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Stanley John Dudrick, titã em cirurgia e nutrição parenteral: definindo a tecnologia disruptiva

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Imagine a 50-year-old patient who develops erythema around the surgical wound on the fifth postoperative day following an exploratory laparotomy requiring multiple bowel resections as a result of a long standing incarcerated ventral hernia that had become symptomatic for several weeks. Imagine that the patient is on a clear liquid diet waiting for the return of bowel function. Imagine that the serum albumin is 2.5 mg/dL and that the patient shows signs of anasarca. Also imagine that while exploring the surgical wound, intestinal contents are observed, and a diagnosis of an entero-atmospheric fistula is made. Fortunately, in modern medicine, this clinical scenario is challenging but not a death sentence. Nowadays, high-complexity hospitals have multidisciplinary teams specialized in the treatment of patients with this type of complications. However, before parenteral nutrition was introduced, patients who could not be feed enterally were doomed to die of starvation.

Now allow me to tell you a story: In the sixties, a first-year surgical resident, an intern, at Pennsylvania Hospital was thinking about changing to a different medical specialty because patients with clinical conditions, such as the one I described above, did not recover from these "successful" operations, and died in the postoperative period(1). This resident was Stanley J. Dudrick, a young man of humble origins, born in the coal mining region in western Pennsylvania. This surgeon in-training worked tirelessly, and against popular wisdom, to develop a method of nourishing patients intravenously. His mentor, Dr. Jonathan E. Rhoads, gave him access to his laboratory, where in collaboration with Dr. Harry M. Vars, an authority on pharmacology(1, 2), Dr. Dudrick was able to reach his full potential and change the world.

It is important to remember that in the academic environment of the mid-twentieth century, total intravenous nutrition was considered an insuperable problem with an inaccessible solution, a "Gordian knot". First, it was said that "feeding entirely by vein was an impossible problem to solve, if it were possible, it would be impractical, and if practical, it would be unaffordable"(2). Dr. Dudrick's work was tedious and unglamorous, but his dedication, creativity, adaptability, and stubbornness led him to solve challenges that had not been resolved in the history of medicine, culminating in the development of a new technology: Total Parenteral Nutrition.

The achievement of a mix of nutrients from solutions with precise concentrations of hypertonic dextrose and protein hydrolysates (1000 calories and 6 g of protein/L, or 1 calorie/mL)(2), that was also chemically stable, was a time-consuming process and full of obstacles. However, once Dr. Dudrick conquered this initial, and almost impossible challenge, the real problems began. It was the way Dr. Dudrick solved these problems what mar-

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ked the difference between the genius and the rest who attempted Total Parenteral Nutrition before him.

Disruptive technology is defined as an innovation that alters the way an industry operates[3], in this case, the medical industry. Making Total Parenteral Nutrition a reality demanded a series of innovations and technological advances that led to regard it and define it—as few advances in history have been able to—as a Disruptive Technology in Medicine. Through some examples I will demonstrate how this colossal effort changed the history of medicine.

1. Use of the appropriate animal model: A decision was made to use Beagle dogs because these wonderful animals had been used by the United States Atomic Energy Commission to conduct experiments. More specifically, they were used to observe the effects of exposure to atomic radiation. Therefore, substantial information on fluid and nutritional requirements were available for this breed. While keeping animals alive with intravenous fluids and nutrients was considered a success, the truly remarkable achievement was that these Beagles were able to normally grow and develop from week 8 to adulthood[1,2]. With this experiment, the perception of what was possible radically changed, and unquestionably it demonstrated that this new technology could be used for growth and development, and not only for life support. Ultimately, its use in neonates would save the lives of millions who could not be fed enterally.
2. Venous access: In clinical practice the traditional venous access required the use of reusable and sterilizable needles. Commercially available plastic catheters made of polyethylene were toxic to tissues, which limited their use for long periods of time. The same happened with Teflon catheters used in the laboratory. In addition, the high osmolarity of the experimental solutions needed to feed patients caused significant damage to peripheral veins. The combination of these factors—which Dr. Dudrick experienced in his own flesh after infusing experimentally on himself with one of these solutions, leading to a severe phlebitis—led Dr. Dudrick to decide to use the jugular vein to access the superior vena cava, this was a statement that went against the belief of the medical establishment, including his mentor Dr. Rhoads, that long-term central venous access was extremely harmful and was contraindicated[4].

   Finally, through trial and error, Dr. Dudrick found that polyvinyl chloride or PVC (obtained from a hardware store and sterilized) worked better and was more durable than any commercially available catheter. In this way, he solved the problem of having a central venous access available for long-term administration of concentrated solutions, which are routinely used in today's hospitals.
3. Filters: The difficulty of sterilizing these solutions rendered intravenous administration of the prescribed nutrients impossible. The caramelization produced by the heating of glucose, and sugars in general, prevented the use of this sterilization method. Dr. Dudrick found a very ingenious solution: The pharmacy at Pennsylvania Hospital used small filters produced by Millipore Corporation to decontaminate ophthalmic solutions from radioactive isotopes, as these solutions could not be sterilized in the autoclave. He learned that these filters were also used in the beer and wine industry to prevent contamination. Dr. Dudrick started using these industrial filters to sterilize liters of his solution. Although the filters permitted to obtain a sterile solution, any contamination present in the infusion system could still cause bacteremia. To solve this problem, another type of filters, this time obtained from the gasoline industry[1], were placed "in-line" or along the infusion system before the solution reached the patient (Figure 1)[5]. The development of this technique and its use changed the world of medicine, and currently, it is difficult to picture modern infusion systems without filters.
4. Infusion pumps: The clinical use of infusion pumps was not a standard. In hospitals, solutions were infused via a gravity system and quantified via the drip method. As a result, in many occasions nurses who were near the end of their shift rushed to complete the volume ordered by increasing the infusion rate, leading to metabolic alterations due to high doses of glucose infused. This situation motivated the use of rudimentary electric infusion pumps (Figure 1). Implementing this technology was not without difficulties. Due to fluctuations in alternating current, electrical peaks modified the infusion rate of the pumps. This led to the design of infusion pumps with surge protective devices and infusion alarms with support of the School of Engineering. These infusion pumps are a standard at hospitals around the world, and nowadays we could not treat our patients without them.
5. Metabolic bed: Parenteral feeding of the first baby, a girl, diagnosed with an intra-abdominal catastrophe was a massive challenge requiring the development

of new technologies to treat and monitor patients. And it was associated with ethical problems never seen before. However, I want to focus on the development of the "metabolic bed". In this patient, the exact nutritional requirements and her response to nutrients administered had to be calculated daily. For this purpose, a bed was designed to collect all excretions. The measurement of excretions allowed to carry out treatment modifications to provide the optimal level of nutrients, fluids, and electrolytes. This type of monitoring not only increased our understanding of human metabolic physiology, but also demonstrated the feasibility and benefits of intensive therapy in medicine. The lives impacted by the decision to implement total parenteral nutrition in a baby changed the way we understood the reach of the medical profession (Figure 1).

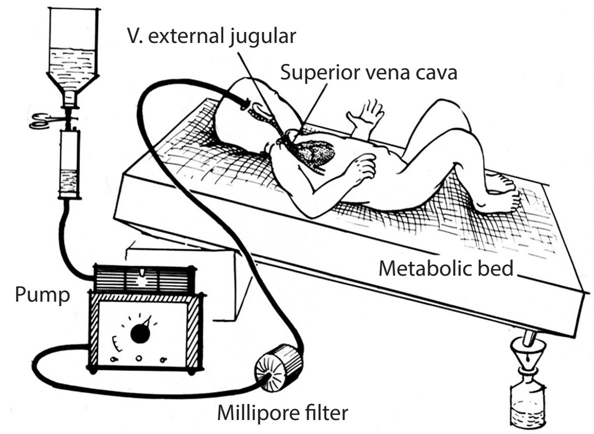

Figure 1. Metabolic bed.

Many other technologies or techniques were implemented and developed by this surgery giant and his team, but the pages in this journal would not be enough to name them all. The important thing here is to recognize that the work of Dr. Stanley John Dudrick changed medicine forever. In the same way we acknowledge that other technological advances such as the Internet and Uber changed the way we see the world, I dare to say that the development of Total Parenteral Nutrition and associated technologies changed the path of modern medicine, which is exactly what defines a Disruptive Technology, similarly to innovations such as asepsis and antisepsis, or the discovery of general anesthesia or antibiotic therapy.

Today, we remember and pay tribute to the life of this titan (Figure 2), a dreamer who was way ahead of his time, whose wonderful legacy changed the course of medicine, impacted the lives of patients, and will continue to reap fruits for generations. Dr. Stanley John Dudrick's legacy will live forever!

Figure 2. Doctors Stanley J. Dudrick and José Mario Pimiento..

Jose Mario Pimiento, MD, FACS. Medical Doctor for the Universidad Nacional de Colombia. In 2000 he met Dr. Dudrick while rotating as a medical student at Bridgeport Hospital, Connecticut. Dr. Pimiento was trained in General Surgery by Professor Dudrick at the Stanley J Dudrick Department of Surgery at the Saint Mary's hospital affiliated with the Yale New Haven Health System. He is a surgical oncologist, who specialized on the upper gastrointestinal tract at the Moffitt Cancer Center, Tampa, one of the National Cancer Institute designated centers in the USA. Dr. Pimiento is a winner of the Stanley J. Dudrick Research Scholar Award granted by the American Society for Parenteral and Enteral Nutrition (ASPEN) in 2019. He maintained permanent contact with his teacher and mentor.

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