

Diabetologia

Up front



Competition for publication in *Diabetologia* continues to grow, and less than 20% of papers are accepted. Of all the high-quality papers that appear in this month's issue I want to draw your attention to five articles that I think are particularly interesting. The articles are summarised here. Our publisher, Springer, has kindly made the full text of each of these papers freely available. I hope you enjoy reading them!

Sally M. Marshall, Editor

Metabolic surgery for the treatment of type 2 diabetes in obese individuals

David E. Cummings, Francesco Rubino

Several bariatric operations dramatically improve glucose homeostasis, causing type 2 diabetes remission in most cases. This results from weight loss and from diverse weight-independent glucose-lowering mechanisms. Results from large, long-term observational studies and numerous randomised clinical trials directly comparing surgery vs medical/lifestyle diabetes therapies uniformly show that surgery achieves better glycaemic control and reduction of cardiometabolic risk, including among people not obese enough to qualify for traditional bariatric surgery. Based on such evidence, bariatric operations are now being repurposed as specific therapy for type 2 diabetes, a practice dubbed 'metabolic surgery'. In a review in this issue (<https://doi.org/10.1007/s00125-017-4513-y>), Cummings and Rubino summarise mechanistic and clinical evidence supporting new guidelines developed during the second Diabetes Surgery Summit, an international consensus conference, for use of metabolic surgery. These recommendations, now ratified by 53 worldwide medical/scientific societies and incorporated into the ADA Standards of Diabetes Care in 2017, suggest considering metabolic surgery for inadequately controlled type 2 diabetes in individuals with a BMI as low as 30 kg/m², or 27.5 kg/m² for Asian individuals.

④ The figures from this review are available as a [downloadable slideset](#).

Medication use for the treatment of diabetes in obese individuals

John P. H. Wilding

People with type 2 diabetes are often also obese, and obesity can complicate type 1 diabetes. The newer glucose-lowering medications, namely the glucagon-like peptide-1 receptor agonists and the sodium–glucose cotransporter 2 inhibitors, also reduce body weight, and new anti-obesity drugs have become available that complement lifestyle weight management. In this issue (<https://doi.org/10.1007/s00125-017-4288-1>), John Wilding reviews the effects of different diabetes medications on body weight, and discusses how a weight-focussed approach to diabetes treatment, including appropriate use of glucose-lowering medicines that help weight loss, and anti-obesity medication, can help optimise outcomes for people with diabetes and obesity. Many novel medicines for obesity and diabetes, including combinations of drugs with complementary modes of action, are in development and may result in a much greater emphasis on this approach in the future.

Translating aetiological insight into sustainable management of type 2 diabetes

Roy Taylor and Alison C. Barnes

The aetiology of type 2 diabetes can now be simply described. The 2008 twin cycle hypothesis postulated that chronic energy

excess leads to a vicious cycle progressively driving up liver fat content, increasing export of triacylglycerols to the pancreas and, in susceptible people, ultimately results in failure of the acute insulin response. In this issue (<https://doi.org/10.1007/s00125-017-4504-z>), Taylor and Barnes summarise studies testing the hypothesis in individuals with a short duration of type 2 diabetes using a low-energy diet and maintenance of reduced body weight. The beta cell defect can now be understood as de-differentiation, caused by cellular metabolic stress and reversible loss of specialised function. Longer-term management highlights the need for effective approaches to dietary advice. It is clear that one diet cannot suit all, therefore, a range of soundly based approaches, tailored to individual preferences, is described. The critical role of family and social circle in achieving sustainable changes in food habits is considered.

Ⓒ The figures from this review are available as a [downloadable slideset](#).

Enteroendocrine K and L cells in healthy and type 2 diabetic individuals

Tina Jorsal, Nicolai A. Rhee, Jens Pedersen, Camilla D. Wahlgren, Brynjulf Mortensen, Sara L. Jepsen, Jacob Jelsing, Louise S. Dalbøge, Peter Vilmann, Hazem Hassan, Jakob W. Hendel, Steen S. Poulsen, Jens J. Holst, Tina Vilsbøll, Filip K. Knop

Hormones from enteroendocrine K and L cells are well-established regulators of glucose homeostasis and appetite. However, it is unclear how these enteroendocrine cells are distributed in the healthy human intestinal tract and whether this distribution is altered in type 2 diabetes. In this issue (<https://doi.org/10.1007/s00125-017-4450-9>), Jorsal et al report the results of anterograde and retrograde double-balloon enteroscopy with frequent mucosal biopsy retrieval (every 30 cm) along the entire intestinal tract in 12 individuals

with type 2 diabetes and 12 healthy individuals. They found that K cells and L cells exhibit specific distribution patterns along the small and large intestine. Furthermore, they show differences between healthy and type 2 diabetic individuals in distribution patterns and expression profiles of K and L cells. These findings provide a reference work for scientists and clinicians and may promote the understanding of the integrative role of the gut in the regulation of glucose metabolism and appetite.

Long-term follow-up of intensive glycaemic control on renal outcomes in the Veterans Affairs Diabetes Trial (VADT)

Lily Agrawal, Nasrin Azad, Gideon D. Bahn, Ling Ge, Peter D. Reaven, Rodney A. Hayward, Domenic J. Reda, Nicholas V. Emanuele, for the VADT Study Group

Nephropathy in type 2 diabetes is associated with a progressive increase in proteinuria, decline in eGFR and eventual renal failure. Whether the pursuit of intensive glycaemic control to reduce the rate of chronic kidney disease (CKD) is worth the effort, cost and patient burden is an important clinical question that many trials have tried to answer. In this issue (<https://doi.org/10.1007/s00125-017-4473-2>), Agrawal et al report the results of an analysis of the Veterans Affairs Diabetes Trial (VADT) and follow-up study. Participants had advanced type 2 diabetes and prevalent cardiovascular disease, and received excellent blood pressure and lipid management. Intensive glycaemic control for a median of 5.6 years resulted in significantly more people maintaining an eGFR above $60 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$ for up to almost 11 years. This benefit was most evident in those with a moderate-to-high risk of CKD at baseline. Drug-specific benefits could not be elucidated, however, the follow-up was much longer than in recent studies on glucagon-like peptide-1 receptor agonists and sodium–glucose cotransporter 2 inhibitors.

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