Careful monitoring of patients with diabetes optimises control and minimises complications

Russell Greene guides us through a range of standard tests and examinations used to ensure patients with diabetes are optimally controlled and have the lowest risk of developing complications.

Why monitor?

Diabetes is the commonest and one of the most severe multi-system diseases.[1,2] With changing lifestyles and the rise in global obesity its prevalence is increasing in both developed and developing countries. Good day-to-day control of blood glucose levels is important — and not just for alleviating the acute symptoms that were the probable reason that the patient first came to medical attention (such as weight loss, and disturbances of consciousness, urination and thirst). The main problems with diabetes, in both type 1 (insulin dependant) and type 2 — the factors that cause disability and premature death — are long-term complications on the cardio-vascular, renal and nervous systems, and on the eyes.[3,4,5] The lesson of major studies of long-term management such as the diabetes control and complications trial (DCCT)[6] and the UK prospective diabetes study (UKPDS)[7] is very clear: good control of blood glucose retards or even prevents long-term complications.

Monitoring involves not just checking blood glucose (BG) levels, but conducting regular checks to detect complications at an early stage (Table 1). It is also necessary, as with all long-term drug therapy, to monitor for possible adverse drug effects. Thus, although abnormalities in BG levels are the key feature of the condition, checking them is only a small part of the comprehensive disease monitoring.

Diagnosis

The confirmation of a diagnosis of diabetes is based on the measurement of BG when fasting and 2h after a standard 75g glucose test meal (the 'glucose tolerance test'). In health the fasting BG (for example, before meals) should stay between 4–7mmol/L and after a meal insulin should be released quickly enough and in sufficient quantity to prevent levels approaching 11mmol/L (this being the level above which glucose would spill over into the urine). Levels outside these ranges are strongly suggestive of diabetes, but obviously borderline cases need repeat testing, and possible primary causes such as pregnancy or steroid medication need to be eliminated. The WHO has also defined two intermediate stages that signify early or potential diabetes, in an attempt to provide early warning of future problems (Table 2), but its value is not universally accepted.

Day-to-day monitoring

Urine testing is rarely used nowadays for routine glucose testing. Although convenient and avoiding the skin puncture that some patients find objectionable, it produces imprecise readings that do not reflect current BG levels. Moreover it provides no information on low BG and thus potential hypoglycaemia. Nevertheless it still may be useful for older, well

Table 1. Regular monitoring of patients with diabetes

Aim	Area monitored	Test or examination
Diagnosis	Biochemical	Plasma glucose (random, fasting), 2h glucose tolerance
Day-to-day control	Biochemical	Blood glucose
Monitor long-term complications control	Biochemical	Glycated haemoglobin, blood lipids, body weight
	Cardiovascular	Blood pressure, ECG, peripheral perfusion (pulses, etc.), symptoms of ischaemia
	Feet	Blisters, sores, chiropody; pulses
	Eyes	Fundoscopy, visual acuity, cataract, intra-ocular pressure
	Renal	Proteinuria; creatinine (clearance)
	Neurological	Sensory, motor and autonomic neurological examination
Monitor drug therapy	Insulin	Injection sites, weight, hypoglycaemic episodes
	Metformin	Renal function (see above)
	Sulphonureas, meglitinides	Weight, hypoglycaemic episodes
	Thiazolidinediones	Cardiac function
	Statins	Liver function, muscle pains

Figure 1. Automated finger pricking device (courtesy of Bayer Diagnostics, with thanks).

stabilized type 2 patients who only need to check occasionally, particularly because the timing is not crucial and passing a stick through the urine stream is easy.

Routine testing for microalbuminuria (proteinuria) is undoubtedly important, but this need not be done by the patient (see renal section below). In addition there are a minority of patients who are prone to ketosis and can use urine sticks to detect ketones.

Blood glucose

Home BG measurement is now the preferred method of self-monitoring, and is the only form suitable for type 1 patients. The procedure has been considerably improved in recent years. There are now minimally invasive semi-automatic skin puncture devices that have made obtaining blood less unpleasant. The depth of the puncture can be altered and the device is spring-loaded (Figure 1). More sensitive strips requiring less blood have been developed, which can be inserted into automated meters that display the result in large easy legible digits (this is useful because many diabetics have some visual impairment). Results can be stored in the meter and downloaded to a computer to show trends (Figure 2).

A particular advantage of BG measurement compared to the old urine glucose methods is that it can detect hypoglycaemia. This can be important for patients who are prone to hypoglycaemia, such as some elderly type 2 patients taking sulphonylureas or insulin dependent type 1 patients aiming for 'tight' control.

Not all patients need to measure their BG daily. Many type 2 patients, if stabilised, need only do so occasionally provided their glycated haemoglobin (see below) is satisfactory. Indeed some evidence suggests that it may produce anxiety or guilt in patients who 'fail' to control it perfectly — and anyway may confer little benefit because not all patients have the knowledge and skill to make appropriate dose adjustments in response.[8]

On the other hand, some type 1 'expert patients' following a basal-bolus regimen measure their BG three or four times daily. They use insulin pens to supply variable doses of short-acting insulin immediately before meals and estimate the dose according to their last BG and the anticipated meal. This system (DAFNE, or dosage adjustment for normal eating) if properly understood affords diabetics great flexibility in balancing and varying diet, activity and insulin dose. The frequency with which other type 1 patients need to monitor will depend on how stable they are, what their usual BG pattern is and how prone they are to hypoglycaemia, but many will only do it a few times per week, either randomly or at specific times such as before meals, in the evening or on rising.

It is important that all patients who use BG monitoring are taught not just how to do it but also how to interpret the results and what action to take according to the result. Apart from the expert patients referred to above, none should alter their insulin dose frequently. Instead, they should modify it gradually if necessary according to several previous results, which would include both peak (post-prandial) and trough (fasting or pre-prandial) readings.

Long-term control

All diabetics should be assessed in a clinic every 6–12 months. The key measure is their glycated haemoglobin-A1c (HbA1c), which indicates their overall long-term control. It measures the proportion of red blood cell haemoglobin that has been affected by a high blood glucose level.

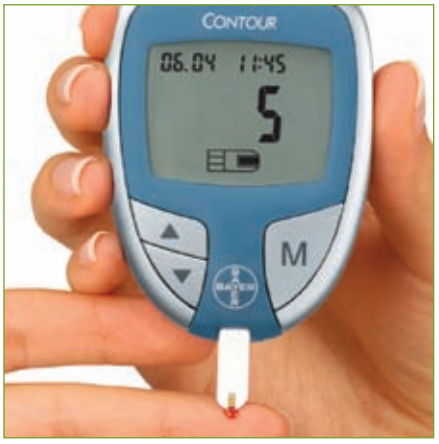

Figure 2. Blood glucose monitoring device (courtesy of Bayer Diagnostics, with thanks).

Table 2. WHO definitions of diabetes mellitus

Class	Plasma glucose (mmol/L)*		
	Fasting		OGTT at 2 hours
Diabetes mellitus	>7	and/or	>11.1
Impaired glucose tolerance	<7	and	7.8–11.1
Impaired fasting glucose	6.1–7		
Normal fasting glucose	<6.1	and	<7.8

**Based on plasma glucose levels, as measured in the laboratory.*
For whole blood (finger prick) figures are approximately 10% lower (for example, 6.1 and 10mmol/L for diabetes mellitus). OGTT=oral glucose tolerance test.

Because the life of a red cell is 120 days it gives a picture of average glucose levels over the past three months. It is now the gold standard for assessing diabetic control,[4] but must be carried out by a laboratory on blood plasma obtained by venepuncture. Non-diabetics normally have a level of <5% glycation; the target for diabetics is <6.5%. Poor control will be revealed by levels above 7.5% despite a patient having perhaps been especially scrupulous controlling their BG over the days or weeks previous to their clinic visit, as shown by the readings stored in their BG meter or recorded in their written record.

Monitoring of potential complications

The complications of diabetes are delayed or mitigated by good control, but because perfect control is not achievable with current technology (short of pancreatic transplantation) some complications will occur eventually to most patients.

Cardiovascular

Control of blood pressure is as important as glycaemic control in limiting complications. The BP targets for antihypertensive therapy are lower for diabetics (130/80mmHg) than non-diabetics because the former are inherently at a higher risk of cardiovascular disease. Examination and checking for symptoms of ischaemic heart disease (ECG, chest pain) and checking peripheral pulses will detect incipient vascular disease (angiopathy). Serum lipids must also be checked to ensure they are low (ideally total cholesterol should be reduced below 5.0mmol/L or by 20–25%, whichever is lower[9] and the patient's weight must be monitored.

Renal

Kidney disease (nephropathy) is a major potential problem and diabetics make up 10–20% of the dialysis/renal transplant population. The key criterion here is the glomerular filtration rate, as calculated from the serum creatinine. Plotting this against time gives a valuable index of any decline in renal function. Early signs of incipient damage are heralded by increasing microalbuminuria, so urine protein is regularly monitored. Other urine tests are not usually necessary unless the patient is prone to ketosis (rare except for some brittle type-1 patients) in which case urinary ketones need monitoring, particularly in times of metabolic stress such as during infections. Some patients may need watching for signs of urinary tract infection.

Feet

Poor peripheral circulation and poor nerve sensation (neuropathy) can permit minor foot lesions to progress rapidly to gangrene and potential amputation. Chiropodists should see all patients regularly, cut toenails, attend to bunions and so on, and recommend suitable footwear.

Eyes

Diabetics are prone to retinal damage (retinopathy), glaucoma and cataract, so ophthalmological examination is essential, including fundoscopy, field tests and intraocular pressure testing. Diabetes is the commonest cause of acquired blindness in developed countries.

Neurological

Neuropathy can involve any peripheral nerves, but sensory nerves in the extremities are often affected first. This is tested by checking different types of sensation (for example, pressure and vibration) at different sites around the body, but particularly the feet. Autonomic neuropathy can cause almost any symptom but cannot easily be monitored prospectively.

Monitoring drug therapy

Diabetes requires lifelong medication so possible adverse effects need to be anticipated.

Insulin

Too-frequent use of the same injection sites can cause unsightly skin damage, so the sites can be inspected and patients advised to rotate them more if problems arise. A history of hypoglycaemic attacks may prompt a reassessment of the dosage regimen, which could be too 'tight' for the patient. Insulin also promotes weight gain.

Metformin

Metformin must be stopped if there is renal impairment, because it makes the patient prone to lactic acidosis.

Sulphonureas and meglitinides

Sulphonylureas and meglitinides (repaglinide and nateglinide) may induce hypoglycaemia and the sulpnonyureas can cause weight gain.

Thiazolidinediones

Thiazolidinediones ('glitazones', such as rosglitazone) have been implicated in liver impairment, heart failure and myocardial infarction, so patients must be watched for signs of these developing.

Statin therapy

Statin therapy requires liver function testing before starting and twice yearly thereafter until one year after the effective dose is reached.

Summary

It is clear that ongoing close and diligent monitoring of diabetic patients is crucial to their being able to enjoy a good quality of life with minimal serious complications. Pharmacists can reduce risk and optimise treatment by ensuring correct monitoring

occurs and patients are as closely involved in their management as possible.

Declaration of competing interests

The author declares he has no competing interests.

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