API-ICP Guidelines on Diabetes 2007

PREAMBLE

The prevalence of type 2 diabetes is increasing all over the world particularly in the developing countries. It has emerged as a major public health problem in our country. The WHO estimated that there were 19.4 million persons with diabetes in India in 1995 and that this number is likely to be 57.2 million in 2025. India has the distinction of having the largest number of diabetics in the world. Studies in 1980 showed higher prevalence rates of type 2 diabetes among migrant Indians in several countries, compared with their native populations and other migrant ethnic groups. Current prevalence rates are 11-12% in the urban Indian adult population. There is evidence that the prevalence of type 2 diabetes is increasing in rural population also.

Type 2 diabetes amongst Indians occurs at a younger age, the age at diagnosis being a decade earlier than in the West. Body mass index is lower by 4 kg/m² for males and 6 kg/m² for females. However abdominal obesity with increased waist to hip ratio is more common. Strong familial aggregation of the disease with high prevalence among first degree relatives and vertical transmission through two or more generations is also noted. The earlier age of onset, delayed diagnosis and improper care lead to an increase in morbidity and mortality resulting in loss of productivity.

Despite the research and the availability of better treatment modalities, the morbidity and mortality is increasing and is a matter of concern.

Managing patients with diabetes effectively, requires a great deal of time, effort and patience. The professional education that increases awareness of the importance of diabetes management is valuable in reducing and preventing complications of diabetes. Diabetes is a serious, common, costly and controllable disease. Controlling diabetes is easier and cheaper than managing its complications.

The task of rendering quality care to our diabetic patients is stupendous and challenging. We do not have a national diabetes care programme. A proper programme will yield rich dividends in terms of prevention of its long term complications and cutting down the morbidity and mortality in diabetics. Our goal should be to preserve the health of the diabetic.

The data from several epidemiological, experimental - human and animal studies and more recently the data from several mega trials like the DCCT, Kumomoto study and the UKPDS have convincingly proved the importance of tight metabolic control in arresting the progression and prevention of microvascular disease.

Hyperglycemia contributes to the increased incidence of macrovascular disease but dyslipidemia, hypertension, central obesity, decreased physical activity and smoking play a major role in accelerated atherosclerosis seen in diabetics.

Therefore, the complete treatment of diabetic patients not only includes meticulous attention to achievement of normoglycemia, but also correction of hypertension and dyslipidemia, correction of body weight and increase in physical activity.

It is desirable to have the fasting and post-prandial blood glucose concentration and HbA1c as close to normal as possible. All the above goals are desirable and can be achieved without significant deterioration in quality of life. Patient education is also an essential goal of any treatment regimen. Patient’s who understand the importance of achieving these goals and their role in preserving health will be motivated to do so.

The American Diabetes Association and the EASD have evolved effective diabetes care programmes, which have succeeded in improving the lot of diabetics in these countries by bringing down the morbidity and mortality. These organizations have brought out consensus guidelines with an aim to achieve the defined goals. Their experience has shown that adopting guidelines by the clinicians improves the outcome of treatment. These guidelines cannot be adopted or copied, for our country. We must evolve our own programme based on our needs. India is a vast country with a heterogeneous population with different religions, cultures, languages, food habits, lifestyles, and traditions. The major portion of this population lives in rural areas with meager facilities in terms of health care delivery. Such a programme should also consider the economic realities of our people - hence such a programme should not only be available but should be affordable for the average Indian.

There is an urgent need for creating and adapting minimal guidelines on diabetes care for our country. Such guidelines once enunciated should be followed and adhered to by all the health care professionals managing
diabetes. In this backdrop, the Indian College of Physicians has decided to bring out the guidelines for the management of type 2 diabetes.

The objectives of these guidelines are:

1. To arrive at an early and proper diagnosis of diabetes.
2. To provide proper treatment to diabetic patients in different situations.
3. To draw up a monitoring programme which should be cost-effective in ensuring good control of diabetes and its associated risk factors to protect the patient from developing complications.
4. To lay down criteria for what is to be considered as ideal, good and acceptable targets to be achieved.
5. To develop a standard education program to be imparted by the family doctor to his patients on each visit.
6. To develop guidelines for early detection of its complications, appropriate measures to arrest and reverse them.
7. Guidelines regarding timely referral to an appropriate specialist and for coordinating with them.
8. To develop guidelines for preventive strategy.
9. To formulate guidelines for establishment of diabetes care centre/clinics and measures to accredit them.

The family physicians and general practitioners bear the burden of carrying out the day to day care in most patients. Therefore it is essential that they be empowered with knowledge and expertise to provide standard care. They should understand goals of therapy and try to achieve the targets of control by using proper management policies. By following the consensus guidelines in their day-to-day practice, they can achieve effective control of diabetes and prevent the development of acute and chronic complications of diabetes.

Effective diabetes self-management is an important concept in the overall control of the disease. Diabetes self-management is a relatively new approach in improving control and thereby helping to prevent its complications. This approach acknowledges that people with diabetes must ultimately take responsibility for the day-to-day management of their disease. Hence, they should receive educational inputs from the diabetic team to empower them to undertake these responsibilities.

The best model for diabetic care is a team approach, comprising of diabetologist/endocrinologist, family physician, diabetes trained nurse, podiatrist, dietician, health educator and various specialists like cardiologist, nephrologist, ophthalmologist specially interested in management of diabetic complications. There should be a close rapport and coordination between the primary care physician and diabetologist. We do not have enough number of trained para-medical personnel. There is a need to initiate the development of training facilities for these paramedical personnel like the diabetic nurse educator, dietician and the podiatrist.

Acknowledgements

I thank the Dean, Dr. Sukumar Mukherjee and the Members of the Faculty Council of the Indian College of Physicians for en trusting me the task of preparing the Indian Guidelines for Management of Diabetes. I chose to be a team of eminent diabetologists of the country - Prof. JK Agarwal, Prof. AK Das, Prof. V Seshiah, Prof. Siddharth N Shah and Professor D Maji to fulfill this task.

We took the help of several other diabetologists across the country who gave us their in puts resulting in a ‘draft of the guidelines’. We circulated this to about 200 reviewers across the country, who gave further valuable suggestions, which we have in corporated and finally we have a consensus document on the “Indian Guidelines for Management of Type 2 Diabetes”.

I sincerely thank the core committee members Professor JK Agarwal, Professor AK Das, Professor V Seshiah, Prof. Siddharth N Shah and Professor D Maji for their keen interest and whole hearted cooperation. We thank the members of the working group for their valuable in puts and the reviewers for their keen interest, critical suggestions and corrections.

I sincerely thanks USV Limited for wholeheartedly supporting us; financially for sponsoring the meetings of the core committee, publication and distribution of the guidelines and scientifically for providing the relevant references.

Prof. BK Sahay

Convenor

Indian Diabetes Guidelines 2002.

REFERENCES

DEFINITION AND EPIDEMIOLOGY

Definition

Diabetes mellitus is a syndrome characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from either an absolute or relative deficiency of insulin secretion and/or action.

*** to incorporate Dr. Munjal’s suggestion

This chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of various organs especially the eyes, kidneys, nerves, heart and blood vessels.

*** definition on prediabetes to be added

Epidemiology (to get from Dr. A.K. Das)

Prevalence of type 2 diabetes mellitus in India is showing a progressively upward trend as depicted in the Table 1.8 The study published by Indian Council of Medical Research (ICMR)5 in 1972 reported a prevalence of 2.3% which has risen to 12.1% in the year 2000 in the urban population.6

The WHO has also projected this rising trend of diabetes.7 The prevalence in India is expected to rise from 19.4 million in the year 1995 to 57.2 million in the year 2025 (Table 2).8 As shown in Table 2, India will have the largest population of diabetics in the world and will continue to have if preventive measures are not implemented.

Genetic predisposition, inherent ethnicity, increased waist to hip ratio with/without obesity, urbanization, migration and life style changes contribute to this rise in Indians.9 Moreover, type 2 diabetes in Indian population may have an onset at a younger age.5,10-12 It is projected that equal number of diabetics are undetected for a long time and hence may present with microvascular and macrovascular complications at the time of diagnosis.13

CLASSIFICATION

An international Expert Committee, working under the sponsorship of the American Diabetes Association was established in May 1995 to review the classification and diagnosis of diabetes mellitus based on etiology. The new classification was published in July, 1997 (Table 3).14 The World Health Organization (WHO) has recently laid emphasis on oral glucose tolerance test (OGTT) and its importance in the classification and diagnosis of diabetes.15

Type 1 Diabetes

a. Immune Mediated Diabetes: This form previously called insulin dependent diabetes, type 1 diabetes or juvenile onset diabetes results from a cellular mediated autoimmune destruction of the beta cells of the pancreas. Markers of the immune destruction of the beta cell include islet cell antibodies (ICAs), autoantibodies to insulin (IAAs), autoantibodies to glutamic acid decarboxylase (GAD 65) and autoantibodies to the tyrosine phosphates, IA-2 and IA-2B. The disease has strong HLA associations. In this form of diabetes, the rate of beta cell destruction is quite variable, being rapid in some individuals (mainly infants and children) and slow in others (mainly adults).

b. Idiopathic Diabetes: Some forms of type 1 diabetes have no known etiologies. Some of these patients have permanent insulinopenia and are prone to ketoacidosis, but have no evidence of autoimmunity. Only a minority of patients with type 1 diabetes fall into this category. However most of those who fall into this category are of the African or Asian origin. Individuals with this form of diabetes suffer from episodic ketoacidosis and exhibit varying degrees of insulin deficiency between episodes.

Table 1: Prevalence of diabetes mellitus in India*** (to be upgraded)

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Place</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1971</td>
<td>Tripathy et al</td>
<td>Cuttack</td>
<td>1.2</td>
</tr>
<tr>
<td>1972</td>
<td>Ahuja et al</td>
<td>New Delhi</td>
<td>2.3</td>
</tr>
<tr>
<td>1979</td>
<td>Gupta et al</td>
<td>Multicentre</td>
<td>3.0</td>
</tr>
<tr>
<td>1984</td>
<td>Murthy et al</td>
<td>Tenali</td>
<td>4.7</td>
</tr>
<tr>
<td>1986</td>
<td>Patej JC</td>
<td>Bhadran</td>
<td>3.8</td>
</tr>
<tr>
<td>1988</td>
<td>Ramachandran et al</td>
<td>Kudremukh</td>
<td>5.0</td>
</tr>
<tr>
<td>1989</td>
<td>Kodali et al</td>
<td>Gangavathi</td>
<td>2.2</td>
</tr>
<tr>
<td>1989</td>
<td>Rao et al</td>
<td>Eluru</td>
<td>1.6</td>
</tr>
<tr>
<td>1991</td>
<td>Ahuja et al</td>
<td>New Delhi</td>
<td>6.7</td>
</tr>
<tr>
<td>1992</td>
<td>Ramachandran et al</td>
<td>Madras</td>
<td>8.2</td>
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<tr>
<td>1997</td>
<td>Ramachandran et al</td>
<td>Madras</td>
<td>11.6</td>
</tr>
<tr>
<td>1998</td>
<td>Shekhar shah et al</td>
<td>Assam</td>
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<tr>
<td>2001</td>
<td>Ramachandran et al</td>
<td>Madras</td>
<td>12.1</td>
</tr>
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</table>

Table 2: Top ten countries for number of persons with diabetes*** (to be upgraded)

<table>
<thead>
<tr>
<th>Year 1995</th>
<th>No. Country</th>
<th>Year 2025 Numbers in Million</th>
<th>No. Country</th>
<th>Number in Million</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. India</td>
<td>19.4</td>
<td>1. India</td>
<td>57.2</td>
<td></td>
</tr>
<tr>
<td>2. China</td>
<td>16.0</td>
<td>2. China</td>
<td>37.6</td>
<td></td>
</tr>
<tr>
<td>3. USA</td>
<td>13.9</td>
<td>3. USA</td>
<td>21.9</td>
<td></td>
</tr>
<tr>
<td>5. Japan</td>
<td>6.3</td>
<td>5. Indonesia</td>
<td>12.4</td>
<td></td>
</tr>
<tr>
<td>7. Indonesia</td>
<td>4.5</td>
<td>7. Mexico</td>
<td>11.7</td>
<td></td>
</tr>
<tr>
<td>8. Pakistan</td>
<td>4.3</td>
<td>8. Brazil</td>
<td>11.6</td>
<td></td>
</tr>
<tr>
<td>9. Mexico</td>
<td>3.8</td>
<td>9. Egypt</td>
<td>8.8</td>
<td></td>
</tr>
<tr>
<td>10. Ukraine</td>
<td>3.6</td>
<td>10. Japan</td>
<td>8.5</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Etiological classification of diabetes mellitus

1. Type 1 diabetes (absolute insulin deficiency)
   a. Immune mediated
   b. Idiopathic
2. Type 2 diabetes (predominantly insulin resistance with relative insulin deficiency)
3. Other specific types
4. Gestational diabetes mellitus (GDM)
This form of diabetes is strongly inherited, lacks immunological evidence of beta cell autoimmunity and is not HLA associated.

**Type 2 Diabetes**

This form of diabetes was previously referred to as non-insulin dependent diabetes or adult on set diabetes. Such individuals have relative (rather than absolute) insulin deficiency. This form of diabetes frequently goes undiagnosed for many years because hyperglycemia develops gradually and in earlier stages is often not severe enough for the patient to develop any of the hyperosmolar symptoms of diabetes. Never the less such patients are at an increased risk of developing macrovascular and microvascular complications and these may be present even at the time of diagnosis. These individuals may be controlled with diet, exercise and oral agents for variable periods of time. How ever, in the course of time they are likely to require insulin for better glycemic control.

**Other Forms of Diabetes**

a. Genetic defects in insulin action  
b. Diseases of the exocrine pancreas – Includes fibrocalculous pancreatopathy  
c. Endocrinopathies  
d. Drug or chemical induced  
e. Infection  
f. Uncommon forms of immune-mediated diabetes  
g. Other genetic syndromes associated with diabetes

**Gestational Diabetes Mellitus (GDM)**

GDM is defined as any degree of glucose in tolerance with on set or first recognition during pregnancy. Six weeks or more after pregnancy ends, the woman should be reclassified into one of the following categories:

1. Diabetes  
2. Impaired fasting glucose  
3. Impaired glucose tolerance  
4. Normoglycemia

In majority of GDM cases, glucose regulation will return to normal after delivery. Clinical recognition of GDM is important because therapy, including diet, exercise, insulin and antepartum fetal surveillance can reduce the associated perinatal morbidity and mortality. Although many patients diagnosed with GDM will not develop diabetes later in life, others will be diagnosed many years post-partum as having type 1 diabetes, type 2 diabetes, impaired fasting glucose (IFG) or impaired glucose tolerance (IGT).

**Special Types of Diabetes in India**

**MODY**

MODY is a uncommon monogenic autosomal dominant variety of diabetes seen in the young described from India. The criteria of which is given in Table (criteria of diagnosis and Types of MODY from [Dr. V. Mohan]________

The WHO classification (1985) had malnutrition related diabetes as a separate class (protein deficient diabetic mellitus (PDDM) and fibrocalculous pancreatic diabetes mellitus (FCPD)). In the recent ADA classification, FCPD has been included in other specific types and PDDM has been deleted. However, this type of diabetes which is modulated by malnutrition is specially seen in India. It is characterized by younger age of on set, BMI < 18.5 kg/m², no pancreatic calcification, relative insulin resistance, non-ketotic but requiring insulin for control of blood glucose.

Low body weight type 2 diabetes mellitus is also seen in our country and is characterized by BMI less than 19 kg/m² and may not require insulin for their glycemic control for a variable period of time. This type of diabetes is not associated with malnutrition. In a multicentric study involving nine cities all over the country (1984-1990), the incidence of lean type 2 diabetes mellitus was observed to be varying from 11-25% at different centres.

**DIAGNOSIS**

The criteria for the diagnosis of diabetes are as follows:

Symptoms of diabetes associated with

a. Random * plasma glucose concentration ≥ 200 mg/dl  
b. Fasting ** plasma glucose ≥ 126 mg/dl  
c. 2 hr plasma glucose ≥ 200 mg/dl during a 75 g OGTT.

For asymptomatic individuals with any one of the above values, a 75 g OGTT is required to confirm the diagnosis.

(*Random is defined as any time of day with out regard to time since the last meal. The classic symptoms of diabetes include polyuria, polydipsia, Polyphagia and unexplained weight loss, **Fasting is defined as no caloric intake for at least eight hours. Plasma glucose should be estimated by glucose oxidase method).

**Oral Glucose Tolerance Test (OGTT) as Specified by WHO**

Procedure

1. The test should be done after at least three days of unrestricted diet (more than 150 g carbohydrate daily) and normal physical activity.  
2. It should be preceded by 10-16 hours of fasting, during which drinking plain water is permitted.  
3. It should be carried out in the resting subject.  
4. Smoking is not allowed on the morning of the test as well as during the test.  
5. Factors that could influence the test’s interpretation must be recorded.
6. Following collection of fasting blood sample, 75 g of glucose should be dissolved in 250-300 ml of water and should be drunk over the course of about five minutes.

7. The another sample is collected 2 hr after the glucose load.

8. The test results are interpreted as given in Table 4. Once diagnosed as diabetes, repetition of OGTT is not required. The diagnosis should not be based on urine sugar alone.

Pre-Diabetes (IFG/IGT)

An intermediate group of subjects, called impaired fasting glucose (IFG) is recognised as those with FPG levels > 110 mg/dl but < 126 mg/dl. Impaired glucose tolerance (IGT) is defined as 2-hr post-glucose levels > 140 mg/dl but < 200 mg/dl. The IGT and IFG group of individuals are important since they have risk of becoming diabetic and are prone to develop macrovascular complications.

SCREENING

In view of the rising trend in the prevalence of diabetes and associated morbidities, it is imperative to screen high risk groups (Table 5) and the population at large. Studies by ICMR19 and UKPDS20 have shown established complications even at the time of diagnosis emphasizing the importance of screening.

<table>
<thead>
<tr>
<th>Table 4 : Diagnostic values for diabetes</th>
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<tbody>
<tr>
<td>Glucose Concentration in mg/dl</td>
</tr>
<tr>
<td>Plasma venous</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Fasting and/or</td>
</tr>
<tr>
<td>2 hr (75 g glucose) post glucose</td>
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</tbody>
</table>

Note: Plasma glucose is 15% higher than the whole blood glucose. In fasting state, venous and capillary glucose are the same, but it differs in the post-prandial state.

<table>
<thead>
<tr>
<th>Table 5: High risk group</th>
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<tbody>
<tr>
<td>a. Family history of diabetes</td>
</tr>
<tr>
<td>b. Overweight / obese (BMI ≥ 23 kg/m²)</td>
</tr>
<tr>
<td>c. Waist circumference &gt;90 cms (in men) &amp; &gt;80 cms (in women)</td>
</tr>
<tr>
<td>d. Waist - hip ratio (0.85 for females and 0.9 for males)</td>
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<tr>
<td>e. History of gestational diabetes mellitus or baby born more than 3.5 kg</td>
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<tr>
<td>f. Hypertension</td>
</tr>
<tr>
<td>g. Dyslipidemia</td>
</tr>
<tr>
<td>h. Impaired glucose tolerance (IGT)</td>
</tr>
<tr>
<td>i. Impaired fasting glucose (IFG)</td>
</tr>
<tr>
<td>j. Vascular disease</td>
</tr>
<tr>
<td>k. Recurrent infections, tuberculosis, non-healing wounds</td>
</tr>
<tr>
<td>l. Skin tags, acanthosis nigricans</td>
</tr>
</tbody>
</table>

Population screening

a. Health check up schemes
b. Insurance screening
c. Employment check up schemes
d. Diabetic detection camps

Tools Recommended for Screening

Even though ideally fasting blood glucose should be performed, an abnormal random plasma glucose value would also indicate diabetes. However, such individuals should be retested at the next visit for establishing the diagnosis of diabetes as per the diagnostic criteria given in Table 4.

CLINICAL ASSESSMENT

Persistent hyperglycemia is the hallmark of all forms of diabetes mellitus. A detailed evaluation optimizes the care required to provide better quality of life for these patients.

The first visit: The very first visit of the patient is fully utilized for a detailed medical history and physical examination. (See Appendix 1 for patient data card).

Medical History

A. Symptoms of hyperglycemia: (polyuria, polydipsia, polyphagia)
   Weight loss, generalized weakness
   Periarthritis
   Delayed healing of ulcers
   Visual disturbances
   Balanitis/balano posthitis, or vulvovaginitis/vaginitis

B. Previous history of ketosis, hyperosmolar coma, hypoglycemia; cerebrovascular complications, coronary events, pancreatitis.

C. Symptoms suggesting development and severity of complications: Facial puffiness, pedal edema; frequency, urgency, dysuria, angina, effort in tolerance, Claudication (vascular/neurogenic), gangrene, amputation,
   Sensory impairment - pain, temperature, gait disturbance in dark,
   Foot ulcers - site, size, source, sepsis, associated cellulitis,
   Infections (prior or current) - skin, dental, genitourinary, pulmonary tuberculosis, Bladder and gastrointestinal function; Orthostatic hypotension,
   Erectile dysfunction ** to reword

D. Evaluation for possible causes of secondary diabetes mellitus.

E. Current nutritional status, eating pattern, adequacy of in take; weight history.
F. Risk factors for atherosclerosis: hypertension, obesity, hyperlipidemia, atherosclerosis in family members.

F1. smoking/tobacco and alcohol use

G. Lifestyle, cultural, psychosocial, educational, economic, activity status and exercise history.

H. Gestational history: hyperglycaemia, delivery of baby > 3.5 kg, toxemia, stillbirth, polyhydramnios or other complications of pregnancy.

I. Family history of diabetes and its complications and other disorders (Hypertension, hyperlipidemia, coronary artery disease)

J. Previous treatment details and their outcomes.

K. Current treatment and glycemic status: medications, compliance, other medications altering glycemic status, frequency of monitoring to achieve glycemic goal.

Physical Examination

- Measures for height, weight, waist circumference and hip circumference, (calculation of BMI, waist circumference and waist-hip ratio)
- Resting pulse, palpation of peripheral pulses including carotid pulses
- Blood pressure, (lying down, sitting up and standing). Ankle pressure measurement and calculation of ankle-brachial index**** wherever indicated
- Presence of pallor, pyrexia, dyspnoea, cyanosis, clubbing, dehydration
- Eye - examination including ophthalmoscopic evaluation reviewed by ophthalmologist
- Oral and dental examination
- Thyroid palpation
- Systemic evaluation
  * Cardiac evaluation
  * Respiratory system examination
  * Abdominal examination
  * Neurological examination with special reference to ankle jerk and peripheral sensation by vibration, pain and touch.
- Foot examination particularly for callosities, interdigital web deformities and ulcers, cracks of skin and foot pulses
- 10 gm mono filament is a sensitive tool to pick up diabetic foot at risk.
- Skin examination

Laboratory Assessment

a. Complete urinalysis: glucose, ketones, protein, sediments
b. CBC (complete blood count): hemoglobin, total leukocyte count, differential leukocyte count, erythrocyte sedimentation rate (ESR)

c. Fasting and 2 hr post-prandial plasma glucose
d. Fasting lipid profile after blood glucose control.
e. Electro cardiogram
f. X-ray chest PA view to see for cardiac size and undetected pulmonary tuberculosis.
g. Serum creatinine, blood urea
h. Test for urinary albumin-creatinine ratio in all patients, if positive than 24 hour urinary protein to be done. Microalbuminuria (if possible)
i. HbA1c (if possible)**

It is the gold standard though it has issues of standardization and cost within our setups.

j. These tests should be done when indicated.

- Sputum for AFB
- Carotid Doppler - IMT
- 2 D-Echocardiography
- Urine culture if sediment is abnormal or symptoms are present
- Serum electrolytes
- Liver function test**
- SGOT/SGPT (if the patient is on glitazones)
- Hs CRF

TMT/Angio (to be given by Dr. Shashank Joshi)

Follow Up Evaluation

Frequency of follow up visits is determined by the control achieved.

First follow up visit: First follow up visit should be scheduled at 2-4 weeks to evaluate blood glucose control and to reinforce diabetic education, diet, exercise and management plan.

Subsequent visits: Once the blood glucose is under control, the subsequent visits should be at three monthly interval to evaluate.

- Improvement in symptoms
- Compliance for diet, physical activity and drugs
- Weight
- Blood pressure
- HbA1c
- Lipid levels if initially abnormal

However plasma glucose (fasting and post-prandial) must be checked every month and if the blood glucose values are high, it must be reported to the physician.

Yearly investigations

- Physical examination including ophthalmoscopic evaluation and fundoscopy by ophthalmologist.
- Renal evaluation as at first visit and
microalbuminuria if possible

- Chest radiography, if required
- Electrocardiogram
- Rest of the investigations as in 3-4 monthly visits
- Evaluation of patient education and diabetes awareness

Note: Echocardiography, Doppler studies for foot pulses, cardiac stress test are to be done in appropriate situations and these need not be repeated with out proper indications. [to come in the box]

**GOALS OF THERAPY**

The goals of management in a diabetic patient are to provide

- Relief from diabetic symptoms and improvement in quality of life
- Prevention of acute complications like diabetic ketoacidosis (DKA), hyperosmolar non-ketotic coma (HONK), hypoglycemia and lactic acidosis
- Prevention of infections
- Prevention of microvascular complications—nephropathy, retinopathy and neuropathy.
- Prevention of atherosclerotic vascular diseases: cardiovascular disease, cerebrovascular disease and peripheral vascular disease.
- Prevention of diabetic foot lesions.

The published data from several experimental, epidemiological, human and animal studies and more recently the data from several megatrials like the DCCT,\textsuperscript{21} Kumomoto study\textsuperscript{22} and the UKPDS\textsuperscript{23} have convincingly proved the importance of tight metabolic control in arresting and preventing the progression of the microvascular complications.

Hypertension represents a major risk for both cardiovascular disease and diabetic nephropathy. Even a modest elevation of blood pressure requires prompt treatment.\textsuperscript{23} It is suggested that a value of 130/85 mm Hg or less is desirable.\textsuperscript{24,25}

Microalbuminuria increase the risk of clinically overt albuminuria and cardiovascular disease.\textsuperscript{26} These should be detected early and treated aggressively.

Therefore the complete treatment of diabetic patients includes correction of body weight and increased physical activity, meticulous attention to achievement of normoglycemia, control of hypertension and correction of dyslipidemia.

The goals are mentioned in the Table 6. All these goals are desirable and can be achieved with out significant deterioration in quality of life. Patient education is also an essential goal of any treatment regimen. Patients who understand the importance of achieving these goals and their role in preserving health will be motivated to do so.

### Table 6: Biochemical and clinical endpoints of diabetes management (to be debated - SRJ)**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting plasma glucose (mg/dl)</td>
<td>&lt;110</td>
<td>126</td>
<td>&gt;126</td>
</tr>
<tr>
<td>Postprandial (2h) plasma glucose (mg/dl)</td>
<td>&lt;140</td>
<td>200</td>
<td>&gt;200</td>
</tr>
<tr>
<td>HbA\textsubscript{1c} (%)</td>
<td>&lt;6.0</td>
<td>7.0</td>
<td>&gt;7.0</td>
</tr>
<tr>
<td>Plasma total cholesterol (mg/dl)</td>
<td>&lt;180</td>
<td>200</td>
<td>&gt;200</td>
</tr>
<tr>
<td>Plasma LDL cholesterol (mg/dl)</td>
<td>&lt;100</td>
<td>130</td>
<td>&gt;130</td>
</tr>
<tr>
<td>Plasma triglyceride (mg/dl)</td>
<td>&lt;150</td>
<td>180</td>
<td>&gt;180</td>
</tr>
<tr>
<td>Plasma HDL cholesterol (mg/dl)</td>
<td>&gt;45</td>
<td>&gt;40</td>
<td>&lt;40</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td>&lt;120/80</td>
<td>130/85</td>
<td>&gt;130/85</td>
</tr>
<tr>
<td>Microalbuminuria (mg/day)</td>
<td>&lt;30</td>
<td>300</td>
<td>&gt;300</td>
</tr>
<tr>
<td>Ideal body weight (%)</td>
<td>&gt;80-&lt;100</td>
<td>120</td>
<td>&gt;120</td>
</tr>
</tbody>
</table>

### PRINCIPLES OF MANAGEMENT

The approach to the management of diabetes has not changed significantly over the years. However, with the development of newer drugs and better understanding of the pathophysiology of type 2 diabetes, the outlook has improved considerably.

The initial step after the diagnosis is made, is lifestyle modification. The patient is advised an appropriate diet and suitable exercise programme, with cessation of smoking and alcohol and initiation of metformin therapy. The response to diet and exercise should be assessed for two months in general. The importance of diet and exercise as a cost-effective measure in the management of diabetes should be understood and imparted to the patients. If adequate glycemic control is achieved, the patient should be motivated to continue the diet and exercise, while monitoring the blood glucose levels at regular intervals.

The choice of drug should be individualized based on the possible underlying pathogenic mechanism in each case. The anthropometric data - weight, height, body mass index (BMI = weight in kg/height in mts\textsuperscript{2}), waist-hip ratio (WHR) should be the guiding factors (see Appendix 2). In obese patients, initiate the therapy with metformin and in non-obese patients, one can initiate the therapy with sulfonylureas, glitazones or insulin, depending on the clinical presentation. When monotherapy fails to achieve adequate control, combination therapy is adopted.

A consensus statement from the ADA and the European Association for the Study of Diabetes on the approach to management of hyperglycemia in individuals with type 2 diabetes has recently been published. Early intervention with metformin in combination with lifestyle changes (MNT and exercise) with continuing, timely augmentation therapy with additional agents (including early initiation of insulin therapy) as a means of achieving and maintaining recommended levels of glycemic control (i.e. A1C <7% for most patients) are highlights of this approach. (Reference: Position Statement: Standards of Medical
However, in certain situations, insulin therapy will have to be initiated soon after the diagnosis. These situations are:
1. When there is an associated infection at the time of diagnosis
2. Myocardial infarction
3. Stroke
4. Ketoacidosis
5. Hyperosmolar coma or pregnancy and
6. When the patient has to undergo surgery.

In all these situations the initial therapy will be with insulin which can be changed after an appropriate time to oral drugs or non-drug therapy. Yet another subset of patients who require such an approach are patients with a high fasting plasma glucose level at on set i.e. greater than 300 mg/dl (>250 mg/dl in lean patients) and patients with marked loss of weight (> 10 kg).

Monitoring is also an important component of management of diabetes. This should include not only the glycemic status but also for risk factors for macrovascular and microvascular disease such as microalbuminuria, hypertension and dyslipidemia.

**NON-PHARMACOLOGICAL MANAGEMENT**

**Diet**

Modification of diet is the most important aspect in the therapeutic plan for patients with diabetes mellitus. Diet therapy consists of the following:
1. Maintenance of proper nutrition
2. Total number of calories ingested
3. Individual food sources that make up these calories
4. Distribution of calories through out the day

Selection, moderation and restriction are the key words in planning. The entire success of dietary modification in a diabetic subject depends on the judicious selection of carbohydrates, adequate protein intake and a determined restriction of total fat in take.

Attainment of optimal body weight results in marked reduction of hyperglycemia and increase in target cell response to insulin. Ideal body weight (IBW) of a person can be calculated by the formula.

IBW (in Kg) = (Height in cm - 100) 0.9

The obese and the over weight must be encouraged to reduce weight. An energy deficit of 500 Kcal daily, will help the patient to reduce 500 gm of weight every week. The next step is to calculate the optimal calories Table 7. Calorie in take based on activity is shown in Table 8.

Any person above 50 years may require 10% less calories for each decade. Children need base line calories of 1000 plus 100 calories for girls and 125 calories for boys, per year of age up to 12 years.

General guidelines for diet planning in diabetes mellitus is given in Table 9.

**Region specific diets of 1200, 1800 and 2200 are highlighted separately in Appendix.**

**Disclaimer on Diabetes Sweets and Chocolates (Shilpa Joshi)**

**Exercise**

Regular exercises form an important component of therapy in patients with type 2 diabetes. However a careful assessment of the expected benefits and associated risks of exercise in individual patients should be made while in corporating an exercise program in the treatment. Appropriate monitoring should be done to avoid complications.

**a. General Principles for Exercise in Diabetics**

- Exercise must be done regularly.
- An exercise schedule should be one that the individual enjoys and which suits his/her needs.
- **Daily exercise is preferable.**
- The patient must be told that well fitting canvas/sports shoes should be worn while walking.
- The duration of exercise should be 30-60 minutes.
- The ideal time is on an empty stomach in the morning or evening (taking into consideration the risk of hypoglycemia).
- Any exercise should have a warming up and cooling down period of 5-10 min.
- Most diabetics may need to reduce the dose of insulin and oral drugs when they exercise regularly.
- Before an exercise programme is initiated, a fair control of diabetes is to be ensured and a thorough clinical evaluation of the patient should be made particularly with regard to complications of diabetes, hypertension, coronary artery disease, peripheral vascular disease, retinopathy and nephropathy.
- The drugs that a patient is receiving should be ascertained and their possible interaction with exercise should be assessed.
It is advisable to individualize the exercise prescription.

Weight Loss para by Dr. Munjal

b. Evaluation of the Patient Before Exercise

Before beginning an exercise program, the individual with diabetes mellitus should undergo detailed medical evaluation with appropriate diagnostic studies.

Cardiovascular system

Before embarking on a moderate to high intensity exercise program, an assessment of the cardiovascular risk status of the individual should be performed.

Any individual with any of the cardiovascular risk factors will need to undergo a graded exercise test.

Retinopathy

For patients who have proliferative diabetic retinopathy, strenuous activity may precipitate vitreous hemorrhages or traction retinal detachment.

These individuals should avoid exercises that involve straining and jarring.

Nephropathy

Patients with overt nephropathy of ten have a reduced capacity for exercise. High intensity of strenuous exercises should there fore be avoided.

Peripheral neuropathy

Peripheral neuropathy results in loss of protective sensation in the feet.

---

**Table 9: Guidelines for diet in diabetes mellitus (to be updated)****

1. **Energy (calories)**
   - 25-30 cal/kg IBW - reduce in obese and increase in underweight
2. **Protein**
   - 0.8 g/kg body weight. Supplement for pregnancy, lactation and growth. Include a small quota of animal proteins - fish, chicken, milk and yoghurt. Avoid cattle meat and eggs
3. **Fats**
   - 20-25% of total calories
   - Saturated: 6-7% of total calories
   - PUFA: 6-7% of total calories
   - MUFA: 6-7% of total calories
   - N6/N3 ratio: 4:1
   - Cooking oil: 0.5 kg/month/person*

   Total fat intake in the form of cholesterol per day = 300 mg.

   Note: When prescribing fat in the diet one should take into account the invisible fat in the diet which nearly contributes to 50% of the required fat. None of the available oils are ideal.26a

   The choice of cooking oil should be as follows.
   a) Use an oil which has a moderate quantity of linoleic acid like ground nut oil, rice bran or sesame.
   b) Use an oil which has high amounts of linoleic acid (safflower oil, sunflower oil, cotton seed, corn oil) along with an oil which has relatively low levels of linoleic acid like palm oil.
   or c) Use any of the above oils with alpha linoleic acid certaining oil like mustard and soya bean oil.

   (* See Appendix 3-5 for content of saturated and unsaturated fatty acids, omega 3:6 content in oils and spices).

4. **Carbohydrates**
   - 55-60% of total calories. Encourage complex carbohydrates i.e. mainly grains, cereals, pulses.

   ****Beans, vegetables and salads.

   Avoid simple and refined carbohydrates like sugar, honey and jaggery.

   Avoid bakery products or deep fried items.

5. **Fruits**
   - Fresh fruits up to 400 g/day. Avoid juices.
   - Ideal fruits are citrus fruits, orange, sweet lime, guava, apple, papaya and watermelon. They provide vitamins, fibre. One portion contains about 40-50 calories. Dry fruits to be avoided.

6. **Dietary fibers**
   - 30-40 g/day preferably from natural sources. Avoid loss from refining and processing. Indian diet is rich in fiber and generally does not require addition of fiber supplements. (See Appendix 6).

7a. **Common Salt**
   - Up to 6 g/day. Reduce intake to 4 g/day in the presence of hypertension, renal failure and heart problems.

7b. **Condiments and spices**
   - Include in diet plan. Provide antioxidants, trace elements, minerals and n-3 fatty acids. (See Appendix 5).

8. **Fenugreek**

9. **Artificial sweeteners**
   - Use of aspartame, saccharose, etc in limited quantity is acceptable. The maximum permitted consumption range from 2-4 mg/kg/day. Avoid in pregnancy and lactation.

9. **Alcohol**
   - Avoid if possible. If not, drastically reduced. It is utilized as carbohydrates. 1 gm of alcohol provides empty calories. Alcohol may exacerbate neuropathy, dyslipidemia, obesity and may worsen the control of diabetes and cause hyperglycemia.

10. **Tobacco**
    - Avoid smoking and use of tobacco in any form.
Significant peripheral neuropathy is an indication to limit weight-bearing exercise. Repetitive exercises in an insensitive feet can lead to ulceration and fractures. It is necessary to advise proper foot wear to these patients. Patients should be taught to monitor for blisters and other potential damage to the feet before and after an exercise session.

**Autonomic neuropathy**

Presence of autonomic neuropathy may limit an individual’s exercise capacity and increase the risk of an adverse cardio vascular event during an exercise.

Hypotension and hypertension are more likely to develop in exercising patients with autonomic neuropathy. These patients also have difficulties in thermoregulation and should be advised to avoid exercises in extremely hot or cold environments and to be careful about their hydration.

c. **Type of Exercises for Diabetic Patients**

The best form of exercise recommended to a diabetic is a step wise increase of aerobic exercises. Plain brisk walking is the simplest and safest of all exercises. It can be started by any one. All the aerobic (isometric) exercises like badminton, tennis and basket ball improve the cardio-respiratory functions and utilize a large portion of muscle mass. On the other hand isometric exercises like weight lifting, sustained and grip are to be avoided in diabetics as they increase the arterial pressure and/or precipitable angina.

d. **Exercise in Special Populations**

Elderly: Many of the elderly patients tend to avoid physical exercise. There is a progressive decline in insulin sensitivity, muscle mass and strength and loss of mineral from the bones with increasing age. Regular physical exercise can prevent and reverse these changes. With exercise a better quality of life is attained in this population with reduction in the burden of chronic vascular disease.

Arthritic patients: To recommend upper body exercises.

Alternative forms of exercises including Yoga may be recommended.

Pregnant ladies: To recommend walking and if not feasible to recommend upper body exercises.

e. **Benefits of Exercise**

Several benefits accrue from a regular exercise schedule. These include:

- Improvement in insulin sensitivity.
- Reduction of hypertension.
- Reduction in weight.
- Improvement in lipid profile: reduces serum triglycerides and increases HDL particularly HDL2 cholesterol.
- Improvement in cardiovascular function.
- Improvement in the sense of physical and mental well being.
- Minimizing calcium loss.
- Improvement in quality of life.

Improving lipid profile and reducing BP is a major benefit of exercise on the cardiovascular risk factors.

f. **Risks of Exercise**

There are several potential risks of exercise for patients with diabetes.

Careful screening for underlying cardiac disease is important in all patients with diabetes before starting any exercise.

Exercise may aggravate several complications of diabetes and hence all patients should be screened thoroughly before initiating exercise.

Patients with proliferative retinopathy may develop vitreous hemorrhages.

Heavy weight lifting and Valsalva maneuver are particularly dangerous.

g. **Special Precautions**

- Feet should be inspected daily (before and after exercise) for cuts, blisters and infections.
- Exercise should be avoided in extreme hot and cold weather conditions.
- Exercise should be avoided during periods of poor metabolic control.
- An exercise program for obese patients with type 2 diabetes should start slowly, build up gradually and include exercises that are familiar to the patient and least likely to cause injuries or worsening of long term diabetic complications.
- Diabetic patients who exercise regularly should always carry quick acting carbohydrate and visible diabetes identification cards to be used in the event of hypoglycemia.

11.2.h. **Role of Yoga**

Several well-planned studies have demonstrated the beneficial effects of yogic practices in diabetics. Table 11 lists the beneficial effects of yogic practices in patients with diabetes. Some of the asanas that were found to produce these benefits are Dhanurasana, Ardhamatsayendrasana, Bhujangasana, Naukasana, Halasana, Paschimotasana, and Shavasana pranayam. (See Appendix 7). However, the patient should be thoroughly evaluated by a physician before undertaking any yogic practices.

**Pharmacological Management**

**Oral Hypoglycemic Agents**

Blood glucose levels are mainly determined by
absorption of glucose from gut, uptake of glucose by peripheral tissues (muscle, adipose tissue, liver, etc.), hepatic glucose output, and the insulin secretion from pancreas (Fig. 1). In diabetics various oral agents act to modify these factors, aiding in the control of hyperglycemia. (Fig. 2, Table 12).

a. Sulphonylureas

- The sulphonylureas bind to specific sulphonylurea receptors on b-cell and increase insulin secretion. All sulphonylureas bind to the 140 kDa sub unit of sulfonylurea receptor whereas glimepiride binds to the 65 kDa sub unit of the sulphonylurea receptor.
- In lean or normal weight individuals, Su are the preferred agents of choice.
- Sulfonylureas are preferably given 15-30 min before meals.
- For optimal release of duodenal insulin releasing factor.

- Therapy should be initiated with lowest effective doses and titrated upwards every one to two weeks until desired control or maximal dosage is reached.
- If no hypoglycemic effect is observed with half the maximal effective dose, then the drug is not likely to be effective combination therapy may be explode.
- Sulfonylureas can be combined with metformin, acarbose, thiazolidinediones and insulin to give synergistic effect. However, they should not be combined with an other sulfonylurea since they act similarly and there is no potentiation of action. Infact there is an increase in side effects.
- About 10 to 20% patients fail to respond to sulphonylureas (primary failure).
- Every year about 5% stop responding (secondary failure).
- Secondary failure may be due to insulin deficiency, but various other factors need to be excluded before it is labelled as secondary failure.
- Factors to be considered before labeling as secondary failure are given in Table 14. In these cases, the failure may be reversible.
- Various clinical trials have failed to conclusively demonstrate superiority of one sulphonylurea over the other, when used in optimal doses. In individual cases, switching over from one sulphonylurea to another may show some benefit but this may not be long lasting.

**Table 10 : Summary of exercise recommendations**

| Screening: Search for vascular and neurological complications including silent ischemic heart disease. |
| Exercise program and type |
| Aerobic |
| Duration | 30-60 minutes |
| Frequency | Daily |
| Avoid complications |
| Warm up and cool down |
| Carefully select the type of exercise and its intensity |
| Patient education |
| Monitoring of plasma glucose by patient and overall program by medical personnel |
| Compliance |
| Making exercise enjoyable |
| Convenient location |
| Positive feedback from involved medical personnel and family |

**Table 11 : Beneficial effects of yogic practices**

- Reduction of blood pressure
- Correction of dyslipidemia
- Reduction of insulin resistance and correction of hyperinsulinemia
- Elimination of stress

**Table 12 : Mode of action of various oral antidiabetic agents**

<table>
<thead>
<tr>
<th>Mode of action</th>
<th>Class of Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing insulin secretion</td>
<td>Sulfonylureas, Meglitinides</td>
</tr>
<tr>
<td>Reduction of insulin resistance</td>
<td>Glitazones, Biguanides</td>
</tr>
<tr>
<td>Decreased hepatic glucose output</td>
<td>Biguanide, Glitazones</td>
</tr>
<tr>
<td>Reduced carbohydrate absorption</td>
<td>Alpha glucosidase inhibitors</td>
</tr>
<tr>
<td>Incretins</td>
<td>DPP-IV Inhibitors (Gliptins)</td>
</tr>
</tbody>
</table>
Side effects

Hypoglycemia is the commonest side effect. Side effects are mild (nausea, vomiting) and generally reversible on discontinuation of treatment. Rarely, skin rashes, leucopenia, anaemia, thrombocytopenia, cholestatic jaundice, Stvensen-Johnson syndrome, granulomatous hepatitis may occur. Weight gain may be seen in patients on sulphonylureas. Hypoglycemia is more likely, prolonged and profound with long acting sulphonylureas i.e. chlorpropamide and glibenclamide. Photosensitivity reaction to sulfonylureas (hyperpigmentation of exposed parts) may occur.

Contraindications

- Renal failure
- Hepatic failure, hepatitis
- Type 1 diabetes

Drug interactions

a. Agents that augment the sulfonylurea action

- Salicylates or NSAIDs
- Sulphonamides
- Trimethoprim
- Fibrates
- MAO inhibitors
- H₂ blockers
- Anticoagulants

b. Agents that attenuate sulfonylurea action

- Alcohol (chronic, moderate use)
- Barbiturates
- Rifampicin
- Beta blockers
- Thiazides
- Corticosteroids
Estrogens
Isoniazid
Nicotinic acid

In elderly patients (> 60 years) short acting sulphonylureas are preferred. Glibenclamide should be used with caution in elderly. Chlorpropamide should not be used in elderly patient and glibenclamide should be used with caution.

b. Non-Sulfonylurea Agents

i. Meglitinide Analogues
- Meglitinide analogues are non-sulphonylurea insulin secretagogues which act on separate non-sulphonylurea receptor binding sites on b-cell and enhance insulin secretion.
- These agents are as efficacious as sulphonylureas when used as monotherapy for treatment of type 2 diabetes.

Repaglinide/Nateglinide
- Repaglinide/Nateglinide is absorbed rapidly (0.5-1 hr) and has a short half life (< 1 hr). Thus it results in a rapid but brief release of insulin.
- The starting dose is 0.5/60 mg, with each meal, increased fortnightly to a maximum of 6/180 mg/day.
- It produces fewer and milder hypoglycemic episodes as compared to sulphonylureas.
- 90% of it is excreted in feces. It can be used in patients with moderate renal insufficiency but is not recommended for severe renal impairment.
- Weight gain is mild when used in newly diagnosed type 2 diabetics.
- May be useful in people with erratic food habits.
- Useful in religious fasting like Ramadan.

ii. Biguanides
- Metformin is the most commonly used biguanide.
- It mediates its effect by enhancing sensitivity of the hepatic and peripheral tissues to circulating insulin as well as decreasing hepatic glucose output. It inhibits the intestinal absorption of glucose and demonstrates anorexic effect.
- The starting dose can be 250 mg twice a day which is increased by 500 mg every two weeks until desired therapeutic goals are achieved or maximum daily doses (2500 mg) are reached.
- It can be used in an effective combination with sulphonylurea and other oral hypoglycemic agents.
- Metformin, being an antihyperglycemic agent, usually produce hypoglycemia when used as monotherapy.
- The UKPDS has demonstrated that use of metformin reduces the risk of macrovascular complications.
- Metformin is now recommended as the first line treatment in obese type 2 diabetics as monotherapy.
- Currently available sustained release and extended release formulations are also effective.

Other effects
- Metformin has a favourable effect on lipids, decreasing triglycerides and LDL cholesterol by 10-15%. Weight loss of 2-3 kg in first six months of treatment has been observed in some studies, whereas in other studies, it has been found to provide a weight stabilizing effect.

Side effects
- Gastrointestinal side effects like abdominal discomfort and diarrhoea occur in 20-30% of patients. These can be minimized if metformin is administered after meals and with slow titration of doses. Lactic acidosis is an uncommon side effect and is reported in the frequency of three to nine cases per 100,000 patient years. It is rare in the absence of other serious hypoxic medical disorders.

Contraindications
- Patients with renal disease (serum creatinine level more than 1.4 mg/dl in females and 1.5 mg/dl in males) ***[to be given by Dr. Munjal]
- Currently the GFR derived from urinary albumin creatinine ratio by using a nomogram [given in the appendix ] is used more to decide the use of metformin.
- Hepatic disease
- Respiratory insufficiency
- Hypoxemic conditions
- Acute myocardial infarction
- Congestive cardiac failure
- Alcohol abuse
- Patients undergoing contrast study, metformin must discontinued for 48 hours and serum creatinine re-checked within two days to ensure that metformin can be continued
- Ketosis prone diabetes
- Acute complications; severe infections, major operations and trauma
- Bad general condition (e.g. malnutrition, dehydration)
- Metformin should be stopped at least three days before elective surgery.

iii. a - Glucosidase inhibitors

Acarbose, Meglitinide, Voglibose
- Acarbose acts by competitively inhibiting a-glucosidase, the enzyme in the small intestine brush border which breaks down oligosaccharides and disaccharides into monosaccharides. Thus the conversion of carbohydrates (starch and sugar) to
glucose is delayed.
- It is especially useful in decreasing post-prandial glucose levels (to the extent of 40-50 mg%).
- It is beneficial in new on set type 2 diabetics when fasting hyperglycemia is mild.
- It can be combined with sulphonylureas and biguanides but its glycemic lowering potency is much less in comparison (0.5).
- The dosage is 25-50 mg once daily increased to 50-100 mg two to three times in a day. It must be ingested with the first bite of food, as the drug must be present in the small bowel with the food for proper effect.
- Hypoglycemia does not occur if used as monotherapy. If hypoglycemia results from combination therapy with sulphonylurea, treatment should be with oral glucose rather than sucrose.
- Meglitinide and voglibose are newer alpha glucosidase inhibitor which have better GI tolerance and they are more selective in their alpha glucosidase inhibitory activity. These drugs are more used in people consuming high carbohydrate diets.

Side effects
- Bloating, abdominal discomfort, diarrhoea and flatulence. These side effects are more pronounced in patients on high carbohydrate diet.

Contraindications
- Inflammatory bowel disease
- Cirrhosis
- Serum creatinine more than 2.0 mg/dl
- Malabsorption
- Intestinal obstruction

Incretins***

iv . Thiazolidinediones (Glitazones)

*** 1 paragraph to be added
- These agents act by inhibition of gluconeogenesis in hepatocytes and by improving insulin sensitivity in adipose tissue and skeletal muscles. This effect is brought about by binding to nuclear peroxisome proliferator activated receptor-gamma (PPAR-\(\gamma\)) leading to increased glucose transporter expression. The action on adipocytes reduces the plasma free fatty acids. This is a major mechanism for restoring insulin sensitivity.
- The dosage of rosiglitazone is 2-8 mg in one to two divided doses while that of pioglitazone is 15 to 45 mg per day.
- Combination with sulphonylurea is as effective as the combination of metformin and sulphonylurea.
- Combination with metformin is synergistic due to complimentary mode of action.

- The onset of action starts from 2-4 weeks of therapy and the maximum effect is observed after 11 weeks.
- Combination of glitazones with insulin can be used with caution.

Precautions
- As a monotherapy, glitazone does not produce hypoglycemia. However in combination, it does so and thus the dose of the other agent must be reduced.
- Treatment with glitazone may lead to resumption of irregular ovulation. Patients may be at a risk of pregnancy.
- Glitazones cause a decrease in hemoglobin and hematocrit. Mean Hb values decline by 2-4%. The changes occurred in the first 4-12 weeks of therapy.
- It should be used with caution in patients with edema.
- Body weight must be monitored. Weight gain up to 3 kgs is allowed.

In preclinical trials, they have been reported to cause plasma volume expansion and preload induced cardiac hypertrophy. It should be used with caution in patients with reduced cardiac reserve.
- Therapy with glitazone should not be initiated if the patient exhibits clinical evidence of active liver disease or the ALT levels exceed 2.5 times the upper limit of normal.
- If ALT levels remain > 3 times the upper limit of normal or if the patient has developed jaundice, glitazone therapy should be discontinued.

Contraindications
- Type 1 diabetes
- Hypersensitivity to glitazones
- Pregnancy
- Lactation
- Pediatric age group
- Dialysis
- Hepatic impairment
- Severe anaemia
- Cardiac failure or history of cardiac failure
- History of MYMA Class III, IV

Side effects
- Mild to moderate hypoglycemia has been reported in patients under going therapy with glitazone in combination with a sulphonylurea or insulin in clinical studies.

Edema was reported in about 4.8% of patients. Edema was reported most frequently in the study in which glitazone was combined with insulin.
- Elevated (≥ 3 times upper limit of normal range)
serum levels of ALT after glitazone treatment was reported in 0.26% patients.

- Adverse events of glitazone when used with metformin are anaemia, weight gain, headache, visual disturbance, arthralgia, hematuria, impotence and edema.
- Adverse events of glitazone when used with sulfonylurea therapy are weight gain, dizziness, flatulence and edema.

**Combination Therapy**

The better understanding of the pathophysiology of type 2 diabetes as well as the development of new drugs with different modes of action has led to the understanding of the rationale for combination therapy.

Type 2 diabetes is caused due to insulin resistance and insulin secretory defects. In any given patient with type 2 diabetes, while one of these two abnormalities may play a predominant role, the other is also frequently present. For an effective management of this disorder both these defects have to be corrected. The drugs available now act at the various sites and overcomes both these primary defects. While metformin and the glitazones improve insulin sensitivity and overcome insulin resistance, the sulfonylureas and meglitinide derivatives stimulate the β-cells to increase the insulin output.

Hence there is a role for a combination of both group of drugs, the insulin sensitizers and the insulin secretagogues. The common practice is to start with monotherapy with either of the two and resort to a combination therapy with the addition of a drug from the other group when adequate glycemic control is not achieved. The usual combinations are SU + metformin, SU + glitazone, SU + insulin, insulin + metformin, glitazone + metformin. Alpha glucosidase inhibitors can be combined with SU, metformin or insulin to correct post-prandial hyperglycaemia.

Currently treatment initiation with combination therapy is also being practiced which is rational.

When fixed dose combination of SU and metformin is used, it should be preferably given before the meals.

In patients with secondary sulfonylurea failure, when there is an inadequate response to the addition of metformin, the options would be either to add insulin to the above combination once at bed time or to stop the oral drugs and add two doses of split mix insulin.

When insulin is added to the SU, a single dose of intermediate acting insulin (usually in a dose of 10-12 units) is given at bed time to provide for basal insulin supplementation. The small dose required at bed time prevents weight gain and prevents hyperinsulinemia. It corrects the hepatic glucose output and brings down the fasting glucose and glucotoxicity, thereby making the oral preparation effective (Fig. 3).

**Role of Indigenous Drugs**

Many patients in our country are motivated to use several alternative systems of medicine like ayurveda, homeopathy, unani or some indigenous drugs. Several drugs have been advocated by alternative medicine practitioners for the treatment of diabetes such as fenugreek seeds, Pterocarpus marsupium, Momordica charantia, Eugenic jambolanca, etc.

These drugs by themselves singly or in combination have inadequate hypoglycemic effects, their exact mode of action is not clear. However, most of these are rich in fibre content and may be effective by interfering and delaying carbohydrate absorption from the intestines.

Interest in the use of fenugreek seeds has been generated by some studies, which have brought out their useful role in diabetic patients. The additional evidence that they reduce triglycerides, might prove their role as a very cost-effective strategy in management of the dyslipidemia in diabetes.

*** (to be send by Dr. Sahay)

There is a need for research and careful evaluation of these in the management of diabetes. Till then their role in the treatment of diabetes will remain inconclusive.

**Insulin Therapy**

**a. Indications of Insulin in Type 2 Diabetes**

- At on set, if FBG is > 250 mg/dl and/or ketonuria
- In stressful situations (acute myocardial infarction, stroke, fulminant infections, trauma)
- During pregnancy
- Peri-operative state
- Hepatic and renal decompensation
- Diabetic ketoacidosis, Diabetic coma, Hyperglycemic & Hyperosmolar state
- Idiosyncrasies to oral anti-diabetic agents
- Secondary failure to OHA
- Diabetics on steroids

**b. Types of Insulin Preparations**

Different types and species of insulins are available. They have different pharmacokinetic properties. Different insulin preparations can be divided based on the species, duration of action and impurities present (Table 15A & B). Insulin type, species, injection technique, insulin antibodies, site of injection and individual patient response differences can affect the onset, degree, and duration of insulin activity. Changing insulin species may affect blood glucose control and should only be done under the supervision of a health professional with expertise in diabetes.

**i. Species of Insulin**

Insulin of bovine or porcine origin were the only commercially available preparations for the first half-century of the insulin era. **Currently only bovine, human**
Fig. 3: Algorithm for the management of type 2 diabetes mellitus.
insulin and analogues are available. The aminoacid sequence of the animal insulin differs from that of human insulin by one (porcine) or three (bovine) amino acid residues as follows:

<table>
<thead>
<tr>
<th>A8</th>
<th>A10</th>
<th>B30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human</td>
<td>Threonine</td>
<td>Isoleucine</td>
</tr>
<tr>
<td>Porcine</td>
<td>Threonine</td>
<td>Isoleucine</td>
</tr>
<tr>
<td>Bovine</td>
<td>Alanine</td>
<td>Valine</td>
</tr>
</tbody>
</table>

### ii. Duration of Action of Insulin Preparations

Insulin is available in short, intermediate and long-acting forms that may be injected separately or mixed in the same syringe (Table 16).

### iii. Purity of Insulins

Purification of insulin reduces the level of antibodies. Immunological reactions to insulin are rare for purified preparations irrespective of species.29

### e. Mixing Insulin

Administration of mixtures of rapid-or short-and intermediate-or long-acting insulin will produce better glycemic control in some patients than use of a single insulin. It is recommended that insulin of the same species should be used for mixing. Regular and lente insulin can be mixed but must be injected immediately.

### f. Use of Syringes

- Conventional insulin administration involves subcutaneous injection with syringes marked in insulin units.
or short acting insulin should be drawn into the syringe first.

**ii. Injection Procedures**
- Injections are given into the subcutaneous tissue.
- Most individuals are able to lightly grip a fold of skin and inject at a 90° angle (Fig. 5).
- Thin individuals or children may need to pinch the skin and inject at a 45° angle to avoid intramuscular injection, especially in the thigh area.

**i. Insulin Pens**
Several pen-like devices and insulin-containing cartridges are available that deliver insulin subcutaneously through a needle. They are easy to use.

**iii. Injection Site**
- Insulin may be injected into the subcutaneous tissue of the upper arm, the anterior and lateral aspects of the thigh, the buttocks, and the abdomen (Fig. 6).
- Rotation of the injection site is important to prevent lipohypertrophy or lipoatrophy. Rotating within one area is recommended (e.g. rotating injections systematically within the abdomen) rather than rotating to a different area with each injection. This practice may decrease variability in absorption from day to day.
- Site selection should take into consideration the variable absorption between sites.

**c. Storage**
- Vials of insulin not in use should be refrigerated. They should not be kept in the freezer compartment.
- Insulin should not be exposed to direct sunlight.
- Excess agitation should be avoided to prevent loss of potency, clumping, frosting, or precipitation.
- Insulin in use may be kept at room temperature to limit local irritation at the injection site, which may occur when cold insulin is used. Once the vial is opened, it should be used for a period of 30 days.
- If refrigeration is not available, insulin should be stored in closed cabinets or under the clothes.
- If regular insulin shows haziness, it indicates bacterial growth and should not be used.

**h. Adverse Effects**
The main problems associated with insulin use are hypoglycemia and weight gain. Weight gain can be substantial, and the amount is generally well correlated with the total daily dose of insulin.

**12.2.j. Initiating Insulin Therapy**
For initiating insulin it is not necessary to hospitalize the patient, it can be done at their home. The dosing has to be individualized depending upon the blood glucose profile and clinical setting. It is better to start with small doses and modify accordingly every three days. Generally the initial starting dose of insulin should be 0.2 units/kg/day.
k. Adding Insulin to Oral Agents

When combinations of oral agents no longer maintain the level of control desired, insulin is needed. Less dose of insulin is needed and less hyperinsulinemia and weight gain occur when one insulin injection is combined with oral agents than with multiple insulin injections.

1. Multiple Insulin Injections

- For less obese patients (BMI < 30), a bed time injection of NPH insulin safely controls fasting hyperglycemia.
- When a single insulin injection plus one or more oral agents no longer maintains good glucose control, two or more injections are needed.
- In contrast to type 1 diabetes, who nearly always requires three or four injections for good control, long duration type 2 diabetes is usually treated with two injections.
- Older persons need careful monitoring to avoid hypoglycemia.
- A regimen of equal amounts of insulin, either NPH and regular insulin mixed by the patients or premixed, taken before breakfast and dinner is a reasonable way to start multiple injections.
- When glitazones are added to insulin regimen, insulin requirements may come down and thus such subjects need to be carefully watched for hypoglycemia.

The alternate routes of delivery under evaluation include intranasal and intrapulmonary.

**MONITORING GLYCEMIC CONTROL**

The importance of glycemic control is well established and has been conclusively proved in both type 1 and type 2 diabetics by DCCT, Kumomoto and UKPDS studies.21-23 As hyperglycemia is strongly associated with the development and progression of diabetic complications, the importance of accurate monitoring of glycemic control cannot be over emphasized.

**Table 17 : Parameters of monitoring**

<table>
<thead>
<tr>
<th>Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine Glucose</td>
</tr>
<tr>
<td>Ketones</td>
</tr>
<tr>
<td>Albumin</td>
</tr>
<tr>
<td>Blood Glucose</td>
</tr>
<tr>
<td>Glycosylated hemoglobin</td>
</tr>
</tbody>
</table>

1.a. Urine Glucose Testing

Although urine glucose testing is pain less and much cheaper than blood glu cose test ing, it is mis -lead ing and there for not rec om mended for rou tine use. It has

limited role in the pres ent day man age ment strategy for diabetes. How ever, some di a be tes pa tients con tinue to use urine test ing. It can be con sidered as an al ter na tive for mon i tor ing their glycemic sta tus since some mon i tor - ing is better than no mon i tor ing. Test strips that quan tify urine glu cose should be used to avoid a false pos i tive re sult. The urine glu cose test ing should be done in the post pran dial state in a sec ond voided spec i men, so that a neg a tive re sult dur -ing this state in di cates ad e quate glycemic con trol. One should watch for hypoglycemia in such sit uations.

1.b. Urine Ketone Testing

Urine ketone test ing is in di cated in the fol low ing :

- At on set of di a be tes in all young pa tients with di a be tes
- Dur ing pe ri ods of poor met a bolic con trol (blood glu cose > 250 mg/dl)
- Dur ing acute ill ness and stress, food de pri va tion (star va tion)
- Dur ing preg nancy (early morn ing sam ple)
- When symp to ms of ketoacidosis are pres ent (such as nau sea, vom it ing and ab dom i nal pain)

1.c. Urine Albumin Testing

Urine al bu min pro vides a fair in di ca tion of kid ney sta tus. If urine al bu min is neg a tive, microalbuminuria should be tested ev ery year.

2.a. Blood Glucose Testing

- Mea sure ment of plasma glu cose is re quired for ini tial di ag no sis of di a be tes.
- Sub se quently, it is done for mon i tor ing the ad e quacy of ther apy.
- The fre quency of test ing de pends upon the type of di a be tes and the ther apy used.32
- Both FPG and PPG should be mea sured.
- Mon i tor ing must be done with the usual diet and drug in take. Ex tra diet or heavy diet should not re place the nor mal diet dur ing mon i tor ing.
- Oral glu cose chal lenge is not re quired dur ing mon i tor ing.
- The targets for glycemic control are summarized in Table 18.

2.a.i. Recommended Frequency for Plasma Glucose Measurements

- The mea sure ment of FPG and 2 hr PPG on a weekly or fort nightly ba sis at start of ther apy. This is to be fol lowed by monthly mea sure ments once sa tisfactory control is achieved.
- How ever, those pa tients with type 2 di a be tes on in su lin ther apy as well as stressed sub jects re quire more fre quent plasma glu cose mea sure ments as in type 1 di a be tes.
Glycated Hemoglobin

- The degree of hemoglobin glycation is proportional to the ambient glucose concentration and is a measure of the average glycemia over the preceding three months.
- HbA1c is the most abundant and correlates best with the degree of glycemia.
- Various factors can alter the HbA1c levels. False high values are observed in situ a tions of increased fetal hemoglobin and uremia whereas falsely low values are observed in hemoglobinopathies and hemolytic anemia.
- A change in HbA1c of 1% would reflect a blood glucose alteration of about 30 mg%.

Table to be added by SRJ***

Compliations

1. Acute Metabolic Complications

1.a. Diabetic Ketosis (DKA)35

Diabetic ketosis is an important cause of mortality and morbidity amongst diabetics. It is a life-threatening situation, awareness, early diagnosis and efficient management are necessary to reduce mortality. In a good center, mortality should not be more than 5% which could be mainly due to un diag nosed diabetes. The treatment of DKA is crucial but should be more than 5% which could be mainly due to underdiagnosis. Treatment of DKA includes fluid resuscitation, electrolyte correction, and insulin therapy. The use of a flow sheet on a timed scale should be maintained.

If a precipitating cause of DKA (such as an infection or myocardial infarction) is detected, its treatment should be started along with the treatment of DKA.

2.a.ii. Self Monitoring of Blood Glucose (SMBG)

- Indications for SMBG in clinical practice are listed in Table 19.
- Type 2 diabetes with altered renal threshold, advanced chronic complications and during period of acute stress.
- Peri-operative state.
- Labile/brittle diabetes.
- Neuroglycopenia without warning, nocturnal hypoglycemia.
- Pregnancy, acute infection and myocardial infarction.
- All cases on intensive insulin therapy.

2.b. Glycosylated Hemoglobin Testing

Glycated proteins such as hemoglobin and serum proteins provide measures of glycemia over an extended period of time depending on their half life in the circulation.

Table 18: Targets Glycemic Control for People with diabetes

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Goal</th>
<th>Additional Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole blood values</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average preprandial</td>
<td>&lt;100</td>
<td>80-120</td>
<td>&lt;80 &gt;140</td>
</tr>
<tr>
<td>glucose (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average bedtime</td>
<td>&lt;110</td>
<td>100-140</td>
<td>&lt;100 &gt;160</td>
</tr>
<tr>
<td>glucose (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma values</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average preprandial</td>
<td>&lt;110</td>
<td>90-130</td>
<td>&lt;90 &gt;150</td>
</tr>
<tr>
<td>glucose (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average bedtime</td>
<td>&lt;120</td>
<td>110-150</td>
<td>&lt;110 &gt;180</td>
</tr>
<tr>
<td>glucose (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>&lt;6</td>
<td>&lt;7</td>
<td>&gt;8</td>
</tr>
</tbody>
</table>

Table 19: Indications for SMBG

- Type 2 diabetes with altered renal threshold, advanced chronic complications and during period of acute stress.
- Peri-operative state.
- Labile/brittle diabetes.
- Neuroglycopenia without warning, nocturnal hypoglycemia.
- Pregnancy, acute infection and myocardial infarction.
- All cases on intensive insulin therapy.

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Table to be added by SRJ***

Compliations

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If a precipitating cause of DKA (such as an infection or myocardial infarction) is detected, its treatment should be started along with the treatment of DKA.
In an unconscious patient, a nasogastric tube should be inserted to keep the stomach empty and prevent vomiting of gastric contents.

**Correction of Dehydration: Fluid and Electrolytes**

Normal saline is the fluid of choice for initial rehydration. On average, one liter should be infused in the first hour. Next, one liter in the next 2 hours. Two liters in the next 4 hours. Two liters in the next 8 hours. i.e. 4-6 liters in 24 hours. The effect of saline should be monitored by blood pressure, CVP, pulse, neck veins, skin turgor. In a situation where serum sodium is 150 mEq/L, hypotonic or half normal saline may be used.

When the blood glucose concentration reaches 250 mg/dl, the fluid should be changed to 5% dextrose-saline with concurrent administration of insulin, in order to avoid hypoglycemia. It takes longer for acidosis to get corrected than blood glucose.

**Fluid Overload**

Care should be taken not to infuse a large amount of fluid too rapidly in elderly patients, in those with existing heart disease especially congestive cardiac failure and in patients with renal failure.

**Table 20: Precipitating factors**

<table>
<thead>
<tr>
<th>Infection</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Omission of insulin</td>
<td></td>
</tr>
<tr>
<td>Unknown cause</td>
<td></td>
</tr>
<tr>
<td>Stressful situations</td>
<td></td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td></td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td></td>
</tr>
</tbody>
</table>

**Table 21: Signs and symptoms of DKA**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyuria</td>
<td>Hyperpnea</td>
</tr>
<tr>
<td>Polydipsia</td>
<td>Hypothermia</td>
</tr>
<tr>
<td>Weakness</td>
<td>Acetone breath</td>
</tr>
<tr>
<td>Lethargy</td>
<td>Acidotic breathing</td>
</tr>
<tr>
<td>Myalgia</td>
<td>Dyspnea</td>
</tr>
<tr>
<td>Headache</td>
<td>Acute abdomen</td>
</tr>
<tr>
<td>Anorexia</td>
<td>Dehydration</td>
</tr>
<tr>
<td>Nausea</td>
<td>Hyporeflexia</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Hypotonia</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Stupor/coma</td>
</tr>
<tr>
<td>Breathlessness</td>
<td></td>
</tr>
</tbody>
</table>

**Potassium Replacement**

The plasma potassium may initially be high in the presence of acidosis. It begins to fall as DKA is treated. Hypokalemia is therefore likely without potassium replacement. There is no definite guideline about when to start potassium replacement. If there is good urinary output, potassium replacement should be started early during the treatment of DKA. Potassium chloride (one ampoule, 10 mEq) should be added in the third bottle of saline. The potassium level should be evaluated every two hours or as necessary. If the response is not adequate, dose must be modified. This should be avoided in the presence of renal failure. ECG monitoring is helpful since tall T waves are indicative of hyperkalemia. Patients not responding to conventional therapy may be looked for other conditions. Ringer lactate and fructose should be avoided in DKA.

**Other Electrolytes**

Bicarbonate may be used in severe cases of acidosis with a pH less than 6.9, bicarbonate levels less than 5 mmol/L, patients with DKA complicating acute myocardial infarction and in patients with lactic acidosis. The risks of bicarbonate therapy are shift of withdrawal of insulin. Fasting Pancreatic Relative D Counter cell failure Insulin K hormone Stress Deficiency A excess Insulin resistance Dehydration

**Insulin**

The standard method is low dose infusion of insulin by the intravenous route after an initial bolus of insulin. If IV infusion of insulin is difficult to perform, hourly in tramuscular (IM) injection of insulin is an alternative method. For an IM administration, the deltoid muscle is preferred. IV insulin therapy is given as an initial dose of 10 units as a bolus, followed by insulin infusion at the rate of 0.1 unit/kg/hour. (50 units of insulin are to be added to 500 ml of normal saline. The infusion is to be run at the rate of 1 ml/min). IM regime involves the use of 0.1 unit/kg/hour of insulin. With these regimens, the plasma glucose level falls (90 mg%) at a predictable rate of around 50 mg/hr. It usually comes down to half the initial value in 6-8 hours. If at the end of 2-3 hours, the plasma glucose values do not show a predictable fall, the dose of insulin infusion is doubled i.e. 12 units/hr. Once the plasma glucose levels come down to 250 mg%, the fluid replacement should be switched over to...
dextrose saline infusions and soluble insulin can be given 4-8 hrs subcutaneously depending on the glucose profile.

Once the sensorium improves and vomiting subsides, the patients is encouraged to take oral feeds and insulin is given by SC route 4-6 hourly depending on the glucose profile. If the patient’s condition does not improve within 24 hours, evaluate for other causes of coma.

1.b. Hyperosmolar Non-Ketotic Coma (HONK)35

It usually occurs in type 2 diabetics. The clinical picture is dominated by profound dehydration, without ketosis or significant acidosis. Plasma glucose levels usually exceed 600 mg/dl.

Clinical Features

- Severe hyperglycemia (plasma glucose > 600 mg/dl)
- Profound dehydration
- Elevated osmolality (more than 320*)
- Absence of ketosis
- Variable neurological signs

Glucose mg | Urea (mg%)  
--- | ---  
18 | 3  

*Osmolality = (Na + K) 2 + 18 + 3

The principles of treatment are similar to those of DKA. The infusion of fluid should first be with ½ normal saline and continued until recovery of extracellular fluid and good urine flow. The same scheme of insulin administration is adequate. However, the patients with HONK are more sensitive to insulin than those of DKA. As with DKA, infusion of glucose should be started when the blood glucose falls to near 250 mg/dl and the replacement of potassium should be started early in the course of treatment.

1.c. Lactic Acidosis

This uncommon condition is usually seen in patients treated with biguanides and have renal, respiratory or hepatic failure. Although the incidence of lactic acidosis is very rare in India, the recognition of this condition is very important. There is severe acidosis but ketosis and dehydration are minimal or absent. In contrast to patients with DKA very large quantities of bicarbonate are needed routinely in these cases, while little hypoglycemic therapy is required. The treatment involves 5% dextrose saline infusion and insulin. Dialysis may have a role in the management. However the mortality is very high. Since large amounts of carbonate are administered, potassium levels must be closely monitored.

1.d Hypoglycemia*

The term hypoglycemia refers to the clinical condition resulting from an abnormally low plasma glucose levels (< 40 mg/dl). Clinically it is characterized by varying degree of neurological dysfunction and is responsive to the administration of glucose.

Predisposing Factors

- Delaying or skipping meals
- Decreased carbohydrate intake
- Increase in the dose of insulin or oral antidiabetic drugs
- Decrease in insulin requirements (after delivery, or with the elimination of stress or control of infection, renal or hepatic insufficiency)
- Sick days
- Undue to unexpected physical strain after taking insulin or oral hypoglycemic drugs
- Alcohol consumption

Hypoglycemia needs to be treated promptly. While it is useful to document the degree of hypoglycemia, this should not delay treatment, and the general advice is “If in doubt, treat”.

Clinical Features

Rapid fall of blood glucose (as with lin) leads to manifestations of the activation of the sympathetic nervous system while a gradual fall (as seen with OHAs) lead to the symptoms due to decreased cerebral function (Table 22).

Persistence of hypoglycemia for over six hours may lead to persistent brain damage. Current attacks may also lead to mental changes in cognitive function.

Management of Hypoglycemia

The Conscious Patient

The treatment involves immediate intake of 10-20 gms of glucose or a rapidly digestible form of carbohydrate orally, followed by a snack of a more slowly digestible form of carbohydrate (equivalent to one slice or bread) to maintain normoglycemia until the next meal. If the patient is on acarbose also, then treat it with glucose.

The Unconscious Patient

A severe hypoglycemic episode can only be treated by intravenous glucose (50-100 ml of 25%/50% dextrose). In responsive patients, parenteral glucagon (0.5-1 mg IM) should be administered. In these patients carbohydrates should be given orally as soon as the patient regains consciousness. The patient must gain

<table>
<thead>
<tr>
<th>Neuroglycopenic</th>
<th>Adrenergic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fainting</td>
<td>Hunger</td>
</tr>
<tr>
<td>Yawning</td>
<td>Perspiration</td>
</tr>
<tr>
<td>Weakness</td>
<td>Rise in BP</td>
</tr>
<tr>
<td>Tingling in the fingers</td>
<td>Tremors</td>
</tr>
<tr>
<td>Diplopia</td>
<td>Headache</td>
</tr>
<tr>
<td>Hysterical behaviour</td>
<td>Palpitation</td>
</tr>
<tr>
<td>Disorientation</td>
<td>Anxiety and nervousness</td>
</tr>
<tr>
<td>Mental confusion</td>
<td>Weakness</td>
</tr>
<tr>
<td>Convulsions and coma</td>
<td></td>
</tr>
</tbody>
</table>

Table 22: Clinical features of hypoglycemia
consciousness within half an hour. Parenteral dexamethasone is also recommended in unresponsive patients. It is important to follow glucose level for at least 24-48 hours in patients where hypoglycemia is induced by long acting sulphonylureas (glibenclamide) or long acting insulin (Lente/NPH). A long term glucose infusion may be necessary and the patient should be hospitalized. Occasional patient may take longer time to cover. Hypoglycemic unawareness is usually seen in type 1 diabetes and may be difficult to recognize. Glucagon although costly and not routinely available is an alternative to treat insulin induced hypoglycemia and later needs oral glucose.

Prevention of Hypoglycemia

Education of patient and family members is a must. Education of the health careproviders in terms of diagnosing diabetes, its management and also diagnosing hypoglycemic episodes early is important.

Recognition***

2. Chronic Vascular Complications
2.a. Macrovascular Complications
2.a.i. Coronary artery disease

Acute Myocardial Infarction (AMI)

In diabetics as compared to non-diabetic subjects,

- The incidence of myocardial in farction is around three times higher and the outcome of AMI is worse.
- Mortality is two times higher in pre-hospital, hospital and post-hospital periods following the episode. This is particularly so in patients be low 60 years of age and in obese females; more so in those with anterior infarctions.40
- Diabetics develop complications of myocar dial infarction more of ten than nondiabetics. These include cardiogenic shock, CHF, conduction disturbances, etc.40-46
- Congestive heartfailure is seen in 44% of diabetic women and 25% of diabetic men.
- Infarct sizes are relatively larger and more of ten anterior.
  * Incidence of silent MI is variable but by all measures more frequent in patients with diabetes.
  * Painless or silent infarcts occur in 20% of diabetics
- Presenting features may be atypical and lead to long lag riod between onset and hospitalization in the intensive coronary care unit (ICCU).47-51
- An estimated 20-40% patients present with atypical fea tures such as confusion, dyspnoea, cough, fatigue, nausea, vomiting and epigastric distress.
- Ketosis (2-4%) or hyperosmolar state (in elderly) may be present at admission.

- Sudden cardiac deaths are more common.
- CABG or PTCA as an intervention may be decided on the merit of individual case.

A major concern in the management of AMI in patients of diabetes is to provide adequate insulin in order to restore glucose utilization and reduce lipolysis and consequent rise in circu lating free fatty acids.

Diabetic retinopathy is no longer a contraindication for thrombolytic therapy.50

Following life saving measures including the admission to intensive coronary care unit (ICCU), specific anti-diabetic therapy has to be started on a priority basis. The infarction may be massive and post-AMI period more stormy.

Diagnosis

On arrival of the patient, random plasma glucose (RPG) is to be estimated immediately. If the patient is not a known diabetic. HbA1c will distinguish between stress hyperglycemia and a diabetic. Urine has to be tested particularly for ketone bodies. In case the plasma glucose is more than 200 mg/dl, short acting insulin is to be started, preferably by IV infusion.

Monitoring for Blood/Plasma Glucose During Infusion

Monitoring is best done at the bedside by glucose monitor. Results thus obtained will guide the rate of insulin infusion from time to time. Beyond this, regular plasma glucose monitoring along with other parameters (electrolytes and ketone bodies) should be done every 4-6 hours for further management. If the serum potassium is less than 3.5 mEq/L, potassium solution has to be added to the insulin infusion device at the rate of 20 mEq/L. Special care has to be taken in case of ketosis, hyperosmolar coma. Nutrients (including dextrose, other resuscitation fluids and essential therapy) should be administered through different IV lines. The revival in the intensified insulin therapy for AMI originated from DIGAMI study51 which achieved favourable results with administration of insulin by infusion. Insulin for first 24 hours of AMI followed by subcutaneous insulin therapy for three months improved the short and long term mortality.

2.a.ii. Cerebrovascular Disease

Stroke

- Diabetes mellitus (chronic hyperglycemia) is an impor tant risk factor for ischemic but not hemorrhagic stroke.
- The relative risk of ischemic stroke is increased on an average by 2-4 fold in the diabetic population.
- The type and distribution of stroke in diabetic patients are not significantly differ ent from that of non-diabetic subjects. Further, to what extent hyperglycemia contributes to promote stroke is not
certain as it is so often associated with hypertension (HTN) and dyslipidemia.

- Framingham study indicates increased cerebral infarction even with mild glucose intolerance.\(^{52-55}\)

Several studies have shown an increase in short and long term morbidity/mortality in diabetics, who have stroke. Hyperglycemia has been observed to worsen the severity of the attack.

**Guidelines for Treatment**

- All stroke victims are likely to be dehydrated and should be started with normal saline at the admission.
- Random plasma glucose (RPG), glycosylated hemoglobin (HbAlc), urea, creatinine, electrolytes, urine for ketones should be tested and an initial value obtained [to distinguish preexisting diabetes from stress hyperglycemia].
- Patient should never be put on dextrose or dextrose saline to start with.
- The rate and total volume of normal saline administered in each patient should be determined after considering the expected total volume loss, renal/heart status and hematocrit.
- Any excess fluid intake may result in development of cerebral edema.
- At times these patients may have complications such as hyperosmolar non-ketotic state or ketoacidosis.

It is very important to note that plasma glucose should not be allowed to fall below 160 mg/dl throughout the therapy. Hyperglycemia raises lactic acid content of cerebral ischemic tissues where as cellular damage occurs in hypoglycemia.

Alongwith maintenance of normoglycemia, a blood pressure above 200/100 mm Hg should be controlled very gradually as acute ing of blood pressure worsens the ischemia and total outcome of the pa tient. Mannitol infusion can be given. However efforts to achieve a good metabolic control should be accompanied by an aggressive approach towards cerebral reperfusion. Hypoglycemia can manifest as stroke.

**2.a.iii. Aspirin Therapy in Diabetes**

People with diabetes have a two to four fold increase in the risk of dying from the complications of cardiovascular disease. Both men and women are at increased risk. Atherosclerosis and vascular thrombosis are major contributors, and it is generally accepted that platelets are contributory. Platelets from men and women with diabetes are often hypersensitive invitro to platelet aggregating agents. A major mechanism is increased production of thromboxane, a potent vasoconstrictor and platelet aggregant. Recommendations on the use of aspirin are given in Table 23.

**2.b. Microvascular Complications**

**2.b.i. Diabetic Nephropathy**\(^{58}\)

Diabetic nephropathy is one of the common est cause of end-stage renal disease (ESRD). This is due to the ing lence of type 2 diabetic, longer life span of diabetic patients and improved therapeutic options and the fact that patients with diabetic nephropathy are being accepted for renal replacement therapy. Prevalence of all grades of proteinuria was seen in 19.7% of type 2 diabetics and amongst them, 5.5% had nephropyathy.\(^{59}\)

The natural history of diabetic nephropathy progresses from normoalbuminuria, through a subclinical stage of urinary albumin excretion called microalbuminuria to overt proteinuria and eventually end-stage renal disease (Table 24).

**Prevalence at Various Stages**

- Acute renal hypertrophy/ hyperfunction Present at diagnosis
- Normoalbuminuria

Most patients in the first 5 years

A higher dose of aspirin are recommended in patient of diabetes with stroke (reference to be searched)

- Incipient nephropathy Occurs after 5-15 years in ~35% of patients
Overt diabetic nephropathy Usually develops in about 35% of patients after 15-25 yrs

End-stage renal disease Final outcome, usually after 25-30 years

Significance of Albuminuria
- Microalbuminuria is a marker of generalized endothelial dysfunction
  - In type 2 diabetes mellitus, microalbuminuria
    - May be non-specific
    - Correlated with systolic hypertension
    - Associated cardiovascular disease
    - Associated peripheral vascular disease
    - Coronary artery disease occurs earlier than ESRD
    - Associated with premature atherosclerosis
    - Abnormal lipid profile
    - Pronounced increased mortality
    - Correction of microalbuminuria in solution may not affect events appreciably

The type 2 diabetes patients with diabetic kidney disease usually die from cardiovascular disease such as coronary artery disease and hence integral management of all risk factors is indicated.

Screening for Albuminuria
- The methods adopted may be
  - 24 hour collection along with measurement of creatinine clearance (mg/24 hours)
  - Timed collection (µg/min)
  - Spot collection to look for albumin to creatinine ratio (møg/mg creatinine). Sample should not be taken in the immediate post-exercise period (Table 25).

In type 1 DM, screening should begin with puberty and after 5 years duration of diabetes. In type 2 DM, however, screening is recommended at the time of diagnosis and if negative, every year. Routine urinalysis should be performed annually. An algorithmic approach is outlined in Fig 8. Treatment Options Modalities of treatment depend on the stage of disease at diagnosis (especially type 1 DM) to prevent onset of nephropathy. Treatment approaches are as outlined in Table 26.

Glycemic Control
- Intensive glycemic control can significantly reduce the risk of developing microalbuminuria and overt nephropathy.
- Metformin should not be used if the serum creatinine is more than 1.4 mg/dl in men and 1.5 mg/dl in women.
- Oral antidiabetic drugs recommended for diabetic nephropathy are glipizide, gliclazide, acarbose, repaglinide and glitazones. However they should be used with caution.

Hypertension Control
- In type 1 diabetes mellitus, hypertension is usually

### Table 24: Stages of diabetic nephropathy

<table>
<thead>
<tr>
<th>Stage</th>
<th>Designation</th>
<th>Main Characteristics</th>
<th>GFR</th>
<th>Albumin Excretion</th>
<th>BP</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Hyperfunction</td>
<td>Large kidney and glomerular size</td>
<td>150</td>
<td>May be increased</td>
<td>Normal</td>
<td>Strict glycemic control reverses the condition</td>
</tr>
<tr>
<td>II</td>
<td>Hypertrophy</td>
<td>Normoalbuminuria</td>
<td>Normal UAE</td>
<td>Normal (often increased in stress situations)</td>
<td>Normal</td>
<td>Strict glycemic control may reduce hyperfiltration</td>
</tr>
<tr>
<td></td>
<td>Normalt</td>
<td>Persistently elevated UAE</td>
<td>130-160</td>
<td>20-200 µg/min</td>
<td>Elevated 3-5% yr</td>
<td>Microalbuminuria stabilized by strict treatment, GFR also stable if HbA₁c is reduced. Prevention of progression is possible</td>
</tr>
<tr>
<td>IV</td>
<td>Overt</td>
<td>Clinical proteinuria</td>
<td>10-130</td>
<td>&gt;200 µg/min</td>
<td>Hypertension</td>
<td>Poor control leads to greater fall in GFR</td>
</tr>
<tr>
<td>V</td>
<td>Uremia</td>
<td>End stage renal failure</td>
<td>0-10</td>
<td>Decreasing</td>
<td>BP is high due to nephron closure</td>
<td>Progression can be retarded by strict glycemic control, BP control</td>
</tr>
</tbody>
</table>

### Table 25: Definitions of abnormal albumin excretion

<table>
<thead>
<tr>
<th>Category</th>
<th>24 collection (mg/24 h)</th>
<th>Timed collection (µg/min)</th>
<th>Spot hour collection (µg/min creatinine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;30</td>
<td>&lt;20</td>
<td>&lt;30</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>30-300</td>
<td>20-200</td>
<td>30-300</td>
</tr>
<tr>
<td>Overt albuminuria</td>
<td>&gt;300</td>
<td>&gt;200</td>
<td>&gt;300</td>
</tr>
</tbody>
</table>

### Table 26: Treatment options for diabetic nephropathy

#### Early Nephropathy
- Glycemic control
- Treatment of systemic and intraglomerular hypertension
- Dietary protein restriction
- Modification of risk factors - smoking and dyslipidemia

#### End Stage Renal Disease
- To provide symptomatic relief, control of hypertension
- Renal replacement therapy
due to the development of nephropathy, while in type 2 diabetes mellitus, hypertension is multifactorial.

- Both systolic and diastolic hypertension can accelerate the progression of diabetic nephropathy and aggressive treatment of hypertension may markedly retard the rate of fall of GFR.

- The goal of treatment in adults is to maintain a systolic BP < 130 mm Hg and a diastolic BP < 85 mm Hg. In patients with isolated systolic hypertension and an initial systolic BP > 188 mm Hg, the initial goal is to reduce it to < 160 mm Hg, and in those with systolic BP 160-179 mmHg, to lower it by 20 mm Hg. If tolerated, further reduction may be attempted.

- Lifestyle modification should play a major role in the treatment which includes cessation of smoking.

- The drug of choice, as per current evidence, is an angiotensin converting enzyme inhibitor (ACEI). This group of drugs has shown benefit in reducing the progression of microalbuminuria in all patients with type 1 DM and in normotensive and hypertensive patients with type 2 DM.

- In normotensive diabetics with normal renal function in the absence of albuminuria, there is not enough evidence for the use of ACEIs.

- Use of betablockers and loop diuretics may be considered in the event of the failure of ACEIs and long acting calcium channel blockers.

- ACEIs should be withheld once the serum creatinine rises above 2 mg/dl or creatinine clearance falls below 30 ml/min.

- The use of AT 2 receptor blockers are indicated:
  * If ACEIs are not tolerated
  * It can be added to ACEIs if the BP control is not optimum.

In the management of hypertension, the specific role of ARBs have been defined presently. Even combination of ACEIs and ARBs is advocated. (Reference from Dr. Sahay)

**Protein Restriction**

- Restriction of protein intake can lead to reduction in the hyperfiltration and intraglomerular pressure and thereby retard the progression of nephropathy. (Use of protein derived from soya bean and its products may be preferable).

- The recommended dietary allowance is 0.8 gm/kg/day. In selected patients with overt nephropathy and falling GFR, a stricter restriction to 0.6 gm/kg/day may be useful.

- Diet recommended for diabetes may not require...
protein restriction.

Other Aspects

- Restriction of salt intake to the extent of 4 g/day (to less than 2 g/day in presence of fluid overload).
- Restriction of phosphate in the diet.
- Use of calcium containing phosphate binders.

Standard treatment for renal disease, as and when indicated, includes, chronic ambulatory peritoneal dialysis, hemodialysis and renal transplantation.

Prevention of Progression of Renal Damage

- Cessation of smoking (any form of tobacco)
- Avoid nephrotoxic drugs
- Prompt treatment of urinary infections and renal
- Caution during contrast study
- Prevention of dehydration
- Use of ACEIs in normotensive diabetics with microalbuminuria retards the progression of microalbuminuria

- Intensive BP control and control of lipids.

2.b.ii. Diabetic Retinopathy

- In India, the prevalence of betic retinopathy is observed to be 23.7% in a study conducted in South Indian urban population. In another study, the prevalence was found to be 34.1%.59 7.3% has been reported to have retinopathy at diagnosis.53
- Retinopathy contributes to almost 20% of the blindness in the general population.
- Diabetic retinopathy is asymptomatic until it is advanced.
- Diabetic blindness is mainly due to maculopathy or proliferative retinopathy. It can also occur due to cataract, glaucoma, and retinal vascular occlusion.
- The presence of proliferative diabetic retinopathy is an indicator of underlying malignant vasculopathy implying a greater risk of death in such individuals from coronary artery disease, nephropathy and stroke. It is estimated that the risk of death in such patients is seven times higher.
- Patients with microalbuminuria have 5-10 times greater risk of developing proliferative retinopathy.
- The main determinant of diabetic retinopathy is the duration of diabetes and quality of glycemic control. Environmental and genetic factors may also play a role (Table 27).
- Once retinopathy is established, tight glycemic control cannot retard its progression.

Pathophysiology

- Retinopathy is due to microvascular disease where there is loss of pericytes and capillary basement membrane thickening which are early signs of abnormalities.

| Table 27: Differences in retinopathy between type 1 and type 2 diabetes mellitus |
|---------------------------------|---------------------------------|
| Type 1                          | Type 2                          |
| Very few patients develop retinopathy in first 5 years | 20% may have changes of retinopathy at onset |
| Don't develop proliferative retinopathy in first 12 years | 10% of these develop proliferative retinopathy |
| Prevalence rises after 8 years of diabetes mellitus | The duration of diabetes mellitus, degree of hyperglycemia, dyslipidemia and hypertension are risk factors |

- Two main pathological processes are capillary occlusion causing ischemia and capillary leak age causing exudation and edema.
- The ischemia produces angioproliferative factors which produces neovascularization and proliferative retinopathy.

Stages of Diabetic Retinopathy

1. Background
- Microaneurysms
- Scattered exudates
- Hard exudates
- Hem or rhages
  - Flame shape
  - Dot and blot
- Cotton wool exudates
- Spots (≤ 5)
- Ve nous di la tion

2. Pre-proliferative
- Rapid increase in microaneurysm count
- Intraretinal microvascular ab nor mal i ties
- Multiple hemorrhages
- Cotton wool spots (> 5)
- Venous beading, looping and duplication

3. Proliferative
- New vessels
  - On disc (NVD)
  - Elsewhere (NVE)
- Fibrous proliferation
  - On disc (FPD)
  - Elsewhere (FPE)
- Hemorrhages
  - Preretinal
  - Vitreous

4. Advanced Diabetic Eye Disease
- Retinal detachment
- Retinal tears
Rubeosis iridis
Neovascular glaucoma
5. Maculopathy
Macular edema
* Focal
* Diffuse
Ischemic maculopathy

Treatment
Periodic ophthalmic checkup
Strict glucose control
Strict control of blood pressure
Lipid control
Cessation of smoking

<table>
<thead>
<tr>
<th>Condition</th>
<th>Recommend Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVD</td>
<td>Pan-retinal photocoagulation before vitreous hemorrhage occurs</td>
</tr>
<tr>
<td>NVE</td>
<td>Pan-retinal photocoagulation before retinal detachment occurs</td>
</tr>
<tr>
<td>Rubeosis iridis</td>
<td>Pan-retinal photocoagulation before neovascular glaucoma develops</td>
</tr>
<tr>
<td>Pre-proliferative</td>
<td>Pan-retinal photocoagulation, of one eye initially</td>
</tr>
</tbody>
</table>

Vitreo-retinal surgery for the ultimate blinding complications of proliferative diabetic retinopathy i.e. severe vitreous hemorrhage, secondary retinal detachment and neovascular glaucoma (Table 28).

Causes of Sudden Blindness in Diabetes
- Retinal detachment
- Vitreous hemorrhage and retinal hemorrhage
- Central retinal vein thrombosis
- Arterial occlusion
- Optic neuritis
- Acute glaucoma

(See Flow Chart)

2.b.iii. Diabetic Neuropathy

Most common and trouble some complication of diabetes mellitus leading to the greatest morbidity and resulting in huge economic burden for diabetic patients and his family.

Diabetic neuropathy is a heterogenous disorder that encompasses a wide range of abnormalities affecting proximal and distal peripheral sensory and motor nerves as well as the autonomic nervous systems.

Clinical Classification
Progressive neuropathies
Reversible neuropathies
Pressure palsies

Progressive Neuropathies
- Distal symmetrical polyneuropathy
  - Pre dominantly sensory
  - Autonomic involvement common (mostly asymptomatic)
  - Clinical motor involvement very rare
- Small fibre neuropathy
  - Autonomic involvement common and usually symptomatic
  - Gradual onset
  - No recovery
  - Associated with increasing duration of diabetes
  - Associated with other chronic diabetic complications
- Reversible neuropathy

Flow Chart for Reviewing Patients with Diabetic Retinopathy

<table>
<thead>
<tr>
<th>Good vision</th>
<th>Poor vision</th>
</tr>
</thead>
<tbody>
<tr>
<td>No retinopathy</td>
<td>Background retinopathy</td>
</tr>
<tr>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Exclude</td>
<td>Retina invisible</td>
</tr>
<tr>
<td>↓</td>
<td></td>
</tr>
<tr>
<td>- Subtle NVD/NVE</td>
<td>Exclude</td>
</tr>
<tr>
<td>↓</td>
<td>- Retinal detachment</td>
</tr>
<tr>
<td>- Macular edema</td>
<td>- Ischemic macular edema</td>
</tr>
<tr>
<td>↓</td>
<td>- Diffuse macular</td>
</tr>
<tr>
<td>- Preproliferative signs</td>
<td>- Neovascular edema glaucoma</td>
</tr>
<tr>
<td>↓</td>
<td></td>
</tr>
</tbody>
</table>
| Review 12 monthly | Review 6 monthly | Refer to ophthalmologist if any of these problems are present or cannot be excluded.

Table 28: Examination of the Eyes in Diabetic patients

<table>
<thead>
<tr>
<th>When to examine</th>
<th>What to do</th>
</tr>
</thead>
<tbody>
<tr>
<td>At diagnosis</td>
<td>Visual acuity</td>
</tr>
<tr>
<td></td>
<td>- distant vision (Snellen chart)</td>
</tr>
<tr>
<td></td>
<td>- near vision (reading chart)</td>
</tr>
<tr>
<td>Annually thereafter</td>
<td>Check pupillary light reflexes for relative after defect</td>
</tr>
<tr>
<td>Biannually if background retinopathy is present</td>
<td>Fundoscopy, through dilated pupils</td>
</tr>
<tr>
<td>Four monthly if mild pre-proliferative changes occur</td>
<td>Specialist ophthalmological investigations</td>
</tr>
<tr>
<td>Immedaitely if any changes in vision or visual symptoms</td>
<td>Slit lamp examination of iris, anterior chamber and retina</td>
</tr>
<tr>
<td></td>
<td>Measurement of intraocular pressure</td>
</tr>
</tbody>
</table>

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Mononeuropathies
- Femoral (amyotrophy)
- Cranial nerve palsies (III and VI)
- Truncal radiculopathies

- Acute diffuse painful neuropathy
  - Stocking disturbance
  - Sudden onset
  - Spontaneous recovery
  - No association with duration of diabetes
  - No association with other chronic diabetic complications

Entrapment Neuropathies
- Median nerve
- Ulnar nerve
- Lateral popliteal nerve
- More common than in the non-diabetic population

Clinical Pattern of Diabetic Peripheral Neuropathy (Figs. 9 - 13).

Fig. 9: Symmetrical diffuse sensory motor neuropathy.
Sensory loss 0 → +++; Pain + → +++;
Tendon Reflexes N; Motor deficit 0 → +

Fig. 10: Acute diffuse painful neuropathy.
Sensory loss 0 → +; Pain + → +++;
Tendon Reflexes N → decreased; Motor deficit 0 → +

Fig. 11: Femoral neuropathy (Amyotrophy).
Sensory loss 0 → +; Pain + → +++;
Tendon Reflexes; decreased 0 → ; Motor deficit + → +++

Fig. 12: Other acute Mononeuropathies.
Sensory loss 0 → +; Pain + → +++;
Tendon Reflexes N; Motor deficit + → +++

Fig. 13: Pressure palsies.
Sensory loss + → +; Pain + → ++;
Tendon Reflexes N; Motor deficit +-- +++

Clinical Presentation of Large Fiber Neuropathies
- Impaired vibration perception (of ten the first objective evidence) and position sense
- Loss of ankle jerk
- Sensory ataxia (waddling gait like a duck)
- Shortening of achilles tendon with pesequimus
- Increased blood flow (hot foot)

Clinical and Subclinical Features of Autonomic Neuropathy (Fig. 14).

Management of Neuropathy
- Control of hyperglycemia
- Aldose reductase in hib i tors (ARIs)
- Tolerestat
- Zenarestat
- Zopolrestat
- Alpha-lipoic acid
- Gamma-linolenic acid
- Aminoguanidine
- Intravenous human immunoglobulin
- Neurotrophic therapy

Management of Autonomic Neuropathy

Postural hypotension
  Supportive garments

Management of Painful Diabetic Neuropathy

Differentiate types of pain

C fibre pain
(Burning, dysthesia, alldynia)

Sympathetic
-Clonidine

Non-sympathetic
-Capsaicin
-Lidocaine
-Mexililte

Antidepressant
Phenothiazines
Amytriptilin
Fluphenazine
Antiepileptics
Gabapentin
NMDA antagonists
Dextromethorphan
Tramadol

Drug therapy : 9-alpha flurohydrocortisone (possible role)

Gastropathy
Multiple small feeds

Fig. 14 : Clinical and subclinical features of autonomic neuropathy.
Mosepride
Domperidone
Erythromycin
Jejunostomy
Cystopathy
Bethanechol
Self catheterization
Gustatory sweating
Topical glycopyrrolate

Since autonomic neuropathy usually occurs alongwith peripheral neuropathy and can have serious cardiorespiratory dysfunction. It is advised that in every diabetic clinic population the autonomic neuropathy may be looked into by doing a battery of cardiovascular bedside tests. Preoperative workup of a diabetic should include this autonomic function test.

Management of Erectile Dysfunction
One must exclude other causes of erectile dysfunction such as drugs, androgen deficiency and psychological factors. Sildenafil citrate can be administered if it not contraindicated. **Patients on nitrate should not take sildenafil citrate.** Intracavernous papavarine injections have shown benefit. Intractable cases may be referred to the urologist.

Beside Assessment of Autonomic Neuropathy
- Postural hypotension
- Pupillary light reflex
- Resting tachycardia
- Post-void distended bladder

2.b.iv. Diabetic Foot Syndrome

Foot problems such as ulcerations, infections, gangrene and amputations are quite common in diabetic subjects. These account for their frequent and prolonged hospitalization, significant morbidity and even mortality. On a rough estimate nearly 20% of all hospital admissions of diabetes are due to foot problems and nearly 5-10% may need foot/leg amputation. Moreover, of all the non-traumatic amputations approximately 50% are related to diabetes.64 The economic and psychological stress for the family and the patient are enormous. However with proper footcare these could be prevented or minimized.

Etiopathogenesis of Foot Lesions in Diabetics

Peripheral vascular disease (PVD), neuropathy (peripheral and autonomic) and infection are the three major etiological factors either singly or in combination. In India, infection plays an important part.65

Clinical Evaluation Guidelines

Ischaemic foot
- History of claudication, rest pain
- Palpation of peripheral pulses
- Ankle-brachial pressire in dex (ABR be low 0.8 indicates ischaemia)
- Dopp ler ul tra sound and other tests

Neuropathic foot
- History of nocturnal pain
- Skin texture, fissuring, dry ness
- Semmes Weinstein microfilament test
- Vibrat ion test and an kle jerk
- Motor power-atrophy
- Biothesiometry
- Nerve con duct ion stud ies

Clinical Spectrum of Diabetic Foot Lesions
- Onychomycosis
- Paronychia
- Infected foot ulcer
- Necrotizing fascitis
- Osteomyelitis
- Charcot’s neuroarthropathy
- Gangrene

Risk Factors for Diabetic Foot Lesion
- Insensitive foot-loss of protective sensation leading to burns or injury
- Altered foot biomechanics - deformed foot
- Increased pressure points - corns, callosities, erythema
- Impaired peripheral circulation - ischemic foot
- Severe nail pathology - in growing nails
- Loss of perspiration - dry skin, fissuring
- Limited joint mobility - ‘intrinsic minus’ foot
- Bare foot walking
- Rat bite
- Edema feet - congestive heart failure, nephropathy
- Past history of foot ulceration, gangrene, amputation
- Epidermophytosis of web space
- Cracks
- Ill-fitting foot wear

Wagner’s Classification of Foot Lesions

Grade 0 : Foot at high risk - no ulceration
Grade 1 : Superficial ulceration
Grade 2 : Deep ulcer ation
Grade 3 : Deep ulceration with infection and osteomyelitis
Grade 4 : Fore foot or localized gangrene
Grade 5 : Extensive gangrene requiring amputation

Measures to Improve Vascular Supply
- Control of diabetes, hypertension, dyslipidemia
• Cessation of smoking/tobacco chewing
• Avoidance of
• Cold exposure, elastic stocking
• Prolonged standing or sitting with crossed legs
• Drugs viz. beta-blockers, dopamine, dobutamine
• Control of congestive heart failure
• Supervised graded exercise

Initial Antimicrobial Therapy

<table>
<thead>
<tr>
<th>Type of Lesion</th>
<th>Anti-microbial therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial ulcer and non-toxic</td>
<td>Ampicillin + cloxacillin</td>
</tr>
<tr>
<td></td>
<td>Ampicillin + clavulanate</td>
</tr>
<tr>
<td></td>
<td>Cephalaxin + ciprofloxacin + metronidazole</td>
</tr>
<tr>
<td>Deep ulcer and toxic</td>
<td>Ampicillin + cloxacillin + metronidazole</td>
</tr>
<tr>
<td></td>
<td>Ampicillin + clindamycin</td>
</tr>
<tr>
<td></td>
<td>Ampicillin + clavulanate</td>
</tr>
<tr>
<td></td>
<td>Amoxyccillin + 3rd generation cephalexin + ciprofloxacin + metronidazole</td>
</tr>
</tbody>
</table>

The choice of antibiotics will ultimately depend on the progression of the foot lesion and culture sensitivity report.

General Management Plan for Infected Foot Lesions

• Immobilization of the extremity, drainage of pus
• Early surgical intervention (if planter mid-compartment is affected)
• Aggressive debridement of necrotic and infected tissue
• Avoid tight bandage in fulminant infection with soft tissue swelling (it prevents pressure necrosis).
• Suspect osteomyelitis in deep lesions especially if bone is felt on probing - confirm by radiography.
• Proper local care of wound, removal of slough and dressing
• Consider use of hyperbaric oxygen therapy wherever indicated.
• Doppler ultra sound to detect vascular pathology

Guidelines for Preventive Measures

• Assess the patient’s knowledge and foot care practices
• Advise essential guidelines for preventive foot care
• Advise to consult the doctor if swelling of foot, color change of toe/nail, pain or throbbing, thick hard skin or corns, breaks in skin, cracks, blisters or sores.
• Identification of foot at risk (low and high risk) and take measure to prevent foot ulceration in them.
• Evaluate for additional risk factors and plan strategies accordingly.

Footwear Advise for the Diabetic Patient

• Hawaii slippers and strap slippers should not be used.
• Sandals are recommended with velcro
• Shoes with broad front should be used.
• Shoes must be roomy
• Use of in soles in early foot lesions
• Foot wear should be ideally purchased in the evening

Foot Care Guidelines for Diabetes

<table>
<thead>
<tr>
<th>Do’s</th>
<th>Don’ts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wash feet daily</td>
<td>Application of hot/cold water</td>
</tr>
<tr>
<td>Inspect feet daily (use mirror)</td>
<td>Soaking foot in warm water</td>
</tr>
<tr>
<td>Keep feet dry especially web spaces</td>
<td>Walking on hot or cold surface/barefoot walking</td>
</tr>
<tr>
<td>Use cotton socks without elastic</td>
<td>Tight shoes</td>
</tr>
<tr>
<td>Canvas shoes/sandals with velcro and MC insole should be used</td>
<td>Self treatment of corn or callus/use of corn caps</td>
</tr>
<tr>
<td>Use broad size well fitting shoes with soft soles, stitched not nailed</td>
<td>Delay in seeking the medical advice Do not cut the nail too short and use nail cutter</td>
</tr>
</tbody>
</table>

Pentoxifylline, clopidogrel.
Low molecular weight heparin for hemodilution and defibrination.
Vascular reconstructive surgery.
Balloon angioplasty.
In India, the neuropathic foot is more common as compared to the ischaemic foot. This diabetic foot can be treated effectively by off loading the body weightby proper foot wear in the grade 0-3 and total contact casting and bedrest in grade 4 along with the use of appropriate antibiotics. These measures can prevent many amputations in neuropathic diabetic foot.
• Use custom made shoes for advanced diabetic lesions.

**SPECIAL SITUATIONS**

1. Infections

The relationship between diabetes mellitus and infections is synergistic66-68 (Table 29). Infections account for nearly 10% and 4% of deaths in type 1 and type 2 diabetics respectively.69 However in developing countries, these infections are relatively more common (Table 30).

**Table 29 : Diabetes and infection : A synergistic combination**

**Effects of diabetes on infections**
- Defective granulocyte, macrophage and lymphocyte function
- Infection is more severe, prolonged and resistant to treatment

**Effect of infections on diabetes**
- Worsening hyperglycemia
- Precipitation of ketoacidosis

**Table 30 : Important infections associated with diabetes**

<table>
<thead>
<tr>
<th>Respiratory</th>
<th>Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>Dermatophytosis</td>
</tr>
<tr>
<td>Mucormycosis</td>
<td>Candidiasis</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Staphylococcal infections</td>
</tr>
<tr>
<td>Empysematus</td>
<td>Carbuncles, paronychia</td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>Soft tissue</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>Necrotizing fasciitis</td>
</tr>
</tbody>
</table>

**Table 32 : The spectrum of diabetes-related candida infection**

<table>
<thead>
<tr>
<th>Infection</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral candidiasis</td>
<td>Topical Imidazoles</td>
</tr>
<tr>
<td>Paronychia</td>
<td>Oral Fluconazole</td>
</tr>
<tr>
<td>Vulvitis</td>
<td>Imidazole suppositories</td>
</tr>
<tr>
<td>Balanitis</td>
<td>Topical Imidazoles</td>
</tr>
<tr>
<td>Esophagitis</td>
<td>Fluconazole</td>
</tr>
<tr>
<td>Urinary tract infection (cystourethritis)</td>
<td>Bladder irrigation with Amphotericin B/oral Flucytosin (for 4 days)</td>
</tr>
<tr>
<td>Invasive/systemic candidiasis</td>
<td>Amphotericin B</td>
</tr>
</tbody>
</table>

**Mucormycosis**

Mucor species cause infection in the immunocompromised, acidic and hyperglycemic states. Rhinocerebral mucormycosis usually presents with facial (periorbital or perinasal) swelling associated with erythema, induration and a bloody discharge. A black necrotic eschar on the nasal turbinate may be an early finding. Later, proptosis, ophthalmoplegia and cranial nerve palsies result. Thrombosis of the cavernous sinus and internal carotid artery may also occur. Tissue biopsy shows characteristic broad, nonseptate, haphazardly branching hyphae. Mortality is about 50%, despite amphotericin B, surgical debridement and hyperbaric oxygen therapy. Pulmonary mucormycosis mimics any chest infection, but the CT scan shows a typical “halo” sign. Amphotericin B is given in increasing doses with a target dose of 1-1.5 mg/kg intravenously daily.

Diabetes and Infection : A Preventable Problem

Infections are a preventable cause of hyperglycemia and ketoacidosis in diabetics.68 The vicious combination of diabetes and infection can be broken by the judicious use of antimicrobial therapy and glycemic control. Near-normal glycemia should be the target in such subjects. Insulin therapy should be instituted, and it is often possible to withdraw insulin and start on oral drugs after the infection has subsided in order to improve patient compliance.

2. Surgery75-76

Surgical intervention in diabetic patients require additional care, gery and diabetes both adversely affect each other. With careful pre-operative assessment and proper preparation, elective surgery can be performed. Choice of appropriate anesthetic agent to avoid metabolic derangement is recommended.
threatening surgical situations can be treated irrespective of blood glucose level with aggressive management of diabetic status. No diabetic should be debarred from the benefit of surgery. Ketoacidosis, osmotic diuresis, electrolyte imbalance and infection alter the surgical outcome. General anesthesia induces a stress and results in secretion of counter-regulatory hormones raising the blood glucose. Spinal and epidural anaesthesia blocks splanchnic supply leading to fall of plasma catecholamine requiring less insulin and thus there is more chance of hypoglycemia. When anesthesia is over, blood glucose starts rising, due to surgical stress. Halothane and enflurane are safer anesthetic agents. Local anesthetic is considered safe in diabetics.

Minor surgery does not require change of medication if there is good glycemic control.

Pre-operative Management (For Major Surgery)

Preoperative Assessment for

- Glycemic status
- Cardiac evaluation
- Hypertension
- Diabetic nephropathy
- Diabetic neuropathy
- Autonomic neuropathy
- Renal parameters

The glycemic control is aimed to achieve a fasting plasma glucose of < 126 mg/dl and a post-prandial glucose of <200 mg/dl.
- In patients with good control on oral antidiabetic drugs, stop OHAs on the day of surgery and put them on IV fluids and insulin.

- In patients on long acting antidiabetic agents, despite good control, stop the drugs 3 days before surgery and admit the patient for insulin therapy.
- Diabetics who are not under control, are to be admitted for stabilizing with insulin. The insulin therapy should be individualised depending on the blood glucose profile. Use of multiple subcutaneous short acting insulin is advisable for effective glycemic control.

On the Day of the Surgery

- The most effective and reliable method of administration of insulin is the IV route. Subcutaneous route is not recommended.
- It is preferable to take the diabetic patients for surgery in the morning as the first case.
- Insulin glucose infusion should be used and blood glucose should be monitored every hourly.
- During surgery, 5% dextrose infusion with appropriate amount of (8-10 units per pint) insulin in the drip or in major surgeries, insulin can be administered by infusion pumps.
- Continuous blood glucose monitoring is recommended.

Monitoring of Blood Glucose

Continuous intra- and postoperative ECG is required in case of patient:

- Above the age of 40 years
- With DKA
- Acid base and/or electrolyte imbalance
- Exposed to hypotension during surgery

CVP measure ment is required in:

- Cardiac surgery
- Dehydration
- Renal failure

Monitor urinary output if necessary by catheter in

- Renal failure
- Hypotension during surgery.

Post-operative Management

In uneventful recovery, the patient can be switched to presurgery antidiabetic therapy after total surgical healing (2-4 weeks). Drugs can be started after at least 4 weeks if there are no complications of surgery.

Use of IV Fluids

1. Dextrose saline/normal saline is used if BP is normal or low.
2. In situations needing fluid restriction, 10% dextrose can be infused instead of 5% dextrose with double the dose of insulin.
3. Avoid Ringer’s lactate solution.
Minor Surgery

The antidiabetic drugs and insulin are stopped on the day of the surgery. Once the surgery is over, and the patient is permitted to resume oral feeds, the antidiabetic drugs are started with half the dose which the patient was originally taking. On the second post-operative day, full dose of the oral antidiabetic drugs and or insulin are started. Currently, cataract surgery and superficial abscess drainage can be performed if the patient is under good control with oral antidiabetic agent without changing over to insulin.

Conclusion

Diabetic patients who are undergoing planned surgery if properly scrutinized and prepared in terms of all the metabolic factors and organ complications, the extra risk for diabetes during or after surgery is negligible. In uncontrolled severe diabetes, the case should be managed as a case of DKA and prepared within a short period. Diabet es is not a contraindication for surgery.

3. Pregnancy and Diabetes

Diabetes and pregnancy encompasses not only a known diabetic marching through pregnancy but also any form of abnormal glucose tolerance developing during gestation. The abnormal glucose tolerance of any etiology, during pregnancy is associated with the high risk of a poor outcome like miscarriages, still-birth, neonates with heavy birth weight, small for dates, children with lethal or morbid congenital malformations.

3.a. Gestational Diabetes Mellitus (GDM)

Gestational diabetes mellitus is defined as any degree of glucose intolerance with the onset or first recognition during pregnancy. The definition applies whether insulin or only diet modification is used for treatment and whether or not the condition persists after pregnancy. It does not exclude the possibility that unrecognized glucose intolerance may have antedated or begun concomitantly with pregnancy. The prevalence may range from 1 to 14% of all the pregnancies depending on the population studied and the diagnostic test employed.

Risk assessment for GDM should be undertaken at the first prenatal visit. Women with clinical characteristics consistent with a high risk of GDM (Table 34) should undergo glucose testing as soon as feasible. If they are found not to have GDM at that initial screening, they should be retested between 24 and 28 weeks of gestation. Women of average risk should have testing undertaken at 24-28 weeks of gestation. Low risk status requires no glucose testing, but this category is limited to those women meeting the characteristics as given in Table 35.

3.b. Screening and Diagnosis

3.b.i. Urine Glucose

Glucosuria is a commonly employed screening test for the detection of glucose intolerance. During pregnancy, the renal threshold for glucose is often lowered, due partly to an eight-fold increase in glomerular filtration of glucose, and partly, to an intermittent tubular defect in glucose reabsorption. Low renal threshold for glucose during pregnancy renders glucosuria less specific for detection of GDM and must not be used as a diagnostic test.

3.b.ii. Blood Glucose

Spot Test: The simplest practical screening procedures, which can be followed is the “Spot Test” based on the study in Madras by Seshiah et al. In their study the +2 SD figure of the spot test blood glucose (corrected to nearest 5 mg) was 85 mg/dl fasting and 105 mg/dl non-fasting. The approximate plasma glucose values will be around 90 mg/dl and 120 mg/dl, respectively. In pregnant women the fasting and non-fasting glucose never exceeded the above figures. Hence any pregnant woman whose plasma glucose value exceeds these cutoff points should be subjected to an oral glucose tolerance test.

O’Sullivan’s Screening Test: The screening test recommended by O’Sullivan and Mahan is to do blood glucose determination one hour after a 50 g oral glucose load, if plasma glucose is more than 140 mg/dl an oral GTT is ordered. It requires 50 g of glucose and the subject has to remain for an additional one hour in the clinic.

American Diabetes Association (ADA) Criteria: The American Diabetes Association in its position statement 2001, recommends Carpenter and Coustan criteria using 100 gm OGGT as shown in Table 36. Alternatively, ADA also recommends that, the diagnosis can be made using a 75 gm glucose load and the glucose threshold values are listed for fasting, 1 hour and 2 hours (Ta ble 36); however, this test is not well validated for the detection of at risk infants or mothers as the 100 gm OGGT. If any
two of the values meet or exceed the cut-off levels the test is positive for GDM. If the test is negative it is repeated during the subsequent trimester, particularly in those who gain excess weight or shown by clinical examination or ultra sound evidence of macrosomia.

**WHO Criteria**: A standard OGTT should be performed after overnight fasting by giving 75 gm of glucose. Plasma glucose is measured at fasting and after 2 hours. Pregnant women who meet WHO criteria for IGT and diabetes are classified as having gestational diabetes mellitus (GDM) (Table 36a).

<table>
<thead>
<tr>
<th>FPG (mg/dl)</th>
<th>2h PG (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGT</td>
<td>&lt; 126</td>
</tr>
<tr>
<td>Diabetes</td>
<td>&gt; 126</td>
</tr>
</tbody>
</table>

**Glycosylated Hemoglobin (GHb)**: GHb is not suitable for screening for gestational diabetes, since it yields false positive results in 41% and false negative in 26%. GHb estimation is useful in pre-gestational diabetes to know the retrospective blood glucose control at the time of conception if performed in the early first trimester. GHb is also useful in monitoring the control during pregnancy but not for day-to-day management. Serum Fructosamine: Like GHb, serum fructosamine is not a useful screening test for gestational diabetes. This test is useful to assess the short-term state of maternal glucose control during the past two weeks.

**3.b.iii. Recommendations**

As per WHO criteria, FPG < 126 mg/dl is normal, whereas by ADA criteria FPG < 95 mg/dl is normal. The 2 hour post plasma glucose of > 140 mg/dl by WHO criteria and > 155 mg/dl by ADA criteria are abnormal. With the effective treatment available, the WHO criteria of 2 hour PPG > 140 mg/dl and ADA criteria of FPG > 95 mgs by identifying a large number of cases have greater potential for prevention of fetal morbidity. Hence, we can adopt FPG > 95 and 2 hour PPG > 140 as diagnostic criteria for GDM.

If any one of the criteria is fulfilled i.e., fasting or 2 hr more than the recommended values, the pregnant woman should be considered as having IABG (isolated abnormal blood glucose) and followed similar to GDM.

If the screen has fasting plasma glucose more than 126 mgs and 2 hr post-glucose more than 200 mgs, probably she has been having undetected diabetes prior to conception (pregestational diabetes) which can be confirmed by glycosylated haemoglobin. The above suggested criteria is only for the diagnosis of GDM. For treatment of glucose intolerance during pregnancy the effort should be to maintain fasting 90 ± 5 mgs and 2 hr post-meal of 120 ± 5 mgs, so that a mean blood glucose around 105 mgs/dl is maintained as this assures best fetal outcome.

1. To reduce neonatal complications like hypoglycemia, hypocalcemia, respiratory distress syndrome, hyperbilirubinemia, polycythemia, intrauterine death etc.
2. To reduce macrosomia
3. To reduce the risk to the mother

**3.c. Management and Monitoring**

The meal plan should allow for appropriate maternal weight gain during pregnancy. Better control is achieved by concentrating on the post-prandial values and not allowing them to exceed 120 mg/dl at 2 hour post-meal. It is practical to check the 2 hour post-breakfast and 2 hour post-lunch glucose levels. Values exceeding 120 mgs/dl require insulin for control. Frequency of monitoring should be twice a week during the initial stage, this is because some patients have severe insulin resistance and may require fairly large doses to achieve control. Once control is established the monitoring can be done every 2 weeks during the second trimester and weekly during the third trimester.

**3.c.i. Diet**

In addition to calculated calories as per the IBW during pregnancy extra caloric requirement is 150, 300 and 450 calories in the first, second and third trimesters, respectively. This requirement can be met with by adding a cup of milk (150 cal) which would provide protein and even calcium.

**3.c.ii. Insulin**

It is mandatory for the mother to learn self injection. Single injection of intermediate acting insulin given in the morning may be sufficient in some cases. When the requirement goes up, multiple shortacting injections will be required to control the blood glucose. Split mixed doses of insulin can also be used. In GDM, in whom insulin is used for the first time it is preferable to choose human insulin. Insulin should be stopped on the day of delivery or caesarean section due to risk of hypoglycemia. Insulin analogues are not recommended during pregnancy based on the present day information.
3.c.iii. Oral Antidiabetic Agents

Agents other than insulin are not advisable. Yet there are many patients who present during pregnancy with good control on sulphonylureas. These patients must be switched to insulin and the risk of congenital abnormalities should be assessed by ultrasonography especially after 14 weeks.

3.d. Delivery

GDM alone is not an indication for caesarean section unless there is macrosomia with probable cephalopelvic disproportion. In Indian settings induction of labor at 38th week is reasonable. After delivery all infants should be checked for hypoglycemia and hypocalcemia and if necessary given glucose intravenously.

3.e. Postpartum

GDM patients should undergo a standard 2 hour OGTT with 75 g of glucose 6 weeks and then 6 months after delivery and thereafter every year. Metaanalysis of available data showed that there is a 40% risk of developing type 2 diabetes at 15 years. The most important predictors for developing type 2 diabetes are a high BMI, the severity of diabetes during pregnancy, early onset during gestations and IGT in the postpartum. There is a small but significant risk of macrovascular disease in these woman; approximately 8% by the age of 60 years.

3.f. Pregnancy in Patients with Preexisting Diabetes Mellitus

Preconception counselling is essential for all diabetic women contemplating pregnancy. Diabetics who become pregnant will have a risk of teratogenecity if the glycemic control is poor during the first 12 weeks of gestation. Hence they should be advised to achieve tight control before conception. During the preconception visit, renal function and the eyes should be checked. Those with established renal disease i.e. proteinuria > 1 g/24 hrs and creatinine clearance < 70 ml/min and those with proliferative diabetic retinopathy may be discouraged from attempting pregnancy because there is a risk of accelerated progression of retinopathy and nephropathy. The patients should be converted to or stabilized on animal/human insulin if on OHA. The fasting and 2 hr post-meal values should be below 95 and 120 mg/dl, respectively. In pregnant diabetics, there is a fall in insulin requirements in the first trimester and then a gradual rise in the second and the third trimester. Thus frequent modification in the dose of insulin is essential. If a patient gets repeated episodes of hypoglycemia, it indicates fetal distress. SMBG must be done atleast daily during pregnancy. Once pregnancy occurs the eyes should be checked every 3 months. In the post-partum period renal status should be reevaluated. There is a risk of pregnancy induced hypertension and the blood pressure should be regularly monitored. Control may be achieved with any suitable combination of short and intermediate acting insulin. The targets are: fasting and pre-meal value of 90 ± 5 mgs/dl; a 2 hr post-meal value of 120 ± 5 mg/dl or less.

3.g. Management of Diabetics in the Post-partum Period

- Insulin is indicated since oral drugs are secreted in the milk.
- Progesterone containing oral contraceptives should be avoided.
- Copper containing IUCD should be avoided due to chances of infection.
- It is preferable for a diabetic mother to complete the family and go for sterilization.

4. Travel Days

Diabetics deserve to enjoy their travel as much as non-diabetics. All that it needs is, some advance planning and application of common sense. The need for modified recommendations in Indian circumstances arises on following counts:

1. Wide variation in availability of different food items in different parts of the country.
2. Poor hygienic standards of food and water served in roadside hotels and restaurants.
3. Wide variation in temperature in different parts of the country.
4. Scanty medical facility available in many of the tourist spots in the country.

Considering these factors following guidelines can be recommended:

1. All efforts should be made to achieve a good metabolic control before the proposed journey. This may not be possible if the journey has to be undertaken at short notice. In such situations the person must seek advice from his or her physician and proceed accordingly.
2. Adequate supply of medicines (OHA/insulin), syringes, needles and alcohol swabs should be ensured. To obviate the eventuality of running out of supply, in case the travel is unexpectedly prolonged, a prescription must be obtained from the treating physician. Generic names of the drugs must be mentioned to avoid confusion on account of wide variability in the brand names. Availability of a prescription is also helpful in case the person is ever questioned about the syringes, needle, medications and other items carried in relation to treatment and monitoring of diabetes.
3. In case of international travel, the following precautions are desirable.
   a. One must obtain medical insurance to meet needs of unexpected emergencies.
   b. It is quite helpful to obtain a list and address of the international diabetes federation.
increased production of ketoacids might contribute to reduced intake of carbohydrates. Simultaneously, hormones leading to a rise in blood glucose inspite of a reduced intake of carbohydrates. Simultaneously, increased production of ketoacids might contribute to reduced intake of carbohydrates. Simultaneously, increased production of ketoacids might contribute to reduced intake of carbohydrates. Simultaneously, increased production of ketoacids might contribute to reduced intake of carbohydrates. Simultaneously, increased production of ketoacids might contribute to reduced intake of carbohydrates. Simultaneously, increased production of ketoacids might contribute to reduced intake of carbohydrates. Simultaneously, increased production of ketoacids might contribute to reduced intake of carbohydrates. Simultaneously, increased production of ketoacids might contribute to reduced intake of carbohydrates. 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1. Early Onset Type 2 Diabetes Mellitus

Characteristics
- Family history
- Obesity
- High plasma glucose values
- Absence of ketoadiposis
- They respond to lifestyle modification and oral hypoglycemic agents
- It can occur as early as the age of puberty.

C peptide values need to be estimated to differentiate it from type 1 diabetes

Malnutrition modulated diabetes mellitus (MMDM) and fibrocalculus pancreatic diabetes (FCPD) have also been described in this age group.

FCPD has a definite marker, whereas MMDM does not have a specific marker.

Patients with MMDM are lean and have a low BMI and require high doses of insulin to achieve normoglycemia and are resistant to ketosis.

2. Maturity Onset Diabetes of the Young (MODY)

There is an other subset of patients who have a strong family history of diabetes running into three generations and onset below 25 yrs of age who are generally asymptomatic and do not develop ketosis. Their BMI is generally normal and they respond to oral drugs.

3. Management of Type 2 Diabetes in the Young Therapy can be initiated with insulin and then revaluated based on the C peptide levels. Those patients with normal C peptide levels can be treated with OHA.

Special precautions need to be taken because the disease starts early and duration may be long.

Diabetes And Hypertension

(FENOFIBRATE WITH LIPIDS LOWERING [UPDATE ON ANTY DRUGS TO NORMAL LIPIDEMIC DIABETES])

Coexistence of hypertension and diabetes is being increasingly recognized. 30-35% of hypertensives are detected to have diabetes. The prevalence of hypertension is 1.5 to 2 times greater in patients with diabetes mellitus compared with matched non-diabetic individuals. More than 40% of diabetics are hypertensive at diagnosis.

Coexistence of diabetes and hypertension increases the risk of macro- and microvascular disease. Blood pressure should be measured in the supine, sitting and standing position in a diabetic patient to detect evidence of autonomic neuropathy. UKPDS has stressed the importance of effective blood pressure control irrespective of the antihypertensive agent used.

Lowering blood pressure to a mean of 144/82 mmHg statistically reduced strokes, diabetes related deaths, heart failure, microvascular complications and visual loss. The study also shows that polypharmacy i.e. use of two or more drugs is required for optimal control. The HOT study in diabetic patients has shown significantly lower risk of cardiovascular disease in those patients as signed to the lowest target blood pressure (< 130/85 mmHg). In the management of diabetic hypertensives, life-style modifications have to be more aggressive. Pharmacological treatment of hypertension in diabetic patients differs due to the effects of certain drugs on the lipid profile, insulin sensitivity and glucose metabolism. ACE inhibitors have been shown to slow the rate of decline in renal function in diabetic patients. The recently reported Heart Outcomes Prevention Evaluation Study (HOPE) emphasised its importance to reduce the risk of complications of diabetes. ACE inhibitors are recommended as first line drugs for management of a diabetic hypertensive. Therapy with ACEIs, should not be initiated in patients with serum creatinine > 3 mg/dl and serum K+ > 5 mEq/L. When a patient is on ACEIs, follow up is required and close watch should be done on the above parameters. If a rising trend is seen, therapy should be withdrawn. ACEIs are contraindicated in bilateral renal artery stenosis and pregnancy. Long acting calcium channel blockers should be used wherever ACEIs are contraindicated. Low dose thiazide diuretics are recommended in mild hypertension and in combination with other antihypertensive agents. Frusemide is recommended in patients with fluid overload and end-stage renal disease. Indapamide is metabolically neutral and can be used in mild hypertension with diabetes.

Beta-blockers potentially mask hypoglycemic symptoms, however at present selective beta blockers are not a major contraindication. Further, there is clear evidence of benefits of beta blockers without intrinsic sympathomimetic activity in diabetic patients after myocardial infarction. Tight metabolic control of diabetes, effective blood pressure control and low protein diet improves overall outcome.

Diabetes And Hyperlipidemia

Mean values of lipoproteins and triglycerides (Tg) level, in healthy controls as observed from different quadrants of India is given in Table 37.

There is global dysfunction of lipoprotein metabolism in type 2 diabetes. The level and metabolism of plasma lipoproteins (Lp) in patients with diabetes mellitus depends on several factors as well as the type of diabetes mellitus. The degree of dyslipidemia is more wide spread (Table 38). Several studies have shown that serum Tg and serum cholesterol values were raised in newly diagnosed type 2 diabetics and longterm diabetics with fair to poor glycemic control. The goals to be achieved in patients with
Management of hyperlipidemia in diabetics shares many factors in common with non-diabetics yet the following points have to be given due attention.

1. Sustained control of glycemic states and maintenance of normoglycemia usually corrects diabetes induced hyperlipidemia.
2. Lifestyle modification i.e. diet, exercise, cessation of smoking and alcohol is an integral part of diabetes management and should favorably influence the lipid profile.
3. If total serum cholesterol or LDL-c is raised, then statins are the drug of choice.
4. Raised Tg levels are first managed by good glycemic control.
5. Reduced HDL levels can be raised with the help of exercise.
6. Bile acid sequestrants to be avoided in patients with fibrocalculus pancreatic diabetes as it can worsen malabsorption.
7. Omega-3 fatty acids (fish oil) can be used since it enhances fluidity of cell membrane and reduces insulin resistance.
8. Fibric acid derivatives especially bezafibrate and fenofibrate are advantageous as they help to increase insulin-sensitivity (Tables 40 and 41).

Table 37: Lipids and lipoprotein normograms in Indian populations (mean value in mg/dl)

<table>
<thead>
<tr>
<th></th>
<th>Triglyceride</th>
<th>Total Cholesterol</th>
<th>HDL-c</th>
<th>LDL-c</th>
</tr>
</thead>
<tbody>
<tr>
<td>East</td>
<td>115</td>
<td>185</td>
<td>42</td>
<td>115</td>
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<td>North</td>
<td>132</td>
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<tr>
<td>West</td>
<td>107</td>
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<tr>
<td>South</td>
<td>132</td>
<td>150</td>
<td>43</td>
<td>101</td>
</tr>
<tr>
<td>South*</td>
<td>119</td>
<td>172</td>
<td>40</td>
<td>108</td>
</tr>
</tbody>
</table>

Table 38: Lipid and lipoprotein abnormalities in type 2 diabetes mellitus

<table>
<thead>
<tr>
<th></th>
<th>LDL-c</th>
<th>HDL-c</th>
<th>Triglycerides</th>
<th>Total cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-c (including small dense LDL)</td>
<td>Normal or raised</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL-c</td>
<td>Low or normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides</td>
<td>Usually increased</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>May be increased or normal</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 39: Lipids and lipoprotein cholesterol levels desirable in patients with diabetes mellitus in India (in mg/dl)

<table>
<thead>
<tr>
<th></th>
<th>LDL-c</th>
<th>Triglyceride</th>
<th>Total chol</th>
<th>HDL-c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes without</td>
<td>&lt; 100</td>
<td>&lt; 150</td>
<td>&lt; 200</td>
<td>&gt; 45</td>
</tr>
<tr>
<td>vascular complication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes with</td>
<td>&lt; 100</td>
<td>&lt; 120</td>
<td>&lt; 180</td>
<td>&gt; 45</td>
</tr>
<tr>
<td>vascular complication</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HOSPITALISATION

In patient care or hospitalization may be appropriate in the following situations:

- Life threatening acute metabolic complications of diabetes like DKA, HONK, hypoglycemia with neuroglycopenia and lactic acidosis.
- Substantial and chronic poor metabolic control that necessitates close monitoring of the patient to determine the etiology of uncontrolled hyperglycemia, with the subsequent modification of therapy.
- Hyperglycemia associated with volume depletion
- Persistent refractory hyperglycemia associated with metabolic deterioration.
- Repeating episodes of severe hypoglycemia (i.e. < 50 mg/dl) despite intervention.
- Instability manifested by frequent swings between hypoglycemia (< 50 mg/dl) and fasting hyperglycemia (> 300 mg/dl)
- Severe chronic complications of diabetes that require intensive treatment or other severe conditions unrelated to diabetes that significantly affect its control or are complicated by diabetes.
- Diabetic foot
- Other acute medical emergencies
Admission for Complications of Diabetes or for Other Acute Medical Emergencies

Chronic cardiovascular, neurological, renal and other diabetic complications may progress to the stage where hospital admission is appropriate. In these situations, the need governing admission for the complication per se (e.g. management of end-stage renal disease) are the primary guidelines for determining whether in patient care is required. However, in applying such guidelines, the fact that diabetes is present must be considered; this may result in patients requiring admission who otherwise might be managed on an outpatient basis. The same is true for other medical conditions (e.g. infarctions) and treatments (e.g. surgery, chemotherapy) in which

1. Diabetes is a confounding factor,
2. Rapid initiation of rigorous control of diabetes can improve outcome (e.g. pregnancy),
3. The primary medical problem or the therapeutic intervention (e.g. large doses of glucocorticoid) can cause a major deterioration in diabetes control, or
4. There is acute onset of retinal, renal, neurological, or cardiovascular complications of diabetes.

**Patient Education**

Diabetes is a chronic disease that requires lifelong treatment after the diagnosis is established. The importance of tight metabolic control has been brought out by several recently concluded trials. The aim of the patient education is

- Make patient knowledgeable about disease
- To build positive attitude towards diabetes
- To make him an active partner in the diabetes team
- Patient empowerment
- Self management
- To enable the patient to make informed choice

Patient participation and compliance in the effective management of diabetes is crucial. A patient who knows different aspects of the disease will be better off than those who are not informed about the disease. In this background patient education is an important and essential component of treatment. This education is imparted in different ways to each patient - this can be given as information during each visit of the patient by his physician or family doctor. It can be given in groups and in diabetic camps where experiences of other patients can be exchanged and it will serve as an important resource. The patient as well as the spouse, siblings and parents of a young patient should get this information. The basic component of this education should stress and address the following issues.

- What is diabetes and why control diabetes: explaining briefly about the advantages of good control in preventing complications, in addition to relief of symptoms and protection from infections.
- How to achieve this control? By diet, exercise and drugs. The importance and the cost-effectiveness of diet and exercise in management of diabetes should be stressed.
- What is the basis of dietary management? Why and how dietary changes are necessary and useful?
- Similarly importance of regular exercise, yoga and the precautions to be taken in exercise planning. Integrating exercise in daily activities of the individual.
- The timing of drug ingestion, insulin administration - timing, injection technique, sites of injection and storage of insulin.
- Monitoring of plasma glucose levels and other co-morbid conditions.
- Information regarding hypoglycemia - how to recognize and correct and measures to prevent recurrence of hypoglycemia in future.
- Audio visual and other patient education material can be kept in the waiting room.
- Emphasis on personal hygiene, foot care.
- General information as regards job, marriage and child bearing.
- Self monitoring of blood glucose training.
- Role of family members in caring for the patient.
- Sick day rules/fasting days.
- Harmful effects of alcohol and smoking (tobacco in any form) and advice regarding cessation.
- Targets for control.
- The role of mass media such as print media; newspapers, electronic media, pharmaceutical industries, TV, internet and diabetic camps.

The physicians can provide this information at every visit to the patient. It may require around 8-10 min. In a diabetes clinic where dietitians, trained nurses, medico-social workers are available, such education can be imparted to the patient. Patient education is a continuous process and must be reinforced at every clinic visit of the patient. (See Appendix 8 for patient information on diet, exercise, self injection, self monitoring, low blood glucose, eyes and feet).

**Prevention of Type 2 Diabetes (Small 2 Lines from IDPP Results May Be Given)**

By the year 2025, diabetes mellitus above 20 years of age is projected to increase by 35% the world over. This means a diabetic population of 200 million by 2025 compared with 135.3 million in 1995.7 The highest increase will be for India - 59% and China - 68%. Our country will have 57.2 million diabetics compared to 19.4 million in 1995. Diabetes will mainly affect the middle aged population (45-64 years).1,3,102 They will live
long enough to develop chronic diabetic complications with a strain on resources in managing the same. With this scenario as the background, any effort to prevent diabetes mellitus assumes significance. Type 2 diabetes develops as a continuum starting with the fully compensated insulin resistance, normoglycemic and asymptomatic state and progressing to impaired glucose tolerance and later frank diabetes. The basic metabolic defect is insulin resistance, non-autoimmune mediated beta cell dysfunction leading to insulin secretory defect and increased hepatic glucose output. Identifying the individuals at greatest risk is essential in planning preventive measures. Prevention of diabetes mellitus has several windows of opportunity. They are divided into three stages:

Primary prevention: To prevent the onset of diabetes.

Secondary prevention: To prevent complications of diabetes in those who are already diagnosed to have diabetes.

Tertiary prevention: To limit the damage caused by diabetic complications in those who already have some degree of complications.

Primary prevention is to prevent the onset of diabetes in high risk individuals (Table 42). The aim should be to enhance insulin sensitivity by

- **Lifestyle Modification**: This involves diet and exercise which has been shown to be beneficial in several studies. The chance of developing diabetes is reduced by at least 50%. The family members should reduce the consumption of refined carbohydrates, fat (particularly saturated fat) and alcohol and discontinue smoking.

- **Insulin Sensitizers**: Some small studies have shown the usefulness of sulfonylureas and phenformin. The results of Diabetes Prevention Program-2 and STOP trial have recently been discussed at the European Association for the Study of Diabetes (EASD) meeting held in September 2001. Intensive lifestyle modification, metformin and acarbose have been found to delay the onset of diabetes in impaired glucose tolerant individuals. The intervention trial involving troglitazone had been discontinued.

- **Avoiding diabetogenic drugs such as beta blockers, steroids, phenytoin, immunosuppressants, thiazide diuretics, pentamidine and dilantin**: Secondary Prevention: The main objective should be to detect early undiagnosed cases. The aim of the therapy should be to reverse the disease or to prevent the progression of the disease. This is done with the help of diet, physical activity, drugs and lifestyle modification process.

**Tertiary Prevention**: The aim is to prevent or limit the damage caused by the disease in the established cases which can be achieved by diet, exercise, drugs, lifestyle modification process and demand management interventions. Here one must monitor, control and screen for complications. The aim is to prevent, arrest or even regress or reverse the complications of diabetes. When treating diabetes, physicians can readily identify the person at risk of developing diabetes or having undetected diabetes (the siblings, children of the patients). Motion that lifestyle modification can markedly reduce the risk of developing diabetes can go a long way in achieving the goal of prevention.

### Table 42: High risk individuals

| Inheritance |
| Age 30 yrs or more |
| BMI > 24 kg/m² |
| Impaired glucose tolerance (IGT) |
| Impaired fasting glucose (IFG) |
| Women with bad obstetrical history/GDM |
| sHypertension |
| Dyslipidemia |

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**References**

14. Report of the Expert Committee on the Diagnosis and
28a. Raghuram TC, Sharma RD, Sivakumar B, Sahay BK. Effect of Biguanides, Basic aspects and clinical uses, In International


29. Katzung BG. Basic and Clinical Pharmacology, 7th Ed. 684-


29. Katzung BG. Basic and Clinical Pharmacology, 7th Ed. 684-


Chandalia HB, Lamba PS. Dyslipidemia and diabetes mellitus. Lipid India 1994;4-16.


Appendix 1

Patient data card

Index no.: ____________________ Date of Registration: ____________________
Name: ________________________ Age: ____________________ Sex: ____________________
Address: ______________________ Age of Onset: ____________________

Occupation: ____________________ Phone: ____________________
Educational Status: ____________________ Activity: ____________________
Duration of Diabetes: ____________________ Socioeconomic Status: ____________________
Smoking: Yes/No: ____________________ No of Packs/Day: ____________________ Years: ____________________
Alcohol : Yes/No: ____________________ Frequency: ____________________ Veg/Non-veg: ____________________
Present Complaints: ____________________ Associated Illness: ____________________

Family H/O diabetes:
Grandparents : Maternal/Paternal: ____________________ Age of onset of complications: ____________________
Uncles/Aunts : Maternal/Paternal: ____________________
Parents ____________________
Siblings: ____________________
Children: ____________________
Consanguinity : Yes/No: ____________________ Spouse diabetic : Yes/No: ____________________
No. of children: ____________________ No. of Diabetic Children: ____________________

Anthropometry: ____________________ Height cm ____________________

<table>
<thead>
<tr>
<th>Date</th>
<th>Height</th>
<th>cm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

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Clinical Examination

<table>
<thead>
<tr>
<th></th>
<th>Date</th>
<th>Pulse</th>
<th>Peripheral pulses</th>
<th>Blood Pressure supine</th>
<th>Blood Pressure Standing</th>
<th>Ankle pressure</th>
<th>Skin lesions</th>
<th>Heart</th>
<th>Lungs</th>
<th>Abdomen</th>
<th>Cranial nerves</th>
<th>Motor system</th>
<th>Sensory system</th>
<th>Autonomic functions</th>
<th>fundus</th>
</tr>
</thead>
</table>

Investigations

<table>
<thead>
<tr>
<th>Date</th>
<th>Complete blood count</th>
<th>Fasting blood glucose</th>
<th>Erythrocyte sedimentation rate</th>
<th>Urea</th>
<th>Creatinine</th>
<th>Triglycerides</th>
<th>High density lipoprotein</th>
<th>Low density lipoprotein</th>
<th>Very low density lipoprotein</th>
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<tbody>
<tr>
<td>Date</td>
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<td></td>
</tr>
<tr>
<td>HbA₁c</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microalbuminur</td>
<td>ia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uric Acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 hr Urinary Protein</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine Clearance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary albumin/creatinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGOT/SGPT (if on Glitazone)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Other investigations:**

- Chest X-ray
- Electrocardiogram
- 2D ECHO:
  - Treadmill Testing:
  - Coronary Angiography:
- Ultrasound scan of abdomen for kidney size:
- Fluorescein Angiography:
- Doppler Studies:

**Diagnosis**

- Diabetes type

**Complications:**
<table>
<thead>
<tr>
<th>Date/year</th>
<th>Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Nephropathy</td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td></td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td>Neuropathy</td>
<td></td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td></td>
</tr>
<tr>
<td>Retinopathy</td>
<td></td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td></td>
</tr>
<tr>
<td>Ketosis/Hyperosmolar non-ketotic lactic acidosis.</td>
<td></td>
</tr>
</tbody>
</table>

Treatment advised:
### Appendix 2: BMI chart

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Height (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>110-114</td>
<td>55-59</td>
</tr>
<tr>
<td>115-119</td>
<td>60-64</td>
</tr>
<tr>
<td>120-124</td>
<td>65-69</td>
</tr>
<tr>
<td>125-129</td>
<td>70-74</td>
</tr>
<tr>
<td>130-134</td>
<td>75-79</td>
</tr>
<tr>
<td>135-139</td>
<td>80-84</td>
</tr>
<tr>
<td>140-144</td>
<td>85-89</td>
</tr>
<tr>
<td>145-149</td>
<td>90-94</td>
</tr>
<tr>
<td>150-154</td>
<td>95-99</td>
</tr>
</tbody>
</table>

### Appendix 3: Fatty acid composition of commonly used oils

<table>
<thead>
<tr>
<th>Saturated</th>
<th>MUFA</th>
<th>PUFA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coconut</td>
<td>86.5</td>
<td>5.8</td>
</tr>
<tr>
<td>Palm</td>
<td>49.5</td>
<td>37</td>
</tr>
<tr>
<td>Groundnut</td>
<td>18</td>
<td>48</td>
</tr>
<tr>
<td>Sunflower</td>
<td>11</td>
<td>20</td>
</tr>
<tr>
<td>Safflower</td>
<td>9.1</td>
<td>12.1</td>
</tr>
<tr>
<td>Mustard</td>
<td>6.8</td>
<td>55.5</td>
</tr>
</tbody>
</table>

### Appendix 4: Omega 6 : Omega 3 content of the commonly used edible oils

<table>
<thead>
<tr>
<th>Oil</th>
<th>N-6</th>
<th>N3</th>
<th>N6 : N3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safflower</td>
<td>73</td>
<td>0.5</td>
<td>146</td>
</tr>
<tr>
<td>Sunflower</td>
<td>49</td>
<td>0.3</td>
<td>163</td>
</tr>
<tr>
<td>Corn</td>
<td>57</td>
<td>0.8</td>
<td>71</td>
</tr>
<tr>
<td>Groundnut</td>
<td>28</td>
<td>0.8</td>
<td>35</td>
</tr>
<tr>
<td>Coconut</td>
<td>1.8</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Ghee (Buffalo)</td>
<td>2</td>
<td>0.9</td>
<td>2.2</td>
</tr>
<tr>
<td>Mustard oil</td>
<td>13</td>
<td>8.6</td>
<td>1.5</td>
</tr>
</tbody>
</table>

### Appendix 5: Rich sources of alpha linolenic acid

<table>
<thead>
<tr>
<th>Cereals and millets</th>
<th>Wheat, bajra</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulses and legumes</td>
<td>Black gram, cowpea, rajmah, soya</td>
</tr>
<tr>
<td>Vegetables</td>
<td>Green leafy</td>
</tr>
<tr>
<td>Spices</td>
<td>Fenugreek, mustard</td>
</tr>
<tr>
<td>Oils</td>
<td>Mustard, soya bean</td>
</tr>
<tr>
<td>Animal foods</td>
<td>Fish</td>
</tr>
</tbody>
</table>

### Appendix 6: Total fiber content of common foods (g/100g)

<table>
<thead>
<tr>
<th>High (&gt; 10)</th>
<th>Medium (1-10)</th>
<th>Low (&lt; 1)</th>
<th>Nil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheat</td>
<td>Rice</td>
<td>Refined</td>
<td>Sugar</td>
</tr>
<tr>
<td>Iowar</td>
<td>Most vegetables</td>
<td>and</td>
<td>Fats/oils</td>
</tr>
<tr>
<td>Bajra</td>
<td>Most fruids</td>
<td>processed</td>
<td>Milk</td>
</tr>
<tr>
<td>Ragi</td>
<td>Coconut</td>
<td>foods</td>
<td>All types of meat</td>
</tr>
<tr>
<td>Maize sesame</td>
<td>Legumes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dals</td>
<td>Fenugreek</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### App 2: Waist/HIP ratio - An important marker for obese type 2 diabetic

<table>
<thead>
<tr>
<th>Waist measurement (cms)</th>
<th>Hip measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>105</td>
</tr>
<tr>
<td>110</td>
<td>115</td>
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<tr>
<td>120</td>
<td>125</td>
</tr>
<tr>
<td>130</td>
<td>135</td>
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<tr>
<td>140</td>
<td>145</td>
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</tbody>
</table>

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