Kinetics of the post-onset decline in zinc transporter 8 autoantibodies in type 1 diabetic human subjects.

Zinc transporter 8 (ZnT8) is a newly discovered islet autoantigen in human type 1A diabetes (T1D). The objective was to document changes in ZnT8 autoantibody (ZnT8A) titer and prevalence after onset of disease in relationship to 65 kDa glutamate decarboxylase antibody (GADA) and islet cell antigen antibody (IA2A). Autoantibody radioimmunoprecipitation assays were performed on sera from three groups: 21 individuals monitored every 3 months from diagnosis for 2.5 yr; 61 individuals monitored at six monthly intervals for 5-12 yr; and a cross-sectional study of 424 patients with T1D of 20-57 yr duration. Circulating C-peptide was determined as an index of residual ?-cell function. ZnT8A titers declined exponentially from clinical onset of T1D with a t(1/2) ranging from 26 to 530 wk, similar to C-peptide (23-300 wk). Life-table analysis of antibody prevalence to 12 yr indicated that ZnT8A measured with either Arg325 or Trp325 probes persisted for a shorter interval than IA2A. Although prevalence of ZnT8A, IA2A, and GADA were comparable at disease onset (70.4 vs. 73.4 vs. 64%), only 6.7% of individuals remained ZnT8A positive after 25 yr compared with 19.5% for IA2A and 25.9% for GADA. Titers of ZnT8A and IA2A in seropositive individuals decreased progressively, whereas GADA remained elevated consistent with
periodic reactivation of GADA humoral autoimmunity. ZnT8 humoral autoreactivity declines rapidly in the first years after disease onset and is less persistent than IA2A or GADA in the longer term. ZnT8A determination may be a useful measure of therapeutic efficacy in the context of immune-based clinical interventions.