Type 2 Diabetes
Practical Targets and Treatments

Third edition

Screening
Diagnosis
Management
Treatment
Monitoring
Education

Jointly supported by an educational grant from Bayer AG and GlaxoSmithKline Pte Ltd to the International Diabetes Federation (IDF) Western Pacific and International Diabetes Institute (IDI), a World Health Organization (WHO) Collaborating Centre for Diabetes.

Endorsed by the WHO Western Pacific Regional Office, IDF Western Pacific Region, Secretariat of the Pacific Community and Western Pacific Diabetes Declaration.

Asian-Pacific Type 2 Diabetes Policy Group
The Western Pacific Declaration on Diabetes

We, the World Health Organization Regional Office for the Western Pacific (WHO/WPRO), the International Diabetes Federation, Western Pacific Region, and the Secretariat of the Pacific Community, the signatories of this document, unite to highlight the serious nature of diabetes, currently estimated to affect at least 30 million people in the region. We, on behalf of people affected by diabetes, jointly call upon all governments, organisations and individuals in the region to undertake the following actions, according to the needs of each country:

1. Recognise the personal, public and economic burden of all types of diabetes and establish diabetes as a priority health concern.

2. Develop and implement national strategies and programmes to prevent and control diabetes, and reduce its risks.

3. Work towards universal access to quality care, training, essential diabetes medications, and other supplies and support for all people with diabetes.

4. Encourage a strategic alliance among governments, international and regional development agencies, health and non-health sectors, mass media, industrial partners, non-governmental organisations, and other stakeholders involved in the prevention and care of diabetes.

5. Recognise and promote the importance of education for people affected by diabetes, health professionals and the general public in the prevention and management of diabetes.

6. Integrate diabetes activities with those of other non-communicable diseases in order to promote healthy lifestyles and environments for the prevention and control of diabetes and its complications.

7. Recognise and address the problem of discrimination against people with diabetes.

8. Encourage research to advance and apply knowledge about the effective prevention, delivery of care and management of diabetes.
The Asian-Pacific region continues to be at the forefront of the type 2 diabetes mellitus epidemic, with consequences to health which threaten to be devastating. It is also becoming increasingly apparent that younger members of our communities are not spared from this disease, with a significant problem emerging in the urbanised young in more affluent parts of the region. Lifestyle changes and urbanisation appear to be the root causes of this problem, and continue to accelerate in the new millennium.

Overwhelming evidence indicates the need for optimal glycaemic control of type 2 diabetes if the impact of long-term microvascular complications is to be minimised. The UK Prospective Diabetes Survey has also highlighted the importance of both good glycaemic control and good blood pressure control. This has been shown to be most relevant in the prevention of stroke and is, therefore, particularly important in this region where stroke is a significant cause of diabetes-related mortality.

Since publication of the second edition of *Type 2 Diabetes Practical Targets and Treatments*, new proposals for the diagnostic criteria and classification of diabetes have been put forward. This third edition produced by the Asian-Pacific Type 2 Diabetes Policy Group is, therefore, timely. It provides an opportunity to update and revise those areas covered in the first and second editions, and to add new information in other areas, particularly with regard to diagnostic criteria and classification, the role of exercise, management of type 2 diabetes in children and adolescents, and management of other cardiovascular risk factors.

These guidelines have the support of the International Diabetes Federation, Western Pacific Region, and have been produced specifically with the needs of our region in mind. It should be emphasised that they are meant to complement rather than replace individual or national guidelines, to add the authority that can be provided by a regional approach as an additional support for national guidelines, and also to provide guidelines for those countries that do not have their own.

I recommend this booklet to you and sincerely hope that it will be used widely by a variety of healthcare professionals in all countries within the region.

Professor Sir George Alberti
International Diabetes Federation
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Preface

The non-communicable diseases (NCD) epidemic has overwhelmed the historical health problems of the Western Pacific Region (WPR) and is now the leading cause of mortality. Within the cluster of NCD, diabetes has become one of the most daunting causes of sickness and death. The current number of people with diabetes in the region is estimated to be 30 million and this number will increase to at least 55 million by the year 2025. Recent data show that the prevalence of diabetes is increasing rapidly in countries where significant socioeconomic changes are occurring, and there is a particularly high prevalence in Pacific Island countries.

However, the news is not all bad. There is now irrefutable evidence that diabetes can be prevented in people at high risk, and that the progression of many of the complications associated with diabetes can be halted. Appropriate diet and physical activity, maintaining a healthy body weight, refraining from tobacco smoking, and proper control of diabetes and blood pressure in people with diabetes will help prevent diabetes and reduce its complications. The means to do this are within the reach of most countries’ budgets. The issue is now not whether but how to deliver these solutions to the people of the region. Each country needs to develop appropriate guidelines for the prevention and control of diabetes, and set up systems to ensure that its guidelines are adhered to.

In some developing countries in the WPR, as many as three out of every four people with diabetes remain undiagnosed. Even when diagnosed, only about two-thirds are undergoing optimal management (non-drug and drug), even in developed countries; and of those undergoing treatment, only one-third are properly controlled.

In partnership with Member States and with the International Diabetes Federation, Western Pacific Region (IDF-WPR) and the Secretariat of the Pacific Community, the World Health Organization (WHO) supported the development of the Western Pacific Declaration on Diabetes in 2000, as well as its associated Plan of Action. As part of this collaboration, the WHO is supporting the development of customised clinical management guidelines for diabetes in Member States. This has now been achieved with WHO support in China, Mongolia, Vietnam and many Pacific Island countries. Other countries and other partners have proceeded with this work such that clinical guidelines will soon be within the reach of most primary-care workers in the region. The next challenge will be to ensure that they are trained in the application of these guidelines, they have the appropriate tools to work with, and that effective control is achieved and sustained.

As an important resource in this work, I am pleased to present this third edition of Type 2 Diabetes Practical Targets and Treatments. This publication is a joint enterprise of the Type 2 Diabetes Policy Group, the IDF-WPR and the WHO Regional
I welcome this new edition of the International Diabetes Federation, Western Pacific Region (IDF-WPR) Type 2 Diabetes Practical Targets and Treatments guidelines.

The IDF-WPR is a vast region, with tremendous variation in living standards and availability of medical services. Yet it has the world’s largest potential and existing number of people with diabetes.

We need to acknowledge that providing a recognised process of care to everyone with diabetes or at risk of diabetes in the Western Pacific Region is a daunting process, and that any set of guidelines must necessarily take into account the vast differences extant in the region in order to be relevant and useful.

Nevertheless, guidelines help to point the way ahead. No matter what our limitations, and no matter how successful we feel we currently are in the fight against diabetes, we must focus on ensuring that we deliver a recognised process of care to as many people with diabetes as possible, and help them all to reach their appropriate treatment goals.

Dr Warren Lee
Chairman
International Diabetes Federation
Western Pacific Region
Chairmen’s Statement

The number of people with diabetes worldwide currently is believed to be about 150 million. By 2025, this number is expected to increase to over 300 million, with the majority of people having type 2 diabetes.

It is well known that most patients with diabetes have type 2. The Asian-Pacific region holds one-third of the world’s population, and includes a variety of ethnic groups. The type of diabetes in this region is predominantly type 2; however, a large pathophysiological difference exists when comparing type 2 diabetes in other ethnic groups with type 2 diabetes in Caucasians.

Following the publication of the European NIDDM Policy Group’s *Desktop Guide for the Management of Non-insulin-dependent Diabetes Mellitus* in Europe, the Asian-Pacific NIDDM Policy Group met on 1 April 1994 with the aim of producing a document for this region. Information was obtained from all of the regional Diabetes Associations and from many key diabetologists. Our aim was to reach a consensus for all the countries involved; it was a difficult task to produce an agreement that has something in common with all of the nations.

However, our ultimate goal was to target the prevention and management of type 2 diabetes, and, thus, a first edition of *Type 2 Diabetes Practical Targets and Treatments* was published. This was updated in 1999 as a result of new suggestions from the World Health Organization (WHO) and the American Diabetes Association (ADA) for diagnostic criteria and classification. Now, in 2002, with the availability of new medications and new data on the prevention of type 2 diabetes, a revised version has become essential. A similar procedure to gain consensus has been followed, and we sincerely hope that this third edition will be an important and useful reference for clinicians and other health professionals involved in caring for people with diabetes.

It has been noted that there is an increasing occurrence of type 2 diabetes in younger age groups than previously, and this issue has been addressed in the current publication. We are fortunate to have the distinguished paediatrician, Professor Martin Silink, provide a youthful perspective on the growing international problem of type 2 diabetes.

In addition, the Western Pacific Declaration on Diabetes 2000–2005 is another new and welcome initiative that will help set the stage for greater awareness of, and action on, type 2 diabetes in this region.
Finally, we would like to extend our sincere thanks to Dr Shigeru Omi, Regional Director of the WHO, Western Pacific Region, and Dr Warren Lee, Chairman of the International Diabetes Federation, the Western Pacific Region, for their active support and collaboration in assisting with the revised guidelines.

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Please see Appendix I
Type 2 diabetes is one of the major public health concerns in both developing and developed countries in the Asian-Pacific region. It has become epidemic in a number of countries, particularly in newly industrialised nations. The direct and indirect social and economic costs of treating diabetes and its complications have the potential to cripple the countries’ healthcare budgets.

The prevalence of type 2 diabetes shows a wide range across adult populations (age 30 years and over) from approximately 2% in the Peoples’ Republic of China to 40–50% in some areas of Papua New Guinea and Nauru. Rates for type 2 diabetes in selected countries in the region are shown in Figure 1. Ethnic groups at particularly high risk of type 2 diabetes are Micronesians, Polynesians, certain Melanesians, migrant Asian Indians and Chinese, and Australian Aborigines.
**Introduction**

Type 2 diabetes is a major cause of premature morbidity and mortality, particularly from cardiovascular disease (CVD), cerebrovascular disease, amputations and renal failure. In many instances, type 2 diabetes is seen clinically as part of the Metabolic Syndrome, a cluster of major CVD risk factors also referred to as ‘Syndrome X’ or the ‘Deadly Quartet’.

Thus, the management of type 2 diabetes must address not only the control of hyperglycaemia but also the other CVD risk factors such as dyslipidaemia, hyperinsulinaemia, hypertension and obesity. Strategies for this approach are provided in this important consensus document.

Many of the complications of type 2 diabetes that contribute to the high cost of the disease, such as foot ulcers resulting in complications, are potentially preventable, and strategies for this and other preventable morbidities associated with type 2 diabetes are also addressed.

Recently, both the American Diabetes Association (ADA) and the World Health Organisation (WHO) have re-examined, redefined and updated the classification (see Appendices III and IV) and criteria for diabetes (see page 10). Both groups met separately, with cross-representation from both parties. The major update in the diagnostic criteria for diabetes mellitus from the previous WHO recommendations is the reduction of the diagnostic value of fasting plasma glucose (FPG) concentration from ≥7.8 mmol/L (140 mg/dl) to ≥7.0 mmol/L (126 mg/dl). For whole blood, the proposed new level was lowered from 6.7 mmol/L (120 mg/dl) to ≥6.1 mmol/L (110 mg/dl).

This change is based primarily on cross-sectional studies demonstrating the development of microvascular and macrovascular complications at the lower glucose levels. In addition, the use of the 1985 WHO criteria to diagnose diabetes found that FPG and 2-hour plasma glucose detect different sectors of the hyperglycaemic state. The WHO FPG criterion for diabetes of 7.8 mmol/L (140 mg/dl) represented a greater degree of hyperglycaemia than the 2-hour plasma glucose criterion for diabetes of 11.1 mmol/L (200 mg/dl), and an FPG of 7.0 mmol/L (126 mg/dl) provided closer parity. The change has been incorporated into this revised version.

Please note that all values cited in this document refer to venous plasma glucose unless otherwise indicated.
Corresponding values for capillary plasma are: for diabetes mellitus, fasting >7.0 mmol/L (>126 mg/dl), 2 hours >12.2 mmol/L (>220 mg/dl); for IGT, fasting <7.0 mmol/L (<126 mg/dl), and 2 hours >8.9 mmol/L (>160 mg/dl) and <12.2 mmol/L (<220 mg/dl); and for IFG >6.1 mmol/L (>110 mg/dl) and <7.0 mmol/L (<126 mg/dl) and, if measured, 2 hours <8.9 mmol/L (<160 mg/dl).

For epidemiological or population screening purposes, the fasting or 2-hour value after 75 g oral glucose may be used alone. 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.

**Note that random glucose cannot be used to diagnose IGT or IFG. Most screening programmes use either a fasting or a random glucose measurement as the first step. However, epidemiological studies have shown that with the current diagnostic thresholds, a significant proportion of people have isolated abnormalities of either the fasting or the post-load state. These people could, therefore, be incorrectly classified as normal by a single screening test, unless an oral glucose tolerance test (OGTT) is performed. In order to reduce the number of people who are missed in this way, it is recommended that an OGTT is performed on all people who have high normal fasting or random glucose values. Recent data suggest that an OGTT should be performed on all people suspected of, or at risk of having, diabetes with an FPG of 5.6–6.9 mmol/L, or a random plasma glucose of 6.5–11.0 mmol/L.
Guide to the Classification of Diabetes

Type 1 or Type 2?

When taken in isolation, blood glucose levels are not useful for classification of diabetes. In fact, no single feature is diagnostic, apart from moderate to heavy ketonuria, which is the hallmark of type 1 diabetes. Some experts may even have difficulty with the initial classification.

In addition, as a result of the recently described condition, latent autoimmune diabetes in adults (LADA), there may be problems in classifying the type of diabetes in young adults. LADA can present initially like type 2 diabetes, but will progress to insulin dependency within months. If there is any uncertainty in diagnosis, a provisional classification should be made and reassessed after an initial response to therapy. Results from a number of studies, including the ASDIAB initiative, indicate that measurement of C-peptide and the antibodies to glutamic acid decarboxylase (anti-GAD) can be useful to assist in making the distinction.

Type 2 Diabetes in Childhood and Adolescence

Type 2 diabetes has emerged recently as a problem among adolescents and young adults, particularly in high-prevalence populations.

Although type 1 diabetes remains the most prevalent form of the disease in children worldwide, it is likely that type 2 diabetes will be the predominant form within 10 years in many populations. Type 2 diabetes has already been reported in children from Japan, Pacific Islands, Hong Kong, Australia (indigenous communities) and southern Asia. Among children in Japan, it is already more common than type 1 diabetes, accounting for 80% of childhood diabetes; the incidence has almost doubled between 1976–80 and 1991–95.

Although type 2 diabetes in Europeans is usually characterised by onset (often asymptomatic) after the age of 50 years, in Pacific Islanders and other high-prevalence groups, such as southern Asians, onset in the 20–30-years
Guide to the Classification of Diabetes

age group is now increasingly common, and it may now be seen in the pre-adolescent child. The majority present insidiously, and have obesity, acanthosis nigricans and asymptomatic glycosuria. A very small minority present more acutely with polyuria, polydipsia and ketosis, requiring transient initial insulin therapy. A family history of type 2 diabetes is also common. As a result of this new and rather alarming scenario, a joint consensus statement has been issued recently by the ADA and the American Academy of Pediatrics (See reference v, Appendix II).

The appearance of type 2 diabetes in a younger age group also raises new issues in the classification of diabetes. The presence of C-peptide and absence of markers of autoimmunity, such as antibodies to GAD, may help to diagnose type 2 diabetes.

The general aims of management are the same for adolescents as they are for adults; however, there are many special problems in dietary and therapeutic management as a result of the complex psychosocial aspects of adolescence. Furthermore, there are only limited data on pharmacological therapies for type 2 diabetes in adolescents and pre-adolescents, although there are recent data confirming the safety and efficacy of metformin. Apart from insulin, however, most pharmacological therapies for diabetes and its associated conditions are not yet approved for use in children.

Lack of adherence to management guidelines is common, and special efforts and skills in dealing with the adolescent age group are needed, since they face the same complications as adults with type 2 diabetes. The prospect of serious microvascular diabetic complications in their early 30s, as well as accelerated macrovascular diseases, is a very real threat.
The Self-Care Programme

The person with diabetes should know:

- The nature of the disorder.
- Symptoms of diabetes.
- Risk of complications and, in particular, the importance of foot care.
- Individual targets of treatment.
- Individual lifestyle requirements and meal planning.
- Importance of regular exercise in treatment.
- Interaction of food intake, physical activity and oral hypoglycaemic drugs, insulin (administration and adjustment of insulin, when appropriate) or other drugs.
- Self-monitoring of blood or urine glucose (only if blood glucose monitoring is not available or practical), and the meaning of blood glucose results, as well as what action needs to be taken.
- How to cope with emergencies such as illness, hypoglycaemia, stress and surgery.
- Women with existing diabetes require special attention during pregnancy.

Education is essential for successful self-care, thus a teaching programme must be offered to each patient.

Management is an active partnership between people with diabetes, their family and their healthcare team.

Other community resources are often available to supplement this.
Monitoring of glucose levels can be done by either blood or urine testing. Blood testing is optimal, but if this is not available then urine testing is an acceptable compromise. The frequency of monitoring will depend upon resources available, either to the individual or the country concerned.

Self-monitoring of glucose levels
Self-monitoring of blood glucose levels should be regarded as essential to improve the safety and quality of treatment. Methods and frequency of self-monitoring depend on the targets and mode of treatment. Blood measurements should be recorded.

Blood glucose self-monitoring
Blood glucose testing is preferable for metabolic control. It is mandatory for patients on insulin or during pregnancy, and desirable for patients on oral antidiabetic drugs. It is also a vital safeguard against hypoglycaemia.

Urine glucose testing
Urine glucose self-monitoring is an alternative to blood glucose self-monitoring only when the latter is not possible. The aim generally is to keep the urine glucose-free.

All patients
- Self-monitoring technique should be checked once or twice per year by the physician or healthcare team. Quality control of tests is essential, particularly if results are inconsistent with glycated haemoglobin or clinical state.
- Extra tests should be performed during illness or prior to strenuous activity.
- Urine ketone tests should be performed during illness or when blood glucose is >20 mmol/L (>360 mg/dl).

Monitoring procedures
- Test:
  - before each meal
  - at bedtime.
- Monitor well-controlled/stable patients on 1 or 2 days per week. This can be less frequent in consistently well-controlled subjects.
- Monitor poorly controlled/unstable patients, or patients during illness, daily until targets of control are achieved.

Urine self-monitoring
Urine glucose self-monitoring is an alternative to blood glucose self-monitoring only when the latter is not possible. The aim generally is to keep the urine glucose-free.

Urine glucose testing
- Does not give warning of impending hypoglycaemia.
- Is not useful in certain situations such as where renal threshold is elevated (e.g. in the elderly) or low as in pregnancy.
- Always check urine ketone during illness.

Blood glucose testing is the optimal monitoring method; however, in certain countries this is not available and urine testing is acceptable.
Effective management of type 2 diabetes cannot be achieved without proper attention to diet and nutrition. This extends to medically associated cardiovascular risk factors such as hypertension, dyslipidaemia and obesity.

**Principles of nutrition**

- Weight control, where appropriate.
- 25–30% of the total dietary energy should come from fats and oils. Less than one-third of this should come from saturated fats with the balance provided by mono- and polyunsaturated fatty acids.
- 55–65% of the total dietary energy should come from complex carbohydrates rather than refined carbohydrates. Complex carbohydrates can be found in some vegetables and wholemeal products.
- Protein should not exceed requirements. No more than 15% total energy should be derived from protein.
- Food selection guided by available foods, which will vary from country to country.
- Distribution of food intake should be as even as possible throughout the day for patients on oral hypoglycaemic agents or insulin.
- Restrict alcohol intake, particularly in obese, hypertensive and/or hypertriglyceridaemic patients. Alcohol may cause hypoglycaemia in patients on sulphonylureas or insulin.
- Non-calorific rather than nutritive (sorbitol and fructose) sweeteners can be used.
- Restrict salt intake to below 10 g/day, particularly in hypertensive patients.
Physical activity plays an important role in the management of type 2 diabetes. Physical activity improves insulin sensitivity, thus improving glycaemic control, and may help with weight reduction.

The common health goal should be to achieve at least 30 minutes of moderate-intensity physical activity every day. This includes activities such as brisk walking, cycling, golf and gardening. Additional health benefits can be obtained by more vigorous activity (such as dancing, jogging, swimming continuous laps, cycling uphill or heavy digging in the garden), or through longer durations of moderate-intensity activities. Strength-developing activities (e.g. weight training) should be encouraged at least twice per week for the major muscle groups of the legs, trunk, arms and shoulders, with the emphasis on using light to moderate resistance, but performing more repetitions (8–12) on each physical activity. Physical activity programmes need to be appropriate for the person’s age, social, economic, cultural and physical status.

Do sparingly

Avoid sedentary activities
e.g. watching television, using the Internet, playing computer games
Management

Do regularly 🏃‍♂️

Participate in leisure activities and recreational sports
e.g. brisk walking, gardening, golf, weight-lifting, cycling, tennis

Adoption of healthy lifestyle practices within daily living, such as taking the stairs rather than the elevator/escalator, or maximising opportunities for vigorous physical activities such as those that would have occurred with traditional lifestyles, e.g. working in fields or plantations, or fishing, should be encouraged. However, careful attention should be given to potential physical activity hazards such as cuts, scratches and dehydration, and special care of the feet should be taken.

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

Do every day 🧘‍♀️

Adopt healthy lifestyle habits
e.g. walk to the shops instead of driving, use the stairs rather than the elevator, walk to office colleagues instead of using the telephone, walk the dog
Treatment of Hyperglycaemia

Drug treatment should be added only when diet, physical activity and education have not achieved individual treatment targets.

NOTE: All sulphonylureas can cause hypoglycaemia. Longer-acting sulphonylureas are particularly hazardous in the elderly, and in the presence of renal or liver disease; therefore, it is advisable to use shorter-acting sulphonylureas. Gliguidone is preferable for subjects with mild or moderate renal insufficiency.

NOTE: Biguanides must not be used in patients with impaired renal function, liver disease or septic shock, or during major surgery because of the risk of lactic acidosis. If creatinine level is above 0.15 mmol/L (150 mg/100 ml), then drug therapy should be stopped. Gastrointestinal intolerance can also occur.

If the patient is very symptomatic or has a very high blood glucose level, diet and lifestyle changes are unlikely to achieve target values. In this instance, pharmacological therapy should be started without delay.

Algorithms showing the treatment of obese and non-obese individuals can be seen on pages 21 and 22.

Sulphonylureas

Traditionally, sulphonylureas have been regarded as the first-line drug treatment in type 2 diabetes patients who are not very obese; for example: tolbutamide; glibenclamide; glimepiride; glipizide; gliclazide; gliguidone; chlorpropamide.

Initial and maximum daily dosages will vary between different countries and ethnic groups. Sulphonylureas can reduce HbA1c absolute values by about 2%.

Biguanides

Biguanides, e.g. metformin and buformin, are useful as first-line therapy in the obese, and are recommended as first-line therapy in non-obese subjects in some countries. The UK Prospective Diabetes Survey (UKPDS) has demonstrated that metformin is able to reduce HbA1c as effectively as sulphonylureas and insulin without significant weight gain, and may have additional cardioprotective properties. Biguanides also do not cause hypoglycaemia.

α–Glucosidase inhibitors

α-Glucosidase inhibitors, such as acarbose, miglitol and voglibose, decrease post-prandial blood glucose and, to a lesser degree, fasting hyperglycaemia, and thus improve overall glycaemic control without mitigation of effect over time. They have a weight-neutral or weight-reducing effect, and can be used as first-line therapy in association with diet, or in combination with sulphonylureas, biguanides and insulin.
Treatment

These drugs may lower HbA$_{1c}$ by about 1%. In order to minimise the gastrointestinal side-effects of $\alpha$-glucosidase inhibitors, a low starting dose is recommended followed by a gradual increase. $\alpha$-Glucosidase inhibitors are generally well tolerated and do not cause hypoglycaemia.

**Thiazolidinediones**

The thiazolidinediones, such as rosiglitazone and pioglitazone, reduce insulin resistance in patients with type 2 diabetes, IGT, and those who are insulin resistant but non-diabetic. Thiazolidinediones increase insulin-stimulated glucose disposal in people with type 2 diabetes and in obese subjects. They sensitise the body to its own insulin by improving cellular response to insulin action; however, they do not enhance insulin production.

Mechanistically and when administered on their own, thiazolidinediones do not cause hypoglycaemia. When administered as monotherapy or in conjunction with other antiglycaemic agents, thiazolidinediones improve glycaemic control in patients with type 2 diabetes. As monotherapy, thiazolidinediones may decrease HbA$_{1c}$ by 1.5%.

Rosiglitazone has shown some significant changes to surrogate markers for cardiac disease, suggesting a long-term beneficial effect, and outcome studies are currently under way to demonstrate this.

Abnormalities in liver function tests (LFTs) were noted in patients treated with troglitazone and, as a result, it has been withdrawn from the market worldwide. Adverse LFTs have not been reported as an adverse effect of rosiglitazone or pioglitazone; nevertheless, it is currently recommended to monitor liver function periodically. Thiazolidinediones should not be initiated in patients with active liver disease or increased transaminase levels. In addition, weight increase and fluid retention may occur as a result of thiazolidinedione therapy.

**Glinides**

A new generation of sulphonylurea-like agents has recently become available in several countries in the region. The compounds, which include nateglinide and repaglinide, appear to stimulate first-phase insulin secretion. Glinides may be used as monotherapy or in combination therapy with biguanides or thiazolidinediones. They reduce post-prandial hyperglycaemia and, when used as monotherapy, do not usually cause hypoglycaemia.
Treatment

Insulin

Insulin is used in patients who present initially with very high blood glucose levels, especially if associated with weight loss. It is also used in patients who have failed to respond to oral therapy who have weight loss and/or persistent hyperglycaemia. Some patients may be asymptomatic. Insulin should be considered as first-line therapy in lean symptomatic subjects if there is uncertainty about the diagnosis of diabetes type. Further details regarding insulin usage appear on page 22. In addition, pages 23 and 24 discuss special situations where temporary insulin therapy may be required.

Combination therapy

Biguanides, sulphonylureas, thiazolidinediones and α-glucosidase inhibitors may be used in combination as oral therapy, or with insulin when treatment targets are not achieved with one agent alone, or when there are clinical reasons for not using insulin. This regimen may also apply to children and adolescents with type 2 diabetes. Combinations of small doses of each drug may also be used to avoid the individual side-effects of each agent.

Treatment of Other

Cardiovascular Risk Factors

Treatent of type 2 diabetes must also address other significant cardiovascular disease risk factors, such as reductions in weight, serum lipids and blood pressure. The evidence for this comes from recent landmark clinical trials including the UKPDS, the Scandinavian Simvastatin Survival Study (4S), the Micro-HOPE study and the Coronary Artery Recurrent Events (CARE) study.

Cessation of cigarette smoking and reduction of alcohol consumption should also be addressed.
Obesity and other determinants

Obesity, particularly central or truncal obesity, is a major factor in insulin resistance and will be an important determinant for choice of appropriate oral hypoglycaemic therapy. The criteria for obesity and its levels of associated risk for diabetes and cardiovascular disease will vary between ethnic groups. For example, acceleration of cardiovascular risks has been demonstrated to be similar between Chinese communities (Hong Kong and Singapore) with body mass index (BMI) values >23 kg/m² and European subjects with BMI >25 kg/m². By contrast, in Pacific Island communities, the opposite may apply. The WHO and other regional organisations have proposed various criteria that are currently under prospective evaluation (see Appendices III and IV). Other factors that may influence choice of therapy include availability, adverse effects, allergy, age and other medical conditions, e.g. renal or liver disease.

The Overweight or Obese Person with Diabetes

TABLE 2
Management algorithm for overweight and obese type 2 diabetes mellitus.

Failure
Add biguanide, TZD or α-glucosidase inhibitor

Failure
Combine two of these or add sulphonylurea or glinide

Failure
Add insulin OR change to insulin**

TZD = thiazolidinedione.
* If control is poor, oral agents may be started early.
** In certain situations, insulin may be required (see text for details).
Obese/Non-Obese

Continue oral hypoglycaemic agents
Intermediate-acting/long-acting insulin after 10 pm
Initial dose 0.2 units/kg
Monitor FPG
Adjust insulin by 2–4 units after a minimum of 3 days†
Aim for FPG 4–8 mmol/L (individualise)

†Proceed to twice daily insulin if control is inadequate.

The Non-Obese Person

with Diabetes

TABLE 3
Management algorithm for normal weight type 2 diabetes mellitus.

Diet, exercise and weight control*

Failure
Add sulphonylurea, biguanide, α-glucosidase inhibitor or glinide

Failure
Combine sulphonylurea or glinide with biguanide and/or α-glucosidase inhibitor and/or add TZD**

Failure
Add insulin OR change to insulin***

TZD = thiazolidinedione.
* If control is poor, oral agents may be started early.
** Use of TZD may be appropriate earlier in patients with features of metabolic syndrome.
*** In certain situations, insulin may be required (see text for details).

Guidelines for combination therapy when commencing insulin.

Continue oral hypoglycaemic agents
Intermediate-acting/long-acting insulin after 10 pm
Initial dose 0.2 units/kg
Monitor FPG
Adjust insulin by 2–4 units after a minimum of 3 days†
Aim for FPG 4–8 mmol/L (individualise)

†Proceed to twice daily insulin if control is inadequate.
Targets/Special Situations

Targets for Control

Many of these targets are based on results from studies conducted in Europe; it is important for individual countries to use these as a basis for the formulation of guidelines targeted at their own populations.

**TABLE 4**
Targets for control.

<table>
<thead>
<tr>
<th></th>
<th>Optimal</th>
<th>Fair</th>
<th>Poor</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma glucose</strong> (mmol/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fasting</td>
<td>4.4–6.1</td>
<td>≤7.0</td>
<td>&gt;7.0</td>
</tr>
<tr>
<td>non-fasting</td>
<td>4.4–8.0</td>
<td>≤10.0</td>
<td>&gt;10.0</td>
</tr>
<tr>
<td><strong>HbA1c</strong> (%)</td>
<td>&lt;6.5</td>
<td>6.5–7.5</td>
<td>&gt;7.5</td>
</tr>
<tr>
<td><strong>Blood pressure</strong> (mmHg)</td>
<td>&lt;130/80</td>
<td>&gt;130/80–140/90</td>
<td>≥140/90</td>
</tr>
<tr>
<td><strong>BMI</strong> (kg/m²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male:</td>
<td>&lt;25</td>
<td>&lt;27</td>
<td>≥27</td>
</tr>
<tr>
<td>female:</td>
<td>&lt;24</td>
<td>&lt;26</td>
<td>≥26</td>
</tr>
<tr>
<td><strong>Total cholesterol</strong> (mmol/L)</td>
<td>&lt;4.5</td>
<td>≥4.5</td>
<td>≥6.0</td>
</tr>
<tr>
<td><strong>HDL-cholesterol</strong> (mmol/L)</td>
<td>&gt;1.1</td>
<td>1.1–0.9</td>
<td>&lt;0.9</td>
</tr>
<tr>
<td><strong>Triglycerides</strong> (mmol/L)</td>
<td>&lt;1.5</td>
<td>&lt;2.2</td>
<td>≥2.2</td>
</tr>
<tr>
<td><strong>LDL-cholesterol</strong> (calculated)</td>
<td>&lt;3.0</td>
<td>2.5–4.0</td>
<td>&gt;4.0</td>
</tr>
</tbody>
</table>

* For equivalent whole blood glucose values, see note on page 10.
** Reference range depends on the method used. For this method, non-diabetic HbA1c <6.0% calibrated to DCCT (Goldstein).
*** As these figures relate to European populations, lipids and BMI should be within the normal range for the population in each country.

See Appendix V for conversion factors between conventional and Système International (SI) units.

Special Situations

Management during illness

Metabolic control may deteriorate rapidly during illness of any kind. As part of their educational programme, it is important to instruct patients on actions to be taken.

- Do not stop diabetes tablets or insulin.
- Maintain fluid intake – clear soups, water, weak tea, etc.
- If unable to take food, substitute with fruit juice, regular soft drinks or other fluids containing glucose.
Special Situations

- Check blood glucose at least four times daily.
- Test for urine ketones at least twice daily.
- If vomiting, diarrhoea or drowsiness persist, a physician should be called immediately.

Pregnancy

During pregnancy, blood glucose levels should be as close to normal as possible to ensure a successful outcome for mother and baby. If consecutive glucose levels exceed 6.7 mmol/L (120 mg/dl), contact physician immediately.

- Check blood glucose four times daily, 2 hours after each meal, aiming to keep the level at <6.7 mmol/L (120 mg/dl).
- Test for urine ketone twice daily.
- Use insulin twice daily or more frequently if glucose levels remain at >6.7 mmol/L (120 mg/dl) after meals.
- Do not use oral hypoglycaemic agents during pregnancy.

Surgery

- Special attention to management is required in the type 2 diabetes patient undergoing surgery. This involves communication between the GP, diabetes specialist, anaesthetist and surgeon.
- Patients with type 2 diabetes should be assessed several weeks prior to surgery for general physical status, degree of diabetes control and suitability for anaesthesia.

The elderly

- Elderly patients may be on multiple drug therapies; therefore, the aim of treatment should be to avoid hypoglycaemia, with control of hyperglycaemia.
- FPG should be <7.8 mmol/L (140 mg/dl), and 2-hour glucose should be <11.1 mmol/L (200 mg/dl). Regular review of nutrition should be conducted by a dietician and exercise should be encouraged.
- When glycaemic targets are not met with diet alone, an α-glucosidase inhibitor or low doses of short-acting sulphonylureas are acceptable.
- Metformin is contraindicated in elderly patients with renal, liver or cardiovascular impairment, and sulphonylureas should be used with caution because of the risk of hypoglycaemia.
Hypoglycaemia is a potentially serious complication of treatment in type 2 diabetes patients, especially among the elderly, people with renal insufficiency and people with severe micro- and macroangiopathy.

Both the UKPDS and the Kumamoto Study (Japan) findings suggest it is still necessary to strictly control blood glucose levels for the majority of type 2 diabetes patients, to prevent retinopathy and nephropathy. However, the risk of hypoglycaemia is increased with strict control as is the chance of weight gain; therefore, flexibility should be exercised in individual cases.

Patients receiving long-acting sulphonylureas or insulin are particularly at risk. The risk is highest at night, in the elderly, and in those patients with renal failure or liver disease.

Causes of hypoglycaemia and response

**Insulin or sulphonylurea overdose**

At the beginning of treatment, the doctor should start with a low dose and gradually increase, adjusting the dose carefully.

**Decrease, delay or omission of meals**

Patients should have a stable amount of food, regular meal times and should decrease drug dosage if they cannot tolerate their usual amount of food.

**Increase of physical exercise**

Extra complex carbohydrates should be eaten before exercising.

**Excessive alcohol intake, particularly without food**

Patients should not drink more alcohol.

Behavioural disturbances and other unusual symptoms are more frequent in the elderly patient during hypoglycaemia. Hypoglycaemia does not occur during dietary, α-glucosidase inhibitor or biguanide therapy. However, the combination usage with other agents may cause hypoglycaemia.

**Action**

If hypoglycaemia is suspected, a blood glucose level measurement is needed to confirm the diagnosis.

**NOTE:** If blood glucose levels cannot be measured, treat as hypoglycaemia.

**The conscious patient**

Administer an oral carbohydrate, such as sugar or glucose, as soon as the patient is conscious.

**NOTE:** Hypoglycaemia induced by the longer-acting sulphonylureas (or long-acting insulin) can be prolonged. It is important to monitor glucose levels for at least 24–48 hours after the patient regains consciousness.

A long-term glucose infusion may be needed and the patient should be admitted to hospital.

**The unconscious patient**

Administer 20 ml 50% glucose intravenously or 0.5–1 mg glucagon intramuscularly. Provide oral carbohydrates as soon as the patient is conscious.

**NOTE:** Hypoglycaemia induced by the longer-acting sulphonylureas (or long-acting insulin) can be prolonged. It is important to follow glucose levels for at least 24 hours.

A long-term glucose infusion may be needed and the patient should be admitted to hospital.
More than two-thirds of type 2 diabetes patients die from cardiovascular disease. The clustering of type 2 diabetes, a well-documented risk factor for CVD, with other established risk factors (including dyslipidaemia, hypertension and abdominal obesity) is now well recognised.

Each risk factor alone conveys significant CVD risk. In combination, they place the person with type 2 diabetes at substantial CVD risk. This clustering has been labelled the Metabolic Syndrome (Figure 2), Dysmetabolic Syndrome or Insulin Resistance Syndrome.

Recognition of these features in people with type 2 diabetes has special importance. Fortunately, there are treatment regimens that can influence all of these risk factors. Weight reduction and exercise reduce both insulin resistance and hyperinsulinaemia, as well as improving glucose tolerance and other CVD risk factors. Smoking should be prohibited and alcohol consumption should be moderated.

Sulphonylureas, insulin, certain antihypertensives and thiazide diuretics should be used with care in these patients to avoid accentuating the other CVD risk factors besides diabetes. Biguanides and α-glucosidase inhibitors are the most appropriate agents if drug therapy is required for lowering glucose. They do not induce weight gain or aggravate lipid levels. This clustering of CVD risk factors lends strong support to an aggressive management approach to control hypertension, dyslipidaemia and obesity for the prevention of CVD in people with type 2 diabetes (see page 20). The potential benefits of thiazolidinediones in this syndrome are also being explored.

The targets for control (Table 4, page 23) need to be achieved as closely as possible.
The Metabolic Syndrome

IGT and type 2 diabetes

Insulin resistance
Hyperinsulinaemia
Hypertension
Increased VLDL triglycerides
Decreased HDL cholesterol
Abdominal obesity
Microalbuminuria
Hypercoagulability

FIGURE 2
The metabolic syndrome.
The most important chronic complications of type 2 diabetes are those affecting blood vessels and nerves.

The microvascular complications (retinopathy, nephropathy and neuropathy) are relatively specific to diabetes and the risk of these (particularly retinopathy) is used to help define the diagnostic criteria for diabetes. The risk of these complications is related to duration of diabetes as well as degree of hyperglycaemia. However, due to delayed diagnosis, these complications may already be present at diagnosis; and coexisting hypertension or dyslipidaemia may exacerbate their risk.

The macrovascular complications (coronary heart disease, cerebrovascular disease and peripheral vascular disease) are not specific to diabetes:

- Diabetes increases the risk of the development of macrovascular complications by 2–4 times. It also predisposes patients to more severe and generalised disease, and to onset of problems at a younger age.
- An increased risk of macrovascular disease is already apparent with degrees of hyperglycaemia below those reaching levels diagnostic of diabetes. For example, there is an approximate two-fold increase in risk of macrovascular disease in those individuals with IGT.
- Hyperglycaemia interacts with other risk factors, such as hypertension and dyslipidaemia, which also occur with increased frequency (30–50%).
- The coexistence of microvascular complications also exacerbates the severity of clinical manifestations. The very high relative risk of lower limb amputation in people with diabetes is an example of the effects of these interactions.

It is vitally important that hyperglycaemia, hypertension and dyslipidaemia are all controlled as effectively as possible to reduce the risk of development or progression of complications.

Once complications have become established, it is no longer sufficient just to treat hyperglycaemia and other risk factors, although this remains important. Additional measures such as laser photocoagulation, use of ACE inhibitors or angiotensin 2 receptor antagonists, foot care education, and treatment may all become necessary. Patients with macrovascular complications should also be considered for low-dose aspirin therapy if no contraindication is present.
Complications

Retinopathy

Type 2 diabetic patients can develop both proliferative and non-proliferative diabetic retinopathy, although it is the latter type complicated by macular oedema that is the leading cause of vision loss.

Every 1–2 years from diagnosis, patients should be checked for visual acuity by examining fundi through dilated pupils. In patients with established retinopathy or long duration of diabetes, examinations may need to be performed more regularly. When retinopathy is detected, fluorescein angiography may be required to assess the severity of retinopathy and the need for laser treatment. Adequate control of hyperglycaemia and hypertension is essential.

Nephropathy

Established diabetic nephropathy is best detected by the presence of 2+ proteinuria on dipstick urinalysis.

Proteinuria usually precedes the development of renal failure by several years as evidenced by rising serum creatinine concentrations. An increase in urinary albumin excretion rate, short of overt proteinuria, is known as ‘microalbuminuria’. This represents an early, subclinical phase of nephropathy and its presence indicates increased risk of progression to overt renal disease, as well as increased risk of macrovascular complications. Intervention at this point, with optimised glucose and blood pressure control, is particularly important to prevent or delay progression.

Although treatment of glucose and lipids remains important, the single most important aggravating factor in nephropathy is hypertension. Decline of renal function can be slowed by tight control of hypertension to levels below 140/80 mmHg (UKPDS data). A number of studies have also shown that either ACE inhibitors or angiotensin-2 receptor antagonists confer additional renoprotection over and above that obtained by blood pressure control alone. Thus, wherever possible one of these agents should be included in the antihypertensive regimen and their use as sole agents may also be considered in patients deemed to be normotensive.
Complications

Diabetic Foot Problems

Diabetic foot problems result from complex interactions between peripheral neuropathy (including autonomic dysfunction), microangiopathy and macrovascular disease, and poor foot hygiene. The relative contributions of each may vary from patient to patient and also may vary in different populations; for example, the contribution from peripheral vascular disease may be less in some Asian populations. As a result, lower limb amputation is one of the most feared complications of diabetes.

People with diabetes are, in general, 15–40 times more likely to require a lower limb amputation compared with the general population, and the comparative risk is even higher in elderly subjects. However, with aggressive management, a substantial proportion of amputations can be prevented.

Peripheral neuropathy with loss of pain sensation is the commonest cause of foot ulceration, closely followed by poor hygiene. This type of neuropathy and ulcer can be completely painless.

Peripheral vascular disease can also cause foot ulceration, which tends to be painful, and plays an important role in neuropathic ulceration by impairing healing. Neuropathic ulcers occur at sites of increased pressure, usually on the plantar surface of the foot. The most common reported site of neuropathic ulcers is the dorsum of the toes, and these are shoe induced. Callus develops as a result of the pressure (Figure 3).

For healing to occur, pressure needs to be reduced (e.g. by removal of callus, and wearing appropriate shoes or a pressure-relieving cast). Vascular ulcers tend to occur at the tips of the toes and on the heel (Figure 4).

For healing to occur, vascular supply may need to be improved. The infection must be treated aggressively, and antibiotic therapy is often required for many weeks or months. The important role of regular debridement of infected and necrotic tissue needs to be emphasised. Failure to heal an ulcer is the common underlying cause of subsequent amputation.
Complications

Routine checking of sensation and pedal pulses are the most important steps in identifying a foot that is at risk of ulceration. In the community, sensation is best tested with the 5.07/10 gm Semmes Weinstein Monofilament, which is a simple and inexpensive procedure. It is calibrated to buckle when a force of 10 gm is exerted (Figure 5).

If a patient cannot feel the pressure, the foot is considered to be insensate. Foot-care education for individuals identified at risk should be more detailed and practical than for other diabetic individuals with intact sensation and circulation.

Treatment of painful neuropathy is unsatisfactory. Useful measures include improving metabolic control and using simple analgesics, tricyclic antidepressants or anticonvulsants for pain relief. Reassuring the patient that pain is in fact not the underlying cause leading to amputation may be advisable.

If glycaemic control is very poor, foot infection and ulceration may occur as a result of poor hygiene, even in the absence of neuropathy or peripheral vascular disease. In this situation, apart from improving glycaemic control, it is important to advise patients to wear shoes to reduce the chance of trauma and, if they wear shoes, also to wear clean socks!

### Practical aspects of assessing patients for complications.

<table>
<thead>
<tr>
<th>Check visual acuity</th>
<th>Examine fundi through dilated pupils</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carry out urinalysis</td>
<td>Check for proteinuria. If present, serum creatinine should be determined. If proteinuria is not present, microalbuminuria should be determined</td>
</tr>
<tr>
<td>Record blood pressure</td>
<td>Palpate pulses of the feet. Use the Semmes Weinstein Monofilament to detect sensory loss. Examine the feet for cracks in the skin, fungal infection, condition of the nails, deformities and evidence of increased local pressure such as callus formation</td>
</tr>
</tbody>
</table>

**FIGURE 5**
Complications

Macrovascular Disease

In type 2 diabetes, 80% of all deaths are due to CVD. An increased risk of macrovascular disease is already present in individuals with IGT. Protection in pre-menopausal women is also lost when diabetes is present. In addition to the overall increased risk, people with diabetes develop more severe and generalised disease, which is associated with a worse prognosis and outcome. Coronary artery disease, cerebrovascular disease and peripheral vascular disease all occur more frequently as a result of diabetes, although ethnic differences may exist that determine which vascular territory is most prone to involvement.

It is important to be constantly on the alert for macrovascular disease. In addition, it should be remembered that, as a result of coexisting autonomic neuropathy, angina and myocardial infarction may be ‘silent’ due to the absence of pain. Unfortunately, also, ischaemic heart disease cannot easily be detected by physical examination.

Resting ECGs have limited value; thus, in patients thought to be particularly vulnerable (e.g. those with additional risk factors such as a strong family history, smoking, hypertension and dyslipidaemia), stress testing is necessary to evaluate cardiac disease.

Smoking greatly increases the risk of macrovascular disease. Control of hypertension and dyslipidaemia, and the use of low-dose aspirin are also effective strategies to reduce the risk of macrovascular events. Some studies, including the 4S study, have shown that the use of HMG-CoA reductase inhibitors to reduce cholesterol is effective in reducing macrovascular events and mortality in diabetic subjects, both with and without known ischaemic heart disease. The benefits appear to be even greater in diabetic subjects when compared with non-diabetic subjects. A common pattern of dyslipidaemia in people with diabetes is elevation of triglyceride with low HDL levels, but relatively unaffected total cholesterol. This pattern may be treated with fibrates, as demonstrated in the Diabetes Athero-Intervention Study (DAIS), although there are less data on the effectiveness of these drugs in reducing morbidity and mortality. Lifestyle measures should not be neglected.
Complications

The HOPE Study, amongst others, has also demonstrated the effectiveness of ACE inhibitors in the prevention of coronary events, and again the beneficial effect may be even more pronounced with diabetes.

**Practical aspects of assessing and managing macrovascular disease:**

- Always include evaluation of macrovascular disease and its risk factors in the assessment.
- Take a detailed history to determine the presence of angina, neurological symptoms, claudication and past episodes of vascular events. Listen for carotid bruit; palpate the pedal pulses; and measure blood pressure.
- Check urine for proteinuria and, in appropriate cases, microalbuminuria.
- Check cholesterol (LDL and HDL) and triglyceride levels.
- Help your patients to give up smoking.
- For secondary prevention, aggressively treat hypertension and dyslipidaemia.
- For primary prevention, aggressively treat hypertension and dyslipidaemia, especially in individuals who are considered to be at high risk of macrovascular events.

Diabetic subjects who suffer a myocardial infarction or stroke have a worse outcome than non-diabetic individuals, both during the acute phase and subsequently. In the context of myocardial infarction, the DIGAMI study has indicated improved short- and longer-term outcomes if intensive insulin therapy is used to establish good glycaemic control. Other preventative measures, such as the use of beta-blockers post-infarction, appear to be equally effective in people with diabetes when compared with the general population. Thrombolytic therapy in the acute phase appears safe in diabetes, even in the presence of retinopathy.
Prevention of Type 2 Diabetes

Lifestyle and Pharmacological Approaches

The rapid escalation of the number of people with type 2 diabetes in the Asian-Pacific region calls for urgent action on prevention. If not, the economic costs of premature morbidity and mortality from diabetes could shatter the healthcare budgets of both developing and affluent nations. By 2010, Asia will be home to 61% of the total global projected number of people with diabetes.

Recent studies have shown the potential for intervention in IGT subjects to reduce progression to type 2 diabetes. One such study is the recently completed Diabetes Prevention Program in the USA. This study showed that, over 3 years, lifestyle intervention (targeting diet and exercise) reduced the risk of progressing from IGT to diabetes by 58%, while the oral hypoglycaemic drug, metformin, reduced risk by 31%. Two other large-scale studies from Da Qing, China, and Finland, have also demonstrated the efficacy of lifestyle interventions. In the Finnish study, the cumulative incidence of diabetes after 4 years was 11% in the intervention group and 23% in the control group. During the trial, the risk of diabetes was reduced by 58% in the intervention group. The reduction in the incidence of diabetes was directly associated with changes in lifestyle.

Several studies provide evidence that the lifestyle approach aimed at high-risk individuals, such as those with IGT, may not be sufficient to prevent all cases of type 2 diabetes. Pancreatic beta-cell function is often already substantially reduced at the time of clinical diagnosis of type 2 diabetes. Even at the earlier stage of IGT, beta-cell function is already impaired and intervention at this stage may be too late to prevent many cases of type 2 diabetes. Also, intensive intervention programmes using well-developed behaviour-modification approaches may show high relapse rates with weight gain and an increase in blood glucose after 1–2 years despite an initially encouraging response. As a result, a number
Prevention of Type 2 Diabetes

of studies are either under way or are being planned to examine whether therapeutic intervention with drugs, such as metformin, α-glucosidase inhibitors, thiazolidinediones and ACE inhibitors, might be used for prevention as well.

The STOP NIDDM study results have been published recently and indicate that acarbose may have a role in preventing type 2 diabetes in IGT subjects. The TRIPOD study has shown that thiazolidinediones will also delay the onset of subsequent diabetes in women with gestational diabetes.

We do not know yet whether treatment of IGT can delay or prevent the appearance of macrovascular disease, the major cause of morbidity and mortality in type 2 diabetes. However, delaying the onset of diabetes in such high-risk subjects will provide some benefit. It may, therefore, be prudent to treat people with IGT with lifestyle advice, at least, or with glucose-lowering agents of proven long-term safety while more data are accumulated.

National governments have been slow to react to the emerging problem of the diabetes and other chronic diseases epidemic. Urgent action is needed to address prevention issues, as has been taken for emerging communicable diseases such as AIDS. The diabetes epidemic will not be prevented by diet and exercise alone. Major and dramatic changes in the socioeconomic and cultural status of people in developing countries, and disadvantaged and minority groups in developed nations, will also be necessary.
Set individual targets for treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight kg</td>
<td></td>
</tr>
<tr>
<td>Height cm</td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
</tr>
<tr>
<td>Blood glucose (fasting/post-prandial) mmol/L (mg/dl)</td>
<td></td>
</tr>
<tr>
<td>Blood pressure (syst/diast) mmHg</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol mmol/L (mg/dl)</td>
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</tr>
<tr>
<td>HDL-cholesterol mmol/L (mg/dl)</td>
<td></td>
</tr>
<tr>
<td>Triglycerides mmol/L (mg/dl)</td>
<td></td>
</tr>
<tr>
<td>HbA₁c %</td>
<td></td>
</tr>
<tr>
<td>Albuminuria* µg/min</td>
<td></td>
</tr>
</tbody>
</table>

Specify and plan first aims and actions with patient

For example:

- Physical activity.
- Nutritional advice.
- Stop smoking.
- Reduce body weight by ____________ kg in ____________ weeks.
- Perform self-monitoring.
- Start record book.

Later visits

- Discuss results, including HbA₁c, and specify next aims and actions with patient.
- Check diabetes record book, discuss results, nutrition and exercise.
- If hypertensive, consider specific treatment; start early if nephropathy (including albuminuria*) is present.
- If dyslipidaemia is present, stress nutritional modifications and consider specific drug treatment.
- Reduce body weight further by ____________ kg in ____________ weeks.

(*Microalbuminuria if resources are available)
### Clinical Monitoring Protocol

<table>
<thead>
<tr>
<th>Test</th>
<th>Initial visit</th>
<th>Follow-up visit</th>
<th>Quarterly visit</th>
<th>Annual visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye: visual acuity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye: fundoscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feet: pulses</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Feet: neuropathy</td>
<td></td>
<td></td>
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<td>BMI</td>
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</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Blood glucose</td>
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<tr>
<td>HbA1c</td>
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<tr>
<td>Cholesterol/HDL-cholesterol</td>
<td></td>
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<tr>
<td>Triglycerides</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albuminuria*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine/BUN</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>ECG</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine microscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- = Conduct test
- = No test required
- = Conduct test if abnormal first visit

(*Microalbuminuria if resources are available)
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Appendices

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Appendix II

The following reports and guidelines have been referred to in this document:


(viii) United Kingdom Prospective Diabetes Study (UKPDS 55). Relationship between ethnicity and glycemic control, lipid profiles, and blood pressure during the first 9 years of type 2 diabetes. *Diabetes Care* 2001; 24(7): 1167–74.


Appendices


Many countries in the region have national guidelines that can be accessed via the individual IDR-WPR member associations (see Appendix I).
### Aetiological classification of disorders of glycaemia*

<table>
<thead>
<tr>
<th>Type 1</th>
<th>(beta-cell destruction, usually leading to absolute insulin deficiency)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Autoimmune</td>
</tr>
<tr>
<td></td>
<td>Idiopathic</td>
</tr>
<tr>
<td>Type 2</td>
<td>(may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with or without insulin resistance)</td>
</tr>
<tr>
<td>Other specific types</td>
<td>Genetic defects of beta-cell function</td>
</tr>
<tr>
<td></td>
<td>Genetic defects in insulin action</td>
</tr>
<tr>
<td></td>
<td>Diseases of the exocrine pancreas</td>
</tr>
<tr>
<td></td>
<td>Endocrinopathies</td>
</tr>
<tr>
<td></td>
<td>Drug- or chemical-induced</td>
</tr>
<tr>
<td></td>
<td>Infections</td>
</tr>
<tr>
<td></td>
<td>Uncommon forms of immune-mediated diabetes</td>
</tr>
<tr>
<td></td>
<td>Other genetic syndromes sometimes associated with diabetes</td>
</tr>
<tr>
<td>Gestational diabetes**</td>
<td></td>
</tr>
</tbody>
</table>

* As additional subtypes are discovered, it is anticipated that they will be reclassified within their own specific category.

** Includes the former categories of gestational IGT and gestational diabetes.

### Disorders of glycaemia: aetiological types and clinical stages

<table>
<thead>
<tr>
<th>Stages</th>
<th>Normoglycaemia</th>
<th>Hyperglycaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal glucose tolerance</td>
<td></td>
<td>IGT and/or IFG</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Types</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Type 1</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autoimmune</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Type 2</strong>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predominantly insulin resistance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predominantly insulin secretory defects</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other specific types</strong>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gestational diabetes</strong>*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* In rare instances, patients in these categories (e.g. Vacor toxicity, type 1 present in pregnancy) may require insulin for survival.

## Appendices

### Appendix V

**Conversion factors between conventional and SI units**

This list is included to assist the reader to convert values between conventional units and the newer SI units (Système Internationale d’Unités) that have been mandated by many journals.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Conventional units</th>
<th>SI units</th>
<th>Conventional to SI units</th>
<th>SI to conventional units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma glucose</td>
<td>mg/dl</td>
<td>mmol/L</td>
<td>0.0555</td>
<td>18.02</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>mg/dl</td>
<td>mmol/L</td>
<td>0.0259</td>
<td>38.61</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>mg/dl</td>
<td>mmol/L</td>
<td>0.0259</td>
<td>38.61</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>mg/dl</td>
<td>mmol/L</td>
<td>0.0113</td>
<td>88.5</td>
</tr>
</tbody>
</table>
Type 2 Diabetes

Practical Targets and Treatments

Third edition

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