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Basic Concepts of Fluid and Electrolyte Therapy

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Basic Concepts of Fluid and Electrolyte Therapy

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Preface

Despite the fact that fluid and electrolyte preparations are the most commonly prescribed medications in hospitals, a number of studies have shown that the knowledge and practice of fluid and electrolyte balance among young doctors is suboptimal, possibly due to inadequate teaching. This is responsible for errors in management, which continue to cause avoidable morbidity and even mortality. It is not the intention of the authors of this book to write a comprehensive textbook dealing with complex problems, but to provide a pocket book for students, nurses and young doctors to help them to understand and solve some of the most common practical problems they face in day-to-day hospital practice. The authors hope that it will also stimulate them to pursue the subject in greater detail with further reading and practical experience. In difficult cases, the young doctor should never hesitate to ask for advice from senior and experienced colleagues.

Dileep N. Lobo

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Foreword

This book, 'Basic Concepts of Fluid and Electrolyte Therapy', fills a long felt need for an up to date pocket guide to the subject. Water and electrolyte balance is crucial for body homeostasis and is one of the most protected physiological mechanisms in the body. While we can survive for months without food, without water intake we die very quickly. Similarly the body has very strong mechanisms to control salt and water balance, an understanding of which has major implications in clinical practice.

Despite salt and water balance being so fundamental for homeostatic control, knowledge and practice of fluid and electrolyte therapy has been shown to be appallingly poor among many health care professionals. The results of such knowledge surveys have been reported by the authors and were surely the reason why they felt the urge to write this book.

Dileep Lobo, Andrew Lewington and Simon Allison are all well renowned experts in this field covering different aspects of the topic: surgery, renal medicine and clinical nutrition. This allows for a broad approach to the concepts of fluid and electrolyte management and gives the book sufficient depth to fulfil the basic needs of all medical specialties.

The book covers the basics in physiology and pathophysiology, how to assess fluid and electrolyte status, a clear overview of fluids used in clinical practice and how to prescribe them, and then moves on to describe and discuss some of the most common clinical problems.

The book is rich in tables and figures that help the reader grasp the fundamentals, both physiological and pathophysiological. It contains examples of how to address clinical situations and to monitor treatment, often with the help of simple cartoons and figures. The authors

have also done a fine job in explaining some of the more complex issues involved, making this book a very useful read for everyone involved in patient care, as well as for students in training for any higher qualifications in the medical professions.

Whether you are a professional in medicine or a student, enjoy this very interesting read, and make use of it in your practice!

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1. Normal Physiology and Anatomy of the Body Fluids

Introduction

When primitive marine unicellular organisms evolved into multicellular organisms and emerged onto land, they faced several physiological challenges including the maintenance of water and salt balance in an environment low in both. Rather than being surrounded by an external sea, they carried with them their own internal sea or extracellular fluid (ECF), in which their cells could bathe in a constant chemical environment, which the great French physiologist Claude Bernard called the 'milieu interieur'. In this environment the cells retain their energy consuming and primeval capacity to pump sodium out and to retain potassium in order to neutralise the negative charges of proteins and other ions.

While fluid balance is usually considered as that between the body and its environment, i.e. external balance, disease also affects the internal balance between the various body fluid compartments, e.g. between the intravascular and interstitial components of the ECF, between the intracellular fluid (ICF) and the ECF, and between the ECF and the gut and other internal spaces.

Normal anatomy and physiology

Water comprises 60% of the body weight of an average adult, although the percentage is lower in obesity, since adipose tissue contains less water than lean tissue. As shown in Fig. 1, the total body water is divided functionally into the extracellular (ECF = 20% of body weight) and the intracellular fluid spaces (ICF = 40% of body weight) separated by the cell membrane with its active sodium pump, which ensures that sodium remains largely in the ECF. The cell, how-

ever, contains large anions such as protein and glycogen, which cannot escape and, therefore, draw in K^+ ions to maintain electrical neutrality (Gibbs–Donnan equilibrium). These mechanisms ensure that Na^+ and its balancing anions, Cl^- and HCO_3^- , are the mainstay of ECF osmolality, and K^+ has the corresponding function in the ICF.

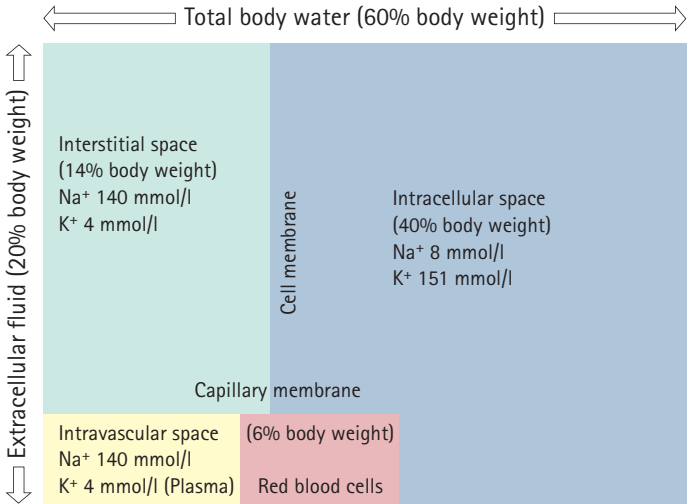


Figure 1: Body fluid compartments with approximate electrolyte concentrations. Red blood cells (haematocrit) account for approximately 45% of total intravascular volume.

The ECF is further divided into the intravascular (within the circulation) and the interstitial (extravascular fluid surrounding the cells) fluid spaces. The intravascular space (blood volume = 5–7% of body weight) has its own intracellular component in the form of red (haematocrit = 40–45%) and white cells and an extracellular element in the form of plasma (55–60% of total blood volume).

The intravascular and extravascular components of the ECF are separated by the capillary membrane, with its micropores, which allow only a slow escape rate of albumin (5%/hr), which is then returned to the circulation via the lymphatics at the same rate, thereby maintaining a steady state of equilibrium (Fig. 2). While the hydrostatic pressure within the circulation tends to drive fluid out, the oncotic pressure of the plasma proteins, e.g. albumin, draws fluid in and maintains the relative constancy of the plasma volume as a proportion of the ECF (Starling effect).

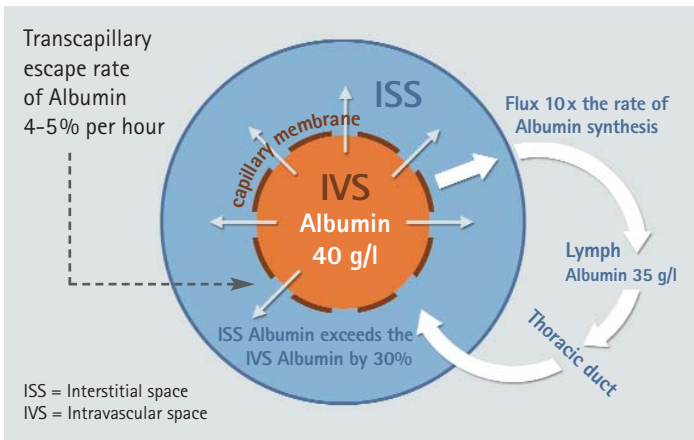


Figure 2: Transcapillary escape of albumin in health.

There is also a clinically important flux of fluid and electrolytes between the ECF and the gastrointestinal (GI) tract involving active secretion and reabsorption of digestive juices (Fig. 3). In health there is a constant flux between these various spaces and important physiological mechanisms ensure a constant relationship between them, which we may term the *internal fluid balance*.

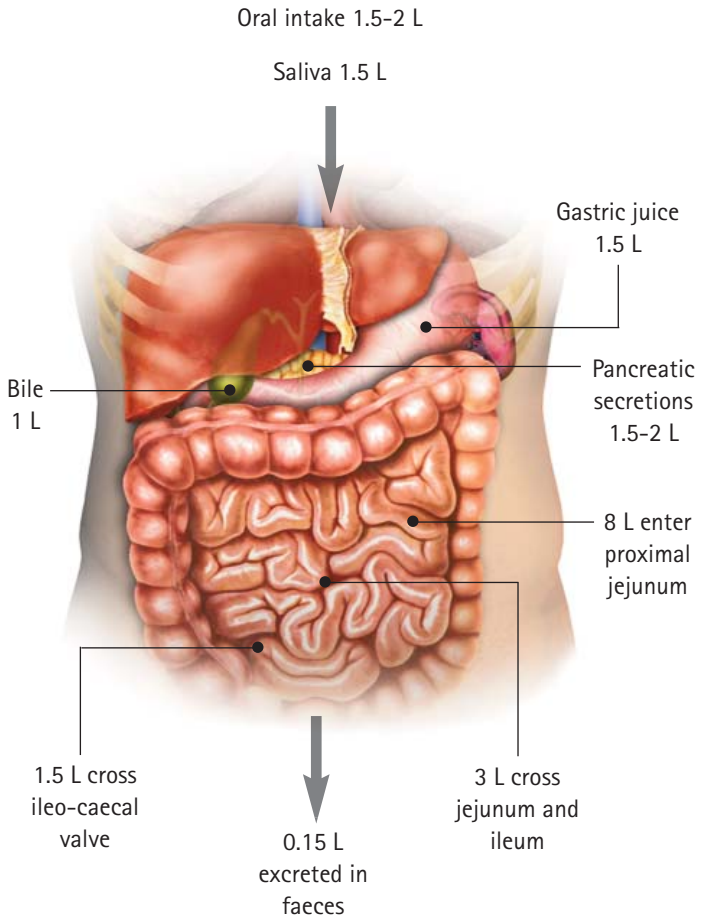


Figure 3: Flux of fluid across the gastrointestinal tract.

The *external fluid and electrolyte balance* between the body and its environment is defined by the intake of fluid and electrolytes versus the output from the kidneys, the gastrointestinal tract, and the skin and lungs (insensible loss). Since the external and internal balances may be disturbed by disease, it is important to understand normal physiology in order to appreciate the disorders, which may occur in patients.

External balance

Values for the normal daily intake and output of fluid and electrolytes are shown in Tables 1 and 2. These are only an approximate guide and may have to be modified in the presence of excessive losses, e.g. of water and salt through increased sweating and insensible loss in hot climates. They may also need to be modified in the presence of disease, e.g. gastroenteritis, which causes abnormal losses of fluid and electrolyte from the GI tract (Fig. 3 and Table 3).

Table 1: Approximate daily water balance in health

Intake (ml)		Output (ml)	
Water from beverages	1200	Urine	1500
Water from solid food	1000	Insensible losses from skin and lungs	900
Metabolic water from oxidation	300	Faeces	100

Table 2: Normal maintenance requirements

Water	25-35 ml/kg/day
Sodium	0.9-1.2 mmol/kg/day
Potassium	1 mmol/kg/day

Table 3: Approximate electrolyte content of gastrointestinal and skin secretions

Secretion	Na ⁺ (mmol/l)	K ⁺ (mmol/l)	Cl ⁻ (mmol/l)
Saliva	40	20	40
Gastric juice	70-120	10	100
Bile	140	5	100
Pancreatic juice*	140	5	75
Small intestine	110-120	5-10	105
Diarrhoea (adult)	120	15	90
Sweat	30-70	0-5	30-70

* Pancreatic juice has a bicarbonate content of 50-70 mmol/l

Intake

Under normal circumstances most of our fluid intake is oral, but remember that all food contains some water and electrolytes and also that water and CO₂ are end products of the oxidation of foodstuffs to produce energy. This metabolic water is a small but significant contribution to net intake. Our drinking behaviour is governed by the sensation of thirst, which is triggered whenever our water balance is

negative through insufficient intake or increased loss. It may also be triggered by a high salt intake, which necessitates the intake and retention of extra water in order to maintain the ECF sodium concentration and osmolality in the normal range.

Although, in the elderly, the thirst mechanism becomes blunted, it ensures, on the whole, that our intake matches the needs of bodily functions, maintaining a zero balance in which intake and output are equal and physiological osmolality (280-290 mOsm/kg) is maintained.

More than a century ago Claude Bernard coined the term '*volume obligatoire*' to describe the minimum volume of urine needed to excrete waste products, e.g. urea, in order to prevent them accumulating in the blood. This concept implies that, if sufficient fluid has been drunk or administered to balance insensible or other losses and to meet the kidney's needs, there is no advantage in giving additional or excessive volumes. Indeed, excessive intakes of fluid and electrolytes may be hazardous under certain circumstances (see below) and overwhelm the kidney's capacity to excrete the excess and maintain normal balance. Salt and water retention becomes clinically apparent in the form of oedema when the ECF has been expanded by at least 2-3 litres.

Output

- Insensible loss: evaporation of water from the lungs and skin occurs all the time without us being aware of it. In our temperate climate the amount so lost is 0.5-1 litre/day. In a warm environment, during fever, or with exertion, we produce additional sweat containing up to 50 mmol/l of salt.
- GI losses: normally, the intestine absorbs water and electrolytes very efficiently so that fluid loss in the stool is as little as 100-150 ml/day, although, in the presence of disease this may be greatly increased (Table 3 and Fig. 3).

■ **Kidney:** this is the main organ for regulating fluid and electrolyte balance as well as excreting the waste products of metabolism, e.g. urea. In this function, its activity is controlled by pressure and osmotic sensors and the resulting changes in the secretion of hormones. The modest daily fluctuations in water and salt intake cause small changes in plasma osmolality which trigger osmoreceptors. This in turn causes changes in thirst and also in renal excretion of water and salt. If blood or ECF volumes are threatened by abnormal losses, volume receptors are triggered (see below) and override the osmoreceptors. In the presence of large volume changes, therefore, the kidney is less able to adjust osmolality, which can be important in some clinical situations.

■ **Water**

Organs, which sense the changes in osmolality of plasma (osmoreceptors), are located in the hypothalamus and signal the posterior pituitary gland to increase or decrease its secretion of vasopressin or antidiuretic hormone (ADH). Dilution of the ECF, including plasma, by intake of water or fluid of osmolality lower than plasma, causes ADH secretion to fall, so that the distal tubules of the renal glomeruli excrete more water and produce a dilute urine (this dilution requires the permissive effect of glucocorticoid upon the distal tubules and is, therefore, lost in adrenal insufficiency - one of the reasons for the hyponatraemia of Addison's Disease). Conversely, dehydration causes the ECF to become more concentrated, ADH secretion rises and the renal tubules reabsorb more water, producing a concentrated urine. In response to dehydration, the normal kidney can concentrate urea in the urine up to a hundred-fold, so that the normal daily production of urea during protein metabolism can be excreted in as little as 500 ml of urine.

In the presence of water lack, the urine to plasma urea or osmolality ratio is, therefore, a measure of the kidney's concentrating capacity. Age and disease can impair the renal concentrating capacity so that a larger volume of urine is required in order to excrete the same amount of waste products. Also if protein catabolism increases due to a high protein intake or increased catabolism, a larger volume of urine is needed to clear the resulting increase in urea production.

To assess renal function, therefore, measurement of both urinary volume and concentration (osmolality) are important, and the underlying metabolic circumstances taken into account. If serum urea and creatinine concentrations are unchanged and normal, then, urinary output over the previous 24 hours has been sufficient, fluid intake has been adequate, and the urinary '*volume obligatoire*' has been achieved.

■ Sodium

Since the integrity of the ECF volume and its proportion of the total body water are largely dependent on the osmotic effect of Na^+ and its accompanying anions, it is important that the kidneys maintain Na^+ balance within narrow limits. If salt depletion occurs, then the ECF, and with it the plasma volume, falls. Pressure sensors in the circulation are then stimulated and these excite renin secretion by the kidney. This, in turn, stimulates aldosterone secretion by the adrenal gland, which acts on the renal tubules, causing them to reabsorb and conserve Na^+ .

Conversely, if the intake of Na^+ is excessive, the renin-aldosterone system switches off, allowing more Na^+ to be excreted, until normal balance is restored. The mechanism for salt conservation is extremely efficient and the kidney can reduce the concentration of Na^+ in the urine to <5 mmol/l. On the other hand, even in health, we are slow to excrete an excess salt load, possibly because our physiology has evolved in the context of a low salt environment and not until modern times been exposed to excessive salt intake. The response of atrial natriuretic peptide to fluid infusions seems to be related more to volume (stretching of the right atrium) than sodium load *per se*.

The mechanism for maintaining sodium balance may become disturbed in disease, leading to Na^+ deficiency or, more commonly, to excessive sodium retention, with consequent oedema and adverse clinical outcome.

■ Potassium (K^+)

Although only a small proportion of the body's K^+ is in the extracellular space, its concentration has to be maintained within narrow limits (3.5–5.3 mmol/l) to avoid the risk of muscular dysfunction or potentially fatal cardiac events. This is achieved by exchange of K^+ in the renal tubules for Na^+ or H^+ , allowing more or less K^+ to be excreted. In the presence of K^+ deficiency, H^+ ion reabsorption is impaired, leading to hypokalaemic alkalosis.

Pathophysiology

Diseases such as gastroenteritis, diabetic ketoacidosis or Addison's disease cause their own specific changes in fluid and electrolyte balance, but there are non-specific changes which occur in response to any form of injury or inflammation, which have important implications for management, particularly of surgical patients.

Response to injury

In the 1930's, Cuthbertson described the metabolic changes, which occur in response to injury (including surgery and sepsis), as an increase in metabolic rate and protein breakdown to meet the requirements for healing. These changes were later shown to be due to neuroendocrine and cytokine changes and to occur in three phases.

The ebb or shock phase is brief and is modified by resuscitation. This gives way to the flow or catabolic phase, the length and intensity of which depends on the severity of injury and its complications. As inflammation subsides, the convalescent anabolic phase of rehabilitation begins. In parallel with these metabolic changes there are changes in water and electrolyte physiology. During the flow phase, there is an increase in ADH and aldosterone secretion leading to retention of salt and water with loss of potassium. These changes are exacerbated by any reduction in blood or ECF volume.

The normal, if somewhat sluggish, ability to excrete an excess salt and water load is further diminished, leading to ECF expansion and oedema. The response to injury also implies that oliguria is a normal response to surgery, and does not necessarily indicate the need to increase the administration of salt and water or plasma expanders unless there are also indications of intravascular volume deficit, e.g. from postoperative bleeding. Salt and water retention after injury can be seen as nature's way of trying to protect the ECF and circulating

volume at all costs. It also explains why sick patients can be so easily overloaded with excessive salt and water administration during the flow phase. Since water as well as salt is retained, it is also easy to cause hyponatraemia by giving excess water or hypotonic fluid. It is important, therefore, to administer crystalloids, not only in the correct volume but also in the appropriate concentration. In the presence of the response to injury, the kidneys are unable to correct for errors in prescribing.

The convalescent phase of injury is not only characterised by the return of anabolism but also by a returning capacity to excrete any excess salt and water load that has been accumulated. These periods have been termed the '*sodium retention phase*' and the '*sodium diuresis phase*' of injury.

Transcapillary escape rate of albumin

The response to injury, stress and sepsis also results in an increase in the size of the pores in the capillary membrane and the transcapillary escape rate of albumin increases from about 5%/h in health to 13-15%/h. This phenomenon can last from several hours to days. Albumin leaks out from the intravascular compartment into the interstitial space and along with it, water and sodium are also drawn into the interstitial space. This results in a net contraction of the intravascular compartment and expansion of the interstitial space (Fig. 4). As the return of albumin to the circulation via the lymphatics is unchanged, the net result is an intravascular hypovolaemia with oedema.

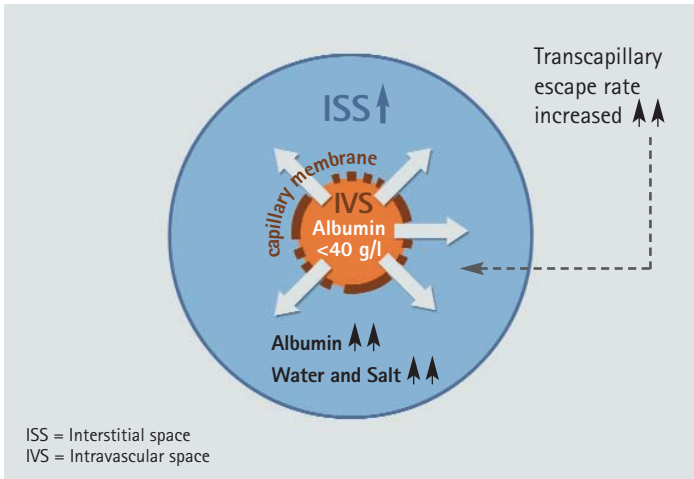


Figure 4: Effects of an increase in the transcapillary escape rate of albumin.

Potassium

K^+ losses after surgery, sepsis and trauma are not only secondary to increased excretion, but also to protein and glycogen catabolism. As intracellular protein is broken down and its constituent amino acids are released from cells, so intracellular negative charges are lost and K^+ , with its balancing positive charges, passes out into the ECF to be excreted. In situations where catabolism is extreme and renal function is impaired, the outflow of K^+ from the cells may exceed the kidney's capacity to excrete it, causing dangerous hyperkalaemia. Conversely, in the convalescent phase, as net intracellular protein and glycogen anabolism is restored, the cells take up K^+ again and the patient's potassium intake has to be increased or else hypokalaemia will develop.

Conclusion

Appropriate fluid therapy depends on an understanding of the underlying physiology and pathophysiology and a consideration not only of external but internal fluid balance.

2. Definitions

Much confusion in the diagnosis and treatment of fluid and electrolyte disorders is caused by loose and ambiguous terminology. The term 'dehydration', for example, meaning lack of water, is often used carelessly and imprecisely to include salt and water lack or, even more confusingly, intravascular fluid depletion. We therefore make a plea for the use of precise diagnostic terms, which indicate clearly the deficit or excess and the treatment required.

Anabolism – the synthesis of large molecules from small ones, e.g. protein from amino acids or glycogen from glucose.

Catabolism – the breakdown of large molecules into small ones, e.g. protein to amino acids or glycogen to glucose.

Total body water (TBW) – percentage of body composition consisting of water, approximately 60% of body weight, less in obesity and more in infants.

Intracellular fluid (ICF) volume – that part of the TBW contained within the cells, approximately 40% of body weight and $\frac{2}{3}$ rds of TBW. Muscle cells contain 75% water and fat cells have <5% water.

Extracellular fluid (ECF) volume – that portion of the TBW outside the cells, approximately 20% of body weight and $\frac{1}{3}$ rd of TBW, sustained osmotically mainly by sodium.

Interstitial fluid volume – that portion of the ECF outside the circulation and surrounding the cells.

Intravascular fluid volume

- the total blood volume consisting of red and white cells and plasma. May be estimated at approximately 5–7% of the body weight.
- the plasma volume is that part of the ECF contained within the circulation and supported oncologically by the plasma proteins, separated from the interstitial fluid by the capillary membrane. Comprises approximately 3–4% of the body weight.
- the effective circulatory volume refers to that part of the ECF that is in the arterial system (normally 700 ml in a 70 kg man – 10% of body weight) and is effectively perfusing the tissues.

Salt – in chemistry this is used to describe a whole family of compounds such as MgSO_4 , FeSO_4 , CaCl_2 , etc. but colloquially and in clinical practice it has come to mean NaCl , and that usage will be followed in this book.

Electrolyte – a substance whose components dissociate in solution into positively (cation) and negatively (anion) charged ions. For example, sodium chloride in solution (saline), dissociates into Na^+ and Cl^- . Other electrolytes of physiological importance include Ca^{2+} , Mg^{2+} , K^+ , PO_4^{2-} , etc. Glucose is not an electrolyte since it does not dissociate in solution. At all times the total number of positive charges balances the number of negative charges to achieve electrical neutrality.

Dehydration – the term 'dehydration' strictly means lack of water, yet it is also used colloquially to mean lack of salt and water or even more loosely to describe intravascular volume depletion. The terms 'wet' and 'dry' are applied to patients with similarly imprecise meaning. We make a plea for confining the use of dehydration to mean 'water lack' and for using unambiguous terms such as 'salt and water depletion', 'blood loss', 'plasma deficit', and so forth, since these are clear diagnoses indicating logical treatments. It may, however, be used legiti-

mately to describe fluid deficit from sweating, remembering that a litre of sweat contains up to 50 mmol Na⁺. This may require salt as well as water replacement under tropical conditions.

Salt and water depletion – this is one of the commonest problems in hospital practice, arising from such conditions as diarrhoea and vomiting, ketotic and non ketotic diabetic decompensation, and diuretic excess. The relative proportion of salt or water lack depends on the source of the loss and the amount of water, which the patient has consumed in order to assuage thirst: it is reflected in the serum concentrations of sodium and chloride.

Intravascular volume depletion – this signifies a deficit in plasma or total blood volume, as in burns or haemorrhage, or a reduction in circulating volume secondary to salt and water loss. The terms 'plasma volume depletion' or 'blood volume deficit' are even more specific.

Salt and water excess – this is most commonly iatrogenic, resulting from excessive administration of saline, but is, of course, a feature of congestive heart failure and other oedema producing conditions. It takes 2-3 litres of salt and water excess before the extracellular fluid is expanded sufficiently for oedema to become clinically apparent. Again, the relative proportions of salt and of water overload, but not the absolute amount of either, are reflected by the serum sodium and chloride concentrations.

Solution – fluid consisting of a solvent, e.g. water, in which a soluble substance or solute, e.g. sugar or salt, is dissolved.

Crystalloid – a term used commonly to describe all clear glucose and/or salt containing fluids for intravenous use (e.g. 0.9% saline, Hartmann's solution, 5% dextrose, etc.).

Colloid – a fluid consisting of microscopic particles (e.g. starch or protein) suspended in a crystalloid and used for intravascular volume expansion (e.g. 6% hydroxyethyl starch, 4% succinylated gelatin, 20% albumin, etc.).

Balanced crystalloid – a crystalloid containing electrolytes in a concentration as close to plasma as possible (e.g. Ringer's lactate, Hartmann's solution, Plasmalyte 148, Sterofundin, etc.).

Osmosis – this describes the process by which water moves across a semi-permeable membrane (permeable to water but not to the substances in solution) from a weaker to a stronger solution until the concentration of solutes are equal on the two sides.

This force is termed osmotic pressure or, in the case of colloids e.g. albumin, oncotic pressure. It is proportional to the number of atoms/ions/molecules in solution and is expressed as mOsm/litre (osmolarity) or mOsm/kg (osmolality) of solution. In clinical chemistry the term 'osmolality' is the one most often used. For example, out of approximately 280-290 mOsm/kg in extracellular fluid the largest single contributor is sodium chloride. This dissociates in solution and therefore its component parts Na^+ and Cl^- exert osmotic pressure independently i.e. Na^+ (140 mmol/kg), contributes 140 mOsm/kg, and Cl^- (100 mmol/kg) contributes 100 mOsm/kg. Additional balancing negative charges come from bicarbonate (HCO_3^-) and other anions. In the intracellular space K^+ is the predominant cation (see below).

Because glucose does not dissociate in solution, each molecule, although much larger than salt, behaves as a single entity in solution and at a concentration of 5 mmol/kg, contributes only 5 mOsm/kg to the total osmolality of plasma.

The cell membrane and the capillary membrane are both partially permeable membranes although not strictly semi permeable in the chemical sense (see below). They act, however, as partial barriers

dividing the extracellular (ECF) from the intracellular fluid (ICF) space, and the intravascular from the interstitial space. Osmotic or oncotic shifts occur across these membranes, modified by physiological as well as pathological mechanisms.

Anion gap – the difference between the plasma concentration of the major cation Na^+ (135–145 mmol/l) and the major anions Cl^- (95–105 mmol/l) and HCO_3^- (22–30 mmol/l), giving a normal anion gap of 5–11 mmol/l.

It is enlarged in metabolic acidosis due to organic acids as in diabetic ketoacidosis, lactic acidosis, renal failure, and ingested drugs and toxins.

$$\text{Anion gap (mmol/l)} = [\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-])$$

The anion gap is normal in hyperchloraemic acidosis (e.g. after excess 0.9% saline administration). It is, therefore, useful in the differential diagnosis of metabolic acidosis, although specific measurement of organic acids such as β -hydroxy butyrate or lactate may also be necessary to define the problem.

Strong ion difference (SID) – Stewart has described a mathematical approach to acid-base balance in which the strong ion difference ($[\text{Na}^+] + [\text{K}^+] - [\text{Cl}^-]$) in the body is the major determinant of the H^+ ion concentration. A decrease in the strong ion difference is associated with a metabolic acidosis, and an increase with a metabolic alkalosis. A change in the chloride concentration is the major anionic contributor to the change in H^+ homeostasis. Hyperchloraemia caused by a saline infusion, therefore, will decrease the strong ion difference and result in a metabolic acidosis.

$$\text{Strong ion difference (mmol/l)} = [\text{Na}^+] + [\text{K}^+] - [\text{Cl}^-]$$

e.g. If Na^+ is 140 mmol/l, K^+ is 4 mmol/l and Cl^- is 100 mmol/l, the SID is 44 mmol/l. The normal range is 38–46 mmol/l.

Base excess – Base excess is defined as the amount of strong acid that must be added to each litre of fully oxygenated blood to return the pH to 7.40 at a temperature of 37°C and a pCO₂ of 40 mmHg (5.3 kPa). A base deficit (i.e., a negative base excess) can be correspondingly defined in terms of the amount of strong base that must be added.

Acidaemia and Alkalaemia – An increase in the H⁺ ion concentration or a decrease in the pH is called acidaemia; a decrease in the H⁺ ion concentration or an increase in the pH is called alkalaemia.

Acidosis and Alkalosis – Processes that tend to raise or lower the H⁺ ion concentration are called acidosis and alkalosis respectively. These may be respiratory, metabolic or a combination of both. CO₂ retention causing a rise in pCO₂ in respiratory failure leads to respiratory acidosis and hyperventilation with a consequent lowering of pCO₂ leads to respiratory alkalosis. Accumulation of organic acids such as lactate or β-hydroxybutyrate or of mineral acidic ions such as chloride cause a metabolic acidosis in which arterial pH falls below 7.4, bicarbonate is reduced and pCO₂ falls as the lungs attempt to compensate by blowing off more CO₂. This is called a compensated metabolic acidosis. Similarly, ingestion of alkalis such as bicarbonate or loss of gastric acid cause a rise in pH and a metabolic alkalosis.

Maintenance – Provide daily physiological fluid and electrolyte requirements.

Replacement – Provide maintenance requirements and add like for like replacement for on going fluid and electrolyte losses (e.g. intestinal fistulae).

Resuscitation – Administration of fluid and electrolytes to restore intravascular volume.

3. Assessment, Measurement and Monitoring

As in all clinical conditions, assessment begins with a careful history and examination, followed by bedside and laboratory tests. The key features of assessment and monitoring of fluid balance are summarised in Table 4.

Table 4: Assessment and monitoring of fluid balance

Parameter	Significance
History	Alerts to likelihood of fluid deficit (e. g. vomiting/diarrhoea/haemorrhage) or excess (e. g. from intraoperative fluids)
Autonomic responses	Pallor and sweating, particularly when combined with tachycardia, hypotension and oliguria are suggestive of intravascular volume deficit, but can also be caused by other complications, e.g. pulmonary embolus or myocardial infarction.
Capillary refill	Slow refill compatible with, but not diagnostic of volume deficit. Can be influenced by temperature and peripheral vascular disease.
Blood pressure	Cuff measurements may not always correlate with intra-arterial monitoring. Does not necessarily correlate with flow. Affected by drugs (important to review medication charts). Nonetheless, a fall is compatible with intravascular hypovolaemia, particularly when it correlates with other parameters such as pulse rate, urine output, etc. Systolic pressure does not usually fall until 30% of blood volume has been lost.
Skin turgor	Diminished in salt and water depletion, but this can also be caused by ageing, cold and cachexia.
Sunken facies	May be due to starvation or wasting from disease, although compatible with salt and water depletion.
Dry mouth	A poor indicator. Compatible with salt and water depletion, but usually due to mouth breathing.
Oedema	The presence of pulmonary oedema should temporise further fluid administration. Peripheral oedema (pedal and/or sacral) occurs in volume overload but can occur in patients with hypoalbuminaemia who are intravascularly deplete (check serum albumin)

Parameter	Significance
Urine output	<30 ml/h (<0.5 ml/kg/h) is commonly used as indication for fluid infusion, but in the absence of other features of intravascular hypovolaemia suggesting a pathological cause, it is usually due to the physiological oliguric response to surgery. Urine quality (e.g. concentration, urine:plasma urea or osmolality ratio) is just as important, particularly in the complicated patient.
Weighing	24-h change in weight (performed under similar conditions) – best measure of change in water balance. Takes account of insensible loss. Simple to carry out by bedside. May be difficult to measure in the critically ill.
Fluid balance charts	Inherently inaccurate in measurement and recording. They do not measure insensible loss. Large cumulative error over several days. Good measure of changes in urine output, fistula loss, gastric aspirate, etc.
Serum biochemistry	Indicates ratio of electrolytes to water in the extracellular fluid. A poor indicator of whole body sodium status. Hyponatraemia most commonly caused by water excess. If change in water balance over 24 h is known, then change in serum sodium concentration can guide sodium balance. Hypokalaemia, on the other hand, nearly always indicates the need for potassium supplementation. Blood bicarbonate and chloride concentrations measured on point of care blood gas machines are useful in patients with acid-base problems including iatrogenic hyperchloraemia. Serum creatinine reflects both muscle mass and renal function. Blood urea reflects renal function and protein catabolism.
Urinary biochemistry	Urinary sodium concentration may reflect renal perfusion and a low value (< 20 mmol/l) is compatible with renal hypoperfusion (pre renal acute kidney injury), although it is also a feature of the response to injury or sodium depletion. Urinary potassium measurement is helpful in assessing the cause of refractory hypokalaemia. Urinary urea excretion increases several fold in catabolic states (e.g. sepsis) and is an indication for provision of additional free water to avoid hypernatraemia and uraemia. Urinary and blood creatinine are combined to measure creatinine clearance to assess renal function.

History

This gives the initial clue to the likely abnormality and the type and degree of deficit, e.g. a background of poorly controlled diabetes, a story of vomiting and/or diarrhoea, diuretics in an elderly patient who is confused, blood loss, burn injury etc.

Examination

Physical signs of fluid deficit are indicative but not specific, and no conclusion should be drawn from any single feature (Table 4). The first indication of a falling intravascular volume is a decrease in central venous pressure (JVP/CVP). With progressive severity, pulse rate increases (Fig. 5), followed by a fall in blood pressure with pallor and sweating. The full-blown picture is called 'shock'. In contrast, pink warm peripheries, with rapid capillary refill after pressure, are usually suggestive of an adequate circulation. Serial measurements of JVP/CVP, pulse, blood pressure and urine output are sufficient to monitor most patients, but in complex cases or critical illness, such bedside examination may need to be supported by invasive techniques for assessing cardiovascular function.

It should also be remembered that shock states due to volume depletion, cardiac causes, or sepsis share many similar features which require expert assessment to distinguish.

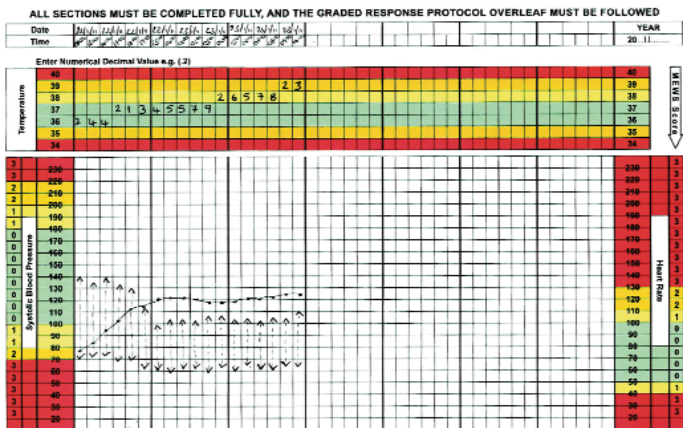


Figure 5: Example of a vital signs chart showing a rising pulse rate and a falling blood pressure, indicating progressive intravascular hypovolaemia secondary to haemorrhage.

Examination of the jugular filling with the patient reclining at 45° should be routine. If the level is elevated above the clavicle, this may signify intravascular over-expansion by administered fluids, congestive heart failure, or both. If, however, no jugular filling is observed, then lower the patient slowly until filling is observed. If filling is still not seen or only seen with the patient nearly horizontal, then this may signify an intravascular volume deficit.

This manoeuvre is particularly valuable in assessing patients still receiving intravenous fluids some days after the acute phase of their illness has subsided and recovery is slow or accompanied by complications. Such patients may have an expanded extracellular fluid (ECF) with oedema due to excess crystalloid administration, but a diminished blood or plasma volume due to continuing leak of blood, protein or serous fluid into wounds or inflamed areas. These findings indicate

the need for colloid to expand the intravascular volume, improve renal blood flow and allow the excretion of the salt and water overload. If, on the other hand, the jugular venous pressure (JVP) is elevated, then immediate cessation of crystalloid administration, with or without diuretics, will correct the underlying imbalance.

Measurements and Investigations

Urine

As described above, the volume and concentration of urine are important indicators of renal function. Oliguria may be physiological post-operatively, or indicative of intravascular or ECF deficit. If this is accompanied by a concentrated urine and a rising blood urea, it is termed pre-renal acute kidney injury (AKI), correctable by appropriate fluid replacement. A persisting low volume and concentration combined with a rising blood urea and creatinine suggest AKI due to intrinsic damage has now developed, necessitating some form of renal replacement therapy (e.g. haemofiltration or haemodialysis). Changes in urine volume must, therefore, be interpreted in the light of accompanying features and circumstances.

Nurses are often instructed to call junior doctors if the postoperative urine output falls below 30 ml/h. As a consequence, the doctor often prescribes extra saline "just to be on the safe side". This commonly results in salt and water overload. In fact, such "oliguria" is usually a physiological response to surgery. While it is important to identify the patient who has become hypovolaemic and to resuscitate adequately, it is unlikely that a patient who appears well with warm pink peripheries and no tachycardia or tachypnoea has need of volume expansion. Urine output in such patients should be averaged over four hours and interpreted in combination with serial trends in vital signs of circulatory adequacy.

Fluid balance charts

These provide useful information about changes in urine output and abnormal losses, e.g. gastric aspirate, but they have inherent inaccuracies. With great care in measurement and recording, they may be helpful in assessing balance over 24 hours. However, an assumption has to be made concerning insensible loss, and errors in measurement and recording are common. The cumulative error over several days can, therefore, be considerable.

Weight

There is no substitute for daily weighing in order to monitor external water balance accurately, yet outside renal units, it is seldom practised. As it is a major safeguard against clinically important errors in fluid volume administration, it is well worth the extra effort and resources required, particularly in complex post-operative cases. It does, of course, only measure external balance, which may conceal significant changes in internal balance between fluid compartments.

For example, in the presence of ileus or intestinal obstruction, large volumes of extracellular fluid may be pooled in the gut and therefore be functionally inert. Weight is, therefore, unchanged despite this clinically important fluid shift, which reduces effective ECF volume and necessitates salt and water replacement. Valuable as weighing is, therefore, it cannot be followed blindly. Like any other parameter, it requires intelligent interpretation in its clinical context and in the light of all the other information available.

Invasive monitoring

Invasive techniques such as insertion of central venous catheters, arterial lines and catheters to measure pulmonary artery wedge pressure are useful to help direct fluid therapy in more complex patients.

Laboratory tests

Haematocrit

Changes in fluid balance cause increase or decrease in the concentration of red cells, e.g. in the acute phase of burn injury, plasma loss may be monitored by frequent haematocrit measurements, which therefore help to guide fluid replacement. Loss of ECF due to gastroenteritis or other causes similarly increases haematocrit. Conversely fluid overload causes a fall in haematocrit due to dilution.

Albumin

The albumin concentration behaves similarly to the haematocrit in response to fluid deficit or excess. Indeed, dilution by infused crystalloids is one of the main causes of hypoalbuminaemia in surgical patients. Another major cause is the increased albumin escape rate from the circulation in response to proinflammatory cytokines (Chapter 1).

Urea

With renal impairment due to either fluid deficit (pre-renal AKI) or intrinsic AKI, blood urea concentration rises, the rate of increase being greater in the presence of post injury catabolism. Urine output measurements are important but are subject to misinterpretation unless other parameters are also considered. It is useful to combine measurement of urine volume with plasma and urine urea or osmolality (mOsm/kg) to assess renal function. The urine to plasma urea ratio has been used in the past to measure renal concentrating function and in normal health can be as high as 100 in the presence of dehydration. With a rising blood urea and creatinine, accompanied by oliguria, urine to plasma urea ratio of <15 can be helpful in defining the transition to intrinsic from pre-renal AKI.

Osmolality

In the presence of AKI, a urine osmolality of >500 mOsm/kg is indicative of a pre-renal cause (e.g. fluid deficit), whereas one <350 mOsm/kg suggests that intrinsic renal damage has developed. Urinary and serum osmolalities are also used in the diagnosis and monitoring of diabetes insipidus and in the monitoring of hyper- and hypo-osmolar states, to ensure that treatment is carefully controlled in order to avoid too rapid changes in serum osmolality with consequent risks of central nervous system damage.

Creatinine

Serum creatinine is a product of muscle metabolism and reflects muscle mass. Normally, therefore, it is higher in a 100 kg muscular man than in a 40 kg elderly woman. For any individual, however, changes in serum creatinine reflect renal function, although this has to fall by more than 50% before the serum creatinine starts to rise. A more sensitive measure of changes in renal function is creatinine clearance, measured as: $\text{Creatinine clearance} = (4 \text{ or } 24 \text{ hr}) \text{ urine creatinine concentration times urine volume divided by plasma creatinine concentration}$.

Sodium

This is expressed as a concentration, i.e. the proportion of sodium to water in the ECF. It is not a measure of the absolute amount of sodium in the body or the need for a higher or lower intake. In fact, the commonest cause of hyponatraemia is dilution by overenthusiastic administration of hypotonic fluids. If, however, water balance is known from daily weighing, then changes in plasma sodium can usually be interpreted in terms of sodium balance. For example, if weight is unchanged, a fall in plasma sodium usually implies that sodium balance is negative and that intake should be increased in the next prescription. On the other hand, if weight has increased by 2 kg and

the plasma sodium has fallen, the balance of water is positive and hyponatraemia is dilutional. The next prescription should include less water and the same sodium intake as before.

An alternative approach to sodium balance is to measure intake and the sodium content of all fluids lost. This however, is difficult to do accurately as well as being more demanding in staff time and resources.

A falsely low serum sodium may be caused by hypertriglyceridaemia, since triglycerides expand the plasma volume but contain no sodium. Similarly hyponatraemia occurs in the presence of hyperglycaemia as in decompensated diabetes, since glucose also acts as an osmotic agent holding water in the ECF. This effect disappears as soon insulin treatment causes cellular uptake of glucose and lowering of its concentration in the blood.

Potassium

The normal serum potassium concentration lies between 3.5 and 5.3 mmol/l. Concentrations rising above 5.5 mmol/l progressively increase the risk of death from cardiac arrest and require urgent treatment which may include extra fluids, intravenous glucose and insulin, bicarbonate, calcium gluconate (to stabilise the myocardium), intrarectal calcium resonium and even renal replacement therapy. Conversely, concentrations below 3.0 mmol/l increase the risk of arrhythmias and indicate the need for potassium supplementation by the oral or intravenous route.

Chloride

Despite the fact that serum chloride measurements do not increase the cost of biochemical screening, many laboratories no longer report serum Cl^- . However, in the differential diagnosis of acidosis, particularly in patients receiving 0.9% saline (with its high chloride content in relation to plasma) intravenously, it may be an important parameter to detect the development of hyperchloraemic acidosis in which the plasma chloride is elevated and bicarbonate reduced.

Bicarbonate

Venous or arterial bicarbonate concentrations indicate acid-base status as described above.

Serial data charts

The sticking of individual reports in the back of notes makes it difficult to detect clinically important trends. The only satisfactory way of monitoring patients with fluid and electrolyte problems is the use of serial data charts on which, each day, important data are recorded, so that changes and trends can be seen at a glance. Our own practice is to record daily weight, serum biochemistry and haematology, etc., on charts, which are kept by the patient's bedside. Although transferring data to such charts is time consuming, it reduces time taken in clinical decision making as well as improving the accuracy of prescribing. It also compels one to look at reports and think carefully about their significance.

Table 5: Reference laboratory values for some commonly measured parameters

	Plasma/Blood
Haemoglobin (g/dl)	13.0-18.0 (men) 11.5-16.5 (women)
Haematocrit (%)	40-54 (men) 37-47 (women)
Na ⁺ (mmol/l)	135-145
Cl ⁻ (mmol/l)	95-105
[Na ⁺]:[Cl ⁻] ratio	1.28-1.45:1
K ⁺ (mmol/l)	3.5-5.3
HCO ₃ ⁻ (mmol/l)	22-30
Total Ca ²⁺ (mmol/l)	2.2-2.6
Ionised Ca ²⁺ (mmol/l)	1.1-1.4
Mg ²⁺ (mmol/l)	0.8-1.2
Glucose (mmol/l)	3.5-5.5
Urea (mmol/l)	2.5-6.7
Creatinine (μmol/l)	60-120
pH	7.35-7.45
PaO ₂ (kPa)	11-13
PaCO ₂ (kPa)	4.7-5.9
Lactate (mmol/l)	0.6-1.8
Albumin (g/l)	33-55
Osmolality (mOsm/kg)	275-295

4. Properties of Intravenous Crystalloids and Colloids

A variety of crystalloids containing salt and/or glucose and of artificial colloids is currently available for intravenous fluid therapy.

A combination of salt containing crystalloids and colloids is currently used during resuscitation to expand the intravascular volume. The properties of some commonly used crystalloids are summarised in Table 9 and must be borne in mind before prescribing intravenous fluids.

The ability of a solution to expand the plasma volume is dependent on its volume of distribution and the metabolic fate of the solute, so that while colloids are mainly distributed in the intravascular compartment, once the dextrose is metabolised, dextrose containing solutions are distributed through the total body water and hence have a limited and transient blood volume expanding capacity (Table 6). Solutions like 5% dextrose and dextrose saline are not meant for resuscitation, but are a means of providing free water when this is appropriate.

Table 6: Volume of infusion required to expand the plasma volume by 1 L

	Infused volume (ml)	Change in interstitial fluid volume (ml)	Change in intracellular fluid volume (ml)
5% albumin	1400-1500	400-500	
25% albumin	250	-750*	
6% hydroxyethyl starch	1400-1500	400-500	
Succinylated gelatin	1400-1500	400-500	
Hartmann's solution or 0.9% saline	4000-5000	3000-4000	
5% dextrose	12000-14000	3000-4000	9000-10000

* Fluid is drawn into the intravascular compartment from the interstitial compartment

Isotonic sodium-containing crystalloids are distributed throughout the ECF (including the plasma) and textbook teaching classically suggests that such infusions expand the blood volume by $1/3^{\text{rd}}$ the volume of crystalloid infused. In practice, however the efficiency of these solutions to expand the plasma volume is only 20-25%, the remainder being sequestered in the interstitial space. Although these solutions are used successfully for this purpose the price paid for adequate intravascular filling is overexpansion of the interstitial space and tissue oedema, which has to be excreted once the acute phase of illness is passed. Solutions of dextrose or of hypotonic saline can cause significant hyponatraemia ($\text{Na}^+ < 130 \text{ mmol/l}$), and care should be taken to avoid this potentially harmful effect, particularly in children and the elderly. Compared to balanced crystalloids, 0.9% saline produces a hyperchloraemic acidosis because its high chloride content compared with plasma (Table 9) causes a reduction in the strong ion difference ($[\text{Na}^+] + [\text{K}^+] - [\text{Cl}^-]$). Hyperchloraemia also causes a reduction in renal blood flow and glomerular filtration, gastrointestinal mucosal acidosis and ileus, cellular dysfunction, impairment in mitochondrial function and worse outcome. Excessive administration of sodium-containing crystalloids causes oedema, which also impacts adversely on outcome. These effects are described in more detail in Chapter 13. For these reasons, in most instances, balanced electrolyte solutions are preferred to 0.9% saline.

Colloids are homogenous non-crystalline large molecules or ultramicroscopic particles dispersed through a fluid, usually a crystalloid. Colloidal particles are large enough to be retained within the circulation and, therefore, to exert an oncotic pressure across the capillary membrane. The ideal colloid should be readily available, have a long shelf life, have no special infusion or storage requirements and be relatively inexpensive. It should be suspended in an isotonic solution, have a low viscosity, be isooncotic with plasma and be distributed exclusively in the intravascular compartment, with a half-life of

6–12 h. The colloid should be metabolised or excreted and should not accumulate in the body. It should not be toxic, pyrogenic, allergenic or antigenic and should not interfere with organ function (e.g. renal or coagulation) or with acid base balance. There is no ideal colloid, that completely fulfils all these criteria, and the colloids used for volume replacement are either naturally occurring (human albumin solution, plasma protein fraction, fresh frozen plasma, and immunoglobulin solutions) or semisynthetic (gelatins, starches and dextrans). In the UK, commonly used colloids include hydroxyethyl starch, succinylated gelatin (Gelofusine), urea-linked gelatin (Haemaccel) and albumin (for selected indications). Dextrans and high molecular weight starches are used seldom or not at all. Older preparations of hydroxyethyl starch are suspended in 0.9% saline while the newer preparations (Volulyte, PVR, Tetraspan) and gelatins (Gelofusine and Haemaccel) are suspended in balanced solutions, making them more physiological. All currently available semisynthetic colloids contain 140–154 mmol Na⁺ and therefore, contribute to the positive sodium balance seen in surgical patients. Although studies on healthy volunteer and on patients undergoing laparoscopic cholecystectomy suggest that the plasma volume expanding capacity of 4% succinylated gelatin and 6% hydroxyethyl starch are similar, studies on patients with burns and those undergoing major surgery suggest that outcomes may be better with hydroxyethyl starch than gelatin.

Albumin solutions are monodisperse as they contain particles of uniform molecular weight (69 kD) while synthetic colloids contain particles of varying sizes and molecular weights in an attempt to optimise the half life (which is directly proportional to particle size) and plasma volume expanding capacity (which is proportional to the number of particles suspended) of the solutions.

There are no indications for using albumin in acute resuscitation. However, concentrated (20–25%) salt poor albumin may be useful in patients in the post-acute phase of illness who are oedematous due

to salt and water overload, but who still have a plasma volume deficit, as it helps draw fluid from the interstitial space into the intravascular space and improves renal perfusion allowing excretion of excess salt and water. Albumin is also used in patients with hepatic failure and ascites. However, the prescription of this expensive preparation should be confined to senior clinicians.

Although, in theory, colloids that are isoosmotic with plasma should expand the blood volume by the volume infused, in practice, the volume expanding capacity of these colloids is only 60–80%. Nevertheless, a given volume of colloid results in greater volume expansion and less interstitial oedema than an equivalent volume of crystalloid. Although, in practice in the UK, we use a combination of crystalloids and colloids for resuscitation, there is, in fact, no firm evidence that the use of colloids rather than crystalloids in the acute phase of injury results in better outcome.

Table 7: Volume effects of some colloids

Colloidal solution	Duration of action	Initial plasma expanding effect (%)
Long acting		
6% HES 450/0.7	24–36 h	100
6% HES 200/0.62	5–6 h	100
Medium acting		
6% HES 200/0.5	3–4 h	100
10% HES 200/0.5	3–4 h	140
6% HES 130/0.40–0.42	4–6 h	100
4% Gelatin	3–4 h	90
Short acting		
3% Gelatin	2–3 h	70
5% Albumin	2–4 h	70–90

HES = hydroxyethyl starch. Properties are dependent on concentration, the weight-averaged mean molecular weight (Mw), the number-averaged molecular weight (Mn), the molar substitution (MS) and the degree of substitution.

Table 8: Advantages and disadvantages of colloids

Advantages	Disadvantages
Smaller volumes than crystalloids are needed for plasma volume expansion	Allergic reactions/anaphylaxis [$<0.4\%$ - least for albumin (0.1%) and hydroxyethyl starch (0.06%)]
Less oedema produced than with crystalloids	Renal toxicity
Potential free radical scavenging effect	Coagulation disturbance
	Pruritus
	May interfere with cross-match

Conclusion

There are good theoretical grounds for using colloids for plasma volume expansion as they cause less salt and water overload and oedema than crystalloids. In practice, we tend to use a combination of the two in varying proportion according to the circumstances. There are very few indications for using 0.9% saline (e.g. chloride deficit from vomiting) and balanced crystalloids are preferred in most circumstances.

Table 9: Properties of commonly prescribed crystalloids

	Plasma*	0.9% NaCl	Hartmann's	Lactated Ringer's (USP)	Ringer's acetate
Na ⁺ (mmol/l)	135-145	154	131	130	130
Cl ⁻ (mmol/l)	95-105	154	111	109	112
[Na ⁺]:[Cl ⁻] ratio	1.28-1.45:1	1:1	1.18:1	1.19:1	1.16:1
K ⁺ (mmol/l)	3.5-5.3	0	5	4	5
HCO ₃ ⁻ / Bicarbonate precursor (mmol/l)	24-32	0	29 (lactate)	28 (lactate)	27 (acetate)
Ca ²⁺ (mmol/l)	2.2-2.6	0	2	1.4	1
Mg ²⁺ (mmol/l)	0.8-1.2	0	0	0	1
Glucose (mmol/l)	3.5-5.5	0	0	0	0
pH	7.35-7.45	4.5-7.0	5.0-7.0	6-7.5	6-8
Osmolarity (mOsm/l)	275-295	308	278	273	276

* Normal laboratory range from Queen's Medical Centre, Nottingham

Plasma-Lyte 148	Sterofundin ISO	0.18% NaCl/4% dextrose	Plasma-Lyte 56 Maintenance	0.45% saline	5% dextrose
140	145	31	40	77	0
98	127	31	40	77	0
1.43:1	1.14:1	1:1	1:1	1:1	-
5	4	0	13	0	0
27 (acetate) 23 (gluconate)	24 (acetate) 5 (malate)	0	16 (acetate)	0	0
0	2.5	0	0	0	0
1.5	1	0	1.5	0	0
0	0	222.2 (40 g)	277.8 (50 g)	0	277.8 (50 g)
4.0-8.0	5.1-5.9	4.5	3.5-6.0	4.5-7.0	3.5-5.5
295	309	284	389	154	278

5. Prescription and Administration

Appropriate fluid and electrolyte prescriptions may be administered orally, enterally, subcutaneously, or intravenously, depending on the clinical situation. Before any prescription is written it is important to ask a number of questions:

- (1) Does the patient need any prescription at all today?
 - (2) If so, does the patient need this for
 - a. resuscitation,
 - b. replacement of losses, or
 - c. merely for maintenance?
 - (3) What is the patient's current fluid and electrolyte status and what is the best estimate of any current abnormality?
 - (4) Which is the simplest, safest, and most effective route of administration?
 - (5) What is the most appropriate fluid to use and how is that fluid distributed in the body?
- (1) If the patient is eating and drinking, the answer is usually no. In the case of a post-operative patient, for example, any intravenous fluids should be discontinued as soon as possible. Intravenous fluids are often continued unnecessarily, leading to fluid overload as well as increased risk of cannula-site sepsis. Nasogastric tubes are only indicated for drainage in the presence of true ileus or gastric dysfunction (e.g. delayed gastric emptying after pancreatic surgery). In the majority of cases, morbidity from nasogastric tubes exceeds any benefit. Gastrointestinal function returns more rapidly post-operatively than previously assumed. The absence of bowel sounds *per se* does not mean that food and drink will not be tolerated. In the past, a combination of naso-gastric tubes and excess intravenous fluids has frequently caused unnecessary delay in reestablishing oral intake, thereby prolonging the length of stay.

Patients receiving artificial nutrition (parenteral or enteral) usually receive an adequate amount of water and electrolytes via the feed and most do not require additional intravenous fluids. It is a common mistake to prescribe intravenous maintenance requirements in addition to the water and electrolyte content of the feed, leading to avoidable fluid overload.

- (2) This question is crucial. Many patients are fluid overloaded because prescriptions based on resuscitation are continued thoughtlessly when maintenance fluids are all that is required. Tables 1 and 2 in Chapter 1 show how low such maintenance requirements are. For example 1 litre of 0.9% saline contains enough salt to meet 2 days' normal maintenance requirements. Intravenous fluid therapy may be needed for resuscitation, replacement or maintenance, depending on the stage of the illness (Fig. 6).

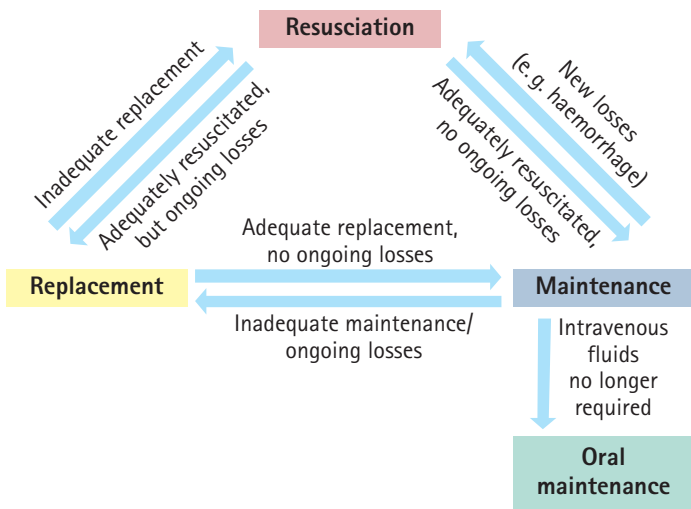


Figure 6: The relationship between resuscitation, replacement and maintenance.

a. *Resuscitation*: In the event of blood loss from injury or surgery, plasma loss e.g. from burns or acute pancreatitis, or gastrointestinal or renal losses of salt and water, a resuscitation regimen is needed to restore and maintain the circulation and the function of vital organs. In this situation, the recommendation is to infuse 500 ml (250 ml if cardiac failure) of a balanced crystalloid stat (e.g. Hartmann's solution or Ringer's lactate) rapidly. If hyperkalaemia is present ($K^+ > 5.5$ mmol/l) or suspected oliguric AKI or rhabdomyolysis 0.9% saline is preferred initially (no potassium in crystalloid). However, there is no evidence that administration of crystalloids containing 3–5 mmol/l of K^+ worsen the hyperkalaemia. The clinical response should be assessed immediately following administration of the fluid bolus in terms of improved peripheral perfusion, decreased pulse rate, rise in blood pressure, rise in JVP and increase in urine output. Further administration will depend on response (Fig. 7). If 0.9% saline has been used initially conversion to a balanced crystalloid can be considered once potassium concentrations are known and good urine output established.

In the case of intravascular fluid losses, colloids or a combination of colloids and crystalloids are appropriate to avoid causing excessive rises in oncotic pressure and potential osmotic nephrosis (renal tubular injury).

Large volumes of 0.9% saline are best avoided, except after gastric losses, because of the risk of producing hyperchloraemic metabolic acidosis and its undesirable sequelae. In the case of major blood loss it is also necessary to cross match and to give packed cells. Early and adequate treatment of the underlying cause of fluid loss, e.g. control of bleeding, is vital. In the severely injured patient, resuscitation of blood loss with packed cells, fresh frozen plasma and platelets in a ratio of 1:1:1 has been shown to be more beneficial than packed cells alone, as this helps correct the associated coagulation defects.

Once resuscitation has been achieved as judged by normalisation of vital signs and urine output or of parameters from more invasive measurements, the prescriber should switch to a maintenance regimen with accurate replacement of any on-going losses. Exceeding such requirements, on the unwarranted assumption that the patient will excrete any excess, is deleterious to outcome and delays recovery.

- b. *Replacement*: any fluid prescription should incorporate not only daily maintenance requirements, but replacement of any ongoing abnormal losses. In the case of a patient with losses from the gastrointestinal tract, e.g. from a fistula or from nasogastric aspiration, the fluid prescription should include the daily maintenance requirements plus like-for-like water and electrolyte replacement of any losses. In order to achieve this, the prescriber should be aware of the approximate electrolyte content of fluid from various parts of the gastrointestinal tract (Chapter 1, Table 3).

- c. *Maintenance*: Maintenance prescriptions should aim to restore insensible loss (500-1000 ml), provide sufficient water and electrolytes to maintain normal status of body fluid compartments, and sufficient water to enable the kidney to excrete waste products 500-1500 ml (Chapter 1, Tables 2 and 3). The average person requires 25-35 ml/kg water, 1 mmol/kg Na and 1 mmol/kg K⁺ per day. Examples of how to provide this maintenance requirement are summarised in Table 10.

Table 10: Examples of maintenance fluid regimens (2-2.5 l/day) suitable for a 70 kg person

	0.18% saline in 4% dextrose (2-2.5 l)	0.45% saline (1-1.5 l) + 5% dextrose (1 l)	Plasmalyte maintenance (2-2.5 l)	Ringer's lactate (1 l) + 5% dextrose (1-1.5 l)	Hartmann's (1 l) + 5% dextrose (1-1.5 l)	Sterofundin ISO (1 l) + 5% dextrose (1-1.5 l)
Water (l)	2-2.5	2-2.5	2-2.5	2-2.5	2-2.5	2-2.5
Na ⁺ (mmol)	60-75	77-116	80-100	130	131	145
Cl ⁻ (mmol)	60-75	77-116	80-100	109	111	127
K ⁺ (mmol)	Should be added	Should be added	26-33	4 (Additional K should be added to the 5% dextrose)	5 (Additional K should be added to the 5% dextrose)	4 (Additional K should be added to the 5% dextrose)
Dextrose (g)	80-100	50	100-125	50-75	50-75	50-75
Ca ²⁺ (mmol)				3	4	2.5
Lactate (mmol)				28	29	
Acetate (mmol)			32-40			24
Malate (mmol)						5
Mg ²⁺ (mmol)			3-4			

-
- (3) The answer to this question is summarised in Chapter 3. Decision making should be informed by all the information available, including history, examination, vital signs, measurements and tests including urine output and concentration and serum biochemistry, fluid balance charts, weight changes, and an understanding of the likely patho-physiological changes. It should not be based just on casual bedside assessment of unreliable and non-specific signs such as dry mouth or diminished skin turgor. Remember, serial weighing is the most accurate measure of external water balance.
- (4) The most appropriate method of administration should be the simplest and safest that is effective (Chapter 6). The oral route should be used whenever possible. In acute situations and in the presence of gastrointestinal dysfunction or large deficits, the intravenous route is the most appropriate. This, however, should be discontinued at the earliest opportunity. Enteral tube administration may be appropriate where swallowing is the major problem. Subcutaneous infusions should be considered, particularly in the elderly, for the management of chronic or recurrent problems.
- (5) The most appropriate fluid to use is that which most closely matches any previous or ongoing losses (Chapter 4). Recent published data favours the use of balanced electrolyte solutions rather than 0.9% saline to replace salt and water deficits, except in the case of losses of gastric juice with its high chloride content. Following intravascular fluid losses, current thinking favours a combination of artificial colloid and balanced electrolyte solutions, supported by packed cells after significant blood loss.

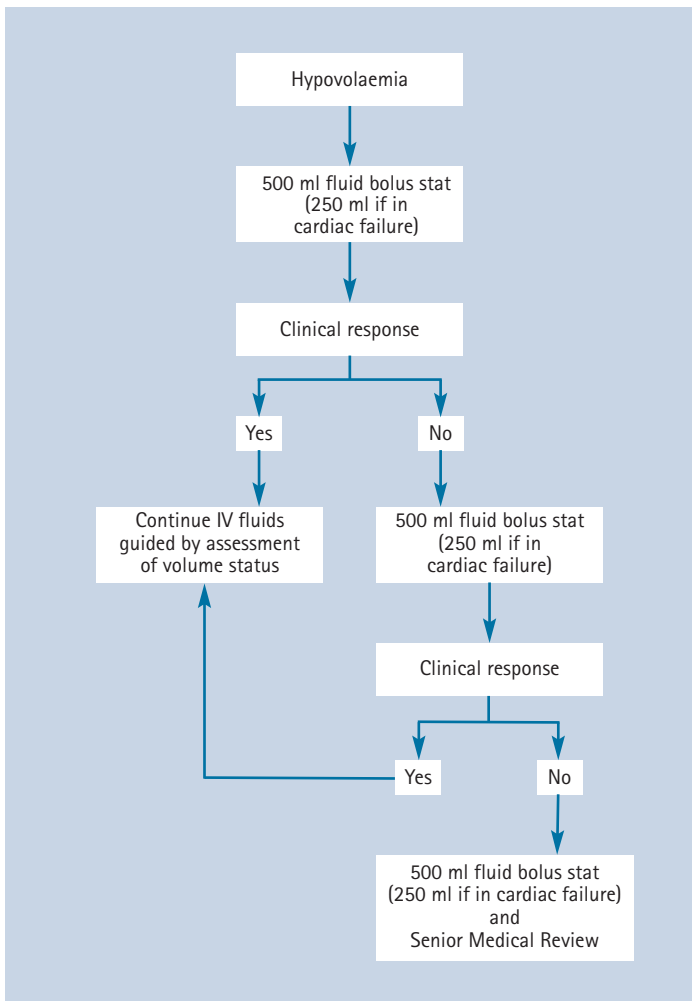


Figure 7: Suggested algorithm for resuscitation of non-haemorrhagic shock.

6. Methods of Fluid Administration

Oral or enteral

The use of oral rehydration solutions to treat diarrhoeal disease in both children and adults is one of the most commonly used treatments worldwide, particularly in developing countries. They can also be useful in the management of short bowel or inflammatory bowel disease in hospital or at home.

These preparations are based on the principle that salt absorption in the small bowel is linked to that of carbohydrate and is, therefore, enhanced by glucose, glucose polymers and starch (e.g. rice water). Some preparations also contain K^+ and an alkalisng agent to counter acidosis. In developing countries, they can be made using locally available materials, with simple measuring devices to ensure the correct proportions of salt, sugar or rice starch, and boiled water. In the UK commercial preparations are available (see British National Formulary), 5 sachets of Dioralyte, for example, reconstituted in 1 litre of water, give Na^+ 50 mmol, K^+ 20 mmol, Cl^- 50 mmol, citrate 10 mmol, and glucose 99 mmol. The WHO formula contains 75 mmol Na^+ . These are suitable for diarrhoeal diseases in children and most adults, although, in short bowel syndrome or inflammatory bowel disease in adults, a more concentrated solution may be required and can be obtained mixing more sachets per litre.

These solutions may also be administered via enteral tubes where oral administration is difficult. Monitoring of oral or enteral fluid treatment follows the same general principles as outlined in Chapter 3. One of the advantages of oral and enteral administration is that it is difficult to give excess fluid owing to limited tolerance. With intravenous fluids it is only too easy to give excess salt and water with

deleterious consequences. On the other hand when fluid losses are very great, the intravenous route may be necessary for resuscitation, replacement and to maintain balance.

Intravenous

Peripheral

Most fluids are infused via a peripheral venous cannula. Such cannulae should be inserted and maintained using meticulous care, technique and protocols, since their potential for causing morbidity and even mortality from infection is often underestimated. Each hospital should have clear guidelines, as part of clinical governance, to ensure optimal care of peripheral cannulae (Fig. 8). Insertion sites should be inspected daily and cannulae removed or resited at the earliest sign of any inflammation. In any case, it is good policy to resite cannulae at least every 72 h.

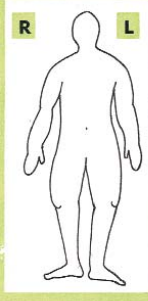
Peripheral Cannula Insertion Sticker		
	Date Inserted	
	Type of Device i.e. Ported, Straight or Butterfly	
	Manufacturer & Product Code	
	Indicate, Site of insertion on picture and also write it here:	
	<i>Please write yes or No in corresponding column</i>	
	YES	NO
Cannula Inserted using Aseptic Technique. (Ensuring strict adherence to HAND HYGIENE , the use of GLOVES, APRONS and the SAFE, DISPOSAL of SHARPS as per NUH guidelines/policies.		
2% chlorhexidine in 70% isopropyl alcohol wipe?		
Sterile, Semi Permeable Transparent Film, dressing used to cover the insertion site?		
Cannula Inserted By:		
Name	Signature	
<i>Please insert sticker into the Patients Medical Notes when completed.</i>		

Figure 8: Example of a sticker used for peripheral cannula insertion.

Central

Modern single or multi lumen polyurethane or silastic cannulae inserted via the internal jugular or subclavian vein have even greater potential than peripheral cannulae to cause morbidity and mortality unless inserted and maintained by skilled staff observing strict protocols.

Sub-cutaneous route (Hypodermoclysis)

This method has been used in paediatrics and geriatrics for many years, but it is so effective for replacing small or medium fluid and electrolyte losses in patients unable to maintain balance by the oral route, that it deserves wider use. One of its virtues is that patients or their carers can be taught to manage it at home. We have found it particularly useful for domiciliary use in adult and elderly patients with salt and water losses from gastrointestinal diseases.

0.9% saline (500–2000 ml daily) or 5% dextrose (500 ml) containing up to 20 mmol K⁺ and/or 4 mmol Mg²⁺ per litre may be infused over 3–4 hours via a fine butterfly cannula inserted into the subcutaneous fat, usually over the torso.

Infusion pumps

When fluid is delivered by either the enteral or parenteral route, what is prescribed is not necessarily what is delivered and patients may receive either too much or too little as a result of inaccuracies in delivery rates. It is now recommended that fluids should be delivered with infusion pumps at predetermined rates, which can be up to 999 ml/h. This increases the accuracy of fluid delivery. Nevertheless, delays in changing fluid bags once they are empty may still lead to inaccuracies.

Table 11: Setting rates of infusions on pumps

Rate of infusion	Duration for delivery of 1 litre
41.7 ml/h	24 h
55.6 ml/h	18 h
83.3 ml/h	12 h
100 ml/h	10 h
125 ml/h	8 h
166.7 ml/h	6 h
250 ml/h	4 h
500 ml/h	2 h
999 ml/h	1 h

Conclusion

In planning fluid replacement it is important to select the safest, simplest and most appropriate route and to monitor this carefully to avoid over- or under-treatment and any potential complications of the method. The aphorism, 'if the gut works, use it' is as appropriate in fluid therapy as it is in nutritional care.

7. Acid-Base Balance

Introduction

Maintenance within narrow limits of the normal acid base composition of the “*milieu interieur*” is essential for the optimal function of tissues. The kidneys together with the lungs and liver play an essential role in the maintenance of normal acid-base balance and arterial blood pH (Table 12). The kidneys remove acid and regenerate bicarbonate, the lungs can regulate the removal of acid (CO_2) by varying respiratory rate and the liver removes and recycles lactate. Therefore, patients with advanced chronic kidney disease (eGFR < 30 ml/min/ 1.73 m²), liver disease or underlying respiratory disease are at increased risk of developing acid-base abnormalities at times of acute illness.

Table 12: Normal arterial blood acid-base measurements

pH	7.35 - 7.45
PaO ₂ (kPa)	10.7-16.0
PaCO ₂ (kPa)	4.7-6.0
HCO ₃ ⁻ (mmol/l)	22 - 26
Base excess (mmol/l)	-2 - +2
Anion gap (mmol/l)	5 - 11

A normal blood pH of 7.35-7.45 is maintained by different buffering systems.

The blood buffering system, which is dependent upon

- the relative proportions of carbonic acid from carbon dioxide (CO_2) and of bicarbonate (HCO_3^-) defined by the Henderson-Hasselbach equation. Note that the pH is determined by the ratio of HCO_3^- to CO_2 .

$$pH = 6.10 + \log \frac{[\text{HCO}_3^-]}{0.03 p\text{CO}_2}$$

- haemoglobin
- phosphate (organic and inorganic)
- bone and its calcium salts

The kidney buffering system which

- controls hydrogen (H^+) and bicarbonate (HCO_3^-) excretion or reabsorption as well as the conversion of ammonia (NH_3) to ammonium (NH_4^+) in the urine.

The lung buffering system which controls

- the carbon dioxide (CO_2) in the blood, increasing expired CO_2 when more is produced or to compensate for metabolic acidosis.

The liver buffering system which

- removes and recycles the large amounts of lactate produced by anaerobic respiration (the Cori cycle).

Disease states can disrupt this finely balanced system resulting in a dangerously low ($\text{pH} < 7.1$) or dangerously high pH ($\text{pH} > 7.6$). Specific patient management will depend upon the clinical status of the patient and correction of the underlying cause. This chapter will pro-

vide a simple description of the most common forms of the simple acid-base disorders. Expert advice should be sought if it is suspected that the patient has a more complex form of acid-base disorder.

Approaches to acid-base balance

There are essentially two different ways to approach acid-base disorders.

- The traditional Schwartz-Bartter approach which accepts the Bronsted-Lowry definition of acids as proton donors and bases as proton acceptors. The hydrogen ion concentration is a function of the ratio between the PCO_2 and the serum bicarbonate (as above). The traditional approach utilises the anion gap calculation to classify acid-base disturbances and is the method used in this chapter.
- The Stewart approach, termed the Strong Ion Difference (SID), is based on the principle that the serum bicarbonate concentration does not alter blood pH. This approach is favoured by intensivists and anaesthetists and is described separately towards the end of this chapter.

Clinical presentation

It is important in every acutely ill patients to consider whether there may be an underlying acid-base disturbance. Serum bicarbonate and chloride are not standard components of all U&E reports and, therefore, may have to be specifically requested. Severe acidaemia ($\text{pH} < 7.1$) results in impaired cardiac function and vascular tone. Severe alkalaemia ($\text{pH} > 7.6$) results in irritability of cardiac and skeletal muscle.

Conditions commonly associated with acid-base disorders include:

- vomiting/diarrhoea
- shock
 - cardiogenic
 - septic
 - hypovolaemic
- acute kidney injury
- respiratory failure
- altered neurological status
 - coma
 - seizures
- decompensated diabetes
- hypo- or hyperkalaemia
 - potassium metabolism is intimately linked with acid-base balance
- prolonged and excessive infusions of saline

If an acid-base disturbance is suspected from clinical features the following investigations should be performed initially:

- Urea, creatinine and electrolytes
- Bicarbonate
- Chloride
- Arterial blood gases (including lactate)

Step-by-step pathway to identify underlying cause

- pH to determine whether acidaemia or alkalaemia
- change in bicarbonate and base excess = metabolic process

-
- change in P_{CO_2} = respiratory process
 - determine whether
 - simple disorder i.e. either metabolic or respiratory process alone
 - mixed disorder i.e. a combination of a metabolic and respiratory process occurring together. There will be evidence of compensatory changes in either bicarbonate or P_{CO_2}
 - calculate the anion gap
 - determined primarily by negative charge on serum proteins, particularly albumin
 - serum anion gap = unmeasured anions – unmeasured cations
 - anion gap = $[Na^+] - ([HCO_3^-] + [Cl^-])$
 - normal anion gap = 5-11 mmol/l
 - in hypoalbuminaemia the normal anion gap is adjusted downward by 2.5 mmol/l for every 10 g/l reduction in serum albumin concentration
 - an increase in anion gap indicates a tendency towards acidosis and a decrease a tendency towards alkalosis.
 - measure blood sugar, serum lactate and/or β -hydroxybutyrate concentrations to determine cause of metabolic acidosis
 - identify and treat the underlying cause

Simple acid-base disorders

Table 13 demonstrates simple acid-base disorders in terms of the primary change in bicarbonate or carbon dioxide, the compensatory changes that occur and the effect on pH. By a simple rule of thumb in simple acid-base disorders the acid-base buffer pair change in the same direction. If they change in the opposite direction the disorder must be mixed.

Table 13: Simple acid-base disorders

	Primary change	Compensation	Effect on pH
Metabolic acidosis	↓ HCO ₃ ⁻	↓ Pco ₂	↓ pH
Metabolic alkalosis	↑ HCO ₃ ⁻	↑ Pco ₂	↑ pH
Respiratory acidosis	↑ Pco ₂	↑ HCO ₃ ⁻	↓ pH
Respiratory alkalosis	↓ Pco ₂	↓ HCO ₃ ⁻	↑ pH

Causes of simple acid-base disorders

The cause of an acid-base disorder is often apparent from the clinical presentation. Metabolic acidosis is best considered as associated with a high anion gap (Table 14) or a normal anion gap (Table 15).

Table 14: Causes of a metabolic acidosis with a high anion gap

Ketoacidosis ■ diabetes
Lactic acidosis ■ tissue hypoxia ■ liver failure ■ metformin
Drug toxicity ■ ethylene glycol ■ methanol ■ salicylate
Kidney disease ■ chronic kidney disease ■ acute kidney injury

Table 15: Causes of metabolic acidosis (hyperchloraemic) with a normal anion gap

Gastrointestinal HCO_3^- loss
■ diarrhoea
■ fistulae
Renal HCO_3^- loss
■ renal tubular acidosis
■ acetazolamide
Infusion of 0.9% saline

Metabolic acidosis with a high anion gap - can be caused by four broad categories of disorders including ketoacidosis, lactic acidosis, poisonings or advanced acute or chronic kidney disease.

Ketosis occurs when there is a lack of insulin or glucose depletion. To compensate fatty acids are oxidised to produce energy which results in the production of ketoacids as a by-product.

- Severe diabetic ketoacidosis occurs secondary to insulin deficiency (Chapter 10)
- Ketosis may also occur with prolonged starvation or in alcoholics

Lactic acidosis is subdivided into

- Type A lactic acidosis - secondary to insufficient oxygen delivery to the tissues
 - hypovolaemic shock
 - cardiogenic shock
 - septic shock
- Type B lactic acidosis - impaired gluconeogenesis causing inability to clear lactate
 - liver failure
 - metformin

Drug toxicity can be subdivided into

- ethylene glycol/methanol
 - metabolism generates glycolate (ethylene glycol) and formate (methanol)
 - elevated osmolal gap (difference between the measured serum osmolality and calculated osmolality)
 - calculated osmolality = $2 \times [\text{Na}^+] + \text{glucose} + \text{urea}$
 - intoxication is likely if the difference between measured and calculated osmolality is greater than 25 mOsm/kg
 - calcium oxalate crystals in the urine suggests ethylene glycol toxicity
- salicylates
 - may result in a metabolic acidosis, respiratory alkalosis or a mixed acid-base disorder

Kidney disease

- chronic kidney disease and acute kidney injury result in reduced
 - excretion of the daily acid load (sulphates, phosphates and organic anions)
 - regeneration of bicarbonate

Metabolic acidosis (hyperchloraemic) with a normal anion gap – the commonest cause is excess 0.9% saline infusion. It can also be caused by gastrointestinal or renal HCO_3^- loss. Rarer causes include inorganic acid intake.

Gastrointestinal HCO_3^- loss results from

- diarrhoea and external fistulae from the pancreas and small bowel
- increased chloride absorption occurs as a compensatory mechanism resulting in a hyperchloraemic metabolic acidosis with a normal anion gap

Renal HCO_3^- loss results from

- renal tubular acidosis (RTA), conditions that are caused by
 - failure to reabsorb HCO_3^- from the proximal tubule (type II RTA)
 - HCO_3^- loss from the distal tubule (type I RTA)
- acetazolamide (carbonic anhydrase inhibitor) which inhibits HCO_3^- reabsorption

Metabolic alkalosis – can occur in association with fluid depletion or mineralocorticoid excess (Table 16). In metabolic alkalosis associated with fluid depletion there is loss of fluid rich in H^+ or Cl^- from the bowel, kidneys or skin. Metabolic alkalosis may occur in hyperaldosteronism, in the absence of fluid depletion, as a result of enhanced renal H^+ secretion.

Table 16: Causes of metabolic alkalosis

Fluid depletion

- vomiting
- gastric suction
- diuretics

Hyperaldosteronism

Cushing's syndrome

Respiratory acidosis – may occur acutely due to respiratory depression secondary to drugs or neurological damage, respiratory muscle weakness, chest injury or acute airways obstruction. In some cases of chronic obstructive airways disease Pco_2 may also be permanently elevated, when it may be partially compensated for by an increase in plasma HCO_3^- .

Existing respiratory disease may be exacerbated perioperatively by atelectasis, respiratory infection, retained sputum, abdominal distension, splinting of the diaphragm, pain from the wound or high doses of opiates. Epidural analgesia may be advantageous in these respects. In severe cases, particularly those with prior lung disease, bronchial suction and mechanical ventilation may be necessary. Chest physiotherapy is also vital in many cases.

Respiratory alkalosis – is due to hyperventilation, causing a low P_{CO_2} and in chronic cases, some compensatory reduction in HCO_3^- . It may be iatrogenic due to deliberate or mistakenly overenthusiastic artificial ventilation, or secondary to anxiety or distress. It may be associated with paraesthesiae, tetany and chest pain.

Management

The principles of management involve correcting any abnormalities of fluid and electrolyte balance (e.g. hypovolaemia, salt and water deficit). The underlying cause for the acid-base disorder (e.g. ketoacidosis, acute kidney injury, sepsis) must be diagnosed and managed promptly. In general, specific therapy to correct the HCO_3^- or P_{CO_2} should only be contemplated if the acid-base disorder is affecting organ function or if the pH is <7.1 or >7.6 .

Patients identified as having a metabolic acidosis secondary to ethylene glycol or methanol intoxication need immediate referral to the renal team for consideration for intermittent haemodialysis to remove the toxin. Additional management should be guided by advice from a poisons centre, but will include the intravenous infusion of alcohol to prevent the breakdown of ethylene glycol and methanol to their toxic metabolites by alcohol dehydrogenase. If available fomepizole, an alcohol dehydrogenase inhibitor is the preferred first line therapy.

Mixed acid-base disorders

These are defined as the presence of more than one acid-base disorder. The patient's history or a lesser or greater than predicted compensatory respiratory or renal response may raise suspicions of mixed acid-base disorder.

A normal pH in the setting of substantial changes in both serum HCO_3^- or arterial Pco_2 indicates a mixed-acid base disorder is present.

Stewart approach to acid-base disorders

The Stewart approach, termed the Strong Ion Difference (SID), is based upon the central tenet that serum bicarbonate does not alter blood pH. Stewart defined acids as ions that shift the dissociation equilibrium of water to a higher concentration of H^+ and a lower concentration of OH^- .

The SID is the difference between the completely dissociated cations and anions in the plasma. It is defined as the difference between the sum of the strong cations, Na^+ , K^+ , Ca^{2+} and Mg^{2+} and the sum of the net charge of the major strong anions, Cl^- and lactate.

$$\text{SID} = (\text{Na}^+ + \text{K}^+ + \text{Ca}^{2+} + \text{Mg}^{2+}) - (\text{Cl}^- + \text{lactate}) = 38\text{-}46 \text{ mmol/l}$$

An increase in the SID is associated with an increase in blood pH, an alkalosis, e.g. vomiting leads to a loss of chloride and a decrease in serum chloride levels resulting in an increase in SID and alkalosis. The Stewart approach therefore explains the alkalosis associated with vomiting as excessive loss of chloride.

A decrease in SID is associated with a decrease in blood pH, an acidosis, e.g. the excessive infusion of saline results in an increase in chloride levels and therefore a decrease in SID and an acidosis. The Stewart approach therefore explains the hyperchloraemic metabolic acidosis associated with excessive saline infusion by the gain of chloride.

8. Oliguria

Introduction

Oliguria is defined as a urine output <0.5 ml/kg/h. It may be physiological (a normal response to surgery/injury) or pathological (secondary to acute kidney injury (AKI)). It is important to establish the cause of AKI with the most common cause being hypovolaemia and/or sepsis resulting in hypoperfusion of the kidneys (Chapter 9). There are other causes of renal hypoperfusion (e.g. cardiac causes), but this chapter will focus on that caused by hypovolaemia.

Physiological oliguria

Oliguria occurring soon after uncomplicated surgery is usually part of the normal physiological response to injury, conserving salt and water in an attempt to maintain intravascular volume. Isolated oliguria in the first 48 hours after uncomplicated surgery does not necessarily therefore reflect hypovolaemia, although it may do so if confirmatory features of intravascular hypovolaemia are present, e.g. tachycardia, hypotension, low central venous pressure (CVP/JVP), decreased capillary refill, etc. (Table 17).

The key clinical question is whether or not the oliguria is secondary to significant intravascular hypovolaemia requiring treatment. It is, therefore, essential that the patient's volume status is assessed carefully (Table 17). Remember that serial changes give more information than single observations. Also remember the importance of charting data in a serial manner and in a way that is easily accessible to the clinician. In difficult cases, particularly intra-operatively, invasive monitoring may be required additionally to guide optimal treatment.

Urine output should be interpreted in the light of these clinical signs and measurements before giving fluid treatment, which may not only be unnecessary, but also deleterious. Unnecessary fluid therapy not only expands the blood volume excessively but also over-expands the interstitial fluid volume, causing oedema and weight gain. The metabolic response to surgery impairs the patient's ability to excrete the additional saline load, making interstitial oedema worse, compromising organ function and increasing the risk of morbidity and mortality. Other consequences are dilution of the haematocrit and serum albumin concentration.

Table 17: Assessment of volume status

Capillary refill time
Pulse rate ■ Beta blockers/diltiazem (prevent tachycardia)
Blood pressure ■ Lying and standing
Jugular venous pressure
Skin turgor (over clavicle)
Auscultate ■ Lungs (pulmonary oedema) ■ Heart sounds (gallop rhythm – hypervolaemia)
Oedema ■ Peripheral/sacral
Urine output
Weight change to assess water balance

Oliguria secondary to AKI

Although it is important not to give excess fluid, failure to recognize and treat hypovolaemia (and pre-renal AKI) adequately may compromise organ perfusion and result in intrinsic AKI. There is evidence that patients with oliguric AKI have more severe tubular damage and a worse outcome.

Once a diagnosis of AKI has been made the underlying cause must be established (Chapter 9). The most common causes are hypovolaemia and/or sepsis leading to hypoperfusion of the kidneys. Clinical examination must be performed to establish the patient's volume status and the source of sepsis must be identified and treated promptly. If the patient is hypovolaemic then appropriate fluid therapy must be given according to a documented management plan, which requires regular review and defined endpoints (Fig. 9).

In a patient with hypovolaemia and oliguric AKI

- consider insertion of a central venous pressure (CVP) line and urinary catheter (not mandatory and could introduce infection) to aid with the assessment of volume status
- resuscitate with IV fluids (fluid challenge)
 - stat fluid bolus of 500 ml (250 ml if cardiac failure) of a balanced crystalloid (e.g. Hartmann's solution or Ringer's lactate) rapidly. If hyperkalaemia is present ($K^+ >5.5$ mmol/l) or suspected oliguric AKI or rhabdomyolysis 0.9% saline is preferred initially (no potassium in crystalloid). However, there is no evidence that administration of crystalloids containing 3–5 mmol/l of K^+ worsen the hyperkalaemia.

-
- assess clinical response to fluid in terms of
 - capillary refill time
 - pulse (reduction in pulse if tachycardic)
 - jugular venous pressure (rise in JVP)
 - blood pressure (rise in BP)
 - pulmonary oedema (if present stop iv fluid)
 - urine output
 - if there is a clinical response to fluid bolus continue with replacement fluids and discuss further fluid therapy management plan with senior member of team.
 - if there is no clinical response and no pulmonary oedema administer further 500 ml of crystalloid, reassess clinically and discuss with senior member of team. Remember to consider postoperative bleeding as a cause for the hypovolaemia and failure to respond to a fluid challenge.
 - if the patient has volume unresponsive oliguric AKI continue with iv fluids cautiously, matching urine output and monitoring for signs of respiratory distress (rising respiratory rate, pulmonary oedema or falling oxygen saturations). Refer to the renal team.

Oliguric AKI secondary to hypovolaemia is either volume responsive or unresponsive. In some cases, despite apparently adequate intravascular volume replacement the patient remains oliguric and unresponsive to any further fluid challenge. At this point, to avoid precipitating pulmonary oedema, no further intravenous fluid should be administered and the patient should be referred to the renal team. In patients who are fluid responsive, further fluid replacement can be prescribed as hourly fluid input equal to the previous hour's output plus 30 ml, with continuous monitoring and frequent review.

Diuretics

A common clinical question with oliguric AKI is whether the administration of loop diuretics (furosemide, bumetanide) improves renal recovery by increasing urine output. Studies have demonstrated that the use of high-dose loop diuretic to increase urine output in patients with established AKI does not decrease the need for renal replacement therapy or improve survival.

Loop diuretics may have a short-term role in managing fluid overload and pulmonary oedema. In these patients intravenous loop diuretics may be used cautiously to try and establish a diuresis and treat the pulmonary oedema. If the patient fails to respond, referral to the renal team is recommended. It must be remembered that high-dose loop diuretics are not without side-effects and may cause permanent hearing loss.

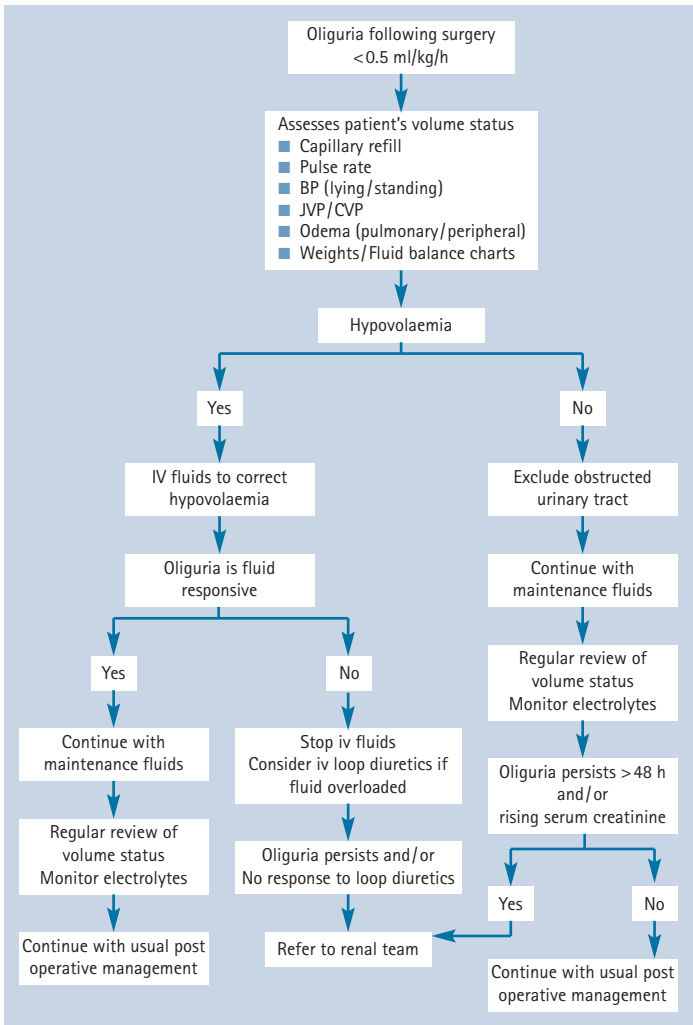


Figure 9: Flow chart for the management of the oliguric surgical patient.

9. Acute Kidney Injury

Introduction

Acute kidney injury (AKI) has replaced the term acute renal failure. It can develop as a consequence of a number of conditions including acute illness, trauma, sepsis or following major surgery. Patients with risk factors are particularly vulnerable to developing the disease (Table 18).

Acute kidney injury is associated with worse patient outcomes and is an antecedent for chronic kidney disease (CKD). It is a medical emergency and should not be regarded as an epiphenomenon without clinical significance.

Table 18: Risk factors for acute kidney injury.

- | |
|---|
| ■ Age >75 years |
| ■ Chronic kidney disease (eGFR < 60 ml/min/1.73m ²) |
| ■ Cardiac failure |
| ■ Peripheral vascular disease |
| ■ Liver disease |
| ■ Diabetes mellitus |
| ■ Hypertension |
| ■ Hypovolaemia |
| ■ Sepsis (hypotension and inflammatory response) |
| ■ Nephrotoxins
(e.g. medications, poisons, iodinated-contrast media) |

Definition

AKI is a result of a rapid fall in glomerular filtration rate occurring over hours or days. The consequences include a failure to regulate fluid and electrolyte balance and a failure to excrete metabolic waste products and drugs.

AKI is defined when one of the following criteria is met;

- Serum creatinine rises by $\geq 26 \mu\text{mol/l}$ within 48 hours or
- Serum creatinine rises ≥ 1.5 fold from a baseline value measured within the previous week or
- Urine output is $< 0.5 \text{ ml/kg/h}$ for > 6 consecutive hours

If serum creatinine concentration has not been measured in the previous week, use the most recent creatinine concentration measured within the last three months. AKI can be staged according to the criteria in Table 19.

Table 19: Stages of acute kidney injury

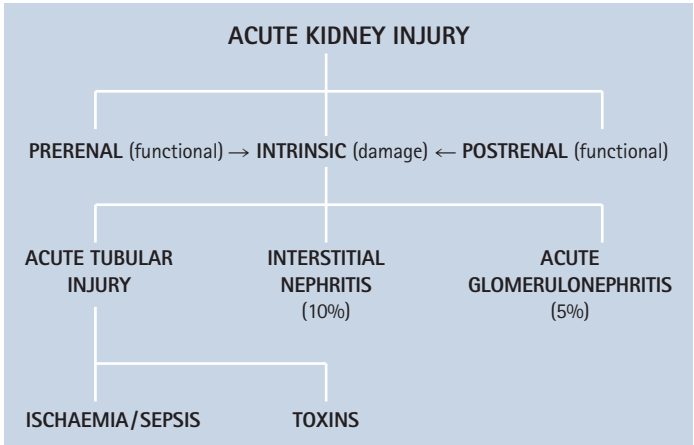
Stage	Serum creatinine (SCr) criteria	Urine output criteria
1	increase $\geq 26 \mu\text{mol/l}$ within 48 h <i>or</i> increase $\geq 1.5\text{--}1.9 \times$ baseline SCr	$< 0.5 \text{ ml/kg/h}$ for > 6 consecutive h
2	increase $\geq 2\text{--}2.9 \times$ baseline SCr	$< 0.5 \text{ ml/kg/h}$ for > 12 h
3	increase $\geq 3 \times$ baseline SCr <i>or</i> increase $\geq 354 \mu\text{mol/l}$	$< 0.3 \text{ ml/kg/h}$ for > 24 h or anuria for 12 h

Any patient who meets the criteria for AKI should have a thorough clinical evaluation, which includes an assessment of volume status, fluid balance and medication chart in order to identify any potential causes for the AKI. In the majority of cases, AKI may be reversible if the cause is identified and appropriate management implemented.

Aetiology of Acute Kidney Injury

If the criteria for diagnosing AKI have been satisfied, it is important to identify its underlying aetiology as this will determine the most appropriate therapy and influence whether early referral to nephrology is necessary. AKI can be considered as pre-renal, intrinsic and post-renal (Fig. 10). Pre-renal and post-renal can both be considered as functional processes that may progress to damage to the parenchyma if not treated promptly.

Figure 10: Classification of AKI



AKI is most commonly secondary to a combination of sepsis and hypovolaemia, which results in hypoperfusion of the kidneys and pre-renal AKI. Failure to correct the hypoperfusion may result in the development of acute tubular injury and intrinsic AKI, classically referred to as acute tubular necrosis (ATN). However it is important to exclude other possible causes so that a rarer aetiology, e.g. vasculitis, is not overlooked (Table 20).

Table 20: Classification and causes of AKI

Pre-renal AKI	Intrinsic AKI	Post-renal AKI
<ul style="list-style-type: none"> ■ intravascular volume depletion <ul style="list-style-type: none"> ■ fever ■ vomiting ■ diarrhoea ■ burns ■ shock (vasodilatation and hypoperfusion) <ul style="list-style-type: none"> ■ cardiogenic shock ■ septic shock ■ anaphylactic shock ■ decreased renal perfusion pressure <ul style="list-style-type: none"> ■ renal artery stenosis/thrombosis ■ congestive cardiac failure ■ liver failure/cirrhosis ■ nephrotic syndrome ■ drugs <ul style="list-style-type: none"> ■ NSAIDs ■ angiotensin-converting enzyme inhibitors ■ angiotensin receptor blockers 	<ul style="list-style-type: none"> ■ tubular injury <ul style="list-style-type: none"> ■ ischaemia/reperfusion injury ■ nephrotoxins <ul style="list-style-type: none"> ■ aminoglycosides ■ cisplatin ■ intravenous iodinated contrast media ■ myoglobin ■ myeloma light chains ■ glomerular <ul style="list-style-type: none"> ■ glomerulonephritis ■ interstitial <ul style="list-style-type: none"> ■ interstitial nephritis <ul style="list-style-type: none"> ■ drugs ■ infections ■ vascular <ul style="list-style-type: none"> ■ atheroembolic disease ■ cholesterol embolisation 	<ul style="list-style-type: none"> ■ blocked urinary catheter ■ retro peritoneal fibrosis ■ kidney stones ■ prostatic disease ■ pelvic tumour ■ renal vein thrombosis ■ iatrogenic injury to both ureters

Clinical Features

There should be a high index of suspicion for AKI, particularly in an acutely ill patient with risk factors. Information about the patient's previous kidney function (e.g. serum creatinine), particularly over the preceding 3 months, is a vital part of the evaluation. As in every other clinical condition, diagnosis is achieved by weighing all the evidence derived from a full history, examination and appropriate investigations. Serial changes in clinical features are often more revealing than single measurements taken at any one time. AKI should be considered as part of the differential diagnosis in patients presenting with the following clinical features (Table 21).

Table 21: Clinical features of patients with suspected AKI and recommended baseline investigations

History	Examination	Investigations
<ul style="list-style-type: none"> ■ risk factors (Table 18) ■ symptoms predisposing to hypovolaemia <ul style="list-style-type: none"> ■ vomiting ■ diarrhoea ■ poor oral intake ■ blood/plasma loss ■ symptoms suspicious of vasculitis <ul style="list-style-type: none"> ■ uveitis ■ skin rash ■ joint pains ■ haemoptysis 	<ul style="list-style-type: none"> ■ general <ul style="list-style-type: none"> ■ weight ■ temperature ■ skin turgor (over clavicle) ■ mucous membranes (misleading if mouth breathing) ■ skin rash (vasculitis) ■ joint swelling (vasculitis) ■ uveitis (vasculitis) 	<ul style="list-style-type: none"> ■ full blood count (FBC) ■ urea and electrolytes (U&Es), including chloride and bicarbonate ■ acid-base status (from arterial or venous blood gas analysis) ■ liver function tests (LFTs) ■ calcium and phosphate ■ urinalysis (prior to urinary catheter) ■ ultrasound of renal tract within 24 hours if obstruction suspected
↓	↓	

History	Examination	Investigations
<ul style="list-style-type: none"> ■ urinary symptoms <ul style="list-style-type: none"> ■ anuria ■ frequent dribbling or passage of small volumes of urine ■ suprapubic discomfort ■ full medication history including <ul style="list-style-type: none"> ■ over-the-counter medications ■ herbal remedies 	<ul style="list-style-type: none"> ■ volume status <ul style="list-style-type: none"> ■ capillary refill ■ pulse rate ■ jugular venous pressure ■ BP (lying and standing) ■ heart sounds (gallop rhythm) ■ lungs (pulmonary oedema) ■ peripheral oedema ■ abdomen <ul style="list-style-type: none"> ■ bladder distension ■ intra-abdominal hypertension ■ rectal or pelvic examination if obstruction suspected 	

AKI can be oliguric (<0.5 ml/kg/h) or non-oliguric. Pre-renal AKI (functional process) is associated with oliguria by virtue of the fact that there is reduced renal perfusion and intact renal tubules which endeavour to preserve salt and water. Patients with pre-renal AKI that evolves to intrinsic AKI (damage) or who experience direct tubular toxicity (e.g. gentamicin, iodinated contrast) may lose the ability to reabsorb fluid and, therefore, are not oliguric maintaining a relatively normal urine output. These patients will require ongoing fluid therapy to maintain an optimal volume status. However, failure to establish adequate renal perfusion in those who are evolving from a pre-renal to intrinsic AKI will ultimately result in oliguria. Therefore, careful continued monitoring is recommended.

Urinary electrolytes

The measurement of urinary electrolytes and osmolality can be used to distinguish pre-renal AKI from intrinsic AKI (Table 22). The measurements of urinary sodium are not accurate if loop diuretics have been administered within the previous 12 hours or there is pre-existing chronic kidney disease.

Table 22: Distinguishing pre-renal from intrinsic AKI

Parameter	Pre-renal	Intrinsic
Urine sodium (mmol/l)	<20	>40
Urine osmolality (mOsm/l)	>500	<350
Urine/plasma urea	>8	<3
Urine/plasma creatinine ratio (index)	>40	<20
Fractional sodium excretion (%)	<1	>2

Management

Prevention

Any patient admitted to hospital who is acutely ill or undergoing major surgery who has been identified as at risk of developing AKI (Table 18) should

- have a daily clinical volume status assessment
- have a daily assessment of the fluid prescription
- have a daily fluid balance chart
- have daily weights
- avoid nephrotoxic agents [e.g. non-steroidal anti-inflammatory drugs (NSAIDs), aminoglycosides]
- have other drugs (e.g. antihypertensive medications such as angiotensin converting enzyme inhibitors, angiotensin receptor blockers) reviewed especially if they develop hypotension and/or sepsis
- have urea, creatinine and electrolytes checked daily until they regain health

Any acutely ill patient with AKI or at high risk for AKI (Table 18) undergoing an iodinated contrast study should

- be discussed with the radiologists with respect to the risk factors and alternative imaging
- have nephrotoxic medication stopped
- have a daily clinical volume status assessment
- have a daily fluid balance chart
- have daily weights
- receive intravenous fluid at 1 ml/kg/hour 12 hours prior to and 12 hours following the procedure (caution if cardiac failure) selecting either
 - 0.9% saline or
 - isotonic (1.4%) sodium bicarbonate solution
- have urea, creatinine and electrolytes monitored for 3-5 days

Treatment

Once a patient has developed AKI, treatment is initially supportive but ultimately dependent upon the underlying cause. Treatment involves the following:

- Identify and treat the underlying cause (not all AKI will be secondary to hypovolaemia and/or sepsis)
- Volume status assessment
 - If hypovolaemic
 - consider insertion of a central venous pressure (CVP) line and urinary catheter (not mandatory and could introduce infection) to aid with the assessment of volume status
 - resuscitate with IV fluids
 - stat 500 ml bolus (250 ml if cardiac failure) of a balanced crystalloid (e.g. Hartmann's solution or Ringer's lactate) rapidly. If hyperkalaemia is present ($K^+ >5.5$ mmol/l) or suspected oliguric AKI or rhabdomyolysis 0.9% saline is preferred initially (no potassium in crystalloid). However, there is no evidence that administration of crystalloids containing 3–5 mmol/l of K^+ worsen the hyperkalaemia.
 - assess clinical response to fluid in terms of
 - capillary refill time
 - pulse (reduction in pulse if tachycardic)
 - jugular venous pressure (rise in JVP)
 - blood pressure (rise in BP)
 - pulmonary oedema
 - urine output (increasing if oliguric)

-
- if no clinical response and no pulmonary oedema administer further 500 ml of crystalloid, reassess clinically and discuss with senior member of team
 - if clinical response to fluid bolus continue with further fluids and discuss further fluid therapy management plan with senior member of team
 - If the patient develops oliguric AKI (< 0.5 ml/kg/24 hrs) despite adequate volume resuscitation consider the patient as having volume unresponsive AKI. Further excessive fluid resuscitation may result in pulmonary oedema.
 - If the patient has volume unresponsive AKI continue with iv fluids cautiously, matching urine output and monitoring for signs of respiratory distress (rising respiratory rate, pulmonary oedema or falling oxygen saturations).
 - Specific treatment of complications of AKI
 - Hyperkalaemia may be associated with
 - muscle weakness, palpitations, paraesthesia
 - ECG changes-loss of P-waves, wide QRS complexes, peaked T waves
 - It must be remembered that unless the cause of the AKI is treated the measures described are only temporary. The potassium will need to be monitored closely until recovery of sufficient kidney function to excrete potassium or RRT.
 - Immediate treatment required if
 - $K^+ > 6.0$ mmol/l with ECG changes or
 - $K^+ > 6.5$ mmol/l with or without ECG changes

■ Immediate treatment

- iv 10 ml 10% calcium gluconate over 2-5 minutes (cautiously, as extravasation can cause tissue damage). This stabilises the myocardium rapidly, but has no effect on serum potassium concentration. Further doses may be required until reduction in plasma potassium concentration is achieved. Onset of action 2-4 minutes. Duration of action 30-60 minutes.

■ Further treatment

- 10u fast acting insulin (actrapid) added to 50 ml of 50% dextrose infused iv over 20 minutes to increase cellular potassium uptake. Blood glucose must be monitored closely. Onset of action 15-30 minutes. Duration of action 4-6 hours.
- 5 mg salbutamol nebuliser (up to a maximum of 10-15 mg back to back) to stimulate cellular potassium uptake. Avoid in patients on beta blockers and/or who have a history of cardiac arrhythmias. Onset of action 30 minutes. Duration of action 2-4 hours.
- Medication review - stop any drugs that contain potassium or interfere with renal excretion of potassium (ACE inhibitors, angiotensin receptor blockers, beta-blockers, potassium sparing diuretics)
- Review potassium intake including intravenous fluids and enteral or parenteral feeds

■ acidosis

- pH 7.2-7.4 – there is very little evidence to support correction with bicarbonate.
- pH <7.2 – isotonic sodium bicarbonate 1.4% solution can be used in stable patients not imminently requiring RRT. Bicarbonate therapy may worsen intracellular acidosis and deliver excessive sodium load. In presence of hypocalcaemia bicarbonate can cause a further reduction in calcium and provoke convulsions. Bicarbonate should only be used when calcium is known, and near normal, and following senior advice. Renal replacement therapy will be required if the patient is hypervolaemic and/or refractory to medical treatment

■ pulmonary oedema

- sit the patient up and provide supplementary oxygen (up to 60%) via venturi face mask. A non-rebreathing (reservoir) mask (15 l/min O₂) may be required if severe pulmonary oedema is present.
- buccal glyceryl trinitrate 2-5 mg works rapidly and can be repeated as frequently as required. If intolerable headache or hypotension develops, this resolves rapidly after removing the tablet from the mouth.
- iv glyceryl trinitrate 50 mg in 50 ml 0.9% saline. Commence at 2 ml/hr and titrate up to 20 ml/hr maintaining systolic BP >95 mmHg.
- iv furosemide can be tried if the patient is haemodynamically stable and adequately intravascularly filled. The dose is dependent on the severity of AKI. Furosemide 160 mg (slow infusion over 1 hour) may be required for severe AKI (stage 3) (Table 19).
- renal replacement therapy if the patient is in extremis ± being ventilated

-
- uraemic encephalopathy
 - renal replacement therapy
 - uraemic pericarditis
 - renal replacement therapy

Medication management

In patients with AKI it is important to identify medications that are normally metabolised and/or excreted by the kidneys, and either avoid or make appropriate dose adjustments. Common examples include:

- penicillins
- cephalosporins
- vancomycin
- morphine (metabolites will accumulate)
- low molecular weight heparin

If the patient is hypotensive there should be a low threshold for withholding antihypertensive therapy which will only exacerbate renal hypoperfusion. Common examples include:

- angiotensin-converting enzyme inhibitors
- angiotensin receptor blockers
- diuretics

Nephrotoxic medications should be avoided if possible (unless life-saving) and include:

- non-steroidal anti-inflammatory drugs (NSAIDs)
- gentamicin
- amphotericin

Referral to nephrologist

- NOT all patients diagnosed with AKI need to be referred
- Prior to referral the following should be performed
 - a thorough clinical history and examination (including fluid balance/volume status assessment)
 - initial investigations (as recommended above)
 - initial supportive management (as recommended above)
- Early renal referral is recommended in the following patients
 - AKI stage 3 ($SCr \geq 3 \times$ baseline value) (Table 19)
 - persistent oliguria and/or rising serum creatinine despite supportive therapy
 - complications refractory to medical treatment
 - hyperkalaemia ($K > 6$ mmol/l)
 - pulmonary oedema
 - acidosis ($pH < 7.15$)
 - uraemic encephalopathy
 - uraemic pericarditis
 - suspicion for primary renal disease
 - absence of defined cause , e.g. sepsis, hypovolaemia
 - systemic features eg rash, uveitis, joint pains, blood and protein on urinalysis
 - paraprotein
 - bloody diarrhoea, haemolysis and low platelets
 - poisoning suspected
 - ethylene glycol
 - methanol
 - lithium

Recovery

The first signs of recovery from oliguric AKI may be an increase in urine output. Alternatively recovery may be heralded by a reduction in the rise in the daily serum creatinine followed by a plateau in its value prior to a fall. Recovery from AKI can result in a polyuric state in some patients with the production of large urine volumes until the capacity of the renal tubule to concentrate urine returns. There must therefore be careful attention to the patient's volume status and fluid requirements.

Patients can be at risk of developing a free water deficit which manifests as hypernatraemia and requires an increased intake of water (intravenous 5% dextrose if unable to take water orally). Failure to address the free water deficit promptly will not only slow renal recovery but will also put the patient at risk of neurological complications. Another potential complication is the development of hypokalaemia, which requires appropriate therapy due to the risk of cardiac arrhythmias and ileus. A balanced crystalloid containing potassium is recommended in this clinical context. If further potassium is required consider infusing dextrose saline (4%/0.18%) with added potassium

Follow up

Acute kidney injury is a recognized antecedent for chronic kidney disease and patients require follow up.

The discharge summary to primary care should summarise:

- the cause of AKI
- risk factors for AKI
- medications stopped and started
- blood pressure (longer term monitoring required)
- kidney function

Refer patients to nephrology left with an estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73 m².

10. The Patient with Diabetes Mellitus

Introduction

Although, with better management of diabetes in recent years, admissions due to loss of control with or without ketosis are less frequent than in former times, nonetheless cases of decompensated diabetes with keto-acidosis (DKA) or hyperosmolar non-ketotic (HONK) syndrome form an important part of every doctor's experience of acute medicine. Similarly, with the rising prevalence of diabetes, particularly type 2, the perioperative fluid and metabolic management of diabetic patients has become increasingly important.

Decompensated Diabetes

Type 1 diabetes: insulin secretion is impaired in most cases by >90%. This means that, with reduced or absent administration of insulin or with increased insulin demand due to intercurrent illness, not only does the blood glucose rise but control over fat and protein metabolism is lost, leading to keto-acidosis (β -hydroxybutyrate being the main keto-acid) and protein catabolism.

Type 2 diabetes: This is associated initially with insulin resistance but only partial loss of secretion. At this stage, there is sufficient circulating insulin to prevent ketosis but not to control the blood glucose. Decompensation is usually associated with HONK in which the blood glucose rises to higher levels than those seen in DKA (it only takes a fraction of the amount of insulin to control ketosis as it does to control blood glucose). With loss of insulin secretion over the years and with severe intercurrent illness type 2 diabetics can develop keto-acidosis, requiring insulin, even though they may be able to revert to tablet treatment afterwards .

DKA and **HONK** represent the two extremes of the spectrum of decompensated diabetes (Table 23), although intermediate cases are not infrequent, depending on the precipitating cause and the percentage loss of insulin secretion. In both situations, hyperglycaemia causes an osmotic diuresis with excessive urinary losses of salt, water, and potassium, leading to ECF and intravascular volume depletion and the risk of prerenal acute kidney injury (AKI).

With both types of decompensation, potassium is lost from cells and excreted in the urine causing a deficit, which only becomes apparent as hypokalaemia once the anabolic effect of insulin treatment is felt. In severe cases the rate of K^+ loss from cells, combined with pre-renal AKI, can cause hyperkalaemia (>5.5 mmol/l) with the risk of cardiac arrest.

The presence of acidosis may present diagnostic problems. Although most cases with ketonuria and features of metabolic acidosis are suffering from ketoacidosis, this cannot always be assumed, particularly where there are other potential causes of acidosis, e.g. renal or circulatory failure. For this reason it is important to measure blood concentrations of lactate and of ketones, particularly β -hydroxybutyrate and chloride, including the anion gap and strong ion difference in order to establish the diagnosis beyond doubt.

Table 23: Features of DKA and HONK compared (approximate values only)

Parameters	Normal range	DKA			HONK
		Mild	Moderate	Severe	
Blood glucose mmol/l	3.5-11.1 (random)	> 14	>14	> 14	>30
Arterial pH	7.35-7.45	7.2-7.3	7.0-7.2	<7.0	>7.3
HCO ₃ ⁻ mmol/l	22-30	15-18	10-15	<10	Normal to slightly reduced
Urine ketones	Absent	++++	++++	++++	±
Anion gap (mmol/l)	5-10	> 10	> 12	> 12	Variable
Serum osmolality mOsm/kg	280-295	280-320	280-320	280-320	>320
Average total losses					
Water (litres)		3-4	4-5	> 5	6-10
Sodium (mmol)		200-280	280-350	> 350	350-700
Potassium (mmol)		200-280	280-350	> 350	> 350

Treatment

Aims

These are similar in both DKA and HONK, although with differences of emphasis.

- Restore the circulation and the ECF deficit by initially rapid fluid infusion. This also has a beneficial metabolic effect reducing the blood glucose, addresses circulatory failure and prerenal AKI, reducing both acidosis and serum K⁺.
- Seek the underlying cause of the diabetic decompensation (e.g. sepsis) and treat it.

Fluids and insulin

- In the absence of shock or oliguria, give 1-2 l of crystalloid (see below) in the first 2 hours, the 1 l over the next 4 hours and 4 l over the next 24 hours. In severe cases, administration should be faster initially, aiming to correct half the fluid deficit within the first 6 hours and the remainder over the ensuing 24 hours. With HONK the fluid deficits are larger (Table 23)
- After the first litre of fluid add KCl 20-40 mmol to each subsequent litre of fluid infused, depending on the changes in serum K⁺ with treatment.
- To avoid precipitating cerebral oedema, the effective serum osmolality should not be reduced at a rate greater than 3 mOsm/kg/h. This is particularly important in cases involving children and the elderly and in the treatment of HONK.
- When the blood glucose has fallen to 14 mmol/l, change to a hypotonic glucose-containing preparation adjusted according to the insulin-induced changes in blood glucose and the serum sodium and osmolality.
- Treat hyperkalaemia and acidosis with fluid infusion, insulin, and, in severe cases (pH < 7.0), with bicarbonate.
- Reduce blood glucose and ketones with insulin infusion. It may take up to 48 hours to clear ketones if DKA is severe. Add 50 U soluble short-acting insulin to 50 ml 0.9% saline in a syringe driver and administer intravenously at 6 U/h i.v., adjusting subsequently to lower the blood glucose at a rate no faster than 4 mmol/l/h.

Monitoring

- Monitor blood glucose, urinary ketones, acid-base status, serum potassium, sodium, chloride and, if appropriate, osmolality, every hour or two initially. Watch particularly for a fall in serum potassium and correct this with increased potassium input to maintain serum K^+ in the range of 3.3–4.5 mmol/l. Monitor clinical status, vital signs, kidney function and urine output.

Fluid prescription

Traditionally, 0.9% saline has been used for resuscitation, followed by 0.45% saline with 5% dextrose and KCl as the volume deficit nears restoration. Recent studies suggest that using a balanced electrolyte solution avoids the hyperchloraemic acidosis associated with administration of 0.9% saline.

Hypotonic solutions pose a risk of too rapid a fall in osmolality unless the plasma sodium and osmolality are monitored carefully and the infusion rate controlled accordingly. It should be remembered that glucose acts like Na^+ as an ECF osmotic agent, so that as the blood glucose falls with insulin treatment, water passes from the ECF to the ICF, thereby concentrating the ECF sodium by 1.6 mmol/l for every 5.6 mmol/l fall in blood glucose. It is common, therefore, particularly in HONK, to see the plasma Na^+ rise with treatment necessitating a switch to a more hypotonic solution. It is at this point that switching from 0.9% to 0.45% saline may be useful gradually to reduce the plasma Na^+ to normal.

Although there is a phosphate deficit in decompensated diabetes, and phosphate levels fall with treatment, phosphate supplementation has not been shown to be beneficial.

*Surgery in the patient with diabetes:
(based on NHS Diabetes recommendations)*

Peri-operative glucose control

For short procedures, involving missing no more than one meal, particularly in type 2 diabetes, the normal treatment may be delayed until post-operatively, with hourly monitoring of blood glucose and treatment with insulin if blood glucose rises above 12.0 mmol/l.

Those expected to miss more than 1 meal, particularly Type 1 patients should receive variable rate insulin infusion (VRII) to maintain blood glucose within the range 4–12 mmol/l as shown by hourly monitoring. Insulin should be administered in 0.45% saline with 5% glucose and 0.15–0.3% KCl via a syringe pump, starting approximately 6 hours preoperatively and continuing post-operatively until normal oral intake is established.

Perioperative fluid and electrolyte management

The principles are the same as those we have outlined for the non-diabetic. In the type 1 diabetic, however, in order to avoid ketosis, it is useful to have a constant rate of infusion of a crystalloid containing 5% glucose with appropriate VRII cover. This can be achieved using 0.45% saline with 5% dextrose and 0.15–0.3% KCl. Alternatively, if a balanced electrolyte solution is preferred, use Plasmalyte Maintenance (Chapter 5).

11. Disorders of Sodium, Potassium, Calcium, Magnesium and Phosphate

Introduction

It is impossible to give a detailed account of all aspects of these electrolytes in a brief chapter such as this. The authors have therefore confined themselves to a short summary of some common aspects. For more detailed treatment the reader is referred to the easily available review articles and books listed under 'Further Reading'.

Sodium (Na^+)

The total body sodium is 3000–4000 mmol, of which only 60% is exchangeable, the remainder being locked mainly in bone. Short-term changes in the serum sodium concentration are usually due to changes in water balance, although, in some cases, salt balance may contribute. This reflects the fact that salt balance is about maintenance of volume, whereas water balance is more concerned with osmolality. Hyponatraemia and hypernatraemia may therefore occur in the presence of positive, negative or zero salt balance. The serum Na concentration on its own, therefore, cannot be used to diagnose the state of Na balance, although if change in water balance is known from serial weighing, then the day to day balance of Na can be inferred from the change in serum Na concentration over the same period (Chapter 3). The principle is best illustrated by some examples:

Hyponatraemia

In severe cases with serum $\text{Na}^+ < 120$ mmol/l, there is a risk of developing cerebral oedema and brain damage, particularly in children and the elderly. Conversely, too rapid correction of severe hyponatraemia may also cause neurological damage (osmotic demyelination). It is advised that hyponatraemia be corrected at a rate not exceeding

10 mmol/l/day. In the differential diagnosis of hyponatraemia, false hyponatraemia should be excluded. In the presence of severe hyperlipidaemia causing milky serum, the serum Na^+ may be falsely low as the lipid expands the ECF but contains no Na^+ .

Similarly hyperglycaemia expands the ECF by its osmotic action and, as the blood glucose falls with treatment, water passes from the ECF to the ICF and the Na^+ concentration rises. Serum Na^+ falls by 1.6 mmol/l for every 5.6 mmol/l increase in plasma glucose. In cases of hyperglycaemia, therefore, the serum Na^+ should be corrected upwards appropriately. It is the corrected value that should guide fluid replacement.

- With positive water and salt balance: This often occurs as a result of infusions of hypotonic fluids post-operatively, following trauma, or during acute illness, when the metabolic response to injury is causing retention of both salt and water, inhibiting the kidneys' ability to correct osmolality by increasing free water clearance. In this situation there is usually a positive sodium balance but, in relation to plasma, a proportionally greater positive water balance. Urinary sodium concentrations are usually low, since with the response to injury the normal physiological relationship between sodium balance and urinary sodium is lost. Treatment consists mainly of stopping intravenous fluids.
- With positive water and normal or slightly negative salt balance. This occurs with inappropriate ADH secretion, classically associated with oat cell carcinoma of the lung, but also caused by a number of other conditions. With the consequent water retention, the serum sodium is diluted, but the urinary sodium is normal or high, as the kidneys respond to the slight hypervolaemia. This condition is often over-diagnosed and should not be confused with the far more common response to injury described above.

-
- With normal water balance and negative salt balance. This classically occurs in Addison's disease with its loss of both mineralocorticoid and glucocorticoid secretion and clinical features of weakness, weight loss, pigmentation and hypotension. Hyponatraemia occurs not only due to renal salt loss, but also due to the kidneys' impaired ability to correct osmolality; firstly because salt loss causes ECF hypovolaemia, which excites ADH secretion and secondly because hydrocortisone has a permissive role in the distal tubule, allowing urinary dilution. In its absence, free water clearance is impaired, the basis for the old Kepler water load test for the condition. Nowadays diagnosis is made simply by measuring serum cortisol levels and their response to Synacthen.
 - With water excess and negative sodium balance. This occurs when excess salt losses from the GI tract or the kidneys (diuretics or tubular disease) are combined with excess water or hypotonic fluid intake by mouth or other routes. The sodium depletion causes hypovolaemia, which, in turn, stimulates not only the renin angiotensin aldosterone system but also ADH secretion, thereby impairing free water clearance and any osmolar correction.
 - In critical illness
In severe catabolic illness e.g. burns, septicaemia etc., cell membrane function may be impaired and the sodium pump affected so that intracellular Na^+ levels rise and those in the ECF fall despite considerable positive Na^+ balance. This has been called the 'sick cell syndrome'. With improved tissue perfusion and oxygenation and correction of underlying sepsis this may resolve. In the past, insulin, glucose and potassium have also been used with effect.

Hypernatraemia

The most common cause is net loss of hypotonic fluid from the GI tract e.g. vomiting and diarrhoea, so that in relation to plasma, pro-

portionately more water is lost than sodium, even though sodium balance is also negative. The same occurs with renal losses due to the osmotic diuresis associated with uncontrolled diabetes. Large fluid losses from sweat, e.g. in the tropics, may also produce the same effect. The rare primary hyperaldosteronism also causes mild hypernatraemia.

Treatment is with hypotonic fluids orally, enterally or intravenously with frequent monitoring of serum biochemistry. Oral water may be sufficient in mild cases. In the presence of diarrhoea oral rehydration solutions may be appropriate. Severe cases should be treated cautiously with hypotonic intravenous fluids (e.g. 5% dextrose, 0.18% saline in 4% dextrose) taking care to avoid too rapid reduction in plasma sodium or osmolality. Correction should be achieved during 48 hours at a rate no greater than 2 mmol/l/h to avoid cerebral oedema.

Chloride (Cl⁻)

This is the main anion of the ECF at a concentration of 95–105 mmol/l. Unfortunately, because most clinical chemistry laboratories gave up reporting the serum chloride as part of routine screening, abnormal states such as hyperchloraemic acidosis have sometimes gone undetected. As a consequence, metabolic acidosis due to chloride has not infrequently been mistaken for other causes of acidosis and inappropriate treatment given. We, therefore, advise that serum chloride should always be measured in the presence of a metabolic acidosis or whenever large volumes of saline have been administered. It is important to remember that while the concentration of Na⁺ in 0.9% saline is 10% higher than that in plasma, the concentration of Cl⁻ is 50% higher. This solution also has a pH of 5.5.

The main cause of hypochloraemic alkalosis is loss of gastric juice (with its high HCl content) by vomiting or gastric aspiration. This is the main indication for giving 0.9% saline.

Potassium (K⁺)

The total body K⁺ lies between 3000 and 3500 mmol and is contained largely in the intracellular space at a concentration of 120–145 mmol/l, where it is the chief cation, balancing the negative charges on proteins and other non-diffusible anions. Only a very small proportion is in the ECF, where its concentration lies crucially in the narrow range 3.5–5.2 mmol/l. The balance of K⁺ across the cell membrane is maintained by the sodium pump combined with the Gibbs-Donnan equilibrium as described in Chapter 1. The normal daily requirements are 1 mmol/kg body weight. The following points are of clinical importance:

Hyperkalaemia: the serum K⁺ rises with renal failure and catabolic states, e.g. the response to injury. During the flow phase of injury, as glycogen and protein are broken down, K⁺ linked to them is released from the cells into the ECF. Conversely, during the convalescent or anabolic phase of injury, the cells take up K⁺ again as glycogen and protein are resynthesised, causing a fall in ECF levels. Serum K⁺ levels also rise in response to internal haemorrhage or tissue damage, e.g. muscle necrosis, as K⁺ is released from dead cells. If acute kidney injury (AKI) and a catabolic state are combined, serum K⁺ levels rise rapidly to dangerous levels, usually accompanied by a metabolic acidosis.

A rise above 6.0 mmol/l risks cardiac arrest and necessitates urgent treatment. With fluid depletion and pre-renal AKI, intravenous fluids may be sufficient, but additional treatment includes bicarbonate as well as insulin and glucose, both of which drive K⁺ back into the cells, but only temporarily (4–6 hours). This is a useful emergency measure which may need repeating. Calcium gluconate also helps to stabilize the heart. If these measures fail or oliguria persists, then calcium resonium rectally or renal replacement therapy should be carried out without delay (Chapter 9).

Hypokalaemia: a fall in serum concentrations below 3.5 mmol/l nearly always reflects K^+ deficiency and is usually accompanied by alkalosis because of the interchange of K^+ , Na^+ , and H^+ in the distal tubule, although, with renal tubular defects and laxative abuse, acidosis may be present. Although the relationship between the degree of hypokalaemia and the total K^+ deficit is not a precise one, in general it takes a loss of 200–400 mmol to reduce the serum K^+ from 4.0 to 3.0 mmol/l and a further loss of the same amount to reduce serum K^+ to 2.0 mmol/l.

Symptoms include muscle weakness and, in more severe cases, as serum K^+ falls below 2.5 mmol/l, paralysis and cardiac arrhythmias. The most common causes of hypokalaemia are GI fluid loss and diuretic therapy. It should also be remembered that patients with diabetic keto-acidosis may have a deficit in excess of 400 mmol even though at presentation the serum K^+ may be high due to acidosis and pre-renal AKI from fluid loss. As the acidosis is corrected and insulin is given, K^+ moves rapidly back into the cells and serum K^+ concentrations plunge to dangerous levels unless adequate K^+ replacement is given (Chapter 9). A similar phenomenon is seen with the refeeding syndrome (Chapter 12).

Immediate treatment should be aimed at raising the serum K^+ to a safe level above 3.0 mmol/l rather than correcting the whole deficit, which can then be done more slowly over the next few days. With mild hypokalaemia (3–3.5 mmol/l), oral supplements at an initial dose of 60–80 mmol/day should be tried, although many patients find oral supplements difficult to tolerate. KCl is preferred to provide Cl^- to correct any accompanying alkalosis. The more easily tolerated effervescent K^+ preparations provide undesirable bicarbonate.

In the presence of alkalosis, the distal tubules continue to excrete K^+ in exchange for H^+ even in the face of a K^+ deficit. In long-term diuretic therapy, a K^+ sparing diuretic or spironolactone should be

added to prevent recurrence. In more severe cases i.e. serum K^+ < 3.0 mmol/l, it is usually necessary to give KCl in saline intravenously. This also provides extra Cl^- to correct alkalosis. The use of dextrose as a vehicle risks lowering serum K^+ still further as it excites insulin secretion and a combination of insulin and glucose drives potassium into the cell. In general, intravenous KCl should not be given faster than 10–20 mmol/h, although higher rates may need to be given to patients with severe hypokalaemia causing paralysis and arrhythmias. Rates as high as 40–100 mmol/h have been given under these circumstances but this should only be done via a central line under high dependency supervision with ECG and biochemical monitoring.

Calcium (Ca^{2+})

There are 1300 g (33,000 mmol) in the body, 99% being in bone and only 1% being freely exchangeable. The normal serum concentration is 2.2–2.5 mmol/l, all except 0.8–1.24 mmol/l being bound to protein, chiefly albumin. With falls in serum albumin due to illness and dilution with intravenous fluids, the measured serum Ca^{2+} should be corrected upwards by 0.02 mmol/l for every 1 g/l fall in serum albumin between 40 and 25 g/l. Ca^{2+} plays a vital role, not only in bone, but also in neural conductivity, muscular conduction and many other physiological and metabolic processes.

Ca^{2+} absorption, excretion and serum concentration are governed by parathyroid hormone, calcitonin, and Vitamin D. Under normal circumstances 240 mmol/day of Ca^{2+} are filtered by the kidney, with all but 2–10 mmol being reabsorbed. Although some vitamin D is derived from food, most is formed in the skin under the influence of sunlight. It is then hydroxylated in the liver and subsequently the kidney to its most active form $1,25(OH)_2D_3$.

Four common aspects of Ca^{2+} disorders deserve a mention here:

Osteomalacia (Rickets in children)

This is due to Vitamin D deficiency caused by lack of exposure to sunlight, malnutrition, some gastrointestinal diseases which cause fat malabsorption, and renal disease causing reduced levels of $1,25(\text{OH})_2\text{D}_3$. It is characterized by typical radiological changes in bone, low serum Ca^{2+} , raised serum PO_4^{2-} , elevated alkaline phosphatase and PTH, and low blood Vit D levels. Treatment is with 0.25-1 mg of 1β -hydroxycholecalciferol daily and, in some cases, calcium supplements.

Osteoporosis

This involves not only thinning of bone calcium but also of its protein matrix. Its causes are multifactorial but include ageing, the menopause, immobility, calcium deficiency, hypogonadism, etc. It is diagnosed radiologically and by bone density measurement. It may be reduced by sex hormone supplements, Ca^{2+} and vitamin D, and exercise, and treated by bisphosphonates.

Hypercalcaemia

Any elevation of serum Ca^{2+} should be investigated thoroughly. Although, in severe cases it may be important to reduce very high levels of Ca^{2+} as soon as possible, the main challenge to the doctor is to distinguish early between malignant causes e.g. secondary malignancy in bone or PTH secreting tumours, and more easily curable 'benign' causes such as hyperparathyroidism, vitamin D intoxication, sarcoid, etc. Primary hyperparathyroidism is associated with elevated PTH levels whereas these are suppressed in secondary malignancy from non PTH secreting tumours.

Mild hypercalcaemia i.e. <3.0 mmol/l is usually asymptomatic, often due to hyperparathyroidism, and may require no active intervention other than monitoring. More severe hypercalcaemia, i.e. >3.0 mmol/l is usually symptomatic in proportion to the magnitude and rapidity of rise of the serum Ca^{2+} . Symptoms include polyuria (due to inhibition of ADH action on the renal tubule), weakness, depression, drowsiness, lethargy, and even coma. It also causes constipation, nausea, vomiting, anorexia and peptic ulcer. Prolonged hypercalcaemia may also cause renal stones and nephrocalcinosis causing chronic kidney disease (CKD). Fluid loss from polyuria may cause prerenal AKI and a further rise in serum Ca^{2+} .

Treatment depends on the severity of the condition, but consists firstly of intravenous saline, which may of itself be sufficient to reduce the serum Ca^{2+} . A loop diuretic may be added and, in severe cases, a bisphosphonate given in at least 500 ml of fluid over 4 hours to avoid nephrotoxicity. Etidronate, 7.5 mg/kg can be given daily in this fashion for 3–7 days with careful monitoring of the serum Ca^{2+} to avoid overshoot hypocalcaemia. Description of the use of other drugs, long-term treatment, and the indications for surgery may be found in appropriate reference works.

Hypocalcaemia

This is usually caused by vitamin D deficiency or hypoparathyroidism, but there are other causes such as chronic kidney disease and acute pancreatitis. It can also be secondary to hypomagnesaemia, which inhibits PTH secretion; so in all cases of hypocalcaemia, the serum Mg^{2+} should also be measured. Falsely low concentrations of total serum Ca^{2+} due to hypoalbuminaemia should be excluded (see above).

Symptoms include neuromuscular irritability causing paraesthesiae, tetany and convulsions. A prolonged QT interval on the ECG may progress to ventricular fibrillation or heart block.

Treatment depends on severity and cause, but may involve vitamin D replacement in the form of 1- α cholecalciferol and/or calcium supplements by the oral or intravenous routes.

Magnesium (Mg²⁺)

This is distributed mainly in bone (500–600mmol) and the ICF (500–850 mmol). Only 12–20 mmol are in the ECF at any given time, at a concentration of 0.7–1.2 mmol/l. It is an important component of many enzyme systems and helps maintain cell membrane stability. The following facts are important to remember.

- Mg²⁺ like Ca²⁺ is bound to albumin and a low serum level should be interpreted in the light of the prevailing albumin concentration
- Mg²⁺ concentration in gastrointestinal fluid varies according to the distance along the intestine. In upper small bowel fluid it is only present at 1 mmol/l, whereas in the distal small bowel it rises to higher concentrations. Significant hypomagnesaemia is therefore more likely to occur from chronic diarrhoea or from distal stomas or fistulae rather than from more proximal GI losses. GI losses are the most common cause of hypomagnesaemia in clinical practice.
- Hypomagnesaemia causes blood PTH levels to fall, with secondary hypocalcaemia. In all cases of hypocalcaemia therefore, the serum Mg²⁺ should be measured. Replacement of Mg²⁺ deficits restores PTH and hence Ca²⁺ levels to normal.
- Overt symptoms of hypomagnesaemia, with neuromuscular irritability, convulsions, and arrhythmias are not usually apparent until the serum Mg²⁺ falls below 0.4 mmol/l, although with milder degrees of hypomagnesaemia patients may experience improved well-being with adequate replacement, suggesting that even mild hypomagnesaemia may cause sub-clinical symptoms.

■ In mild cases of hypomagnesaemia, oral replacement may be sufficient, using magnesium oxide or glycerophosphate. However Mg^{2+} salts are not well absorbed, and in more severe cases it may be necessary to give as much as 160 mmol of $MgSO_4$ intravenously in saline over 48 hours to restore normal concentrations. In patients undergoing intravenous feeding for gastrointestinal failure, daily requirements are 8–12 mmol. An alternative method of replacement, which we have found extremely effective in restoring and maintaining Mg^{2+} levels, as well as replacing salt and water losses, is to give $MgSO_4$ in 0.9% saline subcutaneously (hypodermoclysis) at a concentration of 6–12 mmol/l in up to 2 litres over 4–6 hours every day. This is particularly useful in short bowel syndrome or inflammatory bowel disease and can readily be administered at home by patients or their carers.

Phosphate (PO_4^{2-})

This is an important constituent of food, the normal intake being 800–1400 mg/day. Most is in the ICF, and the normal serum concentration lies between 0.89 and 1.44 mmol/l. Severe hypophosphataemia (<0.32 mmol/l) such as may occur acutely in the refeeding syndrome (Chapter 12) or chronically in diseases of bone and mineral metabolism, risks symptoms of myopathy, dysphagia, ileus, respiratory failure, impaired cardiac contractility and encephalopathy. Severe cases may necessitate cautious intravenous administration of 300–500 ml of Phosphate Polyfusor (Fresenius Kabi, 100 mmol PO_4^{2-} , 19 mmol K^+ and 162 mmol Na^+ /l) or 30–50 mmol of PO_4^{2-} in 1 litre 0.9% saline over 6–12 hours with frequent monitoring of serum PO_4^{2-} and other electrolytes. Excessive or too rapid intravenous administration risks precipitating acute hypocalcaemia and deposition of Ca^{2+} in soft tissues. Less severe cases can be treated orally with 1 g/day phosphate (e.g. Phosphate-Sandoz) replacement.

12. Refeeding Syndrome

Introduction

This is an important condition of insidious onset, which may be lethal or cause serious morbidity. All patients suffering from weight loss or a period of starvation are potentially liable to develop this condition if given large amounts of nutrients, particularly carbohydrate, too rapidly by any route be it oral, enteral or intravenous. The greater the degree of malnutrition or length of starvation, the greater the risk. Even dextrose containing solutions may precipitate it, if administered in large amounts over long periods.

The condition has several components, which may occur separately or in combination. These are hypokalaemia, hypophosphataemia, oedema, hypomagnesaemia, and acute thiamine deficiency causing irreversible brain damage from Wernicke's encephalopathy. It is important to identify patients at risk and take prophylactic measures, rather than waiting until the condition has developed and then treating it.

Hypokalaemia <3.5 mmol/l: (K normal range 3.5-5.2 mmol/l)

Potassium reserves may be already reduced in patients suffering from malnutrition, but carbohydrate administration in any patient excites insulin secretion and drives K^+ from the ECF to the ICF. Particularly in those with diminished K^+ reserves, this may precipitate a sufficient degree of hypokalaemia to cause muscle weakness and/or cardiac arrhythmias. Any patient at risk or who is receiving dextrose containing solutions for prolonged periods should be receiving K^+ supplements and having their serum K^+ measured at the outset and regularly monitored.

Hypophosphataemia <0.7 mmol/l: (normal range 0.74–1.55 mmol/l)

Exactly the same considerations apply as for hypokalaemia. Since glucose taken up by cells requires phosphorylation, carbohydrate administration may precipitate hypophosphataemia. This has been reported in patients receiving intravenous dextrose solutions for several days and can result in decreased respiratory, cardiovascular and neuromuscular function. Symptoms include paraesthesiae, muscular weakness and confusion, sometimes progressing to convulsions and coma. The daily requirement for phosphate is about 20 mmol daily and prevention of hypophosphataemia can usually be achieved by giving 10 mmol of phosphate for every 1000 kcal that the patient receives. Remember 1 litre of 5% dextrose contains 50 g of carbohydrate with an approximate energy value of 200 kcal.

Oedema due to salt and water retention

Malnutrition, like the response to injury, is associated with a reduced capacity to excrete a salt and water load: hence 'famine oedema'. Intake of salt and water in such patients should therefore be restricted to that which maintains zero balance. This should be monitored by daily weighing and serum biochemistry. In a small thin patient for example, fluid intake for maintenance may be as little as 1 litre per day.

Thiamine deficiency

Alcoholic and severely malnourished patients are particularly liable to this complication as they already have low thiamine reserves. Since this is consumed as a cofactor in carbohydrate metabolism, refeeding particularly with carbohydrate may precipitate symptoms of thiamine deficiency including confusion, cerebellar signs with nystagmus, and peripheral neuropathy. These are irreversible once established so that identification of patients at risk and the giving of prophylactic treatment are vital. This latter may be achieved by giving 200 mg of thiamine intravenously at the start, followed by 300 mg daily by mouth or 100 mg intravenously. Thiamine deficiency may also present as wet beri-beri with heart failure.

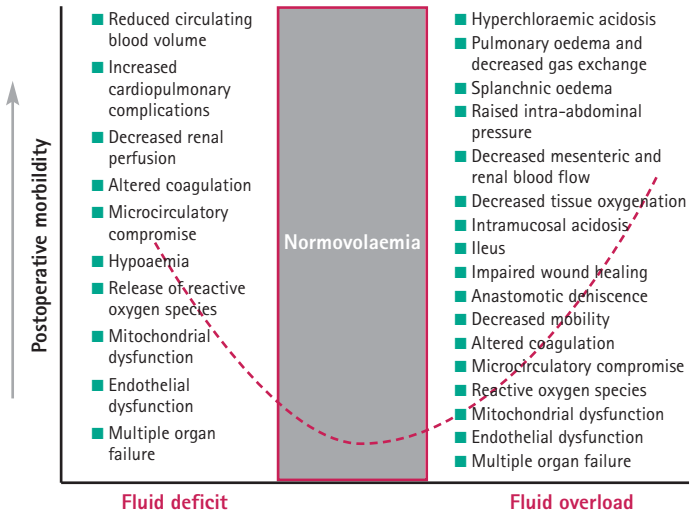
*Hypomagnesaemia, mild 0.5–0.7 mmol/l, severe <0.4 mmol/l:
(normal range 0.7–1.0 mmol/l)*

Magnesium, being involved in the formation of ATP is taken up by cells during refeeding. Deficiency leads to muscle weakness, may cause cardiac arrhythmias, and may cause hypocalcaemia by reducing parathormone levels. It is not necessary in most cases to give prophylaxis except in those cases with prior Mg^{2+} deficiency such as those with short bowel syndrome. Monitoring Mg^{2+} concentrations in patients at risk and giving supplements if levels fall below 0.7 mmol/l is usually sufficient. Daily requirements are 0.2 mmol/kg/d intravenously or 0.4 mmol/kg/d orally. If Mg^{2+} concentrations fall below 0.5 mmol/l then give 24 mmol $MgSO_4$ iv over 24 hours.

13. Fluid Therapy and Outcome

Intravenous fluid therapy is an integral component of perioperative care, but its practice has often been based on dogma rather than evidence, and patients have frequently received either too much or too little fluid. There is a relatively narrow margin of safety for perioperative fluid therapy and either too much or too little fluid and electrolyte (particularly sodium chloride) can have a negative effect on physiological processes, and be detrimental to outcome (Fig. 11). The goal of perioperative intravenous fluid therapy is, therefore, to maintain tissue perfusion and cellular oxygen delivery, while at the same time keeping the patient in a state of as near zero fluid and electrolyte balance as possible.

Figure 11: The dose-response curve for fluid therapy showing the ill effects of imbalance. (With permission from: Varadhan KK, Lobo DN. Perioperative fluid management in enhanced recovery. In: Francis N, et al (eds) Manual of Fast Track Recovery for Colorectal Surgery. Springer, London, 2012)



Prolonged periods of preoperative fasting cause patients to reach the anaesthetic room in a state of fluid depletion, which may be further compounded by indiscriminate bowel preparation, another practice that has not been shown to have a positive effect on surgical outcome. Current anaesthetic recommendations that allow patients to drink clear fluids up to 2 h prior to the induction of anaesthesia prevents preoperative fluid depletion and do not increase aspiration-related complications. On the other hand, the practice of prescribing large amounts of salt containing fluids in the perioperative period causes salt and water overload with adverse effects on surgical outcome.

Although the daily maintenance requirements for sodium and water are estimated at 1 mmol/kg and 25–35 ml/kg to support the integrity of the extracellular fluid volume, it has not been unusual for patients to receive in excess of 5 L water and 700 mmol sodium (and chloride)/day in the early postoperative period. In evolutionary terms, the metabolic response to trauma involves salt and water retention in order to preserve intravascular volume. However, when large volumes of salt containing fluids are administered, most of the excess accumulates in the extravascular compartment and causes oedema, which is detrimental to surgical outcome.

Most of the retained fluid after such infusions accumulates in the interstitial compartment, leading to manifest oedema if overload exceeds 2–3 L. In the face of acute illness, injury, or surgery, and also of severe malnutrition, the capacity to excrete a salt and water load is further impaired, only returning to normal during convalescence. An overload of 0.9% saline in such cases can cause hyperosmolar states, hyperchloraemic acidosis, decreased renal blood flow and glomerular filtration rate, which in turn exacerbates sodium retention. Oedema impairs pulmonary gas exchange and tissue oxygenation, and leads to an increase in tissue pressure in organs such as the kidney which are surrounded by a non-expandible capsule, thereby compromising

microvascular perfusion, increasing arterio-venous shunting and reducing lymphatic drainage, all of which facilitate further oedema formation. Fluid accumulation in the lungs also increases the risk of pneumonia. Removal of excess alveolar fluid is achieved by active sodium transport and the gradient between the hydrostatic and colloid osmotic pressures. Active sodium transport is affected by fluid administration and by the release of proinflammatory cytokines, both of which occur perioperatively. Acidosis impairs cardiac contractility, reduces responsiveness to inotropes, decreases renal perfusion and can be lethal in combination with hypothermia and coagulopathy. Hyperchloraemic acidosis, as a result of saline infusions has been shown to reduce gastric blood flow and decrease gastric intramucosal pH in elderly surgical patients, and both respiratory and metabolic acidosis have been associated with impaired gastric motility. Just as fluid overload causes peripheral oedema, it may also cause splanchnic oedema resulting in increased abdominal pressure, ascites and even the abdominal compartment syndrome. Consequently, this may lead to a decrease in mesenteric blood flow and a further exacerbation of the process, leading to ileus, delayed recovery of gastrointestinal function, increased gut permeability, intestinal failure and even anastomotic dehiscence. Fluid excess may also impair postoperative mobility and increase the risk of deep vein thrombosis, nausea, vomiting, abdominal pain, hyperventilation, headaches, thirst, confusion and diplopia. The literature suggests that, for most purposes, a balanced electrolyte solution is superior to 0.9% saline and a comprehensive review of the use of 0.9% saline for resuscitation has recommended that its routine use in massive fluid resuscitation should be discouraged.

On the other hand, true fluid restriction resulting in underhydration can be equally detrimental by causing decreased venous return and cardiac output, diminished tissue perfusion and oxygen delivery, increased blood viscosity, decreased saliva production with a predis-

position to postoperative parotitis, and an increase in viscosity of pulmonary mucus resulting in mucous plug formation and atelectasis. Induction of anaesthesia in patients with a fluid deficit further reduces the effective circulatory volume by decreasing sympathetic tone. Inadequate fluid resuscitation and decreased tissue perfusion can lead to gastrointestinal mucosal acidosis and poorer outcome.

A recent meta-analysis of patients undergoing major abdominal surgery has shown that patients managed in a state of fluid and electrolyte balance had a 59% reduction in risk of developing complications when compared with patients managed in a state of fluid imbalance (deficit or excess). There was also a 3.4 day reduction in hospital stay in the fluid balance group. Moreover, maximum weight gain was seen in the studies in which the standard group received an excessive amount of fluid. It appears that patients need to gain at least 2.5–3 kg in weight, as a result of salt and water overload, in the postoperative period in order to have a worse outcome than those maintained in a state of zero fluid balance. Avoidance of fluid overload, rather than fluid restriction seems to be the key to better postoperative outcome.

Moore and Shires wrote in 1967, "The objective of care is restoration to normal physiology and normal function of organs, with a normal blood volume, functional body water and electrolytes. This can never be achieved by inundation." This recommendation has never been bettered.

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Basic Concepts of Fluid and Electrolyte Therapy

