

# Paediatric Diabetes – *Advice for Pharmacists*



*Written by Dr Orla Neylon,  
Consultant Paediatric  
Endocrinologist, Dept of Paediatrics,  
UL Hospitals Group, Limerick*

## Why do children get diabetes?

More than 95% of diabetes diagnosed in childhood in Ireland is caused by Type 1 Diabetes (T1D), an autoimmune condition resulting in destruction of the individual's own pancreatic beta cells which leads to absolute insulin deficiency. Similar to other developed countries, the incidence of this condition is rising, particularly in Ireland in the age group 10-14 years old. Individuals are born with a genetic susceptibility to developing T1D, which is then triggered by an inductive environmental event, currently thought to be viral infection e.g. enterovirus, acting which induce autoimmunity via molecular mimicry. Post-diagnosis, individuals with T1D are dependent on insulin replacement therapy for life. It is worth stating that children with T1D did not acquire this as a result of diet or sedentary lifestyle, which is a negative misconception in the lay world that affects them, resulting from confusion with Type 2 Diabetes pathophysiology. Cases of T2D do occur, usually in the post-pubertal age group but not at rates seen in the USA and other countries.

Most notably, 2022 is an important year in the diabetes world, marking the 100 year anniversary of the development of exogenous insulin therapy in Canada by Frederick Banting and Charles Best. Prior to their Nobel prize-winning achievement, all children who developed T1D died, usually within 6-12 months of diagnosis. On the 11th January 1922, Leonard Thompson, a 14-year old boy dying from diabetes in a Toronto hospital, became the first person to receive an insulin injection. Within 24 hours his hyperglycaemia resolved and he lived for another 13 years, eventually dying of complications of pneumonia aged 27.

## How does diabetes present in children?

Without sufficient insulin to facilitate intracellular carbohydrate metabolism, glucose

becomes trapped in the person's bloodstream, which the body attempts to compensate for via renal excretion of glucose. This results in the classic symptoms of clinical diabetes, these being excessive urination, which in turn leads to excessive thirst and weight loss. Without carbohydrate metabolism, cells shift to fatty acid oxidation to generate energy, but manufacture ketones as a by-product. These acidic molecules cause a characteristic sweet-smell from the breath, a flushed complexion and abdominal pain, the latter of which can be very severe. Early symptoms can be subtle and the increased fluid consumption can be mistaken for comfort drinking, especially if a child has just started pre-school or school, or can also be easily misinterpreted during warmer months of the year. The earlier symptoms are recognised and treatment is initiated the better, however approximately 40% of children at diagnosis are in Diabetic Ketoacidosis (DKA), a life-threatening consequence of deteriorating hyperglycaemia which, if left untreated, can result in coma and death. The proportion of newly-diagnosed children in DKA was higher during the past 2 years across the world, due to a combination of inability and reluctance to access healthcare during lockdowns. Compensation for the severe acidosis can result in deep, sighing breathing which has unfortunately been misinterpreted as consistent with acute COVID-19 infection, particularly with resort to telephone consultations during the pandemic. Public education campaigns in countries such as Italy have assisted earlier diagnosis and DKA prevention. Given that Ireland is designated an area of high incidence of T1D in children and adolescents, it is important that all Irish healthcare professionals including community pharmacists be aware of the symptoms of new onset diabetes.

## How is diabetes in children treated?

Once diabetes is diagnosed and a child's condition is stabilised, treatment commences immediately with insulin replacement therapy. The overarching goal of modern diabetes care is the maintenance of blood glucose levels as close to 'target' as possible, using the philosophy of an intensive insulin regimen, balanced with the psychosocial effect of this on the child, parents/carers and wider family. Target blood glucose levels are individualised, but generally in the range of between 4 and 8 mmol/L before a meal and 4 and 10 mmol/L post-prandially. A paradigm shift occurred in diabetes care in 1993 with publication of the Diabetes Control and Complications Trial, a multicentre randomised controlled trial which definitively showed that exposure to hyperglycaemia was directly linked in a dose-response manner to the development of diabetes-related complications; these being micro-vascular disease in the form of retinopathy, nephropathy and neuropathy and macro-vascular disease in the form of stroke and heart attacks. Follow-on studies of

this and other diabetes cohorts, such as the EDIC trial, showed that the benefits of tight blood glucose control were maintained for decades afterwards, with persistent reduction in macro-vascular disease of 57% after 17 years and rate of onset of diabetic retinopathy still 62% lower in the original intensively treated group after 7 years. These findings are persistent in all causes of hyperglycaemia, either from Type 1 or Type 2 diabetes. Diabetic retinopathy is currently the leading cause of acquired blindness in the developed world. The primary measure of glycaemic control in these trials was Glycosylated Haemoglobin, or HbA1c, which subsequently has been used to benchmark glycaemic control and is often available in diabetes out-patient clinics as a point-of-care test. Paediatric targets for HbA1c were recently lowered to 7% (53 mmol/mol) by both the International Society for Paediatric and Adolescent Diabetes (ISPAD) and agreed by the Irish Diabetes Expert Advisory Group. Again, young people may have differing individual targets agreed with their paediatric care team. The economic consequences of diabetes and its related complications are enormous, with 784 million people worldwide predicted to be diagnosed with diabetes by 2045 and, in the US alone, contributing \$237 billion in direct medical costs per year, or 7% of the nation's health care budget which is higher than that spent on cancer (5%) or heart disease/stroke (4%).

Post-diagnosis, children and their parents/carers will often spend up to a week learning the basics of diabetes care, in order to function safely after discharge. The majority of children in Ireland commence a multiple daily injection (MDI) regime, consisting of short-acting insulin before each main meal (usually breakfast, lunch and dinner), with a long-acting insulin usually delivered in the evening. Doses of insulin are calculated according to anticipated carbohydrate intake, exercise and self-monitored blood glucose levels. The variety of insulin analogs available has increased significantly in recent years, along with a significant exponential increase in technologies available, the latter of which are successful in reducing painful injection and finger-pricking burden. Short-acting insulins commonly used include Aspart and Lispro (Novorapid®, Fiasp®, Humalog®) with long-acting options such as Glargine, Detemir, and Degludec (Lantus®, Levemir®, Tresiba®). Insulin regimens are chosen that minimise episodes of hypoglycaemia, mitigate hyperglycaemic excursions and are feasible for the family and young person to administer. Some young people may be on more bespoke regimens using more medium or intermediate insulins and some may be using premixed insulins, although this proportion is lessening. Adolescence is often a particularly challenging time for adherence to the prescribed insulin regimen, along with being a period of endogenous higher insulin resistance secondary to pubertal hormones.

## Teething problems post-diagnosis

After discharge from hospital, young people and their families are supported by hospital-based multidisciplinary teams to incorporate diabetes into their daily lives, learning how to titrate insulin to glycaemic pattern, troubleshoot early issues and manage particular scenarios such as illness, exercise and sports whilst managing burgeoning independence with ongoing education on self-management for events such as sleepovers, self-administration of insulin etc. Since the inception of the national Model of Care in 2015, paediatric diabetes care is organised into integrated practice units comprising a regional centre of reference and a number of additional local units, organised in a hub and spoke model. The majority of units conduct initial support by telephone, with some centres having space to facilitate a 'drop-in' support service and some using more telehealth methods, use of the latter being accelerated by the pandemic.

In the first month after diagnosis, patients are educated to anticipate the temporary 'honeymoon period'. At time of presentation of clinical diabetes, approximately 10-15% of the original beta cell mass is estimated to remain functional. Provision of exogenous insulin allows the beta cells some reprieve and allows them to re-establish intracellular stores of insulin, necessitating a reduction in dose of injected insulin and sometimes a partial remission. This is commoner in children aged >5 years old, those not in DKA at diagnosis and lasts on average 6 to 12 months, as continued immunological destruction of the remaining beta cells does continue. Repeated episodes of hypoglycaemia are common as the dose of insulin is reduced and it is necessary to have extra hypoglycaemia supplies available at this time for prompt treatment. Messages around hypoglycaemia management are important and must be consistent. Hypoglycaemia is generally defined as a blood glucose level of <4 mmol/L and mild/moderate versus severe is not quantified by number, but according to the symptoms displayed by the individual. Severe hypoglycaemia is defined as an episode which results in either loss of consciousness or the individual needing another person's assistance to manage their hypoglycaemic episode. Injectable glucagon is available and should be carried by all people with T1D for this instance, especially those with impaired hypoglycaemia awareness such as younger children. More common are episodes of mild to moderate hypoglycaemia, with symptoms such as pallor, tremor, increased sweating and tachycardia, progressing to confusion and impairment of consciousness without treatment. Treatment consists of 0.3g/kg of a fast-acting glucose source such as Lucozade®, Dextrose tabs, Glucogel®, or Lift® (formerly known as Glucojuice). Options such as chocolate, milk or biscuits are inappropriate treatment options for hypoglycaemia as their fat content renders their absorption too slow. Introduction of the sugar tax in 2017 caused reformulation of many soft drinks, generally meaning that much more volume of the liquid is now required for adequate hypo treatment. This can be difficult for younger children in particular, hence 'Lift®' with 15g per 60ml is an option growing in popularity and available on the long term illness scheme.

Other early issues include needle incompatibility with resultant leakage of insulin and hyperglycaemia and/or ketosis. In general, most insulin products will be compatible with needles made by the



same company and generic substitutions have resulted in administration issues. The recommended needle length for most children is 4 to 5 mm and site rotation is of utmost importance to avoid erratic absorption from lipohypertrophy. If in any doubt, please do not hesitate to liaise with the paediatric diabetes team who will be more than happy to advise.

## Diabetes-related Technologies

The past decade has seen an explosion in technologies, particularly insulin pumps (continuous subcutaneous insulin infusion, or CSII) and continuous glucose monitors (CGM). Insulin pumps are an alternate method of 'intensive treatment' of diabetes which consist of a small pager-sized device worn by the young person on a belt, Velcro pouch or waistband. The family fill insulin into a reservoir in the device which is then infused continuously at pre-set basal rates via a short line and subcutaneous access site to the subcutaneous space. User-activated boluses are administered for food and correction when blood glucose is high, with most devices containing calculators to assist the maths of bolus calculation. Basal rates can be adjusted to account for illness, menstruation or increased activity, increasing flexibility and often improving quality of life for those engaged in their use. Our National Model of Care prioritises insulin pump access for those aged <6 years old, reflecting their increased need given their tendency to hypoglycaemia unawareness, reduced ability to articulate hypoglycaemia symptoms, erratic eating patterns, susceptibility to viral intercurrent illness and requirement for smaller insulin increments. Pump training and initiation is resource heavy, requiring high investment of time for training and support afterwards on the part of both the family and the multidisciplinary team. Fortunately in Ireland, no co-payments are needed and this equipment is funded by our health care system, unlike other first world countries where access to insulin and pumps is not universal.

CGM devices have revolutionised glucose monitoring, previously challenging due to the painful nature of the capillary fingerpricks and disadvantaged as representing an isolated snapshot of glucose control. These devices are placed in the subcutaneous space of the young person using an automatic inserter device and consist of a sensor to estimate

interstitial glucose, along with a transmitter which sends the reading to a mobile phone, insulin pump or other receiver device. Hypo or hyperglycaemia alarms assist detection and some devices allow caregivers to follow glucose levels remotely from their own mobile phones. They generally assess glucose levels at intervals of 5 minutes, either continuously relaying this information to the receiver (Medtronic Guardian® or Dexcom G6®), or intermittently when a user 'flashes' the receiver to read the sensor when indicated (Abbott Freestyle Libre®). The decision as to which device would be suitable to which patient is reached collaboratively by the family and their health care team. Disadvantages include skin hypersensitivity to the adhesive, exacerbation of underlying anxiety by alarms, perceived inaccuracy (interstitial sensed versus true blood glucose) and sensors falling off with activity. Diabetes teams are well versed in troubleshooting these issues and should be consulted in order to maximise the benefit for the child of these expensive systems. These CGM systems are currently funded for the paediatric population and an active campaign is underway nationally to extend eligibility to those aged over 21 with T1D.

The 'holy grail' of diabetes technologies is the interaction of blood glucose information from CGM with insulin delivery with CSII through a functioning algorithm to allow autonomous insulin delivery without user interaction, a.k.a the 'closed loop', or artificial pancreas system. In 2022 two systems with partial closed loop are available in Ireland which adjust basal insulin delivery only. User input is still required for bolus insulin delivery but advancements continue apace in this area.

## Conclusion

T1D is a chronic burdensome illness of childhood which affects quality of life for the young person and their family and is associated with significant complications. Specialist paediatric teams deliver increasingly specialist technological advances to our vulnerable population and encourage proactive management strategies to maximise glycaemic control. Community pharmacies are integral to delivery of this care and an active relationship with patients and their teams is encouraged.

*Next month's issue of IPN will carry a follow-on article looking at the LTI and resources.*