In part 1, part 2, and part 3 of this series, you learned how there are a lot of misconceptions on how insulin works in the body, and how it has been unfairly blamed for weight and fat gain in our society. In this article, I am going to dismantle one of the biggest insulin myths of them all...a myth that has been perpetuated in textbooks and is still taught in college classrooms, despite the fact it was shown to be wrong over 25 years ago.

Insulin Is Not Required for Cells To Take Up Glucose

Are you surprised by the heading above? Many people think that your cells need insulin to take sugar out of the blood. One of the pieces of evidence that is offered for this is the type I diabetic. When a type I diabetic has no insulin, blood sugar skyrockets. This is supposedly because sugar can't get into cells.

However, the above scenario is not what happens in a type I diabetic that has been taken off of insulin. Sugar can get into the cells just fine. There's actually something else going on. A review paper published in the Journal of Anasthesia thoroughly describes how insulin has been misunderstood in its role in blood sugar regulation, and I will summarize this paper here, along with some of my own comments.

A Man Ahead of His Time

In 1916, Sir Edward Schafer, a professor of physiology, published a book called *The Endocrine Organs*. In this book, he hypothesized the existence of what we now call insulin:

> *The results of pancreas extirpation and pancreas grafting are best explained by supposing that the islet tissue produce an Autacoid which passes into the blood stream and effects carbohydrate metabolism and carbohydrate storage in such a manner that there is no undue accumulation of glucose in the blood. Provisionally it will be convenient to refer to this hypothetical substance as insuline.*

Insulin would go onto be discovered 8 years later. Schafer also hypothesized that insulin was created from an inactive precursor:

> *It must however be stated that it has yet to be determined whether the active substance is produced as such in the pancreas or whether it exists there as pro-insuline which becomes elsewhere converted into an active autacoid.*

Pro-insulin was discovered nearly 50 years later. Schafer was truly a man ahead of his time.

Schafer avoided using the term "hormone" to describe insulin. Instead, he used the terms "autacoid" and "chalone." An autacoid was a substance with excitatory action, meaning it stimulated things to happen in your body. An autacoid can be thought of as similar to the gas pedal in your car; you step on the pedal and it stimulates your car to go faster. A chalone was a substance with inhibitory action; it slows things down in your body. A chalone can be thought of as similar to the brake in your car. Schafer correctly hypothesized that insulin acted as both an autacoid and chalone in your body. He also considered that insulin acted as much more of a chalone than an autacoid in your body. In other words, he felt that insulin's inhibitory functions were much more important than its excitatory or stimulatory functions. He would be proven correct many years later.

The Black Age of Endocrinology

However, before Schafer was proven correct, the "Black Age of Endocrinology" ensued. This was the time period between 1950 and 1980, where scientists extrapolated beyond their discoveries. They took *in vitro* animal data (research performed in a test tube or culture), and then assumed that the same thing happens in humans *in vivo* (inside the body). In fact, one of the reasons I am so highly critical of Gary Taubes and his Good Calories, Bad Calories book is that he relies heavily on research from this period, despite the fact that much of what was thought then has either been overturned by better research, or at least significantly altered. Taubes even stated around the 31 minute mark in this interview that he doesn't pay attention to modern research because "all of this should have been obvious decades ago." This is a surprising stance for a science writer; I would think that he would understand that conclusions in science are always tentative. This is particularly true in the nutritional and physiological sciences, where advances in measurement techniques have allowed us to measure and discover things that we could not measure before; this has overturned or modified many hypotheses and thoughts over the years. But I digress.

The Black Age of Endocrinology is what led to the now mistaken belief that insulin is needed for your cells to take up glucose. Experiments in the 1950s showed that insulin could stimulate bits of rat muscle and fat to take up glucose. This data was extrapolated to humans, and it was then incorrectly hypothesized that a lack of insulin results in glucose not being able to get inside your cells, and thus blood glucose climbs to dangerous levels. This erroneous thinking has now been taught in textbooks and college classes all over the world for many years, resulting in dogma. Unfortunately, it is very difficult to overcome dogma, and even though this concept of insulin was shown to be wrong in the 1970's, it still continues to be taught to this day.

Glucose Transport is Not Insulin Dependent

The erroneous hypothesis that insulin withdrawal results in high blood glucose because "glucose can't get into cells" was based on the assumption that insulin is *required* for cells to take up glucose, rather than insulin merely *enhancing* glucose uptake. What the scientists in the 1950s failed to note was how tissues can take up considerable amounts of glucose even when insulin is absent.

Glucose enters your cells via a family of transporters. A primary transporter in muscle and fat cells is known as GLUT-4. Insulin stimulates GLUT-4 to move from the interior of a cell to the cell surface, where the glucose can then bind to the GLUT-4 transporter and enter the cell. However, there are plenty of glucose transporters on the cell surface, even when there is no insulin. In fact, there are enough transporters on the cell surface to allow the cell to get enough glucose to sustain its energy needs. Thus, glucose transport into cells is never truly dependent upon insulin. Insulin enhances the uptake of glucose into cells, but it is not required for it. In fact, when you knock out the insulin receptor in mice so that insulin cannot stimulate glucose uptake into muscle or fat cells (yet you keep the insulin receptor intact on other cells like brain and liver), the animals do not become diabetic and they have normal blood sugars.

What Really Happens in a Type I Diabetic

Metabolic tracer studies have allowed us to learn how insulin operates in humans *in vivo*. When you take a type I diabetic off insulin, blood glucose climbs sharply. However, it's not because glucose can't get into cells. In fact, glucose uptake into cells actually increases. This is because the concentration of glucose in the blood is so much higher than the cellular concentration that glucose must move into the cells (remember, there's already enough glucose transporters on the cell surface even if there's no insulin). So why does blood glucose climb so high? Remember that the amount of glucose in your blood is both a function of how much glucose is entering the blood (the *rate of appearance*), as well as how much glucose is leaving the blood (the *rate of disappearance*). In a fasted diabetic without insulin, all of the glucose is coming from the liver. Remember that your liver helps maintain blood sugar levels when you are fasted by releasing glucose; this glucose comes from both *gluconeogenesis* (the formation of glucose from non-carbohydrate sources, like protein) and *glycogenolysis* (the breakdown of glycogen stored in your liver). Insulin acts as a brake (a chalone as Dr. Schafer described it) on these processes. Thus, when you do not have insulin, you have runaway gluconeogenesis and glycogenolysis. The high blood sugar in an uncontrolled diabetic is thus caused by overproduction of glucose from the liver, not because glucose can't get into cells.

In fact, since insulin is not present, many processes go forth at high rates, completely unregulated. Insulin normally inhibits the production of ketones by your liver; without insulin to slow down ketone production, ketones are produced at high rates, resulting in diabetic ketoacidosis. This is why hyperglycemia and ketoacidosis occur simultaneously. Without insulin, you also have accelerated proteolysis (the breakdown of protein) and lipolysis (the breakdown of fat). The elevated amino acids in the blood provide further substrate for the liver to continue to produce large amounts of glucose. The elevated fatty acids provide substrate for the liver to continue to produce large amounts of ketones.

Thus, insulin is like a traffic cop or a stop light at an intersection. It helps slow down and control traffic. Without a stop light or traffic cop, cars go through the intersection uncontrolled and you get traffic accidents. Likewise, without insulin in the body, gluconeogenesis, glycolysis, proteolysis, ketogenesis, and lipolysis all proceed at high rates without anything to stop them. The end result is hyperglycemia, ketoacidosis, and eventually death.

When you inject insulin into an uncontrolled diabetic, you are now providing a brake on all of the processes mentioned earlier. You inhibit production of glucose by the liver, so blood sugar falls. Because there is no longer hyperglycemia, glucose uptake into cells actually decreases. Lipolysis is inhibited, so free fatty acid concentration falls to near zero. Because there are no longer free fatty acids to make ketones, ketone production slows down. Proteolysis is also inhibited.

Insulin...More of a Traffic Cop Than a Storage Hormone

Metabolic tracer studies have proven what Schafer had hypothesized nearly a century ago...that insulin's main role in the body is inhibitory rather than excitatory. While insulin certainly does have excitatory functions, it is not primarily a "storage hormone" that many individuals claim that it is. Insulin is not needed for your cells to take up and store glucose. Certainly, it enhances uptake, but there is a big difference between enhancing uptake and being needed for uptake.

Of course, this research only tells us what happens when insulin is present versus when it is not present. What about the normal situation of a healthy person, who ingests a meal and sees a rise in blood glucose? What is happening to bring glucose back to normal? And what happens in a type II diabetic in this situation? Learn the answers to these questions by reading part 6 of the series. Also click here to read part 5 where I address comments made by some of the critics of this series.

REFERENCE: Sonksen, P., and Sonksen, J. Insulin: understanding its action in health and disease. *British Journal of Anaesthesia*. 85(1):69-79, 2000.