

The Ten-Year Anniversary of the “Ominous Octet”

Kersthine Andre, MD

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The concept of the “ominous octet” is so commonly discussed in the diabetes world, that we may not remember that this paradigm shift only occurred about 10 years ago. Ralph A DeFronzo, MD introduced the concept of the “ominous octet” in 2009 in the prestigious Banting lecture as well as in the journal *Diabetes*. (2009 Apr;58(4):773-95)

Prior to Dr. DeFronzo’s description in 2009, we generally thought of diabetes as a triumvirate of organs leading to type 2 diabetes mellitus (T2DM). In the triumvirate theory, the three defects leading to diabetes were: 1) decreased insulin production by the beta cell, 2) increased insulin resistance in the muscle, and 3) increased insulin resistance in the pancreas.

Dr. DeFronzo described other core defects in the development of T2DM in addition to those in the **liver**, **muscle** and **beta cells** of the pancreas. He described that **fat cells** have accelerated lipolysis, which further

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The Greater Pittsburgh Diabetes Club – Membership Changes Are on the Horizon

What is new?

Jacqueline Wesche-Thobaben, RN, BSN, CDE, CCRC

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As of January 1, 2020, the membership structure for the Greater Pittsburgh Diabetes Club will change.

Membership dues will remain at \$25 for the year January 1, 2020 through December 31, 2020. This is a bargain given the opportunity to earn 2 CME/CEUs and network with other multidisciplinary clinicians with a special interest in diabetes twice a year. Dues will be accepted through January 31, 2020 only. After this date you will not be able to become a member until the following year.

Educational programs will reflect an increase in the price as follows:

Members: \$15 per educational program
Non-Members: \$40 per educational program

Membership applications will be distributed at the October 29 meeting or you may call Michelle Besanceney at 412-321-5030. ■

Community Events

**Tour de Cure – Ride, Run, Walk - ADA
September 14, 2019, Pittsburgh**

South Shore, Riverfront Park, Southside
Ride – 63, 30, or 12 mi; Run – 5K; Walk – 5K
Visit American Diabetes Association Tour de Cure Pittsburgh for details.

**One Walk – JDRF
September 21, 2019, Pittsburgh
September 28, 2019, Greensburg**

Schenley Park, Flagstaff Hill
Walk 2 miles
Visit jdrf.org/onewalk for details ■

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decreases insulin secretion from the pancreas. Also, in people with diabetes, the **gastrointestinal tract** has decreased production of incretin hormones, which leads to decreased insulin release from the pancreas. In addition to the pancreas beta cells not producing as much insulin, the **alpha cells** of the pancreas release too much glucagon. In the **kidney**, there is increased glucose reabsorption. Also, the **brain** plays an important role in regulating weight. Although insulin usually decreases appetite by its effect on receptors in the hypothalamus, there seems to be insulin resistance in the brain as well.

In addition to describing the eight defects causing diabetes, Dr. DeFronzo described a pathophysiologic approach using initial combination therapy with anti-diabetes agents known to correct established pathophysiologic defects in T2DM rather than the sequential addition of antidiabetes agents as the disease worsened. By using a combination of medications that target different defects, there could be a more effective and physiologic approach in managing patients with T2DM and possibly slow or reverse β cell failure.

The Greater Pittsburgh Diabetes Club is honored to have Dr. DeFronzo as our speaker on October 29, 2019 at the Rivers Casino, North Shore, 6pm. ■

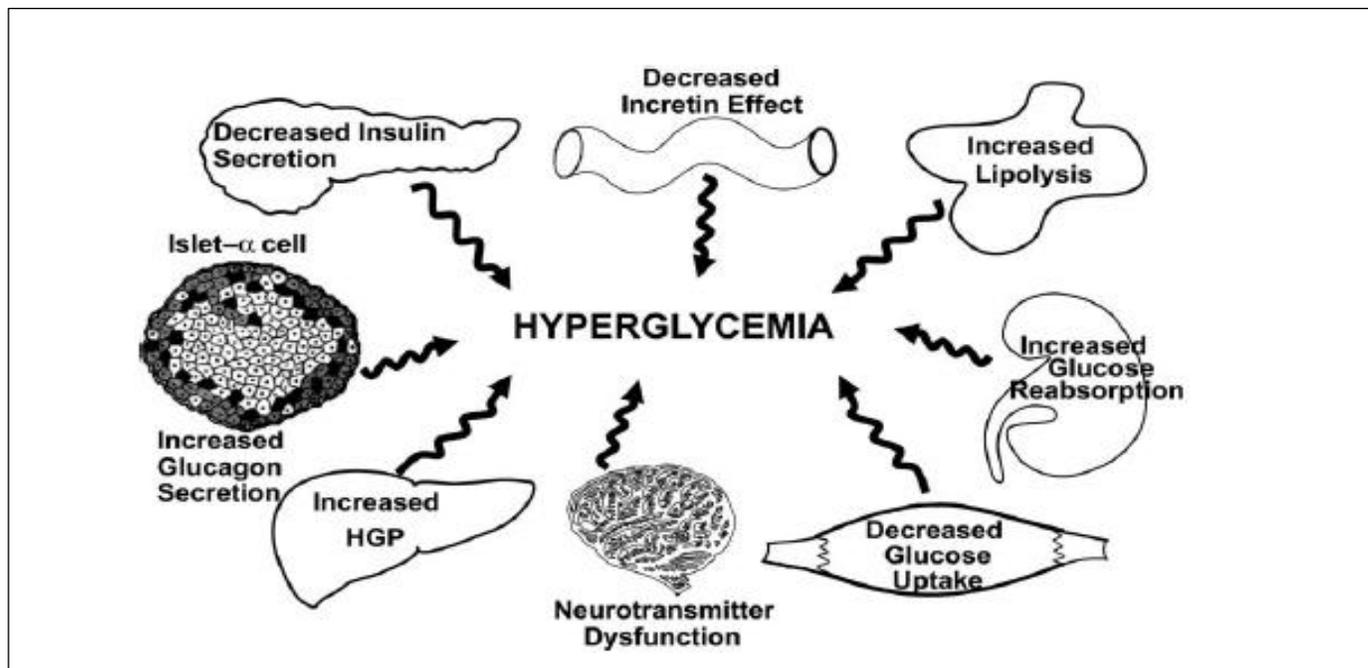
Using JDRF to Make Connections and Find Support for Your Patients

Jamie Kerr, Fellow Type 1
Outreach Manager, JDRF

Everyone knows that JDRF is the leading organization funding Type 1 Diabetes research, but what you might not know is that JDRF also has a lot of programs to benefit those currently living with T1D. JDRF's Outreach program can help those who are newly diagnosed, those who have been living with T1D for years and every level in between.

Most of you have probably heard of the Bag of Hope. The JDRF Bag of Hope is filled with useful resources for both the child who has been diagnosed with T1D and his or her caregivers. Along with educational materials, they have included a special friend — Rufus, the Bear with Diabetes® — to show your child he or she is not alone while learning to take shots and test blood sugar. The bags of Hope can be requested online at JDRF.org and are also distributed 3 times per month at Children's Hospital of Pittsburgh. They have a similar bag for adults, called the T1D Care Kit. The T1D Care Kit features tools and information to educate, support and inspire adults with

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REMIT-DM Trial

David Rometo, MD

Endocrinologist, University of Pittsburgh

The Pittsburgh Innovation Challenge (PInCh) is an annual competition for funding in the medical use of technology. In 2017, the contest had a focus on wearable technology, and Dr. Sandra Sobel of the UPMC Division of Endocrinology, and Chief of Endocrinology at Mercy Hospital, began assembling a team to compete for this grant, using continuous glucose monitoring in a new innovative way; to safely achieve remission of type 2 diabetes shortly after diagnosis.

Studies have been done over the last decade in institutions around the globe using insulin therapy (specifically basal insulin plus pre-meal insulin) to achieve euglycemia quickly after the diagnosis of type 2 diabetes. In a Chinese population, achieving these targets with an insulin pump or multiple injections resulted in diabetes remission that lasted up to 1 year in 50% of the patient's enrolled. Acutely giving the patient all the insulin that their body needs to have normal range glucoses resulted in a significant improvement in their insulin sensitivity, and improvement in their beta cell function.

The duration of insulin therapy in these trials was often less than 1 month. However, the patients required hospitalization, with physicians and nurses checking capillary glucose 7 times/day, administering and titrating their insulin doses in a controlled environment. This type of study has not been repeated, nor the results confirmed, in an American population. And this has not been attempted outside of the hospital or relying upon CGM data.

The team proposed the use of continuous glucose monitor (CGM) while following an insulin titration protocol with basal bolus insulin pens for a period up to 1 month, followed by discontinuation of the insulin and the continuous glucose monitor. The project was titled REMIT-DM: Remission through Early Monitored Insulin Therapy, Duration Month. After several rounds of competition, the team was awarded \$25,000 grant to proceed with the study and the development of this use of technology.

These funds were used to conduct a pilot clinical trial on 10 subjects who were diagnosed with type 2 diabetes in the last 4 years, with an A1c greater than 7, and who were naïve to insulin therapy.

Subjects wear a Dexcom G6 CGM, which requires no calibration, for 30 days. They give 4 injections/day of insulin while on a consistent carbohydrate diet for 3-4 weeks, in the real-world with outpatient medical visits and diabetes education visits before and after this period. They increase their doses according to the CGM values and arrows until fasting glucoses are <95/mg/dL and 2-hour post-prandial glucoses are <125 mg/dL without hypoglycemia, then decrease doses as needed to prevent severe hypoglycemia.

The investigators hope to show that insulin-naïve patients can quickly and safely achieve these glucose targets using CGM and this titration protocol. The subjects will also be followed for 1 year afterward to assess for diabetes remission and to determine its duration. Even if the rate of remission is not as high as in prior trials, this temporary use of CGM and insulin titration protocol can still be tested in other populations that would benefit from quickly obtaining euglycemia: gestational diabetes, pregnancy with preexisting diabetes, patients with long-standing diabetes starting insulin with no expectation of remission, and patients who need glycemic control before surgery.

Programming the titration protocol into a phone app that receives data directly from the Dexcom CGM will likely improve compliance with and safety of dose changes.

Recruitment is almost complete, but if you would like to know more about this trial, please contact: David Rometo MD, E-mail: rometoda@upmc.edu. ■

The investigators of the REMIT-DM study received a \$25,000 grant, hoping to show that insulin-naïve patients can quickly and safely achieve glucose targets using CGM and an insulin titration protocol.

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T1D. Materials include booklets from the My Life, My Diabetes, My Way series, the Calorie King book (for carb counting) and more. The T1D care kits can also be requested on the JDRF.org website, or health care providers can request to have a supply to hand out to patients at their offices.

Another great program that JDRF offers is the T1D Connections program. The T1D Connections program pairs those newly diagnosed with T1D or those needing support with a JDRF Outreach Volunteer. JDRF Outreach Volunteers have a personal connection to T1D. They are caregivers, spouses and other adults who either have T1D themselves—or have a loved one affected by the disease. All of our volunteers understand how overwhelming it can be to adapt to the daily demands of managing T1D and can be there to help the person needing support to get through it.

When it comes to finding support and funding research, JDRF suggests getting involved with the One Walk program. JDRF One Walk is a fun, family friendly event where dedicated walkers, volunteers and

sponsors raise money to make living with T1D safer and healthier until it is no longer a threat. Everyone is welcome to take part—whether you choose to walk on your own or with a family, corporate or school team. As the largest T1D event in the world, it's also an amazing experience filled with activities, entertainment and the celebration of coming together to change the future for everyone living with this disease. The JDRF Western PA chapter hosts two walks annually, one in Pittsburgh and the other in Greensburg. The Pittsburgh walk will take place on September 21 at Schenley Park, and the Greensburg walk will take place the following week on September 28 at the University of Pittsburgh, Greensburg campus. You can find more information and register for the walk at www.walk.jdrf.org.

The staff at the JDRF Western PA is extremely dedicated to providing support and solutions for everyone who needs it. If you are not familiar with what JDRF can do for your patients, please reach out to JDRF to learn ways that they can partner with you to make T1D a little bit less of a burden to all of those that are affected by it. ■



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Professor of Medicine
Chief of the Diabetes Division at the University of Texas
Health Science Center
Deputy Director of the Texas Diabetes Institute,
San Antonio, TX

**Greater Pittsburgh Diabetes Club
Dinner & Presentation
Tuesday, October 29, 2019**

**“Treatment of T2DM: A Sound Approach
based Upon its Pathophysiology”**

Register online:
<https://gpdc-t2dm.eventbrite.com>

Please contact the GPDC if you would like to contribute a future article to the newsletter.

**GREATER PITTSBURGH
DIABETES CLUB**

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