

Guidelines for good practice in the diagnosis and treatment of non-insulin-dependent diabetes mellitus

REPORT OF A JOINT WORKING PARTY OF THE BRITISH DIABETIC ASSOCIATION, THE RESEARCH UNIT OF THE ROYAL COLLEGE OF PHYSICIANS, AND THE ROYAL COLLEGE OF GENERAL PRACTITIONERS

ABSTRACT—The guidelines were prepared by a working party of physicians, general practitioners, specialist nurses, public health physicians, an economist, and a patient. They should be of value in establishing locally agreed guidelines. Non-insulin-dependent diabetes (NIDDM) affects more than 1% of the population, and 70–80% of all people with diabetes have this form of disorder. Care of these patients by general practitioners is rapidly increasing and perhaps the majority will, at least in the early stages, be treated in primary care. The working party encourages the formation of district diabetes committees involving both general practitioners and hospital specialists to support and maintain the best standards of diabetes care.

Diagnosis of diabetes

Non-insulin-dependent diabetes is not a mild disease, as is often thought, but carries considerable morbidity and mortality. Correct management is therefore important from the onset. Diagnosis is usually straightforward, but some common errors are described below. Criteria for diagnosis are as follows.

Presence of symptoms: if classical symptoms are present then only one diagnostic blood glucose level is needed to confirm the diagnosis (Table 1).

No symptoms: in the absence of symptoms two separate diagnostic blood glucose levels are needed for confirmation.

Glycosuria: the presence of glycosuria normally indicates diabetes but the diagnosis must be confirmed by determining blood glucose levels (see 1 and 2 above and Table 1).

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Interpretation of blood glucose levels

1. 'Diagnostic' levels are shown in Table 1.
2. If blood glucose levels are in the 'uncertain' range (Table 1), the test should be repeated, preferably fasting. If they remain in this range, the available options are:
 - a perform a glucose tolerance test;
 - b if the patient is elderly, symptomless, and free from glycosuria, take no further action unless the blood glucose remains near the upper limit of this 'uncertain' range.

Common errors

1. Starting treatment on the basis of glycosuria alone.
2. Diagnosing diabetes by blood glucose strip—this is not adequate for diagnosis of lifelong disease, and a diagnostic laboratory blood glucose must be obtained.
3. Performing a glucose tolerance test when unequivocal 'diagnostic' blood glucose levels have already been demonstrated.

The glucose tolerance test (GTT) (Table 1)

This test is performed in the morning, with the patient fasting, using a 75g glucose load. Results can establish:

- a normal GTT;
- b diabetes;
- c impaired glucose tolerance (IGT);
- d renal glycosuria.

Impaired glucose tolerance (IGT)

This is an unstable state which may revert to normal in approximately one third of cases or progress to diabetes at a rate of about 2% per year. Younger subjects with IGT should be tested for diabetes annually and should reduce other risk factors (eg, smoking, hypertension, hyperlipidaemia, etc). Advice on 'healthy eating' and the achievement of an ideal body weight are also worthwhile. In the symptomless elderly patient IGT can be ignored.

Renal glycosuria

This is defined when glycosuria occurs in a normal glucose tolerance test: it is symptomless and harmless.

Physical examination at diagnosis

A full examination of the patient is a minimum requirement after the diagnosis has been made. This is essential to detect diseases which might cause diabetes (for example, carcinoma of the pancreas), other factors which might precipitate it (especially steroids or various infections), and to discover any of the diabetic complications which are quite commonly present, even at the time of diagnosis. They include retinopathy, foot problems, and neuropathy, and all forms of peripheral and coronary artery disease.

Aims of treatment

The main aims of treatment of NIDDM are:

- a* relief of symptoms;
- b* enhancing the quality of life;
- c* minimising the risks—of the disease
—of the treatment.

Relief of symptoms

Symptoms of diabetes should always be relieved by treatment, and when 'control' is being assessed, evaluation of symptoms must come first. They will generally

abate when fasting blood glucose decreases below 10mmol/l; and patients quickly learn of the association between symptoms and hyperglycaemia. One of the greatest benefits is the increase in energy and improved sense of well-being experienced by most patients, even by those who initially denied symptoms.

Enhancing the quality of life

The diabetes team should give patients and their families sufficient information and education both to gain a realistic perception of the illness and to become independent in its management and thus shape their treatment. Consultations should always explore how patients are coping, not only with their treatment (diet, medication, monitoring), but also how they have adapted in terms of exercise, in family life, and at work. Patients are too often asked to take treatment regarded as 'simple' without any such advice. The diabetes team that has to deliver complex care of this kind needs to include at least a doctor, a nurse/educator, a dietician, and a chiropodist. Many texts give full details of these requirements.

Minimising the risks of the disease

Risks to health and life in diabetes are due on the one hand to the specific diabetic complications, and on the other to the considerable excess of cardiovascular disease associated with an increased mortality. To minimise these problems, attention must centre on several

Table 1. Diagnostic interpretation of blood glucose levels

		SMAC		Finger prick
		Venous blood (mmol/l)	Venous plasma (mmol/l)	Capillary whole blood (mmol/l)
Random levels	Diagnostic	≥ 10.0	≥ 11.1	≥ 11.1
	Uncertain	6.7–9.9	7.8–11.0	7.8–11.0
Fasting levels	Diagnostic	≥ 6.7	≥ 7.8	≥ 6.7
	Uncertain	5.0–6.6	6.0–7.7	5.0–6.6
Glucose tolerance test				
(i) Diabetes	Fasting	≥ 6.7	≥ 7.8	≥ 6.7
	2-hour level	≥ 10.0	≥ 11.1	≥ 11.1
(ii) Impaired glucose tolerance (IGT)	Fasting	< 6.7	< 7.8	< 6.7
	2-hour level	6.7–10.0	7.8–11.1	7.8–11.1

issues and not simply on metabolic control. The recommendations include:

- a* no smoking;
- b* maintenance of normal blood pressure;
- c* good blood glucose control;
- d* attention to plasma lipids.

Regular medical examination is needed to achieve these ends. Targets for metabolic control are shown in Table 2. These targets represent a practical approach to treatment, and adherence to them can be modified according to both the patient's age and degree of compliance. Symptoms must always be assessed when considering the adequacy of control. Appropriate targets should be agreed with each individual patient.

Minimising the risks of treatment

Both over-treatment and under-treatment needlessly increase morbidity and can even be hazardous. These problems apply particularly to the elderly in whom tight control is unlikely to affect morbidity and which is therefore inappropriate. Excessive use of sulphonylureas and insulin in such patients leads to inconvenience and, more seriously, to problems from hypoglycaemia. On the other hand, failure to recommend insulin treatment when it is really needed in older patients results in needless malaise and ill health. Indications for starting insulin are described below.

Conclusions

1. Treatment must aim to alleviate symptoms.
2. Simple risk factors associated with complications should be eliminated.
3. Targets for control should be agreed with the individual patient.
4. Patients should receive sufficient information for them to understand their diabetes and achieve independence.

Starting treatment

Correct treatment from the onset is obviously important, and at first sight appears simple. Diet is always the first method of treatment and there are only a few exceptions to this rule. Yet frequently patients are started on sulphonylurea treatment before instruction on diet has been given, whether or not they are overweight, and sometimes before the diagnosis has been properly established.

Two types of NIDDM

The distinction between *obese* and *non-obese* NIDDM is important in deciding on treatment: a treatment plan is summarised in Table 3. Note the prime role of dietary treatment. When the decision to use an oral hypoglycaemic agent has been made (Table 3), there

Table 2. Targets for metabolic control

	Units	Good*	Acceptable	Poor
Body mass index	kg/m ²	< 25	25–27	> 27
HbA1** (normal 5.0–7.5)	%	< 7.5	7.5–8.8	> 8.8 (> 10.0—very poor)
HbA1c** (normal 4.0–6.0)	%	< 6.0	6.0–7.0	> 7.0 (> 8.0—very poor)
Blood glucose				
—Fasting	mmol/l	< 6.7	< 8.0	≥ 10.0
—Random	mmol/l	4.0–9.0	< 10.0	≥ 10.0
Total cholesterol***	mmol/l	< 5.2	< 6.5	≥ 6.5
HDL-cholesterol	mmol/l	> 1.1	> 0.9	< 0.9
Blood pressure	mmHg	< 140/90***	< 160/95	> 160/95

* This is the ideal and may be difficult, impossible, or unnecessary to achieve in certain patients (eg, in the elderly). Individual targets should be established for each patient.

** Reference ranges for HbA1 vary greatly depending on the method.

*** Less strict target may be appropriate in older patients; age-related charts should be used for younger patients. A stricter target is appropriate for younger patients, especially those with early (microalbuminuria) or established nephropathy.

is a choice between metformin and one of the sulphonylureas. When obesity is clinically obvious (body mass index (BMI) greater than 30), it is appropriate to use metformin. For those whose BMI is in the range 27–30, the choice is determined by factors that include weight loss and/or the presence of symptoms of uncontrolled diabetes (Fig 1).

All patients with newly diagnosed NIDDM should see a dietician if possible. 'Stop-gap' advice in the form of leaflets or booklets is acceptable initially, but if a general practitioner (GP) does not have access to a dietician, the patient should be referred to a hospital diabetic clinic.

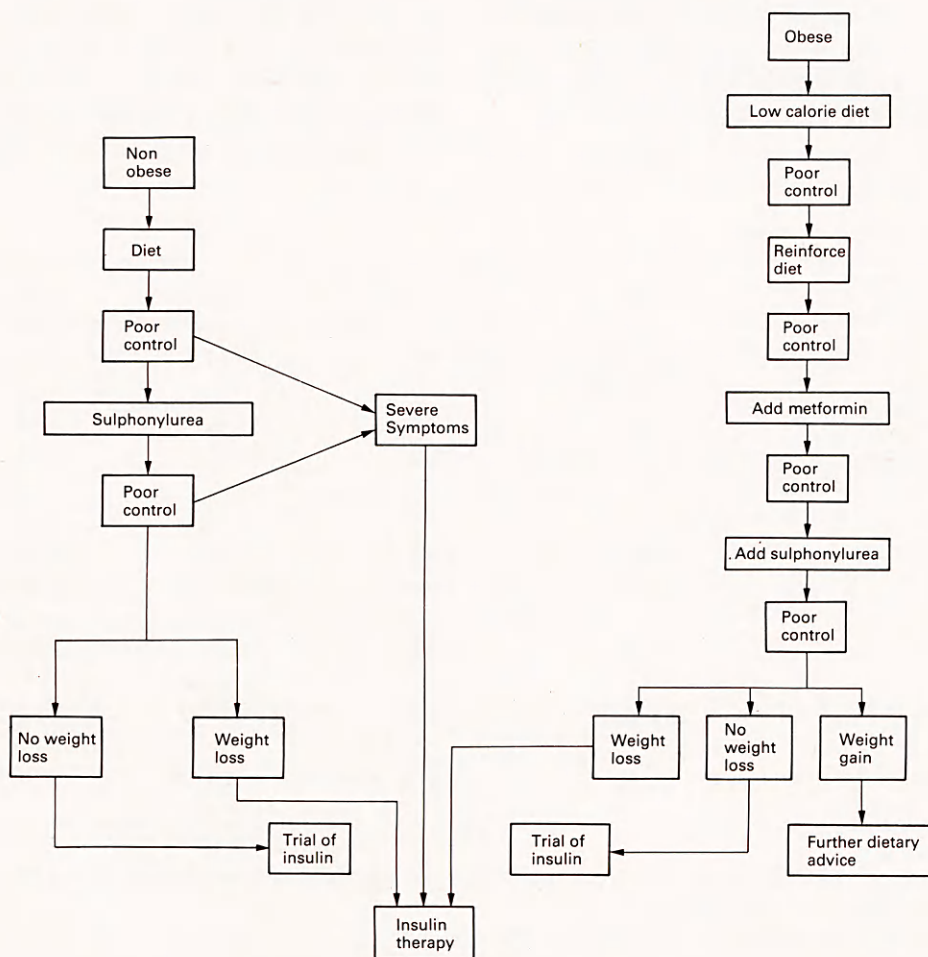
The modern diet for NIDDM is free from refined carbohydrate, but complex high-fibre carbohydrates are encouraged. It is low in fat, and energy-restricted for the obese, but isocaloric with the existing diet for those of normal weight.

Sulphonylureas

There are many sulphonylurea drugs. They work primarily by stimulating insulin release from the pancreas. As insulin is anabolic, their use may be associated with weight gain. They should therefore be used in non-obese NIDDM patients who have failed to achieve acceptable control on diet alone.

1. Glibenclamide (Daonil, Euglucon) is the most popular of the sulphonylureas, though it can cause significant hypoglycaemia—particularly in the elderly and those with renal dysfunction.
2. Gliclazide (Diamicon) is perhaps the most commonly used of the many other sulphonylureas available. It is excreted in the bile and can therefore be used in renal insufficiency. In addition, it is less prone than glibenclamide to cause hypoglycaemia in the elderly.

Fig 1. Treatment scheme for non-insulin-dependent diabetes



3. Glipizide (Glibenese, Minodiab) is an alternative.
4. Tolbutamide (Rastinon) is safe and effective, and has been in use for many years.

Chlorpropamide (Diabinese) is not now normally used because of its long duration of action and tendency to cause serious hypoglycaemia.

Treatment with sulphonylureas should normally start with the lowest dose, which can be increased gradually as needed (Table 3).

The problem of sulphonylurea-induced hypoglycaemia cannot be overemphasised: it is common, and occasionally fatal. Most cases occur in patients taking glibenclamide, though serious problems occur chiefly in the elderly or those with renal dysfunction. This drug should not normally be used in those aged over 70 years, or if there is any degree of renal impairment. Gliclazide, glipizide, or tolbutamide are safer alternatives in this situation. The decision to treat with sulphonylureas thus requires considerable thought, and should not be undertaken lightly. Patients will also need specific information on the symptoms of hypoglycaemia and how to avoid and treat it. If hypoglycaemic symptoms are reported, the drug should be withdrawn or the dose substantially reduced.

Metformin

Metformin (Glucophage) is the only biguanide oral hypoglycaemic drug available in the UK. It has predominantly peripheral actions in lowering blood glucose levels, and to some extent aids weight loss. Metformin should therefore be considered in the overweight NIDDM patient who has failed to achieve adequate control on dietary treatment alone. It should be taken with food to minimise side-effects which are mainly gastrointestinal (nausea, dyspepsia, and particularly diarrhoea). These are less troublesome if small doses are used initially (Table 4). Although blood glucose control improves with metformin, patients rarely feel better while treated with this drug, and sometimes improve when it is withdrawn. The risks of lactic acidosis have been exaggerated, and provided the drug is avoided in the presence of hepatic or renal disease, the risks are minimal. Measurement of serum creatinine as an indicator of renal function is therefore important in metformin-treated patients.

Combination treatment

Failure to achieve adequate control on maximum doses of metformin or sulphonylureas raises the question of 'combination therapy' (sulphonylurea plus metformin). Situations such as this are difficult, and are probably best dealt with by hospital diabetologists. The obese patient, for example, may 'improve control' when sulphonylureas are added to existing metformin therapy—but at the risk of further weight gain. Similarly, the non-obese patient who is clearly hypergly-

caemic on maximum sulphonylurea doses may have metformin added as a fruitless, and even dangerous, 'holding exercise' when insulin is really needed.

Indications for starting insulin

One patient in three developing diabetes after 40 years of age will eventually need insulin: recognition of the need to start insulin, *which can arise at any age*, requires considerable skill if patients are not to suffer protracted and needless malaise, if not actual danger. About 10% of NIDDM patients may each year fail on oral hypoglycaemic drugs and require transfer to insulin. Inappropriate transfer to insulin is also common and can itself lead to needless suffering, especially from hypoglycaemia and weight gain.

Starting insulin needs the considerable expertise of the diabetes team if it is to be properly undertaken, and back-up advice is essential.

Indications for insulin assume that existing treatment is optimal, but has failed to achieve 'control'. They are:

- a obvious need for insulin;
- b prudent trial of insulin;
- c the presence of intercurrent illness.

Obvious need for insulin

There is an obvious need for insulin in the presence of hyperglycaemia in patients with:

- a persistence of symptoms (including lack of energy);
- b continuing weight loss (this may be very gradual over months or even years);
- c persistent ketonuria with or without a or b.

The effect of insulin treatment in most of these patients will substantially improve health and well-being.

Prudent trial of insulin

The decision to start insulin in an apparently symptomless, non-obese patient whose weight is stable, yet who fails to achieve the agreed targets for control appropriate for age and other circumstances, is always difficult. In this situation a three months' trial of insulin can be suggested on the understanding that the patient may choose to return to tablet treatment at the end of the trial period. About half the patients in this category are likely to feel much better, and most will achieve better metabolic control.

The need to improve control is greatest among younger patients in order to reduce the risk of long-term complications; in older patients the improvement in general health is paramount and often rewarding.

When the patient remains poorly controlled yet

Table 3. Oral hypoglycaemic agents: dosage schedules

	Tolbutamide	Glibenclamide	Gliclazide	Metformin
Minimum	500mg bd 500mg tds 1g bd	2.5–5mg om 7.5mg om 5mg bd	40–80mg om 80mg bd 80mg tds	500mg daily 500mg bd 500mg tds
Maximum	1g tds	5mg tds (or 10mg + 5mg)	160mg bd	850mg bd

overweight, the decision is even more difficult. While tighter dietary supervision is the most important treatment for these patients, a few will benefit from the use of insulin. The decision is made along similar lines to those described above, and a two- to three-month trial of insulin can again be valuable in drawing the right conclusion. Insulin is not normally indicated in poorly controlled overweight patients who are actually gaining weight from over-eating: the final result can be needless and excessive obesity.

Insulin in the presence of intercurrent illness

Many disorders, notably infections, increase insulin resistance, and when diabetes control deteriorates as a result, insulin is needed. Following recovery it is normally possible to withdraw insulin and restart the patient's usual treatment.

Steroid therapy always exacerbates hyperglycaemia. Patients need to be carefully monitored, and treated with insulin if the need arises. Patients who need steroids should never be denied their use simply because of diabetes.

Starting insulin

Insulin treatment needs to be introduced by an expert member of the team. Unless the patient is ill, it is usually done as an outpatient, either by the hospital staff or, where expertise exists, in general practice. Twice-daily insulin is normally required, although the health of some elderly patients can be remarkably improved by a single daily injection. Patients need a lot of support when they start insulin, and occasionally hospital admission is needed to provide this level of support.

Diabetes management during illness

Patients should always be instructed to continue their treatment when they are ill; *insulin in particular should be neither reduced nor stopped*. Most patients are likely to need more treatment than usual because of the development of insulin resistance, and some on oral hypoglycaemics will need temporary insulin treatment. More intensive monitoring is needed on these occasions,

and it is unfortunate that so many sick people actually stop their usual monitoring when they feel ill.

Those who are vomiting should replace their carbohydrate intake using fluids, but if vomiting does not resolve quickly, admission to hospital for intravenous fluids is essential.

Screening for complications of diabetes

Diabetes treatment aims to prevent complications where possible, by good management and metabolic control. If complications should occur, their consequences may still be preventable (eg, foot ulcers, decline of vision, progression of renal disease). Systems and techniques of screening for complications, which should usually be undertaken annually, are described elsewhere. Many patients with NIDDM (10–20%) have demonstrable complications at the time of diagnosis, and screening is thus necessary from the onset.

When to refer non-insulin-dependent diabetic patients to hospital diabetic clinics

The following guidelines summarise the situations in which the hospital diabetes team will normally need to be involved.

1. New patients, if practice facilities are insufficient for patient treatment and education.
2. Most patients who become ill with deteriorating diabetic control.
3. Patients with persistent vomiting.
4. Patients in whom control has become a problem, or where hypoglycaemia is severe or frequent.
5. When insulin is needed, especially if the decision is uncertain.
6. Patients with the following complications:

<i>Retinopathy:</i>	Unexplained reduced visual acuity; more than minor background retinopathy; any retinopathy near macula.
<i>Neuropathy:</i>	Impotence; diarrhoea and other auto-

	nostic symptoms; painful neuropathy; other neuropathic syn- dromes, radiculopathies, ocular palsies, etc.
<i>Nephropathy:</i>	Intermittent or continuous proteinuria; raised serum creatinine; uncontrolled hypertension.
<i>Feet:</i>	Ulceration; critical ischaemia.
<i>Large vessel disease:</i>	Unstable angina; transient cerebral ischaemic attacks; claudication.
<i>Major dyslipidaemias.</i>	

Medical audit

These guidelines can be used as a basis for medical audit. For example, medical records of a number of patients with non-insulin-dependent diabetes mellitus can be reviewed to see whether the diagnostic criteria have been satisfied, whether a glucose tolerance test has unnecessarily been done, whether certain key items of information such as a record of the blood pressure and a history of smoking have been entered in the medical record. Treatment policies could also be reviewed against these guidelines. One useful outcome measure is the level of glycosylated haemoglobin, but adverse clinical outcomes should also be considered. For example, an episode of diabetic ketoacidosis should prompt a review, not so much of the immediately precipitating events but rather of the systems of care in the preceding year or so.

Conclusions

Correct diagnosis and treatment of NIDDM represent common problems which need to be solved both in hospital and in general practice. Most patients will be seen first by their GP, and diagnosis and initial treatment will often be successfully applied at the primary care level.

The division of care between the two will clearly depend on the level of expertise and the complexity of the individual case, and this paper presents some guidance regarding this interaction in terms of correct management of NIDDM. Audit of these practices will be important if the highest standards are to be maintained.

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Further reading

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Reprints of this article in booklet form are available on payment of £1.50. Background papers submitted to the working party for use in preparing these guidelines are also available on payment of £4.00 per set to cover costs of photocopying and postage. To obtain copies of the above please write to: The Publications Department, Royal College of Physicians, 11 St Andrews Place, Regent's Park, London NW1 4LE.

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