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Giants of Parenteral Nutrition



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Abstract

Several brilliant scientists and clinicians pioneered parenteral nutrition despite great hurdles and brought the practice into the clinical arena, saving the lives of countless patients. This is a brief summary of a few of those distinguished men who made this possible.

Keywords: parenteral nutrition, enteral feeding, innovative techniques, hyperalimentation

There can be no debate about enteral feeding being the best type of nutritional support for the surgical patient. "If the gut works, use it" is a doctrine that is beyond discussion. Many of the patients are, however, unable to be fed through the enteral route because of either inflammatory bowel conditions or complex surgical situations such as entero-cutaneous fistulas, open abdomen, etc. Fortunately, several brilliant scientists and clinicians pioneered parenteral nutrition, refusing to be grounded by the prevailing dogma in the 1960's, namely: "feeding entirely by vein is impossible; even if it were possible, it would be impractical; and even if it were practical, it would be unaffordable." This communication will focus briefly on a few of those distinguished men who have been credited for saving countless lives through intravenous alimentation.[1-15]

Professor Jonathan Rhoads was the Chairman of Surgery at the University of Pennsylvania (U Penn), between 1959-1972.[1-4] He was so distinguished that was almost simultaneously Chairman of the Department of Surgery of University of Pennsylvania President of the American College of Surgeons, President of the American Surgical Association, President of the American Cancer Society, Chairman of the Board of Managers of Haverford College, a member of the Residency Review Committee, and a member of the American Board of Surgery and the National Research Council. He was also the editor of *Annals of Surgery* and the author of a textbook on surgery. Additionally, he was the editor of *Cancer* for two decades. He was described as a

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"preternatural student, physician, surgeon, teacher, scientist, investigator, innovator, advisor, role model." He was also known for his quick wit: at his 80th birthday reception in Philadelphia, an attendee remarked to him, "Dr. Rhoads, this has been such a wonderful evening that I can hardly wait to celebrate with you on your ninetieth birthday." Dr. Rhoads responded, without a moment's hesitation, "Well then, you had better start taking better care of yourself."[4]

Among his original innovations was the concept of hyperalimentation, in which large quantities of cottonseed oil emulsion were injected intravenously. The excess water load was removed by diuretics. This was among the first forays into the concept of parenteral nutrition.

Eleven of Professor Rhoads' faculty became surgical chairmen and distinguished scientists under his mentorship.[3] One of them was Stanley Dudrick, who was interested in nutrition.[5-6] One day, when three of his professor's patients died despite excellent surgery, Dudrick concluded that the death of these patients was due to their poor nutrition. Since the intestine was not working, there must be some other way to provide nutrition. He presented his idea to Dr. Rhoads, who thought it very interesting, but very difficult to achieve. Dudrick decided to conduct a trial and began to infuse some nutrients diluted in a large amount of water directly into a vein in his arm. The amount of energy that was provided by this was minuscule. He managed to concentrate the amount supplied a little more. The result, however, was disappointing due to the osmolarity of the mixture that the peripheral vein could not tolerate.[5-12]

Professor Rhoads proposed the inguinal vein, but feared the enormous risk of infection. Dudrick then suggested the subclavian or jugular veins, but Rhoads warned of injuring the pleura while accessing the subclavian vein. By 1952, Aubaniac published the first description of percutaneous subclavian venipuncture for the achievement of rapid blood transfusion in severely injured war victims[1,2]; Dudrick learnt from the literature,[1,2] along with other great works of nutritional supplementation. In 1924, Matas used a continuous drip infusion of glucose, and in 1930, Rose discovered the essential amino acids in humans. In 1937, Elman, who came to be known as the "father of IV nutrition," published the intravenous infusion of amino acids as a fibrinogen hydrolysate in man. Dennis, in 1944, reported the support of malnourished IBD patients with glucose, vitamins, and electrolytes. Moreover, in 1945, Zimmermann developed the first polyethylene catheters for IV infusions in humans.[1,2]

Dudrick teamed up with his pharmacist, Henry Vars, and set about designing a dog experiment.[1,2,5, 7-11] They chose beagles because their metabolism was similar to that of humans, and their short hair facilitated

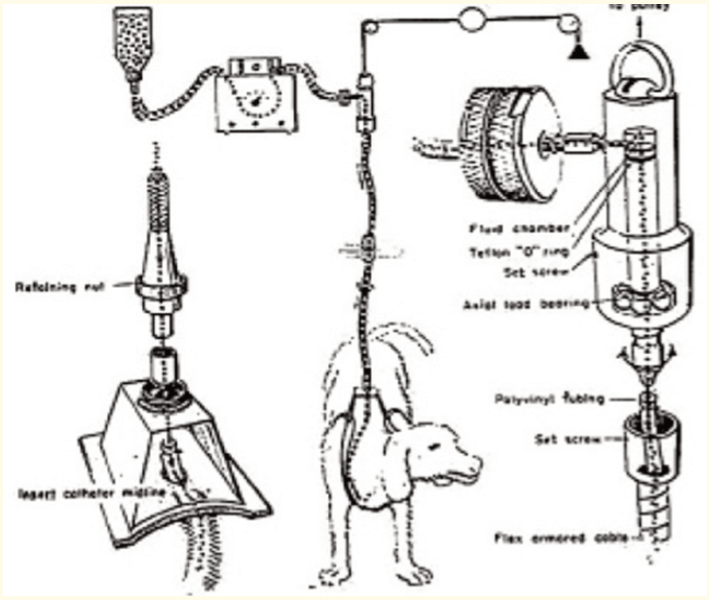

Figure 1 : The basic infusion system in the beagle experiments

easier maintenance of catheters. Several challenges faced them, such as: complete parenteral nutrient solutions did not exist; concentrating substrate solutions was not easy; and the safety and efficacy of long term central venous catherization or infusion of hypertonic solutions had not been established. Maintaining asepsis in the preparation and delivery of nutrient solution was another challenge, as was the metabolic consequences of the infusion.

During a 3-month period prior to initiating the intravenous nutrient infusions in the beagle puppies, a labor-intensive exercise in quantitative physical chemistry was carried out by the scientists. They had to de-

termine the nature and compatibility of the various anions and cations thought to be essential for the growth and development of the puppies. They discovered that there was no vitamin preparation containing all the vitamins required for growth in the puppies. Subsequently, they discovered that the metabolism of dogs needed biotin, choline, and para-amino-benzoic acid (PABA). These had to be added to the solution individually.

All the solutions were initially sterilized by passing them through a Seitzfilter, and ultimately through a 0.22 micropore filter for cold sterilization, since autoclave sterilization inevitably resulted in precipitation of the nutrient solution. Dudrick and his team researched every plastic tubing available at the time. They inserted them subcutaneously in dogs and rats in order to study their reaction. Finally, they settled upon the Irvington Brand polyvinyl tubing, which at the time was in use as insulation for monofilament wire. Aseptic dressings at the skin entry of the intravenous catheter created another problem, as the inorganic iodine was burning the skin. Organic iodine in the form of povidone-iodine, a newly developed formula, became the mainstay in the long-term antiseptic maintenance of central venous catheters.

The experiment was refined step by step, solving each hurdle as it appeared. Figure 1 shows the original sketches of Dudrick. He would check on the beagles every day; one of the beagles, the well-known "stinky," with Dudrick is shown in Figure 2.

The six puppies, fed entirely intravenously, outstripped their control orally fed littermates in weight gain. They matched them in skeletal growth, development, and activity for the study periods of 72 days, 100 days (3 puppies), 235 days, and 256 days. The puppies receiving the 3 experimental diets, which differed primarily in the amount of fat infused, also did well. The two longest-term animals, which were fed entirely by vein for 235 and 256 days, more than tripled their body weights. Dudrick and Rhoads attended the World Nutrition Congress in Hamburg, Germany, where they presented "growth of puppies receiving all nutritional requirements by vein." It was with this study that parenteral feeding was launched.[1,2]

Patient studies were next, and Dudrick perfected the technique of subclavian catheterization in man. He and his colleagues published their results with 12 puppies and six adult patients in "Long Term Parenteral Nutrition with Growth, Development and Positive Nitrogen Balance" in the journal *Surgery* in 1968.[11] These six patients had chronic complicated GI disease. They were supported exclusively by vein with 2,400 to 4,500 calories per day for 10 to 200 days; they received 20 percent glucose, 5 percent fibrin hydrolysate, electrolytes, trace minerals, and vitamins, infused continuously through an indwelling catheter placed percutaneously in the external jugular or subclavian vein. The basic nutrient solution, containing 1,000 calories and 6 Gm. of nitrogen per 1,000 c.c was prepared by the pharmacist from fibrin hydrolysate and anhydrous glucose. Each morning the



Figure 2 : Professor Dudrick and "Stinky"

mineral requirements were determined, and appropriate electrolyte concentrates, vitamins, and trace elements were added. A positive nitrogen balance was achieved in all patients with associated wound healing, fistula closure, weight gain, and increased strength and activity.

A fortuitous circumstance arose with an infant girl at Children's Hospital of the University of Pennsylvania (U Penn).[1,2,5,12] The infant was born with a genetic intestinal problem similar to intestinal atresia. This newborn went on to have an extensive resection of more than 95% of her small bowel with duodeno-ileal anastomosis. Her weight had declined from 5.5 pounds at birth to four pounds at 19 days of age; she was cachectic, hypometabolic, and moribund. A student who had been an intern at the Hospital of the U Penn with Dr. Dudrick heard about his experiment with dogs and contacted him to request a teaching session at his hospital. After the conference, Dudrick was asked if he was willing to use his experimental form of feeding on this baby. Again, fortuitously, Dudrick's colleague, Douglas Willmore, lived near the hospital and took responsibility for the care and supervision of the infant's case.

A make-do IRB (there were no ethics committees at that time) discussed, pondered, and debated; all agreed, the risk of attempting to provide TPN to the infant was worth a try. Accordingly, a polyvinyl catheter was inserted via cut down into her right external jugular vein and advanced distally into her superior vena cava. The proximal end was passed subcutaneously behind her right ear to emerge through the parietal scalp, with the hope of reducing the entry of infectious organisms into the blood stream. The infant was initially infused cautiously with a basic nutrient mixture containing hypertonic dextrose, fibrin hydrolysate, electrolytes, and vitamins. Each day, another nutrient was added to the mixture sequentially so that each formula change can be easily assessed for any adverse reaction. The infusion was delivered continuously by a peristatic pump though a closed intravenous administration system containing an in-line 0.22- micron membrane filter. The infant gained 3.5 pounds in weight and 5.5 cm in length after 45 days of TPN. The circumference of her head increased by 6.5 cm, and she manifested normal activity and development for her age. She was fed for 22 months primarily by vein, and achieved a maximum weight of 18.5 pounds. Eventually, the feeding had to be stopped because the infant was sent home, and subsequently she succumbed to malnutrition. The nutritional, metabolic, and technological experience during her management was unprecedented. The infant became a unique legacy to parenteral nutrition.[5]

Professor Dudrick summarized his trail-blazing experiments step-by-step, and thus they are strongly recommended for every student in surgical nutrition.[1-2] He received many honors and awards for his pioneering work, such as: American College of Surgeons (ACS) Jacobson Innovation Award; ACS Icon in Surgery; American Surgical Association Lance/Karl Award; American Medical Association (AMA) Joseph B. Goldberger Award in Clinical Nutrition; AMA Brookdale Award in Medicine; and the William E. Ladd Medal of the American Association of Pediatrics. He founded the American Society of Parenteral and Enteral Nutrition (ASPEN) in 1975 and served as its first President. He also became the Founding chair of the department of surgery at the University of Texas Medical School in Houston, Texas and served as the chair of the department of surgery at the University of Pennsylvania. Additionally, ASPEN presented him a Lifetime Achievement Award in 2017. ASPEN's Stanley J. Dudrick Research Award was given each year during Dudrick's symposium to stimulate research in the area of nutrition.[5,6]

Over a period, long-term total parenteral nutrition was developed successfully as a safe and efficacious basic feeding technique. It has been credited for having been instrumental in saving countless lives and has defined the role of adequate nutrition in the achievement of optimal clinical results in all ages and in all types of patients when enteral feeding is not an option. The pupils of Rhoads and colleagues of Dudrick went on to contribute to the science of parenteral nutrition and deserve the title of giants of the field. For in-

stance, Douglas Wilmore, as noted previously, was an important contributor to the story of the first infant managed by PN. He was a partner of Dudrick on many studies and publications.[7-12] Moreover, Krieger started the Cleveland Clinic's Nutrition Support Team and a home parenteral nutrition program. He also served as President of ASPEN. Additionally, Harvey Sugerman,[13] the author's chief at the Medical College of Virginia, was a post-doctoral fellow at the University of Pennsylvania and corroborated with Dudrick on several projects; he pioneered gastric bypass surgery and the metabolic studies of morbid obesity. Sugerman became the editor-in-chief of Surgery of Obesity and Related Diseases (SOARD), president of the Western Trauma Association (WTA) and American Society for Metabolic and Bariatric Surgery (ASMBS). Another contemporary of Dudrick, KN Jeejebhoy[14] first reported long-term home parenteral nutrition for 23 months without a complication. Rifat Latifi, [15] the chief editor of the Kosova Journal of Surgery and the inaugural president of the Kosova College of Surgeons, made many contributions in the field and has also co-authored numerous articles and books on the subject with many distinguished pioneers, including a manual on surgical nutrition with Dudrick.

The legacy of Dr. Stanley J. Dudrick and the people who followed in his footsteps has been the key to unlocking the mysteries of parenteral nutrition, thus blessing patients with a chance of recovery from various ailments. In the words of the great man himself, "it is important for us to recall that we all began our lives as human beings in utero, receiving our nourishment entirely by vein, and we must continue our quest to attempt to emulate that ideal model of intravenous feeding for the support of those who might require a period of total parenteral nutrition for sustaining postnatal life."

Conflict of Interest Disclosure Statement

The author has no conflict of interest to declare.

REFERENCES

1. Dudrick SJ. History of Parenteral Nutrition. *J Am Coll Nutr*. 2009;28(3):243–251.
2. Dudrick SJ, Palesty AJ. Historical Highlights of the Development of Total Parenteral Nutrition. *Surg Clin N Am*. 2011;91:693–717. doi:10.1016/j.suc.2011.02.009
3. Barker CF. In Memoriam. Jonathan Rhoads 1907–2002. *Ann Surg*. 2002;235(5):740–744.
4. Dudrick SJ, Daly JM. Jonathan Evans Rhoads, M.D. Renaissance Man of the Twentieth Century. *Cancer*.1997;79(9):1737-1739.
5. Fuchs-Tarlovsky V. Tribute to Stanley John Dudrick, MD, FACS (1935 - 2020). *JCNM*. 2020;3(1):136-142. https://doi.org/10.35454/rncm.v3n1.084
6. Ahuja N. In Memoriam: Stanley Dudrick, MD. Yale School of Medicine. . Published January 23, 2020. Accessed Nov 1, 2021.
7. Dudrick SJ, Steiger E, Wilmore DW, Vars HM. Continuous long-term intravenous infusion in unrestrained animals. *Lab Anim Care*.1970; 20:521–529.
8. Dudrick SJ, Wilmore DW, Vars HM. Long-term total parenteral nutrition with growth in puppies and positive nitrogen balance in patients. *Surg Forum*. 1967;18:356-357.
9. Dudrick SJ, Vars HM, Rawnsley HM, Rhoads JE. Total intravenous feeding and growth in puppies. *Fed Proc*. 1966;25:481.
10. Dudrick SJ, Wilmore DW. Long-term parenteral feeding. *Hospital Practice*. 1968;3:65–78.
11. Dudrick SJ, Wilmore DW, Vars HM, Rhoads JE. Long-term total parenteral nutrition with growth, development and positive nitrogen balance. *Surgery*. 1968;64:134–142.
12. Wilmore DW, Dudrick SJ. Growth and development of an infant receiving all nutrients exclusively by vein. *JAMA*. 1968;203(10):860–4.
13. Travis SF, Sugerman HJ, Ruberg RL, et al. Alterations of red-cell glycolytic intermediates and oxygen transport as a consequence of hypophosphatemia in patients receiving intravenous hyperalimentation. *N Engl J Med*. 1971 Sep 30;285(14):763-8.
14. Jeejeebhoy KN, Zohrab WJ, Langer B. Total parenteral nutrition at home for 23 months, without complication and with good rehabilitation. A study of technical and metabolic features. *Gastroenterology*. 1973; 65: 811-820.
15. Latifi R, Dudrick SJ, editors. *Surgical Nutrition: Strategies in Critically Ill*. Austin, TX: Springer-Verlag/R.G.Landes; 1995.