Age-related islet autoantibody incidence in offspring of patients with type 1 diabetes.

Abstract:
Seroconversion to islet autoantibodies precedes type 1 diabetes. This study aimed to identify periods of high seroconversion incidence, which could be targeted for mechanistic and therapeutic studies. Incidence of islet autoantibodies was calculated in 1,650 genetically at-risk children followed with measurements of islet autoantibodies and thyroid autoantibodies at age 9 months and 2, 5, 8, 11, 14 and 17 years. Peak incidence periods were confirmed in a second cohort of 150 children followed until age 6 years with three-monthly samples up to age 3 years. Islet autoantibody incidence (per 1,000 person-years) was 18.5 until age 9 months, 21 from 9 months to 2 years and <10 for intervals after age 2 years. The second cohort confirmed peak incidence around age 9 months and demonstrated an absence of seroconversion before this age. Seroconversion to insulin autoantibodies occurred earlier than other autoantibodies (p<0.01 against glutamic acid decarboxylase [GAD]-, insulinoma-associated protein 2 [IA-2]- and zinc transporter 8 [ZnT8]-autoantibodies). Early peak seroconversion incidence was most evident in children with high-risk HLA DR3/4-DQ8 or DR4/4-DQ8 genotypes. The age period 9 months to 2 years is associated with a high incidence of activation of type 1 diabetes associated autoimmunity in
genetically at-risk children and should be targeted for effective primary prevention strategies.