VOLUME 2
December, 2018

THE PEDIATRIC JOURNEY

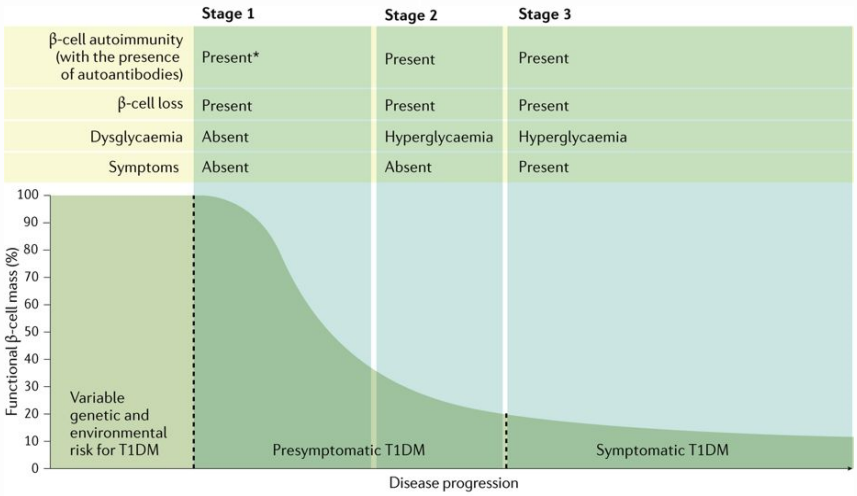
Quarterly Newsletter of Pediatric Practice at

El Paso Children's Hospital | Texas Tech Physicians of El Paso

TYPE 1 DM – PAST, PRESENT AND FUTURE

KRISHNASWAMY J. RAO
MD, MBBS, CHAIR - PEDIATRIC ENDOCRINOLOGY AT TEXAS TECH PHYSICIANS OF EL PASO

FIG 1. - DIABETES PROGRESSION



Nature Reviews | **Disease Primers**

On December 20, 2006, the United Nations (UN) passed a resolution to designate November 14 as World Diabetes Day. The occasion aimed to raise awareness of diabetes, its prevention and complications and the care that people with the condition need. Here we discuss about the past, present and future of type1 diabetes (T1DM), commonly seen in the pediatric population.

Nearly 90000 children are being diagnosed with type1 diabetes (T1DM) each year throughout the world. {Maahs, 2010 #1} T1DM is ubiquitous with the incidence more in Scandinavian and west European countries. Type 1 Diabetes mellitus is due to autoantibodies to β- islet pancreatic cells in 70-90% of cases and genetically predisposed cell destruction in the others. The 4 implicated antibodies are GAD65 (glutamate decarboxlase2, Islet cell, IA-2 (insulinoma associated protein2) and ZNT 8 (zinc transporter 8). Individuals with HLA - DR-DQ MHC antigen genotypes have increased propensity to develop Type 1 DM. The pathogenesis is more of a continuum than in stages and there is a phase of dysglycemia between antibody appearance and symptoms of hyperglycemia (Figure 1). One cannot underestimate the role of environmental factors in modulating the onset of T1DM. The incidence of T1D increases with age in most populations with the highest incidence observed in the 10–14 year olds. 25 percent of people with T1DM are diagnosed as adults. The incidence in T1DM in children is expected to double by 2020 than from 2005. Geographic areas with a high incidence of T1D (populations of European origin) have a male excess, whereas regions with a low incidence (populations of non-European origin) report a female excess. {Karvonem, 1997 #6}

AMERICAN DIABETIC ASSOCIATION DIAGNOSTIC CRITERIA:

- A fasting plasma glucose (FPG) level ≥126 mg/dL (7.0 mmol/L), or
- A 2-hour plasma glucose level ≥200 mg/dL (11.1 mmol/L) during a 75-g oral glucose tolerance test (OGTT), or
- A random plasma glucose ≥200 mg/dL (11.1 mmol/L) in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis.

PRINCIPLES OF MANAGEMENT: Insulin replacement therapy is a must for all children with T1DM. The insulin regime should involve basal insulin (long acting glargine / Detemir) and a pre-prandial insulin (rapid acting –lispro / aspart / glulisine or short acting regular).

Prandial insulin dosing is based on carbohydrate consumption with a meal. Patients are encouraged to eat a balanced diet with approximate daily energy intake fractionated to 50-55% carbohydrate portions, 30-35% fat and 10-15% Protein.

Intensive glucose control is the cornerstone of diabetes management. Blood glucose levels should be checked 4-10 times/day and rapid acting insulin is dosed based on blood sugars. Subcutaneous continuous glucose monitoring is highly recommended. HbA1C should be checked every 3 months. For pediatric patients, the target HbA1C is 7.5%. Lower goal of 7 % is appropriate if achievable without excessive hypoglycemia, impaired quality of life.

COMPLICATIONS: Approximately 32% of patients with T1DM will have or are at high risk for at least 1 complication. The discovery of insulin in 1922 transformed type 1 diabetes from a terminal to a treatable disease. Despite the advances in care, the disease continues to be associated with substantial medical, psychosocial, and financial burden. Hypoglycemia and ketoacidosis are persistent potentially life-threatening complications. Hypoglycemic events requiring treatment assistance from another person occur at rates of 16–20 per 100 person-years. Severe hypoglycemic events leading to loss of consciousness or seizures occur at a rate of 2–8 per 100 person-years. Recurrent hypoglycemia results in an increased likelihood of hypoglycemia unawareness and subsequent severe hypoglycemic events, since recurrent hypoglycemia reduces the glucose concentration that triggers the counter-regulatory responses to return to euglycemia. Hypoglycemia unawareness can improve with education, support, and glucose targets that are aimed at avoiding biochemical hypoglycemia, while maintaining overall metabolic control.

Hypoglycaemic events are associated with adverse effects on cognitive function, and are associated with 4–10% of type 1 diabetes-related deaths. Microvascular complications of the disease manifest primarily as retinopathy, neuropathy, and nephropathy, but also can affect cognitive function and other organs. Hyperglycemia is the primary risk factor for microvascular disease, and reducing HbA 1c through intensive diabetes management, particularly early during disease, is associated with striking (about 70%) reductions in incidence and

Continued on next page >

slower progression of microvascular disease. However, differences in HbA 1c do not fully explain the variation in the incidence of complications and the severity of disease between individuals. Variability in glucose concentrations (both during the day and longer term) and glycosylation rates also probably have a role in interindividual differences. Type 1 diabetes during puberty also appears to accelerate the development of complications. {DiMeglio, 2018 #2}

Macrovascular complications of type 1 diabetes include atherosclerosis and thrombosis in the heart, peripheral arteries, and brain. In contrast with microvascular complications, the risk of cardiovascular complications does not appear to be significantly attenuated by intensive blood sugar control. Diabetic nephropathy, whether manifesting as microalbuminuria, macro albuminuria, or a reduced glomerular filtration rate progressively augments the overall risk of macro vascular complications. Cardiovascular diseases remains the major cause of premature morbidity and mortality, with data suggesting an 8–13-year shorter life expectancy for people with type 1 diabetes than for healthy individuals.

People with diabetes might also have both chronic and acute neurocognitive changes that include decline in cognitive function with detrimental effects on psychomotor speed, cognitive flexibility, attention, and visual perception. Although the pathophysiology of neurocognitive changes is poorly understood, their development has been linked with both microvascular and macrovascular changes and changes in brain structure, neuronal loss, and cerebral atrophy. Risk factors include developing diabetes early in life, chronic hyperglycemia, and repeated hypoglycemia.

An additional noteworthy complication of type 1 diabetes is the patient-reported burden of adverse effects on quality of life. This quality of life impact affects not only the person with type 1 diabetes, but also their family, friends, and caregivers. Fear of hypoglycemia is a prevalent issue, particularly for the families of very young children with type 1 diabetes. Furthermore, poor quality of life is predictive of subsequent poor glycemic control.

TABLE 1 - SECONDARY PREVENTION IN T1DM

Trial	Drug	Phase	n	Outcome	ClinicalTrials.gov identifier
Completed studies					
DPT-1 (REF. 227)	Subcutaneous insulin	III	339	No protective effect	NCT00004984
DPT-1	Oral insulin	III	400	No protective effect	NCT00419562
DIPP (REF. 228)	Intranasal insulin	III	264	No protective effect	NCT00223613
ENDIT (REF. 229)	Oral modified-release nicotinamide	III	552	No protective effect	Not applicable
Ongoing studies					
TN07	Oral insulin	III	400	Ongoing	NCT00419562
INIT II	Nasal insulin	II	110	Ongoing	NCT00336674
TN18	Intravenous abatacept	III	206	Ongoing	NCT01773707
TN10	Intravenous teplizumab	II	170	Ongoing	NCT01030861
DiAPREV-IT	Subcutaneous alum-GAD65	II	50	Ongoing	NCT01122446
DiAPREV-IT2	Subcutaneous alum-GAD65 and oral vitamin D	II	80	Ongoing	NCT02387164
Fr1da	Oral insulin	II	220	Ongoing	NCT02620072
TEFA	Gluten-free diet	II	60	Ongoing	NCT02605148

Alum-GAD65, alum-formulated 65 kDa glutamic acid decarboxylase.

FUTURE PROSPECTS: Every day, scientists all around the world are making progress toward a cure for type 1 diabetes. While it is difficult to say how long it will be before a cure is finally realized, we can reflect on how far we have come since the discovery of insulin in the early twentieth century, and look forward to more new and exciting disease modifying discoveries that will bring us closer to a cure for type 1 diabetes (Table 1).

WHOLE GENOME SEQUENCING AND GENE THERAPY: This is one of the newest programs where we have shown how single-nucleotide polymorphism (SNP) changes in one particular gene called A20 (suspected to be a player in type 1 diabetes) not only contributes to diabetes susceptibility, but also enhances rejection in islet transplantation. Certainly this gene is a target for gene therapy {Chellappan, 2018 #5}.
diabetes and its complications. (References available on request)

TYPE 1 DIABETES IN EL PASO:

Latinos represent the fastest growing immigrant populations in the United States. Most Latino youth with T1D are in suboptimal diabetes control and therefore at high risk for the devastating acute and chronic complications of T1D. Socioeconomic status, access to health care, health literacy, English proficiency, acculturation, family dynamics, mental health, and nutrition are closely inter-related and significantly influence glycemic control and T1DM management. These factors are largely understudied in this population. Better understanding of the factors that influence T1D education, care, and outcomes will shed light on how to best accommodate the needs of this growing group within the existing health system in the United States.

Prior to 2013, children from El Paso with Type 1 diabetes traveled to East Texas and New Mexico in search of diabetes care. Texas Tech physicians and medical staff partnering with the diabetes educators at the American Diabetes Association (ADA) recognized Zachary Bowling Pediatric Outpatient Diabetes Education center (ZPODE) at El Paso Children's hospital are now providing culturally sensitive, comprehensive diabetes education to the diabetic children of our community. We are dedicated to realizing a vision of our world without diabetes and its complications. (References available on request)

VOLUME 2
December, 2018

THE PEDIATRIC JOURNEY

Quarterly Newsletter of Pediatric Practice at

El Paso Children's Hospital | Texas Tech Physicians of El Paso

OUT WITH THE ALTE, IN WITH THE BRUE

BY: LISA AYOUB, MD, FAAP, TEXAS TECH PHYSICIANS EL PASO, HOSPITALIST AT EPCH

As a Hospitalist being called for admitting infants with scary events is not uncommon. As pediatric providers we can all recall countless stories of patients having a concerning episode involving choking, gagging, blue discoloration, tone changes, periodic and irregular breathing and calling it an ALTE or Apparent Life-Threatening Event. We have seen that panic, terror and paralyzing fear in parents eyes. Forty-three percent of healthy infants have had a 20-second apnea episode over a 3-month period and 5% of parents recall seeing an apnea event. Conservatively, 1 out of 250-400 children were hospitalized for an ALTE. According to McGovern et al the most common discharge diagnoses for an ALTE admission was Idiopathic (26-50%), Gastroesophageal Reflux (26-54%), Respiratory infection (8-11%), Seizure (9-11%). Less commonly is Child Maltreatment (1%), Pertussis (0.05-9%), Cardiac arrhythmias (<1%), Bacterial Infection (0-8%), and lastly Metabolic Disorders (1.5%).

Our priority is finding those diagnoses that can lead to harm if left unrecognized or untreated. The fact that ALTE's are common, have a broad differential and can be very anxiety provoking often leads to a cascade of unnecessary testing and treatments. In 2016, the American Academy of Pediatrics published guidelines to replace the term ALTE with Brief Resolved Unexplained Event (BRUE). The guidelines provide an approach to patient evaluation that is based on the risk that an infant will have a repeat event or has a serious underlying disorder. Within the new guidelines there are also management recommendations for lower-risk infants. Low-risk infants are those with reassuring history and normal physical exams. The guidelines do not offer recommendations for higher risk infants, as their history and physical exam would suggest further investigation and treatment.

WHAT IS BRUE?: The term BRUE reflects the BRIEF transient nature and lack of a clear cause while removing the "life-threatening" label. BRUE describes episodes in an infant <1 year old, lasting typically 20-30 seconds up to 1 minute. They RESOLVE meaning the patient is back at baseline after the event with a reassuring history, physical exam and vital signs at the time of examination. Lastly, the event cannot have an identifiable cause. For example a 3 month old with fever, cough, congestion for 3 days presents with history of cyanosis and apnea is not a BRUE. When there are symptoms that provide an identifiable medical condition it is not UNEXPLAINED, hence not a BRUE. The differences between an ALTE and BRUE can be compared in Table 2.

Patients who have had a BRUE should have a careful history and physical exam to determine if there is an underlying disorder. Your history may lead you to child abuse if given an inconsistent story or a cardiac arrhythmia if there is a family history of sudden, unexplained death in a first-degree relative. Patients who have a BRUE may have a recurrent event or a serious undiagnosed condition. The new guidelines help us to figure out the higher risk group from the lower risk group that can be managed safely without extensive diagnostic evaluation or hospitalization.

The criteria for low risk include considerations in regard to age, prematurity, CPR performed, duration of event and whether it was the first event. If the patient is identified as a Lower Risk Patient the management recommendations include caregiver education about BRUE, shared decision-making to guide evaluation, disposition and follow up along with offering resource for CPR training. Interventions that may be considered are pertussis testing, EKG and brief monitoring with continuous pulse oximetry and serial observations. Neither labs nor imaging are recommended. No medications should be prescribed. The Lower Risk Patient need not be admitted to the hospital solely for cardiorespiratory monitoring. The algorithm in the guidelines can help triage your patients and can guide your management. Another handy tool is MDCalc application (also available at www.mdcalc.com) which has a BRUE Criteria Calculator that can be used in daily practice and as an educational tool.

Lastly at EPCH we have incorporated value-based practice as per national guidelines, to reduce costly and unnecessary interventions and provide family centered care. Beyond the guidelines is the art of communication with families to ensure parents are heard, validated and supported during this fear-provoking event. Along with our community providers our Hospitalist group continues to strive to practice evidence based medicine when available while balancing the care of that patient that never reads the book.

TABLE 2 - DIFFERENCES BETWEEN ALTE AND BRUE

Apparent Life Threating Event (ALTE)	Brief Resolved Unexplained Event (BRUE)
An episode in the first year of life that appears potentially life-threatening to the observer. Characterized by some combination of: • Color change (Red, White or Blue) • Apnea • Alteration in muscle tone • Choking or gagging	Event occurring an infant <1 year where the observer reports a **sudden, brief** period of one or more of the following: • **No explanation for event** after appropriate history and physical exam • Pallor or Cyanosis (~~Red~~ White or Blue) • Red is common in healthy babies • Absent, decreased, or irregular breathing • Marked change in tone (hyper- or hypotonia) • Altered level of responsiveness
Based on caregiver's perception that event was life-threatening	Based on the clinician's characterization of features of the event
Can be both a chief complaint and diagnosis • Can have a diagnosis (Ex: meningitis or bronchiolitis) • Can have ongoing symptoms	Diagnosis of exclusion • Excludes patients with explanation or diagnosis (Ex: GER) • Excludes currently symptomatic infants

HIT THE FLU BEFORE IT HITS YOU!

BY: RICARDO REYNA, MD COMMUNITY PEDIATRICIAN, CLINICAL ASSISTANT PROFESSOR-PEDIATRICS TEXAS TECH PHYSICIALS EL PASO

With flu season fast approaching, it's time to roll up your sleeves. There's no denying it, it's flu season. And RSV season. And cold season. It seems everyone probably knows someone who is sick. It's that time of year!

But that doesn't mean it's time to sit back and wait for respiratory illnesses to invade your home. Rather, it's time to play defense.

With 180 pediatric deaths from influenza already reported this season 2017-2018, it is wise to be vigilant. According to a recent AAP News article "Recommendations for Prevention and Control of Influenza in Children, 2018–2019" Sept. 3, 2018, about 80% of the children who died were not vaccinated!!

The American Academy of Pediatrics (AAP) recommends intramuscular inactivated influenza vaccine (IIV) for children in the 2018-2019 season as it has been more consistently effective against most strains of flu in recent seasons, but says the nasal vaccine (LAIV) may be an option for kids who otherwise will not be vaccinated.

The most effective way to prevent and fight influenza is through vaccination. Give yourself a fighting chance and hit back and get vaccinated!

VOLUME 2
December, 2018

THE PEDIATRIC JOURNEY

Quarterly Newsletter of Pediatric Practice at El Paso Children's Hospital | Texas Tech Physicians of El Paso

PREMATURITY AWARENESS AND DIABETES AWARENESS MONTH

There are over 5750 hospitals in the U.S., but fewer than 250 specialize in pediatrics. In November we celebrated prematurity awareness and diabetes awareness month with our staff and community. Our Level IV NICU delivers the most acute prenatal care and our outpatient diabetes education services is the only certified outpatient pediatric diabetes education between Phoenix and Austin. For our physicians, nurses and staff, El Paso children and their families are 100% our mission.

2019 PEDIATRIC GRAND ROUNDS

The First & Third Wednesday of Every Month

Breakfast: 7:30-8 a.m. Grand Rounds: 8-9 a.m.
Academic Education Center (AEC), 2nd Floor, 4800 Alberta Avenue

JANUARY 16th, 2019	Diagnosing and Treating Tourette Syndrome	Keith Coffman, MD.
FEBRUARY 6th, 2019	Retinoblastoma	Amy Schefler, MD.
APRIL 3rd, 2019	Auto-Immune Encephalitis	Eyal Muscal, MD.
	Tuberculosis	Andrea Cruz, MD.