Topics in Gastroenterology 8

EDITED BY

S. C. TRUELOVE

AND

H. J. KENNEDY

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Preface

As with previous volumes in this series, this book is a written version of the annual course in gastroenterology held in January of the current year. It is a great pleasure to thank our contributors whose chapters are based on the lectures they gave in the course.

We are grateful to our publishers, Blackwell Scientific Publications, and in particular to Mr Per Saugman, their Chairman and Managing Director, and to Mr John Robson, their Production Director, with whom it is a pleasure to co-operate.

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Parenteral Feeding

Chapter 1

The development of parenteral nutrition

H. A. LEE

The historical background to parenteral nutrition can be found in reviews by Wilkinson (1963) and Lee (1974). Probably the first attempt at injecting a liquid into the blood stream was made by Dr Robert Boyle in 1659 following a suggestion by Sir Christopher Wren in 1658 that any liquid could be injected into the circulation. Clearly, these ideas arose from the discovery of the circulation by Sir William Harvey in 1625. In 1664 Caspar Scotus injected wine intravenously and then a year later Sir Christopher Wren gave alcohol intravenously. One of the earliest attempts at giving oil intravenously was by Courten in 1679. It is interesting to note that in 1818 James Blundell gave the first successful blood transfusion from one human subject to another.

Probably the first major development in intravenous therapy followed the cholera epidemics of the 1820s and 1830s during which abnormalities in blood chemistry were reported by O'Shaughnessy (1839). As a result of these observations, Dr Latta, a general practitioner working near Leith in Scotland, made up appropriate salt solutions and injected these into stricken cholera patients with considerable success. Then, interestingly, one of the father figures of modern medicine, Claude Bernard, in 1858 recorded his observations on the results of intravenous injection of egg-white into animals. Then, as a result of cholera epidemics, this time in Canada, Hodder (1873) reported his observations following the intravenous injection of milk, the results of which, not too surprisingly, were not very successful. About the same time, Menzel and Perco (1869) carried out comprehensive experiments on animals to which they gave subcutaneous injections of mixtures of oil, beaten eggs, sugar solutions and milk, culminating with the injection of such a mixture into an emaciated patient suffering from Pott's disease. The first report in which glucose was used as a source of calories was pub-

lished in 1899 by Lillienfeld who found that glucose injected intravenously was safe. It fell to Frederich of Leipzig in 1905 to record for the first time the successful maintenance of nutrition by subcutaneous injections of mixtures of water, salts, carbohydrates, fat and peptones for periods varying between 10 and 14 days.

In the early mid-19th century it had been shown that either the administration, or the withholding, of protein could influence nitrogen balance (Bidder and Schmidt, 1852; Voit, 1866). Abderhalden and Rona (1904) were probably the first to show that enzymatically digested protein yielded a solution of peptides and amino acids that could be given intravenously. Some years later, Henriques and Anderson (1913) succeeded in maintaining normal weight in a goat by infusion of such dialysates.

Since then there has been much experimentation with a variety of hydrolysates derived from lactalbumin, bovine serum protein, human serum albumin and horse fibrin. Latterly, casein hydrolysates have been the most commonly used source of protein for intravenous nitrogen administration. However, the early use of protein hydrolysate solutions intravenously was not without setbacks, particularly from toxic reactions. Also, manufacturing difficulties were experienced initially and it was not until the advent of partial enzymatic hydrolysis of protein that preparations containing amino acids and polypeptides were developed without loss of nutritional value or of any of the so-called essential amino acids. This was followed by the development of partial enzymatic hydrolysis coupled with dialysis to remove the larger polypeptides which cause toxic reactions. As a result, Woodyatt *et al.* (1915) and later Rose (1934) suggested the use of parenteral amino acids as a component part of total parenteral nutrition. It was Elman (1937) in St. Louis, U.S.A., who initiated the modern use of protein preparations for intravenous feeding. Shohl and Blackfan (1940) were the first to use a complete mixture of amino acids. Their solution contained 12 dextro and 13 laevo forms of essential and non-essential amino acids and was a modification of a formula proposed by McCoy *et al.* (1935).

The last twenty-five years have seen the development of the pure L form amino acid solutions. These have the advantage of specificity whereas protein hydrolysates contain a fair amount of peptide nitrogen, amonia and other contaminants. Furthermore, there has been an increasing awareness that synthetic crystalline L amino acid solutions need to be balanced, not only with respect to essential amino acids but also in terms of non-essential nitrogen components.

Likewise, in the last two decades there has been a rationalization of the types of substrate used intravenously as a source of energy. Although many different substrates have been investigated, only two need to be considered in modern total parenteral nutrition, namely, glucose and a fat emulsion, such as soybean oil emulsion. Kerr and Pauly (1942) showed that invert sugar could be used intravenously and Wennig (1955) described the use of intravenous honey. Subsequently, sorbitol, xylitol and fructose have all gone through vogues of fashion in intravenous nutrition regimens (Lee, 1974), but really offer no advantages over the other two substrates. Although glycerol has an equal caloric value to glucose and can be given in dilute solution to man (Bowesman, 1938; Sloviter, 1958), it is a dangerous caloric source with serious side-effects.

Alcohol has had its advocates because of its high caloric value of 7 kcal per gram (Rydberg, 1975) but difficulties have occurred because of its known pharmacological effects. Atwater and Benedict (1896) showed that ethyl alcohol could positively affect nitrogen balance and Rice and Strickler (1952) extensively investigated its clinical use. These observations were further extended by Coates (1972), but in current day intravenous feeding alcohol has little, if any, role to play.

Thus, the past twenty years have seen a prodigious amount of experimental work carried out to make comprehensive intravenous feeding a safe and attainable goal, in both the short-term and long-term management of patients who otherwise could not be maintained in nutritional equilibrium. Estimates of patients requiring nutritional support in hospitals vary from 40–50% (Bistrian *et al.*, 1974, 1976; Hill *et al.*, 1977). However, it is likely that only 5–15% of all such patients actually require aggressive nutritional support and of these only 2–4% will need intravenous feeding. Nevertheless, in this nucleus of patients, intravenous feeding may represent the difference between life and death. Many of the technical problems associated with intravenous feeding have been overcome with such modern developments as better silicone catheters, better understanding of catheter maintenance, and the development of safe constant-volumetric intravenous pumps that can be used both in the hospital and in the home.

Probably the most important aspect of intravenous feeding is to be able to recognize the patient who actually requires this type of nutritional support. Having decided that the need exists, it is then important to ascertain the degree of malnutrition that has occurred. This is necessary, not only for defining the problem, but also to confirm that the treatment given is in fact effective. Table 1.1 shows some of

Table 1.1. *Tests for evidence of malnutrition. A profile based on items 1–6 will give a useful guide to nutritional status*

Factor assessed	*Method*	*Evidence of malnutrition*
1. General appearance of patient	Visual assessment	Wasting, Emaciation
2. Body weight in kg and recent loss	Various scales	$>10\%$
3. Triceps skin fold thickness (TST) (fat energy reserves)	Holtain skin fold calipers	<10 mm in males <13 mm in females
4. Mid-arm circumference muscle (MAMC) Muscle protein reserves (MAMC = arm circumf. $-\pi$ TST)	Tape measure in cm	<23 cm in males <22 cm in females
5. Serum albumin (visceral protein)	Routine lab. test	<35 g/l
6. Serum transferrin, Complement C_3 } short half life proteins	Routine lab. test	<2 g/l
7. Retinol binding protein, Thyroxine binding pre-albumin } ultra short half life proteins	Special lab. tests	<40 mg/l <200 mg/l
8. Urinary hydroxyproline	Special lab. test	↑ Collagen turnover
9. Urinary zinc excretion	Special lab. test	↑ due to muscle and collagen breakdown
10. Lymphopaenia	Routine lab. test	$<1{\cdot}2 \times 10^9/1$
11. Plasma amino acid profile	Specialized tests	Changing valine/glycine ratio
12. Urine 3-methylhistidine	Specialized tests	Increased muscle breakdown
13. Hair root morphology	Tweezers and microscope	More telogens and dysplastic hairs

the measurements used and how they are interpreted. Furthermore, it is important to appreciate that such measurements can easily be undertaken by junior medical and nursing staff, are reproducible, and do not require expensive or complicated equipment.

Having ascertained that a patient is in need of this form of treatment, then the question of angioaccess is the next important step. Much has been written about the techniques available for gaining angioaccess (Dudrick and Long, 1977; Parsa *et al.*, 1972). Basically, there are two main methods, both of which require meticulous aseptic technique. One can either choose a peripheral site and use a long catheter (Abbott flexible drum catheter) or go centrally, using a percutaneous venous route to gain access to the subclavian vein, either supraclavicularly or infraclavicularly. When this latter technique is combined with subcutaneous tunnelling, the catheter can be left in place for weeks on end. Angioaccess in such patients must be regarded as their lifeline and be cared for appropriately (Phillips, 1976). Each individual will perfect his own technique and it is presumptuous to say that one method is better than another in experienced hands. Furthermore, the development of silicone catheters, which are non-irritant, means that the catheter can be left in place for a long time (Broviac and Scribner, 1974). There is no real justification for using shunts or fistulae.

With the better development of administration lines the need for 'piggy-backing' is avoided and the risk of infection considerably decreased. Initially, half-litre bottles were used but nowadays there is a choice between one litre bottles or using the 'big bag' (2–3 l) system (Cosh *et al.*, 1977). This latter method has been developed principally as a result of the studies of Solassol and Joyeux (1976), working in Montpellier in France. They have shown that all nutritional requirements can be mixed in a single bag, even including a fat emulsion. For those who are sceptical of such an approach, the use of one-litre bottles and special W giving sets (welded units) enables all ingredients to be given through a single catheter. There is general agreement that intravenous feeding lines should be used solely for feeding purposes and not for giving blood or plasma, or for measuring central venous pressure. The care of catheter lines, in particular of the skin around the entry point, has been described in detail by Colley (1977). A comprehensive review of the technical aspects can be found in Parsa *et al.* (1972).

Having recognized the patient who requires intravenous feeding and having gained angioaccess, the problem then is what to give, how much to give, and over what time. Fortunately, there is now some agreement

about the nutritional requirements of various categories of patient, as shown in Table 1.2. For energy requirements, many would advocate a 50–50 ratio of glucose and fat for energy provision. However, if a patient is known to be septicaemic, or has a known fat intolerance, then more reliance can be made upon concentrated glucose solutions (40–50%), with or without insulin. If insulin has to be given, it can be added to the bottle, even though some will be lost by adhering to the glass surface. Since the aim is to keep the blood sugar below 10 mmol per litre, more soluble insulin can be added if necessary as boluses. The advantages of using a combined fat and glucose regimen are (a) the provision of each substrate is kept well within an individual's tolerance; for example, for a 70 kg man requiring 3,000 kcal per day, this would mean glucose 0·233 g/kg per hour and fat 0·089 g/kg per hour, (b) the volume is kept small, (c) the osmolar load is minimized, being 129 mOsmol/hr, (d) the percentage of energy provided that is lost in the urine is minimal, being less than 5% and (e) minimal monitoring is required and possibly less soluble insulin required.

As for nitrogen sources, it is now generally agreed that there is no single ideal amino acid solution, but there is a range of solutions all of which are adequate. Indeed, Tweedle *et al.* (1973) showed that some of the more modern synthetic crystalline L amino acid solutions, although better defined and with fewer contaminants, were not more effective in maintaining nitrogen balance than the earlier casein/fibrin hydrolysates. Over the past ten years there has been a proliferation of different amino acid solutions said to be necessary for specific situations, but no great variety is required. Indeed, all that is needed is a high nitrogen source solution providing 16–18 g/l, a maintenance solution providing approximately 10 g/l, possibly a specific solution for liver failure (Aguirre *et al.*, 1976) and a further specific one for paediatric use (Lee, 1979 a and b).

Clearly, total intravenous nutrition must take into account not only energy and nitrogen, but also water, electrolytes, fat-soluble and water-soluble vitamins, trace elements, folic acid and phosphate. Each year more is being learned about the so called micronutrients, so that, although we still do not know the precise requirements, such elements as selenium, zinc, chrome, nickel and others may need to be included (Kay *et al.*, 1976; Shenkin and Wretlind, 1978; Aggett, 1979; Van Rij *et al.*, 1979).

The various ingredients need to be combined in optimum ratios, as suggested in Table 1.3. Just as formerly it was inappropriate to talk about 'a drop of water with a pinch of salt' as intravenous solution,

Table 1.2. *Catabolic rates and estimated requirements*

	Protein g(N.g)/day‡	Energy kcal/day	gN/kg body wt	kcal/kg body wt	kcal/gN*
Apyrexial medical patient	45– 75 (7·2–12)	1500–2000	0·16–0·20	30–37	= 170
Post-operative (uncomplicated)	75–100 (12–16)	2000–3500	0·20–0·22	37–45	= 190
Hypercatabolic e.g. burns	> 100 (> 16)	> 3500	0·22–0·30	46–52	= 210

Notes

1. Wide ranges of requirements for each group accentuating risk of underestimating requirements.
2. 1 g nitrogen ≡ 6·25 g protein ≃ 30 g muscle.
3. Many patients breaking down 20 g nitrogen per day ≃ 0·6 kg muscle – hence potential for rapid wasting.

* Recent evidence suggests that in hypercatabolic and normocatabolic patients that the ratio is lower and higher respectively (Woolfson, 1979). However, the generally accepted 200:1 ratio meets most requirements.

‡ Best estimated by measuring urinary urea nitrogen (Lee and Hartley, 1975).