NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Liam's Head Injury:

Is This the Cause of His Frequent Urination?

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Liam has recently suffered a head injury when he fell while skateboarding. Subsequently he has noticed that he is constantly thirsty, that he needs to urinate more frequently, and that his overall urine output is greater than before. Is the head injury associated with his new symptoms? Can he be treated? Answer the questions below after viewing the following video in which Liam meets with healthcare professionals at a local hospital to learn the cause and treatment for his condition: <https://youtu.be/KMtyTy81FDs>.

Vocabulary

Osmolarity: the number of osmoles of a solute per liter of solution. To calculate osmolarity, you need to consider the number of moles of a substance per liter of solution and whether the substance dissociates when in solution. Thus a 1 M solution of glucose has an osmolarity of 1 Osm/L, while a 1 M solution of NaCl has an osmolarity of 2 Osm/L.

Osmolality: the number of osmoles of a solute per kg of water. This term is more common in clinical settings and is used in the video and in some of the questions.

Intracellular fluid compartment: the fluid that is found inside all the cells in the body including blood cells.

Extracellular fluid compartment: the fluid in the body that is outside cells (this includes both the plasma and interstitial fluid) but excludes, for example, fluid in the lumen of the gastrointestinal tract.

Interstitial fluid compartment: the fluid that bathes the cells of the tissues (excluding plasma).

Pathological: associated with a disease or disorder

Questions – Physiology

1. Where is vasopressin (also known as antidiuretic hormone (ADH)) produced and what stimulates its release?
   a. Posterior pituitary, high plasma osmolarity
   b. Hypothalamus, high plasma osmolarity
   c. Posterior pituitary, low plasma osmolarity
   d. Hypothalamus, low plasma osmolarity

2. What is one physiological role of vasopressin?
   a. Decreases blood pressure by binding to receptors on blood vessels
   b. Increases water reabsorption at the distal convoluted tubule and collecting duct
   c. Increases the reabsorption of NaCl to restore plasma osmolarity
   d. Increases heart rate to increase cardiac output

3. After his head injury, Liam starts producing very large volumes of dilute urine. How does his body detect and attempt to compensate for this pathological water loss?
   a. Decreased plasma osmolarity stimulates thirst centers in the hypothalamus
   b. Decreased blood pressure stimulates the release of renin
   c. Increased blood pressure inhibits the release of atrial natriuretic peptide
   d. Increased plasma osmolarity stimulates the release of aldosterone

4. Initially during a fluid deprivation test, Liam is not allowed to eat or drink anything. Predict what would happen to plasma osmolarity and blood pressure during this time.
   a. Both would increase
   b. Plasma osmolarity would increase, and blood pressure would decrease
   c. Both would decrease
   d. Plasma osmolarity would decrease, and blood pressure would increase

5. What response would you expect to occur as Liam's blood pressure decreases during the fluid deprivation test?
   a. His parasympathetic nervous system would become activated
   b. His baroreceptors would increase their firing rate
   c. He would have decreased production of angiotensin II
   d. His sympathetic nervous system would increase his heart rate

6. What physiological response would you expect to occur as Liam's blood osmolarity increases during the fluid deprivation test and before the injection of vasopressin?
   a. The osmoreceptors in the hypothalamus would shrink and decrease their firing rate
   b. The salt permeability of his collecting duct would progressively increase
   c. Activation of osmoreceptors in the hypothalamus would stimulate thirst
   d. The levels of Angiotensin II in the plasma would decrease

7. The nurse will stop a fluid deprivation test if the patient's weight drops by more than 3%, which indicates a deficiency in the ability to conserve body water. In a 70 kg individual, with this deficiency, this would represent about 2 L of water loss. In this circumstance, which fluid shift would have occurred?
   a. More water moving from the interstitial fluid into the plasma
   b. More water moving from the interstitial fluid into tissue cells
   c. More water moving from the plasma into red blood cells
   d. More water moving from the plasma into the Bowman's capsule

8. Halfway through the fluid deprivation test, Liam is injected with vasopressin and is given something to drink. What would happen to his blood osmolarity and rate of urine production?
   a. Both plasma osmolarity and rate of urine production would decrease
   b. Both plasma osmolarity and rate of urine production would increase
   c. Plasma osmolarity would increase, and urine production would decrease
   d. Plasma osmolarity would decrease, and urine production would increase

9. In the video, Dr. Scholey asks Liam whether there is a history of mental illness in his family to help rule out the possibility that he has a condition called psychogenic diabetes insipidus, in which individuals have a normally functioning vasopressin system, but drink abnormally high volumes of fluid. What would you expect to occur in these individuals?
   a. Low circulating levels of atrial natriuretic peptide
   b. Increased release of renin
   c. Low circulating levels of vasopressin
   d. Production of a large volume of urine with a high osmolarity

10. What would you expect to occur over time during the fluid deprivation test in individuals with psychogenic diabetes insipidus as they are deprived of fluids but before an injection of vasopressin?
   a. Their urine production would decrease and their urine osmolarity would decrease
   b. Their urine production would increase and their urine osmolarity would increase
   c. Their urine production would increase and their urine osmolarity would decrease
   d. Their urine production would decrease and their urine osmolarity would increase

11. Another type of diabetes insipidus, termed nephrogenic diabetes insipidus, is found in individuals with a mutation to vasopressin receptor 2 that reduces its function. How would individuals with nephrogenic diabetes insipidus differ from those with central diabetes insipidus?
   a. They would have urine with a higher osmolarity
   b. They would have higher levels of plasma vasopressin
   c. They would produce less urine over a 24-hour period
   d. They would not be as thirsty

12. Refer to Figure 1 (right) that shows the results from a fluid deprivation test of three individuals:
   Individual 1: normal vasopressin production/secretion and vasopressin receptor activity
   Individual 2: complete nephrogenic diabetes insipidus
   Individual 3: complete central diabetes insipidus

   Match the individuals above (numbers) with the expected results (letters) on the figure.
   a. Individual 1=A, individual 2=B, individual 3=C
   b. Individual 1=C, individual 2=B, individual 3=A
   c. Individual 1=A, individual 2=C, individual 3=B
   d. Individual 1=B, individual 2=A, individual 3=C

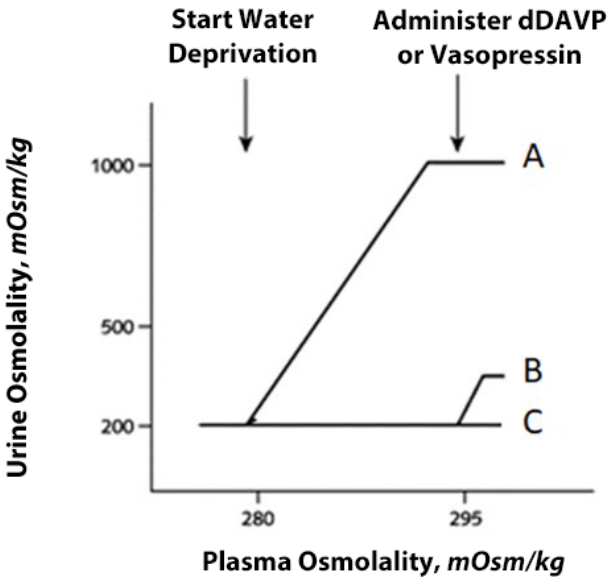

Figure 1. Changes in plasma and urine osmolality in three individuals during a fluid deprivation test. Figure modified from: Sands & Bichet, 2006.

Questions – Cellular and Molecular Biology

13. In the case study video, we learn that the release of vasopressin is impaired in Liam due to a head injury. The amino acid sequence of vasopressin is similar to another hormone found in the body called oxytocin (see Figure 2). Oxytocin is released from the posterior pituitary and stimulates uterine contractions during labor and is needed for lactation. What does the large bracket connecting two of the amino acid residues in each neuropeptide represent? When researchers were developing the drug called desmopressin that was prescribed by the pharmacist to treat Liam, they would have noted differences in which part or parts of these two neuropeptide sequences?

Figure 2. Amino acid sequences of vasopressin and oxytocin.

a. Hydrogen bond; C-terminus
b. Van der Waals forces; N-terminus
c. Hydrophobic interaction; Amino acid residue positions 2 & 7
d. Disulphide bond; Amino acid residue positions 3 & 8

14. Neuropeptide hormones such as vasopressin must interact with the appropriate plasma membrane receptors to exert their action on the body. Given the similarity of the amino acid sequences for vasopressin and oxytocin, which of the following would you predict to be TRUE for distinguishing between the two hormones during interactions with their cell membrane receptor(s)?
    a. The two hormones have similar sequences, but the N and C termini are reversed, thus their overall tertiary structures are completely different from each other.
    b. The residues found at position 8. In vasopressin this residue is large and positively charged, while in oxytocin the residue is medium-sized and non-polar.
    c. The fact that both hormones have a similar tertiary structure characterized by a ring with a 3-amino acid "tail."
    d. None of the above. You would expect vasopressin and oxytocin to either have identical cell membrane receptors or to bind with equal affinity to various types of receptors.

15. Assuming a physiological pH, which of the following amino acids would you expect to enhance affinity of vasopressin for its receptor? (Hint: think about the properties of the R-groups of the classes of amino acids and how these might enhance interactions between the hormone and receptor to enhance binding).
    a. Aspartic acid
    b. Proline
    c. Cysteine
    d. Histidine

16. Vasopressin binds to vasopressin receptors (specifically V2 receptors or V2R) in the plasma membrane of cells in the distal convoluted tubule and collecting duct of the kidney to regulate water reabsorption and urine concentration. Vasopressin also acts on two other types of vasopressin receptors to increase blood pressure under extreme blood loss (V1AR receptors) and to regulate adrenocorticotropin hormone secretion (V1BR also known as V3R receptors). All three of these receptor types belong to a single class of plasma membrane receptors known as G-protein-coupled receptors (GPCRs). Which of the following is a common characteristic of GPCRs?
    a. They are all comprised of a single polypeptide chain with 7 transmembrane helices.
    b. This class of cell membrane receptors interacts with a very limited set of ligands.
    c. Secondary messengers such as cAMP are rarely involved in mediating cell responses.
    d. One signal molecule only activates one specific GPCR.

17. We learn in the video that Liam has central diabetes insipidus caused by a head injury with a resulting loss of vasopressin release, but nephrogenic diabetes insipidus can result from loss-of-function mutations in the V2R vasopressin receptor (other cases are caused by mutations in aquaporin 2). In the case of the V2R receptor, in addition to frameshift or nonsense mutations in the V2R gene, what sort of changes would result in nephrogenic diabetes insipidus?
    a. Misfolding of the receptor and retention in the ER
    b. Inability to interact properly with G-proteins
    c. Inability to interact with vasopressin
    d. All of the above