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MEDIA RELEASE

REDEFINING TYPE 1 DIABETES TO AID EARLY INTERVENTION

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REDEFINING type 1 diabetes as an initially asymptomatic autoimmune disorder rather than a metabolic disorder at the end-stage of the disease would enhance early detection, and increase the opportunities to conduct trials to prevent the disease with increasingly effective agents, according to the authors of a Perspective published in the *Medical Journal of Australia*.

Classic type 1 diabetes remains asymptomatic until the end-stage of the disease, when it is too late to prevent progression to requiring insulin therapy, wrote the authors, Professor Jenny Couper, from the Robinson Research Institute at the University of Adelaide and the Women and Children's Hospital, and Professor Leonard Harrison, from the Walter and Eliza Hall Institute of Medical Research in Melbourne.

"Clinical diagnosis is the end stage of subclinical pathology over months to years, during which time β-cells in the islets of the pancreas undergo autoimmune destruction," they wrote.

"This process begins early in life and is revealed by circulating autoantibodies to islet antigens, which denote pancreatic β-cell or islet autoimmunity. Type 1 diabetes is clinically heterogeneous, but most children who develop type 1 diabetes have detectable autoantibodies before the age of 5 years and many are even younger.

"Children with two or more islet autoantibodies who have a normal blood glucose and who are asymptomatic are defined as having stage 1 type 1 diabetes, encompassing the months to years of subclinical disease," they wrote.

"Stage 2 is the intermediate stage that may last many months, when blood glucose rises transiently without symptoms, especially after food. Stage 3 is the classic presentation of type 1 diabetes with symptoms and fasting hyperglycaemia requiring insulin therapy."

Couper and Harrison wrote that advancing the cause of prevention of type 1 diabetes would require "a paradigm shift" which redefined type 1 diabetes as an autoimmune β-cell disorder (ABCD) that begins with asymptomatic islet autoimmunity (stage 1) and not as a metabolic disorder resulting from end-stage pathology (stage 3).

Early pre-clinical diagnosis of ABCD has been shown to substantially decrease the risk of diabetic ketoacidosis (DKA) and reduce family anxiety at clinical presentation. The shift in the disease's definition would have benefits that include minimising the risk of DKA, decreasing psychological stress in affected families at the time of starting insulin therapy, and earlier initiation of treatment trials with a higher likelihood of preserving insulin production and preventing clinical disease, they wrote.

However, there were also challenges, including the cost of general population screening for islet antibodies and minimising family stress when they learn that their child is at increased risk.

"Only 10% of children presenting with type 1 diabetes have an affected first-degree relative. Therefore, most at-risk individuals with ABCD would need to be identified by general population screening," Couper and Harrison wrote. "At present, the costs of screening and follow-up are likely to outweigh the savings from preventing DKA and potentially alleviating family stress when insulin is eventually needed." However as better individualised therapies to slow progression to diabetes are discovered, the balance of costs will

reduce. The first successful trial to slow down progression from islet autoimmunity to diabetes by about 50% has recently concluded.

“Australia is fortunate in having robust research networks of type 1 diabetes clinicians and researchers that monitor the natural history of type 1 diabetes in genetically at-risk families, screen for ABCD, and conduct intervention trials aiming to slow down or prevent the need to start insulin. These networks are a strong foundation for population screening for ABCD and clinical trials to prevent type 1 diabetes,” they concluded.

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