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The Importance of Good Hydration for Day-to-Day Health

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The role of hydration in the maintenance of health is increasingly recognized. Studies in healthy adults show that even mild dehydration impairs a number of important aspects of cognitive function such as concentration, alertness, and short-term memory. However, due to the lack of suitable tools for assessment of hydration status, the effects of hydration on other aspects of day-to-day health and well-being remain to be demonstrated.

Key words: hydration, health, cognitive function

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INTRODUCTION

The concept of optimal hydration moves us away from the classical idea of nutrition. Indeed, most of us have been educated to approach food and water requirements either in the context of shortage (famine) or excess (feast) or in the context of pathological conditions associated with shortage (malnutrition, dehydration) or excess (obesity, hyperhydration). In terms of energy, for example, the definition of requirements by the WHO[1] only considers optimal requirements in so far as long-term good health is concerned (the energy requirement is the amount of food to be consumed that is compatible with long-term good health) and optimal growth in children. For adults, the target is maintenance of body weight and composition and satisfactory social and economical activity. There is nothing in the terms "maintenance" or "satisfactory" that appears optimal. Gradually, we are heading in the direction of defining and achieving optimal indicators of health (targeting a continuously lower LDL cholesterol is an example) and optimal and personalized nutrition.

As far as water is concerned, although it is the most abundant component of the body, and despite the known health hazards associated with its shortage (death occurring in a matter of days), we are very far away from a definition of optimal water requirements and optimal hydration. There are at least three reasons for this:

1. We are unable to measure hydration accurately and directly, as very briefly shown in this review;
2. Despite the attribution of the Nobel Prize to Peter Agre for the discovery of aquaporins, there is a paucity of evidence-based data connecting optimal hydration and day-to-day health; and
3. Although Haussinger et al.[2-3] have demonstrated that hydration is a key signal for various cellular functions, unfortunately, very few data support this theory at the whole-body level.

DAY-TO-DAY ASSESSMENT OF HYDRATION STATUS

This review will not go into the details of hydration status assessment, since this topic is covered elsewhere in this supplement. Although accurate and precise estimates of body water spaces can be obtained,[5] there are no reference values available for healthy populations. This means that there are no reference values with which to compare measurements, and so healthy people cannot know whether their total or extracellular water is in a good or bad range and a medical practitioner cannot use an evidence-based target value for a rehydration strategy in a dehydrated person. In the studies performed to validate Haussinger's theory, the metabolic changes associated with various situations known to be associated with changes in hydration have been studied. Often, no value for body water space change is provided. It is therefore difficult to relate metabolic changes to quantitative alterations in hydration.

Formulas based on body weight (e.g., Watson's formula[6]) are of no help, since total body water is contained to a large extent in the fat free mass. Therefore, depending on the fatness of the subject, these weight-based formulas will be more or less biased. A database of the reference values for hydration is currently being built (P. Ritz and J. Tichet, unpublished data). This database will give mean values and percentiles for groups of individuals according to age, weight, gender, and body

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composition so that we will be able to define the hydration status of an individual and start to understand why it varies. Furthermore, rehydration strategies will be tested (and eventually validated) in dehydrated patients, and health indicators will be interpreted in the context of hydration. Until then, we will be unable to address the issue of optimal hydration and day-to-day health in a meaningful manner.

Another important issue is the definition of hydration in the fat free mass and the understanding of its variability. Although fat free mass contains most of body's water, the ratio between the two may vary from one individual to another,[5] making some body composition measurements inaccurate. Since body composition is an important health parameter, this technical difficulty represents an important limitation for large, evidence-based studies. Furthermore, when hydration status varies, it becomes virtually impossible to know whether it is the ratio of extra- or intracellular water to fat free mass that is affected, which obviously do not have the same physiological meaning.

HYDRATION AND WELLNESS

Clinical dehydration is often seen in geriatric wards (in about 5% of patients) and is associated with various symptoms.[7] Some of the symptoms reflect the low intravascular water content (e.g., low blood pressure, tachycardia), some are connected to impaired functional status (e.g., confusion, coma, kidney failure, muscular weakness), and some are more tightly associated with the loss of water from tissue (e.g., lasting skinfold). Some others are not specific to dehydration (e.g., general malaise, nausea, headache, urine color). The same is true for hyperhydration, which is often accompanied by elevated blood pressure, edema, changes in urine color, and general malaise, nausea, and confusion. The influence of hydration status on the risk of chronic diseases and on physical performance are addressed elsewhere in this supplement. Although mild dehydration significantly impairs cognitive function, as detailed below, effects on other aspects of general day-to-day health and wellness are not supported by strong evidence.[8]

HYDRATION AND COGNITIVE FUNCTION

The effects of dehydration on cognitive function have been studied in several experiments in which dehydration was achieved by fluid restriction, heat exposure, exercise, or combinations thereof (Table 1). In healthy young adults, fluid restriction over 37 hours without food restriction resulted in a shortage of about 2.7 L of water, leading to body weight loss of 1.8% after 24 hours and 2.7% after 37 hours.[9] Expected changes in osmolarity, plasma electrolyte content, and urine volume occurred. However, it is to be noted that the plasma Na^+ concentration markedly increased after 24 hours (147 mmol/L), indicating that the dehydration obtained was not that mild. Fluid-restricted subjects felt thirstier and experienced greater sensations of dryness of the mouth. Feelings of headache and tiredness were significantly greater (Figure 1), while concentration and alertness were significantly impaired. This was obvious for measurements performed after 24 and 37 hours of fluid restriction when the plasma Na^+ concentration was 147 mmol/L. Similar but weaker effects were reported after 13 hours, when plasma Na^+ concentration was moderately increased (144 mmol/L).

Dehydration to 2.7% body weight loss by heat exposure or exercise has been shown to significantly decrease alertness, concentration, tracking performance, and short-term memory, and increase tiredness and headaches in healthy young adults. Increased reaction time was also observed (the test asked the subjects to identify the color of an object), but the number of correct answers was unchanged.[10,11] In other words, it took a longer time for dehydrated subjects to answer correctly. Perceptual comparison (a test asking the subjects to visually compare the length of two lines) and long-term memory were not influenced by acute dehydration. Fatigue induced a slower response to the test in dehydrated subjects. Comparable effects were observed for dehydration at 2% or more body weight deficit under similar conditions. Arithmetic efficiency, short-term memory, attention, and visuomotor tracking were impaired in healthy young males; impairment was more pronounced at higher levels of dehydration.[12] There were no differences in the effects observed in function between the dehydration methods used (heat stress or exercise).[10-12]

Significant and progressive decreases in concentration and coordination have been observed in healthy young males dehydrated by exercise and heat exposure to 2% to 3% body weight loss, although symbol classification was not affected.[13] Although dehydration of healthy young adults by overnight fluid restriction was shown to result in impaired alertness, visual information processing, reaction time, and spatial and numerical memory were not affected.[14] It should be noted, however, that these experiments were conducted in fit, healthy, young individuals, and need confirmation in the general population. In the only study performed in older subjects (healthy 50- to 82-year-olds), dehydration by overnight fluid restriction was related to slower psychomotor processing speed, poorer attention, and memory performance.[15] Whether mild dehydration further impairs cognitive performance in those subjects in whom baseline performance is altered remains to be validated.

Hormonal theories associating impaired cognition

Table 1. Hydration Status and Cognitive Function

Reference	Subjects	Hypohydration Method	Findings
Shirreffs et al., 2004[9]	15 healthy M/F 30 ± 12 yrs	Fluid restriction for 13, 24, 37 h to 2.7% wt loss at 37 h	Significant decreases in alertness, concentration; significant increase in headache, tiredness
Cian et al., 2001[10]	8 healthy M 27 ± 4 yrs	Heat exposure or exercise for 2 h to 2.7% wt loss	Significant impairment of reaction time, tracking performance, and short-term memory; no effect on long-term memory; no difference according to hypohydration method
Cian et al., 2000[11]	7 healthy M 25 ± 4 yrs	Heat exposure or exercise for 2 h to 2.8% wt loss	Significant cognitive impairment (short-term memory, perceptive discrimination); increased tiredness; no effect on long-term memory; no difference according to hypohydration method
Gopinathan et al., 1988[12]	11 healthy M 20–25 yrs	Heat exposure and fluid restriction to 1%, 2%, 3%, or 4% wt loss	At 2% hypohydration, significant impairment in short-term memory, arithmetic efficiency, attention, and visuomotor tracking; further impairment at increased hypohydration
Sharma et al., 1986[13]	8 healthy M 1–24 yrs	Exercise and heat exposure to 1.4%, 2.3%, or 3.3% wt loss	Significant and progressive decrease in concentration and coordination at 2%–3% hypohydration; no effect on symbol classification
Neave et al., 2001[14]	28 healthy M/F 50–82 yrs	Fluid restriction overnight	Lower hydration status related to slower psychomotor processing speed, poorer attention, and memory performance
Suhr et al., 2004[15]	12 healthy M/F ≥ 20 yrs	Fluid restriction overnight	Significant impairment of alertness; no effect on visual information processing, reaction time, or spatial or numerical memory

and dehydration are developed in the review by Wilson and Morley.[16] The most convincing evidence is from an increased release of arginine vasopressin involving prostaglandin E. Dehydration also induces an increase in plasma cortisol, which is normalized after rehydration. This tends to worsen active learning and compromise short-term memory.[16] This is observed when glucocorticoids are used at pharmacological doses. The authors also suggest a potential role for NO and impaired NO response to dehydration, mainly in the elderly, in impairing cognitive functions.[16] The potential roles for cellular mediators of neuronal death, glutamate metabolism, and cytokine synthesis are still to be proven.[16] There is therefore ample evidence that dehydration is a common precipitating factor of acute confusion, especially in the very young and very old.

HYDRATION AND CONSTIPATION

Constipation can be defined in various ways, such as the number of stools per day, difficulties in defecation, or abnormal fecal retention. A good review on normal stool characteristics is provided by Arnaud.[17] In pigs, a reduction by 20% of water content of digesta from the cecum (91%) to the rectum (71%) resulted in a 240-fold increase in viscosity. Once fecal water content fell below 75%, a small decrease in water content led to a large increase in viscosity. Water from food (approximately

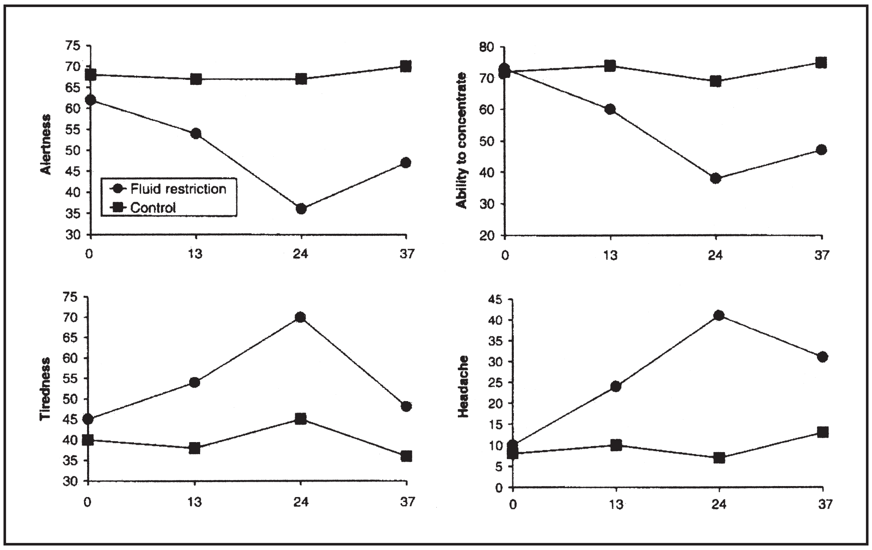

Figure 1. Modifications in subjective sensations induced by acute mild dehydration. (From Cian et al., 2000.[11] Used with permission.)

1 L/d) and from digestive secretions (8 L/d) is absorbed in the small intestine, where absorption capacity is 15 L/d. The colon is able to absorb 5 L/d, and 1.5 L pass through the ileo-cecal valve. Therefore, it seems likely that small changes in fluid intake have little impact on water retention (the amount drunk is small compared with gut secretions).

A comprehensive list of the major causes for constipation cited by Arnaud[17] appears in Table 2. It is clear that a vast number of drugs can be implicated and that inadequate fluid intake is a common cause. However, evidence linking constipation and reduced water intake are scarce, and are more a matter of general wisdom. Numerous articles and textbooks recommend increasing fluid intake to treat constipation. However, in euhydrated children, a 50% increase in fluid intake had no effect on stool frequency or consistency. In the 796 participants of the New Mexico Elderly Health Survey, a trend for lower constipation frequency was observed with increasing fluid intake.[18] Twenty percent of those drinking less than three glasses of fluid a day were affected, as opposed to 15% of those drinking three to five glasses and 11% of those consuming six glasses. In the 1291 out of 21,092 elderly residents who developed constipation, low fluid consumption was the second predictor of constipation.[19] Therefore, it appears more relevant to associate constipation with hypohydration status than with low fluid intake. For chronic constipation, a literature review identified only one study that showed a relationship with liquid deprivation[20]; there are no published studies showing that increasing liquid volume is effective as a treatment in euhydrated subjects with chronic constipation.

HYDRATION CHANGES AND METABOLISM

The cell swelling theory was introduced by Haussinger in the 1990s.[2-4] This new concept in physiology argues that cellular volume is a key signal for the metabolic orientation of cell metabolism, namely, cellular swelling leads to anabolism whereas cellular shrinkage promotes catabolism. In vitro cell swelling is able to inhibit proteolysis, and Haussinger even argues that the anabolic effect of insulin is mediated by cell volume changes. A change in cell volume by 15% inhibits proteolysis by 25%. Cell swelling in hepatocytes is also responsible for an increase in glycogen synthesis, lactate uptake, amino acid uptake, glutamine breakdown, glycine oxidation, ketoisocaproate oxidation, acetyl CoA carboxylase activity, urea synthesis from amino acids, GSH efflux, actin polymerization, and increasing mRNA levels of various genes.[2,21] Cell swelling is also responsible for a decrease in glycogenolysis, glycolysis, glutamine synthesis, urea synthesis from ammonia, mRNA levels of PEPCK (a key enzyme in neoglucogenesis), viral replication, and synthesis of viral proteins. The reverse actions are most of the time true for cellular shrinkage. If we take a bottom-line view, during amino acid starvation, cell shrinkage stimulates glycogenolysis, proteolysis, and expression of PEPCK and inhibits glycogen and protein synthesis. In these circumstances, cell shrinkage results in orienting cell metabolism such that amino acids and glucose are made available for alternative metabolic pathways.

Most of the data available were acquired in cultured rat hepatocytes and perfused liver. It appears that muscle cell swelling is also able to inhibit muscle proteolysis.[22] The rate of glutamine release from rat soleus muscle is dramatically reduced by incubation in a hypoosmolar milieu (146 to 70 mmol/L sodium). The effect is already

Table 2. Major Causes of Constipation (from Amaud 2003[17]; used with permission)

- Diet
- Undernutrition, anorexia
- Inadequate fluid, dehydration
- Low-fiber diet
- Mastication, swallowing, dentition
- Metabolic causes
    - Hypercalcemia
    - Porphyria
    - Hypokalemia
    - Renal acidosis
    - Diabetes mellitus
    - Cystic fibrosis
    - Pregnancy
- Drugs inducing constipation
    - Analgesics
    - Antacids (calcium and aluminum)
    - Anticholinergic agents
    - Anticonvulsants
    - Antidepressants
    - Barium sulfate
    - Diuretics
    - Anti-Parkinson's agents
    - Ganglionic blockers
    - Iron preparations
    - Hypotensives
    - Opiate analgesics
    - Phenothiazines
    - Contraceptive pills
    - Laxatives (long-term)
    - Monoamine oxidase inhibitors
- Endocrine causes
    - Hypoparathroidism
    - Hypothyroidism
- Neurologic and psychiatric causes
    - Paraplegia
    - Cerebral vascular accident
    - Multiple sclerosis
    - Parkinson's disease
    - Depression
    - Psychosis
    - Paranoia
- Rectal anal disorders
    - Anal fissure
    - Anal stenosis
    - Hemorrhoids
- Local lesions of the gut
    - Hernias
    - Aganglionosis (Hirschsprung's disease)
    - Defective electrolyte transfer
    - Obstruction lesions (diverticulosis)
    - Irritable bowel syndrome

significant for a sodium concentration of 120 mmol/L. The phenomenon is fully reversible if sucrose is introduced to restore iso-osmolarity. On the other hand, increasing osmolarity by 10 to 50 mmol/L (by adding sucrose) increases glutamine release, an indicator of proteolysis.

Metabolic changes can also be shown in swollen mitochondria.[23] Mitochondrial swelling (increased matrix volume) is obtained by cultivating hepatocytes in a hypoosmolar milieu, whereas matrix shrinkage results from culture in a hypertonic milieu. Oxygen consumption is decreased in shrunken mitochondria, whereas it is increased during swelling. More importantly, the efficiency of energy conversion in mitochondria is decreased by hyperosmolarity, as evidenced by the decrease of the ratio of ATP produced over oxygen consumed.

Altogether, there is paramount evidence that cell swelling can be considered as an anabolic signal, whereas cell shrinkage is a catabolic signal. This is true for hepatocytes, muscle cells, mitochondria, and also bones and breast cells.[4] There is little doubt that some cells can face large osmolarity changes (e.g., hepatocytes following portal delivery of substrates by the gut or kidney cells along the Henle's tubule). It is suggested that insulin's anabolic effect is almost fully mediated by the swelling it induces, and that part of glucagon's catabolic effect is due to cell shrinkage. The cell swelling theory is therefore very attractive.

In vivo evidence that hydration changes modify metabolism are less convincing and are reviewed in Ritz et al.[24] When plasma volume is artificially increased by 12% to 24%, very few metabolic parameters are changed. Resting energy expenditure, respiratory exchange ratio, neoglycogenesis-glycogenolysis, and glucose utilization are unchanged. Only lipolysis is decreased. A decrease in plasma volume (by diuretics over 4 days) decreases neoglycogenesis and glycogenolysis, while lipolysis is increased.[25] Hypoosmolarity (desmopressin plus water intake) induces a positive water balance by 2 L over 17 hours and reduces proteolysis and leucine oxidation, but increases lipid oxidation and fat oxidation.[9] The discrepancy in the changes in lipolysis (reduced in vitro and after plasma volume expansion, increased by hypoosmolarity) could be induced by the catecholamine response to hypoosmolarity that could blunt the effect of increase water volumes.

When in vitro data are considered, there is little doubt that cell volume (and cell water content) is a second or third messenger relating cellular hydration to metabolism. There are few studies challenging this theory at the whole-body level. It appears that protein metabolism is probably regulated by cellular hydration in humans. Information about the effect of changes in cellular hydration on other metabolic pathways is more questionable, and further studies are necessary to challenge this theory.

CONCLUSIONS

The effects of hydration status on cognitive function are well demonstrated. For other aspects of day-to-day health, there is still not enough evidence to support a link with hydration status, although some health effects can be related to changes in hydration status. It is likely that many aspects of day-to-day health are multifactorial, with perhaps a relatively weak effect of hydration. In order to further demonstrate effects of hydration status on day-to-day health, appropriate tools to assess hydration status and large-scale studies are needed.

PANEL DISCUSSION

Irwin Rosenberg: In struggling with the idea as to whether there is such a thing as "optimal hydration," or to what Dr. Manz refers to as "euhydration," I once wrote an article about optimal nutrition requirements challenging the word "optimal" and asking "optimal for what?" If you don't define that, then it seems to me you are more likely using a marketing term than a scientific concept. So we should either discard the term "optimal" or be examining ways in which to define it with respect to the specific kind of end point or function that we're talking about. To integrate all the potential effects of variation in hydration status without defining them seems to me to be a very large task.

Patrick Ritz: Yes, I fully agree with that. I think Dr. Shirreffs will show us later on during the symposium that physical performance is influenced by hydration. I think we could go in this direction and devise sort of an optimal range of hydration because we know what the optimal function is. If I am a 100-meter runner, I know that I have to run below 10 seconds, for example, so the target function is defined. The difficulty in day-to-day health outcomes such as headache is that there is no easily definable target function. Cognitive performance is very difficult to define and it is also very difficult to obtain some evidence-based data, since we know from clinical practice that when a person is even mildly dehydrated, cognitive performance is reduced. I agree with you: Which function are we defining? Which function are we targeting? For which group? I would say that it is easier for diseased people, but for healthy people it is so difficult to define an optimal function indicator.

Antonio Dal Canton: Do you agree that the concept of "optimal" is different from the concept of "normal"? Different persons actually have such different drinking habits but maintain water balance and a normal content of water. This doesn't mean that they have optimal hydration status, and to define it as you outlined, we need evidence-based measurements of performance, which are very difficult to obtain.

Irwin Rosenberg: Yes, I think that it is important to make that distinction. I think it is also important to make the distinction between what is normal and what is normative. It seems to me, as we heard from Dr. Manz earlier, who was looking at a population data from which normative values might be derived, that normal requires a different level of definition. For the latter, one has to introduce the concept of health or function and, if so, which one? And even then, I think it will continue, as Dr. Dal Canton says, to be a challenge to separate normal from optimal. We need to continue to struggle with those definitions.

Michael Sawka: There are procedures that one can use to control for euhydration or normal hydration. There are several biomarkers (e.g., body weight, urine SG, plasma osmolality) and one can repeatedly measure to establish baseline values on an individual, seeing how they vary day to day, comparing them with normative values, and then, once established for the person, you can define that as indicating euhydration. Once you have established euhydration, then you can study outcome measures and manipulate body water. So from my point of view, I really don't have a lot of difficulty in defining normal hydration, or euhydration. There are biomarkers and criteria that one can use to establish it and I think that the idea of optimal hydration is good in terms of a specific outcome. But I think that for most of the things that you're going to hear during the symposium, at least that I'm aware of, for physical exercise and many other outcomes, that optimal and normal are not very different. They're about the same with a range of fluctuation that does not matter.

Friedrich Manz: Let me just add an example of medical history illustrating the two implications of the term normal: the statistic and the normative meaning. In 1905 Czerny, a famous German pediatrican, wrote that the mean (observed) number of breastfeeding sessions in healthy mothers and infants is six to seven and normal is five! He observed that, in the clinic, infants survived with five feeds of breastfeeding wet nurses. His aim was the survival of the infant, not an optimal quality of life for mother and infant. Unfortunately, this very rigid regimen with several negative side effects spread all over the world.

Eric Jéquier: I would like to comment on the relationship between hydration, either hyper- or hypo-, and metabolism. I think that we have to be prudent with this type of relationship, because hypo-hydration is often linked to hypo-energy intake, and obviously a low energy intake might decrease the respiratory quotient. I would not be surprised if a decrease in respiratory quotient were not at all related to hydration, but perhaps to a concomitant decrease in energy intake, which at a negative energy balance respiratory quotient will decrease. So this is a word of caution about the relationship between hydration and various aspects of metabolism, especially the respiratory quotient.

Patrick Ritz: Yes, I do agree with your comment. However, in these two studies about manipulating osmolality, I think that the food intakes were not affected because the study design was to use an indirect way of changing osmolality but not only changing water or water intake from fluid or from food. And for Dr. Shirreff's studies, the first one I presented was very careful in showing that the energy intakes of these subjects were the same on the two occasions, so there was only fluid restriction.

Antonio Dal Canton: In fact it is very difficult to manipulate osmolality without also changing plasma volume, because even if you add water, pure water I mean, you will increase plasma volume by approximately 30%. It is difficult to distinguish between the two effects. There is also one possible message for laymen that can be taken from this talk. There is some evidence in vivo at the total-body level that if we increase hydration we have a decreasing lipolysis. Many overweight people are waiting for such a message: "Drink more water and you will lose fat."

Patrick Ritz: What is the relationship between metabolism and hydration in obese people, and can we improve anything? Can we just show firstly that there is a relationship between hydration and metabolism? Obviously there are some arguments to show that hydration is changing the metabolism of obese people. I know of no data, but there is a large overweight population to target.

Friedrich Manz: In an experimental study in 14 healthy subjects, the intake of 500 mL of water induced a thermogenic effect of about 100 KJ (Boschmann M, Steiniger J, Hille U, et al. Water-induced thermogenesis. J Clin Endocrinol Metab. 2003;88:6015–6019).

Patrick Ritz: Yes, in that study they used a room calorimeter, and administering 500 mL of water to healthy subjects increased their energy expenditure by about 100 kJ.

Irwin Rosenberg: It's making me wonder whether Dr. Jéquier's observation needs to be taken into account in looking at the relationship between obesity and total body water, but I think we probably need a number of populations to look at.

Antonio Dal Canton: In general, the in vitro findings that the hyperhydration or hypohydration condition influences several cell functions are very interesting. I am talking now from the point of view of any researcher who uses cell culture. It is not so usual, in general, to pay such attention to the osmolality of the culture medium. I understand that we should be very careful in maintaining the osmolality of our media very strictly at normal. This is not so pertinent to the main topic of the symposium, but maybe of interest for anyone who does research with cells and cell cultures.

Patrick Ritz: It is a great deception that this theory cannot yet be proven at the whole-body level, because Haussinger's group has consistently found the same observation: the more the cells are hydrated, the more metabolism is oriented towards anabolism, and the reverse is true. I have even thought that with kidney disease, patients who are going through cycles of fluid expansion and fluid withdrawal are very good models to study these metabolisms, but I have not seen any studies coming out yet.

Friedrich Manz: Pregnancy is an interesting physiologic example of the relationship between anabolism and osmolality. During pregnancy, the set point of vasopressin secretion of the mother is shifted to plasma osmolality levels, which are about 10 mOsm/kg lower than in non-pregnant women. Plasma osmolality of the fetus is even lower by 3 mOsm/kg. Thus, in the fetus, where the anabolic activity of metabolism is at its maximum, plasma osmolality is exceptionally low.

Antonio Dal Canton: Yes, your comment is really appropriate. However, pregnancy is a very special condition in which plasma volume increases, extracellular volume expands, plasma osmolality goes down, plasma renin activity is very, very high (and perhaps increases the thirst sensation), and GFR increases by 100% in some women. So it is a very special condition, but your comment is absolutely appropriate.

Irwin Rosenberg: I wanted to return to the issue of cell volume and swelling and metabolic effects, and the relationship to symptoms in vivo. I am wondering, when dehydration is induced by one means or another, heat, exercise, or whatever, and we see that under conditions of acute dehydration, when there certainly is evidence of functional changes in cognitive function, does brain volume change? Has anyone looked at MRIs under those circumstances? Are we seeing a shrinkage of either extracellular or intracellular volume of the brain?

Michael Sawka: Nose and colleagues (Nose HT, Morimoto T, Ogura K. Distribution of water losses among fluid compartments of tissues under thermal dehydration in the rat. Jpn J Physiol. 1983; 33:1019–1029.) did a study where he dehydrated rats and looked at a variety of different organs. He showed that the brain and most of the organs didn't really change in water content. In fact, what seems to happen with dehydration is that most of the water is lost from the skeletal muscles. That seems to act as the primary reservoir.

Susan Shirreffs: We carried out a pilot study looking at the brain in humans, and at moderate levels of dehydration of around 2% body mass loss with exercise-induced sweating, we saw no changes. We have never followed it up, but again, our observations are in line with those for the brain in the animal model.

Monique Ferry: It is difficult to obtain really good information on hydration with MRI.

Friedrich Manz: Cells of different tissues react in a different way to changes of tonicity. In distal renal tubular cells, an acute increase in urine osmolality only marginally affects cell volume and water content due to the parallel intracellular increase of the concentrations of various organic osmolytes, the so-called "idiopathic osmols," and to the adjustment of the activity of different aquaporin water transport proteins. Similar mechanisms are activated in the cerebrum and the heart. In muscles and red blood cells, however, an increasing plasma osmolality results in cellular shrinkage and loss of water.

Michael Sawka: If you look at dehydrated, healthy 25-year-old humans, you notice that physical fitness level and heat acclimatization level modify the level of loss in terms of intracellular to extracellular water, so it really becomes complex.

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