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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).

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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.

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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]

For discussion of modified formulations of oral rehydration solutions in the treatment of diarrhoea, including the use of cereal-based and low osmolarity preparations, see oral rehydration therapy under Diarrhoea, p.1694.

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Oral versus intravenous rehydration. Although intravenous rehydration is advised for patients with the most severe dehydration (see Diarrhoea, p.1694) it is also widely used in some countries in the management of less severe degrees of fluid loss.[1,2] However, a meta-analysis of 16 randomised controlled studies in children with gastroenteritis (5 of which included children with severe dehydration) found that oral or nasogastric rehydration with an appropriate rehydration solution was at least as effective as intravenous rehydration in terms of weight gain and intestinal losses, and was associated with a lower incidence of adverse effects and a reduced length of hospital stay.[3] The authors concluded that there was no evidence to support the ongoing use of intravenous rehydration in most cases of childhood gastroenteritis.

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Preparations

BP 2008: Oral Rehydration Salts;
USP 31: Oral Rehydration Salts;
WHO/UNICEF: Oral Rehydration Salts.

Proprietary Preparations: some preparations are listed in Part 3.

Bicarbonate

Bicarbonato.

Description. Bicarbonate is an alkalinising agent given as bicarbonate-containing salts (sodium or potassium bicarbonate) or bicarbonate-producing salts (acetate, citrate, or lactate salts). Allowance should be made for the effect of the cation.

Incompatibility. Bicarbonate-producing or bicarbonate-containing solutions have been reported to be incompatible with a wide range of drugs. In many cases this incompatibility is a function of the alkaline nature of the bicarbonate solution. Precipitation of insoluble carbonates may occur, as may production of gaseous carbon dioxide when the bicarbonate ion is reduced by acidic solutions.

Potassium Bicarbonate

E501; Hydrogenuhličitan draselný; Kalii Hydrocarbonas; Kalii Hydrogenocarbobnas; Kalii hydrogenocarbonas; Kalio-vandenilio karbonatas; Kálium-hidrogén-karbonát; Kaliumvätekarbonat; Kaliumvetykarbonaatti; Monopotassium Carbonate; Potasio, bicarbonato de; Potassium, bicarbonate de; Potassium Hydrogen Carbonate; Potasu wodoroweglan; Potasyum Bikarbonat.

$KHCO_3$ = 100.1.
CAS — 298-14-6.
ATC — A12BA04.
ATC Vet — QA12BA04.

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*
Ph. Eur. 6.2 (Potassium Hydrogen Carbonate; Potassium Bicarbonate BP 2008). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; practically insoluble in alcohol. When heated in the dry state or in solution, it is gradually converted to potassium carbonate. A freshly prepared 5% solution in water has a pH of not more than 8.6.
USP 31 (Potassium Bicarbonate). Colourless, odourless, transparent monoclinic prisms or white granular powder. Freely soluble in water; practically insoluble in alcohol. Its solutions are neutral or alkaline to phenolphthalein.

Equivalence. Each g of potassium bicarbonate represents about 10 mmol of potassium and of bicarbonate. Potassium bicarbonate 2.56 g is equivalent to about 1 g of potassium.

Potassium Citrate

Citronan draselný monohydrát; E332; Kalii citras; Kalii Citras Monohydricus; Kalio citratas; Kaliumcitrat; Kaliumsitraatti; Potasio, citrato de; Potassium, citrate de; Potasu cytrynian; Potasyum Sitrat; Trikálium-citrát; Tripotassium Citrate. Tripotassium 2-hydroxypropane-1,2,3-tricarboxylate monohydrate.

$C_6H_5K_3O_7,H_2O$ = 324.4.
CAS — 866-84-2 (anhydrous potassium citrate); 6100-05-6 (potassium citrate monohydrate).
ATC — A12BA02.
ATC Vet — QA12BA02.

Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Int.*, and *US.*
Ph. Eur. 6.2 (Potassium Citrate). Transparent, hygroscopic crystals or a white or almost white granular powder. Very soluble in water; practically insoluble in alcohol. Store in airtight containers.
USP 31 (Potassium Citrate). Transparent crystals or a white granular powder. It is odourless and is deliquescent in moist air. Soluble 1 in 1 of water and 1 in 2.5 of glycerol; almost insoluble in alcohol. Store in airtight containers.

Equivalence. Each g of potassium citrate (anhydrous) represents about 9.8 mmol of potassium and 3.26 mmol of citrate. Each g of potassium citrate (monohydrate) represents about 9.3 mmol of potassium and 3.08 mmol of citrate. Potassium citrate (monohydrate) 2.77 g is equivalent to about 1 g of potassium.

Sodium Acetate

E262; Natrii Acetas; Natrii acetas trihydricus; Natrio acetatas trihidratas; Natrium Aceticum; Nátrium-acetát; Natriumacetat trihydrat; Natriumasetaattitrihydraatti; Octan sodný trihydrát; Sodio, acetato de; Sodium (acétate de) trihydraté; Sodu octan.

$CH_3.CO_2Na,3H_2O$ = 136.1.
CAS — 127-09-3 (anhydrous sodium acetate); 6131-90-4 (sodium acetate trihydrate).
ATC — B05XA08.
ATC Vet — QB05XA08.

Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US.*
US also allows the anhydrous form.
Ph. Eur. 6.2 (Sodium Acetate Trihydrate). Colourless crystals. Very soluble in water; soluble in alcohol. A 5% solution in water has a pH of 7.5 to 9.0. Store in airtight containers.
USP 31 (Sodium Acetate). It contains three molecules of water of hydration or is anhydrous. Colourless, transparent crystals, or a white, granular crystalline powder, or white flakes. It is odourless or has a faint acetous odour. It is efflorescent in warm dry air. Soluble 1 in 0.8 of water, 1 in 0.6 of boiling water, and 1 in 19 of alcohol. pH of a solution in water containing the equivalent of 3% of anhydrous sodium acetate is between 7.5 and 9.2. Store in airtight containers.

Equivalence. Each g of sodium acetate (anhydrous) represents about 12.2 mmol of sodium and of acetate. Each g of sodium acetate (trihydrate) represents about 7.3 mmol of sodium and of acetate. Sodium acetate (anhydrous) 3.57 g is equivalent to about 1 g of sodium. Sodium acetate (trihydrate) 5.92 g is equivalent to about 1 g of sodium.

Sodium Acid Citrate

Disodium Hydrogen Citrate; Disodu wodorocytrynian; E331; Natrium Citricum Acidum; Sodio, citrato ácido de.

$C_6H_6Na_2O_7,1/H_2O$ = 263.1.
CAS — 144-33-2.

Pharmacopoeias. In *Br.*
BP 2008 (Sodium Acid Citrate). A white, odourless or almost odourless, powder. Freely soluble in water; practically insoluble in alcohol. A 3% solution in water has a pH of 4.9 to 5.2.
The BP gives Disodium Hydrogen Citrate as an approved synonym.

Equivalence. Each g of sodium acid citrate (sesquihydrate) represents about 7.6 mmol of sodium and 3.8 mmol of citrate. Sodium acid citrate (sesquihydrate) 5.72 g is equivalent to about 1 g of sodium.

Sodium Bicarbonate

Baking Soda; E500; Hydrogenuhličitan sodný; Monosodium Carbonate; Natrii Bicarbonas; Natrii hydrogenocarbonas; Natriovandenilio karbonatas; Nátrium-hidrogén-karbonát; Natriumvätekarbonat; Natriumvetykarbonaatti; Sal de Vichy; Sodio, hidrogenocarbonato de; Sodium Acid Carbonate; Sodium, bicarbonate de; Sodium Hydrogen Carbonate; Sodu wodoroweglan; Sodyum Bikarbonat.

$NaHCO_3$ = 84.01.
CAS — 144-55-8.
ATC — B05CB04; B05XA02.
ATC Vet — QB05CB04; QB05XA02; QG04BQ01.

Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Int., Jpn, US*, and *Viet.*
Ph. Eur. 6.2 (Sodium Hydrogen Carbonate; Sodium Bicarbonate BP 2008). A white or almost white, crystalline powder. Soluble in water; practically insoluble in alcohol. The pH of a freshly prepared 5% solution in water is not more than 8.6. When heated in the dry state or in solution, it gradually changes into sodium carbonate.
USP 31 (Sodium Bicarbonate). A white crystalline powder that slowly decomposes in moist air. Soluble 1 in 12 of water; insoluble in alcohol. Its solutions, when freshly prepared with cold water, without shaking, are alkaline to litmus; alkalinity increases on standing, agitation, or heating.

Equivalence. Each g of sodium bicarbonate (anhydrous) represents about 11.9 mmol of sodium and of bicarbonate. Sodium bicarbonate 3.65 g is equivalent to about 1 g of sodium.

Sodium Citrate

Citronan sodný dihydrát; E331; Natrii citras; Natrii Citras Dihydricus; Natrio citratas; Natriumcitrat; Natriumsitraatti; Sodio, citrato de; Sodium, citrate de; Sodu cytrynian; Sodyum Sitrat; Trinátrium-citrát; Trisodium Citrate. Trisodium 2-hydroxypropane-1,2,3-tricarboxylate dihydrate.

$C_6H_5Na_3O_7,2H_2O$ = 294.1.
CAS — 68-04-2 (anhydrous sodium citrate); 6132-04-3 (sodium citrate dihydrate).
ATC — B05CB02.
ATC Vet — QB05CB02.

Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Int., Jpn*, and *Viet.*
Int. and *US* specify anhydrous or dihydrate.
Ph. Eur. 6.2 (Sodium Citrate). A white or almost white, crystalline powder or white or almost white, granular crystals; slightly deliquescent in moist air. Freely soluble in water; practically insoluble in alcohol. Store in airtight containers.
USP 31 (Sodium Citrate). It is anhydrous or contains two molecules of water of hydration. Colourless crystals, or a white crystalline powder. The hydrous form is soluble 1 in 1.5 of water and 1 in 0.6 of boiling water; insoluble in alcohol. Store in airtight containers.

Equivalence. Each g of sodium citrate (anhydrous) represents about 11.6 mmol of sodium and 3.9 mmol of citrate. Each g of sodium citrate (dihydrate) represents about 10.2 mmol of sodium and 3.4 mmol of citrate. Sodium citrate (anhydrous) 3.74 g is equivalent to about 1 g of sodium. Sodium citrate (dihydrate) 4.26 g is equivalent to about 1 g of sodium.

Storage. Sterilised solutions when stored may cause separation of particles from glass containers and solutions containing such particles must not be used.

Sodium Lactate

E325; Lactato de sodio; Natrii lactatis; Natriumlaktaatti; Natriumlaktat; Sodium, lactate de. Sodium 2-hydroxypropionate.

$C_3H_5NaO_3$ = 112.1.
CAS — 72-17-3.

Pharmacopoeias. *Chin., Eur.* (see p.vii), and *US* include preparations of sodium lactate.
Ph. Eur. 6.2 (Sodium Lactate Solution). It contains a minimum of 50% w/w of sodium lactate and is a mixture of the two enantiomers in about equal proportions. Sodium (*S*)-Lactate Solution contains a minimum of 50% w/w of sodium lactate, not less than 95% of which is the (*S*)-enantiomer. The solutions are clear, colourless, slightly syrupy liquids. Miscible with water and with alcohol. pH 6.5 to 9.0.
USP 31 (Sodium Lactate Solution). It is an aqueous solution containing at least 50% sodium lactate. A clear, colourless or practically colourless, slightly viscous liquid, odourless or having a slight, not unpleasant, odour. Miscible with water. pH between 5.0 and 9.0. Store in airtight containers.

Equivalence. Each g of sodium lactate (anhydrous) represents about 8.9 mmol of sodium and of lactate. Sodium lactate (anhydrous) 4.88 g is equivalent to about 1 g of sodium.

Adverse Effects and Treatment

Excessive use of bicarbonate or bicarbonate-forming compounds may lead to hypokalaemia and metabolic alkalosis, especially in patients with impaired renal function. Symptoms include mood changes, tiredness, slow breathing, muscle weakness, and irregular heartbeat. Muscle hypertonicity, twitching, and tetany may develop, especially in hypocalcaemic patients. Treatment of metabolic alkalosis associated with bicarbonate overdose consists mainly of appropriate correction of fluid and electrolyte balance. Replacement of calcium, chloride, and potassium ions may be of particular importance.

Excessive doses of *sodium salts* may also lead to sodium overloading and hyperosmolality (see Adverse Effects of Sodium, p.1686). Sodium bicarbonate given