Enhanced Recovery: The Medical Myth-Busting, Evidence-Based Paradigm of the 21st Century

With his 1997 article, "Multimodal approach to control postoperative pathophysiology and rehabilitation", Danish colorectal surgeon, Henrik Kehlet, challenged the surgical and anesthesia worlds to embrace an evidence-based patient-centric approach to perioperative care that would reduce post-operative complications and remarkably improve surgical outcomes. Involving multiple disciplines and modalities, this new paradigm focused on the pathophysiology and reduction of the "surgical stress response." Alternatively called "Fast-track surgery", it would form the basis for the Enhanced Recovery After Surgery® (ERAS®) movement in Europe and the UK. The primary goal was to expedite safely patients' return to their normal level of daily function, thereby drastically reducing hospital lengths of stay (LOS) and healthcare costs without increasing re-admissions.

If Doctor Kehlet's visionary work has earned him the title of "Father of Enhanced Recovery", then Swedish colorectal surgeon, accomplished nutritionist, prolific researcher and President of the International ERAS Society®, Doctor Olle Ljungqvist, would have to be a revered "Uncle." His many early collaborations in and advocacy for the development and standardization of a successful Enhanced Recovery protocol were key. Enhanced Recovery mandated the abandonment of the 160 year-old, non-evidence-based myth that total pre-op fasting from midnight prevented regurgitation and aspiration in healthy patients. It resonated with the 1999 ASA® Fasting Guidelines and their 2011 Update: "Enhancements in the quality and efficiency of anesthesia care include…decreased risk of dehydration or hypoglycemia from prolonged fasting…It is appropriate to fast from intake of clear liquids at least 2 h before elective procedures…" Several studies had confirmed that the consumption of clear liquids 2-3 hours pre-op most often reduced both residual gastric volume and residual gastric acid. Therefore, such ingestion could actually reduce the incidence of the dread regurgitation and aspiration.

But, it was Dr. Ljungqvist's unique focus on the maintenance of an anabolic state in the face of the metabolic stresses of both pre-op starvation and surgery that undoubtedly led to his most profound contribution to the success of the ERAS® effort. He demonstrated that pre-operative oral carbohydrate loading could reduce the post-op insulin resistance (PIR) phenomenon that causes a non-diabetic's post-op metabolic response to mimic that of a type 2 diabetic, resulting in post-op hyperglycemia despite adequate insulin levels. His findings have been replicated in dozens of recent studies.

Dr. Ljungqvist's "Jonathan Rhoads Lecture 2011: Insulin Resistance and Enhanced Recovery After Surgery" offers an excellent overview of the subject and is a must read. In it, he stressed the fundamental effects of insulin not only on glucose but also on fat and protein metabolism, the aberration of which spawns a cascade of post-op complications. He chronicled a search for an oral carbohydrate that could approximate the efficacy of a 20% IV glucose infusion that effectively abolished PIR. To fill that need, Dr. Ljungqvist ultimately formulated and patented a clear 12.5% carbohydrate-rich pre-operative beverage, consisting principally of the complex carbohydrate source, maltodextrin. It is currently packaged in 200 ml plastic bottles; two bottles constitute a recommended serving size. It is not available in the USA.

Wang et al provided an elegant refinement of the intracellular events of PIR in a RCT that compared 3 groups of otherwise healthy colorectal surgery patients, defined by their immediate pre-op nutrition status: 1) an OCH group that consumed 400 ml of a12.5% complex carbohydrate beverage 3 hours prior to anesthesia induction, 2) a placebo group that consumed 400 ml of flavored water at 3 hours at a similar time and 3) a control group that was fasted from 2100 of the previous night. The following parameters were monitored: fasting and post-op blood glucose (BG), HOMA-IR and insulin levels plus insulin receptor (PTK) which activates the main signaling pathway (PI3K)/(PKB) that is responsible for the majority of the metabolic actions of insulin. The hypothesis that pre-op oral carb-loading attenuates PIR by enhancing the PI3K-dependent pathway was confirmed: median post-op insulin and BG levels at 180mg/dl for OCH were significantly lower than for fasting at 208 mg/dl ($P = 0.002$) and placebo at 219 mg/dl ($P = 0.001$) as were HOMA-IR levels ($P < 0.001$). Post-op, PTK activity and median PI3K levels were significantly higher in the OCH group versus the two other ($P < 0.050$).

Due to the eccentricities of the USPTO procedures of the late 90's, nearly simultaneously (about 6,000 miles apart), but completely unknown to each other, another physician was formulating a very similar pre-operative beverage to address a related but very different pre-op patient care issue among outpatients, not inpatients. By the early '90s, nearly 70% of all surgical and invasive diagnostic procedures had migrated from the hospital to the outpatient surgery center (OPSC). The typical OPSC's operating hours were extended from early afternoons to late evenings to accommodate that growth. Per tradition, all patients were expected to fast completely from midnight or for up to 16-18 hours. As the Medical Director of a large and busy OPSC, the creator of ClearFast® was focused on the disturbing physical manifestations of that prolonged total pre-op fast, including hunger, thirst, nausea, headache, anxiety and general discomfort as well as on the significant economic consequences of patients violating that fast. While a fast from solids might have been rationalized, the prohibition of any clear calorie-rich fluids was counter-intuitive.

Both physician-inventors faced the same challenges: a beverage fit for consumption at 2 hours prior to surgery could not contain fats or proteins that are known to delay gastric emptying, making carbohydrates the only available calorie source. A calorie content of less than 200 kcal would not significantly interrupt the starvation process or minimize fasting symptoms. Since rapid absorption was essential, an osmolarity in the physiologic range of less than 300 mOsm and a volume of ≈ 400 ml were targeted. While it is true that 1 gram of any carbohydrate -- simple or complex-- provides 4 kcal of energy, the "osmolar contribution" of 1 gram of a simple sugar such as fructose (M.W. of 180 g/mole) is 14 mOsm or 10 times that of a gram of a typical maltodextrin (M.W. 1,700 g/mole) at 1.4 mOsm. 50 g of fructose in a 400 ml solution would have had an unacceptable osmolarity of approximately 700 mOsm while a 400 ml solution containing 50g of maltodextrin would have an osmolarity of 70 mOsm. Therefore, maltodextrins represented the principal carbohydrate source in both beverages. Though the beverage formulations were very similar, the patents that were issued for each were based primarily on the differences between their "methods claims."

In 2013, Duke University distinguished itself as the earliest adopter of the Enhanced Recovery movement in the USA. It also became the first institution to use ClearFast in its ER effort that year. Since then, the adoption rate has accelerated, prompting think tanks such as The Center for Medical Technology Policy to predict that by 2020, there will be at least a 75% nationwide

hospital adoption of Enhanced Recovery Programs. With that, the "NPO from MN" dinosaur will have slipped into a long-overdue extinction. Pre-op carb-loading will be universally recognized as not only "not bad" but actually "good" for patients!

Enhanced Recovery programs typically focus on the "12 hour pre-op watch" in terms of recommendations for pre-op carbohydrate dosing schedules. The majority propose two servings, each consisting of 355-400 ml containing approximately 13.5-12.5% clear carbohydrate-rich iso-osmolar solutions, on the evening before surgery and a third serving between 2-3 hours prior to surgery. Pre-op carb loading is gaining popularity in the larger OPSC sector as well where single to double dosing occurs, depending on the scheduled surgery time: at least one serving at about 2 hours before surgery with additional servings consumed earlier if surgery is scheduled later in the day. In the OPSC setting, patients are also requesting the carb-rich beverage as their preferred "early recovery" nutrition in the PACU (Post Anesthesia Care Unit) or on arrival at home at a time when other beverages and solids have limited appeal. Some specialists, such as Plastic Surgeons, who practice exclusively in the OPSC setting are tailoring ER protocols to their practice needs and employing a schedule of multiple servings of a carb-rich beverage.

The safety of pre-op carb loading for the known diabetic is a frequently asked question by those contemplating an Enhanced Recovery Program. According to Gustafsson et al and Can et al, Type II diabetics or patients demonstrating insulin resistance (IR) could safely ingest 400 ml of a carb-rich beverage 2-3 hours before surgery as long as they do not have gastroparesis. Many seasoned practitioners of Enhanced Recovery Programs agree that Type I diabetics, ironically, are excellent candidates for such carb loading which removes them from a starved state that would otherwise lead to extremes of hypoglycemia or hyperglycemia. All agree that their glycemic management, from matching pre-op insulin dosing to the ingested carb load to close intra and post-op control are already considered routine.

Predictably, at least one entrepreneurial group has literally rushed to market with a "competitive" pre-op carb-loading product without benefit of any clinical trials or supportive IP. Ironically, its formulation that "empirically" cuts the carbohydrate load of maltodextrin by 50% is based on a probable miss-characterization of the elegant Wang RCT study cited above. The group singles out Wang's OCH group as "patients who may still spike their glucose to 180 mg/dl. At this level there is an approximate doubling of the risk of surgical site infection (SSI), cardiovascular complications, and acute kidney injury." Here is what they failed to recognize in "selectively reporting only one third of the Wang data": median post-op insulin and BG levels at 180mg/dl for the OCH group were significantly lower than for fasting group at 208 mg/dl ($P = 0.002$) and placebo group at 219 mg/dl ($P = 0.001$) as were HOMA-IR levels ($P < 0.001$). Post-op, PTK activity and median PI3K levels were significantly higher in the OCH group versus the two other ($P < 0.050$). It seems that the world will have to await the clinical validation of the claims made about a new powdered product whose reconstitution and chilling on the day of surgery may well present their own challenges to adoption.

Meanwhile, in a perfect world of Enhanced Recovery, there appears to still be an elephant in the room…the undiagnosed pre-diabetics who number as many as 86,000,000 in the USA…who have exaggerated hyperglycemic responses to stresses, especially to surgery. ClearFast applauds and supports organizations that are implementing earlier and better screening and profiling of these so called "non-diabetic patients", including multiple fasting BGs, OGTT, HgA1c levels, physical profiles and health histories, family histories.