Summary

Type 1 diabetes and its increasing incidence in young children becomes a growing problem in pediatric population. Clinical picture of the disease substantially changed in recent years. For decades it was believed that autoimmune beta cell destruction results in complete loss of their function in just few months after the diagnosis – in fact, C-peptide level (a reliable parameter of endogenous insulin secretion) at the disease diagnosis presents a wide spectrum, and the rate of its fall in next years is not linear and may vary. Patients in the partial remission phase present better metabolic control that may result in the delay of chronic diabetes complications development. However, the factors contributing to maintain or loose beta cell function in first months and following years of the disease are still not entirely known. In the future, recognition of those mechanisms may help developing new therapeutic strategies targeted to maintain not only normoglycaemia, but also functioning beta cells producing endogenous insulin.

As the C-peptide molecule became an established insulin secretion biomarker in diabetic patients, in the review "C-peptide and residual β-cell function in pediatric diabetes – state of the art" its utility in clinical practice, as well as the advances in assays measurement is discussed (*Pediatric Endocrinology, Diabetes and Metabolism: 2021, 27 (2), 123-133).*

Beneficial effects of physical activity are confirmed in patients with all types of long-lasting diabetes, including lower insulin resistance and improved laboratory parameters. However, the possibility of exercise to be a factor prolonging remission phase in children with new-onset type 1 diabetes has not yet been thoroughly studied. The aim of the study "Regular physical activity as a physiological factor contributing to extend partial remission time in children with new onset diabetes mellitus - two years observation" was to elucidate the influence of regular physical activity on prevalence of partial remission (PR) and on C-peptide secretion in children newly diagnosed with type 1 diabetes. 125 children diagnosed with the disease were studied prospectively for 2 years: controlled every 3 months and advised to maintain physical activity according to the official recommendations. Anthropometric parameters, HbA_{1c}, C-peptide level and daily insulin requirement (DIR) were analyzed, and patients' physical activity level was assessed using a self-designed questionnaire. 43% of participants were classified as physically-active. In this group, lower HbA_{1c} after 2 years, lower DIR after 3, 6 months, and after 2 years (all $p < 0.05$) were found. At discharge from hospital, the prevalence of DIR < 0.5 U/kg/24 h with near normoglycemia was similar in both groups, however in next months higher PR prevalence in active group was observed and lasted over time resulting in 44% vs 13% after 2

years ($p < 0.001$). C-peptide after 2 years was comparable in both groups, with higher prevalence of clinically significant levels (> 0.2 nmoL/L according to DCCT) in active group: 79.6% vs 61.4% ($p = 0.029$). These data support the view that regular physical activity may essentially contribute to extend PR time in pediatric diabetes, and may therefore lead to a better long-term metabolic control of the disease *(Pediatric Diabetes: 2020, 21, 5, s. 800-807).*

Spontaneous regeneration and stimulated recovery of beta cells might be a possible explanation of partial remission phenomenon. The study "Circulating hematopoietic (HSC) and very-small embryonic like (VSEL) stem cells in newly diagnosed childhood diabetes type 1 - novel parameters of beta cell destruction/regeneration balance and possible prognostic factors of future disease course" aimed to evaluate HSC and VSEL cells mobilization to establish their role in residual beta cell function maintenance and partial remission occurrence in children newly diagnosed with type 1 diabetes. 59 type 1 diabetic patients (aged 6–18 years) and 31 healthy children as a control group were recruited. HSC and VSEL levels were assessed at disease onset in PBMC isolated from whole peripheral blood with the use of flow cytometry and patients were monitored for following 2 years. Basing on C-peptide secretion an assessment of beta cell function was performed. Studied groups were stratified on the basis of VSEL, HSC and/or C-peptide median levels in regard to beta cell function and partial remission. Patients with higher stimulated C-peptide secretion at disease onset demonstrated lower levels of HSC ($p < 0.05$), while for VSEL and VSEL/HSC ratio higher values were observed ($p < 0.05$). After 2 years patients with higher C-peptide secretion presented lower initial levels of HSC and higher VSEL/HSC ratio ($p < 0.05$). Patients with lower values of HSC levels demonstrated a tendency for better partial remission prevalence in the first 3 to 6 months after diagnosis. These clinical observations indicate a possible significant role of HSC and VSEL in maintaining residual beta cell function in type 1 diabetic patients 1 *(Stem Cell Reviews and Reports: 2021, 11 pp).*

In the last study the evaluation of C-peptide levels in relation to clinical parameters in patients with long-standing diabetes was performed. Anthropometric measurements previously acquired laboratory tests, HbA_{1c} and C-peptide levels of 178 diabetic children and adolescents with type 1 diabetes lasting for more than 1 year were analyzed. C-peptide levels were assessed using both classic and "ultrasensitive" methods. In 33,75% patients C-peptide levels > 0.23 ng/ml was found. Those patents were older at the time of diagnosis, experienced longer clinical remission, and required lower total and basal doses of insulin ($p < 0.05$). Preserved C-peptide also correlated with lower mean HbA_{1c} from the last year, but higher HbA_{1c} at the time of the diagnosis. Traditional and ultrasensitive C-peptide tests revealed similar results. Obtained

results confirm that residual beta-cell function may be maintained in young type 1 diabetic patients after few years after diagnosis and is beneficial for their metabolic control.