

PHYSICIAN'S

September
2009

UPDATE

Targeting Diabetes



Children's Mercy
HOSPITALS & CLINICS
www.childrensmercy.org



dear
COLLEAGUES,

This issue of *Physician's Update* highlights the work of our Endocrinology and Diabetes Section.

Over the past two years with the guidance of Dr. Kevin Kelly and a commitment from Children's Mercy, we have grown to become one of the largest Pediatric Endocrine sections in the country, with 12 pediatric endocrinologists on staff and five to six fellows. I have been blessed to be chief of the section during this time of expansion and growth.

Children's Mercy provides comprehensive services for patients with a wide array of endocrine disorders and diabetes, including extensive programs for diabetes, growth and disorders of growth, and obesity. Our diabetes program is one of the largest in the country with over 1,600 active patients and more than 250 new patients each year.

This newsletter highlights some of the activities and recent developments within the diabetes program under the leadership of Dr. Kurt Midyett – a nationally recognized authority on glucose monitoring, our participation in TrialNet, and our research on preventing, treating or curing diabetes and endocrine disorders.

This is a challenging time for pediatric endocrinology with the epidemic of diabetes and obesity, and it is an exciting time since new treatments and approaches are on the horizon.

Sincerely,

Wayne V. Moore MD, PhD
Chief, Section of Pediatric Endocrinology
Children's Mercy Hospital



The Glucose Variability ROLLERCOASTER

Mark Clements, MD, PhD

High average glucose has been commonly believed to be the cause of much of the damage in the bodies of children diagnosed with diabetes.

But research by Mark Clements, MD, PhD, Pediatric Endocrinology, and Assistant Professor of Pediatrics at UMKC School of Medicine, theorizes that the rise and fall of glucose over the day may be the biggest factor, or at least an equally important one.

"It is possible that high blood sugar on average over a long period of time may not only fail to tell us the whole story, but may not be the most important thing in determining our risk for complications in diabetes," says Dr. Clements. "Not all children with good hemoglobin A1c are in good control. Hemoglobin A1c only tells us half the story about the child's risk."

Dr. Clements' research is part of a three-tiered approach.

Tier 1 – Build the animal model to confirm the link between glucose variability and complications

Tier 2 – Evaluate children at an early endpoint to measure the influence of blood glucose control on vascular function

Tier 3 – Study the mechanism by which glycemic variability causes complications

For the past several months, Dr. Clements has been building a model of glucose variability in the diabetic rat and profiling oxidative stress bio markers, gene expression analysis of the white blood cells to look for markers of cardiovascular inflammation, and physiologic markers for cataract formation, proteinuria, hypertension, and tissue damage.

With the animal model built and initial results in hand, the challenge now is to see if the results – and his hypothesis – hold up over time.

"I anticipate by this time next year we will have made significant strides toward controlling the animal's blood glucose for the full six months it takes to understand the impact it has on the end organ disease," says Dr. Clements. "Ultimately our goal is to move back and forth between the animal and the clinic and use this model to not only understand to what degree glycemic variability increases your risk of complications, but also what are some of the vascular players responsible for that risk."

QUESTIONS ABOUT EATING RIGHT WITH DIABETES

At Children's Mercy, diabetes nutrition education plays a key role in helping patients enjoy food while limiting the variances in blood sugar levels.

"Diabetes is not a one-size-fits-all disease, so we are always reading, researching, and providing dietary information," explains Debra McGraw, MS, RD, (Diabetes Educator.)

Here are answers to a couple of the most common questions parents have regarding dietary concerns for children with diabetes.

How do you estimate grams of carbohydrates for foods that don't have a food label?

Children's Mercy provides patients with the CalorieKing book and Web site (www.calorieking.com) to research food information. If the specific information is not available in the book, the hospital helps them break down what the food is composed of and calculate each ingredient on its own or use a weight measure. For example, bread products are typically 15 grams of carbohydrates for a one-ounce

product, while fruit products are typically 15 grams of carbohydrates for four ounces.



What should I do if I dose my child for a certain amount of carbohydrates and then my child eats more or gets full before finishing?

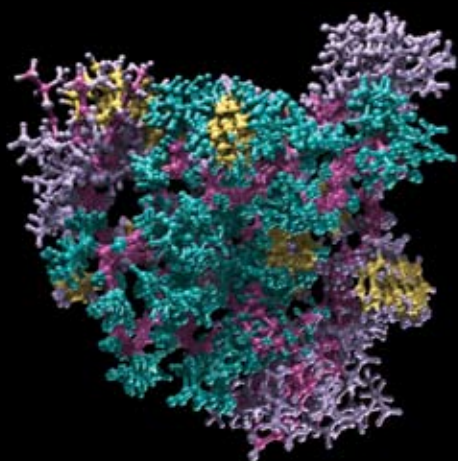
The answer to this is to simply dose insulin again for the extra food if the child is hungrier than expected, and if they get full quicker than expected, they will just need to substitute those extra carbohydrates not eaten but dosed for in another way.

One recommended substitute is milk because it is a liquid; it is not very filling and it is a healthy carbohydrate as opposed to juice or cookies. As long as those extra carbohydrates are consumed within the next 30 to 60 minutes, the child should be fine – meaning not having a low blood sugar later.

For more information about diabetes nutrition or to make a referral to the Children's Mercy Endocrine/Diabetes Outpatient Clinic, please call 816-234-3871.

TRIALNET STUDIES EXPLORE TYPE 1 DIABETES THERAPIES

With the prevalence of type 1 diabetes increasing in pediatrics, Children's Mercy is involved with TrialNet, an international network of researchers who are exploring ways to prevent, delay and reverse the progression of type 1 diabetes.



As a major affiliate of TrialNet, Children's Mercy is performing prevention studies to preserve insulin-producing cells in individuals at risk for type 1 diabetes.

"Our primary goal is exploring new therapies

in subjects with new onset diabetes and their relatives either at risk for type 1 diabetes or high genetic potential for autoimmunity," explains Wayne Moore, MD, PhD, Children's Mercy Section Chief, Pediatric Endocrinology, Professor of Pediatrics, UMKC School of Medicine.

At Children's Mercy, three to five percent of the first and second degree relatives of patients with type 1 diabetes

test positive for the antibodies against components of the beta cell. This indicates high risk for development of diabetes in these individuals and identifies potential subjects for the prevention trials.

In conjunction with TrialNet, the following studies are currently in progress at Children's Mercy:

- Natural History Study – Free screening of relatives of people with type 1 diabetes
- Oral Insulin Trial – Prevention Study
- Nutritional Intervention in Pregnancy – Prevention Study

Additionally, new-onset intervention studies not connected with TrialNet at Children's Mercy include:

- PROTÉGÉ
- START
- Coming soon: ENCORE
- Coming soon: Diamyd

Other clinical trials for the prevention of diabetes and the preservation of beta cell mass are in the pipeline.

To learn more about TrialNet (www.diabetestrialnet.org) and other studies, or to make a referral, please call the Endocrine/Diabetes Office at 816-234-1660.



IT TAKES A TEAM TO MANAGE

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Over the past few years, researchers have noted an alarming rise in the number of children developing diabetes.

That is why Children's Mercy created patient-centric teams - four teams for patients with type 1 diabetes patients and one team for patients with type 2 diabetes patients - to help stem the tide of new patients with type 2 diabetes and to assist with successfully managing patients with type 1 diabetes.

"It takes a team to manage diabetes - the disease is like a big pot and a lot of things go into it," explains Glee Peters, RN, Diabetes Nurse Educator.

What Makes the Teams Special?

Teams are staffed by physicians, registered nurses, nurse practitioners, registered dietitians, psychologists, certified diabetes educators, and social workers specializing in working with kids with diabetes and their families.

"Children's Mercy has a unique approach to diabetes management with our multidisciplinary teams. Other institutions may have a physician and a nurse, but with the sheer number of support personnel, we better manage our patients because we can cover more issues," explains Kurt Midyett, MD, Diabetes Program Medical Director at Children's Mercy, and Assistant Professor of Pediatrics, UMKC School of Medicine.

Additionally, assigning families to a team allows them to talk to the same people consistently and develop a relationship with them instead of feeling like they talk to someone different every time they call who doesn't know them.

Using this comprehensive methodology, Children's Mercy provides the medical, educational, developmental, and emotional support patients need to manage the disease.

Likewise, with the expertise of providers, nurses, dietitians, and additional personnel, referring physicians can feel confident sending their patients to Children's Mercy for diabetes management.

"The hospital bridges care and treatment with community physicians, as we want them to feel comfortable in referring their patients to Children's Mercy. Also, we want the patients to feel that they have access to the most current education and technology that will empower them to manage their diabetes," says Dr. Midyett.



To that end, there is a diabetes doctor on call 24 hours a day to handle emergent diabetes issues so that referring physicians know that they will be called back.

Education is Key

As diabetes is a life-changing event for anyone, especially children, Children's Mercy has established a solid education process for families.

The first time a child is admitted as an inpatient for diabetes, along with medical stabilization, the family is provided with two full days of diabetes education with a nurse and dietitian.

"The education is intense, but it's required. There are so many variables and patterns involved with diabetes regarding what can contribute to blood sugar going up or down—our first focus is to provide a foundation for the family to work with when they go home," explains Debra McGraw, MS, RD, Diabetes Educator.

Following the inpatient stay, families are invited for two additional courses:

- Living with Diabetes
- Adjusting Insulin



Lauren Farrell (center) meets with a Children's Mercy comprehensive, multidisciplinary Endocrine/Diabetes team including (from left to right) Dr. Kurt Midyett, Glee Peters, RN, Stella Vergara-Bagby, RD, Dr. Mark Clements, Cyndy Cohoon, RN, Beth Woodford, RN, CPNP, CDE, and Cathey Donohue, RN, to successfully manage her diabetes.



NEW TECHNOLOGY HELPS NAVIGATE DIABETES

Technology advances in glucose monitors are providing more convenient and effective ways to monitor blood sugar levels to improve patient care.

"The new computerized glucose monitors, offering continuous glycemic level monitoring, are the latest technology in diabetes management to make care more concise and more compassionate," explains Kurt Midyett, MD, Medical Director of Diabetes Program and Assistant Professor of Pediatrics, UMKC School of Medicine.

Additionally, there are high tech models similar to a car's GPS system directing patients to better guidance through ongoing measurement of glucose levels, including

- Updates every five minutes
- A customizable high glucose alert
- Tending screens with 1, 3, 6, 12, and 24 hours of continuous information

Another savvy device that just debuted on the market is a glucose monitor that taps into kids' passion for video games to build consistent blood glucose testing habits.

"The leading-edge monitors are designed to help kids manage this lifelong condition by rewarding them for building consistent blood glucose testing habits and meeting personalized glucose target ranges, which is both exciting and smart," observes Dr. Midyett.

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"Our objective is to get them to the point where they don't need to wait for us to make insulin adjustments for them," adds McGraw.

Treatment Includes Self Management

The standard of care for diabetes at Children's Mercy is intense and aggressive.

"Our primary tool is the insulin pump with our patients. It's the best and most appropriate because it creates opportunities for independence and diabetes management," says Dr. Midyett, adding, "Children's Mercy is special because the hospital is an early adopter of the most current technology available, which benefits our patient population both medically and personally."

The newest tool that will be incorporated into standard practice is glucose sensors, which are inserted underneath the skin and provide continuous information regarding blood sugar levels. This will be a vast improvement over a glucose monitor that simply gives a blood sugar snapshot in time.

"Our philosophy is that patients with diabetes deserve the opportunity to manage their diabetes with the most advanced, up-to-date tools. And at Children's Mercy, that means doing more than other institutions in terms of technology. This is important because the newest technology available is not universal, but it is at Children's Mercy," observes Dr. Midyett.

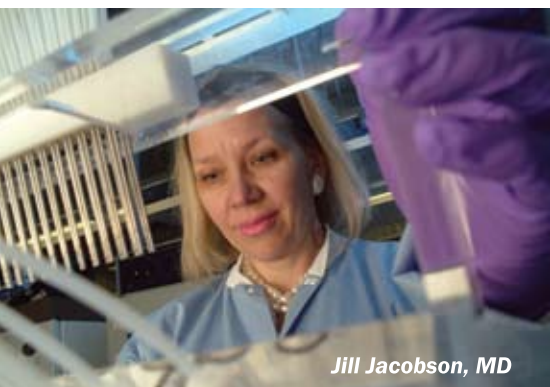
Additionally, Children's Mercy works collaboratively with each diabetes patient to develop a diabetes self-management plan to meet the individual needs, lifestyle and preferences.

To make a referral to the Children's Mercy Endocrine/Diabetes Outpatient Clinic, please call 816-234-3871.

SEX, HORMONES AND G PROTEINS

Autism affects four times as many boys as girls, although no one knows why.

Jill Jacobsen, MD, Pediatric Endocrinologist at Children's Mercy, and Professor of Pediatrics/Endocrinology, UMKC School of Medicine, is leading



research looking at the role of genetic imprinting, and specifically G proteins, in autism spectrum disorders (ASD). The G proteins that are elevated in ASD are controlled by male and female sex hormones, androgen and estrogens.

"G proteins are so called because they function as molecular switches, alternating between an inactive guanosine diphosphate (GDP) and active guanosine triphosphate (GTP) bound state, ultimately going on to regulate downstream cell processes," explains Dr. Jacobsen, adding, "We have recently discovered evidence for higher than normal levels of G proteins in white blood cells from patients with autism or ASD. This finding may be very important for a variety of reasons."

Many key mediators in the brain and nervous system function through these G proteins. It is becoming apparent that measurement of G proteins in white blood cells can indicate the

severity of illness and the responses to therapy in depression, bipolar disorder, and schizophrenia.

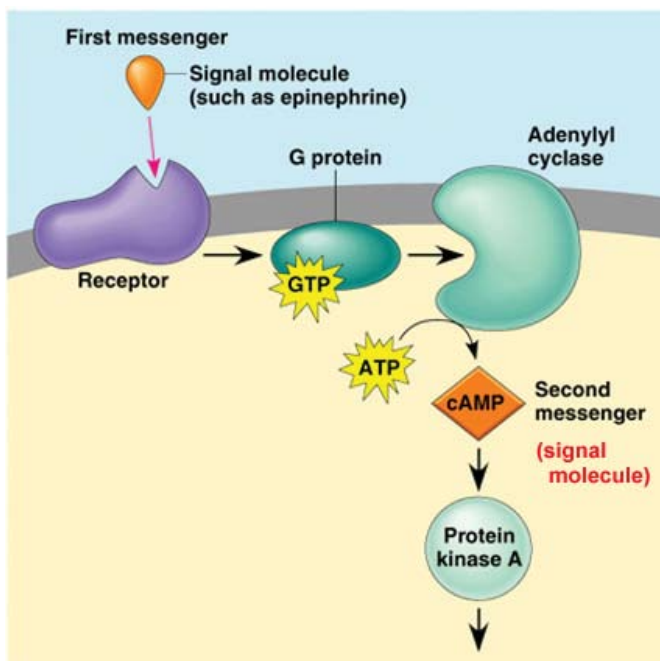
Currently, very little is known about G proteins in ASD; however, it is known that production of the major G protein (called Gs) is controlled by imprinting or epigenetics.

"Epigenetics is a relatively new but important field of genetics that focuses not on the actual sequence of the DNA, but rather the chemical additions, or imprints to DNA that are transmitted from parents to their children," says Dr. Jacobsen.

Children's Mercy research is addressing the potential roles of prenatal hormone exposure (so-called hormonal imprinting) and other forms of imprinting simultaneously.

"We are utilizing our previous findings of elevated G proteins as a marker for autism, as a marker for hormone exposure, as well as a marker of imprinting," says Dr. Jacobsen.

To learn more about Dr. Jacobson's research, contact the Children's Mercy Endocrine/Diabetes Outpatient Clinic at 816-234-3871.



A GROWING PROBLEM

About 5 percent or less of children with truly short stature have an underlying hormone problem. The majority are just some variation of normal, related to familial genetics or a constitutional delay of growth, according to Joseph Cernich, MD, Pediatric Endocrinologist, and Professor of Pediatrics, UMKC School of Medicine.

Signs that there may be a problem include:

- Child's height is in the bottom 3 percent
- Child's growth rate is decreasing
- Child is much lower on growth chart than expected based on height of parents

"If a child is falling off the growth chart and falling behind peers, that is a worrisome sign," says Dr. Cernich.

If there is a concern, Dr. Cernich recommends a bone age x-ray. If further evaluation is needed, call 1-800-GO-MERCY to schedule an Endocrine Clinic appointment. The triage nurses will provide instructions for a panel of lab tests prior to the first visit.



ISLETS HOLD HOPE FOR DIABETES CURE, TREATMENT

The potential of islet transplantation for the treatment or curing of diabetes has been studied since the 1980s, but it wasn't until the Edmonton Protocol of 2000 that scientists achieved their first success.

But that success, using islets transplanted into the liver, proved to be short lived. While 80 percent of patients who had islets transplantation into their livers had reversal in hyperglycemia after one year, by five years the reversal was gone.

Karen Kover, PhD, Children's Mercy Pediatric Endocrinology research scientist who has been studying the use of islets since 1986, theorizes that one of the problems may lie in the transplantation site.

"Looking back, we've asked, why don't islets survive longer in the liver?" says Dr. Kover. "Islets seem to induce liver damage adjacent to the engraftment site and this inflammation may negatively impact islet survival. We now think the liver – while easily accessible – is not a good place for islet transplantation."

Dr. Kover is working with Donna Pacicca, MD, Children's Mercy Orthopaedic Surgeon and Professor of Pediatrics, UMKC School of Medicine, to study transplantation of islets in the bone marrow cavity. Dr. Kover has found that islets transplanted into the tibia bone marrow cavity of laboratory rats do survive and function, although it takes

longer to bring hyperglycemia under control. No long term results are available yet, so Dr. Kover doesn't know how long islets can function at this site or how the islets will affect surrounding bone and bone marrow tissue.

In addition, Dr. Kover is working with Kun Cheng, PhD, Assistant Professor of

Pharmacy at UMKC School of Pharmacy, to address another significant barrier in islet transplantation – the use of toxic anti-rejection drugs to keep the body from attacking transplanted islets. Dr. Kover and Dr. Cheng are evaluating manipulation or blocking of gene expression in transplanted islets to eliminate interaction between islets and immune system cells.

"If we can control the immune response locally at the site of the engraftment, we can eliminate the need for systemic use of anti-rejection drugs which cause side effects due to their impact on the whole immune system," says Dr. Kover.



Karen Kover, PhD



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A PATIENT'S STORY

Phillip Munyan
 14 years old

A memory from a nursing school lesson came in handy in October 2008 when Elaine Munyan realized her 14-year-old son, Phillip, might be diabetic. She noticed Phillip was drinking a lot of water, his vision seemed affected, he was extremely tired and urinating often.

"I recognized that Phillip was presenting symptoms of diabetes, so we were referred directly to Children's Mercy, where he was hospitalized," explains Elaine Munyan.

"We were so overwhelmed, but the staff—physicians, nurses, dieticians, social workers, diabetes educators—were amazing. All of our questions

were answered, the care was phenomenal, and Phillip was only discharged when he was stable and we all felt confident and comfortable with going home."

Phillip continued to manage his diabetes through education courses offered by Children's Mercy and also with the friendships he developed with Ron Hoyler, RN, BA, CDE, Diabetes Nurse Educator and other hospital staff.

"With the help of Children's Mercy, Phillip is doing a great job of managing the disease. In May, Phillip ran 31 miles in four days as part of the Run Across Kansas. We feel like this is terrific progress and it wouldn't be possible without the compassionate care he received at Children's Mercy," says Elaine Munyan.



HOW TO REFER

For Transport, Inpatient Admission or for Consult
 1-800 GO MERCY
 (1-800-466-3729)



Call this number 24 hours a day to mobilize the in-house neonatal or pediatric transport teams, consult with a specialist, or admit a patient directly to Children's Mercy Hospital or Children's Mercy South.

For Specialty Clinic Appointments
 (816) 234-3700 or
 toll free 1-800 800-7300

Nurses with our Physician Appointment line can assist you with scheduling clinic appointments for Children's Mercy Hospital, Children's Mercy South and Children's Mercy Northland.

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