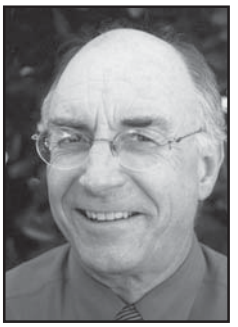
Editorial



Tony Townsend has been a general practitioner for 30 years. Although he has dabbled in medical politics, medical ethics, community-based teaching, university-based teaching, quality improvement and assessment, his passion remains clinical general practice. He is currently a full-time general practitioner in Whangamata.

The metabolic syndrome

Advances in basic medical science have not generally excited me as much as some of the clinical research that seems to be more relevant to my everyday general practice. However, I have followed with great interest the developments resulting from some of the basic scientific and clinical research related to the metabolic syndrome and the relationship of this to diabetes and cardiovascular disease.

Part of my interest stems from having spent several years working in the United Arab Emirates (UAE), a country that developed from a predominantly Bedouin community to an extremely affluent culture in less than thirty years.

Arabs who roamed the desert on camels and survived in a hostile environment on a subsistence diet in the 1950s now drive their Mercs and Beamers from their air-conditioned palaces and pull up outside fast food takeaway shops to order their high calorie meals without stepping out of their vehicles. The prevalence of type 2 diabetes in the 50 to 60 year age group is now around 60% and almost all of this is associated with the metabolic syndrome.

Interestingly, after the age of 60 years the prevalence drops off despite most studies showing that type 2 diabetes prevalence increases with age. Presumably this is due to a marked increase in mortality in the older UAE patients who have this syndrome.

Another stimulus has been the growing awareness that the metabolic syndrome is associated with a wide range of very common, and some less common, conditions including obesity, diabetes, hypertension, cardiovascular disease, cerebrovascular disease, polycystic ovary syndrome and acanthosis nigricans. It is extremely common. Around 24% of US adults are affected[1] and there is every reason to think that New Zealand figures would be similar. And, even more importantly, I am interested because many of the hypotheses and theories explaining this syndrome seem to make such good sense.

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The thrifty gene theory was first proposed by James Neel in 1962.[2] Although his theory has been challenged[3] and the genes (there are certainly more than one) have not yet been fully identified, it seems a sensible explanation for the huge increase in prevalence of type 2 diabetes in Polynesians, Asians, American Indians and Arabs who have moved from a traditional to a more affluent lifestyle. However, the syndrome is not confined to people from developing countries. It has been estimated that by 2025 there will be 300 million diabetic adults worldwide and most of these will be in India, China and the US.[4] It is also disturbing that impaired glucose tolerance associated with insulin resistance has been found to be highly prevalent among US children and adolescents who are severely obese, irrespective of ethnic group.[5]

Genetic susceptibility to the metabolic syndrome is complex and multiple genes have been implicated.[6] These include the peroxisome proliferator-activated receptor gamma (PPARg) and calpain-10 (CAPN10) genes.[7] If the pancreatic beta cells continue to produce sufficient insulin to overcome the cellular resistance to insulin, diabetes will not develop, but other complications of the metabolic syndrome become evident as a result of hyperinsulinaemia, dyslipidaemia, hypertension and a pro-thrombotic environment.[8] As Brotman and Girod have succinctly stated in their recent editorial, *'Even before beta cells fail and type 2 diabetes ensues, the deadly quartet is quietly rehearsing'*.[9]

In this issue we have focussed on the metabolic syndrome in both our editorial and CME sections. We know that reducing glycaemia has the potential to prevent deaths from com-

plications related to diabetes.[10] We also know that lifestyle changes (predominantly diet and exercise) improve outcomes for those patients who have developed diabetes, but it is still unclear as to whether or not treating patients who have the metabolic syndrome without diabetes (i.e. those who have insulin resistance and/or glucose intolerance without frank diabetes) improves their outcome – but it makes sense that it should.

The development of new drugs to specifically treat insulin resistance is exciting. Until now the only available agent that we have had to decrease insulin resistance has been metformin. Too often this has been used as a second-line pharmacological agent rather than a first choice, although the UKPDS has provided clear evidence of the advantages of using metformin as first-line pharmacological therapy in diet-treated overweight patients who have type 2 diabetes.[11] However, metformin treatment has some disadvantages. It is not particularly well tolerated, it is not particularly good at lowering insulin resistance and it should not be used in patients who have impaired renal function. Rosiglitazone will soon be available in New Zealand and Adrian Scott discusses the use of this new agent in the CME section. Drugs such as this – which directly target the susceptibility genes – must improve the outcome for patients who have this syndrome. Once safety profiles are improved, it makes sense that insulin sensitisers should be used at an early stage in the management of insulin resistance and that this should delay or even prevent the progression to diabetes and reduce the burden of cardiovascular disease.

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I will continue to follow developments in the aetiology and management of the metabolic syndrome with interest. I am optimistic that before too long we will be able to significantly improve morbidity and mortality for the large and increasing number of people who are victims of this deadly syndrome. This may not have a great impact on the worldwide diabetes epidemic, but it should help us to improve the outlook for some of our diabetic patients.

The metabolic syndrome

Type 2 DM or IGT and/or insulin resistance with two or more of the following components:

- Raised arterial pressure ≥ 140/90 mm Hg
- Raised plasma triglycerides and/or low HDL cholesterol
- Central obesity and/or BMI ≥ 30
- Microalbuminuria

Definition, diagnosis and classification of diabetes mellitus and its complications, WHO 1999

What's in a name?
Synonyms for the metabolic syndrome

- Reaven's syndrome
- Syndrome X
- The deadly quartet
- The dysmetabolic syndrome
- Insulin resistance syndrome

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