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A Case of Two Runners: Volume and Osmolarity Regulation in Marathoners

Jane and Carla are both running the Boston Marathon. They are 25 years old and have equivalent training regimens and marathon experience. Water and electrolyte-containing sports drinks are available at stations located at each milepost during the race[1].

Data similar for both women:
Pre-race weight: 60 kg (132 lbs)
Avg sweating rate (for race conditions): 1 L/hr
Pace: 8 min/mile

Part 1: After completing 5 miles

A. Carla has ingested a relatively small amount of water from the aid stations. Her total water intake is about 250 ml. For each of the following variables Indicate, at this point in the race, whether each of the following variables will be *increased, decreased or unchanged compared to Carla's resting values*. Explain your answer. Incorporate into your explanation cardiovascular (CV), renal and any other system responses which are appropriate and relevant.
1. Heart Rate
2. Blood Pressure
3. ADH (AVP) [Antidiuretic Hormone (arginine vasopressin)]
4. Angiotensin II
5. Aldosterone

B. Jane has been drinking a full cup of water at every aid station. Her total water intake is about 600 ml. She is beginning to feel the need to urinate. Indicate, at this point in the race, whether each of the following variables will be *increased, decreased or unchanged compared to Jane's resting values*. Explain your answer. Incorporate into your explanation CV, renal and any other system responses which are appropriate and relevant.
1. Heart Rate
2. Blood Pressure
3. ADH (AVP)
4. Angiotensin II
5. Aldosterone

Part 2: After completing 15 miles

A. Carla has been drinking about a full cup of water every 3rd aid station and lesser amounts in between. She's feeling thirsty and occasionally she has a few sips of the sports drink provided at the aid stations. She doesn't want to slow down to drink more. She's ingested about 800 mL of water and sports drink since the start of the race. She's feeling tired and her pace has slowed to 9 min/mile and her sweating rate has decreased to 750 ml/hour. She has urinated once and her urine was dark yellow and low in volume. Indicate, at this point in the race, whether each of the following variables will be *increased, decreased or unchanged compared to Carla's values at mile 5 (Part 1A)*. Explain your answer.

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Incorporate into your explanation CV, renal and any other system responses which are appropriate and relevant.

1. Heart Rate
2. Blood Pressure
3. ADH (AVP)
4. Angiotensin II
5. Aldosterone

B. Jane has read that dehydration is the biggest concern in a marathon. She drinks a full cup of water at most aid stations, and occasionally has a full cup of sports drink too. She's ingested a total of about 4.0 L of water and sports drinks since the race began. At mile 15, she's developing a headache and feeling a bit nauseous. Her pace is still close to 8 min/mile and her sweating rate is about the same or maybe even greater. She's urinated twice and her urine was light in color and of high volume. Indicate, at this point in the race, whether each of the following variables will be *increased, decreased or unchanged compared to Jane's values at mile 5 (Part 1B)*. Explain your answer. Incorporate into your explanation CV, renal and any other system responses which are appropriate and relevant.

1. Heart Rate
2. Blood Pressure
3. ADH (AVP)
4. Angiotensin II
5. Aldosterone

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Part 3: After completing 20 miles

Both Jane and Carla stop running and report to medical personnel for care.

A. Carla's symptoms: Dizziness, nausea, extreme weakness and lethargy.

Vital signs:	HR:	220 beats/min
	BP:	100mmHg/65 mmHg
Blood test:	Plasma [Na^+]:	147 mEq/L
Urine sample:	Urine osm:	1400 mOsm/L
	Urine [Na^+]:	nearly 0 mEq/L

Body Weight: 57.3 kg (126 lbs)

1. What do Carla's symptoms, vital signs and her urine osmolarity and [Na^+] indicate about her body fluid status (dehydrated, euhydrated, hyperhydrated)? Briefly explain.
2. Are Carla's HR and BP higher or lower than expected for someone her age running a marathon? Explain.
3. Explain Carla's urine osmolarity value and urine [Na^+] value.
4. Is her plasma [Na^+] normal? If not, is she hypernatremic or hyponatremic?

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5. Why has she lost considerable weight (4.5% of body weight) in the ~3 hours she's been running?
6. Predict Carla's plasma osmolarity, ADH, angiotensin II and aldosterone compared to a similar runner who has maintained nearly normal hydration.

B. Jane's symptoms: Severe headache, vomiting, lethargy and confusion

Vital signs: HR: 100 beats/min
BP: 140/90

Blood test: Plasma [Na^+]: 125mEq/L

Urine Sample: Urine osmolarity: 100 mOsm/L
Urine [Na^+]: 7mEq/L

Body Weight: 63 kg (138.6 lbs)

1. What do Jane's symptoms, vital signs and her urine osmolarity and [Na^+] indicate about her body fluid status (dehydrated, euhydrated, hyperhydrated)? Briefly explain.
2. Are Jane's HR and BP higher or lower than expected for someone her age running a marathon? Explain.
3. Explain Jane's urine osmolarity value and urine [Na^+] value.
4. Is her plasma [Na^+] normal? If not, is she hypernatremic or hyponatremic?
5. Why has she gained considerable weight (+ 3 kg) in the ~3 hours she's been running?
6. Predict Jane's plasma osmolarity, ADH, angiotensin II and aldosterone compared to a similar runner who has maintained nearly normal hydration.

Variable Measured	**Normal Values**
Plasma [Na^+][2]	135-145 mEq/L
Plasma Osmolality[3] POsm = 2*[Na^+] + [BUN] + [glucose] (concentrations in mmol/L)	280-295 mOsm (can be estimated by 2* [Na^+] = 270-290 mOsm)
Resting Heart Rate[4]	60-80 beats/min
Maximum Heart Rate[5]	~195 bpm
Blood Pressure[6]	Less than 120 mmHg/80 mmHg (but systolic should not be less than 90 mmHg)

References
1. Almond CSD, Shin AY, Fortescue EB, Mannix, RC, Wypij D, Binstadt BA, Duncan CN, Olson DP, Salerno AE, Newburger JW, Greenes DS. Hyponatremia among runners in the Boston marathon. NEJM. 2005; 352: 1550-6.
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3. Hew-Butler T, Verbalis JG, and Noakes TD. Updated fluid recommendation: position statement from the international marathon medical directors association (IMMDA). *Clin J Sport Med*. 2006; 16:283-292.
4. Resting Heart Rate at: http://www.americanheart.org/presenter.jhtml?identifier=4701
5. Target Heart Rates at: http://www.americanheart.org/presenter.jhtml?identifier=4736
6. Blood Pressure at: http://www.nlm.nih.gov/medlineplus/ency/article/003398.htm

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Answer to Volume and Osmolarity Case Study- Hydration in Marathon Runners
(In general, refer to references 7, 8 and 9 for explanations to the physiologic mechanisms described)

Part 1A: At Mile 5 for Carla:

1. Heart Rate

Increased primarily due to the fact that she's exercising and therefore catecholamine levels and sympathetic stimulation are elevated, increasing HR.[7]

2. Blood Pressure

Increased, primarily due to the fact that she's exercising and BP is elevated to maintain increased perfusion of the active tissues. During exercise, the set point for blood pressure is increased.[7]

3. ADH (AVP)

*Increased due to the fact that she's ingested less water than she's lost in sweat. She's lost ~ 670 ml in sweat (1000ml/hour * .67 hour running), but ingested only ~250 ml of fluid. Plasma osmolarity will be increased and a change of as little as 1% in osmolarity will stimulate ADH secretion*[7]*. Volume is also slightly decreased, but a volume change of nearly 10% is required to stimulate ADH, so is not acting at this point.*[8,9]

4. Angiotensin II

Likely to be elevated as sympathetic mediated vasoconstriction during exercise decreases blood flow and therefore GFR to the kidneys. The decreased GFR and afferent vasoconstriction due to sympathetic activation accompanying exercise will stimulate renin release and increased angiotensin II. The current relatively small decrease in blood volume due to sweating may not significantly affect renin release at this time.[7,8,9]

5. Aldosterone

Elevated because angiotensin II is elevated and angiotensin II stimulates release of aldosterone from the adrenal gland.[7,8,9]

Part 1B: At mile 5 for Jane:

1. Heart Rate

Increased primarily due to the fact that she's exercising and therefore catecholamine levels and sympathetic stimulation are elevated, increasing HR.[7]

2. Blood Pressure

Increased, primarily due to the fact that she's exercising and BP is elevated to maintain increased perfusion of the active tissues. During exercise, the set point for blood pressure is increased.[7]

3. ADH (AVP)

Unchanged due to the fact that she's ingested nearly the same amount of water as she's lost in sweat (lost 670 ml, ingested 600 ml). Her plasma osmolarity and volume are both probably within the normal range and therefore not triggering ADH release.[7,8,9]

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4. Angiotensin II

Likely to be elevated as blood flow is decreased to the kidneys and GFR is decreased during exercise. The decreased GFR and afferent vasoconstriction due to sympathetic activation accompanying exercise will stimulate renin release and increased angiotensin II.[7,8,9] *The current relatively small decrease in blood volume due to sweating may not significantly affect renin release.*

5. Aldosterone

Elevated because angiotensin II is elevated and angiotensin II stimulates release of aldosterone from the adrenal gland.[7,8,9]

Part 2A: At mile 15 for Carla (compared to mile 5)

1. Heart Rate

*Increased. Not only is Carla exercising and therefore heart rate is elevated due to increased sympathetic stimulation and catecholamine release; Carla's plasma volume is also decreasing significantly. Her sweat loss at this point is predicted to be ~ 2 L (1L/hour sweating rate * 2 hours running) but she's only replaced 800 ml of fluid. Her loss is 1.2L and her volume is decreasing significantly. Decreased cardiac output as stroke volume decreases will stimulate a compensatory increase in HR via the baroreceptor reflex.*

2. Blood Pressure

Either decreased or normal. Depends upon whether HR can be increased enough to compensate for decreased stroke volume. Since MAP begins to fall when blood volume loss exceeds 20%,and Carla's volume is decreasing due to loss>ingestion, Carla's blood pressure maybe slightly decreased.

3. ADH (AVP)

Increased further (very high). Increased sweat loss, due to hypo-osmotic nature of sweat, increase plasma osmolarity which will increase ADH secretion. Decreased plasma volume, via venous and atrial volume receptors and baroreceptors will increase ADH secretion.

4. Angiotensin II

Increased further. Decreased blood volume and pressure will further increase renin secretion and angiotensin II production as described in Part 1A.

5. Aldosterone

Increased further. Decreased blood volume and pressure and angiotensin II will increased alsosterone release as described in Part 1A.

Part 2B: At mile 15 for Jane (compared to mile 5)

1. Heart Rate

Decreased. Despite the fact that she's exercising and catecholamines and sympathetic stimulation should be increasing heart rate, she has also ingested more fluid than she's lost via sweat (4 L ingested, ~2 L lost). This has increased her blood volume and via the baroreceptor response,

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decreased sympathetic stimulation of the heart and catecholamine release. Her heart rate may still be elevated above rest, but is likely decreased compared to heart rate at 5 miles.[7]

2. Blood Pressure

Increased. As described for 1, Jane's blood volume is increased due to over-ingestion and therefore her blood pressure is likely increased compared to at 5 miles.[7]

3. ADH (AVP)

Decreased. Overingestion of water will dilute the plasma osmolarity and increase plasma volume. Both signals inhibit ADH secretion.[7,8,9]

4. Angiotensin II

Decreased. Due to increased volume, renal perfusion is increased and baroreceptor input is decreased, thereby lowering renin release and angiotensin II production.[7,8,9]

5. Aldosterone

Decreased angiotensin II production also decreased aldosterone production.[7,8,9]

Part 3: After completing 20 miles

Both Jane and Carla stop running and report to medical personnel for care.

A. Carla's symptoms: Dizziness, nausea, extreme weakness and lethargy.

Vital signs:	HR:	220 beats/min
	BP:	100mmHg/65 mmHg
Blood test:	Plasma [Na^+]:	147 mEq/L
Urine sample:	Urine osm:	1400 mOsm/L
	Urine [Na^+]:	nearly 0 mEq/L

Body Weight: 57.3 kg (126 lb)

1. **What do Carla's symptoms, vital signs and her urine osmolarity and [Na^+] indicate about her body fluid status (dehydrated, euhydrated, hyperhydrated)? Briefly explain.**

All symptoms and lab values indicate that Carla is dehydrated.
Extremely high HR and low BP indicate that blood volume and therefore pressure is low stimulating increased sympathetic and decreased parasympathetic stimulation of the heart.[7]
Urine osmolarity at maximum of 1400 mOsm/L indicates that renal water retention mechanisms are maximally activated due to high plasma osmolarity and low plasma volume (low blood pressure).[7,8,9]
Low urine [Na^+] indicates that renal Na^+ and volume retention mechanisms are maximally activated due to low blood pressure.[7,8,9]

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Dizziness, fatigue, weakness and nausea are symptoms related to (1) inadequate perfusion of brain and other tissues as blood pressure falls and (2) the loss of water from cells and cell-shrinkage that occurs because the loss of hypo-osmotic sweat increases the osmolality of the extracellular fluid therefore making the ECF a hypertonic solution.[8]

2. **Are Carla's HR and BP higher or lower than expected for someone her age running a marathon? Explain.**

HR is higher than maximum predicted value for her age and blood pressure is lower than normal and definitely lower than expected for an individual who is exercising, since when exercising, the set point for blood pressure is elevated and maintained at an elevated level.

3. **Explain Carla's urine osmolarity value and urine [Na^+] value.**

ADH levels are maximal due to stimulation by both increased plasma osmolarity and decreased plasma volume and blood pressure. With maximal ADH, free water (water in excess of solute) is reabsorbed from the collecting duct and the urine concentration can reach ~1400 mOsm/L.[7,8,9]

4. **Is her plasma [Na^+] normal? If not, is she hypernatremic or hyponatremic?**

Carla's plasma sodium is not normal but is above 145 mEq/L. She is hypernatremic.

5. **Why has she lost considerable weight (4.5% of body weight) in the ~3 hours she's been running?**

Carla's rate of fluid ingestion is considerably less than her rate of fluid loss via sweat primarily. This body fluid loss is measurable as a body weight change. Greater than 4% body weight loss leads to hypernatremia in most cases.[3]

6. **Predict Carla's plasma osmolarity, ADH, angiotensin II and aldosterone compared to a similar runner who has maintained nearly normal hydration.**[7,8,9]

Osm: Higher: Her plasma osmolarity is estimated to be 2 147 mEq/L = 294 mEq/L, which is elevated. For a normally hydrated runner, [Na^+] between 135-145 mEq/L, the prediction would be at most 2* 145 mEq/L = 290 mEq/L.*

ADH: Higher: plasma osmolarity is elevated and blood volume and pressure are decreased. Both signals stimulate release of ADH. A normally hydrated runner would have nearly normal plasma osmolarity, volume and pressure.

Angiotensin II: Higher. Due to decreased volume and therefore pressure, as described earlier (part 1A and 2A-4)..

B. Jane's symptoms: Severe headache, vomiting, lethargy and confusion

Vital signs: HR: 100 beats/min
BP: 140/90

Blood test: Plasma [Na^+]: 125mEq/L

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Urine Sample:	Urine osmolarity:	100 mOsm/L
	Urine [Na^+]:	7mEq/L

Body Weight: 63 kg (138.6 lb)

1. **What do Jane's symptoms, vital signs and her urine osmolarity and [Na^+] indicate about her body fluid status (dehydrated, euhydrated, hyperhydrated)? Briefly explain.**

All of Jane's symptoms and vital signs indicate that she is hyperhydrated.
HR is low for an exercising individual. 50-85% of maximal HR would be predicted to be 98-166 bpm. She has been running 8 min/miles for ~ 3.5 hours, so her heart rate would be predicted to be higher. Blood Pressure is elevated, which is not abnormal in an exercising individual, but is elevated more than expected considering that she's been sweating and losing volume for the last 3.5 hours.
Urine osmolarity is very low, below normal plasma osmolarity, indicating that rather than retaining water, she is excreting free water. Excretion of free water indicates that plasma osmolarity is low and ADH levels are low[7,8,9], typically due to excess water ingestion causing dilution of the plasma and interstitial fluid.[10]
Her symptoms- headache, vomiting, lethargy and confusion are indicative of hypo-osmolarity. Hypotonicity of the extracellular fluid causes a shift of water into the cells and cell swelling. Increases in cell volume in the brain are of particular concern due to the limitations imposed by the surrounding skull and lead to many of Jane's symptoms (headache, lethargy, confusion .

2. **Are Jane's HR and BP higher or lower than expected for someone her age running a marathon? Explain.**

As described in Part 3-B-1 above, Jane's heart rate is lower and blood pressure is higher than expected. Because she is hyperhydrated, her blood volume is increased, leading to the changes seen via the baroreceptor response..

3. **Explain Jane's urine osmolarity value and urine [Na^+] value.**

Urine osmolarity can range from 50 to 1400 mOsm/kg H_2O[7,8,9]. Because of the excess water she's ingested, Jane is in a state of diuresis and is excreting nearly maximally dilute urine in order to excrete free water and thereby keep plasma osmolarity nearer to normal.

4. **Is her plasma [Na^+] normal? If not, is she hypernatremic or hyponatremic?**

[Na^+] is not normal, which is between 135-145 mEq/L. She is hyponatremic.

5. **Why has she gained considerable weight (+ 3 kg) in the ~3 hours she's been running?**

The weight gain is due to the excess ingestion of water. She has lost about 2.7 L of sweat, but has gained 3 kg of weight.. Since 1 L of water weighs approximately 1 kg, she must have ingested close to 5.7 L of water during the race, much more than she lost.

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6. **Predict Jane's plasma ADH, angiotensin II and aldosterone compared to a similar runner who has maintained nearly normal hydration.**

*Jane's plasma ADH, angiotensin II and aldosterone levels will all be lower than those for an individual who has maintained nearly normal hydration due to her low plasma osmolarity (predicted to be 2*125 = 250 mOsm/kg H2O) and elevated plasma volume and blood pressure; all of which inhibit ADH and renin-angiotensin-aldosterone secretion.*[7,8,9]

Variable Measured	**Normal Values**
Plasma $[Na^+]$[2]	135-145 mEq/L
Plasma Osmolality[3] POsm = 2*$[Na^+]$ + [BUN] + [glucose] (concentrations in mmol/L)	280-295 mOsm/kg H_2O (can be estimated by 2* $[Na^+]$ = 270-290 mOsm)
Resting Heart Rate[4]	60-80 beats/min
Maximum Heart Rate[5]	~195 bpm
Blood Pressure[6]	Less than 120 mmHg/80 mmHg (but systolic should not be less than 90 mmHg)

References
1. Almond CSD, Shin AY, Fortescue EB, Mannix, RC, Wypij D, Binstadt BA, Duncan CN, Olson DP, Salerno AE, Newburger JW, Greenes DS. Hyponatremia among runners in the Boston marathon. NEJM. 2005; 352: 1550-6.
2. Shayman, JA. Renal pathophysiology. Philadelphia: J.B. Lippencott Company, 1995: Chapter 1, Table 1-1, page 4.
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