# DIABETES

# **CLINICAL PRACTICE GUIDELINES FOR PAPUA NEW GUINEA**

July 2012



These Guidelines were developed from a workshop held in Port Moresby on 7<sup>th</sup> September 2009. They form part of a joint HOPE worldwide (PNG) / Papua New Guinea Department of Health program to develop diabetes services in PNG.

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We express our profound gratitude to Professor Stephen Colagiuri for facilitating the workshop, and providing expert advice as the guidelines developed. We also gratefully acknowledge the time and efforts of all contributors.

These guidelines were partly based on the Type 2 Diabetes Clinical Practice Guidelines for Sub-Saharan Africa (published by the International Diabetes Federation Africa Region) and the National Guidelines for the Prevention and Management of Diabetes in Samoa (Department of Health, Samoa, 2002).

For further information on Diabetes in PNG, education resources, and links to relevant published papers, please access the website www.diabetes.hopewwpng.org.pg

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# FOREWORD

Papua New Guinea, like other middle income countries in economic transition, is experiencing a double burden of illness from infectious diseases and lifestyle-related non-communicable diseases. According to a WHO 2005 Report, 80 % of chronic diseases occur in low- and middle-income countries and it is estimated that 7.1 million people will die annually as a result of elevated blood sugar levels.

Diabetes is a systemic disease which can result in a variety of serious complications such as: eye damage leading to blindness, neuropathy resulting in ulcerations and the need for amputations, kidney failure, and substantially increased risk of ischaemic heart disease.

Hospital statistics show that diabetes has increased since 1980. A pilot survey in a working population in Port Moresby in 2008 showed that 10% had a high blood sugar level with no symptoms of diabetes. The STEPs national prevalence study in 2008-9 (funded by WHO) showed that 14.4% of adults aged 15-64 years had a fasting blood sugar level of  $\geq$  6.1 mmol/L. This is indeed a serious situation and this first Standard Treatment Guideline will assist in unifying our efforts to control and manage diabetes in the country.

There has been no standard management and treatment of diabetes in the country and this first edition should be used in all cases unless there are specific professional reasons to do otherwise. This will ensure safe, appropriate and timely management of our patients.

I acknowledge the assistance of Dr Graham Ogle and HOPE *worldwide* (PNG) in securing funding and support from the World Diabetes Foundation, and the guidance of Prof. Stephen Colagiuri and A. Prof. Ashim Sinha to assist us in developing this first Standard Treatment Guideline for diabetes management in PNG.

Dr. Goa Tau Chief Medical Officer

# **PREFACE – DIABETES IN PNG**

Infectious diseases have traditionally dominated health care agendas in PNG. However, non-communicable diseases are becoming increasingly frequent. Diabetes in particular is becoming increasingly common in Papua New Guinea. Certain tribal groups, including Wanigela, Manus and Tolai, have been known to be susceptible for some years. More recently diabetes is also becoming frequent in other parts of the country.

Diabetes itself, and the complications that accompany it, cause considerable morbidity and mortality, resulting in much human distress and also cost to the society. In untreated or poorly managed patients, microvascular complications such as kidney failure, blindness, and foot problems requiring amputation are not uncommon. Diabetes also is a major contributor to cardiovascular disease such as myocardial infarctions and stroke. Much of the morbidity of diabetes is preventable by good glycaemic control, good blood pressure control, and regular examination for complications and timely intervention.

There is evidence that most diabetes in PNG is undiagnosed, and many patients who are diagnosed are not well controlled due to lack of education or resources. The purpose of these Guidelines is to provide standard information for doctors and other health professionals on the diagnosis, treatment, and prevention of diabetes. The Guidelines are comprehensive, and cover all common aspects of the condition.

The Guidelines are based on guidelines developed for Africa and for Samoa, with numerous additions and changes so that they are appropriate for the PNG context. This is the first edition, they will be revised with time.

**ORGANISATION OF DIABETES CARE** 

Papua New Guinea (PNG) does not have formal organised diabetes health-care delivery at the primary level. Even at the secondary and tertiary levels, some staff may lack expertise in diabetes care, and diagnostic equipment and the full range of medications may not always be available.

There is abundant evidence that well-organised diabetes clinics with appropriately trained staff and welldesigned protocols improve the quality of diabetes care. It is therefore suggested that where diabetes clinics do not exist, clinics be established and integrated into the health-care system. Where the clinics do exist, an assessment of the quality of care provided should be done and changes instituted to rectify any deficiencies.

# TABLE 1Optimal staffing and equipment at each level of health care for the appropriate<br/>management of diabetes mellitus

HEALTH-0	CARE LEVEL	PERSONNEL	EQUIPMENT	ACTIVITY
Primary Level	Aid Post	CHW		Community awareness/education on diabetes
	Community Health Post	Above + NO	Urine strips, glucometer, weight scales, height measure, tape measure, monofilament/cotton wool	Early detection diabetes program
	Health Centre	Above + HEO	All above	Above + referral
Secondary Level	District Hospitals	All + MO	<i>All above</i> + tuning fork, patella hammer, ophthalmoscope, Biochem Analyser including HbA1c, lipids	All above
	Provincial hospitals	Above + Physician, Surgeon, Obstetrician, Paediatrician, Ophthalmologist +/- Specialist NO (NCDs), Podiatrist, Dietician	All above	Medication at this level as Category C drugs
Tertiary Level	Regional Hospitals	<i>Above</i> + SMP Physician, Cardiologist, Podiatrist	<i>All above</i> + Fundal camera, retinal laser unit, theatre facilities, cardiovascular diagnostic facilities, dialysis facilities	As above
	Tertiary Hospital	Above + Endocrinologist, Nephrologist	All above	As above

Suggestions for setting up a diabetes clinic are provided in Appendix I (page 39), and indicators to assess quality of care are in Appendix II (page 40).

# ORGANISATION OF DIABETES CARE

### TABLE 1.2 What to do when

Initial Visit3 Month VisitAnnual VisitHistory and DiagnosisRelevant historyHistory and Examination – as atPhysical ExaminationBlood pressureHistory and Examination – as at• Height and Weight (BMI)Blood pressureFoot inspection• Detailed foot examinationFoot inspectionEducation (exercise, avoid• Teeth inspectionNutritional advice (avoid high fat and sugar foods)Nutritional advice (avoid foods highIo fat and sugar)Blood glucose test by meterReview contraceptionEducation (exercise, avoid smoking and alcohol)Nutritional advice (avoid foods high in fat and sugar)Blood glucose test by meterReview contraceptionSECONDARY LEVELAll of the above + MedicationsAll of the above + BiochemistryAs at initial visitECG BiochemistryFurther education and dietary adviceFurther education and dietary adviceAs at initial visit• HbA1cI. Lipids (Cholesterol, Triglycerides, + HDL if available)Further education and dietary adviceAs at initial visit• Urine protein Provide tubal ligation for women not wanting further pregnanciesFURT LARY LEVELAll the above and microalbumin	PRIMARY LEVEL					
Physical ExaminationWeightinitial visit• Height and Weight (BMI)Bood pressureinitial visit• Waist circumferenceFoot inspectionReview contraception• Detailed foot examinationEducation (exercise, avoid smoking and alcohol)Nutritional advice (avoid high fat and sugar foods)Urinalysis for glucose and proteinBlood glucose test by meter Review contraceptionEducation (exercise, avoid smoking and alcohol)Review contraceptionNutritional advice (avoid foods high in fat and sugar)Review contraceptionMedication if HEO or Doctor available, otherwise referral Family planning education, contraceptives if not wanting to fall pregnantAll of the above + BiochemistryAll of the above + MedicationsAll of the above + BiochemistryIbioshemistry • HbA1cIbioshemistry available)• Lipids (Cholesterol, Triglycerides, + HDL if available)All of the above + Biochemistry• Lipids (Cholesterol, Triglycerides, + HDL if available)Further education and dietary advice• Lipids (Cholesterol, Triglycerides, thDL if available)Further education and dietary advice• Creatinine, Sodium, PotassiumFurther education and dietary advice• Further education further pregnaciesFurther education and dietary advice	Initial Visit	3 Month Visit	Annual Visit			
SECONDARY LEVEL         All of the above +       All of the above +       As at initial visit         Medications       Biochemistry       • HbA1c         EVG       • Urine protein       • Urine protein         Biochemistry       • HbA1c       • Urine protein         • Lipids (Cholesterol, Triglycerides, + HDL if available)       • Creatinine, Sodium, Potassium       • Creatinine, Sodium, Potassium         Further education and dietary advice Provide tubal ligation for women not wanting further pregnancies       TERTIARY LEVEL	<ul> <li>Physical Examination <ul> <li>Height and Weight (BMI)</li> <li>Waist circumference</li> <li>Blood pressure</li> <li>Detailed foot examination</li> <li>Teeth inspection</li> <li>Visual acuity</li> </ul> </li> <li>Urinalysis for glucose and protein</li> <li>Blood glucose test by meter</li> <li>Education (exercise, avoid smoking and alcohol)</li> <li>Nutritional advice (avoid foods high in fat and sugar)</li> <li>Medication if HEO or Doctor available, otherwise referral</li> <li>Family planning education, contraceptives if not wanting to fall</li> </ul>	Weight Blood pressure Foot inspection Education (exercise, avoid smoking and alcohol) Nutritional advice (avoid high fat and sugar foods) Blood glucose test by meter Review therapy	initial visit			
MedicationsBiochemistryEye examinations by fundoscopy• HbA1cECG• Urine proteinBiochemistry• Further education and dietary• HbA1cadvice• Lipids (Cholesterol, Triglycerides, + HDL if available)• HDA1c• Creatinine, Sodium, Potassium• HDA1cFurther education and dietary advice• HDA1cProvide tubal ligation for women not wanting further pregnancies• HDA1cHUBA1cHU	r source	SECONDARY LEVEL				
	Medications Eye examinations by fundoscopy ECG Biochemistry • HbA1c • Lipids (Cholesterol, Triglycerides, + HDL if available) • Creatinine, Sodium, Potassium Further education and dietary advice Provide tubal ligation for women	All of the above + Biochemistry • HbA1c • Urine protein Further education and dietary	As at initial visit			
	All the above and microalbumin	TERTIARY LEVEL All of the above	All the above and microalbumin			

### **DEFINITION**

Diabetes mellitus is a group of metabolic diseases characterised by chronic hyperglycaemia, resulting from defects in insulin secretion, insulin action, or both. It is associated with acute complications such as ketoacidosis and hypoglycaemia, as well as long-term complications affecting the eyes, kidneys, feet, nerves, brain, heart and blood vessels.

### DIAGNOSIS

When people present with the classical symptoms of diabetes, diagnosis is usually straightforward. However, diagnosis is more difficult in those with a minor degree of hyperglycaemia, and in asymptomatic subjects. In these circumstances, two abnormal results on separate occasions are needed to make the diagnosis. If such samples fail to confirm the diagnosis it will usually be advisable to maintain surveillance with periodic retesting until the situation becomes clear.

Diagnosis of diabetes must be confirmed biochemically prior to initiation of any therapy. The diagnosis is confirmed by:

- The presence of **symptoms** of hyperglycaemia, such as polyuria, polydypsia, pruritus vulvae, lethargy, and loss of weight, <u>and</u> a random venous plasma glucose of 11.1 mmol/L
- or
- a fasting venous plasma glucose ≥ 7.0 mmol/L

In **asymptomatic** subjects a single abnormal blood glucose result is inadequate to make a diagnosis. The abnormal value must be confirmed at the earliest possible date using either a fasting or random blood sample on another occasion, or a 75 g oral glucose tolerance test.

For clinical purposes the diagnosis of diabetes should always be confirmed by repeating the test on another day, unless there is unequivocal hyperglycaemia with acute metabolic decompensation or obvious symptoms. Between normal glucose tolerance and diabetes, there are two other categories – impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG - see table below for definitions). People with IGT or IFG should be retested after 1 year.

# Table 2.1Values for the diagnosis of categories of hyperglycaemia, measured in mmol/L<br/>(WHO, 2006 and other sources)

	Venous plasma or whole blood glucose (mmol/L)	Capillary whole blood (mmol/L)		
DIABETES				
Fasting	$\geq 7$	≥ 6.1		
or 2h post 75gm glucose load	≥11.1	≥11.1		
IMPAIRED GLUCOSE TOLERANCE (IGT)				
Fasting	< 7	< 6.1		
and 2hr post 75g glucose load	$\geq$ 7.8 and < 11.1	$\geq$ 8.9 and < 12.2		
IMPAIRED FASTING GLYCAEMIA (IFG)				
Fasting	$\geq$ 6.1and < 7.0	$\geq$ 5.6 and < 6.1		
GESTATIONAL DIABETES (GDM)				
If random venous blood glucose level is more than 7, do a glucose profile. Treat as GDM if				

• Fasting > 5.1, *Or* 

• 1-2 hour postprandial level (after mother's normal meals) is > 7 or

• 2 hr post 75g glucose load > 8

### **CLASSIFICATION OF DIABETES**

The classification of diabetes has been revised by the WHO and is based on aetiology (the cause).

Type 1 diabetes	Results from destruction, most commonly autoimmune, of the pancreatic beta cells. Insulin is required for survival.
<i>Type 2 diabetes</i>	Characterised by insulin resistance and/or abnormal insulin secretion, either of which may predominate, both of which are usually present. It is the most common type of diabetes.
Other specific types of diabetes	These are less common and include genetic disorders, infections, diabetes and diseases of the exocrine pancreas,
Contational diabatas	endocrinopathies or as a result of drugs.
Gestational diabetes	<ul><li>endocrinopathies or as a result of drugs.</li><li>Appearing or recognised for the first time in pregnancy.</li></ul>

### **PRESENTATION OF DIABETES**

### Type 1 diabetes

Patients present at a young age (usually their teens or twenties, but earlier presentation may also occur) with rapid onset of severe symptoms, in particular weight loss, thirst and polyuria (excessive urination). Blood glucose levels are high and ketones often present in the urine. If treatment is delayed diabetic ketoacidosis (DKA) and death may follow. The response to insulin therapy is dramatic and gratifying. Type 1 diabetes is rare in PNG, although misclassification of adult patients as "Type 1" is probably relatively common, as being treated with insulin is not the same as being dependent upon insulin for survival.

### Type 2 diabetes

Type 2 diabetes is by far the most common form of diabetes in PNG. Some patients present with the classical symptoms of diabetes including polyuria, polydypsia (excessive drinking), and polyphagia (excessive eating). Additionally, some patients present with sepsis, or, especially in the elderly diabetic coma (hyperosmolar nonketotic states). A minority are asymptomatic and are therefore identified at screening. Some patients do not seek early medical attention because of the insidious nature of the disease and therefore even at diagnosis may present with features of diabetic complications, including visual difficulties from retinopathy, pain and/or tingling in the feet from neuropathy, foot ulcerations, and stroke.

Type 2 diabetes is most common in adults in certain tribal groups (Wanigela, Tolais and other islanders), but can occur in any tribal group. The prevalence is rising as the food and exercise habits of Papua New Guineans change. Type 2 can also occur in adolescents and even older children, particularly in high-risk groups.

### **Gestational diabetes**

Gestational diabetes mellitus (GDM) is diabetes that arises in pregnancy. It reverts to metabolic and clinical normality post-partum, though there is a considerable risk of later Type 2 diabetes. Therefore, GDM must be distinguished from *existing* diabetes in women who become pregnant. The particular importance of GDM is that it is associated with a poor pregnancy outcome especially if unrecognised and untreated. Particular adverse effects include foetal macrosomia (very large baby), eclampsia, intra-uterine growth retardation with low birth weight, birth difficulties, neonatal hypoglycaemia and respiratory distress.

### **PREVENTION OF DIABETES**

In view of the significant rise in the prevalence of diabetes in Papua New Guinea, and the associated morbidity, premature mortality and increasing health costs, prevention is of paramount importance.

The major risk factors for diabetes are shown in the table below.

### Table 2.3Major risk factors for diabetes mellitus

MODIFIABLE	NON-MODIFIABLE
Obesity: general	Age ( $\geq$ 40 yrs)
: central	
Physical inactivity	First degree relative with diabetes
Impaired glucose tolerance / impaired fasting	Previous gestational diabetes
glycaemia	
Dyslipidaemia	Ethnicity
	Hypertension

Evidence from large trials conducted in China, Finland and the USA has shown that the onset of diabetes can be delayed by active lifestyle modification in people at high risk of diabetes. It is currently unknown whether this intervention can totally prevent the onset of diabetes, or its cardiovascular complications.

The components of lifestyle modification should include, but not be limited to:

- Weight loss of 5% 10% if initially overweight
- Return to traditional diet, but avoid the use of excessive coconut cream
- Use low-fat cooking techniques such as steaming, grilling and mumu; roasting of root vegetables in hot ashes
- Reduction in fat intake to < 30% of calories.
- Reduction in saturated fat intake to < 10% of calories.
- Increase in fibre intake to > 15 g/l 000 kcal (traditional PNG diets are high in fibre content).
- Increase in physical activity level: this type of exercise (e.g. brisk walking) should last for at least 30 minutes and should be undertaken at least five times a week see page 19
- Reduction in high levels of alcohol intake to less than one drink per day of any type
- Stop smoking
- Stop chewing of betel nut for non-traditional purposes

# METABOLIC SYNDROME

### **METABOLIC SYNDROME**

Type 2 diabetes and lesser degrees of hyperglycaemia often coexist with hypertension, obesity (particularly "central" or "visceral" obesity), and dyslipidaemia. These components comprise the Metabolic Syndrome, a known cluster of risk factors for ischaemic heart disease, stroke and peripheral vascular disease. The pathogenesis of the syndrome is strongly linked to central obesity and tissue resistance to insulin action arising from genetic pre-disposition or acquired factors, such as obesity and physical inactivity.

The essential components of the Metabolic Syndrome are:

- 1. Central obesity (as measured by waist circumference (see page 12)
- 2. Impaired fasting glycaemia (IFG) or Type 2 diabetes (see page 8)
- 3. Hypertension (BP  $\geq$  130/85)
- 4. Dyslipidaemia (raised triglycerides and/or low HDL-cholesterol)

The presence of three or more of the above essential components constitutes the metabolic syndrome. Formal assessment of insulin resistance is not required to make the diagnosis.

Strong associations of the metabolic syndrome include:

- Polycystic ovary disease
- Acanthosis nigricans (excessive pigmentation +/- skin thickening at the back of the neck)
- Decreased fibrinolytic activity
- Hyperuricaemia
- Proinflammatory state
- Microalbuminuria

### **Management of Metabolic Syndrome**

Treatment of the syndrome consists of managing the various disease components and targeting the pathophysiological derangements of the syndrome: central obesity and insulin resistance. The first line of treatment for all components is lifestyle change: weight loss and increased physical activity. Insulin sensitivity can be improved by non-pharmacological and pharmacological means.

# OBESITY

### **OBESITY**

Over 70% of people with type 2 diabetes are either overweight or obese. Being overweight or obese significantly increases the risk of morbidity and mortality from type 2 diabetes and its co-morbidities. Successful weight reduction has a positive impact on these outcomes. Obesity is also a major component of the metabolic syndrome (see above).

### Measurements for evaluation of obesity are:

- 1. Calculation of overall obesity the body mass index (BMI)
- 2. Determination of central fat distribution by measurement of waist circumference

BMI represents overall fatness. It is derived from the following formula, using the patient's weight in kilograms (kg) and height in meters (m):

$$BMI = Weight (kg)$$
$$Height (m)^{2}$$

For instance, for a man who weights 60 kg and is 160 cm (1.6m) tall, the BMI = 60 divided by  $(1.6)^2$  (the same as 60 divided by 1.6 divided by 1.6) = 23.4

Classification of BMI	$BMI (kg/m^2)$
Underweight	< 19.0
Normal weight	19 - 24.9
Overweight	25 - 29.9
Obesity	$\geq$ 30

The pattern of distribution of the fat in the body (whether mostly peripherally or centrally distributed) is assessed by the use of the waist circumference. Waist circumference should be measured midway between the lower rib margin and the iliac crest. It is a good indicator of central or upper-body obesity. The upper limits of normal are 102 cm in men and 88 cm in women.

Whilst weight loss may be difficult for some to achieve and maintain, it is very beneficial when achieved.

### **General Principles of Obesity Management in Diabetes**

- 1. Assess dietary intake, level of physical activity, BMI, and waist circumference on presentation and monitor regularly
- 2. Integrate weight control measures into the overall management of diabetes and co-morbidities if BMI > 25 and/or waist circumference > 102 cm in men or > 88 cm in women
- 3. Educate families as well as patients
- 4. Involve a nutritionist if available
- 5. Dietary changes and increased level of physical activity are the most economical means to lose weight. Set realistic goals the socio-economic situation will affect ability to comply with dietary advice.
- 6. Maintain records of goals, instructions and weight progress charts

### **MANAGEMENT GOALS**

The goal of management is to improve quality of life and productivity of people with diabetes by:

- Early diagnosis
- Prevention of short-term and long-term morbidities
- Prevention of premature mortality
- Promotion of self-care practices and empowerment
- Reduction of the personal, family and societal burden of diabetes

The successful establishment of the diabetes health-care team and infrastructure to support it is critical for the achievement of these goals. This includes provision of education for health-care professionals and for people living with diabetes.

### **Essential components of care**

Pages 14-20 give full details of management, and page 20 shows an algorithm for care, in steps.

Some cases of diabetes can be managed by education and lifestyle changes – diet and physical exercise – alone (Step 1 in the algorithm on page 22). If these prove inadequate, or if medications are needed immediately, oral glucose-lowering agents can be added, with a single medication (Step 2) or in combination (Step 3). Later, in some patients, insulin needs to be added (Step 4) and in some situations insulin should be started at diagnosis. Finally, more complex insulin regimens may be needed (Step 5).

In addition, management is needed for an accompanying hypertension (page 21) or dyslipidaemia (page 22), as well as prevention and treatment of both microvascular (kidney, eye, nerve and foot) complications and macrovascular complications (pages 24-29).

<b>BIOCHEMICAL MEASURE</b>	OPTIN	IAL
Capillary blood glucose values_(finger-prick)	mmo	l/L
Fasting	4-6	1
2-hr post prandial (after a meal)	4-8	
HbA1c (glycated haemoglobin)	<7	
BMI	<25	5
Blood pressure (if no proteinuria)		
Systolic	≤ 130	
Diastolic	$\leq 80$	
If persistent dipstick for proteinuria		
Systolic	<125	
Diastolic	<75	
Lipids	mmol/L	mg/dL
Cholesterol (Total)	<5.0	<93.6
LDL Cholesterol	<2.0	<46.8
HDL Cholesterol	>1.0	>19.8
Triglycerides	<2.0 <30.6	

### Table 6.1Optimal targets for glycaemic, lipid, and blood pressure control

# MANAGEMENT OF DIABETES

### METHODS FOR MONITORING GLYCAEMIC CONTROL

Clinical and laboratory methods are employed to assess whether the individualised glycaemic targets are being attained. Methods used in PNG will depend on local availability.

HbA1c (glycated haemoglobin) testing is the best method. The test is possible at Port Moresby General Hospital, and should soon be available in five other hospitals around PNG.

If HbA1c testing is not available, the best alternative is a combination of fasting and postprandial plasma glucose, ideally measured in a laboratory, or otherwise with a blood glucose meter.

Glycosuria is a poor means of assessing glycaemic control but in certain clinics this may be the only available tool. In this situation, the second voided specimen of the day should be tested.

Where possible, self-blood glucose monitoring (SBGM) should be encouraged. Results of self-urine testing or blood glucose tests should be recorded in a logbook. The clinic protocol should set out in some detail the parameters to be monitored at the initial visit, regular follow-up visits, and at the annual review.

# **MANAGEMENT OF DIABETES**

### A) **DIABETES EDUCATION**

Diabetes education is the provision of knowledge and skill to people with diabetes that empowers them to render self-care in the management of their diabetes and associated disorders. This is one of the cornerstones of diabetes management, along with diet, physical activity and pharmacotherapy, and is critical in improving the outcome.

### **General Principles**

1. Diabetes education programmes should be locally applicable, simple and effective

2. All members of the diabetes-care team should be trained to provide the education, and be aware of the local myths about diabetes

3. The programme must empower people with diabetes and their families

4. The effectiveness of the programme must be evaluated and modified as necessary

Empowerment of people with diabetes includes their having:

- a broad knowledge of diabetes and its sequelae, and
- the right attitude and resources to provide appropriate self care

### People with diabetes and their families need to know:

- that diabetes is serious, but can be controlled
- that complications are not inevitable they can be prevented
- what foods to eat, how much and how often to eat, how to exercise and its precautions, how and when to take medications
- their metabolic and blood pressure targets
- how to look after their feet, and thus prevent ulcers and amputations
- how to avoid other long-term complications
- that regular medical check-ups are essential
- when to seek medical help, e.g. how to identify hypoglycaemic and hyperglycaemic emergencies and symptoms, as well as signs of chronic complications
- that good glucose control is required before and during pregnancy
- how to make informed choices about their use of traditional medicine

### **B) DIETARY MANAGEMENT**

Effective prevention and care of diabetes cannot be achieved without proper attention to diet and nutrition. This extends to associated cardiovascular risk factors such as hypertension, dyslipidaemia and obesity. Food intake should be distributed as evenly as possible during the day, especially in patients taking tablets or insulin for their diabetes

### Nutrition principles include:

### • Weight control

Limit the overall amount of food. Even too much healthy food can be harmful to one's health.

### • Staple (starchy) foods

Staple foods (starches) give energy to the body, plus vitamins, minerals and fibre. Foods like kaukau, English potatoes, taro, yam, breadfruit, bread, rice, cereal, noodles or pasta are classed as staples, and should be eaten at each meal. Whole meal bread and brown rice are better choices than white bread or white rice.

### • Fruit

Fruit is healthy for everyone, including people with diabetes. Fruit provides essential vitamins, minerals and fibre with very little food energy. Eat fruit instead of drinking fruit juice. Pieces of fruit are more filling. Choose fruit juice with no added sugar (check label), and only drink small amounts.

### • Vegetables

Vegetables are also healthy for everyone, including people with diabetes. They give vitamins, minerals and fibre with virtually no food energy. Green leafy vegetables (aibika) are especially good

### • Protein or body-building foods

Protein foods are fish, meats, poultry, eggs, cheese, and milk. They help the body build tissue and muscle and provide vitamins and minerals.

### • Fats and oils

Only small amounts should be eaten because they have lots of food energy. Animal fats and oils, including fatty meats such as lamb flaps contain saturated fats and cholesterol that are not good for health. Always trim the fat of the meat and remove the skin from chicken. Margarine and butter are also high in fat and should be used in small amounts. Avoid the use of coconut cream.

### • Sugary Foods

Sugary foods are not encouraged in people with diabetes because they are often high in fat and have very few minerals or vitamins. However, small quantities do not worsen diabetes control. However concentrated sugary foods (eg soft drinks) must be avoided.

- Salt intake should be restricted small amounts may be used in cooking but should not be added to meals, particularly in hypertensive patients. Also salty foods should be avoided.
- Alcohol intake Too much alcohol is not good for health. Preferably drink no alcohol but if consumed limit to 1-2 standard drinks a day.

It is good to learn to understand and use the nutrition panel of food products - ingredients are listed from highest to lowest content.

# MANAGEMENT OF DIABETES

### A Typical Meal Plan

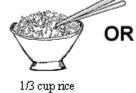
The three main meals of the day should each include the following:

- 2-3 serves of staple foods
- 1-2 serves of fruit
- 2-3 serves of vegetables
- 1-2 serves of protein
- Very little margarine or butter

### Note: Any reduction in food intake is beneficial in overweight people Food Serve sizes:

Examples of one serve of starchy foods is shown in the figure below.









1 slice of bread

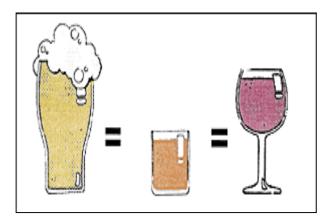
1/2 cup cooked cereal or 3/4 cup dry flakes of cereal

1 small baked potato

### Alcohol – Standard Drink

The following are examples of a standard drink of alcohol:

- 1 glass of beer
- 1 glass of wine
- 1 nip of spirits



# MANAGEMENT OF DIABETES

### C) PHYSICAL ACTIVITY AND EXERCISE

Physical activity plays an important role in the prevention and care of diabetes. Exercise improves blood glucose levels by improving insulin sensitivity and helps with weight reduction.

The goal is to **accumulate** at least 30 minutes of moderate intensity physical activity on most (preferably all) days of the week. Fast walking on a flat surface e.g. to the shop is an excellent form of exercise. Adoption of healthy lifestyle practices within daily living such as taking the stairs at work, or continuing with hard physical labour such as fishing, working in fields or plantations should be maintained and encouraged.

In addition other forms of exercise can also help. Strength-developing activities (weight training) may provide additional benefits. Flexibility exercise is important, especially in older people.

Almost everyone can exercise but the exercise programme must be appropriate to the person's age, social, economic, cultural and physical status.

Care is required for the potential hazards of exercise such as cuts, scratches and dehydration, and special care should be devoted to proper care of the feet.

If exercise is sudden and/or vigorous, people with diabetes should be advised about adjusting food and fluid intake, or medications (insulin or oral agents) in order to avoid hypoglycaemia or dehydration.

### **Types of Physical Activity**

Each person should try to do at least 30 minutes of physical activity each day, five days or more per week

- Walking
- Gardening sweeping leaves, weeding, cutting grass, planting
- House work sweeping, cleaning windows, mopping floors, washing clothes by hand
- Carrying water, fire wood, coconuts
- Sports rugby, soccer, volleyball, basketball etc
- Fishing
- Dancing
- Swimming
- Light / moderate strength-developing exercise eg gym work
- Stretching exercises

Sedentary adults will require a structured exercise programme and should be formally assessed for any underlying physical conditions that may limit the degree and duration of exercise they undertake.

### D) ORAL GLUCOSE·LOWERING AGENTS (OGLAs)

Oral pharmacotherapy is indicated when individualised glycaemic targets are not met by the combination of dietary modifications and physical activity. In some cases, oral pharmacotherapy or insulin is indicated at the first presentation of diabetes, i.e. a fasting blood glucose level > 11 mmol/L or random blood glucose level > 15 mmol/L. Refusal or failure to prescribe OGLAs early may lead to poor control, persistent symptoms, and increased complications rates in the patient, and even a loss of faith in the medical system and a resort to parallel therapies. The OGLAs may be used as monotherapy or in combination therapy as they target different aspects in the pathogenesis of hyperglycaemia in Type 2 diabetes, i.e. increased insulin production and release, decreased insulin resistance and/or decreased hepatic glucose production.

### There are two OGLAs commonly available in PNG – Metformin and Glibenclamide

<u>Metformin</u>	500mg tablets	Starting dose:	500mg daily (1 tablet/day)
		Maximum dose:	1000mg tds (2 tablets 3 times/day)

Metformin is a biguanide. It acts primarily to suppress hepatic glucose output but also causes a modest increase in peripheral insulin-sensitivity. Clinical trials have reported a glucose-lowering effect of **2.2-4.4 mmol/L** with decrease in HbA<sub>1c</sub> of up to **2%**. Because it does not stimulate pancreatic insulin secretion, metformin does not cause hypoglycaemia when used alone. Metformin either maintains or lowers weight and has a beneficial effect on lowering lipid levels. It can cause GI side effects and should be taken with meals and started at a low dose (**500mg daily**). The clinically effective dose range is **1500 mg to 2000 mg/day**, and maximum dose is **3000 mg/day**. Contraindications for metformin include heart (CHF), liver (including alcoholism or alcohol abuse) and kidney diseases (serum creatinine >160 mol/L]) which **increase the risk of lactic acidosis**. Metformin is approved for use during pregnancy.

<u>Glibenclamide</u> ( Daonil)	5mg tablets	Starting dose: 2.5mg daily (Half tablet/day)
		Maximum dose : 10mg BD (2 tablets twice daily)

Glibenclamide (Daonil) is a sulphonylurea. It stimulates insulin secretion from the pancreas. The average glucose lowering effect is **2.8-3.3 mmol/L**, with decrease in HbA<sub>1c</sub> of up to **2%**. The starting dose of glibenclamide is **2.5mg daily, then 2.5mg BD, and** maximum dose is **20 mg/day**. Glibenclamide should be used with caution in renal disease (serum creatinine >200 mol/L) and hepatic dysfunction where the dose may need to be reduced. Glibenclamide and other sulphonylureas are not approved for treatment of hyperglycaemia during pregnancy

### **Combination Metformin and Glibenclamide**

When used in combination, either Metformin or Glibenclamide (Daonil) is used until maximum dose is reached, then the other oral agent is introduced. The second agent may be increased to maximum dose as well. The combination has an average glucose lowering effect of **5.6-6.7 mmol/L** with a decrease of HbA<sub>1c</sub> of **3.5-4%**.

### E) INSULIN THERAPY IN TYPE 2 DIABETES

Insulin therapy is increasingly being used in the successful management of people with type 2 diabetes, either in combination with OGLAs or as a monotherapy so as to achieve optimum glycaemic targets. Initiation of insulin therapy, if indicated, should not be delayed.

### Table 7.1Indications for use of insulin in type 2 diabetes

- Initial presentation with severe hyperglycaemia
- Presentation in hyperglycaemic emergency
- Peri-operative period especially major or emergency surgery
- Other medical conditions requiring tight glycaemic control
- Organ failure (e.g. renal, liver, heart)
- Pregnancy
- Latent autoimmune diabetes of adults (LADA)
- Contraindications to OGLAs
- Failure to meet glycaemic targets with OGLAs (this is the most common reason)

The regimen and dose of insulin therapy vary from patient to patient

- SUPPLEMENTAL THERAPY: NPH insulin administered at 10pm given as a Total Daily Dose calculated by: weight in kg x 0.2 IU of insulin (e.g. 70 kg patient x 0.2 IU = 14 IU insulin). The OGLAs are continued (half maximum dose of sulphonylureas and metformin dose of 2 g/day, or the suphonylureas stopped and metformin continued) and the blood glucose levels are monitored (when possible).
- 2. SUBSTITUTION THERAPY: OGLAs are discontinued (unless the patient is obese where METFORMIN will be continued) and a PRE-MIXED insulin is introduced B.D. at a dosage of 0.2 IU/kg body weight. This is split into 2/3 in the morning and 1/3 in the evening, at 30 minutes before the morning and the evening meals.

If the requirement of insulin exceeds 30 units/day, referral should be considered.

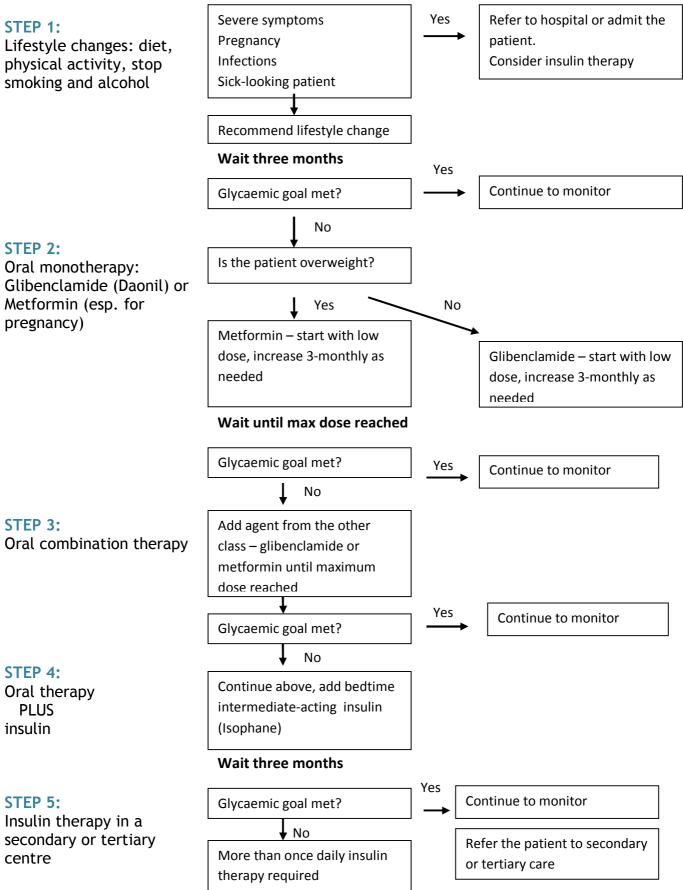
### Table 7.2Time course for action of insulin preparations

INSULIN PREPARATION	ONSET OF ACTION	PEAK ACTION (HOURS)	DURATION OF ACTION (HOURS)	INJECTIONS PER DAY
<b>Rapid-acting analogues</b> (not yet available in the Govt system in PNG)	10-20 min	1-2	3-5	Immediately before meals
<b>Soluble</b> (e.g. Actrapid, Humulin N)	30-60 min	2-4	6-8	30 min. before meals
<b>Intermediate</b> (NPH)	1-2 hr.	5-7	13-18	Once or twice
Lente	1-3 hr.	4-8	13-20	Once or twice
<b>Biphasic mixture</b> 30/70	30 min	2-8	Up to 18 hr.	Usually twice daily
Long-acting analogues (not yet available in the Govt system in PNG)	70 min	no pronounced peak	18-26 hr.	Once

At initiation of insulin therapy and thereafter, appropriate advice on hypoglycaemia, sick days, physical activity, self-monitoring of blood glucose, and diet must be given.

# MANAGEMENT OF DIABETES

### Algorithm on the Glycaemic Management of Type 2 Diabetes



### A) <u>HYPERTENSION IN TYPE 2 DIABETES</u>

Hypertension is frequently associated with Type 2 diabetes and is one of the diagnostic components of the metabolic syndrome. Early and effective treatment of hypertension in Type 2 diabetes prevents cardiovascular disease (CVD), reduces morbidity, mortality, and the rate of progression of renal and retinal disease.

- Determine blood pressure in people with Type 2 diabetes at every visit (measure with a mercury sphygmomanometer and the right-sized cuff with the patient seated)
- Classify blood pressure status using a BP of *130/80* mmHg or more as hypertensive, except if persistent Proteinuria is present, in which case BP should be <125/75
- If hypertensive, perform clinical evaluation to exclude secondary causes of hypertension. If a secondary cause is suspected, refer for comprehensive evaluation
- Monitor serum creatinine and potassium once a year, or more frequently if there is evidence of renal impairment

### What to do

- 1. All people with hypertension should receive non-medication interventions including:
  - weight control
  - regular moderate exercise
  - reduced salt consumption
  - reduced alcohol consumption and advice to avoid binge drinking
  - advice to stop smoking
- 2. If pharmacological intervention is required
  - ACE inhibitors (e.g. Captopril or Enapril) are the preferred agents for treating hypertension in people with diabetes (Captopril dose (25mg tablets) - 12.5mg BD to 50mg TDS or 75mg BD; Enapril 5-10 mg BD
  - Or if ACE inhibitors not available or contraindicated other tablets for hypertension Nifedipine 10-20mg BD, or a beta-blocker in standard doses. Review according to response, refer or gain expert advice if necessary
  - Most people will require more than 1 medication to control blood pressure
  - Avoid combined use of thiazide diuretics and beta blockers which may worsen blood glucose control
  - Common side effects of antihypertensive medication:
    - ACE inhibitors cough
    - Beta blockers slow pulse, cold extremities
    - Calcium channel blockers oedema, palpitations, headache
    - Methyldopa sedation, headache
    - Diuretics electrolyte imbalance, impotence
- 3. Monitor serum creatinine and potassium once a year, or more frequently if there is evidence of renal impairment

# MANAGEMENT OF ASSOCIATED CONDITIONS

AND COMPLICATIONS

### B) **DYSLIPIDAEMIA**

The risk of coronary artery disease and other macrovascular disorders is 2-4 times higher in people with diabetes than in non-diabetic subjects and increases in parallel with the degree of dyslipidaemia.

Aim for Total Cholesterol <5.0 mmol/L, LDL Cholesterol <2.0 mmol/L, HDL >1.0 mmol/L, Triglycerides <2.0 mmol/L (see table page 13)

### Assessment

Measure fasting lipids – total cholesterol and triglycerides, and where possible, HDLC and LDLC as well. *How often:* 

If normal, annually.

If abnormal or on treatment for dyslipidaemia, every 3 - 6 months.

### What to do if results are abnormal:

Use non-pharmacological interventions as initial treatment:

- Improve blood glucose control
- Reduce saturated fat intake
- Ensure regular moderate exercise
- Reduce weight if indicated
- Avoid alcohol intake if triglycerides elevated
- Consider referral to dietician
- Discourage smoking

If the above interventions are unsuccessful after 6 months, refer for pharmacotherapy:

- Statins for raised cholesterol or raised LDL e.g. Simvistatin 20-40 mg daily (1-2 tabs daily)
- Fibrates for raised triglycerides
- Nicotinic acid or fibrates for low HDL

### C) DIABETES AND OTHER CARDIOVASCULAR DISEASES

People with diabetes are 2-4 times more likely to develop cardiovascular disease than people without diabetes.

### The clinical spectrum of cardiovascular disease is:

Coronary heart disease:

- Angina (which may be silent)
- Myocardial infarction
- Congestive cardiac failure
- Sudden death

Cerebrovascular accident:

- Stroke
- Transient Ischaemic Attacks
- Dementia

Peripheral vascular disease:

- Intermittent claudication
- Foot ulcers
- Gangrene

# MANAGEMENT OF ASSOCIATED CONDITIONS

### AND COMPLICATIONS

### Assessment:

- Annual assessment for cardiovascular risk factors.
- Referral to a secondary and/or tertiary institution for evaluation is required/suggested in people presenting with typical, and also atypical but suggestive symptoms of angina, features of congestive cardiac failure, unexplained breathlessness, cardiomegaly, arrhythmias, transient ischaemic attacks or intermittent claudication of the legs.
- Evaluation for coronary artery disease will include ECG, X-ray of the chest (in people with breathlessness) and if warranted an echocardiogram and stress test (if available)
- Evaluation for cerebrovascular disease includes carotid doppler (if available)
- Evaluation for peripheral vascular disease will include dopplers of the lower limbs (if available)

### Management:

- Manage underlying associated cardiovascular risk factors
- Life-style modification
- Initiate aspirin therapy 75-150 mg/day check tablet size as two sizes are available in PNG 100mg (so one tablet per day) and 300mg (so ¼ tablet per day)
- Consider the use of beta-blockers, ACE inhibitors, angiotensin receptor blockers (ARBs) and tight glycaemic control post myocardial infarction
- Coronary angiography, angioplasty or coronary artery bypass graft (CABG) where indicated and available

### **Recommendations for the use of Aspirin**

The use of aspirin in people with Type 2 diabetes reduces vascular events, and is indicated in the following:

- 1. Secondary prevention for coronary and cerebrovascular diseases.
- 2. Primary prevention for people with Type 2 diabetes over the age of 40 years, having:
  - Family history of ischaemic heart disease
  - Cigarette smoking
  - Hypertension
  - Obesity
  - Proteinuria
  - Dyslipidaemia.

However, contraindications may prevent its use, especially the presence or history of peptic ulcers, dyspepsia, heartburn or bleeding. Aspirin should also not be used in uncontrolled (malignant) hypertension

Hemorrhagic stroke must be ruled out before initiating aspirin therapy in patients with acute cerebrovascular accident.

For dosage, see management section above, on this page.

### MANGEMENT OF CHRONIC MICROVASCULAR COMPLICATIONS (KIDNEYS, EYES, NERVES)

These complications (diabetic foot, kidney, eye and nerve) may be present at the time of diagnosis of diabetes, as this is frequently delayed. They can be prevented, or their progression delayed, by optimal treatment of hyperglycaemia and hypertension. Screening for the complications and prompt interventions reduce the risk of major outcomes such as blindness and leg amputations. Prevention and appropriate management of these chronic complications present a considerable challenge in PNG as diagnostic methods for their early detection are either not part of current clinical practice or not available.

### A) NEPHROPATHY (KIDNEY COMPLICATIONS)

Diabetes is becoming one of the most important causes of chronic renal failure. In PNG most patients with diabetic end-stage renal disease die of uraemic complications because of the unavailability of renal replacement therapy facilities.

- Persistent microalbuminuria is a marker for the development of overt nephropathy in diabetes as well as being a well-established marker of increased cardiovascular risk.
- Patients with microalbuminuria who progress to macroalbuminuria (> 300 mg/24 h.) are likely to progress to end-stage renal disease over a period of years.
- Intervention at the stage of microalbuminuria can retard the progression to end-stage renal disease.
- A number of interventions have been demonstrated to reduce the risk and slow the progression of renal disease.

### **Detection and surveillance**

- Check for proteinuria yearly using reagent strips.
- Measure urinary microalbumin excretion yearly (if not proteinuric) and if reagents available using: Semi-quantitative methods (Micral II test strips, Clinitek 50 test strips) or the albumin:creatinine ratio.
- If microalbuminuria is detected, exclude infection by using urine strips to check for nitrites and leucocytes or urine microscopy and culture. Treat infection if present. Re-evaluate for presence of infection at next visit. If there is no evidence of infection retest for microalbuminuria and confirm its presence during the next visit. If proteinuria (trace or greater) is present and there is no infection, confirm at next visit, and if positive, treat and/or refer.
- Measure scrum creatinine annually, and if raised, refer.

# MANAGEMENT OF ASSOCIATED CONDITIONS

### AND COMPLICATIONS

### **General recommendations**

Intensify management of modifiable risk factors Smoking must be stopped Metformin should not be used once the serum creatinine is more than 160 mol/L Treat urinary infections aggressively Avoid drugs toxic to the kidney

### Treatment

- Treat blood pressure aggressively with a target of < 125/75 mmHg
- Use ACE inhibitors or ARBs as first-line drug therapy where possible. These drugs should not be used in pregnancy
- Add diuretics if necessary
- If target blood pressure is not achieved, refer
- Reduce salt intake
- Restrict protein

### B) EYE COMPLICATIONS

Retinopathy is one of the major causes of blindness. Risk factors for retinopathy include poor glycaemic control, nephropathy, hypertension and pregnancy, as well as a long duration of diabetes. Diabetic retinopathy is preventable, and its progression is slowed by improved blood pressure and glycaemic control. Screening for retinopathy and laser therapy can prevent blindness.

### Recommendations

- A full eye examination (preferably after the dilatation of the pupils) including visual acuity and fundoscopy should be performed at the initial visit
- Examinations should be repeated annually, or more frequently if retinopathy is progressing
- A comprehensive eye examination is required in women planning pregnancy, and during the first trimester. Close follow-up is required during pregnancy and for one year thereafter. (This does not apply to women with GDM)
- If retinopathy is present, intensify the management of blood pressure, glycaemia, lipids and stopping smoking
- Give attention to the psychosocial aspects of visual loss when this occurs
- Refer to secondary and/or tertiary care if there is:
  - Unexplained deterioration in visual acuity
  - Cataract
  - Preproliferative, proliferative or exudative retinopathy

### C) **DIABETIC NEUROPATHIES**

Neuropathies arc common complications of diabetes. They play an important role in the increased morbidity and mortality suffered by people with diabetes. Once present, neuropathies are difficult to reverse, but good glycaemic control can reduce symptoms and slow progression. There are three major categories:

- Peripheral neuropathy
- Autonomic neuropathy
- Acute onset neuropathies

# MANAGEMENT OF ASSOCIATED CONDITIONS

AND COMPLICATIONS

### **Clinical Assessment:**

Detailed history: numbness, tingling, pain

Examination of the feet: test for sensation using 10g monofilament, 128 Hz tuning fork or cotton wool (see pages 26-29)

Lying/standing blood pressure (postural hypotension) and pulse

### **General measures:**

Improve glycaemic control

Exclude or treat other contributory factors:

- Alcohol excess
- Vitamin B12 deficiency
- Chronic renal failure
- Poor nutrition

### Treatment

Treatment of symptomatic peripheral neuropathy is extremely difficult Once diagnosed refer to secondary and/or tertiary centre. Some of the drugs used in the treatment of symptomatic peripheral neuropathy or automatic neuropathy are:

- Burning pain: Tricyclic drugs (amitryptyline)
- Lancinating pain: anticonvulsants (Carbamezapine, phenytoin or valproate), tricyclic agents
- Gastroparesis: metoclopropamide ("Maxolon") and domperidone are worth a trial

### D) FOOT PROBLEMS

People with diabetes are at risk of foot ulcers and amputations, which are major causes of morbidity and disability. Education, early recognition, and prompt management can prevent ulcers and amputation.

The most common predisposing factors for ulcers and amputations are:

- Peripheral neuropathy with loss of sensation
- Poor foot hygiene
- Peripheral vascular disease
- Deformities and abnormal biomechanics
- Unsuitable or no footwear

### Cornerstones of management of foot problems:

Identification of the foot "at risk" Regular inspection and examination of the foot at risk Education of health workers, people with diabetes and their families Appropriate footwear Early treatment of non-ulcerative and ulcerative problems Optimise blood glucose, blood pressure and lipid control If the patient smokes, help them to stop

NB - If there are no symptoms it does not mean that the feet are healthy, since the patient can have neuropathy, peripheral vascular disease or even an ulcer without any complaints.

# CONDUCT A FULL EXAMINATION PRESENTATION AND ANNUALLY, OR MORE FREQUENTLY IF RISK FACTORS PRESENT.

### History:

Check for:

- Symptoms of neuropathy (numbness, tingling or pain) and peripheral vascular disease (pain in calves on exercise and at rest)
- History of previous foot problems, such as ulcers or amputations
- Current foot-care practice including barefoot walking, footwear and knowledge

**Examine skin:** Inspect for ulcers, callus, cracking, fragility, dryness, interdigital maceration and nail pathology. Examine lying down and standing up

Vascular: Skin colour, foot and ankle pulses

Neuropathy: Check protective sensation using 10g monofilament

Bones/Joints: Deformities, e.g. claw toes and hammer toes

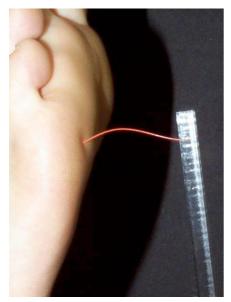
Footwear: Check footwear and socks

### How to examine using the 10 g (5.07 Semmes-Weinstein) monofilament

- Work in a quiet and relaxed setting
- First apply the monofilament on the patient's hands (or elbow, or forehead) so that the patient knows what to expect
- The patient must not be able to see if and where the examiner applies the filament
- Apply the monofilament perpendicular to the skin surface with sufficient force to cause the filament to bend or buckle
- Use the three sites shown below in Figure 8.2
- The total duration of the approach, skin contact, and removal of the filament should be approximately 2 seconds
- Apply the filament along the perimeter of, and not on, an ulcer site, callus, scar or necrotic tissue. Do not allow the filament to slide across the skin or make repetitive contact at the test site
- Press the filament to the skin and ask the patient IF (s)he feels the pressure applied (yes/no) and then WHERE the applied pressure is felt (Left/Right foot).
- Repeat this application twice at the same site, but alternate this with at least one "sham" application, in which no filament is applied (total three questions per site). Protective sensation is present at each site if the patient correctly answers two out of three applications. Protective sensation is absent with two out of three incorrect answers, and the patient is then considered to be at risk of ulceration.
- Encourage the patient during testing.

See pictures on next page for guidance

### Figure 8.1 Monofilament Testing



# Figure 8.2 Monofilament Testing Sites

### **Ankle Pulses**

Figure 8.3 Palpation Dorsalis Pedis Pulse



Figure 8.4 Palpation Posterior Tibial Pulse



At the examination each person's feet must be categorised into: Low Risk or High Risk.

### How often

- Perform routine foot examination every year in all people with diabetes
- Examine feet at more regular intervals in people in other categories (see Table below)

### Table 8.1Interpretation of assessment

INTERPRETATION OF RESULT	WHAT TO DO
Low risk foot	Provide foot care education
Normal sensation, normal pulses, no other abnormality	Examine feet every 12 months
Moderate risk foot	Provide foot care education, advice on appropriate
Neuropathy or	footwear, consider therapy for symptomatic
Absent pulses or	neuropathy, consider further vascular assessment if
Other foot abnormality (except ulcer)	indicated
	Examine feet every 3-6 months
High risk foot	As above and review by foot care service (Diabetic
Past history of ulcer or amputation, or	Clinic/specialist foot care nurse /podiatrist) every 3
'Moderate risk foot' with skin changes,	months
'Moderate risk foot' and unable to self care	
Ulcerated foot – current ulcer	Requires urgent foot care by foot care service
Active foot problem	Treat problem and provide education and regular
Infection, corns, calluses, fissures, nail dystrophy,	follow up
or interdigital maceration	

**Note:** Advise people not to use traditional medicines in the case of foot ulceration or sepsis. Antibiotic therapy should be commenced immediately if there is any evidence of foot sepsis.

### E) SEXUAL DYSFUNCTION

Sexual dysfunction is a well-recognised complication of diabetes. Little information is available on sexual dysfunction in women. In men, erectile dysfunction increases in prevalence with increasing age and has a major psychological impact.

The common causes of erectile dysfunction are psychogenic factors, medications, neurological and vascular.

### Assessment

Ask all people with diabetes whether they are having any sexual dysfunction annually. Refer for vascular investigation if appropriate

### Therapy

If sexual dysfunction is present, counsel the patient and partner, review medications, and refer for special treatment if available

### **GESTATIONAL DIABETES**

- Gestational diabetes mellitus (GDM) is any degree of glucose intolerance first recognised in pregnancy
- If inadequately managed GDM is associated with increased risk of perinatal morbidity and mortality
- Diagnosis and prompt institution of therapy reduces risk of poor pregnancy outcome

### Screening for GDM

When:

- 1. Ideally between 26 and 28 weeks of gestation (or at any time in the 3<sup>rd</sup> trimester if the mother books late).
- 2. Earlier, if there is/are high risk factor(s), and repeat again at 26-28 weeks if the initial test was normal

Whom: Women at high risk for GDM:

- Overweight or obesity (BMI > 30) or weight >85<sup>th</sup> percentile during pregnancy (typically in PNG any mother more than 85 kg)
- Age >35 years
- Ethnicity (high-risk groups Wanigela, Tolai, Buka etc)
- Previous history of GDM
- Persistent Glycosuria on dipstick
- Previous large baby (> 4000 g)
- Poor obstetric history(previous unexplained stillbirth or neonatal death)
- Family history of diabetes
- Known Impaired Glucose Tolerance (IGT) or Impaired Fasting Glycaemia (IFG)
- Polyhydramnios, or fetus feels very big (macrosomic)
- Has been eating non-traditional diet since childhood (eg rice, sugary foods, fatty foods)
- Unexpected pre-eclapmsia i.e. no hypertension in previous pregnancies but now present

### How:

Fasting or 2 hour post-prandial Blood Sugar Level,

### or if possible

75 g OGTT - In the morning after a 10 h. overnight fast with blood sample at 0 h. and 2 h. for measurement of blood glucose.

What level is diagnostic for GDM?

- Post-prandial plasma glucose (2 hours after a normal meal) persistently >7 mmol/L
- OR
- Fasting plasma glucose >5.1 mmol/L
- OR
- 2hr plasma glucose > 8.0 mmol/L

### MANAGEMENT

Ideally GDM is best managed by a combined health-care team (obstetrician, diabetologist or internist, diabetes educator, paediatrician). However this is often not possible, and obstetric doctors may need to manage GDM themselves.

### Glycaemic targets for pregnancy: blood glucose:

- preprandial 3.5 5.5 mmol/L
- postprandial 5 8.0 mmol/L

### PREGNANCY AND PRE-PREGNANCY COUNSELLING IN DIABETICS

- Major congenital abnormalities are important causes of morbidity and mortality in infants of diabetic mothers
- Excellent glycaemic control both before pregnancy and during the 1st to 3rd trimesters has resulted in a marked reduction in the rates of congenital malformation and perinatal morbidity
- But, since many pregnancies are unplanned, there is still an unacceptably high rate of congenital malformations in these infants

### Care before pregnancy

All diabetic clinics should keep careful track of whether their female patients are wanting to get pregnant or not. If not, then provide reliable contraception (e.g. Depoprovera, Pills, IUCD or tubal ligation).

If inquiry reveals that pregnancy is planned:

- Educate on the need for metabolic control before and during pregnancy
- Aim at good glycaemic control (HbA1c < 1% above normal range) before pregnancy is planned
- Teach self-blood glucose monitoring (SBGM) if available
- Tighten glycaemic control
- Use contraception until adequate metabolic control
- Normalise BP (<130/80 mmHg) if hypertensive
- Discontinue ACE inhibitors if being used
- Stop smoking
- Inform that insulin may be required when pregnant and Oral Glucose Lowering Agents (OGLAs), except metformin, will be stopped
- Refer to antenatal clinic as soon as pregnancy is diagnosed

### Pregnancy care

Joint care is preferable, involving an obstetrician, physician, diabetes educator, dietitian, and paediatrician.

Principles of management include:

- Educate on need for strict diabetic diet and regular exercise
- Tight metabolic control with either oral Metformin or Actrapid insulin with each meal and Isophane at 10pm
- Careful monitoring of the pregnancy and screening for pre-eclampsia
- Delivery at term
- Special care with the baby, particularly with regards to risk of neonatal hypoglycaemia

**TYPE 1 DIABETES IN CHILDREN** 

### TYPE 1 DIABETES IN CHILDREN

Type 1 diabetes in children and adolescents is very rare in PNG. The pathophysiological process is different from type 2 diabetes – in type 1 an autoimmune process destroys the insulin-producing ( $\beta$ -cells) in the pancreas.

Symptoms are the same as type 2 – excessive drinking, urination, and eating, also weight loss and sometimes visual disturbances as well. The history is more rapid, and many subjects presenting with diabetic ketoacidosis (see page 37). <u>Diabetic ketoacidosis is a medical emergency.</u> It is often misdiagnosed initially as pneumonia, malaria, typhoid or gastroenteritis.

Patients with type 1 are insulin-dependent from diagnosis. Blood glucose swings are more marked than in type 2. Oral medications such as metformin and glibenclamide are of no benefit, and should not be used.

Complications are essentially the same as with type 1.

Details of management of type 1 diabetes in children are beyond the scope of these guidelines. Type 1 diabetes in children and adolescents is a challenging disorder to manage, and carries a high mortality in developing countries. However, expert care, combined with thorough education of the patient and family, can lead to long-term survival and a good quality of life.

If you diagnose a child with diabetes (type 1 or type 2) – please seek expert advice from senior paediatricians in Port Moresby. <u>www.idf.org/lifeforachild/diabetes-education-resources/english</u> has comprehensive international guidelines and education resources.

The International Diabetes Federation *Life for a Child* program can help with supplies for children with diabetes (type 1 or type 2) in PNG. Please contact HOPE *worldwide* (PNG) or see <u>http://www.diabetes.hopewwpng.org.pg/resources.html</u>

# MANAGEMENT OF TYPE 2 DIABETES DURING SURGERY

Minor surgery can be done at a primary level (e.g. abscesses, ulcers). All other surgery should be referred to a hospital as secondary care is required.

### MANAGEMENT

### Pre operatively:

Delay surgery if possible if glycaemic control is poor:

- HbAlc >9%;
- Fasting Blood Glucose > 10 mmol/L
- Random Blood Glucose > 13 mmol/L

Optimise glycaemic control if surgery is elective.

Screen for complications that may affect surgical risk: - nephropathy, cardiac disease, proliferative retinopathy, neuropathy. Inform surgical team of the complications.

### If on diet and/or oral agent therapy and surgery is minor:

- Omit therapy on morning of surgery
- Resume therapy when eating normally

### If on insulin therapy or poor glycaemic control or major surgery:

Use sliding-scale insulin injections, or if possible the glucose-insulin-potassium regimen

### Table 11.1 Suggested Insulin Regimens during Surgery

- SLIDING SCALE	OPTIMAL - GLUCOSE-INSULIN- POTASSIUM REGIMEN
Injections of short-acting insulin every four hours If BGL give < 8mmol/L no insulin 8-12 mmol/L 4 Units 12-16 mmol/L 8 Units >16 mmol/L 12 Units	<ul> <li>Start at 8 am and stop when eating normally.</li> <li>Monitor blood glucose before, during and after surgery.</li> <li>Aim for blood glucose levels of 6 - 10 mmol/L</li> <li>Add 16 U short-acting insulin and 10 mmol/L potassium chloride to 500 ml 10% dextrose.</li> <li>Infuse IV at 80 ml/h. using a volumetric pump.</li> <li>If obese or initial blood glucose is high consider higher dose (20 U).</li> <li>If very thin or usual insulin dose is low consider lower dose (12 U).</li> <li>If blood glucose high or rising increase dose by 4 U.</li> <li>Continue the infusion until 60 min. after the first meal.</li> </ul>

# **DIABETES AND INFECTIONS**

Some infections are more common in people with diabetes. They can also be harder to cure, due to hyperglycaemia, microvascular disease, and other factors. A relationship with diabetes occurs in two infections of great concern in PNG: tuberculosis and HIV.

### Tuberculosis

Tuberculosis is more common in people with diabetes, and, as diabetes increases in PNG, tuberculosis control may be harder to achieve.

HIV

There have been reports that persons who are HIV positive and not on anti-retroviral therapy, have double the rates of diabetes, compared to persons who are HIV negative.

Highly active anti-retroviral therapy (HAART), including protease inhibitors, have dramatically improved morbidity and mortality rates in HIV infected patients, but may also induce glucose intolerance and diabetes in those at risk.

# ACUTE METABOLIC COMPLICATIONS OF DIABETES

People with diabetes who present with coma or altered levels of consciousness may have one of the metabolic emergencies of diabetes - ketoacidosis, non-ketotic hyperosmolar states, hypoglycaemia, and lactic acidosis. (Other considerations of this presentation include stroke, seizures, trauma, drug overdose, infection, and ethanol intoxication).

The two main diabetic emergencies with elevated blood sugar levels are:

- Diabetic Ketoacidosis
- Hyperosmolar non-ketotic hyperglycaemia

They both carry a high mortality, but with good treatment most recover fully. People with these conditions must be admitted to a hospital.

### 1) DIABETIC KETOACIDOSIS (DKA)

### Precipitating cause:

- Delayed presentation of Type 1 diabetes
- Inappropriate reduction or omission of insulin dose
- Acute infection
- Myocardial infarction (may be silent), stroke
- Trauma, surgery, emotional disturbance

### Symptoms and Laboratory Findings:

- Abdominal pain, vomiting, confused or comatosed, fruity breath (acetone), dehydration
- Serum glucose- elevated: positive (+++) ketones, acidosis (pH<7.3)

### 2) HYPEROSMOLAR NON-KETOTIC HYPERGLYCAEMIA (HONK)

- Usually occurs in Type 2 Diabetes
- HONK takes longer to develop than DKA
- Associated with severe dehydration, diuretics, cerebrovascular and renal diseases

### Symptoms and Laboratory Findings:

- weight loss, dehydration, polyuria, polydipsia, comatose
- serum glucose usually very high: high plasma osmolality 300-400 mosmol/L, no lactic acidosis, negative or mild ketones

### Treatment

See flow chart following page.

# ACUTE METABOLIC COMPLICATIONS OF

DIABETES

### TREATMENT OF DIABETIC EMERGENCIES

# Diabetic Ketoacidosis (DKA) & Hyperosmolar Non-Ketotic Hyperglycaemia (HONK)

Type 1 or 2 Diabetes Mellitus with probable DKA or HONK **Initiate Fluid Management** • 1 litre Normal saline first hour, then 1 litre over next 2 hours continue fluid replacement at about 250mls/hr with Normal Saline for DKA or 0.45% Saline for HONK when BSL<15mmo/l, change IV fluids to 5%Dextrose **Start IV Insulin Therapy** Give IV insulin loading dose Humulin R/Actrapid 10 units stat IV (or IM if IV not • immediately possible) Set up Insulin Infusion (50 units Humulin R/Actrapid in 100mls Normal Saline); running rate initially is 5-10 units per hour Monitor BSL closely every ½ to 1 hour while patient is on Insulin Infusion BSL should fall by 4-5mmol/l per hour, aim for BSL 8-11 mmol/l, and avoid lowering below 8 mmol/l **Other Measures** Consider antibiotics cover if infection Electrolytes (K+ / Na+) Management suspected Normal K+ level: start 20mmol KCL with each litre IV replacement fluids DKA implies Type Low K+ level: start 40mmol KCL with each litre IV replacement fluids 1 diabetes No K+ replacement in chronic renal failure, anuria, or initial K+ level >6mmol/l Severe infection, Hypernatraemia (Na+>150mmol/l) may result from rehydration, and is usually MI, other acute transient. If persistent, hypotonic saline (0.45%) may be used stress can cause DKA in Type 2 diabetes

### **Determine cause of DKA**

• Acute illness

.

- Infection
- Patient not taking insulin
- Degraded insulin from improper storage or insulin past expiration date

### **Determine cause of HONK**

Consider subcutaneous

- Patient not taking medication
- Intercurrent event (eg myocardial infarction)
- Infection (eg foot ulcers)
- Degraded insulin from improper storage or insulin past expiration date
- New treatment started recently that may elevate glucose (eg steroids)

# ACUTE METABOLIC COMPLICATIONS OF

### DIABETES

### 3) <u>HYPOGLYCAEMIA</u>

Hypoglycaemia is a medical emergency and should be treated promptly if serious complications are to be avoided.

The commonest causes of hypoglycaemia are:

- Taking more exercise than usual
- Delay or omission of a snack or main meal
- Poor injection technique
- Administration of too much insulin
- Eating insufficient carbohydrate
- Over-indulgence in alcohol
- Mistake in sulphonylurea dosage

### Acute management:

- 1. Oral glucose if patient is conscious
- 2. If patient is unconscious an IV 50% glucose bolus (40 50 ml) or 100 150 ml of 20% dextrose followed by 8-10% glucose infusion if necessary
- 3. Injectable glucagon can also be administered in unconscious patients
- 4. On recovery give a longer-acting carbohydrate snack
- 5. Prolonged slow IV dextrose infusion (5 10% for 12 24 h.) may be necessary if hypoglycaemia is as a result of long-acting sulphonylureas/long and intermediate-acting insulin or alcohol
- 6. If IV access is impossible, consider nasogastric or rectal glucose; or if available glucagon 1 mg IM
- 7. On recovery, attempt to identify the cause of hypoglycaemia and correct it
- 8. Assess the type of insulin used, injection sites (since lipohypertophy can alter the rate of absorption) and injection techniques
- 9. Enquire into and correct inappropriate habits of eating, exercise and alcohol consumption
- 10. Review of other drug therapy and renal function
- 11. Adjustment of insulin or OGLA dosages if appropriate

# LIVING WITH DIABETES

### **EMPLOYMENT**

A person with diabetes, particularly if using insulin, faces many problems in daily life. Health-care providers should be aware of these problems so that they can give appropriate advice.

The commonest problem is prejudice from employers. Such prejudice is usually because of ignorance and the belief that all people with diabetes have poor work performance and have regular interruptions as a result of hypoglycaemia. This causes some people with diabetes to try to conceal their diabetes from their employers and workmates. This must be discouraged as concealment may result in grave consequences in case of attacks of hypoglycaemia.

Shift work and irregular working hours can present problems but these can be overcome. A person with diabetes, depending on their qualifications, could apply or be eligible for most jobs.

### DRIVING

Hypoglycaemia is one of the common medical causes of road accidents. There is often discrimination against a person with diabetes applying for a driving license. All drivers must act responsibly and schedule their medications and eating pattern to avoid hypoglycaemia.

Commercial drivers on insulin and insulin secretagogues should be advised to inform their employers and the licensing authorities.

### Advice to drivers:

- Inform insurance company
- Always keep glucose or sweet eatables in the vehicles
- Never drink alcohol and drive
- Never drive if a meal has been missed

### Insurance

Most people with diabetes are asked to pay additional premiums for life assurance and sickness insurance. Some are denied insurance outright. There should however be unbiased access to insurance policies (life or sickness) at a reasonable cost.

### SPORTS, RECREATIONAL AND OCCUPATIONAL EXERCISE

- Treatment with insulin and OGLAs do not preclude vigorous sports and exercise, unless there is underlying heart disease or significant microvascular complications, e.g. advanced retinopathy
- There is a possibility of hypoglycaemia as a consequence of exercise or vigorous sports
- Hypoglycaemia may even occur some hours after exercise, possibly because the liver and muscles are still replenishing glycogen stores
- Exercise or sports may need to be accompanied by extra food or adjustment in OGLA or insulin dosage
- If vigorous sporting activity is being considered, the person should not have any contraindication to such activity and be in good metabolic control. Detailed advice from a health provider should be sought to reduce the risk of hypoglycaemia

# APPENDIX I

### **Requirements for a primary level diabetes clinic**

### STAFF

- HEO or Doctor
- Nurses
- Diabetes educator and dietitian if possible

### CLINIC REQUIREMENTS

- 1. Clinic room with nearby toilet
- 2. Furniture and fittings
  - Doctors table
  - Nurses table
  - Examination couch with sheets and screen
  - Storage cupboard/cabinet
- 3. Equipment
  - Clinical practice guidelines
  - Blood glucose meter with strips
  - Urine test strips
  - Refrigerator
  - Tape measure
  - Weight scale
  - Height measure
  - Sphygmomanometer with 2 cuff sizes
  - Stethoscope
  - Monofilament
  - Reflex hammer and/or Tuning fork (128 Hz)
  - Education posters and leaflets
  - Emergency treatment tray
- 4. Maintaining an inventory and statistics
  - Inventory book of equipment, supplies and literature, so clinic can remain well stocked
  - Monthly clinic statistics of new patients and follow-up

### Monitoring the quality of care

Periodic monitoring of the quality of care provided, and instituting changes to rectify deficiencies that are identified should form an integral component of health-care delivery. This requires the setting of target standards based on the National guidelines.

### Some examples of indicators for monitoring include:

MEASUREMENT	CALCULATE			
PROCESSES OF CARE				
Blood pressure measurements at every visit	Percent of patients screened in 1 year			
Feet examinations	Percent of patients screened in 1 year			
Screening for proteinuria/microalbuminuria	Percent of patients screened in 1 year			
Screening for retinopathy	Percent of patients screened in 1 year			
Education given	Percent of patients educated in 1 year			
INTERMEDIA	<b>TE OUTCOMES</b>			
HbA1C levels	Percent of patients achieving target			
Blood glucose levels	Percent of patients achieving target			
Blood pressure levels	Percent of patients achieving target			
Cholesterol levels	Percent of patients achieving target			
Triglyceride levels	Percent of patients achieving target			
HDL levels	Percent of patients achieving target			
Blood pressure control in hypertensives	Percent of patients achieving target			
Retinopathy	Percent of patients with retinopathy			
TRUE OUTCOMES				
Leg Amputations	Incidence			
Stroke	Incidence			
Blindness	Incidence			
End-stage renal failure	Incidence			
Myocardial infarction	Incidence			
RISK FACTOR CONTROL				
Smoking	Percent of patients smoking			
Obesity	Percent of patients obese			
Physical activity	Percent of patients exercising			

Forms that can be used in Clinics

### DIABETES REGISTER FORM - INITIAL DIABETES ASSESSMENT

Date:	Centre:				
Name:			_Sex:	Age:	DOB:
Type of DM: 1 / 2 /G	DM	Hospita	l No		
Date Diagnosed:			_Village:		
Family Hx of DM			_Occupatio	on:	
Alcohol:			_Smoking:		
Relevant Medical Hx:					
<u>Treatment</u>					
Glibenclamide:					
Metformin:					
Insulin:					
Blood pressure medicat					
Other:					
Weight:				aist circumfe	rence
Blood Pressure:	HbA	1c	_Blood Sug	ar:	
Blood glucose meter / L	.aboratory; Fasting /	Non-Fastin	B		
Problems:					
General:					
• Feet:					
pulses D Pedis	post	tibial			
Nerves: symptoms :	:				
Monofilament (L)	(R)				
Reflexes : AJ (L)	(R)	Others :	impotence	e,	
• Vascular (CVA / IHE	D / Hypertension / etc	:.)			
Cholesterol :					
-					_Cr
Visual Acuity : (L)	(R)	Fundi (L	)	(R)	
Hospital admissions	s related to DM :				
Dr /RN/ other			Date :		

## **DIABETES REGISTER FORM - CONTINUING ASSESSMENT**

Name:	DOB:	Date of diagnosis		
DATE				
Weight (aim BMI <25)				
Blood Pressure (aim BP ≤130 / 80)				
BSL / Glucose (fast / non-fast)				
HbA <sub>1c</sub> (aim ≤ 7%)				
Lifestyle (smoke, diet, alcohol, exercise)				
	Feet			
Monofilament				
Pulses				
Skin infection				
Ulcer, amputation				
	Eyes			
Visual Acuity				
Fundi				
To Ophthalmologist				
	Kidneys			
Dipstick urinalysis for proteinuria				
BUN				
Creatinine (N<130 μmol/l)				
	Lipids			
TC: (N<5.0 mmol/l)				
HDL:(N>1 mmol/l)				
LDL:(N< 2.0				
mmol/L)				
TG: (N<2 mmol/l)				
Treatment/Change				

### FASTING FOR RELIGIOUS PURPOSES

All the major religions recommend or command one form of fasting or another. Fasting for religious purposes is possible in certain circumstances in people with diabetes.

### **General Principles**

- The health provider should be consulted on whether fasting is safe, given medical grounds
- Advice from the religious leader should also be sought as to whether (s)he can be exempted
- Check the level of glycaemic control using HbA1c or fasting blood glucose. Those in very poor control should be discouraged from fasting
- Drug dosage review is required for patients with fasting blood glucose ≤5mmol/L
- If on insulin or insulin secretagogues, drugs dosages and timing will require adjustment during the period of food denial to meet calorie intake
- A total fast (from food and water) is not recommended for people with diabetes. Adequate hydration is important even during the period of fasting
- Self-blood glucose monitoring is optimal for people with diabetes who elect to fast. Once-a-day monitoring is adequate for patients on diet only or diet with metformin.
   In patients on glibenclamide, SBGM should be done at least three times a day. Doctor and patients should agree on how to handle abnormal results of SBGM before start of fast.
- If hyperglycaemia is marked, testing should be more frequent and the urine tested for ketones
- Vigorous activity should be avoided during period of fast
- People who fast should have ready access to their health-care providers during the period of fast
- Clear guidelines should be set as to when to terminate the fast, e.g. frequent hypoglycaemia, intercurrent infection

A normal fast or the "Common fast" is when the fasting person abstains from all foods (solid or liquid) for a limited time, except that they can drink water at any time.

In partial fast, the so-called "Daniel fast", the subjects abstain from selected foods and drinks. The foods consumed usually consist of fruits, vegetables and water. Choosing to fast or to omit a certain meal each of the fasting days is also taken as partial fast.

The purpose of fasting can also be met by denying oneself other pleasures and entertainment. The pleasure fast involves setting aside one's favourite form of entertainment such as watching TV, listening to the radio, newspapers, etc. for the fasting period.

If a person with diabetes intends to fast:

I. If the type of diabetes or treatment precludes any of the traditional type of fasting, then another form of fasting, e.g. pleasure fast, can be chosen

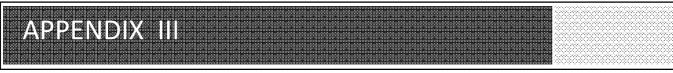
2. If medically eligible to fast, the fast that best suits the person's type of diabetes should be selected in consultation with the health-care provider

3. If patient is on insulin, a partial fast is preferred to absolute or normal forms of fasting

### Ramadan (fast of the Moslem faith)

Patients on metformin can continue taking the usual doses at the usual times. If on glibenclamide (Daonil), this should be taken before breaking the fast and not before dawn.

For Type 2 patients on Insulin, if on once daily insulin before bed, this can be given as usual. If on twice daily short- and intermediate-acting insulin: Before the dawn meal, give the usual evening dose of short



acting insulin without any intermediate acting insulin. Before the evening meal give the usual morning dose of short-acting and intermediate-acting insulin.

# The Table below summarises broad suggestions to Christians and others who elect to embark on fasting during lent or a similar occasion:

TREATMENT REGIMEN	FASTING REGIMEN	WHEN TO TAKE ANTIDIABETIC AGENTS
Diet only	Normal or partial fast	Not applicable
Metformin	Normal or partial fast	With meals
Sulponylureas –	Partial fast	Before meals
glibenclamide		
Daily intermediate or long-	Partial fast	Before first meal
acting insulin		
Multiple insulin doses using	Avoid fasting, or pleasure	Not applicable
intermediate and short-	fast	
acting		
Complex medications	Pleasure fasting	Not applicable



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