

# Avoiding common problems associated with intravenous fluid therapy

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## Waterlogged in hospital

**TO THE EDITOR:** I am an 81-year-old retired medical practitioner; in 2006, I underwent resection of the sigmoid colon. At the time of surgery, before I used the bowel flushing preparation, my weight on my bathroom scales was 72.5 kg. After I used the flushing preparation, on the morning of the operation, my weight on the same scales was 70.5 kg and, on my return home on Day 8 after the operation, it was 81 kg.

About Day 4 of my hospital stay, my legs, scrotum and chest became oedematous. From my weight at home on Day 8, the extent of this oedema was about 10 kg, equivalent to about 10 L. While in hospital, I received a continuous saline infusion. When I asked for an explanation of my waterlogged condition, I was told that the drip interacted with the body's fluid balance, so that a balance should have been maintained.

I am comparatively well, but I am concerned that when the oedema first appeared my medical attendants accepted it as a usual occurrence. Despite it causing considerable discomfort and mild breathlessness, they saw no need to investigate further. A recently graduated surgeon confirmed that, in the hospital where he worked, he has seen similar oedema, which he maintains was necessary to sustain blood pressure and life.

Does my case represent a current clinical problem that is yet to be aired?

Retired Medical Practitioner  
(name and address supplied)

## ABSTRACT

- Inappropriate intravenous fluid therapy is a significant cause of patient morbidity and mortality and may result from either incorrect volume (too much or too little) or incorrect type of fluid.
- Fluid overload has no precise definition, but complications usually arise in the context of pre-existing cardiorespiratory disease and severe acute illness.
- Insufficient fluid administration is readily identified by signs and symptoms of inadequate circulation and decreased organ perfusion.
- Administration of the wrong type of fluid results in derangement of serum sodium concentration, which, if severe enough, leads to changes in cell volume and function, and may result in serious neurological injury.
- In patients whose condition is uncomplicated, we recommend a restrictive approach to perioperative intravenous fluid replacement, with initial avoidance of hypotonic fluids, and regular measurement of serum concentration of electrolytes, especially sodium.

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Intravenous fluid therapy has been used for almost 200 years and remains a fundamental part of hospital patient care.<sup>1</sup> However, approaches to the administration of water and sodium vary,<sup>2,3</sup> with justification for any particular intravenous fluid regimen being based primarily on physiological concepts rather than evidence. Inappropriate administration of intravenous fluids — either the incorrect volume (too much or too little) or the incorrect type of fluid — is a significant cause of patient morbidity and mortality. Here, we recommend strategies to avoid inappropriate intravenous fluid therapy.

## Volume replacement

The goal of volume replacement is to prevent or restore impaired circulatory function secondary to ineffective vascular volume. Volume replacement is commonly guided by one of two strategies:

- fixed fluid replacement regimens, adjusted by individualised assessment of fluid losses; and
- variable, algorithmic approaches, where volume replacement is optimised by targeting a specific circulatory parameter.<sup>4,5</sup>

## Fixed fluid replacement regimens

Fixed fluid regimens predominate in common clinical settings and include:

- standard perioperative fixed fluid replacement regimens, as described in student texts, which usually advocate 3 L per day of fluid of varying composition;<sup>5</sup>

- restrictive fluid regimens, which have long been advocated for postoperative management of pneumonectomy and lobectomy, and more recently for bowel surgery;<sup>6–9</sup> and
- liberal acute fluid resuscitation in severe burns.<sup>10</sup>

In general, fixed fluid regimens should be considered guides to safe volume replacement, with the actual amounts to be given determined by clinical response, including serial observations of heart rate, blood pressure and urine output. However, clinical assessment of volume requirement and clinical response are confounded by extremes of age, pre-existing disease, severity of acute illness or major surgery, and a continuum of general physiological changes, ranging from the normally adaptive stress response to life-threatening systemic inflammation with shock.<sup>11–14</sup> Recent studies support the safety of more restrictive perioperative fluid regimens in uncomplicated elective surgery (Box 1).

## Algorithmic approaches

Recent evidence also suggests that volume replacement targeting a specific circulatory parameter may improve patient outcome.<sup>15–17</sup> These targets involve invasive monitoring of cardiac chamber filling pressures (central venous pressure and pulmonary artery wedge pressure) and cardiac output. Recent ultrasound techniques, such as continuous transoesophageal Doppler, allow less invasive monitoring of circulatory parameters, such as stroke volume. These regimens are necessarily restricted to critically ill patients in intensive care units and will not be discussed further here.

**1 Examples of common restrictive postoperative fluid regimens\***

| Setting  | Initial intervention          |
|--|-------------------------------|
| Significant likelihood of inadequate volume state without sodium administration  | 2–3 L isotonic saline daily   |
| <ul style="list-style-type: none"> <li>• Large bowel surgery (hemicolectomy, abdominoperineal resection)</li> <li>• Abdominal aortic surgery</li> <li>• Large bowel losses (vomiting, fistula or diarrhoea)</li> </ul> |                               |
| Nil oral, low risk of volume depletion   | 1.5–2 L isotonic saline daily |
| <ul style="list-style-type: none"> <li>• Peripheral vascular surgery (femoral–popliteal bypass)</li> <li>• Uncomplicated hernia repairs</li> <li>• Cholecystectomy</li> </ul>  |                               |

\* Assuming the patient is not critically ill, has normal renal and cardiac function and weight of 70 kg. ◆

**Disturbances of volume**

In both fixed and targeted regimens, there is a risk of either insufficient or excessive volume replacement. This risk is likely to be small in previously healthy patients with minimal acute illness. However, a patient's tolerance to relative hypo- or hypervolaemia decreases with increasing severity of acute illness<sup>18</sup> (Box 2 and Box 3).

Inadequate volume replacement is defined as the failure to restore an adequate vascular volume for effective nutrient, metabolite and gaseous exchange in the tissues. The consequences of hypovolaemia are likely to be related to the magnitude of volume loss, timing and adequacy of volume replacement, and clinical context.

Extreme hypovolaemia manifests clinically as shock, which may be treated with crystalloids or colloids. A recent Australian study showed that, in intensive care patients, use of either 4% albumin or 0.9% (isotonic) saline for fluid resuscitation resulted in similar outcomes at 28 days.<sup>20</sup> Of note, the ratio of the volume of albumin to saline administered was about 1 : 1.4.

The clinical impact of a lesser degree of hypovolaemia can range from thirst and postural hypotension, increased incidence of perioperative nausea and vomiting, through to prolonged hospitalisation.<sup>21–23</sup>

There is no universally accepted definition of over-resuscitation or “fluid overload”,<sup>5,13,24</sup> which is often understood to mean respiratory or heart failure secondary to excessive positive fluid balance.

Symptoms and signs attributed to fluid overload are likely to be determined by the magnitude of positive fluid balance, the severity of underlying cardiorespiratory disease and the nature and severity of acute illness. Limited human data exist, but volunteer studies suggest that infusion of more than 2–3 L isotonic saline in euvoemic humans results in symptoms of mild nasal stuffiness, periorbital discomfort and a small, asymptomatic decrease in lung mechanics and gas exchange.<sup>25,26</sup>

As volume loading increases, maintenance of the plasma oncotic pressure may become important in protecting against pulmonary oedema. Acute illness is often associated with hypoalbuminaemia, and it has been shown that when filling pressure is increased, a low plasma oncotic pressure allows pulmonary oedema to develop at lower filling pressures.<sup>27</sup>

Excessive administration of saline may be tolerated by an otherwise healthy patient, but additional acute physiological changes, such as altered perioperative sodium and water metabolism, increased capillary permeability, hypoalbuminaemia, and impaired pulmonary mechanics, increase the risk of symptomatic respiratory failure.

**Recommendations**

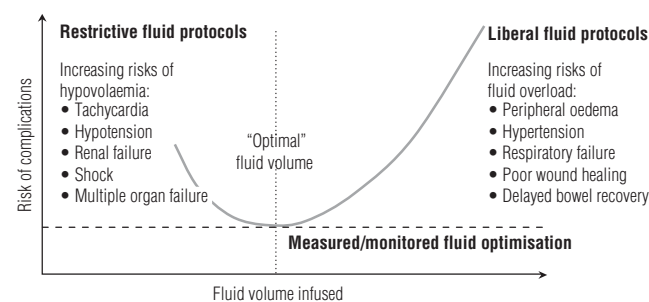
- Unless clearly indicated, a more restrictive approach should be taken to maintenance fluid administration than the “mandatory 3 L per day” that is frequently prescribed (Box 1).
- An ill patient whose condition is complicated may benefit from a targeted fluid replacement strategy.
- When assessing a patient's volume status and the relative risks of insufficient or excessive volume replacement, pre-existing cardiorespiratory and renal disorders, and the severity of pathophysiological changes associated with the acute illness itself must be taken into account.
- If fluid overload is suspected, fluid restriction and/or diuretic therapy may be indicated; however, in more complex clinical situations attempts to achieve a negative fluid balance are not necessarily sufficient, effective or appropriate, as there may be a maldistribution of fluid and, while the patient overall may have fluid overload, there may still be a deficit of fluid in the vascular compartment.

**Types of fluid administered**

The type of fluid administered may be considered incorrect if it causes excessive changes in effective osmolality (tonicity).

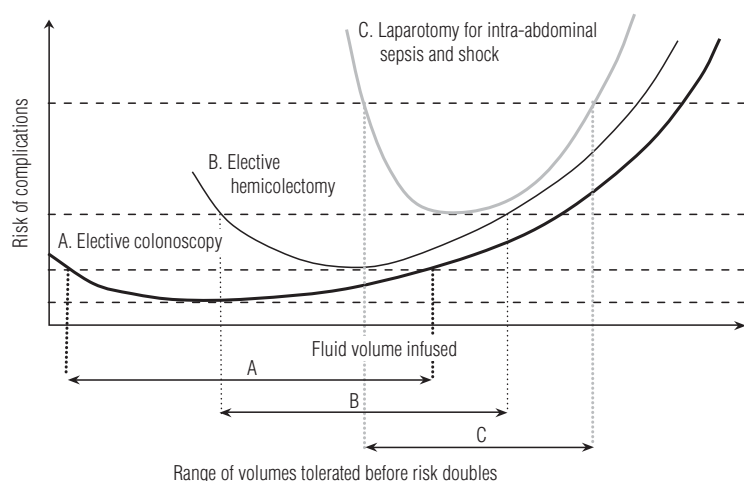
If two solutions are separated by a barrier permeable to water only, then water will move from the compartment of low osmolality to that of higher osmolality until the fluids on either side of the barrier share the same osmolality. This redistribution of water between the intracellular and extracellular fluid (ICF and ECF) compartments leads to rapid changes in cell volume, with consequent cellular dysfunction or injury. This is particularly important

**2 Hypothetical curve of the risk of fluid therapy-related complications versus volume of fluid infused**



Risk is associated with both persistent hypovolaemia and iatrogenic fluid overload, although the actual and relative risks of these two extremes may be difficult to quantify in individual patients. Restrictive and liberal fluid protocols aim to minimise the risks of fluid overload and hypovolaemia, respectively. However, by failing to take into account individual patient differences, these protocols may produce their own complications. Monitored fluid administration individualises fluid requirements but, given the lack of an ideal monitor for volume replacement, does not necessarily determine the optimal fluid volume to minimise risk. (Figure adapted from Ayus and Arieff.<sup>19</sup>) ◆

### 3 Hypothetical risk versus volume replacement curves for an individual patient in different clinical scenarios



*Curve A: Low-risk clinical context, such as elective colonoscopy, where optimal fluid requirements are minimal, and the patient can tolerate significant variations in volume replacement.*

*Curve B: The same patient in a slightly higher-risk context, such as elective colectomy. The volume for optimal fluid replacement is likely to be higher than in Scenario A, and the tolerance for error slightly lower, given the larger volume and pathophysiological changes associated with surgery.*

*Curve C: The same patient in a high-risk clinical context, such as urgent laparotomy for intra-abdominal sepsis and hypotension. Fluid requirements are likely to be high, and the patient is unlikely to tolerate significant deviations from this amount.*

*Even with optimal volume replacement in each of these scenarios, the risks associated with fluid therapy are likely to increase with the severity of the acute illness. (Figure adapted from Ayus and Arief.<sup>19</sup>)* ◆

in the central nervous system, where it results in clinically significant symptoms and signs.

Hypotonic fluids, such as 5% glucose and 4% glucose in 0.18% saline have low (or no) effective solutes when added to the ECF and cause net water movement into cells. Hypertonic fluids, such as 3% saline, added to the ECF cause net water movement from cells. Isotonic (0.9%) saline is isotonic to normal ECF and causes no net water movement. Hartmann's solution is mildly hypotonic,<sup>28</sup> having a calculated osmolality of 273 mOsm/kg, but a measured osmolality (by freezing point depression) of only 254 mOsm/kg.

Disorders of tonicity most commonly result from the accumulation or loss of total body water. Therefore, hyponatraemia usually indicates relative water overload, and hypernatraemia indicates dehydration (water depletion).

#### Hyponatraemia

Hyponatraemia (serum sodium concentration <135 mmol/L) is the most common electrolyte disorder in hospitalised patients.<sup>29</sup> Symptoms of hyponatraemia include headache, lethargy, decreasing level of consciousness and seizures. Death can result from cerebral oedema. Permanent neurological abnormalities may occur with rapid decreases in sodium concentration below 125 mmol/L, or too rapid correction of sodium concentration back towards this level (osmotic demyelination syndromes).

Hypotonic fluid administration to fasting postsurgical patients is the main cause of hyponatraemia in adults and children in hospital.<sup>19,30-33</sup> The perioperative stress response, pain, nausea and vomiting all lead to increased secretion of antidiuretic hormone (ADH) which results in inappropriate accumulation of free water from "routine" administration of hypotonic fluids in susceptible individuals. The duration of the effect is from 12 hours after minor surgery to 4 days after major surgery.<sup>13</sup>

Fatal cases of hyponatraemia in otherwise healthy patients have led to publications questioning the routine use of hypotonic intravenous fluids and proposing they be replaced with isotonic saline in hospitalised patients.<sup>34-37</sup>

Hyponatraemia should be avoided by not administering hypotonic fluids to patients while they have increased ADH secretion. Once hyponatraemia occurs, management is determined by the

cause and severity, the time over which it developed, and the presence of neurological symptoms.<sup>29,38</sup> Initial management of acute hyponatraemia without neurological symptoms includes the cessation of all fluids that can exacerbate hyponatraemia. If the patient is euvolaemic or hypervolaemic, then the hyponatraemia is likely to result from inappropriate ADH secretion (SIADH, syndrome of inappropriate ADH) or excessive free water administration. Importantly, patients with SIADH can produce hypertonic urine, and thus neither isotonic (0.9% NaCl solution) nor hypotonic fluids should be administered, as they will exacerbate the hyponatraemia.<sup>29</sup> Acute hyponatraemia associated with severe volume depletion (eg, diarrhoea or diuretic use) often corrects spontaneously when the volume depletion is restored with isotonic saline or colloids.<sup>39</sup> Hypertonic solutions should only be considered for asymptomatic acute hyponatraemia if a standard approach does not adequately correct the hyponatraemia. The rate of correction of serum sodium concentration in asymptomatic patients with acute hyponatraemia should be gradual and not exceed 8 mmol/L per day.<sup>29</sup> Neurological symptoms and persistent or worsening hyponatraemia despite standard treatment should prompt referral to a physician experienced in treatment of acute hyponatraemia.

Severe acute hyponatraemia (serum sodium concentration <125 mmol/L) associated with neurological symptoms such as headache, drowsiness or seizure is a medical emergency that may result in death from cerebral oedema. The initial treatment goal should be rapid elevation of serum sodium concentration until acute neurological symptoms are controlled, usually by the administration of hypertonic saline (eg, 3% NaCl solution). This is followed by slower correction, as per the treatment of hyponatraemia without neurological symptoms. Permanent brain injury and death due to osmotic demyelination following symptomatic hyponatraemia and its correction are well described.<sup>29,40,41</sup> Approaches to the rate of correction of serum sodium in this setting have been recently reviewed.<sup>37,42,43</sup>

Chronic hyponatraemia is often associated with medication or severe organ failure, particularly cardiac or liver failure. Specific treatment of chronic hyponatraemia is not required provided hyponatraemia is not symptomatic or severe (serum sodium

concentration < 125 mmol/L). Optimising management of the underlying condition and addressing drug causes is the mainstay of treatment in this setting.

### Recommendations

- Measure serum sodium concentration daily in all patients receiving maintenance fluids.
- Use a staggered regimen for fluid administration, giving isotonic fluids (eg, 0.9% NaCl solution) during the period of high ADH secretion (24–96 hours, depending on the circumstance) and introduce hypotonic fluids only later or if hypernatraemia develops.
- Completely avoid all hypotonic fluids in patients whose serum sodium concentration is low or falling rapidly (by >8 mmol/L per day).
- Acute decreases in serum sodium concentration below 125 mmol/L with neurological symptoms should be considered a medical emergency, and treatment should include prompt, controlled correction of serum sodium concentration.
- Rapid correction of chronic or asymptomatic hyponatraemia is not indicated.

### Hypernatraemia

Hypernatraemia (serum sodium concentration > 145 mmol/L) is much less common than hyponatraemia and occurs when there is either excessive water loss from the ECF (most common) or excessive sodium gain (uncommon, and associated with hypervolaemia). Normal renal concentrating function and thirst often prevent hypernatraemia developing, but these can be impaired in infants and elderly and critically ill patients, increasing the propensity for hypernatraemia.<sup>44</sup> Usually, the onset of hypernatraemia is gradual and results from insufficient replacement of free water loss from urine, skin (eg, fever, severe exercise, burns) or bowel (severe diarrhoea). However, diabetes insipidus due to either insufficient ADH release (central diabetes insipidus) or decreased renal distal tubular response to ADH (nephrogenic diabetes insipidus) can cause more rapid rises in serum sodium concentration because of large urinary losses of free water. Brain injury (central) and chronic lithium use (nephrogenic) are the two most common causes of diabetes insipidus.

Hypernatraemia that results from sodium accumulation in excess of water is less common, but may occur in patients with trauma, burns and brain injury who are resuscitated with hypertonic saline (eg, 3% NaCl solution).

Symptoms directly attributable to hypernatraemia are neurological and range from lethargy, weakness, and irritability, to seizures, obtundation and death in severe cases. Severe or permanent neurological dysfunction is more likely to occur with acute increases in serum sodium concentration above 160 mmol/L.<sup>45,46</sup>

Hypernatraemia secondary to water loss is managed by treating the specific cause for ongoing water loss, and is corrected by the administration of hypotonic fluids. These usually contain glucose (eg, 5% glucose, or 4% glucose in 0.18% NaCl solution) and may cause hyperglycaemia in patients with diabetes or if given in excessive quantities. If hyperglycaemia and hypernatraemia are severe, sterile water can be administered intravenously, but this requires central venous access as peripheral administration leads to red cell haemolysis.<sup>47</sup> Central diabetes insipidus requires administration of the ADH analogue desmopressin (2–4 µg intravenously) to control urinary free water loss, whereas the nephrogenic form is managed by removing the cause of renal ADH unresponsiveness, if possible, and increasing the intake of hypotonic fluids.

Hypernatraemia secondary to excessive hypertonic fluid administration is managed by ceasing hypertonic fluid intake and, if necessary, increasing urinary sodium excretion with diuretics plus hypotonic fluid replacement of urinary volume loss.

### Recommendations

- Acute increases in serum sodium concentration above 150 mmol/L should be assessed for a cause and corrected.
- Diabetes insipidus is important to recognise as it can cause large, rapid losses of free water with a rapid rise in serum sodium concentration.
- In hypernatraemia, as in hyponatraemia, the rate of correction should be proportional to the rate of onset of the hypernatraemia, taking into account the presence and severity of neurological symptoms (maximal rate of correction 10 mmol/L per day). Overly rapid correction may result in cerebral oedema, seizures or death.

### Conclusion

Intravenous fluid therapy is common and has frequent non-trivial complications with regard to volume and tonicity. Disorders of the two states may coexist, and we advocate considering each state separately in formulating an approach to management.

Volume complications tend to follow large errors in volume replacement and primarily relate to the cardiorespiratory system and peripheral perfusion. Disorders of tonicity may occur independently of volume state abnormalities, and complications are primarily neurological.

Avoidance of these complications is predicated on careful clinical estimation of the volume, composition and rate of intravenous fluid replacement, and diligent monitoring of clinical response, supplemented with daily estimations of electrolyte concentrations and renal function.

### Competing interests

None identified.

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