SUMMARY

LDL-apheresis is a method of extracorporeal elimination of LDL-cholesterol. LDL-cholesterol is known to activate inflammatory processes leading to atherosclerosis. The study was divided into two parts. THE AIM OF THE FIRST PART was to evaluate 1000 LDL-apheresis procedures based on immunoadsorption in 9 patients (median age was 57, range 19-61 years) with severe familial hyperlipidemia refractory to conventional treatment. Blood cells separators Cobe Spectra (COBE BCT, USA) were used to separate patients' plasma. Immunoadsorption was performed by means of ADA or Adasorb (Medicap, Germany) and columns LDL-Lipopak (Pocard Ltd., Russia). Before and immediately after the procedure, blood samples were taken and serum levels of lipoproteins and some other parameters were tested. **Results:** Median of the treatment duration was 6,7 (range 2,9 - 8,5) years, median interval between two apheresis procedures was 17 (4 – 294) days, in familial hypercholesterolemia homozygots 14 days. One procedure took 3,8 (1,0 - 5,6) hours. Median volume of processed plasma was 7000 ml, i.e. 99 (15 - 156) ml/kg of body weight. Median blood flow 70,0 (45,0 – 70,0) ml/min., median plasma flow was 34,5 (20,3 - 38,2) ml/min. Median total cholesterol decrease was 70 %, LDL-cholesterol 86%, Lp(a) 74%, HDL-cholesterol 26%, triacylglycerides 59%, both hemoglobin and hematocrite 7%, thrombocytes 9%, plasma viscosity 15% after one procedure. Median number of procedures performed per one pair of columns was 49 (11-109) and one pair of columns was used 2,6 years. The adverse events were mostly mild and represented by vaso-vagal events and manifestation of citrate related toxicity. The selectivity and efficiency of immunoadsorption did not change during the usage of columns. The new air removing system from columns was developed. **CONCLUSION:** Our modification of LDL-immunoadsorption is effective, selective and safe. According to our experience, LDL-apheresis procedures should not take more than 4 hours. The quality of columns LDL-Lipopak is stable during the treatment.

IN THE SECOND PART OF THIS STUDY, the effect of two consecutive LDL-apheresis procedures on selected indicators of atherogenesis activity was tested.

a)Soluble P- and E-selectin and monocytic chemoattractant protein-1 (MCP-1) levels. **Results:** In the group of patients described above, a significant ($p < 0,05$) decrease of elevated serum P-selectin levels (median 31% a 30%), a marker of endothelial (and thrombocyte) activity, and of normal levels of MCP-1 (median 22% a 41%) were observed. Levels of E-selectin, a specific marker of endothelium activation, were not elevated and did not change after the LDL-apheresis. MCP-1 was adsorbed in columns. **Conclusion:** For the first time, the effect of LDL-immunoadsorption on P- and E-selectin and MCP-1 levels was described. Elimination of those molecules by columns was evaluated.

b)Urinary neopterin and microalbuminuria. In 10 patients with severe dyslipidemia (median age 48 years, range 19-61 years), treated with LDL-immunoadsorption (n=8) or plasma filtration (n=2) using filters Evaflux 4A (Kuraray, Japan), levels of urinary neopterin, a specific marker of macrophage activation, and microalbuminuria, an indicator of generalized vascular dysfunction, were investigated between two LDL-apheresis procedures. **Results:** No significant changes of the urinary neopterin levels and microalbuminuria were observed, except a significant ($p < 0.006$) decrease of urinary neopterin/creatinine ratio in the evening after the LDL-apheresis. This decrease showed significant negative correlation with the pre-apheretic levels of total and LDL-cholesterol and with their decrease after the apheresis ($p < 0.05$). Microalbuminuria correlated positively with total and LDL-cholesterol levels before the apheresis and with the evening urinary neopterin/creatinine ratio after the apheresis. **Conclusion:** A single LDL-apheresis procedure did not significantly affect microalbuminuria. The decrease of urinary neopterin in the evening after the apheresis corresponds with the diurnal rhythm of neopterin excretion and was less pronounced in patients with more severe hypercholesterolemia, probably because their macrophage activity was less influenced by LDL-apheresis, and possibly because of narrowing of circadian variation of neopterin excretion as a result of elevated basal neopterin production from atherosclerotic plaques. The correlations between microalbuminuria, neopterin and pre-apheretic cholesterol concentrations indicate a possible connection between microvascular dysfunction, macrophage activity and severity of hypercholesterolemia.

c)C-reactive protein (CRP), serum neopterin, CD40 ligand (CD40L) and soluble endoglin. **Results:** In the other study but in the identical group of patients, a significant decrease ($p < 0,05$) of normal levels of high-sensitivity CRP (median decrease 34% and 40%) CD40L, a mediator of T-lymphocyte effect on inflammatory process (40% and 38 %) and decrease of elevated levels of endoglin, a marker of endothelial activation and/or damage (26% and 21%) were observed after LDL-apheresis, in contrast to serum neopterin level, which was normal and did not change. CD40L level correlated with total ($r_s = 0,721$, $p = 0,016$) and LDL-cholesterol ($r_s = 0,818$, $p = 0,002$). **Conclusion:** Original observation of CD40L and endoglin levels in extracorporeal LDL-elimination was performed. Serum neopterin was for the first time evaluated in the case of LDL-immunoadsorption. Elimination of those molecules by columns and filters was tested.

CONCLUSION OF THE SECOND PART OF THE STUDY: Elevated levels of parameters described above reflect the presence of atherosclerosis, since other disorders, known to elevate these markers, were excluded. The decrease after LDL-apheresis was partly caused by hemodilution. MCP-1 was adsorbed in columns, elimination of other molecules was not proved. The possible role of the decreased production or increased degradation of these molecules was not quantified. Despite the cause, the decrease of these immunologicaly active molecules may contribute to the positive effect of LDL-apheresis on atherogenesis.