given by intravenous infusion but must be administered slowly to avoid causing hyperkalaemia and associated cardiac toxicity; plasma-potassium concentrations should be closely monitored and ECG monitoring may be required. The choice of salt for oral potassium replacement depends on co-existing acid–base and electrolyte disturbances. Potassium chloride is generally the drug of choice for the treatment of hypokalaemia in patients with metabolic alkalosis with hypochloraemia, whereas a salt such as the bicarbonate may be preferred in patients with hyperchloraemic acidosis as in some renal tubular acidoses. Hypokalaemia secondary to hypomagnesaemia requires magnesium replacement therapy.

References.

1. Halperin ML, Kamel KS. Potassium. *Lancet* 1998; **352:** 135–40.
2. Gennari FJ. Hypokalemia. *N Engl J Med* 1998; **339:** 451–8.
3. Cohn JN, *et al.* New guidelines for potassium replacement in clinical practice: a contemporary review by the National Council on Potassium in Clinical Practice. *Arch Intern Med* 2000; **160:** 2429–36.

BARTTER'S SYNDROME. Bartter's syndrome is a set of closely related disorders thought to result from inherited defects in ion transport in various sections of the renal tubule.[1,2] Patients exhibit hyperplasia of the juxtaglomerular cells, hypokalaemia and metabolic alkalosis, and excess aldosterone, prostaglandin, and renin production. Symptoms are primarily those of the hypokalaemia, including muscle weakness; polyuria and enuresis, and growth retardation in children, can occur. In contrast to other hyperreninaemic states, patients do not have hypertension or oedema.

Treatment rarely completely corrects hypokalaemia. Potassium supplementation may be given, while a cyclo-oxygenase inhibitor such as indometacin, or an ACE inhibitor such as captopril, can produce benefit.[2] Spironolactone and propranolol have also been tried and magnesium salts may be given if there is hypomagnesaemia.[2]

1. Guay-Woodford LM. Bartter syndrome: unraveling the pathophysiologic enigma. *Am J Med* 1998; **105:** 151–61.
2. Amirlak I, Dawson KP. Bartter syndrome: an overview. *Q J Med* 2000; **93:** 207–15.

DIURETIC-INDUCED HYPOKALAEMIA. Reduced potassium concentrations may result from the use of potassium-losing diuretics, particularly thiazides and loop diuretics. Clinically significant hypokalaemia is unlikely at the doses used in hypertension and the routine use of potassium supplements is no longer recommended. However, the concomitant use of a potassium-sparing diuretic such as amiloride or, less usually, a potassium supplement, may be necessary in patients at risk of hypokalaemia (see also Hydrochlorothiazide, Effects on Electrolyte Balance, p.1308).

HYPOKALAEMIC PERIODIC PARALYSIS. Hypokalaemic periodic paralysis is an inherited disorder in which episodes of hypokalaemia with muscle weakness or paralysis appear to be associated with a shift in potassium from the extracellular to the intracellular fluid. Acute attacks are treated with potassium, given orally or intravenously. Prophylaxis with acetazolamide has been found to reduce the frequency and severity of attacks.[1,2]

1. Ahlawat SK, Sachdev A. Hypokalaemic paralysis. *Postgrad Med J* 1999; **75:** 193–7.
2. Bond EF. Channelopathies: potassium-related periodic paralyses and similar disorders. *AACN Clin Issues* 2000; **11:** 261–70.

Sodium Homoeostasis

Sodium is the principal cation in the extracellular fluid and is responsible for the maintenance of the extracellular fluid volume and osmolality. In addition, sodium is also involved in nerve conduction, muscle contraction, acid–base balance, and cell nutrient uptake. A usual plasma concentration of sodium would be expected to be within 135 to 145 mmol/litre.

Sodium homoeostasis is complex and closely associated with fluid balance. The osmolality and volume of the extracellular fluid are tightly regulated. Small changes in osmolality (plasma-sodium concentrations) are corrected by alteration of extracellular volume. This balance of plasma osmolality is achieved by the secretion or suppression of antidiuretic hormone (ADH; vasopressin), which primarily controls water excretion by the kidney. A tendency towards hyponatraemia suppresses ADH secretion and promotes renal loss of water; an increase in ADH secretion increases water reabsorption by the renal distal tubules. Changes in extracellular volume will also affect ADH release independently of osmolality. In addition, changes in extracellular volume result in modulation of the renal excretion of sodium.

Total body sodium content is regulated by renal sodium excretion, which can vary widely depending on dietary intake. Various mechanisms are involved in controlling renal sodium excretion including the renin-angiotensin system, glomerular filtration rate, and natriuretic factors. A reduction in extracellular fluid volume leads to the production of angiotensin II which stimulates the secretion of aldosterone. Aldosterone promotes the reabsorption of sodium ions by the distal tubules. There may be significant effects on sodium homoeostasis if adrenal insufficiency or mineralocorticoid excess disturb this mechanism.

Hypernatraemia. Hypernatraemia is an abnormal rise in the plasma-sodium concentration with a simultaneous rise in plasma osmolality. It is generally associated with volume depletion when water intake is less than water losses through renal or extrarenal routes. The causes include impaired thirst, as in coma or essential hypernatraemia, osmotic diuresis (solute diuresis), as in diabetic ketoacidosis (see Diabetic Emergencies, p.435) or after drugs such as mannitol, and excessive water losses, either from the kidney, as in diabetes insipidus (p.2179), or extrarenally, for example because of excessive sweating or diarrhoea.

Hypernatraemia can also occur after excessive oral sodium intake (but this is uncommon) and after inappropriate use of intravenous sodium chloride.

The clinical manifestations of hypernatraemia are caused by the effect of increased plasma osmolality on the brain and include somnolence, confusion, respiratory paralysis, and coma. CNS symptoms are more severe when hypernatraemia develops rapidly. If there is volume depletion, other symptoms such as hypotension, tachycardia, and symptoms of circulatory insufficiency may occur as well. A high volume of dilute urine is seen in patients with abnormal renal water conservation, whereas a low volume of concentrated urine is expected in patients with impaired thirst or excessive extrarenal water loss.

Treatment of hypernatraemia usually requires water replacement, and drinking water may be sufficient for some patients. In more severe conditions, glucose 5% may be given by slow intravenous infusion. Alternatively, some recommend the use of sodium chloride 0.9% if volume depletion is severe. Care is required, as too rapid correction can induce cerebral oedema, particularly in chronic conditions.

If the total body sodium is too high, loop diuretics may be used to increase sodium excretion, with fluid losses being replaced by an infusion of glucose 5% and potassium chloride. It has also been suggested that dialysis may be necessary if there is significant renal impairment, if the patient is moribund, or if the serum-sodium concentration is greater than 200 mmol/litre.

References.

1. Adrogué HJ, Madias NE. Hypernatremia. *N Engl J Med* 2000; **342:** 1493–9.
2. Kang S-K, *et al.* Pathogenesis and treatment of hypernatremia. *Nephron* 2002; **92** (suppl): 14–17.
3. Reynolds RM, *et al.* Disorders of sodium balance. *BMJ* 2006; **332:** 702–5.

Hyponatraemia. Hyponatraemia, an abnormal fall in the plasma-sodium concentration, usually with a simultaneous fall in the plasma osmolality, is not uncommon, and may occur in diseases as diverse as heart failure, cirrhosis, adrenocortical insufficiency, hyperglycaemia, and AIDS.

The kidney is able to conserve sodium, and sodium depletion due to low salt intake is rare. Sodium depletion may occur if there are abnormal losses, either from the gut as a consequence of repeated diarrhoea and/or vomiting or from the kidney, for example, due to various renal disorders or the overuse of diuretics (see under Hydrochlorothiazide, Effects on Electrolyte Balance, p.1308).

The most common cause of hyponatraemia is dilution. This may result from excessive fluid intake, for example the ingestion of large volumes of water in patients with primary polydipsia (psychogenic polydipsia). More often, however, it is a result of reduced water excretion, as in renal impairment or the syndrome of inappropriate secretion of antidiuretic hormone (SIADH—p.2182). Postoperative hyponatraemia is a frequent complication which can be exacerbated by the inappropriate intravenous use of hypotonic,[1] or even isotonic,[2] fluids.

Hyponatraemia due to sodium depletion in the presence of volume contraction may cause orthostatic hypotension and circulatory insufficiency. Dilutional hyponatraemia can be asymptomatic but headache, confusion, nausea, vomiting, somnolence, and weakness may occur. If severe, cerebral oedema may lead to respiratory arrest, convulsions, and coma. CNS symptoms are more common when the condition is acute.

Therapy is guided by the rate of development and degree of hyponatraemia, accompanying symptoms, and the state of water balance, and should also take into account the underlying cause. Mild asymptomatic hyponatraemia does not usually require specific therapy. Chronic mild to moderate sodium depletion, such as occurs in salt-losing bowel or renal disease, may be treated with oral sodium chloride supplements while ensuring adequate fluid intake.

When there is substantial volume depletion, volume replacement is necessary and intravenous sodium chloride 0.9% is often used.[3-5]

Chronic dilutional hyponatraemia, which is often asymptomatic, can generally be managed by correcting the underlying disease; water restriction may also be necessary and drugs that interfere with the action of ADH such as demeclocycline or lithium carbonate may be useful in SIADH.[3-6] Furosemide plus oral sodium chloride supplements have also been used.[7]

Acute symptomatic hyponatraemia (water intoxication) is generally associated with plasma-sodium concentrations below 120 mmol/litre and requires more aggressive therapy. This involves giving hypertonic or isotonic sodium chloride intravenously, often with a loop diuretic such as furosemide, especially if fluid overload is likely to be a problem.[4,6,7] The aim is to render the patient asymptomatic, with a plasma-sodium concentration of 120 to 130 mmol/litre; the plasma-sodium concentration should not be corrected to normal values nor should hypernatraemia be allowed to develop.[1,6,7] Plasma-sodium concentrations and the total body-water volume should be monitored throughout.

A rare neurological syndrome known as central pontine myelinolysis (osmotic demyelination) has been associated with the over-rapid correction of symptomatic hyponatraemia, particularly if the condition is well established. However, there is no consensus about the optimal administration of intravenous sodium chloride, and a number of regimens have been suggested. Generally, it has been recommended that the rate of correction of plasma-sodium should be 0.5 to 1 mmol/litre per hour, and not exceeding 2 mmol/litre per hour; maximum corrections have included 8 mmol/litre per 24 hours,[7] 12 mmol/litre per 24 hours or 18 mmol/litre over the first 48 hours,[6] and 20 mmol/litre in the first 48 hours.[1] Some[1,5] have given more specific recommendations depending on the severity of symptoms, suggesting that patients with severe symptoms, such as seizures, respiratory arrest, or neurogenic pulmonary oedema, require rapid correction in the first few hours, aiming for an initial increase in plasma-sodium of 2 to 4 mmol/litre, followed by a continuous infusion.

More recently, the vasopressin receptor antagonist conivaptan has become available for the management of euvolaemic and hypervolaemic hyponatraemia. It must be given intravenously, and other vasopressin receptor antagonists that are orally active are under investigation.[5,6]

1. Moritz ML, Ayus JC. Hospital-acquired hyponatremia—why are hypotonic parenteral fluids still being used? *Nat Clin Pract Nephrol* 2007; **3:** 374–82.
2. Steele A, *et al.* Postoperative hyponatremia despite near-isotonic saline infusion: a phenomenon of desalination. *Ann Intern Med* 1997; **126:** 20–5.
3. Yeates KE, *et al.* Salt and water: a simple approach to hyponatremia. *CMAJ* 2004; **170:** 365–9.
4. Reynolds RM, *et al.* Disorders of sodium balance. *BMJ* 2006; **332:** 702–5.
5. Verbalis JG, *et al.* Hyponatremia treatment guidelines 2007: expert panel recommendations. *Am J Med* 2007; **120** (suppl 11A): S1–S21.
6. Cawley MJ. Hyponatremia: current treatment strategies and the role of vasopressin antagonists. *Ann Pharmacother* 2007; **41:** 840–50.
7. Adrogué HJ, Madias NE. Hyponatremia. *N Engl J Med* 2000; **342:** 1581–9.

Dialysis Solutions

Soluciones para diálisis.

Pharmacopoeias. In *Eur.* (see p.vii), which includes separate monographs for solutions for haemodialysis, haemofiltration and haemodiafiltration, and peritoneal dialysis.

Dialysis and Haemofiltration

Dialysis and filtration solutions are solutions of electrolytes formulated in concentrations similar to those of extracellular fluid or plasma. They always contain sodium and chloride and bicarbonate or a bicarbonate precursor. In addition, they often contain calcium and magnesium, and rarely potassium. Glucose may be added as an osmotic agent. These solutions allow the removal of water and metabolites and the replacement of electrolytes.

In *haemodialysis*, the exchange of ions between the solution and the patient's blood is made across a semipermeable membrane, primarily by diffusion. Excess fluid is removed by ultrafiltration achieved by a pressure gradient. Membranes are either derived from cellulose (e.g. cuprophane) or are synthetic. Bicarbonate rather than a bicarbonate precursor is increasingly preferred as the bicarbonate source in haemodialysis since the problems of precipitation of calcium and magnesium have been overcome by changes in dialysis technique. Acetate is still used in some dialysers, but is thought to have vasodilator and cardiodepressant actions, and may not be converted to bicarbonate fast enough for high-flux haemodialysis or in patients with liver disease. Haemodialysis solutions are provided in a sterile concentrated form for dilution with water before use; this water need not be sterile.

In *peritoneal dialysis*, the exchange is made across the membranes of the peritoneal cavity primarily by diffusion. Excess fluid is removed by ultrafiltration achieved by the use of osmotic agents such as glucose. The problems of calcium bicarbonate precipitation have not yet been overcome, and lactate is generally used as the bicarbonate precursor. Peritoneal dialysis solutions must be sterile and apyrogenic.

In *haemofiltration*, blood is filtered rather than dialysed. Metabolites are removed by convective transport, and excess water by hydrostatic ultrafiltration. Fluid and electrolytes are replaced by direct intravenous infusion. Most haemofiltration solutions use acetate or lactate as the bicarbonate source. Haemofiltration solutions must be sterile and apyrogenic.

Adverse Effects

Adverse effects occurring during *haemodialysis* include nausea, vomiting, hypotension, muscle cramps, and air embolus. Effects related to vascular access include infection, thrombosis, and haemorrhage. Adverse effects occurring during *haemofiltration* are similar to those for haemodialysis.

The most common adverse effects associated with *peritoneal dialysis* include peritonitis, hernias, hyperglycaemia, protein malnutrition, and catheter complications.

Long-term complications in dialysed patients, some of which may relate to renal failure itself, include haemodialysis-related amyloidosis, acquired cystic kidney disease, and accelerated atherosclerosis. Dialysis dementia is a special hazard of aluminium overload. Long-term peritoneal dialysis results in progressive structural changes to the peritoneal membrane ultimately resulting in dialysis failure.

◊ References.

1. Himmelfarb J. Hemodialysis complications. *Am J Kidney Dis* 2005; **45:** 1122–31.

Aluminium overload. Accumulation of aluminium in patients on dialysis may result in dialysis dementia, anaemia, and aluminium-related bone disease (see also p.2254). Sources of aluminium include the water used for preparation of dialysis fluids and aluminium-containing phosphate binders used in treating renal osteodystrophy (p.1086). It is therefore important that water used for the preparation of dialysis fluids has a low aluminium concentration; Ph. Eur. 6.2 specifies a limit for aluminium of 10 micrograms/litre. Non-aluminium-containing phosphate binders such as calcium acetate or calcium carbonate may be preferred for long-term therapy. Aluminium overload in patients on dialysis has been treated with desferrioxamine (p.1441).

Copper toxicity. Liver and haematological toxicity has occurred as a result of absorption of copper from dialysis fluids (see Adverse Effects of Copper, p.1935).

Haemodialysis-induced cramp. Muscle cramps (see Muscle Spasms, p.1887) commonly occur during haemodialysis procedures and between sessions. Cramping usually affects the lower extremities, causing severe pain, and is a common reason for avoiding or stopping haemodialysis. The aetiology is not clear but possibly related to hypovolaemia, hypotension, changes in plasma osmolality, and hyponatraemia.[1]

Non-pharmacological measures to treat cramp during haemodialysis include the local application of moist heat and massage, and stretching the affected muscle. Hypotension should be corrected, by slowing or stopping ultrafiltration, and possibly giving isotonic or hypertonic sodium chloride infusion.[1] Adjustment of the dialysate sodium concentration during dialysis, or the use of a dialysate containing bicarbonate instead of one containing acetate, are other measures that may be used to reduce hypotension and cramp. Midodrine has also been recommended for the management of hypotension.[2] Hypertonic solutions of sodium chloride or glucose may be used to raise plasma osmolality; mannitol has also been used but may accumulate in the extracellular space.[1]

Quinine has been widely used for the prevention of haemodialysis-induced cramp, but it can cause serious adverse effects and such use has been discouraged.[1] Other treatments that have been tried as prophylaxis include carnitine, creatine, and vitamins C and E. However, information on these is limited and data on long-term efficacy and safety are lacking.[1] There is also limited evidence that a traditional herbal medicine, shao-yao-gan-cao-tang (shakuyaku-kanzo-to), comprising extracts of peony and liquorice roots, may be of benefit for both prevention and treatment of haemodialysis-induced cramp.[1]

1. Kobrin SM, Berns JS. Quinine—a tonic too bitter for hemodialysis-associated muscle cramps? *Semin Dial* 2007; **20:** 396–401.
2. National Kidney Foundation. Maximizing patient adherence to the hemodialysis prescription. In: NKF-K/DOQI clinical practice guidelines for hemodialysis adequacy: update 2000. Available at: http://www.kidney.org/professionals/kdoqi/guidelines_updates/doqiuphd_vi.html#15 (accessed 09/11/07)

Hypersensitivity. For anaphylactic reactions associated with the use of ethylene oxide for the disinfection of dialysis equipment, see p.1643.

Infections. Patients undergoing haemodialysis are at risk of infections from microbial contamination of dialysis fluid, and from inadequate care of vascular access sites. Maximum microbial counts and limits for endotoxins have been specified for water used in dialysis fluids. Bicarbonate-based dialysis solutions are more susceptible to microbial growth than acetate-based solutions.

Peritonitis is common in patients receiving peritoneal dialysis. The risk of infection may be minimised by using disconnect systems, good aseptic technique, and by good care of catheters. Treatment of bacterial peritonitis requires intraperitoneal antibacterials, which are usually added to the dialysis fluid (see p.184).

Dialysis equipment should be regularly disinfected with agents such as formaldehyde (p.1645) or ethylene oxide (p.1643), but for mention of ethylene oxide anaphylactoid reactions, see p.1643.

Metabolic complications. The high concentrations of glucose in peritoneal dialysis solutions required to form an osmotic gradient can lead to weight gain, hyperglycaemia, hyperlipidaemia, and increased protein loss. Alternative osmotic agents such as icodextrin (p.1937) can be used, and amino acid-based solutions are also available.

References.

1. Burkart J. Metabolic consequences of peritoneal dialysis. *Semin Dial* 2004; **17:** 498–504.

Precautions

Peritoneal dialysis is not appropriate for patients with abdominal sepsis, previous abdominal surgery, or severe inflammatory bowel disease.

Haemodialysis should be used with caution in patients with unstable cardiovascular disease or active bleeding. During haemodialysis and haemofiltration, heparin (see Extracorporeal Circulation, p.1304) or epoprostenol (Uses, p.1280) are required to prevent clotting of the blood in the extracorporeal circuit.

Dialysis solutions should be warmed to body temperature with dry heat because wet heat carries a risk of microbial contamination.

Interactions

The effects of dialysis and filtration procedures on drug concentrations in the body can be complex. More drug may be removed by one dialysis technique than another. In general, drugs of low molecular weight, high water solubility, low volume of distribution, low protein binding, and high renal clearance are most extensively removed by dialysis. For example, aminoglycosides are extensively removed by dialysis procedures, and extra doses may be needed to replace losses. Specific drug dosage adjustments for dialysis procedures may be used where these are known. For drugs where the effect of dialysis is unknown, it is usual to give maintenance doses after dialysis. Dialysis has been used to remove some drugs in the treatment of overdosage and poisoning (see below).

Dialysis-induced changes in fluids and electrolytes have the potential to alter the effects of some drugs. For example, hypokalaemia predisposes to digoxin toxicity.

In patients undergoing peritoneal dialysis, drugs such as insulin and antibacterials may be added to the dialysis fluid. Consideration should be given to the possibility of adsorption of drugs onto the PVC bags.

◊ References.

1. Aronson JK. The principles of prescribing in renal failure. *Prescribers' J* 1992; **32:** 220–31.
2. Cotterill S. Antimicrobial prescribing in patients on haemofiltration. *J Antimicrob Chemother* 1995; **36:** 773–80.
3. Aronoff GR, *et al. Drug prescribing in renal failure: dosing guidelines for adults*. 4th ed. Philadelphia: American College of Physicians, 1999.

Uses and Administration

Dialysis and filtration procedures are used in renal failure to correct electrolyte imbalance, correct fluid overload, and remove metabolites. They also have a limited role in the treatment of overdosage and poisoning. The two main techniques are haemodialysis and peritoneal dialysis; haemofiltration is used less frequently. The choice of technique will depend on the condition to be treated, the clinical state of the patient, patient preference, and availability.

Haemodialysis is more efficient than peritoneal dialysis at clearing small molecules such as urea, whereas peritoneal dialysis may be better at clearing larger molecules. Haemodialysis is considered to be less physiological as it alternates periods of high clearance with periods of no clearance.

Haemodialysis is usually performed intermittently (often 3 times a week); a typical session takes 3 to 5 hours. More recently high-flux dialysers have been developed which have reduced the time required for dialysis sessions.

Peritoneal dialysis may be performed continuously or intermittently. Continuous ambulatory peritoneal dialysis (CAPD) is the most commonly used technique. Patients remain mobile, except during exchanges, and can carry out the procedure themselves. There is always dialysis solution in the peritoneal cavity, and this is drained and replaced 3 to 5 times daily. Continuous cycle peritoneal dialysis (CCPD) is similar, except that exchanges are carried out automatically overnight, and patients do not have to carry out any exchanges during the day. Intermittent peritoneal dialysis (IPD) requires the patient to be connected to a dialysis machine for 12 to 24 hours 2 to 4 times a week. During this time, dialysis solution is pumped into and out of the peritoneal cavity, with a dwell time of about 10 to 20 minutes.

Haemofiltration is usually performed as a continuous technique and, as it is not portable, its principal use is in intensive care units. It may also be used intermittently as an adjunct to haemodialysis in patients with excess fluid weight gain. Continuous arteriovenous or venovenous haemodiafiltration (CAVHD or CVVHD) combines dialysis and filtration.

Assessing serum concentrations of urea or creatinine before the next dialysis session is not a good measure of the adequacy of the dialysis, so various other measures have been developed including the urea reduction ratio and urea kinetic modelling. The use of such measures is more established for haemodialysis than for peritoneal dialysis.

◊ References.

1. Zucchelli P, Santoro A. How to achieve optimal correction of acidosis in end-stage renal failure patients. *Blood Purif* 1995; **13:** 375–84.
2. Carlsen DB, Wild ST. Grams to milliequivalents: a concise guide to adjusting hemodialysate composition. *Adv Ren Replace Ther* 1996; **3:** 261–5.

3. Passlick-Deetjen J, Kirchgessner J. Bicarbonate: the alternative buffer for peritoneal dialysis. *Perit Dial Int* 1996; **16** (suppl 1): S109–S113.
4. Pastan S, Bailey J. Dialysis therapy. *N Engl J Med* 1998; **338:** 1428–37.
5. Ifudu O. Care of patients undergoing hemodialysis. *N Engl J Med* 1998; **339:** 1054–62.
6. Mallick NP, Gokal R. Haemodialysis. *Lancet* 1999; **353:** 737–42.
7. Gokal R, Mallick NP. Peritoneal dialysis. *Lancet* 1999; **353:** 823–8.
8. Fischbach M, *et al*. Hemodialysis in children: principles and practice. *Semin Nephrol* 2001; **21:** 470–9.
9. Schröder CH. The choice of dialysis solutions in pediatric chronic peritoneal dialysis: guidelines by an ad hoc European committee. *Perit Dial Int* 2001; **21:** 568–74.
10. Teehan GS, *et al*. Update on dialytic management of acute renal failure. *J Intensive Care Med* 2003; **18:** 130–8.
11. Locatelli F, *et al*. Optimal composition of the dialysate, with emphasis on its influence on blood pressure. *Nephrol Dial Transplant* 2004; **19:** 785–96.
12. Lameire N. Volume control in peritoneal dialysis patients: role of new dialysis solutions. *Blood Purif* 2004; **22:** 44–54.
13. Maduell F. Hemodiafiltration. *Hemodial Int* 2005; **9:** 47–55.
14. Nanovic L. Electrolytes and fluid management in hemodialysis and peritoneal dialysis. *Nutr Clin Pract* 2005; **20:** 192–201.
15. Saxena R. Peritoneal dialysis: a viable renal replacement therapy option. *Am J Med Sci* 2005; **330:** 36–47. Correction. *ibid*.; 110.
16. Ikizler TA, Schulman G. Hemodialysis: techniques and prescription. *Am J Kidney Dis* 2005; **46:** 976–81.

Acute renal failure. Acute renal failure is characterised by a rapid decline in kidney function, and has a variety of causes.[1-7] It is often classified by origin as *prerenal* (e.g. due to hypovolaemia such as that associated with shock, burns, or dehydration; congestive heart failure; or renal artery obstruction), *renal* (such as acute tubular necrosis or interstitial nephritis of various causes, including nephrotoxic drugs and infections), or *postrenal* (acute urinary tract obstruction). The prognosis depends on the underlying disease, which should be identified and treated if possible, but the mortality may still be as high as 60%, particularly after surgery or trauma and in patients who become oliguric. Management is essentially supportive in the hope that renal function will recover. Complications of acute renal failure include extracellular volume overload and hyponatraemia, hyperkalaemia, metabolic acidosis, hyperphosphataemia and hypocalcaemia. Those complications requiring urgent treatment, often including the use of dialysis, are severe hyperkalaemia (p.1669), pulmonary oedema, pericarditis, and severe metabolic acidosis (p.1667). The use of dialysis before clinical signs of uraemia is a matter of debate since it does not appear to hasten recovery *per se*,[1] but all save the shortest episodes of acute renal failure will require some form of renal replacement therapy with dialysis or filtration. Intermittent haemodialysis and peritoneal dialysis are both used, but the newer haemofiltration techniques have theoretical advantages in terms of volume control and cardiovascular stability, and are increasingly preferred.[2,8,9]

Numerous drugs have been tried in attempts to attenuate renal injury or hasten recovery in patients with acute tubular necrosis due to ischaemia or nephrotoxins.[1,5,10,11] These include drugs to increase renal blood flow (e.g. low-dose dopamine, atrial natriuretic peptide, or prostaglandins), drugs to increase urine flow and protect the epithelial cells (mannitol and loop diuretics, calcium-channel blockers), or the use of chelating agents or antidotes against specific nephrotoxins. Consistent clinical benefit has not, however, been shown.

Acute renal failure is reversible in about 95% of patients who survive the complications. A few patients who survive acute renal failure will require long-term dialysis or kidney transplantation (p.1813).

1. Brady HR, Singer GG. Acute renal failure. *Lancet* 1995; **346:** 1533–40.
2. Morgan AG. The management of acute renal failure. *Br J Hosp Med* 1996; **55:** 167–70.
3. Evans JHC. Acute renal failure in children. *Br J Hosp Med* 1994; **52:** 159–61.
4. Klahr S, Miller SB. Acute oliguria. *N Engl J Med* 1998; **338:** 671–5.
5. Dishart MK, Kellum JA. An evaluation of pharmacological strategies for the prevention and treatment of acute renal failure. *Drugs* 2000; **59:** 79–91.
6. Ashley C, Holt S. Acute renal failure. *Pharm J* 2001; **266:** 625–8.
7. Lameire N, *et al*. Acute renal failure. *Lancet* 2005; **365:** 417–30.
8. McCarthy JT. Renal replacement therapy in acute renal failure. *Curr Opin Nephrol Hypertens* 1996; **5:** 480–4.
9. Joy MS, *et al*. A primer on continuous renal replacement therapy for critically ill patients. *Ann Pharmacother* 1998; **32:** 362–75.
10. Albright RC. Acute renal failure: a practical update. *Mayo Clin Proc* 2001; **76:** 67–74.
11. Pruchnicki MC, Dasta JF. Acute renal failure in hospitalized patients: part II. *Ann Pharmacother* 2002; **36:** 1430–42.

Chronic renal failure. Chronic renal failure is the irreversible, usually progressive, loss of renal function that eventually results in end-stage renal disease (ESRD) and the need for renal replacement therapy (dialysis or renal transplantation). The rate of decline in renal function is generally constant for each patient and is usually monitored by measuring serum-creatinine concentrations as an indirect index of the glomerular filtration rate (GFR). In its early stages when the patient is asymptomatic, progressive loss of renal function is described as diminished renal reserve or chronic renal insufficiency. When the limits of renal reserve have been exceeded and symptoms become apparent, it is termed chronic renal failure or overt renal failure. When renal function is diminished to such an extent that life is no longer sustainable (GFR less than 5 mL/minute), the condition is termed ESRD or uraemia. Many diseases can lead to ESRD, the most common being diabetes (p.433), glomerulonephritis (p.1504), and hypertension (p.1171).

The management of patients with chronic renal failure prior to ESRD involves measures to conserve renal function and compensate for renal insufficiency. Methods to slow the progression of renal failure include the treatment of hypertension (p.1171), reduction of proteinuria, and the reduction of hyperlipidaemia (p.1169). ACE inhibitors (p.1199) or angiotensin II receptor antagonists (see Losartan, p.1328) are used for the reduction of proteinuria and the control of hypertension. Dietary protein restriction (see Renal Failure, p.1923) has also been used for control of proteinuria, but conclusive evidence for a renal protective effect is lacking. Anaemia (p.1063), hyperphosphataemia (p.1669), secondary hyperparathyroidism (p.1087), and renal osteodystrophy (p.1086) often require active treatment. Nephrotoxic drugs, including NSAIDs, should be avoided.

The choice between haemodialysis, peritoneal dialysis, and organ transplantation is considered, and the patient prepared, before it is actually required. In patients for whom transplantation is the preferred option, dialysis may still be required while waiting for a kidney. Kidney transplantation is discussed on p.1813. There are differences between countries in the choice of dialysis technique for patients with ESRD. For example, in-centre haemodialysis is used in about 80% of patients in the USA, whereas CAPD is used in over 50% of patients in the UK. Overall survival appears to be similar between the 2 techniques, but more patients on CAPD will eventually require a change to another dialysis method because of treatment failure.

Unlike renal transplant patients, dialysis patients still require replacement therapy with hormones that are usually produced by the kidney. Thus, recombinant erythropoietin and hydroxylated vitamin D analogues are commonly given.

References.

1. NIH. Morbidity and mortality of dialysis. *NIH Consens Statement* 1993; **11:** 1–33.
2. Friedman AL. Etiology, pathophysiology, diagnosis, and management of chronic renal failure in children. *Curr Opin Pediatr* 1996; **8:** 148–51.
3. Steinman TI. Kidney protection: how to prevent or delay chronic renal failure. *Geriatrics* 1996; **51:** 28–35.
4. Walker R. General management of end stage renal disease. *BMJ* 1997; **315:** 1429–32.
5. McCarthy JT. A practical approach to the management of patients with chronic renal failure. *Mayo Clin Proc* 1999; **74:** 269–73. Correction. *ibid*.; 538.
6. Morlidge C, Richards T. Managing chronic renal disease. *Pharm J* 2001; **266:** 655–7.
7. Currie A, O'Brien P. Renal replacement therapies. *Pharm J* 2001; **266:** 679–83.
8. Ruggenenti P, *et al*. Progression, remission, regression of chronic renal diseases. *Lancet* 2001; **357:** 1601–8.
9. Renal Association. *Treatment of adults and children with renal failure: standards and audit measures*. 3rd ed. London: Royal College of Physicians of London and the Renal Association, 2002. Also available at: http://www.renal.org/Standards/RenalStandards_2002b.pdf (accessed 26/04/05)
10. Taal MW. Slowing the progression of adult chronic kidney disease: therapeutic advances. *Drugs* 2004; **64:** 2273–89.
11. Meguid El Nahas A, Bello AK. Chronic kidney disease: the global challenge. *Lancet* 2005; **365:** 331–40.

Electrolyte disturbances. Haemodialysis with magnesium-free dialysis solution has been used to remove magnesium from the body in severe hypermagnesaemia (p.1668). Similarly, haemodialysis, and sometimes peritoneal dialysis, has been used in treating hypercalcaemia (p.1668), hyperkalaemia (p.1669), hypernatraemia (p.1670), and hyperphosphataemia (p.1669).

Overdosage and poisoning. Haemodialysis, or less often peritoneal dialysis, can be used to remove some substances from the body after overdosage or poisoning. Substances most readily removed have a low molecular weight, low volume of distribution, low protein binding, high water solubility, and high renal clearance. Examples of agents for which haemodialysis may have a role in the treatment of severe overdosage include alcohol (p.1626), ethylene glycol (p.2300), methyl alcohol (p.2024), lithium (p.403), and salicylates such as aspirin (p.20). Dialysis may be particularly important when poisoning with these agents is complicated by renal failure.

Preparations

Ph. Eur.: Solutions for Haemodialysis; Solutions for Haemofiltration and for Haemodiafiltration; Solutions for Peritoneal Dialysis.

Proprietary Preparations: some preparations are listed in Part 3.

Oral Rehydration Solutions

Soluciones de rehidratación oral.

Oral rehydration solutions have 4 main constituents:

- electrolytes—typically sodium chloride and potassium chloride
- a bicarbonate source to correct or prevent metabolic acidosis, such as sodium bicarbonate or sodium citrate
- water to replace fluid losses
- a carbohydrate source to maximise absorption of fluid and electrolytes—typically glucose, although cereal-based formulations may also be used.

They are most commonly available as oral powders (oral rehydration salts) that are reconstituted with water before use, but effervescent tablets and ready-to-use oral solutions are also available.

Adverse Effects

Vomiting can occur after taking oral rehydration solution, and may be an indication that it was given too quickly. If vomiting occurs, administration should be halted for 10 minutes then resumed in smaller, more frequent, amounts.

The risk of hypernatraemia or overhydration with oral rehydration solutions is low in patients with normal renal function. Overdosage of oral rehydration solutions in patients with renal impairment may lead to hypernatraemia and hyperkalaemia.

Precautions

Oral rehydration salts or effervescent tablets should be reconstituted only with water and at the volume stated. Fresh drinking water is generally appropriate, but freshly boiled and cooled water is preferred when the solution is for infants or when drinking water is not available. The solution should not be boiled after it is prepared. Other ingredients such as sugar should not be added. Unused solution should be stored in a refrigerator and discarded within 24 hours of preparation.

Oral rehydration solutions are not appropriate for patients with gastrointestinal obstruction, oliguric or anuric renal failure, or when parenteral rehydration therapy is indicated as in severe dehydration or intractable vomiting.

Uses and Administration

Oral rehydration solutions are used for oral replacement of electrolytes and fluids in patients with dehydration, particularly that associated with acute diarrhoea of various aetiologies (p.1694).

The dosage of oral rehydration solutions should be tailored to the individual based on body-weight and the stage and severity of the condition. The initial aim of treatment is to rehydrate the patient, and, subsequently, to maintain hydration by replacing any further losses due to continuing diarrhoea and vomiting and normal losses from respiration, sweating, and urination. Initial rehydration should be rapid, over 3 to 4 hours, unless the patient is hypernatraemic, in which case rehydration over 12 hours is appropriate.

For adults, a usual dose of 200 to 400 mL of oral rehydration solution for every loose motion has been suggested. The dosage for children is 200 mL for every loose motion, and for infants is 1 to 1.5 times their usual feed volume. Normal feeding can continue after the initial fluid deficit has been corrected. Breast feeding should continue between administrations of oral rehydration solution.

Sodium content and osmolarity. The original standard WHO oral rehydration solution contained 90 mmol/litre of sodium and 111 mmol/litre of glucose.[1-3] While it has been used safely and effectively,[4] it does not reduce the volume or duration of diarrhoea,[3] and solutions with reduced sodium content and osmolarity have been suggested to be more effective.[1,2] WHO and UNICEF now recommend a solution containing 75 mmol/litre of sodium and 75 mmol/litre of glucose, with a reduced osmolarity.[4] However, there have been concerns that the reduced sodium content of this formulation may increase the risk of hyponatraemia in patients with cholera,[3,5,6] and especially in adults.[4] WHO and UNICEF have stated that hyponatraemia may also occur with the standard WHO formulation, and that there is no evidence to suggest that this transient hyponatraemia has had significant adverse clinical consequences for cholera patients.[4] Solutions containing less sodium have been recommended in more developed countries: 60 mmol/litre in Europe,[7] and 45 to 90 mmol/litre in the USA.[8]