Understanding Clinical Dehydration and Its Treatment

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Dehydration in clinical practice, as opposed to a physiological definition, refers to the loss of body water, with or without salt, at a rate greater than the body can replace it. We argue that the clinical definition for dehydration, ie, loss of total body water, addresses the medical needs of the patient most effectively. There are 2 types of dehydration, namely water loss dehydration (hyperosmolar, due either to increased sodium or glucose) and salt and water loss dehydration (hyponatremia). The diagnosis requires an appraisal of the patient and laboratory testing, clinical assessment, and knowledge of the patient's history. Long-term care facilities are reluctant to have practitioners make a diagnosis, in part because dehydration is a sentinel event thought to reflect poor care. Facilities should have an interdisciplinary educational focus on the prevention of dehydration in view of the poor outcomes associated with its development. We also argue that dehydration is rarely due to neglect from formal or informal caregivers, but rather results from a combination of physiological and disease processes. With the availability of recombinant hyaluronidase, subcutaneous infusion of fluids (hypodermoclysis) provides a better opportunity to treat mild to moderate dehydration in the nursing home and at home. **(J Am Med Dir Assoc 2008; 9: 292–301)**

Keywords: Dehydration; long-term care; hyperosmolar dehydration; hyponatremia dehydration; education; prevention; recombinant hyaluronidase; subcutaneous infusion of fluid; hypodermoclysis

> *"Water . . . Not necessary to life,*
> *But rather life itself . . ."*
> *de Saint-Exupery A. Wind, Sand and Stars. 1939. Galantiere L, translator, 1967, Harcourt Brace & Co., Orlando, Fl.*

Dehydration is considered a sentinel event in long-term care. Few diagnoses generate as much concern about its causes and consequences as does dehydration. The public, including regulatory agencies and lawyers, seem to believe that dehydration represents neglect by the nursing home staff and/or physician. This negative perception may lead to a failure to aggressively diagnose and treat dehydration early in its evolution. The area is further confused by a lack of understanding of the pathogenesis of dehydration and of its definition. The purpose of this review is to provide a logical clinical definition of dehydration (which differs from its use by physiologists), to define the criteria for its diagnosis, and to provide a treatment framework. Most importantly, this review stresses that the vast majority of persons develop dehydration because of disease processes and that dehydration is rarely due to neglect. The risk of dehydration in older persons is due to increased fluid losses coupled with decreased fluid intake related to decreased thirst.

The concept that old age is associated with dehydration is not a new one.[1] Homer suggested that old age is like a dried olive branch. Aristotle pointed out that "one should know that living beings are moist and warm . . . however old age is dry and cold." Galen continued this theme by writing that "Aging is associated with a decline in innate heat and body water." Galen's most pertinent observation was that dehydration is difficult to diagnose, and this remains true today. A recent study found that the diagnosis

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Table 1. *Physiological Functions of Water*

- Aqueous environment to allow chemical reactions to occur within cells
- Waste product removal (urine and feces)
- Aqueous medium for transport of nutrients, gases, and hormones
- Thermoregulation (sweat)
- Lubricant for joints
- Shock absorber (intravertebral discs)

of dehydration was not supported by laboratory data in 40% to 80% of patients diagnosed with dehydration.[2] The reasons for this are multifactorial, including varying criteria for diagnosis of dehydration, poor education about dehydration among many physicians, and fiscal incentives for hospitals to diagnose dehydration.

THE REGULATION OF WATER METABOLISM

Water plays a key role in maintaining multiple physiological functions (Table 1). Water comprises 55% to 65% of body mass. Two thirds of the water in the body is intracellular, predominantly in lean tissue. Of the remaining one third of body water that is extracellular, only 25% is intravascular, representing a mere 8% of total body water. With aging, there is a decline in total body water, in both the extracellular and intracellular fluid volume.[3,4] This decline in total body water and the alterations in water regulation with aging leads to increased vulnerability of older persons to heat stress. Morgan et al[5] found that in response to heat and exercise, older persons lose more intracellular fluid and less interstitial fluid in an attempt to maintain intravascular volume. The factors involved in the regulation of water in humans are shown in Figure 1A.

Studies using positron emission tomography (PET) scans and functional magnetic resonance imaging (MRI) have shown that multiple sites in the brain in addition to the classical circumventricular organs and the median pro-optic nucleus are involved in the regulation of thirst.[6] The day-to-day regulation of fluid intake is predominantly under the control of osmoreceptors that alter thirst through the dopamine-mu opioid neurotransmitter interaction in the brain (Figure 1B). A decrease in opioid system activity has been shown to play a role in decreased thirst in older persons.[7] When hypovolemia occurs, the baroreceptors can further activate thirst. Angiotensin II drives fluid intake in animals and plays a role in the decreased thirst with aging, although its role is less clear in humans.[8] Relaxin from the uterus also increases fluid intake and plays an important role in the drive for an increased fluid intake during pregnancy.

In their classical study, Phillips et al[9] demonstrated that fluid restriction results in relatively less stimulation of thirst and fluid intake compared to older persons. They found a similar decrease in thirst following an infusion of hypertonic saline in older persons compared with younger ones.[10] Heat exposure and exercise are also associated with decreased thirst and fluid intake in older persons.[11–13]

Besides the failure to drink adequate fluid in response to dehydration, older persons also develop a higher serum osmolality in response to fluid deprivation.[14] This is due to changes in renal function with aging. In general, aging is associated with a reduced glomerular filtration rate, increased proximal tubular renal absorption, decreased free water clearance due to a loss of distal tubular diluting capacity, and a decline in maximal fluid concentrating ability.[15] Animal studies have shown that aging results in a decrease in Aquaposin-2 in response to a decline in the activity of arginine vasopressin (AVP)-V2 receptor.[16] Finally, AVP basal secretion is increased but the normal nocturnal rise that occurs with AVP is blunted with aging. This failure for AVP to rise in the evening is the explanation for the nocturia that occurs in most older persons.

These physiological changes that occur with aging place the older person at major risk for dehydration.

DEFINITION

Classically, the medical literature has distinguished 2 forms of total body water fluid loss: (1) dehydration, which refers to a loss of body water mainly from the intracellular compartments, and (2) volume depletion, referring to a loss of extracellular fluid clinically affecting the vascular tree and interstitial compartment.[17,18] While physiologically this makes eminent sense, most clinicians tend to use the term dehydration for any loss of total body water. For this reason, we believe it has become more practical to define dehydration by its clinical use and then redefine the 2 forms of loss of total body water under this rubric.

Thus, we suggest that dehydration be defined as a complex condition resulting in a reduction in total body water. This can be due primarily to a water deficit (water loss dehydration) or both a salt and water deficit (salt loss dehydration). Dehydration due to a water deficit is either hypernatremic or hyponatremic when it occurs in the presence of hyperglycemia. Dehydration due to a salt and water deficit is hyponatremic (or rarely isotonic) (Figure 2). In most cases, dehydration is due to disease and/or the effects of medication and NOT primarily due to lack of access to water. Clinically, it cannot be defined by a single symptom, sign, or laboratory value.

Osmolality can be directly measured or calculated from the formula:

$$\text{Osmolality} = 2 \times (\text{Na} + \text{K (mmol/k)} + \frac{\text{plasma glucose (ng/dL)}}{18} + \frac{\text{BUN (ng/dL)}}{28}$$

For clinical purposes the blood urea nitrogen (BUN) should be excluded from the calculation because BUN is freely permeable to cells. When BUN is excluded, this is referred to as the Effective Osmolality. Osmolality is considered to be elevated when it is greater than 300 mmol/kg. Between 295 and 300 can be considered to suggest impending dehydration. Water-losing dehydration results in an elevated serum osmolality. In all cases, either serum sodium or glucose levels must be elevated. When both water and salt are lost, dehydration is associated with hyponatremia and low osmolality. The ma-

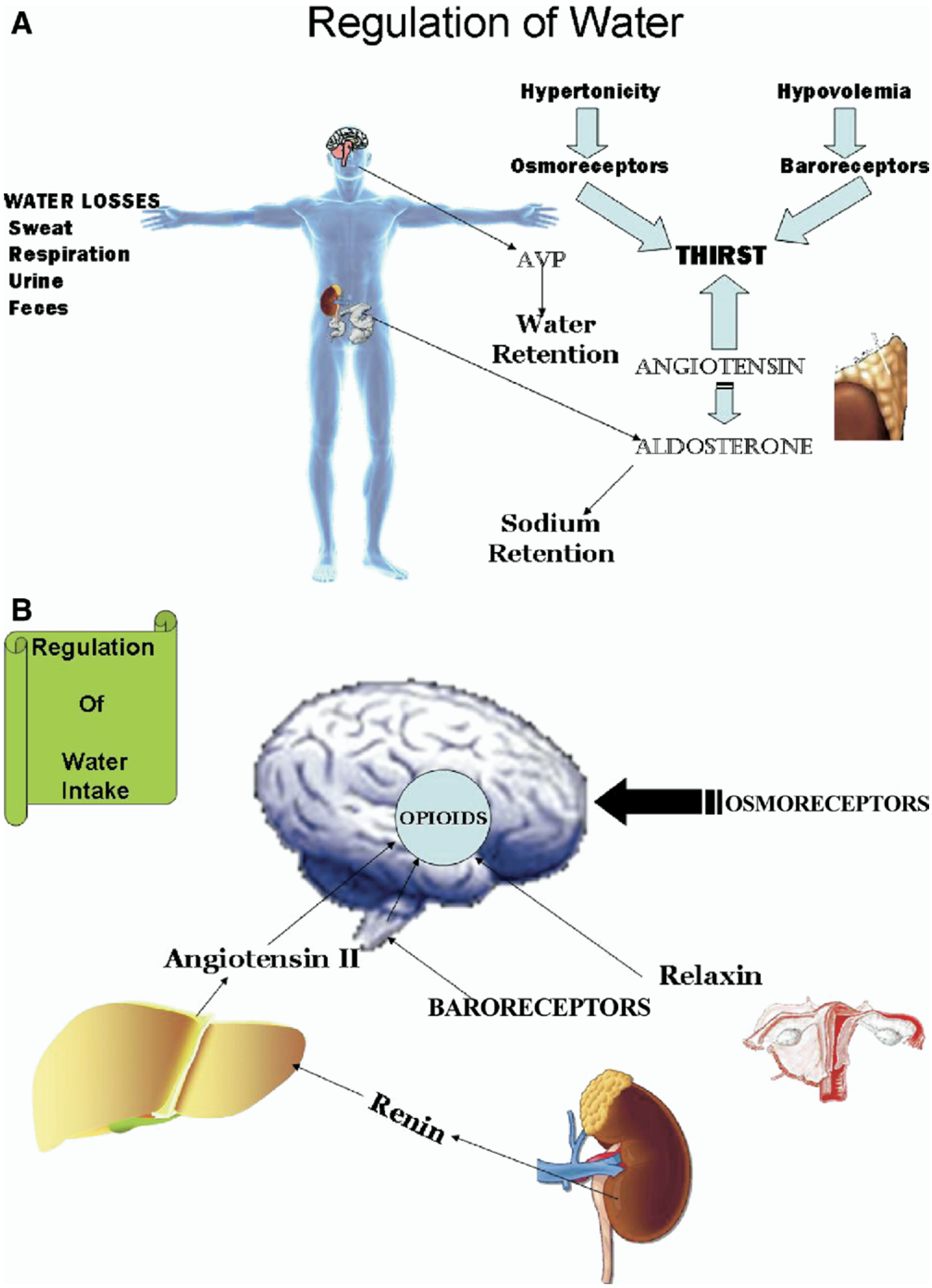

Fig. 1. *(A)* Peripheral factors involved in the regulation of water metabolism. *(B)* Central factors involved in the regulation of water intake.

jority of these patients will have a metabolic alkalosis and elevated BUN/creatinine ratio and uric acid. Urine sodium levels may be low or increased.

While most cases of dehydration have an elevated BUN/creatinine ratio, there are many other causes of an elevated BUN/creatinine ratio (Table 2). Thus, an elevated BUN/creatinine ratio alone cannot be used to diagnose dehydration.

When a person is hyponatremic, the differential diagnosis includes the syndrome of inappropriate antidiuretic hormone (SIADH). In a study of 119 residents in a long-term care facility with a serum sodium determination, 53% of the residents had at least 1 episode of hyponatremia (serum sodium less than 135 mg/dL) in the preceding year. A water-loading test was normal in only 5 (22%) of 23 selected subjects with hyponatremia, suggesting that the majority of the tested subjects had features consistent with SIADH.[19] In contrast to dehydration, SIADH does not have an elevated BUN/creatinine ratio and elevated uric acid. SIADH is accompanied by increased urine sodium, but sodium-losing dehydration may also have this finding when it is caused by diuretics or salt-losing nephropathy.

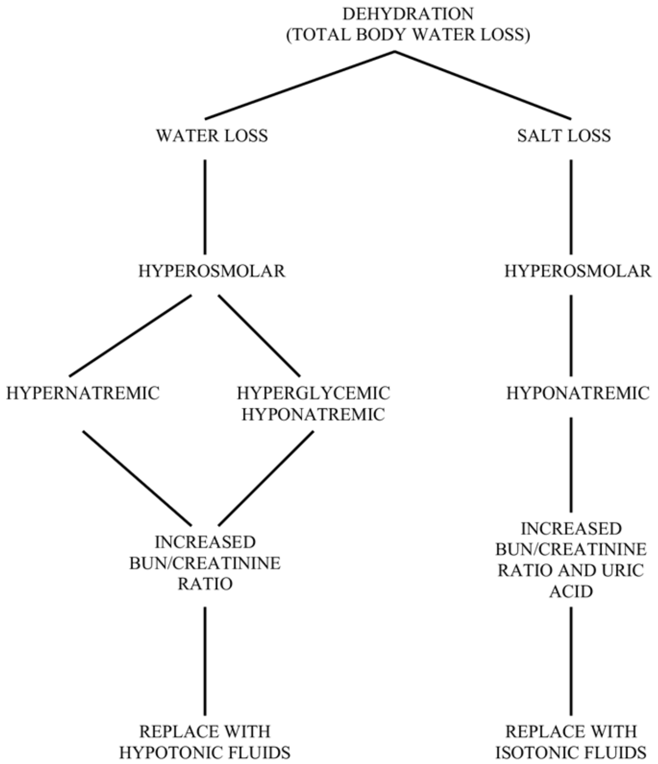

Fig. 2. *The types of dehydration.*

The presence of orthostasis suggests dehydration. In addition, fluid overload states, eg, cirrhosis and congestive heart failure, are often associated with hyponatremia. The criteria for SIADH syndrome are shown in Table 3.

EPIDEMIOLOGY

The studies examining the presence of dehydration are confounded by imprecise diagnoses and varying study methodologies. Miller et al[21] in a study of older African Americans (mean age 79.7 years) living in the community found an elevated BUN/creatinine ratio in 10% and an elevated sodium level in only 1%. They identified persons who were depressed and those who had impaired function as having increased risk for dehydration. Dehydrated individuals performed poorly on timed tests, one leg stand, "Get Up and Go," and the physical performance test. And most importantly, especially for the long-term care resident, dehydrated individuals had a poorer quality of life.

Table 2. *Etiologies of an Elevated BUN/Creatinine Ratio*

- Dehydration
- Renal failure
- Bleeding
- Congestive heart failure
- Sarcopenia (muscle loss)
- Increased protein intake
- Glucocorticoids
- Licorice

Table 3. *Criteria for Diagnosis of Syndrome of Inappropriate Antidiuretic Hormone (SIADH)*

Essential
- Plasma osmolarity less than 275
- Urinary osmolarity greater than 100
- No signs of volume depletion, no edema
- Urinary sodium greater than 40
- Normal thyroid function, normal adrenal function
- No diuretics

Supplemental
- Uric acid less than 4
- BUN less than 10
- Fractional excretion of sodium greater than 1%
- Failure to correct hyponatremia with 0.9% saline
- Correction of hyponatremia with fluid restriction
- Low AVP levels

Adapted from Ellison and Bert.[20]

Two other community studies have reported a much higher prevalence of dehydration in community-dwelling seniors. Using calculated osmolality in the National Health and Nutrition Examination Survey (NHANES) III population, Stookey[22] found that 28.4% of persons 70 to 90 years old had a plasma osmolality greater than 300 mmol/L and another 39.8% between 295 and 300 mmol/L. The Duke Established Populations for Epidemiologic Studies of the Elderly surveys reported that approximately 50% of older adults had elevated plasma tonicity.[23] The most likely reason for this increased prevalence of hypertonicity is the high prevalence of elevated glucose levels in older persons.[24]

In hospitals, 7.8% of older persons have the diagnosis of dehydration.[24] It is associated with a dramatically increased mortality rate.[25–27] Diagnoses associated with dehydration included respiratory illnesses, fever, diabetes mellitus, heart failure, and frailty.

Using the Minimum Data Set, the point prevalence of dehydration in Missouri Nursing Homes was 1.4% compared with 1.2% in Iceland and 0.8% in Ontario.[28] Dehydration is associated with increased mortality in nursing homes.[29,30] Demented patients are more likely to develop dehydration.[30] Infection, fever, and oral problems are strongly associated with the development of dehydration in nursing homes.[30–32] Dehydration increases the likelihood of persons with stroke requiring transfer back to the hospital.[33]

Mentes and Culp[34] followed 35 nursing home residents (mean age 82 years) for 6 months. A dehydration episode occurred in 31%, based on hospitalization for dehydration (n = 4), intravenous fluids in the nursing home (n = 2), or a BUN/creatinine ratio greater than 25:1 (n = 5). Dehydration was most common in those who had difficulty drinking or in those who feared incontinence. The next most common group was those who were dysphagic or physically dependent. The limitation of the study was that it used elevated BUN/creatinine ratio or hospitalization as the criteria to diagnose dehydration.

Some causes of dehydration are iatrogenic; for example, persons undergoing colonoscopy bowel preparation develop moderate dehydration.[35] This may be in part because fluid

Table 4. *Consequences of Dehydration*

• Weight Loss • Constipation • Falls • Delirium • Drug toxicity • Orthostasis • Delayed wound healing • Renal failure • Postprandial hypotension • Infections (urine and respiratory) • Seizures • Myocardial infarction • Hospitalization • Death

requirements of older persons are underestimated by physicians.[36] The potential consequences of dehydration are listed in Table 4.

DEHYDRATION AND DELIRIUM

Recently, it has been suggested that the assessment of mental status should be the sixth vital sign.[37] It is well accepted that dehydration commonly precipitates delirium.[38,39] Persons in nursing homes with agitated or aggressive behavior are more likely to have anorexia, weight loss, and dehydration.[40] Dehydration and infections are major causes of acute confusion in nursing homes.[41]

A general schema of the progressive effects of variable degrees of dehydration on behavior has been suggested:

- Persistent subclinical dehydration is associated with anxiety, panic attacks, and agitation.
- Fluctuation in tissue hydration results in inattention, hallucinations, and delusions.
- Severe dehydration leads to somnolence, psychosis, and unconsciousness.

In general, central nervous system symptoms are present when dehydration results in a 1% loss of body weight and are very prominent at 5% loss.[42]

Wilson and Morley[43] found in their review of the literature that dehydration can alter cognition through intracellular effects, intravascular volume depletion, and extracellular effects. Intracellular effects include an increase in local cytokine production, glutamate toxicity, mitochondrial dysfunction, altered pharmacokinetics of drugs, and increased anticholinergic burden. Intravascular volume depletion results in cerebral hypoperfusion, cardiac ischemia and thromboembolic disorders. Extracellular effects include uremia, contraction alkalosis, and electrolyte imbalance.

IDENTIFYING DEHYDRATION

Clinical symptoms and signs of dehydration generally have poor sensitivity and specificity.[44] This requires a high index of suspicion to make the diagnosis. Chassagne et al[30] identified orthostasis, decreased skin turgor (subclavian and forearm), tachycardia, dry oral mucosa, and recent change in consciousness (delirium) as factors associated with dehydration in the nursing home. However, none of these factors were diagnostic. Skin turgor is not reliable because of the loss of subcutaneous tissue with aging. Dry axilla is fairly useful if present, with a positive likelihood ratio of 2.8.[45] In a meta-analysis, dry axilla had a sensitivity of 50% and a specificity of 82%. Similarly, absence of a dry tongue makes it unlikely that the person is dehydrated, but its presence is not a useful diagnostic clue.

Factors that have a sensitivity of greater than 80% are dry mucous membranes in mouth and nose, and longitudinal furrows on the tongue. A specificity of over 80% was conferred by orthostasis, speech incoherence, extremity weakness, dry axilla, and sunken eyes. While orthostasis is a popular indicator of dehydration, it has multiple other causes. Sunken eyes also had a sensitivity of 62%.

While physical examination may suggest the presence of dehydration, ultimately, nursing homes and physicians should not rely on any clinical signs and symptoms to indicate that dehydration is present, or rely on the absence of such signs and symptoms to indicate its absence. In the final analysis, the diagnosis of dehydration is biochemical (established via diagnostic testing).

Urine has been used to diagnose disease since Susruta originally tested "sugar" in urine to diagnose diabetes mellitus.[46] By the 16th century, urine color charts had been developed to diagnose disease. Urine color charts have been developed to assess hydration status in extreme environments.[47] A study in elderly hospitalized veterans found that urine color had a moderate correlation with urine specific gravity.[48] A small study in the nursing home suggested that urine color had a good correlation with urine specific gravity and dehydration status in residents with adequate renal function (>50 mL/min). The correlations were better in females than males.

The minimum data set has 12 triggers for dehydration/fluid maintenance and 7 additional risk factors. The American Medical Directors Association (AMDA) Dehydration and Fluid Maintenance Clinical Practice Guideline lists 19 clinical conditions and 8 environmental factors that put an individual at risk for dehydration.[49] Its hydration status assessment tool lists 12 subjective factors and 8 objective factors to help make the diagnosis of dehydration. Mentes et al[50] developed a dehydration risk appraisal checklist consisting of 3

Table 5. *Simple Screen for Dehydration*

• **D**rugs, eg, Diuretics • **E**nd of life • **H**igh fever • **Y**ellow urine turns dark • **D**izziness (orthostasis) • **R**educed oral intake • **A**xilla dry • **T**achycardia • **I**ncontinence (fear of) • **O**ral problems/sippers • **N**eurological impairment (confusion) • **S**unken eyes

personal characteristics, 10 significant health conditions, 6 medication factors, 8 questions regarding intake, and 4 laboratory abnormalities. All of these screens are complex and unfortunately identify the vast majority of nursing home residents as being at risk for dehydration. While this may be true, it minimizes the effective use of a risk assessment tool.

In an attempt to simplify this situation, the members of the Dehydration Council created the DEHYDRATIONS mnemonic to increase awareness of dehydration (Table 5). The Council is planning to develop a scoring system and test its utility in the nursing home. A recent study demonstrated that physicians misdiagnose dehydration in at least a third of patients admitted to hospital.[2]

In the final analysis, the diagnosis of dehydration is biochemical. Any person suspected of being dehydrated needs at a minimum to have blood urea nitrogen, sodium, creatinine, glucose, and bicarbonate measured. In addition, osmolality should either be directly measured or calculated. If the sodium is elevated, it is likely that the person has water loss dehydration and needs free water, usually in the form of a 5% dextrose solution. An elevated osmolality in the presence of hyponatremia and elevated glucose suggests a hyperosmolar state due to hyperglycemia. Pseudohyponatremia may be due to hypertriglyceridemia or mannitol infusion and is treated with free water and insulin. If the person is hyponatremic and hyposmolar, and uric acid is elevated in the presence of a metabolic alkalosis, salt loss dehydration is likely presented, provided the person is not fluid overloaded. This condition of dehydration can be effectively treated with isotonic saline.

MANAGEMENT OF DEHYDRATION

Recognizing the difficulty of diagnosing dehydration, that it is typically due to underlying disease processes (or to excessive diuresis), and that it can develop very rapidly, it is essential that facilities are routinely vigilant about fluid maintenance. This requires increasing the role of certified nursing assistants in risk assessment and making dehydration part of nursing's daily checklist. Such vigilance includes increased awareness of risk factors for dehydration, eg, fever, hot weather, diuretics, vomiting, and diarrhea. When a resident's fluid intake decreases or when the urine becomes dark, this needs to be recognized and investigated promptly. Fluids need to be offered regularly and methods to increase an individual's likelihood of ingesting them explored. This approach to the prevention of dehydration is summarized in Table 6.

Table 6. *Prevention of Dehydration*

- Ongoing educational focus on dehydration
- Increase awareness of factors responsible for dehydration, eg, fever, hot weather, vomiting and diarrhea, medications
- Report decreased intake and dark urine
- Provide straws and cups that residents can use
- Offer fluids regularly
- Provide preferred beverages
- Use swallowing exercises and cuing before thickening liquids
- Encourage persons with urinary incontinence not to restrict fluids
- Hydration cart
- Use frozen juice bars
- Encourage family involvement in increasing fluid intake

When a person has hypernatremic hyperosmolar dehydration, the estimated fluid deficit should be calculated:

$$\text{Fluid deficit} = \left[\frac{\text{serum sodium}}{140}\right] \times \text{bodyweight}^{*}\,(\text{kg}) \times 0.5 - (\text{bodyweight [kg]} \times 0.5)$$

* "Bodyweight" refers to baseline bodyweight before fluid losses occurred.

This formula presumes that the predehydration body weight is known, which can be problematic in older persons. Fluid replacement consists of the estimated fluid deficit plus urine output and insensible fluid loss (~500 mL/day). In the presence of severe hyponatremia, the serum sodium should be corrected over a few days (no greater than 1 mEq/hour) to avoid cerebral pontine myelinolysis.

Once a person is dehydrated, replacement of fluid orally in the nursing home may be difficult. In a study of 63 incontinent nursing home residents, subjects were randomized to receive 16 weeks of 4 verbal prompts daily to drink fluids in between meals, 8 weeks of 8 verbal prompts daily to drink fluids in between meals, or 8 weeks of 8 verbal prompts daily to drink fluids in between meals using their beverage of preference. In response to the verbal prompts, 81% of subjects increased their average daily fluid intake. An additional 21% of subjects increased their average daily fluid intake only when their preferred beverage was offered. The average increase in fluid intake was less than 5 ounces in a third of subjects. Another third increased their fluid intake from 5 to 20 ounces per day, and a quarter of subjects showed a decrease in their fluid intake. Significant improvement in serum osmolality and BUN/creatinine ratio was only observed in residents increasing oral intake more than 5 ounces per day.[51] The improvement in average daily fluid intake correlated directly with cognitive status, with the greatest benefit occurring in residents with higher cognitive function.

Individuals with mild or moderate dehydration who can drink and do not have significant mental or physical compromise due to the fluid loss may be able to replenish losses orally. Otherwise, it has been commonplace to use intravenous fluid replacement, which often requires hospitalization.

SUBCUTANEOUS INFUSION

Recently, for persons with mild to moderate dehydration, hypodermoclysis has reemerged as an option for hydrating persons in the nursing home and at home.

Candidates for subcutaneous infusion include persons with signs of mild to moderate dehydration. Subcutaneous infusion is not appropriate for persons who have severe dehydration requiring hospitalization, manifest or imminent shock or hypotension, need for administration of a parenteral pharmacological agent, severe heart failure, acute myocardial infarction, generalized edema, skin infection, or allergic skin diseases at injection sites. Normal saline (0.9%), half-normal saline

Table 7. *Medications That Can Be Administered via Subcutaneous Infusion*

- Morphine
- Haloperidol
- Chlorpromazine
- Insulin
- Potassium chloride
- Theophylline
- Phenobarbital
- Metoclopramide
- Hydrocortisone
- Penicillins
- Streptomycin

(0.45%), 5% glucose in water infusion (D5W), or Ringer's solution have been used for subcutaneous infusion. The achievable volume has been variously reported to be 1500 mL per day, or up to 3000 mL per day using 2 sites. In a study of 60 residents in a long-term care facility with dementia and mild to moderate dehydration, more subjects receiving intravenous fluids were agitated (80%) compared with 37% of subjects receiving subcutaneous fluids. No difference was found in amount of fluid administered or in improvement of dehydration parameters.[52]

The administration of fluids, electrolytes, and drugs subcutaneously, with or without hyaluronidase, has been used for over 50 years. This technique has been particularly well used in dehydrated children. A number of studies in older persons have directly compared subcutaneous infusion to intravenous administration of fluids and found little difference in their efficacy in mildly to moderately dehydrated patients.[51,53–55] One of these studies concluded that subcutaneous infusion was superior in confused patients and those with difficult venous access.[55] Another found that agitation occurred half as often in those receiving subcutaneous infusion compared with those receiving fluids intravenously.[52] One study found an equivalent improvement in orientation regardless of the infusion technique. Dasgupta et al[56] reported a much higher rate of complications in long-term care residents receiving intravenous fluids. Most impressive were the data reported by Schen and Singer-Edestein,[57,58] who carried out hypodermoclysis in 634 patients reporting only occasional fluid overload, 5 cases of subcutaneous edema, 2 of ecchymosis, and 1 infection.

Hyaluron is a large repeating sugar polymer found in interstitial tissue. It forms a barrier to movement of molecules in interstitial space. It has a high turnover rate of more than 5 g/day in humans. Hyaluronidase, which was originally identified as a "spreading factor" in 1928, is the enzyme that degrades hyaluron resulting in an opening of the interstitial space and a decreased resistance to bulk fluid flow. The first patients were treated with bovine hyaluronidase by Hechter[59] in 1947. Numerous studies in the early 1950s demonstrated the safety and efficacy of hyaluronidase.[60–63] Originally, the hyaluronidase extracts were bovine and then ovine. After the identification of the hyaluronidase gene in 1993, human recombinant hyaluronidase (Hylenex) was introduced into the clinical arena in 2005. Subcutaneous infusions with hyaluronidase allow an infusion rate of over 300 mL/hour compared with placebo rates of 82 to 148 mL/hour (Baxter, Inc.: data on file, 2007). Placebo infusions result in severe edema in 26% and moderate in 69% compared with infusions with hyaluronidase having moderate edema in only 17% of persons. There is less pain and discomfort with hyaluronidase and 92% of subjects and investigators preferred hyaluronidase to placebo. Constans et al[64] reported that subcutaneous infusion with hyaluronidase results in a smaller arm circumference.

Lipschitz et al[65] demonstrated that radioactive technetium pertechnate and triticem injected at the site of the infusion is absorbed into the blood supply within 60 minutes. They also found that the technetium gamma activity had been totally absorbed from the infusion site within 75 minutes.

Subcutaneous infusions with hyaluronidase have become particularly popular in palliative care.[66–72] Side effects have included local skin irritation and occasional itching, site bleeding, and infection.[64] In this arena, subcutaneous infusion has been used to provide drugs such as opiates and chlorpromazine as well as fluids and potassium. Table 7 provides a list of medications compatible with subcutaneous infusion and hyaluronidase.

Table 8 compares subcutaneous infusion to intravenous therapy. With the availability of recombinant hyaluronidase, subcutaneous infusion appears to be an old approach with a new twist to improving quality of life in persons in long-term care settings. Table 9 gives detailed instruction for starting subcutaneous hydration with hyaluronidase.

CONCLUSION

Dehydration is common in older persons and is associated with poor outcomes including increased mortality and an

Table 8. *Subcutaneous Infusion or Intravenous Therapy? (Adapted from Hussain and Warshaw.[72])*

Subcutaneous Infusion	Intravenous Therapy
1. Easy to initiate	Harder to initiate
2. Can be done with limited training	Needs trained personnel
3. Easy to restart	Difficult to restart
4. Infection rare	Cellulitis and septicemia
5. Minimal bruising	Multiple bruises
6. Easier to maintain (unlikely to need restraints)	Difficult to maintain (restraints often requested)
7. Reasonable volume can be delivered	Greater volumes can be delivered
8. Fluid overload rare (but sometimes localized edema)	Fluid overload a problem
9. High staff and patient acceptance	Variable acceptance
10. Can be done at home by family member (eg, palliative care)	Cannot be done at home
11. Can be used to deliver some drugs (eg, opiates)	Better drug delivery system
12. Very cost effective	Less cost effective

adverse effect on quality of life. Dehydration occurs because physiological changes associated with aging interact with a variety of disease processes. Dehydration is rarely due to neglect. Older persons fail to recognize the need to drink more in response to fluid loss. Older persons have an increased risk of dehydration, despite the availability of fluids, because of impaired thirst mechanisms and urinary, skin, and respiratory loss of fluids. Persons at greatest risk for dehydration include persons with fever or infections, impaired cognitive status, impaired renal function, and poor oral intake ("sippers") and those who take medications that impact fluid and electrolyte balance.

This article has proposed to redefine dehydration as total body water loss to make the term compatible with general clinical usage instead of the more restricted definition used in physiology. Clinical signs and symptoms have limited value in allowing a clinician to make the diagnosis of dehydration, and therefore should not be relied on either to screen for, or to diagnose, dehydration. Instead, the diagnosis of dehydration should be made with laboratory measurements, clinical assessment, and knowledge of the patient's history. Two types of dehydration can be identified: (1) water loss dehydration (hyperosmolar) and (2) salt loss dehydration (hypoosmolar). Long-term care facilities should have ongoing interdisciplinary educational activities about the prevention of dehydration in view of the poor outcomes associated with it. Physicians, facility staff, and consultant pharmacists must pay close attention to individuals who are getting medications such as diuretics, ACE inhibitors, and angiotensin receptor blockers, as inadequate monitoring of fluid and electrolyte balance and the patient condition may lead to dehydration regardless of facility efforts to maintain hydration.

Table 9. *Starting Subcutaneous Hydration With Hyaluronidase (Adapted from Farr and Campbell.[73])*

Swab the infusion site with betadine or alcohol. (Potential sites include the pectoral area [men], lateral lower abdomen, thighs, and scapular area.)
Place a 22- or 24-gauge angiocatheter subcutaneously. Advance catheter to its hub, remove the metal stylus, leaving the silastic tubing in place, and secure. Alternatively, place a 25- or 27-gauge SC button, after priming with fluid, and secure. Cover with sterile, occlusive dressing.
Use infusate-primed tubing to connect the bag to the catheter. Immediately before fluid infusion, deliver 150 IU rHuPH20 by steady push over 1 minute via a Y-port proximal to the catheter site.
To administer infusion by gravity flow, hang the infusion bag so that the meniscus of the fluid is higher than the catheter, and adjust the fluid drip rate as prescribed. A pump set to a specified rate may also be used, but this adds to the cost of therapy and requires specialized expertise.
Check after 1 hour to make sure that the infusion rate is correct, and that the infusion site shows no sign of edema, leakage or disconnection, or fluid collection distal to the site. Check the patient for signs of fluid overload.

Often, dehydration can be treated with oral rehydration or by subcutaneous infusion, without requiring hospital transfer. The availability of recombinant hyaluronidase has made subcutaneous infusion a more accessible and acceptable method to treat mild to moderate dehydration in long-term care.

Finally, the public, academic, political, legal, and regulatory discourse about dehydration needs to change. While dehydration may occur because of inadequate care, it also occurs despite appropriate care, which is similar to many other conditions and negative outcomes in susceptible individuals, including other emotionally charged outcomes such as pressure ulcers. In addition, the condition is often misdiagnosed based on superficial assessment or misinterpretation of laboratory test results. Because of common misunderstanding or an incomplete evaluation of the patient and circumstances, the diagnosis should be reviewed and verified before intervention (including hospital transfer or hospital admission), and should not be used to presume poor care. Presuming "guilt" without a rational appraisal and understanding of the patient and his or her circumstances does not improve care at any time. An approach to dehydration including an earlier rather than delayed diagnosis benefits the patient and the health care team and should serve us all better in the future.

'Tis a little thing
To give a cup of water; yet its draught
Of cool refreshment, drained by fevered lips,
May give a shock of pleasure to the frame
More exquisite than when nectarean juice
Renews the life of joy in happiest hours.
Sir Thomas Noon Talfourd (1795–1854)
Ion Act 1 Sc 2

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REFERENCES

1. Morley JE. A brief history of geriatrics. J Gerontol A Biol Sci Med Sci 2004;59:1132–1152.
2. Thomas DR, Tariq SH, Makhdomm S, Haddad R, Moinuddin A. Physician misdiagnosis of dehydration in older adults. J Am Med Dir Assoc 2003;4:251–254.
3. Rikkert MGMO, Hoefnagels WHL, Deurenberg P. Age-related changes in body fluid compartments and the assessment of dehydration in older age. In: Arnaud M, Vellas BJ, Albarede JL, Garry PJ, eds. Hydration and Aging. New York, NY: Springer Publishing Company; 1998:13–32.
4. Bossingham MJ, Carnell NS, Campbell WW. Water balance, hydration status, and fat-free mass hydration in younger and older adults. Am J Clin Nutr 2005;81:1342–1350.

5. Morgan AL, Sinning WE, Weldy DL. Age effects on body fluid distribution during exercise in the heat. Aviat Space Environ Med 2002;73: 750–757.
6. Egan G, Silk T, Zamarripa F, et al. Neural correlates of the emergence of consciousness of thirst. Proc Natl Acad Sci U S A 2003;100(25):15241–15246.
7. Silver AJ, Morley JE. Role of the opioid system in the hypodipsia associated with aging. J Am Geriatr Soc 1992;40:556–560.
8. Silver AJ, Morley JE, Ishimaru-Tseng TV, Morley PM. Angiotensin II and fluid ingestion in old rats. Neurobiol Aging 1993;14:519–522.
9. Phillips PA, Rolls BJ, Ledingham JG, et al. Reduced thirst after water deprivation in healthy elderly men. N Engl J Med 1984;311:753–759.
10. Phillips PA, Bretherton M, Johnston CI, et al. Reduced osmotic thirst in healthy elderly men. Am J Physiol 1991;261:R166–R171.
11. Miescher E, Fortney SM. Responses to dehydration and rehydration during heat exposure in young and older men. Am J Physiol 1989;257(5 Pt 2):R1050–R1056.
12. Mack GW, Weseman CA, Langhans GW, et al. Body fluid balance in dehydrated healthy older men: Thirst and renal osmoregulation. J Appl Physiol 1994;76:1615–1623.
13. Zappe DH, Bell GW, Swartzentruber H, Wideman RF, Kenney WL. Age and regulation of fluid and electrolyte balance during repeated exercise sessions. Am J Physiol 1996;270(1 Pt 2):R71–R79.
14. Rolls BJ, Phillips PA. Aging and disturbances of thirst and fluid balance. Nutr Rev 1990;48:137–144.
15. Hodak SP, Verbalis JG. Abnormalities of water homeostasis in aging. Endocrinol Metab Clin 2005;34:1–12.
16. Tian Y, Serino R, Verbalis JG. Downregulation of renal vasopressin V2 receptor and aquaporin-2 expression parallels age-associated defects in urine concentration. Am J Physiol Renal Physiol 2004;287:F797–F805.
17. Feig PU, McCurely DK. The hypertonic state. N Eng J Med. 1977; 297(27):256–277.
18. Mange K, Matsuura D, Cizman B, et al. Language guiding therapy: The case of dehydration versus volume depletion. Ann Int Med 1997;127: 848–853.
19. Miller M, Morley JE, Rubenstein LZ. Hyponatremia in a nursing home population. J Am Geriatr Soc 1995;43:1410–1413.
20. Ellison DH, Bert T. Clinical practice. The syndrome of inappropriate antidiuresis. N Engl J Med 2007;356(20):2064–2072.
21. Miller DK, Perry HM 3rd, Morley JE. Associations among the Mini Nutritional Assessment instrument, dehydration, and functional status among older African Americans in St. Louis, MO, USA. Nestle Nutr Workshop Ser Clin Perform Programme 1999;1:79–86.
22. Stookey JD. High prevalence of plasma hypertonicity among community-dwelling older adults: Results from NHANES III. J Am Dietetic Assoc 2005;105:1231–1239.
23. Stookey JD, Pieper CF, Cohen HJ. Is the prevalence of dehydration among community-dwelling older adults really low? Informing current debate over the fluid recommendation for adults aged 70+ years. Publ Hlth Nutr 2005;8:1275–1285.
24. Mazza AD, Morley JE. Update on diabetes in the elderly and the application of current therapeutics. J Am Med Dir Assoc 2007;8:489–492.
25. Warren JL, Bacon WE, Harris T, McBean AM, Foley DJ, Phillips C. The burden and outcomes associated with dehydration among US elderly. Am J Public Health 1994;84:1265–1269.
26. Snyder NA, Feigal DW, Arieff AI. Hypernatremia in elderly patients. A heterogeneous, morbid, and iatrogenic entity. Ann Intern Med 1987; 107:309–319.
27. Palevsky PM, Ghagrath R, Greenberg A. Hypernatremia in hospitalized patients. Ann Intern Med 1996;124:197–203.
28. Jensdottir AB, Rantz M, Hjaltadottir I, Guomundsdottir H, Rook M, Grando V. International comparison of quality indicators in United States, Icelandic and Canadian nursing facilities. Int Nurs Rev 2003;50: 79–84.
29. O'Neill PA, Faragher EB, Davies I, Wears R, McLean KA, Fairweather DS. Reduced survival with increasing plasma osmolality in elderly continuing-care patients. Age Ageing 1990;19:68–71.
30. Chassagne P, Druesne L, Capet C, Menard JF, Bercoff E. Clinical presentation of hypernatremia in elderly patients: A case control study. J Am Geriatr Soc 2006;54:1225–1230.
31. van der Steen JT, Mehr DR, Kruse RL, Ribbe MW, van der Wal G. Dementia, lower respiratory tract infection, and long-term mortality. J Am Med Dir Assoc 2007;8:396–403.
32. Weinberg AD, Pals JK, McGlinchey-Berroth R, Minaker KL. Indices of dehydration among frail nursing home patients: highly variable but stable over time. J Am Geriatr Soc 1994;42:1070–1073.
33. Kind AJ, Smith MA, Frytak JR, Finch MD. Bouncing back: Patterns and predictors of complicated transitions 30 days after hospitalization for acute ischemic stroke. J Am Geriatr Soc 2007;55:365–373.
34. Mentes JC, Culp K. Reducing hydration-linked events in nursing home residents. Clin Nurs Res 2003;12:210–225; discussion 226–228.
35. Sanders G, Mercer SJ, Saeb-Parsey K, Akhavani MA, Hosie KB, Lambert AW. Randomized clinical trial of intravenous fluid replacement during bowel preparation for surgery. Br J Surg 2001;88:1363–1365.
36. Price JD, Sear JW, Venn RM. Perioperative fluid volume optimization following proximal femoral fracture. Cochrane Database Syst Rev 2004; (1):CD003004.
37. Flaherty JH, Rudolph J, Shay K, et al. Delirium is a serious and under-recognized problem: Why assessment of mental status should be the sixth vital sign. J Am Med Dir Assoc 2007;8:273–275.
38. Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. JAMA 1996;275:852–857.
39. Mentes J, Culp K, Maas M, Rantz M. Acute confusion indicators: Risk factors and prevalence using MDS data. Res Nurs Health 1999;22: 95–105.
40. Leger JM, Moulias R, Robert P, et al. Agitation and aggressiveness among the elderly population living in nursing or retirement homes in France. Int Psychogeriatrics 2002;14:405–416.
41. Cacchione PZ, Culp K, Laing J, Tripp-Reimer T. Clinical profile of acute confusion in the long-term care setting. Clin Nurs Res 2003; 12:145–158.
42. Lieberman HR. Hydration and cognition: A critical review and recommendations for future research. J Am Coll Nutr 2007;26(5 Suppl):555S–561S.
43. Wilson MM, Morley JE. Impaired cognitive function and mental performance in mild dehydration. Eur J Clin Nutr. 2003;57(Suppl 2):S24–S29.
44. McGee S, Abernethy WB 3rd, Simel DL. Is this patient hypovolemic? JAMA 1999;281:1022–1029.
45. Eaton D, Bannister P, Mulley GP, Connolly MJ. Axillary sweating in clinical assessment of dehydration in ill elderly patients. BMJ 1994;308: 1271.
46. Kim MJ, Rolland Y, Cepeda O, Gammack JK, Morley JE. Diabetes mellitus in older men. Aging Male 2006;9:139–147.
47. Armstrong LE, Soto JA, Hocker FT, Casa DJ, Kavouras SA, Maresh CM. Urinary indices during dehydration, exercise, and rehydration. Int J Sport Nutr 1998;8:345–355.
48. Wakefield B, Mentes J, Diggelmann L, Culp K. Monitoring hydration status in elderly veterans. Western J Nurs Res 2002;14:132–142.
49. American Medical Directors Association. Dehydration and fluid maintenance: Clinical practice guidelines 2001. Biol Res Nurs 2006;7:197.
50. Mentes JC, Wakefield B, Culp K. Use of a urine color chart to monitor hydration status in nursing home residents. Biol Res Nurs 2006;7:197–203.
51. Simmons S, Alessi C, Schnelle J. An intervention to increase fluid intake in nursing home residents: Prompting and preference compliance. J Am Geriatr Soc 2001;49:926–933.
52. O'Keefe ST, Lavan JN. Subcutaneous fluids in elderly hospital patients with cognitive impairment. Gerontology 1996;42:36–39.
53. Challiner YC, Jarrett D, Hayward MJ, Al-Jubouri MA, Julious SA. A comparison of intravenous and subcutaneous hydration in elderly acute stroke patients. Postgrad Med J 1994;70:195–197.
54. Ferry M, Leverve X, Constans T. Comparison and subcutaneous and intravenous administration of a solution of amino acids in older patients. J Am Geriatr Soc 1997;45:857–860.

55. Slesak G, Schnurle JW, Kinzel E, Jakob J, Dietz K. Comparison of subcutaneous and intravenous rehydration in geriatric patients: a randomized trial. J Am Geriatr Soc 2003;51:155–160.
56. Dasgupta M, Binns MA, Rochoon PA. Subcutaneous fluid infusion in a long-term care setting. J Am Geriatr Soc 2000;48:795–799.
57. Schen RJ, Singer-Edelstein M. Subcutaneous infusions in the elderly. J Am Geriatr Soc 1981;29:583–585.
58. Schen RJ, Singer-Edelstein M. Hypodermoclysis. JAMA 1983;250: 1694–1695.
59. Hechtor O. Reconstitution of the dermal barrier to fluid diffusion following administration of hyaluronidase. Proc Soc Exp Med 1947;13:14–18.
60. Burket LC, Gyorgy P. Clinical observations on the use of hyaluronidase. Ann N Y Acad Sci 1950;52:1171–1179.
61. Forbes GB, Deisher RW, Perley AM, Hartmann AF. Effect of hyaluronidase on the subcutaneous absorption of electrolytes in humans. Science 1950;111:177–179.
62. Schwartzman J. Hyaluronidase: A review of its therapeutic use in pediatrics. J Pediatr 1951;39:491–502.
63. Anonymous. Hyaluronidase and hypodermoclysis. JAMA 1953;151: 644–645.
64. Constans T, Dutertre J-P, Froge E. Hypodermoclysis in dehydrated elderly patients: Local effects with and without hyaluronidase. J Palliative Care 1991;7:10–12.
65. Lipschitz S, Campbell AJ, Roberts MS, et al. Subcutaneous fluid administration in elderly subjects: Validation of an under-used technique. J Am Geriatr Soc 1991;39:6–9.
66. Dolal S, Bruera E. Dehydration in cancer patients: To treat or not to treat. J Support Oncol 2004;2:467–479.
67. Fainsinger RL. The use of hypodermoclysis for rehydration in terminally ill cancer patients. J Pain Symptom Manage 1994;7:298–302.
68. Bruera E, Legris MA, Kuehn N, Miller MJ. Hypodermaclysis for the administration of fluids and narcotic analgesics in patients with advanced cancer. J Pain Symptom Manage 19990;5:218–220.
69. Storey P, Hill HHJ, St Louis RH, Tarver EE. Subcutaneous infusions for control of cancer symptoms. J Pain Symptom Manage 1990;5:33–41.
70. Waldmann CS, Eason JR, Rambohul E, Hanson GC. Serum morphine levels. A comparison between continuous subcutaneous infusion and continuous intravenous infusion in postoperative patients. Anesthesia 1984;39:768–771.
71. Pirrello RD, Chen CT, Thomas SH. Initial experiences with subcutaneous recombinant human hyaluronidase. J Palliat Med 2007;10: 861–864.
72. Hussain NA, Warshaw G. Utility of clysis for hydration in nursing home residents. J Am Geriatr Soc 1996;44:969–973.
73. Farrand S, Campbell AJ. Safe, simple subcutaneous fluid administration. Br J Hosp Med 1996;55:690–692.