Review Article

Nutritional support of the hospitalized patient

Part I. Background, methodology and techniques

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Summary

The technique of parenteral nutrition is available at most hospitals in the RSA, and can be administered successfully by medical staff if the advice provided here is followed in an obsessional way. Close co-operation between nurses, physicians, surgeons and pharmacists is the key to success, and the development of a 'team approach' cannot be under-emphasized.

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Malnutrition in the hospitalized patient

Malnutrition is commonly associated with acute and chronic illness, and the reason is twofold: firstly, malnutrition lowers host-defence,[1-8] and secondly, the sick patient loses his appetite and suffers 'catabolic' losses of protein and energy.[9-13] A series of large studies on the nutritional status of medical and surgical patients in hospitals in the USA[14,15] and Europe[8,16] were necessary to awaken the clinician to the enormity of the problem. These studies demonstrated that between 40% and 60% of patients in westernized communities had significant depletion of their body stores of protein and energy. By extrapolation, it is likely that a similar proportion of inpatients will be affected in hospitals for White South Africans. Initial studies have shown the rate to be far higher, reaching 80% among males and 55% among females, in hospitals for urbanized Blacks.[17] Up to a decade ago such findings would have been treated with indifference, as they were accepted as an integral part of the disease process which could only be reversed on recovery. However, present-day techniques of hyperalimentation have made it possible to maintain nutritional status in the face of serious disease. This is of vital importance because malnutrition is associated with a wide range of immunological defects[1-5] resulting in decreased host resistance and wound healing, and culminating in increased mortality rates.

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Historical background of parenteral nutrition

The history of the practice of intravenous nutrition is fascinating — one of the earliest attempts known was that of Sir Christopher Wren, to whom so much of the architectural elegance of London can be attributed, being best known as the architect of St Paul's Cathedral. In 1656 he ran a series of experiments, injecting nutrients into the veins of dogs. He used a goose quill attached to a pig's bladder for the intravenous administration of a solution containing ale, opium and wine! The results of these experiments, as well as the attempts of others to transfuse animal blood into human beings, were disastrous for reasons that now appear obvious.

It was not until the pioneering work of Lister (1870) and Pasteur (1877) on the identification of bacterial contamination and the use of sterile techniques that a solution with a reasonable chance of success could be designed. Dextrose-containing solutions began to be used in postoperative management after the appearance of the work of Kausch[18] in 1911, which was followed by the introduction of sterile protein hydrolysate solutions by Hendriques and Anderson[19] in 1913. However, progress towards total parenteral nutrition was slow, and it was really only after Dudrick demonstrated in 1969 that beagle puppies could develop normally on solely intravenous nutrition consisting of hypertonic glucose, a complete spectrum of synthetic amino acids, vitamins, minerals and trace elements administered via long cannula into the subclavian vein, that intravenous nutrition became recognized as a possible alternative to that by the normal route.[20]

The metabolic response to acute illness

The acute stress reaction that accompanies illness results in a change in hormonal regulation; this permits an alteration in metabolism which optimizes the chances of successful recovery. Insulin resistance and increased catecholamine, corticosteroid and glucagon secretion characterize the reaction.[21] Endogenous metabolic pathways are switched from a predominance of substrate conservation to substrate mobilization from tissue stores. This allows for the accelerated protein synthesis required for tissue repair. The increased demand for energy is provided for by increased fat mobilization and gluconeogenesis. While endogenous protein breakdown is increased to satisfy the extra demand for amino acids (in the absence of dietary intake), the increased flux of amino acids also results in extra substrate being available to oxidative pathways, this resulting in increased hepatic gluconeogenesis, urea synthesis and excretion. This accounts for the well-known catabolic response to acute illness, originally thought to be insensible 'nitrogen-wasting' but now recognized as an appropriate response to acute injury since it is associated with increased visceral (as opposed to skeletal) protein synthesis.[13] It

has long been known that the presence of malnutrition with depletion of protein stores suppresses the catabolic response,[22] and in these patients resistance to disease is decreased and mortality rates are elevated.[8,23] The import of this simple observation is that if body stores and dietary intake are lacking, nutritional support may be life-saving. Parenteral nutrition has been shown to reduce the need for gluconeogenesis by providing exogenous glucose.[18,24] The consequent reduction in urea formation and excretion explains the well-known 'protein-sparing' effects of glucose (Fig. 1).[25] In severely stressed patients it will be necessary to accompany the glucose infusion with exogenous insulin in order to prevent hyperglycaemia.[26] In addition, the infusion of amino acids with the intravenous diet can replace the need for mobilization of body protein stores.[13] While the latter effect will not reduce protein or amino acid oxidation, it will spare body protein stores, thus balancing output by input. Combination of the above two approaches, i.e. infusion of glucose plus amino acids, maximizes protein sparing and synthesis (Fig. 1).[13] This forms the basis of most present-day parenteral nutrition regimens.

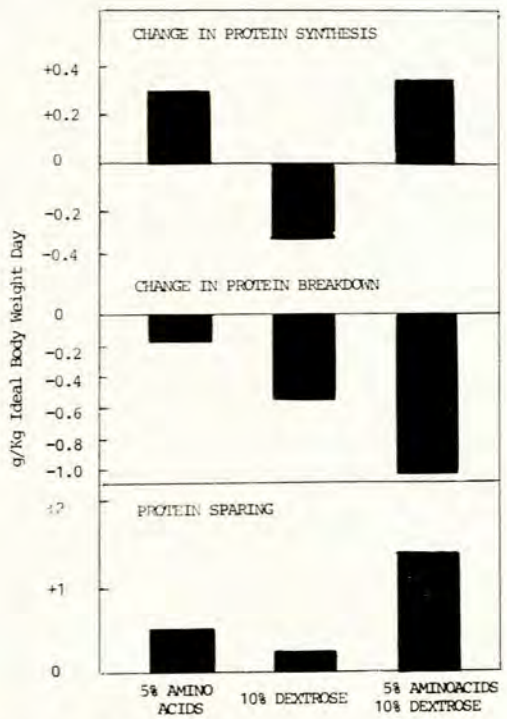

Fig. 1. The effect of amino acids and glucose on postoperative protein turnover and protein sparing.

Assessment of nutritional status

Gross malnutrition is usually obvious but occasionally the situation is complicated, e.g. with loss of lean body mass marked by fluid retention and oedema, and if this is the case more objective measurements of nutritional status are required.[8] In these patients the total body weight might be normal or even artificially increased, and more objective measurements (such as triceps skinfold thickness and mid-arm circumference) which are less affected by the presence of oedema should be employed. These tests are also valuable in assessing response to a particular nutritional support regimen selected.

Hallmarks of protein/calorie malnutrition

Clinical appearance: Muscle wasting.

Weight loss in ward exceeds 10% of total body weight, or weight at admission < 80% of that expected for the patient's height.

Triceps skinfold thickness measurement correlates with the fat stores. Ideally, control values for the population or racial group studied should be obtained. Reductions to below 60% of normal signify severe deficit.[8,14,15] In the absence of controls values below 10 mm for males and 13 mm for females may be used to indicate the need for nutritional support.[27]

Arm muscle circumference on its own provides a rough guide to loss of muscle bulk when compared with age- and sex-matched standards.[27] However, it is better to subtract the contribution made by subcutaneous fat to provide an indirect measurement of arm muscle area. Calculations are easily made from nomograms.[28]

Biochemical indicators: (*i*) plasma albumin < 35 g/l;[8,14,15] (*ii*) serum transferrin or total iron-binding capacity < 1,5 g/l; (*iii*) total plasma proteins < 50 g/l; and (*iv*) retinol-binding protein[29,30] and pre-albumin.[29-31]

Immunological markers: Total lymphocyte count < 1 500/μl.[8,14,15] Skin tests: intradermal injections of common antigens, e.g. *Candida albicans*, streptokinase/streptodornase, tuberculin and mumps virus antigen. Delayed hypersensitivity reactions are measured at 48 and 72 hours;[6] loss of reactivity occurs in prolonged starvation and is reversed by refeeding.[7]

The clinician must be made aware of some difficulties in the absolute interpretation of the above nutritional markers. Racial differences can vary body composition, and specific defects can be induced by disease. Consequently, no single test should be used as proof of nutritional depletion — supportive evidence must be obtained from the remaining indices. As a general rule anthropometric standards should be developed for the community under study,[27] although this approach may be complicated by baseline abnormalities such as obesity in the First World and undernutrition in Third World countries.[17] Body composition may be affected by disease; fluid retention, for example, can invalidate weight for height measurements.[8] Triceps skinfold thickness and mid-arm circumference measurements are less severely affected, but can result in overdiagnosis of malnutrition since some individuals are thin but healthy. Biochemical indicators can also be misleading, the classic example being the hypoalbuminaemia due to liver disease. Albumin, transferrin, retinol-binding proteins and pre-albumin are all synthesized within the liver and may be suppressed in liver failure.[32] However, the hypo-albuminaemia of chronic liver disease is probably of dual aetiology, since malnutrition and total body protein depletion are common in such patients.[8] On the other hand, plasma albumin concentrations can be within the normal range in marasmic patients, since skeletal protein is sacrificed to maintain visceral protein synthesis.[33] Pre-albumin and retinol-binding protein concentrations have been shown to be more sensitive indicators of body protein depletion and more responsive to refeeding.[30,31] Plasma globulins are synthesized extrahepatically, but levels may be 'artificially' increased because of chronic infection. Of the immunological defects associated with malnutrition, many can also be consequences of disease, e.g. disorders of the reticuloendothelial system, hypersplenism and liver disease.[8]

Indications for nutritional support

Support should not be reserved for malnourished patients, but ideally should also be used to prevent depletion in patients who cannot eat. It is easier to prevent loss than to induce anabolism in sick patients. Significant in-hospital depletion is commonly taken to be a weight loss of greater than 10% of admission weight.[33] Consequently, nutritional assessment is extremely important on admission and at weekly intervals. Measurements are easy to take and can be performed in conjunction with the completion of the usual general nursing observations.

Choice of method of nutritional support

Roughly, methods can be divided into 'enteral' and 'parenteral' techniques. In order to decide which approach to use, the reasons for anorexia or decreased body-cell mass must be investigated.

Enteral nutrition

If the gastro-intestinal tract is intact and functional, enteral feeding must be attempted. All too often patients with severe weight loss are directly referred for parenteral feeding. However, various liquid formula diets are currently available that are well tolerated by some patients who are unable to eat a normal ward diet. Enteral nutrition is cheaper and, where successful, more efficiently utilized than parenteral solutions.

Initially the patient should be allowed to drink the solution, usually a volume of 2 litres divided into 3 - 6 portions. If this is unsuccessful, 'tube-feeding' should be attempted.[34] Fine-bore Silastic tubes that are easy to insert and well tolerated for prolonged periods (i.e. 3 - 4 weeks) are now available. Infused at a constant rate over 24 hours via such tube systems, the liquid formula diet is better tolerated than in bolus form, since the absorptive capacity of the gut will be maximized. Diarrhoea will indicate intolerance, most commonly caused by osmotic load or disaccharide intolerance. The solution should then be reduced to half-strength and gradually increased back to full strength after the diarrhoea has stopped for 3 days. In the event of further diarrhoea lactose-free solutions should be tried. Only then should failure lead to total parenteral nutrition.

Parenteral nutrition

Unlike the enteral solutions parenteral diets are not fully formulated but require admixing either at the bedside or in the hospital pharmacy. The ideal would be the designing of a single solution that has the composition of the digested and absorbed normal enteral diet. Such a solution is at present unavailable in South Africa because of factors relating to instability.

The major differences between a normal diet and those commonly used for parenteral nutrition is the form in which energy is supplied, i.e. fat is replaced with carbohydrate. The main explanation is one of cost, but glucose/amino acid solutions are also more stable than fat emulsion/amino acid solutions. Such combinations of glucose and amino acids have been shown to be strongly anabolic, both in the healthy and in the acutely stressed postoperative patient.[11,13,26] Protein sparing can be achieved by the simple use of amino acids alone,[11,12] but the progressive addition of glucose in turn progressively enhances the amount of nitrogen retained.[24] As described earlier, the problem is that the higher the concentrations of glucose used, the higher the osmolarity and therefore the tendency to induce thrombophlebitis. Consequently, solutions with a final glucose concentration of greater than 10% should never be given via a 'peripheral' vein; central venous catheterization is mandatory. The alternative is to keep the glucose concentration down and use fat emulsions (e.g. Intralipid 10% — osmolarity 250 mOsm) as the major energy source. This is termed the 'peripheral system'.

Peripheral system. A degree of 'protein sparing' can be achieved by low-kilojoule regimens consisting of combinations of hypotonic glucose (5%) and amino acids (3,5%).[11,12] However, these regimens rarely maintain nitrogen balance, and cannot maintain energy balance. Alternatively, energy balance can be achieved by the addition of a 10 - 20% fat emulsion. This mixture has a considerably lower osmolarity and is reasonably well tolerated for periods of up to 7 - 10 days. Note that the two solutions must be given simultaneously — amino acids given on their own in concentrations greater than 3,5% are poorly tolerated by peripheral veins. Generally the tolerance level for peripheral veins is taken to be 600 mOsm.[35] However, there are a few reports of solutions of higher osmolarity being used successfully, provided cortisol 5 mg/l is added.[36] Most authorities accept that there is a place for peripheral hyperalimentation in patients requiring intravenous feeding for less than 2 weeks.

Central system. The solutions given here, for example 4,5% amino acids and 25% glucose, are hypertonic (osmolarity 1 900 mOsm) and must only be given via a central vein catheter. The rate of blood flow within central veins is sufficiently high to cause rapid dilution of the total parenteral nutrition solution. This allows far more flexibility in the composition of the solutions used. The mixtures should be tailored to meet individual requirements, as explained in the next section. Glucose remains the major energy source. However, caution is necessary to avoid exceeding the energy requirements (as was previously advocated in burn patients) in order to suppress catabolism. This results in a high respiratory quotient and excessive carbon dioxide production from oxidation of the excess glucose; in sick patients (e.g. those in intensive care) this can precipitate respiratory failure.[37] Estimation of the energy requirement is therefore clearly important, and is described in the next section. Essential fatty acid deficiency can be prevented by the infusion of 1 litre of 10% Intralipid solution each week.[38]

The 3-litre bag system. This is a relatively new development. Its usefulness and efficacy have been proven in Europe and it is associated with significant reductions in complications.[38,39] Similar encouraging results have been obtained at our unit in Durban.[40] It allows for a more controlled infusion which may be changed only once a day, this resulting in an important reduction in nursing time and supervision. Preliminary studies from Europe suggest that, provided the solution is used within 24 hours, Intralipid may be mixed with the glucose and amino acid constituents to provide up to 50% of the total energy requirement.[41] However, further studies on the stability of this solution under local conditions are awaited. The container consists of a sterile 3-litre capacity PVC bag with sealed inlet and outlet tubing. Various combinations of nutrient solutions can be admixed either under gravity flow or with the use of a special perspex evacuation chamber (Travenol). This shortens the process considerably. The mixing can be performed in a side-ward, but is probably best handled under sterile lamina-flow conditions by the hospital pharmacist.

The team approach

Most hospitals in Europe and the USA have now adopted this. Since parenteral nutrition cannot be regarded as primarily a medical or a surgical subspecialty, the obvious answer is to form a team. Included within the team are a physician and surgeon who select the patients, insert the central venous catheters and supervise day-to-day management, a pharmacist who supplies and mixes the various solutions under appropriate sterile (lamina-flow) conditions, a nurse who ensures adequate supervision of drip infusion rates, changes the bottles and giving-sets, redresses the cannula entry site and collects 24-hour urine specimens, and finally a dietitian to advise on nutrient requirements. Such a team allows a strict protocol of management to be followed, which has resulted in dramatic decreases in complication rates.[38,39,41-43] The results of one such team[41] are used to illustrate this point (Table I).

Central venous catheterization

It would be fair to say that if it were not for the fears of clinicians concerning the insertion and care of central venous lines, parenteral nutrition would be far more commonly used. However, the technique in itself is relatively simple, but must be performed

TABLE I. THE TEAM APPROACH — PATIENT COMPLICATIONS[41]

	With team approach (Group A)	Without team approach (Group B)
Complications of catheter insertion		
Pneumothorax	0	47 (12%)
Haemothorax	0	9
Pleural effusion	0	3
Brachial plexus injury	0	3
Subclavian artery injury	0	7
Catheter embolism	0	5
Catheter malposition	9 (3,17%)	52 (13,2%)
Hydromediastinum	0	2
Metabolic complications		
Electrolyte imbalance	6	59
pH imbalance	6	31
High ammonia level	2	17
Trace element deficiency	2	8 (clinical symptoms)
Hyperglycaemic non-ketotic dehydration	0	11 (8 died)
Folate deficiency	8	?
Essential fatty acid deficiency	0	9 (clinical symptoms)
Rebound hypoglycaemia	0	17 (2 died)

under the strict conditions outlined below. In this way central venous catheterization can be safe and effective with minimal risk of complications.

Method

Infraclavicular subclavian vein cannulation is preferred for nutrition catheters. Ideally all such catheters should be inserted in the operating theatre, but if placement is done in the ward strict aseptic techniques must be used. A 35 cm silicone catheter with detachable hub is recommended (Vygon). The patient is placed in the Trendelenburg position at 15 - 20° from horizontal, and the skin over the right anterior chest wall is cleaned with chlorhexidine and then povidone-iodine. A small roll is placed between the shoulder blades, the patient's arms being at the side and the head turned to the opposite side to aid insertion of the catheter. The physician is gloved, gowned and masked.

Infiltration of subcutaneous local anaesthetic is extended from the midpoint below the clavicle to a convenient point on the flat anterior chest wall approximately 8 cm inferomedially. A 0,5 cm incision is made below the mid clavicular point and the needle and cannula are advanced (immediately below the clavicle), aiming medially for a point just above the suprasternal notch. Once the subclavian vein has been entered the needle is withdrawn, leaving the plastic sheath within the vein itself. The silicone catheter with the stilette *in situ* is introduced until 10 cm remains protruding. The patient is asked to bear down while the catheter is passed. Both the stilette and the plastic sheath can now be removed *in toto* leaving only the silicone catheter in the vein. The needle and sheath are now reinserted 8 - 10 cm below the original puncture site and pushed up to the incision below the midclavicle. Great care is necessary to prevent damage to the silicone catheter by the advancing needle. The needle is again removed, leaving the plastic sheath protruding through the skin. The catheter is passed down the sheath retrogradely until it emerges from the puncture wound at the end of the sheath. The cannula is removed, the detachable hub fitted to the catheter and the hub connected to a giving-set. Free return of the blood is checked by lowering the bottle, and the catheter hub is then fixed to the skin with 2 nylon sutures. A third nylon suture closes the skin incision. The sites of skin puncture are sprayed with povidone-iodine spray, and povidone-iodine ointment is applied around the exit site. A small gauze swab should cover the skin incision and the catheter hub, and the whole area is sealed with a clear plastic adhesive membrane.

A chest radiograph is taken to check the catheter position and exclude the possibility of complications of insertion before any hypertonic solution is given. Infusion should therefore begin with an isotonic solution (e.g. Plasmalyte L).

Care of the line is as important as the insertion procedure. The giving-set and adhesive dressings must be changed every 3 days. The skin must be mechanically cleansed using acetone and povidone-iodine. Iodine ointment must be applied to the exit site at each change. Skin swabs and blood samples from the catheter are cultured weekly. The skin must be inspected for inflammation, erythema, drainage and crusting. It is generally wise to keep the line for the administration of nutrient solutions only: central venous pressure monitoring, blood administration and blood sampling for routine laboratory tests must be avoided.

Calculation of patients' requirements

The levels of protein and energy required change in association with the metabolic upset. The aim of nutritional support must be to balance losses. Excessive support can be as hazardous to the patient as starvation.[37] Consequently, both dietary input and excretion rates must be accurately monitored. Since the major excretory organ of the body is the kidney, valuable information pertaining to body losses can be calculated from the rate of excretion of various urinary constituents. This underlines the extreme importance of training nursing staff in the ward to collect *complete* 24-hour urine samples.

For maintenance in health. Requirements have been calculated in relation to age, sex and physical activity. For the average 65 kg male participating in light activity 40 - 60 g protein and 11 300 kJ (2 700 Kcal) of energy should maintain the nitrogen and energy balance.[44] For the standard 55 kg female 40 - 50 g protein and 8 370 kJ (2 000 Kcal) should suffice. In addition, 2 - 3 litres of fluid are required together with 70 mmol Na^+, 50 mmol K^+ and the recommended dietary allowance (RDA) of vitamins[45] and trace elements.[46]

In sickness requirements vary and should be assessed in the following manner. In practice the normal requirement as calcu-

lated above is provided until individual balances can be achieved in the following manner:

Protein balance. Twenty-four hour urine samples should be collected and analysed in the routine laboratory for urea content. From this the rate of protein oxidative (or 'catabolic') losses may be estimated as follows:

6,25 (24 h urinary urea (mmol/d) x 28/1000).

To this figure should be added an estimated allowance for non-urea nitrogen losses, e.g. via urinary ammonia, faeces and skin, of approximately 22 g/d.[10] The protein balance can then be calculated from the difference between dietary intake and the above calculation of protein losses.

Energy balance. The conventional method for calculating the expected basal energy expenditure is the Harris-Benedict equation: (*i*) for women = 65,5 + (9,6 x W) + (1, 8 x H) — (4,7 x A); and (*ii*) for men = 66 + (13,7 x W) + (5 x H) — (6,8 x A), where W = body weight in kg, H = height in cm, and A = age in years. Since acute stress will be associated with increased metabolic expenditure, energy intake will have to be higher to maintain balance. One method of quantifying the increase is illustrated in Fig. 2. Alternatively, ..ctual energy expenditure may be calculated from oxygen consumption rates, particularly in intensive care patients. One litre of oxygen consumption is approximately equal to 20 kJ.

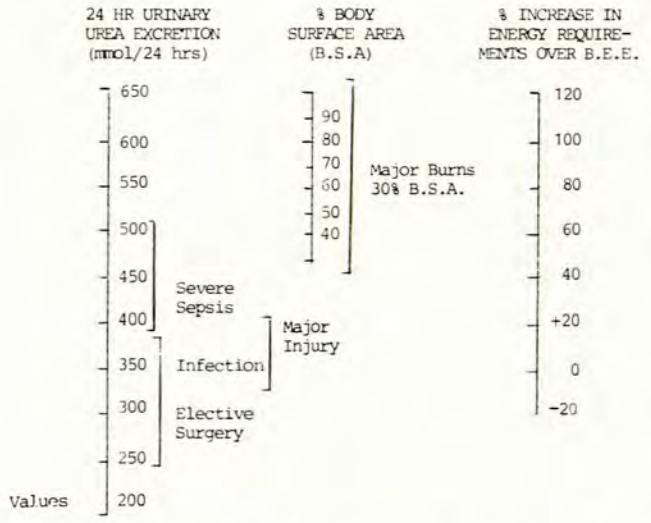

Fig. 2. The relationship between urinary urea excretion and energy requirements (BEE = basal energy expenditure).

Total fluid and electrolyte balance. In patients with normal hydration this can be calculated as the previous day's urine output plus 500 ml. In dehydrated patients fluid volumes should be increased up to 3-6 l/d. In shocked patients central venous pressure measurements must be used to gauge the volume requirements. In the presence of fluid retention and oedema the total fluid intake should be kept at 1 000 - 1 500 ml/d. Routine measurements of both plasma and urinary sodium and potassium will facilitate the maintenance of the electrolyte balance.

Micronutrient balance. As little is known of the exact requirements of vitamins in disease, it is conventional to provide the RDA quantities, except in the case of liver disease where 1,5 - 2 times the RDA is given. The use of total parenteral nutrition has revealed further information on the importance of trace elements in health.[46] The basic intravenous fluids used contain minimal quantities of these elements, as impurities and failure to supplement with zinc, copper, chromium, iodine, selenium and iron has resulted in the clinical manifestation of deficiency.[46] Fresh-frozen plasma is commonly given as a source of trace elements. However, recent sample analysis has demonstrated the inadequacy of this approach and supported the use of more complete commercial mixtures (e.g. Addamel; Saphar Laboratories, Industria, RSA).[47]

Major complications

The incidence of serious complications in well-managed patients is small (e.g. catheter sepsis occurs in less than 5% of catheter insertions). The most important and common complications are outlined below. The reader is referred to the literature for further details of other recognized but rare complications.[48]

Hyperglycaemia. This is the most common and most important metabolic complication. As stated earlier, sick patients are commonly glucose-intolerant and will develop hyperglycaemia when concentrated glucose solutions are infused. In practice the addition of soluble insulin to the nutrient solution is the most effective mode of control.[49] Control is also facilitated if a constant glucose concentration and pumped infusion rate is used. Blood glucose is particularly difficult to control in acutely ill patients receiving corticosteroids. Fig. 3. illustrates such a situation, where a patient with acute ulcerative colitis was being treated with corticosteroids, bowel rest and total parenteral nutrition. Initially various bottles of varying glucose content were used, resulting in serious fluctuations of blood sugar levels ('uncontrolled' period). The regimen was then standardized to contain fixed glucose (25%) and insulin (30 U/l) concentrations. Infusion of this solution at a constant pumped rate resulted in satisfactory control ('controlled' period). In intolerant patients insulin should initially be added at 20 U/l of 25% glucose solution, with 6-hourly 'sliding-scale' insulin for cover. Further additions may be necessary to hold the blood glucose concentrations below 14 mmol/l. Under these conditions electrolytes must be checked daily, as additional potassium may be necessary. Care must be taken to prevent a sudden cessation of infusion; this can be associated with rebound hypoglycaemia.[33]

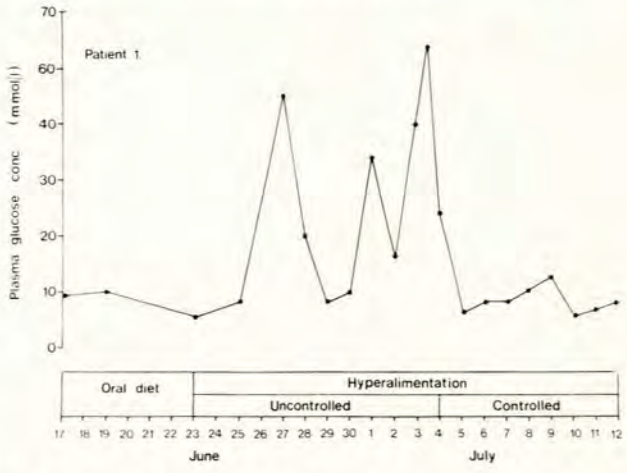

Fig. 3. Plasma glucose concentrations in a patient with acute ulcerative colitis during an oral diet; 'uncontrolled' and 'controlled' hyperalimentation.

Blocked catheter. The most frequent cause of this is stagnation of fluid within the line due to delayed change-over of bottles. Manual or 'tap' control of the infusion rate is notoriously unreliable and, in the absence of 'perfect' nursing supervision, should be avoided by either using a 'dial-a-flow' mechanism or by the incorporation of an infusion pump (e.g. IVac and IMed models). The choice of pump is important. If the multiple-bottle system is used, only a volumetric cassette-type pump will be suitable (e.g. IMed Model 922), while with the 3-litre container peristaltic drip-regulated models (e.g. IVac Model 530) may also be used. This approach has been shown to reduce complications signifi-

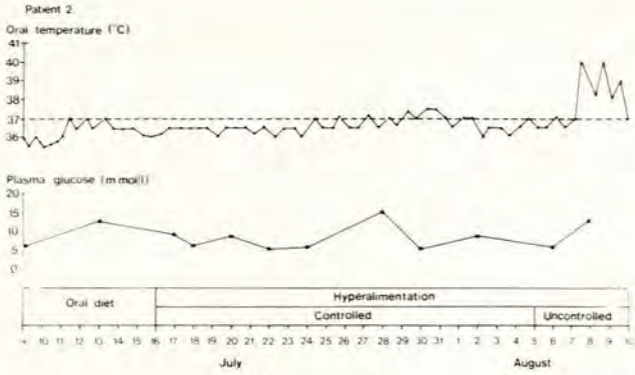

Fig. 4. Temperature chart and blood glucose concentrations of a patient with intestinal tuberculosis during an oral diet, 'controlled' and 'uncontrolled' hyperalimentation.

cantly, and thus prove its cost-effectiveness.[50] Fig. 4 illustrates the problem of associated pump failure, blocked catheter and consequent catheter sepsis in a patient requiring prolonged total parenteral nutrition for intestinal tuberculosis (the 'uncontrolled' period). The addition of heparin in concentrations of 2 000 U/l of fluid has been shown by some workers to prolong catheter life by decreasing thrombotic occlusion and embolism.[51,52] Such quantities do not result in a significant bleeding tendency.

Catheter-related sepsis. In inexperienced hands most catheters will become infected sooner or later, occasionally with fatal results. In experienced hands the acceptable incidence rate is only 3%.[53] The majority of infections will result from poor local catheter care. Organisms invade the catheter from the skin. The following examinations are essential in the exclusion of catheter sepsis: (*i*) clinical examination; (*ii*) full blood count, white cell count and blood culture (peripheral); (*iii*) swab from catheter entry site; (*iv*) blood culture taken from central line; (*v*) culture of urine, sputum, etc.; and (*vi*) appropriate radiographs, ultrasound examination, etc. If there is an obvious source of infection (wound infection, pneumonia, urinary tract infection, intra-abdominal abscess) this should be treated while parenteral nutrition is continued. If there is no clear source of infection the giving-set and infusate should be changed. If the fever continues for 24 hours the central venous catheter should be removed and the tip of the cannula cultured for bacteria and fungi. Catheter-related sepsis usually settles after withdrawal, without the use of antibiotics. The catheter should be removed from any patient with a positive blood culture. Parenteral nutrition should then be continued via a peripheral vein for a period of at least 3 days, before reinserting a central line on the other side.

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