From the Journals

Urine or blood ketones?

Brewster S, Curtis L, Poole R. Urine versus blood ketones. *Practical Diabetes* 2017; 34: 13–15.

Ketonuria is part of the diagnostic criteria for diabetic ketoacidosis (DKA); but how reliable is urine ketone testing? This question is particularly important as bedside meters are now available for blood ketone measurement – indeed, currrent United Kingdom (UK) guidelines for DKA diagnosis and management recommends blood rather than ketone measurement. This useful review article discusses the advantages of blood ketone testing. The three ketone bodies are beta-hydroxybutyrate (BOH), acetoacetate, and acetone. In DKA, BOH is the predominant ketone (about 80%). This is measured by blood ketone meters, but urine strips measure acetoacetate only. As DKA is treated successfully, BOH is oxidised to acetoacetate, so blood ketone levels will accurately reflect DKA resolution, but urine tests will remain positive despite clinical and metabolic improvements. Other advantages of blood ketone meters are that they give a quantitative result, and do not rely on a urine sample, which can sometimes be difficult to obtain. The downside, however, as may be expected is that blood testing is relatively expensive.

The artificial pancreas?

El-Khatib H, Bolliro C, Hillard MA et al. Home use of a bihormonal bionic pancreas versus insulin pump therapy in adults with type 1 diabetes: a multicentre randomised crossover trial. *Lancet* 2017; 389: 369–380.

Standard insulin treatment of type 1 diabetes is sometimes described as "open loop". This means that insulin doses are decided upon by patients and/or healthcare workers depending on self-monitoring of blood glucose levels. It is not a very satisfactory system – hence the quest for "closed-loop" systems, either pancreas transplantation (segmental or islet cell) or the "artificial pancreas". The latter is an external or implantable device which infuses insulin in response to continued measurement of tissue glucose levels, the doses being decided by computerised algorithms. Such devices have been intermittently tested for some time, and have been becoming smaller and more sophisticated. This recent Lancet study reports a trial of a "bihormonal" system (i.e. delivering both insulin and glucagon), compared with standard open-loop insulin treatment. The trial was short-term (two 11 week periods) but there was improvement in glycaemic control and reduction in hypoglycaemia in the automated delivery group. This confirms previous studies, and suggests that larger trials (at least 6 months) are now needed. An accompanying Lancet editorial comments that the focus should now move to "commercialisation and real-world application". In fact, an automated insulin-only delivery system (Medtronic Minimed 670G) was approved for use in the USA in 2016. We will certainly be hearing more of this fascinating technology.

Atypical ketosis-prone diabetes

Lontchi-Yimagou E, Nguewa JL, Assah F et al. Ketosis-prone atypical diabetes in Cameroonian people with hyperglycaemic crisis: frequency, clinical and metabolic phenotypes. *Diabetic Medicine* 2017; 34: 426–431.

'Atypical ketosis-prone' diabetes is a form of diabetes seen in Africa, or in African migrants. It is characterised by an abrupt onset with hyperglycaemia or ketoacidosis (DKA), followed by periods of partial or complete remission. The causes of this syndrome, and whether it is a variant of type 1 (T1DM) or type 2 (T2DM) diabetes remain uncertain. This paper from Cameroon has investigated a group of classical T2DM patients (n = 124) with a group with ketosis-prone diabetes (n = 49). The latter group included 34 in the ketotic and 15 in the non-ketotic phase of disease. Investigations carried out included assessment of endogenous insulin secretion (C-peptide) and insulin resistance (HOMA). There were no significant differences between the type 1 and non-ketotic phase atypical diabetic patients. However, the ketotic-phase patients had lower BMI, lower C-peptide and lower HOMA-IR values. The authors conclude that atypical ketosis-prone diabetes is likely to be a variant of T2DM rather than T1DM. It also appears to be associated with transiently reduced insulin secretion at the time of and just after diagnosis, as well as during subsequent ketotic phases. The cause of the syndrome remains, however, mysterious.

Vitamin d and diabetic complications

Samefors M, Scragg R, Lanne T, Nystrom FH, Ostgren CJ. Association between serum 25(OH)D3 and cardiovascular morbidity and mortality in people with type 2 diabetes: a community-based cohort study. *Diabetic Medicine* 2017; 34: 372–379.

One of the possible explanations for the relatively low incidence of type 1 diabetes (T1DM) in the tropics is the "sunshine hypothesis" – that high levels of vitamin D may protect against T1DM. This would explain the increasing incidence as one moves more northerly or southerly from the equator. A new vitamin D-related report may have relevance to type 2 diabetes (T2DM) and its complications in the tropics. This paper studied a cohort of 698 people in Sweden with T2DM and followed them for over 7 years. Serum levels of 25(OH)D3 (vitamin D) were measured at baseline, and correlated with the later development of cardiovascular complications. Both cardiovascular mortality and morbidity was strongly associated with lower vitamin D levels (Hazard Ratio 0.98, p = 0.001), and the association remained after adjusting for other cardiovascular risk factors (e.g. obesity, hypertension etc). Cardiovascular complications of T2DM are seen much less frequently in Africa than in Europe, and the results of this Swedish study may suggest a new "sunshine hypothesis" – that high vitamin D levels in African T2DM patients may protect them from cardiovascular complications.