Home Parenteral Nutrition

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Edited by

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Preface

This Book has been designed to cover all the aspects of Home Parenteral Nutrition (HPN) on basis of the evidence-based medicine but also on the experience of worldwide experts in this field. We are deeply grateful to all the contributors – physicians, surgeons, nurses, dieticians, pharmacists – who contributed to the realization of this Book.

HPN was initiated by some pioneers in the early seventies in North America and in Europe and was initially conceived to provide nutrition to patients who were suffering of life threatening chronic intestinal failure. Progressively, the HPN use was extended to patients with advanced cancer who were enable to eat. HPN being at the edge of medical, ethical, psychological issues, a multidisciplinary approach is mandatory for taking care of these patients.

For these reasons, we felt useful to collect all the knowledge in this field – covering all these aspects of such treatment – in a book. The main objective of this Book on HPN is to share the knowledge and the expertise of clinical researchers in this field with all the teams following patients on HPN.

The first part provides an overview on the history of HPN in the world and the epidemiology in different areas around the world, raising some differences in the use of HPN throughout various countries.

The second part is dealing with the most frequent clinical conditions in which HPN can be initiated, from the short bowel syndrome to the cancer patient.

Part III is devoted to HPN complications but mainly conceived to provide recommendations for preventing these complications.

In the part IV, the authors detailed practical issues – requirements, teaching, monitoring, etc – of HPN including the contribution of pharmacists, dieticians, nurses and physicians.

A special section (V) has been reserved to HPN in children. Indeed, the use of HPN in pediatrics – infants or adolescents – has its specific

concerns ; exchange of knowledge between pediatricians and physicians for adults is obviously a wonderful source for improving our daily practice.

Finally in the part VI, some miscellaneous issues of HPN has been debated. A special interest has been given to intestinal transplantation that is considered in some patients who are on HPN; progress in this field could change our strategy in the next future.

This Book is also dedicated to our HPN patients who – in some way – also participated for improving the practice of HPN in sharing their experience and feelings with the nutritional teams.

We also underline the role of the ESPEN-Home Artificial Nutrition working group that supported the project of this Book, but also provided the opportunity to create a network on HPN in Europe.

Finally we wish to thank CABI Publishing for the joined effort to produce a moderne and updated Book that – we hope – will be of interest for each people being involved in a HPN programme.

Federico Bozzetti Michael Staun André Van Gossum

Part I

Parenteral Nutrition: an Overview

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1 History of Parenteral Nutrition

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Introduction

Although the modern era of home parenteral nutrition (HPN), using central venous catheters to treat patients with disease, began almost four decades ago, its origins are almost four centuries old. A number of authors, including several pioneers in the field, have reviewed various aspects of parenteral nutrition (PN): some focused on nutrients and nutritional requirements (Levenson *et al.*, 1984; Shils, 1984; Winters *et al.*, 1984), others on pharmaceutical developments (Hardy, 1995), fluid administration (Barsoum and Kleeman, 2002), access routes, paediatric PN (Winters *et al.*, 1984) or on combination of these (Meng, 1976; Dudrick, 1977; Macht, 1980; Rhoads *et al.*, 1981; Hartmann, 1985; Wretlind and Szczygiel, 1998; Vinnars and Wilmore, 2003). Here, a very brief overview is provided, with a focus on HPN.

Terminology

PN involves the administration of nutrients using routes other that the gut. This could include infusion of nutrients into veins, arteriovenous shunts, subcutaneous tissue, muscle or bone. Although all of these access routes have been tried at one time or another, PN usually involves the intravenous route, and for patients on HPN it almost invariably involves central venous catheters. The term hyperalimentation, introduced by Jonathan Rhoads in the USA, implies that patients can be given nutrients in excess of their normal requirements, even if they are sick or unconscious. The term 'artificial gut' was used by Scribner *et al.* in 1970 (Scribner *et al.*, 1970) to describe the use of PN to treat patients with intestinal failure (analogous to renal failure or cardiac failure).

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Early Historical Developments

Since venous access is of key importance to the practice of PN, its history can be justifiably said to begin with the discovery, in 1628, of the circulatory system (Harvey, 1628) by William Harvey. By 1658 Sir Christopher Wren and colleagues had reported on the effects of infusing ale, wine, opium and oil to dogs, using hollowed-out goose quills, which acted as needles/catheters, and a pig's bladder which acted as a reservoir. For example, Sir Christopher Wren wrote: 'I injected wine and ale into the mass of blood of a living dog by vein in good quantities, till I made it drunk'.

Some key historical events leading to the successful introduction of PN, first in hospital, and then in the community, are summarized in Box 1.1. It lists the developments under different headings ('General', 'Venous access', 'Macronutrients' (fats, carbohydrates and proteins/amino acids) and 'Other nutrients'), although the developments overlapped in time and were interdependent. Developments in PN, and ultimately in HPN, were facilitated by a better understanding of the metabolic response to trauma, sepsis and other diseases, as well as a better understanding of the nutritional fluid and electrolyte needs of these conditions and their effects on acid-base regulation. Understanding the chemical structure, stability and biological effects of a variety of nutrients that were discovered in the latter part of the 19th century and first half of the 20th century was also very important. However, before PN could become widespread and used to treat patients at home, it was essential that the nutrients could be delivered in a safe and predictable way.

Patients and Indications

The first case of home PN took place in 1969, and was managed by Shils and colleagues in New York, USA (Shils *et al.*, 1970). It involved a 37-year-old woman with a short bowel syndrome, who was given PN for a period of 7 months. She was readmitted for small bowel transplantation, but she died from post-operative complications (see Chapter 3, this volume). This patient was infused through an arteriovenous shunt, which became infected and blocked. Most of the subsequent cases of HPN in the USA and other countries involved central venous catheters.

The first patient to receive HPN in Canada started treatment in 1970, following an almost complete bowel resection due to mesenteric vessel thrombosis (Langer *et al.*, 1973). The patient survived for another 20 years. Another patient, who started HPN in Canada in 1972, probably holds the record for being on HPN the longest (over 32 years; see Chapter 4, this volume).

Following these landmark events, HPN began to be practised in the 1970s more widely in North America and, for the first time, in several European and other countries, such as Australia. With the exception of

Box 1.1. Some key chronological developments leading to PN and HPN

General

1628: discovery of the circulatory system reported by William Harvey.
1658: intravenous infusion of alcohol, lipid and opium into animals reported (experiments began in 1656).
1831: successful intravenous administration of a solution (essentially saline solution) for treating excessive fluid losses due to cholera (Latta, 1831).
1923: Seibert's work on pyrogens (Seibert, 1923, 1963), led to the subsequent description of principles and methods for providing pyrogen-free intravenous fluids.
1904: subcutaneous PN (fat, glucose electrolytes and peptones) in humans (Freidreich, 1904).
1955–1965: peripheral and sometimes central PN was used by clinicians for limited periods (5 or 10% glucose, protein hydrolysates and intravenous fat) (Levenson *et al.*, 1984).
1967: successful intravenous nutrition over prolonged periods, allowing normal growth in beagle puppies (Dudrick *et al.*, 1967).
1967: successful prolonged central venous PN with 20–25% dextrose and 4–5% amino acid solution.
1969: home PN in USA (Shils *et al.*, 1970).
1970: home PN in Canada (Langer *et al.*, 1973).
1970s: home PN in several European and other countries (see text).
1972: introduction of the 'all-in-one' bag for long-term use, which is now routinely used in HPN (Romieu *et al.*, 1972).
1970 to present: evolution of HPN in different ways in various countries (Elia and Baldwin, 1999; Moreno *et al.*, 2001) (see text).
2003: International Organization for Standardization (ISO) produced a document (ISO 14698-1) outlining a strategy for implementing ISO 14644 (limits to particles and bacteria in the environment). This development arose from an outbreak of bacterial contamination in PN bags.

Venous access

1658: hollowed-out goose quills used as needles for intravenous infusions.
1940s: variable success at administrating 15–20% dextrose solutions to humans (Dennis, 1944; Dennis *et al.*, 1948); phlebitis was a problem.
1949: hypertonic dextrose and protein solutions given successfully through central venous catheters in dogs (Meng and Early, 1949; Rhode *et al.*, 1949).
1952: description of central (subclavian) vein cannulation (Aubaniac, 1952), although catheters threaded centrally had been reported as early as 1944 (Levenson *et al.*, 1984).
1967: use of a technique for placement of central venous catheters for hypertonic PN in humans (Dudrick *et al.*, 1968, 1969).
1969: arteriovenous shunt used for venous access in the first patients on home PN in the USA (Shils *et al.*, 1970).

Macronutrients

Carbohydrate

1843: Claude Bernard showed that sugar solutions could be safely given parenterally to animals (Foster, 1899) (later, he injected glucose into one of his own veins).

Box 1.1. *Continued*

1887: Landner proposed that glucose could be used as part of a regimen for 'artificial nutrition'.
1896: successful intravenous infusion of glucose in man (Biedl and Kraus, 1896).
1915: Woodyatt *et al.* reported that up to ~0.85 g glucose/kg/h could be supplied intravenously to humans without resultant glycosurea (Woodyatt *et al.*, 1915).
1967: Long-term hypertonic glucose infusions in humans (Dudrick *et al.*, 1968).

Protein/amino acids

1870–1900: infusions of milk into man, but severe systemic reactions could occur.
1913: successful infusion of non-allergenic protein hydrolysate to nourish a goat for 16 days (Henreiques and Anderson, 1913).
1937: similar and more extensive successes with protein hydrolysates in animals (Elman and Weiner, 1939).
1939: a solution of 2% casein hydrolysate and 8% dextrose was infused into a patient without reaction (Elman, 1937).
1940: synthetic crystalline amino acids infused into infants reported (Schohl and Blackfan, 1940).
1964: crystalline amino acid solution introduced in Germany (Bansi *et al.*, 1964).
1970s: crystalline amino acids replaced commercial protein hydrolysates.
1980s: dipeptides, such as glycyl-glutamine or alanyl-tyrosine, were developed to stabilize unstable amino acids (e.g. glutamine) and solubilize amino acids with poor solubility (e.g. tyrosine). These are used in some commercial preparations today.

Fat

1678: intravenous administration of lipid in animals reported by Christopher Wren.
1869: subcutaneous injection of fat in dogs without adverse effects (Menzel and Perco, 1869).
1869: subcutaneous injection of fat into man suffering from malnutrition and Pott's disease.
1915: first fat emulsion given intravenously to animals (Murlin and Riche, 1915).
1920: first fat emulsions given intravenously to paediatric patients in the USA (Rhoads, 1975).
1961: safe and effective intravenous lipid emulsion (Intralipid) developed by Wretlind in Sweden (Schuberth and Wretlind, 1961). This was approved in most European countries by 1963, but not in North America until 1977.
1964: Food and Drug Administration in the USA banned fat emulsions derived from castor oil and cotton seed oil due to adverse reactions.
1980 to present: new types of lipid emulsions developed, including those containing medium-chain triglycerides, fish oils and structured lipids, but these have not been widely used.

Alcohol

1658: alcohol infused in animals.
1970s: alcohol was included in some commercial PN preparations, and used widely in some centres.
1980 to present: intravenous nutritional products containing alcohol were withdrawn at a time when the practice of HPN was growing in many countries.

Other nutrients

See text.

Solassol *et al.* in France, who by 1973 had already reported the use of long-term intravenous feeding in 75 patients (Solassol *et al.*, 1974), HPN in Europe was generally slow to develop. For example, in Britain, the first reports of HPN appeared in the late 1970s.

The commonest indication for HPN in different countries, which mainly involved adults, was the short bowel syndrome due to surgical resections, in patients with Crohn's disease, and mesenteric vascular disease. Over time, the age distribution of patients increased to encompass more (often younger) children and older adults – trends that are continuing in several countries today. At the same time, the indications for HPN widened. HPN began to be used for an increasing number of paediatric conditions, such as autoimmune enteropathy, necrotizing enterocolitis and congenital malformations. In some countries, such as the USA, it was also used for a growing number of patients with HIV, and in both the USA and many other countries it began to be used increasingly to support patients with malignant conditions. However, international differences in the indications for HPN became apparent. For example, although the proportion of patients given HPN because of malignant disease has steadily increased in the UK, the proportion has been relatively small (< 5% among those who started HPN in the period 1996–2000, and < 5% among those who received it at a given point in time during the same period) (Elia and Baldwin, 1999). In contrast, in other European countries the figures were several-fold greater (Van Gossum *et al.*, 1999).

It has also became apparent that the prevalence of HPN (per million of population) varied considerably between countries (Elia, 1995; Elia and Baldwin, 1999; Elia *et al*, (2001)) and was related to economic factors: lowest in low-income countries, such as several African countries and in India, intermediate in Western European countries and highest in the USA.

The success of PN in human patients led to its use in animal patients (veterinary medicine), such as dogs and horses, although this practice has not become widely used.

Developments in Preparation, Setting up and Infusing PN

In the 1970s the administration of PN, including HPN, often involved multiple bottles (dextrose, amino acids, saline, fat emulsion). This was tedious, time consuming and increased the risk of errors and complications, such as catheter-related infections. In addition, the composition of vials containing vitamins and micronutrients was not optimal for long-term intravenous use. For example, the first patient on HPN (Shils *et al.*, 1970) was reported to have received four different commercial vials of vitamins, which were believed to be necessary, as well as eight other types of solutions (a fat emulsion was not included in the initial formulation). Infusion schedules were also frequently complex.

Commercial companies took up the challenge of producing new formulations that simplified the administration. Such developments which

have taken place since the 1970s were also made possible by pharmaceutical developments and appreciation of specific patient needs:

1. Large plastic bags ('all-in-one' bags), which allowed nutrients to be mixed together and delivered all nutrients together over a prescribed period of time. Although the use of 'all-in-one' bags in the community was first reported in 1972 (Romieu *et al.*, 1972), their use did not become widespread until the 1980s. The compatibility of nutrients had to be carefully assessed to avoid, for example, precipitation of calcium phosphate, or destabilization of lipid emulsions by divalent cations. This field of investigation led to the development of pre-nutrients, such as organophosphates, which were stable and soluble and did not cause precipitation. Once within the body, the organophosphates, such as glucose phosphate, or glycerol phosphate, were hydrolysed to yield free phosphate and either glucose or glycerol.
2. Multilayered bags, which were studied in the 1990s, were found to limit the diffusion of oxygen that was responsible for degradation of the following: (i) some amino acids, such as cysteine; (ii) some vitamins, such as vitamin C, especially in the presence of the catalytic effect of copper; and (iii) some drugs, such as ranitidine. Such bags are now routinely used for HPN in many countries.
3. Backpacks and plastic 'vests', which allowed the infusate to be carried in plastic vests or backpacks while the patient remained mobile, e.g. able to work outside their home. The infusate is delivered into a central vein via a lightweight portable infusion pump, which is also carried in the backpack.
4. Infusion pumps. Many of the initial infusion pumps, which were designed for use on hospital wards, were bulky, noisy and not ideal for home use. Therefore, new pumps were designed that were smaller, lighter and more user-friendly for home use.
5. Administration stands. Some of the stands were found to be unsuitable for use over certain surfaces in the home. For example they were bulky, had small wheels and could not easily be moved up or down different floors, or across surfaces covered with certain types of carpets. In the UK a patient organization, 'PINNT' (Patients on Intravenous and Nasogastric Nutrition Therapy), identified these problems and designed their own stand and pump system. Now, many patients use their tailor-made portable, lightweight and practical system.

Delivery of feeds and accessories

The feed and administration sets were initially delivered to the patient's home from hospital, although in many countries this practice has been largely taken over by commercial companies, whose role varies from delivery of feeds and accessories to total care, including clinical/nursing care. To allow international travel, some companies have established a network of care, so that patients can travel abroad to work or have holidays. Feeds and accessories are delivered according to individual patient specifications.

Nutrients

Key developments in the use of macronutrients (amino acids, carbohydrate, fat and alcohol) in HPN are summarized in Box 1.1. The trends in the 1970s were to replace protein hydrolysates with mixtures of synthetic L-amino acids, which could more easily be standardized to meet quality control criteria, and to replace alternative carbohydrates such as fructose (and to a much more limited extent other carbohydrates such as sorbitol) with glucose, which was always the most widely used carbohydrate. In the USA, the adverse effects of administering castor and cotton seed oils (fever, coagulation problems, back pain, jaundice) led to their ban in 1964. This also led to a slower introduction and use of smaller quantities of lipid emulsions compared to many European countries, when a safe lipid preparation emerged from Sweden in 1961 (Schuberth and Wretlind, 1961). Later, alcohol was introduced but withdrawn from commercial intravenous preparations, mainly in the 1970s, because of concern about potential adverse effects on the liver and brain.

A historical review of other nutrients in HPN is beyond the scope of this brief article, but three points are summarized below:

1. The quantity of some nutrients delivered to patients on PN (including HPN) was sometimes less than the amount prescribed. This was due to degradation (e.g. oxidation of vitamin C) or adsorption of nutrients onto the bags. It was found that photo-degradation of certain vitamins, notably vitamin A, could be reduced by administering the infusion overnight, covering the bag with a light, impermeable material and by using an all-in-one bag containing lipid emulsions, which limited the transmission of light.
2. The profile of trace elements and minerals for PN use was different from that for oral nutrition due to their variable absorption, which in healthy subjects ranges from less than 10% (e.g. chromium, manganese) to almost 100% (e.g. sodium, potassium fluoride). A range of nutrient deficiencies and some toxicities, due to inadequate or excess provision of the nutrients, was described within a few years of the introduction of PN in hospital and at home.
3. The term 'total parenteral nutrition' (TPN) is still used today, but it has now largely been replaced by the term 'parenteral nutrition' (PN), since it was recognized that several nutrients were not (and are still not) included in routine PN, e.g. carotenoids, choline, taurine, glutamine, fructose and certain fish oils.

Finally, in some patients, the 'artificial gut' (PN) has been replaced by a transplanted gut (Langnas, 2004). A study in Pittsburgh, USA, involving 169 patients, reported 75% survival at 1 year, 54% at 5 years and 42% at 10 years. There is still some way to go with intestinal transplantation, but in the future it may become a much more common and realistic option for patients on long-term HPN.

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