Parenteral replacement of fluids and electrolytes: the basics

Many conditions, from severe burns to diarrhoea, or simply an inability to drink enough fluid, can result in dangerous fluid and electrolyte losses. John Sexton and Mohamed H. Rahman explain why maintaining optimum fluid balance is essential and how it can be restored.

The average adult is made up of around 60 per cent water by weight. Water is the medium by which nutrients, waste products, electrolytes, hormones and proteins are moved around the body, and water soluble electrolytes and products of metabolism are excreted (dissolved in urine). Fluid is lost mainly by excretion through the kidneys, but smaller (“insensible”) losses occur in sweat, faeces or expired air, or via cell reactions. Each day, the average adult typically needs to drink about 2L of fluid to replace losses and, normally, the oral route is the only source of fluid intake.

Two-thirds of body water is found inside cells (the intracellular fluid compartment; IFC) giving them their physical structure and facilitating metabolic processes. The remaining third (the extracellular fluid compartment; EFC) is divided between the blood (plasma) and the fluid between cells (interstitial fluid) in an approximately 1:2 ratio.

Cell membranes are freely permeable to water but the movement of electrolytes is controlled (eg, by sodium-potassium pumps), resulting in varying electrolyte concentrations in the IFC and EFC. The different fluid compartments of the body of a typical 70kg adult are shown in Figure 1 (p572).

Integrated mechanisms exist to maintain fluid homeostasis (and the related sodium balance), to ensure that there is minimal fluctuation in blood volume, osmolality and organ perfusion. Blood is filtered at the glomeruli of the kidneys and the filtrate passes through the nephrons into the collecting ducts and eventually through the ureters into the bladder. A typical glomerular filtration rate of 150ml/min results in about 150L of filtrate in 24 hours, so in an adult who voids 2L of urine daily over 98 per cent of the fluid has been reabsorbed before it leaves the kidney, and the filtrate passes through the nephrons into the collecting ducts and eventually through the ureters into the bladder. The body is extremely sensitive to small changes in the volume of water it contains, and especially to the volume of the plasma compartment, on which the maintenance of blood pressure and organ perfusion depends.

Changes in increased sodium concentration leads to both transient thirst stimulation and ADH secretion, leading to an increase in body water and a normalisation of extracellular sodium concentration. Other important hormones modify sodium, including renin, angiotensin, aldosterone and β-natriuretic peptide. Blood volume and pressure are also influenced by vasoactive substances (eg, catecholamines) and changes in sympathetic nerve outflow. When hypovolaemia is detected by the kidney, renin is released leading to the activation of angiotensin II, a potent vasoconstrictor, (which itself modifies ADH release) and the secretion of aldosterone from the adrenal glands. Aldosterone is a natural mineralocorticoid which leads to the conservation of both sodium and water in the renal tubules.

The body is extremely sensitive to small changes in the volume of water it contains, and especially to the volume of the plasma compartment, on which the maintenance of blood pressure and organ perfusion depends. Dehydration, whether due to reduced fluid intake or increased fluid losses will be detected as a rise in serum osmolality, which, in turn, will lead to the release of ADH from the posterior pituitary. This release may be augmented by receptors in the blood vessels that detect a fall in blood volume (hypovolaemia) and a
subsequent fall in blood pressure. These same mechanisms also stimulate thirst.

If oral fluid intake is reduced or stopped for more than short periods the body will not be able to maintain fluid homeostasis. The time taken for this to occur will depend on the individual, and frail elderly people tend to be affected sooner. Fortunately, most cases of mild dehydration respond quickly to increased fluid intake and serious consequences are averted. For some patients however, drinking will not be sufficient to replace deficits or is unsuitable for other reasons (e.g., non-availability of the enteral route due to deficits or is unsuitable for other reasons (e.g., drinking will not be sufficient to replace deficits or is unsuitable for other reasons (e.g., non-availability of the enteral route due to intractable vomiting).

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Fluid replacement is intended to correct acute losses or maintain homeostasis (of blood volume, fluid levels, organ perfusion and function), or both. Patients who need parenteral fluid and electrolyte replacement might include:

- Those in whom there has been prolonged failure of oral intake (e.g., mucositis, poor self care or poor care by others)
- Those with excessive losses (e.g., in profuse diarrhoea or vomiting, exposure to extreme heat, burns patients and profound diuresis [seen in diabetes insipidus or, more commonly, diabetic ketoacidosis, where uncontrolled serum glucose has led to a massive osmotic diuresis secondary to glucose entering the urine as the renal threshold is exceeded])
- Those in whom the oral route is not available (e.g., people who cannot drink because of head or neck surgery or unconsciousness due to surgery, accident or illness, or who cannot absorb fluid enterally because of gastrointestinal problems)

Parenteral fluids are usually administered by the intravenous route, although the subcutaneous route (hypodermoclysis; see Panel 1) is sometimes used to maintain hydration in cases where long-term venous access is a problem.

Intravenous fluid administration

If intravenous fluid replacement is necessary, a doctor, nurse or other trained practitioner can insert a cannula into a small vein in the back of the patient’s hand or forearm to achieve venous access. Alternatively, a catheter can be inserted into a large vein (e.g., in the neck), possibly using a surgical procedure to locate the vein, and this is known as a central line. Central lines are used where peripheral sites are not available, hypertonic or irritant fluids

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**Panel 1: Hypodermoclysis**

The administration of fluids subcutaneously is known as hypodermoclysis. Because the typical parenteral fluids on the market in the UK are all licensed as intravenous fluids, hypodermoclysis is an “off-label” technique (under the prescriber’s responsibility).

Standard isotonic glucose and sodium chloride 0.9 per cent solutions are routinely administered in this manner at volumes of up to 2L per site over 24 hours. Substantial literature exists on the subject but good evidence and comparative studies are scant.

Subcutaneous administration of fluids may be preferred in cases where prolonged administration of parenteral fluids is required and the use of a nasogastric tube has been considered and rejected. It is especially popular in elderly patients who are not drinking (e.g., after a stroke or in palliative care). The main advantage over intravenous administration is that subcutaneous administration systems are less difficult to insert, can be easily repositioned by nurses (especially useful in nursing homes, hospices and domiciliary situations), and can be located in body areas less likely to allow a confused patient to pull the line out.

A disadvantage of hypodermoclysis is that it is unsuitable for rapid administration of large volumes of fluid or to correct severe electrolyte deficiencies (see main text). Despite this, substantial references exist to using bags containing potassium at up to 40mmol/L, although 27mmol/L is more common — even though potassium solutions are considered to be iritant, they can still be used. It was formerly common to inject the enzyme hyaluronidase around the injection site to aid absorption, but this practice has fallen out of favour.

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**Which fluid?**

Parenteral administration of water is generally avoided because it is hypotonic compared with the body’s tissues and fluids, and would damage the vasculature and the cells contained within the circulation. The two major categories of intravenous fluids are colloids and crystalloids.

**Crystalloids**

Crystalloids are solutions containing small molecules that pass freely through semi-permeable membranes. The two crystalloids most often used in the UK are glucose and sodium chloride. Solutions are available in varying strengths, but the two most common are isotonic glucose (dextrose) 5 per cent and sodium chloride 0.9 per cent (often inaccurately referred to as “normal saline”). Mixtures of glucose and saline are also available to allow a greater degree of flexibility.

Many hospitals use compound sodium lactate (Hartmann’s solution), which bears a closer resemblance to plasma, especially in terms of chloride ions, and is less likely to cause fluid overload problems due to a lower sodium content. (Hartmann’s solution contains buffers, which are metabolised by the liver to produce bicarbonate, that enable the slight acidosis that sometimes follows general anaesthesia to be corrected.)

Isotonic fluids will not damage the cells lining the blood vessels or cells in the blood because they exert the same effective osmotic pressure as plasma. As a result, they can be
administered safely into small veins without damage and a peripheral cannula can be left in a vein for several days before it needs re-sting. Hypertonic glucose (strengths above 10 per cent and up to 50 per cent) is available, most commonly for use in intravenous feeding regimens and the acute management of hypoglycaemia. Prolonged administration is usually through a central catheter into a larger vein, such as the subclavian or jugular vein, with a greater flow of blood to dilute the solution and to prevent, as far as possible, damage to the vein wall. Colloids Colloids (also called plasma substitutes) have large molecules that are retained initially within the blood because they are too big to diffuse easily through the blood vessels into other fluid compartments. They are, therefore, most suitable for use as plasma expanders in shock and trauma where the aim is primarily to maintain or expand blood volume and improve end organ perfusion. They are mainly used in intensive care and accident and emergency situations, but are sometimes used on general wards under specialist supervision. Examples of colloids include albumin, dextrans, gelatin and etherified starch.

The traditional use of albumin in trauma has declined in recent years following evidence that outcomes were often worsened. (It was presumed that in shock blood vessel permeability increased, allowing leaking out of molecules into interstitial fluids and giving rise to hypovolaemia. The use of albumin was thought to maintain blood pressure because the molecules would stay in the plasma compartment). The use of dextrans has also decreased because they have been associated with a higher risk of venous thromboembolism. Gelatin and etherified starch (a range of heta-, penta- and tetra- starches is available) are probably the most commonly used colloids. Starches are now available in a balanced carrier solution (similar to Hartmann’s solution, as opposed to a sodium chloride 0.9 per cent base) and these are gaining popularity.

How much fluid? An adult with severe dehydration, such as that secondary to uncontrolled hyperglycaemia (where there has been massive osmotic diuresis) or due to severe burns, may need 10L or more of fluid in the first 24 hours of therapy. However, once any initial deficits are corrected, most patients in the maintenance phase will require 2 or 3L per day — larger patients tend to need 3L and smaller ones 2L. A few older patients or those with fluid overload secondary to heart or renal failure may be “fluid restricted” and require as little as 1L daily if overload is to be avoided — special considerations are required. Giving fluid requires care because it is possible to give too much, pushing the patient into oedema. Several formulae to calculate total fluid requirement exist (weight and height are usually factors), but are not used frequently on general wards because they are no substitute for good clinical observation and judgement. Whatever the formula determines, a patient who shows clinical signs of dehydration (eg, loss of skin elasticity, low blood pressure, sunken eyes) needs more fluid, and one who is fluid overloaded (eg, swollen ankles or oedema in lungs, raised jugular venous pulse) needs less.

Once a patient is fluid replete, empirical methods are most frequently used to estimate fluid needs. Good nursing practice involves maintaining a fluid balance chart for patients requiring fluid restriction or replacement, on which all inputs and outputs of fluid are recorded. These charts, however, are notoriously inaccurate and it is important to establish that all urinary excretion is collected and recorded, and that any diarrhea, vomiting losses or surgical drain losses are included. Similarly, parenteral replacement fluids, drinks, and fluids contained in administered intravenous drugs or blood products must be documented. Once the net losses of the patient have been established, it should be replaced with the same volume plus about 500ml to cover insensible losses. Glucose 5 per cent and sodium chloride 0.9 per cent intravenous infusions are available as 50ml, 100ml, 250ml, 500ml, and 1L bags but for most patients, the desired daily fluid volume can be rounded to the nearest litre. This allows the fewest bags to be used, reducing costs, workload and risks. Smaller bags are most appropriate for the intermittent infusions used to administer intravenous drug therapy.

Panel 2: Typical daily intravenous fluid regimens for short-term fluid replacement

<table>
<thead>
<tr>
<th>Example 1: Fit young man, weight 70kg</th>
<th>Example 2: Small frail elderly female patient, weight 50kg</th>
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<tbody>
<tr>
<td>1L sodium chloride 0.9% with 40mmol potassium (over eight hours)</td>
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</tr>
<tr>
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This regimen provides 3L fluid, 150mmol of sodium, and 80mmol potassium over 24 hours. This regimen provides 2L fluid, 150mmol of sodium, and 40mmol potassium over 24 hours. (This may still be too much sodium for this patient, and some hospitals use mixtures of glucose/saline to get a more suitable sodium load, at the expense of simplicity.)
**Electrolyte requirements**

Glucose 5 per cent infusion is essentially water because the small amount of glucose it contains is rapidly taken up into cells unless there is a failure of insulin. A deficit of water is likely to affect electrolyte concentrations and blood tests are required to assess and monitor the patient.

Sodium and potassium are the most common electrolytes replaced in therapy. Most patients need about 2mmol/kg/day of sodium and 1mmol/kg/day of potassium. Sodium chloride 0.9 per cent (9g NaCl in 1L) contains 153mmol each of sodium and chloride ions and 1L will, therefore, meet the daily sodium needs of the typical patient. The remaining fluid requirement can then be supplied as glucose 5 per cent. For example, if a patient needs 3L of total fluid daily, this could be supplied as 1L of sodium chloride 0.9 per cent with two 1L bags of glucose 5 per cent. Each bag would be given over eight hours, at an easy to calculate 125ml/h, or 2ml/min. Unless a patient is in heart or renal failure, the exact regimen is not that critical, especially for short periods, because oral diets also vary.

Potassium is more problematic. The amounts of sodium and potassium in the body are similar, but most potassium is stored intracellularly so the plasma level is low compared with sodium (most of which is found extracellularly). Small shifts in the serum potassium (normal range 3–5mmol/L) are more dangerous to the heart than small changes in sodium concentration (normal range 135–145mmol/L). Careful adjustment of potassium load is important, especially in renal failure, which can cause it to accumulate.

Both glucose 5 per cent and sodium chloride 0.9 per cent are available commercially with pre-added potassium chloride, typically at 0.2 per cent (27mmol/L) or 0.3 per cent (40mmol/L). The practice of adding potassium to fluid bags on wards has been abandoned in the UK because of a series of deaths from poor mixing (“layering”) of bags or accidental bolus administration of neat potassium chloride ampoules mistaken for sodium chloride.

At 1mmol/kg/day of potassium a patient might be expected to require 50–70mmol/day. This could be met by using two or three bags containing 27mmol/L or one or two bags of 40mmol/L, plus potassium-free solutions to the required total fluid requirement. Two sample regimens for different patients are illustrated in Panel 2 (p573). Monitoring via blood tests is usually daily for acute patients.

- Patients with low measured serum potassium levels or high gastrointestinal fluid losses (which are rich in potassium) will need more, and those with higher potassium levels or reduced renal excretion will need less, and possibly none at all if levels are within the reference range.

- If there is established hypokalaemia, intravenous therapy can be designed to correct the potassium concentration as much as to administer fluid, but the British National Formulary warns against using glucose as the initial carrier fluid. This is because potassium is taken into cells under the action of insulin, and the insulin response to glucose infusions may cause plasma potassium to fall further. Conversely, in conditions such as diabetic ketoacidosis (in type 1 diabetes mellitus) and hyperosmolar non-ketotic coma (H O N K), an absolute or relative failure of insulin allows both plasma glucose and potassium to rise because there is a shift out of cells, accompanied by dehydration due to the osmotic diuresis secondary to the hyperglycaemia. As insulin is replaced and blood sugar levels fall, initial hyperkalaemias are also corrected by intra-cellular shifting and the true severe potassium deficit secondary to the osmotic diuresis is uncovered. At this point, despite the initial dangerous hyperkalaemia, fluid bags containing potassium will be required to prevent the development of hypokalaemia.

The complex calculation and administration of fluid replacement therapy in addition to administration of multiple drug therapy is routinely seen in hospitals requiring careful thought about maximum dilution volumes, rates of administration, fluid compatibility etc, and ward pharmacists often engage with doctors at ward level in devising such regimens.

**Long-term needs**

Patients can be maintained on intravenous or subcutaneous fluids for several days. Their fluid needs and replacement of the major electrolytes (sodium and potassium) are satisfied and organ perfusion and function are maintained, and enteral fluid and nutrition can be gradually reintroduced. Patients who are not able to eat or drink effectively after a few days will require nutritional support. It should be noted that in the longer term, parenteral fluids are inadequate replacements of a normal oral diet because:

- Inadequate calories are being supplied (2L of glucose 5 per cent infusion contains 100g of glucose [400kCal] and the patient will starve. Protein will be used as fuel, impairing any wound healing and recovery.)

- Although sodium and potassium are replaced, other electrolytes, such as phosphate, magnesium and calcium, and trace elements are not usually supplied

- They contain no fat or water soluble vitamins so deficiency syndromes will arise

- They contain no fat and, therefore, no essential fatty acids, and no nitrogen source to replace oral protein.

It is for these reasons, and also to prevent the development of gut stasis, that oral nutrition and fluids need to be encouraged as quickly as possible. If this is not possible, enteral fluids and nutrition can be given through nasogastric, gastrostomy or jejunal tube. A small number of patients, mostly those without a functioning gastrointestinal tract, will require parenteral feeding and fluids (ie, total parenteral nutrition). This will be discussed in a future CPD article.