of HDL cholesterol. We divided FH patients into 3 groups: 1 - free of CHD; 2 - with stable CHD; 3 - with progressive CHD. LDL/HDL ratio was 5.2±0.45, 7.7±0.89, and 10.4±0.78, respectively. Genetic study found 1 patient with homozygous FH, 1 patient with apoB-100 (FDP) gene mutation that was revealed for the first time in Saint-Petersburg. We expected to find mutations of LDL-receptor gene (FH-Helsinki and FH-North Karelia) that are responsible for 70% of all FH cases in Finland, but found only 1 case of FH-North Karelia mutation in Petrozavodsk. Most of revealed mutations of LDL-receptor gene were unique i.e. found only in 1 family. This suggest the absence of a strong founder effect associated with FH in the North-West Region of Russia. Due to high heterogeneity of FH-causing mutations, we failed to establish interrelations between type of mutation and severity of atherosclerosis complications.
Conclusions: High level of HDL cholesterol is the only one proved lipid factor preventing atherosclerosis development in patients with verified FH.

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03. Lipids - 03.09 Managing familial hypercholesterolemia

EAS19-0488.
FIVE YEAR EXPERIENCE OF INTENSIVE LIPID-LOWERING TREATMENT OF 14 YEARS OLD BOY WITH HOMOZYGOUS FAMILAIL HYPERCHOLESTEROLEMIA:A CASE REPORT

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Background and Aims: Homozygous FH (homoFH) is severe lipid disorder with extremely high level of LDL-C and poor prognosis due to fast progression of CVD. We report a case of 14 years old boy with homoFH treated with statin+ezetemibe+i-PSCK9 over 5 years.
Methods: Patient was treated in academic hospitals and routine medical care.
Results: Patient V .I, (boy, 14 years old) was initially consulted in Jan 2013 with baseline LDL-C of 19.9 mmol/l massive eruptive xanthomata, arcus lipoidea and Achilles tendon thickening> 2 sm. DNA test revealed two mutations of LDL receptor (C68F and C270X) and alone with typical clinical features diagnosis of homoFH was established. Initial examination of patient also revealed intensive stenosis of carotid arteries (45-50%) . Echocardiography examination showed initial stenosis of estuary of aorta. Stress ECG has not showed signs of ischemia of coronary arteries. Treatment with rosuvastatin 20 mg/day was commenced with subsequent dose increase to 40 mg/day (November 2013) and then combination therapy rosuva 40+ezetemib 10 mg/day (since Sept 2015). There were no elevation in activity of AST, Alt and CK during treatment. In march 2016 injection of evalocumab 420 mg/month was added and resulted a moderate effects on lipids and good tolerability. The lowest LDL-C level was detected in September 2018 of 4.61 mmol/l and fast regression of xanthomata was observed by June 2016. Coronary angiography performed in November 2018 demonstrated clean coronary arteries
Conclusions: Thus, triple combination therapy allowed to maintain LDL-C reduction by 60% and stabilize atherosclerosis in patient with severe homoFH.

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EAS19-0542.
FH PHENOTYPE: MONOGENIC, POLYGENIC OR OTHER CAUSES?

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Background and Aims: Familial Hypercholesterolaemia (FH) is a monogenic lipid disorder caused by mutations in *LDLR*, *APOB*, and *PCSK9* genes. However, 50% of individuals with clinical FH do not have a mutation in one of these 3 genes, so other causes for their phenotype must exist. The aim of this work was to characterise the origin of the FH phenotype in a cohort of patients with clinical diagnosis of FH.
Methods: A total of 731 clinical FH patients have been referred to our laboratory. *LDLR*, *APOB*, *PCSK9*, *APOE*, *LIPA*, *LDLRAP1*, *ABCG5*/8 genes were studied. The 6-SNP LDL-C genetic risk score (GRS) for polygenic hypercholesterolaemia was validated in our population and applied to our cohort.
Results: We have identified a mutation causing disease in 38.7% of the patients, 13.7% were found to have high GRS (>75th), and 0.8% other lipid disorders. This additional causes of the FH phenotype increased the rate of patients where the cause of hypercholesterolaemia has been identified to 54%. If all variants of uncertain significance were pathogenic, the identification rate would increase to 59%. The monogenic causes of the FH phenotype are: *LDLR* variants in 91% of the patients, *APOB* variants 5%, *PCSK9* variants 1% and 2% are due to other causes (*LIPA*, *APOE* and *ABCG5/8)*.
Conclusions: Patients with some other monogenic causes for dyslipidaemia (eg. LALD, sitosterolaemia*)*, need a completely different management approach than patients with monogenic FH. This study suggests that all known causes of the FH phenotype should be investigated in FH cohorts for a best patient management and prognosis.

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EAS19-0643.
APOLIPOPROTEIN M AND HIGH-DENSITY LIPOPROTEIN SUBFRACTION LEVELS IN NEWLY DIAGNOSED, UNTREATED FAMILIAL HYPERCHOLESTEROLEMIA

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Background and Aims: Familial hypercholesterolemia (FH) is an autosomal dominant disorder with extremely high plasma total- (TC) and LDL-cholesterol (LDL-C) levels and increased risk of premature cardiovascular disease. Although the HDL-cholesterol (HDL-C) level is usually in the high-normal range, the structure and function of the HDL particle is impaired. The HDL-associated apolipoprotein M (ApoM) has several anti-atherogenic properties and was found to be decreased in FH. However, its level was not studied in untreated FH patients.
Methods: 56 newly diagnosed, untreated patients with heterozygous FH and 32 healthy controls were enrolled. Serum lipid parameters, ApoM levels and HDL subfractions were evaluated. ApoM level was detected by ELISA. Lipoprotein subfractions were measured by gel electrophoresis (Lipoprint). FH was diagnosed using Dutch Lipid Network Criteria.
Results: Significantly higher TC, LDL-C, triglyceride and Lp(a) levels was found in FH patients compared to the controls. ApoM level was significantly higher in patients compared to controls: 3.56 (3.2-3.9) vs. 3.02 (2.7-3.2) μg/ml ($p<0.01$). We found significant positive correlations between ApoM levels and small HDL subfraction levels both in all subjects ($p<0.001$) and in FH patients ($p=0.05$). In multiple regression analysis ApoM level was best predicted by TC level ($\beta=0.57$; $p<0.001$).
Conclusions: Measurement of ApoM level in FH may contribute to understand the role of HDL structure and function in enhanced atherogenesis observed in FH patients.
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