

Type 2 diabetes not just a touch of sugar

Type 2 diabetes is more often than not associated with other cardiovascular risk factors; hence it is better considered a syndrome than simply a biochemical diagnosis.

PAT J. PHILLIPS

MB BS, MA(Oxon), FRACP,
MRACMA, GradDipHealthEcon(UNE)

Dr Phillips is Senior Director,
Endocrinology, North Western
Adelaide Health Service,
The Queen Elizabeth Hospital,
Woodville, SA.

Type 2 diabetes is diagnosed according to blood glucose biochemistry, but nearly all patients with type 2 diabetes have at least one of the following associated features:

- central overweight (or 'overwaist')
- hypertension
- dyslipidaemia
- a prothrombotic tendency.

For the purposes of prevention and treatment, it is useful to view type 2 diabetes as a syndrome so that all risk factors for cardiovascular events can be assessed and managed. Taking this approach, there is overlap with features of the metabolic syndrome. Some experts would see the metabolic syndrome as a precursor or early stage of type 2 diabetes.

Progression of glycaemia

Impaired glucose metabolism is very common. About one in four adult Australians have abnormal glucose metabolism: 4% have diagnosed diabetes, 4% have undiagnosed diabetes, and 16% have impaired glucose tolerance or impaired

fasting glucose (so-called 'pre-diabetes').¹ But all 24% have the same condition – just at different stages of its development.

As we age, our insulin resistance increases and our capacity to secrete enough insulin to overcome this resistance decreases (Figure). For a while, our pancreatic beta cells meet the challenge, but at some stage they may not and blood glucose will start climbing. Initially, the blood glucose may still be in the normal range, just higher than it was earlier in life. Then it might move into the range for impaired glucose tolerance and, finally, into the range for diabetes (Table).²

When impaired glucose metabolism progresses and diabetes is diagnosed, this may seem like a clear endpoint. However, type 2 diabetes continues to progress: insulin resistance increases, insulin capacity decreases, and the metabolic mess continues to worsen.

Progression beyond glycaemia

As age increases and blood glucose metabolism is increasingly impaired, other progressive changes

IN SUMMARY

- About one in four adult Australians have abnormal glucose metabolism: 4% have diagnosed diabetes, 4% have undiagnosed diabetes, and 16% have impaired glucose tolerance or impaired fasting glucose.
- Nearly all patients with type 2 diabetes have at least one of the following associated features: central overweight, hypertension, dyslipidaemia and/or a prothrombotic tendency.
- A healthy lifestyle can slow the progression of impaired glucose tolerance to diabetes.
- In the beginning, type 2 diabetes is often controllable by lifestyle change alone, but as the disorder progresses so should treatment.
- Interventions can make a difference at all stages of the development and progression of type 2 diabetes.

Type 2 diabetes

continued

are also occurring. It is useful to consider the ABCs when managing patients with type 2 diabetes:

- A_{1c} (glycosylated haemoglobin)
- Blood pressure
- Cholesterol
- Smoking
- Salicylates.

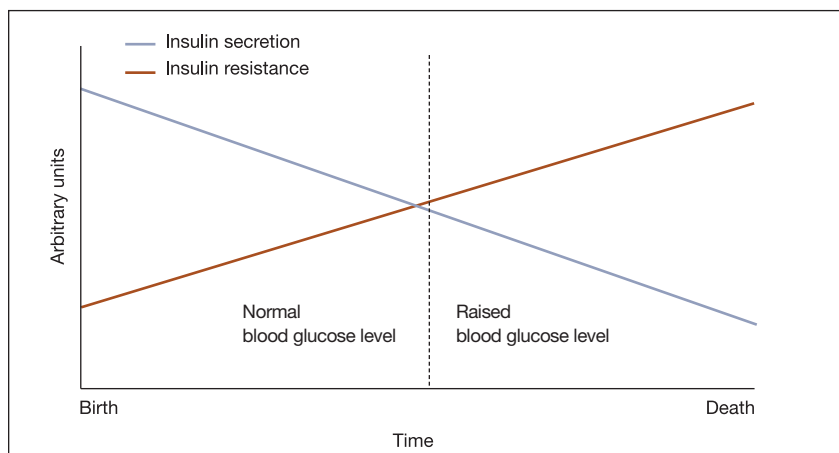


Figure. With increasing age, insulin resistance increases and insulin secretion decreases. Initially the blood glucose level is normal but when the lines intersect the blood glucose level progressively rises.

A_{1c}

Type 2 diabetes is said to often be controllable by lifestyle change alone. This is true – in the beginning – but as the disorder progresses so should treatment. Over time, oral hypoglycaemic agents are needed, then increasing doses and additional oral agents, and then insulin. In the United Kingdom Prospective Diabetes Study (UKPDS), 50% of participants required insulin within six years of diagnosis to maintain $A_{1c} \leq 7\%$.³ Even with increasing treatment, overall blood glucose tends to rise over time. The UKPDS showed that A_{1c} increased by 1% each seven years despite 'intensive treatment'.⁴

Blood pressure

Initially, blood pressure increases but remains within the normal range, which is arbitrarily defined as $<130/80$ mmHg in people with diabetes² and $<140/90$ mmHg in others. Some young people with type 2 diabetes have systolic blood pressure below 100 mmHg; their blood pressure will take longer to increase into the 'abnormal' range, but their risk will be progressively increasing before this.

In the past, increasing blood glucose and blood pressure were accepted to be part of normal ageing. (Remember the old 'rule' that the upper limit of normal systolic blood pressure was 100 plus your age?) But blood pressure (like blood glucose) doesn't have to increase with age – for example, it often doesn't in those members of our indigenous population who maintain their traditional lifestyle and don't adopt an unhealthy one with overweight/overwaist and underactivity.

When 'hypertension' is diagnosed, blood pressure has already been increasing for years. Initially, it may be controlled with lifestyle modification, but then medication is needed and then more and more medication is needed. In the UKPDS, blood pressure was held constant (unlike blood glucose, which increased), but increasing medication was required to achieve this.⁵

Cholesterol

Dyslipidaemia is progressive and the associated cardiovascular risk also increases progressively. Interventions have been shown to be effective in reducing cardiovascular risk – two statins (simvastatin and atorvastatin) have been shown to reduce the risk of cardiovascular events by 25 to 40% in people with type 2 diabetes, one other cardiovascular risk factor and total cholesterol over 3.5 mmol/L (i.e. almost all people with type 2 diabetes).^{6,7}

Smoking and salicylates

Quitting smoking is the best health decision any smoker can make – especially a smoker who has the high cardiovascular risk associated with the syndrome of type 2 diabetes.

Taking an aspirin a day does keep heart attacks away.⁸

Table. Oral glucose tolerance test results^{2*}

	Preprandial glucose (mmol/L)	Postprandial glucose (mmol/L)	Comments
Normal	<6.1	<7.8	No excess macro- or microvascular risk
Impaired fasting glucose	6.1 to 6.9	–	Excess macrovascular risk
Impaired glucose tolerance	–	7.8 to 11.0	
Diabetes	>6.9	>11.0	Excess macro- and microvascular risk

* Plasma glucose before (fasting) and two hours after a 75 g glucose load.

Progressive syndrome, progressive risk

All clinical features associated with type 2 diabetes tend to progress, and so does the risk of further health problems. Even

within the 'normal range' for cardiovascular events, there is an increase with increasing risk factors. Cardiovascular events among patients with impaired glucose tolerance are less frequent than among

patients with diabetes, but more frequent than for the general population. Risk increases as impairment of glucose metabolism worsens.

Rates of cardiovascular events increase with time after a diagnosis of diabetes is made. This is partly because of time itself (getting older), but cardiovascular events also increase because risk factors are associated with progressive tissue damage and often the risk factors themselves get progressively worse.

Prevention

The progression of type 2 diabetes and associated features as well as the increasing cardiovascular risk is all a bit depressing. If it is inevitable, why shouldn't patients move on and enjoy the life they have rather than spending time restricting their lifestyle, taking pills, seeing health professionals and having tests?

The 'F factors' predisposing to type 2 diabetes are known: Forty, Family history and Fat (some also add Fitness). We can't change our age or genes, but our risk of diabetes can be greatly reduced if we change our fatness (and fitness) through healthy lifestyle behaviours. Results from the Diabetes Prevention Program, a randomised trial of 3234 people with impaired glucose tolerance, have shown that a dopting a healthy lifestyle can delay progression of glycaemia.⁹ Over an average follow up of almost three years, the absolute risk of progression to diabetes was reduced by 60% in those receiving a lifestyle modification program and by 30% in those receiving metformin (850 mg twice daily), compared with those receiving conventional treatment. The number needed to treat to prevent one person from developing diabetes in the next three years was five for the lifestyle program and ten for metformin.

We now know that interventions can make a difference at all stages of the development and progression of type 2 diabetes. Children of parents with type 2 diabetes don't have to gain as

much weight as they do now. Early diagnosis of diabetes allows interventions to slow progression of cardiovascular risk factors. When complications occur, such as microalbuminuria, multiple interventions have been shown to greatly reduce the risk of macro- and microvascular events.¹⁰

Final comments

Our role as health professionals and educators is to identify people who can improve their future health and give them the information and opportunity to do so. We can work with them to integrate their chosen interventions into their daily routine so they can get on with their lives.

Perhaps the most important step is for us to convince ourselves of the value of identifying features associated with type 2 diabetes at all stages of development. We may need to change some of our beliefs that were formed before we knew interventions can make a difference. But once we are convinced, we can choose the level of intervention we wish to practise. Then we can incorporate these interventions into our daily professional work and get on with our jobs. **MT**

References

1. Dunstan D, Zimmet P, Welborn T, et al, on behalf of the AusDiab Steering Committee. Diabetes and associated disorders in Australia 2000: the accelerating epidemic. Melbourne: International Diabetes Institute; 2001.
2. Harris P, Joyner B, Mann L, Phillips P, Snowdon T, Webster C. Diabetes management in general practice 2005/6. 11th ed. Canberra: Diabetes Australia and RACGP; 2005.
3. Turner RC, Cull CA, Frighi V, Holman RR. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). UK Prospective Diabetes Study Group. JAMA 1999; 281: 2005-2012.
4. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight

patients with type 2 diabetes (UKPDS 34) .

Lancet 1998; 352: 854-865 [erratum in: Lancet 1998; 352: 1558].

5. Adler AI, Stratton IM, Neil HA, et al. Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study. BMJ 2000; 321: 412-419.

6. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002; 360: 7-22.

7. Colhoun HM, Betteridge DJ, Durrington PN, et al; CARDS investigators. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin

Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. Lancet 2004; 364: 685-696.

8. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients . BMJ 2002; 324: 71-86 [erratum in: BMJ 2002; 324: 141].

9. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002; 346: 393-403.

10. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med 2003; 348: 383-393.

DECLARATION OF INTEREST: Dr Phillips has received research and travel grants, acted on advisory boards and been involved with clinical trials and seminars sponsored by a range of pharmaceutical companies. He does not think that these associations have influenced the content of this article.