CURRENT OPINION

Considerations in the Use of Body Mass Change to Estimate Change in Hydration Status During a 161-Kilometer Ultramarathon Running Competition

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Abstract Hydration guidelines found in the scientific and popular literature typically advise that body mass losses beyond 2% should be avoided during exercise. In this work, we demonstrate that these guidelines are not applicable to prolonged exercise of several hours where body mass loss does not reflect an equivalent loss of body water due to the effects of body mass change from substrate use, release of water bound with muscle and liver glycogen, and production of water during substrate metabolism. These effects on the body mass loss required to maintain body water balance are shown for a 161-km mountain ultramarathon running competition participant utilizing published data for the total energy cost, exogenous energy consumption and percentage from each fuel source, average participant body mass, and the extent of soft tissue fluid accumulation during an ultramarathon. We assumed that total energy derived from protein ranges from 5 to 10%, all exogenous energy is used to support the energy cost of the race, glycogen utilization ranges from 300 to 500 g, water linked with glycogen ranges from 1 to 3 g per g of

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glycogen, and the mass of the bladder and gastrointestinal tract is unchanged from pre-race to post-race body mass measurements. These calculations show that the average participant of 68.8 kg must lose 1.9–5.0% body mass to maintain the water supporting body water balance while also avoiding overhydration. Future hydration guidelines should consider these findings so that the proper hydration message is conveyed to those who participate in prolonged exercise.

Key Points

A given change in body mass does not reflect an equal change in hydration status. This effect becomes very important in prolonged exercise of several hours.

The determination of proper body mass loss to maintain the water supporting body water balance must consider the effect of body mass changes from substrate use, release of water bound with glycogen, and the production of water during substrate metabolism.

The present calculations demonstrate that the average participant of a 161-km mountain ultramarathon running competition must lose 1.9–5.0% body mass to maintain the water supporting body water balance while also avoiding overhydration.

1 Introduction

Recent hydration guidelines published by scientific organizations indicate that cognitive and physical performance deteriorates when more than 2% body mass has been lost during exercise [\[1–7](#page-6-0)]. Guidelines also link these levels of body mass loss during exercise with impaired management of thermal stress $[2, 4, 5]$ $[2, 4, 5]$ $[2, 4, 5]$ $[2, 4, 5]$ $[2, 4, 5]$ $[2, 4, 5]$, increased risk for the development of exercise-induced muscle cramping $[2-5]$, and acute kidney injury from rhabdomyolysis [[2\]](#page-6-0). Owing to these concerns, several guidelines in the scientific literature advise that body mass losses beyond 2% should be avoided during exercise $[1-7]$.

Avoidance of body mass losses greater than 2% during exercise is now the common message seen by the general public when seeking hydration advice. Hoffman and coworkers [[8\]](#page-6-0) recently showed that among the top 141 websites identified by Internet searches on hydration guideline terms, 44 (64%) of the 69 websites commenting about proper body mass loss during exercise indicated that no more than 2% should be lost. An additional 17 (25%) indicated that no more than 0–1% should be lost, and six (9%) indicated no body mass loss should occur. In other words, 67 (97%) of 69 websites providing recommendations indicated that the proper body mass loss during exercise was some amount less than 2%.

Despite the prominence of hydration recommendations indicating that body mass loss beyond 2% should be avoided during exercise, there has not been universal acceptance of these guidelines under all exercise circumstances. Not only has it been challenged that endurance exercise performance is necessarily impaired from a 2% body mass loss [\[9–13](#page-6-0)], but an association of such levels of body mass loss with development of heat illnesses [[14,](#page-6-0) [15\]](#page-6-0) and muscle cramping [\[16–18](#page-6-0)] has also been questioned. A basis for resistance to such hydration guidelines is that a 2% loss in body mass does not reflect an equal change in body water. In fact, it has been demonstrated that total body water can be maintained despite a loss in body mass of $\sim 2.0\%$ among soldiers during a 14.6-km march [[19\]](#page-6-0) and among participants of a 21-km running race lasting an average of 2.2 h [[20\]](#page-6-0). In a longer running event of 56 km lasting an average of 5.7 h, mean body mass fell by 2.5 kg (3.6%) but total body water fell by only 1.6 L [[20\]](#page-6-0). This discrepancy between change in body mass and change in body water is because a number of different factors will separately influence these two entities during exercise, so they are not interchangeable. In reviewing these factors, Maughan et al. [[21\]](#page-6-0) concluded that "A significant loss of body mass—perhaps of the order of 1–3% of pre-exercise mass—may be incurred without an effective hypohydration resulting''. Unfortunately, this information has largely been ignored.

Our intention with the present work is to demonstrate that a change in body mass during extreme endurance running does not necessarily reflect an equivalent change in effective body water. In doing so, we outline the sources of mass change that must be recognized in order to use body mass change as a reflection of hydration state, and we use data from an ultramarathon running event to perform the calculations necessary to demonstrate an appropriate mass change during such exercise to properly maintain the water supporting body water balance. We hope that this illustration will stimulate the propagation of more accurate and coherent hydration advice to participants at risk for over- or under-hydration during prolonged exercise.

2 Sources of Mass Change During Prolonged Exercise

Even though change in body mass may be a useful approximation for change in hydration status for the active individual who is performing relatively short bouts of exercise (up to \sim 1 h), a given change in body mass does not reflect an equal change in hydration status [[21\]](#page-6-0). In other words, a 1-kg decrease in body mass does not mean that there has been a reduction of 1 L in body water. This effect becomes very important in prolonged exercise of several hours, so the sources of body mass change and their effect on body water need to be understood.

Body mass can be altered during exercise by a number of factors, as displayed in Fig. [1.](#page-2-0) Increases in body mass from water intake and subsequent gastrointestinal water absorption have a comparable effect on total body water. Decreases in body mass from sweating, emesis, respiratory water loss, transcutaneous water loss, and the combination of urine production and urination are also reasonably wellreflected by comparable decreases in total body water. Menstruation could be another very minor consideration that would have a comparable effect on body mass and total body water. Ultimately, such changes in total body water are also reflected in changes of intravascular volume.

In contrast to these factors that comparably affect body mass and intravascular volume, water of oxidation ultimately adds to both intravascular water and body mass, but since the effect varies with relative substrate use, the relationship between change in body mass and change in intravascular water is complex. Other sources of error in the assumption that body mass change and intravascular water change are interchangeable include mass loss from substrate use, release of water bound with muscle and liver glycogen, and the development of peripheral edema. While each of these errors is small when considered individually,

Fig. 1 Schematic showing the factors that increase (*entering arrows*) or decrease (exiting arrows) intravascular water, total body water, and body mass. Intravascular water overlaps completely with total body water, which also overlaps completely with body mass since intravascular water is a component of total body water, and total

the combined effect can be important, particularly during prolonged exercise. Pertinent issues in this regard are discussed in Sects. 2.1[–2.6.](#page-3-0)

2.1 Endogenous Substrate Mass

Utilization of stored energy is an obvious source of mass loss during exercise. Stored carbohydrate, fat, and protein contribute to the metabolic needs during exercise, with the relative contribution depending primarily on the exercise intensity and duration [[22–24\]](#page-6-0), fitness level of the individual [[25,](#page-6-0) [26\]](#page-6-0), and preceding exercise and nutritional status [[27–30\]](#page-6-0). Regardless, the predominant fuels used during endurance exercise are carbohydrates and fats. Protein only contributes about 1–10% of the total energy production during prolonged exercise [[31](#page-6-0)].

The extent of carbohydrate stored as glycogen will depend very much on prior diet and exercise as well as on body mass and body composition, but may amount to about 350–700 g in the muscle and about 100 g in the liver [\[22](#page-6-0)]. Conservatively, 400 g of this glycogen could be mobilized during prolonged exercise [[32](#page-6-0), [33\]](#page-6-0), producing 4.1 kcal/g of glycogen (Table 1). The remaining energy turnover that is not met by exogenous sources comes from stored fat producing 9.3 kcal/g, and a small amount from stored protein

body water is a component of body mass. Those factors displayed within boxes affect intravascular water, but do not change total body water and body mass. For simplification, gastrointestinal water is considered to be part of the total body water pool. GI gastrointestinal

producing 4.1 kcal/g. With knowledge of the total energy requirement of the exercise, extent of glycogen utilized, and exogenous sources consumed during the exercise, the mass loss resulting from the oxidation of stored fat and protein can be calculated.

2.2 Water Release as a Result of Glycogen **Oxidation**

Water is stored in association with glycogen, although the relative amount is not entirely clear, and the amount of water per gram of glycogen probably varies with tissue glycogen content and almost certainly differs between skeletal muscle and liver [[21\]](#page-6-0). A very large number of studies on the association between glycogen storage and water storage in the liver were published in the 1930s and 1940s, and these studies suggested that about 2–3 g of water was stored with each gram of glycogen in rat liver [\[34](#page-6-0), [35\]](#page-6-0). More recent studies of rabbit liver have suggested that the amount may be closer to 1 g $[36]$ $[36]$. In studies of human skeletal muscle, it was estimated that 3 g of water was stored with each gram of muscle glycogen [[37\]](#page-6-0), but it seems unlikely that this is a constant [\[38](#page-6-0)]. Regardless of the ratio of water stored with glycogen, the water that is released as the glycogen content of tissues is reduced is

Table 1 Energy, water of oxidation and net mass change for 1 g of each substrate used during exercise (adapted from Maughan et al. [\[21\]](#page-6-0))

Substrate	Energy (kcal)	Water of oxidation (g)	Net mass change (g)
Carbohydrate	4.1	0.60	-0.40
Fat	9.3	1.13	$+0.13$
Protein	4.1	0.39	-0.45

Note that the formation of sulfate, phosphate, and nitrogenous compounds from protein metabolism will influence the net mass change, and will vary depending on the amino acid composition of the protein. The data shown here are for mixed meat protein. The fat data are for palmitate

mass that must be lost in order to avoid expanding the water pool supporting body water balance.

2.3 Water of Oxidation

Aerobic metabolism uses oxygen derived from ambient air to generate carbon dioxide, which is lost to the atmosphere in expired air, and water, which adds to the body water pool supporting body water balance. Protein oxidation also produces non-volatile compounds of sulfur, nitrogen, and phosphorus which will contribute in the short term to body mass. The water of oxidation and net mass change from different fuel sources are shown in Table [1](#page-2-0). As with the water released from glycogen metabolism, an equal body mass to the mass of water generated from endogenous substrate oxidation must be lost in order to maintain a constant amount of water supporting body water balance. While the mass of water generated from exogenous substrate oxidation reduces the necessary water intake to maintain hydration, retention of this water would be reflected by a comparable increase in body mass, and does not represent additional mass that must be lost from baseline body mass to maintain a constant water pool supporting body water balance.

2.4 Urine and Fecal Mass

Any change in mass of urine and feces between body mass measurements must be considered when using mass change to estimate change in hydration status. For instance, if urine or feces are produced during exercise and not eliminated before the post-exercise measurement of body mass, then the additional mass of the accumulated urine and feces must be subtracted from the post-exercise body mass measurement in considerations related to change in hydration status. During running exercise, the rate of urine production will be modest and in the order of 40–55 mL/h [\[39](#page-6-0), [40](#page-6-0)], so even if voiding does not occur immediately prior to the post-exercise body mass measurement, the effect of urine production during a relatively short period of exercise can generally be ignored. Furthermore, if little or no nutrition is taken in during the exercise and the bowels are not evacuated between body mass measurements, then the mass of fecal production is not a consideration. However, during long bouts of exercise, changes in mass of urine and feces might become an important consideration if the bladder and bowels are not evacuated prior to the pre-exercise body mass measurement but are evacuated during exercise, or if urine or feces accumulate during the exercise and are not eliminated prior to the postexercise body mass measurement.

2.5 Peripheral Edema

During some forms of exercise, fluid may accumulate in the interstitial compartment of certain body areas due to gravitational and centripetal forces, and as a result of an inflammatory response from repetitive trauma. Little is known about the magnitude of this effect, but it appears to be quite modest even under extreme conditions. In studies performed at 100-km ultramarathons, one reported no change in pre-race to post-race right foot volume [\[41](#page-6-0)]; however, another study found statistically significant increases in pre-race to post-race subcutaneous tissue thickness in the hand and ankle, though the mean volume increase of one lower leg of 0.02 L was not statistically significant [[42\]](#page-7-0). While any water associated with the development of peripheral edema would still contribute to the total water pool of the body, it does not contribute to the intravascular fluid compartment, so an equal mass of water must be gained to sustain water balance and maintain hydration.

2.6 Distribution of Water

The presumption is that water released from glycogen and water produced from substrate oxidation will be distributed throughout the body water pool according to local osmotic, oncotic and hydrostatic gradients. Unlike high-intensity exercise, which results in a large increase in intracellular osmolality in active muscles due to the accumulation of glycolytic intermediates and endproducts, endurance exercise results in relatively little disturbance to the osmolality of tissues [[43\]](#page-7-0). So, this water should contribute not only to the total water pool of the body, but also to the intravascular fluid compartment in order to sustain water balance and maintain hydration.

3 Illustration from an Ultramarathon

The required change in body mass to maintain the water supporting body water balance can be calculated from knowledge of total energy requirement and exogenous sources consumed during the exercise, coupled with assumptions about the amount of endogenous glycogen metabolized, the amount of water linked with glycogen, the percentage of energy derived from protein, changes in bladder, stomach and bowel mass, and the extent of soft tissue fluid accumulation.

Table [2](#page-4-0) shows calculations of expected body mass change for an 'average runner' participating in a 161-km mountain ultramarathon under a range of reasonable assumptions. In this illustration, the total energy cost was estimated to be 14,500 kcal based on prior studies at the

Table 2 Required change in body mass to sustain body water balance to maintain euhydration during a 161-km mountain ultramarathon under various conditions. Italicized text in the section outlining the

conditions is used to show adjustments relative to the 'average runner'. See text for support for the defined conditions for the 'average runner'

event [[44–46\]](#page-7-0). The total exogenous energy consumption and percentage from each fuel source, as well as the mean body mass of the 'average runner' completing the distance in 27 h was derived from another study at this event [\[47](#page-7-0)]. In this illustration, we also assumed that soft tissue fluid accumulations amounted to 40 g [[42\]](#page-7-0), and all exogenous energy was used to support the energy cost of the race. We also assumed that the mass of the bladder content was unchanged from pre-race to post-race body mass measurements, which is reasonable since athletes generally void as needed during this type of event. With regard to changes in the mass of gastrointestinal tract content, we assumed this to also be insignificant since runners commonly evacuate during the race and the types of nutrition consumed during these events will produce limited fecal mass.

We show calculations for 5 and 10% of total energy being derived from protein [\[31](#page-6-0)], and for a range of glycogen utilization of 300–500 g and water linked with glycogen of 1–3 g per g of glycogen. We also include calculations for a range of exogenous energy consumption of 30% more to 30% less than the 'average runner', which was roughly 1 standard deviation above and below the mean of the study population [[47\]](#page-7-0).

Based on these calculations, we determine that the 'average runner' should lose 4.2% body mass to maintain the water supporting body water balance. Variation in the percent of total energy derived from protein oxidation has 248 M. D. Hoffman et al.

minimal effect across the 5–10% range we examined. Yet, if less water is linked with glycogen or if less glycogen is utilized, then the necessary body mass loss decreases. On the other hand, greater glycogen utilization and less caloric intake during the event results in a need for greater body mass loss. Considering a variety of realistic assumptions, the expected body mass that must be lost to sustain body water balance to maintain euhydration was calculated to be 1.9–5.0%. Not surprisingly, top performers at the 161-km mountain ultramarathon from which the example pertains have been found to have body mass losses in this range [\[48](#page-7-0), [49](#page-7-0)].

4 Implications of the Findings

Contributions to the water supporting body water balance from water release with glycogen oxidation and the generation of water with substrate oxidation provides an example of the remarkable effectiveness of the body at responding to prolonged exertion. As a result of these mechanisms, the magnitude of fluid requirement during exercise is decreased, and so the risk for hypohydration and resulting impairments in performance and thermoregulation are also reduced. While the effect of these mechanisms may be limited in short-duration exercise where they are also less critical, they become important considerations in prolonged exercise. Without consideration of these effects, universal hydration recommendations based on change in body mass that are not adjusted for very prolonged exercise will be erroneous.

Endurance athletes currently receive conflicting and confusing messages about hydration needs for very prolonged exercise. Excessive concern and attention paid to avoiding hypohydration can be a stimulus for overhydration [\[50–54](#page-7-0)]. Among athletes, this is particularly true in environments where there is a common belief that a performance advantage will result from avoiding hypohydration [[55\]](#page-7-0). As a result, overhydration has been quite common among endurance athletes. For instance, 25–29% of finishers of a prestigious 161-km mountain trail ultramarathon in 2013 and 2014 had a mass gain or $\langle 1\%$ mass loss during the race based on body mass measurement immediately before the race start [[49,](#page-7-0) [56\]](#page-7-0). Additionally, another 50–58% of finishers had lost $\leq 4\%$ body mass during the race. Based on the present calculations, there should be clear concern about a high prevalence of overhydration in this population of athletes.

Overhydration during exercise can have serious consequences. Exercise-associated hyponatremia (EAH) has a primary etiology of overhydration. While the incidence of symptomatic EAH among those who overhydrate during exercise is low [[13,](#page-6-0) [57\]](#page-7-0), when EAH becomes symptomatic,

the individual is at considerable risk if the condition is not recognized promptly and treated properly. EAH-related deaths have been reported in association with various endurance competitions, including marathons, a 612-km canoe race, and an Ironman triathlon, as well as during prolonged hiking and various shorter-duration activities [\[58–60](#page-7-0)]. Unfortunately, at least four deaths from EAH since 2014 make it evident that the issue remains relevant [\[60–63](#page-7-0)].

Besides the potential for development of EAH from overhydration, excessive fluid intake during ultra-endurance exercise can also impair performance through unnecessary fluid carriage (which reduces the power to mass ratio), delays for drinking and filling fluid containers, and pauses required for urination. Excessive fluid intake, resulting in unabsorbed fluid in the upper gastrointestinal tract, can also induce gastrointestinal symptoms that commonly interfere with exercise performance [\[64](#page-7-0)]. Furthermore, we are not aware of any evidence that overhydration is protective against hyperthermia or muscle cramping. Therefore, both performance and health are optimized by proper hydration—that is, avoiding either significant hypohydration or overhydration.

5 Conclusions

The present work demonstrates that universal guidelines to avoid body mass loss of over 2% during exercise are not suitable to circumstances when the exercise is prolonged running of several hours. Body mass losses of 1.9–5.0% appear to be required in order to sustain body water balance to maintain euhydration when the exercise lasts for \sim 25–30 h. Without such body mass losses, athletes are at risk for becoming overhydrated during such exercise. This should be recognized in future hydration guidelines in order to properly educate ultra-endurance athletes so they can prevent unnecessary fluid intake that might not only impair exercise performance, but can also result in serious health consequences.

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Compliance with Ethical Standards

Conflict of interest Martin D. Hoffman, Eric D. Goulet, and Ronald J. Maughan declare that they have no potential conflicts of interest that are directly relevant to the content of this article.

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References

- 1. American College of Sports Medicine, Armstrong LE, Casa DJ, et al. American College of Sports Medicine position stand. Exertional heat illness during training and competition. Med Sci Sports Exerc. 2007;39:556–72.
- 2. American College of Sports Medicine, Sawka MN, Burke LM, et al. American College of Sports Medicine position stand. Exercise and fluid replacement. Med Sci Sports Exerc. 2007;39:377–90.
- 3. American Dietetic Association; Dietitians of Canada, American College of Sports Medicine, Rodriguez NR. American College of Sports Medicine position stand. Nutrition and athletic performance. Med Sci Sports Exerc. 2009;41:709–31.
- 4. Casa DJ, Armstrong LE, Hillman SK, et al. National Athletic Trainers' Association position statement: fluid replacement for athletes. J Athl Train. 2000;35:212–24.
- 5. Casa DJ, Clarkson PM, Roberts WO. American College of Sports Medicine roundtable on hydration and physical activity: consensus statements. Curr Sports Med Rep. 2005;4:115–27.
- 6. Kreider RB, Wilborn CD, Taylor L, et al. ISSN exercise & sport nutrition review: research & recommendations. J Int Soc Sports Nutr. 2010;2(7):7.
- 7. Thomas DT, Erdman KA, Burke LM. American College of Sports Medicine joint position statement. Nutrition and athletic performance. Med Sci Sports Exerc. 2016;48:543–68.
- 8. Hoffman MD, Bross TL 3rd, Hamilton RT. Are we being drowned by overhydration advice on the Internet? Phys Sportsmed. 2016;44:343–8.
- 9. Cotter JD, Thornton SN, Lee JK, et al. Are we being drowned in hydration advice? Thirsty for more? Extrem Physiol Med. 2014;3:18.
- 10. Goulet ED. Effect of exercise-induced dehydration on endurance performance: evaluating the impact of exercise protocols on outcomes using a meta-analytic procedure. Br J Sports Med. 2013;47:679–86.
- 11. Goulet ED. Effect of exercise-induced dehydration on time-trial exercise performance: a meta-analysis. Br J Sports Med. 2011;45:1149–56.
- 12. Hoffman MD, Cotter JD, Goulet ED, et al. VIEW: is drinking to thirst adequate to appropriately maintain hydration status during prolonged endurance exercise? Yes. Wilderness Environ Med. 2016;27:192–5.
- 13. Noakes TD, Sharwood K, Speedy D, et al. Three independent biological mechanisms cause exercise-associated hyponatremia: evidence from 2,135 weighed competitive athletic performances. Proc Natl Acad Sci USA. 2005;102:18550–5.
- 14. Noakes T. Fluid replacement during marathon running. Clin J Sport Med. 2003;13:309–18.
- 15. Noakes TD. Drinking guidelines for exercise: what evidence is there that athletes should drink ''as much as tolerable'', ''to replace the weight lost during exercise'' or ''ad libitum''? J Sports Sci. 2007;25:781–96.
- 16. Hoffman MD, Stuempfle KJ. Muscle cramping during a 161-km ultramarathon: comparison of characteristics of those with and without cramping. Sports Med Open. 2015;1:8.
- 17. Maughan RJ. Exercise-induced muscle cramp: a prospective biochemical study in marathon runners. J Sports Sci. 1986;4(1):31–4.
- 18. Schwellnus MP, Nicol J, Laubscher R, et al. Serum electrolyte concentrations and hydration status are not associated with exercise associated muscle cramping (EAMC) in distance runners. Br J Sports Med. 2004;38:488–92.
- 19. Nolte HW, Noakes TD, Van Vuuren B. Protection of total body water content and absence of hyperthermia despite 2% body mass

loss ('voluntary dehydration') in soldiers drinking ad libitum during prolonged exercise in cool environmental conditions. Br J Sports Med. 2011;45:1106–12.

- 20. Tam N, Nolte HW, Noakes TD. Changes in total body water content during running races of 21.1 km and 56 km in athletes drinking ad libitum. Clin J Sport Med. 2011;21:218–25.
- 21. Maughan RJ, Shirreffs SM, Leiper JB. Errors in the estimation of hydration status from changes in body mass. J Sports Sci. 2007;25:797–804.
- 22. Cermak NM, van Loon LJ. The use of carbohydrates during exercise as an ergogenic aid. Sports Med. 2013;43:1139–55.
- 23. Romijn JA, Coyle EF, Sidossis LS, et al. Regulation of endogenous fat and carbohydrate metabolism in relation to exercise intensity and duration. Am J Physiol Endocrinol Metab. 1993;265:E380–91.
- 24. van Loon LJ, Greenhaff PL, Constantin-Teodosiu D, et al. The effects of increasing exercise intensity on muscle fuel utilisation in humans. J Physiol. 2001;536:295–304.
- 25. Holloszy JO, Coyle EF. Adaptations of skeletal muscle to endurance exercise and their metabolic consequences. J Appl Physiol. 1984;56:831–8.
- 26. Romijn JA, Klein S, Coyle EF, et al. Strenuous endurance training increases lipolysis and triglyceride fatty acid cycling at rest. J Appl Physiol. 1993;75:108–13.
- 27. Betts JA, Williams C, Boobis L, et al. Increased carbohydrate oxidation after ingesting carbohydrate with added protein. Med Sci Sports Exerc. 2008;40:903–12.
- 28. Gonzalez JT, Veasey RC, Rumbold PL, et al. Breakfast and exercise contingently affect postprandial metabolism and energy balance in physically active males. Br J Nutr. 2013;110:721–32.
- 29. Wallis GA, Dawson R, Achten J, et al. Metabolic response to carbohydrate ingestion during exercise in males and females. Am J Physiol Endocrinol Metab. 2006;290:E708–15.
- 30. Yeo WK, Carey AL, Burke L, et al. Fat adaptation in well-trained athletes: effects on cell metabolism. Appl Physiol Nutr Metab. 2011;36:12–22.
- 31. Tarnopolsky M. Protein requirements for endurance athletes. Nutrition. 2004;20:662–8.
- 32. Bergström J, Hermansen L, Hultman E, et al. Diet, muscle glycogen and physical performance. Acta Physiol Scand. 1967;71(2):140–50.
- 33. Hermansen L, Hultman E, Saltin B. Muscle glycogen during prolonged severe exercise. Acta Physiol Scand. 1967;71(2):129–39.
- 34. McBride JJ, Mason Guest M, Scott EL. The storage of the major liver components; emphasizing the relationship of glycogen to water in the liver and the hydration of glycogen. J Biol Chem. 1941;139:943–52.
- 35. Pukett HL, Wiley FH. The relation of glycogen to water storage in the liver. J Biol Chem. 1932;96:367–71.
- 36. Geddes R, Harvey JD, Wills PR. The molecular size and shape of liver glycogen. Biochem J. 1977;163:201–9.
- 37. Ollson KE, Saltin B. Variation in total body water with muscle glycogen changes in man. Acta Physiol Scand. 1970;80:11–8.
- 38. Sherman WM, Plyley MJ, Sharp RL, et al. Muscle glycogen storage and its relationship with water. Int J Sports Med. 1982;3(1):22–4.
- 39. Dion T, Savoie FA, Asselin A, et al. Half-marathon running performance is not improved by a rate of fluid intake above that dictated by thirst sensation in trained distance runners. Eur J Appl Physiol. 2013;113:3011–20.
- 40. Rogers G, Goodman C, Rosen C. Water budget during ultraendurance exercise. Med Sci Sports Exerc. 1997;29:1477–81.
- 41. Cejka C, Knechtle B, Knechtle P, et al. An increased fluid intake leads to feet swelling in 100-km ultra-marathoners—an observational field study. J Int Soc Sports Nutr. 2012;9(1):11.
- 42. Bracher A, Knechtle B, Gnädinger M, et al. Fluid intake and changes in limb volumes in male ultra-marathoners: does fluid overload lead to peripheral oedema? Eur J Appl Physiol. 2012;112:991–1003.
- 43. Lundvall J, Mellander S, White T. Hyperosmolality and vasodilatation in human skeletal muscle. Acta Physiol Scand. 1969;77(1):224–33.
- 44. Cuddy J, Slivka D, Hailes W, et al. Total energy expenditure, body water turnover, hydration status, and blood composition during the Western States 100. Med Sci Sports Exerc. 2009;41:S336–7.
- 45. Dumke CL, Shooter L, Lind RH, et al. Indirect calorimetry during ultradistance running: a case report. J Sports Sci Med. 2006;5:692–8.
- 46. Ruby BC, Cuddy JS, Hailes WS, et al. Extreme endurance and the metabolic range of sustained activity is uniquely available for every human not just the elite few. Comp Exer Physiol. 2015;11:1–7.
- 47. Stuempfle KJ, Hoffman MD, Weschler LB, et al. Race diet of finishers and non-finishers in a 100 mile (161 km) mountain footrace. J Am Coll Nutr. 2011;30:529–35.
- 48. Hoffman MD, Hew-Butler T, Stuempfle KJ. Exercise-associated hyponatremia and hydration status in 161-km ultramarathoners. Med Sci Sports Exerc. 2013;45:784–91.
- 49. Hoffman MD, Stuempfle KJ. Hydration strategies, weight change and performance in a 161 km ultramarathon. Res Sports Med. 2014;22:213–25.
- 50. Coler C, Hoffman MD, Towle G, et al. Hyponatremia in an 85-year-old hiker: when depletion plus dilution produces delirium. Wilderness Environ Med. 2012;23:153–7.
- 51. Frizzell RT, Lang GH, Lowance DC, et al. Hyponatremia and ultramarathon running. JAMA. 1986;255:772–4.
- 52. Gardner JW. Death by water intoxication. Mil Med. 2002;167:432–4.
- 53. Garigan TP, Ristedt DE. Death from hyponatremia as a result of acute water intoxication in an Army basic trainee. Mil Med. 1999;164:234–8.
- 54. Pearce EA, Myers TM, Hoffman MD. Three cases of severe hyponatremia during a river run in Grand Canyon National Park. Wilderness Environ Med. 2015;26:189–95.
- 55. Winger JM, Hoffman MD, Hew-Butler TD, et al. The effect of physiology and hydration beliefs on race behavior and postrace sodium in 161-km ultramarathon finishers. Int J Sports Physiol Perform. 2013;8:536–41.
- 56. Hoffman MD, Stuempfle KJ. Is sodium supplementation necessary to avoid dehydration during prolonged exercise in the heat? J Strength Cond Res. 2016;30(3):615–20.
- 57. Hoffman MD, Stuempfle KJ, Sullivan K, Weiss RH. Exerciseassociated hyponatremia with exertional rhabdomyolysis: importance of proper treatment. Clin Nephrol. 2015;83(4):235–42.
- 58. Anonymous. Bushwalker died from drinking too much water. The Sydney Morning Herald. 2012 Sep 17. [http://www.smh.com.](http://www.smh.com.au/national/bushwalker-died-from-drinking-too-much-water-20120917-2621c.html) [au/national/bushwalker-died-from-drinking-too-much-water-](http://www.smh.com.au/national/bushwalker-died-from-drinking-too-much-water-20120917-2621c.html)[20120917-2621c.html.](http://www.smh.com.au/national/bushwalker-died-from-drinking-too-much-water-20120917-2621c.html) Accessed 31 Mar 2017.
- 59. Hew-Butler T, Rosner MH, Fowkes-Godek S, et al. Statement of the third international exercise-associated hyponatremia consensus development conference, Carlsbad, California, 2015. Clin J Sport Med. 2015;25:303–20.
- 60. Krabel H. Athlete dies after IM Frankfurt. Slowtwitch.com. 2015. [http://www.slowtwitch.com/News/Athlete_dies_after_IM_Frank](http://www.slowtwitch.com/News/Athlete_dies_after_IM_Frankfurt_5190.html) [furt_5190.html.](http://www.slowtwitch.com/News/Athlete_dies_after_IM_Frankfurt_5190.html) Accessed 9 Jan 2017.
- 61. HS football player dies from drinking too much fluid. WYFF4. com. 2014. [http://www.wyff4.com/news/hs-football-player-dies](http://www.wyff4.com/news/hs-football-player-dies-from-drinking-too-much-fluid/27409692)[from-drinking-too-much-fluid/27409692.](http://www.wyff4.com/news/hs-football-player-dies-from-drinking-too-much-fluid/27409692) Accessed 9 Jan 2017.
- 62. Lilley K. West Point grad dies after hospitalization during Ranger School. Army Times. 2016 Jul 28. [http://www.armytimes.com/](http://www.armytimes.com/story/military/2016/07/28/west-point-grad-dies-after-hospitalization-during-ranger-school/87660358/) [story/military/2016/07/28/west-point-grad-dies-after-hospitalization](http://www.armytimes.com/story/military/2016/07/28/west-point-grad-dies-after-hospitalization-during-ranger-school/87660358/)[during-ranger-school/87660358/.](http://www.armytimes.com/story/military/2016/07/28/west-point-grad-dies-after-hospitalization-during-ranger-school/87660358/) Accessed 9 Jan 2017.
- 63. Williams A. Jackson Prep football player dies. WAPT News. 2014. [http://www.wapt.com/news/central-mississippi/jackson/](http://www.wapt.com/news/central-mississippi/jackson/jackson-prep-prays-for-hospitalized-football-player/27712666) [jackson-prep-prays-for-hospitalized-football-player/27712666.](http://www.wapt.com/news/central-mississippi/jackson/jackson-prep-prays-for-hospitalized-football-player/27712666) Accessed 9 Jan 2017.
- 64. Hoffman MD, Pasternak A, Rogers IR, et al. Medical services at ultra-endurance foot races in remote environments: medical issues and consensus guidelines. Sports Med. 2014;44:1055–69.