cell membrane will have proportional changes in the ECFV. If a disturbance causes ECF osmolarity to increase, water will flow out of the cell and into the extracellular space to balance the osmotic gradient; however, the total body osmolarity will remain higher than what is typical, and the cell will shrink. If a disturbance were to cause a decrease in ECF osmolarity, then water will move from the ECF into the ICF to attain an osmolar equilibrium; however, the total body osmolarity will remain lower than normal, and the cell will swell. Third, were isosmotic fluid to enter the extracellular space, then there would be no net changes in the ICF, and the ECFV will increase. Related Testing Much of this information can appear abstract, especially when talking about compartments that are more of a theoretical space. Therefore, it is crucial to have a way to physically measure the volumes of the different compartments. The way to measure the different spaces is by using the indicator-dilution method.[9] The theory behind this is that to measure the volume of a specific compartment; one must introduce into the body measurable substances that are distributed uniformly to a compartment of interest. Using this method, individual volumes can be measured directly, and others can be measured by subtracting the volumes of related compartments. This information can then be quantified by using the equation Volume (V) = Amount (substance injected)/Concentration (measured after equilibration).[10] The following compartments can be measured as followed: Total body water (TBW) - To measure, you have to inject radioactive titrated water or antipyrine. The idea behind this is that water gets uniformly distributed among all the different compartments. So if one can measure the radioactive water, it follows you to determine the TBW. Extracellular fluid volume (ECFV) - To measure this volume, labeled inulin, sucrose, mannitol, or sulfate can be injected. These are large molecules and are therefore impermeable to the cell membrane and will only be able to diffuse to the plasma and interstitial spaces. Blood volume - Red blood cell volume can be measured with 51Cr-tag RBCs or by using the formula: Calculated Blood volume= Plasma volume X 100/ [100-(0.87 X Hct %)], where 0.87 is the trapping factor. Plasma volume (PV) - Can be calculated using radioiodinated serum albumin (RISA) or Evans Blue dye, as they are specific to the plasma space. Intracellular fluid volume - Cannot be measured directly but can be calculated by subtracting ECFV by TBW, as the latter two variables are measurable. Interstitial fluid volume - Cannot be measured directly but can be calculated by subtracting PV by ECFV, as the latter two variables are measurable. Clinical Significance Aside from the significance of the study of water balance has on our physiologic understanding of the human body, the idea behind it is commonly seen in pathology and is presented clinically on a daily basis. Various conditions lead to an imbalance of water in the different compartments of the body; the specific imbalance can show in different ways and can be treated differently as well. The following presents five clinical scenarios where alterations in water balance can present. Each will have an accompanying analysis of ECF volume, ECF osmolarity, ICF volume, and ICF osmolarity. Diarrhea - Diarrhea can be caused by a myriad of pathogens, but classically is associated with isosmotic volume contraction.[11] As the fluid lost is isosmotic, there will be no net effect on intracellular fluid, and the only change will be a decrease in ECF volume with osmolarity remaining unchanged. Diabetes Insipidus - In this condition, the body is either unable to produce ADH, or the kidneys cannot respond to it, leading to a hyperosmotic volume contraction. In either case, there is a decrease in free water reabsorption from the distal tubules leading to free water loss.[12] In this scenario, the osmolarity of the ECF increases, leading to an inflow of water from the ICF to the ECF, leading to ICF volume constriction. However, this flow of water across the membrane into the ECF compartment is not enough to compensate for the loss of free water; thus, there is constriction of the EFV as well. Lastly, as water is lost from the ICF compartment, the osmolarity of the ICF will increase. The same changes would be expected in severe burns, as well as excessive sweating, where there is excessive loss of free water as well. SIADH - Conversely, there is excessive free water retention in SIADH, so the results will be the antithesis of what is seen in diabetes insipidus, leading to hypoosmotic volume expansion. In this condition, there is excess free water reabsorption in the distal tubule of the kidney leading to a decreased osmolarity of the ECF as well as an expansion of the ECFV.[13] Due to the decrease in ECF osmolarity, water will flow into the ICF compartment leading to an expansion of the ICFV and decreased osmolarity of the intracellular fluid. Adrenal Insufficiency - In this case, there is low aldosterone, primarily leading to decreased tubular sodium absorption, resulting in hypoosmotic volume contraction.[14] In this case, there are sodium and water loss, leading to decreased ECFV and decreased ECF osmolarity. Due to this decreased osmolarity, water shifts into the intracellular compartment leading to ICFV expansion. Due to the decreased solute reabsorption, there is decreased ICF osmolarity as well. Uremia - Often found in kidney failure. BUN can increase. However, an isolated state of increased urea would not cause a shift in the volume of either compartment, nor would it lead to a change in osmolarity. The reason for this is that these changes are only accompanied by the addition or subtraction of free water or the addition or subtraction of an osmotically active particle, meaning a particle that cannot freely cross the cell membrane.[15] As urea can freely cross the cell, it is considered to be non-osmotically active and, therefore, would not change osmolarity, thereby not leading to any shift of water balance. Review Questions Access free multiple choice questions on this topic. Comment on this article. References 1. Lobo DN. Fluid and electrolytes in the clinical setting. Nestle Nutr Workshop Ser Clin Perform

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