

The diabetes epidemic: addressing diagnostic and therapeutic challenges

"Diabetes not only represents a public health problem with increased cardiovascular disease morbidity and mortality, but also poses major economic challenges for healthcare systems around the globe."

Diabetes mellitus (DM) has become the modern-time epidemic that continues to increase rapidly, affecting millions of people around the globe [1-7]. In the USA, the number of adults who reported having been diagnosed with DM was 9.9% in the year 2009, adding to this figure the substantial number of cases of undiagnosed diabetes, this number approaches 14% of the population and is projected to be 33% by the year 2050 [8]. Worldwide, over 285 million people have diabetes, with projected increase to 366 million diabetics by the year 2030 [7]. Diabetes not only represents a public health problem with increased cardiovascular disease (CVD) morbidity and mortality, but also poses major economic challenges for healthcare systems around the globe. In the USA, for example, in 2007 diabetes-related costs amounted to US\$253 billion, including direct medical cost and indirect costs such as absenteeism, loss of productivity and early mortality [7].

Healthcare providers are faced with major challenges in diagnosis and management of diabetes and its complications, particularly early recognition of chronic kidney disease, the main cause of end-stage renal disease and renal replacement therapy, and a major contributor to early mortality from CVD in the diabetic population [9-11].

In this themed issue of *Therapy*, we discuss selected 'hot topics', addressing therapeutic and diagnostic challenges as well as opportunities for CVD risk reduction. These articles are written by scholars with particular expertise and insights in the field. In this issue, the Heinz Drexel group discuss in a comprehensive review the current evidence for combination lipid therapy in people with diabetes [12]. While statins are a wellestablished, lipid-lowering therapy for people with diabetes that is associated with CVD risk reduction as well as pleotropic effects above and beyond lipid lowering [13], residual CVD risk remains unacceptably high in the diabetic population despite statin therapy [14]. Therefore, combination lipid-lowering therapy addressed in this issue by Drexel *et al.* appears to be a logical option in this high CVD risk diabetic population.

Obesity remains one of the major risk factor for diabetes and CVD with up to 90% of diabetic patients being overweight or obese at diagnosis [15]. These patients generally continue to gain weight throughout the course of their illness in a way that seems inevitable [16] and thus enter into a vicious cycle of weight gain and poor glycemic control. Ironically, some of the major therapeutic agents for diabetes, such as insulin, as well as oral antidiabetic agents, such as sulfonylureas, lead to substantial weight gain with potential perpetuation of such a vicious cycle of weight gain and poor glucose control, sending the wrong message to patients who are often asked to lose weight. This therapeutic dilemma is addressed in a review by our group providing insights into weight gain associated with insulin therapy and highlighting therapeutic strategies that could potentially mitigate weight gain associated with such therapy [17].

Complementary to our article is the special report by Sonnett et al. on incretin-based therapies and their future in Type 2 diabetes [18]. These agents, contrary to insulin, sulfonylureas and thizolidinediones, are associated with substantial weight loss, such as the case with GLP-1 agonists including exenatide and liraglutide, or at least weight neutral, as with the DPP IV inhibitors sitagliptine and saxagliptine. Beneficial weight effects make these agents attractive options in Type 2 diabetes where the majority of patients are obese [19]. In fact, this feature prompted the endorsement of early introduction of these agents for the treatment of Type 2 diabetes [20]. Future implications of these therapeutic agents are addressed in the special report in this issue [18].



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Finally, in a review of cutting-edge information, the Whaley-Connell group presents an insightful discussion on the role of novel biomarkers in diagnosis of early diabetic kidney injury [21]. The use of these markers, including neutrophil glutinase-associated lipoprotein, kidney injury module-1 and podocin might lead to early recognition and treatment of diabetic kidney disease, therefore preventing one of the major complications of diabetes.

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Bibliography

- 1 Ayach BB, Korda H: Type 2 diabetes epidemic in First Nations people of Canada. *Ethn. Dis.* 20, 300–303 (2010).
- 2 Davis GA: The epidemic of diabetes for SC. *SC Nurse* 17, 1 (2010).
- 3 Low LC: The epidemic of Type 2 diabetes mellitus in the Asia-Pacific region. *Pediatr. Diabetes* 11, 212–215 (2010).
- 4 Moore PA, Zgibor JC, Dasanayake AP: Diabetes: a growing epidemic of all ages. J. Am. Dent. Assoc. 134, 11S–15S (2003).
- 5 Wiegand S: Type 2 diabetes in children: a new epidemic in Europe? *MMW Fortschr. Med.* 152, 42–45 (2010).
- 6 Wilmot EG, Davies MJ, Yates T, Benhalima K, Lawrence IG, Khunti K: Type 2 diabetes in younger adults: the emerging UK epidemic. *Postgrad. Med. J.* 86, 711–718 (2010).
- 7 Wylie-Rosett J: The diabetes epidemic: what can we do? J. Am. Diet Assoc. 109, 1160–1162 (2009).
- 8 Danaei G, Friedman AB, Oza S, Murray CJ, Ezzati M: Diabetes prevalence and diagnosis in US states: analysis of health surveys. *Popul. Health Metr.* 7, 16 (2009).
- 9 Collins AJ, Kasiske B, Herzog C et al.: Excerpts from the united states renal data system 2003 annual data report: atlas of

end-stage renal disease in the united states. *Am. J. Kidney Dis.* 42(6 Suppl. 5), A5–A7, S1–S230 (2003).

- 10 McCullough PA, Li S, Jurkovitz CT et al.: CKD and cardiovascular disease in screened high-risk volunteer and general populations: the Kidney Early Evaluation Program (KEEP) and National Health and Nutrition Examination Survey (NHANES) 1999–2004. Am. J. Kidney Dis. 51, S38–S45 (2008).
- 11 Whaley-Connell AT, Sowers JR, McFarlane SI *et al.*: Diabetes mellitus in CKD: Kidney Early Evaluation Program (KEEP) and National Health and Nutrition and Examination Survey (NHANES) 1999–2004. *Am. J. Kidney Dis.* 51, S21–S29 (2008).
- 12 Saely CH, Drexel V, Vonbank A, Drexel H: Lipid management in Type 2 diabetes: the case for combination therapy? *Therapy* 8(2), 129–141 (2011).
- 13 McFarlane SI, Muniyappa R, Francisco R, Sowers JR: Clinical review 145: Pleiotropic effects of statins: lipid reduction and beyond. *J. Clin. Endocrinol. Metab.* 87, 1451–1458 (2002).
- 14 Judge EP, Phelan D, O'Shea D: Beyond statin therapy: a review of the management of residual risk in diabetes mellitus. *J. R. Soc. Med.* 103, 357–362 (2010).
- 15 McFarlane SI, Banerji M, Sowers JR: Insulin resistance and cardiovascular disease. J. Clin. Endocrinol. Metab. 86, 713–718 (2001).

- 16 Tremble JM, Donaldson D: Is continued weight gain inevitable in Type 2 diabetes mellitus? J. R. Soc. Promot. Health 119, 235–239 (1999).
- 17 Provilus A, Abdallah M, McFarlane SI: Weight gain associated with antidiabetic medications. *Therapy* 8(2), 113–120 (2011).
- 18 Sonnett TE, Robinson JD, Bowen KA: Incretin-based therapies and their future in Type 2 diabetes mellitus. *Therapy* 8(2), 143–152 (2011).
- 19 Fonseca VA, Zinman B, Nauck MA, Goldfine AB, Plutzky J: Confronting the Type 2 diabetes epidemic: the emerging role of incretin-based therapies. *Am. J. Med.* 123, S2–S10 (2010).
- 20 Rodbard HW, Jellinger PS, Davidson JA *et al.*: Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology consensus panel on Type 2 diabetes mellitus: an algorithm for glycemic control. *Endocr. Pract.* 15, 540–559 (2009).
- Buddineni JP, Chaudhary K, Whaley-Connell A: Biomarkers in diabetic kidney disease. *Therapy* 8(2), 121–127 (2011).