From the Symposia

It’s always been a mystery why some people develop type-1 diabetes at a very young age while others develop it as adults. Dr. George Eisenbarth of the Barbara Davis Center explained that the age at which type-1 diabetes appears can be predicted based on the level (not just the presence) of insulin autoantibodies, as well as the age at which autoantibodies first appear. Good reasons to make use of TrialNet for early screenings for those at high risk.

Efforts are being made to develop glucagon in a stable liquid form for easier emergency injection and potential use in a closed-loop system. The keys appear to be keeping the glucagon solution at a non-acidic level (pH 10) for an extended period of time before use. Buffers such as glycine and lactose have been shown to be useful for preventing degradation.

In closed-loop studies, the accuracy of the various CGM (continuous glucose monitoring) systems has been evaluated. MARD (Mean Absolute Relative Difference) between the sensors and fingerstick values were as follows (lower numbers mean better sensor accuracy):

- Dexcom G4 (not yet commercially available): 11%
- Freestyle Navigator (no longer available in the U.S.): 12%
- Dexcom 7+: 16%
- Medtronic Enlite (not yet commercially available in the U.S.): 17%
- Medtronic Sof-Sensor: 20%

Reducing glycemic variability is gaining importance as research shows the link between high variability and development of complications. Perhaps the best way to assess variability is through COEFFICIENT OF VARIANCE (CV). This is simply the standard deviation divided by the average glucose. The higher the CV, the more variability there is in the glucose values. CV has been shown to correlate directly with risk of hypoglycemia. For most people with type-1 diabetes (not including those who are pregnant), a CV of less than .33 is highly desirable.

Speaking of glycemic variability, a couple of new approaches have been shown to be effective for reducing post-meal blood sugar spikes. Making lunch the “high carb” meal and breakfast & dinner lower-carb meals produces the least peaking throughout the day. Also, consuming one’s vegetables before the starchy foods helps to reduce the post-meal peak.

In a Canadian study evaluating the impact of adding strength training to a cardiovascular exercise program, people with type-1 diabetes actually saw limited benefit. Strength did improve along with waist-to-hip ratio, but no differences were observed in terms of the number of hypoglycemia events, A1c, body mass index, cholesterol levels or total insulin requirements.

In order for closed-loop systems to work more effectively, researchers have learned that insulin needs to work much faster. Several approaches are showing promise: Warming the site of
insulin infusion makes the insulin peak 30-50 minutes sooner. The “Insupatch” heating element is being used to achieve this. Studies at Yale Medical Center showed that insulin reached peak action 30 minutes earlier when the skin was warmed to 38°C, and more than 50 minutes earlier when warmed to 40°C. Pre-treatment of the infusion site with the hyaluronidase enzyme helps to break down absorption barriers, allowing insulin to act more quickly. Studies are also looking at micro-needle infusion (infusing insulin near the capillaries just below the skin surface rather than into the fat layer) and intraperitoneal insulin delivery, whereby insulin is delivered directly into the abdominal cavity by way of a catheter.

GLP-1 is an injectable “incretin” hormone that has proven blood sugar and weight control benefits for those with type-2 diabetes. The use of GLP-1 replacement therapy in adults with type-1 diabetes was recently evaluated. Exenatide (brand name Byetta and new long-lasting Bydureon) reduced post-meal glucose peaks, fasting blood sugar, insulin requirements and weight, but A1c levels did not change significantly in type-1s. It was concluded that exenatide could be a highly useful tool for reducing glucose variability in type-1s.

1,5 AG (also called Glycomark) measures the degree of glucose variability over a 10-14 day period. It is well known that post-meal glucose peaks can contribute to excessive fetal growth during pregnancy, which may lead to malformation and a difficult birth. In a study conducted in Poland, 1,5 AG was found to be associated with newborn weight, even after A1c was controlled for. Use of 1,5 AG during third trimester, in particular, can be useful for predicting large birthweight in pregnancies complicated by diabetes.

There is strong evidence that free fatty acids (cause by a high-fat diet) impair insulin sensitivity. Researchers at Joslin Diabetes Center set out to quantify this effect. They found that a meal high in fat (containing 60 grams of fat) required nearly 50% more total insulin than a meal containing 10 grams of fat, even though the carb amounts in the meals were identical. A separate study in children with type-1 showed that insulin pump users with suboptimal A1cs had diets much higher in fat those with A1cs below 8.5%. No such connection was found between protein intake and A1c.

**From the Research Posters**:  
* these are not posters in the literal sense (no Farrah Fawcett swimsuit scenes); they are small-scale research studies displayed in a bulletin-board format for review and discussion by the conference attendees.

A group of physicians in the U.K. studied the effects of basal insulin reductions during exercise in patients with type-1 diabetes. They found that the standard 50% basal reduction was insufficient to prevent hypoglycemia in most cases. Instead, an 80% reduction, starting 30-90 minutes pre-exercise, reduced the incidence of hypoglycemia significantly.

Another group studied the glucose levels of elite endurance athletes with type-1 diabetes and without diabetes before, during and after cycling races. Both the cyclists with diabetes and those without diabetes showed marked elevations in glucose levels on race days as well as during recovery. This confirms the experience of many non-elite-athletes whose glucose levels rise during and after competitive events.

According to research conducted in California and supported by Animas corporation, for those with type-2 diabetes who still produce some of
their own insulin, nearly 80% can get by with a single, flat basal setting on their insulin pumps.

For those challenged to control glucose levels when using prednisone (or similar steroids) post-transplant or post-surgery, splitting the dose to twice daily results in less of a blood sugar “spike” at 6-18 hours, but also more stable glucose levels through the entire day.

Not sure what we can do about this, but epidemiologists in Pittsburgh found that people with type-1 diabetes who have high “Type-A” personality scores have much lower rates of death than those who fit a “Type-B” profile. This held true even after variables such as A1c, hypertension, smoking, body size and blood lipids were controlled for.

A group in Minneapolis performed matching tests between A1c obtained in a hospital lab and the A1cNow+ home kit. They found that the A1cNow+ device was significantly different from the lab in a majority of cases, with an overall tendency to underestimate true A1c levels.

Medtronic has supported research to find out whether glucose sensors are affected by the proximity of insulin infusion. Preliminary results indicate that sensor performance is unaffected when insulin from a pump is infused within about an inch of the sensor. This may open the door for development and approval of an infusion device and sensor in the same unit.

The DPP-4 inhibitor sitagliptin (brand name Januvia) was tested in adults with type-1 diabetes. After 16 weeks, those using sitagliptin in addition to their usual insulin program a reduction in post-meal glucagon levels. However, little difference was seen in A1c, insulin requirements and weight.

A group of clinicians in upstate New York evaluated the effectiveness of the GLP-1 medication liraglutide (brand name Victoza) in patients with type-1 diabetes. Adding liraglutide to the usual insulin program decreased the amount of time with blood sugar greater than 200 mg/dl by 45%, and time above 250 by 62%. There was a 25% reduction in insulin requirements, and significant weight loss. In a follow-up study with overweight patients with type-1 diabetes, over a 6-month period, A1c levels fell by approximately .4%, bolus (but not basal) insulin decreased by nearly 20%, and blood pressure improved significantly.

Use of pramlintide (brand name Symlin) was studied in young adults at Yale Medical Center. After 3 weeks, the average insulin requirement was fell by 32%, mainly due to reduced bolus needs. Average glucose levels dropped 19%. No severe hypoglycemia or major gastrointestinal distress was reported.

In order to better understand characteristics of people with type-1 diabetes, the T1D Exchange Clinical Registry, supported by the Helmsley Charitable Trust, has collected data from thousands of patients at dozens of diabetes treatment centers. Here are some of the findings:

- For those with diabetes <20 years, approximately 5% are being treated for retinopathy, nephropathy or neuropathy. At 20-40 years, approximately 17% are being treated. Longer than 40 years, 30%.

- Factors associated with lower A1c levels include older age, being married, having a higher education/income, private insurance, pump use, sensor use, and more frequent blood glucose monitoring.
• A1c appears to be best in older adults, and worst in teenagers and young adults. Average A1c for kids under age 13 was 8.2%; age 13-19: 8.7%; age 20-25: 8.2%; age 26-64: 7.6%, and age >64: 7.4%.

From the Exhibit Hall:

Tandem Diabetes is starting to take orders for their t-Slim insulin pumps. The pump has the look and feel of a tiny iPhone, and the web-based download software looks very smooth.

The 4th generation Dexcom CGM (Dexcom G4) shows a great deal of promise. In pre-market closed-loop studies, its accuracy was within 11% of laboratory glucose values, and 93% of the data points were within 20% of the actual glucose readings. The sensor filament is smaller and shorter than the current dexcom sensor, and the transmitter is much stronger – sending the signal up to 25 feet (albeit the battery in the transmitter won’t last as long, and will only be warranted for 6 months). The receiver features a bright LED display that provides much more detail and better resolution than the current receiver.

The new Asante Pearl pump, set for release in the next 6-9 months, not only has the advantage of using prefilled 3ml insulin cartridges; it also has a very early occlusion detection system. And the upfront cost of under $1000 looks good for those with substantial out of pocket copays and deductibles.

Insulet is close to receiving FDA clearance on their new OmniPod and PDM (hoping for release in the second half of 2012). The new pod is 34% smaller and 25% lighter than the original, with a quieter cannula insertion. It is glued more completely to its adhesive patch, and sports a blue cannula for easier viewing through its window. The PDM sends a stronger signal (up to 5 feet), and the IOB calculation includes boluses given for food (yea!). Best of all, there will be no cost to upgrade from the old to the new pods and PDMs.

Novo Nordisk is gearing up to release a new ultra-long-acting insulin called Degludec (brand name Tresiba. No, I didn’t think up that name). Studies have shown that its action lasts approximately 48 to 72 hours. When taken daily, it produces a very flat level of basal insulin in the bloodstream, starting 2-3 days after initiating treatment. Although preliminary research failed to show improvements in A1c for those using Degludec compared to Glargine (Lantus), lower fasting blood sugar levels and less incidence of nighttime hypoglycemia have been seen in those using Degludec.

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