Discussion of the complications of intravenous fluids may be considered under two basic headings: first, complications of access to the circulation, and secondly, complications of the intravenous fluids themselves.

Complications of Access to the Circulation

The commonest complication, thrombophlebitis at the site of insertion of an intravenous fluid cannula into a peripheral vein[1], may arise because routine ward management of intravenous cannulae frequently leaves much to be desired and the puncture site is contaminated with bacteria. Thrombophlebitis is also related to the chemical and physical properties of the fluids given. Administration of hypertonic fluids into peripheral veins causes damage to the venous endothelium, followed by inflammation, swelling and obstruction of the vein.

Cannulation of major veins is associated with more severe complications. Haemorrhage is rare but must be considered, particularly when cannulating the central veins by means of direct subclavian puncture; both haemotherax and pneumotherax may occur and have, on occasion, proved fatal. Central vein thrombosis may also occur. Major peripheral veins such as the subclavian vein may thrombose, usually when a long intravenous catheter is inserted from a peripheral vein towards the central veins and the tip is left in the subclavian vein or the axillary vein. If hypertonic solutions are infused, severe thrombophlebitis and subclavian vein thrombosis may develop.

Insertion of relatively hard PVC catheters into the right side of the heart may cause acute bacterial endocarditis or perforation of the atria and the ventricles, resulting in fatal cardiac tamponade. Fortunately, these complications are rare.

Management

The first step is prevention of peripheral thrombophlebitis, but this is not easy. The first rule is strict asepsis in the insertion of the cannula because in most cases the infecting organisms arise from the patient’s own skin rather than from the intravenous fluids. The incidence of thrombophlebitis is not altered by using millipore filters to remove organisms within the fluid[2]. When a catheter becomes infected and causes symptoms such as pyrexia it should be removed and replaced by another catheter. It is futile to attempt to treat such sepsis with antibiotics.

When hypertonic fluids have to be administered, as in intravenous feeding, the use of a central vein is mandatory. In a central vein, the flow of blood is so great that the osmolality of the fluid is diluted fast enough to prevent significant damage to the venous endothelium. This does mean, however, that the increasing risks of central vein catheterisation must be faced, but if a patient is sick enough to require continued administration of hypertonic fluids, the risks of catheterisation have to be accepted and can be minimised.

Where possible, the most acceptable route of catheterisation of a central vein, both for the patients and clinician, is to use the subclavian vein approach from either above or below the clavicle. When this is done by an experienced operator under strict asepsis, the results are excellent and the complication rate minimal. It is, however, not a procedure to be undertaken on an occasional basis, otherwise the complication rate soon becomes unacceptable. But even in the most careful hands and under the strictest asepsis, the use of the routine subclavian catheter results in a useful catheter life of between 18 and 28 days only, particularly in patients with chronic sepsis, who frequently develop septic foci on the catheter, thus necessitating its removal. We have recently overcome this problem by using sialastic catheters placed in situ at surgical operation and tunnelled to a peripheral puncture site so that minimal infection occurs. We have had these catheters in place in such patients for longer than a year and our American colleagues have had similar catheters in situ for up to three years. The catheters are the Broviac[3] or the Hickman catheters, both eminently suitable for the purpose, but they must be inserted under full sterile operating theatre precautions.

It is essential to use radiology to ensure the correct placement of the catheter in the right atrium or the superior vena cava. Without the use of X-rays, catheters can become misplaced in the axillary vein of the same or the opposite side, or in the jugular vein, where the unnecessary infusion of hypertonic solutions can do great harm. When the catheters are satisfactorily positioned, they are acceptable to the patient in terms of comfort, and easy to manage provided a strict protocol of asepsis is used in the handling of the catheter.

Complications of Intravenous Fluids

The complications of intravenous fluids can be divided
into those that occur early and those that occur late. Most of the early complications arise in patients who are receiving isotonic or hypertonic intravenous fluids at and around the time of surgery, or during the management of an acute illness. The late complications occur in those patients receiving intravenous feeding as a result of long-standing chronic disease, or delayed recovery from a major illness.

**Early Complications**

**Over and Underhydration.** Probably the commonest complications of intravenous fluid management in general are simple overhydration and underhydration, usually the result of carelessness in the management of fluid balance and inaccurate calculations of the day-to-day gains and losses of fluid. It is not unusual to see the clinician rubbing his hands with glee at the sight of a patient gaining weight, but careful analysis of his input chart shows an inescapable correlation between the 1 kg/day gain in weight in the patient and the one litre positive water balance which, if it continues, will surely end in disaster. Underhydration also is a significant cause of clinical problems and, once again, the risk can be eliminated by careful management of fluid balance.

**Electrolyte Homeostasis.** Disorders in electrolyte homeostasis can also be controlled by careful management of the patient's fluid balance status and by regular measurement of the serum electrolytes. It is essential to know the losses of electrolytes in urine, fistula and drain fluid, and be aware of the insensible losses of relevant electrolytes. The relevant electrolytes not only include sodium, potassium, chloride and bicarbonate, but also calcium, magnesium and phosphate, which are becoming increasingly important in the day-to-day management of nutritionally depleted and injured patients.

**Complications of the Administration of Carbohydrates.** Glucose is the commonest carbohydrate that is administered and it is usually given in homeopathic quantities as 5 per cent dextrose. However, any patient who continues for a significant length of time on intravenous fluids, and is failing to take adequate quantities of calories and nitrogen by mouth, must have replacement of his nutritional requirements by vein. It is when we enter the field of intravenous feeding that we get a wide range of problems caused by excesses or deficiencies in the basic nutritional substrates.

When glucose is used as an energy source, hyperglycaemia can occur together with hyper-osmolality. Neither of these complications should be allowed to occur, because patients undergoing intravenous feeding need to be very carefully monitored, with measurements of blood and urine sugars. If hyperglycaemia does occur, it should be treated with insulin. The prime consideration is the number of calories that the patient needs as carbohydrate. The amount required should be given. If the patient subsequently gets hyperglycaemia, he should be given insulin in sufficient quantities to keep the blood glucose normal. Diabetic patients should be treated on exactly the same basis.

Hypophosphataemia is a manifestation of an electrolyte disorder which is actually enhanced by the administration of calorie sources such as glucose[4-6]. It is well recognised that in the malnourished patient the infusion of glucose can cause a very rapid decline in serum phosphate concentration. Because of the demand for phosphate by cells for phosphorylation of glucose, adequate quantities of phosphate must be provided with any glucose solution to ensure that hypophosphataemia does not occur. Fructose has also been used as a calorie source. It has been argued that it is better tolerated by patients after injury but it does have the risk of causing lactic acidosis, particularly in the neonate, so it is not considered to be as satisfactory as glucose. Some animal studies have shown that elevated levels of sorbitol may cause cataracts. Cataracts in the diabetic patient may be due to conversion of the excessive quantities of glucose by polyol pathways into sorbitol crystals deposited in the lens.

Finally, there is evidence to suggest that the malnourished cannot tolerate large quantities of glucose. We have shown that when glucose is infused into normal healthy people, plasma glucose and osmolality rise and cell volume falls concomitantly[7]. However, the reverse occurs in the malnourished, so that there is a degree of cell swelling. The reason for this is not clear. It is possible that the metabolism of glucose is not normal, with a fall in intracellular energy supply. This may affect sodium pumping, thus enhancing cell swelling. The administration of excessive quantities of dextrose to malnourished patients may cause some degree of intracellular overhydration during glucose infusion, which may be manifested as cerebral oedema[8].

**Complications of Fat Emulsion.** The fat emulsions in current use are soya bean emulsions, which are relatively trouble-free. However, the first emulsions we used clinically were cotton-seed emulsions, which were associated with frequent and severe adverse effects[9], mainly coagulation disorders. But there is a moderate incidence of pyrogenic reactions during the clinical use of fat emulsions[10]. Other manifestations, such as nausea, vomiting, flushing, dyspnoea, apprehension, cyanosis and hypotension can occur. Although the solutions are tested very carefully, there is some evidence to suggest that the current pyrogenic tests miss endotoxin contained in fat emulsion products and that the presence of endotoxins is the explanation for these clinical phenomena.

Spuriously low concentrations of serum electrolytes will be recorded on the hyperlipidaemic blood samples taken from patients being infused with fat emulsions. The lipid moiety has to be removed, otherwise the fat will coat the electrodes in the analytical apparatus. There is some clinical evidence of fat deposition in blood vessels. We and others have seen a thin layer of fat deposited in the major veins of patients who have been receiving large quantities of fat for long periods of time.
Complications of Amino Acid Solutions. Metabolic acidosis related to intravenous feeding, and particularly the amino acid solutions, has been recognised for many years. Hyperchloraemic metabolic acidosis is associated with infusion of amino acids with a relatively high concentration of chloride. A second type of metabolic acidosis is more subtle and it has been suggested that it is due to an abnormally large intake of titratable acid[11], or alternatively, to infusion of amino acid formulations that have a particularly wide cation gap.

Leucocytosis has been observed in a number of patients receiving amino acids but it settles immediately the amino-acid infusion is discontinued. Like many drugs, the amino acids are liable to cause marrow depression manifested particularly by thrombocytopenia; fortunately, this complication is rare.

In patients with liver disease, administration of excessive amino acids containing high concentrations of aromatic amino acids can precipitate metabolic encephalopathy. It has also been suggested that amino acid solutions that contain a large quantity of glutamic acid can, in susceptible individuals, give rise to a syndrome similar to that which arises in people sensitive to monosodium glutamate[12]. It has therefore been suggested that solutions containing glutamic acid should be avoided.

Finally, cholestasis and jaundice have been seen relatively frequently in patients undergoing long-term intravenous feeding[13] and both protein hydrolysate and crystalline amino acid solutions have been associated with cholestatic jaundice. Although the jaundice can be quite severe, it usually resolves spontaneously when intravenous feeding is stopped.

Late Complications

These syndromes are mainly confined to patients with bowel disease who require intravenous feeding on a long-term or semi-permanent basis.

The syndromes are due to excess or deficiency. The most straightforward are those due to excess quantities of fluid or electrolytes. When using solutions containing fairly large quantities of calcium, phosphate, magnesium and potassium, and primarily designed for the undernourished patient, it is not unusual to encounter raised levels of these substances in the normally nourished patient who is on intravenous feeding for a long period of time. Great attention must be paid to monitoring such patients to prevent these excess syndromes occurring, as they can cause serious adverse effects.

A variety of deficiency syndromes may occur in the patient undergoing long-term intravenous feeding.

Essential fatty acid deficiency causes skin rashes and delayed wound healing[14, 15]. It may be treated simply by giving intravenous fat emulsion containing adequate quantities of essential fatty acids; the clinical response is frequently quite dramatic.

Vitamin deficiency is quite common because many of the currently available vitamin preparations do not contain adequate quantities of all the necessary vitamins. In particular, folic acid is frequently omitted and can result in folic acid deficiency anaemia and jaundice[16].

The importance of the trace elements in the long-term management of patients on intravenous fluids is becoming more obvious[17]. Zinc is now routinely replaced because zinc-deficient skin abnormalities used to be seen in the patients on long-term feeding. Similarly, copper and chromium are replaced, as these can cause anaemia and glucose intolerance respectively. The whole spectrum of trace elements is now under intensive study, and patients on long-term total intravenous feeding are turning into experimental studies for specific trace element deficiencies. As more and more bizarre syndromes present themselves they are found to respond to the administration of further trace elements. The most recent trace element to be intensively studied is selenium; there is some evidence that it can cause syndromes not unlike multiple sclerosis and muscular dystrophy.

Prevention of Complications of Intravenous Fluids

The main preventive measures are to monitor the patient carefully by regular measurement of biochemical, haematological and body compositional parameters, and to be aware of the possible complications. Very careful attention must be paid to methods of administering fluids so that excessive quantities are not given accidentally. The use of accurate flow control devices or intravenous feeding pumps in patients who are particularly unstable is recommended.

If meticulous attention is paid to technical detail in administration, and great care is taken in the assessment and day-to-day management of the patients, the complications of intravenous fluids may be minimised. Intravenous feeding then becomes an acceptable long-term method of maintaining the patient in adequate fluid, electrolyte and nutritional homeostasis. Techniques have improved to such an extent that we are now in a position to be able to send patients home on intravenous feeding and maintain an acceptable way of life for many months, or even years, at a time.

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Sir Thomas and the Marquis

The Dorchester library is perhaps the most precious of the College's possessions. The exciting tale of its acquisition was told by Dr Charles Newman in the Journal (1970, Vol. 4, p. 234). This year marks the three hundredth anniversary of the death of Henry Pierpoint, Marquis of Dorchester, a little man with a furious temper. His thirst for omniscience is shown by the breadth and scope of his library. He knew a lot about medicine, for which the public ridiculed him but the College made him the first honorary Fellow in 1658. Accepting this honour he acknowledged the excellence of the medical profession and lavished sweetmeats on all present. The idea that he would leave his library to the College grew slowly but the Marquis did nothing. In May 1680, he nearly killed himself with a huge dose of opium, taken in error. Then, in November, his habit of rubbing himself all over with salt started his last illness because he rubbed a bit of skin off his ankle, the whole leg swelled and became gangrenous. Dr Edward Browne was his physician, whose father, Sir Thomas Browne, knew what was happening and alluded to the Marquis in many of the letters addressed to his son Edward at Salisbury Court, next the Golden Balls, London. 'If the profits of the next year are not up to this, I would not have you discouraged; for the profits of no practice are equal or regular: and you have had some extraordinary patients this year . . .' 'I am glad you can please my L.M of Dorchester when you go to him . . . You have surely much obliged him by his last recovery.' (August and September 1680.) And on 29th November he wrote: 'I am sorry to understand that your good friend my L. marquis is fallen so ill againe and is in a coma, or some soporous disease, and threatening apoplexis and palsie; perhaps his last mistaken draught of the opiat left some ill impression on his brayne. Tis well that hee hath declared that he will give his librarie to the colledge, whether he live or dye.' He added: 'I hope you will bee well considered for your paynes and sitting up.'

On 3rd December he wrote: 'I hope my L. marquis is recovered, you saying nothing of him in your last. I presume it is a noble librarie, and consisteth of usefull booke, which may bee of good advantage to those who have leasure to passe their time in a publick librarie, and because there are most good authors, it may bee usefull to others, as not being in every private man's librarie. It may serve for others to looke after anything in them upon occasion.' However, five days later the Marquis died. 'I am sorry to understand that my L. marquess of Dorchester is dead', wrote Sir Thomas on 13th December. 'I hope his librarie is assured unto the colledge, which I hear is a good and fayre and profitable one. Unto the physician who liveth in the colledge it may be of good use, because hee is neere it, and may make use of it daye and night; unto others it may bee servicable to read any booke, or looke into it upon occasions, the bookes being of the best or most scarce editions.' On 4th March 1681 Sir Thomas came back to the subject of the library. 'Thinke the colledge is much obliged to you for what you have done towards the procuring of my lords librarie. And I hope such care will bee taken as that you may soone have the possession of it. It were well if you could so contrive the business as to be at little charge for a librarie keeper, for there is not like to bee any constant studying in it, men being diverted by the avocations of their profession.' Sir Thomas was ever a realist.