Intravenous fluid resuscitation is an important component of anaesthesia and critical care practice. The end point is to increase intravascular volume to augment cardiac output and organ perfusion. Failure to resuscitate patients adequately may lead to multi-organ dysfunction syndrome and, eventually, death. History, clinical signs and haemodynamic indices can all aid in the diagnosis of hypovolaemia although only the latter is reliable. Fluid challenge is a very practical and reliable way to diagnose and correct hypovolaemia.

Fluid resuscitation may be attempted with either colloid or crystalloid solution. The benefits of each type of fluid have been widely debated for many years and controversy continues as to whether crystalloid or colloids are preferred for intravascular volume replacement. However, both fluids are capable of correcting hypovolaemia. All patients require a predictable volume (usually 1500–2000 ml/24 h) of maintenance fluid, which is usually given as a combination of nutritional fluid and crystalloid. Colloid fluids are reserved for supplementation of the intravascular volume.

### Hypovolaemia

The extracellular fluid volume is determined by the absolute amount of sodium and water that are present, and constitutes ~35–40% of total body water in normal subjects. The extracellular volume is regulated by alterations in sodium excretion primarily attributable to activity of the renin–angiotensin–aldosterone system, the sympathetic nervous system, and secretion of atrial natriuretic peptide.

Hypovolaemia refers to any condition in which the extracellular fluid volume is reduced and, when severe, leads to a clinically apparent reduction in tissue perfusion. Hypovolaemia is most important when there is a reduction in intravascular volume. Hypovolaemia can be absolute or relative (Table 1). Absolute hypovolaemia refers to the actual loss of volume from the extracellular space. Relative hypovolaemia refers to an inappropriate redistribution of body fluids or dilatation of the intravascular space resulting in a decrease in the effective intravascular volume.

### Diagnosis of hypovolaemia

The diagnosis of hypovolaemia can be based on history, clinical examination, invasive and non-invasive diagnostic procedures.

### History and examination

A history of any known cause of hypovolaemia (Table 1) may aid in the diagnosis. However, apart from dramatic volume loss that requires emergency fluid replacement, the history is usually of little help in predicting the scale of hypovolaemia.

Clinical signs of hypovolaemia (reduced skin turgor, oliguria, tachycardia and hypotension) are late indicators. The presence of these signs signifies hypovolaemia of a degree that requires urgent intervention. The absence of these signs does not exclude hypovolaemia. The diagnosis of lesser degrees of hypovolaemia (covert hypovolaemia), which require treatment for maintenance of tissue perfusion and avoidance of organ dysfunction is difficult clinically. Clinical assessment is dependent on

### Table 1 Causes of absolute and relative hypovolaemia

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<tr>
<th>Absolute hypovolaemia</th>
<th>Relative hypovolaemia</th>
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<tr>
<td>Haemorrhage</td>
<td>Capillary leak</td>
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<tr>
<td>Burns</td>
<td>Inflammation</td>
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<tr>
<td>Diarrhoea</td>
<td>Burns</td>
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<td>Polyuria</td>
<td>Trauma</td>
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<td>Evaporation</td>
<td>Anaphylaxis</td>
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<td>Surgery</td>
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<td>Sweating</td>
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<td>Spinal surgery</td>
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<td>Anaesthesia</td>
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Key points

- Hypovolaemia can lead to multi-organ dysfunction syndrome and death.
- The clinical diagnosis of hypovolaemia is unreliable, often leading to significant delays in treatment.
- Both colloid and crystalloid can be used to correct hypovolaemia.
- Minimally invasive tools are now available to monitor haemodynamics and promote early correction of hypovolaemia.
- Fluid challenge is a very practical and reliable technique to diagnose and correct hypovolaemia.
patient position, there being an increase in plasma volume and therefore a minimization of clinical signs associated with supine positioning. Where hypovolaemia is suspected in a supine patient, lifting the legs and watching for an improvement in the circulation is a useful indicator. Severe hypotension induced by the administration of drugs with vasodilator properties (e.g. sedatives) might indicate significant hypovolaemia. Routine physical assessment alone, including blood pressure, heart rate, and urine output, often fails to show the true haemodynamic status of the compromised patient. Several studies have demonstrated that clinicians were able to predict haemodynamic status accurately, on the basis of physical assessment and clinical findings alone, in only ~50% of cases. Many factors may contribute to these findings, including physiological compensatory mechanisms that often mask the true extent of hypovolaemia.

Measurement of blood volume
The gold standard for the diagnosis of hypovolaemia is the measurement of blood volume. Techniques available rely on the principles of indicator dilution, usually involving radioisotopes as the indicators. Most techniques are not practical as they do not lend themselves to rapid, bedside estimation and, therefore, preclude rapid intervention. Furthermore, true estimation of blood volume requires an indicator that is detectable before it distributes outside the circulation. The only indicator that can currently be used in this fashion, mixing with the whole circulation before any loss from the circulation, is radio-chromium labelled red blood cells. The development of methods based on carbon monoxide labelled red cells is more promising. Measuring blood volume in hypovolaemic patients is not currently a clinically useful technique. Even if we had a reliable method of measuring blood volume at the bedside, normal blood volume is a poor indicator of physiological requirement and is dependent on body composition, being lower in obese patients. We therefore rely on surrogate markers of volume status.

Central venous pressure
The central venous pressure (CVP) is the most popular and most commonly used surrogate marker of volume status. Its popularity is based on ease of measurement but there are a number of pitfalls. CVP is dependent on venous return to the heart, right ventricular compliance, peripheral venous tone and posture. A normal CVP does not exclude hypovolaemia and the CVP is particularly unreliable in pulmonary vascular disease, right ventricular disease, patients with tense ascites, isolated left ventricular failure and valvular heart disease. In patients with an intact sympathetic response to hypovolaemia, the CVP may fall in response to fluid as their compensatory venoconstriction is reduced. Critically ill patients often have abnormally high or low CVP measurements, and treatment is often aimed at maintaining a slightly higher than normal CVP to ensure sufficient blood return to the heart. Unfortunately, a single CVP measurement has limited significance and administration of fluid to achieve fixed CVP targets has little to do with ensuring the patient has received a correct amount of fluid. Trends in CVP response to fluid administration provide important information about the patient’s response to fluid resuscitation.

Pulmonary artery wedge pressure and cardiac output
The pulmonary artery catheter (PAC) allows directly measurement of the cardiac output (CO), stroke volume (SV), pulmonary artery pressures and the mixed venous oxygen saturation. Pulmonary artery wedge pressure (PAWP) provides similar information regarding fluid status as the CVP along with similar pitfalls. As the purpose of fluid resuscitation is to provide optimal blood flow to maintain tissue perfusion, measurement of PAWP without assessment of CO cannot be justified. As with CVP measurement, the absolute level of PAWP does not confirm or exclude hypovolaemia. Left ventricular disease may increase the level of PAWP required for an adequate circulating volume. Interpretation of PAWP requires caution in ventilated patients as increased intrathoracic pressure falsely increases the PAWP reading. PAWP is a useful indicator of hypovolaemia where CVP is high and PAWP is significantly lower (e.g. selective right ventricular dysfunction, chronic airflow limitation). Many clinicians have limited knowledge of how to make use of data from a PAC in a clinical setting. It is now well established that use of the PAC is frequently associated with inaccurate measurements. Furthermore, even when measurements are accurate, benefit could only be gained when appropriate decisions are made based on these measurements. The difficulty in interpretation of the waveforms and the lack of an understanding of the relevance of each variable obtained may lead to inappropriate intervention and subsequent adverse results.

Pulmonary artery catheterization is known to be associated with significant complications and has even been suggested as a cause of increased mortality. A number of less invasive methods of CO and SV measurement are now available. Bioimpedance is a completely non-invasive method of assessing blood flow and volume status. Its main drawback is the need for critical electrode placement and inaccuracy in capillary leak, tachycardia and environments where there is electrical interference. It is not widely used in the operating theatre or critical care settings. Another completely non-invasive method of assessing CO relies on a modified Fick equation to derive CO from changes in exhaled carbon dioxide during rebreathing. Its major limitation is a time lag of ~3 min for a physiological change to be displayed and requirement for mechanical ventilation with constant minute ventilation. The technique assumes no intrapulmonary shunt and requires a correction for estimated shunt fraction.

Pulse contour analysis assesses changes in CO according to changes in the size and shape of the arterial pressure wave. Calibration requires measurement of CO by another technique. Two readily available techniques are a modification of the dye dilution technique using lithium as the indicator or thermodilution. Rather than measuring CO with a PAC, these techniques rely on indicator dilution from central venous injection to arterial cannula.
measurement. The techniques are inaccurate in cases of aortic regurgitation, intra-aortic balloon counterpulsation, severe peripheral vascular disease and in hypothermic patients. Recalibration is needed more frequently during haemodynamic instability.

Oesophageal Doppler monitoring provides real-time measurements and visualization of blood flow from the left side of the heart. It requires significantly less insertion time than the PAC, can be done by trained nursing staff and carries significantly less risk of complications. Oesophageal Doppler monitoring has few contraindications but these include coarctation of the aorta or patients treated with intra aortic balloon counterpulsation (not accurate) and patients with oesophageal pathology. Although the probe is similar in size to a Ryle’s tube, sedation may be required to aid patient tolerance of the probe.

As with other surrogate markers of volume status, knowledge of the absolute CO or SV does not confirm or refute hypovolaemia. More important is the response of CO and SV to fluid therapy. CO is only adequate when it provides sufficient tissue perfusion.

Measurement of tissue perfusion

Treatment of volume status is not required if tissue perfusion is adequate. Global assessment of tissue perfusion is based on demonstration of the absence of anaerobic metabolism (i.e. no lactic or metabolic acidosis). However, the presence of lactic acidosis does not necessarily indicate an inadequate circulation (e.g. liver dysfunction) and the absence of lactic acidosis does not guarantee adequate perfusion of all tissues.

The gut mucosa is one of the earliest tissues to be compromised in hypovolaemia. Gastric tonometry provides a simple, minimally invasive method of assessing the adequacy of perfusion. It is based on the assumption that the \( P_{aco_2} \) in the lumen of a hollow viscus will equilibrate with the \( P_{aco_2} \) in the superficial mucosa of the organ. Mucosal \( P_{aco_2} \) increases in mucosal hypoperfusion. Originally, mucosal \( pH \) (pHi) was calculated from mucosal \( P_{aco_2} \) and arterial bicarbonate (Henderson–Hasselbalch equation) on the assumption that tissue and arterial blood bicarbonate concentrations are similar. pHi is low in the presence of mucosal hypoperfusion.

Newer devices rely on rapid assessment of mucosal \( P_{aco_2} \), which is compared with end-tidal \( P_{aco_2} \) (\( E_{aco_2} \)) to provide semi-continuous monitoring of the difference. The greater the difference, the greater the degree of mucosal hypoperfusion. The assumptions around arterial and mucosal bicarbonate, now known to be a source of error, are no longer required. \( E_{aco_2} \) is assumed to reflect \( P_{aco_2} \). While this may be true in most elective surgical cases, it is a limitation of the device in the critical care.

Sublingual \( P_{aco_2} \) (\( PsL_{aco_2} \)) measurements can be obtained by placing a disposable sensor under the tongue with the sensor element facing the sublingual mucosa. Within 5 min, a \( PsL_{aco_2} \) measurement is recorded. Increases in \( PsL_{aco_2} \) directly correlate with decreases in sublingual blood flow, mirroring the decreases in flow seen in both the stomach and the oesophagus. Studies in animal models have demonstrated increases in \( PsL_{aco_2} \) are correlated with decreases in arterial blood pressure and cardiac index, with corresponding increases in serum lactate during both haemorrhagic and septic shock. Current technology allows single readings only, which makes monitoring using this method difficult and expensive.

The use of i.v. fluids

For a long time, clinicians have used filling pressures to guide fluid resuscitation therapy in patients with central venous or pulmonary artery catheters. Most have used absolute values of CVP or PAWP as targets for fluid therapy. Establishing goals for these filling pressures is difficult and is not physiological because end-diastolic filling depends on physiological factors other than filling pressure. Furthermore, filling pressures are dependent on venous tone in addition to cardiac end-diastolic pressure.

Using fluids to correct hypovolaemia is a dynamic process that requires ongoing evaluation of clinical and haemodynamic indices. Thus, the use of the fluid challenge provides a successful method of adjusting fluid volume to the patient’s need.

The fluid challenge

The fluid challenge is a method of safely restoring circulating volume according to physiological need rather than using fixed haemodynamic end-points. Fluid is given in small aliquots to produce a known increment in circulating volume with assessment of the dynamic haemodynamic response to each aliquot. No fixed haemodynamic end-point is assumed and the technique provides a diagnostic test of hypovolaemia (via an appropriate positive response of the circulation to fluid) and a method of titrating the optimal dose of fluid to the individual’s requirement.

The response of SV and/or CVP (or PAWP) should be monitored during a fluid challenge. The basis of the fluid challenge is to achieve a known increase in intravascular volume by rapid infusion of a bolus of colloid fluid (200 ml). Colloid rather than crystalloid should be used because rapid extravasation of crystalloid to the interstitial space makes it impossible to know that we have achieved a defined increment in intravascular volume that lasts long enough for measurements to be made. The change in CVP or PAWP after a 200 ml increment in intravascular volume depends on the starting circulating volume. Where intravascular volume is low, CVP will not increase with a small increment in blood volume whereas a significant increase in CVP will be seen as the starting intravascular volume increases (Fig. 1). The same is true for PAWP. A 3 mm Hg increase in CVP or PAWP represents a significant increase and is probably indicative of an adequate circulating volume. It is important to assess the clinical response and adequacy of tissue perfusion in addition; if either are inadequate, it is appropriate to monitor SV before further fluid challenges or considering further circulatory support.

In the inadequately filled left ventricle, a fluid challenge will increase SV (Fig. 1). Failure to increase SV with a fluid challenge
Fluid resuscitation

![Stroke volume vs PAWP/CVP graph]

**Fig 1**. The response of stroke volume, CVP or PAWP to a 200 ml increment of blood volume. In the hypovolaemic patient, no significant increase in CVP or PAWP would be expected but an increase in stroke volume would be expected. In the optimally filled patient, an increase in CVP or PAWP with no significant increase in stroke volume would be expected.

may indicate a circulation that is unresponsive to fluid or an inadequate challenge. If the PAWP or CVP fails to increase significantly (by at least 3 mm Hg) while SV fails to increase, the increment in circulating volume filled the depleted peripheral vascular space and did not increase cardiac filling. In this case, the fluid challenge should be repeated. SV rather than CO is monitored during a fluid challenge because an appropriate fall in heart rate in response to a fluid challenge may result in a decrease in CO despite an increase in SV. Fluid challenges should be repeated while the response (increasing SV or no increase in CVP) suggests continuing hypovolaemia.

Studies have demonstrated that intraoperative fluid optimization guided by oesophageal Doppler monitoring significantly improved outcomes, as evidenced by a 30–40% decrease in duration of stay. These studies have been performed in different surgical populations, including cardiac, orthopaedic and general surgery. All of the studies used similar algorithms involving fluid challenges to guide volume administration. After baseline oesophageal Doppler values had been obtained, a fluid challenge was given. If the SV increased by >10%, the patient was considered to be volume responsive and fluid challenges were repeated until no further increase in SV was noted. At this point, the patient was considered to be unresponsive to fluid. No further fluid challenges were given unless the SV decreased by >10%.

**Choice of i.v. fluid**

The choice of replacement fluid depends, in part, upon the type of fluid that has been lost. Blood is indicated in patients who have lost blood and the main purpose of blood transfusion is to restore oxygen-carrying capacity. However, the restoration of circulating volume with any fluid is more critical and urgent than the restoration of oxygen carrying capacity. Fresh frozen plasma and other blood components are indicated in patients with severe coagulopathy but these fluids should not be used for volume replacement.

Both crystalloid and colloids have been used to replace extracellular fluid deficit. Crystalloid solutions such as lactated Ringer’s solution and sodium chloride 0.9% (normal saline solution) do not possess oncotic properties, so only ~25% of the infused volume is retained in the intravascular space. When crystalloid is used to correct hypovolaemia, lactated Ringer’s solution is recommended as the first-line therapy because it closely resembles physiological body fluid in terms of electrolyte concentration and oncoticity. The use of normal saline may lead to hyperchloraemia and metabolic acidosis. Crystalloid fluids fill both the interstitial and intravascular spaces. Advantages of crystalloid fluids include cost and non-allergenic properties. Disadvantages include excessive tissue oedema.

Colloids include the plasma substitutes: human serum albumin (5% and 25%), dextran, gelatin and hydroxyethyl starch (HES). Colloid solutions contain large, molecules, which (compared with crystalloid) stay within the intravascular space and exert an oncotic force to maintain plasma volume. Potential disadvantages of colloid solutions are cost, risk of developing coagulopathy and rare allergic reactions.

The controversy over the type of fluid (crystalloid vs colloid) to be used in volume resuscitation is well known. Both crystalloid and colloid fluids are capable of restoring circulating volume. Some benefits from using colloid are the more rapid plasma volume expansion and the lower risk of pulmonary and systemic oedema. Although colloids are more expensive than crystalloid, their effect on the circulating volume lasts much longer and smaller volumes are required. Crystalloid supporters argue that leakage of colloid into the interstitial space contributes to oedema formation. There is no evidence that leakage of colloid molecules to the interstitium has any effect but limited research in this area has been performed. There is good evidence that suggests that, even for very short periods of time, rapid infusion of colloid is significantly more able to increase blood volume (and by inference cardiac output) than is the same volume of crystalloid even when the crystalloid is given very rapidly. This is particularly important in a clinical scenario in which hypotension is immediately life threatening. Recent studies suggest that intra-operative fluid resuscitation with predominantly colloids appears to improve the quality of postoperative recovery compared with crystalloid. Specifically, colloid administration was associated with a lower incidence...
and severity of nausea, vomiting and use of rescue antiemetics. Crystallloid-resuscitated patients also experienced more severe pain, periorbital oedema, and double vision.

Although the crystallloid–colloid controversy has not focused on the specific colloid used, it is increasingly clear that different colloid molecules have different effects. The available solutions have different physical and chemical properties and different side-effect profiles.

Gelatins are polypeptides with a relatively small average molecular weight. They are a degradation products of animal collagen and therefore inexpensive and readily available. Gelatins are appropriate as the fluid of first choice in volume resuscitation. HES compounds are synthetic polymers derived from amylopectin, a branched polysaccharide. Various HES solutions are currently available ranging from low to high molecular weight and low to high degree of substitution. High molecular weight HES preparations with greater hydroxyethyl substitution reduce levels of coagulation factors, fibrinogen, factor VIII, and Von Willebrand’s factor and reduce platelet function. It is hypothesized that complex polysaccharides precipitate certain coagulation factors making the factors unavailable to the coagulation cascade. Lower and medium molecular weight HES show less interference with coagulation. Medium and high molecular weight HES solutions are better retained than gelatins and therefore provide for intravascular retention in cases where capillary leak is present.

Albumin is not routinely used for volume resuscitation. However, some physicians use it for volume resuscitation when hypoalbuminemia is present. The many theoretically useful properties of albumin make a rapid return to normal serum values an attractive proposition. However, these properties are minor effects of albumin and there are better treatments available to deal with them. To date, the available literature implies that we might do more harm than good infusing albumin.

Dextrans are composed of linear polysaccharide molecules. Low molecular weight dextran can improve the microvascular circulation by decreasing blood viscosity and coating vascular endothelial cells to minimize platelet and red blood cell aggregation. However, the same mechanisms can cause considerable impairment to the coagulation system and may produce bleeding.

Key references


See multiple choice questions 80–83.