ISPAD Consensus Guidelines for the Management of Type 1 Diabetes Mellitus in Children and Adolescents
Consensus Guidelines
2000

ISPAD Consensus Guidelines for the Management of Type 1 Diabetes Mellitus in Children and Adolescents

ISPAD
INTERNATIONAL SOCIETY FOR PEDIATRIC AND ADOLESCENT DIABETES

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Novo Nordisk subsidiaries
In addition, the guidelines can be viewed at the following internet sites:
www.ispad.org
www.novo.dk


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Foreword

Globally, diabetes is a disease in evolution. These global changes in diabetes are also affecting children and adolescents, and the incidence of all types of diabetes is rising. In many parts of the world type 1 diabetes in childhood is increasing by 3–5% per annum whilst type 2 diabetes is declaring itself in younger and younger age groups. These children have a lifetime of diabetes ahead, and the new International Society for Pediatric and Adolescent Diabetes (ISPAD) Consensus Guidelines are aimed at providing health care providers with clear guidance in both acute and chronic care.

ISPAD is a professional organization whose aims are to promote science (clinical and basic), education and advocacy in childhood and adolescent diabetes. The strength of ISPAD lies in the scientific clinical expertise of its membership in childhood and adolescent diabetes (550 members from over 70 countries). This international breadth of experience is reflected in these guidelines, which can be adapted or adopted by health professionals looking after children and adolescents in any country. The guidelines are thus a consensus of best practice recommendations from around the world and reflect the art of medicine as well as the latest in evidence-based information.

Guidelines need to be living documents and to reflect the changing nature of a disease, clinical practice as well as new knowledge. These guidelines are much expanded from the ISPAD Consensus Guidelines for the Management of Insulin-Dependent (Type 1) Diabetes (IDDM) in Childhood and Adolescence which were published in 1995. The new edition recognizes the emerging problem of type 2 diabetes and addresses all forms of diabetes affecting children and adolescents.

The International Diabetes Federation, which represents member diabetes associations from over 130 countries in all continents, has warmly endorsed these guidelines. The guidelines will be freely available to all health professionals with a special interest in childhood and adolescent diabetes and will be distributed in a printed as well as an electronic format (www.ispad.org). It is hoped that the guidelines will stimulate each country to develop appropriate standards of care for childhood and adolescent diabetes and result in improved delivery of care.

A task as important as this could not have been achieved without the dedication and hard work of many people. In writing this foreword on behalf of ISPAD, I wish to thank all of those who gave so willingly of their time and expertise. I wish to pay particular tribute to Dr Peter Swift for his outstanding editorship in collating the many contributions and promoting debate in order to achieve consensus, and to Dr Ragnar Hanas not only for his editorial contributions but also for posting the drafts on the website that he has developed for ISPAD. The process of developing the guidelines required the support of industry, and on behalf of ISPAD I wish to thank Novo Nordisk for its generous financial backing, for its global vision and for its commitment to education in childhood and adolescent diabetes.

Martin Silink  
President ISPAD
Introduction

We as pediatric diabetes specialists believe that the needs of children and adolescents with diabetes and their families are very special and are different from those of adults. This belief is enshrined in both the International Diabetes Federation (IDF) philosophy (see p123) and in the first International Society for Pediatric and Adolescent Diabetes (ISPAD) Consensus Guidelines published in 1995. In contrast, the *IDF Type 1 (Adult) Diabetes Desktop Guide*, 1998 (ISBN 0 7017 0080 7) shows distinctive differences from the pediatric guidelines.

The 1995 ISPAD Consensus Guidelines have been translated into many different languages and formed the basis of the handbook produced by the Australian Paediatric Endocrine Group (APEG, 1996, ISBN 0 646 28302 2), which remains a rich source of information and guidance.

These publications acknowledge the fact that children and families require an holistic approach to their care and have helped to ‘pave the way for practical, flexible, age-appropriate management, to ensure the well-being of the child and adolescent, who should be able to participate in all normal life activities at home, at school and in employment, and to minimize psychological and long-term complications’ (Laron, ISPAD Consensus Guidelines, 1995).

These revised guidelines for the new millennium are more comprehensive, contain new sections and place education at the center of clinical management.

Education provides not only a knowledge base but also when it is delivered in a style which is patient-centered and appropriate for the age and maturity of the young person and the culture of the family, it becomes the vehicle for optimal self-management, the key to success.

Clinical guidelines are defined as ‘systematically developed statements to assist practitioners and patients in decision-making on the most appropriate health care for specific clinical circumstances’. Childhood diabetes is a condition for which clinical guidelines are entirely appropriate because there are — huge variations both worldwide and within countries in the acceptance of diabetes as a major chronic disease of childhood — massive inequalities in the provision of resources.
— major differences in management strategies
— wide discrepancies in outcomes and cost-effectiveness.

The guidelines are based on a wide consensus of clinical practice. They were drafted by international writing teams, modified by experts in different specialties from many countries, debated at the annual ISPAD meeting in 1999, and were reviewed by members via the internet and the ISPAD website.

We hope therefore that the guidelines will be widely consulted and will be used to
— improve awareness among governments, state health care providers and the general public of the serious long-term implications of poorly managed diabetes and of the essential resources needed for optimal care
— assist individual care givers in managing children and adolescents with diabetes in a prompt, safe, consistent, equitable, standardized manner in accordance with the current views of experts in the field.

With regard to the contentious issue of an evidence base for the guidelines, it was agreed by consensus that references should not be included nor should we attempt to classify the levels of scientific evidence for the following reasons — the guidelines are essentially clinical and are based on consensus opinion — evidence at the higher levels of controlled trials was either not available or not easily applicable to many aspects of childhood diabetes Nevertheless, in support of the recommendations and statements in the guidelines we intend to publish as soon as possible referenced resource papers.

These guidelines are not strict protocols nor are they the final word. They will evolve as new information becomes available. They will be viewed from many different perspectives and interpreted in various ways not only in different countries but also in different centers within individual countries.

We sincerely hope that the guidelines will improve the understanding and clinical management of diabetes in young people by all those who have the privilege and shared responsibility of caring for children and adolescents with diabetes.

Peter G.F. Swift
Editor in Chief, ISPAD Consensus Guidelines 2000

Practical editorial points

• Throughout the text we have used ‘international English’
• Whenever the words ‘child’ or ‘children’ are used they most often also mean ‘and adolescents’
• Whenever the word ‘parent’ is used it most often also means ‘all close care givers’
• DCCT = Diabetes Control and Complications Trial
• BG = whole blood glucose level
• Units of measurement of BG = mmol/l
  When 1 mmol/l = 18 mg/100 ml or 18 mg/dl
• HbA1c means the ‘c’ fraction of glycated hemoglobin HbA1c
Endorsement

Diabetes mellitus is a chronic disease, the seriousness of which is still often not recognized, although the complications that the condition implies can be very damaging as well as costly and are often brought on by a lack of knowledge about the condition and lack of adequate care.

Diabetes is also one of the most frequent chronic diseases in childhood, which not only affects the child himself, but also involves his immediate environment. His parents do not always know how to react and feel insecure about the child’s future. Teachers and friends often do not know how to respond when a child has diabetes. As a direct consequence, the child often feels isolated and stigmatized.

The first ISPAD Consensus Guidelines for the management of children and adolescents with diabetes published in 1995 were a very valuable tool. We therefore very much welcome this updated version of the Consensus Guidelines on diabetes in children and adolescents and sincerely hope that they will contribute to the improvement in care and living conditions of the child with diabetes.

Maria L de Alva
IDF President
Definition, epidemiology, diagnosis and classification

Definition

Diabetes mellitus is a metabolic disorder of multiple etiology, characterized by chronic hyperglycemia due to defective insulin secretion or insulin action or both

◊ The ancient words diabetes mellitus described the ‘flowing over of sweet urine’ associated with the characteristic symptoms of polyuria (accompanied by polydipsia) and the confirmatory diagnostic feature of glycosuria
◊ In childhood and adolescence, diabetes is most often associated with a genetically determined predisposition, the presence of autoimmune markers, aggressive beta-cell destruction, severe insulin deficiency, and the urgent need for insulin replacement therapy because of the risk of ketoacidosis
◊ Historically various terms have been used to describe this type of diabetes
  – juvenile diabetes
  – ketosis-prone diabetes
  – autoimmune diabetes
  – insulin-dependent diabetes mellitus (IDDM)
    and, with recent international agreement (WHO, 1998)
  – type 1 diabetes
◊ Characteristic features of type 1 diabetes in comparison with type 2 diabetes are shown in Table 1

Epidemiology

◊ Incidence studies most often define the onset of type 1 diabetes as the date of the first insulin injection, because of the variable time between onset of symptoms and diagnosis
◊ New case incidence varies greatly between different countries, within countries, and between different ethnic populations (Figure 1)
◊ In countries with higher incidence, the age of onset indicates that
  – diabetes under the age of 1 year is extremely uncommon
  – incidence increases with age
  – there may be a minor peak at age 4–6 years
  – there is a major peak at age 10–14 years
◊ In many countries the total incidence of type 1 diabetes has been shown to be increasing
In some countries the incidence has also increased significantly in children under the age of 5 years.

There is no clear pattern of inheritance of childhood diabetes although there is familial aggregation due to the association of type 1 diabetes with certain genetic markers.

In the higher incidence countries the risks to relatives of developing the disease when a member of the family has type 1 diabetes, are as follows:

- risk to child/adolescent of a father with type 1 diabetes ~7%
- risk to child/adolescent of a mother with type 1 diabetes ~2%
- risk to identical twin of a child with type 1 diabetes ~35%
- risk to sibling of a child with type 1 diabetes ~3-6%

---

**Definition, epidemiology, diagnosis and classification**

Table 1: Characteristic features of type 1 compared with type 2 diabetes in young people.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Throughout childhood</td>
<td>Pubertal (or later)</td>
</tr>
<tr>
<td>Onset</td>
<td>Most often acute, rapid</td>
<td>Variable: from slow, mild (often insidious) to severe</td>
</tr>
<tr>
<td>Insulin dependence</td>
<td>Permanent, total, severe</td>
<td>Uncommon, but insulin required when oral hypoglycemic agents fail</td>
</tr>
<tr>
<td>Insulin secretion</td>
<td>Absent or very low</td>
<td>Variable</td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>Genetics</td>
<td>Polygenic</td>
<td>Polygenic</td>
</tr>
<tr>
<td>Race/ethnic distribution</td>
<td>All groups, but wide variability of incidence</td>
<td>Certain ethnic groups are at particular risk</td>
</tr>
<tr>
<td>Frequency (% of all diabetes in young people)</td>
<td>Usually 90%+</td>
<td>Most countries &lt;10% (Japan ~80%)</td>
</tr>
<tr>
<td>Associations</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Autoimmunity</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Ketosis</td>
<td>No</td>
<td>Strong</td>
</tr>
<tr>
<td>Obesity</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Acanthosis nigricans</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

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Figure 1: Annual incidence rates for childhood type 1 diabetes (0- to 14-year age group) in different regions of the world. [Source: Verge CF, Thesis, University of Sydney, 1994]
Diagnosis

- In the majority of young people the diagnosis of type 1 diabetes should be made without difficulty and with urgency
- The symptoms of thirst, excessive drinking and urination should prompt immediate confirmatory tests for
  - heavy glycosuria (>55 mmol/l; 1.0 g/dl)
  - possible ketonuria (often >4 mmol/l; 0.4 g/l acetoacetate)
  - random hyperglycemia (BG ≥11.1 mmol/l; 200 mg/dl)

◊ In some countries and in certain circumstances diabetes may be of slower onset and present diagnostic difficulties
◊ In contrast, some forms of type 2 diabetes present acutely with ketoadidosis
◊ If the diagnosis of diabetes is uncertain the following investigations may help

1. Repeated random tests for BG, glycosuria and HbA₁c
2. Measurement of islet cell autoantibody markers, e.g. ICA, GAD, IA2 and IAA
3. Review of risk factors
   - family history of type 1 or type 2 diabetes
   - obesity (type 2)
   - autosomal dominant history suggesting genetic defects of beta-cell function
4. Oral glucose tolerance test (OGTT)
   - in fasting state (but only after previously normal carbohydrate intake)
   - glucose orally 1.75 g/kg body weight (maximum 75 g)

Diagnostic criteria are the same for children as for adults (American Diabetes Association, 1997; WHO, 1998) (Table 2)

<table>
<thead>
<tr>
<th></th>
<th>Impaired fasting glycermia (IFG)</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting plasma glucose (mmol/l)</td>
<td>≥6.1 to &lt;7.0</td>
<td>≥7.0 (whole BG ≥6.1)</td>
</tr>
<tr>
<td>2-h Plasma glucose (mmol/l)</td>
<td>—</td>
<td>≥11.1</td>
</tr>
</tbody>
</table>

*In asymptomatic patients the diagnosis must only be made on the basis of at least two separate abnormal measurements of significant hyperglycemia
Classification

Although in most countries type 1 is the predominant form of diabetes in young people, diabetes is a heterogeneous disease. The recommended etiological classification by the American Diabetes Association (1997) and the WHO Expert Committee on the Classification and Diagnosis of Diabetes (1998) is shown in Table 3

Type 2 diabetes

◊ Previously known as non-insulin-dependent diabetes (NIDDM)
◊ In adults it is common and is the predominant form of diabetes
◊ In children it is uncommon but is being reported more frequently in many countries in association with rising rates of obesity
◊ Occurs more commonly than type 1 diabetes in Japanese children, and certain ethnic groups are at high risk, e.g. Native Americans and Canadians, Mexican/Hispanic Americans, African-Americans, South Asian Indians in India and Europe, Pacific Islanders, Australian Aborigines

Onset

◊ 80–90% are obese at the time of diagnosis (in the absence of obesity, consider genetic defects of beta-cell function)
◊ Most children and adolescents are asymptomatic or have minimal symptoms at diagnosis
◊ Occasionally ketoacidosis may develop in association with infections or other major stress

Etiology

◊ Unknown
◊ Genetic (polygenic) factors are important
  [Identical twins have 100% concordance for type 2 diabetes
  Positive family history is likely especially when parents tested with OGTT]
◊ Lifestyle factors such as overeating and little exercise may have an important influence
◊ The sequence of intrauterine growth retardation (thrifty phenotype or genotypic variation) → excess postnatal nutrition → obesity → hyperinsulinemia and insulin resistance → diabetes, hypertension, cardiovascular disease (metabolic syndrome) has major worldwide implications
Definition, epidemiology, diagnosis and classification

Table 3: Etiologic classification of diabetes mellitus

**Type 1 diabetes mellitus** (beta-cell destruction, usually leading to absolute insulin deficiency)
- Immune-mediated
- Idiopathic

**Type 2 diabetes mellitus** (may range from predominantly insulin resistance with relative insulin deficiency to predominantly secretory defect with insulin resistance)

**Gestational diabetes mellitus** (onset or recognition of glucose intolerance in pregnancy)

**Other specific types**

<table>
<thead>
<tr>
<th>Genetic defects of beta-cell function</th>
<th>Genetic defects in insulin action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosome 12, HNF-1α (formerly MODY 3)</td>
<td>Type A insulin resistance</td>
</tr>
<tr>
<td>Chromosome 7, glucokinase (formerly MODY 2)</td>
<td>Leprechaunism</td>
</tr>
<tr>
<td>Chromosome 20, HNF-4α (formerly MODY 1)</td>
<td>Rabson-Mendenhall syndrome</td>
</tr>
<tr>
<td>Mitochondrial DNA</td>
<td>Lipoatrophic diabetes</td>
</tr>
<tr>
<td>Others</td>
<td>Others</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diseases of the endocrine pancreas</th>
<th>Endocrinopathies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatitis</td>
<td>Acromegaly</td>
</tr>
<tr>
<td>Trauma, pancreatectomy</td>
<td>Cushing's syndrome</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Glucagonoma</td>
</tr>
<tr>
<td>Thalassemia</td>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td>Hemochromatosis</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>Fibrocystic pancreatopathy</td>
<td>Somatostatinoma</td>
</tr>
<tr>
<td>Neoplasia</td>
<td>Aldosteronoma</td>
</tr>
<tr>
<td>Others</td>
<td>Others</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infections</th>
<th>Uncommon forms of immune-mediated diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital rubella</td>
<td>‘Stiff-man’ syndrome</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Anti-insulin receptor antibodies</td>
</tr>
<tr>
<td>Others</td>
<td>Others</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug- or chemical-induced</th>
<th>Other genetic syndromes sometimes associated with diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vacor</td>
<td>Down syndrome</td>
</tr>
<tr>
<td>Pentamidine</td>
<td>Klinefelter syndrome</td>
</tr>
<tr>
<td>Nicotine acid</td>
<td>Turner syndrome</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>Wolfram syndrome (DIDMOAD)</td>
</tr>
<tr>
<td>Thyroid hormones</td>
<td>Friedreich's ataxia</td>
</tr>
<tr>
<td>Diazoxide</td>
<td>Huntington's chorea</td>
</tr>
<tr>
<td>Beta-adrenergic agonists</td>
<td>Laurence-Moon-Biedl syndrome</td>
</tr>
<tr>
<td>Thiazine</td>
<td>Myotonic dystrophy</td>
</tr>
<tr>
<td>Dilantin</td>
<td>Porphyria</td>
</tr>
<tr>
<td>Alpha-interferon</td>
<td>Prader-Willi syndrome</td>
</tr>
<tr>
<td>Others</td>
<td>Others</td>
</tr>
</tbody>
</table>

DNA, deoxyribonucleic acid; HNF, hepatic nuclear transcription factor; MODY, maturity-onset diabetes in the young
Principles of management

The aim is to prevent long-term vascular complications:

◊ Reduction in energy intake to recommended values in order to control weight gain or reduce obesity
◊ Exercise and healthy lifestyle
◊ Oral hypoglycemic agents, e.g. sulfonylureas and metformin (also consider thiazolidinediones and possibly alpha-glucosidase inhibitors)
◊ Insulin treatment should not be delayed if good glycemic control is not achieved by the above measures, particularly in the adolescent who is still growing

Screening

• **Routine screening** for glycosuria in most populations is not cost-effective
• **Selective screening** or monitoring of urine or BG in populations or individuals at high risk may be advisable

◊ All Japanese children have regular school urine screening partly because of the higher incidence of type 2 diabetes
◊ Differentiation between non-obese type 2 and type 1 diabetes may be helped by measuring islet cell autoantibodies

Community implications and prevention

The increasing prevalence of type 2 diabetes, as rates of obesity also increase in certain populations, is a cause of great concern

• Research is needed to understand the biology of this phenomenon
• Programs to prevent obesity are urgently needed
Genetic defects of beta-cell function (formerly known as maturity-onset diabetes in the young, MODY subtypes)

**Characteristics**

◊ Early-onset hyperglycemia before age 25 years
◊ Monogenic, autosomal dominant mode of inheritance — at least two, preferably three, generations exhibiting a similar phenotype (although older relatives may not be diagnosed until older age)
◊ Non-insulin-dependent for at least 5 years after diagnosis of diabetes
◊ Impaired insulin secretion
◊ Absence of severe ketosis

Some forms of these defects in beta-cell function may present with severe osmotic symptoms and may be misdiagnosed as type 1

**But**

– Not severely ketotic
– Family history (autosomal dominant)
– Good metabolic control with low insulin dose

Table 4: Classification of the three most common genetic defects

<table>
<thead>
<tr>
<th>Gene defect</th>
<th>HNF-1α</th>
<th>Glucokinase ‘glucose sensor’ gene</th>
<th>HNF-4α</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromosome location</td>
<td>12q</td>
<td>7p</td>
<td>20q</td>
</tr>
<tr>
<td>Mutations</td>
<td>Multiple</td>
<td>Multiple</td>
<td>Multiple</td>
</tr>
<tr>
<td>Frequency in large series</td>
<td>65%</td>
<td>10–15%</td>
<td>5%</td>
</tr>
<tr>
<td>Onset of hyperglycemia</td>
<td>Puberty–adulthood</td>
<td>In utero, from birth</td>
<td>Puberty, young adults</td>
</tr>
<tr>
<td>Severity of hyperglycemia</td>
<td>Progressive, may become severe</td>
<td>Mild, persistent</td>
<td>Progressive, may become severe</td>
</tr>
<tr>
<td>Pathophysiology</td>
<td>Beta-cell dysfunction</td>
<td>Beta-cell dysfunction</td>
<td>Beta-cell dysfunction</td>
</tr>
<tr>
<td>Microvascular complications</td>
<td>Frequent</td>
<td>Abnormal glucose sensing Rare</td>
<td>Frequent</td>
</tr>
</tbody>
</table>

HNF-1α, hepatic nuclear transcription factor-1α; HNF-4α, hepatic nuclear transcription factor regulating HNF-1α
Other variants

◊ Until recently specific genetic diagnosis was not possible in 15–20% of families with defects of beta-cell function, however
  – A fourth variant is associated with defects in the insulin promoter factor (IPF1) — in the homozygous state associated with pancreatic agenesis
  – A fifth variant is associated with mutations in HNF-1β — resulting in renal abnormalities particularly cystic kidney disease, which is normally congenital

Management

◊ Depends on underlying genetic disorder
◊ Children and adolescents with glucokinase or transcription factor mutations only require healthy eating recommendations initially to achieve good glycemic control
◊ Progressive beta-cell deficiency in some children with transcription factor mutations results in the need for oral hypoglycemic agents. HNF-1α variants may exhibit sensitivity to small doses of sulfonylureas (with the risk of hypoglycemia)
◊ One-third of patients with mutations in HNF-1α may require insulin treatment, but this is usually in adulthood

Other specific types

Diseases of endocrine pancreas

Cystic fibrosis-related diabetes

◊ Longer survival of cystic fibrosis (CF) patients results in 10–30% of 15- to 25-year-olds developing diabetes
◊ Screening for hyperglycemia, glycosuria and/or HbA1c is recommended as part of the annual review of CF patients and particularly if steroid treatment is used
◊ Insulin treatment will improve hyperglycemia and help to prevent catabolic weight loss in CF especially during intercurrent infections
◊ High dietary energy intake is recommended including high fat and high complex carbohydrate
**Thalassemia**

◊ Iron overload affecting beta-cell function and the decreasing insulin sensitivity of puberty are thought to contribute to the risk of diabetes in young people with thalassemia

◊ Some studies suggest that treatment with high doses of insulin is required if iron levels remain high

**Fibrocalculous pancreatopathy and other diabetes in developing countries**

◊ Atypical diabetes in young people occurs in some developing countries

◊ Previously named malnutrition-related diabetes mellitus (MRDM), it may be characterized by lean body mass, relative ketosis resistance and superimposed nutritional deficiencies

◊ There may be calcification of the pancreas, or protein deficiency pancreatic diabetes

◊ The ketosis ‘resistance’ may reflect later onset, less severe type 1 diabetes in children who survive long enough to reach medical attention

**Other genetic syndromes associated with diabetes**

**Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, Deafness (DIDMOAD) syndrome (Wolfram syndrome)**

◊ Insulin-dependent diabetes mellitus usually presenting in the first decade

◊ Insidious onset of diabetes insipidus, deafness and visual impairment

◊ Non-autoimmune genetic condition, usually autosomal recessive

◊ Potentially progressive deterioration in neurological function with cerebral atrophy and psychological disturbances in the third or fourth decade

◊ Gene localized to chromosome 4p

**Prader-Willi syndrome**

◊ Severe obesity is associated with a high incidence of secondary diabetes in the second decade

◊ Weight reduction is extremely difficult

◊ The diabetes is type 2, usually responding poorly to oral hypoglycemic agents; most patients require insulin
Presentation and phases of diabetes

Type 1 diabetes in childhood and adolescence is characterized by the following phases

• Prediabetes
• Presentation of diabetes
• Partial remission (or ‘honeymoon’)
• Permanent insulin dependency

Prediabetes

Definition

A state preceding the clinical onset of diabetes by months or even years, characterized by the presence of antibodies to several islet cell antigens which are often, but not always, predictive of the development of type 1 diabetes. The antibodies have been used as markers to identify people at risk of developing type 1 diabetes

Immunological markers

◊ Islet cell autoantibodies (ICA) at a high titer (>20 JDF units) predict a 40–60% risk of type 1 diabetes over the next 5–7 years

◊ When multiple autoantibodies are present the risk prediction rate increases greatly, e.g. glutamic acid decarboxylase (65 kD GAD isoform) plus IA2 antibodies predict a risk of >70% over 5 years. Insulin autoantibodies (IAA) at high titer may also increase the risk prediction

Genetic markers

◊ Certain HLA markers, particularly when identical to those of a family member with diabetes, indicate increased risk

Examples of genetic markers conferring increased risk

HLA DR3–DQA1*0501-DQB1*0201
HLA DR4–DQA1*0301-DQB1*0302
Presentation and phases of diabetes

Examples of genetic markers conferring decreased risk

HLA DR2–DQA1*0102–DQB1*0602

Insulin secretion

◊ During the phase of prediabetes, before clinical onset of diabetes, beta-cell destruction progresses and insulin secretion diminishes. In the research setting using a standard ICARUS protocol, insulin secretion has been tested by the IV glucose tolerance test. Severely impaired first-phase insulin release confers an almost 100% risk of type 1 diabetes over the next 5 years.

Presentation

◊ Diabetes in young people most often has a sudden and acute onset with polyuria, polydipsia and evidence of ketosis
◊ A minority of young people have a slower onset with symptoms presenting over several months

Additional clinical presentations

◊ Recent-onset or persistent enuresis
◊ Abdominal pain with or without vomiting
◊ Vaginal candidiasis
◊ Poor weight gain or weight loss
◊ Fatigue, irritability, decreasing school performance
◊ Recurrent skin infections

Diagnostic difficulties at onset

◊ Young infants with hidden symptoms
◊ Hyperventilation misdiagnosed as pneumonia
◊ Abdominal pain or vomiting misdiagnosed as abdominal ‘migraine’ or appendicitis
◊ Enuresis or polyuria misdiagnosed as urinary infection
◊ Polydipsia misdiagnosed as habit or psychogenic drinking
**Partial remission phase**

**Definition**

The phase after the diagnosis of type 1 diabetes during which there may be continuing and effective secretion of endogenous pancreatic insulin

◊ Often called the ‘honeymoon period’ when glycemic control seems inappropriately easy
◊ Has been defined in the past as when the insulin dose required to maintain excellent metabolic control is less than 0.5 units/kg body weight per day
◊ Approximately 30–60% of children and adolescents demonstrate a partial remission phase most often during the first 1–6 months after starting insulin treatment
◊ Opinion has varied about whether insulin treatment should be withdrawn temporarily during this phase
◊ Currently there is no clear evidence of any treatment strategy which significantly prolongs the partial remission phase (there is weak evidence to suggest that maintenance of normal BG levels with insulin injections helps to protect islet cell function)
◊ Beta-cell function becomes almost unmeasurable in the great majority of children by 1–2 years after diagnosis

**Permanent total insulin dependency**

◊ When beta-cell function becomes unmeasurable, the individual is then totally dependent on exogenous insulin injections
◊ Total pancreatic insulin deficiency is one of the factors causing erratic swings of glycemia in many young people with diabetes


**Diabetes education**

Education is the keystone of diabetes care and management

The Diabetes Control and Complications Trial (DCCT) provided clear evidence that
- successful intensification of management reduces microvascular complications
- intensification of management requires effective diabetes self-management
- effective self-management requires frequent and high levels of educational input and continuing support

**Universal principles**

Every person with diabetes has a right to comprehensive expert practical education

- Children and adolescents, their parents and other care providers should all have easy access to and be included in the educational process
- Diabetes education should be delivered by health care professionals with a clear understanding of the special and changing needs of young people and their families as they grow through the different stages of life
- Educators (doctors, nurses, dieticians and other health care providers) should have access to continuing specialized training in diabetes education and educational methods. This should be the responsibility of each nation/state and be a national priority
- The priorities for health care professionals in diabetes education may not match those of the child and family. Thus diabetes education should be based on a thorough assessment of the person’s attitudes, beliefs, learning style, ability and readiness to learn, existing knowledge and goals
- Diabetes education needs to be adaptable and personalized so that it is appropriate to each individual’s age, stage of diabetes, maturity and lifestyle, culturally sensitive and at a pace to suit individual needs
- Diabetes education needs to be a continuous process and repeated for it to be effective
- Diabetes education is the interface between research and clinical practice. It should be planned, documented, monitored and evaluated regularly by the diabetes care team
- Research into diabetes educational methods is important in improving clinical practice
Content of education program

The content and pace of education are determined by the model of care utilized (e.g. ambulatory care compared with inpatient management). Therefore the following guidelines on survival skills and continuing education can only act as a template on which to develop an appropriate curriculum.

A practical, simplified, written summary of most of the sections in these ISPAD Guidelines should provide the basis of an educational curriculum.

At diagnosis: survival skills

1. Explanation of how the diagnosis has been made and reasons for symptoms.
3. The need for immediate insulin and how it will work.
4. What is glucose? — normal BG levels and glucose targets.
5. Practical skills: insulin injections, blood and/or urine testing and reasons for monitoring.
6. Basic dietetic advice.
9. Diabetes at home or at school, including the effects of exercise.
10. Identity cards, necklets, bracelets, etc.
11. Membership of a diabetes association and other available support services.
12. Psychological adjustment to the diagnosis.
13. Details of emergency telephone contacts.

Continuing educational curriculum

- Continuing education will take place most often in an ambulatory (clinic, community, domiciliary) setting. Where staffing levels, expertise and local circumstances do not permit this, educational programs may be carried out in the hospital environment, either by individual teaching or in groups.
- The educational program should utilize appropriate patient-centered, interactive teaching methods for all people involved in the management of diabetes, particularly the affected child or adolescent.
Diabetes education

Continuing curriculum

1 Pathophysiology, epidemiology, classification and metabolism
2 Insulin secretion, action and physiology
3 Insulin injections, types, absorption, action profiles, variability and adjustments
4 Nutrition: meal planning; local systems of regulation of carbohydrate, fat, proteins and fiber; coping with special events and eating out; growth and weight gain; ‘diabetic foods’; sweeteners; drinks; exercise and food
5 Monitoring, including glycated hemoglobin and the targets of control
6 Hypoglycemia and its prevention, recognition and management, including glucagon
7 Intercurrent illness, hyperglycemia, ketosis and prevention of ketoacidosis
8 Micro- and macrovascular complications and their prevention. The need for regular assessment
9 Exercise, holiday planning and travel, including educational holidays and camps
10 Problem-solving and adjustments to treatment (matching insulin, food and exercise)
11 Smoking, alcohol and drugs
12 School, college, employment and driving vehicles
13 Sexuality, pregnancy, childbirth and contraception

Education and age group

Infants and toddlers

◊ Acknowledging the total dependence on parents and care providers for injections, food and monitoring
◊ Advising on unpredictable erratic eating and activity levels
◊ Recognizing that hypoglycemia is more common and may be more severe. Education on prevention, recognition and management is a priority

School age children

◊ Learning to help with and developing skills in injections and monitoring
◊ Recognizing hypoglycemic symptoms and understanding self-management
◊ Adapting diabetes to school programs, school meals, exercise and sport
◊ Advising parents on the gradual development of the child’s independence and progressive hand-over of responsibility

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Adolescents

◊ Promoting independent, responsible self-management appropriate to the level of maturity and understanding
◊ Discussing emotional and peer group conflicts
◊ Teaching strategies for dealing with dietary indiscretions, illness, hypoglycemia, sports, etc
◊ Negotiating targets, goals and priorities and ensuring that the tasks taken on by the adolescent are understood and accepted
◊ Developing strategies to manage transition to adult services

Knowledge about diabetes does not necessarily correlate with good metabolic control. Successful education not only instills knowledge, it must also empower and motivate the young person to use knowledge and practical skills in problem-solving and self-management

Mode of education and resources

◊ Methods of delivering education and the use of educational resources will depend on local experience and facilities. Education will be dominated initially by individual teaching, and in most countries, backed up by written guidelines, booklets and other media which should be appropriate to the child’s age
◊ Written materials for parents should use appropriate language and a style that is easily comprehensible (it is suggested that this should be at the level of a popular local or ‘tabloid’ newspaper)
◊ When available, videos, computer games, etc, might be used, all of which should be coordinated through the pediatric diabetes care team
◊ Other methods of delivering education might include group teaching sessions with young people and/or parents and/or other care providers, role plays, television, radio or tape learning, friendship or school groups, organized diabetes association meetings, and in particular an opportunity to participate in holiday or camping experiences

Educational holidays and camps

◊ For many years organized specialized camps and educational activity holidays for young people with diabetes have been an important feature of diabetes care in many parts of the world
◊ Originally camps were introduced to help children from underprivileged
families, but are of proven short-term benefit to children and adolescents of all backgrounds in terms of improving self-management skills, bolstering self-confidence and enhancing independence
◊ It has not been possible to measure the longer term benefits of camps

**Primary aims**

◊ To provide an enjoyable holiday for children with diabetes in a safe environment
◊ To engage young people in a variety of interesting and exciting supervised activities to demonstrate their compatibility with diabetes

**Secondary benefits**

◊ Experiential learning of social and practical skills
◊ Gaining self-confidence and independence; feeling less isolated
◊ Learning better self-management of diabetes
◊ Sharing experiences with other young people outside the home environment
◊ Respite for the parents
◊ Educational value for the organizers and leaders

**Organization and planning**

Diabetes holidays are organized in many different ways and with differing objectives, from predominantly educational, to sports-orientated (e.g. water sports, skiing, specialized sports), dietetic groups, skills training (e.g. pottery, sewing, painting) and many other models. Camps may be specific for different age groups; their client group may be local, regional, national or international; they may be family weekend groups of high educational value for newly diagnosed young children; or they may be leadership outward bound holidays for adolescents

- All group holidays must have the security of **meticulous and safe planning**, written guidelines, led by expert and experienced personnel with careful documentation not only of the young person’s diabetic management (e.g. reduction of insulin and increased carbohydrate for days of high activity and the importance of BG monitoring) but also of any unexpected organizational problems
- At the end of the camp, careful communication with parents and local medical personnel will help to highlight the successes and failures of the holiday so that the young person with diabetes can gain optimal benefit from the camping experience
Outpatient management/ambulatory care

From the first day of diagnosis the child or adolescent with diabetes and the family should be cared for by members of a team of specialists. All members of the team should have training, expertise and understanding of both diabetes and pediatrics, particularly child and adolescent development.

Essential members of the multidisciplinary diabetes care team

- **Pediatrician** specializing in diabetes/endocrinology (or a physician with a special interest in childhood and adolescent diabetes)
- **Diabetes specialist nurse and/or diabetes educator**
- **Dietician**

Other health care professionals should be part of the specialist team, or at least there should be easy access to

- Psychologist/psychiatrist/counselor trained in pediatrics and with some knowledge of childhood diabetes
- Pediatric social worker
- Chiropodist/podiatrist with knowledge of childhood diabetes

These recommendations will be impossible in areas of low population density or where childhood diabetes rarely occurs. In these circumstances, and where the number of children with diabetes is small, care is likely to be provided by a locally based pediatrician/physician. These practitioners should have ready access to facilities and advice provided by the diabetes care team in regional centers of excellence. Where practical the annual review might best be performed in the regional center.

General aims of the diabetes care team should be to provide

- Expert practical guidance and skill training
- Consistent and repeated educational advice
- An understanding of, and support for, the psychosocial needs of the family

**Diabetes is a condition requiring skilled self-management in the home and local environment. Therefore the diabetes care team**
Outpatient management/ambulatory care

should have the resources to develop strong links, clear communication and common working practices with

◊ The child and family at home
◊ The young person at school/college
◊ Primary health care providers
◊ Other pediatricians and health care providers in areas of low population density

The organization of the diabetes care team, its size and situation will depend on geographical and demographic characteristics

◊ The teams from district or regional centers might organize outreach clinics when there are difficulties for children and families travelling to the regional centers

The specific aims of the diabetes care team should be to provide

◊ Specialized hospital medical care
◊ Expert comprehensive ambulatory care of diabetes and associated pediatric conditions
◊ Expert advice on issues related to diabetes such as exercise, travel and sickness
◊ Screening for complications
◊ Emergency telephone or other support 24 hours a day

Generally accepted good clinical practice for the successful management of children and adolescents

At onset

◊ Provision of easy access (24-h a day) to diabetes care team for rapid diagnosis and initiation of treatment
◊ Availability of accepted written protocols for management of DKA and other types of presentation of childhood diabetes
◊ Provision of practical guidance at diagnosis, including dietary management
◊ Domiciliary/outpatient/ambulatory management of children at the time of diagnosis is possible in some centers but can only be recommended when 24-h access to senior experienced members of the diabetes care team is available

The importance of providing ‘a good start’ with confident, clear, positive messages, support and advice cannot be overemphasized
The first 6 months

◊ Frequent contact with the diabetes care team is necessary to help in managing the changing requirements of diabetes in its early phases
◊ Contact may be by frequent clinic appointments, home visits, telephone or other methods

Follow-up consultations

• It is common practice for children and adolescents to be reviewed in outpatient clinics at least three or four times a year, or more if particular difficulties in managing diabetes are recognized

Clinic visits with members of the diabetes care team should include assessment of

◊ General health and wellbeing
◊ Height and weight (entered on appropriate growth charts)
◊ Intercurrent health problems (infections, disabilities, enuresis and other pediatric and developmental problems)
◊ Insulin types, dose, injection devices, injection sites
◊ Glycemic control
◊ Dietary management
◊ Hypoglycemia
◊ Changes in developmental performance, education (particularly school absences/problems), leisure and sport activities and psychosocial progress
◊ Information on driving, employment, smoking, sex, drugs and alcohol

It is good clinical practice to organize an annual review of

◊ Physical development and wellbeing with particular emphasis on
  – growth
  – injection sites
  – puberty
  – associated conditions (goiter/thyroid disease; celiac disease; skin or foot problems)
◊ Nutritional plan and dietary management
◊ Complications screening including blood and urine tests, blood pressure measurement, eye tests

Transition to adult clinics

◊ The age of transfer to an adult clinic will vary according to local circumstances and traditions
Recommendation

It is good clinical practice for pediatric diabetes care teams to organize age-banded adolescent or young adult clinics jointly with their adult specialty colleagues.

Record-keeping, audit, quality assurance and information services

Many models of care exist which aim to improve communication between the child/adolescent/family and diabetes care teams. These models should also include methods to evaluate the quality of the diabetes services provided and the outcomes of management.

Examples of useful clinical management tools include:

◊ Personal hand-held records, monitoring diaries
◊ BG monitoring machines (± computer/telephone links)
◊ Clinic data sheets (hard copies and computer databases)
◊ A register or database including:
  – incident cases
  – clinic attendances
  – clinical review and complications screening

The WHO Basic Information Sheet for Children and Adolescents is an important template for the central collection of clinic data (Figure 2).

Out of clinic activities

The diabetes care team may well be involved in helping to organize:

◊ Local (and national) support groups
◊ Resources (information leaflets/books, audio/video tapes equipment)
◊ Nutritional games/experiments/innovations
◊ Discussion groups, activity days, visits, lectures, holidays, camps
Figure 2: The WHO Basic Information Sheet for Children and Adolescents
Assessment and monitoring of metabolic control

The DCCT provided clear evidence in adults and adolescents that

◊ Better metabolic control is associated with fewer and delayed microvascular complications
◊ Optimal glycemic control could only be assessed and maintained by frequent and accurate monitoring
◊ In younger children, clear targets of glycemic control are less certain but there is good evidence that suboptimal levels of metabolic control at all ages are associated with a higher risk of both acute and long-term complications
◊ In very young children with diabetes, improvements in measures of glycemic control must be balanced against the potentially increased risks of severe hypoglycemia

Assessment of glycemic control

Aims

• To assess with accuracy and precision the level of glycemic control achieved by individuals so that they may benefit from attaining the most realistic glycemic targets
• To collect data on glycemic control from each diabetes center for comparison with stated local, national and international standards so that the performance of the multidisciplinary diabetes care team may be improved

Monitoring of BG

• In most diabetes centers it is recognized that self-monitoring of blood glucose (SMBG) is an essential tool in the management of childhood and adolescent diabetes because it

◊ Helps to monitor immediate and daily levels of control
◊ Detects hypoglycemia
◊ Assists in the safe management of hyperglycemia
◊ Has educational value in assessing BG responses to insulin, food and exercise
**Equipment**

Appropriate monitoring equipment is essential (see Summary of essential requirements)

**Timing of SMBG**

BG is best measured

- At different times in the day to show levels of BG in response to the action profiles of insulin, food intake and exercise. In this way, changes may be made in management to improve BG profiles
- To confirm hypoglycemia and to monitor recovery
- During intercurrent illness to prevent hyperglycemic crises
- In association with vigorous sport or exercise

The number and regularity of SMBG should be individualized depending on

- Availability of equipment
- Acceptance by the young person
- The type of insulin regimen

**Frequent, accurate SMBG is the only method by which optimal glycemic control can be achieved by intensified management regimens**

**Targets (Table 5)**

**Monitoring of urine glucose**

It is recognized that in many countries urine glucose monitoring is the only monitoring method available and that it

- Provides useful but different information from SMBG
- Reflects glycemic levels over the preceding several hours
- Is related to the renal threshold for glucose, which in children is approximately 9–10 mmol/l
- Can be less traumatic than SMBG for some children

**Predominantly negative tests for glycosuria with infrequent hypoglycemia may indicate satisfactory metabolic control**
**Assessment and monitoring of metabolic control**

### Limitations of urine glucose monitoring

- Uncertain correlation with BG levels
- Inability to detect hypoglycemia
- Less valuable as an educational tool
- Unhelpful in hyperglycemic crises because of the lag phase between recovery and changes in urine glucose

### Table 5: Target indicators of glycemic control

<table>
<thead>
<tr>
<th>Level of control</th>
<th>Ideal (non-diabetic)</th>
<th>Optimal</th>
<th>Suboptimal</th>
<th>High risk (action required)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical assessment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raised BG</td>
<td>Not raised</td>
<td>No symptoms</td>
<td>Polyuria, Polydipsia, Enuresis, Poor weight gain, Poor school attendance</td>
<td>Blurred vision, Cramps, Poor growth, Delayed puberty, Skin or genital infections, Signs of vascular complications</td>
</tr>
<tr>
<td>Low BG</td>
<td>Not low</td>
<td>Few mild, no severe hypos</td>
<td>Episodes of severe hypoglycemia (unconscious or convulsions)</td>
<td></td>
</tr>
<tr>
<td><strong>Biochemical assessment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preprandial or fasting BG (mmol/l)</td>
<td>3.6–6.1</td>
<td>4.0–7.0&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&gt;8.0</td>
<td>&gt;9.0</td>
</tr>
<tr>
<td>Postprandial BG (mmol/l)</td>
<td>4.4–7.0</td>
<td>5.0–11.0</td>
<td>11.1–14.0</td>
<td>&gt;14.0</td>
</tr>
<tr>
<td>Nocturnal BG&lt;sup&gt;c&lt;/sup&gt; (mmol/l)</td>
<td>3.6–6.0</td>
<td>Not &lt;3.6</td>
<td>&lt;3.6 or &gt;9.0</td>
<td>&lt;3.0 or &gt;11.0</td>
</tr>
<tr>
<td>HbA&lt;sub&gt;1c&lt;/sub&gt; (%) (DCCT standardized)</td>
<td>&lt;6.05</td>
<td>&lt;7.6</td>
<td>7.6–9.0</td>
<td>&gt;9.0</td>
</tr>
</tbody>
</table>

<sup>a</sup>These population-based target indicators must be adjusted according to individual circumstances. Different targets will be appropriate for various individuals such as young children, those who have experienced severe hypoglycemia or those with hypoglycemic unawareness.

<sup>b</sup>If fasting morning BG is <4 mmol/l, consider the possibility of antecedent nocturnal hypoglycemia.

<sup>c</sup>These figures are based on clinical studies but no strict evidence-based recommendations are available.

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*ISPAD Guidelines 2000*
Assessment and monitoring of metabolic control

Target

- As many urine tests as possible should show no glycosuria without the occurrence of frequent or severe hypoglycemia

Equipment

◊ Most centers use specific glucose-oxidase strips which are relatively inexpensive and convenient
◊ Some non-specific reducing agent methods are used such as Clinitest tablets or Benedict's test. These are less convenient to use
  [They are also potentially dangerous if the chemical reagents are in contact with the skin or gastrointestinal tract]

Monitoring of urinary ketones

- It is good clinical practice to advise urinary ketone measurement during episodes of uncontrolled hyperglycemia, insulin deficiency, intercurrent illness ('sick days') and impending ketoacidosis
  [Some centers advise regular ketone testing before breakfast as an indicator of antecedent insulin deficiency (the dawn phenomenon)]

Equipment

◊ Tablets or urine testing strips for ketone testing are available that detect increased levels of urinary acetoacetate (present in lower concentrations than β-OH butyrate)
  [New blood ketone strips measuring β-OH butyrate in electronic monitoring devices are on clinical trial]

Guideline for ketone testing

- Illness with fever and/or vomiting
- If BG rises above 15 mmol/l in an unwell child
- Episodes of drowsiness
- Abdominal pains or rapid breathing
- Before breakfast to detect overnight insulin deficiency

Glycated hemoglobin

◊ Glucose attaches itself to the molecule of hemoglobin (Hb) during the life-cycle of the circulating red cell, forming glycated hemoglobin (HbA₁ or HbA₁c)
◊ HbA₁c level reflects levels of glycemia over the preceding 6–12 weeks
Assessment and monitoring of metabolic control

HbA1c monitoring has been shown to be the most useful measure in evaluating metabolic control and is the only measure for which good data are available in terms of its relationship with later microvascular complications.

Recommendation

Facilities for the measurement of HbA1c should be available to all centers caring for young people with diabetes.

- Frequency of measurement will depend on local facilities and availability, but good clinical practice would suggest that there should be four to six measurements per year in younger children, three to four measurements per year in older children, and a minimum of one measurement per year in all children.

Equipment and facilities

- A normal reference range for non-diabetic children should be available.
- There should be regular quality control comparisons with national and DCCT standards.
- It is preferable that a capillary method for collecting the child’s blood is available and that the HbA1c result is available at the time of the clinic visit so that adjustments in management may be based on that information.

Targets

- For each individual the target should be the lowest achievable HbA1c without the occurrence of frequent or severe hypoglycemia (see Table 5 for specific target indicators of glycemic control).
  - A proportion of children should expect to achieve an HbA1c within the normal reference range at some time in the first year after diagnosis (during the partial remission phase).
  - The DCCT showed that as HbA1c rises above 7.5% (or more than approximately 120% above the upper level of the normal reference range), the risk of later microvascular complications increases steeply. [In the DCCT intensive treatment group of adolescents, fewer than 50% achieved a mean HbA1c <8% (reference range <6.05%)].

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**Fructosamine and other glycated products**

◊ Fructosamine measures the glycation of serum proteins such as albumin and reflects glycemia over the preceding 3–4 weeks. It is therefore used for the assessment of shorter periods of control than HbA1c.
◊ Fructosamine has not been evaluated in terms of vascular risk

**Record-keeping**

• It is common practice for a monitoring diary, logbook or some type of electronic memory device to be used to record patterns of glycemic control and adjustments to treatment
• The record book is useful at the time of consultation and should contain

◊ BG levels
◊ Time and date
◊ Insulin dosage
◊ Special events affecting glycemic control (e.g. illness, parties, exercise, menses, etc)
◊ Hypoglycemic episodes and description of severity

Monitoring records should not be used as a judgement but a vehicle for discussion on the causes of variability and strategies for improving glycemic control

In many countries, facilities and equipment for monitoring are very expensive. However, it must be recognized by nations, states and health care providers that without accurate monitoring the risks of acute crises and long-term vascular and other damaging complications are greatly increased, leading to high levels of health costs and personal disability
Insulin

Insulin availability

◊ Children and adolescents with type 1 diabetes are dependent on insulin for survival
◊ ISPAD and IDF are working towards universal insulin availability for all children and adolescents with diabetes (see Summary of essential requirements) and are promoting universal insulin labeling

Insulin treatment must be started as soon as possible after diagnosis (usually within 24 h if ketonuria is present) to prevent metabolic decompensation and diabetic ketoacidosis

Insulin formulation and species

◊ Many formulations of insulin are available; most have some role in the management of type 1 diabetes (Table 6).
◊ Most children are prescribed human insulins because of their availability through modern manufacturing techniques using recombinant DNA technology and because of their low immunogenicity

Porcine or bovine preparations may be cheaper and more readily available in some parts of the world. They are not inferior in clinical efficacy to human insulins. Some locally manufactured preparations have greater immunogenicity, and high titer antibodies may alter pharmacodynamics by acting as insulin-binding proteins. This is particularly relevant when using older bovine insulins

Short-acting insulin

• Short-acting (soluble, regular) insulin is used as an essential component of most daily replacement regimens either
  – in combination with intermediate-acting insulin in a twice-daily regimen
  or
  – as pre-meal bolus injections in basal-bolus regimens (20–30 min before meals)
• Soluble is the only insulin suitable for IV therapy
Soluble insulin is used in the following crisis situations
– diabetic ketoacidosis
– control of diabetes during surgical procedures
– hyperglycemic episodes at home (e.g. during intercurrent illness)

### Rapid-acting insulin analogs

Several novel insulin analogs are being developed. Two rapid-acting monomeric types are currently available for children. They have a rapid onset and shorter duration of action than soluble insulin (see table)

- Rapid-acting analogs can be given immediately before meals because there is evidence that the rapid action not only reduces postprandial hyperglycemia but that postprandial and nocturnal hypoglycemia may also be reduced. In selected children they offer the useful option of being given after food to toddlers who are reluctant to eat
- Rapid-acting analogs may also be used during sick days with hyperglycemia and potential ketosis
- Rapid-acting analogs are most often used as prandial or snack boluses in combination with longer acting insulins given twice or more times daily

### Recommendation

All children should have soluble or rapid-acting insulin available for crisis management

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**Table 6: Types of insulin preparations and suggested action profiles**

<table>
<thead>
<tr>
<th>Insulin type</th>
<th>Onset of action (h)</th>
<th>Peak of action (h)</th>
<th>Duration of action (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid-acting analogs</td>
<td>0.15–0.35</td>
<td>1–3</td>
<td>3–5</td>
</tr>
<tr>
<td>Short-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular/soluble</td>
<td>0.5–1</td>
<td>2–4</td>
<td>5–8</td>
</tr>
<tr>
<td>Intermediate-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Semi-lente (pork)</td>
<td>1–2</td>
<td>4–10</td>
<td>8–16</td>
</tr>
<tr>
<td>Isophane NPH</td>
<td>2–4</td>
<td>4–12</td>
<td>12–24</td>
</tr>
<tr>
<td>IZS lente type</td>
<td>3–4</td>
<td>6–15</td>
<td>18–24</td>
</tr>
<tr>
<td>Long-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultralente type</td>
<td>4–8</td>
<td>12–24</td>
<td>20–30</td>
</tr>
<tr>
<td>Analog</td>
<td>2–4</td>
<td>none</td>
<td>24</td>
</tr>
</tbody>
</table>

NPH, neutral protamine Hagedorn insulin; IZS, insulin zinc suspension

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**Intermediate-acting insulins**

- The action profiles of these insulins make them suitable for twice-daily regimens and for pre-bed dosage in basal-bolus regimens

Two principal preparations are used

- Isophane NPH (neutral protamine Hagedorn) insulins
- Crystalline zinc acetate insulin (insulin zinc suspensions [IZS] or lente insulins)

Isophane insulins are extensively used in children, mainly because of their suitability for mixing with soluble or rapid-acting insulins in the same syringe, vial or cartridge without interaction

- When soluble insulin is mixed with lente preparations it reacts with excess zinc, blunting its short-acting properties

**Long-acting insulins**

- Ultralente® and Ultratard® insulins were designed to have a duration of action of more than 24 h to meet basal insulin requirements and therefore could be used in basal-bolus injection regimens. Their action profile in children appears to be extremely variable and they may have to be injected twice daily to meet basal insulin requirements
- A long-acting insulin analog has recently become available

**Pre-mixed insulin preparations**

- Pre-mixed insulins (fixed ratio mixtures of soluble and isophane) are popular in some countries particularly for prepubertal children on twice-daily regimens. Although they reduce potential errors in drawing up insulin, they remove the flexibility offered by separate adjustment of the two types. Such flexibility is useful for children with variable food intake
- There is no clear evidence that pre-mixed insulins in young children are less effective, but there is some evidence of poorer metabolic control when they are used in adolescents
- Pre-mixed insulins with soluble:isophane in different ratios, e.g. 10:90, 15:85, 20:80, 25:75, 30:70, 40:60 and 50:50, are available in various countries from different manufacturers
- Pre-mixed insulins are most commonly used in pen injector devices
- Pre-mixed insulins may be useful when compliance (or adherence) to the regimen is a problem
Insulin concentrations

◊ The most widely available insulin concentration is 100 IU/ml (U 100)
◊ Treatment with U 40 (40 IU/ml) or other concentrations such as U 500 are also acceptable subject to availability and special needs
◊ Care must be taken to ensure that the same concentration is supplied each time a new prescription is made
◊ Very young children occasionally require insulin diluted with diluent obtained from the manufacturer, but special care is needed in dilution and drawing up the insulin into the syringe

Insulins must be administered by insulin syringes (or other injection devices) calibrated to the concentration of insulin being used

Storage of insulin

The individual manufacturer’s storage recommendations and expiry dates must be adhered to. These usually suggest that

• Insulin must never be frozen
• Direct sunlight or warming (in hot climates) damages insulin
• Unused insulin should be stored in a refrigerator (2–8°C)
• After opening, an insulin vial should be discarded after 3 months if kept at 2–8°C or after 1 month if kept at room temperature
• In hot climates where refrigeration is not available, cooling jars or a cool wet cloth around the insulin will help to preserve the insulin activity

Recommendation

It is advisable that a small supply of spare insulin should be readily available to all children and adolescents so that supply is uninterrupted

Injection sites

The usual injection sites are

◊ Front of thigh/lateral thigh (the preferred site because of ease of access, administration and for slower absorption of longer acting insulins)
◊ Abdomen (the preferred site when faster absorption is required, and it

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Insulin

May be less affected by muscle activity on exercise
◊ Buttocks (upper outer quadrant – may be useful in small children)
◊ Lateral aspect of arm (in small children with little SC fat, IM injection is more likely and it may cause unsightly bruising)

• Cleaning or disinfection of skin is not necessary unless hygiene is a real problem. Infection at injection sites is uncommon

Recommendation

Children and adolescents should be encouraged to inject consistently within the same site at a particular time in the day, but must avoid injecting repeatedly into the same spot to prevent lipohypertrophy

Problems with injections

◊ Local hypersensitivity reactions to insulin injections are uncommon but when they do occur, formal identification of the insulin (or more rarely preservative) responsible may be possible with help from the manufacturer, or a trial of an alternative insulin preparation may solve the problem
◊ Lipohypertrophy with the accumulation of fat and fibrous tissue in lumps underneath the skin is common in children
◊ Lipoatrophy is now uncommon since the introduction of highly purified insulins
◊ Painful injections are a common problem in children. Check angle and depth of injection to ensure injections are not being given IM
◊ Leakage of insulin is common and cannot be avoided. Encourage slower withdrawal of the needle from the skin, stretching of the skin after the needle is withdrawn, or pressure with a clean finger over the injection site
◊ Bruising and bleeding are more common after IM injection or tight squeezing of the skin
◊ Bubbles in insulin should be removed whenever possible. If the bubble is not big enough to alter the dose of insulin it should not cause problems

Insulin absorption

◊ Insulin activity profiles show substantial variability both day to day in the
same individuals and between individuals, particularly children
◊ The onset, peak effect and duration of action depend upon many factors
which significantly affect the speed and consistency of absorption

**Young people and care providers should be aware of the following factors which influence insulin absorption**

◊ Age (young children, less SC fat → faster absorption)
◊ Fat mass (large SC fat thickness, lipohypertrophy → slower absorption)
◊ Dose of injection (small dose → faster absorption)
◊ Site and depth of injection (abdomen faster than buttock; buttock faster
  than leg; superficial injection → slower absorption)
◊ Exercise (leg injection, leg exercise → faster absorption)
◊ Insulin concentration, type and formulation (lower concentration →
  faster absorption)
◊ Ambient and body temperature (higher temperatures → faster
  absorption)

• Faster absorption results in shorter duration of action

**Administration of insulin**

*Injection technique*

◊ **Injections by syringe** are usually given into the deep SC tissue through
  a two-finger pinch of skin at a 45–90° angle
◊ The pinch of skin is used to avoid the risk of administering insulin IM
◊ The SC fat layer should be thicker than the needle length. Very short
  needle lengths (e.g. 5 or 8 mm) are now available in some countries and
  they are particularly useful for young, slim children
◊ All suspensions of insulin (e.g. NPH, IZS, pre-mixes) must be resuspended
  before injection by rolling or inverting the vial or pen injector device (10
  times) so that the cloudy suspension mixes thoroughly and uniformly
◊ **Pen injector technique** requires careful education including the need to
  ensure that no airlock or blockage forms in the needle; a wait of 5–10
  seconds after pushing in the plunger helps to ensure complete expulsion
  of insulin through the needle

*Self-injection*

◊ It should be emphasized that a proportion of people with diabetes have
  a severe and long-lasting dislike of injections, which may influence their
  glycemic control
**Insulin**

- There is great individual variation in the appropriate age for children to self-inject
- The appropriate age relates to developmental maturity rather than chronological age
- Most children over the age of 10 years either administer their own injections or help with them
- Younger children sharing injection responsibility with a parent or other care provider may help to prepare the device or help push the plunger and subsequently under supervision be able to perform the whole task successfully
- Self-injection is sometimes triggered by an external event such as overnight stay with a friend, a school excursion or diabetes camp
- Parents or care providers should not expect that self-injection will automatically continue and should accept phases of non-injection and the need to provide help
- Younger children on multiple injection regimens may need help to inject sites that are difficult to reach (e.g. buttocks) to avoid lipohypertrophy

**Recommendation**

Regular checking of injection sites, injection techniques and skills remains the responsibility of parents, care providers and health professionals

**Self-mixing of insulin**

When a mixture of two insulins is drawn up (e.g. soluble mixed with isophane), it is most important that there is no contamination of one insulin with the other in the vials. To prevent this the following principles apply

- There is no uniformity of advice but most often it is taught that clear insulin (short-acting) is drawn up into the syringe before cloudy insulin (intermediate- or long-acting)
- If the cloudy insulin is lente type, the mixture must be administered immediately otherwise the short-acting component interacts
- Insulins from different manufacturers should be used together with caution as there may be interaction between the buffering agents
- NPH and lente insulins should never be mixed
- Rapid-acting insulin analogs may be mixed in the same syringe as NPH or lente
Devices for insulin delivery

**Insulin syringes**

◊ Plastic fixed-needle syringes with small dead space are preferable to glass syringes
◊ Syringes are available in a variety of sizes in different countries and should enable accurate dose delivery, but it is desirable for small dose, 1 unit per mark syringes (e.g. 0.3 ml) to be available for small children
◊ Plastic fixed-needle syringes are designed for single use (but many children and adolescents successfully re-use them without a significant increase in risk of infection). Re-use should be discouraged if there is concern about hygiene

• **Insulin syringes must have a measuring scale consistent with the insulin concentration (e.g. U 100 syringes)**
• **Syringes must never be shared with another person because of the risk of acquiring blood-borne infection (e.g. hepatitis, HIV)**
• It is advisable that all children and adolescents with diabetes should know how to administer insulin by syringe because other injection devices may malfunction

**Disposal of syringes**

• Appropriate disposal procedures are mandatory
◊ Specifically designed and labeled ‘sharps containers’ may be available from pharmacies and diabetes centers
◊ Special needle clippers (e.g. Safeclip®) may be available to remove the needle and make it unusable
◊ Without a sharps container, syringes with the needles removed may be stored and discarded in opaque plastic containers or tins for garbage collection

**Subcutaneous indwelling catheters**

◊ Such catheters (e.g. Insuflon®) inserted using topical local anesthetic cream may be useful to overcome problems with painful injections
◊ These catheters are used in some centers for introduction of multiple injection therapy

**Pen injector devices**

◊ Pen injector devices containing insulin in prefilled cartridges have been designed to make injections easier and more flexible. They eliminate the need for drawing up from an insulin vial, the dose is dialled up on a
digital scale and they may be particularly useful for insulin administration away from home, at school or on holiday
◊ Special pen injection needles of small size are available and may cause less discomfort on injection
◊ Pen injectors of various sizes and types are available from the pharmaceutical companies. Availability is a problem in some countries and although pen injectors may improve convenience and flexibility they are a more expensive method of administering insulin
◊ Pen injector devices are useful in children on multiple injection regimens or fixed mixtures of insulin but are less acceptable when free mixing of insulins is used

Automatic injection devices

◊ Automatic injection devices are useful for children who have a fear of needles. Usually a loaded syringe is placed within the device, locked into place and inserted automatically into the skin by a spring-loaded system
◊ The benefits of these devices are that the needle is hidden from view and inserted rapidly through the skin
◊ Automatic injection devices for specific insulin pen injectors are now available

Jet injectors

◊ High pressure jet injection of insulin into the skin has been designed to avoid the use of needle injection
◊ Jet injectors may have a role in cases of needle phobia
◊ Problems with jet injectors have included a variable depth of penetration, bruising, variable absorption of insulin, and cost

Subcutaneous insulin infusion pumps

◊ The use of external pumps is increasing and is proving successful even in young infants for stabilizing difficult diabetes
◊ Insulin pump treatment may be hazardous when education and adherence to therapy is inadequate because of the smaller depot of SC insulin and the risk of ketoacidosis
◊ Only short-acting or rapid-acting insulin analogs are used in the pumps

The use of pumps should be restricted to centers with special experience and expertise. Twenty-four-hour access to the center should be provided
Insulin regimens

No insulin injection regimen satisfactorily mimics normal physiology

- The choice of insulin regimen will depend on many factors including: age, duration of diabetes, lifestyle (dietary patterns, exercise schedules, school, work commitments, etc), targets of metabolic control and, particularly, individual patient/family preferences
- At least two injections of insulin per day are advisable in most children. Occasionally, particularly during the partial remission phase in younger children, one injection per day maintains satisfactory glycemic control
- Most regimens include a proportion of soluble short-acting or rapid-acting insulin analog, but some young children or those in the partial remission phase maintain satisfactory metabolic control on intermediate or long-acting insulins alone

Recommendation

Whatever insulin regimen is chosen it must be supported by comprehensive education appropriate for the age, maturity and individual needs of the child and family

Principles of insulin therapy

- To provide sufficient insulin throughout the 24 h to cover basal requirements
- To deliver higher boluses of insulin in an attempt to match the glycemic effect of meals

Frequently used regimens

- Two injections daily of a mixture of short and intermediate-acting insulins (before breakfast and the main evening meal)
- Three injections daily using a mixture of short and intermediate-acting insulins before breakfast; short-acting insulin alone before an afternoon snack or main evening meal; intermediate-acting insulin before bed; or variations of this
- Basal-bolus regimen of short-acting insulin 20–30 min before main meals (e.g. breakfast, lunch and the main evening meal); intermediate or long-acting insulin at bedtime
- Basal-bolus regimen of rapid-acting insulin analog immediately before

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main meals (e.g. breakfast, lunch and main evening meal); intermediate- or long-acting insulins at bedtime, probably before breakfast and occasionally at lunchtime

◊ **Insulin pump regimes** are regaining popularity with a fixed or variable basal dose and bolus doses with meals

None of these regimens can be optimized without frequent assessment by BG monitoring

**Daily insulin dosage**

Daily insulin dosage varies greatly between individuals and changes over time. It therefore requires regular review and reassessment

Dosage depends on many factors such as

◊ Age
◊ Weight
◊ Stage of puberty
◊ Duration and phase of diabetes
◊ State of injection sites
◊ Nutritional intake and distribution
◊ Exercise patterns
◊ Daily routine
◊ Results of BG monitoring (and glycated hemoglobin)
◊ Intercurrent illness

Guideline on dosage

- During the partial remission phase the daily insulin dose is often <0.5 IU/kg per day
- Prepubertal children (outside the partial remission phase) usually require 0.7–1.0 IU/kg per day
- During puberty, requirements may rise substantially above 1 IU/kg per day

The ‘correct’ dose of insulin is that which achieves the best attainable glycemic control for an individual child or adolescent

**Distribution of insulin dose**

The distribution of insulin dose across the day shows great individual variation
Insulin

- Children on twice-daily regimens often require more (perhaps two-thirds) of their total daily insulin in the morning, and less (perhaps one-third) in the evening.
- On this regimen approximately one-third of the insulin dose may be short-acting insulin and approximately two-thirds may be intermediate-acting insulin, although these ratios change with greater age and maturity of the young person.
- On basal-bolus regimens, night-time intermediate-acting insulin may represent 30–50% of total daily insulin: 50–70% as rapid or short-acting insulins divided up between three to four pre-meal boluses (when using rapid-acting insulin for pre-meal boluses, the proportion of basal insulin may be higher).

**Insulin dose adjustments**

**Soon after diagnosis**

◊ Frequent advice by members of the diabetes care team on how to make graduated alterations of insulin doses is of high educational value.
◊ Insulin adjustments should be made until target BG levels are achieved.
◊ If frequent BG monitoring is not possible, urinary tests are useful especially in the assessment of nocturnal control.

**Later insulin adjustments**

◊ On **twice-daily insulin regimens**, insulin dosage adjustments are usually based on recognition of daily patterns of BG levels over the whole day or a number of days, or in recognition of glycemic responses to food intake or energy expenditure.
◊ On **basal-bolus regimens**, flexible or dynamic adjustments of insulin are made before meals and in response to frequent BG monitoring. The new analogs may require postprandial BG tests to assess their efficacy.

| Health care professionals have the responsibility to advise parents, other care providers and young people on adjusting insulin therapy safely and effectively. This training requires regular review, reassessment and reinforcement |

**Advice**

◊ Elevated BG level before breakfast → increase pre-dinner or pre-bed intermediate or long-acting insulin (BG tests during the night might ensure that this change does not result in nocturnal hypoglycemia).
◊ Rise in BG level after breakfast → increase pre-breakfast short or rapid-acting insulin.
Elevated BG level before evening meal → increase pre-breakfast intermediate-acting insulin or increase dose pre-lunch of short or rapid-acting insulin if on basal-bolus regimen
Rise in BG level after evening meal → increase pre-evening meal short or rapid-acting insulin

In addition

Unexplained hypoglycemia requires re-evaluation of insulin therapy
Hyper- or hypoglycemia occurring in the presence of intercurrent illness requires a knowledge of ‘sick day management’
Day-to-day insulin adjustments may be necessary for variations in lifestyle routine especially exercise or dietary changes
Various levels of exercise require adjustment of diabetes management
Special advice may be helpful when there are changes of routine, travel, school outings, educational holidays or other activities which require adjustment of insulin doses

Development of skills in the independent adjustment of insulin doses varies greatly among young people and families. To facilitate these skills 24-h telephone access to personnel experienced in pediatric diabetes care should be available. This assists not only general diabetic management and safe insulin adjustment but also provides invaluable support during illness and other crises. In this way, admissions to hospital may be prevented

Dawn phenomenon

BG levels tend to rise in the hours of the morning (usually after 5.00 am) prior to waking. This is called the dawn phenomenon. In non-diabetic individuals the mechanisms include increased nocturnal growth hormone secretion, increased resistance to insulin action and increased hepatic glucose production. These mechanisms are more potent in puberty
In individuals with type 1 diabetes, fasting hyperglycemia is predominantly caused by waning insulin levels, thus exaggerating the dawn phenomenon. Research studies have not confirmed Somogyi’s idea that the rising BG is due predominantly to counter-regulatory hormones
Correction of fasting hyperglycemia is likely to require an adjustment of the insulin regimen to provide effective insulin levels throughout the night and the early morning, for example by the use of
– intermediate-acting insulin later in the evening or at bedtime
– a longer acting evening insulin
– insulin pump treatment
Nutritional management

Nutritional management is one of the cornerstones of diabetes care and education

◊ Achieving a balance between food intake, insulin levels and energy expenditure is an essential prerequisite for achieving glycemic control. Methods for accomplishing this show wide variations and are often complex and controversial
◊ Nutritional advice must be adapted to cultural, ethnic and family traditions and to the individual requirements of the child
◊ The psychological significance of feeding patterns, appetite and tastes of the child must not be underestimated

1. It is recognized that different countries and regions have widely varying dietary habits. These consensus guidelines are based on a number of national and international position statements and on current available evidence. Further research is required in some areas

2. Modern dietary recommendations for young people with diabetes are essentially healthy eating recommendations suitable for the general population and therefore should be applicable to the whole family

3. Several of the recommendations are associated more with reducing cardiovascular risk than specifically helping to improve glycemic control

Aims of nutritional management

• Provide sufficient and appropriate energy intake and nutrients for optimal growth, development and good health
• Encourage healthy lifelong eating habits whilst preserving social, cultural and psychological well-being
• Achieve and maintain the best possible glycemic control
• Achieve and maintain ideal body weight. This includes the strong recommendation for young people to take regular physical exercise
• Prevent and treat acute complications of diabetes such as hypoglycemia, hyperglycemic crises, illness and exercise-related problems
• Help to prevent micro and macrovascular complications
Nutritional management

Nutritional support, education and advice

Recommendations

1. A specialist pediatric dietician with experience in childhood diabetes should be available to provide advice to parents and young people as soon as possible after diagnosis to promote a secure and supportive relationship.

2. Simple advice should be given at the first meeting followed by more detailed education in later weeks.

3. Education should be individualized and appropriate for the age and maturity of the child to help engage the child in active learning.

4. Advice should be available to the other caregivers, e.g., extended family, schoolteachers, babysitters.

5. The dietician should be part of the children’s multidisciplinary diabetes care team.

6. Dietary messages throughout the team must be consistent.

The dietician will be expected to:

- Take a **dietary history** including:
  - Pre-existing family dietary habits, traditions, and beliefs
  - The child’s usual appetite, food intake, energy, carbohydrate distribution, mealtimes
  - The child’s daily activities, including the impact of nursery/school/college/work and exercise schedules

- Give consistent diabetes **education**
- Promote a **healthy lifestyle**
Main nutritional recommendations

These are based on adult recommendations. Children <5 years require a more energy-dense diet; children >5 years should be encouraged to adopt adult nutritional guidelines.

Recommendations

1. Distribution of food energy and carbohydrate intake to balance insulin action profiles and exercise (and adjustment of insulin doses to varying food patterns).

2. Total energy needs to be sufficient for growth but to avoid obesity.

3. Total daily energy intake should be distributed approximately as follows:
   - **Carbohydrate >50%**
     - encourage complex unrefined higher fiber carbohydrate
     - moderate sucrose intake
   - **Fat 30–35%**
     - less than 10% saturated fat
     - less than 10% polyunsaturated fat
     - more than 10% monounsaturated fat
   - **Protein 10–15%**
     - decreasing with age

4. Fruit and vegetables (five items per day are recommended)

Food guide pyramid

◊ The pyramid displays diet recommendations in a diagrammatic form (Figure 3).

Energy balance

◊ Energy intake varies greatly with the availability of food and according to age, appetite, growth rate, puberty, energy expenditure and environmental influences such as ambient temperature.

◊ Although energy intake may be regulated by appetite, when food is in

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abundance excess energy intake causes obesity which, when accompanied by diabetes, increases cardiovascular risk
◊ At diagnosis, appetite and energy intake are high to restore the preceding catabolic weight loss, but should be reduced when weight is restored
◊ In puberty, energy intake and nutritional demands increase substantially along with significant increases in insulin dosage

Guidelines on food components

Carbohydrates

◊ The proportion of carbohydrate as a percentage of total energy intake varies enormously around the world but there is agreement that carbohydrate should not be restricted
◊ In some countries where carbohydrate forms 60–70% of intake, excellent glycemic control is achievable

- Meals containing complex carbohydrate from sources such as whole grains (wheat, corn, maize), potatoes, rice or pasta are particularly recommended
Carbohydrate sources containing **soluble fiber** should be strongly encouraged (see below)

**Quantitation of carbohydrate**

Many methods of counting carbohydrate have been used and many are still commonly used in pediatric practice
- e.g. Exchanges
  - Portions/servings
  - Grams
  - Glycemic index
  - Carbohydrate : insulin ratio

Although exchanges and gram counting would appear to have an educational value, there is little evidence that parents (and particularly young people) can understand or implement such diets in the long term. Unless rigorously reviewed, there is a danger that such dietary ‘prescriptions’ will lead to carbohydrate constraint as the child grows, and may lead to disordered eating behavior (including eating disorders).

However, some practical quantification of carbohydrate is necessary as part of intensification of management. Parents and young people should be able to visualize amounts and types of carbohydrate using educational tools such as the “plate model” or “size of hand model”. In this way it may be possible to estimate the glycemic impact of various types of food.

**The insulin dose and action profile needs to be balanced against the expected carbohydrate intake**

For example
- twice-daily insulin regimens of short and longer acting insulins require regular and frequent carbohydrate intake (often as ‘snacks’) to prevent hypoglycemia during inevitable periods of hyperinsulinemia
- multiple injection regimens of pre-meal short or rapid-acting insulins enable a more flexible or dynamic approach
- most insulin regimens require carbohydrate intake before bed to prevent nocturnal hypoglycemia
- increased exercise and sport require extra complex carbohydrate before, during and after exercise to balance increased energy needs and prevent hypoglycemia

**Fiber**

- Soluble fiber found mainly in vegetables, legumes, oats and fruits may be particularly useful because it reduces the speed of carbohydrate absorption and may improve lipid metabolism
- Insoluble fiber found in grains and cereals promotes healthy bowel function
Nutritional management

◊ A reasonable target for total fiber intake for children above 2 years is an amount equal (in grams) to the child’s age plus 5 g/day
◊ Increased fiber intake should be introduced slowly to prevent abdominal discomfort
◊ Increased fiber intake should be accompanied by an increase in fluid intake

Sucrose

◊ Can provide up to 10% of total energy intake (no more than that advised for the general population)
◊ Moderate amounts can be included as part of mixed meals without causing hyperglycemia
◊ Sucrose-sweetened drinks or sweets eaten at inappropriate times may cause significant hyperglycemia and should be avoided
◊ May be used to prevent or treat hypoglycemia before and during physical exercise
◊ Denial of sucrose-containing foods may have important psychological implications

Fructose

◊ The major fruit sugar, does not greatly elevate blood glucose
◊ In excess may elevate triglyceride levels
◊ As a sweetening agent is not recommended
◊ Naturally occurring sources, fruits and vegetables, are recommended

Fats

◊ Are the most energy-dense food substance and are important components of lipid membranes
◊ Serum cholesterol is a predictor of macrovascular risk. Although dietary cholesterol is not the most important determinant of serum cholesterol, a diet low in total fat with emphasis on decreasing saturated and transunsaturated fatty acids is recommended. Saturated fats are found in animal produce such as whole milk, cheese, butter and red meats. Transunsaturated fatty acids are found in manufactured confectionary such as biscuits, cakes and chocolates
◊ Polyunsaturated fatty acids derived from vegetable origins such as corn, sunflowers, safflower, soybean, seeds and oils, or from oily marine fish may reduce lipid cardiovascular risk factors. Unsaturated fatty acids of the n-3 variety found in oily fish and certain vegetable oils are thought to be particularly beneficial
◊ Monounsaturated fatty acids (particularly cis-configuration) found in olive, sesame, rapeseed and some nut oils may be beneficial in controlling
lipid levels and convey some protection against cardiovascular disease. They are recommended replacements for saturated fats.

In societies where total energy intake is compromised or where there is a predominant vegetable/fish diet, the intake of fat may be greater than the recommended 35%. However, this higher fat intake may be composed of low saturated fat and high levels of n-3 polyunsaturated fats. In South-East Asia the traditionally high carbohydrate, low fat diet comprises only 20–30% fat. In contrast, South Asian cooking methods of deep fat frying with ghee, a saturated form of fat, increase the total fat intake significantly and in addition to local high fat milk may increase cardiovascular risk especially when in association with diabetes.

**Protein**

◊ Worldwide intake of protein varies greatly depending on economy and availability
◊ Is an essential source of nitrogen
◊ Intake decreases during childhood from approximately 2 g/kg per day in early infancy to 1 g/kg per day for a 10 year old, and to 0.8–0.9 g/kg per day in later adolescence
◊ Can only be used for growth if the total energy intake is sufficient
◊ Sources of vegetable protein such as beans, legumes and lentils, which are lower in saturated fat and higher in fiber and complex carbohydrate, should be encouraged but are difficult to incorporate when not part of the indigenous diet
◊ When persistent microalbuminuria, raised blood pressure or established nephropathy occurs, excessive protein intake may be detrimental and therefore intake should be at the lower end of the scale. Protein restriction in adolescence should not be allowed to interfere with normal growth and requires expert management by a dietician

**Vitamins, minerals and antioxidants**

◊ Supplements of vitamins, minerals or trace elements are not usually recommended unless nutritional assessment confirms significant deficiencies
◊ Optimum vitamin status should be maintained for cardiovascular protection
◊ Many fresh fruits and vegetables are naturally rich in antioxidants (tocopherols, carotenoids, vitamin C, flavonoids) and should be strongly encouraged in young people with diabetes
Nutritional management

**Salt**

◊ Sodium chloride is added to many processed and ‘fast foods’
◊ In many countries, salt intake is in excess of recommendations
◊ In adults, less than 6 g/day is recommended (except in very hot countries) but evidence is not available for children

**Alcohol**

◊ Alcohol is dangerous in children and prohibited in many cultures
◊ Excess alcohol intake may induce a prolonged hypoglycemic effect
◊ Carbohydrate should be eaten before, during and after alcohol intake
◊ Special care should be taken to prevent nocturnal hypoglycemia

**Special labeled ‘diabetic’ foods**

◊ Are not recommended or necessary because they are expensive, calorie-dense, high in fat and may contain sweeteners with laxative effects
◊ Lower sugar or sugar-free products are more suitable

**‘Bulk’ sweeteners**

◊ Added sweeteners such as dextrins or sugar alcohols (e.g. sorbitol, mannitol) are added to commercial foods to improve sweetness and palatability
◊ They are all energy-containing, and affect the level of BG. They may also produce a laxative effect and are not recommended as sweeteners

**Artificial or intense sweeteners**

◊ Saccharin, aspartame, acesulfame K, cyclamates, alitame and sucralose are used in low sugar or sugar-free products to improve sweetness and palatability
◊ Acceptable daily intakes have been established in some countries

**Meal planning and review**

◊ The dietician should advise on planning, content and timing of meals and snacks (particularly carbohydrate intake) in the context of each child’s individual circumstances, lifestyle and the insulin action profiles
Particular attention should be paid to the energy profile of snacks, encouraging low fat carbohydrate choices.

It is unlikely that meal planning will be successful unless the whole family is involved in making appropriate changes based on healthy-eating principles.

**Recommendations**

1. The *initial* nutritional plans should be reviewed by the specialist pediatric dietician within a month or so after diagnosis.

2. Thereafter contacts will depend on local arrangements, but as a minimum should include annual reassessments to keep pace with the child's height, weight, diabetes management, lifestyle changes, developmental stages and the identification of specific dietary problems such as weight loss, obesity and eating disorders.

**Special groups, events and problems**

All care givers, school staff and friends should be aware of the child’s diabetes and have an understanding of the recognition and management of hypoglycemia paying special attention to the following age groups.

**Infants and toddlers**

- Breastfeeding of infants should be encouraged.
- Frequent small meals (‘grazing’) may promote better glycemic control, depending on the insulin regimen.
- Participation in family meals may promote improved cooperation.
- A variety of tastes, colours and textures should be encouraged.
- Food substitutes and flexibility in food intake and insulin (e.g. rapid analogs) may be useful for episodes of food refusal or ‘sickness’.

**Schoolchildren**

- Require advice on prevention of hypoglycemia. Food planning for episodic or planned physical activity is advisable.
- Need to double their energy intake for optimal growth between ages 6 and 12 years.
- Should receive specific holiday and travel advice, particularly for school events.
**Nutritional management**

**Adolescents**

◊ Weight monitoring is important in the early recognition of weight loss or excessive weight gain.
◊ Excessive weight gain (and obesity) may be associated with attempts to obtain excellent glycemic control by matching insulin levels with food intake. Careful review of insulin dosage, energy input and output is advisable to help resolve this difficult problem.
◊ Poor growth may be a sign of insufficient energy intake, inappropriate or missed insulin doses and/or poor glycemic control.
◊ Rebellion, binges and erratic eating behavior may require expert (psychological) support and counseling.
◊ The association between weight loss and eating disorders needs to be recognized.
◊ Advice on drinking alcohol and food intake is important in certain societies.

**Parties, festivities and special events**

◊ Special dispensation is usually given to children with diabetes during fasts such as Ramadan.
◊ Parents are recommended to advise other care givers on food preferences and low sugar drinks.
◊ Occasional sugary food treats may not provoke hyperglycemia if physical activity levels are also high or insulin dose adjustments are made.
◊ Advice on additional (short or rapid-acting) insulin may be useful to prevent or treat hyperglycemia.
◊ Friends and other care givers should know how to recognize and treat hypoglycemia.

**Education, training, audit and research**

◊ Pediatric dieticians should be trained not only in nutrition and diabetes care but in communication skills, psychology and behavior modification techniques.
◊ Audit and evaluation of dietary advice are often deficient and may be assisted by regular dietetic data collection and the use of databases.
◊ More research is needed on nutritional management and to provide evidence on its effectiveness.
Diabetic ketoacidosis

Diabetic ketoacidosis (DKA) is the commonest cause of diabetes-related deaths in children

Most deaths in DKA occur as a result of cerebral edema

Deaths and neurological morbidity should be avoidable by

- Reducing the incidence of DKA by
  - earlier diagnosis at onset
  - appropriate management of diabetes during intercurrent illness
  - recognition that recurrent DKA is often caused by insulin omission

- Optimal management of DKA

No protocol for DKA has been shown to eliminate the risk of cerebral edema. These consensus guidelines are believed to be the safest available in the light of current evidence and clinical practice

Recommendations

1. In centers treating DKA, a clear, unambiguous, written protocol, adapted to local circumstances, should always be immediately available

2. A senior specialist/consultant physician with experience in managing DKA in children should be consulted for advice

Definition

These guidelines are recommended for children with

- Heavy glycosuria (>55 mmol/l) and ketonuria
- Hyperglycemia (BG >11 mmol/l)
- pH <7.3
- Bicarbonate <15 mmol/l and who are

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**Diabetic ketoacidosis**

5% or more dehydrated
± vomiting
± drowsy

◊ In rare cases the BG is not elevated

◊ Children <5% dehydrated and not clinically unwell usually tolerate oral rehydration and SC insulin

**Recommendation**

Children and adolescents who develop DKA as defined above should be managed in centers with experience of such treatment, where vital signs, neurological status and laboratory results can be monitored and evaluated frequently

**Emergency assessment**

**Confirm the diagnosis**

- Characteristic history
  - polydipsia, polyuria
- Biochemical confirmation
  - glycosuria
  - ketonuria
  - BG
  - pH
- Clinical assessment
  - full examination paying special attention to

◊ **Severity of dehydration**
  - 3% just detectable
  - 5% dry mucous membranes, reduced skin turgor
  - 10% capillary return 3 seconds or more, sunken eyes
  - 10%+ shock, poor peripheral pulses

Clinical assessment of dehydration may be difficult especially in young children. Severity of dehydration is often overestimated
Diabetic ketoacidosis

◊ Evidence of acidosis
  – hyperventilation
◊ Assessment of conscious level (and examine pupils and retinal fundi)

Recommendation

Optimal management of children with severe DKA (pH <7.1, hyperventilation, in shock, depressed level of consciousness, persistent vomiting, age <5 years) is in an intensive care unit or at least in a children’s ward specializing in diabetes care

Immediate investigation

- Weigh child whenever possible (or obtain recordings from recent visits)
- Capillary BG (often inaccurate in the presence of poor peripheral circulation and severe acidosis)
- Venous BG, electrolytes and urea
- Capillary, venous or arterial blood gases
- As indicated: full blood count (leukocytosis is a common feature of DKA), HbA₁c, urine culture, throat swab, chest x-ray, blood cultures. Height measurement or estimation is of value if calculation of body surface area is required
  [Retrospectively a fluid input >4 l/m² per 24 h has been suggested as a risk factor in cerebral edema]

Resuscitation

In shock with poor peripheral pulses, or coma

- Oxygen 100% by face mask
- Normal saline 0.9% 10 ml/kg over 10–30 min (should be repeated if peripheral pulses remain poor)
  [Albumin 4–5% solution 10 ml/kg or other volume expanders may be used but there is no evidence that they are preferable]
- Nasogastric tube to drain stomach if there is vomiting ± impaired consciousness

In most DKA protocols the fluid for resuscitation is not included in the calculations for later deficit dehydration.

If the child is in a location 1 h or more from a specialist center, Normal saline 0.9% should continue at 10 ml/kg per h for 1–2 h (thereafter 5 ml/kg per h)
Diabetic ketoacidosis

Clinical observations and monitoring

Careful and frequent clinical monitoring to detect warning signs of complications is of paramount importance

- **Hourly**
  - pulse rate, respiratory rate, blood pressure
  - accurate fluid input and output (when level of consciousness is impaired a urinary catheter may be necessary). Test each urine specimen for glucose and ketones
- **Hourly or more frequent** neurological observations
- **ECG monitoring** in severe DKA to assess T-waves
  [There is no evidence but it would seem logical after resuscitation to nurse patients with the head of the bed raised in an attempt to reduce CSF pressure]

Rehydration and insulin management

**Fluids**

The cause of cerebral edema during treatment remains unclear. However, too rapid reduction in intravascular osmolality may aggravate the process. It seems prudent therefore that rehydration should occur more slowly in children with DKA than in other causes of dehydration

Proceed with urgency but with caution

**Use either: Fluid calculation (model 1)**

**Requirements = Deficit + Maintenance**

- Calculate **DEFICIT = estimated % dehydration \times body weight (kg and equivalent in ml)**
- Calculate **MAINTENANCE (ml)** (Table 7)
• Then add **DEFICIT** to **48 h MAINTENANCE** and replace this volume evenly over 48 h as **Normal saline 0.9% initially**

**Or use: Fluid calculation (model 2)**

Covers **MAINTENANCE + 10% DEFICIT** given evenly over 48 h in children of all sizes

- 6 ml/kg per h for children weighing 3–9 kg
- 5 ml/kg per h for children weighing 10–19 kg
- 4 ml/kg per h for children weighing >20 kg (up to maximum of 250 ml/h)

These calculations will usually cover ongoing losses which in most cases do not need additional replacement, but excessive continuing fluid losses might need replacing if the severity of dehydration is not improving

• **When the BG falls to 12–15 mmol/l** the infusion should be changed to a fluid containing glucose, the most commonly recommended being **saline 0.45% (or 0.9%) with glucose 4–5%** (or glucose 5% with added sodium chloride 80 mmol/l or more)

**Oral fluids**

• In severe dehydration and acidosis only allow sips of cold water or ice to suck
• Oral fluids (e.g. fruit juice/oral rehydration solution) should only be offered after substantial clinical improvement and no vomiting
• Oral fluid volume should be subtracted from the IV calculations

**Potassium**

◊ Total body potassium is always substantially depleted in DKA
◊ Serum/plasma potassium may be low, normal or high
◊ If serum potassium is not available before the completion of resuscitation, ECG monitoring is recommended before potassium is added to the infusion fluid

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**Table 7: Calculation of maintenance fluid volumes for different ages.**

<table>
<thead>
<tr>
<th>Approximate age (years)</th>
<th>Weight (kg)</th>
<th>Maintenance fluid (ml/kg per 24 h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>3–9</td>
<td>80</td>
</tr>
<tr>
<td>1–5</td>
<td>10–19</td>
<td>70</td>
</tr>
<tr>
<td>6–9</td>
<td>20–29</td>
<td>60</td>
</tr>
<tr>
<td>10–14</td>
<td>30–50</td>
<td>50</td>
</tr>
<tr>
<td>&gt;15</td>
<td>&gt;50</td>
<td>35</td>
</tr>
</tbody>
</table>

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*Diabetic ketoacidosis*
Diabetic ketoacidosis

- Start potassium replacement as soon as resuscitation is completed and the ECG does not show elevated T-waves (or if serum potassium is not elevated)
- **Potassium chloride 40 mmol** is usually added to each liter of saline infusion
  [Phosphate or acetate salts of potassium may also be used but there is no evidence that they are preferable]

**Insulin**

**DKA is caused by insulin deficiency, either relative or absolute**

- Insulin should not be started until shock has been successfully reversed by emergency resuscitation and a saline/potassium rehydration regimen begun (this avoids sudden influx of potassium from plasma into cells, with danger of cardiac arrhythmia)
- During the first 60–90 min of initial rehydration the BG may fall substantially even without insulin treatment
- **Insulin by continuous low-dose IV infusion is the optimal method**
  [An initial bolus of insulin is not recommended]
- A solution of **soluble insulin 1 unit/ml made up in Normal saline** is best by electronic pump
- Recommended initial insulin dose = **0.1 units/kg per h**
  [Some recommend 0.05 units/kg per h particularly for younger patients]

◊ When syringe pumps are not available a separate low-dose infusion may be given, e.g. soluble insulin 50 units in 500 ml Normal saline (i.e. 1 unit insulin per 10 ml saline), the bag being changed every 24 h to avoid inactivation of insulin
◊ When insulin infusion methods are not available the use of hourly IM/SC injections of soluble or rapid-acting insulin 0.1 units/kg has been shown to be effective
◊ After resuscitation the typical rate of fall of BG is 4–5 mmol/h
- When BG falls to 12–15 mmol/l, change to the glucose saline infusion (as above) to maintain BG in the desired range of 8–12 mmol/l
- If BG rises again above 15 mmol/l, increase the insulin infusion by 25%
- If BG falls to <8 mmol/l, or falls too rapidly, increase the concentration of glucose to 10% (or more) with added saline
- The insulin infusion rate should only be decreased if the BG level remains below the target range despite glucose supplementation
- Do **not** stop insulin infusion or decrease below 0.05 units/kg per h

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• because a continuous supply of both insulin and glucose substrate is needed to promote anabolism and reduce ketosis

**Bicarbonate**

There is no evidence that bicarbonate is either necessary or safe in DKA. Bicarbonate should not be used in the initial resuscitation

• **Potential hazards** of bicarbonate therapy
  – exacerbation of CNS acidosis
  – hypokalemia and altered calcium ionization
  – excessive osmolar load
  – tissue hypoxia
• Persistent acidosis is likely to be caused by inadequate resuscitation, inadequate insulin effect or sepsis
• Bicarbonate may be considered for treatment of impaired cardiac contractility in persistent severe shock
  [If bicarbonate is considered, proceed with caution giving 1–2 mmol/kg bicarbonate over 60 min]

**Monitoring progress**

**Capillary BG**
Monitor hourly (cross-check every 2 or 4 h against laboratory venous glucose)

**Laboratory tests**
Electrolytes, urea, BG and blood gases should be repeated every 2–4 h until acidosis is reversed

**Sodium and osmolality**

◊ Despite the depletion of total body sodium in DKA, the elevated osmolality in the hyperglycemic state results in a dilutional effect on the measured sodium
**Diabetic ketoacidosis**

Corrected sodium can be calculated from

\[
\text{Corrected Na} = \text{Measured Na} + 2 \times \left( \frac{\text{BG} - 5.5}{5.5} \right)
\]

[This calculation may be useful when concerns arise with abnormal measured sodium levels]

◊ Serum sodium often rises as the BG falls. Theoretically, sodium should rise by 2 mmol for every 5.5 mmol fall in BG, resulting in a slower fall in osmolality

◊ Serum osmolality can be measured directly or calculated from

\[
\text{Serum osmolality (mOsm)} = 2 \times (\text{Na} + \text{K}) + \text{BG (mmol)}
\]

[Retrospectively a fall of serum osmolality >3 mOsm/kg per hour has been suggested as a risk factor in cerebral edema although the evidence is weak]

A fall in serum sodium has been noted in a number of studies as one of the few laboratory correlates of impending cerebral edema

- If serum sodium fails to rise, and particularly if it falls, a careful re-evaluation of the fluid replacement is required. Consider increasing the concentration of sodium chloride and observe with increased vigilance for signs of cerebral edema
- An initial serum sodium >150 mmol/l might prompt an even slower rehydration rate than 48 h

**Potassium**

- The potassium infusion should be titrated to maintain serum potassium within the laboratory normal range

**Urine output**

If this is inadequate (< 1.5 ml/kg/h) the cause must be sought (e.g. acute renal failure, continuing shock, urinary obstruction, bladder retention). If fluid retention is occurring there is some evidence that a single dose of a loop diuretic might be helpful in promoting water diuresis
Complications

Cerebral edema

◊ Approximately 0.4–1% of children with DKA develop cerebral edema with a high mortality/morbidity
◊ Cerebral edema most commonly occurs in the first 24 h after starting rehydration when the general condition of the child might seem to be improving. Vigilant observations throughout the 24 h must not diminish
◊ In many cases warning signs/symptoms occur which should prompt the emergency administration of mannitol

Warning signs/symptoms of cerebral edema

• Headache and slowing of heart rate
• Change in neurological status (restlessness, irritability, increased drowsiness, incontinence) or specific neurological signs (e.g. cranial nerve palsies)
• Rising blood pressure, decreased O₂ saturation

◊ More dramatic changes such as convulsions, papilledema and respiratory arrest are late signs associated with extremely poor prognosis

Action

• Exclude hypoglycemia
• If warning signs occur at any time of day or night, give immediate IV mannitol 1 g/kg over 20 min (i.e. 5 ml/kg 20% solution)
• Halve rehydration infusion rate until situation is improved
• Nurse with child’s head elevated
• Move to intensive care unit as soon as possible
• Alert anesthetic and senior pediatric staff (if assisted ventilation is required maintain PCO₂ above 3.5 kPa)
• Consider continuation of mannitol infusion 0.25 g/kg per h to prevent rebound increase in intracranial pressure (or repeat bolus doses every 4–6 h)
• Cranial imaging should only be considered after child has been stabilized. Intracranial events other than edema may occur, e.g. hemorrhage, thrombosis, infarction

Mannitol should be immediately available during the treatment of DKA
Diabetic ketoacidosis

Hypoglycemia and hypokalemia
Avoid by careful monitoring and adjustment of infusion rates

Aspiration pneumonia
Avoid by nasogastric tube in vomiting child with impaired consciousness

Other associations with DKA
These require specific management, e.g. continuing abdominal pain (due to liver swelling/gastritis/bladder retention — but beware appendicitis), pneumothorax ± pneumomediastinum, interstitial pulmonary edema, unusual infections (e.g. TB, fungal infections), hyperosmolar hyperglycemic non-ketotic coma, ketosis in type 2 diabetes

Transition to SC insulin injections

• Oral fluids should be introduced only when substantial clinical improvement has occurred (mild acidosis/ketosis may still be present)
• When oral fluids are tolerated, IV fluid should be reduced
• Insulin infusion may be continued with adjustments to cover oral carbohydrate intake or
• Insulin by SC injection may be started when oral intake is tolerated
• The dose and type of SC insulin given will depend on local circumstances
• To prevent rebound hyperglycemia do not stop the IV insulin infusion until 60 min after the first SC injection of short or rapid-acting insulin

Algorithm for the management of DKA (see next page)

Recurrent DKA

◊ Associated with inadequate insulin levels
◊ Commonly due to insulin omission

• Parents and young people should learn how to recognize impending DKA and treat urgently with additional short or rapid-acting insulin
• Parents and young people should have easy 24-h access to emergency advice and treatment
Algorithm for the management of diabetic ketoacidosis

Immediate assessment

Clinical history
- Polyuria
- Polydipsia
- Weight loss (weight)
- Abdominal pain
- Tiredness
- Vomiting
- Confusion

Clinical signs
- Assess dehydration
- Deep sighing respiration (Kussmaul)
- Smell of ketones
- Lethargy/drowsiness and vomiting

Biochemical Signs
- Ketones in urine
- Elevated blood glucose
- Acidaemia
- Take blood for blood gases, electrolytes, urea
- Other investigations as indicated

Diagnosis confirmed

Diabetic Ketoacidosis

Contact senior staff

Resuscitation
- Airway/nasogastric tube
- Breathing (100% O₂)
- Circulation (saline 0.9% 10 ml/kg over 10-30 min until circulation restored. May be repeated)

IV therapy
- Calculate fluid requirements
- Correct over 48 hours
- Saline 0.9%
- ECG for elevated T-waves
- Add KCl 40 mmol/l fluid

Low dose continuous insulin infusion
- 0.1 U/kg per hour
- (consider 0.05U/kg per hour for a young child)

Critical observations
- Hourly blood glucose
- Hourly fluid input and output
- Neurological status at least hourly
- Electrolytes 2 hours after start of IV therapy
- Monitor ECG for T-waves changes

Acidosis not improving
- BG 12-15 mmol/l or BG falls >5 mmol/hour

Re-evaluation
- IV fluid calculations
- Insulin delivery systems and dose
- Need for additional resuscitation
- Consider sepsis

IV therapy
- Change to saline 0.45% + glucose 4 or 5%
- Adjust insulin infusion (not < 0.05 U/kg per hour)
- Adjust sodium infusion to promote an increase in serum sodium

Exclusive
- Hypoglycaemia
- is it cerebral edema?

Improvement
- Clinically well, tolerating oral fluids

Transition to SC insulin
- Start SC insulin then stop IV insulin 60 min later

Management
- Give IV mannitol 1 g/kg
- Restrict IV fluids by 50%
- Call senior staff
- Move to ICU
- Consider cranial imaging only after patient stabilized

Adapted from:
Dunger et al. Publ Karger, 1999
Diabetes and illness

Sick day management

◊ Although children whose diabetes is under good metabolic control should not experience more illness or infections than children without diabetes, those with poor metabolic control may have decreased immunity to a variety of different infections
◊ Illness associated with fever tends to raise BG because of higher levels of stress hormones, gluconeogenesis and insulin resistance
◊ Illness associated with vomiting and diarrhea (e.g. gastroenteritis) may lower BG, with the possibility of hypoglycemia

Recommendation

The diabetes care team should provide clear guidance on managing diabetes during intercurrent illnesses to avoid the complications of
– Dehydration
– Ketoacidosis
– Hypoglycemia

Guidance should include advice on the following

• Never stop insulin
  ◊ But advice should be available on alterations of insulin dose

• More frequent monitoring
  ◊ Frequent BG testing facilitates optimal management during illness
  ◊ Urinary ketone tests will guide management
  ◊ Adequate supplies of BG and ketone test strips should be available to avoid complications during intercurrent illness

• Loss of appetite
  ◊ Replacing meals with easily digestible food and sugar-containing fluids

• Maintaining hydration
  ◊ Hyperglycemia, fever and excessive glycosuria increase fluid losses
Specific medical advice

Treating fever, malaise and headache with antipyretics such as paracetamol.

Vomiting may be caused by:
- (a) the illness itself when the BG may be low
- (b) lack of insulin when the BG will be high and ketones may develop.

Consider treatment of vomiting with a single injection of an anti-emetic to help oral intake of carbohydrate.

Sugar-free medicines for young children are advisable but not essential.

Infections associated with hyperglycemia with or without ketosis

Recommend additional doses of short or rapid-acting insulins with careful monitoring to reduce BG, prevent ketoacidosis and avoid hospital admission.

The dose and frequency of injection will depend on the age of the child, the level and duration of hyperglycemia, the severity of ketosis and previous experience with alterations of insulin.

**Example** Sick child, BG 15–20 mmol/l (± ketosis): advise 10–20% of total daily insulin dose (or 0.1 U/kg) as short or rapid-acting insulin every 2–4 h until BG falls to <15 mmol/l. Thereafter any additional doses might be 5–10% of the total daily dose.

Infections associated with hypoglycemia

These infections are often associated with nausea, vomiting ± diarrhea. Advise replacing meals with frequent small volumes of sugary drinks and careful BG monitoring.

Reduction of insulin dose by 20–50% may be required.

If hypoglycemia (and nausea or food refusal) persists, an injection of glucagon may reverse the hypoglycemia and enable oral fluids to be re-established.
Diabetes and illness

Recommendation

In a child with intercurrent illness urgent specialist medical or nursing advice must be obtained when
- The diagnosis is unclear
- Vomiting is persistent (particularly in young children)
- BG continues to rise despite increased insulin
- Hypoglycemia is severe
- Ketonuria is heavy and persistent
- The child is becoming exhausted, confused, is hyperventilating, dehydrated or has severe abdominal pain

◊ When metabolic control is persistently unsatisfactory or if BG monitoring is inadequate or unavailable, intercurrent infections may be more frequent and more severe, it would then seem mandatory to
  - advise more frequent urinary glucose and ketone testing
  - give clear guidance on alterations of insulin dosage to prevent ketoacidosis

◊ If sudden repeated episodes of hyperglycemia with vomiting occur, it should be recognized that this may be due to omission or inadequate administration of insulin (see recurrent DKA)
Hypoglycemia

- Hypoglycemia is the most frequent acute complication in type 1 diabetes
- Mild hypoglycemia may cause a variety of reversible signs and symptoms characteristic of neurological dysfunction, from transient dizziness or cognitive impairment to excitation of peripheral nerves or even temporary hemiplegia
- Severe prolonged hypoglycemia with convulsions has the potential, particularly in young children, to cause permanent CNS impairment
- Hypoglycemia provokes significant anxiety in children, adolescents, parents and other care givers
- Hypoglycemia is an important limiting factor in attempts to achieve near-normoglycemia

Definition

There is no consistent or agreed definition of hypoglycemia for the diabetic child

- In theory, hypoglycemia is the level of BG at which physiological neurological dysfunction begins
- In practice, neurological dysfunction can be symptomatic or asymptomatic, and the level at which it occurs
  - varies between individuals
  - may vary with time and circumstances
  - is affected by antecedent hypoglycemia

Clinically, hypoglycemia causes **signs and symptoms** of

**Autonomic activation** (hunger, trembling of hands or legs, palpitations, anxiety, pallor, sweating)

- **BG threshold** for autonomic (counter-regulatory) activation
  - experimentally has been shown to be at a higher BG level in children than adults
  - varies with level of metabolic control
    - poor control — threshold for autonomic activation is at a higher BG level
    - good control — threshold for autonomic activation is at a lower BG level
  - may be lowered by antecedent hypoglycemia
  - is lowered by sleep

**Neuroglycopenia** (impaired thinking, change of mood, irritability, dizziness, headache, tiredness, confusion and later convulsions and coma)
Hypoglycemia

◊ **BG threshold** for cognitive impairment is usually between 2.6 and 3.5 mmol/l (plasma glucose 3.1–4.0 mmol/l)

**Neuroglycopenia may occur before autonomic activation (causing hypoglycemic unawareness)**

**Recommendation**

The level of BG should be maintained above 4 mmol/l

**Grading of severity**

**Mild (grade 1)**

- Child or adolescent is aware of, responds to and self-treats the hypoglycemia

Children aged below 5–6 years can rarely be classified as grade 1 hypoglycemia because they are usually unable to help themselves

**Moderate (grade 2)**

- Child or adolescent cannot respond to hypoglycemia and requires help from someone else, but oral treatment is successful

**Severe (grade 3)**

- Child or adolescent is semi-conscious or unconscious or in coma ± convulsions and may require parenteral therapy (glucagon or IV glucose)

**Predisposing factors**

**Hypoglycemia is the result of a mismatch between insulin, food and exercise**

- Altered routine (missed or erratic meals, changes in physical activity, alterations or errors in insulin dosage or absorption)
- Younger age (<6 years)
• Lower HbA1c [see below]
• Total deficiency of endogenous insulin
• Antecedent hypoglycemic episodes
• Hypoglycemic unawareness
• Defective glucagon and catecholamine counter-regulation (longer duration)
• Alcohol ingestion

Good evidence now exists that in diabetes centers where excellent metabolic control is achieved (with lower mean HbA1c levels) the frequency of severe hypoglycemia may be less than in some other centers achieving less satisfactory levels of control

Consequences

**Brain dysfunction**

◊ Severe prolonged episodes with convulsions in younger children have the potential to harm the developing brain including the occurrence of secondary epilepsy
◊ Transient episodes have important implications for school and social wellbeing including
  – decreased awareness and cognitive deficits
  – injury or accident during an episode
  – fear of hypoglycemia with consequent deterioration of glycemic control
◊ The development of hypoglycemic unawareness should raise the possibility of antecedent unrecognized hypoglycemia, particularly during the night

**Nocturnal hypoglycemia**

◊ Is frequent, often prolonged, usually asymptomatic and does not necessarily disturb sleep patterns
◊ Counter-regulatory responses may be impaired during sleep
◊ Should be suspected if
  – pre-breakfast BG is low
  – confusional states, nightmares or seizures occur during the night, or impaired thinking, lethargy, altered mood or headaches are experienced on waking
◊ Can only be confirmed by BG tests at regular intervals during the night
◊ The association with subsequent hypoglycemic unawareness may be
reversed by maintaining BG above 3 mmol/l during the night
◊ Is not regularly predictable on the basis of a bedtime BG level
   (predictability is improved by BG measurement towards midnight)

Although many parents of younger children gain reassurance by maintaining bedtime BG levels above 6 mmol/l and ensuring that a bedtime snack is eaten, this should not be at the expense of causing high overnight BG levels

**Exercise and hypoglycemia**

◊ When adequate insulin levels are present, muscular activity lowers BG during, immediately after, and/or several hours after exercise
◊ The BG-lowering effect is extremely variable and its severity depends on many factors
◊ When BG levels are high because of inadequate insulin levels, exercise may lead to a further rise in BG
◊ Recommendations for individuals can only be made on the basis of their age, size, individual experience and ‘trial and error’

**Light or brief exercise**

- A small intake of rapidly absorbed carbohydrate is usually recommended prior to exercise

**Intensive, strenuous or prolonged exercise**

- Careful monitoring of BG levels is recommended to help in matching insulin and food to the intensity of exercise
- Reduction of insulin should be considered
- Extra slowly absorbed complex carbohydrate will be necessary especially at bedtime following strenuous exercise in the afternoon or evening [The bedtime snack also containing fat and protein may help to prevent nocturnal hypoglycemia]

**High-risk and/or high-activity exercise or sport when hypoglycemia would be potentially dangerous**

(e.g. water sports, climbing, skiing, diving, etc)

- BG monitoring is extremely valuable
- BG targets for near-normoglycemia may be temporarily relaxed
Extra rapidly absorbed carbohydrate must be available throughout the period of strenuous exercise
Reduction of insulin dose should be considered
Delayed and nocturnal hypoglycemia may be prevented by special attention to increased snacks especially before sleep

**Before and during activities such as riding bicycles in traffic or driving vehicles, the prevention of hypoglycemia is extremely important**

**Recommendations**

1. BG monitoring should be performed to provide information about glycemic levels during and after exercise or sport to enable individual algorithms to be devised
2. Young people with diabetes should perform strenuous exercise in the presence of a companion or supervisor familiar with the recognition and treatment of hypoglycemia and with an immediate supply of rapidly absorbed carbohydrate

**Prevention**

Requires

- **Education** of young people, their parents and other care givers with particular attention to
  - early warning signs and symptoms
  - the usefulness of BG monitoring
  - effects of increased exercise
  - preventative effects of higher fiber, higher carbohydrate foods and snacks
  - management of hypoglycemic episodes
  - review of individual insulin management
  - taking special care when routines are altered, such as holidays, travel or changes of season
  - repeated advice that a source of glucose or sucrose must always be immediately available
- **Assessment** of episodes, particularly
  - food intake (daytime and bedtime snacks; pre- and post-exercise carbohydrate intake)
Hypoglycemia

- insulin action profiles (e.g. rapid-acting insulin analog to reduce post-meal or nocturnal hypoglycemia; splitting evening short/rapid and bedtime intermediate-acting insulin doses)
- nocturnal (2.00–4.00 am) BG measurements

- Review of glycemic targets for those at high risk (e.g. young children and those with hypoglycemic unawareness)

Treatment

Mild or moderate (grade 1 or 2)

- Immediate oral rapidly absorbed simple carbohydrate
  e.g. 5–15 g glucose or sucrose (tablets/sugar lumps)
  100 ml sweet drink (glucose/sucrose drinks, cola, etc)
- Wait 10–15 min if no response ...
- Repeat oral intake as above
- As symptoms improve or normoglycemia is restored, the next meal or oral complex carbohydrate should be ingested (e.g. fruit, bread, cereal, milk)

BG measurements are the only way to confirm hypoglycemia if the diagnosis is uncertain, for example in children who may mimic the symptoms of hypoglycemia in order to be allowed to eat sweet foods. BG measurements also confirm the return of BG towards normal after hypoglycemia

Severe (grade 3)

- Treatment is urgent
- Severe hypoglycemia with loss of consciousness ± convulsions (particularly if there is vomiting) is most safely and rapidly reversed by injection of
  **Glucagon**  0.5 mg for age <12 years
  1.0 mg for age 12+ years
  [or 0.1–0.2 mg/10 kg body weight]
  best given IM (or deep SC)
  If glucagon is unavailable or recovery is inadequate ...
  **IV glucose** should be administered slowly by trained personnel over several minutes to reverse the hypoglycaemia
  e.g. glucose 10–30% at a dose of 200–500 mg/kg (glucose 10% is 100 mg/ml)
  If the hypoglycemia is not associated with vomiting nor severe enough to remove the swallowing, spitting or gag reflexes, it is usually effective to
give concentrated sugar as glucose gel/syrup/honey/jam carefully by mouth

[The evidence is not strong that massaging the outside of the cheek against the gum facilitates buccal absorption of glucose. It is likely that some of the sugar is swallowed and absorbed lower in the gastrointestinal tract]

In the recovery phase after severe hypoglycemia

• Close observation and BG monitoring are essential because vomiting is common and recurrent hypoglycemia may occur

The child will then usually require

• additional oral carbohydrate and/or
• IV infusion of glucose
e.g. glucose 10% 2–5 mg/kg per min (1.2–3.0 ml/kg per h)

Recommendations

1. An immediate source of glucose or sucrose must always be immediately available to young people with diabetes

2. Equipment for BG measurement must be available to all young people with diabetes for immediate confirmation and safe management of hypoglycemia

3. Children, adolescents, parents, schoolteachers and other caregivers should receive education on the recognition and management of hypoglycemia

4. Glucagon should be readily accessible to all parents and caregivers, especially when there is a high risk of severe hypoglycemia. Education on administration of glucagon is essential

5. Children and adolescents with diabetes should wear some form of identification or warning of their diabetes
Psychological, social and financial issues

Psychosocial factors are the most important influences affecting the care and management of diabetes

◊ Diabetes in a young person has a profound impact on family life. It has the potential to cause serious personal and family distress
◊ Pre-existing psychological, social or financial problems in individuals and families are likely to be accentuated by the stress of caring for a young person with diabetes
◊ The cultural, environmental, developmental and personal circumstances of the child and family should receive high priority in diabetes care including a careful assessment at the time of diagnosis
◊ Attention focused only on metabolic control, with neglect of psychosocial influences is to be strenuously avoided
◊ Poor metabolic control is commonly associated with psychological and social difficulties. Appropriate and timely intervention may be the most effective way to improve control

The young person

• Each individual should be assessed on the basis of age, stage of development, maturity, and emotional and social wellbeing
• Each child’s situation in the family and the social environment (particularly nursery, school or college) needs to be recognized
• Young people should have equal opportunities in any type of school/college activity
• Apart from a few necessary exceptions, young people with diabetes should have equal opportunities in employment
• The diabetes care team should provide age-appropriate advice and education not only on diabetes itself but also on how to cope with
  − psychological stress, e.g. feeling different, bullying, jealousy, peer group pressures, discrimination
  − diabetes in daily life, e.g. at school, with friends, eating behavior, becoming independent
Parents and other family care givers

Recommendation

◊ At diagnosis parents, grandparents and other close care givers often pass through stages of grief, fear, guilt, anger, denial, resentment, bargaining and depression before adapting to the requirements of the condition
◊ These feelings may re-emerge at later dates, particularly when faced with crises such as hypoglycemia, diabetic ketoacidosis, intercurrent illnesses or worries about behavior, schooling, marriage, insurability, etc.

Recommendation

◊ Parents should be invited to stay with their child in hospital at all times

◊ Parents (particularly of young children) fear both hypoglycemia and the long-term consequences of hyperglycemia
◊ Diabetes may cause extreme frustration because perfect control is never achieved and is constantly changing in childhood and adolescence
◊ Parents worry about the balance between retaining responsibility, being overprotective, and allowing increasing independence
◊ Grandparents and other relatives may have considerable difficulties in understanding diabetes, the different priorities for the affected child and the need for consistency in management to avoid family conflicts
◊ Babysitters or other temporary care givers of children with diabetes should receive specific instructions on dealing with diabetes from the parents or the diabetes care team

Siblings

◊ The diabetes care team should recognize that siblings may exhibit many different and strong emotions about their brother/sister with diabetes
◊ The care team may need to provide specific information, counseling and

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**Psychological, social and financial issues**

- support for siblings exhibiting guilt, fear, jealousy, embarrassment or sadness
- Parents, siblings, other relatives and care givers all require accessible, consistent and skilled psychosocial support systems to improve their sense of understanding, self-efficacy and personal influence over the child’s diabetes

**Recommendation**

The diabetes care team should receive training in the recognition, identification and provision of information and counseling on psychological and social problems related to diabetes

**Social and financial provision**

- **Parents** should be allowed time off work at the time of diagnosis to enable them to have uninterrupted access to their child and the diabetes care team
- **Housing and child care**: extra practical and financial support may be required to enable the young person with diabetes to be cared for in a safe environment which does not inhibit the management of diabetes
- **Economic support**: family or state-aided support may be required to provide uninterrupted supplies of insulin, equipment and nutrition. Some countries provide disability, travel and telephone allowances or other state benefits to offset the extra costs of care
- Parents should be advised of local or national **diabetes associations** and other voluntary/charitable organizations which may provide support at many levels, e.g. information and education, support groups, educational holidays/camps, financial help, etc.
- Attempts should be made to raise **public awareness** of the special needs of children with diabetes and the affected families. This should include
  - recognizing the early symptoms of diabetes in young people
  - prompt diagnosis
  - the urgency of treatment by an expert pediatric team
  - acknowledging the psychological, social and financial burden of diabetes on the child and family
  - the importance of reducing the short and long-term medical and psychosocial complications
- Families with serious social and financial deficits require expert assessment and support by professionals trained in social work, and in some cases there may be a need for special residential accommodation
Recommendation

| Children and adolescents should have the same social rights as their non-diabetic peers, and no stigma nor discrimination should be attached to diabetes |

Nursery, school and college

◊ Diabetes should not alter a child’s academic potential
◊ Diabetes should not be the cause for being excluded from any type of activity nor for non-attendance at nursery, school or college
◊ Education and the social integration within schools and colleges is of fundamental importance

School staff require advice to ensure that the following priorities are understood

- Safety is paramount especially when participating in sports, school excursions or camps
- Any discrimination or stigmatization is unacceptable
- Full participation and opportunities in all academic, social and sporting activities should be encouraged
- Development of self-esteem and confidence in school activities is likely to have positive effects on the management of diabetes

Parents should be able to visit their child’s school and with members of the diabetes care team provide information on

◊ Recognition and management of hypoglycemia (including advice on emergency treatment for loss of consciousness, seizures or severe vomiting, and to provide emergency telephone numbers)
◊ Avoiding delays in meals and snacks
◊ Allowing extra snacks or drinks occasionally at different times from the child’s peers and particularly in relation to exercise/sport
◊ Allowing children taking academic examinations to eat a snack or measure the BG level
◊ Encouraging the young child to eat all carbohydrate requirements at appropriate times
◊ Encouraging younger children to report hypoglycemia to staff
◊ Encouraging parents and children to discuss diabetes openly with peers, school staff and friends

Psychological, social and financial issues

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Psychological, social and financial issues

Recommendations

1. A supply of rapidly absorbed sugar must be immediately available in the child’s classroom or place of work

2. During or following hypoglycemia at school a child must not be left unaccompanied or be expected to walk to a ‘medical room’

3. Teachers should be aware that cognitive function may be affected for some hours after hypoglycemia
Adolescence

◊ The transitional phase of development between childhood and adulthood which incorporates the biological changes of puberty imposes unique challenges to the individual with diabetes and the diabetes care team
◊ Although the majority of adolescents adapt well to the difficult challenges of puberty, it must be recognized that their health care and emotional needs are distinctly different from those of younger children or older adults

Recommendation

Special facilities in the diabetes service should be made available for adolescents and young adults

• The major risks to the adolescent with diabetes include
  ◊ Persistent or progressively unsatisfactory metabolic control
  ◊ Risk-taking behavior
  ◊ Recurrent DKA
  ◊ Acceleration of microvascular complications
  ◊ Failure of attendance at clinics particularly at the time of transition from pediatric to adult diabetes service

• The deteriorating metabolic control in adolescence may be a consequence of
  ◊ Inadequate insulin dose increments in response to accelerating growth and body weight
  ◊ Hormonal changes associated with puberty
  ◊ Psychological and social difficulties
  ◊ Missed insulin injections
  ◊ Inappropriate eating behavior or eating disorders

Optimal care of the adolescent with diabetes

Optimal care should provide

• An environment that
  ◊ Allows a trusting relationship to develop between the adolescent and the diabetes care team
Helps the adolescent to clarify priorities particularly where there is conflict between the needs of diabetes management and the adolescent’s social development and peer activities

Provides expertise in identifying the physiological changes of puberty, their effect on insulin dose and the frequent difficulties of weight control and dietary regulation

Provides regular screening for early signs of complications

Recognizes the emerging maturity of the adolescent, encourages self-reliance and allows consultations to be increasingly directed towards the adolescent rather than the parents. **Emerging independence is best pursued gradually**

Maintains the trust of parents in helping them in their changing role from full responsibility towards cooperative care of the adolescent

Identifies and recognizes the need for specialized psychological counseling in some situations

- **Appropriate styles of education** that

- Offer a variety of educational opportunities including open-ended adolescent-orientated discussion and negotiation, age-appropriate written materials, videos, the use of the Internet, peer involvement and group learning, and other activities outside the clinic

- Enables the adolescent to learn from mistakes without moral judgment

- Encourages the adolescent to make decisions about diabetes management with appropriate advice

- Opportunities for teenage diabetes **holidays, camps and other recreational activities** including

- Information on availability of camps, teenage support groups, discussion meetings and other recreational activities

- Promotion of these activities and ensuring that they are safe, well-organized and have adequate medical input, supplies and emergency procedures

- Information on traveling with diabetes (particularly to foreign countries) and high-activity pursuits

- **Organized transition** to adult care which involves

- Negotiation and liaison between the pediatric and adult services including, when possible, the organization of joint clinics

- Deciding on the optimal age and stage of development for transition to joint care or transfer to adult care depending on local services and agreements

- Preparing the adolescent for transfer in advance
Ensuring that there is no hiatus in care at the time of transfer and that the young person is not lost to follow-up care

Young people with diabetes who are lost to follow-up care have a high risk of vascular complications

**Recommendation**

The diabetes service should have mechanisms in place to identify and locate all young people who fail to attend follow-up consultations

- Advice on **sexual health** including
  - A non-judgmental approach to sexual activity
  - Advice on contraception
  - Prevention of hypoglycemia during or after intercourse
  - Advice on genital hygiene, monilial infection, menstruation and sexually transmitted diseases (STDs)

- **Pre-pregnancy counseling** with emphasis on
  - The importance of good glycemic control before pregnancy, particularly the risks to the developing embryo and fetus
  - Understanding the importance of good control throughout pregnancy particularly avoidance of hypoglycemia and ketoacidosis
  - Discussion of genetic implications of diabetes to the young person and partner

- Access to expert **pregnancy management** should include
  - Cooperative management by an obstetrician and physician with special experience in diabetes and pregnancy
  - Delivery of the baby in a hospital able to provide expert perinatal and neonatal care

Adolescent girls with diabetes should be aware of the extreme importance of a planned pregnancy. Poor glycemic control around the time of conception increases the prevalence of fetal malformation
Adolescence

- Advice on **alcohol, smoking and drugs** including encouragement to refrain from smoking and under-age alcohol, and firm advice on the dangers of addictive drugs
  
  ◊ Adopting a realistic advisory approach to alcohol rather than an absolute ban
  ◊ Information on the dangers of alcohol particularly in young adolescents, its effects on the liver by inhibiting gluconeogenesis, and the possibility of delayed hypoglycemia
  ◊ Advice on preventing nocturnal hypoglycemia after drinking alcohol in the evening. This should include advice on eating food while drinking, maintenance of good hydration, measurement of BG level before bedtime, and eating before bedtime to minimize the risk of hypoglycemia during sleep
  ◊ Warning adolescents on the dangers of binge drinking, particularly the risks of vomiting, aspiration and DKA

**Friends and relatives of adolescents with diabetes who drink alcohol should understand that hypoglycemia might be confused with intoxication and that it is important to eat carbohydrate before sleep**

- Firm advice about **smoking** as an additional risk for the vascular complications of diabetes
- Helping the adolescent who does smoke to stop by providing specific advice

- Information on **driving** including
  
  ◊ Provision of supportive information about diabetes for potential employers when applying for a job
  ◊ Prevention of hypoglycemia whilst driving (particularly if hypoglycemic unawareness is a problem) by BG monitoring and appropriate food intake
  ◊ Encouraging stable metabolic control (particularly avoidance of severe hypoglycemia), which helps driving licence authorities in some countries to award a driving licence
  ◊ Regular visual acuity and retinal checks

- Advice on **employment** including
  
  ◊ Advice on informing potential employers about diabetes when applying for a job
  ◊ Not concealing diabetes if asked about health
  ◊ The value of a good medical report from the diabetes care team which
may reassure employers that diabetes should not be a disadvantage in employment
◊ Advice on those careers which may be unavailable to persons with diabetes, e.g. armed services, police, public service driver or pilot. These regulations vary between countries
◊ Reassurance to employers that young people with diabetes make good employees if they have shown mature self-care, self-discipline and responsibility

Recommendation

Employers should not exclude young people from employment on the basis of diabetes alone

Contraception

◊ If an unplanned pregnancy in an adolescent girl with diabetes occurs in the setting of poor metabolic control, the risk of congenital malformations, spontaneous abortion, fetal death and macrosomia is greatly increased
◊ When a diabetic girl becomes sexually active she should do so with knowledge of how to avoid an unplanned pregnancy

A planned pregnancy in a person with diabetes in good metabolic control and in good health carries risks which are not substantially greater than those in the general population

The diabetes care team should be sensitive to the religious and cultural influences affecting an individual’s choice of contraceptive method

Barrier methods

◊ Worldwide safe sex, STD and HIV campaigns have made adolescents more aware of barrier methods, particularly condoms
◊ **Condoms** offer the greatest protection against STDs to the whole genital tract (less against herpes), and substantial protection against pregnancy
◊ **Diaphragms**, sometimes worn continuously by women, offer added protection to the condom but on their own provide less effective contraception than the condom and do not protect against vaginal infection
◊ **Spermicidal gels** probably increase the effectiveness of barrier methods
**Oral contraceptives (OCs)**

◊ In the past, OCs were thought to have an adverse effect on metabolic control and lipid profiles and increase the risks of hypertension, cardiovascular and thromboembolic diseases
◊ Newer OCs with a lower estrogen dose (<50 µg ethinylestradiol) and alternative progestogens (Table 8) reduce these risks but may be more expensive
◊ Young people with diabetes on OCs should be monitored regularly, particularly blood pressure, side effects such as headaches, mood changes, breast changes, genital infections
◊ Starting OCs may slightly increase insulin requirements
◊ If acne or hirsutism are problems, the use of an OC containing cyproterone acetate may be helpful
◊ **Progesterone-only** OCs may provide insufficient contraception for teenagers with erratic lifestyles
◊ In some circumstances if there is the possibility of an unwanted pregnancy it may be beneficial to advise sexually active young people about the availability of the ‘morning after’ hormone pill

**Table 8: Examples of OCs with a lower estrogen content**

<table>
<thead>
<tr>
<th>Estrogen</th>
<th>Progestogen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Second-generation OCs</strong></td>
<td></td>
</tr>
<tr>
<td>Ethinylestradiol 30 µg</td>
<td>Levonorgestrel 50–150 µg</td>
</tr>
<tr>
<td>Ethinylestradiol 30–35 µg</td>
<td>Norethisterone 500–1500 µg</td>
</tr>
<tr>
<td><strong>Third-generation OCs</strong></td>
<td></td>
</tr>
<tr>
<td>Ethinylestradiol 30 µg</td>
<td>Desogestrel 150 µg</td>
</tr>
<tr>
<td>Ethinylestradiol 30 µg</td>
<td>Gestodene 75 µg</td>
</tr>
</tbody>
</table>

**Intra-uterine devices (IUDs)**

◊ IUDs are not suitable for nulliparous girls
◊ IUDs provide no protection against STDs
Vascular complications

Microvascular complications

◊ Children and adolescents with diabetes are at risk from progressive microvascular damage
◊ Early vascular changes are subclinical but can be detected by sensitive testing methods
◊ The prepubertal phase of diabetes contributes to the risk of vascular damage
◊ Puberty accelerates the progression of microvascular complications
◊ Improvements in glycemic control reduce the risk of retinopathy, nephropathy and neuropathy

Risk factors for the development of microvascular complications

• Younger age at onset
• Longer duration of diabetes
• Poor glycemic control
• Family history of diabetes complications
• Higher blood pressure (not necessarily to hypertensive levels)
• Smoking
• Abnormal lipid levels

Recommendation

Awareness in families, children and adolescents of potential long-term complications is a fundamental part of diabetes education. Such information should be provided to children at a rate appropriate to their level of understanding and maturity.

Positive encouragement should be provided to emphasize that

• From the onset of diabetes the aim is to achieve the best possible metabolic control to reduce the risk of blood vessel complications
• Any level of sustained improvement in glycemic control reduces the risk of microvascular complications
Vascular complications

- The DCCT found that for every 10% improvement in HbA1c (e.g. 8 vs 7.2%) there is a 44% reduction of risk

There is no HbA1c threshold below which diabetes complications will not occur

Diabetic eye disease

Retinopathy

- Diabetic retinopathy remains the most common cause of acquired blindness in young and older adults
- Early retinopathy is asymptomatic but may be detected by sensitive methods (e.g. fundus photography or fluorescein angiography) in a large proportion of young people with diabetes duration of more than 10 years

Fluorescein angiography is not performed in many pediatric centers but is a sensitive method of detecting early functional vascular abnormalities of the retina which are potentially reversible by improvements in metabolic control. There is good evidence that serial fundus photography, which is less invasive, is equally effective in the monitoring of retinopathy

Types of retinopathy

Early or background retinopathy

- Microaneurysms
- Hemorrhages
- Hard and soft exudates
- Intra-retinal microvascular abnormalities (IRMA)

Background retinopathy is non-vision-threatening. It may remain stable for years, may sometimes regress, or may progress to more severe retinopathy

Vision-threatening retinopathy

- Macular edema (rare in children)
- Pre-proliferative retinopathy (vascular obstruction, progressive IRMA, infarctions of the retinal nerve fiber layer causing cotton wool spots)
- Proliferative retinopathy (new vessel formation of retina and/or vitreous)
Vascular complications

posterior surface). New vessel formation is responsible for further retinal and vitreous hemorrhage, fibrous reactions and subsequent retinal detachment

**Recommended screening procedures**

◊ Clinical examination of the eyes and ophthalmoscopy should be performed soon after diagnosis to exclude cataract formation or other disorders. At this early stage, ophthalmoscopy provides the added educational opportunity of linking good control with prevention of eye problems. Expert ophthalmological advice should be sought if the examination is not entirely normal

◊ Visual acuity will usually be determined at times of expert eye examination to rule out refractive and other errors not necessarily associated with diabetes itself

• **Screening for retinopathy** by ophthalmoscopy is not a sensitive method of screening for retinopathy and there are few data to support its effectiveness. It is best performed through pharmacologically dilated pupils* by a trained observer (diabetologist, specialist nurse, optometrist or ophthalmologist)

• **Fundus photography** (preferably stereoscopic several field views through dilated pupils) has been shown to be a safe, non-invasive and sensitive screening procedure. Photography has the advantage over simple ophthalmoscopy of providing a hard copy capable of being compared with subsequent photographs and transferable to other clinics

**Recommendation**

<table>
<thead>
<tr>
<th>Age of retinopathy screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Prepubertal onset of diabetes: 5 years after onset or at age 11 years, or at puberty (whichever is earlier), and annually thereafter</td>
</tr>
<tr>
<td>• Pubertal onset of diabetes: 2 years after onset, and annually thereafter</td>
</tr>
</tbody>
</table>

* Pupil dilation by: cyclopentolate 1% + phenylephrine 2.5% or tropicamide 1% ± phenylephrine 10%
Vascular complications

Further retinopathy monitoring

- Progression of retinopathy to more than 10 microaneurysms
  **Recommend**
  evaluation by experts in interpreting retinal photographs and
  ophthalmological management
- Advanced background retinopathy, macular edema or proliferative
  changes
  **Recommend**
  immediate referral for expert ophthalmological management

Prevention and intervention

- Improve BG control
- Strongly discourage smoking
- Encourage healthy exercise
- Monitor microalbuminuria and blood pressure as these complications are
  associated with retinopathy in adolescents
- Ophthalmological management: laser photocoagulation is effective in
  preventing visual loss in proliferative retinopathy; focal laser
  photocoagulation is beneficial in eyes with macular edema

◊ There is evidence that angiotensin-converting enzyme (ACE) inhibitor
  treatment should be considered in progressive retinopathy
◊ Tight metabolic control after prolonged unsatisfactory control may
  worsen retinopathy initially, followed by later benefits in reducing the
  risks of further progression of retinopathy

Other eye complications

◊ Cataracts have been described very soon after the onset of diabetes. They
  are rare but may occur more often in adolescents with a long history of
  polyuria before diagnosis. Cataracts later in diabetes are a consequence
  of prolonged poor metabolic control
◊ Refractive errors and blurring of vision occur during major changes in
  glycemia (e.g. following prolonged hyperglycemia before diagnosis and
  during stabilization). They are usually transient
◊ Glaucoma and other eye diseases are rare in the pediatric age group
Diabetic kidney disease

Nephropathy

◊ Diabetic nephropathy and end-stage renal failure have been a major cause of mortality amongst young adults with type 1 diabetes
◊ In recent decades a decrease in clinical nephropathy in some countries probably reflects improvements in diabetes management and glycemic control
◊ Increasing and persistently elevated urinary albumin excretion may predict later diabetic nephropathy
◊ Elevated blood pressure is an associated feature of diabetic kidney disease

Microalbuminuria

◊ The 95th centile for albumin excretion in non-diabetic children is 7.2–7.6 µg/min
◊ Persistent microalbuminuria is defined in a minimum of two out of three consecutive urine specimens
  Albumin excretion rate (AER) 20–200 µg/min in timed overnight urine collections
  or
  AER 30–300 mg/24 h in 24-h urine collections
◊ Alternative definitions
  Albumin/creatinine ratio (ACR) 2.5–25 mg/mmol (spot urine) (Europe)
  [3.5–25 mg/mmol has been proposed in females because of lower creatinine excretion]
  ACR 30–300 mg/g (spot urine) (North America)
  Albumin concentration 30–300 mg/l (early morning urine)

Other causes of microalbuminuria need to be excluded, e.g. glomerulonephritis, urinary tract infection, intercurrent infections, menstrual bleeding, vaginal discharge, orthostatic proteinuria and strenuous exercise

Microalbuminuria screening

• Screening may be performed by early morning urine albumin concentration or spot urine ACR or by timed urine collection
• Abnormal screening values should be confirmed by repeated sampling to demonstrate persistent microalbuminuria
Recommendation

**Microalbuminuria monitoring**

- Abnormal screening tests should be repeated, as pediatric studies have shown that apparently ‘persistent’ microalbuminuria may disappear
- Urinary albumin tests should be accompanied by measurements of blood pressure at least annually
- Blood pressure values should be compared with age-appropriate centile charts. Confirmation of hypertension may be assisted by 24-h ambulatory blood pressure measurements
- When persistent microalbuminuria is confirmed, screening for retinopathy, neuropathy and lipid abnormalities is also recommended

**Prevention and intervention**

- Improve BG control
- Strongly discourage smoking
- Encourage healthy exercise
- Discourage excessive nutritional protein intake (recommended maximum of 1.0–1.2 g/kg body weight per day)
- Intervention for hypertension: no clear consensus but blood pressure should probably be maintained at less than the 95th centile for age and maturity

◊ Persistent and progressive albuminuria has been found to be improved by the use of ACE inhibitors. Progression to overt nephropathy may be delayed but their place in protecting long-term renal function in young people has not yet been established. There is early evidence that even without hypertension, ACE inhibitors should be considered when persistent microalbuminuria has been confirmed

◊ The introduction of ACE inhibitors must be combined with monitoring of renal function. ACE inhibitors are not licenced for use in pregnancy

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Vascular complications

**Age of microalbumin screening**

- Prepubertal onset of diabetes: 5 years after onset or at age 11 years, or at puberty (whichever is earlier), and annually thereafter
- Pubertal onset of diabetes: 2 years after onset, and annually thereafter
Diabetic nerve disease

**Neuropathy**

◊ Clinical neuropathy is rare in children and adolescents with satisfactory glycemic control
◊ Sensitive tests can detect subclinical neurological abnormalities, the natural history of these being unclear

• In the presence of poor diabetic control young people should be questioned and examined in relation to
  – symptoms of numbness, pain, cramps and paresthesia
  – skin sensation, vibration sense and light touch
  – ankle reflexes

In specialist centers, abnormalities in the autonomic nervous system have been reported which include postural change in blood pressure, heart rate responses to Valsalva maneuver, sophisticated tests of cardiovascular reflexes, plus pupillary reflex changes. The significance of such findings is uncertain but would make close monitoring and improvements in glycemic control mandatory

**Macrovascular complications**

◊ Large vessel disease such as coronary artery atherosclerotic disease does not often manifest in children or adolescents but has its beginnings in early childhood
◊ Macrovascular disease is accelerated by diabetes, dyslipidemia, raised blood pressure and smoking, and is associated with obesity
◊ Macrovascular complications are the commonest cause of premature death in adults with diabetes

The evolution of macrovascular disease may be reduced by

• Improved metabolic control of diabetes
• Blood pressure control
• Treatment of dyslipidemia (e.g. familial hypercholesterolemia)
• Not smoking
• Participation in healthy exercise
**Associated conditions and other complications**

**Growth and development**

- **Impaired growth and delayed pubertal development** may occur in the following circumstances:
  - Poor metabolic control
  - Inadequate nutritional intake
  - Hypothyroidism
  - Celiac disease
  - Other conditions not associated with diabetes

**Recommendation**

Regular monitoring and assessment of growth are an essential part of good diabetes management.

**Autoimmune disorders**

- Islet cell antibodies and other autoantibodies can be found in a high proportion of children prior to the onset of type 1 diabetes
- More children with type 1 diabetes also have other detectable organ-specific autoantibodies (e.g., thyroid, antigliadin, adrenal) than are found among the general population
- Family members of children with diabetes are more likely to have autoantibodies and other manifestations of autoimmune disease than the general population

**Risk factors for the development of associated autoimmune disorders**

- Age (older)
- Sex (female)
- Duration of diabetes (longer)
- Presence of other organ-specific autoantibodies
- Family history of autoimmune disease (genetic predisposition)
Associated conditions and other complications

Children and adolescents with diabetes have an increased risk of developing other autoimmune disorders

Thyroid disease

- Thyroid autoantibodies (TAAB), particularly microsomal antibodies, occur in up to 20–30% of young people with type 1 diabetes
- A palpable or visible goiter may be present in 10–20%
- Most young people with a goiter and positive TAAB have (Hashimoto’s) thyroiditis but the majority are euthyroid
- Absence of TAAB does not preclude later development of thyroid disease

Hypothyroidism

- Overt hypothyroidism occurs in 1–5% of young people with type 1 diabetes
- Compensated hypothyroidism — asymptomatic, normal thyroxine level, modestly raised thyroid-stimulating hormone (TSH) — occurs in 1–10%

Diagnostic pointers

- Goiter
- Increased weight gain (facial fullness)
- Decreased growth rate
- Tiredness, lethargy

Hypothyroidism may not significantly affect metabolic control

Definitive diagnosis

Low total (or free) thyroxine; raised TSH

Treatment

L-Thyroxine with TSH monitoring
Associated conditions and other complications

Thyrotoxicosis

◊ Diagnosed less frequently than hypothyroidism in association with diabetes
◊ May be transient and occasionally precedes hypothyroidism (or vice versa)

Diagnostic pointers

• Agitation
• Tachycardia
• Weight loss
• Heat intolerance
• Tremor
• Possibly increasingly unstable metabolic control

Definitive diagnosis

Raised total (or free) thyroxine, raised triiodothyronine, with TSH suppressed below normal range (raised TSH receptor-stimulating antibodies)

Treatment

Anti-thyroid drugs such as carbimazole, methimazole, propylthiouracil

Recommendations

1. Regular clinical examination of the thyroid gland in all young people with diabetes for detection of goiter
2. Close to the time of diagnosis of diabetes, thyroid function and thyroid antibody tests should be performed as a baseline or to uncover asymptomatic thyroid disease
3. Repeat thyroid function tests should be performed if a child with diabetes develops a goiter, has slow growth velocity, has symptoms suggestive of thyroid disease or has high titers of thyroid antibodies
4. Many centers repeat the thyroid function tests as part of an annual review
Celiac disease

◊ Occurs in 1–10% of children and adolescents with type 1 diabetes (prevalence is 10–50 times greater than in the general population and this varies between different geographical regions)
◊ Should be considered whenever a child with diabetes has gastrointestinal signs or symptoms including diarrhea, abdominal pain, flatulence, dyspeptic symptoms or recurrent aphthous ulceration
◊ Is often asymptomatic
◊ Non-gastrointestinal presentations are not uncommon, e.g. poor growth, iron deficiency anemia, delayed puberty, unexplained recurrent hypoglycemia (particularly with poor weight gain), dermatitis herpetiformis

Immunological tests

◊ Antiendomysial IgA antibody (EMA) is the most specific test
◊ EMA should be combined with total IgA level to exclude false-negative results
  [Antigliadin IgG and IgA antibodies are sensitive screening tests but are less specific]
◊ Seroconversion to positive EMA after onset of diabetes predicts later celiac disease but this may take months or years to develop

Definitive diagnosis

◊ Jejunal biopsy showing villous atrophy
◊ A normal mucosa in a seropositive child does not preclude later development of celiac disease. Seropositive patients require regular reassessment

Treatment

Definitive biopsy diagnosis mandates a gluten-free diet (GFD), which should reverse signs and symptoms

◊ GFD may improve growth and wellbeing in previously ‘asymptomatic’ patients
◊ GFD may or may not alter insulin requirements
◊ GFD may or may not alter metabolic control
◊ GFD should be associated with disappearance of EMA
Associated conditions and other complications

Screening

◊ Controversy exists as to the need for and frequency of screening tests to detect clinically asymptomatic cases of celiac disease
◊ In some geographical areas annual screening for celiac disease is recommended

Recommendations

1. Consider the possibility of celiac disease in any child or adolescent with gastrointestinal symptoms, unexplained poor growth or anemia
2. Immunological screening should be considered close to the time of diagnosis of diabetes and repeated if clinical circumstances suggest the possibility of celiac disease

Other autoimmune associations

Adrenal insufficiency

◊ Adrenocortical autoantibodies can be detected in 2–4% of young people with type 1 diabetes
◊ Adrenal insufficiency occurs rarely in children with diabetes but must be suspected where there are decreasing insulin requirements, unexplained hypoglycemia, weight loss, lethargy or increasing skin pigmentation

Polyglandular autoimmune disorders

◊ Approximately 25% of patients with one autoimmune disease may develop another autoimmune disease during their lifetime
◊ Other associated conditions include
  – vitiligo
  – alopecia
  – hypoparathyroidism
  – hypergonadotropic hypogonadism
  – pernicious anemia
Associated conditions and other complications

Skin conditions

**Lipoatrophy**

◊ Now uncommon with the use of highly purified human insulins
◊ Said to be improved by injecting soluble insulin around the affected area

**Lipohypertrophy**

◊ A common problem due to repeated injection into the same site
◊ Insulin absorption from these areas is more erratic and unpredictable
◊ Improves with better rotation of injection sites

**Necrobiosis lipoidica diabeticorum**

◊ Purplish-red slightly raised or atrophic skin lesions with occasional pale or ulcerating center (usually lower limbs)
◊ May be present at or before the onset of diabetes
◊ Cause unknown, treatment controversial and prognosis uncertain

Feet

◊ Diabetes-related foot problems usually occur in older people with neuropathy and vascular complications
◊ Discussion of potential problems with the feet is advisable to avoid or treat
  – trauma and infection
  – ingrowing toenails (and paronychial infection)
  – tinea pedis (athlete’s foot)
  – biomechanical problems (ill-fitting footwear)
  – callus formation (look for limited joint mobility)

Limited joint mobility

◊ Is demonstrated by opposing the hands in a ‘praying position’ which demonstrates the inability to straighten the interphalangeal and metacarpophalangeal joints. There may be limited mobility of wrists, elbows, feet, neck and spine
Associated conditions and other complications

- May be associated with thickening of the skin
- Severe forms more often associated with persistently poor metabolic control
- Treatment is unsatisfactory

Dental problems

- Periodontal disease may be a problem in some children
- Dental checks are an important part of general health care

Other associations

Type 1 diabetes is more common in young people with other syndromes and disorders (see Table 3 & pp 19–20)
Management of children with diabetes requiring surgery or fasting

Children with diabetes requiring a surgical procedure

◊ Must be admitted to hospital for general anesthesia
◊ Need insulin, even if fasting, to avoid ketoacidosis
◊ Should receive a glucose infusion when fasting before an anesthetic to prevent hypoglycemia

Recommendations

1. Surgery on children and adolescents with diabetes should only be performed in centers with dedicated pediatric facilities for the care of young people with diabetes

2. To ensure the highest levels of safety, careful liaison is required between surgical, anesthetic and children’s diabetes care teams before admission to hospital for elective surgery and as soon as possible after admission for emergency surgery

Elective surgery

• Operations are best scheduled early on the list, preferably in the morning
• Admit to hospital the afternoon prior to surgery for morning and major operations, or early morning for minor operations later in the day
• Earlier admission is important if glycemic control is poor
• Admission should be to a pediatric diabetes or pediatric surgical ward

Evening prior to surgery

• Frequent BG monitoring is important especially before meals and snacks and before bedtime (and check urinary ketones)
• Usual evening or bedtime insulin(s) and bedtime snack should be given
• Ketosis or severe hyperglycemia will necessitate correction, preferably by overnight IV infusion, and might cause a delay in surgery
Morning operations

- No solid food from midnight
- Clear fluids may be allowed up to 4 h preoperatively (check with anesthetist)
- Omit usual morning insulin dose
- Start IV fluid and insulin infusion at 6.00–7.00 am (Table 9)
- Hourly BG monitoring preoperatively; half-hourly during operation and until woken from anesthetic
- Hourly BG monitoring for 4 h postoperatively
- Aim to maintain BG between 5 and 12 (Table 9)
- Continue IV infusions until the child tolerates oral fluids and snacks (this may not be until 24–48 h following a major operation)
- Change to usual SC insulin regimen or short/rapid-acting insulin before the first meal is taken
- Stop insulin infusion 60 min after the SC insulin is given
- For minor operations it may be possible to discharge from hospital after the evening meal if the child is fully recovered

Table 9: Infusion guide for surgical procedures

1. Maintenance fluid guide
   - Glucose 10%, saline 0.18%
   - If infusion is required for more than 12 h, add potassium chloride 20 mmol to each liter and monitor electrolytes
     [If glucose 10%, saline 0.18% is not available, add sodium chloride 15 mmol to 500 ml glucose 10% for an equivalent solution]

<table>
<thead>
<tr>
<th>Body weight</th>
<th>Fluid requirement/24 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–9 kg</td>
<td>100 ml/kg</td>
</tr>
<tr>
<td>10–20 kg</td>
<td>Add 50 ml/kg</td>
</tr>
<tr>
<td>20 kg</td>
<td>Add 20 ml/kg (max 2000 ml female, 2500 ml male)</td>
</tr>
</tbody>
</table>

2. Insulin infusion
   - Add soluble insulin 50 units to 50 ml saline 0.9%, making a solution of 1 unit/ml; attach to syringe pump and label clearly
   - Start infusion at 0.05 ml/kg/h (i.e. 0.05 units/kg/h)
   - Aim to maintain BG levels between 5 and 12 mmol/l by adjusting insulin infusion hourly
   - Do not stop insulin infusion if BG <5 mmol/l as this will cause rebound hyperglycemia; reduce the rate of infusion
   - The insulin infusion may be stopped if BG <3 mmol/l, but only for 15 min
Afternoon operations

- Give one-third of the usual morning insulin dose as short-acting insulin if the operation is after midday.
- Allow a light breakfast; clear fluids may be allowed up to 4 h preoperatively
- Start IV fluids and insulin infusion at midday at the latest (Table 9)
- Then as for morning operations (above).
  [Alternatively IV insulin infusion may be started at breakfast time]

Emergency surgery

◊ DKA may present as an ‘acute abdomen’
◊ Acute illness may precipitate DKA (with severe abdominal pain)

- Nil by mouth
- Secure IV access
- Check weight, electrolytes, glucose, blood gases and urinary ketones preoperatively
- If ketoacidosis is present, follow protocol for DKA and delay surgery until circulating volume and electrolyte deficits are corrected
- If there is no ketoacidosis, start IV fluid and insulin infusions as for elective surgery

Minor procedures requiring fasting

For short procedures (with or without sedation or anesthesia) and when rapid recovery is anticipated, a simplified protocol may be organized by experienced diabetes/anesthetic personnel and may include either
  – early morning procedure (e.g. 8.00–9.00 am) with delayed insulin and food until immediately after completion
  or
  – reduce (e.g. give / of) usual insulin dose or give repeated small doses of short/rapid-acting insulin

Glucose 5–10% infusion and frequent BG monitoring are recommended in all these situations
Summary of requirements and specific recommendations

Essential requirements

- All health care providers at local, regional and national levels have a duty to ensure that children and adolescents receive an uninterrupted supply of
  - Insulin of reputable quality (may be human or animal)
  - Syringes and/or insulin pens and/or injector devices and needles, which are essential for the proper administration of insulin
  - Blood and urine testing equipment, which is essential for monitoring metabolic control

- All children, adolescents, their families and other care givers should have access to
  - Age-appropriate support, care and education in diabetes with the aim of enhancing self-management for young people
  - Health care professionals with experience and expertise in the management of both diabetes and child health care
  - Twenty-four-hour advice and support for safe and effective diabetes management including acute emergencies
  - Written (or electronic) information and guidelines on the management of the different phases of diabetes in childhood and adolescence

- All health care providers at local, regional and national levels should be aware of
  - The enormous personal, social and psychological burdens of childhood diabetes on the individual and on families
  - The potentially devastating long-term consequences of poorly managed diabetes including the substantial financial costs to individuals and to health care services
  - The need for adequate technical, financial and human resources to improve the total management of young people with diabetes
Summary of essential requirements and specific recommendations

Specific recommendations

**Diagnosis and presentation**

◊ There is a need for greatly increased awareness of the symptoms of diabetes both in the general public and by health care professionals

◊ Prompt diagnosis and rapid treatment are essential if the complications of diabetic ketoacidosis (DKA) are to be avoided

◊ Weight loss, increased thirst or excessive urination in a child must always be investigated immediately by at least a urinary glucose test

◊ There is a need for greater awareness, accurate assessment and methods of prevention of the less common forms of diabetes, particularly the increasing prevalence of obesity-related type 2 diabetes in certain ethnic groups

◊ Children developing diabetes in locations remote from specialized centers require particular attention to ensure safe, consistent care and continuing management

**Early management**

◊ **Education** is the keystone to successful management. It needs to be structural, adaptable and personalized, patient-centered, appropriate to the level of maturity and understanding of the young person and family, culturally sensitive

◊ Educational messages require repetition, and the curriculum should be regularly re-evaluated

◊ From the first day after diagnosis, the care, education and emotional support for the young person and the family should be provided by a team of specialists, all of whom should have received specialist training in both diabetes and pediatrics (particularly child and adolescent development)

◊ The **multidisciplinary diabetes care team** for children and adolescents should include the following essential members

  – pediatrician specializing in diabetes/endocrinology (or physician with a special interest in childhood and adolescent diabetes)
  – diabetes specialist nurse or diabetes educator
  – pediatric dietician with special expertise in diabetes
  – and there should be easy access to services for children provided by
  – social workers, counselors/psychologists/child psychiatrists, ophthalmologists and podiatrists

◊ Resources should be made available for the diabetes care team to be based in specialized regional children’s diabetes **centers of excellence**

◊ In areas of low population density or where diabetes occurs rarely, the numbers of children with diabetes will be small. In these circumstances care
Summary of essential requirements and specific recommendations

is likely to be provided by a locally based pediatrician/physician who should have easy access to facilities, advice and the possibility of annual review by the diabetes care team based in the regional center of excellence

◊ The importance of ‘a good start’ to the early education of the young person with diabetes cannot be overemphasized and is more likely to be provided by teams frequently dealing with diabetes and working in centers of excellence

◊ Most children developing diabetes will be admitted to hospital for immediate management but if 24-h community facilities are available, domiciliary management has been shown to be successful

◊ Parents or other care givers should be invited to stay with their children in hospital at all times

Crisis and emergency management

◊ It is good clinical practice for young people and care givers to receive advice on how to adjust insulin to maintain glycemic control especially during episodes of intercurrent illness, hyperglycemia or hypoglycemia. It is recommended that
  – short/rapid-acting insulin should always be available for crisis management
  – insulin should never be stopped except on the advice of an experienced member of the diabetes care team
  – young people should always carry with them a supply of glucose or sucrose, particularly during exercise and sport
  – glucagon should be immediately available to care givers

◊ Recognition of the earliest signs of both hypoglycemia and DKA are essential parts of the educational curriculum. All care givers including relatives, babysitters, teachers, sports instructors and youth leaders should have easy access to such information, particularly the management of hypoglycemia

◊ Equipment and skills for monitoring BG and ketone levels are essential for the optimal management of diabetic emergencies

◊ Independent adjustment of insulin doses by young people and parents is facilitated by 24-hour access to members of the diabetes care team

◊ Centers managing young people with DKA must always have available
  – a written protocol
  – senior medical personnel experienced in the management of DKA to provide emergency advice
  – a specialized children's inpatient facility (with access to intensive care facilities whenever possible)
  – specialist children's nurses trained to perform frequent, careful, clinical monitoring
  – laboratory facilities able to provide rapid, frequent, biochemical measurements
Outpatient management, monitoring and metabolic control

◊ Regular, uninterrupted, consistent follow-up of young people for the optimal management of their diabetes should be provided by the diabetes care team

◊ Frequent reassessments are recommended in the first weeks and months after diagnosis to enable optimal metabolic control to be achieved. Thereafter it is common practice to organize at least three or four visits per year to a children’s specialist diabetes clinic, but more frequently if glycemic control is unsatisfactory

◊ Frequent, accurate self-monitoring of BG is the optimal method of measuring short-term glycemic control and is of good educational value. It is the only method by which optimal glycemic control can be achieved by intensified management regimens

◊ It is good clinical practice to organize an annual review with assessment of
  – growth, development, education and psychosocial change
  – injection sites and techniques
  – glycemic control
  – puberty
  – nutritional plan and dietary management
  – associated conditions (goiter/thyroid dysfunction, dyslipidemia, celiac disease, skin or foot problems)
  – complications screening

◊ Facilities for the measurement of glycated hemoglobin (preferably HbA1c) should be available to all centers caring for young people with diabetes. There should be regular quality control comparisons with national standards and those set by the Diabetes Control and Complications Trial

◊ It is good clinical practice to measure HbA1c at least three or four times each year, preferably by capillary collection methods and available at the time of the clinic visit

◊ For each individual the targets of optimal metabolic control should be the lowest achievable blood or urinary glucose profiles and HbA1c levels without the occurrence of frequent or severe hypoglycemia

◊ The diabetes care team and voluntary organizations should be encouraged to develop out-of-clinic activities such as support groups, educational events, holidays and camps

Summary of essential requirements and specific recommendations

Nutritional management

◊ Specialist dietetic advice should be available at the time of diagnosis and regularly afterwards to provide essential dietetic advice for achieving glycemic control, which is to distribute the intake of food energy and carbohydrate to balance insulin action profiles and exercise levels
Total energy intake must be sufficient for optimal growth but to avoid obesity. Total energy intake should be distributed as follows:
- Carbohydrate >50% (mainly complex unrefined higher fiber carbohydrate)
- Fat 30–35% (<10% saturated fat)
- Protein 10–15% (decreasing with age)
Fruit and vegetables are strongly recommended, distributed throughout the day.

**Psychosocial and financial issues**

It should be recognized that psychosocial factors are the most important influences affecting the care and management of childhood diabetes. There must be no stigma attached to, nor discrimination against, children and adolescents with diabetes. They should have equal opportunities and social rights in education, schools, colleges, employment and insurance schemes.

Care givers should have easy access to expert advice on the financial and social support available from local services, the state and voluntary organizations.

**Adolescence**

Special facilities should be developed for adolescents and young adults to help manage their own diabetes in an optimal environment and to negotiate the difficult transition between children’s and adult services. It is good clinical practice to organize joint transition clinics with the involvement of both pediatric and adult diabetes care teams.

Specific advice should be made available to adolescents on the influence of diabetes on puberty, growth, vascular complications, metabolic control and exercise, and information made available on pregnancy, contraception, smoking, alcohol, drugs, driving and employment.

**Vascular complications**

Awareness of potential long-term microvascular complications is a fundamental part of diabetes education and should be provided at a rate appropriate to the young person’s understanding and maturity. Positive encouragement should be provided to emphasize that improvements in metabolic control reduce the risks of complications.
Screening recommendations

Retinopathy and nephropathy

- Prepubertal onset of diabetes
  - 5 years after onset, or
  - aged 11 years, or
  - at puberty (whichever is earlier)
- Pubertal onset of diabetes
  - 2 years after onset and annually thereafter

Assessments should include at a minimum
- retinal examinations through dilated pupils (preferably with retinal photography)
- microalbuminuria measurements
- blood pressure measurement
- clinical review of possible neurological dysfunction

Associated conditions

◊ Height and weight monitoring is an essential part of diabetes care
◊ Assessment of associated autoimmune and other conditions should be performed at an annual clinic review (see above)

Surgery

◊ A written protocol should be available in all centers caring for young people with diabetes to ensure the safe management of children and adolescents undergoing surgical procedures. The protocol should be agreed between anesthetic, surgical and pediatric staff

Audit, training and research

◊ Health care providers and diabetes care teams should ensure that there is a comprehensive population-based diabetes register (either manual or computerized) which includes the names of all young people within a particular area or region. Regular register reviews and audits will assist in the evaluation of standards, assessment of outcome and identifying young people who default, and thus help to ensure their consistent support and surveillance
◊ Improvements in the training of specialists who provide care for children and adolescents is essential. Training should include not only diabetes care but education theory, psychology, counseling and the mechanisms of behavior change
Research initiatives which help to investigate not only the etiology, development and prevention of diabetes and its associated complications but also optimal methods of care and management should be encouraged at local, national and international levels. Training in research methods and specific training fellowships in pediatric diabetes will help in promoting such research.
International declarations

International diabetes federation’s philosophy on childhood and adolescent diabetes

In 1992 the IDF in recognising the special needs of children and adolescents with diabetes established a Task Force working closely with ISPAD (formerly ISGD) and as a result formulated the following philosophy, accepted as policy by both IDF and ISPAD.

“As they grow, children and adolescents with diabetes have special and changing needs. These needs must be recognised and addressed by the general public and health professionals alike. While their dependence on insulin and their need for food and appropriate nutrition is the same as IDDM adults, there are major physiological, medical, psychological, social and emotional differences.

These differences arise from the stages of growth and development through which young people pass. Babes in arms, toddlers, school children and adolescents with their developing independence must each be considered differently. Children are not self-sufficient, they depend on their family and are strongly influenced by their immediate surrounding (i.e. their home, siblings, peers). When diabetes mellitus occurs in childhood, it has the potential to be profoundly destructive of normal individual and family relationships.

All young people with diabetes have the right to competent medical management and diabetes education by a team of individuals who have expertise in and an understanding of the medical and psychosocial needs of young people and their families. A child cannot fight for these rights. It is, therefore, the responsibility of society to provide all necessary support to the child and the family: This should include medical, social, public, governmental and industrial resources and efforts.”

ISPAD Task Force: Lorna Mellor, Harold Rifkin, Margaret McGill, Martin Sillink

ISPAD declaration of KOS

On September Fourth, Nineteen Hundred and Ninety Three, on the Island of Kos, the members of the International Study Group of Diabetes in Children and Adolescents (ISGD), assembled at their nineteenth annual international scientific meeting and in the process of transforming ISGD into the International Society for Pediatric and Adolescent Diabetes (ISPAD), renewed their Hippocratic oath by proclaiming their commitment to
implement the St Vincent Declaration to promote optimal health, social welfare and quality of life for all children and adolescents with diabetes around the world by the year 2000. They took this unique opportunity to reaffirm the commitments by diabetes specialists in the past and, in particular, unanimously pledged to work towards the following:

- to make insulin available for ALL children and adolescents with diabetes
- to reduce the morbidity and mortality rate of acute metabolic complications or missed diagnosis related to diabetes mellitus.
- to make age-appropriate care and education accessible to & children and adolescents with diabetes as well as to their families
- to increase the availability of appropriate urine and blood self-monitoring equipment for ALL children and adolescents with diabetes.
- to develop and encourage research on diabetes in children and adolescents around the world.

**The St Vincent Declaration**

Representatives of government health departments and patients’ organisations from all European countries met with diabetes experts under the aegis of WHO Regional Offices for Europe and the International Diabetes Federation (IDF), European region, in St Vincent, Italy on 10–12 October 1989. They unanimously agreed on the following recommendations and urged for their implementation in all countries throughout Europe.

“Diabetes mellitus is a major and growing European health problem, a problem at all ages and in all countries. It causes prolonged ill-health and early death. It currently threatens at least ten million European citizens.

It is within the power of national governments and health departments to create conditions in which a major reduction in this heavy burden of disease and death can be achieved. Countries should give formal recognition to the diabetes problem and deploy resources for its solution. Plans for the prevention, identification and treatment of diabetes and particularly its complications – blindness, renal failure, gangrene and amputation, aggravated heart disease and stroke – should be formulated at local, national and European regional levels. Investment now will earn great dividends in reduction of human misery and in massive savings of human and material resources.

General goals and five-year targets (listed below) can be achieved by the organised activities of the medical services in active partnership with diabetic citizens, their families, friends and workmates and their organisations in:

- The management of their own diabetes and education for it.
- The planning, provision and quality audit of health care.
- National, regional and international organisations for disseminating information about health maintenance.
- Promoting and applying research.
**General Goals for Children and Adults with Diabetes**

- Sustained improvement in health experience and a life experience approaching normal expectation in quality and quantity.
- Prevention and cure of diabetes and its complications by intensifying research effort.

**Five-year Targets**

- Elaborate, initiate and evaluate comprehensive programmes for the detection and control of diabetes and its complications with self-care and community support as major components.
- Raise awareness in the population and amongst health care professionals of the present opportunities and the future needs for the prevention of diabetes and its complications.
- Organise training and teaching in diabetes management and care for people of all ages with diabetes, for their families, friends and working associates and for the health care team.
- Ensure that care for children with diabetes is provided by individuals and teams specialised in the management of both diabetes and children, and that families with a diabetic child get the necessary social, economic and emotional support.
- Reinforce existing centres of excellence in diabetes care, education and research.
- Promote independence, equity and self-sufficiency for all people with diabetes, i.e. children, adolescents, those in the working years of life and the elderly.
- Remove hindrances to the fullest possible integration of the diabetic citizen into society.
- Implement effective measures for the prevention of costly complications:
  a) Reduce new blindness due to diabetes by one third or more.
  b) Reduce the number of people entering end-stage diabetic renal failure by at least one third.
  c) Reduce by one half the rate of limb amputations for diabetic gangrene.
  d) Cut morbidity and mortality from coronary heart disease in the diabetic by vigorous programmes of risk factor reduction.
  e) Achieve a pregnancy outcome in the diabetic woman that approximates that of the non-diabetic woman.
- Establish monitoring and control systems, using state-of-the-art information technology for quality assurance of diabetes health care revision and for laboratory and technical procedures in diabetes diagnosis, treatment and self-management.
- Promote European and international collaboration in programmes of diabetes research and development through national, regional and World
International declarations

Health Organisation (WHO) agencies and in active partnership with diabetes patients’ organisations.
• Take urgent action in the spirit of the WHO programme ‘Health for All’ to establish joint machinery between the WHO and the International Diabetes Federation (European region) to initiate, accelerate and facilitate the implementation of these recommendations.”

At the conclusion of the St Vincent meeting, all those attending formally pledged themselves to strong and decisive action in seeking implementation of the recommendations on their return home.
Since 1989 further implementation and evaluation meetings have been held in Budapest (1992), Athens (1995), Lisbon (1997) and Istanbul (1999), where representatives of ISPAD have helped to formulate recommendations on behalf of children and adolescents.
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