MANAGEMENT OF DIABETES MELLITUS
STANDARDS OF CARE AND
CLINICAL PRACTICE GUIDELINES

Edited by

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INTRODUCTION

Available data from many countries of the Eastern Mediterranean Region (EMR) indicate that diabetes mellitus has become a problem of great magnitude and a major public health concern. Studies have demonstrated that, in some countries, diabetes affects up to 10% of the population aged 20 years and older. This rate may be doubled if those with impaired glucose tolerance (IGT) are also included.

The manifestations of diabetes cause considerable human suffering and enormous economic costs. Both acute and late diabetic complications are commonly encountered. Long-term complications represented by cardiovascular diseases, cerebrovascular accidents, end-stage renal disease, retinopathy and neuropathies are already major causes of morbidity, disability and premature death in countries of this Region.

The development of long-term complications is influenced by hyperglycaemia. Poor control of diabetes accelerates their progression. Thus, to prevent complications, good control of diabetes is essential and the management of diabetes should therefore aim to improve glycaemic control beyond that required to control its symptoms. Intensified therapy and maintaining near-normal blood glucose levels can result in considerable reduction in the risk of development of retinopathy, nephropathy and neuropathy.

However, despite the high prevalence of diabetes and its complications and the availability of successful prevention strategies, essential health care requirements and facilities for self-care are often inadequate in this Region. Action is needed at all levels of health care and in the various aspects of diabetes care to bridge this gap and to improve health care delivery to people with diabetes. Education of the health care team on the management of diabetes and on how to educate people with diabetes is one major aspect that requires strengthening.

Even though resources vary widely within the Region, the primary resource in diabetes care is now recognized to be the people with diabetes themselves, supported by well trained and enthusiastic health care professionals. This resource can be strengthened nearly everywhere by education.
The recommendations contained in this document have been developed to serve as general guidelines for better management of diabetes and improved patient care. They are based on up-to-date scientific knowledge and clinical practice but take into consideration the regional situation and focus on the active role of people with diabetes in the management of their own disease.

Needless to say, health systems and resources vary from one country to another and accordingly these guidelines have to be modified and adapted to local needs and circumstances. They must be acceptable both to the professionals who shall be using them and to the people with diabetes.

Medicine is an ever-changing science and advances and new developments in diabetes care and clinical practice will continue to take place. Thus revision of the guidelines will be necessary as new knowledge is gained.
Basic principles

• Correct diagnosis is essential. Thus emphasis should be placed on using appropriate diagnostic criteria.
• Treatment should not only consider lowering the blood glucose level but also should focus on the correction of any associated CVD risk factors such as smoking, hyperlipidemias, and obesity as well as monitoring of blood pressure and treatment of hypertension.
• Management of non-insulin-dependent diabetes mellitus (NIDDM) requires teamwork. The doctor should work closely with the nurse and other members of the diabetes health care team, whenever available, and with the person with diabetes.
• Self-care is an essential strategy. Education of the person with diabetes and his/her family is the cornerstone of management. Without appropriate education, the desired therapy targets are difficult, or even impossible to achieve. People with diabetes should be encouraged and enabled to participate actively in managing and monitoring their condition.
• Good control is important. Self-monitoring improves the quality and safety of therapy.
• The health care system should ensure that people with diabetes have access to the basic requirements essential to practise self-care.
• Record-keeping is critically needed and should be considered a basic requirement for the management and follow-up of all cases.
• Objectives and priorities of treatment must be tailored to individual needs; therapy targets should be individually determined for each case.
General objectives of diabetes management

- To relieve symptoms
- To correct associated health problems and to reduce morbidity, mortality and economic costs of diabetes
- To prevent as much as possible acute and long-term complications; to monitor the development of such complications and to provide timely intervention
- To improve the quality of life and productivity of the individual with diabetes

Diagnosis

The diagnosis of diabetes carries considerable consequences and should therefore be made with confidence. If the patient has classical symptoms (such as increased thirst and urine volume, unexplained weight loss, pruritus vulvae or balanitis) or drowsiness or coma, associated with marked glycosuria, the diagnosis can be readily established by demonstrating fasting hyperglycaemia. If the fasting blood glucose concentration is in the diagnostic range shown in Table 1, an oral glucose tolerance test (OGTT) is not required.

In such instances however, a confirmatory test should be performed as incomplete fasting may give rise to spurious diagnosis.

The diagnosis can also be established if a random blood glucose estimation exceeds the diagnostic values indicated in Figure 1.

An OGTT is performed if the diagnosis is uncertain and the blood glucose values are in the equivocal range. It is often sufficient to measure the blood glucose values only after fasting and 2 hours after a 75 g oral (anhydrous) glucose load. The diagnostic criteria are shown in Table 1.

The requirements for diagnostic confirmation for a person presenting with severe symptoms and gross hyperglycaemia will differ from those of the asymptomatic patient whose blood glucose levels are just above the diagnostic cut-off values. For the asymptomatic patient, at least one additional test result with a value in the diabetic range is desirable.

Clinical diagnosis should never be based on the presence of glycosuria alone. The diagnosis of diabetes in pregnancy follows the same criteria.
TABLE 1. Diagnostic values for the oral glucose tolerance test (OGTT)

<table>
<thead>
<tr>
<th></th>
<th>Glucose concentration, m mol/litre (mg/d)</th>
<th>Whole blood</th>
<th>Plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Venous</td>
<td>Capillary</td>
<td>Venous</td>
</tr>
<tr>
<td><strong>Diabetes mellitus</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting value</td>
<td>=6.7</td>
<td>(=120)</td>
<td>=7.8</td>
</tr>
<tr>
<td></td>
<td>(=120)</td>
<td>(=120)</td>
<td>(=140)</td>
</tr>
<tr>
<td>2 hours after glucose load</td>
<td>=10.0</td>
<td>(=180)</td>
<td>=11.1</td>
</tr>
<tr>
<td></td>
<td>(=180)</td>
<td>(=200)</td>
<td>(=200)</td>
</tr>
<tr>
<td><strong>Impaired glucose tolerance</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting value</td>
<td>&lt;6.7</td>
<td>(&lt;120)</td>
<td>&lt;7.8</td>
</tr>
<tr>
<td></td>
<td>(&lt;120)</td>
<td>(&lt;120)</td>
<td>(&lt;140)</td>
</tr>
<tr>
<td>2 hours after glucose load</td>
<td>6.7-10.0</td>
<td>(120-180)</td>
<td>7.8-11.1</td>
</tr>
<tr>
<td></td>
<td>(140-200)</td>
<td>(140-200)</td>
<td>(160-220)</td>
</tr>
</tbody>
</table>

Once the diagnosis is confirmed, an attempt should be made to classify the type of diabetes. Distinction between the two major types of diabetes can be difficult. However, the following generally favour the diagnosis of insulin-dependent diabetes mellitus:

- acute onset
- onset at young age (20 years and younger)
rapid weight loss
ketonuria.

Factors favouring a diagnosis of non-insulin-dependent diabetes mellitus:

- absence of classical symptoms of diabetes
- older age of onset (over 30 years)
- presence of obesity.

Maturity onset diabetes of youth (MODY) is a rare type of diabetes that may be inherited as an autosomal dominant condition. It is characterized by onset at young age and correction of hyperglycaemia without insulin.

**Initial assessment**

A standardized form should be used for recording clinical data and the results of investigations. Record-keeping is important to ensure good quality of care and is essential for follow-up and monitoring.

Clinical assessment on presentation should be performed by a physician in all cases.

A full history is needed. In addition to the presenting symptoms, emphasis should be placed on:

- risk factors of cardiovascular diseases, such as smoking, hypertension, obesity, hyperlipidaemia and family history
- symptoms of cardiovascular complications including angina, heart failure and claudication
- visual symptoms
- symptoms of neuropathic complications such as numbness, pain, muscle weakness, gastrointestinal symptoms including diarrhoea, impotence and bladder dysfunction
- drug history
- past history
- gestational history.

A complete examination is part of the minimum requirements. Certain aspects of the physical examination should receive special attention. These include:

- height and weight measurements
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- blood pressure (lying and standing positions to detect postural change)
- cardiovascular examination for abnormal signs and assessment of peripheral pulses
- examination of the lower limbs for peripheral pulses, sensation, ankle jerk and foot lesions
- ophthalmoscopy with dilated pupils.

*Laboratory assessment should include:*
- a blood glucose measurement as a minimum requirement to confirm the diagnosis
- urine examination for ketones, protein and glucose
- serum creatinine measurement in all hypertensive patients and those with proteinuria
- electrocardiography and measurement of total serum cholesterol and triglycerides in high-risk individuals
- HBAIC measurement and quantitative measurement of urine protein as optional investigations that may be performed as part of the initial assessment where facilities and resources allow.

*Treatment*

The major components of the treatment of diabetes are:

1. **diet (combined with exercise if possible)**

2. **oral hypoglycaemic therapy**

3. **insulin treatment**

*Education* of the person with diabetes is an essential component of management in every case. To ensure appropriate management, the basic knowledge and skills should be acquired by the patient and his family and the health care team should work closely with the patient to achieve this objective and to promote self-care. The person with diabetes should also be involved in setting therapeutic targets for weight, blood pressure and blood sugar control. Basic educational requirements for the person with diabetes and his family are outlined on page 10.
Drug therapy should also be considered at this stage in the presence of marked hyperglycaemia or when the condition is associated with infection or other intercurrent illnesses.

Unless contraindications are present. The choice between BG and SU may also depend on the degree of hyperglycaemia.
Management strategies

Ideally, the initial management of NIDDM should be based on dietary therapy combined with increased physical activity, if possible. However, pharmacologic therapy (oral hypoglycaemic drugs or insulin) may be considered in the presence of marked hyperglycaemia.

The treatment scheme in Figure 3 can probably be appropriately applied in most cases.

Therapy targets

Therapy targets should be determined and fully discussed with the person with diabetes at the initial phase of management. In addition to achieving an optimal body weight, Table 2 represents targets that may be considered.

<table>
<thead>
<tr>
<th>TABLE 2. Therapy targets</th>
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<tbody>
<tr>
<td><strong>Value</strong></td>
</tr>
<tr>
<td>Symptoms</td>
</tr>
<tr>
<td>Plasma glucose level in mg/dl (mmol/L)</td>
</tr>
<tr>
<td>Fasting</td>
</tr>
<tr>
<td>Postprandial</td>
</tr>
<tr>
<td>Glycated Hb level (% of upper limit)</td>
</tr>
<tr>
<td>Total cholesterol level in mg/dl (mmol/L)</td>
</tr>
<tr>
<td>Triglyceride level in mg/dl (mmol/L)</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
</tr>
</tbody>
</table>

Basic educational requirements

The person with diabetes should acquire adequate knowledge and skills in the following:

- individual therapy targets
- individual nutritional requirements and meal planning
- type and extent of exercise and physical activity
- interaction of food intake and physical activity with oral hypoglycaemic drugs/insulin
- improvements in lifestyle, for example harmful effects of smoking, obesity and alcohol intake
self-monitoring and significance of results and actions to be taken
- how to cope with emergencies (illness, hypoglycaemia)
- how to avoid complications and detect them at an early stage, e.g. how to take care of the feet.


**Dietary treatment**

Diet is a basic part of management in every case. Treatment cannot be effective unless adequate attention is given to ensuring appropriate nutrition.

**Dietary treatment should aim at:**

- ensuring weight control
- providing nutritional requirements
- allowing good glycaemic control with blood glucose levels as close to normal as possible
- correcting any associated blood lipid abnormalities
- ensuring consistency and compatibility with other forms of treatment if used, for example oral agents or insulin.

**The following principles are recommended as dietary guidelines for people with diabetes:**

- Dietary fat should provide 25-35% of total intake of calories but saturated fat intake should not exceed 10% of total energy. Cholesterol consumption should be restricted and limited to 300 mg or less daily.

- Protein intake can range between 10-15% total energy (0.8-1 g/kg of desirable body weight). Requirements increase for children and during pregnancy. Protein should be derived from both animal and vegetable sources.

- Carbohydrates provide 50-60% of total caloric content of the diet. Although it has been traditionally recommended that carbohydrates should be complex and high in fibre, more emphasis should be placed on the total amount of carbohydrates consumed than the source of carbohydrate.
Excessive salt intake is to be avoided. It should be particularly restricted in people with hypertension and those with nephropathy.

Artificial sweeteners are to be used in moderation. Nutritive sweeteners (sorbitol and fructose) should be restricted.

The same precautions regarding alcohol intake that apply to the nondiabetic population also apply to people with diabetes. Additionally, however, alcohol tends to increase the risk of hypoglycemia in those taking antidiabetic drugs and should be particularly avoided in those with lipid abnormalities and patients with neuropathy.

Except in special conditions like pregnancy and lactation, routine vitamin and mineral supplementation is generally not needed in people with a well balanced diet. There is, at present, no definite evidence to confirm that such treatment has any benefits.

**Meal planning**

- Assessment of dietary intake and individual needs of those with diabetes should be made as part of the initial management. Under optimal circumstances, this task is the responsibility of an experienced dietician, in consultation with the treating physician. However, after appropriate training the physician and the nurse can take on this responsibility in places where dietitians are not available.
- Meals and food intake should be planned in relation to economic factors and local circumstances concerning availability and cultural and social values. Special consideration should be given to meal planning during the month of Ramadan.
- Dietary counselling should be a continuing process to be reinforced during each visit by all members of the health care team.
- Meals should be evenly distributed throughout the day. Consistency of food timing and energy intake from day to day should be emphasized, especially by those taking insulin.

**Exercise**

Physical activity promotes weight reduction and improves insulin sensitivity, thus lowering blood glucose levels.

Together with dietary treatment, a programme of regular physical activity and exercise should be considered for each person. Such a programme must be tailored to the individual’s health status and fitness. People should, however, be educated about the potential risk of hypoglycaemia and how to avoid it.
Drug treatment

Oral hypoglycaemic drugs (OHD) are considered only after a regimen of dietary treatment combined with exercise has failed to achieve the therapy targets set.

There are two major groups of OHD: sulphonylureas (SUs) and biguanides (BGs). SUs act by stimulating insulin release from the beta cells and also by promoting its action through extrapancreatic mechanisms. BG exert their action by decreasing gluconeogenesis and by increasing the peripheral utilization of glucose.

Several SU preparations are marketed in countries of the Eastern Mediterranean Region. Selection of a specific SU preparation will depend on factors such as availability, cost, and the physician’s experience. However, this group of drugs may be represented by glibenclamide or tolbutamide.

SUs can cause hypoglycaemia and their use should therefore be closely monitored in the elderly and in those with nephropathy. Tolbutamide is a short-acting SU and may be selected in patients with renal impairment.

Glibenclamide may be given in an initial dose of 1.25-2.5 mg which can be increased up to a maximum daily dose of 15 mg. For tolbutamide, the initial daily dose is 0.5 g which can be increased, if necessary, to 1.5 g in divided doses.

Metformin is the only BG preparation now marketed in most Eastern Mediterranean Region countries. Metformin is primarily used in the obese not responding to dietary therapy. The starting dose is 500-850 mg with or after food, once daily, which can be increased to 500 mg tds or 850 mg bd. Because of the risk of lactic acidosis, it is contraindicated in:

- patients with impaired renal function
- elderly people above the age of 70 years
- patients with heart failure, hepatic impairment, or predisposition to lactic acidosis.

For the same reason, treatment with metformin should be discontinued during surgery, severe infections and intercurrent illnesses.

SUs may be combined with metformin when therapy targets are not achieved with either drug alone.

Both SUs and BGs should not be used during pregnancy or breast-feeding.

Some traditional and herbal therapies may be shown to lower blood glucose levels, but their long-term efficacy and safety have not been studied and they are therefore not recommended.
In people with NIDDM, insulin is indicated in the following situations:

- when diet and oral hypoglycaemic drugs fail to control hyperglycaemia and achieve therapy targets;
- diabetes during pregnancy when diet alone is inadequate;
- when oral hypoglycaemic drugs are contraindicated;
- during stressful conditions such as infection and surgery.

Further guidelines on insulin treatment are included in the section on the management of IDDM.

**Monitoring glycaemic control**

Glycaemic control should always be monitored. The absence of symptoms alone should not be taken as an indicator of good control.

- Self-monitoring should be encouraged.
- Methods and frequency of monitoring depend on the type of treatment, the local facilities available, and therapy targets set.
- Methods include:
  - urine glucose testing;
  - blood glucose measurements;
  - other tests like glycated haemoglobin (HbA1c) or fructosamine measurement;
  - urine ketones should also be tested during intercurrent illnesses and periods of poor control.

Blood glucose testing is more informative and safer than urine testing. It is particularly important in poorly controlled cases, those on insulin or when hypoglycaemia is suspected.

Glucose meters may be used but are not essential. Blood glucose testing using visually read strips can be equally reliable in suitably trained hands.

Frequency of blood glucose testing should be determined by the person with diabetes in consultation with the physician and nurse. Intensified testing is needed during pregnancy and in special cases when strict glycaemic control is to be ensured.
**Insulin**

**People with diabetes should**
- be taught self-monitoring techniques
- have their skills checked periodically and reinforced. The precision of blood glucose measurement should be verified at least every six months
- keep a record of self-monitoring results
- be assisted in acquiring knowledge and developing skills that enable them to modify treatment according to the results of self-monitoring.

**Urine glucose testing**
- may be an effective tool for monitoring diabetes control in situations where frequent blood glucose testing is not possible, although it provides no information on hypoglycaemia;
- is an alternative in people refusing blood testing;
- may by an acceptable method of monitoring in elderly people with a stable condition and for those in whom strict glycaemic control is not important;
- is generally unreliable during pregnancy.

**Guidelines for urine testing**
- use a second-void urine specimen
- The goal is a persistently negative test (in people with normal renal threshold)
- Check blood glucose if urine >2% 
- Check urine ketones when:
  - blood glucose is consistently >300 mg 
  - urine glucose is consistently >2% 
  - during intercurrent illnesses
- Frequency of urine glucose testing:
  - daily at fasting
  - before main meals and at bedtime once weekly in stable patients and more frequently in poorly controlled cases.
**Insulin**

**Diabetes and other illnesses**

Metabolic control may deteriorate during infections, stressful conditions and other intercurrent illnesses. Both the health care team and the person with diabetes should take note of this fact and take action to avoid complications.

**Actions to be taken:**

- More frequent monitoring of urine and blood glucose
- Monitoring of urinary ketones
- Recognition of symptoms and signs of ketoacidosis (vomiting and other gastrointestinal symptoms, dehydration, etc.) and early referral to a specialist.

**Hypoglycaemia**

Hypoglycaemia is a common complication of drug treatment and is a particular risk in insulin-treated patients. Severe episodes can lead to serious complications and may be potentially fatal if left untreated.

Hypoglycaemia is likely to occur under the following circumstances:

- omission of meals or inadequate food intake
- with unaccustomed physical exercise
- overtreatment with insulin or sulphonylureas
- ingestion of alcohol particularly without food
- diminishing insulin requirements due to impaired renal function.

**Treatment of hypoglycaemia**

- Hypoglycaemia is a medical emergency and should always be treated promptly.
- Blood glucose should be measured, using glucose-sensitive reagent strips to confirm the diagnosis in suspected cases. But if this measurement is not immediately available, treat as hypoglycaemia.
Insulin

- In mild cases, the person with diabetes should be instructed to deal with such episodes by having a rapidly absorbable carbohydrate or sweetened drink which may have to be repeated as necessary.
- If the patient is confused and uncooperative or unconscious, give 10-20 grams of 20% or 50% glucose intravenously.
- When intravenous therapy is not available or possible, give glucagon, 1 mg, intramuscularly or subcutaneously.
- Hypoglycaemia due to sulphonylureas and long-acting insulins may be prolonged. Therefore it is important that frequent measurements of blood glucose are made to assess the effectiveness of therapy and to safeguard against recurrence of hypoglycaemia.
Insulin

MANAGEMENT OF

INSULIN-DEPENDENT

DIABETES MELLITUS

(IDDM)

The principles, guidelines and recommendations made for NIDDM generally apply to IDDM. However, the following guidelines focus on aspects of the management of IDDM which should receive additional emphasis or require detailed recommendations.

Organization of care

Emphasis should be placed on:

- empowering the person with diabetes to take an active part in the management and monitoring of his/her condition;

- ensuring availability and easy access to the minimum standards of diabetes care, particularly insulin and facilities for self-care and monitoring;

- providing adequate education of the person with diabetes and his family concerning all aspects of management;

- developing an organized system of health care and regular follow-up with record-keeping in all cases;

- ensuring referral to a diabetes health care team with experience in dealing with children whenever possible;

- providing adequate time for the health care consultation and easy and immediate access to medical advice in emergency situations; and

- ensuring regular review of self-management skills, particularly those required for insulin injection; regular enquiry on the occurrence of potential side effects of therapy and inspection of injection sites for local complications.
**Insulin**

**Specific objectives**

In addition to the objectives outlined under the management of NIDDM, a specific goal in the management of IDDM in children is to ensure normal growth and development of the child. Additional emphasis is also needed to alleviate anxiety and to prevent adverse psychological effects on the child and his/her family. Emphasis should be given to providing support to the family of a child with diabetes.

**Initial assessment**

The same principles under NIDDM generally apply to IDDM. However, attention should also be given to thyroid function and thyroid function tests may therefore be part of the initial assessment in some places. The assessment is also modified in children and adolescents with diabetes. Investigation for long-term complications is not indicated at the initial stage. Children should be cared for by paediatricians, whenever possible. Height and weight should be measured. **Growth should be monitored periodically.**

**Dietary therapy**

In addition to its general objectives, dietary therapy should also aim to:

- match food intake with insulin therapy to avoid excessive swings in blood glucose levels; and
- avoid hypoglycaemia.

**Meal planning should receive adequate emphasis in IDDM**

- Food intake should meet the requirements for normal growth and development.

- Calories should be distributed into main meals and regular snacks, taking into consideration local circumstances and the type of insulin therapy. Generally, the person should have three main meals with snacks in between and at bedtime but the frequency and energy content of the snacks depends on the treatment and calorie requirements.

- People with diabetes should be trained to adjust their calorie intake and insulin according to self-monitoring results and modify it with physical exercise. Additional carbohydrate intake is required to prevent hypoglycaemia which may result from prolonged or unaccustomed physical activity.

- The general principles of dietary treatment of NIDDM also apply to IDDM.
Insulin

Insulin therapy

Treatment with insulin is one aspect of management in which adequate education of the patient cannot be overemphasized. Close cooperation between the patient and his family and members of the health care team is absolutely essential.

Insulin therapy aims at:

- achieving good metabolic control by mimicking physiological insulin secretion as much as possible; and
- minimizing the risk of hypoglycaemia.

Matching insulin requirement with carbohydrate intake and physical activity and combining it with frequent self-monitoring are prerequisites for a successful therapeutic strategy in IDDM.

Insulin preparations of any species may be used.

Two major types of insulin preparations are usually used: short- and intermediate-acting. Except in occasional circumstances, long-acting insulins are generally not needed.

The strength of insulin and the calibration of syringes should be uniform throughout the country, for example U-100, in order to avoid confusion.

Insulin is usually given by the subcutaneous route. Intravenous or intramuscular routes may be used in emergencies such as in cases of diabetic ketoacidosis. The use of other routes such as intraperitoneal or nasal is still in the experimental stage.

Insulin regimens

- The majority of patients will require more than one daily injection if good glycaemic control is to be achieved. However, a once-daily injection of an intermediate acting preparation may be effectively used in some patients.

- Twice-daily mixtures of short- and intermediate-acting insulins is a commonly used regimen.

- In some cases, a mixture of short- and intermediate-acting insulins may be given in the morning. Further doses of short-acting insulin are given before lunch and the evening meal and an evening dose of intermediate-acting insulin is given at bedtime. Other regimens based on the same principles may be used.

- A regimen of multiple injections of short-acting insulin before the main meals, with an appropriate dose of an intermediate-acting insulin given at bedtime, may be used, particularly when strict glycaemic control is mandatory.
**Insulin**

The dose of the insulin preparations is adjusted according to frequent monitoring of blood glucose levels. Blood glucose monitoring should be intensified during intercurrent illness and other stressful conditions and the insulin dose may have to be increased.

**Insulin delivery techniques**

- Plastic disposable syringes with a fixed needle are recommended. They may be reused as long as the needle remains sharp and precautions are taken to prevent contamination. Washing of syringes or wiping the needle with alcohol or any other antiseptic should *not* be practised. Glass syringes, appropriately sterilized, may be used if plastic syringes are not available.
- Other insulin delivery devices may be useful, but are not essential. Insulin injection pens are reliable and easy to use. Pump treatment, providing continuous subcutaneous insulin infusion (CSII), may also be used in some specialized centres, but it is expensive, may cause complications and requires experience and prompt and efficient maintenance facilities which are rarely available in this region.
- Implantable insulin pumps are still in the experimental stage.
- Injections should be given into the deep subcutaneous tissue at a 45° angle or at a 90° angle when the subcutaneous layer is greater than the needle length.
- Rotation of injection sites is recommended to reduce insulin injection site damage.
- Absorption from the abdomen is faster than from thighs or upper arms and may be preferred for short-acting preparations.
- The knowledge and skills required by the patient for administration of insulin therapy should be periodically evaluated. Areas of emphasis include knowledge of insulin types and names, knowledge of safe storage conditions, the ability to administer correct insulin doses and the ability to prevent, recognize and treat hypoglycaemia.
- A special identification card or bracelet is recommended.

**Therapy targets and self-monitoring**

The therapy targets recommended for NIDDM may also be used for IDDM. However, once again it is important to emphasize that the therapy targets should be set on an individual basis after discussion and in consultation with the person with diabetes. Efforts to meet these targets should be intensified before and during pregnancy and in people with microalbuminuria.
Insulin

Self-monitoring is essential for adjusting insulin regimens and should therefore be practised by all IDDM patients.

Follow-up

Emphasis should be placed on the importance of regular follow-up. During follow-up visits, education should be reinforced, growth monitored, blood glucose monitoring results reviewed and measurement of HbAIC, urine glucose and ketones made. Following puberty, and more than five years after diagnosis, annual eye examination with assessment of the retina and testing for microalbuminuria are recommended.
LONG-TERM

COMPLICATIONS

Eye complications

Diabetic retinopathy is a leading cause of visual disability. Significant retinopathy is rarely encountered in the first five years of insulin-dependent diabetes mellitus, nor before puberty. However, over the subsequent two decades, the vast majority of people with diabetes develop retinal changes. In those suffering from NIDDM, up to 20% may be found to have retinopathy at the time of first diagnosis of diabetes and most develop some degree of retinopathy over subsequent decades. Hypertension is an established risk factor for macular oedema and is associated with the presence of proliferative retinopathy.

Good control of diabetes results in reduction in the occurrence of retinopathy. Timely laser photocoagulation has been demonstrated to prevent a major proportion of severe visual loss associated with proliferative retinopathy. It has also been shown to be of considerable benefit to patients with macular oedema.

Since retinopathy is not the only manifestation of diabetic eye disease, attention should also be given to glaucoma, cataract and other abnormalities likely to occur in diabetes.

In every case, eye assessment should include the following:
- History of visual symptoms, glaucoma and cataract;
- physical examination: visual acuity testing, unaided and, if necessary, with glasses and/or pinhole-lens examination for cataract, ocular pressure; and
- pupil dilation with 2.5%-10% phenylephrine and/or 1% tropicamide, and/or cyclopentolate eye drops, followed by fundus examination by direct ophthalmoscopy.
**Insulin**

Further assessment should be performed every one-to-two years. If retinopathy is detected, follow-up should be arranged in one year or more frequently, if required.

**To prevent retinopathy and visual loss, the following are recommended:**

- promoting good glycaemic control in all diabetic individuals
- controlling blood pressure
- detecting and treating glaucoma at an early stage
- detecting and treating cataract
- detecting and providing timely treatment of potentially serious retinal changes

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**Nephropathy**

Diabetic nephropathy is a major cause of death among people with diabetes and an important cause of morbidity and increased health care costs due to diabetes. It leads to end-stage renal disease requiring dialysis or renal transplantation.

**This complication may be prevented and progression can be slowed by:**

- strict glycaemic control
- vigorous treatment of hypertension
- avoidance of nephrotoxic drugs and early and effective treatment of infection.

The onset of clinical nephropathy is manifested by proteinuria. However, an earlier marker of the onset of nephropathy is the presence of microalbuminuria (defined as an overnight excretion of 20-200 microg/min or excretion of >30 mg/24-hr) on more than one occasion.

**The following action should be taken:**

- People with diabetes should have their urine tested for protein at initial assessment and periodically at annual reviews.
- In the absence of proteinuria, a test for microalbuminuria is recommended where local resources permit.
- In the presence of microalbuminuria or gross proteinuria:
  - full assessment of renal function should be performed periodically
Insulin

- Treatment of hypertension should be instituted as early as possible and good control should be achieved. Emphasis should be given to avoidance of nephrotoxic drugs and early and effective treatment of infection.

- Optimal diabetes control should be ensured.

Dietary modifications in the form of reduced protein intake and salt restriction should be considered if the need arises.

Neuropathy

Neuropathy is a common complication of diabetes. It causes clinical manifestations and disabilities of diverse spectrum and considerable severity. Both peripheral nerves (sensory and motor) and the autonomic nervous system can be affected. Patients present with distal symmetrical polyneuropathy, focal neuropathy or manifestations of autonomic involvement such as gastroparesis, constipation, diabetic diarrhoea, bladder dysfunction, impotence and orthostatic hypotension.

During the initial assessment, the person with diabetes should be questioned about symptoms of neuropathies. Screening for autonomic neuropathic involvement is particularly important prior to general anaesthesia.

Peripheral nerve affection together with peripheral vascular disease predispose to foot ulcers and infection. If not detected early, these lesions may progress to gangrene and result in amputation.

Neuropathic involvement can be prevented or delayed by good glycaemic control. Foot complications can be avoided by good foot care and detection of early lesions (see below).

Pain due to neuropathy can be severe and distressing and often requires attention. If it persists in spite of good blood glucose control, drug treatment may be indicated. Analgesics may be given but if ineffective, tricyclic antidepressants such as amitriptyline may also be used for this purpose. Reassurance that pain will eventually decrease with time is needed.

Diabetic gastropathy, caused by autonomic involvement, is often manifested by troublesome gastrointestinal symptoms such as heartburn, nausea and vomiting. Symptoms may be relieved by agents promoting gastric emptying such as metoclopramide or domperidone.
Insulin

**Foot care**

Severe foot lesions requiring amputation are one of the major complications of diabetes.

The two main approaches to prevention are: (1) identification of high-risk individuals, and (2) early detection of foot lesions: for example, trauma, infection or ulcers.

**Intensified foot care should be ensured for patients at high risk, such as those with:**

- symptoms and/or signs of neuropathic involvement
- evidence of peripheral vascular disease
- nephropathy or significant retinopathy
- foot deformities and chronic orthopaedic or rheumatic disorders, and
- poor hygiene.

**Instructions on foot care should be an integral part of any educational activity on diabetes. They should focus on:**

- Self-examination
- avoidance of trauma
- cessation of smoking, and
- wearing properly fitting shoes.

Efforts should be intensified in respect of high-risk people. Health-care professionals, other than doctors, at the primary health care level should be trained to identify such individuals and recognize early lesions. Patients with suspected or confirmed abnormalities should be sent for medical consultation.
Insulin

Cardiovascular diseases

Cardiovascular diseases (coronary heart disease and strokes) are the leading causes of death in the diabetic population. Risk factors for the development of macrovascular disease are frequently found in people with diabetes.

The initial assessment of the newly diagnosed NIDDM individual should always include:

- clinical screening for risk factors of cardiovascular diseases (CVD); for example, hypertension, smoking, obesity, and hyperlipidemia
- screening for early signs of cardiovascular abnormalities
- a baseline electrocardiogram
- serum lipid measurement, whenever possible.

Activities to reduce CVD risk factors should be an integral part of the management plan.

The management plan should include:

- prevention and cessation of smoking
- correction of other CVD risk factors, good control of hypertension and effective treatment of hyperlipidemia
- nutritional advice to reduce weight, lower saturated fat and avoid excess salt in the diet and to discourage the use of alcohol, particularly in individuals with hypertriglyceridemia.
- promotion of physical activity and exercise.

Hypertension

Hypertension is commonly associated with diabetes and may complicate it. Other conditions are important independent risk factors for cardiovascular, renal, cerebral and peripheral vascular disease.

Hypertension should be detected early and treated aggressively if its contribution to increased morbidity and mortality in diabetes is to be avoided.
Insulin

*Guidelines for the management of hypertension in diabetes*

- Unless the blood pressure is severely elevated, diagnosis should usually be based on high blood pressure (BP) measurements made under standard conditions on at least three occasions.

- Blood pressure is elevated when the BP is persistently >140 mmHg systolic and/or >90 mmHg diastolic.

- BP should always be examined in the supine and standing positions to detect postural changes.

- The presence of target-organ damage (e.g. retinal, renal or cardiovascular) should be evaluated.

- **Other modifiable cardiovascular risk factors should be checked.**

- In general, the goal of blood pressure treatment should be to maintain BP at <140 mmHg systolic and <85 mmHg diastolic.

- Treatment should initially be based on nonpharmacological therapy, namely weight reduction, dietary modification, increased physical activity and smoking cessation.

- The aim of dietary therapy should focus on a low salt intake (sodium intake of less than 100 mmol/day), and low saturated fat to reduce the risk of CVD. For overweight individuals, calorie reduction to achieve gradual weight loss should be planned together with regular physical exercise. Alcohol increases plasma triglyceride levels; excessive consumption can also lead to a further rise in blood pressure.

- Drug treatment should be considered only if the therapy targets are not reached with nonpharmacological measures. An exception to this recommendation is severe hypertension (systolic of >180 or diastolic of >110) when drug treatment should be considered on presentation.

**Drugs used to lower blood pressure in diabetes**

There are several classes of antihypertensive drugs. Each class has potential advantages and possible drawbacks.

*Thiazide diuretics* and *B-blockers* have been shown to reduce cardiovascular morbidity and mortality in diabetic and nondiabetic subjects. Thiazides in small daily doses (12.5–25 mg hydrochlorothiazide or chlorthalidone) are effective. Side effects, such as hyperglycaemia, hypokalaemia, hypomagnesaemia and hyperuricaemia, may develop but are minimal with such low doses.
Insulin

In addition to reducing cardiovascular morbidity and mortality in population-based studies, B-blockers have also been shown to reduce the recurrence of myocardial infarction and sudden death. However, their use may be associated with an adverse effect on lipid status and blood glucose control. B-blockers may interfere with the awareness of, and recovery from, hypoglycaemia. They may also cause worsening of peripheral vascular disease by causing vasospasm.

Angiotensin—converting enzyme (ACE) inhibitors have been shown to reduce microalbuminuria and delay the onset and progression of diabetic nephropathy. They have no adverse effects on lipid status or glucose levels but may cause hyperkalemia in patients with renal impairment and in those taking potassium-sparing drugs or potassium supplement. ACE inhibitors are contraindicated in pregnancy and should therefore be used with caution in women of childbearing age. In people with renal artery stenosis, ACE inhibitors may induce impairment of renal function.

Calcium channel blockers have no adverse effects on lipid and glucose metabolism.

a-1 receptor blockers have no adverse effects on lipids or glucose control but may cause postural hypotension and should be used with caution, particularly in people with autonomic neuropathy. This also applies to other sympatholytic drugs.

In conclusion, available evidence indicates that ACE inhibitors, calcium channel blockers and a-1 receptor blockers can be effectively used to lower blood pressure. Small dose thiazides can also be effective and have been shown to have a cardioprotective effect. The favourable cardioprotective action has also been documented with 13 blockers but in this case cardio-selective preparations in low doses are preferred and caution should be exercised in patients particularly predisposed to hypoglycemia. Low-dose methyldopa may be considered in some cases particularly in the treatment of hypertension during pregnancy. At any rate, the choice of the antihypertensive drug used will be determined individually and by the presence or absence of other associated conditions like CVD, nephropathic or neuropathic complications. It is also important to consider the cost of treatment as a factor influencing drug choice since many of the drugs mentioned above may be beyond the reach of some patients.
Insulin

**DIABETES AND PREGNANCY**

Good glycaemic control has special importance during pregnancy. Maternal and perinatal complications can be reduced if good control is achieved before and during conception. Good biochemical control before pregnancy is important since hyperglycaemia seems to be a major factor in the development of congenital malformations and the risk of these malformations is highest during the first eight weeks of gestation.

**Guidelines for the management of diabetes during pregnancy**

- Intensive education and management of the woman with diabetes should start several months before conception to ensure strict control during the early weeks of pregnancy. Pregnancy may have to be deferred until optimal control is achieved.

- Women well controlled on oral hypoglycaemic drugs should be changed over to insulin and achieve optimal blood glucose control before conception.

- Those well controlled on diet alone may continue on such therapy as long as they are carefully monitored to assess the need for insulin.

- Therapy targets, prior to conception, should be achieved. Treatment should aim at having preprandial and postprandial glucose levels which are close to normal as well as normal or near normal glycated haemoglobin levels (if such measurement is available).

- Full clinical assessment is needed. Renal and retinal complications should be looked for. Ophthalmoscopy and testing for urinary albumin should be repeated during pregnancy.

- During pregnancy, frequent follow-up is needed to ensure that therapy targets are met without significant hypoglycaemia. Review every two to four weeks is generally recommended but should be more frequent if required.
**Insulin**

- Early morning urine should be tested for ketones, if indicated, to rule out starvation. Urine glucose measurement, however, is no longer reliable during pregnancy because of changes in the renal threshold.
- Insulin is preferably given three to four times per day. Some patients may be controlled with two daily injections of a mixture of short- and intermediate-acting insulin.
- Delivery should be planned jointly by the physician and the obstetrician. It can take place at term without surgical intervention but earlier induction or caesarian section may be needed for obstetric reasons.
- Following delivery, frequent blood glucose monitoring is needed to avoid hypoglycaemia and to adjust the insulin dose which diminishes dramatically at this stage.
- Postpartum follow-up and counselling will be needed in all cases.

**Screening for diabetes during pregnancy**

A substantial proportion of women of childbearing age develop gestational diabetes mellitus (GDM). GDM is defined as diabetes which is first detected during pregnancy. In order to prevent maternal and perinatal complications of diabetes, early detection of glucose tolerance abnormalities during pregnancy is important. Another advantage in screening for GDM is the fact that women who develop glucose intolerance during pregnancy will run a higher risk of developing diabetes in the future; thus, detection of this abnormality provides the possibility of preventive intervention.

The following recommendations on screening for GDM during pregnancy in the Eastern Mediterranean Region were made during the First WHO Regional Meeting on Diabetes in 1992:

**Screening is recommended at two stages during pregnancy:**

- All pregnant women should be screened for diabetes during the first antenatal visit by testing for glycosuria. A positive test is an indication for further assessment by a 75 g oral glucose tolerance test.
- At 24-28 weeks of gestation, women at high risk of developing GDM or IGT should be screened by means of an oral glucose tolerance test, using 75 g glucose load. Those at high risk include women with:
  - previous GDM or IGT
  - a family history of diabetes
  - obesity
Insulin

- adverse obstetric history
- history of giving birth to a big baby
- history of a congenital malformation affecting the newborn in a previous pregnancy.

The WHO criteria for the diagnosis of glucose tolerance abnormalities can be used during pregnancy.

These recommendations may be modified in different countries of the Region according to local circumstances and resources. They are also subject to change as more knowledge is gained on the importance of the various risk factors in determining the predisposition to GDM.
Many references have been consulted in the preparation of these guidelines. The following deserve special mention:


ANNEX

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