Parenteral nutrition in renal failure

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THE MODERN management of acute oliguric renal failure includes careful control of fluid, electrolyte, vitamin and calorie intake. Such treatment is designed to maintain the constancy of the 'milieu intérieur' and prevent excess catabolism. With the advent of treatment using extracorporeal haemodialysis and peritoneal dialysis techniques the survival rate of such patients has been considerably increased.

Nevertheless, in patients with prolonged renal failure secondary to trauma, gross sepsis or surgical operation in whom a strict oliguric renal failure regime has to be maintained in addition to repeated haemodialysis, severe wasting and evidence of malnutrition have become increasingly apparent. Lawson *et al.* (1962) designed a diet containing 1200-1400 calories with 30-40 g first-class proteins in about 650 ml fluid. Lawson *et al.* (1962) and Kille & Lawson (1963) have also shown that provision of up to 40 g first-class protein in the diet does not significantly increase the daily increment of blood urea. More recently, Berlyne *et al.* (1966) have designed a diet for the treatment of acute renal failure containing 2000 calories, 18 g protein and minimal amounts of sodium and potassium in 500 ml fluid. Furthermore, this diet contains adequate amounts of all essential amino acids, except methionine, of which a supplement is given, and also a 3-day rotation in menu. Again, Silva *et al.* (1964) in the treatment of patients with hypercatabolic acute renal failure with daily haemodialysis permitted 60 g protein, 2500 calories and 1500 ml fluid in the diet. Recently, the use of high liquid glucose concentrates in the management of acute renal failure (Parsons & Fore, 1963) has helped supply more calories in a smaller volume of fluid virtually free of electrolytes but does not compensate for the absence of protein.

However, not infrequently one has to treat patients with hypercatabolic renal failure in whom only a parenteral route for nutrition is possible. This until recently has usually meant giving hypertonic glucose or fructose solutions via a catheter into the inferior vena cava. Even so, it has been extremely difficult to give sufficient calories by this means in the fluid volumes allowed and complications such as thrombophlebitis have been common. Use of the superior vena cava (Thoren, 1964) appears to lessen the incidence of thrombophlebitis.

The use of amino acid solutions and fat emulsions seemed to be an ideal approach and a leading article in the *British Medical Journal* in 1961 commented upon the latter 'that fat emulsions offer a compact and reasonably safe source of calories for intravenous administration'. Shuttleworth (1963) considered that intravenous fat therapy would be a valuable addition to the management of difficult post-operative problems but that more clinical evaluation was required. Their usefulness in many clinical situations have now been shown (Schuberth & Wretling, 1961; Schuberth, 1964; Freuchen & Ostergaard, 1964; Wretling, 1964; Lawson, 1965; Sherwood Jones & Peaston, 1966). There have been reservations about the use of parenteral nutrition in the management of acute renal failure and Schuberth (1964) gave the latter as a contra-indication to its use. Birke (1964) quotes Alwall when describing the great difficulties which arise in managing acute renal failure with parenteral nutrition, despite the great need for such therapy in this situation.

Kille & Lawson (1964) reported on two cases where the efficiency of haemodialysis seemed to have been impaired when intravenous fat emulsions were being given. In one instance the dialysing membrane was covered with a thin layer of fat. Sherwood Jones, Robinson & McConn (1963)

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and Lawson (1965) suggested respectively that fat emulsions should not be given less than 48 and 6 hr prior to haemodialysis. There have been few reports on the specific application of parenteral nutrition to the management of acute renal failure (Alwall, 1964; Lee & Shortle, 1965; Lee & Sharpstone, 1965).

We report here our experiences with fat emulsions and amino acid solutions in the treatment of patients with acute and chronic renal failure. The nutritional solutions used were amino acid mixtures (10% 'aminosol'; aminosol-fructose-ethanol) and 10% and 20% soya bean oil emulsions ('Intralipid').

Results

The number and range of clinical states in which we have used complete parenteral nutrition are shown in Table 1. In all instances a parenteral route alone was available for maintenance of nutrition either because oral or intragastric feeding was absolutely contraindicated or because the oral route was not possible. The range of duration of continuous parenteral nutrition varied from 6 to 31 days with a mean of 12.5 days. In our present series of cases we initially did not exceed a dose level for fat emulsions of 2.5 g/kg body weight/day. More recently we have consistently used a dose range of 3–5 g/kg body weight/day, again without any side effects. Formal fat clearances were not carried out but that the patient was eliminating the infused fat emulsion from the circulation was ascertained by taking a morning specimen of blood, centrifuging and checking the plasma for turbidity, prior to infusing the daily intravenous fat requirement.

We have not met any examples of acute or chronic toxic effects. Rapid infusions of 500 ml of 10% and 20% soya bean oil have been given over 20–45 min (0.24–0.16 ml/kg/min for 70 kg patient), whilst recording blood pressure, pulse, respiratory rate and temperature. No pyrexial reactions or effects upon the cardiorespiratory system were seen.

Liver function has been studied in ten patients receiving complete parenteral nutrition for periods varying from 6 to 23 days. Serum bilirubin, serum transaminases, alkaline phosphatase and flocculation tests were all recorded prior to and serially after starting parenteral nutrition. In only one patient was there a significant change in any of these parameters measured, where the serum glutamic pyruvate transaminase rose from 13 to 47 units after 6 days.

The question of whether infusions of fat emulsions during the management of renal failure might interfere with haemodialysis, if it was re-

TABLE 1
Patients treated with complete parenteral nutrition for at least 6 days

Clinical conditions	Number
Trauma	2
Severe burns (60%)	2
Septic abortion, renal failure, paralytic ileus	4
Peritonitis	5
Carcinoma of cervix, chronic renal failure	1
Carcinoma of oesophagus (pre-operatively)	1
Cellulitis, septicaemia and acute renal failure	2
Acute renal failure and pancreatitis	3
High intestinal obstruction	1
Bronchopneumonia and generalized debility	2
Carcinoma of bladder	1
Carcinoma of prostate	1
Advanced chronic renal failure	6
Intensive care patients with head injuries	3
Post-operative	6
Pyelonephritis and pregnancy	1
Septicaemia and jaundice	1

quired, by coating the artificial kidney membrane and so altering membrane permeability, has been studied by measuring clearances. Fat emulsions have been infused immediately prior to and during dialysis with a Kolff twin coil artificial kidney. In other cases, fat emulsion has been infused only during the second half of a haemodialysis. Tables 2, 3 and 4 show that urea and uric acid clearances are not altered by fat infusions but that there is a slight reduction in phosphate clearances. Table 5 shows the total amounts of urea, uric acid, phosphate removed during dialyses, all dialyses having a mean duration of 6 hr. Exchanges of sodium, potassium and bicarbonate ions across the membrane have likewise been unaffected by fat infusions. Similar results have been obtained (not included in tables) with a Kiil artificial kidney.

From a laboratory standpoint there are certain precautions to be noted. Problems encountered were largely due to mechanical interference resulting from the viscous quality of the fat emulsions. Thus there was a tendency for sludging in the atomizer of the flame photometer, soot formation over the glass and adhesion of material to the plastic walls of the automatic pipette thus reducing the bore and internal volume. Also sludging and blockage of the dialyser compartment in the AutoAnalyzer sometimes occurred. Most of these difficulties are overcome by shaking the plasma with two aliquots of ether to extract the fat. The peptides in the amino acid solutions result in a higher total protein figure when estimated by the

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TABLE 2
Urea clearance (ml/min)

	Blood urea (mg/100 ml)		
	101-200	201-300	301-400
With 'Intralipid'	98 (n=30) $\pm$ 18	114 (n=25) $\pm$ 25.1	116 (n=10) $\pm$ 22.3
Without 'Intralipid'	105 (n=31) $\pm$ 30.1	121 (n=42) $\pm$ 25.2	111 (n=16) $\pm$ 25.1

TABLE 3
Phosphate clearances (ml/min)

	Blood phosphate (mg/100 ml)	Phosphate clearances
With 'Intralipid'	8.6 (n=39) $\pm$ 2.85	70 $\pm$ 22.85
Without 'Intralipid'	7.3 (n=58) $\pm$ 1.99	89 $\pm$ 36

TABLE 4
Uric acid clearances

	Serum uric acid (mg/100 ml)	Uric acid clearances
With 'Intralipid'	8.6 (n=16) $\pm$ 2.0	87 $\pm$ 15.46
Without 'Intralipid'	10.6 (n=33) $\pm$ 3.1	96 $\pm$ 12.3

TABLE 5
Amounts of urea, phosphate and uric acid removed per dialysis

	With 'Intralipid'	Without 'Intralipid'
Starting blood urea (mg/100 ml)	344 (36) $\pm$ 75	349 (36) $\pm$ 51.72
Urea removed (g)	81 $\pm$ 30.54	84 $\pm$ 27.74
Starting plasma phosphate (mg/100 ml)	11.6 (18) $\pm$ 4.27	10.0 (23) $\pm$ 2.71
Phosphate removed (g)	1.8 $\pm$ 0.85	2.05 $\pm$ 0.61
Starting serum uric acid (mg/100 ml)	11.52 (14) $\pm$ 2.87	10.6 (16) $\pm$ 2.1
Uric acid removed (g)	2.58 $\pm$ 0.43	2.2 $\pm$ 0.44

Biuret reaction. Again, occasional specimens taken during intravenous amino acid administration gave rise to turbidity in the diazo reaction for bilirubin. The presence of fat emulsion interferes with the colorimetric estimation of haemoglobin.

The only clinical difficulty, which was rarely encountered, was thrombophlebitis following administration of aminosol. This was usually then avoided by either running in aminosol and fat emulsions simultaneously through larger veins, or infusing the aminosol alone faster or changing the infusion site daily.

Case R.J. Illustrative cases

An 18-year-old girl was admitted to another hospital with acute abdominal pain. At laparotomy on 30 December 1964 a perforated appendix

and peritonitis were found; an appendicectomy was done. She was not able to take anything orally and by 6 January 1965 had developed paralytic ileus. She was managed by intravenous infusions and intestinal aspiration. Although her blood urea rose she did not become oliguric. She became very toxic, acidotic, uraemic and hypokalaemic. When transferred to us on 12 January 1965 she was cachectic and there was dehiscence of the lower part of the abdominal wound. She required haemodialysis and her serum biochemical values were restored to normal. It can be seen from Fig. 1 that this patient had received no nitrogen and scarcely any calories since her hospital admission. She was starving and in gross negative nitrogen balance. Her uraemic state resulted from three factors: (1) mild non-oliguric renal failure, (2)

FIG. 1. Daily caloric and nitrogen intake, weight and blood urea changes and 24-hr urine output in patient R.J. Note cessation of further weight loss after starting i.v. nutrition. Mean daily increment of blood urea not increased by i.v. feeding and no change in renal function.

severe post-operative hypercatabolic state accentuated by infection, and (3) dehydration. On 12 January 1965 her abdominal wound burst and inspection of the wound edges showed almost complete disappearance of fat from the subcutaneous tissues and dark brown discoloration of muscle. With complete parenteral nutrition, using amino acid solutions and fat emulsions, there was a remarkable overall improvement. There was no

FIG. 2. Temperature, blood urea, serum bilirubin and white blood cell count changes in patient M.W. Note relatively small loss of weight and well-being of patient in spite of prolonged hectic fever, two operations and discharging fistula.

improvement in renal function during this time. She was finally discharged in February.

This patient is an example of starvation in a post-operative patient with attendant complications. Parenteral nutrition and haemodialysis to a lesser extent were life-saving measures.

Case M.W.

A 28-year-old female developed a pelvic abscess, Gram-negative septicaemia, renal failure and jaundice following a right oophorectomy for a pseudomucinous cystadenocarcinoma and an appendicectomy on 10 August 1965. The course of her illness is shown in Fig. 2. Post-operatively she developed a wound infection and a pyrexia of 103°F which did not respond to chloramphenicol. Next, vomiting, watery diarrhoea, hypotension, oliguria and jaundice occurred. On admission to this unit on 20 August 1965 investigation results were: WBC 22000/mm³, blood urea 126 mg/100 ml, serum bilirubin 2 mg/100 ml, blood

TABLE 6
Daily parenteral nutrition of M.W.

Solution	Volume (ml)	Calories	Nitrogen (g)	Sodium (mEq)	Potassium (mEq)
Soya bean emulsion 20%	1000	2000			
Aminosol-fructose-ethanol	1000	875	4.25	54	
Aminosol 10%	500	160	6.5	80	
Normal saline	1500			230	
Potassium chloride					107
Vitamins i.v.					
Total per 24 hr	4000	3035	10.75	364	107

TABLE 7
Daily parenteral nutrition of H.S.

Solution	Volume (ml)	Calories	Nitrogen (g)	Sodium (mEq)	Potassium (mEq)
Aminosol-fructose-ethanol	750	660	3.2	38	—
Soya bean emulsion 20%	1000	2000	—	—	—
Aminosol 10%	250	80	3.0	40	—
Blood	250	70	2.2	40	2
Vitamins i.v.					
Total	2250	2810	8.4	118	2

FIG. 3. Blood urea changes and daily fluid balance in patient H.S. Note how frequent haemodialysis permitted of adequate parenteral nutrition. Mean daily increment in blood urea 92 mg/100 ml. The cross-hatched columns represent fluid intake, the blank columns urine output and the blocked columns water removed by haemodialysis.

cultures negative. Because of persistent vomiting parenteral nutrition was begun with 3-4 litres of fluid daily, including 1 litre 20% 'intralipid', 1 litre aminosol-fructose-ethanol, and sodium, potassium and vitamin supplements (Table 6). Her pyrexia settled on ampicillin and with general improvement parenteral nutrition was stopped after 5 days. She entered the diuretic phase and her blood urea fell. Drug sensitivity led to clinical deterioration, pyrexia and increasing leucocytosis. Chemotherapy was changed and parenteral feeding resumed. High fever persisted over the next 10 days with development of a faecal fistula. Her general condition, however, remained remarkably

good, her diuresis continued, the blood urea did not rise and the serum bilirubin varied between 1.5 and 3.0 mg/100 ml. At laparotomy on 6 September 1965 4 weeks post-operatively, some collections of pus were drained, adhesions divided and the faecal fistula closed. After laparotomy, the fever subsided but faeces still poured from the abdominal drains. One week after laparotomy, renewed pyrexia of 102°F and hypotension indicated a Gram-negative septicaemia, which responded dramatically to ampicillin and hydrocortisone. Finally, 5½ weeks after her original operation, parenteral nutrition was discontinued and her weight was only 4 kg down. Her subsequent progress was uneventful, the faecal fistula closed, the serum biochemistry returned to normal and she was discharged 8 weeks after her first operation.

Thus, this patient's nutrition was satisfactorily maintained throughout a complicated post-operative course. During 23 days of complete parenteral nutrition a total of forty-two bottles of 20% 'intralipid' and over fifty bottles of amino acid solution were given. When the infection was eradicated, she very soon became ambulant and was discharged shortly after.

Case H.S.

This 38-year-old male was referred from another hospital with acute oliguric renal failure secondary to major trauma following a 70 ft fall. His main injuries were fractured femur, fractured pelvis, fractured radius, ruptured liver and torn perineum. He was markedly hypercatabolic with a mean daily increment in blood urea of 92 mg/100 ml. Oral feeding was precluded by the early onset of paralytic ileus. With frequent haemodialyses every 48 hr, a mean volume of 2500 ml was ultrafiltered per dialysis allowing for adequate parenteral nutrition (see Fig. 3 and Table 7).

Case J.B.

This 6-year-old patient, weighing 17.8 kg, had an open heart operation for a ventricular septal

FIG. 4. Blood urea and daily fluid balance in patient J.B. Fluid balance symbols as for Fig. 3. Note how ultrafiltration during haemodialysis in initial stages permitted of adequate parenteral nutrition. Initial weight 17.8 kg, final 16.3 kg. O, Operation; D, haemodialysis.

defect using a cardiopulmonary bypass. During the operation the blood pressure was satisfactorily maintained throughout but a severe degree of haemoglobinaemia developed. Immediately following operation she became oliguric with an associated rapid rise in blood urea. There was also a severe anaemia as a result of the haemolytic process. The child became very ill, extremely anorexic and nauseated. She would not tolerate a gastric tube and thus parenteral feeding was the only means for maintaining nutrition. She required haemodialysis on three occasions during which she was transfused with blood and deliberately dehydrated to allow volume space for parenteral nutrition (see Fig. 4). She made a rapid, uneventful recovery and required but a short convalescent period.

Discussion

In many clinical situations such as severe burns, sepsis or trauma there is a high rate of endogenous protein breakdown which can rapidly lead to a negative nitrogen balance and marked wasting (Macallum, 1910; Cuthbertson, 1960; Lawson, 1965). Such a negative nitrogen balance can in turn lead to reduced serum protein levels (Sachar, Horwitz & Elman, 1942), accelerated rate of rise of blood urea, rapid weight loss (Sachar *et al.*, 1942), impaired wound healing (Hartzell, Winfield & Irwin, 1941) and a poor resistance to infection (Sako, 1942). Many of these complications can be

avoided by a high calorie and adequate nitrogen intake (Abbott *et al.*, 1957; Parsons & Fore, 1963; Hadfield, 1965a; Lawson, 1965).

Such patients are often unable to take an adequate oral diet on account of anorexia, vomiting or ileus and nutrition must be provided partially or completely by the intravenous route; attention was brought to this by a leading article in the *British Medical Journal* in 1961. Particular problems of parenteral nutrition are met in the management of acute oliguric renal failure. It is well known that proteins are a poor source of calories and further that deamination processes during protein metabolism result in a rise of blood urea which is particularly undesirable in patients who have impaired renal function. Alternatively fat emulsions provide a valuable small-volume source of calories and are a useful adjunct in the management of renal failure. That such intravenously administered fat is rapidly catabolized has been shown by the balance studies of Abbott *et al.* (1957) and $^{14}\text{CO}_2$ elimination after giving ^{14}C labelled fat (Geyer, Chipman & Stare, 1948). Furthermore, it is important to appreciate that with parenteral nutrition the aim is not merely to provide calories but rather a balanced 'diet' containing all the essential constituents of a normal one (Lee & Shortle, 1965). This would include the minimal daily requirements of all the essential amino acids (Rose & Wixom, 1957), an optimum balance of about 200 calories/g nitrogen for maximum protein sparing and re-synthesis (Calloway & Spector, 1954; Abbott *et al.*, 1957), approximately 10% of the total caloric intake as carbohydrate and a minimal daily calorie intake (Hegsted, 1964). Since glucose intolerance is a feature of renal failure (Westervelt & Schreiner, 1962), whilst there is a normal fructose tolerance (Kennedy *et al.*, 1964) it is expedient to use fructose as the carbohydrate source. Many renal-failure patients are also post-operative, when decreased glucose utilization is known to occur (Hayes & Brandt, 1952). Not only is there an optimum ratio to be achieved between calories and nitrogen supplied but it has also been shown that the maximum effect toward restoring a positive nitrogen balance is obtained by giving calories and nitrogen simultaneously (McNair, O'Donnell & Quigley, 1954; Lawson, 1965). In addition adequate electrolytes and vitamins must be supplied. By combination of the intravenous preparations described in this paper it is possible to design a parenteral regime to meet all requirements (see 'Appendix').

The complete absence of side-effects in patients treated over several weeks with continuous parenteral nutrition has been a most encouraging

feature. The noticeable well-being of patients on such therapy (Rausch, 1948) with the absence of features such as nausea, vomiting, lethargy and weight-loss contrasts markedly with patients treated along the lines of former regimes who rapidly become enfeebled and cachectic (Lee & Shortle, 1965; Kennedy *et al.*, 1963). However, Lawson (1965) found little evidence of subjective improvement in his series but suggested that bodily discomforts following surgical procedures overshadowed the clinical picture. Our studies do not permit of a comparison to be made of survival rates with and without parenteral nutrition. However, in this series no patient died as a result of malnutrition which is quite different from our experience in similar cases treated prior to the introduction of parenteral nutrition. We feel that cases such as R.J. and M.W. would not have survived or progressed so well without the use of parenteral nutrition.

The nitrogen loss in post-operative states (Brunschwig, Clark & Corbin, 1942) is not related so much to the nature of the disease but more to the length of time for which the patient has been without food. Obviously, if the patient's general condition is good and his nutritional state normal it is of little importance if the patient is without sustenance for a day or two. However, in any disease state it is often impossible to predict the duration of starvation and active measures to forestall a decrease in body protein with its attendant symptoms and complications should be instituted. By such means not only is the mortality rate reduced (Krishnan, Narayanan & Sankaran, 1944; Varco, 1946) but also the morbidity rate. If the loss of body weight is greater than 30% the chance of survival is very poor (Lawson, 1965). Bohmansson (1944) showed that the incidence of complications is higher and the convalescent period longer in undernourished surgical patients than in those adequately nourished.

Earlier suggestions that fat emulsions interfere with membrane permeabilities of artificial kidneys (Kille & Lawson, 1963) and that the use of such emulsions prior to haemodialysis should be restricted (Sherwood Jones *et al.*, 1963; Lawson, 1965) are not supported by our findings. No significant changes in clearances studied were found and particular advantage of this point should be taken in the management of hypercatabolic renal failure where frequent dialysis and parenteral nutrition are required. There appears to be a slower rate of elimination of infused fat emulsion in uraemic states which does not increase following heparin administration (Lawson, 1965) as in normal subjects (Becker, Rall & Grossman, 1955). However, this finding cannot be considered a

contra-indication to the use of intravenous fat in this situation.

Many of the disadvantages seen with the earlier cotton seed oil emulsions such as acute allergic responses and long-term effects such as the 'overloading syndrome' (Shuttleworth, 1963; Wretling 1964; Schuberth, 1964) have not been met with in our patients using soya bean oil emulsion. Reports on prolonged use of fairly high dosage intravenous soya bean oil emulsion are few (Lawson, 1965; Hadfield, 1965b). Lawson (1965) used soya bean oil emulsion at a dose of almost 3 g/kg/body weight/day for periods varying from 8 to 36 days. He found no significant change in BSP clearances, serum bilirubin or serum transaminases (SGOT) levels. In two cases from which he obtained liver biopsies on days 30 and 36 the only change seen was heavy pigmentation of the Kupffer cells. Our findings in respect of liver function have been similar. The fluctuations in serum bilirubin seen in case M.W. were attributed to the patient's infection (Eley, Hargreaves & Lambert, 1965) and not to the fat infusions. Hadfield (1965b) has used soya bean oil emulsion in a dosage of up to 12 g/kg body weight/day in the treatment of a case of fulminating ulcerative colitis without side effects. Likewise, we have been impressed by the absence of side effects when using moderately high doses (3–5 g/kg body weight) in renal failure patients.

Many of our patients so treated have been examples of acute hypercatabolic renal failure with paralytic ileus. Until recent times, the question of daily fluid volume requirements seriously hampered the application of parenteral nutrition to this type of case. However, daily peritoneal dialysis (Pringle & Smith, 1965) or haemodialysis (Silva *et al.*, 1964) or at least frequent haemodialysis, allows removal of sufficient body fluid so that parenteral nutrition provides no problem from a pure volume standpoint. This is equally applicable to paediatric practice (Lee & Sharpstone, 1966) where parenteral nutrition often affords a valuable addition to therapeutic management (Chaptal *et al.*, 1964). Again, the electrolyte contents of some amino acid solutions do not prove a problem and electrolyte stability is maintained by frequent dialysis and appropriate composition of the dialysing fluid. Normally, the electrolyte contents of these parenteral solutions are considered part of the daily replacement regime and the chief cation under consideration is sodium. All contain but negligible amounts of potassium, indeed it often needs to be added. The solutions used here did not have any effect upon the acid-base balance of our patients (Wretling, 1948).

In this study, there were two reasons for not attempting to measure nitrogen balance. Firstly, there is a large literature on the ability of amino acid solutions to reduce the degree of negative balance or maintain positive nitrogen balance (Lidstrom & Wretling, 1951; Elman, 1947; Abbott & Albertsein, 1963; Larsen & Brockner, 1965), and secondly, that many of our patients were hypercatabolic. In addition many patients had infections for varying periods, variable pyrexias, anaemia and metabolic acidosis as part of their uraemic picture. In such patients, various factors influencing nitrogen balance come into play at varying times but tending to decrease with time, such as tissue destruction, wound healing, hormone responses to stress, involuting uterus and absorption of large amounts of extravasated blood. Thus for many of the same reasons it has not been possible in the majority of cases to compare the daily rate of blood urea rise, but in those cases where it has, parenteral nutrition (nitrogen) has not accelerated urea production. However, cautious interpretation of daily blood urea increments is required for the reduction in protein breakdown with time is not necessarily dependent on the diet used (Maher & Schreiner, 1961; Berlyne *et al.*, 1966).

Further it is important to realize that even forced feeding of patients during the post-operative catabolic phase will not completely abolish the negative nitrogen balance. The extent of the negative nitrogen balance can be considerably reduced by provision of adequate calories and amino acid nitrogen (Wadstrom & Wiklund, 1964; Lawson, 1965; Johnston, 1965). Some workers (Moore & Ball, 1952) express the view that provision of protein and calories are valueless during brief catabolic periods because loss of nitrogen is unavoidable and there is a decreased utilization of protein. There is some evidence that the retention of amino-acids is greater 5 days after operation than at 3 days and thus it has been suggested that intravenous nutrition might be started at the 4th or 5th post-operative day. Nevertheless, there is evidence that amino acids infused during the catabolic phase following injury are utilized by the body (Larsen & Brockner, 1965). ¹⁵N-labelled glycine given post-operatively can be detected in the framework of tissue protein very quickly (Johnston, 1965). Thus, on balance, even if all the nitrogen supplied in the immediate post-operative period is not utilized, nevertheless the degree of negative nitrogen balance is very much reduced (Freuchen & Ostergaard, 1964; Lawson, 1965) and this can only be of benefit to the patient.

A particularly important aspect of nitrogen balance in renal failure presents in those patients being treated by peritoneal dialysis. Here, considerable protein losses occur (Boen *et al.*, 1962; Berlyne *et al.*, 1964) with a fall in plasma albumin which is replenished only very slowly (Berlyne *et al.*, 1964). Current studies (Berlyne & Lee, 1966) show that considerable quantities of amino acids (including all the essential ones) appear in the peritoneal dialysate. Since the amino acid pool is only of the order of 1–3 g, with a half-life time of about 1 hr, considerable leaching out of amino acids occurs and their replacement is essential. In patients not able to feed normally, parenteral nutrition achieves this aim but the replacement therapy should be given at the end of the procedure or between peritoneal dialyses rather than during the dialysis when the infused amino acids may be leached out rapidly.

In an attempt to meet the anuric patient's protein requirement Alwall (1964) recommends giving intravenous aminosol during haemodialysis in an attempt to replete the tissues with amino acids and protein and ultrafiltrating the excess fluid. However, the low molecular weight of the amino acids makes it extremely likely that most of them will diffuse out into the dialysate and, again, it would seem advantageous to dehydrate the patient first and supply the amino acids intravenously after the procedure. The fat emulsions, as previously indicated, can be safely given during dialysis.

Blagg, Parsons & Young (1963) studied the effect of giving glucose and protein in the dietary management of acute renal failure. They found that protein of high biological value did not appear to increase the rate of urea production but they used suboptimal caloric intakes incapable of supplying basal metabolic requirements. Likewise studies by Lawson *et al.* (1962) suggested a similar conclusion, though their control and test periods were not strictly comparable.

Not infrequently, a patient with chronic renal failure who has been well maintained by dietary measures, suddenly deteriorates as a result of some intercurrent illness and becomes progressively uraemic with nausea, anorexia and vomiting. Many of these patients are dehydrated. Treatment by a dialysis procedure is not always feasible. We have found that parenteral nutrition with amino acids and fat emulsions often remarkably improves these patients, not only rehydrating them but reducing their catabolic state and obviating the need for a dialysis. Similar but more elaborate studies with similar results have been made by Giordano and his colleagues (Giordano, 1963). On several occasions we have treated patients with advanced chronic renal

failure by complete parenteral nutrition and then been able to start them on a Giordano-Giovanetti dietary regime without the need for an intervening peritoneal dialysis (Shaw *et al.*, 1965).

The daily caloric requirements for man have been calculated (Hegsted, 1964) and approximate to 1900 calories for an 80 kg man per day. A table indicating approximate daily requirements of other dietary constituents is shown in the Appendix. It must again be emphasized that on any dietary regime protein must be present otherwise gross wasting will occur. In a regime devoid of protein, the patient will lose labile body protein stores from viscera and blood, and later from less labile protein stores in viscera and muscles (Munro, 1964).

Whilst there may not be complete agreement as to the precise daily requirement of the various dietary constituents in acute disease states, nevertheless modern parenteral nutrition allows a good attempt of achieving a near ideal. Furthermore, such regimes can be maintained over prolonged periods without risk to the patient. Although this paper deals primarily with parenteral nutrition in the management of renal failure, the principles outlined here can be applied to any clinical situation.

Summary

The application of parenteral nutrition to the management of renal failure has been studied. The solutions used have been casein hydrolysates and soya bean oil emulsions. The effects of such emulsions upon artificial kidney membrane clearances have been studied and no significant changes found. Patients have been treated with complete parenteral nutrition for 6–31 days without any acute or chronic toxic effects being seen. As a result of using parenteral nutrition in the cases described, there has been an obvious overall improvement in their general well-being, marked loss of weight has not occurred and convalescence has been considerably shortened. The report is a predominantly clinical investigation and the prin-

ciples outlined apply to any clinical situation. It is concluded that amino acid solutions and fat emulsions provide a valuable adjunct to the management of renal failure, that they are safe even over relatively long periods at moderately high dosage and do not decrease the efficiency of haemodialysis.

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Appendix

Most calculations for daily requirements of dietary constituents were based on the following table (Schuberth, 1964) although for individual cases it was considerably modified, particularly with reference to fluid allowance.

Basic daily minimum caloric requirements and dietary source

	Per kg body weight	For 70 kg man
Water (ml)	25–35	1500–2500
Calories	25–30	1750–2100
Protein (g)	1	70
Carbohydrate (g)	2	140
Fat (g)	2	140

The amino acid solutions used were mixtures derived from a dialysed, enzymatic casein hydrolysate and thus contained all essential amino acids. The amino acid mixtures contain about two-thirds free amino acids of which nearly 40% are essential, and one-third low molecular weight dialysable peptides. The carbohydrate content of high calorie amino acid mixture is fructose, an advantage when considering the glucose intolerance of uraemia and post-operative states. The remaining calories were derived from alcohol, 1 g corresponding to 7.1 calories.

The soya bean oil emulsions ('Intralipid') have the following composition: 20% emulsion con-

	Calories/l	N ₁ (g/l)	Protein (equiv.)	Na+ (mEq/l)	K+ (mEq/l)
Aminosol-fructose-ethanol					
Aminosol	100	4.25	25.6	54	0.15
Fructose	600				
Ethanol	175				
Aminosol 10%	320	12.75	78.6	160	0.5
Soya bean emulsion 10%	1100	0		0	0
Soya bean emulsion 20%	2000	0		0	0
4.3% dextrose	180	0		0	0
10% fructose	400	0		0	0

	Calories	N ₂ (g)	Protein equivalent (g)	Na+ (mEq)	K+ (mEq)
E.g. 700 ml 10% aminosol	224	8.9		112	3.5
300 ml aminosol fructose-ethanol	263	1.3	64	16	0.15
1000 ml 'Intralipid' 20% (2.5 g/kg)	2000	—		—	
Total	2487	10.2		128	0.3

tains 200 g of soya bean oil, 12 g of egg yolk phosphatides, 25 g of glycerol made up to a volume of 1000 ml with distilled water. The main fatty acid constituents of soya bean oil are linolenic acid, linoleic acid, oleic acid and palmitic acid with a small proportion of others. The particle size of this emulsion does not exceed 0.5 μ .

Example of fluid restriction

Fluid allowance was 2000 ml/day. Patient weighs 80 kg. Post-operative oliguric renal failure. Requirements based on 30 calories/kg would be 2400 calories (see table above).

In such a regime, the additional vitamin and electrolyte requirements can be added to the amino acid solution. Such a regime fulfils the best requirements for utilization of the nutrients, i.e. a minimal 200 calories : 1 g N₂ ratio, an optimum fat supply and almost 10% of the total calorie intake is as carbohydrate in the form of fructose.

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