In 2007 a National Patient Safety Agency alert ("Promoting safer use of injectable medicines") drew attention to the safety and effectiveness of intravenous treatment. Most discussions around implementing the alert have focused on injectable drugs, but IV fluids should not be overlooked. Pharmacists review prescribed medicines critically, but their reviewing and monitoring of IV fluids tends to be less consistent. This is an area where pharmaceutical expertise can, and should, be applied systematically.

IV fluids are among the most commonly used therapies in hospitals, yet they are often prescribed with little regard for actual fluid and electrolyte requirements, despite the fact that under- and overdosing can have serious consequences. The responsibility for most IV fluid prescribing is typically given to the most junior members of the medical team, many of whom are unaware of the contents of common IV fluids.

Recent consensus guidelines for good perioperative fluid prescribing (GIFTASUP) underline the importance of tailoring fluid input to physiological needs and haemodynamic status. The guidelines also provide recommendations on the choice of fluid in a range of clinical situations; when it comes to prescribing IV fluids, one size definitely does not fit all.

In this article, we have confined our discussion to IV fluid therapy for adults.

### Summary

Intravenous fluids are commonly prescribed in hospitals. Despite this, many clinical pharmacists lack confidence when reviewing orders for IV fluids. Fluid therapy fails, broadly, into two categories — replacement and maintenance.

Fluid replacement involves, in the short term, administration of large volumes of fluid. Generally, once a sufficient amount of fluid had been replaced, patients are switched to maintenance treatment. Maintenance fluids should closely match physiological needs, in terms of water, sodium and potassium.

### Fluid replacement and resuscitation

The situations where fluid replacement and resuscitation are required are discussed in the accompanying article (p274).

It is generally agreed that large volumes of fluid are needed in the short term. Isotonic crystalloid solutions are often recommended in the first instance (unless a patient has had a significant haemorrhage with a haemoglobin level below 7g/dl, in which case a blood transfusion may be necessary). GIFTASUP promotes the use of "balanced" crystalloid solutions, eg, compound sodium lactate (Hartmann’s solution) over the traditional sodium chloride
(NaCl) 0.9%. This is because of the risk of hyperchloraemic acidosis, which may occur as a result of the physiologically high level of chloride found in NaCl 0.9%-based fluids.

Box 1 shows the amount of volume expansion of each compartment (ie, intravascular, interstitial, intracellular) that can be expected from common fluids. Crystalloid solutions leak rapidly into the interstitial space and can cause significant tissue oedema. Not only can this be uncomfortable, but it can also reduce mobility and compromise organ function. For example, there is evidence that crystalloid infusions cause small bowel oedema and this can impair gastrointestinal function by causing intolerance to enteral feeding and postoperative nausea and vomiting. Also, increased cerebral oedema can worsen the prognosis for patients who have undergone brain surgery or those with head trauma.

Colloid solutions (eg, containing starches, gelatin, albumin) are also effective for volume replacement. They are advantageous because they provide volume expansion while limiting risk of fluid overload and oedema; however there is no evidence that this leads to any benefit in patient survival (see Box 3 on p280 of the accompanying article).

Fluid maintenance

Once the goals of fluid resuscitation have been achieved, the level of fluid administration should be adjusted for maintenance treatment. Overloading with salt and water during resuscitation is often unavoidable and can take days or weeks to resolve, so it is important to switch as soon as possible to a regimen that matches physiological needs more closely, to avoid further overloading.

The basal requirements for an adult patient are:

- 1–1.4 mmol/kg/day of sodium
- 0.7–0.9 mmol/kg/day of potassium
- 30 ml/kg/day of water

A worked example of how these requirements can be met using the weight-based guidelines for a 60 kg and an 80 kg patient is shown in Box 2. These maintenance regimens are designed to provide typical amounts of sodium, potassium and water for a healthy young adult.

Box 1: Effect of 1L fluid on body compartments

<table>
<thead>
<tr>
<th>FLUID</th>
<th>EXPANSION OF IVF (ml)</th>
<th>EXPANSION OF ISF (ml)</th>
<th>EXPANSION OF ICF (ml)</th>
<th>SODIUM CONTENT (mmol/L)</th>
<th>OSMOLARITY (mOsm/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl 0.9%</td>
<td>250</td>
<td>750</td>
<td>0</td>
<td>154</td>
<td>308</td>
</tr>
<tr>
<td>NaCl 0.45%</td>
<td>167</td>
<td>500</td>
<td>333</td>
<td>77</td>
<td>154</td>
</tr>
<tr>
<td>Glucose 5%</td>
<td>83</td>
<td>250</td>
<td>667</td>
<td>0</td>
<td>252</td>
</tr>
<tr>
<td>Glucose 5% with NaCl 0.45%</td>
<td>167</td>
<td>500</td>
<td>333</td>
<td>77</td>
<td>432</td>
</tr>
<tr>
<td>Albumin 5%</td>
<td>1,000+</td>
<td>0</td>
<td>0</td>
<td>154</td>
<td>310</td>
</tr>
<tr>
<td>Hetastarch 6% in NaCl 0.9%</td>
<td>1,000+</td>
<td>0</td>
<td>0</td>
<td>154</td>
<td>310</td>
</tr>
</tbody>
</table>

The values for hetastarch in NaCl and albumin solutions indicate their ability to expand the volume in IVF by more than the amount of fluid administered

More recent guidelines have simplified the basal requirements for an adult patient to:

- 50–100 mmol/day of sodium
- 40–80 mmol/day of potassium
- 1.5–2 L/day of water

Some caution is required because the recommendations are based on body weight, therefore they tend to overestimate the requirements for obese patients.

Adjustments need to be made to correct pre-existing deficits and replace unusual losses (eg, from drains or fistulas — see below). In addition, pre-existing medical conditions need to be taken into account. Elderly patients are more likely to have cardiac, respiratory or renal impairment, and have a lower reserve capacity than younger patients. Other at-risk groups include patients with:

- Cardiac disease — tissue perfusion may be reduced and there is a risk of fluid retention and overload
- Renal disease — it may be difficult to remove excess fluid, so there is a risk of fluid overload
- Cerebrovascular disease — patients are likely to have complex requirements and it may be difficult to maintain electrolyte and fluid balance

Replacing losses

Where patients are losing fluid through gastrointestinal (GI) drains or fistulas, maintenance regimens need to be adjusted accordingly to account for this volume. Box 3 (p288) lists the typical contents of the various GI fluids and explains how these can be used to calculate an additional requirement.

Excessive losses from gastric aspiration or vomiting should be treated with an appropriate crystalloid solution plus a suitable potassium supplement. GIFTASURe recommends balanced crystalloids rather than NaCl 0.9% for replacement of GI losses or following excessive diuretic use.

Response to injury

Normal fluid and electrolyte homeostasis is disturbed after injury (eg, trauma, surgery) and this can affect the
way in which infused electrolytes and fluids are handled. The changes are complex and poorly understood, with the exception of vascular leakage and the role of antidiuretic hormone, which should be considered when planning or reviewing treatment.

**Vascular leakage** Inflammation, resulting from sepsis, trauma or burns, causes a sharp increase in vascular permeability. Leakage of plasma proteins, electrolytes and water from the intravascular compartment into the interstitial space occurs consequently. Vascular permeability returns to normal over the subsequent 12 hours, but affected patients can require large amounts of IV fluid to maintain adequate tissue perfusion. Crystalloids are commonly used although colloid solutions can also be given, in smaller quantities, to restore intravascular volume.

**Antidiuretic hormone** In the immediate postoperative period, there is intense activation of antidiuretic hormone and the renin-aldosterone-angiotensin system. This results in active sodium retention and a low urine output. The capacity to excrete salt and water returns to normal over the following few days. If urine output is used to determine organ perfusion, it will be underestimated and fluids may be over-prescribed as a result.

**Factors affecting blood pressure**

Low blood pressure can be an early sign that a patient does not have enough circulating volume (an indication for being prescribed more IV fluids). Other factors that affect blood pressure may also need to be considered.

**Concurrent drugs** Some drugs that affect blood pressure (eg, diuretics, antihypertensives) can potentiate postoperative hypotension and influence IV fluid treatment. Practitioners can accidentally prescribe more fluid than necessary for these patients, in the belief that the changes are complex and poorly understood, with the exception of vascular leakage and the role of antidiuretic hormone, which should be considered when planning or reviewing treatment.

**Analgesia** Low blood pressure can be caused by epidural analgesia. It is easy to assume for hypotensive patients who have recently received an epidural that their low blood pressure is drug-induced. However, hypovolaemia is the cause of low blood pressure.

**Box 3: Fluid loss through gastrointestinal drains**

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Sodium content (mmol/L)</th>
<th>Potassium content (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric</td>
<td>45–100</td>
<td>30–45</td>
</tr>
<tr>
<td>Intestinal</td>
<td>120</td>
<td>20</td>
</tr>
<tr>
<td>Bile*</td>
<td>140</td>
<td>5</td>
</tr>
<tr>
<td>Pancreatic*</td>
<td>130</td>
<td>15</td>
</tr>
</tbody>
</table>

* May also contain large amounts of bicarbonate

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**Reviewing IV prescriptions**

IV prescriptions should be reviewed at the same time as all other prescribed medicines, including parenteral and non-parenteral medicines and fluids, and undertaken with knowledge of a patient’s diagnosis and pathophysiological status. Reviewing one prescribed item or section of a prescription in isolation does not provide a clear picture of the patient’s treatment, and pharmacists should aim to review patients comprehensively whenever possible. Pharmacists should consider:

- The type of fluid and administration rate
- Whether there are any contraindications to the fluid prescribed
- How the fluid is to be administered (ie, what type of pump will be used)
- What drugs are also being administered
- Whether fluid or drugs are to be administered through a central line or a peripheral line
- Any duplication of therapy
- Whether there is any ambiguity in the prescription

Experienced pharmacists often recognise patterns in prescribing. Being familiar with common IV fluid regimens helps when undertaking a prescription review.

**Sodium content of medicines** When calculating the daily requirement of sodium for a patient, pharmacists should remember that certain IV medicines deliver a considerable sodium load. In addition, many IV medicines are added to infusion bags that contain NaCl. Such as:

- Vancomycin 1g in 250ml NaCl 0.9%, given twice a day — 77mmol of sodium per day
- Benzylpenicillin 1.2g in 100ml NaCl 0.9%, given four times a day — 75mmol
- Clarithromycin 500mg in 250ml NaCl 0.9%, given twice a day — 78mmol
- Piperacillin/tazobactam 4.5g in 50ml NaCl 0.9%, given three times a day — 51.3mmol
- Metronidazole 500mg in 100ml NaCl 0.9%, given three times a day — 39mmol (can vary depending on brand)
**Box 4: Lessons learnt through case examples**

**Lesson 1 — Prescribe a full fluid regimen, not “bag-by-bag”**

An 87-year-old woman was admitted on a Friday to a surgical ward with suspected acute cholecystitis. The consultant instructed a junior doctor to start intravenous fluids. Her biochemistry was reviewed on Monday and plasma sodium found to be 154mmol/L (normal range 135–145mmol/L). On investigation it was found that she had been initially prescribed 1L of sodium chloride (NaCl) 0.9% over 12 hours on Friday and that this prescription was repeated for the entire weekend. Different doctors had continued prescribing NaCl 0.9%, most likely due to the nursing staff requesting further bags of fluid.

This case demonstrates the need to plan fluid replacement regimens and not prescribe on a “bag-by-bag” basis. In this case the issue was compounded by different doctors prescribing without referring to daily blood results. Such events can easily occur in busy clinical areas.

**Lesson 2 — Always use infusion pumps for continuous infusions**

An 80-year-old woman was admitted to an acute medical ward with community-acquired pneumonia. She was started on IV fluids since she was unable to eat or drink. Four days later she was found to be in acute heart failure with a 4L positive fluid balance since admission (her fluid output being 4L less than the amount of fluid received). Diuretic therapy was initiated and her heart failure resolved.

The initial IV fluid regimen had been for 2L of glucose 4% / NaCl 0.9% with potassium 20mmol/L over 24 hours, but the charts showed that a higher volume of infusion fluid had been administered.

It was discovered that all these infusions had been administered by gravity set without the aid of an infusion device. It appears that infusions intended for administration over a 12-hour period had been given over 8–10 hours, resulting in more fluid than intended being administered.

**Lesson 3 — Do not interpret individual biochemical results in isolation**

An 83-year-old, 60kg man underwent hemicolectomy for bowel cancer. During the procedure he lost 300ml of blood, but was given 500ml of a colloid solution and 2L of a crystalloid solution. At the end of the operation, his blood pressure was 100/60mmHg, and his haemoglobin was 7.2g/dl (normal 11.5–16g/dl). He was prescribed two units of packed cells (red blood cells in a reduced volume of plasma).

He was moved to the high dependency unit where he was found to have a 4L positive fluid balance. He was also oliguric, producing 10–15ml/h of urine instead of the expected 30ml/h (0.5ml/kg/h), hypotensive and oedematous. His low urine output was interpreted as being due to poor renal perfusion. He was therefore prescribed 1L of NaCl 0.9% and 2L of glucose 5% / NaCl 0.45% every 24 hours for the next three days.

During this time he remained oliguric and also started to vomit.

This case illustrates the danger of interpreting single measurements in isolation. It is likely that the low haemoglobin measured at the end of the operation was the result of plasma dilution, since his blood loss had been modest. His oliguria in the postoperative phase was more likely due to his body retaining large amounts of sodium in response to trauma, rather than low renal perfusion. Consequently, the prescribed fluids may have worsened his condition.

Rather than concentrating on individual parameters in isolation, the clinicians should have evaluated the patient’s full clinical picture and response to therapy.

**Further learning**

Some administration systems are complex and sound knowledge of different giving sets, connectors and taps is essential (further information on infusion devices is available on the Medicines and Healthcare products Regulatory Agency website or in an article by Quinn). Examples of problems that can occur with patients receiving IV fluid therapy, and some of the lessons that can be learnt, are described in Box 4.