Health is funding the TODAY study (Treatment Options for Type 2 Diabetes in Adolescents and Youth). It will compare different treatment options, including changes in eating habits and physical activity and different combinations of medications, which include metformin and rosiglitazone. Metformin is the only oral medication FDA approved to treat type 2 diabetes in children. Doses range from 1000-2000 mg daily. The main side effects are gastrointestinal in nature and are minimized by taking the medication with food. Metformin is contraindicated in individuals with renal disease or conditions that lead to a hypoxic state (CHF, respiratory distress, sepsis) because of an increased risk of lactic acidosis. It is recommended to stop metformin prior to surgery or any radiological procedure that requires radiocontrast material, until a normal creatinine is confirmed after the intervention. Rosiglitazone is an anti-diabetes medication that decreases insulin resistance, which lowers plasma glucose and insulin levels. It has been used extensively in adults but not in children. It may have an added benefit of preserving beta cell function and ameliorating diabetes, but further studies need to be done.

The TODAY study seeks young people between the ages of 10 and 17 who have had type 2 diabetes for less than 2 years. They will be asked to be more active, eat healthy foods, check their blood glucose, and take metformin or rosiglitazone twice daily, and visit a study center regularly for 2 to 5 years. Parents and family members will be asked to help the child with TODAY study activities. The children will be given free medical exams, diabetes care, diabetes medication and supplies. Our team consists of a pediatric endocrinologist, diabetes nurse educators and dieticians who will help the children stay in good health and learn how to best manage the disease.

In adults with impaired glucose tolerance and at risk for developing diabetes mellitus, lifestyle intervention consisting of walking 25 minutes per day and following a healthy diet and losing an average of 7% of their body weight decreased the risk of progressing to diabetes by 75% ( ). At this time, we recommend intensive lifestyle interventions that follow the American Academy of Pediatrics guidelines for exercise and diet. After evaluating these children, we refer them to our Healthy Lifestyle Program, directed by Dr. Denise Woodall-Ruff.

* Enrollment for the TODAY Study will continue through April 2007. We hope to recruit 750 participants across the country. The Joslin Diabetes Center is one of twelve sites across the nation. For more information go to www.todaystudy.org or call Kelly Duncan at 315-464-3878.
As we increasingly move children out of the hospital and into the home to complete their care, coordination with home nursing, social work, schools, and similar agencies becomes essential.

Type 2 Diabetes, Metabolic Syndrome, and the TODAY Study

Robert Izquierdo, MD, pediatric endocrinologist

Type 2 diabetes and metabolic syndrome, once considered adult diseases, are now striking children and teenagers at an alarming rate. Children as young as 8 years are being diagnosed, with the average age being 13. A major concern is that patients diagnosed in childhood and adolescence will develop macrosomic and microvascular complications such as renal and cardiovascular disease in adulthood. This rise in type 2 diabetes and metabolic syndrome is temporally related to the increase in obesity in children. It is more common in children of certain ethnic/racial groups (American Indian, Hispanic, African Americans, Asia/Pacific Islanders) than those with a family history of type 2 diabetes. In most cases the disease starts with excess weight gain and insulin resistance, a state in which muscle and fatty tissue do not respond properly to the actions of insulin and as a response the pancreatic beta cell secretes more insulin. This results in a normal plasma glucose with a high serum insulin level. With time, the beta cells fail to secrete enough insulin to overcome the insulin resistance, and plasma glucose begins to rise above the normal fasting and postprandial ranges (impaired glucose tolerance) to a state of diabetes in which clinical symptoms appear.

Presenting “Susan”
Susan is a 14-year-old Caucasian girl who went to her pediatrician with a vaginal yeast infection. She has nocturia twice a night and has been experiencing thirst frequently. She had not lost weight. Her menstrual cycles have always been irregular. However, she was not taking medications. Her mother and maternal aunts were diagnosed with diabetes at ages 37 and 42, respectively. Review of systems revealed that she had two periods in the past year. She had menarche at age 12 and her menstrual cycles have always been irregular.

Susan’s height was 63 inches, weight 186 pounds, and body mass index (BMI) 32. Her physical examination was unremarkable. She had moderate severe acanthosis nigricans that extended to the lateral neck. A urinalysis revealed the presence of trace amounts of ketones and 500 mg/dl of glucose. The best and easiest screening test for diabetes mellitus is a fasting plasma glucose. A level of 126 mg/dl or higher suggests diabetes and a level of 100-125 mg/dl suggests pre-diabetes. In fact, Susan’s fasting sugars were 148 and 137 mg/dl.

Susan was diagnosed with type 2 diabetes. Surprisingly, evidence for this includes obesity, a strong family history of diabetes, and acanthosis nigricans (a sign of insulin resistance). She did not have weight loss, which is commonly seen in patients with type 1 diabetes. Her urinalysis showed only a trace amount of ketones, which is unusual in patients with type 1 diabetes who often have significant ketosis and a large amount of ketones in their urine. Occasionally, it is difficult to distinguish between type 1 and type 2 diabetes. In these circumstances, serum antibodies to GAD 65, ICA 512, and insulin, which are commonly present in type 1 diabetes, may help point us in the proper direction.

In Susan, oligomenorrhea was very suggestive of polycystic ovarian syndrome, and further evaluation confirmed PCOS. As much as a third of patients with polycystic ovarian syndrome have insulin resistance and up to 10% have frank diabetes mellitus. Other conditions that may need to be addressed include hypertension, osteohypertrophy, and dyslipidemia. The most common lipid abnormalities seen in these patients include low HDL cholesterol and elevated triglyceride levels. LDL cholesterol may be normal or may not be elevated. Many of our children with type 2 diabetes have elevated ALT and AST that end up being secondary to a “fatty liver” or further evaluation. The long-term consequences of hepatic steatosis is a concern. Susan had candidal vulvovaginitis, which occurs frequently in females with diabetes, because moderate hyperglycemia impairs the cellular immune response.

A New Approach: The TODAY Study

Because type 2 as a childhood disease is relatively new, there are no large-scale studies to suggest the best treatment options. That is why the National Institutes of Health...