## Hallmarks in the History of Enteral and Parenteral Nutrition : From Antiquity to the 20th Century

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Review

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# Hallmarks in the History of Enteral and Parenteral Nutrition: From Antiquity to the 20th Century

**Frank Vassilyadi, BSc[1]; Alkistis-Kira Panteliadou, MD[2]; and Christos Panteliadis, PhD[3]**

## Abstract

Parenteral nutrition (PN) and enteral nutrition (EN) have a very long history, emerging in the ancient world and developing throughout the common epoch. This history dates back as far as 3500 bc to the ancient Egyptians, Indians, and Chinese. Their medical practices were the first reports of enteral feeding therapy, provided via rectum with enemas of wine, milk, whey, wheat, and barley. Hippocrates and Plato, in ancient Greece, were the first personalities to emphasize the importance of diet on health. In the following centuries, Erasistratus and Herophilus described the first notion of the circulatory system, and Oribasius and Celsus described the role of nutrition and disease. There is a great historical gap between the times of Galen (2nd century), who elaborated on the circulatory system; Ibn Zuhr (12th century), who constructed the first model of PN; and Capivacceus (16th century), who placed the first tube for EN. The 17th–19th centuries showed major developments in modern nutrition elements. Steps toward artificial nutrition began in 1628 with the detailed description of blood circulation by William Harvey; however, most of the advances in enteral and parenteral feeding techniques, solutions, and formulas took place in the 20th century. Over the last decade of the 20th century, research focused on metabolic control, multitude formulas, timing and the combination of EN and PN for intensive care patients. (*Nutr Clin Pract*. 2013;28:209-217)

## Keywords

enteral nutrition; parenteral nutrition; history

Enteral nutrition (EN) and parenteral nutrition (PN) are integral parts of clinical therapies. The purpose of EN and PN is to provide the body with essential nutrients, to maintain structural components, and to promote physical development when feeding by mouth is not possible. It is known that if an adult does not eat for over 14 hours, metabolic catabolism begins (ie, the breakdown of protein), resulting in the breakdown of amino acids to fuel gluconeogenesis. This situation increases postoperatively and after trauma in order to mobilize energy reserves to compensate for increased endogenous needs.

Hospitalized patients are often poorly nourished: of patients admitted to the hospital, 25%–50% have preexisting poor nutrition status, whereas a further 25%–30% of those who remain in the hospital tend to develop malnutrition. The nutrition status of the patient before surgery plays an important role toward a successful postsurgical outcome. Poor nutrition affects all organs of the human body, with the exception of the adult brain. It is therefore important that malnourished patients be supported by gastrointestinal or intravenous (IV) feedings. Children, especially infants and babies whose main source of nutrition is the mother's milk, are at high risk during protein catabolism because their energy reserves are minimal in comparison to the average adult. This is a notion that has existed since ancient times and is still relevant today.

Over the centuries, experimentation and research have contributed to a greater understanding of nutrient requirements. Methods have been updated to more accurately access the gastrointestinal tract, new materials have been developed (such as equipment, tubes, and containers), and knowledge has increased about digestion, absorption, and use of macro- and micronutrients. Today, mixed feeding (enteral-parenteral) is being applied to more patients, especially to those who are hospitalized in critical care.

The aim of this historic review is to demonstrate a historical progression in both EN (Table 1) and PN (Table 2), the former finding its roots more than 3000 years ago and the latter being documented for the first time in the 12th century AD. This review was mainly compiled using online journal databases and books found in university libraries. The majority of the ancient texts were written in Greek or German, which we read and translated.

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**Table 1.** Historic Timeline of Enteral Nutrition.

| Date | Contributor | Contribution | Reference |
|---|---|---|---|
| 1550 BC | Ancient Egyptians | RE of milk, whey, wine, and barley broths delivered as food or medication | 6, 7 |
| 300 BC | Hippocrates | RE of ptisan, oxymel, hydromel, and wines | 15 |
| 100 BC | Lykos | RE of barley and wheat in patients who could not be fed orally | 18, 19 |
| 50–25 BC | Celsus | RE of barley, wheat, milk, eggs, and deer marrow for patients with dysentery or gastric diseases | 20 |
| 1598 | Capivacceus | EF using a hollow tube to push liquid down the esophagus | 26 |
| 1617 | Aqua Pendente | EF using a small silver nasopharyngeal tube to feed patients with tetanus | 27 |
| 1646 | von Helmont | EF using a leather, flexible transnasal tube | 28 |
| 1790 | Hunter | First to use EN for therapeutic purposes | 37 |
| 1837 | Egeberg | First gastrostomy in dogs for the purpose of feeding | 47 |
| 1849 | Sedillot | First gastrostomy in humans—unsuccessful | 47 |
| 1858 | Busch | Fed a diet of eggs, flour, meat, and meat broth via the jejunum | 50 |
| 1876 | Verneuil | First successful gastrostomy in humans | 47 |
| 1878 | Surmay | First successful jejunostomy | 51 |
| 1882 | Bliss | RF of President Garfield, who lived for 79 days after being shot | 67 |
| 1894 | Stamm | Standardized the gastrostomy technique | 48 |
| 1895 | Eiselberg | Modified the jejunostomy technique, which is still used today | 57 |
| 1910 | Einhorn | Developed a weighted nasogastric tube that could pass into the duodenum | 69 |
| 1915 | Gross and Held | Developed a weighted nasogastric tube that could pass into the jejunum | 72 |
| 1980 | Gauterer et al | Described the first endoscopic placement of a gastrostomy tube | 115 |

EF, enteral feeding; EN, enteral nutrition; RE, rectal enema; RF, rectal feeding.

## Before the Common Era

The word *diet* comes from an ancient Greek word meaning "way of life."[1] Archaeological finds have shown that vegetarian-type diets date as far back as the sixth century BC.[2] This was the lifestyle of choice by followers of the Orphic movement in ancient Greece, including the Pythagoreans.[3,4] The words *vegetarianism* and *vegetable*, however, were not used until the end of the 19th century, when they were established in 1847 at the newly founded Vegetarian Society by Frances Kemble.[5] Other foods consumed in ancient times included bread, corn, and pap (ie, porridge) with the later addition of rice and maize. In times of hunger and famine, there was a shortage of food in which people were starving, became sick, and were in need of food. The first people to overcome this challenge with artificial nutrition were the ancient Egyptians.

One of the first references to artificial nutrition can be found in the Ebers Papyrus, written in hieratic Egyptian in 1550 BC. It is among the most important medical papyri of ancient Egypt and constitutes the most voluminous record of known ancient Egyptian medicine. The Ebers Papyrus was purchased at Luxor (Thebes) in the winter of 1873–1874 by Georg Ebers and can now be found in the library of Leipzig University in Germany. This document describes EN in the form of rectal enemas (using small tubes made from clay or ceramic pipes tied to animal bladders), which would deliver milk, whey, wine, and barley broths as a form of food and/or medication.[6,7] Similarly, the Edwin Smith Papyrus (which dates back to 1500 BC) describes the view of the polymath Imhotep that food and nutrition should both be considered a form of medication.[8] In the same period, traditional Indian medicine (also known as Ayurvedic medicine) details the importance of dietary patterns in the prevention of disease and health status. This notion can also be seen in traditional Chinese teachings, which were accredited to the "Yellow" Emperor Huang Ti 4500 years ago.[9,10] These ancient records of artificial nutrition were confirmed by the "Father of History," Herodotus, an ancient Greek historian who was born in Halicarnassus in the fifth century BC and reported in his historical papers, *Historien II 77*, that the ancient Greeks and Egyptians administered nutrition in the form of rectal enemas.[1,10-12] This route of delivery continued to be preferred throughout history until the early 1900s.[13]

In ancient Greece, Hippocrates (460–370 BC) was both a physician and a medical writer who established a renowned school on the island of Cos, in which Asclepius studied medicine: this school also functioned as a center for medical advice, prognosis, and healing. Hippocrates, through the Hippocratic Oath and his work *Corpus Hippocraticum* (which contains the core medical texts of his school), implies that "Hippocratic" medicine was practiced by a group of professional physicians bound to the 4 treaties on nutrition, one being *On Regimen in Acute Diseases*.[14] In this treaty, he describes regimes for various diseases, in addition to the importance of choosing a regime based on the patient's diet prior to getting ill. Regimes include ptisan (gruel made from barley), oxymel (a mixture of honey and vinegar), hydromel (honey and water), and wines of various types, which were administered by rectum. In his

**Table 2.** Historic Timeline of Parenteral Nutrition.

| Date | Contributor | Contribution | Reference |
|---|---|---|---|
| 300 BC | Herophilus and Erasistratus | First description of the circulatory system | 15 |
| 1091–1161 | Ibn Zuhr | Early attempt at "nourishing" a human with the aid of hollow silver needle | 25 |
| 1628 | Harvey | Detailed description of blood circulation | 28 |
| 1658 | Wren | IV device made from goose quill that infused wine, ale, and opiates into a dog | 31, 32 |
| 1710 | Courten | Infusion of vinegar, salts, and urine into a dog with no adverse effects; dog died when infusing olive oil | 34 |
| 1733 | Hales | IV infusion of water, leading to discovery of dropsy | 36 |
| 1831 | Latta | IV infusion of saline solution to successfully treat cholera | 41, 42 |
| 1843 | Bernard | IV infusion of sucrose that was soon detected in the patient's urine | 44 |
| 1869 | Menzel and Perco | SC infusion of fat, milk, and camphor into dogs showing high doses of fat can be given without diverse effects | 58 |
| 1873 | Hodder | IV infusion of milk to treat cholera | 43 |
| 1875 | Krug | Fed a patient suffering from anorexia nervosa with SC injections of oil and protein | 46 |
| 1904 | Friedrich | Administered PN by SC infusion of peptone, fat, glucose, and salt | 74 |
| 1909 | Abderhalten | First successful attempt at PN | 75 |
| 1911 | Kausch | Infused glucose postoperatively | 78 |
| 1913 | Henriques and Andersen | Achievement of positive nitrogen balance in a goat fed animal protein IV | 76 |
| 1915 | Woodyatt et al | Used infusion pump for constant infusion of IV glucose | 80 |
| 1934 | Rose | Identification of essential amino acids in humans | 91 |
| 1936 | Elman | Successful IV infusion of enzymatically hydrolyzed proteins to dogs and humans | 92 |
| 1939 | Shohl | IV infusion of hydrolyzed proteins with glucose and laevulose—satisfactory results | 94 |
| 1949 | Rhode et al | Successful infusion of adult dogs with PN | 103 |
| 1963 | Schuberth and Wretlind | Successful testing of fatty emulsion containing soya oil and egg yolk phospholipids | 97 |
| 1964 | Bansi et al | IV supply of synthetic L-amino acid | 111 |
| 1967 | Dudrick et al | Successful infusion of beagle puppies with PN | 102 |
| 1968 | Wilmore and Dudrick | Successful long-term infusion of an infant with PN | 105 |
| 1973 | Hofert et al | First amino acid formula designed for infants | 112 |
| 1974 | Grotte et al; Borresen and Knutrud; Jurgens et al | Designed programs of PN with emulsified fat for infants and children | 99–101 |
| 1983 | Wretlind | Developed a synthetic formula solution called Vamin for postoperative patients | 113 |
| 1987 | Panteliadis et al | Designed formula of middle-chain and long-chain triglycerides, containing taurine | 96 |

IV, intravenous; PN, parenteral nutrition; SC, subcutaneous.

works *On Diet*, Hippocrates denotes the importance of diet on medicine: "let thy food be thy medicine, thy medicine be thy food."[11,15-17]

Oribasius (400–320 BC), a Greek medical writer and the personal physician of the Roman emperor Julian the Apostate, depicted his main work in *Collectiones*, a massive compilation of excerpts from medical writers of the ancient world. It consisted of 72 books, of which only 25 survive today. In book *II 245f*, Oribasius refers to Lykos, a physician who lived in Neapolis around 100 BC, as using enemas of barley and wheat in patients who could not be fed orally.[18,19]

Further confirmation of the use of nutrition enemas in ancient years comes from the ancient Roman epoch. Aulus Cornelius Celsus was a Roman encyclopedist and physician who lived in Gallia Narbonensis between 25 and 50 BC. In his work *De Medicina*, he suggests that enemas with barley, wheat, milk, eggs, and deer marrow should be used in patients with dysentery or gastric diseases.[20] Celsus is also credited with the first classical reference of nutrition enemas when describing stomach problems, stating that "the last resource is the introduction into the bowel from below either barley or spelt gruel since that too supports the patient's strength."[15]

## The Common Era Prior to the 19th Century

One of the first accounts documented in this period came from Soranus of Ephesus (150–200 AD), a Greek physician in Alexandria and Rome and the founder of obstetrics and gynecology, who wrote a treatise entitled *Gynecology*.[21] In his chapter on nutrition, he describes the importance of breastfeeding and recommends that mothers follow this regimen for feeding their infants.[21,22] In the same period, Aelius Galenus (131–201 AD) was greatly influenced by the works of Hippocrates. Galen, for the first time, described the difference between venous and arterial blood. He also explained that the circulatory system consists of 2 one-way systems that are separate from each other.[23,24]

The earliest documented attempt at PN was in 12th-century Sevilla, Spain, by an Arab surgeon named Ibn Zuhr (1091–1161), who supplied "nourishment" to a human with the aid of a hollow silver needle of his own design. It is not clear whether the attempt was successful or the exact contents of the so-called nourishment, but it is noteworthy that such an attempt was made so early in history.[25]

Early development of EN, however, did not begin until 1598 when Capivacceus, a Venetian physician, was the first to report enteral feeding using a hollow tube to push liquid down a patient's esophagus.[26] Later, in 1617, Fabricius ad Aqua Pendente passed a small silver nasopharyngeal tube to feed a patient with tetanus.[27] This technique was improved by von Helmont, in 1646, who used a flexible transnasal tube made from leather for esophageal feeding [28]; however, this technique was traumatic, and the material used for the tube was rigid, leading to its dismissal.[29]

One of the greatest advances in the field of medicine and PN has been the description of the circulatory system by William Harvey (1578–1657), an English physician who published his work on the presence of the circulatory system in 1628. He was not the first, however, to describe the circulatory system (in the third century BC, Herophilus was the first to distinguish between veins and arteries, noting that the latter pulse while the former do not, whereas Erasistratus mapped the course of veins throughout the human body[15,23]) but was the first to elaborate on the topic in detail. Harvey suggested that whatever enters the bloodstream circulates around the body and, as a result, the nutrients that are ingested reach all of the body's tissues via a capillary network of the blood's circulation.[30] This historical moment paved the way for future research in PN. Using this novel notion, Sir Christopher Wren (the famous chief architect of St Paul's Cathedral in London) successfully invented a working IV device made of goose quill and porcine urinary bladder. In 1658, he used this to intravenously infuse wine, ale, and opiates into a dog.[31-33]

In 1710, Courten published a paper with his studies on IV administration. He infused vinegar, salts, and urine into the veins of dogs and saw no adverse effects, but when administering olive oil, the dog died within hours. Courten speculated that the dog may have possibly died due to pulmonary fat embolism, which led him to the conclusion that fats require special manipulation before being infused.[34] Gauthier, in 1717, invented a technique to distill water,[35] which, in 1733, led to Stephen Hales's account of "dropsy" in humans after having infused water intravenously.[36]

In 1790, a surgeon named John Hunter (1728–1793) was the first to use EN for therapeutic purposes[37,38]: in particular, he administered nutrients via a tube made of whale bone and wrapped in eel skin connected to an animal bladder that served as the pump.[39] This led to the study of metabolism, which was initiated by the founder of modern chemistry, Antoine-Laurent Lavoisier (1743–1794), and subsequently the discovery of glucose by Lobowitz in 1792,[40] which would later be studied by Claude Bernard and Landerer.

## The 19th Century (1800s)

In the 19th century, rapid progress was being made in experimental medicine and PN. In 1831, Thomas Latta was the first to successfully infuse IV saline solutions containing a hypotonic solution of sodium, chloride, and bicarbonate to treat patients with cholera.[41,42] Cholera treatment was also explored later in 1873 by Hodder, who successfully infused 2 of 3 cholera patients with milk.[43]

In 1843, Claude Bernard (1813–1878), a French physiologist and founder of endocrinology, used IV access to administer a solution of sucrose, egg proteins, and milk (among other nutrients). He also noticed that the IV administration of sucrose (and not glucose) was soon detected in the patient's urine.[33,44] In 1859, he described the importance of glucose in normal metabolism and homeostasis, calling his concept *Milieu Intérieur* (the environment within).[44] Later, in 1887, Landerer stated that "glucose may serve as part of a regimen for artificial nutrition."[45] It took many years, however, to further advance this area of study: many experiments failed, mainly due to localized pain and fever, from where the term *glucose fever* was coined.[46]

A surgical approach to feeding was performed for the first time in 1837 by Egeberg, a Norwegian surgeon. He performed a gastrostomy in dogs for the purpose of feeding and providing medication. This breakthrough led to human gastrostomies: the first attempt in 1849 by Sédillot was unsuccessful, whereas the first successful attempt was in 1876 by Verneuil.[47] Later, in 1894, Stamm standardized the technique of gastrostomy.[48,49]

Feeding via the jejunum was first described by Busch,[50] who, in 1858, fed a diet of eggs, flour, meat, and meat broth by intermittent instillation to a woman with a jejunal fistula. The first jejunostomy, however, was not performed until 1878 by Surmay[51] and subsequently in 1885 by Robertson,[52] Lee and Gould,[53] and Golding-Bird[54] independently. High mortality rates[55] led to the modification of the technique in 1892 by Maydl,[56] who used solid food, and in 1895 by Eiselberg,[57] whose technique is still being used today.

Throughout the 19th century, significant experiments took place on the subcutaneous infusions of nutrients. In 1869, Menzel and Perco[58] administered fat, milk, and camphor subcutaneously to dogs, showing that high doses of fat can be given without diverse effects. In 1875, Krug fed a patient who had anorexia nervosa with subcutaneous injections of oil and protein extract, and in 1876, Whittaker used milk, beef extract, and cod liver oil for a similar type of patient.[46]

The effects of body surface area on heat production were studied by the French scientist Richet in 1885.[49,59] Another French scientist, Langlois,[60] in 1887 explored the effects of environmental and body temperatures on heat production. In Italy, infant metabolism was studied independently in the late 1800s by Mensi[61] and Poppi[62] using closed- circuit calorimetry.

This same research was also conducted in Czechoslovakia by Scherer,[63] in 1896, and Babak.[64]

In that same period, Florence Nightingale (one of the pioneers of modern nursing) was especially interested in EN. When the first nursing schools were founded in the United States, she tasked students to study nutrition regimes for therapeutic purposes in hospitalized patients.[65] She is quoted as saying, "You cannot diet a patient from a book; you cannot make up the human body as you would a prescription."[66]

Toward the end of the 19th century, enemas such as milk, red wine, blood, and others would still be administered per rectum[11,67,68] using a piece of pipe with a bladder tied to one end. The most famous case of rectal feeding was that of President Garfield, in 1882, after he was shot during an assassination attempt and lived for 79 days.[67] In the following century, the preferred route of feeding would slowly shift from rectal enemas to gastric and small bowel feedings.[13]

## The 20th Century (1900s) to Present

Enteral feeding saw a turning point in development in the early 1900s. In 1910, Einhorn[69] developed a weighted nasogastric tube that was able to pass into the duodenum. This initial design was associated with a number of intolerances, and an improved designed was developed independently by Morgan[70] and Jones,[71] who administered their solutions "drop by drop" rather than as bolus. A larger tube with a heavier weight was designed by Gross and Held[72] to reach the duodenum faster, and later, they developed a tube that passed into the jejunum. In 1917, the newly founded American Association of Dietology under the leadership of Lenna Cooper and Lulu Graves (First Meeting October 1917 in Cleveland, Ohio) presented the basic principles of dietology and EN.[17,73]

The first theoretically and experimentally well-documented attempt at administering PN was made in 1904 by Friedrich,[74] who administered PN for the first time by subcutaneous infusion of peptone (derivative of animal milk proteins that have undergone proteolytic digestion), fat, glucose, and salt but would later abandon the method as it was too painful for patients. The first successful attempt at PN was made in 1909 by Abderhalten et al,[75] who artificially nourished a 9-year-old boy. Soon later, Henriques and Andersen[76] achieved positive nitrogen balance in a goat that was intravenously fed with animal proteins, and, independently, Van Slyke and Meyer[77] experimented with animal proteins in dogs. In 1911, Kausch[78] infused a postoperative patient with glucose, based on a previous discovery made 10 years earlier by Biedl and Kraus,[79] who administered glucose to a human for the first time, but not for nutrition purposes. In 1915, Woodyatt et al[80] reported using an infusion pump to ensure a constant infusion of IV glucose.[46] A rate of 0.85 g per kilogram of body weight per hour was defined as "appropriate" (ie, not too high as to cause glycosuria) and was used later, in 1924, by Mattas[81] as a continuous-drip infusion in humans.

Research was also being conducted in basal metabolism. The first investigation published on the gaseous metabolism of infants was conducted by Edmund Robert Forster (1878–1933) in Munich.[82] The carbon dioxide production of 2 infants, 14 and 16 days of age, was measured in an open-circuit calorimeter. Rubner and Heubner later used the apparatus in their classic studies of daily energy requirements of normal and atrophic infants. Max Rubner (1854–1932) pioneered the studies on substrate oxidation and formulated the law of body surface area (ie, the theory that the metabolic rate per 0.67 power of the body's surface area is the same for both large and small animals, independent of body size). He also formulated the rate-of-living theory where animals with a slower basal metabolism have a longer life span. He determined the exact caloric "heat-producing" values for carbohydrates (4.1 kcal/g), fat (9.3 kcal/g), and protein (4.1 kcal/g) following an experiment in rabbits where he found that protein can replace fat as an energy source.[83-85] In 1918, Harris and Benedict estimated the basal metabolic rate in men and women using direct calorimetry. The formula they suggested is still used today, with only minor modifications.[86] In 1925, Talbot calculated a higher basal metabolism (by observing a higher level of heat production) in children.[87] In 1932, Max Kleiber, in his influential monograph, challenged Rubner and explained that the basal metabolic rate was not proportional to the 0.67 power of surface area but instead to the 0.75 power.[88,89]

Around the same time, a scientist named Alfred Bosworth created an infant formula that was milk based (a new concept at that time). This idea had stemmed from the Moores and Ross Milk Company that was established in Columbus, Ohio. The focus of this company had been the home delivery of bottled milk, until a new direction was proposed by Bosworth.[90] This led to another milestone in PN, which was the identification of essential amino acids in humans by William Rose in 1934.[91] In 1937, Robert Elman[92] successfully infused enzymatically hydrolyzed proteins intravenously to dogs and humans. In comparison with the proteins received orally, the body immediately used the proteins received intravenously. The same investigator also emphasized the significance of these amino acids as an energy source.[93] In 1943, Shohl reported that the IV infusion of solutions of hydrolyzed proteins with glucose and laevulose in patients after major or minor surgical procedures yielded satisfactory results; however, positive nitrogen balance was only rarely achieved.[94] This was due to what Cuthbertson[95] defined as a catabolic reaction, which takes place when the human organism is in a diseased state. Another problem was the composition of the solution: isotonic glucose solutions and hypertonic solutions of up to 10% were well tolerated compared with those of 15%, which caused superficial venous thromboses and other skin complications. PN should be designed in such a way that it would suffice for patients who cannot receive nutrition orally or for preoperative patients. Such patients need at least 1400 kcal/d to meet their metabolic demands. This was attempted with the use of lipids since they have the highest caloric value and are not related to thrombotic complications. Although the emulsified fats had been tested for IV administration, they were finally abandoned because it was found that lipid microparticles led to the formation of microspheres and triggered subsequent embolic events.[33]

In the 1940s, numerous investigators tried to determine the best formula for a mixture of homogenized lipids with carbohydrates that would supply high amounts of energy with the least possible side effects. For example, infants with enteral dysfunctions should consume formula diets with protein hydrosylate, corn oil, dextrimaltose, vitamins, and minerals.[33]

The next step in artificial nutrition was to determine the necessary volume of fluids and restrict the use of diuretics. The first diuretics contained mercury and showed an increased risk of deteriorating renal function. After the 1950s, safer diuretics were developed, and as a result, infusions of up to 5 L of fluid per day were possible. Meanwhile, many interesting studies were published. It was shown that, in many cases, enteric fistulas would close if patients were treated with PN. Similarly, promising results were shown in patients having undergone major surgical procedures, patients with severe burns, and victims of multiple trauma. Finally, there were excellent results in premature newborns in the intensive care units (ICUs).[96]

In 1960, a Swedish company produced a fatty emulsion that contained soya oil and egg yolk phospholipids as an emulsifier. Three years later, it was tested by Schuberth and Wretlind[97] and Hallberg et al[98] in hospitalized patients with great success. As a result, PN with fat and glucose as a nonprotein energy source was the method of choice in many hospitals. Grotte et al[99] in Sweden, Børresen and Knutrud[100] in Norway, and Jurgens et al[101] in Germany designed programs of PN with emulsified fat for infants and children. The same authors published programs for PN via peripheral or central venous catheters.

In the late 1960s, Dudrick, Wilmore, Vars, and Rhode achieved a historical landmark in parental nutrition. They successfully infused adult dogs and beagle puppies with PN, which led to a successful attempt in human infants.[102-104] The first successful clinical application of PN was conducted postoperatively by Dudrick[104] on 6 malnourished adults. The first long-term case of PN feeding was performed by Wilmore and Dudrick[105] in 1968, reporting the successful feeding of a 1-month-old infant postoperatively using only PN for 5 months. This case led to advances in measuring serum amino acids and fatty acids using the automated analyzers and chromatographic methods, significantly improving the administration of solutions according to the specific needs of the human body, and as a result, the programs of IV nutrition were further modified.[104-109] PN would become the preferred source of artificial nutrition for surgical patients in the 1970s and 1980s.

The first teams of dietary support were organized in major hospital centers in the early 1970s. These teams consisted of physicians, nurses, dieticians, and pharmacists. Their role was in the dietary support of patients in need of EN or PN.[110]

The first to use an intravenously supplied synthetic L-amino acid (composed mostly of glycine) was the German scientist Bansi in 1964.[111] The first amino acid formula that was especially designed for infants was presented by Hofert et al in 1973.[101,112] Due to the high level of ineffectiveness of glycine toward nitrogen balance, Wretlind,[113] in 1983, developed a more complete synthetic solution called Vamin, which was much more effective in postoperative patients. Subsequent studies showed that the use of synthetic amino acids had minor complications compared with hydrolyzed proteins. Moreover, synthetic amino acids were used by the body in a more efficient way. In 1987, a formula of middle-chain and long-chain triglycerides was presented by Panteliadis et al.[96] In addition, this infant formula contained taurine, which is an essential amino acid for premature infants. Further development in the area of artificial nutrition involved improvement in the knowledge of catheters and continuous administration pumps. ICUs were better equipped and medical and nursing staff accumulated increasing experience, which contributed significantly to the restriction of mechanical, infectious, and metabolic complications of PN. In recent years, many formulas of different amino acid compositions have been manufactured, and PN has been widely used. According to Kinney, PN is not only an effective treatment modality but also an important method for the investigation of metabolic derangement during acute illness or trauma.[33]

In the 1980s, Hirschhorn reviewed the historical, physiological, clinical, and epidemiological evidence that supported a method of therapy for children's diarrhea that may be recommended for general acceptance. The understanding and use of fluid and nutrition therapy of acute diarrhea in childhood have progressed over the years to a point where acute mortality can be reduced to nearly zero.[114] At the same time, Gauterer et al[115] described the first endoscopic placement of a gastrostomy tube. This new technique was simple, safe, rapid, and particularly useful in high-risk patients because the gastrostomy was performed without the need for a laparotomy. The original description was made in children; however, it has become a popular method of EN in all age groups.

Further development in artificial nutrition was accomplished with the support of the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.), founded in 1976, and whose first president was Stanley Dudrick. Its purpose is to encourage communication between investigators in the area of EN and PN. One of the most important leaders of A.S.P.E.N. was Jonathan E. Rhoads, who provided the Society with research and programmatic guidance. He mentored many physicians and other healthcare professionals and served as the senior scientist in the development of PN. The Society began publishing a scientific journal in 1977, the *Journal of Parenteral and Enteral Nutrition*, and a clinical practice journal in 1985, *Nutrition in Clinical Practice*. The A.S.P.E.N. Rhoads Research Foundation was developed in 1992 to honor

Rhoads and continues to fund basic and clinical nutrition research.[116]

The past 2000 years have shown significant research and experimentation in the field of artificial nutrition, whose roots began developing over 5000 years ago with the ancient Egyptians. This review has incorporated the earliest available documents from the field of artificial nutrition into a comprehensive review that details the progression in research from enemas of barley broth used in antiquity up until the 20th century, when physicians began to control the timing and the combination of EN and PN administered to patients.

## References

1. Edelstein L. Antike Diätetik. *Die Antike*. 1931;7:255-270.
2. Spencer C. *The Heretic's Feast: A History of Vegetarianism*. London: Fourth Estate Classic House; 1993.
3. Martin L. *Hellenistic Religions: An Introduction*. New York: Oxford University Press; 1987.
4. Walters K, Portmess L. *Religious Vegetarianism: From Hesiod to the Dalai Lama*. Albany: State University of New York Press; 2001.
5. Kemble F. *Journal of a Residence on a Georgian Plantation in 1838-1839*. New York: Harper & Brothers; 1864.
6. Joachim H. *Papyrus Ebers: The First Complete Translation From the Egyptian*. Berlin, Germany: G. Reimer; 1890.
7. Scholl R. *Der Papyrus Ebers. Die größte Buchrolle zur Heilkunde Altägyptens* (Schriften aus der Universitätsbibliothek 7). Leipzig, Germany: Leipzig University Press; 2002.
8. Ebell B. *The Papyrus Ebers: The Greatest Egyptian Medical Document*. Copenhagen, Denmark: Levin & Munksgaard; 1937.
9. Anderson E. *The Food in China*. New Haven, CT: Yale University Press; 1988.
10. Estes J. *Food as Medicine*. Cambridge, UK: Cambridge University Press; 2000.
11. Harkness L. The history of enteral nutrition therapy: from raw eggs and nasal tubes to purified amino acids and early postoperative jejunal delivery. *J Am Diet Assoc*. 2002;102:399-404.
12. Lysen L. *Enteral Equipment*. Philadelphia, PA: WB Saunders; 2003.
13. Harkness L. *The History of Medical Nutrition Therapy in the Treatment of Gastrointestinal Disorders*. Boca Raton, FL: CRC Press; 2011.
14. Adams F. *The Genuine Works of Hippocrates*. New York: William Wood and Company; 1891.
15. Fidanza F. Diets and dietary recommendations in ancient Greece and Rome and the school of Salerno. *Prog Food Nutr Sci*. 1979;3:79-99.
16. Kalde S, Heise J. Praxis der künstlichen enteralen Ernährung in der Pädiatrie (Teil I). *Kinderkrankenschwester*. 2004;23:160.
17. Todhunter E. Some aspects of the history of dietetics. *World Rev Nutr Diet*. 1973;18:1-46.
18. Grant M. *Dieting for an Emperor: A Translation of Books 1 and 4 of Oribasius' Medical Compilations With an Introduction and Commentary*. New York: Brill Academic; 1997.
19. Browning R, Nutton V. *Oribasius*. Oxford, UK: Oxford University Press; 2003.
20. Langslow D. *Medical Latin in the Roman Empire*. Oxford, UK: Oxford University Press; 2000.
21. Rose V. *Sorani Gynaeciorum vetus translatio latina*. Leipzig, Germany: Teubner; 1882.
22. Temkin O. *Soranus' Gynecology*. Baltimore, MD: Johns Hopkins University Press; 1956.
23. Skiadas P, Lascaratos J. Dietetics in ancient Greek philosophy: Plato's concepts of healthy diet. *Eur J Clin Nutr*. 2001;55:532-537.
24. Grant M. *Galen on Food and Diet*. New York: Routledge; 2000.
25. Abdel-Halim R. Contributions of Ibn Zuhr (Avenzoar) to the progress of surgery: a study and translations from his book Al-Taisir. *Saudi Med J*. 2005;26:1333-1339.
26. Randall H. *The History of Enteral Nutrition*. Philadelphia, PA: WB Saunders; 1983.
27. Aquapendente F. *Oeuvres chirurgicales de Hierosme Fabrice de Aquapendente*. Lyon, France: Jean Antoine Huguetan; 1670.
28. Rosenfield L. The last alchemist—the first biochemist: J. B. van Helmont (1577-1644). *Clin Chem*. 1985;31:1755-1760.
29. Dukes C. A simple mode of feeding some patients by nose. *Lancet*. 1876;2:394.
30. Harvey W. *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus*. Francofurti, Italy: Sumptibus Fitzeri; 1628.
31. Dorn H, Mark R. The architecture of Christopher Wren. *Sci Am*. 1981;245:160-173.
32. Oldenburg H. An account of the method of conveying liquors immediately into the mass of the blood. *Bull NY Acad Med*. 1939;15:624.
33. Rhoads J, Dudrick S. *History of Intravenous Nutrition*. Philadelphia, PA: Saunders; 1986.
34. Courten W. Experiments and observations of the effects of several sorts of poisons upon animals made at Montpellier in the years 1678 and 1679 by the late William Courten. *Philos Trans R Soc Lond*. 1712;27:485-500.
35. Wyatt J. *The Repertory of Arts, Manufacturers and Agriculture*. Vol XXIV. Second Series. London: JB Nichols and Son; 1814.
36. Long E. The oldest fundamental investigations of the origin of dropsy. In: Neuberger M, Farrison F, eds. *Essays in the History of Medicine*. New York: Medical Life Press; 1930.
37. Hunter J. *Dictionary of National Biography*. London: Smith, Elder & Co; 1885-1900.
38. Stevenson L. John Hunter, Surgeon-General 1790-1793. *J Hist Med Allied Sci*. 1964;19:239-266.
39. Keoshian L, Nelsen T. A new design for a feeding tube. *Plast Reconstr Surg*. 1969;44:508-509.
40. Lusk G. *Nutrition*. New York: PB Hoeber; 1933.
41. Latta T. Affording a view of the rationale and results of his practice in the treatment of cholera by aqueous and saline injection (letter to the Secretary of the Central Board of Health, London). *Lancet*. 1831;2:274-277.
42. Latta T. Relative to the treatment of cholera by the copius injection of aqueous and saline fluids into the veins. *Lancet*. 1832;2:274.
43. Hodder E. Transfusion of milk in cholera. *Practitioner*. 1873;19:517.
44. Bernard C. *Introduction à l'étude de la médecine expérimentale*. Paris, France: Baillière; 1865.
45. Watt J, Watt C. *The Chemist*. Vol 2. London: R. Hastings; 1855.
46. Vinnars E, Wilmore D. History of parenteral nutrition. *JPEN J Parenter Enteral Nutr*. 2003;27:225-231.

47. Cunha F. Gastrostomy: its inception and evolution. *Am J Surg*. 1946;72: 610-634.
48. Hemmeter J. *Diseases of the Stomach: Their Special Pathology, Diagnosis and Treatment*. Philadelphia, PA: Blakiston Son & Co; 1897.
49. Wolf S. *Brain, Mind and Medicine From Charles Richet*. New Brunswick, NJ: Transaction; 1993.
50. Busch W. Beitrag zur physiology der verdauungsorgane. *Virchow Arch Path Anat*. 1858;14:140.
51. Surmay M. De l'enterostomie. *Bull General Ther*. 1878;94:445.
52. Robertson G. A case of fibrous stricture of the pylorus, enterostomy, death. *Br Med J*. 1885;1:376-377.
53. Lee R, Gould P. Cancer of the pylorus and duodemum: jejunostomy; death. *Lancet*. 1885;2:1092-1093.
54. Golding-Bird C. Jejunostomy. *Br Med J*. 1885;2:1063-1064.
55. Rosenak S, Hollander F. Surgical jejunostomy for alimentation: a historical review. *Clinics*. 1944;3:638-662.
56. Maydl K. Ueber eine neue methode zur ausfuhrung der jejunostomie and gastroenterostomie. *Wien Med Wochenschr*. 1892;42:740-743.
57. Eiselsberg A. Ueber ausschaltung inoperabler pylorous-stricturen nebst bemerkungen uber die jejunostomie. *Arch Klin Chir*. 1895;50: 919-939.
58. Menzel A, Perco H. Uber die Resorption von Nahrungsmitteln vom Unterhautzellgewebe aus. *Wien Med Wochenschr*. 1869;19:517.
59. Richet C. Recherche de calorimeter. *Arch Physiol*. 1885;15:237.
60. Langlois P. Contribution a l'etude de la calorimetrie chez l'homme. *J Anat Physiol*. 1887;28:400.
61. Mensi E. Il ricambio respiratorio nel Neonato umano. *Giorn R Accad Med Torino*. 1894;57:301.
62. Poppi E. *Il ricambio materiale e il ricambio respiratorio nell'atrofia infantile*. Bologna, Italy; 1900.
63. Scherer F. Die Respiration des Neugeborenen und Säuglings. *Jahrb Kinderheilk*. 1896;43:471.
64. Babak E. Über die Wärmeregulation der Neugeborenen. *Arch Physiol*. 1902;89:154.
65. Nightingale F. *Notes on Nursing: What It Is and What It Is Not*. London: Harrisson; 1839.
66. Hwalla N, Koleilat M. Dietetic practice: the past, present and future. *East Mediterr Health J*. 2004;10:716-730.
67. Bliss D. Feeding per rectum: as illustrated in the case of the late President Garfield and others. *Med Rec*. 1882;22:64.
68. Brown-Sequard C. Feeding per rectum in nervous afflictions. *Lancet*. 1878;1:144.
69. Einhorn M. Duodenal alimentation. *Med Rec*. 1910;78:92-94.
70. Morgan W. Duodenal alimentation. *Am J Sci*. 1914;148:360-368.
71. Jones C. Duodenal feedings. *Surg Gynecol Obstet*. 1916;22:236-240.
72. Gross M, Held I. Duodenal alimentation. *JAMA*. 1915;65:520-523.
73. Grant J. *Historical Perspectives in Nutritional Support*. Philadelphia, PA: Grune & Stratton; 1988.
74. Friedrich P. Die kunstliche subcutane Ernahrung in der praktischen Chirurgie. *Arch Klin Chir*. 1904;73:507-516.
75. Abderhalten E, Frank F, Schttenlehn A. Über die Verwertung von tief abgebautem Eiweiß im menschlichen Organismus. *Z Physiol Chem*. 1909;63:215.
76. Henriques V, Anderson A. Über parenterale Ernährung durch intravenöse Injektion. *Hoppe-Seylers Z Physiol Chem*. 1913;88:357-369.
77. Van Slyke D, Meyer G. The fate of protein digestion products in the body, III: the absorption of amino-acids from the blood by the tissues. *J Biol Chem*. 1913;16:197-212.
78. Kausch W. Über intravenöse und subcutane ernährung mit traubenzucker. *Dtsch Med Wochenschr*. 1911;37:8.
79. Biedl A, Kraus R. Über intravenöse Traubenzucker infusionen an Menschen. *Wien Klin Wochenschr*. 1896;9:55-58.
80. Woodyatt R, Sansum W, Wilder R. Prolonged and accurately timed intravenous injection of sugar. *JAMA*. 1915;65:2067-2070.
81. Mattas R. The continued intravenous drip. *Ann Surg*. 1924;5:643-641.
82. Forster E. Amtlicher Bericht der 50 Versammlung Deutscher Naturforscher und Aerzte. Munich, Germany;1877.
83. Rubner M. Über den Einfluss der Körpergrösse auf Stoff- und Kraftwechsel. *Z Biol*. 1883;19:536-562.
84. Blaxter K. *Energy Metabolism in Animals and Man*. Cambridge, UK: Cambridge University Press; 1989.
85. Chambers W. Max Rubner: June 2, 1854–April 27, 1932. *J Nutr*. 1952;48:1-12.
86. Harris J, Benedict F. A biometric study of human basal metabolism. *Proc Natl Acad Sci U S A*. 1918;4:370-373.
87. Talbot F. Basal metabolism of children. *Physiol Rev*. 1925;5:477-517.
88. Huyssen V, Lacy R. Basal metabolic rates in mammals: taxonomic differences in the allometry of SMR and body mass. *Comp Biochem Physiol A*. 1985;81A:741-754.
89. White C, Seymour R. Mammalian basal metabolic rate is proportional to body mass. *Proc Natl Acad Sci U S A*. 2003;100:4046-4049.
90. Van Slyke L, Bosworth A. A volumetric method for determination of casein in milk. *Ind Eng Chem*. 1909;1:768-771.
91. Rose W. The significance of the amino acids in nutrition. *Harvey Lect*. 1934;1934:30-49.
92. Elman R. Amino acid content of the blood following intravenous injection of hydrolyzed casein. *Proc Soc Exp Bio Med*. 1937;37:437-440.
93. Elman R, Weiner D. Intravenous alimentation with special reference to protein (amino acid) metabolism. *JAMA*. 1939;112:796-802.
94. Shohl A. Nitrogen storage following intravenous and oral administration of casein hydrolysate to infants with acute gastrointestinal disturbance. *J Clin Invest*. 1943;22:257-263.
95. Cuthberston D. Historical background to parenteral nutrition. *Acta Chir Scand*. 1980;498(suppl):1-11.
96. Panteliadis C, Kremenopoulos E, Soumpasi V, Avgoustidou P. Erfahrungen mit MCT-haltigen Fettermulsionen bei Frueh-und Neurebonene. *Infusions-Therapie*. 1987;14:38-40.
97. Schuberth O, Wretlind A. Fat emulsions for intravenous nutrition: pharmacological and clinical experiences. *Nord Med*. 1963;69:13-17.
98. Hallberg D, Schuberth O, Wretlind A. Experimental and clinical studies with fat emulsion for intravenous nutrition. *Nutr Dieta*. 1966;8:245-281.
99. Grotte G, Esscher T, Hambraeus L, Meurling S. Total parenteral nutrition in pediatric surgery. *Ann Anesthesiol Fr*. 1974;15:65-73.
100. Børresen H, Knutrud O. Intravenous feeding in pediatric surgery and pediatrics: a summary of 7 years of research and routine. *Tidsskr Nor Laegeforen*. 1974;94:613-623.

101. Jurgens P, Dolif D, Panteliadis C, Hofert C. Controlled parenteral nutrition of premature infants. *Adv Exp Med Biol*. 1974;46:178-198.
102. Dudrick S, Wilmore D, Vars H. Long-term total parenteral nutrition with growth in puppies and positive nutrition balance in patients. *Surg Form*. 1967;18:356-357.
103. Rhode C, Parkins W, Tourtellote D, Vars H. Method of continuous intravenous administration of nutritive solutions suitable for prolonged studies in dogs. *Am J Physiol*. 1949;59:409-411.
104. Dudrick S. A 45-year obsession and passionate pursuit of optimal nutrition support: puppies, pediatrics, surgery, geriatrics, home TPN, ASPEN, et cetera. *JPEN J Parenter Enteral Nutr*. 2005;29:272-287.
105. Wilmore D, Dudrick S. Growth and development of an infant receiving all nutrients exclusively by vein. *JAMA*. 1968;203:140-144.
106. Silberman H, Freehauf M, Fong G. Parenteral nutrition with lipids. *J Am Med Assoc*. 1977;238:1380-1382.
107. Mullen J, Hargrove W, Dudrick S, Fitts W, Rosato E. Ten years experience with intravenous hyperalimentation and inflammatory bowel disease. *Ann Surg*. 1978;187:523-529.
108. Dudrick S, Wilmore D, Steiger E. Spontaneous closure of traumatic pancreatoduodenal fistulas with total intravenous nutrition. *J Trauma*. 1970;10:542-553.
109. Shaw S, Elwyn D, Askanazi J, Iles M, Schwarz Y, Kinney J. Effects of increasing nitrogen intake on nitrogen balance and energy expenditure in nutritionally depleted adult patients receiving parenteral nutrition. *Am J Clin Nutr*. 1983;37:930-940.
110. Wesley J. Nutrition support teams: past, present and future. *Nutr Clin Pract*. 1995;10:219-228.
111. Bansi H, Juergens P, Mueller G, Rostin M. Metabolism in intravenous administration of nutritional solutions, with special reference to synthetically composed amino acids solutions. *Klin Wochenschr*. 1964;42: 332-352.
112. Hofert C, Panteliadis C, Dolif D, Jurgens P. Bilanzierte parenterale Ernährung von Frühgeborenen. *Msch Kinderheilk*. 1973;121:525-530.
113. Wretlind A. Die Historische Entwicklung der parenteralen Ernaehrung. *Klinische Ernaehrung*. 1983;11:3-6.
114. Hirschhorn N. The treatment of acute diarrhea in children: an historical and physiological perspective. *Am J Clin Nutr*. 1980;33:637-663.
115. Gauterer M, Ponsky J, Izant M. Gastrostomy without laparatomy: a percutaneous, endoscopic technique. *J Pediatr Surg*. 1980;15:872-875.
116. Vanek V. A.S.P.E.N.—past, present, and future. *JPEN J Parenter Enteral Nutr*. 2008;32:535-562.