

Diabetes Mellitus

Clinical Practice Guidelines

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PREFACE

Like the rest of the world, diabetes continues to be a major health problem in Pakistan. Diabetes is a life-long disorder, and the better it is managed, the better the outlook for a long and healthy life, but no one should be expected to follow a lot of restrictions and advice unless their purpose is fully understood. This book has been written as a practical guide to the management of diabetes for the benefit, I hope, of clinicians. It is based on my larger book on Diabetes (in Urdu). I hope this handbook will be helpful to those with charge of diabetics and also that it will be valuable, either in general practice or in hospital. The reader will find the chapter on Diabetes and Ramadan useful as not much is written on this subject in general medical text books.

This Handbook addresses in a straightforward manner what the clinician needs to know.

Feb, 1998 Karachi

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Introduction

In the last decade diabetes has emerged as major health problem in Pakistan. The national diabetes prevalence survey conducted by the DAP and WHO collaborating centre Karachi in collaboration with WHO has shown that over 10% of the people in the age group of 25 years and above are diabetic and an equal number are suffering from impaired glucose tolerance (IGT).

The incidence of childhood diabetes (type 1) continues to be very low in Pakistan and there has been no apparent increase during the last 30 years. The manifestations of diabetes cause considerable human suffering and enormous economic costs.

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 Pakistan. Action is needed at all levels of health care and in the various aspects of diabetes care to bridge the gap and to improve health care delivery to people with diabetes.

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.

The recommendations contained in this hand book have been developed to serve as general guide lines for better management of diabetes and improved patient care. They are based on up-to-date scientific knowledge and clinical practice.

Needless to say that 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.

Definition

Diabetes mellitus is a group of metabolic diseases characterized by Chronic hyperglycaemia with disturbances of Carbohydrate, fat and protein metabolism resulting from defects in Insulin Secretion, Insulin action or both. The severity of its Symptoms is largely determined by the degree to which the insulin action is deficient. Characteristically, the diabetic has a

long term risk of developing progressive disease of the retina and kidney, damage to the peripheral nerves, and aggravated atherosclerotic disease of the heart, legs and brain.

Classification

Clinical Classes

- * Insulin dependent diabetes mellitus (IDDM) – Type I
- * Non-Insulin dependent diabetes mellitus (NIDDM) – Type II
- * Gestational diabetes mellitus (GDM)

The classes, Insulin dependent diabetes mellitus and non-Insulin dependent diabetes mellitus recognize the fundamental Clinical differences in these two major forms of the disease and the vital clinical and therapeutic importance of whether or not the subject is dependent on exogenous insulin to preserve life.

Diagnosis

When symptoms of thirst, polyuria with glycosuria and weight loss are present, a single measurement of blood glucose is usually all that is required to establish the diagnosis and more formal tests are unnecessary. This may also be the case when symptoms and signs are few. A clearly raised fasting glucose concentration (venous plasma) in excess of 126 mg/100 ml or a 2 hours post meal blood glucose in excess of 200 mg/100 ml unequivocally establishes the diagnosis. However, a standard oral glucose tolerance test (OGTT) should be performed when random blood glucose values are equivocal or when there are special indications.

ORAL GLUCOSE TOLERANCE TEST (OGTT):

OGTT is the only form of glucose tolerance testing recommended for the diagnosis of diabetes, and is the only test for IGT.

OGTT must be among the most over-used procedures in every day diagnostic practice. When it is necessary to carry out this test, it should be performed as follows:

The subject should be consuming a diet, containing more than 150 gm carbohydrates for at least 3 days before the test. After 8-14 hours overnight

fast, fasting blood sample is taken and the subject then drinks the glucose load dissolved in 250 to 300 ml of water over the course of 5 minutes. The recommended glucose load is 75 gm for adults and 1.75 gm/kg body weight to a maximum of 75 gm for children. A further blood sample should be taken 2 hours after the glucose drink. The patient should sit comfortably and not smoke during the test. Any medications, medical disorders, adverse reactions to testing or other special features should be noted as they may affect the validity or interpretation of the test. The values of diagnostic glucose concentrations for diabetes mellitus are given in Table 1.

Table 1: Values of diagnosis of diabetes mellitus

	Glucose concentration, mmol/l (mg/dl)		
	Whole blood	Plasma	
	Venous	Capillary	Venous
Fasting	≥ 6.1 (110)	≥ 6.1 (110)	≥ 7.0 (126)
or			
2-h post glucose load			
or both	≥ 10.0 (180)	≥ 11.1 (200)	≥ 11.1 (200)

In the absence of diabetic symptoms, at least two abnormal values are required to establish the diagnosis of diabetes mellitus.

The old OGTT, requiring half hourly blood glucose estimation for two and a half hours or more has been replaced by the above modified OGTT.

IMPAIRED GLUCOSE TOLERANCE (IGT):

Impaired glucose tolerance is present when the fasting levels are less than those specified in Table 1 and 2 hour value fall within the specified range, Table 2. For the diagnosis of IGT, blood sugar estimation 2 hours after glucose load is necessary.

Table 2: Values for diagnosis of Impaired Glucose Tolerance (IGT)

	Glucose concentration, mmol/l (mg/dl)		
	Whole blood		Plasma Venous
	Venous	Capillary	
Fasting concentration (if measured)	< 6.1 (110)	< 6.1 (110)	< 7.0 (126)
and 2-h post glucose load	6.7-9.9 (120-179)	7.8-11.0 (140-199)	7.8-11.0 (140-199)

IGT recognizes the existence of a zone of diagnostic uncertainty and includes individuals who used to be classed as chemical, borderline, subclinical or early diabetics. The justification for distinguishing IGT from normal is based on long-term follow-up results which show that annually 2-4% of patients in this group develop unequivocal diabetes. There is a comparable likelihood that some will revert, apparently spontaneously, to normal tolerance. The risk of developing clinically significant diabetic retinopathy and nephropathy in this IGT group has been shown to be virtually zero but, by contrast, they share a doubling of the risk of coronary heart disease with unequivocal diabetics. The designation IGT spares a large number of people, particularly older ones, the unjustified stigma and disadvantages attached to being formally diagnosed as diabetic. In pregnancy, IGT must be taken very seriously and should be treated as diabetes.

**Table 3: Targets for Control of diabetes in men
and non pregnant women**

Time	Ideal	Acceptable
Fasting/preprandial	70-105 mg/dl	80-120 mg/dl
Postprandial (2 h)	80-120 mg/dl	80-150 mg/dl
Bedtime	100-140 mg/dl	100-160 mg/dl

Table 4: Targets for Control of diabetes in pregnant women

Time	Glucose
Fasting / Preprandial	70-100 mg/dl
Postprandial (2 h)	80-120 mg/dl

TREATMENT

The primary objective of the treatment of all types of diabetes are:

- * To alleviate symptoms of hyperglycemia
- * To achieve optimum control and thus improve the quality of life
- * To prevent acute complications and to reduce long term complications.
- * To reduce mortality.
- * To treat associated disorders

The treatment plan for all types of diabetes includes

- * Diet and Nutritional Recommendations
- * Exercise
- * Education
- * Oral hypoglycaemic Drugs
- * Insulin
- * Management of associated conditions and complications

DIET AND NUTRITIONAL RECOMMENDATIONS

The first line of treatment is diet combined with exercise

A. Goal of Diet Therapy

- * To provide adequate amounts of all nutrients
- * To achieve and maintain ideal body weight
- * To normalize blood sugar and blood lipids
- * To prevent or delay the complications of diabetes

B. Recommendations

Calories should be prescribed according to the individual requirements, taking into account the age, activity and body weight. The following table gives the recommendations for calories, proteins, carbohydrates and fats.

Recommendations	1000 Cal/day (Obese)	1500 Cal/day (Medium built)	2000 Cal/day (Thin built)
15% of the total Calories as Proteins	38 g/day	56 g/day	75 g/day
55- 60% of total calories as CHO	138-150 g/day	206-225 g/day	275-300 g/day
25- 30% of total Calories as Fat	28-33 g/day	42-50 g/day	56-67 g/day

Carbohydrate Intake

Carbohydrates should provide 55-60% of the total calorie intake. At least 80% of the total carbohydrates should come from complex starches like cereals (rice, wheat, bread, oats) legumes (beans, lentils) and vegetables and root tubers (potato)

Protein Intake

Proteins should provide 15% of the total calorie intake. The recommended dietary allowance is 0.8 g/kg body weight except in elderly subjects, pregnant women and children who may require more. In case of diabetic nephropathy protein intake has to be reduced to 0.5 g/kg body weight. White meat like fish, chicken, low fat milk, cottage cheese and legumes should form part of the protein.

Fat and Cholesterol intake

Total fat consumption has to be restricted to 25-30% of the total calories. Cholesterol consumption has to be limited to less than 300 mg per day. Replacement of saturated fats with unsaturated fats may slow the progression of atherosclerosis.

Salt intake

Normal salt intake is allowed except in hypertensive persons and in those with cardiac failure when salt intake is reduced.

Alcohol

Alcohol on an empty stomach can enhance the blood sugar lowering action

of insulin and causes hypoglycaemia. Restriction of alcohol intake is particularly important to those who are obese, hypertensive and those with uncontrolled diabetes and hyperlipidaemia.

Vitamins and Minerals

If the individual is eating a normal well-balanced diet, there is no need for supplements of vitamins and minerals except in elderly patients who may need them.

Artificial sweeteners

The use of artificial sweeteners is not strongly advised as it is better, in the long term, for the person with diabetes to get away from the taste of sugar. Noncaloric sweeteners like aspartame and saccharine can be used in limited amounts.

The food intake should be distributed as evenly as possible throughout the day.

EXERCISE

Exercise is extremely important in the management of diabetes because of its effects on the blood glucose and free fatty acids. Exercise burns calories and helps to control weight, ease stress and tension, and maintain a feeling of well-being. Regular exercise improves the body's response to insulin and makes oral hypoglycaemic drugs and insulin more effective. It also promotes circulation, lowers cholesterol and triglyceride levels, thus reducing the risk of cardiovascular disease.

Persons with diabetes, especially the young ones, should be encouraged to lead a normal life and to participate in sports and exercise programme that other people are doing. Generally they should not be excluded from physical activities or games, unless there are complications. The parents, teachers and coaches should be sufficiently informed about diabetes and physical activities.

Before starting any exercise programme, the health provider should do a thorough physical examination to find out whether or not it is safe to exercise.

The person with diabetes should be advised to:

- * Start activities slowly and then work up to a goal over a 6-8 week

period.

- * Wear proper foot wear and other appropriate protection equipment
- * Avoid exercise in extreme hot conditions and immediately after heavy meals (2 hours wait is essential)
- * Avoid exercise during period of severe hyperglycaemia. (e.g. when blood sugar is above 270mg in IDDM).
- * Reduce medication prior to exercise when necessary (Insulin in IDDM)
- * Consume Carbohydrates 30–40 minutes before exercise, especially if blood sugar is below 100mg.
- * Additional precautions should be taken for those with complications e.g. those with sensory neuropathy or vasculitis.
- * For those who are unfit or who have not been active for sometime, low intensity activities like walking should be started for at least four to six weeks initially for 10 to 15 minutes, gradually building up to 30–40 minutes.
- * For people with NIDDM, daily walk for 30–40 minutes on empty stomach. 120 steps per minute is very useful. If it is not possible to undertake daily walk, do it at least three days in a week.

EDUCATION

Education is a vital aspect of the care of persons with diabetes. Diabetes education is the transmission of information through:

Knowledge:

a. Of understanding diabetes

A brief explanation of the condition and the need for insulin injection or oral hypoglycaemic agents should be given in a simple language.

b. Of hypoglycaemia

It is important for persons with diabetes to know the symptoms of hypoglycaemia, its causes and its treatment. Advice should include carrying sugar or sweets or fruit juices and snack foods in case of delayed meals.

c. Of diet

Information about certain diets and healthy eating habits, should be explained clearly to persons with diabetes and their families. The importance of 3 meals and 3 snacks containing carbohydrates, in insulin and tablet(s) treated patients should be stressed.

d. Of exercise

Stress the importance of regular exercise in making oral hypoglycaemic drugs and insulin more effective and its role in weight reduction. Exercise also promotes circulation, lowers cholesterol and triglyceride levels, thus reducing the risk of cardiovascular disease.

e. Of identification

persons with diabetes should be advised to always carry their diabetes care booklet, so that in case of an emergency everyone will know what medication or insulin injection is being received and treatment can take place immediately.

f. Of good hygiene.

All persons with diabetes must receive adequate instructions on personal hygiene, especially with regard to care of the feet, skin and teeth.

Practical Skills

a. Insulin Injection Technique

Self insulin injection should be encouraged so that the people with diabetes can manage their condition without being too dependent on health professionals. This will give them more freedom and boost their morale. In the case of children, parents/family members should be taught. However when they reach the proper age and maturity (8 - 10 years), they should be taught self injection. This also applies to the elderly persons with diabetes and persons with physical defects.

b. Self Blood Glucose Monitoring.

Self blood glucose monitoring is an integral part of the treatment. It involves active participation of the person with diabetes in management.

Before starting the actual training in self-monitoring it is mandatory to make an assessment of the person's knowledge of diabetes. Procedures should be checked under observation.

Frequency of self monitoring will depend on many factors, like the type of diabetes, therapeutic scheme, the degree of metabolic control desired, the person's willingness to participate and the availability of equipment.

Persons with diabetes should be encouraged self blood glucose monitoring and should be explained about the benefit of having their blood glucose monitored. **Education is not part of the treatment, it is the Treatment.**

ORAL HYPOGLYCAEMIC AGENTS (O H A)

The three groups of oral hypoglycaemic agents available in Pakistan are:

1. Sulphonylureas
2. Biguanides
3. Alfa Glucosidase inhibitors

Oral hypoglycaemic agents should be used only when diet and education have failed to achieve individual treatment goal. O H A are used only in the treatment of hyperglycaemia in non-insulin dependent diabetic (NIDDM) patients. They have no role in the treatment of insulin dependent diabetes (IDDM).

SULPHONYLUREAS

Sulphonylureas are the first line drug treatment in NIDDM patients who are not very obese. The following sulphonylureas are available in Pakistan

Glibenclamide	(Daonil, Euglucon, Glicon)
Glipizide	(Glibinese, Minidiab)
Gliclazide	(Diamicron, Diclazide, Nidornil, Nodibet)
Chlorpropamide	(Diabenese)

	Initial daily dose	Maximum daily dose
Glibenclamide	2.5 – 5 mg	5 – 15 mg
Glipizide	2.5 – 10 mg	10 – 30 mg
Gliclazide	80 – 160 mg	160 – 320 mg
Chlorpropamide	250 – 375 mg	375 – 750 mg

All Sulphonylureas can cause hypoglycaemia. Longer-acting sulphonylureas (chlorpropamide) are particularly hazardous in the elderly. Renal insufficiency may require dose reduction.

Before using Sulphonylureas, the patient must be advised that: (1) they do not replace the need for continued strict dieting (2) their use does not imply

that the diabetes is 'mild' and therefore not liable to complications in the years ahead: (3) they may not be effective for an indefinite period. On average about 6-10% of NIDDM patients fail to respond to sulphonylureas every year. Thus on an average about 90% NIDDM patients will not be controlled on O H A after 10 years of onset of diabetes. In fact, it has been observed that the oral agents may assist in the control of diabetes for an average of 8 years and after that in these patient use of insulin becomes necessary for blood sugar control.

Two sulphonylureas must not be combined while treating diabetes.

BIGUANIDES

The commonest use of biguanides has been in combination with sulphonylureas. If therapy with sulphonylureas alone is not sufficient, then additional administration of biguanides can produce further blood glucose lowering effect. Biguanides are also useful as first line drug treatment in the very obese. The Biguanides available in Pakistan are: Metformin. Glucophage. Biguanil and Tabophage. Biguanides must not be used in patients with impaired renal function, septic shock, acute myocardial infarction or during major surgery, because of the risk of lactic acidosis. If creatinine rises, stop the drug. Gastro intestinal intolerance can also occur (upto 20% of patients), but can be minimized by starting therapy at a low dose (500 mg or 850 mg daily) and increasing slowly as tolerance develops. Recognised problems include dyspepsia, anorexia, diarrhoea and occasionally unpleasant metallic taste. Patients may also complain of general malaise. These side effects often limit the dose which a patient can tolerate. The incidence of gastrointestinal intolerance increases if the dose of Biguanide exceeds (500 mg per day). Biguanides should always be taken immediately after meals or during meals.

α -GLUCOSIDASE INHIBITORS (ACARBOSE)

Competitive, reversible inhibition of α glucosidase and pancreatic α amylase by acarbose delays carbohydrate digestion, prolongs digestion time, and reduces the rates of glucose absorption. As a result, the post prandial rise in blood glucose is dose dependently decreased, and insulin secretion is attenuated. They are therefore useful particularly in those with normal fasting glucose levels.

This group has been introduced in Pakistan as Glucobay and is available in

50 mg and 100 mg tablets. The dose is 50–100 mg three times a day to be taken at the beginning of breakfast, lunch and dinner. Common side effect is gaseous distention.

COMBINATION THERAPY

Biguanides and Sulphonylureas may be used in combination when treatment goals are not achieved with either agent alone. Combinations of small doses may also be used to avoid side effects of either agent. α glucosidase inhibitors (Glucobay) may also be used in conjunction with other oral hypoglycaemic drugs.

THE OBESE PERSON WITH TYPE II DIABETES

Healthy lifestyle
Diet, exercise and weight control



SUCCESS



FAILURE

Add: biguanide and/or
 α glucosidase inhibitor



SUCCESS



FAILURE

Add: Sulphonylurea



SUCCESS



FAILURE

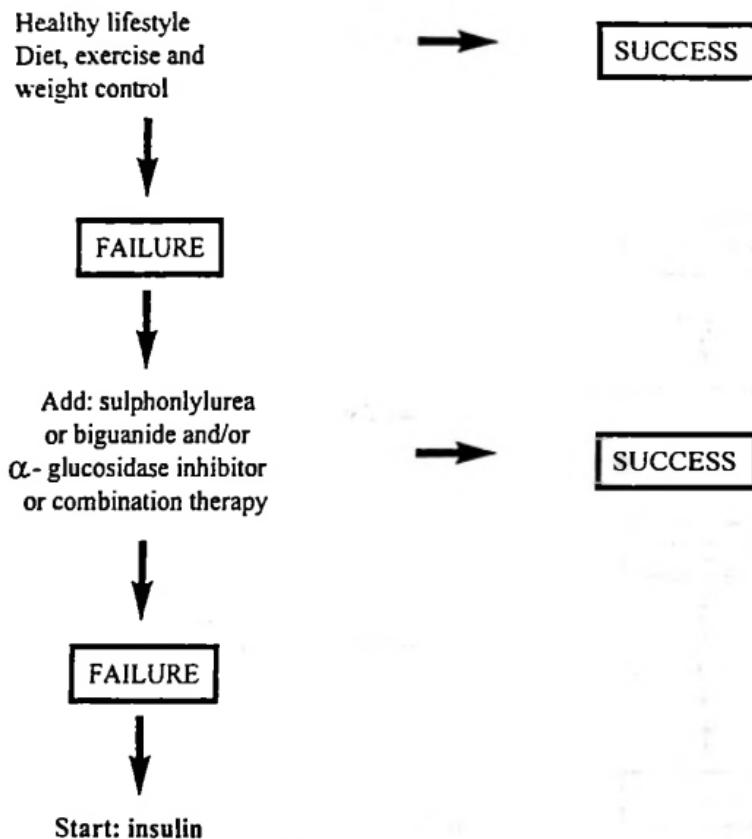


Start: insulin

Targets

“Success” = maintenance of appropriate body weight and normoglycaemia.
if “Success” is achieved, review need for continuing medication.

THE NON-OBESE PERSON WITH TYPE II DIABETES



Targets

“Success” = maintenance of appropriate body weight and blood glucose. .
if “Success” is achieved, review need for continuing medication.

INSULIN THERAPY

Indication for insulin therapy:

- * When hyperglycaemia has not been controlled by diet and oral hypoglycaemic drugs
- * When the diet has failed during pregnancy
- * During stressful situations like the presence of infection, trauma, surgery and myocardial infarction.
- * Presence of ketones in urine with hyperglycaemia.

Types of Insulin Preparation

- * Short acting
- * Intermediate acting
- * Long acting
- * Mixed insulin preparation (short and intermediate acting).

Types of insulin preparation	Onset of action	Peak	Duration
1. Short-acting, with rapid onset of action. Available as Regular-Actrapid (clear in appearance) The only type that can be administered intravenously.	30-60 Min.	2.4 hrs	4-6 hrs
2. Intermediate acting (cloudy) available as NPH - Isophane-Insulatard.	2-4 hrs	6-16 hrs	12-18 hrs
3. Long-acting - (cloudy) Slow onset of action with prolonged duration. Ultralente (zinc suspension).	3-8 hrs	10-30 hrs	36 hrs
4. Mixed Insulin preparation (cloudy) Convenient for patients with poor visual acuity or hand coordination who are unable to mix doses of insulin correctly. Available as Mixtard 30- Humulin 70/30. (70% NPH + 30% Regular)	30 min.	2-12 hrs	24 hrs.

Insulin dose

- * There are no fixed rules of insulin dosages, but average requirements are often 0.5-1.0 U/kg/day.
- * The majority of patients will require more than one daily injection if good glycaemic control is to be achieved.
- * Twice-daily injections of mixed 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 evening meal and an evening dose of intermediate-acting insulin is given at bedtime. This may be used, particularly when strict glycaemic control is mandatory.

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

Injection sites

- * The abdominal wall or front of the thighs are ideal sites for self injection of insulin.
- * Insulin can also be injected in the upper outer areas of the arms & buttocks. **NEVER INJECT INSULIN IN FOREARM OR CALF.**
- * Rotation of injection sites should be encouraged within these areas to reduce the chance of lipoatrophy and lipohypertrophy which can interfere with insulin absorption.

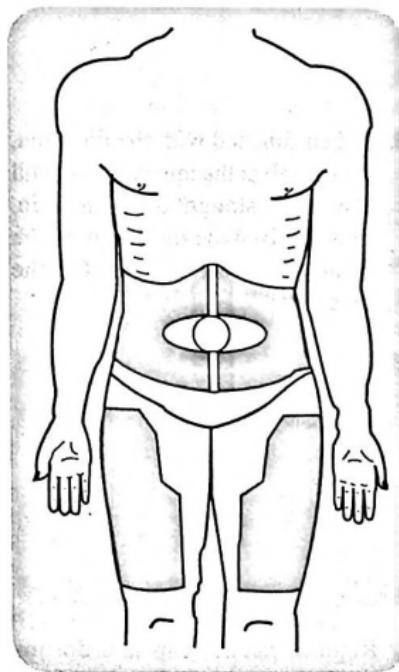
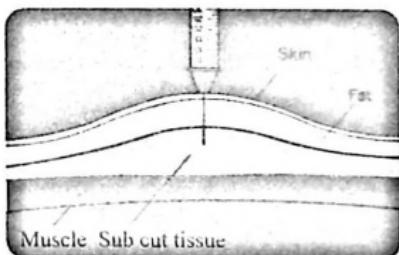
Injection Technique

- * Cleaning of injection site is generally not necessary. However Dettol or warm water Swab can be used to clean the injection site. Move the swab in a circular motion. Start from the centre and move out ward.
- * Injections should be given into the deep subcutaneous tissue into a broad pinch of skin at 90 degree angle.

1. Carefully pick up the syringe, without allowing the needle to touch anything. Or, if you have replaced the needle shield to protect the needle, remove it. Gently pinch up a two inch fold of skin. With one quick motion, inject the needle into the skin. The usual injection angle is 90 degrees but in thin persons or children it could be 45 degrees.

INJECTING INSULIN

Injection Sites



which is below that. Body areas where adequate subcutaneous tissue is found include: the abdomen, except the area around the umbilicus; the front and outer side of the thighs; the upper outer area of the arm, the buttocks. The abdominal wall or thighs are ideal sites for self injection of insulin. Rotation of injection sites should be encouraged within these areas to reduce the chance of lipoatrophy and lipohypertrophy which can interfere with insulin absorption.



1. Choose an injection site where there is adequate subcutaneous tissue. This type of tissue is located between the fat layer just under the skin and the muscle layer
2. Clean the injection site with an antiseptic or warm water swab. Do not use methylated spirit as it will harden the skin. Move the swab in a circular motion. Start from the centre and move outward.

INJECTING INSULIN



the insulin should be completed in 3 to 5 seconds.



3. Carefully pick up the syringe, without allowing the needle to touch anything. Or, if you have replaced the needle shield to protect the needle, remove it. Gently pinch up a two inch fold of skin with one quick motion, inject the needle into the skin. The usual injection angle is 90 degree, and in thin persons or children 45 degree.



4. Release the two inch fold of skin. Use one hand to hold the barrel of the syringe steady, and with the other hand push on the plunger to inject the insulin. The injection of

5. When finished with the injection, hold swab at the injection site. Pull the needle straight out of the skin, and gently wipe the site with the swab. DO NOT MASSAGE the area.



6. Replace needle cap and do not wash the syringe. Same syringe can be used several times without risk of infection.

2. Release the two inch fold of skin. Use one hand to hold the barrel of the syringe steady, and with the other hand push on the plunger to inject the insulin. The injection of the insulin should be completed in 3 to 5 seconds.
3. When finished with the injection, hold a swab at the injection site. Pull the needle straight out of the skin, and gently wipe the site with the swab. DO NOT MASSAGE the area.

- * Injection sites and skills should be checked regularly and more often where blood glucose control is suboptimal.

Insulin Storage

- * Insulin should be refrigerated but never frozen or exposed to direct sunlight or heat. The insulin should be removed from the refrigerator at least 30 minutes before the time of the injection to reduce painful sensation. If refrigeration is not available, insulin can be safely kept in water cooler (with out ice) or in a clay Pitcher which should be kept in a cool area.

Special circumstances

- * Insulin should never be omitted during intercurrent illness. Extra insulin is often required and if possible self-monitoring should be intensified.
- * Less insulin may be taken before predicted exercise.

Appropriate adjustments (including changes to cope with time zones) may be necessary when travelling.

Complication of insulin therapy

- * Hypoglycaemia

Hypoglycemia occurs when blood sugar becomes very low (less than 50 mg/dl) as a result of poor intake of food, increased metabolic demands or as a complication of treatment with insulin or oral hypoglycaemic agents. Early warning signals of low blood sugar include dizziness, lightheadedness, sweating, tremors and hunger. Later on, patients may present with behavioural and sensorial changes and subsequently coma and even convulsions if uncorrected. Unfortunately, some patients especially those with neuropathy, do not experience the early warning signs. These

patients would usually be found already unconscious. These patients are said to have "Hypoglycemia unawareness"

It is important that these early warning signals be picked up so that treatment may be given immediately. If the patient is still conscious with the above symptoms, he may be given candy or any sugar containing beverage such as coke or juice so that blood sugar can be raised as soon as possible after which the patient must be fed. However, if the patient is already unconscious, never force any food or drink because this will just cause the patient to choke resulting in more complications. Unconscious patients are best treated with intravenous glucose or glucagon if available.

Insulin allergy / hypersensitivity

Occasionally local or sometimes generalized urticaria occurs due to beef insulin, particularly with those containing protamine. Anti-histamines and desensitization may be helpful, but it is better to switch to human insulin.

Immune insulin resistance

Insulin treated patients develop a titre of circulating anti-insulin antibodies (IgG). This results in high insulin requirements. Shifting to human insulin which is less antigenic may lead to reduction in the insulin requirements.

SELF-MONITORING AND SELF-MANAGEMENT

Self-monitoring fulfills a number of important roles in diabetes self care. It is recommended for all IDDM patients. It helps to document the diabetic control achieved, provides reassurance and information required for appropriate changes in therapy, warns against metabolic disturbances and provides a powerful tool to understand the effects of behavioural changes.

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.

The following tables give simplified methods for adjusting the amount of insulin when monitoring blood glucose at home for patients receiving twice daily injection of short and intermediate-acting insulin.

If blood glucose results are too high for two days or more:

Before breakfast	Before lunch	Before dinner	At bed time
Increase next evening's intermediate acting insulin	Increase next morning's short-acting insulin	Increase next morning's intermediate acting insulin	Increase-next evening's short-acting insulin.

If blood glucose results are low for two days or more:

Before breakfast	Before lunch	Before dinner	At bed time
Reduce evening's intermediate acting insulin	Reduce morning's short-acting insulin	Reduce morning's intermediate-acting insulin	Reduce evening's short-acting insulin.

NOTE

- * Increase or decrease insulin by 2 units at a time.
- * Ask the patient to consult his/her doctor if frequent (more than two) changes are needed.

Gestational Diabetes Mellitus (GDM)

Definition

Carbohydrate intolerance resulting in hyperglycaemia of variable severity with onset or first recognition during pregnancy. The definition applies irrespective of whether or not insulin is used for treatment or the condition persists after pregnancy. It does not exclude the possibility that unrecognised glucose intolerance may have antedated.

Diagnosis

An oral glucose tolerance test (OGTT) should be performed after overnight fasting of 8-14 hours. Fasting blood sugar may not be done because it is not reliable in pregnant women. Plasma glucose is measured 2 hours after 75 G glucose load. The diagnosis of diabetes mellitus and impaired glucose tolerance (IGT) is based on WHO criteria as in table 1 & 2 on page 3 & 4. However IGT in pregnancy should be treated as diabetes mellitus.

Six to eight weeks after the pregnancy ends, the OGTT should be repeated and the woman can be reclassified as diabetes mellitus, IGT or normal glucose tolerance.

Screening for diabetes 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. All pregnant women should be screened for diabetes during the first antenatal visit by testing for glycosuria. A positive test is an indication for confirmation by a 75 g oral glucose tolerance test.

A repeat screening is performed at 24-28 weeks of gestation, in order to detect pregnancy induced diabetes mellitus. If screening of all pregnant women is not possible then women with the following high risk factors should be screened.

- Previous GDM or IGT
- Family history of diabetes
- obesity
- Adverse obstetric history
- History of giving birth to big baby ≥ 3.5 kg
- History of a congenital malformation affecting the newborn in a previous pregnancy.

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. Known diabetics who are on oral hypoglycaemic agents (OHA) should be changed over to insulin before conception. OHA should not be used during pregnancy.
- * 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 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.
- * The target blood sugar levels for diabetes control in pregnancy are; fasting blood sugar (venous plasma) below 100mg and postprandial (2h) below 120mg.
- * 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.

LONG-TERM 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 of 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.

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

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 urinary protein excretion of $> 500\text{mg}$ or urinary albumin excretion of $> 300\text{ mg}$ in 24 hours. However, an earlier marker of the onset of nephropathy is the presence of microalbuminuria, defined as an overnight excretion of 20-200 microgram of albumin per minute or excretion of 30 - 300 mg of albumin in 24 hours 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 clinical proteinuria:
 - Full assessment of renal function should be performed periodically
 - 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 modification 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.

Pain due to neuropathy can be severe and distressing and requires attention. If it persists inspite 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.

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

Instruction 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.

Effort 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.

Cardiovascular diseases

Cardiovascular disease (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 disease (CVD); for example, hypertension, smoking, obesity, and hyperlipidaemia
- * 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:

- * cessation of smoking
- * correction of other CVD risk factors, good control of hypertension and effective treatment of hyperlipidaemia
- * 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 hypertriglyceridaemia.
- * promotion of physical activities and exercise.

Hypertension

Hypertension is commonly associated with diabetes and may complicate it. Both 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.

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) measurement made under standard condition on at least three occasions.
- * Blood pressure is elevated when the BP is persistently ≥ 140 mmHg systolic and/or ≥ 90 mm Hg diastolic
- * BP should always be measured 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.
- * Dietary advice should focus on low salt intake 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 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 > 180) or (diastolic >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 β -blockers have been shown to reduce cardiovascular morbidity and mortality in diabetic and nondiabetic subjects. Thiazide 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.

In addition to reducing cardiovascular morbidity and mortality in population based studies. β -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. β -blockers may interfere with the awareness of, and recovery from, hypoglycaemia. They may 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 hyperkalaemia in patients with renal impairment and in those taking potassium-sparing drugs or potassium supplements. 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.

α -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 α -1 receptor blockers can be effectively used to lower blood pressure. Small dose thiazide can also be effective and have been shown to have a cardioprotective effect. The favourable cardioprotective action has also been documented with β blockers but in this case cardioselective preparations in low doses are preferred and caution should be exercised in patients particularly predisposed to hypoglycaemia. 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.

Diabetes and Ramadan

Ramadan is that Holy month of fasting when all Muslims desire to obtain the divine favors and blessings. Alterations in the mealtimes, daily routines and use of certain traditional foods at Iftar and Sehri is also the feature of this month.

As diabetes and its treatment is related to diet control, proper timings of

meals and medicines, the diabetic patients would like to know, from the medical point of view, if it is possible for them to fast during the month of Ramadan. If so, then what are the precautions that will enable them to fast as well as keep diabetes under good control.

Islam is a religion which does not believe in strictness under special circumstances and according to the situation permits Muslims certain favors and leniency. Keeping this in view, the advice given below for the month of Ramadan is appropriate from medical point of view.

Fasting in Ramadan will depend on the control and the type of treatment being given. According to the treatment received, the diabetic patients can be divided into three groups.

Group 1: Patients in whom blood sugar is under control on diet only

If you belong to this group you can fast, provided you continue with your diet control. Obese patients belonging to this group can reduce weight by fasting which in turn will lead to better control of diabetes. Diet means eating healthy food, eating enough and having regular meals. Diabetics should avoid becoming over weight.

The advice regarding diet during Ramadan is basically same as on normal non fasting days.

The adjustments to your diet are based on the following two principles.

- i) Avoid sugar, very sweet foods and drinks.
- ii) If you are overweight, loose weight by reducing intake of all those foods which provide energy in excess of your requirement. Diabetics should therefore avoid foods containing sugar and fatty foods (1 G of fat contains 9 calories of energy as against 4 calories of energy in 1 G each of carbohydrates and proteins.)

Weighing your food is usually not necessary; you can use common house hold measures such as tablespoons, dessertspoons, or teaspoons, cups or fistful of flour or rice (an average Pakistani female fist holds 42G of the flour and 44G of uncooked rice.)

Special diabetic foods are expensive and not really necessary for people with diabetes.

If you like eating sweet foods, it is better to include fresh fruits in your meal plan.

Avoid very sweet fruits like mangoes, grapes, dates and tinned fruits.

All vegetables including those which grow under the soil are good for you. Eat plenty of salad and vegetables including Potatoes, but avoid fried Potatoes.

You may find the following meal plan useful during Ramadan.

You may open fast with small amount of chick peas (Chola) or one oil fried vegetable Samosa or two Pakora and water or Tomato juice. Eat full meal after Maghrib prayers.

Take plenty of vegetables both cooked and uncooked., Dal, roti, boiled rice, yoghurt, fish or meat or both (if blood lipids are high, avoid red meat i.e. mutton and beef). Finish your meal with fresh fruit. If you like you can take a glass of skimmed milk with dinner or at bed time. In practice roti of whole wheat flour is as good as roti made of Gram, Maize and Millet flours.

Same principles should be followed for sehr meal. Avoid vermicelli (Khajla and Pheni). Instead whole wheat cereals or porridge may be taken.

Group 2: Patients in whom blood sugar is under control on diet and blood glucose lowering tablets (Oral hypoglycaemic drugs).

If you belong to this group you can also fast. You will have to continue with your diet control and in addition follow the advice given below regarding your oral hypoglycaemic drugs.

- a) If you are taking oral tablets in single dose in the morning, then you should continue with the same dose in Ramadan but the tablets should now be taken at the time of breaking fast (Iftar).
- b) If you are on twice daily doses, during Ramadan you will continue with the two doses but with the following modifications in the timings and quantity of drugs.

- i) The morning tablets taken on normal days should be taken at the time of Iftar. The dose will remain the same.
- ii) The second dose is taken at the time of starting your fast (Sehr) but reduce this dose to half of your usual evening dose.
- iii) If you are taking tablets three times a day then you should first consult your doctor, as the dose and the timings of your tablets will have to be adjusted so that you are able to control your diabetes on twice daily doses. If on your doctor's advice you can do this and your diabetes is under control, you can fast, otherwise not. While fasting you will have to follow the same instruction as given above regarding the timing and the dose of your tablets.

Group 3: Patients who are on insulin

If you are on insulin treatment you are not a suitable candidate for fasting. Your blood sugar levels can fluctuate considerably (i.e. blood sugar level can increase or decrease). The control of your sugar levels depends on a continuous balance between the dose of insulin administered and the food intake all day long. During fasting you can therefore develop hyperglycaemia and ketosis or sudden hypoglycaemia which can be dangerous and life threatening.

General Instructions:

Your daily food intake should be as advised by your doctor as it is calculated according to your energy requirements while controlling your blood glucose at the same time. While fasting, do not forget that you are a diabetic and the traditional foods (usually sweets and high calorie fatty foods) cooked during Ramadan are not suitable for you. Divide your daily food intake in two equal portions. Take one portion at Iftar and the other at Sehr. The meal at sehr should be delayed as much as possible, i.e. the meal should be taken within the last 30 minutes before beginning of fast.

Blood glucose control is achieved not only by diet control and medication but also by daily exercise. During Ramadan routine activity should not be reduced but some rest may be taken in the afternoon.

Exercise is good for keeping physically fit and healthy. Exercise helps diabetics by reducing their blood glucose levels thus decreasing their need

for medication (tablets or insulin). All diabetics should exercise regularly such as 30 minutes daily brisk walk (120 steps per minute) on empty stomach. During Ramadan the best time for walking is before sehr. Get up early., do brisk walk for 30 minutes, eat your meal and begin fast.

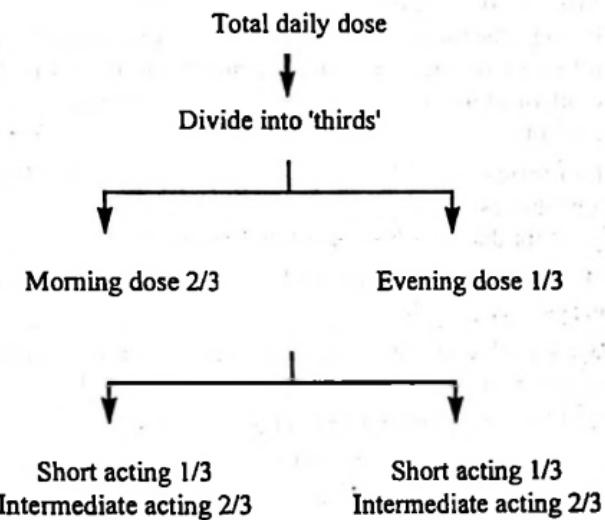
If you strictly observe these instructions, check your blood sugar levels regularly and follow doctor's advice, you will be able to fast during Ramadan and not face any unusual problems. All diabetics should remember that: "Little knowledge is not a dangerous thing. The diabetic who knows the most about his disease, lives longest".

Every diabetic, therefore, should aim to be his own doctor, of course under the supervision of a physician.

STARTING INSULIN: THE RULE OF THIRDS

1. Total daily dose = $0.5 \times$ body weight in kilograms

- 2.



EXAMPLE

- a) 72 kg patient
- b) total daily dose = 0.5×72
= 36 units
- c) Divide into thirds = 12 units
- d) Inject 24 units am
Short acting 8 units
intermediate acting 16 units
- e) Inject 12 units pm
Short acting 4 units
intermediate acting 8 units

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Morning dose

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Evening dose

DIABETES **10 COMMANDMENTS**

1. All diabetic children need insulin for treatment and survival. Oral hypoglycaemic drugs have no role in the treatment of children with diabetes.
2. Most of the adult diabetics can be controlled on diet and/or oral hypoglycaemic drugs during first 6 to 8 years of diabetes. Every year in 6 to 10% of adult diabetics the oral hypoglycaemic drugs will fail to control blood sugar and they will then require insulin for optimal control.
3. Diabetics should avoid sugar and sugar rich food and drinks. Vegetables which grow under soil such as carrot, radish, potatoes, are good for diabetics because of their high fibre contents.
4. Over weight diabetics must loose weight and should take low caloric meals.
5. Brisk walk daily for 30 minutes, 120 steps per minute before meals is good for control of diabetes and cholesterol levels.
6. Oral hypoglycaemic drugs should not be given to pregnant diabetics. These patients should be controlled on diet and/or insulin.
7. Acceptable control of blood sugar, fasting blood sugar below 120 mg and blood sugar 2 hours after meal below 150 mg is necessary to avoid chronic complications of diabetes which can adversely affect kidneys, eyes, nervous system and blood vessels of the legs, heart and brain.
8. Testing of sugar in the urine either for diagnosis or control has no value in adult diabetics. They must check their blood sugar to monitor their control.
9. Children with diabetes should test their blood sugar at least once a week and adults at least once a month, but more frequently if their diabetes is out of control.
10. Those patients who need to be on insulin for short periods, such as during pregnancy, infections and surgery, should preferably be on human insulin if they can afford it. Otherwise beef insulin is as good as human insulin for patients who need it on long term basis and also for short duration.

HINTS FOR LOSING WEIGHT

1. Avoid frying food - boil, stew or bake.
2. Use very little oil during cooking or serving.
3. Avoid salad dressings use vinegar or lemon juice instead.
4. Avoid oily 'take-aways' and thickened gravies and sauces.
5. Do without sugar completely, use sweeteners if necessary.
6. Drink plenty of water or sugar-free fluids.
7. Don't take excessive milk, cheese or eggs.
8. Use a smaller plate and avoid second helpings.
9. Weigh weekly, not daily, using same scales.
10. NEVER use slimming pills, 'formula' drinks etc.

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Many references have been consulted in the preparation of these guidelines. The following deserve special mention:

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