# Parenteral Nutrition in Acute Metabolic Illness

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edited by

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# Preface

The clinical and metabolic consequences of major trauma, complicated surgery, gastrointestinal failure and severe infections are well recognized. With their increasing debility the management of such patients becomes more difficult. The central role of nutrition in the care of these patients is becoming increasingly appreciated. There can be no excuse for failing to meet nutritional demands simply because a patient cannot take food orally or through a nasogastric tube. To allow starvation and severe wasting (negative nitrogen balance) with its attendant *sequelae* to occur is tantamount to clinical incompetence. The value of complete parenteral nutrition in containing and reversing many of the consequences of hypercatabolic states has become very evident over the past twenty years.

The apparent "ideal" post-operative treatment of 2 litres 5% dextrose and 1 litre normal saline daily still so widely practised should be brought under careful scrutiny. Careful examination will then show how totally inadequate such a regime is for many patients. A considerable amount of research endeavour has been directed to improving parenteral nutrition so that there are now available very safe and efficient intravenous nutrient solutions. It is now possible to devise total parenteral nutrition regimes meeting all major and minor requirements over prolonged periods.

The purpose of this book is to present an up-to-date account of the pharmacological, biochemical and clinical advances in intravenous nutrition. The basic facts of intermediary metabolism, water and electrolyte requirements as applied to parenteral nutrition have been set out in the first section. This is followed by a section of applied physiopathology explaining the disturbances of metabolism in severely ill patients. Anyone involved in the management of intensive care patients whether at clinical or laboratory level or purely from a research standpoint will find material of interest in this book. This volume will also serve as a comprehensive source of reference in this field.

Those involved primarily with the clinical management of patients will find guidelines set out as to the most appropriate nitrogen and caloric source solutions to use, in what ratios they should be given, and what potential hazards to be wary of. The sections on clinical applications of parenteral nutrition, and on techniques and solutions should dispel any fears that those unfamiliar with this treatment may

have. Every effort has been made to indicate what sort of patients will benefit from this treatment and how best it is given. The decision to start parenteral nutrition demands careful assessment and thought, but it is a logical step and capable of measurement. There are hazards of parenteral nutrition, but most of these are avoidable. To start parenteral nutrition regimes where not indicated or without assessing all the patient's metabolic requirements will only lead to disillusionment. Parenteral nutrition must be seen as part of the overall metabolic management and not in isolation.

There are two important chapters dealing specifically with the special application of parenteral nutrition regimes and techniques in paediatrics. This is an interesting and still developing area of intravenous nutrition and much work remains to be done.

Though the currently available solutions for complete intravenous nutrition have proved their worth there is still room for improvement particularly with the formulation of nitrogen source solutions. Further developments, as hitherto, will depend upon close collaboration between the pharmaceutical industry, clinicians, laboratory personnel and other non-clinical para-medical disciplines.

Finally, I would like to thank all my co-authors for their enthusiasm and diligence in making this book possible.

H. A. LEE

*January 1974.*

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# Section I
# Introduction

# 1

# Historical Review of Parenteral Nutrition

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Though parenteral nutrition now forms part of accepted general medical practice in acute medical and surgical illness, it is really only in the last 25 years that the appropriate advances have been made. Parenteral nutrition has progressed from the saline–dextrose regimes to present-day comprehensive intravenous nutrition supplying all the essential nutrients. The origins of parenteral nutrition go back to the seventeenth century when, in 1658, Sir Christopher Wren, the well-known scientist and architect, had predicted that it should be possible to inject any liquid into the blood stream. His friend, Dr. Robert Boyle, proved the possibility in 1659 when he injected opium into the veins of a dog. In 1664 Caspar Scotus (Fortescue-Brickdale, 1904) gave wine (ethyl alcohol) intravenously and a year later, Sir Christopher gave alcohol intravenously. Probably one of the earliest intravenous injections of oil was given by Courten in 1679.

Other early attempts at intravenous nutrition can be read in the review by Wilkinson (1963). He recounts the observations of O'Shaughnessy during the cholera epidemics of the late 1820's and early 1830's who noticed that his cholera patients seemed to develop a deficiency of salts in their blood. On this evidence, Dr. Latta, a general practitioner from Scotland, made up solutions of the appropriate salts and administered them, it seems with considerable success, to patients stricken with cholera.

The first account of parenterally administered fat appears in 1869 by Menzel and Perco, who carried out comprehensive animal experiments and then gave subcutaneous injections of a fat to an emaciated

patient suffering from Pott's disease. Hodder, working in Toronto, tried the effect of intravenous fat in the form of milk as part of his overall treatment of cholera. Leube (1895) administered camphor oil to cardiac patients and suggested that it might be useful as a source of calories. However, Henderson and Crofutt (1905) concluded that no beneficial metabolic effects were achieved when fat was given either subcutaneously or intraperitoneally.

During the first half of this century, parenteral nutrition had been largely based on the intravenous use of dextrose. Dextrose has been extensively studied since 1896 (Biedle and Krause) and is probably the most commonly employed parenteral nutrient other than water itself. This is not surprising when the central role of glucose in overall metabolism, its low cost, its natural occurrence in blood and its plentiful abundance are considered. Another hexose, fructose, has also been extensively investigated as it also occurs naturally in animal tissues as phosphorylated derivatives. Considerable amounts of fructose are consumed in the diet as sucrose or honey. In 1942, Kerr and Pauly showed that invert sugar (containing equal amounts of glucose and fructose) could be substituted for glucose. However, it has never been conclusively shown that either invert sugar or fructose have material advantages over glucose which is well-proved as a nitrogen-sparing nutrient. Wennig (1955) reporting from Europe, described the use of intravenous honey, but this has not been further investigated. In the light of a vast amount of investigatory work there seems little need to look for a hexose substitute when glucose in particular and to a lesser degree fructose, have proved so satisfactory.

In the last decade, some workers have experimented with intravenous sorbitol and more recently, xylitol. Though sorbitol at least is non-toxic this has not been shown to have any advantage over glucose or fructose. As for xylitol, recent reports from Australia warn of adverse reactions to this substance and deaths have been recorded. Currently, in Germany, work is in progress to determine whether the diols might be a useful intravenous source of calories.

Glycerol, which has an equal caloric value to glucose, has also been investigated as a possible intravenous nutrient. In dilute solution and moderate daily dosage this substance is well tolerated in man (Bowesman, 1938; Sloviter, 1958). However, large doses result in toxic reactions such as haemolysis, hypotension and central nervous system disturbances. Currently, the main use of glycerol in intravenous nutrition is as a stabilizer for fat emulsions and not as a caloric source. It is not considered a suitable substitute for the hexoses.

Alcohol, because of its high caloric value of 7 cal/kg, has also

received considerable attention as an intravenous caloric source. Though it is recognized that as a result of its pharmological effects it could never be used as a sole caloric source, nevertheless, it is a useful addition to many intravenous nutrition regimes. Atwater and Benedict (1896) demonstrated that oral ethyl alcohol had a beneficial effect on nitrogen balance. Rice and Strickler (1952) investigated the clinical use of alcohol and stressed its value in attaining daily caloric intake as an additive to many intravenous solutions particularly glucose and protein hydrolysates and emphasized its wide margin of safety. Coats (1972) has also reported on the clinical use of intravenous alcohol and has shown that up to 100 g (700 cal) per day can be safely given.

Following the early unsuccessful attempts to give intravenous fat, the first systematic investigations on the role of intravenous fat emulsions were carried out in Japan in the decade 1920 to 1930. These Japanese workers used lecithin as the emulsifying agent and reported good tolerance in animals (Yamakawa, 1920; Sato, 1931; Baba, 1931). The fat emulsion used was based on castor oil. In 1935, Holt, Tidwell and Scott reported some success with the clinical use of intravenous fat emulsions in the treatment of marasmic children. However, the idea of using intravenous fat emulsions did not gain popularity partly because the emulsions were relatively unstable but more especially because serious toxic reactions occurred.

A fat emulsion consists of a suitable triglyceride oil, an emulsifying agent, water, and a tonicity agent such as glucose or sorbitol. An important breakthrough in the search for a suitable emulsifying agent came in 1943 when McKibbin, Hegsted and Stare introduced soya bean phosphatides. These substances have retained their importance up to the present day. Later, McKibbin, Pope, Thayer, Ferry and Stare (1945) introduced the synthetic stabilizer polyoxyethylene-propylene (Pluronic F68) and were thus able to reduce the amount of soya bean phosphatides required in emulsions.

There can be little doubt that an important driving force in the further research and development of a suitable fat emulsion developed under the auspices of the American Army Medical Services through its research and development command. In charge of this work was Colonel Huber who with a small group of collaborators formed what was then known as "Task Force on Intravenous Alimentation". This group investigated and extensively used a fat emulsion called "Lipomul" which was based on a cotton seed oil. A symposium held in Kalamazoo (Symposium on Intravenous Fat Emulsions, 1957) reported on the clinical and experimental experiences with this fat emulsion which

appeared to cause only a few acute side-effects. However, not long after, the first reports began to appear of the long term effects of such infusions giving rise to the so-called fat-overloading syndrome. This syndrome comprised fever, anorexia, malaise, vague abdominal pain, bleeding phenomena, anaemia, jaundice and hepatosplenomegaly. Such reports caused any enthusiasm on the development of fat emulsions to dwindle rapidly. Thus, in his preface to a whole edition of the *American Journal of Clinical Nutrition* in 1965 devoted to the use of intravenous fat emulsions, J. F. Mueller commented that as yet no safe intravenous fat emulsion was available in the United States.

Up to that time a prodigious amount of work had been carried out not only to find the most suitable fat emulsion but also the best stabilizers and several excellent reviews summarizing all this work have been published (Geyer, 1960; Schuberth and Wretlind, 1961; Edgren and Wretlind, 1963; Wretlind, 1964; Hallberg, Holm, Obell, Schuberth and Wretlind, 1967). However, at about the same time, in Scandinavia, Wretlind and a group of collaborators had been investigating the value of another fat emulsion derived from soya bean oil. Following his researches, Wretlind was able to report to the Kungalv Conference (1962) that with a soya bean oil emulsion it had proved possible to cover the total basal caloric requirements in dogs for relatively long periods without any side effects. At the same conference, Schuberth also reported on his considerable clinical experience with intravenous fat emulsions and on the apparent safety of the soya bean oil emulsion in complete intravenous nutrition regimes. Over the next few years, increasing numbers of reports appeared confirming the complete safety of soya bean oil emulsion both in the short term and long term parenteral feeding and without any occurrence of the over-loading syndrome. More recently, Allen and Lee (1969), Prague Conference (1969) and Wilkinson (1972) have reported that in physio-pathological terms soya bean oil emulsions are completely safe and among some of the safest materials used in clinical medicine. Thus the quest for an adequate safe caloric source has ended with the modern day fat emulsions. Though the soya bean oil emulsions have largely superseded cotton seed oil preparations it must at the same time be admitted that with improved manufacturing processes and better emulsifying agents even the current day cotton seed oil emulsions have a far better record than at the time when Allen and Lee (1969) were making their review.

The background to amino acid therapy centres on the development of protein hydrolysates and the preparation of crystalline amino acid solutions. From the early mid-nineteenth century, it had been known