Triple Your Pleasure

Three pancreatic hormones may be necessary to fully close the loop.

By Gary Scheiner MS, CDE

Medusa. The Hydra. The 2010 Philadelphia Phillies starting rotation. All considered 3-headed monsters of epic proportion. Another 3-headed beast is in the works, and it will be very good news for all of us who treat and live with diabetes.

Today's closed loop systems pump rapid-acting insulin into the subcutaneous fat where it takes time to work: typically 15 minutes to start, an hour to peak, and 3-4 hours to finish. Compare that to a healthy pancreas which secretes insulin directly into the bloodstream where it starts working in seconds and finishes in just a few minutes. So even with sophisticated mathematical algorithms to interpret the sensor data and predict what's going to happen next, the closed loop systems currently being used in clinical trials fail to prevent post-meal blood sugar "spikes" and can't shut down insulin secretion soon enough to prevent lows during and after physical activity.

One company's solution is to have the user anticipate when a meal will be consumed and program the closed loop pump to deliver a preparatory bolus the same way we've always done. Other companies are looking at ways to make the insulin start and finish working much faster. But all are missing an important point: Glucose regulation involves the interplay of multiple hormones, not just insulin.

Following our column theme (and my favorite book title) *Think Like A Pancreas*, let's consider what a pancreas really does, at least when it comes to glucose regulation. Besides producing insulin, the islet cells of the pancreas also secrete **glucagon** in response to falling blood glucose levels, and **amylin** when food enters the stomach.

Glucagon is important to the prevention of hypoglycemia. Once glucagon is secreted by the pancreas, it rushes directly to the liver where it causes the immediate release of glucose into the bloodstream. Along with other "counterregulatory" hormones such as epinephrine and cortisol, glucagon keeps blood sugar from dropping too low even under the most extreme conditions.

Amylin's actions are focused around post-meal blood sugar control. When amylin is secreted, it affects the nerves that control gastric emptying, slowing down the rate at which food digests. It also blocks hunger by stimulating the "satiety" center of the brain and keeps glucagon from being secreted right after eating. Through these three mechanisms, amylin works in tandem with insulin to keep blood sugar from rising much (if at all) after eating.

Now imagine this. What if a closed loop system could incorporate a pump that secretes not one, not two, but THREE hormones: insulin in a steady basal manner; insulin and amylin in larger amounts (boluses) when blood sugar starts to rise; and glucagon when blood sugar starts to drop or reaches a critical low level. Sounds far fetched? Maybe not.

Several insulin pump companies are in the early stages of developing multi-chamber pumps. Some of the current insulin manufacturers and a few start-up companies are formulating ways to make insulin work much faster. A new company has developed a glucagon formulation that is stable in liquid form at room temperature.

And the commercially available amylin hormone (Symlin), although not government-approved for use in this manner, has been delivered successfully by many individuals through an insulin pump.

So where does that put us today? Well, nowhere exactly. This type of triple-chamber system is still years off. But it does provide a model upon which we can examine how we manage glucose levels today. Symlin is readily available for those who experience blood sugar spikes after meals (or incessant hunger). Although complex to master, Symlin can be successfully incorporated into most diabetes management plans. But it will require some patience and willingness to carefully titrate doses and tolerate a few side effects in the early going.

Glucagon is also readily available, but nobody expects us to use it as tool for managing day-to-day drops in blood sugar. However, it can be used in a traditional manner to treat severe lows, as well as mild/conscious lows when administered in small doses using standard insulin syringes. But before getting to that point, we can certainly examine how we treat our lows. Are you using the most rapidly-digesting carbohydrate possible (dextrose)? Are you making good use of the *predictive* value of continuous glucose monitoring so as to prevent lows before they happen?

When it comes to your insulin, are you giving it time to work before your food kicks in? Pre-bolusing (giving insulin a little while before eating) is a very effective technique for reducing post-meal spikes. And when extreme highs occur, consider using i.m. (intramuscular) injections of insulin to bring the blood sugar down as quickly as possible.

Hey, you may not have a perfectly functioning pancreas, but at least you can think like one!

Editor's note: Gary Scheiner is a Certified Diabetes Educator with a private practice, Integrated Diabetes Services, based near Philadelphia. He works with individuals and their families on intensive diabetes management via phone and e-mail throughout the world. Gary has had Type-1 diabetes for 25 years, and currently uses Symlin, insulin pump therapy and continuous glucose monitoring to manage his diabetes. He can be reached at 877-735-3648, or gary@integrateddiabetes.com. His website is www.integrateddiabetes.com