

Editorial: Diabetology: Feature Papers 2021

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We begin this editorial with a discussion about insulin. Stuart Brink [1] has been involved with paediatric patients with type 1 diabetes for many years and is clearly very knowledgeable and passionate about the subject. He begins with a short history of the idea of pancreatic secretion being involved in the control of glucose, before discussing the Toronto laboratories extraction and their first treatment of Leonard Thompson. He moves from beef and porcine insulin to human insulin, into the modern era of modified insulin molecules to make them short acting or long acting, as well as the demonstration that better glucose control with multiple injections leads to reduced complications both during the trial as well as 20–30 years later. The DCCT was a landmark trial, which pushed clinicians and patients to tighten control, and with that, obtain better measures of control, from sensors to pumps. Technology has expanded dramatically to help with this, has along with newer insulins to gain better control with fewer hypos. Stuart describes how to manage patients transitioning from older insulins to newer analogues or how to start new patients on these regimes, and this provides practical guidance for new clinicians. He also provides some guidance on the use of data analysis from CGMS and how best to use it. Common CGM devices are well described, both freestanding and linked to insulin pumps. He describes advances in inhaled insulin and ultrafast and ultraslow insulins, all of which await full development and approval. Finally, he discusses the thorny issues of availability of insulin for financially distressed parts of the world and what current solutions are available.



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Immune Mechanisms in Type 1 Diabetes

Sanjay Rathod [2] has written an elegant review of the immune mechanisms of destruction of beta cells and potential methods of keeping destructive autoimmunity in check. The key point is that the immune system is hardwired to recognise self-antigens and to develop an immune response to them, which is kept under control by T-reg cells—i.e., this immunity is in a non-reactive tolerant state. Thymic tolerance eliminates lymphocytes producing high-affinity antibodies, as well as those not reacting to self-antigens, but it also tolerates lymphocytes producing medium-affinity antibodies. The presence of infection, inflammation or tissue damage may allow the medium-affinity antibodies to become destructive.

Although immune modulation studies have been pursued for over 35 years, no single study has demonstrated clinical effectiveness with an acceptable safety profile, but there have been several hopeful studies that have led to a better understanding of the mechanisms of beta cell destruction.

For T-cell modulation, two anti-CD3 agents (Teplizumab, Otelexizumab) have shown modest clinical benefits by reducing T-cell activation and reducing T-effector cell numbers. Rituximab, an CD20 B cell blocker, also has clinical benefits. Therapies involving CTLA-4-IgG1 chimeric proteins acting as decoy receptors for CD80/86 reduce T-cell activation, as do LFA-3-IgG1 chimeric proteins. TNF antagonism and combination cyclophosphamide for immune suppression along with ATG and GCSF for T-reg stimulation also have clinical benefits.

A single 14-day regimen of Teplizumab (anti-CD3, a pan T cell marker) delayed the onset of autoimmune T1D by 24.4 months when compared to a placebo-treated group, and

29 percent of treated patients had HbA1c levels less than 7% and insulin dose requirements of less than 0.5 U/kg per day. This drug now has FDA-expedited status.

Many other potential pathways are discussed, including modulating IL17 cytokine levels and increasing IL2 levels to enhance T-reg cells to damp down the cytotoxic T cells. A new technique currently in clinical trials is to generate cytolytic CD4 T cells that specifically target antigen-presenting cells (APC) with Beta-cell-specific antigens. This destroys the APC cells as well as T cells activated by the APCs.

The other five papers in this special edition covered a wide variety of topics in people with type 2 diabetes, from focus groups in rural Pakistan to the use of the FINDRISC questionnaire in young people in Tanzania [3–7], the use of ultrasound to measure median nerve size, a meta-analysis of studies of the renal tubular marker N-Acetyl- β -D-glucosaminidase to assess early diabetic nephropathy, as well as a study of COVID-19-associated mucormycosis in patients with diabetes. Ultrasound was not helpful as a diagnostic tool, nor was FINDRISC in young people. Urine NAG was best at differentiating normal people from those with normo and microalbuminuria.

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References

1. Brink, S.J. Insulin Past, Present, and Future: 100 Years from Leonard Thompson. *Diabetology* **2022**, *3*, 117–158. [[CrossRef](#)]
2. Rathod, S. Novel Insights into the Immunotherapy-Based Treatment Strategy for Autoimmune Type 1 Diabetes. *Diabetology* **2022**, *3*, 79–96. [[CrossRef](#)]
3. Ansari, R.M.; Harris, M.F.; Hosseinzadeh, H.; Zwar, N. Experiences of Diabetes Self-Management: A Focus Group Study among the Middle-Aged Population of Rural Pakistan with Type 2 Diabetes. *Diabetology* **2022**, *3*, 17–29. [[CrossRef](#)]
4. Malindisa, E.K.; Balandya, E.; Mashili, F.; Njelekela, M. Is the FINDRISC Tool Useful in Screening Type 2 Diabetes and Metabolic Syndrome in an African Setting? Experience among Young Adults in Urban Tanzania. *Diabetology* **2021**, *2*, 240–249. [[CrossRef](#)]
5. Guillen-Astete, C.A.; Luque-Alarcon, M.; Garcia-Montes, N. Ultrasound Assessment of the Median Nerve Does Not Adequately Discriminate the Carpal Tunnel Syndrome among Patients Diagnosed with Diabetes. *Diabetology* **2021**, *2*, 226–231. [[CrossRef](#)]
6. Driza, A.R.; Kapoula, G.V.; Bagos, P.G. Urinary N-Acetyl- β -D-glucosaminidase (uNAG) as an Indicative Biomarker of Early Diabetic Nephropathy in Patients with Diabetes Mellitus (T1DM, T2DM): A Systematic Review and Meta-Analysis. *Diabetology* **2021**, *2*, 272–285. [[CrossRef](#)]
7. Sharma, M.; Vanam, H.P.; Panda, N.K.; Patro, S.K.; Arora, R.; Bhadada, S.K.; Rudramurthy, S.M.; Singh, M.P.; Koppula, P.R. Deciphering the Neurosensory Olfactory Pathway and Associated Neo-Immunometabolic Vulnerabilities Implicated in COVID-Associated Mucormycosis (CAM) and COVID-19 in a Diabetes Backdrop—A Novel Perspective. *Diabetology* **2022**, *3*, 193–235. [[CrossRef](#)]