Carol Rees Parrish, R.D., M.S., Series Editor

Intravenous Fluids: It's More Than Just "Fill 'Er Up!"

Eugene C. Corbett, Jr.

This review highlights several important considerations in the management of intravenous fluids, specifically sodium and water administration. It emphasizes the fact that these are not only the key elements of routine intravenous fluid orders, but also body nutrients, which require administration within certain limits so as to avoid the adverse consequences of either excess or deficit. Included is a review of basic sodium and water distribution, regulation, and excretion. The sodium content of various salt-containing fluids and supplements are presented as well as a common example in which unintended but excessive intravenous sodium was provided. General principles underlying the administration of sodium and water are described.

INTRODUCTION

The goal of intravenous fluid (IV) administration is to carefully achieve and maintain a euvolemic and isotonic environment within the body as well as to provide for a variety of nutritional and pharmacologic interventions. The selection of an appropriate IV solution is dependent upon the fluid volume and electrolyte status of the individual patient as well as any additional specific therapeutic goal. Consideration also needs to be given to the ability of the individual patient to sustain fluid volume changes that result from intravenous administration of salt and water. Avoiding extracellular volume excesses in the elderly is one example of this. The purpose of this article is to review basic water and sodium metabolism and relate it to the choice of IV fluid as a function of the volumetric status of the "typical" hospitalized patient and their serum sodium concentration. For discussion of clinical conditions related to sodium aberrations, the reader is referred to additional pertinent literature (1–3, Table 7). It is a point of emphasis in this review that sodium and water are nutrients. As such, there are upper and

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Eugene C. Corbett, Jr., M.D., FACP, Bernard B. and Anne L. Brodie Professor of Medicine, Professor of Nursing, Division of General Medicine, Geriatrics & Palliative Care, University of Virginia Health Science Center, Charlottesville, Virginia.

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Table 1
Potential Sources of Fluid Excess or Loss in Hospitalized Patients

Intake
- Intravenous fluids
- Medications given via IV drip
- Water flushes given with crushed medications
- Water flushes to keep tubes patent
- Water contained in tube feedings or TPN

Output
- Stool/Urine
- Chest tubes
- Percutaneous drains
  - Biliary /Pancreatic
- Wound drainage
- Ostomies
- Naso/oro gastric tube suction
- Excessive drooling/sialorrhea
- Fistulas
  - Enterocutaneous
  - Spit fistulas
- Insensible losses
- *Accelerated* insensible losses including:
  - Burns
  - Tracheostomies
  - Fever
  - Kinair beds

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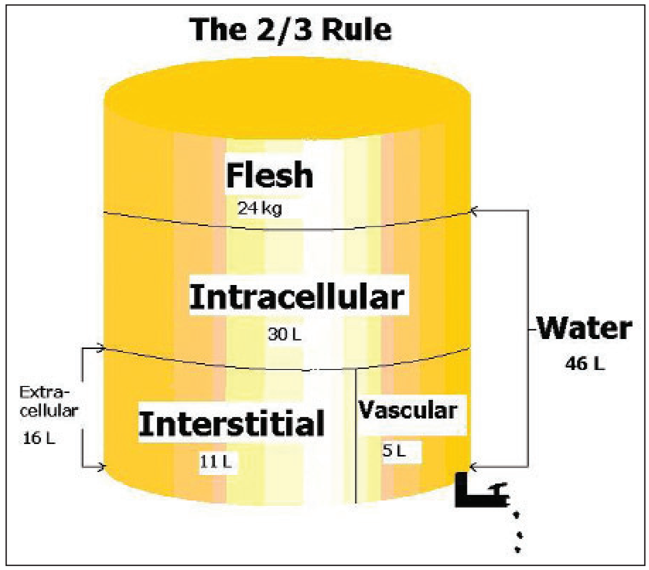

Figure 1. The distribution of body water within a euvolemic 70 kg (154 lb.) person. Used with permission from the University of Virginia Health System Nutrition Support Traineeship Syllabus (8).

Remember that 1 kg of water weight equals 1 liter as follows:

Flesh	24 Kg
Water	46 L
Intracellular	30 L
Extracellular	16 L
Interstitial	11 L
Vascular	5 L

lower limits to the amounts that are needed in order to maintain ideal physiologic homeostasis (4–5).

WATER

For the purpose of considering the fluid and electrolyte status at any one time, it is useful to imagine the body as a cylinder containing four compartments (Figure 1). Water free mass ("flesh") represents, on average, one-third of the body volume. The remaining two-thirds in a normal weight individual represent water volume. In turn, approximately two-thirds of the total body water is contained in the intracellular space, with the remaining third in the extracellular compartment. This latter space is further subdivided into the interstitial and the vascular spaces. In a normal individual, the interstitial space contains about two-thirds of the extracellular volume. The vascular space, the smallest of the body's fluid compartments, represents approximately one-third of the extracellular volume and about one-ninth of the body's water space overall.

Maintenance of the euvolemic state requires replacement of normal daily volume losses. These include primarily insensible and renal losses, the former including solute-free pulmonary water loss ("free water"). Because the kidney's water concentrating ability spans a large range and continually adapts to variations in water intake availability (e.g., urine specific gravity can vary between 1.001 to 1.040, or between 30 to 1200 mOsm/L), estimation of *approximate* water requirements using the "2/3 rule" is normally sufficient in the clinical setting (Figure 1). Because there is an upper limit to renal solute concentrating ability, as well as a mandatory loss of insensible free water, most individuals require a minimum of 1.5 to 2 liters of water replacement per day as follows:

1. **Renal excretion: minimum 1 liter daily.**
   In a 24-hour period, the human body under normal conditions produces about 1000–1500 milliosmoles of ionic and molecular waste for renal excretion. The upper limits of renal concentration ability are reached at about 1200–1500 milliosmoles/liter. Under conditions of illness and therapeutic intervention, fluid requirements increase for solute excretion, e.g. increased waste excretion due to enhanced catabolism, pharmacologic degradation products, increased acidotic excretion.
2. **Minimal insensible loss is approximately 0.5 to 1 liter daily.**
   Whereas renal fluid losses are a mix of water and solute waste, pulmonary water loss is solute-free water vapor. This is termed "insensible" loss because of the fact that it is not normally observed nor directly measured. Factors that increase insensible water loss include fever, increased ventilatory rate, tracheostomy, mechanical ventilation as well as enhanced sweating (Table 1).
3. **Miscellaneous.**
   Miscellaneous fluid losses: minor amounts of water are lost through the gastrointestinal tract, usually less than 150 mL/24 hrs. Such losses can increase considerably under illness conditions.

Thus, with an intake of approximately 2 liters of water per day (equivalent to an IV infusion rate of about 85 mL/hr), normal body water homeostasis can be maintained in the absence of exaggerated fluid gains or losses. For the average person on oral intake, about half of this comes from ingested fluids while the other half is contained within foods that are eaten.

Disease processes and care interventions add an additional challenge to the body's ability to maintain a euvolemic state. These include water losses that result from diarrhea, vomiting, increased sweating and enhanced insensible loss, or the diuretic effects of drugs (Table 1). Gains in body fluid volume can result from cardiac failure, impairment in renal or hepatic function (low albumin), impaired capillary endothelial function in the setting of sepsis/trauma/ARDS, excessive water retention, the effect of drugs, or excessive sodium intake.

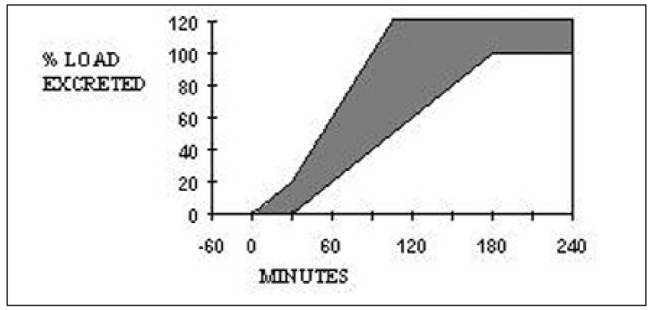

Figure 2. Water elimination. The effect of a standard water load on renal function. Shaded areas indicate the range of values obtained in 24 healthy adults. A water load of 20 ml per milogram of bodyweight was given between 0 and 30 min. The bottom panel indicates cumulative excretion expressed as a percentage of the total. From Felig, Endocrinology & Metabolism, 3rd edition, 1995, figure 9-22, pg. 423. With permission from McGraw Hill Companies.

Under normal physiological conditions, neurohumoral adjustments to changes in the body's water intake and losses begin to occur within minutes. For example, the intake of free water beyond the body's euvolemic need is generally eliminated within three hours of ingestion (Figure 2). On the other hand, vomiting results in an almost immediate increase in antidiuretic hormone (vasopressin) levels and the initiation of renal water conservation.

SODIUM

The body's fluid volume is regulated to maintain an isotonic (iso-osmolar) state in all water compartments. The extracellular compartments of the body are dominated by sodium (~140 mEq/L) and chloride (~100 mEq/L). In contrast, the intracellular compartment dominated by potassium (~150 mEq/L) and phosphate (~50 mEq/L). Thus, over 90% of dissolved body sodium is contained within the *vascular* and *interstitial* spaces, while over 90% of body potassium is located within the *intracellular* space. In addition,

Table 2
Sodium Distribution in the Body

Compartment or Tissue	*Sodium Distribution*
Plasma	11%
Interstitial	29%
Connective Tissue	12%
Bone	43%
• Exchangeable	14%
• Non-Exchangeable	29%
Intracellular	2.5%
Transcellular	2.5%
Total	100%

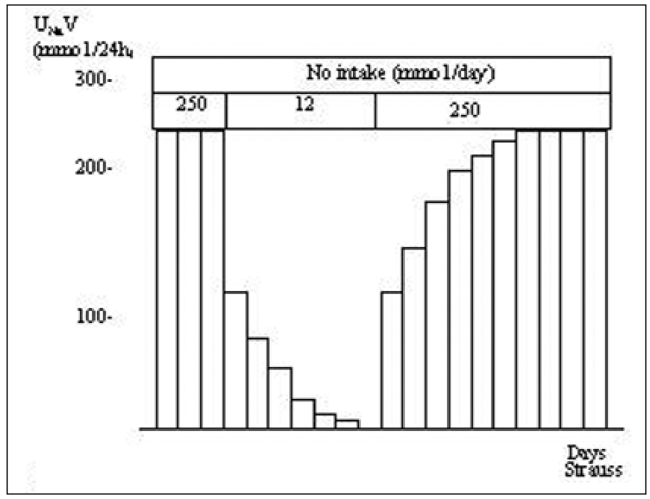

Figure 3. Sodium elimination. Urinary sodium excretion (mmol/day), predicted by the model (appendix, equation 2), following a step change in sodium intake from 250 mmol/day to 12 mmol/day and back to 250 mmol/day. It is assumed that about 12 mmol/day is lost by non-renal routes. From reference 7. With permission from Elsevier.

variable amounts of sodium are stored in bone, approximately half of which remains physiologically available (Table 2).

Typically, the amount of ***sodium excretion*** in an individual on a daily basis is equivalent to their average sodium intake. Thus the amount of sodium excretion in 24 hours varies from individual to individual over a large range. In the United States this is generally between 40 and 450 mEq (mmol). Under experimental conditions, human sodium conservation can be maintained with as little as 5–10 mEq intake in 24 hours due to the ability of the kidney to tightly conserve sodium (6). Potassium excretion also varies with intake. However, in contrast to the ability of the kidney to conserve sodium even at very low intake levels, renal potassium conservation is more limited. Thus, under conditions of no potassium intake and normal renal function, renal losses continue at a minimum level of approximately 20 mEq daily (also known as the "renal potassium leak").

Moreover, whereas water conservation and excretion regulatory mechanisms operate almost on a minute-to-minute basis, adjustments in renal excretion to daily variations in sodium intake typically take a *number of days* to respond (Figure 3) (7). For example, when a hospitalized patient receives an intravenous infusion which contains an amount of sodium *in excess* of their normal average intake, a number of days will pass before their sodium excretion begins to match this higher intake level. The ramifications of the resulting sodium accumulation can be significant for patients who normally subsist on lower sodium intake levels such as the elderly population.

As an illustration, consider an elderly woman who is admitted to the hospital for dehydration secondary to pneumonia whose normal average sodium intake is 100 mEq daily (2300 mg), a figure in the midrange of the Recommended Dietary Allowance (RDA). On admission to the hospital, an IV infusion of normal saline (containing 154 mEq sodium/liter) is begun at the rate of 150 mL/hr. After 24 hours, she no longer appears dehydrated and her infusion rate is decreased to 125 mL/hr for another two days after which it is discontinued because of adequate oral intake. Over the 72-hour period of IV infusion, she has received a total of the following intravenous ingredients:

- 9.6 liters of water
- 1,478 mEq of sodium (34,000 mg!)

In contrast to her normal living circumstance in which she would have cumulatively taken in 300 mEq (6900 mg) of sodium over the same time period of 72 hours, this three-day infusion of normal saline exceeded her usual intake by about 1,178 mEq (27,100 mg) of sodium. In adjusting this value to account for what was needed to correct for her level of dehydration

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Table 3
Electrolyte Content of IV Solutions, per Liter

Fluid	*Na*	*K*	*Glucose*	*Tonicity*	*mOsm/liter*
0.9 NS*	154	0	0	Slightly hypertonic	304
0.45 NS	77	0	0	Hypotonic	154
0.25 NS	38	0	0	Hypotonic	77
Lactated Ringers (LR)	130	4	0	Isotonic	280
D_5W	0	0	50 gm	Hypotonic	0**
D_5W 0.45 NS	77	0	50 gm	Hypotonic	154**
0.9 NS + 150 mEq $NaHCO_3$	308	0	0	Very Hypertonic	616

*One liter of 0.9 NS contains approximately 2 teaspoons of table salt.
**Note: the 50 grams of dextrose in a liter bottle equates to an osmolarity of 277 mOsm/L. However, the dextrose is rapidly metabolized and does not contribute to serum osmolarity unless the patient is hyperglycemic.
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Table 4
Comparative Sodium Levels

	Sodium Content		
Source	*mEq*	*mg*	*NaCl (mg)*
Lowest required intake (6)	5/day	115	287
Recommended Dietary Allowance (RDA)	47–147	1,100–3,300	2750–8250
1 liter 0.9 normal saline	154	3,542	8,855
U.S. intake, range per day	50–450	1,150–10,350	2,875–25,875
0.45 NS Infusions			
75 mL / hr × 24 hrs	138	3,188	7,970
100 mL / hr × 24 hrs	185	4,250	10,625
125 mL / hr × 24 hrs	231	5,313	13,282
0.9 NS Infusions			
75 mL / hr × 24 hrs	277	6,371	15,927
100 mL / hr × 24 hrs	369	8,487	21,217
125 mL / hr × 24 hrs	462	10,626	26,565
150 mL / hr × 24 hrs	554	12,742	31,855
Addition of $NaHCO_3$ to 0.45 & 0.9 NS Infusions/ Liter*			
75 mEq in 0.45 NS	152	3,496	8,740
150 mEq in 0.9 NS	304	6,992	17,480

*Only occasionally ordered. The astute pharmacist will call attention to the hypertonic sodium load.
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on admission (a typical dehydration range would be 2%–5% body weight), at most, about one-third of her total infusion was actually needed to bring her to euvolemic status. Thus, the remainder of the infused sodium (2/3 × 1178 = 785 mEq Na) represents an amount equivalent to seven or more additional days of intake beyond her usual amount. Because of the normal delay in adjustment of her renal sodium excretion to match the new intake level, her extracellular sodium content has therefore been increased by approximately 785 mEq. This results in an isotonic volume expansion of about 6 liters (785 mEq/140 mEq/L = 6L). This represents an excessive intake of 18,000 mg of sodium, or approximately 12 teaspoons of table salt! If her IV infusion had been continued for a longer period of time, or at a higher infusion rate, an additional amount of sodium would have been infused and accumulated in her extracellular compartment.

Particularly in patients with limited cardiac, renal or hepatic function, such excesses in volume expansion can lead to interstitial edema and its cardiopulmonary consequences. Of additional concern, if her oral intake of water was also compromised because of limited water access, *her free water intake requirement would not have been met*, potentially leading to hypernatremia (3) and the discomfort of excessive thirst. Adverse outcomes such as these are preventable with careful avoidance of excessive sodium infusion and provision of free water. The choice of the appropriate amount and concentration of hydration fluid requires the same care as the selection of a correct medication dose.

Tables 3 and 4 indicate sodium content levels in standard IV fluids and at commonly ordered infusion rates. For comparison, the RDA for sodium intake is between 47–147 mEq (1,100–3,300 mg) per day (5). Because actual dietary sodium intake in the United States is generally higher than this and varies between 50 and 450 mEq per day (1,150–10,350 mg), sodium deficiency is rarely observed.

It is important to emphasize that a liter of normal saline contains 154 mEq (3,542 mg) of sodium, an amount that is just above the upper Recommended Dietary Allowance range. This is equivalent to an amount just under two teaspoons of table salt per liter. In comparison, the average concentration of sodium in the extracellular body compartment is ~140mEq/liter.

Table 5
Salt and Salt Substitutes

1 mEq (mmol) Na = 23 mg Na
1 mg Na = 2.5 mg *NaCl*

	Per teaspoon		
Product	*mEq*	*mg*	*NaCl (mg)*
Salt	100	2300	5750
Sea Salt	95	2176	5440
Garlic salt	89	2050	5125
Garlic powder	0.04	1	2.5
Black pepper	0.04	1	2.5
Lemon Pepper	28	487	1217
Morton Lite Salt	48	1100	2750
Morton Salt Substitute	0	0	0
No Salt	0.9	20	50
Nu-Salt	0	0	0
Mrs. Dash seasonings	0	0	0
Chef Paul Prudhomme Magic Salt Free All Purpose Blend Seasoning	0	0	0
AlsoSalt	0	0	0
Blue Crab Bay Herbs for Seafood	0	0	0
Soy sauce	15	343	857
Low sodium soy sauce	9	200	500
Vinegar	0	0	0
Mustard	3	65	162
Dill pickle (1 spear)	40	928	2320
Beef bouillon (1 cube)	38	864	2160

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Thus, normal saline contains no free water and is slightly hypertonic to normal body osmolarity. For comparative interest, Table 5 contains the sodium content of common salt substitutes.

MAINTENANCE FLUID REQUIREMENTS FOR IV INFUSION

For the average person who is euvolemic, iso-osmolar (isotonic) and limited to IV replacement alone (NPO),

Table 6
Sodium Concentration in Body Fluids

Body Fluid	*Concentration*
Serum	135–145 mEq/L
Saliva	10–55 mEq/L
Gastric juice	10–100 mEq/L
Pancreatic juice	120–140 mEq/L
Bile	120–160 mEq/L
Intestinal	105–145 mEq/L
Stool / diarrhea	1–100 mEq/L
Skin	1–80 mEq/L

a *minimum* of two liters of IV is recommended. The equivalent of one liter of 0.9% normal saline contains sufficient sodium replacement for a 24-hour period in the typical clinical circumstance. The remainder of the intravenous volume replacement can be provided in the form of free water as represented in a solution of 5% dextrose in water (D_5W). An equivalent example of a minimum standard IV "maintenance fluid" for 24 hours would be achieved with an order of D_5 in half-normal (0.45) saline to run at 85 mL per hour. This would provide approximately two liters of volume with 156 mEq of sodium plus an additional liter of free water replacement over a 24-hour period. Writing for 75, 100 or 125mL/hr of 0.45 NS, would provide respectively 1.8, 2.4 and 3 liters of volume in 24 hours. The obvious advantage of using 0.45 normal saline is that it contains half free water.

GENERAL RECOMMENDATIONS FOR IV FLUID SELECTION

The following guidelines are recommended for achieving and maintaining a euvolemic and isotonic internal environment under most clinical circumstances (Table 7):

1. ***Achieving Euvolemia***
   a. From a comparison of an individual's normal with their current body weight and clinical examination, determine the patient's volume status and estimate if any, the degree of variation from euvolemia;
   b. If *euvolemic*, only maintenance fluids need to be prescribed, as in the patient who may be NPO;
   c. The *dehydrated* patient will require an estimated amount of isotonic fluid (Table 3) to bring them to normal volume status. Following achievement of this, maintenance fluid replacement should then be instituted;
   d. Volume replacement because of additional clinical volume loss (diarrhea, blood loss, vomiting/NG suction, exaggerated insensible loss (fever)) needs to be estimated from clinical examination, measured intake/output volume, body weight and the sodium content of the specific fluid lost (Table 6);
   e. The *volume expanded* patient generally requires maintenance free water volume replacement and very limited sodium intake, as well as diuresis as indicated by the clinical circumstance. If they are isotonic or hypertonic, fluid replacement should be limited to free water replacement only. This will also help to facilitate sodium excretion (natriuresis).
2. ***Achieving Isotonicity* (iso-osmolar status)**
   a. Tonicity of body fluids can be measured directly (serum osmolarity), or estimated approximately from the serum sodium concentration ($[Na] \times 2 + 10$), or more exactly from the formula $[Na] \times 2 + \text{glucose}/18$;
   b. The *isotonic* patient requires only maintenance sodium replacement unless they are also dehydrated (see 1c,d above);
   c. The *hypertonic* (*hypernatremic*) patient requires additional free water replacement according to the following formula:

      Average Total body water (TBW) = $0.66 \times$ body weight (kg)

      Water deficit = $\text{TBW} \times \{\text{Serum [Na]} - 140\} / 140$

      Generally it is best to give no more than half of the calculated deficit over 12 hours and recalculate the deficit based upon repeated clinical measurements. Examples include patients with renal (diabetes insipidus) or extrarenal volume losses (vomiting, diarrhea).

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Table 7
Examples of Sodium and Water Abnormalities

Hyponatremia with Hypovolemia
(Decreased Total Body Water [TBW] and Na; relatively greater decrease in Na)
- Extrarenal losses
  - GI: vomiting, diarrhea, fistulas, ostomies
  - Third-space losses: pancreatitis, peritonitis, small-bowel obstruction, rhabdomyolysis, burns, post-operative period
- Renal losses
  - Diuretics
  - Osmotic diuresis (glucose, urea, mannitol)
  - Mineralocorticoid deficiency
  - Salt-losing nephropathies

Hyponatremia with Euvolemia
(Normal TBW; near-normal total body Na)
- Hypothyroidism
- Glucocorticoid deficiency
- States that increase release of ADH (postoperative, narcotics, pain, emotional stress)
- Syndrome of inappropriate ADH secretion
- Primary polydipsia

Hyponatremia with Hypervolemia
(Increased total body Na; relatively greater increase in TBW)
- Extrarenal disorders
  - Congestive heart failure
  - Hepatic cirrhosis
- Renal disorders
  - Nephrotic syndrome
  - Acute renal failure
  - Chronic renal failure
- Syndrome of inappropriate ADH secretion

Hypernatremia with Hypovolemia
(Decreased TBW and Na; relatively greater decrease in TBW)
- Extrarenal losses
  - GI: vomiting, diarrhea
  - Skin: burns, excessive sweating
- Renal losses
  - Diuretics medications
  - Osmotic diuresis (glucose, urea, mannitol)
  - Diabetes Insipidus

Hypernatremia with Euvolemia
(Relatively decreased TBW; increased total body Na)
- Inability to access free water
- Patients on tube feeding
- Cannot reach water glass
- NPO on isotonic IV fluids only

Hypernatremia with Hypervolemia
(Increased TBW, greater increase in Na)
- Hypertonic IV fluid administration without free water
- Total parenteral nutrition with inadequate free water
- Mineralocorticoid excess

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d. The *hyponatremic* patient requires a determination of whether the hypotonic state needs correction, and if so, whether water restriction or sodium supplementation is required:
   1. No correction is generally necessary if [Na] is >130 mEq/L and not trending downward (stable);
   2. Water restriction (generally 1200–1500 mL/day) is required if a diagnosis of the syndrome of inappropriate antidiuretic hormone secretion (SIADH) applies, especially if the [Na] is <130 mEq/L and/or is trending downward;
   3. Sodium supplementation is generally indicated only for the rare patient who is considered truly sodium depleted. Typically these patients are also volume depleted and generally respond to isotonic volume replacement (they are not free water deficient).

CONCLUSION

Achievement and maintenance of a euvolemic and isotonic internal environment requires careful adjustment of water and sodium intake that reflects the excesses and/or deficits of these physiologically linked nutrients. Optimal care of the fluid status of an individual also requires an appreciation of the limits of sodium and water handling which can vary from patient to patient depending upon such factors as age, renal and cardiac function, and variations in their otherwise routine intake of sodium. Under most clinical circumstances, careful attention to amounts of infused sodium and water in conjunction with appropriate clinical assessment will provide for optimal establishment and maintenance of the patient's fluid status. Standard assessment methods include physical examination, serum electrolytes, and accurate body weight and fluid intake and output measurements. Consistent application of these principles will insure that the internal fluid environment of the patient remains normal and adverse outcomes are otherwise avoided. ■

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