TYPE 1 DIABETES MELLITUS IN CHILDREN AND ADOLESCENTS IN INDIA

CLINICAL PRACTICE GUIDELINES 2011

INDIAN SOCIETY FOR PEDIATRIC AND ADOLESCENT ENDOCRINOLOGY

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PREFACE

The burden of childhood diabetes is increasing year by year in India, as it is in Western countries. However, our basic pediatric training, due to competing claims of issues of greater public health impact on the limited training time available, does not provide the skills for ambulatory chronic care of the child with diabetes. Yet, here is an example of a disease which, if well looked, after can allow a long and productive life for our patient. In recognition of a felt need, the Indian Society for Pediatric and Adolescent Endocrinology (ISPAE) has prepared this practical "guidelines" for the benefit of pediatricians, physicians, diabetes educators and medical students in India.

These guidelines aim to provide clear practical instructions on how best to look after a patient of pediatric diabetes in the Indian setting.

It is proven beyond doubt that the closer one comes to perfect blood glucose control, the lower the risk of developing the long term complications that contribute to diabetes morbidity and mortality. Even with the best available treatment, however, it may not be possible to achieve normal metabolic milieu; hence certain arbitrary criteria are laid down to indicate good control. These criteria must be individualized based on patient characteristics as the day to day management of diabetes is largely dependent on the patient. Thus patient education forms a constant theme in the background of this book. The market is flooded with a variety of insulins and insulin administration devices. The latest and the most expensive insulin or device is not necessarily the best for every case. The treating doctor must be equipped with the knowledge to make the right choice on a case to case basis. Nutritional management, physical exercise, assessment of long term control and tests to screen for microvascular and macrovascular complications and comorbidities associated with type 1 diabetes, the two acute complications of hypoglycemia and diabetic ketoacidosis, and management during sick days, are some of the other chapters which all will find useful. Special attention has been paid to psychosocial aspects, keeping in mind the tender age of our patients and the fact that diabetes management is a task for the whole family.

The preparation of these guidelines was entrusted to a team of pediatric endocrinologists and diabetologists from different parts of our vast and diverse country. The team includes those who manage the poor, less literate patients in public hospitals as well as those who deal with the well to do, highly educated patients in the private sector. Each chapter has been written by a single author but incorporates inputs from all members of the writing and editorial group.

The guidelines are divided in 23 chapters, each dealing with a specific aspect of type 1 diabetes. Each chapter is complete in itself and the reader can read the chapters in any sequence. We hope that the ISPAE guidelines will be read by all those who care for children; that reading the guidelines will result in earlier diagnosis of diabetes and scientific approach to its management, thus ensuring a longer, healthier life for children afflicted with this disease.

Aspi J Irani
P S N Menon
Vijayalakshmi Bhatia

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INTRODUCTION

Aspi J. Irani

Several excellent guidelines are available for the management of type 1 diabetes mellitus (T1DM) in children and adolescents. These include the ISPAD guidelines (2009), Australasian guidelines (2005), Canadian Diabetes Association guidelines (2008) and the American Diabetes Association guidelines (2011). One may therefore ask – what was the need for publishing the present set of guidelines?

The present Indian Society for Pediatric and Adolescent Endocrinology (ISPAE) guidelines summarizes the current scientific data on the subject and offers guidance on how best to apply the same for optimum results in the Indian scenario. These guidelines have been written keeping in mind the situation prevailing in our country and the constraints under which we work.

T1DM is the commonest metabolic-endocrine disease in children and adolescents. There has been a significant increase in the number of new cases in the past few years. However, a practicing pediatrician in India is not likely to encounter more than a couple of new cases each year.

Our country has certain circumstances and requirements, some common to other developing nations and some unique .There are very few specialized pediatric endocrinologists in our country. Most pediatric patients with diabetes are managed by the general pediatrician, the internist or the "adult" diabetologist or endocrinologist.

Very few centers are able to provide a team based approach for management of diabetes in the pediatric age group. A 24-hour helpline for these patients is virtually non-existent. Little attention is paid to the psychosocial needs of the patients. There are very few diabetes support groups. Most schools in our country are neither geared for nor willing to take up any responsibility for caring for the child with diabetes.

The different types of foods we consume in various parts of our vast country and lack of sufficient data on carbohydrate content of our foods poses a major challenge. The joint family system creates a problem especially with meal planning. The same system, if properly harnessed, can afford parents the benefit of additional support and assistance in managing diabetes.

Poverty, absence of government funding and illiteracy are some of the other important hurdles in the management of T1DM. Misconceptions about the disease,

and its victims, are rampant. Blind faith in alternative systems of medicine often leads patients to omit insulin therapy with disastrous results. Availability of the latest medications and devices for management of diabetes is no longer a problem. The challenge lies in making these available to all classes of patients and ensuring that they are utilized appropriately so as to derive maximum benefit.

For all the above mentioned reasons, the ideal therapeutic approach may not always be the most practical one to follow. This booklet on guidelines for diabetes management by the ISPAE has been prepared with the abovementioned factors in mind.

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DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Anna Simon

SUMMARY

- Diabetes mellitus should be suspected in a variety of clinical situations including failure to gain weight, weight loss despite good appetite, and recurrent infections, in addition to classical features of diabetes and ketoacidosis.
- The revised criteria proposed for diagnosis of diabetes include HbA1c $\geq$6.5% as a criterion, in addition to plasma glucose levels.
- Even though type 1 diabetes accounts for most cases in childhood, other types of diabetes are being increasingly diagnosed now.
- Type 2 or other etiologies of diabetes should be suspected in presence of autosomal dominant history, presence of syndromic features, deafness, optic atrophy, abdominal pain, or acanthosis nigricans.
- Insulin-requiring hyperglycemia in the first three months of life is known as neonatal diabetes mellitus. Approximately half of the cases are transient, which resolve spontaneously. The most common form of permanent neonatal diabetes is activating mutations of Kir6.2 (KCNJ11) and SUR1 (ABCC 8) subunits of KATP channel or mutations of Insulin Promoter Factor-1 or FOXP3 gene.

CLINICAL FEATURES OF T1DM

- Polyuria, polydipsia, nocturia or secondary enuresis in association with glucosuria and ketonuria
- Failure to gain weight or weight loss despite increased appetite
- Persisting glucosuria
- Presence of candidial vaginitis or balanitis or recurrent skin infections
- Diabetic ketoacidosis or rarely hyperosmolar coma

CRITERIA FOR DIAGNOSIS OF DIABETES

The criteria recently proposed by the American Diabetic Association (ADA) for the diagnosis of diabetes are given in **Table 1** below.

TABLE 1. Criteria for the Diagnosis of Diabetes (ADA 2011)

1. Fasting plasma glucose (FPG) ≥126 mg / dL (7.0 mmol / L). Fasting is defined as no caloric intake for at least 8 hours.*

OR

2 2-hr plasma glucose ≥200 mg / dL (11.1 mmol / L) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

OR

3. HbA1c ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg / dL (11.1 mmol / L).

**In the absence of unequivocal hyperglycemia, criteria 1–3 should be confirmed by repeat testing.*

An oral glucose tolerance test (OGTT) should not be performed in children and adolescents if diabetes can be diagnosed using fasting, random or post-prandial criteria. It is rarely indicated in making the diagnosis of T1DM in childhood and adolescence. If doubt remains, periodic re-testing should be undertaken until the diagnosis is established.

CLASSIFICATION OF DIABETES MELLITUS

An etiological classification of diabetes in children is given below.

I. Type 1 Diabetes Mellitus (T1DM)

(β cell destruction or insulin deficiency)

A. Immune mediated

B. Idiopathic

II. Type 2 Diabetes Mellitus (T2DM)

(Insulin resistance with variable insulin deficiency)

III. Other Specific Types

A. *Genetic defects of β cell function*

MODY 1 (20q12-q13.1, HNF-4α)

MODY 2 (7p15-p13, glucokinase)

MODY 3 (12q24.2, HNF-1α, TCF-1)

MODY 4 (13q12.1, IPF-1)

MODY 5 (17cen-q21.3, HNF-1β, TCF-2)

MODY 6 (2q32, *NeuroD1*, beta2)

Mitochondrial DNA mutation

DIDMOAD - Wolfram syndrome (WFS-1/chromosome 4)

Chromosome 7, KCNJ11 (Kir6.2) SUR, IPF-1, FOXP3

Others

B. *Genetic defects of insulin action*

Leprechaunism

Rabson–Mendenhall syndrome

Lipoatrophic diabetes

Type A insulin resistance

Others

C. *Diseases of the exocrine pancreas*

Cystic fibrosis related diabetes

Pancreatectomy/trauma

Fibrocalculous pancreatopathy

Pancreatitis

Hemochromatosis

Irradiation

D. *Endocrinopathies*

Cushing disease

Hyperthyroidism

Acromegaly

Pheochromocytoma

Somatostatinoma

E. ***Drug/chemical induced***

Glucocorticoids

Cyclosporine

L-asparaginase

Nicotinic acid

Diazoxide

Thiazides

Vacor

Pentamidine

F. ***Genetic syndromes with insulin resistance / insulin deficiency***

Prader-Willi syndrome (chromosome 15)

Down syndrome

Turner syndrome

Friedreich's ataxia

IV. Gestational Diabetes Mellitus

ETIOLOGICAL DIAGNOSIS

Though T1DM is the most common cause of diabetes in childhood and adolescence, there is increasing recognition of the occurrence of T2DM and other rarer genetic forms of diabetes in recent years. The differentiation between T1DM, T2DM and monogenic forms of diabetes is important for planning the therapeutic strategy.

Type 1 Diabetes Mellitus (T1DM)

T1DM usually presents with polyuria, polydipsia, weight loss and easy susceptibility to ketosis. It is also characterized by the dependence on exogenous insulin to preserve life, the presence of circulating antibodies to cytoplasmic and cell-surface components of islet β cells and its association with certain HLA loci and other autoimmune diseases. In Caucasians, serological markers of an autoimmune pathologic process, including islet cell antibodies (ICA), GAD_{65}, IA-2, IA- 2β, or insulin autoantibodies (IAA), are present in $> 90\%$ of individuals with T1DM (type 1A). However, the corresponding figures are much lower in Indian studies, therefore the absence of these markers does not rule out T1DM. This antibody negative variety of type 1 DM is also called type 1B DM.

Clinical and Laboratory Features of Other Forms of Diabetes

The possibility of other types of diabetes must be suspected when there is:

- An autosomal dominant family history of diabetes
- Presence of syndromic features, associated deafness or optic atrophy
- Features of insulin resistance (acanthosis nigricans or polycystic ovary syndrome)
- Requirement of very little insulin or no insulin outside the honeymoon phase
- History of exposure to drugs toxic to β cells or known to cause insulin resistance
- Onset below the age of 6 months

Some of the clinical and laboratory features differentiating the rarer forms of diabetes from T1DM are described below and shown in **Table 2**.

TABLE 2. Differentiation of T1DM, T2DM and Monogenic Diabetes

Characteristic	***Type 1***	***Type 2***	***Monogenic***
Genetics	Polygenic	Polygenic	Monogenic
Age of onset	6 months to adolescence	Usually pubertal	Often post pubertal except glucokinase and neonatal
Clinical presentation	Most often acute, rapid	Variable	Variable
Autoimmunity	Yes	No	No
Ketosis	Common	Uncommon	Common in neonatal forms, otherwise uncommon
Insulin secretion	Decreased / absent	Variable	Variably decreased
Insulin sensitivity	Normal	Decreased	Normal
Insulin dependency	Permanent	Episodic	Variable
Obesity	Population Frequency	Increased frequency	Population frequency
Acanthosis nigricans	No	Yes	No

Type 2 Diabetes Mellitus (T2DM)

T2DM is a polygenic disease with multiple risk factors. The possibility of T2DM should be considered in children and adolescents who

- Who are obese
- Who have family history of T2DM
- Who have evidence of insulin resistance (acanthosis nigricans or polycystic ovary syndrome)
- Whose fasting insulin and C-peptide levels are normal or elevated

In an overweight adolescent who had recent onset hyperglycemia without ketosis, it may not be very clear whether the diabetes is type 1 or 2. In such cases it may be relatively safer to start treatment with insulin rather than oral antidiabetic agents. There is a place for testing autoantibodies in such situations, even though they are reported to be less prevalent in Indian studies.

Maturity Onset Diabetes of the Young (MODY)

These are a group of disorders with a monogenic defect in β cell function. They are important to diagnose as their treatment, natural course, associated features and nature of genetic counseling are different from type 1 or type 2 DM.

Clinical features which suggest a diagnosis of monogenic diabetes:

1) If the patient apparently has very mild hyperglycemia and does not seem to require insulin (ie, appears like type 2 DM), but yet is not obese and has no acanthosis, and may have diabetic family members who are not obese.

2) If the patient requires insulin and is non-obese (thus appearing like type 1 DM), but is below 6 months of age or has a parent with diabetes

Tests which can give a clue to the presence of monogenic diabetes:

1) If the child appears to have type 1 DM but islet antibodies are negative, particularly at onset of DM, and / or there is evidence of C peptide production beyond 3 years from diagnosis of DM.

2) If the child appears to have type 2 DM but there is no evidence of insulin resistance and fasting C peptide is in the normal range.

Fibrocalculous Pancreatic Disease with Diabetes (FCPD)

In India, in adolescents, especially those who do not present with ketosis , one must be alert for the diagnosis of FCPD. Some helpful features include:

- associated symptoms of pancreatic disease, abdominal pain and malabsorption
- evidence of pancreatic calcification

Ultrasound of pancreas is useful but may not always be diagnostic. The implications of having FCPD include the need to test for exocrine pancreatic function and for enzyme replacement in addition to insulin, the occurrence of intermittent episodes of pancreatitis, and an increased risk for pancreatic carcinoma.

DIDMOAD Syndrome (Wolfram syndrome)

DIDMOAD syndrome is characterized by diabetes insipidus, diabetes mellitus, optic atrophy and deafness. The disease has an autosomal recessive

inheritance with the gene mapped on chromosome 4 (WFS 1). WFS1 has a role in β cell and neural tissue survival.

Neonatal Diabetes

Insulin-requiring hyperglycemia in the first three months of life is known as neonatal diabetes mellitus. Most affected infants have intrauterine growth retardation (IUGR) and other clinical features such as polyuria with glucosuria, dehydration, failure to thrive and rarely DKA.

Neonatal diabetes can be classified as:

A. Transient - without recurrence

B. Transient - with recurrence

C. Permanent from onset

Approximately half of the cases are transient which resolve spontaneously. This is often due to delay in maturation of pancreatic â cells. In patients with transient neonatal diabetes mellitus, permanent diabetes may appear later in life.

About 50% of cases are of the permanent form and may additionally present with dysmorphic features, muscle weakness and epilepsy. The most common form of permanent neonatal diabetes is due to activating mutations of Kir6.2 (KCNJ11) , SUR1 (ABCC 8) subunits of KATP channel or mutations of Insulin Promoter Factor-1 (chromosome 7), or FOXP3 gene. These forms of neonatal diabetes are responsive to pharmacological doses of the oral sulphonylurea, glibenclamide.

Other rarer forms of permanent neonatal DM are

- Pancreatic agenesis (homozygous mutation of IPF1 or glucokinase gene) – may present with exocrine manifestation like malabsorption.
- IPEX syndrome (immune dysregulation, polyendocrinopathy, enteropathy, X-linked)
- Wollcot-Rallison syndrome associated with multiple epiphyseal dysplasia, renal and hepatic impairment and ectodermal dysplasia.

Stress Hyperglycemia

Stress hyperglycemia is common in children and adolescents and is reported in about 5% of children presenting to an emergency department. Severe hyperglycemia detected in children with acute infections, respiratory distress, shock, trauma or surgery is usually transient and may require treatment. Stress hyperglycemia by itself is not diagnostic of diabetes. Reported incidence of progression to overt diabetes varies from 0% to 30% and hence it is recommended that patients be screened for diabetes at regular intervals.

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PRINCIPLES AND GOALS OF MANAGEMENT

Aspi J. Irani

SUMMARY

- Daily, lifelong insulin injections are essential for the survival of children with Type 1 diabetes mellitus (T1DM).
- Medical nutritional therapy, planned physical activity and self monitoring of blood glucose and urine ketones are other very important aspects of treatment.
- Hospitalization for initial management and education is required in most, though not in all, newly diagnosed cases.
- Management of childhood diabetes needs a team approach. The patient must have round-the-clock access to a team member.
- Patients and their families must be educated in self management of diabetes, including prevention and first aid management of diabetes related emergencies (hypoglycemia and ketosis).
- Psychosocial problems must be anticipated and addressed.
- A childhood and adolescent diabetes support group must be established in each city.
- Even with the best available treatment, it is not possible to achieve a normal metabolic milieu. The goals of treatment therefore are to keep the child symptom free, ensure normal growth and development, with HbA1c as close to the normal range as possible.
- The lower the HbA1c value, the lower the risk for development / progression of long term microvascular and macrovascular complications. However, the risk of hypoglycemia rises sharply.
- The therapeutic plan and goals of therapy should be individualized depending on the patient's abilities, motivation, finances, age, daily schedule and the availability of medical services.
- Regular screening for long term complications and co- morbidities must be undertaken.
- There is no medication other than insulin for control of diabetes, though in selected cases metformin and amylin may have some role.
- At present there is no cure for T1DM, but it should be controlled to the best possible extent.

Type 1 diabetes mellitus (T1DM) is caused by autoimmune or idiopathic destruction of the insulin producing β cells in the pancreas. **Exogenous insulin** (available since 1921) **is essential for the survival of children and adolescents with T1DM.** Insulin is available only in injectable form. Inhaled insulin and buccal insulin were introduced recently, but have now been withdrawn from the market worldwide.

Replacement of the missing hormone, insulin, is only one aspect of management of diabetes in children and adolescents. **Equal importance must be given to each of the four "therapeutic pillars"** which include :

1. Insulin therapy
2. Meal planning (medical nutritional therapy)
3. Planned physical activity
4. Self monitoring of blood glucose and urinary or blood ketones

Diabetes is perhaps the only chronic childhood disease in which **the patients (child and family) need to play the key role in day to day management.** They must be taught :

1. How to inject insulin (including injection sites and site rotation)
2. How to test blood glucose and urine ketones
3. How to record, analyze and act on the home monitoring results
4. Principles of "healthy eating" and meal planning to prevent swings in blood glucose
5. How to plan physical activity so as to prevent hypoglycemia, and finally
6. Everything about prevention, early recognition and first aid management of the diabetes related emergencies: ketoacidosis and hypoglycemia

In a disease requiring active and intelligent participation of the child and family, patient education as well as compliance are most important. Intensive and ongoing education of the patient in self-management of diabetes is essential. Not providing self-care education constitutes sub-standard care. Ideally this should be supplemented with a round-the-clock telephone helpline. To ensure patient compliance, attention must be paid to the emotional state of the child and family. **Together, patient education and emotional stability constitute the foundation on which the four pillars of diabetes management rest.**

The patient and family members are invariably in a state of shock and denial at the outset. They are overcome with the "why us?" feeling and the need to blame a person or event for the diabetes. As there is so much to learn and so

much responsibility to shoulder, the parents feel helpless and confused. There is anxiety and worry about the child's future – education, employment, marriage, childbearing, acute and long term complications of DM and the expected life span. These **emotional upheavals and "unspoken" fears must be anticipated and addressed.** Stress must be laid on the strong possibility of a bright future provided diabetes is well controlled.

In order to provide the full range of services, **management of childhood diabetes needs a team** – the team should include a pediatric endocrinologist or a pediatrician with special interest in diabetes, a dietician, a psychologist, a social worker and a nurse educator. The team should ideally also include senior patients and their family members who can be the best counselors, educators, social workers and above all "role models" for the "new entrants".

Maintaining contact with the patient at regular intervals (preferably with a 24 hour helpline) per se improves the level of control. This is possible in our country on the telephone and via SMS, fax and e-mail.

A childhood and adolescent diabetes support group should be established in each city. This is useful for group education and counseling. It also enables patients to procure diabetes related paraphernalia at lower cost on account of bulk purchase. They can help each other by sharing their ideas and experiences. The group can work towards creating informed awareness about this relatively rare disease and securing a fairer deal from schools, colleges and employers.

The medical team must communicate with school authorities to ensure that the child is not treated differently from other children and at the same time the staff members must take care to avoid situations that predispose to hypoglycemia. The staff should be in a position to identify hypoglycemia early and manage the same should the need arise.

Hospitalization for initial management is mandatory if the child is dehydrated, vomiting, breathless, or has abdominal pain, or is drowsy (features of ketosis). In patients who are not in ketosis at presentation, the following would be indications for hospitalization:

1. The child below 5 years of age
2. When parents are emotionally disturbed or incapable of administering insulin and checking blood glucose at home
3. When the residence is far away from the medical center and/or there are no adequate means of communication

If hospitalization is required, the child should be managed in the pediatric ward, never in a ward for adult patients.

Ideally one would like to achieve normal blood glucose and a normal metabolic milieu all the time. This is not possible even with the most sophisticated treatment available today. Thus, **one should strive to achieve the following arbitrary goals:**

1. The child should be leading a normal and happy childhood.
2. The child should be asymptomatic (with no seizures, unconsciousness or confusional state due to hypoglycemia, no symptoms of high blood glucose, no ketoacidosis).
3. The child should be growing and maturing normally, with participation in normal school curricular and extra-curricular activities, and no school absenteeism.
4. The child should remain free of the long-term microvascular and macrovascular complications which are known to impact the quality of survival and shorten the life span of patients with T1DM.

Whereas the first three goals are relatively somewhat easier to achieve, the last goal is the most challenging.

The **"Diabetes Control and Complications Trial" (DCCT)** which compared the outcome in two groups of adolescents and adults (a "conventional treatment" group and an "intensified treatment" group) showed that:

1. Those on intensified management had a lower HbA1c (8.1% vs. 9.8%) which in turn resulted in a 50-60% reduction in onset as well as progression of the long-term microvascular complications of nephropathy and retinopathy.
2. There was no lower threshold level of HbA1c below which the complications did not develop. Any sustained improvement in HbA1c was shown to reduce the risk.
3. When individual patients in the two groups were compared the risk of complications was lower in the "intensified treatment" group, even in those with identical HbA1c values. The reduced swings of blood glucose may have accounted for this observation.
4. The benefits of intensified management, however, came at the cost of a 300% higher incidence of hypoglycemia and of weight gain in the intensively treated group.

Later studies, including the **"Epidemiology of Diabetes Interventions and Complications" (EDIC) trial** have shown that:

1. Intensified management also lowers the risk of macrovascular complications.

2. The beneficial effects of a period of good control continue to accrue even if the same degree of control is not sustained subsequently.
3. With the newer insulins and monitoring methods which became available after the conclusion of the DCCT trial, the adverse effects of intensified management (hypoglycemia and weight gain) have considerably reduced.
4. It is difficult to achieve the level of control as in the DCCT even though we now have better management tools; this is perhaps because it is not easy to maintain the same level of 24 hour access to medical advice and guidance as was done in the DCCT.

From the DCCT and the EDIC trials it is clear that **one should strive to achieve as perfect a level of control as possible (reflected by the HbA1c) with minimum swings in blood glucose.** A low HbA1c with frequent hypoglycemic episodes is not acceptable.

It must be stressed that **there is no single best way to manage diabetes**. Since patient participation is so crucial, the goals of management must be set, taking into account the level of motivation and intelligence of the patient and the family, their financial status, the child's age, the daily schedule of the child and parents, and the availability of medical services.

Thus, the intelligent, rich and motivated older patient may opt for the insulin pump or a basal bolus insulin regimen using analogs (3-5 injections a day), perform 5-8 blood glucose tests a day and use a meal plan based on carbohydrate counting. At the other extreme, the underprivileged, uneducated or poorly motivated patient can be managed on two injections a day of premixed insulin with little or no home monitoring and diet instructions covering "healthy and consistent eating" and a "traffic signal diet." However, the majority of patients would fall in between these two extremes; they can learn to mix regular and NPH insulins, inject 2-4 times a day and test blood glucose 1-2 times daily. Thus, **the treatment plan must be individualized**.

Regular annual screening for subclinical evidences of microvascular complications, predisposing factors for macrovascular complications and T1DM associated co-morbidities must be a part of clinic evaluation. Early detection and prompt remedial action can go a long way in improving the long term outcome.

Besides insulin, it is possible that **amylin** (another hormone produced by the β cells and which regulates postprandial glycemia and glucagon output) may have a role in T1DM management. Obese adolescents with T1DM and especially those who develop polycystic ovarian disease may benefit from addition of **metformin** to counter the added factor of insulin resistance. No other drugs have any role to play in blood glucose control in patients with T1DM.

A permanent cure for T1DM is not available at present. Several therapeutic modalities, including stem cells, are being explored but are still experimental. T1DM is not a curable disease; however, it can and should be controlled to the best possible extent.

INSULIN THERAPY

Aspi J. Irani

SUMMARY

- Insulin replacement therapy is essential for the survival of children with T1DM.
- For day to day management insulin is injected subcutaneously, two or more times a day. It can be injected with a syringe, a disposable pen, a reusable pen or it can be given as a continuous subcutaneous infusion (the insulin pump).
- Short acting human insulin or a rapid acting analog (to provide a "bolus" to cover post meal glycemia) as well as an intermediate acting human insulin or long acting basal analog (for basal insulin supply) are both essential for day to day management. Insulin pumps use only a rapid acting analog for both bolus as well as basal phases. In treatment of DKA only short acting human insulin is used.
- Basal bolus regimens involve taking 3 or more injections a day but give more flexibility of lifestyle and better control than the split-mix regimen.
- The choice of regimen should be based on the assessment of the patient's motivation, capability and financial position.
- The usual dose of insulin varies between 0.5-1.5 units / kg / day according to the stage of diabetes and the age and maturation of the child.
- The correct techniques of storing insulin, mixing insulins and injecting insulin should be taught to all patients.
- Hypoglycemia and lipohypertrophy are the two main complications of insulin therapy encountered with the newer preparations. With a little bit of care both can be prevented.

Type 1 diabetes mellitus (T1DM) is a hormone deficiency disease and treatment is directed at replacing the missing hormone, in this case, insulin. Insulin replacement therapy as practised today is far from being perfect for it is very difficult to mimic the pattern of endogenous insulin secretion. Exogenously administered insulin first enters the systemic circulation rather than the portal circulation and liver; it is given in a predetermined dose in anticipation of a meal rather than in response to changing glycemia with a meal; it has a long half life

allowing limited flexibility; the action profile of a given insulin preparation may vary in the same patient from day to day.

Insulin is essential for the survival of patients with T1DM. All children with T1DM require daily life-long insulin therapy.

Insulin is available only in injectable form. Inhaled insulin and buccal insulin which were introduced a few years ago have been withdrawn from the market.

Three varieties of diabetes with onset in childhood may not require insulin therapy:

- *Those presenting with diabetes below 6 months of age:* 30-50% of cases may be due to genetic mutations affecting insulin secretion and may respond to sulfonylurea group of drugs.
- *T2DM:* now seen with increasing frequency in obese adolescents (especially in those with acanthosis nigricans and a strong family history of T2DM). This is treated with oral hypoglycemic agents, particularly metformin.
- *Maturity onset diabetes of the young (MODY):* should be suspected if mild diabetes develops with a family history of non-insulin dependent diabetes beginning below 25 years of age in three successive generations.

TOTAL DAILY DOSE (TDD) OF INSULIN

In the management of DKA a dose of 0.1 unit / kg / hour of short acting insulin given as an intravenous infusion should be appropriate in the majority of cases.

When the patient recovers from DKA, the insulin requirement may initially be as high as 2-3 units / kg / day for the first few days, because of elevated levels of stress hormones, increased appetite and need to restore depleted body stores of protein and glycogen.

As the patient enters the honeymoon phase, the dose comes down to 0.5 units / kg / day or less; some may require virtually no insulin. However, it is preferable to continue with a very small dose once or twice a day. The honeymoon phase lasts for 3-12 months, rarely up to 24 months.

As the intensification phase sets in (this may happen gradually or it may be abrupt if precipitated by an infection) the requirement rises to 0.7-1.0 units / kg / day in prepubertal children and 1.0-1.5 units / kg / day in pubertal children (on account of the anti-insulin effects of growth hormone and sex steroids).

INSULIN PREPARATIONS AVAILABLE IN INDIA

In India, the conventional short acting insulin (regular or soluble) and intermediate acting insulin (NPH) are available. These insulins are manufactured by recombinant DNA technology and are structurally identical to the insulin

produced in the human body (as against the animal pancreas extracted beef and porcine insulins used till recently). All available insulins are now highly purified.

The intermediate acting *lente* insulin and long acting *ultralente* insulin are no longer available.

The newer insulin analogs (so called "designer insulins") are also available in India: these include the rapid-acting analogs Lispro, Glulisine and Aspart; and the long acting basal analogs Glargine and Detemir. Since the effect of the rapid acting analogs lasts only for 2-4 hours, they can sometimes give pre-meal hyperglycemia. A recent study has hinted at a higher risk of malignancy in patients on Glargine monotherapy. This study however was inconclusive and at variance with other studies showing a lower risk of malignancies when Glargine was used with other insulins.

Available premixed insulins include mixtures of regular with NPH (in the ratio 50:50 and 30:70) and of soluble rapid acting analogs with a protaminated suspension of the analog (in the ratio 30:70 in the case of Aspart insulin and 25:75 or 50:50 in the case of Lispro). Premixed insulins have the disadvantage that the individual components cannot be adjusted in different amounts or in different directions.

The time-action profiles of the various insulin preparations are shown in **Table 1**.

TABLE 1. The Time Action Profiles of the Various Insulins Available in India

Insulin	*Onset (Hr)*	*Peak (Hr)*	*Duration (Hr)*
Rapid acting analogs	0.25	1	3-4
Human regular	0.5-1	2-4	6-8
Human NPH	1-3	6-8	12-16
Glargine	1	Nil	11-24
Detemir	1	3-9	6-23

RAPID ACTING ANALOGS VS. REGULAR INSULIN

The rapid acting analogs have a quicker onset of action, a higher peak effect and a brief "tail" of action. This gives them certain advantages over regular insulin:

1. In view of the *quicker onset of action*, analogs can be injected just before eating. Studies have shown that the injection can be given even after completion of a meal without significant compromise in efficacy, though this should not be done routinely. Regular insulin must be given 20-30 minutes before eating. (This "lag time" would need to be longer if the pre-meal BG is raised.) Thus the analogs are especially useful in young children who cannot be relied upon to eat after the insulin shot, or in those who have a short lunch break

at school and hence must inject and eat immediately. During outings the patient can estimate the type and amount of food or snacks that he would be ingesting and then take an appropriate dose of the analog.

2. The *quicker onset when injected subcutaneously* also makes the analogs the preferred choice in sick day management and in insulin pumps though not in DKA when the IV route is used (the time action profile is the same for both varieties of insulins when given IV).
3. The *higher peak action* achieved gives better post meal glucose control with the analogs.
4. Because of the *shorter "tail" effect* the analogs are associated with lesser risk of hypoglycemia especially at nights and there is less need for mid-meal snacks.
5. The absorption of the analogs is more consistent from different injection sites whereas regular insulin is absorbed faster from the abdomen than from the buttocks and slowest from the thighs.
6. Switching to analogs may help in resolution of lipoatrophy when it occurs with regular insulin (this is in any case rare with the use of highly purified "human" insulins).

Although they have several advantages (as listed above), long term studies have shown little change in the HbA1c with use of the analogs. Further, the analogs are 3-4 times more expensive than regular insulin. (Refer **Table 2**) It should also be noted that the requirement for basal insulin is higher when analogs are used for pre-meal boluses, since the "tail effect" of regular insulin provides some basal effect. Therefore they should be offered only to families who can easily afford them.

TABLE 2. Cost of Insulin Preparations Available in India

Insulin	***Cost (In Rupees per Unit)***
Human insulin (in vial)	0.40
Human insulin (in pen cartridge)	0.70
Human insulin (in disposable pen)	0.95
Rapid acting analog (in vial / cartridge)	1.45
Rapid acting analog (in disposable pen)	1.89
Long acting basal analog, Glargine	2.95
Long acting basal analog, Detemir	3.30

Note that the long acting basal analogs cost 7-8 times more than human insulin. The rapid acting analogs cost 3.5 times more than human insulin. Insulin in a vial costs much less than the same insulin in a cartridge and insulin is most expensive in a disposable pen.

LONG ACTING ANALOGS VS. NPH INSULIN

The long acting analogs were developed to address three problems associated with NPH insulin:

1. NPH insulin has *a distinct peak of action* 6-10 hours after injection. This necessitates ingestion of a snack to prevent hypoglycemia in the daytime and also increases the risk of night-time hypoglycemia. The long acting analogs are relatively peakless hence there is less need for snacks (and therefore reduced chances of obesity) and night-time hypoglycemia is significantly reduced.
2. NPH insulin *does not cover 24 hours* hence 2-3 injections a day are necessary when it is used as the basal insulin. Glargine covers 24 hours in most children and adolescents though in 20-30% of patients two doses may be needed.
3. NPH has a *25-50% variability of action from day to day* in the same individual. The long acting analogs have a more consistent time action profile in a given patient.

The long acting analogs however have the following disadvantages:

1. The cost is very high being 6-8 times more than that of NPH.
2. The manufacturer's guidelines state that Glargine, being acidic in pH, cannot be mixed in the same syringe with other insulins. Recent studies however have shown that mixing with rapid acting insulins does not affect the action of either insulin, thus reducing one needle prick.
3. Some children experience a burning sensation at the injection site with glargine insulin.
4. If accidentally injected intramuscularly, it's time action curve resembles that of regular insulin (this can cause night-time hypoglycemia if the insulin is given in the late evening.)

STORING INSULIN

Insulin vials should be refrigerated at 2-8^{o}C. They should never be frozen; should this happen inadvertently, the vial would have to be discarded.

In households that do not have a refrigerator, insulin should be kept in a cool, dry place away from sunlight and away from other sources of heat (such as the stove). It can be stored in an earthenware pitcher or *matka*. At 4-8^{o}C, full potency is retained till the expiration date stated on the vial. However, a vial in use (after the seal has been punctured) should not be used beyond three months if refrigerated. If kept at room temperature, it retains full potency for only four weeks. Insulin pens in use need not be refrigerated but should be kept in a cool,

dry place. Insulin should ideally be brought to room temperature before injecting since cold insulin may be painful.

The shelf life and viability of insulin in opened cartridges for insulin pens and pre-filled insulin pens ranges from 7-30 days, the shorter shelf life is for the cartridges containing premixed insulins. Patients should be advised to refer to the manufacturer's guidelines.

Visual inspection of an insulin vial can provide information about its damage due to improper storage. Regular insulin, the rapid acting analogs and Glargine are clear. NPH insulin and levemir have a cloudy appearance. If the clear insulin appears cloudy or has particulate matter it should be discarded. If the cloudy insulin appears thick, discolored, or has solid floating particles, or solid residue at the bottom of the vial, it should be discarded.

During travel insulin can be carried in a thermos flask (wrapped in a plastic pouch to prevent direct contact with ice) or in a "cool pack". During air travel insulin should not be kept in the check-in baggage.

INSULIN INJECTION: PEN OR SYRINGE?

Insulin can be injected with an insulin syringe or pen. Pens may be disposable or reusable.

In India, insulin in vials may be available in two concentrations (40 IU/mL and 100 IU/mL). It is extremely important to ensure that the insulin syringe has the same number of subdivisions as the strength of insulin preparation in use (i.e. 40 IU syringe for 40 IU insulin vial and 100 IU syringe for 100 IU insulin vial).

Insulin in vials (for use with a syringe) is cheaper (refer **Table 2)** than the same insulin supplied in cartridges for use in the pen.

Syringes are preferred to pens for patients who need to mix two types of insulins in varying proportions. In general, syringes and vials are preferred for those on split-mix regimens. The pen is more suitable for those on a basal-bolus regimen, though the morning dose of basal and bolus can be mixed in the syringe, with the pen being used for daytime boluses.

Insulin syringes with 30G-31G gauge needles are almost pain free and can be reused (till the needle becomes blunt) provided they are handled with clean hands and stored in the door of the refrigerator. The needle should never be cleaned with spirit.

Insulin pens are an "attractive toy" which most children prefer to the syringe. The needles are shorter, reducing the chance of intramuscular injections. They are very convenient to use: they do away with the need for carrying insulin vials and filling a syringe before each shot. Injections using the pen are near-painless.

The pen can be carried in the pocket and one merely has to "dial the dose and inject". Pen needles can also be used multiple times.

A half unit pen is also available and this is very useful for small children for fine tuning of insulin dose.

WHO SHOULD ADMINISTER THE SHOT?

Children above the age of 8 years can inject themselves. Self injection is less painful and psychologically less traumatic for the child.

In younger children the parents should administer the shot, while the child can participate in the process of drawing insulins in the syringe.

When children and adolescents inject themselves, parental supervision is extremely important to ensure compliance.

It is suggested that all parents must be made to first poke themselves with the insulin syringe in order to make them realize that the injection is not really painful. When children see their parents injecting themselves their fears too are dispelled.

INJECTION SITES

Insulin is injected subcutaneously in the anterolateral thigh, the anterior abdominal wall (leaving out 2 inches from all sides of the navel) and the upper outer region of the buttocks. The deltoid region is not ideal for the pediatric patient as self injection is difficult and also because there is little subcutaneous fat in this region.

Insulin is absorbed fastest from the abdomen, then from the upper arms, followed by the thigh region. Absorption is slowest from the buttocks.

SITE ROTATION

The injection area should remain the same for a given time of the day (e.g. If the pre-breakfast dose is being injected in the abdomen, it should not be given in the thigh or buttocks).

Systematic site rotation within the selected area is however very important to prevent lipohypertrophy, which is not only cosmetically disturbing but also leads to erratic insulin absorption.

Within a given area not more than 2-3 doses should be injected in a month at the same point. To achieve this, in each area 10-15 spots must be marked in such a way that there is a distance of two fingers width between any two spots. This can be done on a transparent plastic sheet and the spots numbered from 1-10 or 1-15 and again from 15-30 or 10-20 and 20-30.

SEQUENCE FOR DRAWING TWO TYPES OF INSULIN IN THE SYRINGE

The vial of cloudy insulin should be gently rotated between the palms (never shake the vial). It is essential to inject air in each insulin vial prior to drawing insulin in the syringe (exception: when in an aircraft, there is no need to inject air). The amount of air injected should equal the dose of insulin to be withdrawn. The vials should be placed on a flat surface when injecting air. A separate syringe can be used for injecting air, this reduces blunting of the needle used for insulin administration. Air ***need not be injected into a cartridge***.

When drawing insulin in the syringe, the vials are held upside down and the short acting insulin is taken first followed by the longer acting insulin. This sequence must be strictly followed.

INJECTION TECHNIQUE

The injection is given in the subcutaneous tissue (for this the skin must be pinched up) at an angle of 45-90^{o} to the surface (the smaller angle for the thinner child). The needle should be first brought down to touch the skin surface and then slowly allowed to glide in. After injecting one should wait for 5-10 seconds and then release the pinch before withdrawing the needle; these steps are important to prevent insulin from leaking out from the injection site. Do not massage the injection site.

Elaborate videos demonstrating the steps in use of various insulin pens can be accessed on the websites of the manufacturers.

DISPOSAL OF SHARPS

Patients and families must be taught about proper disposal of needles and lancets. If a pre disigned sharps disposal box is not easily available for purchase, empty powder boxes can be used to break of the needle. The needle falls in to the powder box & the rest of the syringe can be thrown in the waste. Used lancets too can be stored in small inexpensive screw cap plastic containers and thrown along with the container once it is full.

INSULIN REGIMENS

Short acting insulin (or preferably a rapid acting analog) is used alone only in management of DKA, in the insulin pump (continuous subcretaneous insulin infusion, CSII) and for supplements on “sick days”. Insulin is used IV or IM only in management of DKA. For day to day management it must be injected SC.

For routine day to day management, patients use rapid or short acting insulin together with intermediate or long acting insulin. The latter insulin alone may rarely suffice in children in the remission phase.

Broadly, there are 2 regimens for giving insulin:

1. *Split-mix regimen* in which 1 insulin covers 1 time period and
2. *Basal-bolus regimen* in which intermediate or long acting insulin is used as "basal" to suppress hepatic glucose production in the fasting state and rapid or short acting insulin is injected before each major meal to cover post meal glycemia (the so called "bolus").

The basal-bolus regimens are more physiological and give greater flexibility; however, they involve taking a greater number of shots.

Split-Mix Regimen

In these regimens one type of insulin covers one time period: the pre-breakfast short acting covers the period from breakfast to lunch while the intermediate acting works between lunch and dinner; the evening short acting covers the period from dinner to bedtime / midnight while the intermediate acting covers the period from bedtime to pre-breakfast.

- *2 injection regimen:* The patient takes two injections, one pre-breakfast and the other pre-dinner. Generally 2/3rd of the TDD is given before breakfast and 1/3rd before dinner. Each injection is a mixture of rapid or short acting insulin and NPH in the ratio 1:3 for the morning dose and 1:1 or 1:2 for the evening dose.
- *3 injection regimen:* If, on the 2 injection regimen, the BG at 2-3 am is in the normal range with elevated fasting (pre-breakfast) levels, stepping up of the pre-dinner intermediate acting insulin to control the pre-breakfast BG may cause nocturnal hypoglycemia. In such cases it is common to split the evening dose with the short acting being administered before dinner and the intermediate acting at bedtime.
- *1 injection regimen:* rarely used, only in the remission phase. A single pre-breakfast injection of intermediate acting / short + intermediate acting insulin / long acting basal analog may give reasonably good control. We do not recommend starting a patient on this regimen; however as the patient enters the honeymoon phase and insulin requirement drops, the evening shot may become redundant. When on 1 injection, ensure that the blood glucose is in normal range both when the insulin action peaks (late evening) and when the action wears off (pre-breakfast).

Basal-Bolus Regimen

The basal-bolus regimens are more physiological and if implemented correctly (with frequent SBGM, corrective supplemental doses of insulin and carbohydrate counting for pre-meal bolus calculation) can give better control. These regimens

use rapid or short acting insulin to cover meals and NPH or a basal analog to provide basal insulin (to regulate hepatic glucose output in the fasting state). The common regimens in use are:

- *Regular insulin three times a day before each major meal and NPH insulin only at bedtime or preferably pre-breakfast plus bedtime:* 40-50% of the TDD is given as NPH and 50-60% as regular insulin. 70% of the calculated NPH requirement is given at bedtime and the remaining 30% pre-breakfast. The regular insulin is given in three divided doses in proportion to the carbohydrate content of the meal it is supposed to cover.
- *Regular insulin three times a day before each major meal (the doses being distributed as discussed above) and Glargine or Detemir once or twice a day:* Most children can be controlled on a single dose of Glargine; in the case of Detemir, the majority will need two daily doses. About 50% of the TDD is given as the long acting analog.
- *Lispro, Aspart or Glulisine insulin before each major meal or large snack (3-5 doses a day) and either NPH or preferably a long acting analog for basal insulinemia:* It should be noted that the proportion of bolus to basal insulin is lower when the short acting analogs are used. (Regular insulin itself contributes to basal insulinemia.)
- *Continuous subcutaneous insulin infusion (CSII) or the open loop insulin pump:* It has the advantage that it uses only a rapid acting analog as a continuous infusion for both basal and bolus doses. Since there is no subcutaneous depot of insulin, there is considerable flexibility. The basal dose too can be varied for different periods of the day (some pumps have provision for programming 48 basal rates through the day, though the majority of patients require only four). The bolus can be delivered as a normal bolus, a square wave bolus (for a prolonged meal or a meal with high fat content) or a dual wave bolus (for meals with both rapidly and slowly absorbed carbohydrates and for correcting elevated BG before a meal). The basal insulin infusion can be discontinued during physical activity. Since there is no insulin depot in the body in pump users, mechanical failure of the pump can lead to rapid onset of DKA. Insulin pumps can give excellent control if all other aspects of diabetes self management (in particular, meal planning with carbohydrate counting, frequent home based blood glucose monitoring with corrective action) are intensified.

It must be noted that the TDD and the distribution of the TDD during the day as indicated in the discussion so far refers to the starting dose. This has to be modified and fine tuned on an ongoing basis with the help of self monitoring of blood glucose (SMBG).

Choice of Insulin Regimen

The choice of regimen would depend on multiple factors: the age of the child, stage of diabetes, financial condition of the family, school timings, motivation of child and parents, and feasibility of giving multiple shots.

The split-mix regimens are the most commonly used in children as they are simple for the patient and require fewer daily injections (See **Table 3**). These regimens are appropriate for children who have a fairly constant lifestyle (waking and sleeping hours; school and play and meal timings).

When good control cannot be achieved, the patient should be switched to a basal-bolus regimen. The latter regimens can be started at the outset in patients who can afford the additional cost and are also motivated not only to take multiple shots (including an afternoon dose) but also to perform frequent SMBG and act on the results.

TABLE 3. Insulin Regimens for Children and Adolescents with T1DM

The horizontal columns indicate the time of insulin administration. The vertical rows indicate the insulin regimen and the insulin preparation given at each of the indicated times.

Common Insulin Regimens	***Pre-breakfast***	***Pre-lunch***	***Pre-dinner***	***Bedtime***
Split-mix regimen (2 injections a day)	Regular *or* rapid acting analog *plus* NPH	-	Regular *or* rapid acting analog *plus* NPH	-
Split-mix regimen (3 injections a day)	Regular *or* rapid acting analog *plus* NPH	-	Regular *or* rapid acting analog	NPH
Basal-bolus regimen (using human insulins)	Regular *plus* NPH	Regular	Regular	NPH
Basal-bolus regimen (using a combination of human insulin and analogs)	Regular	Regular	Regular	Glargine* *or* Detemir
Basal-bolus regimen (using analogs)	Rapid acting analog	Rapid acting analog	Rapid acting analog	Glargine*
Basal-bolus regimen (using analogs)	Rapid acting analog *plus* Glargine *or* Detemir	Rapid acting analog	Rapid acting analog	Glargine *or* Detemir

**Though Glargine was originally recommended at bedtime, it can be given at any other (constant) time of the day. Some patients may require two doses of Glargine in a day.*

INSULIN SENSITIVITY FACTOR AND INSULIN TO CARBOHYDRATE RATIO

Insulin sensitivity factor is the extent to which the BG is expected to drop (in mg/dl) with 1 unit of regular insulin or rapid acting analog. This factor can be derived by dividing a constant factor (1700) by the patient's TDD.

The insulin:carbohydrate ratio (or the grams of carbohydrate for which 1 unit of rapid or short acting insulin are needed) is calculated by dividing the constant 500 by the TDD.

Intelligent use of these ratios in calculating the pre-meal bolus dose of insulin can help improve the HbA1c significantly.

COMPLICATIONS OF INSULIN THERAPY

As all insulins available currently are highly purified, the problems of immunoresistance, lipoatrophy and allergy are very rare, unlike in the past. Lipohypertrophy is encountered in patients who do not follow site rotation (see section above).

NUTRITIONAL MANAGEMENT

Aspi J. Irani

SUMMARY

- A dietician with special interest in pediatric diabetes must be part of the diabetes management team.
- Children and adolescents with T1DM do not need a special diet (exceptions are those with obesity, hypertension, hyperlipidemia, nephropathy and celiac disease).
- Caloric requirement is calculated as for any non-diabetic child. Normal growth is the best indicator of caloric sufficiency.
- Meal planning is of utmost importance :
  - to match insulin, exercise and meals,
  - to regulate intake of dietary items that can increase risk of hypertension, macrovascular and macrovascular disease,
  - to prevent hypoglycemia especially in relation to exercise and during night hours and
  - to prevent hypoglycemia and ketoacidosis during intercurrent illnesses.
- Fixed timings and carbohydrate content for each meal from day to day is necessary for patients on split-mix insulin regimen. They can be given a calorie exchange list to avoid monotony.
- Those on basal-bolus regimen can have considerable flexibility in their meal timings and content with the intelligent application of carbohydrate counting and insulin to carbohydrate ratio.
- 50-60% of calories should be provided as carbohydrate. Sucrose is no longer forbidden but its use is better minimized. Complex carbohydrates and foods with low glycemic index give better postprandial control.
- A high fiber diet may confer some benefit in children above 2 years of age.
- Salt intake should be regulated to reduce risk of hypertension.

- 30% of calories should come from fats, with restriction of saturated fats to <10% and elimination of trans fatty acids.
- Protein intake should not be higher than the recommendation for healthy children. Protein restriction is needed if microalbuminuria develops.
- Sweeteners may be used if necessary. Diabetic snacks are not recommended.
- Routine vitamin and mineral supplementation is not required.
- Instructions on "eating out" must be provided.

A dietician with special experience in pediatric diabetes should be part of the team caring for the patient with T1DM.

Routinely, children with diabetes do not need a restrictive or special diet. They should be advised to eat all healthy foods in right amounts and avoid food items which are considered harmful to health. In fact, the entire family should convert to eating the same healthy food. The "silver lining in the dark cloud" when a child is diagnosed with diabetes is that the overall health of all other family members would improve if this simple guideline is followed.

Careful meal planning is a must for children and adolescents with T1DM.

ROLE OF MEAL PLANNING

Meal planning is necessary in T1DM for the following reasons:

- To ensure normal growth and prevent obesity (the latter being very common in adolescent girls with T1DM.)
- To match food intake to the action profile of insulin (though whenever possible one should try to select an insulin regimen to match the child's preferred eating pattern.)
- To regulate the intake of food items that would predispose to hypertension, microvascular and macrovascular disease, all of which are commoner in T1DM than in the general population.
- To prevent the progression of certain complications if detected at an early stage.
- To prevent hypoglycemia, especially at nights and in relation to exercise.
- To help prevent ketoacidosis or hypoglycemia during intercurrent illnesses.

INDICATIONS FOR A SPECIAL DIET

Children with T1DM do not need a special diet except under certain circumstances. A special diet is necessary only for those who are obese (reducing

diet), develop microalbuminuria (mild protein restriction), hypertension (salt restriction), hyperlipidemia (special fat restricted diet: reduce fat intake to 25% of total calories, saturated fat to <7% and increase consumption of monounsaturated fatty acids or MUFA and omega-3 fatty acids), celiac disease (gluten elimination) or pernicious anemia (vitamin B12 supplementation).

CALORIC REQUIREMENT

The caloric requirement is higher than normal soon after diagnosis and after recovery from DKA. This phase lasts till the pre-illness weight has been regained (being the period of catch up growth after a state of "starvation amidst plenty").

At other times, the caloric requirement of a child with T1DM is calculated as for any non-diabetic child of the same age, weight, sex and race and level of activity.

It must be noted that the child's appetite and growth are more important determinants of caloric adequacy than any formula.

IMPORTANCE OF GROWTH PLOTTING

Growth must be plotted on appropriate growth charts once in 6 months.

Inadequate weight gain or weight loss (detected on serial growth plotting) would point to the possibility of insufficient caloric intake or insufficient insulin doses. Adolescent girls may try to miss insulin when they realize it leads to weight loss. Other causes to be considered include poorly controlled diabetes, hyperthyroidism, celiac disease, Addison's disease, an associated chronic illness such as tuberculosis or an eating disorder.

Excessive weight gain could be due to overeating, especially intake of junk foods (with over-insulinization). Other causes include hypothyroidism and frequent hypoglycemia with over-correction.

THE MEAL PLAN

The meal plan should be finalized in consultation with the patient and parents. The plan should be built around the child's preferred eating habits (timing and type of meals). In order to ensure compliance, changes should be made in the child's pre-illness meal timings and habits only if essential. This is now possible thanks to the more flexible basal-bolus insulin regimen, coupled with frequent SBGM, knowledge of carbohydrate counting and intensive patient education.

In a child on the *split-mix insulin regimen,* meal timings and carbohydrate content should be constant for a given meal from day to day. Ideally there should be three main meals, two mid-meal snacks to cover the peak hours of insulin action plus a bedtime snack to prevent nocturnal hypoglycemia.

A calorie exchange list should be provided to avoid monotony. The child can be given a sample diet and for each item in the sample diet a list of alternatives with similar carbohydrate and calorie content is provided. The exchange list divides foods in six groups: milk, vegetable, fruit, fat, cereal or bread, pulse or meat. An item from one group can be exchanged only for any other item from the same group in the amount specified.

If the child is started on a *basal-bolus regimen* (especially with the use of insulin analogs) it is possible to have greater flexibility: meals can be delayed or even omitted, and the carbohydrate intake can be varied from day to day. To make this possible, the patient is taught the *carbohydrate content (count)* of various foods.

Individualized insulin to carbohydrate ratio is established for different parts of a day. This ratio can be calculated roughly using the formula 500 divided by TDD: this gives the grams of carbohydrate for which 1 unit of rapid acting insulin is required. Using this ratio, the patient takes a bolus insulin dose just before eating, after estimating the amount of carbohydrate in the meal.

PERIODIC REVIEW OF MEAL PRESCRIPTION

Children and adolescents with T1DM should visit a dietician once in 6 months as meal requirements may change rapidly on account of fast growth, puberty and frequent changes in activity and school schedules in this age group. Patients should also periodically weigh foods to have a better concept of portion sizes and they should be supplied with standardized measures such as spoons, *katoris*, and cups and so on.

ROLE OF SELF BLOOD GLUCOSE MONITORING (SBGM)

SBGM plays an important role in fine tuning the meal plan. This tool should be used by the patient to study the effects of various foods and physical activities on blood glucose levels in different situations. Experience gained from SBGM is the best guide for perfecting the meal plan.

DIET IN INFANTS AND TODDLERS

In the first 6 months exclusive breast feeding or a humanized infant formula is recommended. After 6 months, weaning foods in the form of cereals and pulses, fruits, vegetables and meats should be gradually introduced. In infants below 2 years of age a grazing diet is most appropriate.

After 9 months of age, the rate of weight gain, and consequently the appetite, decline significantly, causing parental anxiety. Parents must be informed that this is natural. Further, they must be counseled that babies at this age are negativistic and so forced feeding or coaxing may prove counterproductive, leading to food refusal and a difficult behavioral problem.

Toddlers eat best by imitation and hence the infant above 9-12 months should be made to sit with the mother (if not the entire family) to eat. Toddlers are attracted by the appearance of the food; hence decorating the meal can go a long way in improving compliance. Meal times should be pleasant. Toddlers will cannot resist temptation: unhealthy snacks and junk foods should therefore not be kept in the house ("out of sight is out of mind") and under no circumstances should these be offered as rewards.

WHAT IS HEALTHY EATING?

1. Carbohydrates

50-60% of the total calories in the diet should be derived from carbohydrates. Carbohydrates are consumed as fruits, vegetables, cereals, legumes (peas, beans or lentils) and milk. The traditional Indian diet is high in carbohydrate.

Low carbohydrate diets are not recommended as carbohydrates are important sources of energy, fiber, vitamins and minerals.

Carbohydrates are the chief proximate principal in food that influences blood glucose. Insulin needs to be matched to the carbohydrate intake (rather than calorie content) at each meal. For this it would be ideal to teach patients the carbohydrate content of common foods and snacks and establish insulin to carbohydrate ratio for different times of the day for each patient. Those on a basal-bolus regimen can calculate the pre-meal insulin to match the anticipated carbohydrate intake at each meal. If a patient is on a split-mix regimen taking a fixed insulin dose from day to day, the carbohydrate content too should be fixed for a given meal from day to day.

Digestible carbohydrates are classified as starches and sugars. Starches are complex carbohydrates; they are slowly digested and absorbed and hence do not produce a rapid or sharp rise in blood glucose. They also contain other nutritional components and fiber. They are consumed in natural or in refined forms – the former should be preferred. Sugars (glucose, fructose, lactose and the table sugar or sucrose) occur naturally in foods (fruits, milk, and vegetables) or may be added in manufacturing or before consumption – they produce sharper swings in blood glucose.

Up to 10% of the total calories may be consumed as "added sugar" so long as it is part of a fiber rich meal, and spaced out through the day. However, sucrose provides only "empty" calories, has an adverse effect on dental health and snacks with sucrose (e.g. mithai, ice creams and chocolates) are usually also high in saturated fat content. Hence, in general, we prefer to advice our patients against adding sucrose to beverages or eating sucrose containing snacks, but they may occasionally be permitted specifically for the prevention of hypoglycemia before

prolonged exercise, as total denial would encourage non-compliance. Such snacks should not be given for reversal of acute hypoglycemia, as the fat content slows down sugar absorption.

Foods that produce lower postprandial blood glucose (PPBG) excursions are to be preferred, these foods are said to have a low *glycemic index (GI).* The GI compares PPBG response to constant amounts of different carbohydrate containing foods. It measures the rise above fasting in BG area in first 2 hours after ingestion of 50 g of the carbohydrate under study compared with the response to a reference food (glucose or white bread). Please note that the GI of white bread (maida) is the same as of glucose!

Foods with a low GI are those that produce lower rise in BG over the first 2-3 hours after ingestion.

- Examples of *low GI foods* include oats, barley, beans, lentils, legumes, soybeans, kidney beans, cashew nuts, pasta, noodles, strawberries, apple, orange, fructose, full cream milk and yogurt.
- *Foods with high GI* include white bread, white rice, puffed rice, *bajra, jowar, ragi,* maize, semolina, tapioca, cornflakes, baked potato, and honey.
- *Foods with moderate GI* include sugar, *basmati* rice, honey, popcorn, ice cream, dried rice noodles, black gram, green gram and croissants.

GI depends on multiple factors other than the type of carbohydrate – these include the style of cooking, state of ripeness, degree of processing and macronutrient distribution of the meal of which the carbohydrate is a part. A recent meta-analysis showed a 0.4% decline in HbA1c with low GI foods as against high GI foods.

2. Fiber

Indigestible carbohydrates present in food are designated as "dietary fiber" or "unavailable carbohydrates". A fiber intake equal to the child's age in years plus 5 g is known to be beneficial. The traditional Indian diet is naturally high in fiber content.

To increase fiber intake, patients should be advised to consume whole fruits with skin and edible seeds, vegetables, legumes, oats, beans and whole grain cereals.

Soluble fiber (found in dried beans, peas, oat bran, barley, apples, prunes, citrus fruits, watermelon, carrots and potatoes) improves total and LDL cholesterol levels by binding to bile salts, slows carbohydrate absorption by delaying gastric emptying thus giving a flatter blood glucose curve and may reduce insulin requirement. Insoluble fiber (present in whole wheat products, fruit skin, green

beans, dark green leafy vegetables, and seeds and nuts) helps bowel movement and prevents constipation.

A high fiber diet is not recommended in children below 2-3 years of age as they need a calorie dense diet.

Certain precautions need to be taken when going on a high fiber diet – introduce gradually; step up water intake; anticipate flatulence, abdominal cramps and bloating; and provide supplements of calcium and trace elements particularly iron and zinc.

3. Protein

Protein intake should be 15% (12-20%) of the caloric requirement. Higher protein intakes are not recommended. The protein requirement is 2 g/kg at 1 year, 1 g/kg at 10 years and 0.8-0.9 g/kg in adolescence.

Proteins from animal sources (fish, milk, egg white, poultry and meats) are of better quality than those from vegetarian sources (soya, beans, and lentils) as they provide all essential amino acids. However, proteins from vegetarian sources are accompanied with fiber and complex carbohydrates and contain less of saturated fat in contrast to those from animal sources, which are more likely to be associated with higher salt and saturated fat content. When consuming non-vegetarian sources of protein, skin and visible fat should be removed. Soya foods have been shown to reduce LDL cholesterol and triglycerides.

If microalbuminuria develops, protein intake should be restricted to 10% of the total calories since increased glomerular perfusion or filtration is a key factor in progression to nephropathy. Microalbuminuria cannot be prevented by consuming a lower than normal protein diet.

4. Fat

Fats should provide 30% of total calories (higher in infants below 2 years of age). All fats provide the same number of calories (9 per g), but some are beneficial to the cardiovascular system while others can be harmful. Hence attention needs to be paid to both the amount and the quality of fat in diet.

Saturated fat consumption should not exceed 10% of the total calories. Higher intakes are associated with increased risk of cardiovascular disease. Saturated fats are the main components of LDL cholesterol. They raise serum total cholesterol (LDL as well as HDL). They are chiefly derived from animal sources including dairy products. They are found in egg yolk, flesh foods, poultry skin and in those fats that are solid at room temperature (butter, *ghee,* cream, palm oil, coconut oil). Non-vegetarian foods with low saturated fat content are fish, lean meat and poultry without skin and fat. In patients with raised LDL cholesterol the saturated

fat intake needs to be further reduced to below 7% of total calories while cholesterol intake should be less than 200 mg per day.

The unsaturated fats are classified as polyunsaturated and monounsaturated fatty acids. They are mainly derived from plant and vegetable sources. These fats have beneficial effects on LDL cholesterol and in the case of MUFA, also on HDL cholesterol. They help to reduce the risk of cardiovascular disease.

Polyunsaturated fatty acids (PUFA) should make up 10% of calories. These are essential fatty acids (not synthesized in the body). They are classified as omega-6 and omega-3 fatty acids.

Omega-6 PUFA is found in various cooking oils (safflower, sunflower, soya, cottonseed, corn, peanut and sesame) and in pulses, vegetables, cereals, nuts, seeds, eggs and poultry.

Omega-3 PUFA may have a beneficial influence on coronary heart disease, serum triglycerides and the immune system and are found particularly in cold water fatty fish. About 250 gm of fish should ideally be consumed every week. For the vegetarian, flaxseeds, walnuts, soybean, canola oil, kidney beans, tofu, broccoli, spinach, cauliflower, and Chinese cabbage are good sources of omega-3 fatty acids.

Monounsaturated fatty acids (MUFA) should make up 10-15% of the total calories. They are found in olive, canola, groundnut, peanut, sesame, rice-bran and mustard oils and in almonds and avocados. A diet using monounsaturated fat rather than carbohydrate to lower saturated fat in diet gives better postprandial blood glucose levels with equivalent lowering of LDL cholesterol; however it may cause undesirable weight gain and does not significantly improve HbA1c levels.

Trans fatty acids are produced by heating liquid vegetable oils in presence of hydrogen (partial hydrogenation) to make them less liquid and are found in processed foods, commercially prepared fried fast foods and baked products. They not only raise the LDL cholesterol but also lower HDL cholesterol, making them even more dangerous than saturated fats. There is no documented beneficial role for them in the human body. Patients must be told to avoid any product containing "hydrogenated oil" or "partially hydrogenated oil".

5. Salt

Children with T1DM are more likely than non-diabetic children to develop hypertension. They also are more likely to consume higher amounts of salt as the stress is on a "non-sweet" diet. It would be prudent to restrict salt to 2 g per 1000 calories. Further restriction may be indicated if hypertension sets in.

Patients should be advised to restrict canned or packaged foods, baked

products, pickles, pappad, sauces, and Chinese foods. They can use flavor enhancers such as herbs, lemon juice, vinegar, spices, onions, tamarind, and green pepper.

6. Vitamin and Mineral Supplementation

Routine provision of vitamins and minerals is not indicated except in patients who are on a restrictive diet, or have celiac disease, pernicious anemia or achlorhydria.

Potassium supplementation is important for patients recovering from DKA till they reach the pre-DKA weight.

Diabetes puts body tissues under increased oxidative stress. However, there is no evidence that increasing dietary consumption of antioxidants improves health outcomes. Fresh fruits and vegetables are good natural sources of anti-oxidants.

7. Sweeteners

Sweeteners are classified as nutritive and non-nutritive. Of the nutritive sweeteners, fructose contains calories similar to sucrose but with a lower GI: fructose has a GI of 29 as against 69 of sucrose. However, added fructose may have an adverse effect on serum lipids and hence its use as a replacement for sucrose in the diet is not recommended.

The sugar alcohols such as xylitol, sorbitol and mannitol contain half the calories of sucrose and have a better GI. They are considered safe, though in excess, they may cause diarrhea.

The nutritive sweeteners are included in diabetic snacks. Diabetic snacks may not have an important role any longer as sucrose is no longer "out of bounds". Further these snacks are often high in calories and saturated fat content.

The non-nutritive (artificial) sweeteners are virtually calorie free. These include aspartame, sucralose, stevia, saccharin, and acesulfame potassium. All are fairly safe in amounts recommended by the American Diabetes Association, but most children can do without them.

MEAL PLANNING ON "SICK DAYS"

When the child is unwell, anorexia may lead to hypoglycemia while elevated levels of the counter-regulatory hormones can cause hyperglycemia and even ketoacidosis. Meal planning plays an important role in preventing both hypoglycemia and ketoacidosis during intercurrent illnesses. (See Chapter 12: Sick Day Management for more details.)

If the illness is accompanied with appearance of ketones and a blood glucose level above 180 mg / dL, the child should be coaxed to have plenty of salty liquids

to compensate for polyuria, prevent dehydration, and replace salt loss in urine.

On the other hand if blood glucose is below 180 mg/dL, with presence of ketones in urine or blood the patient should be encouraged to have sweet liquids to prevent hypoglycemia while insulin administration can be continued to correct the ketosis.

On sick days small, frequent meals and cool liquids of child's choice are better accepted and tolerated.

PREVENTION AND MANAGEMENT OF HYPOGLYCEMIA

All children with diabetes must carry 2 sweets (boiled candy) or a plastic pouch with 3-4 teaspoons of powdered sugar or glucose for prompt ingestion in case of symptoms of hypoglycemia. Children must also carry a fruit or a few biscuits with them when in school or college, in case for some reason there is a delay in returning home for a meal. (See Chapter 10: Hypoglycemia for more details.)

Patients must be instructed on the importance of ingesting a snack prior to unaccustomed (not part of daily schedule) physical activity: approximately 15 g carbohydrate for 30 minutes exercise. This snack should provide a readily absorbable form of carbohydrate plus a sustained supply of carbohydrate for prolonged activity. (See Chapter 9: Exercise and Physical Activity for more details.)

Additional bedtime snack to prevent delayed post-exercise hypoglycemia after intense evening exercise is also important. The role of the nocturnal snack cannot be over-stressed as frequency of hypoglycemia is highest at night in sleep. The bedtime snack should have a low glycemic index with some protein and fat to cover the long hours of fasting during sleep.

EATING OUT

Children and particularly adolescents will need to eat out periodically under peer pressure (if not personal choice). The dietician must check with the patient the eating houses that are likely to be frequented and then guide them on the most appropriate items to order at each such place and the carbohydrate content of those meals or snacks. With knowledge of the carbohydrate content of the eatables and the child's individual insulin to carbohydrate ratio it is possible to ensure that the blood glucose is not adversely affected when eating out.

COMPLIANCE WITH THE MEAL PLAN

Compliance with the meal plan is difficult to achieve. This is due to various factors which must be carefully addressed. These factors include faulty cooking and eating habits of the family, emotional state of the child, forced feeding by parents, exposure to TV ads, food faddism, peer pressure when eating away from

home, sharing of food or snacks in school, frequent parties, unrealistic "standardized" diet prescriptions and an eating disorder to mention a few. Each of these issues has been discussed earlier in this article. Appropriate counseling of both parents, siblings and in a joint family the grandparents is necessary. Informing the school authorities about the dietary needs of the child (not missing a meal and additional snack before unaccustomed activity) is essential.

SPECIAL DIABETIC PRODUCTS

Diabetic cookies, pies, cakes, and candies mislead the diabetic patient into believing that decreased sucrose or sugar intake is all that is needed to regulate blood glucose levels. Patients must be taught how to read and interpret food labels. Most of the "diabetic" snacks are high in calories and fat – they belong to the times when sucrose was forbidden and have no role in modern nutritional management of T1DM.

HOME MONITORING OF CHILDREN WITH DIABETES

M Vijayakumar

SUMMARY

- Type 1 diabetes is characterized by fluctuating blood sugars from day to day.
- Yet, to prevent or minimize long term complications, it is important to keep as many of the blood sugar readings in or near the normal range as possible, particularly in adolescents and adults.
- Monitoring sugars at home with the help of a glucometer allows the patient and family to adjust insulin doses for hypoglycemia, high blood glucose, unplanned exercise, and ketosis on sick days.
- Home BG testing involves high cost of strips as well as the pain of finger pricks 2 to 4 times a day. However, since urine glucose will be positive only if BG is above 200 mg/dl, and also will not diagnose hypoglycemia, the expenditure and pain are considered justified due to the high dividends obtained for the short as well as long term health of the child.
- Blood glucose goals are much more liberal for young children below about 6 years of age, as repeated hypoglycemic insult to the developing brain has tremendous risk for permanent cognitive impairment.
- Monitoring urine ketones with the help of ketone strips enables home management of mild ketosis associated with sick days.

Diabetes is a condition which requires regular, if not constant monitoring and action. At home the child and/or parents should monitor the glycemic status, presence of ketones, diet pattern, and danger signals of acute complications and make necessary adjustments in insulin dose and diet especially during unaccustomed activities and during sick days.

SELF MONITORING OF BLOOD GLUCOSE (SMBG)

In childhood diabetes, morbidity and mortality will be effectively reduced by practices that maintain blood glucose levels within a strictly defined range. It not only reduces acute complications such as hypoglycemia and hyperglycemia, but delays the onset and slows the progression of diabetic retinopathy, nephropathy

and neuropathy. This is possible only by daily monitoring of blood glucose and regular monitoring of HbA1c.

Self monitoring of blood glucose (SMBG) is thus an important part of day to day management of T1DM and decreasing long term complications.

Advantages of SMBG

The major benefits of regular SMBG include the following:

1. It gives a detailed account of glucose levels at different times of the day thus enabling the patient and/or parents to act according to the value obtained and maintain a more or less constant blood sugar level throughout day and night. It also helps them to adjust their diet and exercise pattern based on the levels obtained.
2. It improves patient's ability to recognize acute complications such as hypoglycemia and hyperglycemia and act at an earlier time, thus preventing mortality and morbidity (e.g. effects on cognitive function).
3. It can also be used to monitor recovery in hypo/hyperglycemia.
4. Strict maintenance of blood sugar by SMBG is associated with improved health outcomes such as reduction in the levels of HbA1c, and reduction in the incidence of long term microvascular and macrovascular complications.
5. The use of SMBG during exercise improves insulin management and diet adjustment so that there is decreased risk of hypoglycemia during and after exercise.
6. It is a valuable tool to assess glycemic status during an intercurrent illness and can prevent a hyperglycemic crisis.

Instruments Needed for SMBG Measurement and Record

- Glucometer
- Strips
- Lancet
- Cotton pad
- Notebook (diary or log book)

Technology

Most glucometers employ the oxidation of glucose catalyzed by the enzyme glucose oxidase or glucose dehydrogenase (GDH). The older glucometers used the colorimetric method using glucose oxidase. Most recent glucometers use an electrochemical method. Test strips contain a chemical which alters after coming

in contact with glucose in the blood drop, which can be measured by the sensor in the meter. Test strips sucks out a reproducible amount of blood by capillary action. The glucose in blood reacts with the enzyme present in the strip (usually GDH) and gets oxidized. It generates an electric current with the help of a mediator reagent, ferricyanide. This electrical charge is measured by a sensor in the glucometer (coulometric method).

Coding

Since test strips may vary from batch to batch, the user should enter the code found on the vial of test strips. By entering the code into the glucometer, the meter will be calibrated to that batch of test strips. Otherwise it will lead to getting wrong values.

Accuracy

Glucose levels of plasma are generally 10-15% higher than glucose measurements in the whole blood, which is even more after food intake. Home blood glucometers measure glucose in whole blood while most of the lab tests measure glucose in plasma.

Glucometers use capillary blood while lab tests use venous blood. Capillary blood can give a slightly higher reading than the venous blood.

Putting all these factors together, there will be a difference of 10-15% between the two methods. If the difference is more, we have to make sure that the glucometer is working properly. Hence periodic cross checking with a reliable lab result is a must. Periodically the doctor or diabetes nurse-educator should crosscheck the glucometers used by the patients by comparing with standard glucose control solutions usually provided by the meter manufacturers to the hospital or clinic.

Method

The technique varies from meter to meter and can be read by meticulously following the instructions supplied with the instrument or from the websites of the manufacturers**.**

1. Set the glucometer, test strip, a lancet and pad.
2. Wash hands to prevent infection, rub the hands together to keep them dry and make blood flow easier.
3. Decide the site to be punctured – usually fingertips. Hands and forearm are rarely used as these sites are slower to reflect falling blood glucose levels. Only selected meters can be used for alternate site testing.
4. Turn on the glucometer and place the test strip in the meter when it is ready.

Watch the indicator for placing the blood in the strip.

5. Pierce the fingertip with the lancet and obtain a drop of blood. Lancet is preferable to the needle.
6. Place the drop of blood on the strip.
7. Wait for a few seconds to get the reading.
8. Write down the result in the diary or log book.
9. Press the finger with gauze pad if it still bleeds.
10. Dispose the lancet in a puncture proof container and keep the glucometer and test strips in a clean and dry place.

Timing of SMBG Measurements and Guidelines for Insulin Adjustment:

SMBG should be done many times every day – before breakfast (fasting), before lunch, before dinner and at bed time. It should be done at around 2-3 AM at least once in a week. These readings should be used for adjusting the insulin dose.

There are two types of adjustments in insulin dose based on blood glucose levels.

- If the pre-meal sugar is high, then the regular or rapid acting insulin dose to be taken for that meal is to be adjusted upwards. This adjustment is valid for any type of regimen.
- The second (preventive) type of adjustment is to be done if high or low reading is observed over a few days. The type of adjustment will differ with the regimen. Adjustments should be made not only in insulin, but also diet, and/or exercise, aimed at preventing the high blood sugar levels (**Table 1.**)

TABLE 1. Preventive Insulin Adjustment in Split-Mix Insulin Regimen

SMBG reading	***Insulin to be altered***
Fasting	Night NPH *
Pre-lunch	Morning regular
Pre-dinner	Morning NPH
Bed time	Night regular

* Before increasing the night NPH insulin, possibility of Somogyi phenomenon should be kept in mind and glucose estimation should be done at 2-3 AM.

TABLE 1A. Preventive adjustments in Basal Bolus Regimes using Analogs

SMBG reading	***Insulin to be altered***
Fasting and pre-meals	Long acting analog
Post meal	Rapid or regular before that meal

BLOOD GLUCOSE GOALS

The target blood glucose varies based on the age of the child. Different norms have been laid down for various age groups. Young children may suffer more from severe hypoglycemia, and therefore goals of blood glucose levels may be set higher than those for older children and adolescents **Table 2** highlights the 2011 recommendations of the American Diabetes Association..

TABLE 2. Target Blood Glucose Levels

Time	*Blood glucose levels age < 6 years*	*Blood glucose levels age 6 - 12 years*	*Blood glucose levels age > 12 years*
Fasting and pre-meal	100- 180 mg/dL	90 - 180	90- 130 mg/dL
Bed time and midnight	110 - 200 mg/dL	100 - 180	90 - 150 mg/dL

MONITORING IN SPECIAL SITUATIONS

A short description about the points to be noted while monitoring blood glucose in some special situations is given below.

- ***Exercise*** – SMBG should be taken ideally before, during and after the exercise and action should be taken accordingly. Monitoring **several hours after the exercise** and before going to bed and also at 2-3 AM is important after strenuous activities as chance of late hypoglycemia is high. (See Chapter 9 for more details.)
- ***Hypoglycemia*** – The child should be educated to do SMBG whenever he / she is experiencing warning symptoms/signs of hypoglycemia and do necessary actions. SMBG should be repeated at 15 and 30 minutes to assess the response. If the child had a severe attack, subsequent monitoring is needed because of the chance of recurrent hypoglycemia. (See Chapter 10 for more details.)
- ***Sick days*** – SMBG should be monitored every 2-4 hours, often along with ketones. Insulin dose should be enhanced if glucose level is >180 mg/dL and decreased if <80 mg/dL. (See Chapter 12 for more details.)
- ***DKA*** – Capillary blood glucose should be checked hourly. (See Chapter 11 for more details.)
- SMBG should be used to study the influence of different foods and activities on blood glucose.

DISADVANTAGES OF SMBG

1. ***Cost of the glucometer and the reagent strips*** – They are expensive and most of our patients cannot afford them. But without adequate monitoring there

are more chances that acute and chronic complications and related disabilities would make health care costs high. If patients can afford a few strips a month, testing can be reserved for sick days and hypoglycemia episodes, and perhaps 2 to 4 tests a day for 2 to 3 consecutive days, to get an idea of the pattern of sugars.

2. ***Pain of needle prick –*** Children have to undergo multiple needle pricks a day which will make them and their parents unhappy with the regular monitoring.

3. ***Infection*** – There is a chance of infection, if good aseptic precautions are not taken care of during monitoring.

HOW TO MAINTAIN A DIARY OR LOG BOOK?

The diary or log book should ideally contain the following details as given in **Fig 1.**

Name: Age (Date of birth): Address: Phone / Mobile No {Patient): Phone / Mobile No (Parents):	Clinic Number: Weight: Height: Insulin regimen and insulin dose:

Date	*Fasting*	*Pre-lunch*	*Pre-dinner*	*Bed time*	*2-3 AM*	*Other time*	*Insulin adjusted*	*Remarks*

Fig 1. A Model Diabetes Diary or Log Book

URINE SUGAR MONITORING

Before the emergence of blood glucose monitoring, urine sugar monitoring was used all over the world and diabetic children and their families were able to maintain reasonably good control. Blood glucose monitoring has now replaced urine monitoring in most of the developing countries. But overemphasis on blood sugar monitoring and discarding the practice of urine sugar testing in our patients could result in no monitoring at all. Hence using urine sugar testing in conjunction

with blood sugar monitoring is an option when patients cannot do frequent blood glucose monitoring in our setting.

Urine sugar tests determine whether glucose is present in urine. Glucose will overflow into the urine when renal threshold for glucose is attained which is 180 mg/dL (10 mmol/L) of plasma.

Methods

1. Glucose oxidase method

Glucose oxidase reacts with glucose to yield gluconic acid and hydrogen peroxide. These reagents are impregnated in the paper strips. The steps of the test include the following:

1. Collect a small amount of urine.
2. Dip the test strip in the urine sample.
3. Read the test result in the specified time, by comparing the color change on the test strip with the color change in the reference chart.

2. Benedict's Test

Benedict's reagent is used to detect the presence of reducing sugars like glucose and galactose in urine. The reagent is a mixture of sodium carbonate, sodium citrate, and copper sulfate. Blue copper (Cu^{2+}) ions are precipitated as red copper oxide if heated in presence of a reducing sugar. The steps of the test include:

1. To 5 ml of Benedict's reagent, add 8 drops of urine.
2. The mixture is boiled and cooled.
3. Depending on the color of the mixture (blue, green, yellow, orange or red) the concentration of glucose can be estimated.

Benedict's test is more inconvenient compared to urine glucose strips and does not offer any cost advantage.

Advantages of Urine Sugar Testing

1. Cheap
2. Easy to perform
3. It does not require any instrument or battery.
4. It is a non-traumatizing method.
5. It is not associated with disposal issues.

Disadvantages of Urine Sugar Testing

1. Urine glucose testing does not reflect the blood sugar level at the time of

testing. It gives an indication of blood sugar level over the past several hours, since urine may be present in the bladder for few hours. Blood sugar level may have changed during that period.

2. Urine sugar test will give a positive value only if glucose is present in urine, when blood sugar crosses the renal threshold (180 mg/dL or 10 mmol/L). Hence it cannot differentiate between a normal blood glucose level and a dangerously low blood glucose level.
3. Volume and concentration of urine can vary in different situations, like when the patient is having vomiting or dehydration due to diarrhea. In these situations it can produce abnormal results.
4. Since only color change can be read and interpreted, it won't give an accurate value. Only a rough estimate of sugar level is obtained.
5. Renal threshold may be lower in some children, like children with renal diseases. They show abnormal results even if blood sugar level is normal.

Recommendations for Urine Sugar Monitoring

1. Urine glucose monitoring is not a substitute for blood sugar monitoring but can be used as an alternative method of monitoring of glycemic status of an individual where blood glucose monitoring is not accessible, affordable or child is not co-operative due to pain.
2. It can be used separately or in conjunction with blood glucose monitoring.
3. The goal would be to maintain the urine glucose as "nil".

Because it is significantly cheaper than blood glucose monitoring, it has a very important role to play in occasions where people cannot afford blood glucose monitoring.

Increasingly, emphasis is being given to blood sugar monitoring without much publicity given to the valuable role of urine glucose monitoring. This lack of information will result in health care professionals downgrading or becoming less aware about the usefulness of urine sugar monitoring in appropriate circumstances.

Hence urine sugar monitoring should continue to be available throughout the world. We should not discard this test as obsolete, but education about its role and appropriate use should be a part of diabetes education.

MONITORING KETONE BODIES

Under normal conditions, fat is broken down to fatty acids and glycerol, fatty acids being converted to acyl CoA. If glucose is present, acyl CoA can enter tricarboxylic acid cycle. In conditions where glucose is lacking, liver converts the

acetyl CoA to ketone bodies. They circulate as â-hydroxybutyrate, acetoacetate and acetone and decrease the blood pH (acidosis). Many enzymes that govern our metabolic process require normal pH (7.35-7.45). Hence in acidosis, metabolic function is blocked.

Conditions precipitating ketosis

1. Infection or illness
2. Stressful situation like surgery
3. Inadequate insulin levels – due to missed dose, improper storage of insulin, malfunction of pumps
4. Hypoglycemia

Symptoms that make ketone testing mandatory

- Fever with tiredness and loss of appetite
- Signs of dehydration
- Nausea and vomiting
- Rapid, deep, and sighing respiration
- Abdominal pain
- Drowsiness or loss of consciousness

If blood sugar is persistently >250 mg/dL, ketone body measurement is a must even if the child is asymptomatic.

Measuring Ketone Bodies

- Ketone bodies can be measured by urine tests or blood tests.
- Urine tests are freely available but blood tests are not frequently done in most of the labs.
- Urine tests measure acetoacetate and blood tests, β-hydroxybutyrate.

Advantages of blood ketone estimation

1. In acute ketosis, β-hydroxybutyrate (BHOB) levels become very high compared to acetoacetate (AcAc) and as a result the normal BHOB: AcAc ratio (1:1) may go up as high as 10:1. In response to treatment, β-hydroxybutyrate level decreases faster. Since urine tests detect mainly acetoacetate, these acute changes cannot be appreciated.
2. Elevation of blood β-hydroxybutyrate precedes elevation of urine acetoacetate and hence by detecting blood ketones, DKA can be diagnosed early.

3. Urine ketones tests can remain positive for 24 hours after control of DKA (due to conversion of BHOB to AcAc which can be measured in urine). This may lead to over-treatment of DKA.

Thus blood levels of â-hydroxybutyrate are a better indicator of a patient's metabolic status during the detection and treatment of DKA.

Urine Ketone Estimation - Methods

1. Rothera's test

- Saturate 5 mL of urine with ammonium sulphate.
- Add a few crystals of sodium nitroprusside and shake.
- Add liquor ammonia from the side of the test tube.
- Formation of purple ring at the junction indicates a positive test.
- Intensity is measured from +1 to +4.

Sodium nitroprusside detects both acetone and acetoacetate, but does not detect β-hydroxybutyrate.

2. Paper strip test (ketostix)

These contain sodium nitroprusside, aminoacetic acid and disodium phosphate. A positive test is indicated by the development of purple color.

- The strip consists of a thin piece of plastic film, with a reagent pad on one end.
- The strip is either dipped into a urine sample or passed through the stream while the patient is voiding.
- The pad is allowed to react for exactly 40 or 60 seconds (depending on the manufacturer's guidelines.)

The resulting color is then compared to a graded shade chart.

CLINIC MONITORING

Anna Simon

SUMMARY

- Clinic visits for a child with diabetes should consist of meetings with a team, not just a doctor.
- The diabetes management team consists of a pediatric diabetes specialist, diabetes educator, dietician, psychologist and social worker. In India, many teams may be incomplete due to lack of trained personnel.
- History should include aspects of schooling, sports, social issues and diabetes knowledge, as well as aspects of diabetes care particularly hypoglycemia.
- Examination should include assessment of growth and puberty, in addition to examination for diabetes related long term morbidity.

Children and adolescents with T1DM should be routinely cared for by an experienced multidisciplinary team consisting of

- A pediatric endocrinologist or diabetologist or a pediatrician with special interest in diabetes,
- A diabetes nurse-educator,
- A dietitian and
- A social worker.

The team would benefit by the addition a clinical psychologist or psychiatrist. Experienced parents of children with diabetes and elder (grown-up) childhood onset diabetics might help the team in counseling.

Co-ordinated effort by this multidisciplinary team is essential to achieve the treatment goals of

- Achieving satisfactory biochemical control,
- Maintaining growth and development,
- Preventing acute complications,
- Preventing or delaying late onset complications and
- Ensuring emotional stability of the child and the family (**Fig 1**).

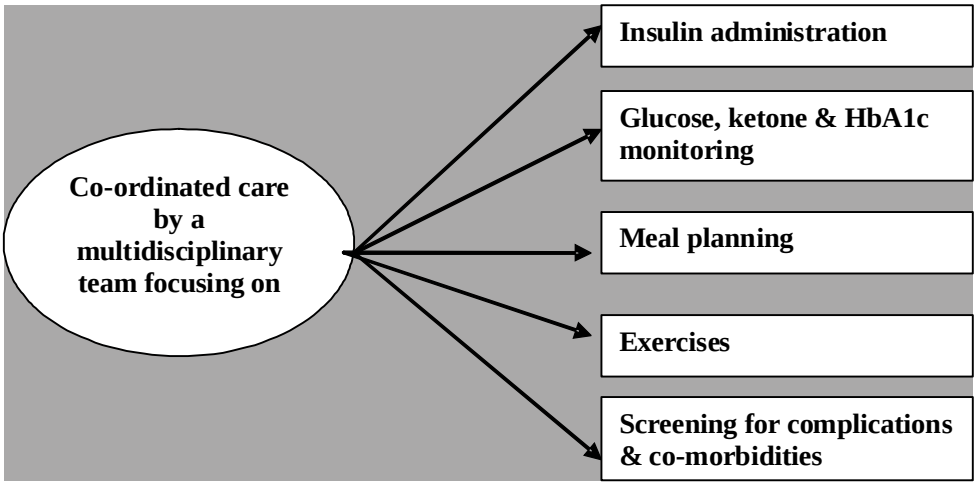

Figure 1. Multidisciplinary Team Care for Diabetic Children

Frequent regular follow-up visits every 2-3 months are important for achieving the targets planned with therapy. Clinic visits may have to be more frequent during the first few months following diagnosis. Also the details of HBGM can be communicated to the physician or diabetes nurse-educator every two weeks by telephone, email or fax for assessing adequacy of insulin dosing schedule and if required dosage adjustments.

HISTORY

The clinical assessment begins with eliciting history regarding the following:

- General well-being.
- Any recent events disturbing the child's life-style.
- Reviewing the results of self monitored blood glucose (SMBG) estimations (ideally daily or at least a minimum of 3-4 consecutive days of monitoring every month.)
- Review of insulin therapy with particular attention to adequacy of insulin, injection technique and rotation of injection sites.
- Review of dietary behavior and exercise.
- Any experiences of hypoglycemia, and its causes, such as skipping of meals, uncovered exercise, missed snack (suspect hypothyroidism, celiac disease or adrenal insufficiency with unexplained hypoglycemia or requirement for reduction in insulin dosage.)
- Any polyuria or polydipsia.

- Review of any associated medical condition especially other autoimmune disorders such as thyroid disease, adrenal insufficiency and celiac disease.
- Review of any symptom suggestive of long term complications.
- Underlying psychopathology: features of depression, over-eating and altered sleep rhythm.

PHYSICAL EXAMINATION

Growth

Exact measurement of height, weight and pubertal assessment is an integral part of the examination. Height and weight should be monitored carefully and plotted on a growth chart at least twice a year. Any deviation from the norm should be identified early and appropriate remedial measures should be undertaken. Poor glycemic control can result in poor linear growth, inadequate weight gain and/or delayed puberty and skeletal maturation. Conversely, excessive insulin therapy can result in excess weight gain.

Blood Pressure

Blood pressure (BP) measurement using an appropriate size cuff and with the patient seated and relaxed should be part of every diabetes physical examination. Hypertension is defined as systolic or diastolic BP >95th centile for age, sex and height percentile, measured on three separate occasions. Children with hypertension should be evaluated for renal functional status and urinary albumin excretion

General and Systemic Examination

This should focus on insulin injection sites, palpation of the liver, eliciting the deep tendon reflexes (DTR) and sensations, foot inspection, thyroid gland, liver size, limited joint mobility (LJM) and fundus examination.

ANNUAL REVIEW

The ISPAD (International Society for Pediatric and Adolescent Diabetes) recommends that annual review for long term complications should commence from the age of 11 years after 2 years duration and from the age of 9 years after 5 years duration. The American Diabetes Association recommends it annually after 5 years duration, after the age of 10 years.

Nephropathy

The earliest sign of diabetic nephropathy is microalbuminuria. Microalbuminuria is defined as the persistent urinary excretion of albumin in the range of 30-300 mg/day. Microalbuminuria if treated early can prevent or even reverse progression of renal disease. The presence of microalbuminuria calls for

improved glycemic control, attention to normalization of BP and lipid profile, and treatment with ACE inhibitors if necessary.

Retinopathy

Assessment for retinopathy should be done by an ophthalmoscope through dilated pupils by an experienced person. Stereoscopic fundus photography and fluorescein angiography are more sensitive in detecting background or proliferative retinopathy. If significant retinopathy is present, more frequent reviews by the ophthalmologist is necessary. Risk factors for diabetic retinopathy include longer duration of diabetes, poor metabolic control, presence of microalbuminuria, hypertension, abnormal lipid profile and higher BMI. Interventions should include improving glycemic control and addressing associated risk factors. Laser therapy should be considered for proliferative retinopathy or maculopathy.

Cataracts

Clinical examination of the eye for cataracts should be done soon after diagnosis.

Refractive Errors

Transient refractive errors can occur with changes in blood glucose levels.

Neuropathy

Neuropathy is rare in children and adolescents with T1DM. The most common neuropathic complication with diabetes is generalized sensorimotor polyneuropathy, which occurs insidiously, first manifesting as sensory loss and later motor weakness. A history of paresthesia, numbness or persistent pain and examination of light touch with graded monofilaments will help in diagnosis.

Macrovascular Disease

Hypertension and atherosclerosis are major risk factors for macrovascular disease. It is important to regularly screen and maintain BP in the normal range ($< 120/80$ mmHg or $< 90^{th}$ centile for age, sex and height). If persistently $\geq 130/80$ mmHg (or $\geq 95^{th}$ percentile), antihypertensive treatment is started. Lipid profile should be performed at onset, after blood glucose control, if there is family history of hypercholesterolemia, and at age 10 years, if there is not. Thereafter, if the result is normal, it should be repeated after 5 years. Treatment with a step 2 AHA (American Heart Association) diet should be started if hypercholesterolemia is detected and statins is to be considered if needed, beyond the age of 10 years.

Screening for Associated Autoimmune Disorders

This is recommended at diagnosis and thereafter every 1-2 years or whenever the clinical assessment demands.

- *Autoimmune thyroid disease* – Deceleration of height velocity, delayed puberty or a goiter may point towards hypothyroidism. The diagnosis of hypothyroidism is confirmed by elevated TSH level and low free T4 levels. Anti-thyroid antibodies (anti-thyroid peroxidase and / or anti-thyroglobulin) are usually demonstrable in the serum. (See Chapter 8 for details.)
- *Celiac disease* – Poor glycemic control, hypoglycemia and poor weight gain, symptoms of malabsorption and concurrent iron deficiency will point towards the diagnosis. Screening for celiac disease with antibodies to tissue transglutaminase should be done at the time of diagnosis and every 2-3 years thereafter. (See Chapter 8 for details.)
- *Primary adrenal insufficiency* – occurs rarely.
- *Vitiligo*.

CONCLUSIONS

Time and space must be provided for individual consultations with the nurse-educator, dietitian and social worker during every clinic visit. Every visit is an opportunity for continuing and reinforcing diabetes education.

Each clinic visit should be concluded by outlining an individualized plan incorporating school timings, eating habits, cognitive ability and emotional maturity. The plan should contain the following:

- Reiteration of treatment goals.
- Agreement or revision of insulin dose, meal plan and exercise schedule.
- New treatment for any associated conditions or complications.
- Appointment date for next consultation.

LABORATORY MONITORING

Anna Simon

SUMMARY

- Glycosylated hemoglobin (HbA1c) is the single most important laboratory monitoring for a child with T1DM.
- Thyroid disease, celiac disease, may have to be screened for.
- Microvascular complications screen includes microalbuminuria and lipid profile.

Hemoglobin A1c (HbA1c)

Measurement of HbA1c every 3 months prior to the clinic visit is an excellent method to judge adequacy of insulin therapy. HbA1c best correlates with the mean blood glucose level over the previous 8 to 12 weeks and this value needs to be interpreted in the context of self monitored blood glucose (SMBG) readings and clinical findings. HbA1c along with SMBG helps to determine the requirement for insulin adjustment. The aim is to keep the HbA1c as close to normal. Targets for HbA1c are to be given with careful attention to avoid severe hypoglycemia. Based on DCCT results, the general goal is to keep the HbA1c in all patients <7.5%, but a realistic goal for infants and toddlers would be >7 and < 8.5)

Continuous Glucose Monitoring (CGM)

In an occasional patient with poor glycemic control, 72 hrs of continuous glucose monitoring is very useful for planning management, as this will allow the study of the effect of food, exercises and insulin timing on glucose levels (See Chapter 16 for more details.)

Urine for Microalbuminuria

Microalbuminuria is defined as the persistent urinary excretion of albumin in the following range:

- Albumin excretion rate (AER) between 20-200 μg/min or AER 30-300 mg/ 24 hr urine
- Albumin concentration 30-300 mg/L (early morning sample)
- Albumin/creatinine ratio 30-300 mg/g (spot urine)

Screening for microalbuminuria should be done annually from the age 11 years after 2 years duration and from 9 years after 5 years duration of diabetes, as per recommendations of the International Society for Pediatric and Adolescent Diabetes (ISPAD).

Microalbuminuria if treated early can prevent or even reverse progression of renal disease.

The presence of microalbuminuria calls for improved glycemic control, attention to normalization of blood pressure and lipid profile and treatment with ACE inhibitors if necessary.

Serum Lipids

Screening for fasting lipid profile should be performed in all children with T1DM aged over 10 years. If normal, the test should be repeated every 5 years.

Hyperlipidemia should be managed by strict glycemic control, dietary intervention (weight reduction, if obese and reduction of saturated fat intake) and an exercise schedule. Treatment with a statin can be considered if the above measures fail. There is limited experience with fibrates, bile acid sequestrants and nicotinic acid in children.

SCREENING FOR ASSOCIATED AUTOIMMUNE CONDITIONS

Thyroid Disease

Upto 20% of patients with T1DM have positive anti-thyroid antibodies (anti-thyroid peroxidase and/or anti-thyroglobulin antibodies) and 2-5% with T1DM develop autoimmune hypothyroidism. Hypothyroidism usually manifests by deceleration of growth, pubertal delay, goiter, poor glycemic control or unexplained hypoglycemia.

Anti-thyroid antibodies are checked at the time of diagnosis and if positive, patients require screening for hypothyroidism yearly or whenever clinical suspicion arises. If the test is positive, anti-thyroid antibodies need not be repeated. The diagnosis of hypothyroidism is confirmed by elevated TSH and low free T4 levels.

Screening of thyroid function with TSH is to be done every 2 years in asymptomatic patients without a goiter or in patients who are negative for autoantibodies.

Hyperthyroidism is less common and can occur as the hyperthyroid phase of Hashimoto's thyroiditis or Graves' disease.

Celiac Disease

Celiac disease occurs in 1 -10% of children and adolescents with diabetes. It is usually associated with unexplained hypoglycemia or a reduction in insulin

requirement. It should also be suspected when there is poor growth, poor glycemic control, iron deficiency anemia or gastrointestinal symptoms. Celiac disease can often remain asymptomatic.

Screening for celiac disease with antibodies to tissue transglutaminase should be done at the time of diagnosis and every 2-3 years thereafter. If antibodies are positive, a small bowel biopsy is necessary to confirm the diagnosis. If celiac disease is confirmed, a gluten free diet should be advised.

9

EXERCISE AND PHYSICAL ACTIVITY

Anna Simon

SUMMARY

- Physical activity should be considered as an important aspect of management of T1DM.
- Regular physical activity has been demonstrated to improve glycemic control, physical fitness and muscle strength and psychological well-being. Children participating in sports or programmed exercises should be supervised and should have access to sweetened drinks and snacks.
- Extra caution should be taken when undertaking solo sports or events in water (or mid-air).
- Blood glucose levels should be monitored before, during and after physical activity.
- Do not inject insulin into a site that will be heavily involved in muscular activity.
- Extra carbohydrate intake and/or reduction of insulin dosage may be necessary; previous experience and blood glucose monitoring will help to determine the appropriate adjustments required with diet and insulin therapy.
- A general recommendation is that for every 30 min of moderate to intensive sport or physical activity, 15 g or an extra serving of carbohydrate should be consumed.
- Extra carbohydrates should be taken if blood glucose is <100 mg/dL at bedtime and check blood glucose at 3 AM as well.
- Strenuous physical activity should be avoided if blood glucose concentration is >250 mg/dL, especially if ketones are present. This will require insulin supplementation as well.

The management of T1DM focuses on insulin therapy, planned diet, physical activity and monitoring therapy. Physical activity is not just organized sports; it includes walking, playing, dancing and other activities of daily living. The benefits of physical activity in people of all age groups with chronic diseases are well known and accepted. Physical activity by improving known risk factors for atherosclerosis (obesity, hypertension and hypercholesterolemia will benefit

patients with diabetes who are at increased risk for macrovascular disease.

The major benefits of physical activity in T1DM can be listed as follows:

- Decreases blood glucose levels before and after exercise.
- Reduces insulin dosage.
- Increases insulin sensitivity.
- Controls blood pressure and increases cardiovascular function.
- Improves lipid profile.
- Promotes psychological well-being.

Despite these physical and psychological benefits, the occurrence of acute complications like hypoglycemia with physical exercise is common. An understanding of the metabolic changes occurring with physical activity in T1DM is necessary to individually modulate insulin therapy and diet plan before and after exercise to avoid these complications.

METABOLIC AND HORMONAL RESPONSES DURING PHYSICAL ACTIVITY IN T1DM

1. Influence of Exercise on Glucose Metabolism

There is increased blood flow to the muscles during exercise to facilitate the increased demand for oxygen, energy substrates and carbon dioxide removal. This increased glucose demand activates complex hormonal responses involving insulin and the counter-regulatory hormones (glucagon, cortisol, GH and catecholamines).

2. Subverted Physiological Regulation of Insulin

The lack of endogenous insulin secretion makes children with T1DM totally different from non-diabetic children. In children with T1DM, the peripheral insulin concentration depends on the dose and type of injected insulin, site of the injection and time elapsed after the injection. Thus physiological suppression of insulin is not achievable in T1DM.

3. Blunted Response of Counter-Regulatory Hormones

Several studies have also demonstrated a blunted counter-regulatory hormonal response to exercise in patients with T1DM.

COMPLICATIONS DURING AND AFTER PHYSICAL EXERCISE IN T1DM

1. Exercise Hypoglycemia

This is the most common and important complication with physical activity in T1DM and is defined as glucose levels <70 mg/dL. During exercise, there is

increased peripheral glucose uptake and also an increased absolute or relative concentration of insulin. Excessive insulin absorption due to the increased blood flow through muscles during exercise especially if the injection is into the working muscle aggravates the over-insulinization.

Factors predisposing to the occurrence of hypoglycemia include:

- Low glycemic trends / previous hypoglycemia,
- Exercising during the peak insulin action,
- Long duration or high intensity sports,
- Aerobic exercises tend to decrease blood glucose both during and after the exercise,
- Anaerobic exercises cause a transient initial rise in blood glucose (first 30-60 min) followed by hypoglycemia,
- Injection into working muscle, leading to enhanced absorption
- Intake of inadequate food or food with low glycemic index before exercise and
- Autonomic involvement

Late-onset hypoglycemia, which develops 5-24 hrs after exercising, is mainly due to:

- Increased insulin sensitivity and
- Depletion of muscle and liver glycogen stores.

2. Exercise Hyperglycemia and Ketosis

This occurs mainly in poorly controlled T1DM performing high intensity exercises. The blood glucose level before exercise (> 250 mg / dL ± ketones) is the major determinant for developing exercise hyperglycemia.

Factors predisposing to hyperglycemia include:

- High glycemic trend,
- Delaying exercises from last insulin injection,
- Prolonged low intensity exercises promoting lipid utilization and ketosis.
- Inadequate hydration.

3. Chronic Complications

Though rare, physical activity may adversely affect diabetes related complications (See Table 1.)

TABLE 1. Chronic Complications Associated with Physical Activity and Exercise

Predisposing Factor	***Complication***
Rise of blood pressure during exercises	Increased risk of retinal and vitreal hemorrhage and retinal detachment
Physical exercises	Increased proteinuria
Diabetic neuropathy	Increased risk for foot ulcers, articular and tissue injury Decreased cardiovascular rate to physical activity Exaggerated orthostatic hypotension Induction of angina

MANAGEMENT STRATEGIES TO PREVENT EXERCISE-INDUCED COMPLICATIONS

Hypoglycemia can be prevented with insulin dose reduction and dietary modification when exercise is pre-planned. Extra calorie intake is the only option when exercise is unplanned and sporadic. Additional blood glucose monitoring at bedtime and 3 AM are warranted, especially after unaccustomed physical activity.

1. Diet Management during Exercise in T1DM

- Complex carbohydrates 70% to increase muscle and liver glycogen stores. No increased fat intake, to prevent ketosis.
- 15 g of extra carbohydrate for every 30 min of moderate to intense activity.
- Prolonged exercising may require calorie intake *before*, *during* and *after* the exercise.
- Additional low GI food at bedtime if blood glucose is $\leq$ 100 mg / dL.

2. Insulin Adjustments with Exercise in T1DM

Insulin levels are influenced by multiple factors and therefore dosing adjustments have to be done on an individual basis. Factors affecting insulin levels are the dose and type of insulin, timing of the injection, site of injection, duration and intensity of physical exercise, emotional stress, and fitness status.

For prevention of hypoglycemia:

- For pre-planned physical activity consider reducing pre-meal insulin by 30-50% or delaying activity to avoid exercising during peak levels of insulin action.

- With prolonged exercise, consider reducing evening intermediate or long acting insulin by 20-50% to prevent late onset hypoglycemia.
- If on insulin pump – for short periods of exercise, stop insulin infusion by discontinuing the device before and during exercise and for pre-planned exercises, consider reducing by 50% of the basal infusion rate from 60 min prior to exercise. Also consider reducing the overnight infusion rate by 10-30% to prevent late onset hypoglycemia.

Exercise hyperglycemia:

- If blood glucose levels are >250 mg/dL and ketones are *negative*, insulin supplementation is required before exercise.
- If blood glucose levels are >250 mg/dL and ketones are *positive*, insulin supplementation and delaying exercise till urinary ketones are negative is advised.

HYPOGLYCEMIA

Anju Virmani

SUMMARY

- Hypoglycemia in a child with diabetes is defined at a BG < 70 mg/dl. In an infant or toddler, BG should be maintained above 100 mg/dl.
- Treatment should aim for best possible glycemic control, without significant hypoglycemia.
- The child, family, school staff and other caregivers should be educated about suspecting, confirming and managing hypoglycemia.
- Ideally the child should have an I-card or wear some form of identification indicating diabetes.
- Sugar or glucose 1 to 3 tsf, is useful to immediately raise BG, followed by a small snack. Glucagon (0.3 to 0.5 mg S/C for a young child, 1.0 mg for an older child) should be available at all times.
- Prevention of hypoglycemia includes attention to bedtime and midnight BG, delayed hypoglycemia after exercise, hypoglycemia unawarenss syndrome.
- Pathological causes include hypothyroidism, celiac disease, renal failure.

Hypoglycemia ("hypo") is the commonest acute complication of diabetes control in children. It is usually defined as a blood sugar < 70 mg/dL, but in toddlers, action should perhaps be taken at levels <100 mg/dL. Repeated episodes can cause cognitive dysfunction, especially in the very young child.

CAUSES

Hypoglycemia is commonly due to:

- Excessive insulin action,
- Inadequate or delayed food intake, or
- Excessive or unplanned exercise.

Hypos can occur with several regimens. The split-mix regimen, comprising two shots of regular and NPH insulin often leads to hypoglycemia if mid-meal snacks are not taken, or at night.

Conversely, attempts at very tight glycemic control can also increase the number of hypo episodes.

Hypos are particularly common in the honeymoon phase. If the child is admitted, insulin dose should be reduced by 10% at the time of discharge, to prevent hypos which may occur with the increased activity at home.

The next sharp drop in blood glucose (BG) levels comes when the initial glucotoxicity settles down, so insulin requirements also fall rapidly. Frequent BG monitoring is especially important in the first few weeks after diagnosis to prevent these hypos.

Later in life, if hypos suddenly and unexpectedly increase in frequency, one should think of hypothyroidism, celiac disease, renal compromise and / or failure, or rarely hypoadrenalism. All these conditions are more common in T1DM.

In general, throughout the lifetime of a person with diabetes, constant vigil is needed, with frequent BG monitoring, proper rotation of injection sites and judicious use of analogs a insulin pumps where they can be afforded, to reduce the frequency of hypos.

CONSEQUENCES

Hypoglycemia can result in abnormal behavior, drowsiness, convulsions, coma, or if prolonged, death. It can be so frightening that the diabetic child and his / her family may refuse to try for tight glycemic control for fear of hypoglycemia. Recurrent hypoglycemia can lead to *hypoglycemia unawareness,* increasing the risk of later episodes.

Severe hypoglycemia is more likely in :

- Toddlers and very young children,
- Adolescents, especially when they are rebelling,
- Those with longer duration of diabetes, and
- Those with low HbA1c values.

SYMPTOMS AND SIGNS

Symptoms and signs of hypoglycemia may be

- *Adrenergic:* uneasiness, shakiness, palpitations, and / or cold sweats.
- *Neuroglucopenic:* difficulty in vision, hearing, or concentrating, slurred speech, confusion, dizziness, abnormal gait, drowsiness, coma, seizures, death ("dead in bed").
- Headaches, mood swings, poor school performance, nightmares, and depression, apart from the classical symptoms.

- *Transient neurologic deficits:* hemiplegia and aphasia, which can occur with prolonged hypoglycemia.

Some Caveats

1. Symptoms and signs do not correlate well with BG levels, and may vary from person to person, and episode to episode.
2. Marked symptoms may occur if the BG drops sharply ("pseudohypoglycemia"), so it is important to test BG whenever possible to confirm if the level is indeed low. Otherwise, patients often treat themselves for adrenergic symptoms merely because there is a drop in BG from high to normal values.
3. Conversely, a hypo maybe missed and BG appears to be normal or even high if rebound hyperglycemia occurs quickly, or testing is delayed.
4. The accuracy of capillary testing is less in the low range.

Therefore though there is no specific cut-off value for defining hypoglycemia, most people would consider levels below 70 mg/dL as diagnostic, and aim to keep BG above 90 mg/dL. In very young children, higher levels are targeted at, because symptoms may not be picked up easily. Adrenergic symptoms and counter-regulatory responses are lesser

- During sleep,
- After an episode of severe hypoglycemia,
- In those with tight control, and
- In those with long duration of diabetes.

In fact, if adrenergic symptoms are very mild or ignored, then neuroglucopenic symptoms may be the first indication of trouble *("**hypoglycemia unawareness**"*). Hypoglycemia unawareness may occur in a child having repeated episodes of hypoglycemia. It is often reversible, with hypoglycemia awareness returning once there are less hypos with less strict control of blood sugars. It is therefore important to encourage ongoing frequent BG monitoring, especially before and after exercise, during illnesses, and periodically in the middle of the night. Continuous glucose monitoring systems (CGMS) have provided a wealth of information about glucose patterns in individual patients, and may be useful occasionally (see Chapter 16). In children who do not test frequently for financial or other reasons, families should be asked to be vigilant, and make sure BG is tested when hypoglycemia is suspected.

Severity

1. *Mild or moderate* hypoglycemia is defined as when the patient can manage to treat him/herself. This may be
   - Symptomatic ("documented symptomatic hypoglycemia"), or
   - Asymptomatic: Asymptomatic episodes are important because they increase the risk of severe hypoglycemia and of hypoglycemia unawareness.
2. *Severe* hypoglycemia: is defined as when the patient has altered sensorium (coma or convulsions) and so needs help for management (glucagon or IV glucose)

MANAGEMENT

The aim of treatment is to normalize BG levels to above 100 mg/dL.

Mild to Moderate Hypoglycemia

If the BG is more than 60 mg/dL and the sensorium is normal, the child should be given:

1. 5-15 g of carbohydrate orally. This should preferably be in the form of free sugars, because the presence of fat delays the absorption of the sugar. Thus the child can be given glucose, sugar, regular cold drink (not diet drink), if not available, juice or honey.
2. This is followed after 10-15 minutes by a retest of BG, and then
   - If still low, repeat glucose administration.
   - If >100 mg/dL, give a snack e.g. glass of milk, fruit, sandwich, glucose biscuits, chocolate, etc., to make sure that the BG does not dip again.

Severe Hypoglycemia

This needs urgent action. The management include the following steps:

1. **Injection of *glucagon***, if available, given intramuscularly or subcutaneously: 10-30 μg/kg: 0.5 mg for children younger than 10 years of age; 1 mg for older adolescents. If sensorium improves, a snack should be given (as above); to make sure BG does not dip again.
2. If glucagon is not available, the child should be put in a lateral position to prevent aspiration and **a thick paste of glucose (glucose powder with a few drops of water)** smeared onto the dependent cheek pad. Sugar or any other powdery substance or thin liquids like a glucose solution or honey should NOT be given forcibly to the semi/unconscious child.

3. If the child is in a medical facility, then **IV infusion of 10% dextrose** should be started: 5 mL/kg, (or I/V push of 2 ml/kg 25% dextrose) till sensorium stabilizes and the child can tolerate oral intake comfortably. At this time, a snack should be given, as above. Observation for 12-24 hours is needed because vomiting or a recurrence may occur.
4. Rest: No further strenuous physical activity should be allowed.

PREVENTION

Special attention must be paid to high risk groups which include:

- Very young children and toddlers.
- Children with low HbA1c.
- Children on low cost regimens (NPH absorption is very variable and can be associated with a significant risk of hypos. The risk of hypos is lower with insulin pumps, and with basal-bolus regimens using insulin analogs.)
- When treatment regimen or daily routine is changed (e.g. small child moves from play school to regular school; class teachers no longer supervise eating of tiffin; or during preparation for a sports day or a cultural evening, etc.)
- Athletes.
- When hypoglycemia has occurred recently.
- Children with significant autonomic neuropathy.
- Associated diseases: renal failure, possible hypothyroidism, hypocortisolism, or celiac disease.

SOME PRACTICAL HINTS

- *BG should be checked frequently in the day for all children,* but more often in high risk groups or times, e.g. during and after strenuous sport. It should also be checked at 2-3 AM periodically, and 10-12 hours after alcohol ingestion. Mid-meal snacks are important for those on NPH insulin.
- The close family members, as well as teachers, bus driver, sport teacher, coach should all be aware of the symptoms, and the action required to be taken. Extra carbohydrate is necessary for every 45 minutes of sports or play. Two or three sweets in pillow packs and a packet of glucose biscuits must always be available, in the child's pocket AND school bag, in the school bus or van, in the sports teacher's locker, and in the school medical room, etc.
- The child and family must be asked if they are carrying a diabetes identity card, a sample of which is appended below.

- Families should be encouraged to keep Inj. Glucagon at home or when traveling. Glucagon is now available in India, and may be life-saving.
- Families should be encouraged to keep a thick paste of glucose in a sealed box at home. They should also be encouraged to obtain glucose gel from abroad, as this is convenient when traveling.
- BG testing must be done when traveling or during sports. They must know that carbohydrate must be given (15 g, contained in 3 tsf sugar or about 120 ml juice, raises sugar by about 20 mg/dL) and exercise should be stopped if BG dips.
- Patients should be encouraged to take milk at bedtime, unless of course hyperglycemia is occurring at night.
- During routine visits, prevention and treatment strategies should be briefly asked for, doubts clarified and knowledge gaps filled. *Families must be reminded that emergencies occur without warning.*
- After each episode of hypoglycemia, the insulin-diet-exercise regimen should be reviewed to identify triggers so they can be avoided in the future.
- Prevention is important as repeated episodes can interfere with school performance and sports, cause long term cognitive dysfunction, cause hypoglycemia unawareness, prevent the parents from trying for tight glycemic control due to anxiety, result in accidents, and even death (e.g. "dead in bed").

NOCTURNAL HYPOGLYCEMIA

This should be suspected if the child

- Has nightmares,
- Wakes up confused or with a headache,
- Has low or unexpectedly high fasting BG, or low bedtime sugars.

A bedtime glass of milk may be useful, especially after strenuous play in the evening. Insulin doses should be aggressively reduced to prevent nocturnal hypoglycemia.

11

DIABETIC KETOACIDOSIS

Anurag Bajpai

SUMMARY

- Diabetic ketoacidosis (DKA) is a life-threatening condition requiring early diagnosis and appropriate treatment.
- DKA should ideally be managed in a center equipped to treat the condition under the supervision of an experienced pediatrician. In resource-poor settings stabilization followed by early referral to a higher center is recommended.
- Laboratory tests should be interpreted with caution due to known fallacies.
- Children younger than 2 years and those with severe DKA should be managed in an ICU.
- Close clinical and laboratory monitoring is essential for successful management of DKA.
- Hydration is the mainstay of management of DKA. Rapid and excessive fluid administration should however be avoided due to the risk of cerebral edema.
- Insulin should be withheld in the initial hydration phase.
- Continuous intravenous infusion of insulin is the standard of care for pediatric DKA. In resource-poor settings intermittent intramuscular insulin may be used. Intravenous bolus of insulin should be avoided.
- Potassium replacement is required in children with DKA even if the initial potassium levels are normal.
- Bicarbonate should be used only in children with pH less than 6.9 and cardiac compromise.
- Resolution of acidosis is the primary criteria for reduction of insulin infusion rate.
- Mannitol and dextrose should be available at bedside of all patients with DKA for emergent treatment of cerebral edema and hypoglycemia.

- Cerebral edema should be considered in all patients with sudden deterioration of neurological and clinical status.
- Insulin infusion should be discontinued 30 minutes after the administration of subcutaneous insulin.
- Appropriate management during sick days and invasive procedures is essential for prevention of DKA.

DKA is the most severe acute complication of diabetes mellitus. Previously believed to be limited to subjects with T1DM, DKA has been increasingly observed in T2DM and maturity onset diabetes of young (MODY). Early identification and management is essential to limit the extent of mortality and morbidity associated with DKA.

EPIDEMIOLOGY

Thirty to forty percent freshly diagnosed children with T1DM present with DKA. This figure varies from 16-67% depending on geographical, racial and socioeconomic factors. *Although large epidemiological data from India is lacking, the figure is substantially higher than the developed countries.* In children with established T1DM the risk of development of DKA is 13 episodes per 1000 T1DM patient years. This usually occurs due to omission of insulin or inadequate management during stress or infection. Children on insulin pumps are prone to develop DKA even after short duration of interruption of pump therapy due to line blockage or pump failure.

PATHOPHYSIOLOGY

DKA is the end result of absolute or relative insulin deficiency combined with excess of counter-regulatory hormones like glucagon, catecholamines, cortisol and growth hormone (GH). The disorder is usually precipitated by infection, stress and trauma, conditions associated with increased insulin requirement and higher level of counter-regulatory hormones. DKA is characterized by increased production of ketoacids and hyperglycemia. Accumulation of ketoacids produces acidosis in these subjects, which in turn produces Kussmaul breathing (acidosis), abdominal pain (acidosis) and fruity odor (acetone). Hyperglycemia results in increased urinary water losses due to osmotic diuresis and dehydration. Osmotic diuresis is associated with increased urinary losses of sodium, potassium and phosphate, leading to significant deficits of these electrolytes. Potassium levels are of special concern as correction of metabolic acidosis following therapy and administration of insulin leads to intracellular migration predisposing the individual to severe hypokalemia.

DIAGNOSIS

There is a need for high index of suspicion for DKA. DKA should be considered in the presence of *any of the following:*

- Acute diabetic presentation – polyuria, polydipsia, weight loss
- Unexplained encephalopathy
- Acute abdomen
- Unexplained dehydration with polyuria
- Acidotic breathing

Differential Diagnosis

DKA should be considered in the differential diagnosis of the following conditions:

Clinical

- *Encephalopathy* – CNS infection, severe malaria, poisoning
- *Acute abdomen* – Pancreatitis, appendicitis
- *Dehydration* – Gastroenteritis
- *Tachypnea* – Bronchial asthma, pneumonia

Laboratory

- *Hyperglycemia with acidosis without ketosis* – Renal failure, septicemia
- *Ketoacidosis without hyperglycemia* – Starvation, salicylate poisoning, organic acidemia

CRITERIA FOR DIAGNOSIS

DKA should be diagnosed only in the presence of *all of the following:*

- *Hyperglycemia* – Blood glucose > 200 mg/dL (11.1 mmol/L)
- *Metabolic acidosis* – pH < 7.3, serum bicarbonate < 15 mmol/L, Base excess > - 5 mmol/L
- *Ketosis* – Blood ketone > 3 mmol/L *or u*rine ketone > 2+

Table 1 describes the various differentiating features of the severity of DKA.

Fallacies in Blood Tests

- Blood sugar may be normal at presentation in children with recurrent vomiting, reduced carbohydrate intake and those who have received some treatment.
- Venous blood gas is unreliable in children with hemodynamic compromise.

Table 1. Classification of Disease Severity

Features	*Mild*	*Moderate*	*Severe*
Dehydration	< 5%	5-10%	> 10%
Blood glucose	200-250 mg / dL	250-300 mg / dL	> 300 mg / dL
pH	7.2-7.3	7.1-7.2	< 7.1
Bicarbonate	10-15 mmol / L	5-10 mmol / L	< 5 mmol / L
Base excess	–5 to –10 mmol / L	–10 to –15 mmol / L	< –15 mmol / L
Treatment *Insulin* *Fluid correction* *Setting*	 Subcutaneous Over 6-10 hours Emergency	 Infusion Over 48 hours Inpatient	 Infusion Over 72 hours Intensive care (ICU)

- Measured sodium levels are erroneously lower in the presence of hyperglycemia and should be corrected according to the formula below:

$$\textbf{Corrected sodium} = \textbf{Measured sodium} + \frac{(\text{Glucose mg/dL} - 100)}{100} \times 1.6$$

- Amylase levels may be elevated in DKA and should not be considered a pointer to pancreatitis.
- Elevated total leukocyte count is common in DKA and not a marker of infection.
- While interpreting the results of urine ketone sticks one needs to consider the following caveats:
  - They measure acetoacetate and not b-hydroxybutyrate, the major ketone in DKA.
  - They get rapidly denatured if exposed to room air.

MANAGEMENT

Setting

DKA is a life threatening condition and should ideally be managed in a hospital equipped with facilities for intravenous infusion and measurement of blood gas and electrolytes. The child should be managed by a pediatrician experienced in the treatment of DKA. *Children younger than 2 years of age and those with severe DKA should be managed in an ICU setting.* We realize that this is not feasible in many setups in India and have therefore also provided guidelines for resource-poor settings. All efforts should however be made to transfer the patient to appropriate centers after initial stabilization.

Clinical Evaluation

- *Airway, breathing and circulation* (ABC)

- *Weight* – All calculations should be based on current weight and not on that from previous records.
- *Level of dehydration* – 5-10% (often overestimated in DKA)
- *Identification of precipitating factor*
  - **First presentation** – Infection
  - **Known case** – Missed insulin dose, infection, insulin pump malfunction
- *Hemodynamic status* – Blood pressure, heart rate, capillary refill time
- *Neurological status*
  - Level of consciousness
  - Pupils (dilated and fixed in the presence of cerebral herniation)
  - Cranial nerves (sixth nerve palsy suggestive of cerebral edema)
  - Fundus (papilledema suggestive of cerebral edema)
  - Deep tendon reflexes (brisk suggestive of raised intracranial tension)

Investigations

- **Serum sodium (Na)**
  - *Status* – Deficit (20% of total body sodium, 4-6 mmol/kg)
  - Sodium levels are falsely reduced in hyperglycemia (use corrected sodium)
  - *Implication* – Rapid decline is a risk factor for cerebral edema
- **Serum potassium (K)**
  - *Status*
    - **Intracellular** – Deficit (20% of total body potassium, 3-6 mmol/kg)
    - **Extracellular** – Elevated due to acidosis and insulin deficiency
  - *Implication* – Treatment of DKA is associated with risk of hypokalemia due to intracellular shift secondary to reversal of metabolic acidosis and correction of insulin deficiency.
- **Plasma osmolality**
  - *Status* – Elevated (300-350 mOsm/kg)
  - *Estimation* – Effective plasma osmolality

    Effective osmolality- 2 (Na + K) + <u>Glucose (mg/dL)</u> mOsm/kg

- *Implication:* Aim is to have gradual fall in osmolality of 2 mOsm/kg/hour. More rapid fall than this is a risk factor for cerebral edema

- **Blood lactate**
  - *Status* – Normal (0.4-1.8 mmol/L)
  - *Implication* – Lactic acidosis in DKA should prompt evaluation for cerebral edema, infection or hemodynamic compromise
- **Serum phosphate**
  - *Status* – Deficit (0.5-1 mmol/kg)
  - *Implications* – Hypophosphatemia may be associated with decreased responsiveness to insulin and lactic acidosis
- **Infection screening**
  - *Complete blood examination:* Transient leukocytosis is common in DKA. Consider infection only in the presence of persistent leukocytosis and fever.
  - *Urine examination*
  - *Blood and urine cultures*
  - *Chest X ray* in the presence of persistent tachypnea and chest signs
- **Renal function tests** – High urea indicative of severe DKA
- **Electrocardiography** – For evidence of hypo/hyperkalemia

STEPS IN MANAGEMENT

A. Initial Stabilization

- Assess adequacy of airway, breathing and circulation
- **Fluid** – 10 ml/kg normal saline over 1 hour only (repeat if required) in children with hemodynamic instability. No role of colloids at this stage.
- Oxygen therapy in the presence of shock
- Respiratory support if required
- Nil by mouth
- Insertion of nasogastric tube and urinary catheter in unconscious patients

B. Specific Management

1. ***Fluid therapy:*** Fluid therapy forms the mainstay of treatment for DKA. Significant improvement in clinical condition and blood glucose can be

achieved by fluid resuscitation alone. Rapid and excessive fluid intake is however a risk factor for developing cerebral edema and should be avoided. The aim is to provide maintenance requirement and deficit evenly over 48 hours. In most cases the fluid deficit is 5-8%. The fluid requirement is usually around 3-3.5 L/m^2/day (**Table 2**). Care should be taken to avoid fluid administration more than 3.5 L/m^2/day due to the risk for cerebral edema. The amount of fluid replacement given in other centers prior to referral should be considered while calculating fluid requirements. In children with severe DKA and very high plasma osmolality fluid correction should be planned over 72 hours.

Table 2. Guidelines for Fluid Infusion Rate (ml/Hour) in DKA

Weight	*Level of dehydration*			*Weight*	*Level of dehydration*		
	Mild/Nil	*Moderate*	*Severe*		*Mild/Nil*	*Moderate*	*Severe*
5 kg	24	27	31	**38 kg**	101	125	156
7 kg	33	38	43	**40 kg**	104	129	162
8 kg	38	43	50	**42 kg**	107	133	168
10 kg	48	54	62	**44 kg**	110	137	174
12 kg	53	60	70	**46 kg**	113	141	180
14 kg	58	67	79	**48 kg**	116	146	186
16 kg	64	74	87	**50 kg**	119	150	191
18 kg	70	80	95	**52 kg**	122	154	197
20 kg	75	87	104	**54 kg**	124	158	203
22 kg	78	91	110	**56 kg**	127	162	208
24 kg	80	95	115	**58 kg**	130	167	214
26 kg	83	100	121	**60 kg**	133	171	220
28 kg	86	104	127	**62 kg**	136	175	226
30 kg	89	108	133	**64 kg**	139	179	232
32 kg	92	112	139	**66 kg**	142	183	238
34 kg	95	116	145	**68 kg**	145	187	244
36 kg	98	120	151	**70 kg**	148	191	250

2. ***Insulin:*** Insulin should be started only after around 1-2 hours of hydration as blood glucose falls rapidly even without insulin. Early insulin treatment is associated with a drastic fall in plasma osmolality, hypokalemia and increased risk of cerebral edema.

- **Route**
  - *Continuous intravenous infusion* – Preferred route. Initial insulin bolus should be avoided as it is a risk factor for cerebral edema.

- *Preparation*
  - Insulin infusion should be given using a dedicated intravenous line.
  - The intravenous tubing should be flushed with insulin as insulin binds to plastic tubing.
  - Regular insulin should ideally be given using an infusion pump. Dissolve 50 units of insulin in 50 ml normal saline. Rapid acting insulin analogs have no advantage over regular insulin when used as an infusion.
  - *Burette set may be used if infusion pump is not available with 50 units of regular insulin dissolved in 500 ml normal saline.*

- **Infusion rate**
  - *Initial*
    - **Mild DKA, infant, severe hypokalemia** – 0.05 unit/kg/hour
    - **Moderate, severe DKA** – 0.1 unit/kg/hour
  - *Subsequent modification*
    - **Reduction** – The insulin infusion rate should be reduced after resolution of acidosis. The infusion rate should then be decreased by 0.02 unit/kg/hour.
    - **Increase** – The dose should be increased if fall in glucose is less than 50 mg/dl/hour. The dose should be increased in quantum of 0.02 IU/kg/hour. Wait for at least 30 minutes before modifying the dose again.

Options for resource poor settings

If the facility for intravenous insulin is not available, intramuscular insulin can be used. The first dose should be 0.3 unit/kg, followed by 0.1 unit/kg hourly. ***Recurrent intravenous boluses of insulin should be avoided due to high risk of cerebral edema.*** Subcutaneous insulin is not recommended due to decreased absorption in the setting of poor perfusion.

3. *Electrolyte management*

- ***Sodium***
  - Most patients have significant sodium deficits (4-6 mmol/kg). Slow rise in sodium levels in the setting of rapid fall in glucose is a risk factor for cerebral edema.

- The sodium content in fluid should be no less than 77 mmol/L (half normal saline). Normal saline (154 mmol/L) should be used in the first six hours of hydration. Thereafter the sodium content in the fluid should be between 77-154 mmol/L.

- ***Potassium***
  - Significant total body potassium deficit occurs in DKA (3-6 mmol/kg).
  - Extracellular potassium levels may however be high due to acidosis and insulin deficiency. There is thus a risk of life threatening hypokalemia during treatment following the correction of insulin deficiency and resolution of metabolic acidosis.

    Management
  - Potassium replacement should be started in the initial hydration phase (20 mmol/L) in the rare scenario of hypokalemia at presentation. Insulin should be deferred until serum potassium is above 3.5 mEq/L.
  - In all other situations potassium replacement should be started after the initial hydration at the time of initiation of insulin infusion.
  - Potassium infusion should be started at a dose of 40 mmol/L unless serum potassium is > 6 mmol/L, the patient is anuric or ECG changes of hyperkalemia are present.

- ***Dextrose***

  Rationale
  - Hyperglycemia resolves prior to correction of acidosis
  - Decreasing insulin infusion rate with lowering of blood glucose would prolong duration of acidosis

  Management
  - Initial fluid – Dextrose free
  - Add dextrose according to blood glucose
    - *< 15 mmol/L (270 mg/dL)* – 5% dextrose
    - *< 11.1 mmol/L (200 mg/dL)* – 10% dextrose

4. *Acid base management*

Rationale – Alkali treatment should be avoided as
- Acidosis resolves with hydration and insulin
- Rapid correction of acidosis associated with risk of

- Hypokalemia (intracellular shift of potassium)
- Lactic acidosis due to left-ward shift of oxygen dissociation curve and decreased tissue oxygen delivery

Alkali treatment

- *Indications*
  - pH less than 6.9 with hemodynamic compromise
  - Severe hyperkalemia (serum potassium more than 6.5 mmol / L with ECG changes)

  Plan
  - Sodium bicarbonate 1-2 mmol / kg as infusion over 4 hours
  - Should be diluted in half normal saline

  Adverse effects
- Hypokalemia (intracellular shift of potassium)
- Cerebral edema (osmotic effect)
- Cerebral acidosis (low brain penetration of bicarbonate)

MONITORING (TABLE 3)

- **Clinical**- Hourly
  - *Neurological status* – Level of consciousness, pupil

TABLE 3. Monitoring chart for diabetic ketoacidosis

Parameter	***Time hour***									
	0 hr	**1 hr**	**2 hr**	**3 hr**	**4 hr**	**5 hr**	**6 hr**	**8 hr**	**10 hr**	**12 hr**
Clinical										
Sensorium	√	√	√	√	√	√	√	√	√	√
Blood pressure	√	√	√	√	√	√	√	√	√	√
Hydration	√	√	√	√	√	√	√	√	√	√
Heart rate	√	√	√	√	√	√	√	√	√	√
Laboratory										
Blood glucose	√	√	√	√	√	√	√	√	√	√
pH	√	×	×	×	√	×	×	√	×	√
Bicarbonate	√	×	×	×	√	×	×	√	×	√
Lactate	√	×	×	×	√	×	×	√	×	×
Anion gap	√	×	×	×	√	×	×	√	×	×
Sodium	√	×	×	×	√	×	×	√	×	√
Potassium	√	×	×	×	√	×	×	√	×	√
Osmolality	√	×	×	×	√	×	×	√	×	√

- *Hemodynamic status* – Heart rate, blood pressure, respiratory rate
  Fluid input and output

- **Laboratory** – Hourly
  - Blood glucose
  - *Venous blood gas* – pH, bicarbonate, lactate, base excess
  - *Electrolytes* – Sodium, potassium, anion gap
  - Plasma osmolality
  - Blood ketone (no role of urine ketones)

- **Expected Response (Table 4)**
  - **Blood glucose**
    - *Hydration phase* – Rapid decrease
    - *Continuation phase* – Decrease by 50-100 mg/dL/hour
    - *Reasons for poor response*
      - Dilute insulin
      - Insulin sticking to intravenous tubings
      - *Action* – Prepare new insulin infusion with new IV tubing.
  - **Metabolic acidosis**
    - Recovery over 6-12 hours
    - *Reasons for persistent acidosis*
      - Infection
      - Lactic acidosis
      - Cerebral edema resulting in hemodynamic instability
    - *Actions*
      - Exclude infections, consider antibiotics
      - Evaluate for clinical features of cerebral edema
  - **Serum potassium** – Reduction in serum potassium
  - **Plasma osmolality**
    - *Desired response* – Gradual decrease
    - Fall more than 2 mOsm/kg/hour risk factor for cerebral edema

- **Serum sodium**
  - *Desired* – Increase by 3 mmol/L per 100 mg/dL fall in glucose
  - Inadeguate increase is a risk factor for cerebral edema
- **Ketones**
  - Rapid decrease in blood ketones
  - Urine ketones may persist for up to 48 hours as
  - Urine ketosticks measure acetoacetate
    - β-hydroxybutyrate is the main ketone in DKA
    - β-hydroxybutyrate converted to acetoacetate during treatment

Table 4. Laboratory Parameters and Response to Treatment in DKA

Parameter	*Expected*	*Concern*	*Action*
Blood sugar	Decrease by 50-100 mg/dL/hour	Decline > 100 mg/dL/hour Decline < 50 mg/dL/hour	Add dextrose to IV hydration fluid Prepare fresh infusion, flush tubing with insulin
Blood pH	Resolution by 12 hours	Persistent at 12 hours	Exclude infection, shock, lactic acidosis
Serum sodium	Increase	Increase < 2 mmol/L/hour	Increase sodium concentration in fluid
Serum potassium	Gradual decrease	Hypokalemia	Increase potassium concentration in fluid
Anion gap	Resolution by 12 hours	Elevated at 12 hours	Exclude lactic acidosis, consider infection
Plasma osmolality	Stable	Decrease by > 2 mOsm/kg/hour	Increase sodium concentration, decrease fluid rate
Blood count	Decrease	Persistently elevated	Exclude infection
Blood urea	Decrease	Persistently elevated	Exclude renal failure

DISCONTINUATION OF ACUTE TREATMENT

- **Indications** – Normal hydration status, sensorium, and blood gas, and acceptance of food.
- **Protocol**
  - Consider continuing infusion till the time of oral feeds are established.
  - **Regular Insulin (0.25 unit/kg)** should be given 30 minutes before eating. Alternatively the child may be started on a split mix or basal bolus regime.
  - Discontinue insulin infusion 30 minutes after insulin to provide overlap. Early discontinuation of insulin is associated with recurrence of hyperglycemia.

- Monitor blood glucose after one hour and two hourly thereafter for six hours.
- **Ongoing insulin-** The decision for insulin regime should be individualized based on institutional preference, age, socio-economic status and family dynamics (please refer to the section on insulin regimens– Chapter 4). ***In most cases initial insulin requirements are substantially high (> 2 unit/kg/day) in the first weeks of treatment.***

COMPLICATIONS

Table 5 lists the common complications likely to occur following DKA.

Table 5. Complications Following DKA

Acute	*Chronic*
Cerebral edema	Growth hormone deficiency
Infection- Bacterial, fungal	Mental retardation
Hypoglycemia	Diabetes insipidus
Hypokalemia	
Acute respiratory distress syndrome	
Venous thrombosis	

1. Cerebral Edema

Cerebral edema is the most serious complication of DKA and the most common cause of death. The incidence of clinical cerebral edema is 0.5-1.0%. Radiological features are however present in most cases of DKA.

- **Risk factors**
  - **Patient related**
    - Age less than 5 years
    - Severe disease – Severe acidosis, high plasma osmolality, low CO_2 and high blood urea
  - **Treatment related**
    - Insulin – Insulin bolus, multiple intravenous injections
    - Fluid – Excessive volume (> 4 L / m^2 / day), hypo-osmolar fluid
    - Alkali treatment
- **Onset** – Usually 4-12 hours of treatment (may be present at diagnosis)
- **Indicators of diagnosis**
  - Persistent hemodynamic instability

- Worsening in clinical condition after initial improvement
- **Clinical features**
  - Early – Headache, vomiting, drowsiness, irritability, hypertension with bradycardia
  - Late – Unconsciousness, focal neurological deficits, papilledema, fixed dilated pupils

- **Diagnosis-** Clinical, no need to confirm with imaging. Neuroimaging should however be considered after stabilization in patients with persistent neurological features, to exclude rhinocerebral mucormycosis and cortical venous thrombosis.
- **Treatment**
  - Mannitol – 0.25-1 g / kg intravenous push *or*
  - Hypertonic saline – 10 ml / kg of 3% saline over 10 minutes
  - Fluid restriction – Reduce fluid rate to 50%
  - Head end elevation
  - Hyperventilation – Impending respiratory failure
- **Outcome** – Following clinically evident cerebral edema
  - Mortality – 20-30%
  - Morbidity – 30% (long term neurocognitive deficits)
- **Prevention**
  - Avoid insulin bolus
  - Fluid therapy
  - Use fluid boluses judiciously
  - Fluid replacement < 4 L / m^2 / day
  - Gradual correction in children with high plasma osmolality
  - Avoid sodium bicarbonate unless pH < 6.9
  - Use normal saline in children with high plasma osmolality

2. Infections Associated with DKA

- Agents – Bacteria, fungi (rhinocerebral mucormycosis, aspergillosis)
- Indicators
  - Persistent fever and leuckocytosis

- Black nasal discharge (mucormycosis)
- Hemoptysis (pulmonary aspergillosis)

- **Diagnosis** – Blood culture, chest X ray, sputum culture. It is always better to send blood, urine, and other suspicious secretions for culture at the beginning of therapy.
- **Treatment**
  - **Bacterial infection** – Antibiotics
  - **Fungal infection** – Itraconazole, amphotericin B

PREVENTION OF DKA

- Primary
  - High index of suspicion for T1DM.
  - Frequent sugar monitoring and careful management during sick days and invasive procedures in children and adolescents with T1DM.
  - Close sugar monitoring and rapid correction of hyperglycemia of patients on insulin pumps. All children on insulin pump should have access to vials/pens of rapid acting insulin. They should be used if there is no response to one correctional bolus.
- Secondary
  - Early diagnosis of ketoacidosis.
  - Careful fluid and insulin management.
- Tertiary
  - Early identification and treatment of cerebral edema.
  - Appropriate treatment of infections.

SICK DAY MANAGEMENT

Aspi J. Irani

SUMMARY

- Never omit insulin when sick. Insulin dose can be reduced if child is anorexic or vomiting with BG below 100 mg/dL.
- Follow BG and urine or blood ketones. These should be checked every 2-4 hours. Never go by the appetite alone.
- Give additional supplements of rapid acting analog or regular insulin when ketones are raised with BG above 180 mg/dL.
- If child cannot eat his usual diet, give plenty of liquids orally in frequent small sips. Offer sweetened liquids when BG is less than 180 mg/dL and salty liquids when BG is above 180 mg/dL.
- Consider "mini dose glucagon" if BG is less than 80 mg% with raised ketones and child cannot accept or retain oral liquids. If this is not practical, hospitalization for intravenous dextrose may be required.
- Hospitalize urgently for impending DKA if child has more than 3 vomits, significant abdominal pain, drowsiness or breathlessness.
- It is the responsibility of the medical team to ensure that every patient is fully conversant with these "sick day" guidelines. Clear written instructions should be given to the family and the school authorities.

Children with diabetes are not more susceptible to infections than those without diabetes, provided the diabetes is in good control. If diabetes is poorly controlled, infections tend to be more severe and unusual infections can develop.

The line of treatment of any illness in a child with diabetes does not differ from that in a child without diabetes. Whenever possible it is preferable to use tablets or sugar-free syrups; however, if this is not possible then one should not hesitate to use sugar containing syrups as the influence on blood glucose (BG) would be marginal.

When children with diabetes develop an infection or other severe illness there are two factors that can adversely affect diabetes control:

1. ***The release of stress hormones and cytokines in response to the illness:*** These raise BG *despite poor oral intake* and can lead to ketoacidosis (DKA). This is

often seen during illnesses which are associated with fever. (See Chapter 11 Diabetic Ketoacidosis.)

2. ***Anorexia, nausea, vomiting or diarrhea:*** When these dominate the clinical picture, without a febrile response, hypoglycemia commonly develops. It is important to note that vomiting without diarrhea, if associated with raised BG, is often due to insulin deficiency per se. (See Chapter 10 : Hypoglycemia.)

   The net effect of the two opposing factors (which can be present together in a given illness) is difficult to predict and hence *a safe rule is to follow the BG and ketones (in urine or blood) rather than the appetite in planning insulin therapy on sick days.* For this, blood glucose and ketones should be checked frequently (every 2-4 hours).

DKA is by far the commonest diabetes-related cause of death in children and adolescents with T1DM. The commonest cause of DKA in a known diabetic (other than insulin omission) is lack of knowledge of sick day management.

It is important to educate the patient and family members about handling sick days to prevent DKA, dehydration, and hypoglycemia. These guidelines should be given in writing; they should be clear and should be reinforced periodically, at least during each clinic visit.

MANAGEMENT OF DIABETES DURING A SICKNESS

1. Monitoring on Sick Days

Blood glucose and ketones must be checked every 2-4 hours.

If the patient does not have a BG meter then they may use BG strips that can be read by visual comparison. Urine glucose testing may be employed only as a last resort.

There is only one meter available in India that checks blood ketones and the cost of each ketone strip is very high (Rs. 150/- approximately). In practice therefore most patients depend on the less reliable urine ketone tests. Blood ketone test measures β-hydroxybutyrate (BOHB) which is the predominant ketone body in DKA. The urine test measures acetoacetate (AcAc). In normalcy, the ratio of BOHB to AcAc is 1:1 while in DKA it can be as high as 10:1. Hence, urine tests underestimate the degree of ketosis.

Blood testing reflects the glucose or ketone level at the time of testing and gives a precise measurement whereas urine tests reflect the average level since the time urine was last passed. Unlike urine, blood has the added advantage that it can be drawn whenever needed.

A blood glucose level above 180 mg/dL signifies insulin deficiency and the need for additional insulin. Presence of ketones in urine or blood would mean

either carbohydrate deficiency due to poor intake (in which case the simultaneous BG would be less than 100 mg/dL) or significant insulin deficiency (when associated with BG over 180 mg/dL).

2. Insulin on Sick Days

Insulin should never be completely omitted even if child refuses to eat.

Insulin dose can be reduced only when BG is below 80 mg/dL and the child cannot eat. In this case, the short or rapid acting insulin dose is omitted while the intermediate or long acting insulin is continued as usual. If however, the urine ketones are also positive (more than trace), the dose of the intermediate or long acting insulin (as the case may be) should be reduced by 20-30%. **Table 1** summarizes the reductions in routine insulin dose to prevent hypoglycemia.

TABLE 1. Reduction in Usual Insulin Dose to Prevent Hypoglycemia on "Sick Days"

Blood glucose	***Urine ketones***	***Action***
<80 mg/dL	Absent / trace	Omit regular insulin or rapid acting analog if oral intake is poor. Continue NPH / long acting basal analog
<80 mg/dL	> trace	*Also* decrease NPH or long acting basal analog by 20-30%

When BG is over 180 mg/dL the patient needs a supplement of short or rapid acting insulin immediately. This additional dose is calculated as a percentage of the total daily dose (TDD). (TDD refers to the sum of all insulins taken in 24 hours on routine days. See Chapter 4 : Insulin Therapy.) The supplement may range from 5-20% of TDD depending on the BG and the ketone levels. It is always given as regular insulin or rapid acting analog. As a rough guide, when BG is over 180 mg/dL with absent or trace urinary ketones, a supplement of 5-10% of TDD may be taken; the supplement should be 10-20% if ketones are small or moderate and 20% if ketones are large. **Table 2** gives at a glance the calculation of insulin supplements when BG is above 180 mg/dL.

Subsequently retesting is done at 2-4 hours intervals with supplements taken whenever indicated.

When taking serial supplements it must be remembered that some of the previous dose may not have been absorbed or may not have acted as yet. With rapid acting analogs the rate of absorption is 30% per hour, hence at the end of 2 hours 60% would have been absorbed while 40% is yet to commence working and this amount should be subtracted from the calculated amount of the next supplement.

TABLE 2. Insulin Supplements (Expressed as a Percentage of TDD) to Prevent DKA on "Sick Days"

Blood glucose	*Urine ketones*	*Blood ketones*	*Extra insulin* (% of TDD**)*
> 180 mg / dL	Absent / trace	<0.6 mmol / L	5-10%
180-400 mg / dL	Small / moderate	0.6-1.5 mmol / L	10-15%
> 400 mg / dL	Small / moderate	0.6-1.5 mmol / L	15-20%
180-400 mg / dL	Large	>1.5 mmol / L	20%
> 400 mg / dL	Large	>1.5 mmol / L	20%

**Supplements are given as regular insulin or preferably as a rapid acting analog.*
***TDD or total daily dose of insulin refers to the sum of all insulins taken on a routine day.*

Insulin requirement may go up during the incubation period of an illness. Increased requirement may last for as much as a week after recovery from the illness.

3. Diet on Sick Days

The patient who cannot eat his regular meals should be offered plenty of salty liquids (such as rice kanji, vegetable soup, dhal soup, buttermilk, milk without sugar or chicken soup) if BG is above 180 mg / dL and sweet liquids (non-diet soft drinks without fizz, fruit juices, milk with sugar, WHO-ORS or melted ice-cream) if BG is below 180 mg / dL.

These liquids must be taken in small and frequent sips to minimize chances of vomiting. Further, it should be kept in mind that an anorexic child is more likely to accept items of his / her choice. Cool liquids are preferred as they are less likely to induce nausea or vomiting.

4. Mini Dose Glucagon Rescue

If the BG is below 60 mg / dL with more than trace ketones in urine and patient cannot accept or retain any oral liquids, glucagon (if available) can be injected in a dose of 10 μg per year of age (minimum dose: 20 μg and maximum: 150 μg). For this, dissolve glucagon in the diluent provided (1 ml = 1000 μg) and inject intramuscularly using a 100 IU insulin syringe. One unit (1 IU) would provide 10 μg; hence inject 2-15 units depending on age. This mini dose raises BG by 60-90 mg / dL for a period of 60 minutes without aggravating nausea. Glucagon can be repeated in double the dose if BG does not rise sufficiently after 20-30 minutes.

If the patient does not have glucagon (many patients in our country may not afford glucagon and unfortunately it is also not freely available at all times), then the child would need to be hospitalized for intravenous dextrose to maintain BG.

5. Do not Delay Hospitalization when there are Signs of Impending DKA

Hospitalization may be required either for impending severe hypoglycemia (as discussed above) or impending DKA.

If the child vomits more than 3 times, is drowsy, has significant abdominal pain or is breathless, immediate hospitalization for intravenous fluids and insulin infusion, is a must. It must be remembered that the single most important factor that correlates with mortality in DKA is the duration of the process.

Every patient must be familiar with these guidelines for managing diabetes when sick: what to check; how frequently to check; how much of extra insulin to take; when to reduce insulin; what oral intake is appropriate; and when to rush to hospital.

13

PSYCHOSOCIAL ASPECTS

M. Vijayakumar

SUMMARY

- Attention to psychological issues is as important as insulin administration, meal planning, self blood glucose monitoring (SBGM) and exercise.
- Stages of shock and grief at the time of diagnosis, progressing to disbelief, denial, anger, false hopes, confusion and depression later; and finally resolution and acceptance, may all occur. Financial worries may loom large..
- Clinically significant depression is not uncommon.
- Psychological evaluation, recognition of abnormal coping, and intervention, may help prevent major crises.
- Support groups are helpful in allowing "senior", experienced families to come to the help of families with a newly diagnosed child.

Diabetes influences the lifestyle, personality, emotional and physical well-being of the child. Diagnosis of diabetes and a routine of daily insulin injections coupled with monitoring blood glucose levels, diet adjustments and exercise may contribute to emotional disturbances both in the child and the family.

In addition frequent and extreme fluctuations in blood sugar levels and the psychosocial effects of a chronic disease are often associated with deficits in academic performance especially in children with poor glycemic control. For children with diabetes, life will not be normal if their learning and school performance are compromised by cognitive deficits resulting from the disease.

Psychological factors are important influences affecting the care and management of diabetes. Developing effective stress management and problem solving skills is as important for successful therapy as are insulin administration, meal planning, self blood glucose monitoring (SBGM) and exercise.

The diagnosis of diabetes poses considerable challenges and stress for children and families. Research findings indicate that children with diabetes and their parents are at risk for adjustment problems during the initial period of adaptation after the diagnosis. When adjustment problems exist, children are at higher risk for continued adjustment difficulties. Therefore there is a great need, at the time

of initial diagnosis, to assess the developmental, behavioral and psychological history of children with diabetes and their families.

Assessment should occur both at the time of diagnosis and periodically thereafter. If problems are identified, early interventions should be initiated. Psychological therapies can have a considerable impact on the outcome of diabetes management.

Psychosocial Impact at the Time of Diagnosis

Any potentially life-threatening condition has some psychosocial impact, and that of diabetes is profound. Family members often experience the classic stages of shock and grief at the time of diagnosis progressing to disbelief, denial, anger, false hopes, confusion and depression later; and finally resolution and acceptance.

Unresolved grief leads to family becoming dysfunctional in some cases. On the other hand, denial may lead to delay in starting treatment as parents "shop" for second opinion. Denial and false hopes may lead to omission of insulin and trials with alternative medicines. Although most families reach grief resolution, chronic sorrow and depression will be there for a long time, probably life-long.

Diabetic control and usual family functioning are difficult during this period and require support from the medical team. These periods of grief may reappear during the time of life-threatening complications such as DKA or severe hypoglycemia.

Depression, Anxiety and Fear

When diabetes is diagnosed, parents and children suddenly feel depressed and may be in a state of shock. Parent's expectations shift as their once normal child has a serious illness with its acute and chronic complications and need life-long management with rigorous monitoring. The child may have negative experiences of hospitalization, injections and diet restrictions. Overprotective attitude and the grief of parents often transmit to the child.

Diabetic children and adolescents may have fears too – about insulin injection, self pricking for blood tests, hypoglycemia, revealing to peers, managing at school, career, marriage, life span and long term complications. These can be overcome only by appropriate diabetes education programs and group sessions.

Many parents especially mothers of newly diagnosed children are at risk of psychological adjustment problems. Clinically significant depression is noted in one-third of the mothers. One-fourth of parents have met the criteria of post-traumatic stress disorder. Pre-existing psychological, social, or financial problems are likely to be accentuated by the stress of caring for a young person with diabetes. Psychological maladjustments in parents are associated with poor glycemic control in their child.

Children will have difficulty in classrooms adjusting restrictions caused by the disease and school routines and often worry about getting a hypoglycemic attack, the most dreaded of all complications to the child and parents. Many parents spend sleepless nights. They are anxious about the first aid available at school in case of emergency and the competency of school staff in recognizing and treating hypoglycemia.

Financial Constraints

Financial burden is a major factor denying adequate care and hence producing mental agony to the parents and to the child. Costs of insulin and the strips are the usual culprits and frequent clinic visits add to the problem. Some children are actually aware of the financial strains within the family and they try to compromise, like taking less insulin, reuse syringes and lancets, and test blood glucose fewer times than recommended in order to save money which will lead to poor glycemic control.

Childhood diabetes support groups can help families in a number of ways – bulk purchase of insulins and test strips; donations for therapy from individuals and corporate firms; cheaper investigation packages from a laboratory and so on.

Feeling Different

One of the greatest desires of a child in school is to mingle freely with peers. Children with diabetes feel different from their friends because of diet restrictions and frequent monitoring. Some may be reluctant to eat snacks, do blood sugar monitoring and manage hypoglycemic symptoms in front of their classmates resulting in failure of adequate sugar control. If a common meal is served, they will have problems when they are not able to eat all foods their classmates eat, like ice cream, sweets etc. These factors will produce a tremendous negative effect on their self esteem. An ongoing diabetes education program can help to solve many of these issues.

Independence Issues

Parents may be overprotective of a child who wants normal independence and the child never attains the independence his / her peers enjoy. Conflicts develop between the parents and the children and this leads to oppositional behavior and rebellion. Sometimes it even becomes the ultimate conflict in the family. One of the tasks of adolescent period is to achieve independence from the parents gradually, but with diabetes, the task becomes more difficult.

Family Functioning

Quality of life of all the family members is affected by diabetes. Parents of

youth with diabetes have more conflicts and financial problems. Improved metabolic control is associated with better family communication, agreement about family responsibility and supportive behavior. Family relations are linked with regimen adherence. Parental warmth is predictive of better adherence. Youths should receive active support from the family and friends.

Single parenthood is associated with poor metabolic control. Stress factors such as divorce, family arguments, violence or abuse can lead to elevated blood sugar levels.

Families play the key role in the adjustment of children to diabetes and its complications. Not only parents, but the grandparents and sibling and other close relatives should be involved in the management and education programs. Impact of diabetes depends on the background, structure, and functioning of family as a whole.

In low income families, limited access to health providers and high costs of health care affects diabetic control and family stability.

A history of diabetes and its complications among patient's relatives can significantly affect the outlook of both the diabetic children and their parents.

Stress and Coping

Children with high life stress tend to have worse glycemic control. Youth in poor metabolic control perform poorly with stress, while children in good glycemic control have high levels of self efficacy and engage in active coping. Maladaptive coping is associated with poor regime adherence.

Infants and toddlers are dependent on their parents for care. This puts parents, especially the mother in our society, under a great deal of stress. Even adjustment from initial hospitalization to home can be difficult unless the parents have been properly prepared.

Support groups can help parents manage the stress and cope with feelings of guilt anxiety and fear. Health care providers can help by promoting the development of clinical services, education materials and support groups for families living with diabetes. Meeting people with same condition and having the opportunity for exchanging ideas have important therapeutic value.

Neuropsychological Deficits

Neuropsychological deficits are observed few years after the diagnosis. These include:

- Reduced speed of information processing, decrements in conceptual reasoning and acquisition of new knowledge.

- Defective memory and learning capacity.
- Poor performance on various measures of intelligence, attention, processing speed and long term memory.
- Weakness in attention executive functioning.

Major predictors in these changes include onset of diabetes prior to four years, recurrent severe hypoglycemia and hyperglycemia. Better glycemic control and quality of life are seen in children when parents, school personnel and friends receive some training in diabetes management and guide these children effectively in preventing and treating diabetic complications.

Depression and Other Psychiatric Disorders

Depression is common among children with diabetes. It is usual to find sadness, anxiety, loneliness and isolation. Children find difficulties in controlling blood sugar because of failure to follow strict diet advice and insulin administration and often labeled as non-adherent, by the parents and health care workers. This disappoints them and guilt, feeling of failure and depression ensue. They feel that their parents and caretakers have lost their faith in them. This may even lead to manipulating blood sugar results.

Because of diet restriction, diabetic children, especially adolescent girls may develop abnormal eating habits, Usual among them are anorexia, bulimia, and insulin omission.

Other psychological problems include anxiety, poor self esteem and high levels of stress. The major factor leading to these problems is poor metabolic control. Children with recurrent DKA are more likely to have psychiatric disorders compared to children in good metabolic control. Repeated hospitalization adds to depression.

Both internalized and externalized behavioral problems are high in children with diabetes. Boys with diabetes become more aggressive than normal children. High level of family conflict acts as a predictor of behavioral problems.

Social Support

Social support from family members is important. Family members who provide high level support for diabetes care have children who adhere better to the regime. Compared to younger children, older children and adolescents get less family support. When youth attribute negative peer reactions to their self care, they are more likely to have adherence difficulties and increased diabetes stress, which in turn worsens glycemic control.

Special Problems of Adolescent Children

Puberty imposes unique challenges on the individual with diabetes, their family and health care personnel. Their health problems and emotional needs are entirely different from younger children. These issues are discussed in detail in Chapter 22.

RECOMMENDATIONS

Psychological Assessment

- ***A multidisciplinary team*** is needed for the care of children with diabetes. Help of mental health professionals, interested in issues of childhood diabetes, preferably a child psychologist, should be sought whenever needed.
- The diabetic health care team should maintain constant, uninterrupted contact with patients and family members.
- ***Assessment of developmental progress*** in all areas of life (physical, intellectual, mental, social, academic and emotional) should be done frequently.
- ***Routine assessment and follow up*** of children are needed. This includes children's knowledge about diabetes, insulin administration skills, regimen adherence, complications as well as psychological problems faced by the child and parents.
- ***Identification of psychological adjustment problems***, depression, eating disorders, and other psychiatric disorders should be conducted at regular intervals by health professionals. These assessments are particularly important in young children not achieving treatment goals or who exhibit poor metabolic control (high HbA1c, recurrent hypoglycemia or DKA.)
- Diabetic care team should provide ***age appropriate advice and education*** not only on diabetes but also how to cope with psychological stresses like feeling different, discrimination, peer group pressure etc.
- Be a ***patient listener*** to a child with diabetes regarding his doubts. Assure them that they will be heard, will be treated and adult supervision will be available.

Routine Diabetes Care

- ***Insulin administration and glucose monitoring*** should be carried out with ***least discomfort*** possible to ease the psychological trauma.
- ***Preventing severe hypoglycemia and ketoacidosis*** are crucial. Special attention must be given to under-5 children who experience frequent severe

hypo- or hyperglycemia since such occurrences are associated with learning disabilities.

- Children and adolescents should ideally be managed in a separate clinic and ward for them rather than those for adults with diabetes and long-term complications.

Care at School

- ***School performance*** of children should be evaluated, especially those with recurrent hypoglycemia and early onset diabetes. They should be specially evaluated and treated for learning disabilities.
- Work to ***minimize differences with other students*** whenever possible, rather than singling out any child because of diabetes. Diabetes should not be the cause for being excluded from any type of ***activity in school.***
- ***Teachers and school staff*** must be educated about diabetes. Considerations must be given to appropriate teacher-pupil relationship so that children with diabetes do not get singled out as misfits in the class room.
- Teachers should be given instructions regarding how to recognize and manage ***hypoglycemia***. A supply of rapidly absorbed sugar must be immediately available in the class room. He / she should not be left alone during and after the episode.
- Diabetic children should take active participation in all available academic and social activities. Young people should have equal opportunities in any type of school / college activity and if possible in employment also.
- ***Safety*** is paramount especially when participating in sports, school excursion or camps.

Family Counseling

- The health care team should aim to provide preventive interventions for the family. ***Parents*** should be aided in identifying their own stress and doing relieving techniques like practicing yoga, meditation or relaxation technique.
- They require ***emotional support*** mainly after diagnosis, after a life-threatening complication (DKA or severe hypoglycemia) or during adolescent period.
- ***Psychological, behavioral interventions*** should be made available for patients and families exhibiting conflict, disordered communication, behavioral and psychiatric difficulties.
- Parents of children with diabetes should be encouraged to ***visit their child's school*** to discuss specific needs with teachers, the principal and other staff. If possible, health care personnel may also visit school.

Society and the Diabetic Child

- ***Economic support –*** Economic support aided by government or voluntary organizations may be required to provide uninterrupted supply of insulin, equipment and nutrition.
- Parents should be given information about voluntary or charitable organizations, which may provide support like information and ***education, support groups, educational camps, financial helps*** etc.
- Attempts should be made to raise ***public awareness*** of special needs of children with diabetes and affected families.

Adolescent with Diabetes (see also Chapter 22)

- Understanding the physiological and psychological development of adolescence is important. ***Risk taking activities*** like omitting insulin doses and hence achieving poor metabolic control are common***.***
- ***Differences in lifestyle and need for independence*** in the young patient must be appreciated.
- Developing a ***trusting relationship with the adolescen and*** Gradual transition to ***co- operative care with the adolescent are useful***.
- Encouraging the young to ***refrain from smoking, alcoholism and drug abuse*** and ***prevention of hypoglycemia while driving*** are important concerns.

Management of Specific Psychological Illnesses

- ***Have a high index of suspicion towards mental illnesses like anxiety, depress*****ion, eating disorders, and drug abuse and give spe**cialized counseling.
- The HEADS technique (Home, Education, Activities during spare time, Drug use, Sexual activities) is helpful while analyzing psychological problems.
- ***Overt psychological problems or psychiatric disorders*** in the child or family members should receive support from diabetic care team and expert attention from a social worker, ***psychologist or psychiatrist*** trained in child and family therapy.

14

PROCEDURES AND SURGERY

M. Vijayakumar

SUMMARY

- The counterregulatory hormones rise during surgery or other stress, and result in high BG and ketones.
- Diabetes increases the risk of infections, and influences wound healing, therefore excellent BG control is desirable prior to elective surgery.
- Insulin doses may have to be adjusted from the night before major surgery, and on the morning of a minor surgery. **Insulin must never be completely missed.**
- Attention must be paid to fluid and electrolyte balance.

IMPLICATIONS OF COEXISTING DIABETES MELLITUS IN A CHILD DUE FOR AN INVASIVE PROCEDURE

- Invasive procedures including surgery and anesthesia are stressful situations. These lead to release of ACTH, glucagon, catecholamines, and growth hormone (GH), in a magnitude directly proportional to the severity of stress. Their concentration gradually decreases during recovery period.
- The effect of these counter-regulatory hormones is to increase gluconeogenesis, lypolysis and glycolysis, resulting in high blood glucose and ketones.
- In normal subjects, insulin secretion increases to balance the effect of counter-regulatory hormones. In T1DM, patients are unable to produce insulin, hence cannot balance the effect of these hormonal changes. Hence they are more prone for hyperglycemia and ketoacidosis.
- Decreased caloric intake or over-treatment with insulin may decrease glucose levels resulting in hypoglycemia.
- Hypoglycemia is particularly dangerous for a sedated or anesthetized patient, as it makes it difficult to identify the warning signs such as drowsiness and if left undetected, could lead to permanent brain damage.
- The impact of diabetes on surgical outcome depends on:
  - Glycemic control,
  - Presence or absence of long term diabetic complications or

- Concurrent infections.

- Deciding factors in the management are:
  - Nature and severity of the invasive procedure,
  - Extent of diabetes, its complication and glycemic control and
  - Concurrent illness present in the child.

Influence of Glycemic Control on the Outcome of Surgery

- In children with good glucose control, wound healing is good.
- If diabetes is not under control, there is increased susceptibility to infection as a result of impaired leukocyte function (decreased chemotaxis, impaired phagocytic activity of granulocytes and decreased intracellular killing of organisms).
- Therefore, in elective conditions, optimization of glycemic control before the procedure or surgery and identification and treatment of diabetic complications that may affect the surgical management is ideal.
- However, since majority of procedures are done on an emergency basis, good glycemic control may not always be possible.

EVALUATION OF CHILDREN WITH T1DM PRIOR TO INVASIVE PROCEDURES

Clinical Evaluation

- ***History:***
  - Good history which should include the duration of the disease, treatment regime, adherence to treatment and presence of complications.
  - Inspection of patient's insulin and blood glucose log records, including HbA1c.
  - Complete and accurate drug history – other than insulin.
- ***Examination:***
  - Attention to all systems especially cardiovascular and nervous system, including autonomic system.
  - Record vitals including BP, respiratory rate, heart rate, and temperature.
  - Check the status of thyroid.

Essential Laboratory Investigations before the Procedures

1. Minor procedures

- Blood – Complete blood counts including ESR

- Serum electrolytes – Sodium and potassium
- Renal function tests – Blood urea and creatinine
- Urine
  - Proteins – Possible renal complication, microalbuminuria
  - Microbiology – To rule out urinary infections
  - Ketones – Poor control of diabetes.

2. Additional investigations in a major procedure

- Coagulation profile – This should include plasma prothrombin time (PPT) and activated partial thromboplastin time (APTT).
- Arterial blood gases
- Serum ketones
- Blood culture
- ECG
- X-ray chest – To screen for pulmonary infections, including tuberculosis.

SPECIAL ISSUES WHILE PLANNING THE PROCEDURE

The regimen adopted depends upon:

- Nature of the surgical procedure
- Expected duration of fasting
- Pre-existing insulin regimen.

Instructions Given to the Patients before an Elective Procedure

- Patients are advised to do strict glucose monitoring 4-5 times a day for at least 2 days prior to the procedure. If blood sugar cannot be maintained properly, procedures should be deferred, if possible.
- Encourage to continue taking clear liquids until 2 hours before a major procedure. If this is not possible, an IV maintenance infusion is started so that the child does not have fluid deficit during the procedure.
- Usually if major anesthesia is planned, no solid food should be taken overnight, i.e. fasting for 8 hours.

Do not Omit Insulin Altogether before the Procedure

- A common error in the management of diabetic children who is having poor intake is to completely withhold insulin therapy.

- Insulin requirements are often higher than normal, even when fasting, and missing insulin doses can have very serious consequences, including DKA.

Timing of the Procedure

- Procedures should be scheduled as early in the day as possible, often as the first procedure. This allows the patient maximum recovery time to restart oral intake and subsequent insulin therapy.

Choice of Anesthesia

Local anesthesia is preferred as far as possible since

- It reduces the stress response.
- Hypoglycemia can be detected early since the patient is awake.
- Post-operative nausea is reduced.
- Easier post-operative diabetic control.

INSULIN REGIMENS TO USE DURING SURGERY

Minor Procedures (Classic "Non-tight Control" Regimen)

- When the procedure is only brief, and full oral intake is possible early after the procedure, one can monitor hourly blood glucose and give the subcutaneous insulin.
- If long acting analogues are used, full dose should be given in the evening before the surgery. If NPH or lente is in use, one half of the morning dose is given before the surgery.
- Once they recover from the procedure, patients can have 50- 60% of usual insulin with a meal and blood glucose is monitored carefully.
- Sedation – benzodiazepines, opioids, and barbiturates do not alter glucose metabolism much.

Major Procedures

- Preferred method is continuous intravenous insulin infusion.

Advantages of Continuous Intravenous Insulin Infusion (Tight Control Regimen) during a Procedure

- Continuous intravenous insulin infusion is used in surgery and other emergencies. Improved glycemic control is noticed with continuous insulin infusion over conventional subcutaneous administration of NPH insulin.
- In operative settings absorption of insulin from subcutaneous tissue is slow, erratic and unpredictable secondary to poor perfusion of this region.

- ***Combined insulin and dextrose infusion:*** This is a less flexible method poorly suited to major procedures. It is generally not adequate for T1DM who are prone for wide swings of blood sugar.

Technique of Continuous Intravenous Insulin Therapy

- Separate continuous insulin and glucose infusions (5% dextrose) are the standard therapy coupled with hourly monitoring of plasma glucose.
- Infusions are adjusted to allow adequate insulin infusion rates, while maintaining plasma glucose in the range of 100-180 mg/dL (5.5-11.1 mmol/L). (See **Table 1.)**
- Start the infusion at least 2-3 hours before the surgery. For early morning surgery and that needing improved glycemic control, infusion is started in the night before surgery. Allowing more time between the start of insulin infusion and surgery will allow more time for titration to the desired level of control.
- Insulin administered, consists of a standard solution of insulin (50 units of regular insulin in 50 ml of normal saline – one unit in one ml) delivered by an infusion pump. (You can also use 50 units in 500 ml i.e. 1 unit in 10 ml; this may be easier to use in an infusion pump.)
- Flush 3-5 ml through IV line before connecting to the child because insulin binds to IV tubing and flushing it helps in saturating the binding sites.
- 5% dextrose containing solution is started at the rate of 1500 ml/m^2/day. It can be given by another IV line or by piggy backing it with insulin infusion pump.
- Insulin level should be monitored hourly and monitoring should be started at least 4 hours before the procedure to allow glucose levels to stabilize.

TABLE 1. Guidelines for Intravenous Insulin Coverage during Surgery (Intravenous Sliding Scale)

Blood glucose level (mg/dL)	***Insulin infusion (unit/kg/hour)***
< 120	0
121- 200	0.03
200- 300	0.06
300- 400	0.08
> 400	0.10

- Increased insulin may be needed in obese children, children with sepsis and in children on steroids.

- Plasma half life of IV insulin is only 5 minutes. Hence it can be stopped temporarily if sugars are below 120 mg/dL during the procedure and restarted if it comes up.
- There is no role for administration of intermittent large intravenous insulin doses. This can result in big swings in glucose concentration and a greater chance of lipolysis and ketogenesis.
- ***If blood glucose is below 80 mg/dL during the procedure,*** stop insulin and administer intravenous bolus of 50% dextrose 1 ml/kg bodyweight and wait for 30 minutes. Restart by a lesser unit/kg (70% of the previous infusion rate) once the sugar level increases.
- Patients with insulin pumps should have them turned off in the perioperative period and replaced by continuous infusion regime.

FLUID AND ELECTROLYTES

- ***Ensure adequate hydration*** – Fluid correction in diabetic children is similar to non-diabetic children. For calculating maintenance fluid requirement, Holliday and Segar's formula can be used – for first 10 kg, maintenance fluid requirement is 100 ml/kg/day; for next 10 kg it is 1000 ml + 50 ml/kg and for next 10 kg it is 1500 ml + 20 ml/kg.
- ***For volume replacement,*** non glucose containing crystalloid solutions should be ***administered separately through another site***. Ringer's lactate is not a good option since lactate is a glucogenic precursor and makes glucose correction difficult.
- ***Potassium replacement*** is needed (20 mEq/L) which can be adjusted based on serum potassium level. Electrolytes should be checked every 6-12 hours.

POST-OPERATIVE PRECAUTIONS AND CARE

- ***IV insulin*** should be continued after the procedure till the child is able to take orally. Then subcutaneous insulin can be given and IV insulin is tapered. Since IV insulin works fast and subcutaneous insulin is slower to act, subcutaneous insulin should be given 30 minutes before meals and IV insulin should be stopped 30 minutes after the subcutaneous dose.
- The requirement of subcutaneous insulin may be high early in the post-procedural days and gradually comes down.
- The child should not be discharged until blood glucose levels are stable and oral intake is well tolerated.

UNIVERSAL PRECAUTIONS TO BE OBSERVED DURING PROCEDURES (INCLUDING FINGER PRICKS)

- Devices should be restricted to individual use.
- Never reuse needles, syringes and lancets.
- Dispose of the used finger prick devices and lancets at the point of use in approved sharp containers – usually blue in color.
- Dispose your own sharps yourself; never pass used sharps to another person.
- During exposure-prone procedures, minimize the risk of injury by ensuring that the operator has the best possible visibility. E.g. by positioning the patient, adjusting good light source and controlling bleeding.
- Protect fingers from injury by using forceps instead of fingers for guiding suturing.
- Never recap, bend or break disposable needles.
- Multidose insulin vials should be assigned to individual patients and labeled appropriately.
- Assign separate glucometers to individual patients.
- Glucometers and other instruments should be cleaned regularly and whenever contamination with blood or body fluid is suspected.
- Store individual patient supplies and equipment within patient's rooms whenever possible.
- Wear gloves during finger prick, administration of insulin, and other procedures involving potential exposure to blood and body fluids.
- Change gloves between patient contacts; discard the gloves in appropriate places.
- Perform hand hygiene; give attention to all 6 areas while doing hand washing.
- Provide full hepatitis vaccination to all patients and if possible, check and document post-vaccination titers.
- Whenever possible, consider *Hemophilus influenza B* (HiB), pneumococcus, varicella and hepatitis-A vaccines.

REDUCING PAIN IN PEDIATRIC PROCEDURES

- ***Blood draws and intravenous lines –*** EMLA is a combination of lignocaine and prilocaine, which comes in both a cream and disc formulations. The cream must be used with an occlusive dressing. EMLA results in anesthesia

down to 3-4 mm, but it takes 60 minutes to achieve maximum effect. EMLA can cause vasoconstriction, which make vein cannulation more difficult.

- ***Lumbar puncture*** – EMLA to be applied to the lower back 60 minutes before the procedure. The use of 1% lignocaine into the skin overlying the interspace is done before the procedure.
- ***Wounds requiring suture repair*** – LET is a combination of lidocaine, epinephrine and tetracaine and is available as a gel. If further anesthesia is needed for a deeper effect, lignocaine injection is used. Maximum safe dose of lignocaine without epinephrine is 4 mg/kg and with epinephrine is 5-7 mg/kg.
- ***Bone marrow aspiration, pleural tap*** – IV midazolam 0.2 mg/kg 15 minutes prior to the procedure. Action lasts for one hour. It can also be used as IM, oral, rectal and nasal route.
- ***Diagnostic radiology procedures including MRI*** – Inj pentobarbital IV 1-6 mg/kg 10-15 minutes before the procedure.
- ***Fracture reduction, thoracotomy tube insertion*** – Inj ketamine IV 1-2 mg/kg loading dose and 0.25-1 mg/kg maintenance every 15 minutes.

15

CONTINUOUS SUBCUTANEOUS INSULIN INFUSION (INSULIN PUMP)

Anurag Bajpai

SUMMARY

- An insulin pump, the size of a small mobile phone, pumps regular insulin or rapid acting analog, through a plastic tubing and butterfly needle, into a subcutaneous site. The pump can be programmed with different basal rates, say high rates to counter early morning dawn phenomenon, or low rates to counter exercise induced hypoglycemia. Boluses are given just prior to meals and large snacks.
- Insulin pumps have the advantage of providing good glycemic control with lower frequency of hypoglycemia and better quality of life.
- Careful patient selection and intensive education is essential for successful insulin pump treatment.
- Children on insulin pumps should check blood glucose levels at least four times a day (pre-meal and at bedtime).
- Emergent correction of hyperglycemia is mandatory for prevention of DKA in children on insulin pump.
- Insulin injection using a syringe or pen should be used to correct hyperglycemia in children on insulin pumps in the presence of ketosis.

All currently available insulin regimens are unable to replicate the pattern of physiological insulin secretion. Under physiological circumstances, insulin is secreted at a basal rate to suppress hepatic glucose production with extra insulin released in the portal circulation in response to meal. While none of the currently available systems allows portal delivery of insulin, continuous subcutaneous infusion of insulin (CSII) using an insulin pump comes closest to physiological insulin replacement.

PRINCIPLE

Insulin pumps are electronic devices that inject insulin using a subcutaneously inserted catheter. The pump delivers insulin at a preset rate (basal rate) and gives insulin boluses along with meals (meal bolus) and in the presence of hyperglycemia (correction bolus). Rapid acting insulin analogs are used in CSII due to their rapid onset and short duration of action.

PATIENT SELECTION

Insulin pumps are indicated in children with inadequate glycemic control despite multiple daily injections. They are particularly helpful under following circumstances:

1. Infants and toddlers with erratic eating habits
2. Recurrent unpredictable hypoglycemia
3. Active life style with inconsistent meal times and levels of physical activity
4. Excessive glycemic excursions

Careful patient selection is mandatory for successful CSII therapy. Parents should be counseled that insulin pumps are not quick fix solutions for diabetes and the commitment required is much greater for pumps than that for intermittent injections. Thus a family finding it difficult to manage with split-mix regimen is extremely unlikely to succeed with insulin pumps. Another major limitation of pump therapy is the cost (approximately Rs 1.5 lakhs at initiation and Rs 5,000 per month at the time of writing).

Pre-requisites for initiating insulin pump treatment

Before starting insulin pump therapy, it is important to ensure the following basics:

1. Motivation on the part of the child and family.
2. Willingness to perform a minimum of four blood glucose measurements every day.
3. A good knowledge of carbohydrate counting and glycemic index.
4. An understanding of sick day and hyperglycemia management
5. Availability of a center with expertise in initiation and management of insulin pumps.

INITIATION OF PUMP THERAPY

Initiation of insulin pump therapy requires intense education of the child and family spread over multiple sessions. Close review of blood glucose logs by health professionals during the first couple of weeks is highly recommended. Continuous blood glucose monitoring (CGM) could be very helpful during this period (See Chapter 16).

Patient education

A comprehensive review of patient and family's knowledge about diabetes should be undertaken. Following issues specific for insulin pumps need to be stressed.

- Pump functions – Different modes, setting of basal rates, retrieval of data
- Technique of catheter insertion
- Carbohydrate counting
- Calculation factors
- Management during sick day and exercise
- Management of hyperglycemia.

INITIATION OF INSULIN TREATMENT

The total daily dose of insulin should be reduced by 20% while starting on insulin pump. The calculation of basal dose, insulin to carbohydrate ratio and correction factor is based on the total daily dose as highlighted below.

Basal dose – Total daily basal dose should be 40-50% of the total daily dose (TDD). This should initially be evenly distributed throughout the day. This is then modified according to premeal blood glucose levels in quantum of 10%. Subsequently different basal rates may be required for different periods of the day.

Lower basal rates are usually required in the late evening / midnight (between 8 PM and 2 AM) and during the day (between 10 AM and 4 PM). Higher basal rates are often needed in the early evening (from 4 PM to 8 PM) and morning hours (from 2 AM to 10 AM). Many prepubertal children need a higher basal rate late in the evening (9 PM to 12 midnight).

Bolus dose – The dose of meal bolus is determined by the estimated carbohydrate content of the meal and pre-meal blood glucose level. The meal bolus can be given as a linear dose (all insulin released immediately), square wave (insulin released over a time period of 30-60 minutes) or a combination of both. Square wave bolus is recommended for a high fat meal high fat, while the linear dose is the indicated for a high glycemic index meal.

Insulin to carbohydrate ratio represents the amount of carbohydrate (in grams) covered by 1 unit of insulin. This is estimated by dividing 500 by the total daily dose of insulin. Higher insulin to carbohydrate ratio is recommended for young children while lower levels may be required for adolescents.

Insulin to carbohydrate ratio = 500 ÷ Total daily dose of insulin g / unit

Correction bolus is determined based on *insulin sensitivity (correction factor)*. This provides information about the amount of blood glucose (in mg / dL) lowered by 1 unit of insulin.

Correction factor = 1700 ÷ Total daily dose of insulin mg / dL / unit

The dose of meal bolus is calculated as below.

$$\text{Meal bolus} = \frac{\text{Anticipated carbohydrate intake (g)}}{\text{Insulin to carbohydrate ratio}} + \frac{\text{Blood glucose} - 180}{\text{Correction factor}}$$

The correction factor can also be used to estimate a negative correction in the presence of hypoglycemia (in a patient on 50 units of insulin a day, giving 1 unit less at meal times should allow the blood glucose to rise by 36 mg/dL). Correction bolus should also consider the amount of *residual insulin* which represents the amount of remaining insulin of the bolus. This is determined by the assumption that 30% of insulin bolus is used up every hour.

In most pumps, these formulae are loaded by the health care professional. The patient only needs to feed the carbohydrate count and blood glucose levels and the calculation is performed by the insulin pump.

FOLLOW-UP

Follow-up of children on insulin pump treatment should include close monitoring of insulin pump sites and skin for any evidence of infection. Blood glucose records should be reviewed and the dose of insulin adjusted. Total daily dose, basal dose, bolus dose and number and amount of correctional boluses should be reviewed. While changing the total daily dose the correction factors and insulin to carbohydrate ratio should be appropriately adjusted. Patients should be informed about the need for careful monitoring and dose adjustments, on a regular basis.

DOSE MODIFICATIONS

Glucose monitoring should be done at least four times a day (pre-meals and bed time). More frequent monitoring may be required in children with poor control. The basal rate is adjusted according to pre meal blood glucose levels. Post meal blood glucose provides information about the appropriateness of meal bolus. Insulin to carbohydrate ratio should be reduced in children with persistent post-meal hyperglycemia.

HYPERGLYCEMIA MANAGEMENT

Careful management of hyperglycemia is mandatory to prevent the development of DKA in children on insulin pumps. This is important as insulin pumps deliver rapid acting insulin only, with no cover of basal insulin. Thus even small interruptions in insulin pump infusion can lead to the development of DKA. All children on insulin pump should therefore stock syringe-vial/pens of short/rapid acting insulin. Correctional insulin boluses are required if blood sugar is more than 180 mg/dL. Ketones (urine or blood) should be checked in children with blood glucose more than 270 mg/dL. The pump should not be used to correct

hyperglycemia when ketones are present and insulin should be given via pen or syringe. In the absence of ketones single correctional bolus could be given by the pump as illustrated below.

$$\text{Dose} = \frac{\text{Blood glucose mg/dL} - 180}{\text{Correction factor}} - \text{Residual insulin}$$

Individuals with persistent hyperglycemia 1 hour after the bolus should receive short or rapid acting insulin using a pen or syringe (0.25 unit/kg). The dose of rapid acting analog should be repeated every 4 hours (6 hours for short acting insulin) till the pump failure has been corrected. The pump should be carefully examined for battery status, the amount of insulin in the reservoir, the site and the patency of the catheter. The catheter should be removed and new tubing should be inserted if these measures are unsuccessful.

ADVANTAGES

Insulin pumps are associated with better glycemic control, lower insulin dose resulting in reduced hypoglycemia and weight gain and greater flexibility in life style. A meta-analysis of 12 randomised controlled trials , mainly in adults but with some adolescents, reported that pump patients had lower mean HbA1c by 0.51% and lower insulin requirements by 14% compared to patients on optimized insulin injections. Overall, hypoglycemia is much less frequent with pumps than in intensive injection regimens. Observational studies have reported significant improvements in HbA1c, reduction in hypoglycemia and higher satisfaction. The capability of insulin pump to react to real time changes in blood glucose (closed loop system) is expected to provide significant advancement in the insulin treatment.

DISADVANTAGES

High cost is an important limitation in the use of insulin pump. The approximate cost of insulin pump is Rs 1.5 lakh at initiation with approximately Rs 5000 monthly expenses on consumables and insulin. There is also a need for close monitoring of blood glucose to avoid hypoglycemia and hyperglycemia. The risk of development of DKA with pump dysfunction should also be considered.

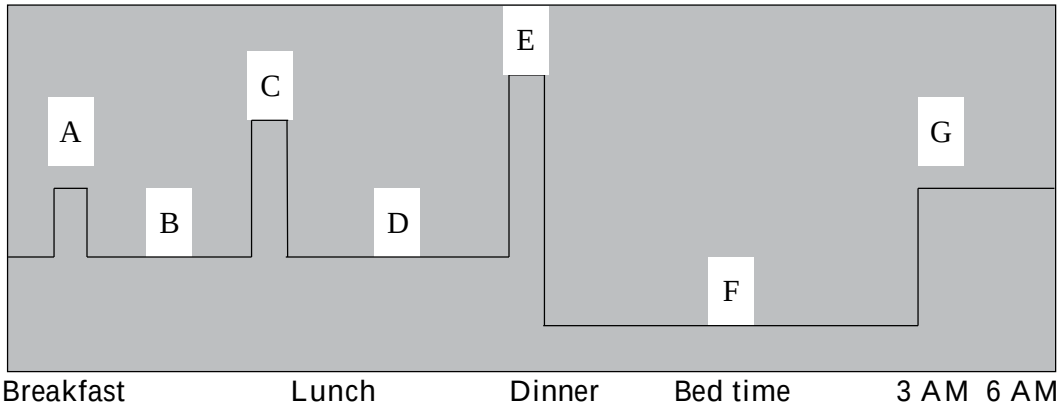

Figure 1. Continuous subcutaneous insulin infusion. Rapid acting insulin is continuously infused with intermittent meal boluses using an insulin pump. Initially basal insulin (40-50% of insulin dose) is distributed evenly over 24 hours. Insulin boluses are given before each meal according to premeal blood glucose and carbohydrate content of the meal. In this example, pre-breakfast bolus A has been adjusted downwards to account for a very small breakfast the child eats before school. The pre-dinner bolus E has been adjusted upward compared to the pre-lunch bolus C, as his pre-dinner blood sugar was high. His basal rate for the night, F, has been adjusted lower, to prevent midnight hypoglycemia. The basal rate for the early hours of the morning, G, has been programmed higher, to prevent dawn phenomenon related hyperglycemia.

ILLUSTRATIVE CALCULATIONS

Insulin plan for a child on split-mix regimen on 50 units insulin per day.

- **Initial calculations**
  - Total daily dose on subcutaneous insulin = 50 units
  - Total daily dose on insulin pump (reduce dose by 20%)= 50 – 10 = 40 units
  - Total daily basal dose (50% of daily dose) = 20 units
  - Initial hourly basal insulin rate = 20 ÷ 24 = 0.8 unit/hour
  - Insulin to carbohydrate ratio = 500 ÷ 40 = 12.5 g/unit
  - Correction factor = 1700 ÷ 40 = 42 mg/dL/unit
- **Meal bolus**
  - ***Parameters***
    - Pre-meal blood glucose = 270 mg/dL
    - Anticipated carbohydrate intake = 75 g

- ***Calculation***
  - Insulin required to correct hyperglycemia = (270 – 180) ÷ 36 = 2.5 units
  - Insulin required for carbohydrate intake = 75 ÷ 12.5 = 6 units
  - Bolus = Correction factor + Correction = 6 + 2.5 = 8.5 units

- **Correction bolus**
  - ***Parameters***
    - Blood glucose two hour post-meal = 305 mg/dL
    - Pre-meal insulin 5 units
  - ***Calculation***
    - *Residual insulin* – 30% used per hour (2 units remaining at two hours)
    - *Correction dose* = (305 – 180) ÷ 42 = 3 units
    - *Correction required* = (3 – 2) = 1 unit

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CONTINUOUS BLOOD GLUCOSE MONITORING

Anurag Bajpai

SUMMARY

- Continuous glucose monitoring systems (CGMS) measure interstitial fluid glucose continuously. By calibrating the system with 2 to 4 capillary BG values, continuous "blood glucose" values can be read off without extra pricks.
- They are indicated in children with uncontrolled diabetes and significant glycemic excursions.
- Real time glucose monitoring would be of help in preempting and preventing diabetic emergencies like severe hypoglycemia and DKA.

Regular self blood glucose monitoring is pivotal for successful management of children with diabetes mellitus. Intermittent glucose monitoring by glucometers provides only a limited glimpse of blood glucose profile and frequently misses asymptomatic hypoglycemia and overnight glycemic excursions. These limitations led to the development of continuous blood glucose monitoring (CGM) systems.

CGM is especially helpful in patients with erratic glycemic control and during initiation and continuation of pump treatment. They also help in identifying asymptomatic hypoglycemia and the cause of morning hyperglycemia (Dawn phenomenon versus Somogyi effect).

Both invasive and non-invasive CGM systems are available.

INVASIVE CGM

These systems measure interstitial blood glucose via an indwelling sensor in the subcutaneous tissue of the abdomen or buttocks. Three to 4 capillary BG measurements are performed daily and used to calibrate the CGM instrument, which therefore can equate the measured interstitial glucose reading to blood glucose readings. The systems commonly used for short term retrospective analysis (Medtronic MiniMed CGMS) make measurements over 72 hours, which are then downloaded onto the workstation computer at the doctor's office and the BG trends of the 72 hour period examined.

Real time continuous glucose monitoring (RT-CGM) systems are also available that provide continuous information about "blood glucose" (hence called "real time" which can be seen by the patient and used to execute changes in insulin or

food). They are also equipped with alarms to indicate rapid decrease or increase in blood glucose levels to preempt the development of hypoglycemia and diabetic ketoacidosis.

NON-INVASIVE CGM

Electrochemical enzyme sensor. This device is worn like a wristwatch (GlucoWatch Biographer). Glucose is extracted non-invasively via reverse iontophoresis for collection in a gel disc biosensor.

Infrared spectroscopy. Infrared spectroscopy technology is also being developed to measure blood glucose non-invasively.

ADVANTAGES

CGM is superior to intermittent glucose monitoring in the identification of post-meal hyperglycemia and asymptomatic hypoglycemia. It is a useful adjunct to pump therapy. Recent studies have shown improved glycemic control and higher patient satisfaction with CGM use in children on insulin pumps.

DISADVANTAGES

These systems are relatively imprecise and need to be validated with 3 – 4 capillary blood glucose measurements per day. Otherwise, their only disadvantage is their high cost.

CGM systems represent significant advances in the management of children with DM. Further innovations and improved precision of these systems in future are expected to result in much tighter glycemic control without the risk of hypoglycemia. These efforts are expected to culminate in the development of a closed loop system, where blood glucose measurements by RT CGM drive the insulin pump, which acts as an artificial β cell.

TRAVEL AND HOLIDAYS

Aspi J. Irani

SUMMARY

- Before planning a long journey, a check up is advisable.
- Facilities for medication, food, emergencies, should be found out prior to travel.
- Cool transport of insulin, general non-diabetes related medication, food, clean footwear are some items whose availability should be ensured.
- Extra exercise may necessitate decrease in doses
- Air travel has a set of precautions including letters to be carried and planning for changing time zones.

There is no restriction on travel for children with T1DM; however, several precautions need to be taken before and during a long journey. Careful planning is essential to make travel safe and trouble free.

PREPARATION BEFORE DEPARTURE

Planning should begin well in advance. The child with diabetes must undergo a detailed health check-up to detect and treat any problems that may need medical attention. One should ensure that diabetes is adequately controlled and education in self management of diabetes must be reinforced. Necessary vaccines for travel to a particular country must be administered as early as possible.

The patient should be provided with:

- Clear, detailed, written guidelines on management of hypoglycemia and sick days.
- Contact numbers of members of the medical team for telephonic advice in case of any emergency.
- Contact details of a doctor specialized in childhood diabetes, in the area or country that is being visited.
- A letter explaining the medical condition and treatment needs for the reference of the physician who may be consulted during the trip.
- A prescription for insulin in case the patient runs out of stock during the trip.

Patients must purchase an extra stock of all diabetes related supplies. These should be distributed in two separate bags. They should be carried in a sturdy case that can be placed in the bags in such a way that there is no risk of damage.

If traveling by air, these supplies should be carried in hand, preferably distributed in two plastic bags, separate from the hand baggage. A bag for medical supplies and equipments would not be counted as carry-on luggage. The doctor's formal prescription and the chemist's original bill (both tallying with the medical supplies being carried) must also be available for security check at airports.

Insulin may be carried in insulated containers or cool packs or in a thermos that has been pre-cooled; but one must ensure that the insulin does not freeze.

The patient should also take along:

- A pair of comfortable shoes and foot care products including creams and bandages.
- Emergency drugs for non-specific ailments (diarrhea, vomiting and fever).
- A diabetes identification card translated in the local language, if visiting a different state in India or a foreign land.
- A few plastic pouches containing 3-4 teaspoonful of powdered sugar.
- Food: in India, it may not be possible to buy safe food everywhere, and the bus/train/flight may often be late.

The patient must learn some important phrases in the local language of the city or country being visited, to make it possible to convey messages for getting medical help and for ordering meals (e.g. "I have diabetes", "I am experiencing a hypo", "I need sugar", and "I need insulin" and so on).

SECURITY CHECKS AT AIRPORTS

The security personnel at the airport should be informed at the outset that the child has diabetes.

It is necessary to furnish a detailed medical prescription stating that the child has T1DM and needs to carry life-saving supplies including insulin, injection devices; blood glucose meter and test strips; finger pricking devices; glucagon kit; urine ketone strips; alcohol swabs; sharps disposable containers; eatables that do not need refrigeration and in selected cases, an insulin pump.

One must ensure that the original pharmaceutical labels are retained on the insulin vials and the manufacturers' labels are intact on all the other equipments and materials. The glucagon kit should also be carried in the original box.

PRECAUTIONS DURING A FLIGHT

Insulin should never be kept in check-in luggage as temperature in the luggage hold is not regulated and hence there is risk of freezing or overheating.

In the aircraft an aisle seat would be preferred as it gives easy access to the toilet as also to insulin stored in carry-on case.

The flight attendant or at least one other person on the flight and seated nearby should be informed that the patient has diabetes.

On a long journey, the patient should get up and move about every hour or so to prevent deep vein thrombosis. The patient should drink plenty of liquids to remain well hydrated. Alcoholic drinks and drinks containing caffeine should be avoided.

Blood glucose should be checked every 4-6 hours during the journey.

When in flight there is no need to inject air or one may need to inject only half the amount of air in the insulin vial.

PRECAUTIONS AT DESTINATION

Blood glucose levels are likely to be lower on vacations due to reduced stress, more activity and different types of meals. For this reason, frequent blood glucose tests and knowledge of dose adjustments is important.

All the diabetes supplies must be carried in a back-pack when on a day's sightseeing trip or outing. One should also carry enough drinking water.

A diabetes identification card must be kept in the child's pocket at all times along with a plastic pouch containing powdered sugar. The card should be translated in the local language if visiting a different state in India or a foreign land. This card may also help in getting priority in queues in amusement parks and during other such outings.

If at all insulin needs to be purchased in a foreign country, it should be noted that in many countries insulins may be available only in 100 IU/ml strength.

INSULIN DOSE ADJUSTMENTS WHEN CROSSING TIME ZONES

The detailed itinerary with the timings of departure and arrival at various destinations, duration of each journey and differences in time between the places to be visited should be available.

Adjusting insulin dose and timings becomes necessary when crossing more than 5 time zones during eastward or westward travel. With eastward travel the day becomes shorter and with westward travel it becomes longer.

During long journeys patients must keep their wristwatch unadjusted to display the time at the place of departure till the beginning of the first full day at the destination. This will help them understand better when insulin and meals are due.

Adjusting insulin dose and timings is easier if the patient is on a basal-bolus regimen with insulin analogs (or on the insulin pump) rather than on the split-mix regimen.

In a patient on a basal-bolus regimen with glargine (as basal) and either regular insulin or a rapid acting analog (as bolus): During a long journey eastward or westward across multiple time zones, the basal insulin glargine can be continued at the corresponding time at the place of arrival. The bolus doses should be taken as usual before each meal in an amount calculated from the carbohydrate content of each meal.

In a patient on the split-mix regimen – when traveling westward, the day becomes longer. To cover meals during the extra hours gained (and after the action of the insulin taken before departure wears off), supplements of rapid or short acting insulin would need to be taken once in 4-6 hours. The patient can switch back to the normal routine on the next morning (local time) after arrival. Till then, it is advisable to keep the watch displaying the time at the place of departure.

In a patient on the split-mix regimen – when traveling eastward, the day is shortened. Before or soon after departure the patient can take the usual morning or evening dose (as the case may be). 10-12 hours later, he/she can take the next usual full dose of regular insulin (to cover a meal) with half or two-third of the usual NPH dose (since that segment of the day will be shorter). The remaining one-third or half of NPH (along with the full dose of regular insulin) can be added on to next 10-12 hourly dose. From the second morning of arrival, at the local time, the patient can start taking the routine insulin doses. Till this time, the patient must keep his watch unadjusted to display the time of the departure point.

Another approach is to take only regular insulin every 4 hours till the body adjusts to the new schedule.

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DIABETES CAMPS

Aspi J. Irani

Residential camps wherein children and adolescents with diabetes, their parents, and the medical team stay together for 3-4 days, should be an essential and regular part of the diabetes management protocol.

The chief aim of the camps in India has been to bring together the patients and the medical team in a relaxed atmosphere, for group education in diabetes self management and to discuss and solve their psychosocial problems.

There are some differences in priorities between the camps conducted in the western countries and those conducted so far in India. The primary stress abroad is on providing children with diabetes a safe environment to participate in challenging physical activities under guidance and supervision.

The first residential camp ever for children with diabetes mellitus was conducted by Dr. Leonard F. C. Wendt near Detroit in the USA in 1925. In India, the first camp was held in the year 1983 at Khandala, a hill station near Mumbai, by the Juvenile Diabetes Foundation, Maharashtra Chapter.

The residential camps should be supplemented with "Day Camps" and "Adventure Camps".

THE NEED FOR CAMPS

T1DM is the only chronic childhood disease in which the patients have to play the key role in day to day management. Patients must learn to inject insulin and test blood glucose and urine ketones. They should have a sound knowledge of meal planning and activity planning. They need to be well versed with the prevention, early recognition and first aid management of diabetic ketoacidosis and hypoglycemia. Finally, they must know how to integrate this information into their daily lifestyle.

This elaborate and practical education cannot be imparted in a busy clinic: it requires plenty of time and a team effort. It is best imparted when the educators and the patients stay together for a few days in a relaxed atmosphere.

Children with diabetes and their families are invariably under tremendous emotional stress. There is shock, resentment, anger, guilt, the "why only us?" feeling, false hopes, anxieties about the future, a feeling of hopelessness and of course, financial worries. When a large number of children and parents come

together and discuss their problems in the presence of a psychiatrist or clinical psychologist who acts as a catalyst, it can work wonders with their stress levels.

Siblings too suffer because of the restrictions imposed on the family's eating habits and lifestyle, the added stresses in the house and the extra attention received by the child with diabetes. Grandparents tend to have their own outdated views on what is good for the child and what is not. In joint families, this can lead to conflicts and may pose major hurdles. In selective cases, it is important to invite siblings and grandparents to attend the camp.

SELECTION OF THE CAMP SITE

The camp site should be a holiday resort so as to provide a relaxed atmosphere. The entire premises should be booked so that campers can be spared from prying eyes and awkward questions. It should be easily accessible by road. It should be comfortable with sufficient number of bathrooms and adequate water supply so that proceedings can begin on time each day. A large playground is a must so that children can have fun. There should be a minimum of two halls to conduct educational sessions. There should be facilities for cooking food suitable for the campers. All these requirements should be available at a reasonable cost. The same place should preferably be available every year so that time is not lost in adjusting to a new setting.

SUMMER CAMPS OR WINTER CAMPS?

In our country, winter camps are preferred as the weather is pleasant and there is usually no water shortage at the holiday resorts. Further, families often prefer to visit their native place or go on long vacations during the long summer holidays.

WHO SHOULD ATTEND THE CAMPS?

Children and adolescents with diabetes and their parents must attend the camp. Adolescents with previous camp experience may attend alone to enable them develop a sense of independence. It is a good idea to take along siblings and grandparents in selected cases.

A few married adults with onset of diabetes dating back to childhood must be a part of the camp: those who are doing very well will serve as role models and a source of inspiration; those who are not doing so well and regret their initial casual approach to diabetes management will serve as a subtle warning.

The medical team should include the doctors (child diabetologist and psychiatrist), nutritionists, clinical psychologists, diabetes educators, play therapists (to keep the little children busy during the educational sessions) and volunteers.

CAMP ACTIVITIES

Camp activities should include education in self management of diabetes by means of lectures, demonstrations, educational games and competitions; informal psychotherapy and "problem solving" sessions, besides games and entertainment programs.

To perfect injection and testing techniques: Children should take their insulin injections and check urine ketones and blood glucose in a common hall under supervision. This helps them to perfect their techniques, learn from mistakes of others and also gives the newer patients the self confidence to inject themselves or prick themselves for checking blood glucose.

Interactive lecture sessions: Sessions on record keeping, insulin dose adjustments, insulin supplements, meal planning, hypoglycemia and sick day management should be age appropriate. These should be interactive sessions rather than monologues.

Meal planning education: It is best to have a nutritionist explain before each camp meal the nutritional properties of the various items being served, the best methods of cooking and other aspects of healthy eating. Before play time, patients are given a snack and an explanation as to why it is needed and what would be appropriate for a given level and duration of anticipated activity. Those on the split-mix regimen can be taught the use of "exchange lists" whereas sessions on "carbohydrate counting" should be conducted for those on basal-bolus regimens and insulin pumps.

***Camp exhibition*:** All medications, equipments and gadgets used in management of T1DM along with relevant information pertaining to them can be displayed. There should also be exhibits showing the food preferences for prevention of exercise induced hypoglycemia and nocturnal hypoglycemia, treatment of hypoglycemia and sick day options.

Educational games and competitions: Children can be asked to enact plays in which all practical aspects of hypoglycemia and sick day management are woven into a story. Quiz contests between parents and children or between groups of children can be very entertaining and educational.

"Tackling the disturbed mind": The issues to be discussed include:

- What is the cause of diabetes?
- Does diabetes impact the educational capabilities of the child?
- What should be told to the school authorities?
- How does one reveal the diabetes state to peers?

- What sort of jobs would be most suitable?
- How difficult would it be to obtain or maintain a job?
- What are the chances of finding a life partner and should one reveal the diabetes state before finalizing marriage?
- What problems can arise during pregnancy and what are the risks to offsprings?
- What is the importance of good control?
- What are the long term complications and can these be prevented or arrested if detected early?
- What is the expected life span?
- Will diabetes ever be curable?
- How can the childhood diabetes group work towards bringing down the cost of diabetes management?

These sessions may be conducted separately for the adolescents and for the parents with a combined session before the termination of the camp.

Interaction with sibling and grandparents: They should be taught how to inject insulin and glucagon, how to measure blood glucose and the early recognition and first aid management of hypoglycemia. The grandparents need to be convinced about the various scientific aspects of diabetes management and an attempt should be made to enlist their cooperation. Siblings should receive a patient hearing and counselling with regard to the problems and difficulties they face because of the atmosphere in the house on account of the child with diabetes.

POST-CAMP BENEFITS

At the conclusion of the camp, the participants should have accepted that:

- T1DM cannot be cured but can and should be controlled well with insulin injections, meal planning, regular planned activity and SMBG.
- No other system of medicine has any effective treatment to offer.
- There is no basis for guilt for pricking the child often or imposing restrictions on the child's eating habits as these are essential for the child's long term good health.
- Patients should have acquired a better understanding of the disease and a thorough practical knowledge of its day to day management, so that they feel less confused and helpless.

- Having met so many others with the same problem, the feeling "why us" should be replaced with "I am not alone".
- Patients should establish enduring friendships which would be of mutual benefit in the long run.
- They should work together as a group to improve the lot of their children.
- They should be better placed to handle psychosocial pressures.
- Having met and interacted with seniors who are married and well settled in life, their anxieties about their own future should have been eliminated to a large extent. They should no longer feel inferior.

Adventure Hikes and Competitive Sports

Strenuous planned physical activities may not be possible during the 3-4 days of residential camps. However, adventure hikes and sports days should be separately organized to supplement these camps. This would serve the dual purpose of teaching children how to manage diabetes in such situations and at the same time give them the confidence that no physical activity is beyond them.

Day Camps

Day camps are less time consuming, more economical, and easier to plan and conduct. These should become a routine in centers which do not have facilities to organize residential camps.

Camp Research

The camp gives an ideal opportunity to conduct research as a large number of children and their families are accessible at one time.

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INFORMING THE SCHOOL AUTHORITIES

Aspi J. Irani

Children spend a large part of their day in school. Staff members and some close school mates of the child with T1DM should be familiar with the special needs of the child.

It is recommended that a social worker belonging to the medical team should meet the school authorities in person and also hand over written guidelines for care of the child or adolescent with T1DM.

The following messages need to be conveyed to the school authorities:

- T1DM is not a contagious disease. It is not caused by overeating or lack of physical activity or any other act of omission or commission on the part of the child or the family members.
- ***The child with diabetes needs to take 2-4 injections of insulin each day, check blood glucose, eat healthy food at fixed timings and take certain precautions prior to physical exercise.***
- A child with well controlled diabetes can lead a near normal life. The child with T1DM should not be treated differently from other children.
- ***Diabetes does not affect the academic performance, provided it is well controlled.*** Diabetes will not affect the extracurricular activities of the child, provided certain pre- and post-activity precautions are observed.
- The child with diabetes does need some special care and attention, but this must be provided in an unobtrusive manner.
- ***Teachers and close friends should be familiar with the symptoms of high blood glucose,*** in particular, polyuria and polydipsia. If the child frequently asks for permission to drink water or visit the rest room he/she should not be denied permission; however, the parents should be alerted as these are indicators of poor diabetes control.
- ***Teachers and close friends should be conversant with the early symptoms and the first aid management of hypoglycemia.*** If the child complains of hypoglycemia or is found to be drowsy, confused or behaving in an erratic manner, he/she should be promptly given 3 teaspoons of glucose powder or powdered sugar (which the child must carry in a plastic pouch in his/her

pocket at all times). This should be followed with a snack in the form of a fruit, sandwich or biscuits (which also the child should carry in his / her school bag at all times).

- ***Teachers must be aware that the child needs to eat on time;*** meals should never be skipped or delayed, even if for some reason the child needs to be detained in the school beyond routine timings.
- ***The child must be allowed to consume an extra snack*** before, and at times even after, unaccustomed physical activity.
- ***Child should be granted permission to check blood glucose,*** if he / she has been advised by the doctor to perform tests during school hours.
- ***Ideally the school should have a nurse*** who can administer and / or supervise the administration of a morning or afternoon dose of insulin (if indicated), check blood glucose (when needed) and administer a shot of glucagon (in case of severe hypoglycemia). Frequent communication between the nurse and the medical team can lead to improvement in control of diabetes.
- ***The staff at school must have the telephone numbers of the child's parents and medical team members in case of any emergency.***

DIABETES SELF MANAGEMENT PATIENT EDUCATION

Anurag Bajpai

SUMMARY

- Diabetes education is the cornerstone to successful management of children with T1DM.
- Centers caring for children with T1DM should develop written and structured program for 'Diabetes Self Management Patient Education'.
- The diabetes self management patient education program should be individualized according to the age, stage of diabetes, socioeconomic and educational status and cultural values of the patients and their families.
- Diabetes education team should at the minimum comprise of a diabetic educator and a dietician.
- No child with T1DM should be discharged from the hospital without the understanding of survival skills of insulin injection, blood glucose testing and hypoglycemia by the patient and the family.
- Diabetes self management patient educational material written in lay terms in local language should be provided to the family.
- Families should be encouraged to join patient support groups for T1DM, at enrolment.

'Diabetes Self Management Patient Education Program' is the cornerstone for success in the management of children with T1DM. The lack of ongoing assistance from diabetes support staff in resource-poor settings like India mandates greater empowerment of families with T1DM in self management. ***The education program should encompass all aspects of the disease and needs to be individualized according to the age, education, socio-economic status and cultural background of the patient.*** These guidelines aim to provide an overview of a diabetes self management education program for Indian children. They should be individualized as per the needs and resources of centers caring for children with diabetes.

AIMS

Diabetes self management education program aims to empower the child and the family in independent management of diabetes. The family should be trained to handle special circumstances and identify and correct acute complications especially, hypoglycemia and DKA. They should also understand the predisposing factors and measures to prevent short and long-term complications of the disease.

GUIDING PRINCIPLES

Diabetes self management education program is as much an art as science and requires immense patience on the part of the educating team. The program should include the child with diabetes and both the parents or caregivers.

Burdening of family with too much information at a time significantly limits patient retention. This should be avoided by giving education in a ***structured and phased*** manner***.***

The availability of written structured education program individualized to the center's needs ensures uniformity of the education program. Education handouts and/or leaflets written in local language should be provided to the families.

The program should be interactive and not didactic to ensure ongoing feedback.

The first few days following discharge are crucial given the significant changes in insulin requirement, nutrition and levels of physical activity. The families should therefore have ongoing access patient helpline to resolve these issues.

Children diagnosed at a young age should be re-educated at a later age to ensure adequate understanding of the disease.

PERSONEL AND DURATION

Diabetes education requires a multidisciplinary team involving the primary treating doctor (pediatrician or pediatric endocrinologist), diabetic educator, dietician and social worker. Diabetes educator forms the core of the team and provides a forum for interaction with other members of the team. The team should be modified according to the availability of resources but at the least should include a diabetes educator and a dietician.

The program should be spread over 3-4 days to provide ample time for understanding all the aspects of the disease.

FORMAT

The diagnosis of diabetes usually comes as a big shock to the family. Most

people think of diabetes as an adult disease and are not aware about T1DM. The prospect of life-long daily injections coupled with the guilt about the cause of the disease is quite disconcerting for the family. There is usually a strong urge to seek 'permanent cure' using alternate therapies. The initial contact with the family should be used to allay the fears and guilt of the parents and to emphasize that insulin is the only form of treatment for T1DM.

The diabetes self management educational program should be prioritized in to primary (essential survival skills; *'must know'*), secondary (*'shall know'*) and tertiary *('can know'*) levels. Enrollment in a patient support group and meeting with other diabetic families is particularly helpful at this time point.

Table 1 provides a summary of the different levels of diabetes self management education program. **Table 2** provides an overview of the structured day-wise format for a diabetes self management patient education program.

Primary Education (Must Know)

This covers the most important aspects essential for care of children with T1DM. ***No child should be discharged from medical facility without imparting these skills.***

- ***Disease***
  - Role of glucose and insulin in body and normal blood glucose levels.
  - The cause of disease (insulin deficiency) and symptoms.
  - Emphasis that diabetes is a life-long disease with numerous short and long-term complications.
  - Parent's guilt should be allayed by reassuring them that the disease was not caused by any act of commission or omission by the family.
  - Normal outcome is possible with good control. Examples of role models from different fields of society go a long way in this regard.
- ***Treatment***
  - Insulin is the only form of treatment.
  - Daily multiple injections are required throughout life.
  - No role of alternative medicines like oral antidiabetic drugs, homeopathy, ayurvedic or unani medicines.
- ***Practical skills***
  - Insulin storage (see Chapter 4)
  - Overview of different insulin concentrations in vials and syringes (U 40 and U 100)

- Self monitoring of blood glucose (SMBG)

- ***Nutrition***
  - Healthy feeding pattern
  - Meal plan – Frequent meals with mid-meal snacks

- ***Follow-up***
  - Honey-moon phase and the need for reducing insulin dose during this period
  - *Hypoglycemia* – Clinical features and treatment
  - *Sick day guidelines* – Never skip insulin during illness
  - Features of diabetic ketoacidosis

Secondary Education (Shall Know)

These aspects should be imparted to all the families.

- ***Disease***
  - Role of insulin and a brief overview of glucose homeostasis
  - Difference between type 1 and type 2 DM
  - Pathophysiology – Cause of T1DM
  - Long term complications of DM (nephropathy, neuropathy and cardiac disease)

- ***Treatment***
  - Forms and source of insulin
  - Time course of action of different insulins
  - Insulin injection devices

- ***Practical skills***
  - Insulin modifications
  - Insulin guidelines for sick day management
  - Anticipatory management of physical activity

- ***Nutrition***
  - Recommended dietary allowance (RDA) for macronutrients and calorie
  - Food exchanges
  - High fiber diet

- Culturally acceptable foods

- ***Follow-up***
  - Self monitoring –
    - Glucometer and log books
    - Glycemic goals
    - Ketone monitoring
  - Role of HbA1c in monitoring of sugar control
  - Prevention of hypoglycemia
  - Physical activity program
  - School planning and time sheet
  - Long term complications

Tertiary Level (Can Know)

This covers finer aspects of diabetes management and should be targeted to educated and highly motivated families and children.

- ***Disease***
  - Effects of insulin deficiency
  - No need for excessive restriction Classification of diabetes
  - Autoimmunity and its role in T1DM
  - Disease associations of T1DM (hypothyroidism and celiac disease)
- ***Treatment***
  - Insulin regimens
  - Overview of insulin pens and pumps
  - Newer insulins – Oral and inhaled insulins - status of research
  - Hope for the future- islet cell transplant, stem cell transplant
- ***Practical skills***
  - Glucagon injection for hypoglycemia
  - Proactive management of ketosis
  - Indications for hospitalization

TABLE 1. Levels of Diabetes Self Management Education

Category	*Primary*	*Secondary*	*Tertiary*
Disease	Life-long disease Normal outcome possible Allay guilt and reassure	Role of insulin T1DM vs. T2DM Pathophysiology Complications	Effects of insulin deficiency Classification of diabetes Autoimmunity Disease associations
Treatment	Insulin is the only treatment Daily injections No role for alternative medicines	Insulin preparations Time course Injection devices	Insulin regimens Insulin pens & pumps Newer insulins Hope for the future
Practical skills	Insulin storage Injection technique SMBG	Glycemic targets Insulin modifications Time sheet	Physical activity Ketone monitoring Glucagon injection
Nutrition	Healthy eating Avoid simple sugars Mid-meal snacks	RDA for age Food exchanges High fiber intake	Carbohydrate counting Insulin to carb ratio Glycemic index Eating out
Follow-up	Honey-moon phase Hypoglycemia Sick day guidelines	SMBG- Checking logs and meters Role of HbA1c Complication screen Physical activity	Diabetes diary and log DKA prevention CBGM

- ***Nutrition***
  - Carbohydrate counting and calorie content of common products
  - Glycemic index
  - Insulin to carbohydrate ratio for children on basal bolus and insulin pumps
  - Adjustments for eating out
- ***Follow-up***
  - Diabetes diaries and log
  - Annual complication screening
  - Continuous glucose monitoring systems
  - Planning for travel, examinations and camps

TABLE 2. Structured day wise format for Diabetes Self Management patient education

Day	*Disease*	*Treatment*	*Nutrition*	*Practical skills*
1	Role of insulin Life-long disease Allay guilt and reassure	Insulin is the only treatment No role for oral drugs	Healthy eating Frequent meals	Insulin storage Injection sites
2	Classification Complications Cause	Insulin regimens Site and rotation Injection devices	Age specific RDA Diet chart	Insulin mixing Insulin injection Time sheet
3	Hypoglycemia Sick day	Glycemic goals Dose adjustment	Food exchanges Glycemic index	Glucose testing Urine ketones
4	Feed back Education quiz	Honey-moon phase Practical guidelines	Carbohydrate count Insulin to carb ratio	DKA prevention Glucagon Diabetes log and diary

Diabetes education is the most important, though often neglected part of diabetes management of children. Formulation of standardized Diabetes Self Management Patient education module individually targeted to the centers needs is important to achieve this goal.

DIABETES IN TODDLERS

Aspi J. Irani

SUMMARY

- Toddlers present with more acute and severe symptoms of insulinopenia compared to older children.
- They eat unpredictably, hence hypoglycemia is a greater possibility.
- Repeated hypoglycemia to the developing brain must be avoided at all costs. Therefore the goals of therapy are relaxed for this age group, if so needed.
- The availability of glucagon at home is of greatest importance in this age group.

The term "toddler" refers to a child in the age group of 1 to 3 years, a small child who is just learning to walk and talk. In recent years there has been a spurt in incidence of T1DM in this age group. This section outlines some of the important aspects of diagnosis and management of diabetes in toddlers.

DIAGNOSIS

The diagnosis of T1DM is often missed till late in this age group. Awareness and a high index of suspicion are important for early diagnosis.

Diabetes must be suspected in any toddler presenting with:

- The classical triad of polyuria, polydipsia and polyphagia;
- Dehydration and polyuria;
- Weight loss and polyphagia; Kussumal's breathing ("air hunger") with normal findings on examination of respiratory and cardiovascular systems (due to metabolic acidosis);
- Candida dermatitis in diaper area, resistant to treatment.

INITIAL MANAGEMENT

At diagnosis, it is advisable to hospitalize the patient (even if non-ketotic) for a day or two to provide basic education in diabetes self management. One should arrange for the new family to be visited in the hospital or soon after discharge by a patient from the same locality to provide much needed emotional support and guidance in the early weeks after diagnosis. The latter should not only be well

versed in diabetes self management but also emotionally well adjusted.

INSULIN THERAPY

A split-mix regimen with 2 or 3 injections of insulin a day may be used in a toddler who has a predictable meal intake However, toddlers are often picky eaters, and it would be less stressful for the parents if a basal-bolus regimen is used. A rapid acting insulin analog can be given *after* the meal and in a dose based on the amount of carbohydrate consumed. Lispro insulin given after a meal has been shown to be as effective as when given before the meal and is more effective than pre-meal regular insulin. The basal insulin can be provided by either NPH insulin given once or twice a day or glargine insulin given in a single daily dose. For the basal insulin, glargine at bedtime has been shown to be superior to NPH insulin given twice a day.

Many centers have reported good results with use of the insulin pump (CSII) in the toddler age group: a significant drop in HbA1c, several fold reduction in episodes of hypoglycemia and greater confidence and independence in parents (reflected by reduction in parent contact with the medical team).

MEALS

Toddlers are fastidious eaters, and have a highly variable appetite from day to day. Rigid meal plans never work and have no role in a toddler with diabetes. A variety of foods should be offered at meal time, so that child is more likely to select an item. Food should be decorated well as eating is largely psychological. Forced feeding should be strictly avoided as this will only lead to food refusal. Parents must ensure that meal times are pleasant. Toddlers prefer self feeding. Parents should set limits on time allowed for a meal. “Out of bounds” dietary items should not be kept in the house to avoid temptation. Food should never be used as a reward.

PREVENTION OF HYPOGLYCEMIA AND MANAGEMENT GOALS

Severe and frequent hypoglycemia, below the age of 3 years, can lead to permanent cognitive, intellectual and learning defects. MRI scans of such children have shown a significant incidence of mesial temporal sclerosis (MTS), a defect that is never observed in normal children.

Recognition of hypoglycemia can be difficult in this age group. The toddler may become pale, cranky, start to sweat, or tremble, let out a particular cry, become clumsy, or develop a bluish tinge of lips or fingers. A temper tantrum may be the chief symptom of hypoglycemia.

Prevention of hypoglycemia is the most important aim of management in this age group. A delicate balance needs to be struck between what is desirable

(good but safe level of blood glucose) and what is practical to achieve. Higher target blood glucose of 110-220 mg/dL would seem appropriate in toddlers. The target HbA1c in this age group should be 8 to 8.5 %. In addition, it is important that the child should be leading a normal, happy childhood, and growing and developing normally.

GUIDELINES FOR INJECTIONS AND HOME BLOOD GLUCOSE MONITORING

Parents must adopt "matter of fact" approach when performing the unpleasant tasks of injecting insulin and checking blood glucose. They should be firm but gentle. Delaying tactics on part of the child and attempts to bargain must be ignored. Parents must ensure that insulin, glucometer, strips etc are ready before going to the child. The child should know when he/she is about to be injected so that he/she is not scared every time the parents approach. Injections should not be given to the child when in bed. Distractions such as television or songs can be used. Child should be allowed to participate in some routines such as choosing the blood glucose strip or the finger to prick. Parents should make it a point to display love for the child after giving the injection or a prick. All grown-up persons in the house should take turns to inject so that the child does not feel that one parent is causing all the pain; also the child can be managed in the absence of one or both parents.

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DIABETES IN ADOLESCENTS

Anju Virmani

SUMMARY

- Many aspects of adolescence impact diabetes management, often adversely.
- The presence of a chronic condition like diabetes places great demands on the psychology of the youngster.
- The special issues include physical and emotional changes, insulin resistance and glycemia, academic and career issues, privacy, confidentiality and freedom, and transition to adult care.

Adolescence is the period of transition from childhood to adulthood. There are numerous aspects of adolescence which impact upon diabetes management, often adversely. Likewise, the presence of a chronic condition like diabetes places great demands on the psychology of the youngster who is already going through a difficult period of his or her life. Recognition of these issues, and paying attention to them as the child with diabetes grows into an adult, will allow for smooth transition through these difficult years.

Some of these aspects are discussed below

- ***Physical changes:*** The adolescent growth spurt provides a significant proportion of the adult height of an individual, and linear growth may be adversely affected by poor glycemic control during this period.. Puberty may be delayed if glycemic control is poor. Body image assumes importance during adolescence and eating disorders may begin to manifest. Some adolescents, especially girls, realizing that poor control helps them lose weight, intentionally miss insulin doses.
- ***Glycemia and complications***: There is significant insulin resistance during adolescence. Thus higher insulin doses to the tune of 1.5 to 2 units/kg/day may be needed for about 2 to 3 years, and often a need for more frequent injections. All other risk factors including diabetes duration being the same, puberty gives a greater risk for microvascular complications. Thus, for children whose diabetes onset is during the adolescent period, complications screening is recommended after diabetes duration of just 2 years rather than 5 years.
- ***Mental and emotional changes***: Risk taking and mood swings are an integral

part of growing up. They reduce compliance with diabetes self care and worsen control. The adolescent's need for peer approval and to move away from the family also interfere with communication within the family, and add to the stress of this period.

- ***Social and cognitive development:*** This new maturity may mean that the young patient with diabetes realizes the full impact of diabetes upon the rest of his / her life, which may causes depression, denial, or other mental health problems. Social independence and development of self-esteem may be restricted by diabetes. The adolescent may need privacy (especially from parents) during examination and also history taking or discussion.
- ***Academic and career issues:*** These are worries for the adolescent, and are impacted, often negatively, by diabetes.
- ***Financial independence:*** This is delayed and reduced by diabetes. Many of them feel resentful of the financial burden diabetes imposes.
- ***Experimentation:*** The adolescent may try smoking, alcohol, other drugs, or sexual exposure, with a negative impact on general health as well as glycemic control.
- ***Transition of care:*** The diabetic adolescent is likely to be referred to an adult clinic, and may have a difficult time adjusting to the new caregivers and the more impersonal atmosphere of adult clinics.

Adolescents tend to have higher A1c levels in general, more frequent episodes of ketoacidosis as well as hypoglycemia.

The aim of the diabetes care team should be to provide care such that growth and physical and emotional development are normal, complications reduced, and discrimination avoided. Ideally, transition programs should be made to help the adolescent move from the pediatric to the adult clinic. The age at which this transition should be made should depend on the maturity and wishes of the patient and of the family. In actual practice, the unfortunate lack of enough trained pediatric endocrinologists has meant that many concerns are unmet, and patients move randomly to whatever service is available and most convenient, rather than ideal.

The adolescent should be offered:

1. ***Physical privacy*** during history or examination, with adequate chaperons if relevant. Consultations in large OPDs can be very embarrassing for the young person.
2. ***Personal privacy*** - some time for direct talking to the doctor / team member without the parents in the room.

3. ***Advice relevant to changing needs***, e.g. adequate protein, iron, calcium and vitamin D intake.

4. ***Monitoring of growth and puberty*** to ensure they are progressing at a normal pace, and advice about handling pubertal changes.

5. Explanation that ***higher insulin doses*** may be needed to compensate for the insulin resistance of puberty. Some girls may do well with small doses of metformin, especially if they develop obesity and / or PCOD.

6. Encouragement to take ***more frequent injections*** or, if the financial situation permits and other factors are conducive, change over to the insulin pump, to increase flexibility in life style, which is very important at this age.

7. ***Warnings*** about tackling and preventing acute and chronic complications.

8. ***Monitoring*** of blood pressure, eye changes, lipids, microalbuminuria, at regular intervals to enable early detection of microvascular complications.

9. Sensitivity to the possibility of ***eating disorders***, and ***risk taking behavior***, and ongoing counseling for preventing and / or solving these problems.

10. Explicit age- and maturity- appropriate discussion on how to cope with ***peer pressure*** to experiment with smoking, alcohol, other drugs, or sexual exposure, and advice on contraception if they are (or likely to be) sexually active. They should be discouraged from smoking, binge drinking, or taking drugs from an early age.

11. ***Complete confidentiality when giving advice on contraception.*** Indian families are often unwilling to bring up the topic of sexuality or contraception, so extreme care and sensitivity are needed. Giving contraceptive and other such advice without parental involvement is legally a grey area for adolescents below the age of 18 years, but may be crucial.

12. Encouragement to the family members to give adolescents the ***greater freedom*** they need, while keeping the channels of communication open, no matter how difficult the adolescent gets. Break down of communication could mean even worse compliance and even total loss to follow up.

13. Discussion about ***driving*** involving the family. They must fully understand the importance of being able to handle hypoglycemia (suspecting, testing, treating, preventing), as even mild hypos can disrupt driving. They must be aware of the very high risk of drinking and driving, more so with hypoglycemia, for accidents, including fatal accidents.

14. Opportunities to ***meet older persons*** with type 1 diabetes, so they can realize that careers, marriage, parenthood, etc. are all possible with diabetes.

15. ***Career counseling*** so they can maximize their potential, and allow them to achieve financial independence as well as self esteem. Some career options are not open to persons with diabetes. Unfortunately, at present diabetes debars one from all government jobs in India.
16. Frank discussion of what the issues bothering the patient are, e.g. looks, sexuality, etc. and understanding these from the patient's perspective.
17. Empathy along with firmness as regards compromises in care, e.g. if the adolescent is not willing to test often, or if the intake of junk food goes up.
18. Involvement of the adult physicians, counselors, gynecologists, and other medical personnel they may need to see, so that transition is easier and smoother.
19. Clear instructions on which emergency service to contact in case of need.

THE FUTURE

Anurag Bajpai

SUMMARY

- A structured program should be developed for transition of adolescents with T1DM to adult care.
- Young adults with T1DM should be counseled against risk taking behaviors like smoking and consumption of alcohol and illicit drugs.
- Counseling on reproductive health, academics and career are integral to management of young adults with T1DM.
- Although the patients should be educated about the latest developments in the treatment of diabetes, the need for long term insulin should be emphasized.

The future of T1DM as well as that of children affected with the condition appears bright thanks to the tremendous advances in management of the condition. There are ever expanding hopes for disease prevention, near physiological insulin replacement, minimally invasive insulin delivery systems and potential cure. However despite this leap in the science of diabetes, the art of managing children with diabetes remains a challenge. Central to this is the need to tailor the management according to the changing requirements of different phases of life. This section elaborates the key aspects of post- adolescent management of T1DM and makes an attempt to gaze through the crystal ball of T1DM.

THE FUTURE OF CHILD WITH T1DM

T1DM is a life-altering disease affecting all aspects of life. Advances in management have however provided the opportunity of achieving lifetime goals for children affected with the condition. This requires ongoing interaction with the patient with a continuing age-appropriate education program.

Ongoing medical care

Continuation of quality medical care is central to successful outcome of young adults with T1DM. *The transition from family oriented pediatric care to treatment targeted adult care is often disconcerting and frequently results in the discontinuation of medical care.* The transition should therefore happen only after the achievement of physical, social and psychological maturity by the young adult. *Stabilization of*

insulin regimen and screening for complications should be performed prior to transfer to adult care. Transition provides an opportunity for re-education of the young adult about self management of diabetes. Adult health care providers willing to and equipped for the management of young adults with T1DM should be identified. Shared care by both pediatric and adult health care providers should be done in the initial phase.

Academics

Children with T1DM should be encouraged to achieve their full academic potential. This requires a close interaction between health care provider, parents and the educational institution. *Information about the disease, special needs of the child and identification and management of hypoglycemia should be provided to the school authorities.* In particular, the need for carrying snacks and glucometer during examination should be emphasized. Physiological regimens (basal-bolus or insulin pump) should be considered in children with unpredictable lifestyle and eating patterns.

Career

Occupational counseling is integral to T1DM management. Children should be informed at an early stage about careers such as armed forces, commercial driving, pilot and fire fighting where T1DM may be considered an impediment. Letter of support may be required to allay the anxieties of the employers.

Risk taking behaviors

Health care providers should strive to educate patient and family about these behaviours.. Smoking increases the risk of microvascular complications and should be discouraged. The adverse effects of alcohol consumption including hypoglycemia and dyslipidemia should be addressed. Consumption of illicit drugs should be identified and rectified.

Reproductive health

Reproductive health forms an important aspect of long term care for T1DM. *The young adults should be educated about methods of prevention of reproductive tract infections and unwanted pregnancy.* Contraceptive needs should be addressed in a confidential and non-judgmental manner. Barrier contraception should be encouraged as it in addition provides protection from reproductive tract infections. Oral contraceptives are associated with adverse metabolic effects and increased risk of microvascular complications. The risk is however lower for oral contraceptives with low estrogen content. Intrauterine device and progesterone implant should be avoided due to the risk of pelvic inflammatory disease and adverse metabolic effects respectively.

Girls should be reassured that outcome of pregnancy is very good provided all the pre-pregnancy care is taken. *The need for careful pre-pregnancy planning with good glycemic control, folic acid supplementation and discontinuation of ACE inhibitors need to be emphasized to girls with T1DM.*

FUTURE OF T1DM

Living with T1DM is not the same as a decade ago and would not be the same a decade later. The changes in the management of the condition are happening at a brisk pace and it is important for physicians caring for T1DM to keep abreast with them. Some of these advances are highlighted below.

Hope for prevention

The efforts for prevention of T1DM have completed a full circle. Large studies have failed to show benefit of oral and subcutaneous insulin, nicotinamide and immunosuppressive agents in preventing the development of T1DM. The outcome of ongoing research using inhaled insulin, vitamin D analogs, delayed cow milk exposure and newer immunosuppressant is also far from encouraging.

Hope for monitoring

Severe hypoglycemia remains a major hindrance in achieving good glycemic control. Continuous glucose monitoring with real time sensors have added a new dimension to T1DM management. These systems with in-built alarms provide the opportunity to achieve near normal blood glucose levels while avoiding hypoglycemia. While their use is currently limited by high cost, they are expected to play an important role in future. Prediction of long term complications using advanced glycation products is expected to provide opportunity to prevent and treat them at an early stage.

Hope for treatment

The aim of T1DM management is to provide near physiological insulin replacement using minimally invasive measures. Insulin analogs and continuous subcutaneous infusion of insulin have gone a long way in achieving this goal. The need for parental administration however represents a formidable barrier. Inhaled insulin, considered a big breakthrough in T1DM management, was withdrawn due to market considerations. *Phase III trials of oral insulin IN-105 are ongoing and if successful would be a welcome development for children with T1DM. Ultralong acting insulin analogs injected once a week are in the pipeline and would further reduce the burden of T1DM.* Finally the development of sensor augmented pump therapy is expected to achieve the long sought goal of developing artificial pancreas.

Hope for cure

Given the need for lifelong treatment in T1DM, it is only expected that most

patients seek permanent cure from the malady. Unfortunately no such cure is available at the moment. *The efforts at developing cure for T1DM are directed towards reversing the autoimmune process or restoration of â cell mass.* Immunosuppressive agents (steroids, cyclosporine A, azathioprine, anti-thymocyte globulin and anti-CD3 antibody) have resulted in only partial and transient response. Moreover these strategies are limited by significant adverse effects. Recently autologous stem cell transplant after high dose immunosuppression has been utilized to reset the immune process with some success in young adults with T1DM. These strategies are limited by the fact that over 95% of â cell mass is destroyed by the time of diagnosis of the disease.

The other, more appealing, approach for cure for T1DM involves restoration of â cell mass using pancreatic, islet cell or stem cell transplantation. Pancreatic transplant is a major endeavor requiring long term immunosuppression and clearly out of question for adolescents with T1DM. Studies have failed to show long term remission with islet cell transplantation T1DM. *There is currently no evidence of efficacy of stem cell therapy in the cure of T1DM.* Thus while the parents should be counseled about the feasibility of cure of T1DM in the foreseeable future, they should be cautioned about the tall claims of cure of the disease by mushrooming stem cell centers.

T1DM is going through an exciting phase. *The advances in management over the last 80 years have enabled the transition of this fatal disease to easily manageable condition with hope for long term cure. At the moment insulin however represents the one and only treatment for the disease.*

SUGGESTED READING

WEBSITES FOR OTHER GUIDELINES:

1. Clinical practice guidelines: Type 1 diabetes in children and adolescents.

   Prepared by the Australasian Pediatric Endocrine Group for the Department of Health and Ageing. These guidelines can be downloaded from the National Health and Medical Research Council website: www.nhmrc.gov.au/publications.

2. ISPAD Clinical Practice Consensus Guidelines 2009 Compendium. The complete set of guidelines can be found at www.ispad.org.

3. Position statement: Standards of Medical Care in Diabetes—2011: American Diabetes Association. These guidelines are available at care.diabetesjournals.org and can be read in Diabetes Care, Vol. 34, Supplement 1, January 2011.

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3. An ambulatory stabilization program for children with newly diagnosed type 1 diabetes. Srinivasan S, Craig ME, Beeney L, Hayes R, Harkin N, Ambler GR, Donaghue KC, Cowell CT: *Med J Austr* 2004; 180:277-280.

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These guidelines on practical diabetes management in childhood have been written specially keeping in mind the social and economic conditions in which our patients live and we work. Nevertheless, every attempt has been made to refer to international texts and clinical practice guidelines as recent as 2011. The handbook should be useful to pediatricians, pediatric endocrinologists and endocrinologists, diabetologists and physicians, nurse educators, dieticians and counselors.

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