

Commentary

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How to select optimal maintenance intravenous fluid therapy

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Summary

Hyponatraemia is the commonest electrolyte abnormality in hospitalized patients. If the plasma sodium concentration (P_{Na}) declines to ~ 120 mM in <48 h, brain cell swelling might result in herniation, with devastating consequences. The volume and/or the composition of fluids used for intravenous therapy often contribute to the development of

acute hyponatraemia. Our hypothesis is that the traditional calculation of the daily loss of insensible water overestimates this parameter, leading to an excessive daily recommended requirement for water. We offer suggestions to minimize the risk of iatrogenic hyponatraemia.

Introduction

Hyponatraemia is defined as a plasma Na^+ concentration (P_{Na}) <136 mM.¹ While this could result from a deficit of sodium (Na^+), it is most often due to a surplus of water (Figure 1, Table 1). To create a positive water balance,^{1,2} input of water must exceed output. A low water output is usually due to the release of vasopressin, often because of non-osmotic stimuli (Table 2).³ When this occurs, patients cannot produce the large water diuresis that prevents a fall in their P_{Na} .⁴ In fact, vasopressin acts throughout the 24-h period in normal volunteers despite episodic intake of water (Figure 2). Hence normal humans rarely have a water diuresis unless their arterial P_{Na} falls below 136 mM. In contrast, when hospitalized adults⁴ and paediatric⁵ patients have a P_{Na} that is <136 mM, they do not have a dilute urine because of renal actions of vasopressin, released in response to non-osmotic stimuli.

Outline of the problem

Intravenous fluid administration is common and more than 75% of currently recommended maintenance fluids are given in the form of electrolyte-free water (0.2% saline).^{6,7} Because patients who are ill often have non-osmotic stimuli for the release of vasopressin, it is not surprising that hyponatraemia is the commonest electrolyte disorder in hospitalized patients, in part due to this electrolyte-free water input.⁸ A large fall in the P_{Na} in <48 h should cause cell swelling because the ICF volume is inversely related to the P_{Na} (Figure 1).¹ Because brain cells occupy approximately 2/3 of the intracranial volume, brain-cell swelling is very likely to increase intracranial pressure and predispose to brain herniation, since the brain resides in a rigid bony structure and there is only a small volume of intracranial water that can be lost when there is a small rise in intracranial pressure (the volume in the cerebrospinal fluid).⁹ Children are at greater risk

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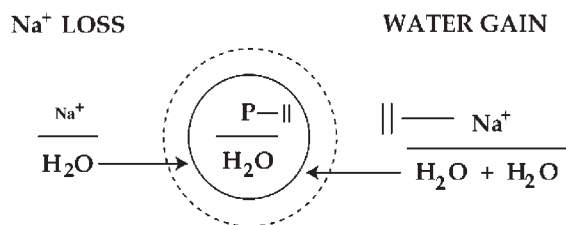


Figure 1. Water movement across cell membranes. The solid circle represents the normal ICF volume and the dashed circle represents the expanded ICF volume when hyponatraemia is present. Water channels permit the cell membranes to be permeable to water. Osmotic forces are immense. Therefore, independent of whether hyponatraemia is due to a negative balance for Na^+ as shown on the left, or a positive balance for water shown on the right, the ICF volume will rise to the same extent because the number of particles restricted to the ICF compartment (P) does not change appreciably in most cells, and Na^+ ions are restricted to the ECF compartment for the most part.

because their brains have a larger ICF volume (more cells) per total skull volume. Nevertheless, not all causes of acute hyponatraemia are associated with brain cell swelling. For example, when a patient undergoes a transurethral resection of the prostate, lavage fluid may enter the vascular compartment and be retained in the ECF compartment.¹⁰ If this fluid contains osmoles such as sorbitol or mannitol that remain extracellularly, the ECF volume will be expanded by an iso-osmotic, Na^+ -free solution. Because most of these solutions are half-isotonic, there will be a modest degree of expansion of the ICF compartment. Accordingly, little of this added Na^+ -free water will enter cells and cause brain-cell swelling despite the large fall in P_{Na} .¹¹ Hence it is important to include in the clinical analysis the condition that caused the hyponatraemia, and not simply treat a laboratory P_{Na} value.

Our view is that a fall in the P_{Na} is preventable if intravenous fluid therapy is tailored to

Table 1 Physiological classification of hyponatraemia

I. Deficit of Na^+ in the ECF compartment

1. Non-renal loss of Na^+ (sweat, gastrointestinal tract)
2. Renal loss of Na^+ :
 - Lack of a stimulator for Na^+ reabsorption (e.g. aldosterone)
 - Presence of an inhibitor (e.g., ECF volume expansion or a diuretic)
 - Inborn errors that interfere with the normal reabsorption of Na^+

II. Surplus of electrolyte-free water in the ECF compartment

1. Determine the source of electrolyte-free water:
 - Gastrointestinal tract
 - Intravenous fluids
 - Urine (need to excrete urine with a $Na^+ + K^+$ concentration $>P_{Na}$ or the infused fluids⁴)
2. Determine why there is too little excretion of electrolyte-free water:
 - Vasopressin is present (see Table 2)
 - Vasopressin can be absent
 - Low distal delivery of filtrate ('trickle-down hyponatraemia'⁴⁶)
 - Renal failure

Note that hyperglycaemia and/or high mannitol-like solutes in plasma might be contributing to the degree of hyponatraemia.

Table 2 High vasopressin levels in patients with hyponatraemia

1. Causes that are readily reversible:
 - Low 'effective' circulating volume to cause the release of vasopressin
 - Anxiety, stress, pain, nausea
 - Drugs causing nausea (e.g. many of the currently used chemotherapeutic agents), the central release of vasopressin (e.g. morphine, barbiturates, 'ecstasy') or enhancement of the renal effects of vasopressin (e.g. certain oral hypoglycaemics, non-steroidal anti-inflammatory agents, anticonvulsants such as carbamazepine)
 - Endocrine causes (e.g., hypothyroidism, adrenal insufficiency)
 - Exogenous dDAVP, oxytocin
2. Causes that cannot be reversed rapidly:
 - Vasopressin-producing tumours
 - CNS or lung lesions (may cause 'reset osmostat')
 - Granulomas
 - Certain metabolic lesions (e.g. porphyria)

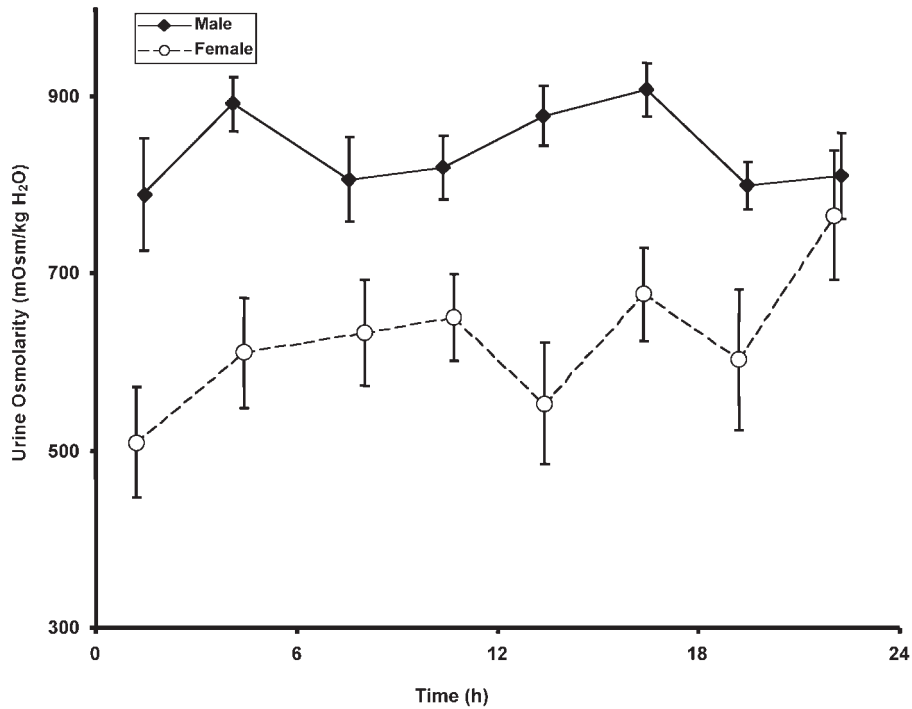


Figure 2. Diurnal variation in the urine osmolality. Data were gathered in 75 volunteers (aged 17–64 years). Voluntary voiding occurred at 2-h intervals for the 16 h while awake and when the subject woke up at night to void. There were no restrictions on water intake, diet, or activity. No subject took medications. The males ($n=45$) are depicted by the solid diamonds connected by a solid line and the females ($n=30$) by the open circles connected by a dashed line.

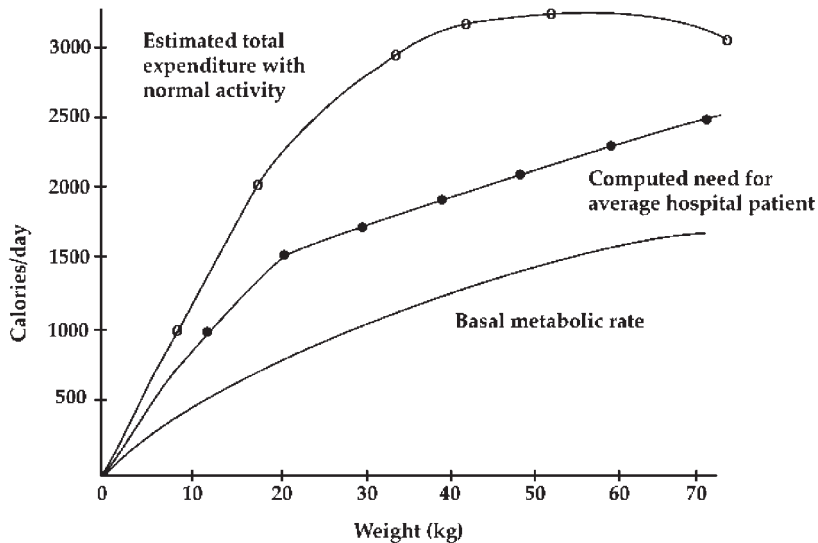


Figure 3. Comparison of energy expenditure in the basal and ideal state. This figure was redrawn, based on a publication by Holliday and Segar.¹⁵ The upper and lower lines were plotted from the data of Butler and Talbot.⁴⁷ Weights at the 50th percentile level were selected for converting calories at various ages to calories related to weight. The computed line was derived from the following equations: ages 0–10 kg, 100 cal/kg; 10–20 kg, 1000 cal +50 cal/kg for each kg over 10 kg; 20 kg and up, 1500 cal/kg +20 cal/kg for each kg over 20 kg.

the needs of individual patients.⁵ Hence the first question to ask is why do we currently infuse so much hypotonic saline.

Usual reasons for intravenous fluid administration

There are five common reasons to infuse intravenous fluids (Table 3). Only the last two deal directly with the development of hyponatraemia, and they will be emphasized.

(i) Defend normal blood pressure

A reduced ECF volume, if accompanied by haemodynamic collapse, has a greater initial priority than all but the most serious degrees of expansion of the ICF volume. Isotonic saline is the initial therapy, but hypertonic saline should be given if there is both a low ECF volume and an acutely low P_{Na} , as seen in people with excessive sweat loss accompanied by a large intake of water.^{12,13}

Patients who are anaesthetized usually have a fall in blood pressure in the absence of a contracted ECF volume because anaesthetic agents diminish venous tone.⁴ An infusion of isotonic saline helps avoid this type of hypotension.

(ii) Return the ICF volume to normal

In a patient with acute hyponatraemia, the ICF volume in the brain rises and could become dangerously high with a more prominent decline in the P_{Na} . Shrinking the ICF volume becomes an urgent priority only when there are CNS symptoms or a P_{Na} in the mid-to-low 120 mM range.

When there is a large water deficit in the ICF compartment (indicated by a $P_{Na} > 140$ mM), electrolyte-free water (often 5% dextrose in water or D₅W) should be infused. Care should be taken to avoid inducing a significant degree of hyperglycaemia.¹⁴

(iii) Replacing ongoing renal losses

This therapy is directed at patients who do not have an antecedent condition that led to the retention of salt and water.

(iv) Giving maintenance fluids to match insensible losses

The traditional guidelines for maintenance fluid infusion focus on the need to replace insensible loss of water for heat dissipation—the latter was related to caloric expenditure based on data and deductions published almost 50 years ago,¹⁵ and was reiterated recently^{16,17} These authors stated: ‘Maintenance requirements for water in individuals is determined by their caloric expenditure. By means of the following formula (summarized in Figure 3) the caloric expenditure of hospitalized patients can be estimated with sufficient accuracy by weight alone. Significant deviations from this relation exist, including excessive obesity, the elderly, and patients with infections.’ Notwithstanding, alternative views have been expressed,^{5,18} because traditional recommendations require that hypotonic saline be infused. We emphasize that there is a danger in infusing a large volume of electrolyte-free water because it will accumulate when vasopressin acts, providing that there is not a very large volume of sweat.

Table 3 Indications for the prescription of intravenous fluids

I. Highest priority

- a) Defend haemodynamics
 1. Re-expand a severely contracted ECF volume
 2. Prevent a fall in blood pressure when venous tone is low (e.g., anaesthesia)
- b) Return the ICF volume towards normal
 1. Acute hyponatraemia that is symptomatic
Infuse hypertonic saline to raise the P_{Na} by 5 mM in 1–2 h
 2. Chronic hyponatraemia with a seizure
Infuse hypertonic saline to raise the P_{Na} by 5 mM, but maximum is 8 mM/day; a lower target should be set if the patient is malnourished or K^+ -depleted
 3. Chronic asymptomatic hyponatraemia
Raise the P_{Na} by up to 8 mM/day, slower rate if the P_K is low in a malnourished patient

II. Moderate priority

1. Re-expand a modestly contracted ECF volume
Replace ongoing losses
Avoid oliguria
Match estimated electrolyte-free water loss in sweat and in the GI tract

Moreover, it is not uncommon for patients to seek medical care and arrive in hospital with a low P_{Na} because they drank electrolyte-free water while vasopressin was released secondary to their illness (Table 2). It would be a grave error to give them electrolyte-free water. In the next section, we shall provide evidence to suggest that the classical calculations of losses of insensible water lead to an overestimation of the need for hypotonic fluid administration. This error is compounded by a perceived need to excrete a larger urine volume with a more 'comfortable' urine osmolality.¹⁵

(v) *The need for glucose as a fuel for the brain*

A theoretical advantage of infusing 2 l of D₅W is that this infusion provides 100 g of glucose, which is almost equivalent to the 120 g of glucose oxidized daily by the brain.¹⁹ The unstated assumption is that this infused glucose is not oxidized by other organs, which in turn is dependent on their ability to oxidize fatty acids,²⁰ because fatty acid oxidation inhibits the oxidation of glucose.²¹ Therefore, if the infusion of glucose raises the plasma glucose concentration sufficiently to stimulate the release of insulin,²² little of this infused glucose will be available for oxidation in the brain, because of the antilipolytic actions of insulin. On the other hand, if glucose were needed (i.e. to prevent the development of hypoglycaemia and/or to minimize protein catabolism), it need not be given as D₅W with its electrolyte-free water load—rather glucose could be added to infused saline.

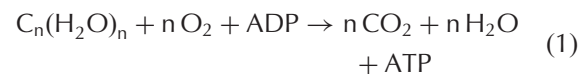
Analysis of insensible water loss

Heat is produced continuously by intermediary metabolism.²³ This heat must be dissipated to avoid a life-threatening rise in body temperature. Part of this vital function is served by evaporation of surface water from the skin and the respiratory tract. While this rationale is correct, we question whether the recommendations derived from it are correct from a quantitative perspective.¹⁵

Water production by metabolism and its loss via the lungs

We begin with this component of water balance to largely dismiss it as a factor that would change the P_{Na} . Our rationale is as follows—

metabolic production of CO₂ and water occur in a 1:1 proportion during the oxidation of carbohydrates (C_n(H₂O)_n) (equation 1) and fatty acids (–CH₂)_n (equation 2). Moreover, these two end-products are eliminated together in alveolar air in a 1:1 proportion, providing that the arterial pCO₂ is close to 40 mmHg (Figure 4).²³ The reason for this parallel excretion of water and CO₂ is that the partial pressures of water vapour and CO₂ are virtually equal in alveolar air (47 and 40 mmHg) and in inspired air (close to zero after air is warmed to 37°C²⁴). Therefore, water loss via exhaling alveolar air is equal to its metabolic production, so these two pathways can be ignored unless the patient is hyperventilating and/or is on a ventilator and is inspiring humidified air warmed to body temperature.²³ Only water evaporation from the upper respiratory tract results in a negative water balance.



Water loss in sweat

This type of water loss is the major reason to administer electrolyte-free water to hospitalized patients. We emphasize that an exogenous source of water should be replaced only in patients who have a $P_{Na} > 140$ mM, indicating a deficit

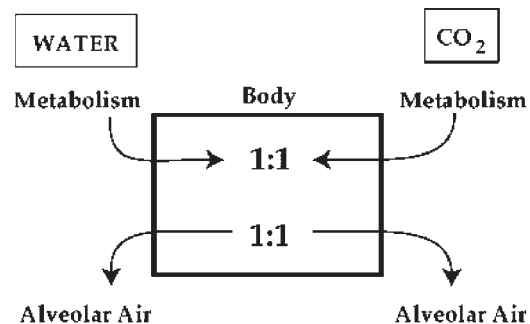


Figure 4. Fate of metabolic water. The body is depicted by the large rectangle. Events describing water are shown to the left while events describing CO₂ are shown to the right of this rectangle. Production of water and CO₂ (top arrows) as well as their loss (bottom arrows) are both in close to a 1:1 proportion. Hence there is no net change in water balance as a result of metabolism and alveolar ventilation.

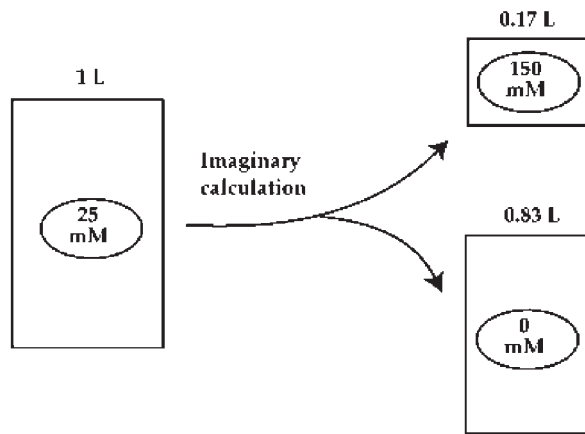


Figure 5. The electrolyte-free water content of sweat. The larger rectangle to the left of the arrows represents 1 l of sweat. Its Na^+ concentration is 25 mM, shown in the oval inside that rectangle. An imaginary calculation is performed where the 25 mmol of Na^+ are restricted to a volume of 1/6 l to have a final concentration of 150 mM. The remaining 5/6 l is electrolyte-free water.

of intracellular water. Sweat usually contains 15–30 mmol of Na^+ per litre.^{25,26} Hence when 1 l sweat containing 25 mM Na^+ evaporates, there is a loss of 0.83 l electrolyte-free water (Figure 5). This link between water evaporation (heat dissipation) and caloric expenditure (heat production) is the cornerstone for the traditional prescription for maintenance fluid administration.¹⁵ These two components are analyzed in the following paragraphs.

(a) Heat dissipation

In a healthy, fed, 70 kg adult male in steady state, approximately 2500 kcal are ingested and expended each day. The volume of insensible water loss is close to 1 l/day, but this causes a loss of only slightly >500 kcal.²⁴ Hence ~2000 kcal of heat are removed daily by conduction and convection. The exact quantitative contribution of these latter routes of heat loss depends on environmental factors such as temperature, air circulation, humidity, cutaneous blood flow, clothing, etc. Hence they cannot be quantified from general guidelines.

When additional heat loss is needed, there is an increased production of sweat together with its evaporation. Therefore an appreciable volume of sweat can be anticipated during exercise or a febrile state, unless heat loss by conduction and/or convection can be augmented. Conversely, little water loss in sweat might occur when caloric expenditure declines, if there is little change in heat loss by conduction and convection.

(b) Heat production

There are three classes of nutrients, carbohydrate, fat, and protein.²³ On a typical Western diet, oxidation of carbohydrates and fatty acids generate ~85% of the adenosine triphosphate (ATP) needed to perform biological work. The limiting factor for oxidation of these fuels is the availability of adenosine diphosphate (ADP) in cells.²⁷ Thus the rate of fuel oxidation is dependent on how quickly ADP is regenerated during biological work and/or if oxidative phosphorylation is uncoupled.^{28,29}

There are three categories of biological work: biosynthetic, mechanical, and electrical work. To digest food, enzymes must be synthesized. For absorption of nutrients, there is a need for ion transport.³⁰ During the conversion of dietary fuels to storage forms of energy, there is biosynthesis of proteins,³¹ glycogen, and triglycerides. Hence it is not surprising that caloric expenditure is much lower when there is little physical activity (e.g. bed rest) and little dietary intake. In quantitative terms, there is a 50% decline in daily caloric expenditure during prolonged fasting with inactivity.¹⁹ If a hospitalized patient is afebrile, does not eat, and is physically inactive, much less heat production can be anticipated, and thereby there is a diminished need for water infusion to match its loss by evaporation.

Caloric expenditure (heat production) exceeds that needed for metabolic work if there is uncoupling of oxidative phosphorylation. This form of heat production is catalysed by uncoupler proteins.^{28,29} The major uncoupler proteins that have an impact on the endogenous heat production in human subjects are those in skeletal muscle—their estimated contribution to energy metabolism in the rat is about 25% of resting energy turnover.²⁸ Moreover, the uncoupler proteins in skeletal muscle rise 5–10-fold during caloric deprivation.³² This topic is discussed in more detail in reference.³³

In summary, it is unlikely that the contribution of uncoupler protein-catalysed energy metabolism will be constant in a patient, and it should be extremely difficult to predict their total caloric expenditure while receiving much of his/her caloric supply from endogenous sources. Therefore relating body needs for electrolyte-free water in an *individual* patient is dependent on unreliable criteria—*estimated* energy expenditure based on body weight.¹⁵

Analysis of electrolyte-free water loss in the urine of hospitalized patients

The kidneys regulate the excretion of water and Na^+ by independent mechanisms.

(i) Excretion of water

In most hospitalized patients, there will be very little if any excretion of electrolyte-free water, because vasopressin makes the later parts of the distal nephron permeable to water.³ Exceptions to this rule occur in diabetes insipidus, during a glucose- or urea-induced osmotic diuresis,³⁴ and when there is a major renal concentrating defect.

(ii) Generation of electrolyte-free water

The infusion of isotonic saline can lead to a positive electrolyte-free water balance when this salt load is excreted in hypertonic form. The most common example of this type of generation of electrolyte-free water is when a large volume of isotonic saline is infused to prevent an appreciable fall in blood pressure in anaesthetized patients.⁴ Later, when the level of the anaesthetic agent declines, the rate of excretion of $\text{Na}^+ + \text{K}^+$ rises due to a higher central venous pressure and the urine becomes hypertonic due to actions of vasopressin (Figure 6). Quantitatively, close to half of the infusate can be *desalinated* because the urine Na^+ plus K^+ concentration can rise to $\sim 300 \text{ mM}$.⁴ Therefore, a large urine volume is not a 'good urine output' because it leads to the net addition of electrolyte-free water to the body, and thereby the development of acute hyponatraemia.⁴ In this setting, measures to lower the urine Na^+ plus K^+ concentration include a loop diuretic or inducing an osmotic diuresis with urea or mannitol.^{35–37}

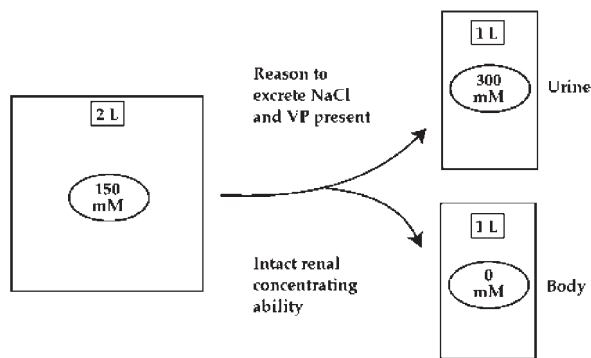


Figure 6. Desalination of administered isotonic saline. The larger rectangle to the left of the arrows represents the infusion of 2 l of isotonic saline; the concentration of Na^+ is shown in the oval inside that rectangle. A similar depiction is used for the excretion of Na^+ and water and they are shown to the right of the arrows. To have a concentration of Na^+ in the urine that is 300 mM, vasopressin (VP) must act and there must be a reason to excrete NaCl. The remaining 1 l of electrolyte-free water is retained in the body.⁴

Excretion of concentrated urine and extra renal work

One reason proposed to infuse electrolyte-free water to hospitalized patients is to minimize the work of the kidney.¹⁵ Energy is expended for active, but not passive reabsorption of Na^+ .³⁸ While it has been suggested that work is required to excrete concentrated urine,³⁹ we doubt that extra renal work was required for this task. Our rationale is that normal kidneys reabsorb 99.5% of filtered Na^+ , whether or not the final urine is concentrated (see Appendix for more discussion). Water reabsorption in the kidney is passive, and is controlled by the induction of water permeability of luminal membrane of the distal nephron⁴⁰—this requires the expenditure of very little energy, so it can be ignored in the overall quantitative analysis of renal work.

Design of a prescription for intravenous fluid administration

It is important to recognize that intravenous fluid prescriptions should be *individualized*. The priorities for the infusion of fluids are summarized in Table 3. Focusing on maintenance fluid administration, our view is that caloric expenditure should *not* be used to quantify its need.¹⁵

1. What are the indications and contraindications to infuse hypotonic fluids?

Do not infuse hypotonic solutions if the P_{Na} is $< 138 \text{ mM}$ unless the patient is having a rapid water diuresis and you want to limit the rise in P_{Na} . Rather, hypotonic fluids should be given to match the daily loss of electrolyte-free water in sweat in a patient who has a $P_{\text{Na}} > 138 \text{ mM}$. This volume is $< 1 \text{ l/day}$ unless the patient is febrile. There are two circumstances to infuse electrolyte-free water rapidly: first, when the P_{Na} is significantly $> 145 \text{ mM}$ and if the patient is symptomatic. It should be noted that the P_{Na} can rise transiently by $\sim 15 \text{ mM}$ during a seizure.⁴¹ Second, replace renal loss of electrolyte-free water in a large water or osmotic diuresis, or if there is a non-renal loss via the gastrointestinal tract or the skin. The goal will be to create a positive balance for electrolyte-free water. To lower the P_{Na} by 1 mM, the positive balance of electrolyte-free water should be $((1/P_{\text{Na}}) \times \text{total body water})$, usually 50–70% weight depending on skeletal muscle and adipose

tissue mass). For example, in a 50 kg person who has 28 l total body water, a positive balance of 0.2 l of electrolyte-free water would lower the P_{Na} from 140 to 139 mM.

2. Do certain patients have unique factors that place them at greater risk of developing a more severe decline in their P_{Na} when given a particular volume of electrolyte-free water?

The answer is yes, and two factors should be considered. The first is the age of the patient, because brain cell number decreases with age, placing children and young adults at greater risk. The second factor concerns skeletal muscle mass relative to body weight, because 50% of body water is in skeletal muscle in normal subjects. Therefore in patients who have marked muscle atrophy due to disuse, nutritional problems, and/or a disease that involves skeletal muscle, much less electrolyte-free water needs to be retained to cause a serious decline in P_{Na} and, as a result, a greater degree of swelling of brain cells if the hyponatraemia is acute.

Concluding remarks

Patients who receive intravenous fluids often have a fall in their P_{Na} in hospital. This provides a rationale to re-evaluate current recommendations for intravenous therapy. Once adequate blood pressure is established, deficits and ongoing losses should be replaced. General guidelines that follow from the underlying physiology discussed in this paper are as follows. Do not give hypotonic solutions if the patient has a surplus of water in cells (a $P_{Na} < 138$ mM in the absence of hyperglycaemia). Do not administer isotonic saline in the absence of an indication to do so, because electrolyte-free water may be generated by desalination (Figure 6).⁴ In this context, a 'good urine output' can be a danger sign. The P_{Na} should be examined before infusing >1–2 l hypotonic intravenous solutions. Be aware of occult source of oral water administration (e.g. ice chips to treat a dry mouth). Be even more cautious when planning intravenous therapy for young patients and those with a small muscle mass. Do not advise subjects to drink a large quantity of water if they are taking drugs such as 'ecstasy' that are known to cause the release of vasopressin independent of the P_{Na} (reviewed in reference 42).

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Appendix: a more detailed analysis of renal work

Renal work is almost exclusively due to active reabsorption of Na^+ in individual nephron segments, providing that Na^+ that was reabsorbed by a transcellular route,⁴³ including the Na-K-ATPase—3 Na^+ pumped per ATP hydrolysed.⁴⁴

The proximal convoluted tubule

Not every Na^+ that enters proximal convoluted tubule cells is exported via the Na-K-ATPase. For example, when Na^+ is reabsorbed via H^+ secretion to reabsorb filtered HCO_3^- , one-third of the Na^+ that exits these cells is passively linked to 3 HCO_3^- ($\text{Na}(\text{HCO}_3)_3^{2-}$). The resting membrane potential, a by-product of the Na-K-ATPase flux, drives this passive reabsorption of Na^+ . In quantitative terms, this passive process accounts for ~10% of proximal convoluted tubule Na^+ reabsorption.

Loop of Henle

The active reabsorption of Na^+ is in the thick ascending limb of the loop of Henle and involves the Na-K-2 Cl cotransporter. This Na-K-2 Cl cotransporter flux reabsorbs one Na^+ and two Cl^- ions. The second Na^+ is reabsorbed passively through the tight junctions between cells, driven by a lumen-positive voltage, because these junctions are permeable to Na^+ . Thus this half of Na^+ reabsorption in the thick ascending limb of the loop of Henle bypasses the Na-K-ATPase and does not directly require the hydrolysis of ATP.

The reabsorption of Na^+ in the medullary thick ascending limb of the loop of Henle is necessary for both concentrating *and* diluting the urine. A higher medullary interstitial osmolality is important when the urine is maximally dilute, because it leads to the reabsorption of almost 2/3 of the 60l of filtrate delivered daily from the proximal convoluted tubule in the descending thin limb of the loop of Henle.⁴⁵ This places an upper limit on water diuresis.

Distal nephron segments

Because all the reabsorption of Na^+ in the distal nephron traverses cells and because there is no passive transport of Na^+ across basolateral membranes that leads to a bypass of the Na-K-ATPase, more energy would need to be expended by the kidney to reabsorb the same amount of Na^+ daily by the kidney if less Na^+ were reabsorbed in its thick ascending limb.